Anesthesia Review

for DNB Students

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Appa, Amma, Sowmya, Jay and Sai



AT THY LOTUS FEET

Preface

It was during my postgraduate years that I realized that the subject of anesthesiology does not have a comprehensive and examination-oriented book. The pursuit of DNB as a postgraduation degree itself is an arduous task, owing to the difficult work schedule, and high expectations from the students at the time of examinations. This problem is compounded manifold for the subject of anesthesiology, as it is a discipline in which the students have to have a wide base of knowledge.

Most of the textbooks available today are not student-friendly as there is a lot of information in them, from which the examinee has to pick and retain in memory only those details which are necessary. As a result, there is a whole lot of unwanted information to which he is subjected, which may be confusing at the time of examinations. Secondly, there is no single textbook which gives all the details in an examination-oriented format. As a result, the student is forced to study from several different textbooks spanning multiple subjects. Also, owing to the importance of knowledge of various clinical guidelines, it becomes mandatory for the anesthesiology examinee to be familiar with the latest guidelines across a wide variety of disciplines. I have attempted to address these problems by compiling a book, which is student-friendly, well researched and is based on the most recent clinical practice guidelines.

This book has been written to cater to the DNB anesthesiology board examinations in a comprehensive and point-based system. Also, most of the references are from standard textbooks in order to prevent confusion arising due to numerous research papers published in the recent past.

Therefore, the information has been provided in a highly concise, crisp and readable manner to help you crack the anesthesiology boards.

Hope you enjoy reading it and wishing you all the best to crack your boards!!

Kaushik Jothinath

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CHAPTER

1

Neuroanesthesia

PHYSIOLOGY OF ICP[1,2,3]

Properties

- Total skull volume = 1475 ml
- Total brain volume = 1300 ml
- CSF volume = 150 ml
- Blood volume = 110 ml
- ECF volume = 75 ml.

Normal ICF Pressures

- 10–15 mm Hg in adults and young children
- 3–7 mm Hg for young children
- 1.5–6 mm Hg for term infants
- > 20 mm Hg = raised ICP.

Factors Determining ICP

- *Monroe-Kellie doctrine:* In the setting of a nondistensible cranial vault, volume of blood, CSF and brain tissue must be in equilibrium
- Normally, a small increase in volume is compensated by:
  - Elastance of intracranial components
  - Translocation of CSF and venous blood into CSF space and extracranial veins.
- *Intracranial compliance* refers to the degree of increase in ICP in response to an increase in volume of intracranial contents.

Effects of Raised ICP

- Cerebral ischemia due to a reduction in CPP
- Impaired autoregulation—lower limit of autoregulation is raised with increasing ICP
- Herniation of brain:
  - Through open cranium
  - Subfalcine herniation
  - Uncal herniation
  - Tonsillar herniation.
- Hemodynamic changes: *Cushings reflex*

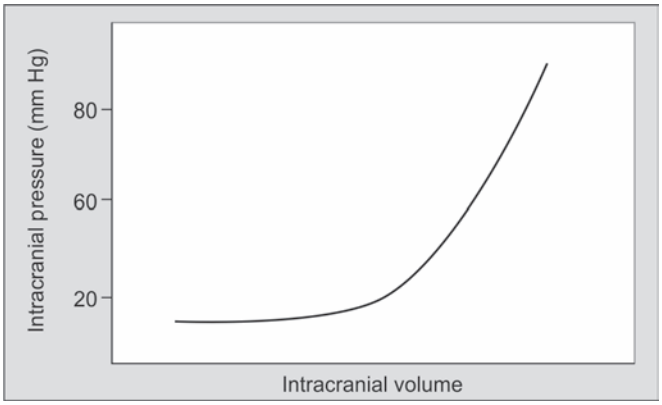


Fig. 1.1: Cerebral compliance curve

Causes of Raised ICP

Physiological

- Intubation, fever, seizures
- Excess fluids, hypertension
- Head down tilt
- Hypothermia
- Hypoventilation
- Hypoxia and hypercarbia

Pathological

Intracranial (Primary)

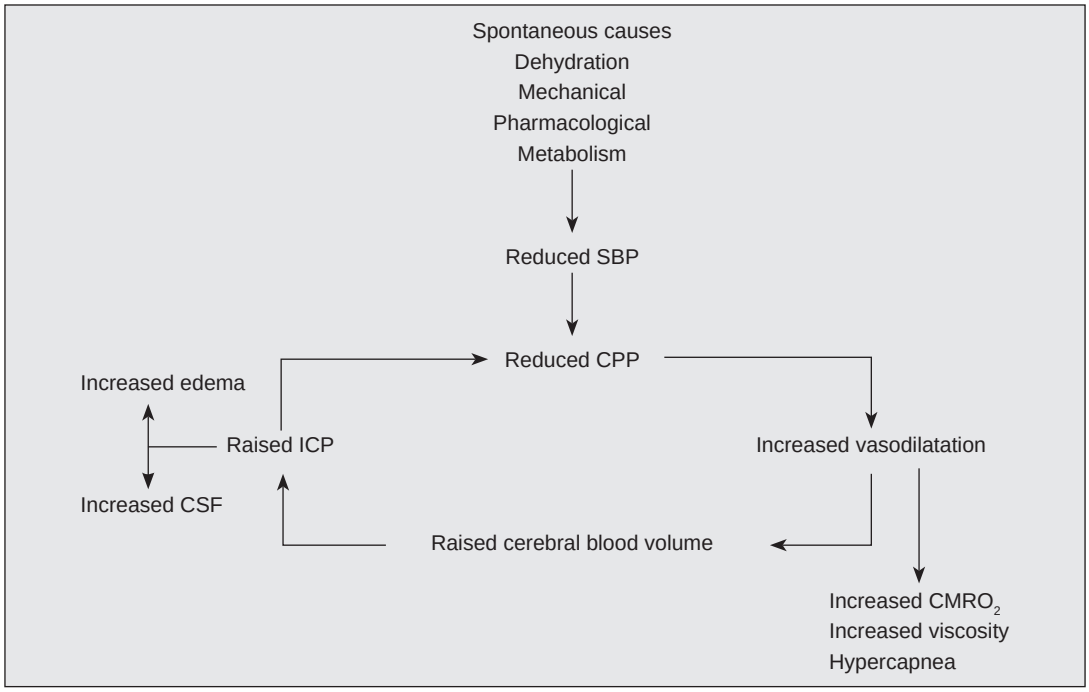
- Increased brain substance:
  - Tumor
  - Abscess
  - Hematoma

- Increased CSF volume:
  - Hydrocephalus
  - Benign intracranial hypertension
  - *Pseudotumor cerebrii*
  - Blocked shunt.
- Increased blood volume:
  - Increased cerebral blood flow—hypoxia, hypercarbia, volatile agents
  - Increased cerebral venous volume:
    - Raised thoracic pressure
    - Venous obstruction in neck
    - Coughing.
- Increased ECF volume:
  - Cerebral edema
  - Nontraumatic intracerebral hemorrhage
  - Trauma-epidural/subdural hematoma, cerebral contusion.

Extracranial (Secondary)

- Airway obstruction
- Hypoxia
- Hypercapnea
- Hypertension (pain/cough)
- Hypotension
- Seizures, fever
- Drugs and metabolic causes:
  - Volatile anesthetic > 1 MAC
  - Hepatic encephalopathy.

Pathophysiology



Anesthetic Drugs and ICP[1]

S. No.	Drug	Effect on ICP	Mechanism
1	Induction agents		
	Thiopentone	Reduces CBF, CBV and ICP	Cerebral vasoconstriction
			Reduced $CMRO_2$
	Propofol	Reduces CBF, CBV and ICP	Cerebral vasoconstriction
			Reduced $CMRO_2$

Contd...

Contd...

S. No.	Drug	Effect on ICP	Mechanism
	Ketamine	Increases ICP	
2	Opioids	Increase ICP	Cerebral vasodilatation
			Systemic hypotension
3	Nitrous oxide	Increases ICP	Cerebral vasodilatation
			Reversed with IV anesthetic

Contd...

Contd...

S. No.	Drug	Effect on ICP	Mechanism
4	Volatile agents	Reduce ICP at < 1 MAC	Vasodilatation and reduced CBF
		Increase ICP at > 1 MAC	Vasodilatation and increased CBF
5	Succinylcholine	Increases ICP	Muscle fasciculations

CEREBRAL BLOOD FLOW[1,2,3,7]

Introduction: CNS receives 12–15% of cardiac output, although it represents only 2% of total body weight. This is due to the high cerebral metabolic rate

Normal Values

Gray matter has a higher CBF (80 ml/100g/min) than white matter (20 ml/100g/min)

Parameter	Normal
CBF	45–55 ml/100g/min
CBF	≃ 750 ml/min in adult
$CMRO_2$	3–3.5 ml/100g/min
Cerebral vascular resistance	1.5–2.1 mm Hg/100g/min/ml
ICP (supine)	8–12 mm Hg
CPP	80–100 mm Hg
CBF: $CMRO_2$ ratio (flow metabolism coupling)	14–18

Factors Affecting CBF[1]

- Chemical/Metabolic/Humoral:
  - PaO_2
  - $PaCO_2$
  - $CMRO_2$:
    - Arousal/pain, temperature
    - Seizures, anesthetics.
  - Vasoactive agents:
    - Anesthetics, vasodilators
    - Pressors.
- Myogenic:
  - Autoregulation
  - Mean arterial pressure.
- Rheological: Blood viscosity
- Neurogenic Pathways:
  - Extracranial sympathetic and parasympathetic pathway
  - Intra-axial pathways

Factors Affecting CBF

Metabolism

- Increase in $CMRO_2$ increases CBF
- CBF increases with seizures, pain, anxiety, acidosis
- CBF decreases with coma, hypothermia, alkalosis, anesthetic agents
- CBF and $CMRO_2$ coupling is called *Flow-Metabolism coupling*
- When $CMRO_2$ increases, local byproducts of metabolism increase:
  - K^+ ions
  - H^+ ions
  - Lactate, adenosine
  - ATP
- Thus, CBF increases as well
- For each mm Hg rise in $PaCO_2$, CBF increases by 1.8 ml/100gm/min

$PaCO_2$

- Hypocapnea causes cerebral vasoconstriction and a reduction in cerebral blood flow
- Changes are more in gray than in white matter due to increased vascular density
- CO_2 dissolves with H_2O in CSF and forms H_2CO_3 The H^+ ions generated cause vasodilation of CBV
- One mm Hg rise in $PaCO_2$ causes increase in CBF of 1–2 ml/100g/min
- At $PaCO_2$ > 90 mm Hg, narcosis occurs
- At $PaCO_2$ < 20 mm Hg, cerebral ischemia with left shift of Hb dissociation curve occurs.

PaO_2

- Not an important determinant of CBF
- Effects mediated through lactic acid and other metabolic products of acidosis
- CBF begins to increase when PaO_2 < 50 mm Hg or when cerebral venous PO_2 reduces from 35 to 30 mm Hg.

Temperature

- Hypothermia decreases $CMRO_2$ by ≃ 5% for every degree celsius but does not uncouple $CMRO_2$ and CBF
- Hyperthermia increases CBF and $CMRO_2$.

Viscosity

- Not a target of manipulation, unless HCT ≥ 55%
- No effect on CBF when HCT is between 30–50%
- CBF will increase with reduction in HCT below 30%
- In focal cerebral infarcts, a HCT of 30–35% will cause optimal delivery of O_2.[1]

Anesthetic Agents[3]

S. No.	Agent	Effect
1	Inhalational agents	Reduce CBF at < 1 MAC
	Halothane = enflurane > desflurane >	Increase CBF at > 1 MAC
	isoflurane > sevoflurane	***Luxury Perfusion*** occurs at > 1 MAC when
		CBF increases but $CMRO_2$ decreases
2	Nitrous oxide	Increases CBF by cerebral vasodilation
3	Intravenous anesthetics:	
	Ketamine	Increases CBF
	Thiopentone	Decreases CBF
	Propofol	Decreases CBF
	Etomidate	Decreases CBF
	Benzodiazepines	Decrease CBF
4	Opioids	
	Morphine	Increases CBF due to histamine release
	Fentanyl and others	Modest reduction in CBF and $CMRO_2$
		May increase CBF if systemic hypotension
5	Nondepolarizing muscle relaxants	Increase CBF at high doses due to histamine release
6	Succinylcholine	Increases CBV due to fasciculation induced increase in CVP
7	Lidocaine	1.5–2 mg/kg boluses
		Effective in controlling acute rise in ICP
8	Droperidol	Reduces CBF without significant change in $CMRO_2$
9	Dopamine, adrenaline	Increase CBF

Monitoring CBF[3]

Quantitive Global and Regional CBF

- ***Kety-Schmidt technique***:
  - N_2O wash out technique
  - ***Gold standard***
  - Cannulation of jugular bulb necessary
  - Measures global hemispheric blood flow and derives $CMRO_2$.
- Radioactive Xenon washout:
  - Xe^{133} administered by IV/inhalation (less common)
  - Multiple detectors next to head measure CBF
  - Accuracy impaired in low flow conditions
  - Areas with no flow cannot be detected (***look through phenomenon***).
- Stable Xenon CT:
  - Stable xenon inhaled and CT scan taken
  - Stable xenon is expensive and at 30% causes significant cerebral vasodilation.
- CT perfusion scan:
  - Computer examines transit time of contrast and derives regional CBF
  - Allows assessment of patients response to hyperventilation or increased BP.
- Position emission tomography:
  - Measures regional CBF, CBV, $CMRO_2$ and glucose consumption
  - Expensive.
- Laser Doppler
  - For local CBF, where continuous CBF monitoring is done with laser Doppler flow probes
  - Probe implanted via burr hole into parenchyma
  - Measures CBF only in a volume of 1 mm^3.

Semiquantitive/Qualitative CBF

- Single photon emission computed tomography (SPECT):
  - Using Tc^{99} injected intravenously
  - Noninvasive, involves less radiation than a CT scan
  - Regional distribution of blood can be quantified but not absolute CBF
  - Useful to assess ischemia secondary to vasospasm
- Transcranial Doppler USG:
  - Low frequency (2 MHz) pulsed wave probe is used
  - Insonation of basal cerebral vessel done through acoustic cranial window
  - Can detect emboli, vasospasm
  - Quantifies risk of cerebral ischemia during carotid cross clamping.

CEREBRAL AUTOREGULATION[1,2,3,7]

Introduction

- Physiological response whereby CBF remains constant over a wide range of BP due to alterations in cerebrovascular resistance
- CBF closely autoregulated between MAP 70–150 mm Hg.[1]

Mechanism

Robin Hood Phenomenon

- Blood vessels surrounding an ischemic area are already maximally dilated
- If $PaCO_2$ rises in these areas, vasodilation of normal vessels around these areas occurs
- This causes an intracerebral steal phenomenon, reducing blood flow to ischemic areas
- Reduction in $PaCO_2$ which normally constricts cerebral BV diverts blood to disease areas
- Areas of focal ischemia receive more CBF in this manner.

Myogenic Hypothesis

- Changes in CPP cause direct change in tone of vascular smooth muscle
- Maybe due to nitric oxide release
- Also due to autonomic innervation of cerebral blood vessels.

Metabolic Coupling

- Occurs when metabolic demands of tissues exceeds cerebral blood flow
- Tissue metabolites which are released cause vasodilation which increase blood flow
- Due to *Flow-Metabolism Coupling*

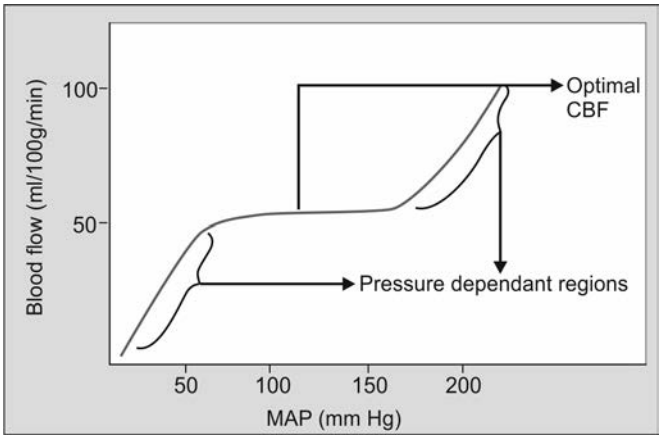


Fig. 1.2: Cerebral autoregulation

Factors Affecting Autoregulation

Hypertension

- In patients with chronic HTN, autoregulation curve shifts to right
- Upper limits of autoregulation are higher
- BP which may be adequate in a normal patient may cause ischemia in a hypertensive patient
- Shift of autoregulation curve is modified by long term antihypertensive therapy.

Hypotension

- Autoregulation is impaired during hypotension
- As BP returns to normal, a reactive hyperemia occurs.

Chemical Sympathectomy

- Used along with sodium nitroprusside/trimethophan
- May extend lower limit of tolerable hypotension.

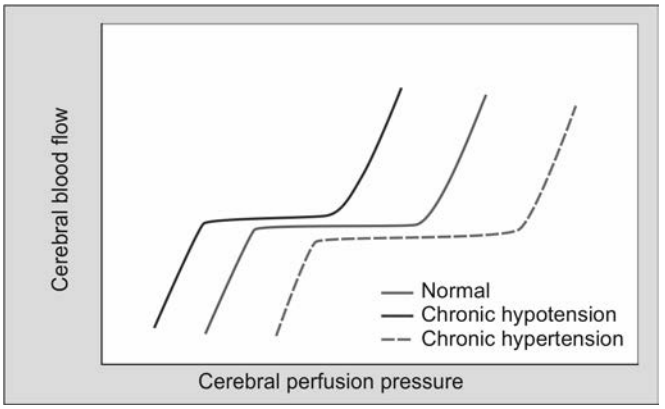


Fig 1.3: Autoregulation in hypertension

Autoregulation Impaired in

- Areas of relative ischemia
- Surrounding mass lesions
- After grand mal seizures
- After head injury
- During episodes of hypoxia/hypercarbia
- Volatile anesthetics
- Brain tissue acidosis:
  - Hypoxia
  - Hypercarbia
  - In areas surrounding infarcts.

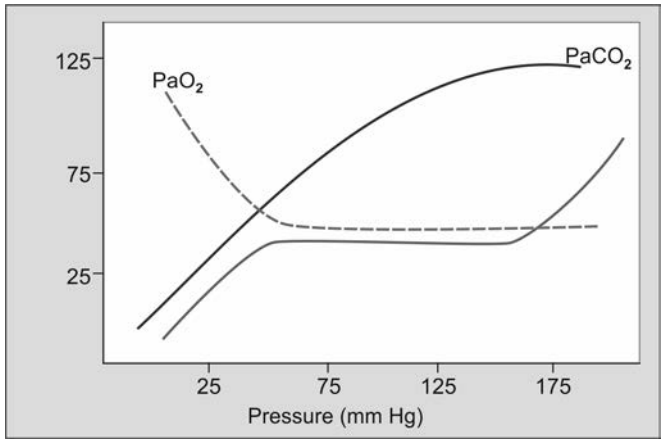


Fig. 1.4: Cerebral autoregulation

Types of Autoregulation

- Static autoregulation: Response to slow changes in arterial BP/CPP
- Dynamic autoregulation: Response to rapid changes in arterial BP/CPP.

Autoregulation Testing

Used in patients with TBI/SAH with impaired cerebral autoregulation

- Relationship between BP and flow velocity:
  - Negative correlation between changes in BP and flow velocity when autoregulation is intact
  - State of autoregulation determined by monitoring BP and flow velocity simultaneously.
- Transient hypermic response:
  - When autoregulation is intact, compression of extracranial internal carotid artery for 7–10 seconds will cause transient hypermic response in ipsilateral middle cerebral artery.
- Dynamic autoregulation
  - When auto regulation is intact, sudden deflation of inflated thigh cuff will cause a brief reduction in MCA flow velocity.
- Static autoregulation
  - When autoregulation is intact, elevation of BP below upper limit of autoregulation using phenylephrine will not affect cerebral artery flow velocity.

THERMOREGULATION[1,2,3,7]

Introduction

Thermoregulation involves control of basal metabolic rate, muscular activity, sympathetic activity, vascular tone and hormonal activity balanced against exogenous factors, which determine the need for body to create heat or to adjust heat transfer to the environment.

Pathways of Thermoregulation

Afferent Sensing Pathways

Thermosensitive cells from:

- Hypothalamus and other parts of brain
- Spinal cord
- Deep thorax

Deep abdomen
Skin surface (each 20% input)
↓
A δ fibers (cold)
↓
C fibers (warm)
↓
Anterior spinothalamic tract
↓
Hypothalamus (preoptic region)

Central Regulation

- Integrated normal input from skin surface and deep tissues compared by hypothalamus
- Input compared with threshold temperature for each thermoregulatory response
- Interthreshold range is the core temperature between first cold induced (vasoconstriction) and warm induced (sweating) response
- No autonomic thermoregulatory response occurs in this range (normally 0.2 °C)
- Mediators – 5 HT, acetylcholine, PGE, neuropeptides.

Efferent Responses

- Behavioural responses
  - Assume body positions which oppose skin surfaces
  - Voluntary movements.
- Vasoconstriction: Heat loss
- Nonshivering thermogenesis: Especially in newborn
- Shivering:
  - Increases heat production by 100–200%
  - Occurs after vasoconstriction
  - Does not occur in newborn and is ineffective in children up to several years old.

Thermoregulatory Responses in Unanesthesized Individuals

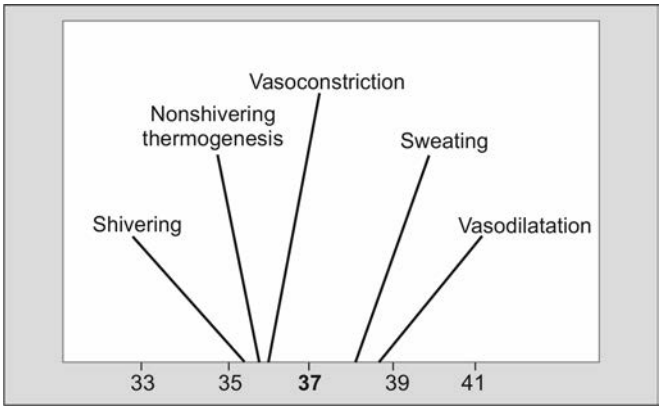


Fig. 1.5: Normal thermoregulatory responses

Thermoregulation During General Anesthesia

Phases of Thermoregulation[1]

Phase I: Redistribution Phase

- During first hour of GA
- Largest drop in core temperature occurs (0.5–1.5 ºC)
- Due to:
  - Vasodilatation caused by volatile anesthetics
  - Heat distribution from core to periphery along temperature gradient.

Phase II: Linear Phase

- Linear reduction in core temperature
- Due to heat loss exceeding heat production (0.83 kcal/kg/hr)
- Occurs for next 2–4 hours after GA
- Heat loss by radiation > convection > evaporation > conduction.

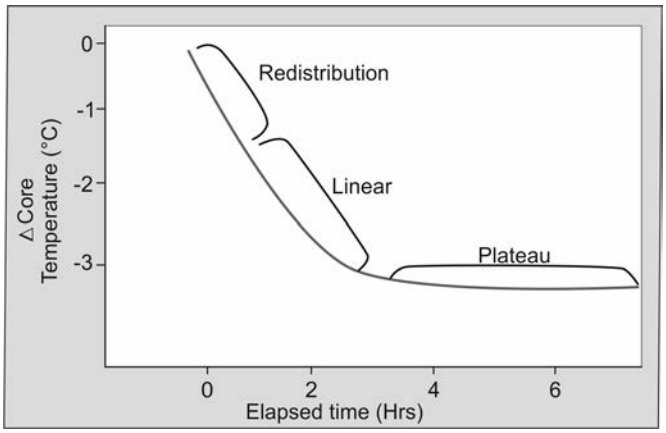


Fig. 1.6: Thermoregulation during GA

Phase III: Plateau Phase

- After 3–4 hrs of GA, core temperature stops reducing
- Represents normal steady state when heat loss equals heat production
- Occur when thermoregulatory vasoconstriction sets in
- Reduces heat loss from body
- Absent in peripheral/autonomic neuropathy.

Altered Efferent Responses During General Anesthesia

- Interthreshold range 2–4 ºC
- Behavioral regulation not relevant
- Nonshivering thermogenesis not significant in adult
- Shivering impaired due to muscle paralysis
- Volatile anesthetics, propofol, dexmedetomidine and alfentanil reduce vasoconstriction and shivering threshold.

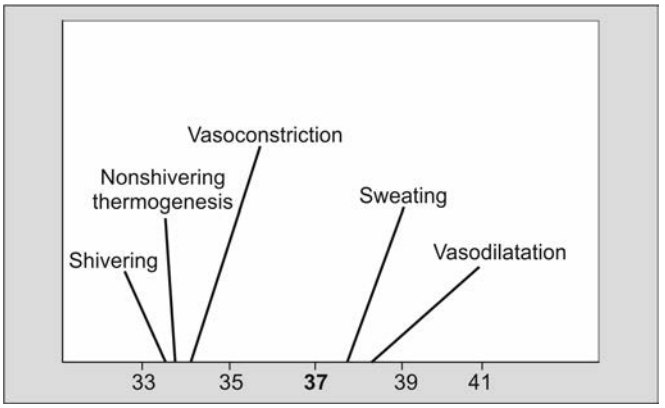


Fig. 1.7: Thermoregulatory response during GA

Thermoregulation During Regional Anesthesia

Phases of Thermoregulation[1]

Phase I: Redistribution Phase

- Core temperature reduces during first hour due to vasodilatation.

Phase II: Linear Phase

- Occurs as heat loss exceeds heat production.

Phase III: Plateau Phase

- *Absent*
- No plateau phase present as RA blocks blood vessels in legs
- Prevents any thermoregulatory vasoconstriction.

Altered Efferent Responses

- RA inhibits tonic cold signals from legs to thermoregulatory center

- Brain interprets this as warming of legs
- Thus, it reduces the vasoconstriction and shivering threshold
- Interthreshold range increases to 0.8 ºC
- Peripheral vasoconstriction and shivering is inhibited in blocked areas but occurs in muscle mass proximal to these areas
- Regional anesthesia itself impairs thermoregulatory center
- Absence of behavioural regulation as this is largely determined by skin temperature rather than core temperature
- Thus even though core temperature reduces, skin temperature increases
- Patient does not feel cold inspite of reduced core temperature.

Thermoregulation in Combined General-Regional Anesthesia

- Core temperature does not plateau in combined GA-RA
- Thus, it continues to decrease throughout surgery
- Core temperature management and monitoring is very important in these cases.

Thermoregulation in Newborn

- No shivering/effective vasoconstriction occurs
- Have a larger surface area to weight ratio which increases heat loss
- Also have less subcutaneous fat for insulation
- Very effective *Nonshivering Thermogenesis*
- No thermoregulatory sweating.

SHIVERING[1,2,3,7]

Introduction

- Oscillatory muscular thermoregulatory response which increases heat production by up to 600% above basal level in response to a reduction in core temperature.
- Normal body temperature – 36.8 ± 0.4 ºC.[8]

Risk Factors

- Young age
- Low core temperature preoperatively – *most important predictor*
- Male sex
- GA > RA
- Propofol > thiopentone.

Etiology

Increased Heat Loss

- Evaporation during skin preparation
- Radiation and convection from skin
- Low ambient temperature (< 21 ºC)
- Cold IV fluids and irrigation fluids
- Humidification of gases.

Redistribution

- Due to peripheral vasodilatation (Regional anesthesia/volatile anesthetics)
- Reduced thermoregulatory threshold
- Sepsis induced vasodilatation/allergy.

Altered Thermoregulation

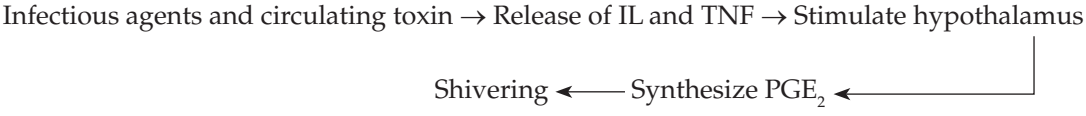
- Paralysis and anesthesia impaired shivering and behavioural regulation
- Impaired thermoregulatory vasoconstriction.
- Absent nonshivering thermogenesis in anesthetized adults
- Volatile anesthetics interfere with hypothalamic thermostat
- Reduced basal metabolic rate (0.83 kcal/kg/hr)

Incidence

- Up to 40%
- 65% after general anesthesia
- 33% after regional anesthesia.

Pathogenesis

- Elicited when preoptic region of hypothalamus is cooled
- Stimulation of κ-opioid, NMDA and 5-HT receptors occurs
- Efferent signals from hypothalamus descend via medial forebrain bundle
- Mesencephalic reticular formation and medullary reticular formation exert descending influence on spinal cord which increases muscle tone
- Spinal α motor neurons are the final common pathway for shivering
- Also, spinal cord function recovers faster than brain function
- This results in spinal reflexes manifested as clonic activity.



Pathophysiology

EMG demonstrates two distinct patterns:

- Tonic Pattern:
  - Resembles normal shivering
  - 4–8 cycles/min with waxing and waning pattern
  - Simple thermoregulatory responses to hypothermia.
- Clonic Pattern:
  - Resembles pathological clonus
  - 5–7 Hz burst patterns
  - Not a normal component of thermoregulatory shivering
  - Occurs specifically on recovery from volatile anesthetics.

Factors Affecting Shivering

- Pain
- Adrenal suppression
- Uninhibited spinal reflexes
- Pyrogens
- Thermoregulatory factors.

Shivering Assessment

Bedside Shivering Assessment Scale

Score	Type of shivering	Location
0	None	No shivering on palpation of masseter/neck/chest muscles
1	Mild	Shivering localized to neck and thorax only
2	Moderate	1+ shivering involving gross movement of upper extremities
3	Severe	Involving gross movements of trunk, upper and lower extremities

Effects of Shivering and Hypothermia

Central Nervous System

- Altered mental status
- Decreased MAC (5–7% per 1 ºC cooling)
- Increased residual sedation
- Increased residual paralysis
- Delayed awakening
- Slow EEG with increased SSEP latency
- Protects against cerebral ischemia
- Increased IOP and ICP
- Decreases $CMRO_2$ by 8%.

Cardiovascular

- Increased release of norepinephrine and epinephrine
- Increases peripheral and pulmonary vascular resistance
- Decreases venous capacitance and cardiac output
- Increases heart rate and blood pressure
- Increases chances of MI
- Increased Troponin I levels
- Dysrhythmias (VF, if < 28 ºC).

Altered Coagulation

- Platelet sequestration
- Decreased platelet function
- Decreased clotting factor function
- Increased blood loss and blood transfusion.

Impaired Wood Healing

- Poor wound healing
- Increased postoperative infection
- Impaired phagocytosis and oxidative killing
- Impaired chemotaxis
- Moderate hyperglycemia.

Oxygenation

- Shift of oxyhemoglobin dissociation curve to left
- Increased oxygen consumption (100–200%) and CO_2 production
- Increased tissue hypoxia and metabolic acidosis
- Jeopardized marginal tissue grafts.

Others

- Impaired renal function
- May interfere with planned procedure (MAC like ESWL, colonoscopy)
- Decreases reliability of pulse oximetry, ECG and IBP monitoring
- Incidental trauma
- Wound pain by stretching incision site
- Decreased drug metabolism—interferes with recovery from anesthesia.

Prevention

- Maintain OT temperature between 21–23 ºC
- Maintain intraoperative normothermia
- Adequate prewarming for 30 minute prior to regional anesthesia
- Ketamine 0.5 mg/kg IV before GA/RA
- Ondansetron 8 mg IV given during induction of anesthesia prevents Post Anesthetic Shivering (PAS)

- Correct underlying problems—sepsis and hypothermia
- Warming IV fluids and irrigating solutions:
  - 1 unit of blood or 1 liter crystalloid at room temperature reduces mean body temperature by 0.25 ºC
  - Withhold reversal of intraoperative muscle relaxation in intubated patients.

Treatment

Rewarming

- Active rewarming: Two types available
  - Circulating water mattresses:
    - Not very effective
    - Only little heat is lost from back into the foam covering OT table
    - Combination of heat and reduced perfusion of the back can cause burns.
  - Forced air warmers at 40–43 ºC - *most effective*
  - Radiant infrared lamps.
- Passive rewarming:
  - Maintain OT temperature at 21–23 ºC
  - Insulators like cotton blankets, surgical drapes, plastic sheets, reflective composites (*space blankets*) used to cover head and body surface
  - Single layer of each reduces heat loss by 30%
  - Using multiple layers or prewarming insulators not very useful
  - Cover head of infants with blankets/aluminium foil.

Humidification

- Limited role as only 10% of heat produced is lost via respiratory tract
- Respiratory loss remain almost constant during anesthesia
- Thus, fraction of heat lost during major surgeries reduces drastically
- HME in breathing circuits (infants and children).

Supplemental Oxygen

Drugs

- Opioids:
  - Meperidine
    - 0.35–0.4 mg/kg (12.5–25 mg IV)
    - Central κ opioid action
    - ***Most effective***
  - Tramadol – 25–50 mg or 0.1–0.2 mg/kg IV
  - Butorphanol–1–2 mg IV
  - Fentanyl
  - Alfentanil 250 µg IV.
- 5-HT Antagonists:
  - Action based on ***Monoamine Theory of Thermoregulation***
  - Ketanserin 10 mg IV.
- α_2 Agonists
  - Clonidine 1.5 µg/kg or 75 µg IV
  - Dexmedetomidine 0.2–1.5 µg/kg/hr
  - Decreases vasoconstriction and shivering threshold.
- Anticholinergics:
  - Physostigmine 0.04 mg/kg IV
  - Chlorpromazine 10–25 mg IV.
- NMDA Antagonists
  - Orphenadrine
  - Ketamine–0.5 mg/kg IV
  - Magnesium sulfate 30 mg/kg IV or 500 mg/hr infusion.
- Analeptics
  - Doxapram 100 mg or 1.5 mg/kg IV
  - Methylphenidate.
- Others
  - Propofol 10–50 µg/kg/min
  - Nefopam 0.15 mg/kg IV
  - If uncontrolled, IV vecuronium 0.1 mg/kg IV followed by mechanical ventilation.
- Associated with Sepsis
  - PG synthetase inhibitors [Acetaminophen (PR), aspirin]
  - Glucocorticoids.

NONSHIVERING THERMOGENESIS (NST)[1,2,3,7]

Introduction

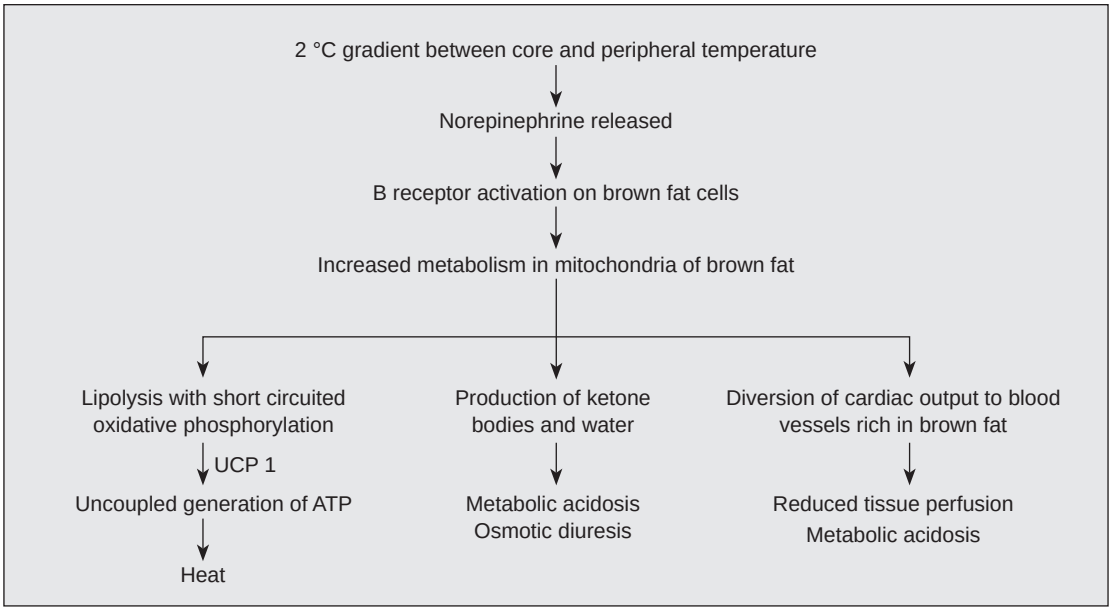
- Represents the primary mechanism in newborn to respond to heat loss by increasing metabolic heat production 100% without producing mechanical work
- *Chemical thermogenesis.*

Physiology

- NST occurs up to 3–6 months of age
- Occurs predominantly in brown fat or Brown Adipose Tissue (BAT)
- Other sites of NST–liver, skeletal muscle, brain and white fat

- Norepinephrine, glucocorticoids and thyroxine are chief mediators for NST
- NST can be inhibited by
  - Surgical sympathectomy
  - Ganglionic blockers
  - Beta blockers
  - Volatile anesthetics.

Mechanism[3]



Brown Fat

- Brown fat is adipose tissue with high vascularity
- Constitutes 2–6% of infants total body weight
- Ample source of blood vessels imparts brown colour to the fat tissue
- Also richly innervated by sympathetic nervous system
- Sites with brown fat:
  - Between scapulae
  - Axilla
  - Around sternum
  - Around kidneys, adrenals
  - Major blood vessels of thorax and abdomen.

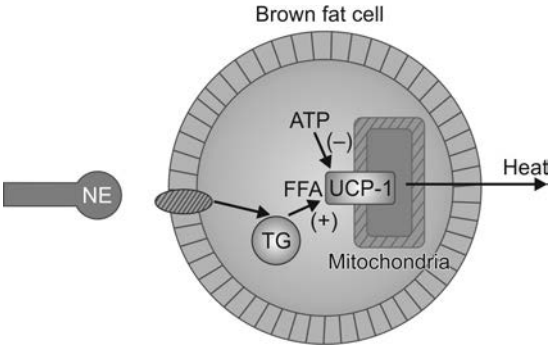


Fig. 1.8: Brown fat metabolism

- Causes of insufficient BAT:
  - Preterm infants
  - Intrauterine Growth Retardation (IUGR)
  - Infants exposed to prolonged cold stress.

Efficacy

- Increases heat production by up to 200% in infants
- Not effective in anesthetized adults
- Shivering is primary mechanism of heat production in adults
- Heat production increased only slightly in non-anesthetized adults.

Prevention

- Important as it causes increased hypoxia and metabolic acidosis
- Maintain neutral thermal environment
- Skin surface warming:
  - Hot water warmers
  - Infrared radiant heaters
  - Convection heaters
  - Use plastic wrap/covers/hats to reduce heat loss from head and other areas
  - Use of head caps useful in infants in contrast to adults.

- Prevent heat losses
  - Transport newborn in incubator and not bed with overhead heaters
  - Increase OT temperature to maximum levels (around 26 ºC if tolerable)
  - Air humidification
  - Place patient on forced air warming blanket to reduce conductive heat loss
  - Use of warm IV fluids-place fluid warmer close to IV access site.

SHIVERING DURING ANESTHESIA[1,2,3,7]

Introduction

- Thermoregulatory response which increases the heat production in response to a reduction in the core body temperature
- Normal body temperature: 36.8 + 0.4 ºC.

Incidence

- Up to 40%
- 65% after general anesthesia
- 33% after regional anesthesia.

Risk Factors

- Young age
- Low core temperature preoperatively
- Male sex
- GA > RA
- Propofol > thiopentone

Etiology

- Increased heat loss
  - Evaporation during skin preparation
  - Radiation and convection from skin
  - Low ambient temperature(< 21 ºC)
  - Cold IV and irrigation fluids
  - Humidification of gases.
- Redistribution
  - Due to peripheral vasodilation
  - Reduced thermoregulatory threshold
  - Sepsis induced vasodilation/allergy.
- Altered thermoregulation
  - Reduced basal metabolic rate
  - Paralysis and anesthesia impaired shivering and behavioral regulation
  - Impaired thermoregulatory vasoconstriction
  - Volatile anesthetic interference with hypothalamic thermostat
  - Absent nonshivering thermogenesis during anesthesia.

Pathogenesis

- Postanesthetic shivering occurs due to:
  - Infective agents and circulating toxins release of IL1 and TNF $\alpha \longrightarrow$ stimulate hypothalamus $\longrightarrow$ synthesize $PGE_2 \longrightarrow$ shivering
  - Stimulation of K opioid, NMDA, 5HT receptors
  - Spinal cord function recovers faster than the brain. This causes uninhibited spinal reflexes manifested as clonic activity.

Characteristics

EMG demonstrates 2 distinct patterns:

1. **Tonic Pattern**
- Resembles normal shivering
- 4–8 cycles per min with waxing and waning patterns
- Simple thermoregulatory response to hypothermia.

2. **Clonic Pattern**
- Resembles pathological clonus
- 5–7 Hz bursting pattern
- Not a normal component of thermoregulatory shivering
- Occurs specifically on recovery from volatile anesthetics.

Effects of Shivering and Hypothermia

Central Nervous System

- Altered mental status
- Residual paralysis
- Delayed awakening
- Reduced MAC (5–7% reduction per 1 ºC cooling)
- Protects against cerebral ischemia
- Raised IOP and ICP
- Reduced $CMRO_2$.

Cardiovascular System

- Increased epinephrine and norepinephrine levels
- Increased peripheral and pulmonary vascular resistance
- Increased heart rate and BP
- Increased chances of MI
- Dysrhythmias (VF if < 28 ºC).

Coagulation

- Platelet sequestration
- Reduced platelet function
- Reduced clotting factor function
- Increased blood loss.

Impaired Wound Healing

- Poor wound healing
- Impaired phagocytosis

- Impaired oxidative killing
- Impaired chemotaxis
- Moderate hyperglycemia.

Oxygenation

- Shift of ODC to left
- Increased oxygen consumption (100–200%)
- Increased CO_2 production
- Increased tissue hypoxia
- Metabolic acidosis—jeopardises marginal tissue grafts.

Others

- Impaired renal function
- May interfere with planned procedure (MAC like ESWL)
- Reduced reliability of pulse oximetry, ECG and BP monitoring due to vasoconstriction and shivering
- Incidental trauma
- Wound pain by stretching incision site
- Reduced drug metabolism—contributes to delayed recovery.

Prevention

- Maintain OT temperature between 21–23 ºC
- Maintain intraop normothermia
- Adequate prewarming for 30 min prior to regional anesthesia
- Ketamine 0.5 mg/kg IV before GA/RA
- Correct underlying problems: Sepsis, hypothermia
- Warming IV fluids and irrigating solutions
- Withold reversal of neuromuscular relaxants in intubated patients.

Treatment

Rewarming

- Active rewarming:
  - Circulating water mattresses:
    - Not very effective
    - Only very little heat lost from back
    - Combination of heat and reduced perfusion of back can cause burns.
  - Forced air warmers: *Most effective*
  - Radiant infrared lamps.
- Passive rewarming:
  - Maintain OT temperature at 21–23 ºC.
  - Cotton blankets, surgical drapes, plastic sheets, reflective composites (*'space blankets'*)
  - Cover head of infants with blankets or aluminium foils.

Humidification

- Limited role
- Important during major surgeries as respiratory loss remains constant over prolonged periods
- HME in breathing circuits to prevent
- Supplemental O_2 in recovery room.

Drugs

- Opioids:
  - Meperidine 0.35–0.4 mg/kg IV
    - *Most effective*
    - Through central K opioid action.
  - Tramadol 25–50 mg IV
  - Butorphanol 1–2 mg IV
  - Fentanyl and alfentanyl.
- 5HT antagonists:
  - Ketanserin 10 mg IV.
- $Alpha_2$ agonists:
  - Clonidine 1.5 mics/kg or 75 mics IV
  - Dexmedetomidine.
- Anticholinergics:
  - Physostigmine 0.04 mg/kg IV
  - Chlorpromazine 10–25 mg IV.
- Others:
  - Propofol
  - Magnesium sulfate 30 mg/kg IV
  - Nefopam 0.15 mg/kg IV.
- Shivering associated with sepsis:
  - PG synthetase inhibitors (aspirin, paracetamol)
  - Glucocorticoids.

TESTS OF AUTONOMIC NERVOUS SYSTEM[1,2,3]

Introduction

Tests to measure response of organ systems under autonomic nervous system to stimulation.

Indications

- Syncope
- Central autonomic degeneration (e.g. Parkinsonism)
- Pure autonomic failure
- Postural tachycardia syndrome
- Autonomic and small fiber peripheral neuropathies
- Diabetic neuropathy
- Hereditary neuropathy
- Sympathetically mediated pain
- Evaluating response to therapy.

Patient Preparation

- Refrain from heavy meals, coffee and nicotine 3–4 hours before testing
- Withhold anticholinergic medication 24–48 hours before test
- Withhold medications with α and β activity 24–48 hours before test
- Patients to wear loose fitting clothes.

ELECTROPHYSIOLOGICAL METHOD

Heart Rate Recording

- Three lead ECG with electrodes on anterior chest wall
- Reference electrode at midaxillary line at T_4 level
- Tests of heart rate variability measured as R-R interval.

Blood Pressure Recording

- Continuous or intermittent recording
- Brachial/wrist/finger cuffs used
- Plethysmography and arterial tonometry for non invasive recording.

PARASYMPATHETIC FUNCTION TESTS

Heart Rate Response to Valsalva Maneuvre

Procedure

- Baseline BP and heart rate measured 3 minutes before test
- Patient takes deep inhalation, complete exhalation followed by deep inhalation again
- Patient then exhales deeply into a mouth piece for 15 seconds
- Mouth piece connected to pressure transducer to measure expiratory pressure
- Expiratory pressure maintained at 40 mm Hg
- BP and heart rate measured throughout the maneuver and for 60 seconds after maneuver
- Average of two trials taken for analysis.

Interpretation

- $\text{Valsalva Ratio} = \dfrac{\text{Maximum heart rate}}{\text{Minimum heart rate}}$
- Normal ratio > 1.21.

Summary

Stimulus	Expiration of 40 mm Hg for 15 seconds
Afferent	Baroreceptors, glossopharyngeal, vagus nerves

Contd...

Contd...

Central	Nucleus Tractus Solitarius
Efferent	Vagus and sympathetic nervous system
Response	Maximum: Minimum heart rate > 1.21

Contraindications

- Geriatric patients
- Respiratory disease
- H/o recent retinal surgery.

Misinterpretation

- Hypovolemia
- Medical deconditioning
- Hypothyroidism.

Respiratory Sinus Arrhythmia

Procedure

- Done with patient supine
- Breathing at rate of 6 breaths/min with slow inspiration and expiration
- This provides maximum heart rate variability
- Six to eight cycles are recorded in one/two trials
- Timed breathing potentiates sinus arrhythmia
- Reduced heart rate variability with respiration seen with autonomic disease.

Results

- $\text{E/I ratio} : \dfrac{\text{Sum of longest R-R intervals}}{\text{Sum of shortest R-R intervals}}$
- Normal value : Mean difference of 15 bpm

Summary

Stimulus	Deep breathing (6 breaths/min)
Afferent	Pulmonary receptors, cardiac mechanoreceptors
	Vagus N, Glossopharyngeal N
	Respiratory center
Central	Nucleus Tractus Solitarius
Efferent	Vagus N
Response	HR increase during inspiration
	HR decreases during expiration

Misinterpretation

- Poor respiratory effort
- Hypocapnea
- Salicylates
- Positioning
- Obesity.

Heart Rate Response to Standing

- Baseline heart rate measured in supine position
- Patient asked to stand up quickly
- Heart rate variability measured for atleast 1 minute of active standing.

Interpretation

- 30:15 ratio : $\frac{\text{HR at 15 seconds of standing}}{\text{HR at 30 seconds of standing}}$
- Normal ratio > 1.

Summary

Stimulus	Decreased central blood volume
Afferent	Baroreceptors, Ergoreceptors
	Vagus N, Glossopharyngeal N
Central	Nucleus Tractus Solitarius
	Rostral Ventrolateral Medulla
Efferent	Vagus N
Response	Heart rate increases at 15 seconds
	Heart rate decreases at 30 seconds

Misinterpretation

- Hypovolemia
- Medical deconditioning
- Hypothyroidism.

SYMPATHETIC FUNCTION TESTS

Blood Pressure Response to Sustained Hand Grip

- Sustained hand grip measured by dynamometer
- Blood pressure measured every minute for 5 minutes
- Initial diastolic BP subtracted from DBP just before release of hand grip
- Normal value > 16 mm Hg.

Blood Pressure Response to Standing

- Patient moves from supine to standing position
- Standing systolic BP subtracted from supine SBP
- Normal value < 10 mm Hg.

Tilt Table Test

Procedure

- Patient lies supine on tilt table and belt placed around waist
- BP and heart rate measured throughout the test
- Baseline BP recorded for atleast 3 minutes
- Patient tilted slowly to 60–80 upright angle
- Patient told to report any symptoms
- Patient returned to horizontal supine position
- HR and BP monitored till returns to baseline

Interpretation

- Normal values:
  - No symptoms
  - Decrease in systolic BP < 20 mm Hg
  - Decrease in diastolic BP < 10 mm Hg.

Summary

Stimulus	Decreased central blood volume
Afferent	Baroreceptors
	Vagus N, Glossopharyngeal N
Central	Nucleus Tractus Solitarius
	Rostral Ventrolateral Medulla
	Hypothalamus
Efferent	Sympathetic vasomotor
Response	Fall in SBP with tilting
	Fall in DBP with tilting

Sympathetic Skin Response (SSR)

Procedure

- Standard EMG instrument used
- Sweep speed of 10 sec and band pass filter of 1–2000 Hz used
- Small recording electrode attached to palmar and dorsal surface of hands and feet
- Stable baseline recorded before administering stimulus (electrical/loud noise)
- Sympathetic Skin Response noted
- Recordings can be obtained simultaneously from hands and feet
- 3–4 trials obtained.

Interpretation

- *Normal response:* Monophasic or biphasic deflection which habituates with time
- *Abnormal response:* Absent SSR.

Others

Silastic Imprint Test

- Plastic/silicon film applied to area of sweat gland activity
- Iontophoresis or cholinergic agent given to provoke glands

- Film is removed and number, volume and density of sweat glands studied.

Thermoregulatory Sweat Test

- Indicator like alizarin red applied to patients body
- Patient placed in thermally controlled environment
- Core temperature raised above baseline
- Pattern of color changes expressed as percentage of body surface area calculated.

Quantitative Sudomotor Axon Reflex Test: (Q-Sart)

- Test measures postganglionic sympathetic function
- Small plastic cup placed on skin of arms/legs/both
- Temperature and amount on sweat under skin measured
- Iontophoresis or cholinergic agent used to stimulate sweat glands
- Response measured using sudorometer
- Measures:
  - Resting skin temperature
  - Resting sweat output
  - Stimulated sweat output.

Microneurography

- Intraneural measurement of muscle sympathetic nerve activity
  - Sympathetic outflow to muscle at rest and stimulation measured.

GLASGOW COMA SCALE[1,8,10]

Introduction

Neurological scale which records conscious state of a person for initial and subsequent assessment.

Published in 1974 by ***Bryan Jennett and Graham Teasdale***

Components

S. No	Components	Score
I	**Eye opening**	
	Opens eyes spontaneously	4
	Opens eyes to speech	3
	Opens eye to painful stimuli	2
	No response	1
II	**Motor response**	
	Spontaneous/Purposeful	6
	Localizes pain	5

Contd...

Contd...

S. No	Components	Score
	Withdraws to pain	4
	Abnormal flexion to pain (decerebration)	3
	Abnormal extension to pain (decortication)	2
	No response	1
III	**Verbal response**	
	Oriented and Talks	5
	Disoriented and talks	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No response	1
IV	**Verbal response–intubated**	
	Seems to be able to talk	5
	Confused conversation	4
	Questionable ability to talk	3
	Generally unresponsive	1
V	**Verbal response–pediatric (0 to 2 Yrs)**	
	Oriented, Babbles and coos appropriately	5
	Cries consolably	4
	Cries inconsolably/Screaming in pain/ Persistent crying	3
	Grunts/Moans to pain	2
	No Response	1

Procedure

- Painful stimuli used:
  - Supraorbital pressure
  - Earlobe pinch
  - Trapezius squeeze
  - Sternal rub
  - Nailbed pressure.
- Decorticate/extensor response:
  - Abducted arm
  - Internal rotation of shoulder
  - Pronation of forearm
  - Wrist extension.
- Flexor/decerebrate response:
  - Adducted arm
  - Internal rotation of shoulder
  - Pronation of forearm
  - Wrist flexion.

Uses

- Risk stratification of patients in TBI
- Prediction of outcome based on 24 hours GCS score

- As part of other ICU scoring systems:
  - APACHE
  - SAPS II
  - SOFA
  - WFNS.

Disadvantages

- Response cannot be elicited in
  - Severe facial injury/orbital injury (eye opening response)
  - Injury to limb (motor response)
  - Intubated patients (vocal response)
  - Alcohol intoxication
  - Drug abuse/overdose
  - Shock
  - Spinal cord injuries
- Limited application in children below 36 months
- Long-term prognosis cannot be predicted on this alone
- Does not check memory of patient.

Recent Advances

- ***Abbreviated GCS/AVPU Scale:***
  - A = alert
  - V = responds to vocal stimuli
  - P = responds to painful stimuli
  - U = unresponsive
- ***Ranchos Los Amigos Scale:*** To evaluate TBI patients
- Rappaport coma scale.

Level	Response
I	No response
II	Generalized response
III	Localized response
IV	Confused–agitated
V	Confused–inappropriate
VI	Confused–appropriate
VII	Automatic–appropriate
VIII	Purposeful–appropriate

Prognostication

S. No.	Prognosis	Score	Description
I	Mild disability	13–15	
II	Moderate disability	9–12	Loss of consciousness > 30 mins
			Physical/cognitive impairment

Contd...

Contd...

S. No.	Prognosis	Score	Description
			May/may not resolve
			Benefit from rehabilitation
III	Severe disability	3–8	Comatose
			Unconscious state
			No meaningful response
			No voluntary activities
IV	Vegetative state	3	Sleep–Wake Cycles
			Arousable but no interaction
			No localized response to pain
V	Persistant vegetative state	3	Vegetative state > 1 month
VI	Brain death	3	No brain function

HORNERS SYNDROME[1,2,3]

Introduction

Also called: ***Claude Bernard Horner syndrome Oculosympathetic palsy***

Etiology

- Hemispherical lesions:
  - Lateral medullary lesions
  - Multiple sclerosis
  - Cavernous sinus thrombosis.
- Brainstem lesions:
  - Vasculitis
  - Encephalitis
  - Pontine glioma.
- Cervical cord lesions:
  - Syringomyelia
  - Intramedullary gliomas
  - Ependymomas.
- D1 root lesions:
  - Pancoast tumor (tumor in apex of lung)
  - Cervical rib
  - Klumpkes palsy—avulsion of lower brachial plexus
  - Neurofibromatosis type I.
- Sympathetic chain:
  - Neoplastic
  - Thyroid/laryngeal surgery
  - Massive goiter/thyroid carcinoma
  - Thoracic aortic aneurysm.

- Miscellaneous:
  - Congenital
  - Migraine
  - Orbital lesions
  - Middle ear infections.
- Procedural:
  - Nerve blocks
  - Cervical plexus block
  - Stellate ganglion block
  - Interscalene block
  - During tube thoracostomy.
- Components:
  - Ptosis
  - Miosis
  - Anhydrosis (Ipsilateral)
  - Enophthalmos
  - Loss of ciliospinal reflex
  - Conjunctival redness.

Anatomy

Three orders of neurons in sympathetic chain:

- Ist order neurons:
  - From hypothalamus to lateral grey matter in thoracic spinal cord.
- IInd order neurons:
  - Preganglionic neurons from spinal cord to superior cervical ganglion.
- IIIrd order neurons:
  - Postganglionic from superior cervical ganglion to pupils and blood vessels of eye.
- Oculomotor N supplies elevator of eyelid (Mueller's muscle)
- Nasociliary N supplies blood vessels
- Long ciliary N innervates pupils
- Site of lesion is on ipsilateral side of symptoms.

Clinical Features

In All Patients

- Partial Ptosis: Due to loss of innervation to Mueller's muscle
- Miosis:
- Anhydrosis:
  - Involves entire side of face in common carotid A area
  - Only medial side of forehead and side of nose if distal to CCA bifurcation.
- Enophthalmos
- Loss of ciliospinal reflex
  - Afferent C2 C3
  - Pupils fail to dilate when back of neck is pinched
  - Inconsistent
  - Blood shot conjunctiva.

In Some Patients

- *Anisocoria:* Affected pupil dilates slower than normal pupil
- *Heterochromia iridis:*
  - More often in children
  - Difference in color between 2 eyes
  - Lack of sympathetic stimulation affects melanin pigmentation in superficial stroma of iris.
- *Hortons headache:* Horners syndrome + Cluster headache
- *Harlequin effect:*
  - Flushing of ipsilateral side of face due to dilatation of subcutaneous blood vessels
  - Seen on exercising.

Variants

- Raeder paratrigeminal syndrome:
  - Episodic retrobulbar/orbital pain
  - Miosis
  - Ptosis
  - No associated cranial N findings.
- Central lesions affect sweating over entire head neck arm and upper trunk on I/L side
- Lesions in lower neck affect sweating over entire face
- Lesions above superior cervical ganglion may not affect sweating at all.

Investigations

Pharmacological Test

- Cocaine drop test:
  - Cocaine dilates normal pupils
  - Mydriatic failure in Horners syndrome.
- Apraclonidine test:
  - Test of choice
  - Reversal of mydriasis on affected side of Horners syndrome.
- Paredrine test:
  - Localizes cause of miosis
  - Amphetamine dilates pupils if IIIrd order neurons are intact
  - No effect if IIIrd order neurons are affected, pupils remain constricted.
- Dilation Lag Test.

Nonpharmacological Tests

- X-ray chest
- MRI head neck and chest
- MR angiography for carotid artery dissection.

Treatment

Treat the cause.

GUEDEL'S STAGES OF ANESTHESIA[1,2,3]

Introduction

- Described by ***Arthur E Guedel*** in 1920 with ether
- Regarded obsolete now due to use of rapid acting IV induction agents and muscle relaxants
- Depth estimated with BIS/entropy
- With thiopentone induction patient directly enters Stage III, Plane II.

Prerequisites

- For use with sole inhalational anesthetic ether
- Premedicated with atropine
- IV anesthetic agents/morphine/muscle relaxants not used.

Stages

Plane	Extent	Description
Stage I: Stage of analgesia and amnesia		
	Beginning of induction to LOC	Loss of memory intellect perception of time, space
		Sensation of pain present
		Altered reaction to pain
		Used for minor surgeries
		IInd stage labor analgesia/ dental procedures
Divided into 3 planes by Joseph F Artusio		
I		Patient does not experience amnesia/analgesia
II		Complete amnesia, but only partial analgesia
III		Complete analgesia and analgesia
Stage II: Stage of delirium/excitement		
	LOC to onset of regular breathing (RB)	Loss of eyelash reflex
		Other reflexes intact

Contd...

Contd...

Plane	Extent	Description
		Struggling coughing vomiting possible
		Irregular respiration with breatholding
		Patient should not be stimulated
		Reaction to stimulus maybe violent and injurious
Stage III: Stage of surgical anesthesia		
	Onset of RB to respiratory paralysis (RP)	
Divided into 4 Stages:		
I	Onset of RB to cessation of eye movement	Loss of eyelid and conjuctival reflex
		Loss of swallowing reflex
		Marked eyeball movement possible
II	Cessation of eyeball movement to commencement of intercostals palsy	Loss of corneal and laryngeal reflexes
		Pupil centrally fixed middilated reactive to light
		Increased secretion of tears
		Automatic and regular respiration
		Loss of movement to skin stimulation
III	Commencement to completion of intercostal palsy	Loss of light reflex
		Pupils dilated
		Persistence of diaphragmatic respiration
		Progressive intercostal palsy
		Desired plane for surgery
IV	Intercostal palsy to diaphragmatic palsy	
Stage IV: Stage of medullary paralysis		
	Stoppage of respiration till death	Medullary paralysis
		Respiratory arrest and vasomotor collapse
		Pupils widely dilated, muscles relaxed

PERIOPERATIVE CEREBRAL PROTECTION[1,2,3,6]

Introduction

Neuroprotection is defined as the treatment initiated before the onset of ischemia, intended to modify intra-ischemic cellular and vascular biological responses to deprivation of energy supply so as to increase tolerance of tissue to ischemia.

Physiological Basis

- Central nervous system consumes 20% of O_2 at 150 µmol/100g/min
- CNS consumes 25% glucose at 30 µmol/100 g/min
- Cerebral metabolism is divided into:
  - Functional component:
    - Comprises 60% of neuronal O_2 use
    - Important for generating action potentials
    - Maybe assessed using EEG
    - Anesthetics (thiopentone, propofol, etomidate and volatile anesthetics) reduce functional component
    - Thus, ideal anesthetics produce at the most a 60% reduction in O_2 use.
  - Cellular integrity component:
    - Only hypothermia reduces functional and integrity component
    - No effect of anesthetics on integrity component.

Ischemic Events

Anticipated Events

- Cerebral aneurysm clipping:
  - Incidence of infarction reduced in patients receiving neuroprotective agents.
- Cartoid endarterectomy
  - Neuroprotection reduces frequency and severity of perioperative stroke
  - Use of surgical shunt, barbiturate coma, anticoagulation and maintaining high MAP with fluids and vasopressors.
- Cardiopulmonary bypass.

Unanticipated Events

- Cardiac arrest
  - Mild hypothermia reduces neurological morbidity and mortality
  - The 2005 International Emergency Cardiac Care Guidelines.
- Spontaneous stroke.

Neuroprotective Interventions

Physiological Interventions

- Hypothermia
  Mechanisms of action:
  - Reduces functional and integrity components of cerebral metabolism
  - Increases blood brain barrier stability
  - Preserves ATP and reduces calcium influx
  - Maintenance of ion homeostasis
  - Reduced levels of excitatory amino acids and free radicals.
- Guidelines for use:
  - *2005 IECC guidelines:* Mild hypothermia reduces neurological morbidity and mortality
  - IHAST II (Intraoperative Hypothermia for Aneurysms Surgery Trial)—mild hypothermia not beneficial in patients undergoing cerebral aneurysm surgery
  - Hypothermia improves outcome following global cerebral ischemia
  - No such effect is seen following focal ischemia
  - Beneficial temperature threshold is 33–35 ºC
  - Deep hypothermia < 20 ºC if prolonged cardiac arrest.
- Disadvantages
  - Reduced metabolism of drugs
  - Coagulation abnormalities
  - Cardiac rhythm disturbances
- Examples
  - Deep hypothermic circulatory arrest where at temperatures of 15–18 ºC, intact cerebral function may be regained after up to 60 minutes of complete global ischemia.
  - When core body temp is < 20 ºC, circulatory arrest of < 30 mins appears to be well tolerated
  - Most prospective trials did not show any benefit of hypothermia (33 ºC) induced within 8 hours of injury and maintained for 48 hours.
- Cerebral perfusion pressure
  - Maintain normotension
  - Cerebral blood flow is autoregulated over a CPP of 60–150 mm Hg
  - Maintain CPP between 50–70 mm Hg *(BTF 2007)*
- Arterial CO_2 levels
  - Maintain normocapnea
  - l kPA (7.5 mm Hg) change in $PaCO_2$ causes a 15 ml/100g/min change in CBF
  - Prolonged hyperventilation is not advised
  - Only brief periods of hyperventilation $PaCO_2$ < 35 mm Hg advised when acute neurological deterioration *(BTF 2007)*

- Glycemic control
  - Hyperglycemia increases infarct size, as glucose is metabolized anaerobically to release lactic acid
  - Lactic acid contributes to acidosis in neuronal tissues causes neuronal necrosis
  - American Endocrinology Association Guidelines:
    - Perioperative glycemic levels: 90–130 mg%
    - ICU glycemic levels: 110–180 mg%
    - Intraoperative glycemic levels: < 150 mg%
- Seizure prophylaxis
  - Untreated seizures can produce neuronal necrosis
- Maintain Normal pH.

Pharmacological Interventions

Barbiturates

- Considered gold standard of brain protective anesthetics during focal ischemia
- Hypothermia is for global ichemia and barbiturates for focal ischemia
- Mechanism of action:
  - Metabolic suppression
  - Favorable redistribution of cerebral blood flow to ischemic areas (Robin-Hood effect)
  - Membrane stabilization
  - Free radical scavenging
  - Altered ion homeostasis
  - Reduced glutamate activity
  - Reduced intracellular calcium
  - Increased GABA activity and NMDA antagonism.
- High doses which produce isoelectric EEG with maximal EEG suppression have equivalent cerebral protective effects as smaller doses (one third isoelectric EEG dose)
- Disadvantages:
  - Not useful if hemodynamically unstable
  - Reduced cardiac contractility
  - Systemic hypotension
  - Compromises cerebral oxygen delivery.

Propofol

- Produces burst suppression of EEG, thus reducing $CMRO_2$ by 50%
- Useful for mild insults and less for moderate-severe insults
- Mechanism of action:
  - Increased GABA activity
  - Free radical scavenging
  - Limits lipid peroxidation.

Volatile Anesthetics

- Isoflurane effective in mitigating mild-moderate ischemic insult
- May be effective when applied during ischemic insult
- Also effective when given as preconditioning therapy
- Seroflurane also useful: No trials to guide clinical practice.

Newer Approaches

Statin Therapy

- Inhibit 3 hydroxy 3 methyl glutaryl COA (HMG–CoA)
- Neuroprotective actions:
  - Improved endothelial function
  - Antithrombotic
  - Anti-inflammatory.

Erythropoietin

- Mitigates lipid peroxidation
- Prevents apoptosis.

MALIGNANT HYPERTHERMIA[1,2,3,6]

Introduction

Pharmacogenetic syndrome occurring during anesthesia with volatile halogenated alkanes and succinylcholine causing rapidly increasing body temperature and extreme acidosis due to acute loss of control of intracellular calcium levels.

Incidence

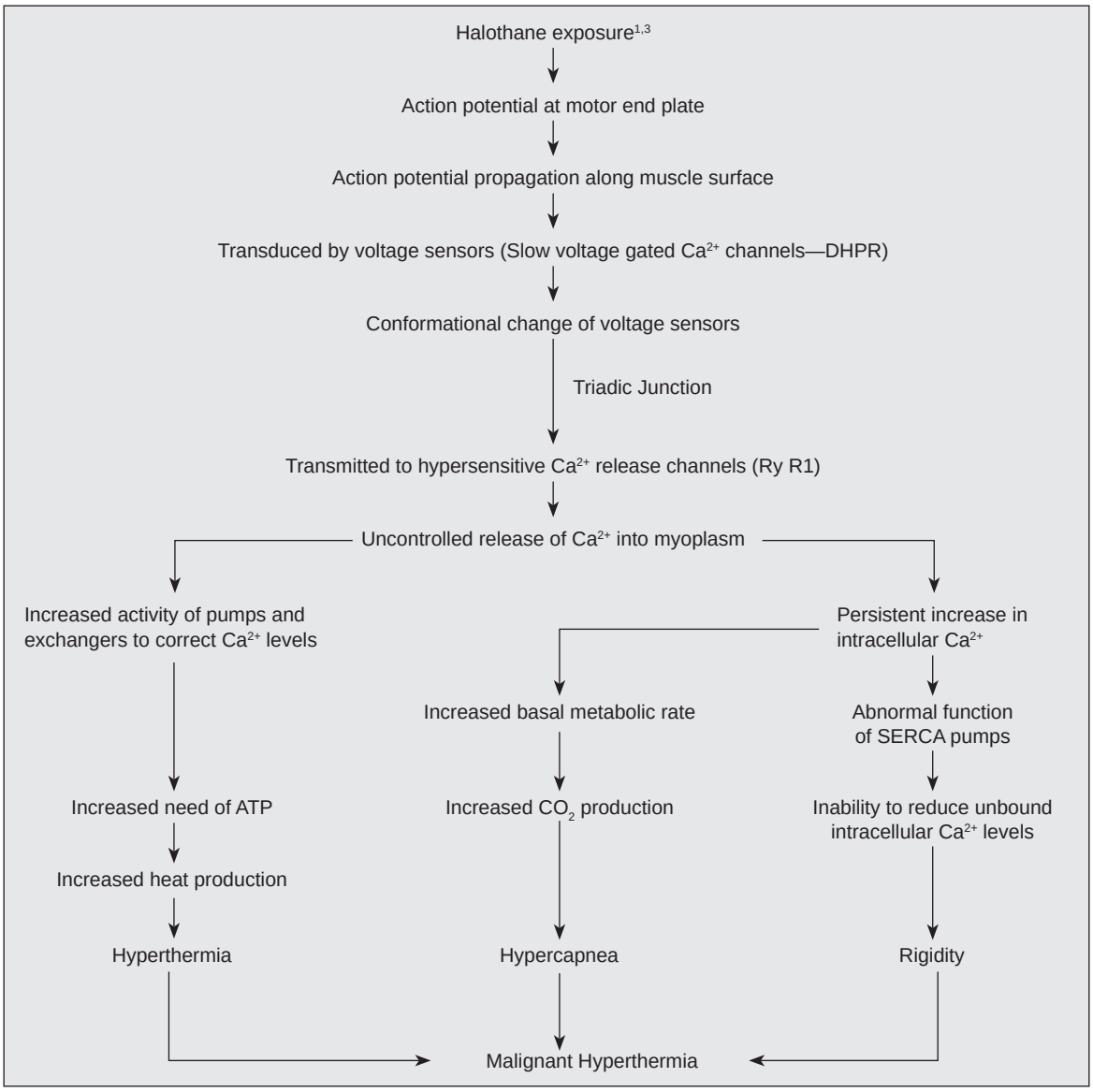
- 1:14 000
- Increased to 1:2500 in squint surgeries
- Most common in children and adolescents.

Etiology

- Autosomal dominant with variable penetrance
- Occurs due to multiple mutations in:
  - Skeletal muscle Ca^{2+} release channel *(R_yR_1-type I)*
  - L-type calcium channel
  - Dihydropyridine receptor (DHPR)
  - Some suggest polygenic mutation

Pathophysiology

- Occurs due to abnormal functioning of calcium release units (CRU)
- CRU is a macromolecular assembly of interacting proteins which participate in Excitation–Contraction coupling
- Ryanodine receptor is a central part of CRU
- Occurs from increased sensitivity to:
  - Volatile anesthetics
  - Succinylcholine
  - Caffeine
  - Ryanodine
  - 4 chloro-m-cresol
  - K^+ depolarization.



Risk Factors for Malignant Hyperthermia

Neuromuscular Disorders

- Strabismus, ptosis
- Meningomyelocele
- Hypoplastic mandible, poor dental enamel, cleft palate
- Myotonic dystrophy, muscular dystrophy
- Pectus carinatum
- Kyphoscoliosis

- Osteogenesis imperfecta
- Clubfoot.

Syndromes

- ***Duchennes*** muscular dystrophy
- ***Beckers*** dystrophy
- ***King***–Denborough syndrome
  - Short stature
  - Mental retardation
  - Cryptorchidism
  - Kyphoscoliosis
  - Pectus deformity
  - Slanted eyes
  - Low set ears
  - Webbed neck
  - Winged scapulae.
- Arthrogryposis multiplexa congenita
- Periodic paralysis.

Surgeries

- Tonsilectomy, adenoidectomy, dental surgery
- Orthopedic surgery (joint dislocation)
- Ophthalmic surgery (squints)
- Head and neck surgery.

Body Habitus

- Short, stocky stature (Marfanoid features too)
- Bulky muscles, rounded belly
- Muscle hypertrophy, atrophied muscle groups, muscle cramps
- Intolerance to caffeine.

Clinical Features

Classic Malignant Hyperthermia

- Acute onset of symptoms
- If succinylcholine is used fulminant MH within 5–10 minutes possible
- Can be delayed upto 4 hours postoperatively

Use of succinylcholine/halothane followed by:

- Hypermetabolism
  - Increased $ETCO_2$ with adequate ventilation most sensitive sign
  - $ETCO_2$ may be > 100 mmHg
  - Increase O_2 consumption with decreased SpO_2
  - Tachypnea, cyanosis, mottling of skin
  - Unexpected metabolic acidosis (pH may be < 7)
  - Central venous desaturation.
- Hyperthermia
  - Fever (> 1 ºC rise every five minutes)
  - Sweating
  - Increased body temperature > 38.8 ºC with no obvious cause
  - Core temperature may exceed 43 ºC
  - Temperature may not increase if heat loss exceeds production/cardiac output decreases early.
- Sympathetic Activity
  - Tachycardia–cardinal and earliest sign
  - Hypertension
  - Arrhythmias.
- Muscle Damage/Rigidity
  - Masseteric spasm
  - Generalized rigidity
  - Increase creatinine kinase, myoglobinemia, myoglobinuria
  - Hyperkalemia, hypernatremia, hyperphosphatemia.
- Complications
  - Acute renal failure
  - DIC
  - Cardiac failure – pulmonary edema
  - Cerebral edema, coma, paralysis
  - Hepatic failure.

VARIATIONS IN PRESENTATION

- MH Associated with less muscle rigidity
- MH Associated with less hyperthermia
- Masseteric rigidity/masseteric spasm (MMR)

Introduction

Jaw muscle rigidty which limits muscle flaccidity after administration of succinylcholine

Etiology

- Due to presence of slow tonic fibers in masseter and lateral pterygoid
- These muscles respond to depolarizing muscle relaxants with contracture.

Clinical Features

- May be mild spasm or very rigid (jaws of steel)
- More common in children and young adults
- May occur even after pretreatment with defasciculating dose of NDMR
- It is less common after IV induction
- Most common after IV succinylcholine but can occur with any IV agent[3]
- Flaccid paralysis of peripheral nervous system
- Frank MH supervenes in 30% cases and is more if MMR associated with rigidity of chest and other limb muscles.

Differential Diagnosis

- Myotonic syndrome
- TM joint dysfunction
- SCH underdose
- Not allowing sufficient time for SCH action
- Malignant hyperthermia.

Treatment

Severe Rigidity

- Discontinue anesthetic and postpone surgey
- Dantrolene 1 mg/kg
- Monitor for 12–24 hrs
- Creatinine kinase at 6, 12, 24 hours and longer if required
- Symptomatic treatment.

Moderate Rigidity

- Halt surgery/continue with nontriggering agents depending on situation.

Mild Rigidity

- Continue anesthetic with proper monitoring.

Factors Affecting Severity

- Depends on 4 variables:
  - Genetic predisposition
  - Absence of inhibiting factors
  - Presence of anesthetic/nonanesthetic triggers
  - Presence of potentiating environmental factors.
- Factors delaying onset of MH:
  - Mild hypothermia
  - Preadministration of barbiturates, propofol, nondepolarizing MR.

Triggering Agents

Unsafe

- Ether, Cyclopropane, Methoxyflurane
- Halothane, enflurane
- Isoflurane
- Sevoflurane, Desflurane (lesspotent)
- Succinylcholine
- Potassium
- Avoid phenothiazines[3]
- Caffeine, ryanodine
- K^+ depolarization.

Safe to Use

- Nitrous oxide
- Opioids, barbiturates, benzodiazepines
- Ketamine, propofol, etomidate
- Nondepolarizing muscle relaxants, neostigmine
- Local anesthetics (even amides)
- Antibiotics
- Antihistaminics, droperidol
- Propranolol
- Vasoactive drugs
- May also be triggered by exercise, heat, anxiety and anoxia.

Intraoperative Diagnosis

Usually occurs within minutes of using succinylcholine/volatile agents.

It can occur immediate postoperatively but usually not beyond 4 hrs postoperatively:

- Unexpected increase in $ETCO_2$
- Unexplained tachycardia, arrhythmias
- Unstable BP
- Tachypnea, cyanosis, if spontaneous ventilation
- Increased temperature, sweating, mottling of skin
- Muscle rigidity
- Metabolic/respiratory acidosis
- CO_2 absorbent becomes warm to touch as the reaction with CO_2 is exothermic.

Investigations

- Hyperkalemia, increased ionized calcium
- Hyperphosphatemia, serum Na^+ and Mg^{2+}
- Decreased pH and PO_2, increased PCO_2 (pH < 7), decreased MvO_2
- Increased CK > 20000 IU/L (monitor every 6 hrs for 24 hrs)
- Increased myoglobin, lactate, pyruvate, LDH, aldolase.

Larach's Clinical Grading Scale[3]

Muscle Rigidity

• Generalized rigidity	15
• Masseteric rigidity	15

Myonecrosis

• CK > 20000 (with succinylcholine)	15
• CK > 10000 (without succinylcholine)	15
• Cola colored urine	10
• Myoglobin is urine > 60 µg/l	5
• Serum K^+ > 6 mEq/l	3

Respiratory Acidosis

• $ETCO_2$ > 55 with controlled ventilation	15
• $PaCO_2$ > 60 with controlled ventilation	15

- $ETCO_2$ > 60 with spontaneous ventilation 15
- Inappropriate hypercarbia 15
- Inappropriate tachypnea 10

Temperature

- Rapid increase in temperature 15
- Inappropriate temperature > 38.8 ºC 10

Cardiac Involvement

- Inappropriate tachycardia 3
- VT or VF 3

Sum of > 50 implies D_6 (almost certainly Malignant Hyperthermia).

Sum of 35–49 implies D_5 (very likely to be Malignant Hyperthermia).

Differential Diagnosis

- Pheochromocytoma:
  - Very high hypertension (Pheochromocytoma > thyrotoxicosis > MH)
  - No associated muscle rigidity and acidosis.
- Thyrotoxicosis:
  - High HTN compared with MH
  - No associated muscle rigidity and acidosis.
- Sepsis:
  - Persistant rigidity is rare (rigors associated with fever may be present)
  - Treated effectively with NSAIDs, antibiotics and cardiovascular support
  - MH does not respond to such treatment.
- Mitochondrial myopathies
- Rhabdomyolysis
- Muscular dystrophy
- Neuroleptic malignant syndrome
- Contrast dye/drug anaphylaxis
- Drug abuse/toxic overdose
- Heat stroke
- Diabetic coma, hypokalemic periodic paralysis
- Serotonin syndrome: Drug induced hyperthermia
- Hypoxic encephalopathy (Brainstem/hypothalamic injury).

Screening/Predictors of MH

- Plasma CK values: (> 20000 IU/L)
  - If increased in close relatives of patients with MH, considered to have MH (without contracture testing)
  - If normal on several occasions it has no predictive value and contracture studies are necessary
  - Nonspecific test.
- *Caffeine Contracture Test:*
  - Diagnostic of malignant hyperthermia
  - Skeletal muscle biopsies (1–3 g) taken from vastus lateralis muscle
  - Muscle divided into strips measuring 15–30 mm × 2–3 mm width and 2–3 mm thickness
  - Strips are mounted in muscle bath apparatus
  - Strips are then stimulated at 0.1–0.2 Hz to check for muscle viability
  - Halothane and varying concentrations of caffeine are added to different muscles strips
  - Ryanodine and 4-chloro-m-cresol have also been used
  - Patients susceptible to MH show contractures at much lower concentration of halothane and caffeine.
- Nuclear magnetic resonance spectroscopy (using forearm ischemia):
  - Evaluates ATP depletion during graded exercise
  - MH patients have greater breakdown of ATP and creatine phosphate.
- Single muscle fiber contracture studies
- In vivo microdialysis:
  - Small quantities of caffeine/halothane injected through microdialysis catheter into thigh muscle
  - Samples of local CO_2 and lactate levels taken.
- DNA testing for mutations in R_yR_1 using B—lymphocytes
- Electromyography, motor unit counting and microscopic examination of muscle.

Treatment

Discontinue Trigger

- Discontinue all anesthetic agents
- Secure another anesthesia machine with ambu bag support
- E cylinder of oxygen kept ready
- Change tubing and soda lime too
- Hyperventilate with
  - 100% FiO_2
  - Minute ventilation ≥ 10 l/min
  - O_2 flow ≥ 10 l/min.

Monitor

- *Pulse oximeter;* IBP unstable
- *$ETCO_2$;* Urine output
- *ECG;* CVP (individualized)
- *Temperature;* ABG/electrolytes
- *Coagulation;* INR, PT, platelet count, FDP, fibrinogen
- Muscle tone.

Secure

- Wide bore IV cannula
- Arterial line/CVP
- Foleys catheter (as every 20 mg dantrolene has 3 gms mannitol)
- Nasogastric tube.

Dantrolene[1]

- 2.5 mg/kg IV Q5-10 mins until symptomatic improvement or total dose of 10 mg/kg
- Continue at 1 mg/kg IV Q6H for 24–48 hrs to prevent relapse.

Control Hyperthermia

- Iced IV fluids
- Cool body surface—cooling blanket packed with ice
- Ice packs on groin and axilla
- Gastric, rectal, wound and peritoneal lavage with iced saline.
- Stop cooling at 38 ºC to prevent hypothermia
- Cold peritoneal dialysis/cardiopulmonary bypass if intractable.

Symptomatic

- Acidosis—soda bicarbonate 2–4 mEq/kg IV
- Cardiac glycosides and inotropes
- Antiarrhythmics—lidocaine IV useful
- Calcium channel blockers when used with dantrolene causes cardiac arrest
- Hyperkalemia:
  - Insulin 0.15 IU/kg IV
  - Glucose - 1 ml/kg 50% dextrose
  - Calcium gluconate 10% 10 ml over 10 mins if unstable
  - Dantrolene is best to reverse hyperkalemia.

Diuresis

- Mannitol 0.5 g/kg or furosemide 1 mg/kg IV
- Maintain urine output ≥ 1 ml/kg/hr.

Postoperative Care

- Monitor:
  - Cardiovascular and respiratory stability
  - Urine output
  - Coagulation profile
  - Acid base and electrolytes.
- Keep body temperature ≤ 38 ºC
  - Administer dantrolene 1 mg/kg IV Q6H
  - Continue dantrolene for at least 24 hrs after successful treatment of episode
  - Maintain urine output ≥ 1 ml/kg/hr
  - Symptomatic treatment of muscle pain
  - Give soda bicarb to maintain alkaline urine.

ANESTHESIA FOR MH SUSCEPTIBLE PATIENTS

Choice of Anesthetic Technique

- RA/NAB safe and preferred technique
- TIVA is safe
- If GA used, nontriggering anesthetic technique
- Epidural anesthesia safest technique for C-section without dantrolene prophylaxis.

Technique of General Anesthesia

- Preop preparation:
  - Adequate reassurance and counselling
  - Adequate premedication to produce low normal heart rate
  - Premedication with opioids, benzodiazepines, barbiturates
  - Anticholinergics and antihistaminics safe
  - Avoid phenothiazines
  - Routine dantrolene prophylaxis not recommended
  - 5 mg/kg/24 hrs IV or PO if required
  - Alternately, 2.5 mg/kg 15–30 mins IV before surgery
- OT preparation
  - Ventilator preparation
  - Equipment for rapid ABG and electrolyte measurement
  - Cooling aids
    - Hypothermic blanket
    - Crushed ice
    - Cold saline
    - NG tube
    - Foleys catheter.
  - MH cart with:
    - Soda bicarb
    - Dantrolene, sterile water
    - Mannitol/furosemide
    - Antiarrhythmics
    - Insulin, 50% dectrose
    - Calcium gluconate.
  - Monitors:
    - Pulse oximeter
    - ECG
    - Capnogram
    - NIBP
    - Temperature monitor

- Machine preparation[1]
  - Vapour free anesthesia machine
  - Remove/seal vaporizers
  - Change soda lime
  - Replace fresh gas flow hose, reservoir bag
  - Use fresh circuit
  - Flush machine with 10 l/min flow for 10 mins
  - Use disposable circuit where possible.
- Induction
  - Fentanyl 2 µg/kg + midazolam/thiopentone 3–4 mg/kg
  - Intermediate acting Non-Depolarizing Muscle Relaxants (NDMR) for muscle relaxation
  - Ventilate with O_2 and N_2O
  - Topical anesthesia of larynx and vocal cords with local anesthetic spray if required during intubation.
- Maintenance
  - O_2 + N_2O + fentanyl 1 µg/kg boluses+ NDMR
  - MH unlikely if no signs of MH in 1st hour intraop with safe technique.
- Postoperative
  - Vigilant monitoring
  - Minimum PACU stay of 4 hrs recommended
  - Adequate IVF and oral intake reduces chances of fever due to dehydration.

TREATMENT OF RAISED ICP[1,2,3,10]

Introduction

- Goal of treating ICP is to maintain a Cerebral Perfusion Pressure (CPP) of 50–70 mm Hg
- Brain Trauma Foundation 2007 guidelines—BTF 2007.

Management Goals

Airway: Early tracheal intubation if GCS < 8 or unable to meet respiratory goals.

Respiratory

- Avoid hypoxia, maintain SpO_2 > 97%, PaO_2 > 80 mm Hg
- Maintain $PaCO_2$ between 35 to 37 mm Hg
- Hyperventilation with $PaCO_2$ between 30 to 35 mm Hg only if indicated.

Cardiovascular

- Avoid hypotension, maintain MAP > 80 mm Hg
- Replace intravascular volume
- Avoid hypotonic and glucose containing solutions
- Use blood as necessary, reverse existing coagulopathy
- Vasopressors, as necessary to maintain cerebral perfusion pressure.

Central Nervous System

- Monitor ICP, avoid ICP > 20 mm Hg
- Maintain CPP > 60 mm Hg
- Adequate sedation and analgesia
- Hyperosmolar therapy
- Maintain serum sodium < 155 mEq/l, Posm < 320 mosm/l
- CSF drainage
- Treat seizures
- Barbiturate coma, decomporessive craniectomy, hypothermia for refractory raised ICP.

Metabolic

- Monitor blood glucose
- Aim for blood glucose 108–180 mg/dl
- Avoid hyperthermia
- DVT thromboprophylaxis.

GENERAL MEASURES

Airway

- Intubation if altered consciousness to:
  - Reduce risk of aspiration
  - Maintain oxygenation and ventilation.
- *PEEP < 10 cm H_2O* recommended
- Use ICP and CVP monitoring if higher PEEP required
- PEEP may increase ICP as it increases intrathoracic pressure and reduces cerebral venous outflow.

Sedation

- Barbiturates used if hemodyamically stable
- Propofol is an alternative but only for short-term
- Propofol infusion syndrome (PRIS) occurs on long-term
- Treatment guided by EEG burst suppression
- Inhalational agents: Isoflurane dose < 1 MAC recommended.

Anticonvulsants

Phenytoin 15 mg/kg IV at < 50 mg/min.

SPECIFIC MEASURES

Reduce Brain Water: Osmotherapy

Mechanism of action:

- Establishes osmotic gradient across blood brain barrier to reduce brain ECF
- Reduces brain water content and CSF pressure in 20 mins

- Compensatory cerebral vasoconstriction in response to an increase in cerebral blood flow
- Rise in BP causes autoregulatory cerebral vasoconstriction and reduction in cerebral blood volume.

Mannitol

- 0.25–1 g/kg over 10–15 minutes
- Sudden exposure to high osmolarity can cause vasodilation and increase CBF
- Up to 2 g/kg can be tried if serum osmolarity > 320 mosm/kg.

Hypertonic Saline

- 7.5% or 3% at 20–40 ml/hr can be used
- Some studies say hypertonic saline more effective than mannitol
- Efficacy yet to be proven
- No electrolyte disturbance as occurs with mannitol
- Brisk diuresis is absent as with mannitol
- Can cause:
  - Osmotic demyelination
  - Rebound increase in ICP
  - Coagulopathies
  - Volume overload
  - Electrolyte abnormalities and renal failure.
- Should be given via central line
- Tapered off slowly to prevent rebound hyponatremia
- Mixture of sodium chloride and sodium acetate used if hyperchloremic acidosis occurs.

Mannitol with 0.5–1 mg/kg frusemide may be more effective than mannitol alone.

Other alternatives: Urea, glycerol, sorbitol, HS-dextran.

Remove CSF

- External ventricular drain, ventriculostomy
- Subarachnoid catheter/screw
- Lumbar drain
- Maybe difficulty if ventricular collapse associated with edema
- Trauma and infection may occur
- Shunt procedures.

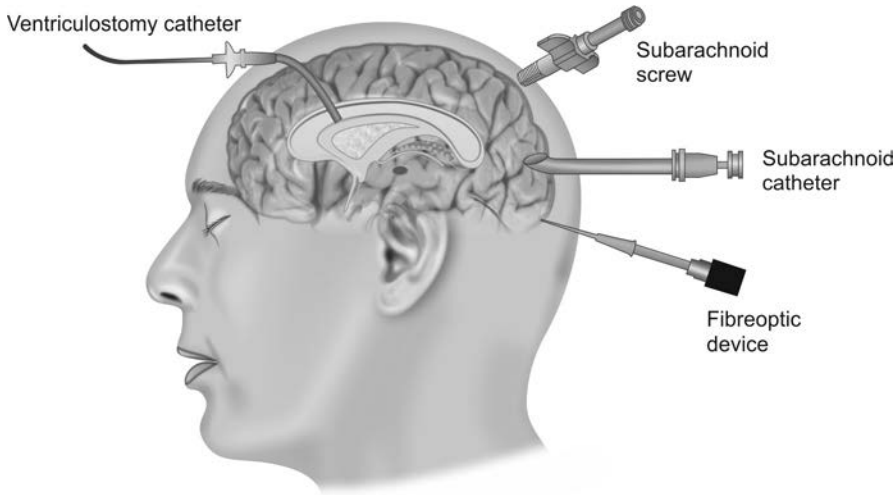


Fig. 1.9: Raised ICP: Interventions

Reduce Cerebral Blood Volume

Position

- Neutral head position
- 15–30° elevation of head end recommended—increases venous drainage
- Avoid flexing/turning head to avoid IJV obstruction
- Abdominal decompression as increased IAP reduces venous outflow from lumbar veins.

Hyperventilation: BTF 2007 Guidelines

- Indications:
  - Brief periods of hyperventilation ($PaCO_2$< 35) when acute neurological deterioration
  - Prolonged hyperventilation only in refractory intracranial hypertension
  - To improve surgical field.

- Avoided in:
  - First 24 hrs after Traumatic Brain Injury (TBI)
  - Hyperventilation in first 24 hrs compromises cerebral perfusion when CBF is already low.
- Guidelines:
  - Level of hyperventilation controversial
  - Limit reduction in $PaCO_2$ to 25 mm Hg as:
    - Below 25 mm Hg, very little additional benefit
    - Increased chances of cerebral ischemia due to vasoconstriction.
  - If chronically hyperventilated (> 2 days) avoid rapid restoration of $PaCO_2$
  - In craniotomy patients, $PaCO_2$ to be increased after retractors are removed to minimize residual pneumotocele.
- Disadvantages:
  - Hyperventilation causes cerebral vasoconstriction
  - This reduces CBF when $CMRO_2$ is high
  - Therefore increased chances of cerebral ischemia
  - CBF and ICP return to normal in 8–12 hrs due to reduction in CSF bicarbonate levels by altered function of carbonic anhydrase.

Increase MAP

- Adequate IV resuscitation to maintain euvolemia
- Phenylephrine, dopamine and norepinephrine used to ensure CPP between 60–70 mm Hg
- Intraoperative BP maintained within 10% of awake values.

Excise Mass Lesions

- Tumor/hematoma excision
- This is most definitive treatment.

Other Measures

Steroids

- 4 mg dexamethasone QID
- Not recommended in head injury management protocols routinely
- Restores blood brain barrier and reduces edema
- Improves viscoelastic property
- Takes 48–72 hrs to act
- Administer 48 hrs before surgery for action to be apparent.

Hypothermia

- Head injured patients with mild hypothermia (< 35 ºC) had better outcomes
- Not routinely recommended
- Reduces ICP and CBF and also attenuates biochemical reactions occurring at time of injury
- Increases risk of pneumonia, wound infections, and coagulopathies.

Cerebral Vasoconstrictors

- Dihydroergotamine is precapillary vasoconstrictor
- Used in refractory intracranial hypertension in patients with TBI
- Limited experience.

Refractory Intracranial Hypertension

- High dose barbiturate *(Pentobarb coma)*.
- Thiopentone 10–15 mg/kg IV
- Aggressive hyperventilation
- Surgical options:
  - Hemicraniectomy
  - Frontal/temporal lobectomy
  - Decompressive craniectomy
  - Decompressive exploratory laparotomy.

ANESTHESIA FOR RAISED ICP[1,2,3,6]

Anesthetic Considerations

- Maintain CPP around 50–70 mm Hg
- Avoid increase in CBF and ICP
- *Loose brain* which facilitates access to lesion
- IPPV to control $PaCO_2$ and good oxygenation.

Preoperative Evaluation

Clinical Features

- Early:
  - *Headache:* Focal neuro deficits
  - *Vomiting:* Papilledema, blurred vision
  - Seizures
  - Headache which is postural and awakens patient at night.
- Late:
  - Hypertension, bradycardia, Cheyne-Stokes breathing (Cushings triad)
  - Agitation, drowsiness, coma
  - Apnea
  - Ipsilateral followed by bilateral pupillary dilation
  - Decorticate followed by decerebrate posturing
  - Obtain history of medication to reduce ICP.

Investigations

- Routine blood—Complete blood count, coagulation profile, blood group and type

- RFTS and LFTS
- X-ray skull: Silver beaten appearance
- CT/MRI:
  - Midline shift, obliteration of sulci
  - Ventricular effacement/enlargement, edema.

Preoperative Preparation

- Dehydration and dyselectrolytemia due to vomiting and diuresis corrected
- Continue steroid therapy if patient is on chronic steroid therapy
- Loading dose of phenytoin 15 mg/kg IV
- Loss of consciousness and any focal neuro deficits documented
- Avoid sedation in drowsy patients
- In awake patients, benzodiazepines on night before and morning of surgery
- IV fluids at < 30 ml/kg/day if cerebral edema present.

Induction

- Thiopentone 3–5 mg/kg or propofol 1.5 mg/kg + fentanyl 2–3 µg/kg + vecuronium 0.15 mg/kg
- Rapid inhalational induction in children
- Rapid sequence induction with cricoid pressure and scholine of difficult airway
- Smooth unhurried induction to avoid increase in ICP
- Avoid coughing and straining
- IV lidocaine 1–1.5 mg/kg to avoid raised ICP at intubation
- Avoid obstructing neck with ETT ties to avoid increasing venous pressure.

Monitoring

- *Pulse oximetry;* Foleys catheter
- *$ETCO_2$;* Temperature
- *ECG;* Neuromuscular monitoring
- *NIBP/IBP;* Central Venous Pressure
- ICP monitoring.

Ventilation

- Controlled mandatory ventilation
- Normocapnia/mild hypocapnea (30–35 mm Hg)
- Avoid PEEP
- If used, PEEP < 10 mm Hg recommended.

Position

- 15–30º head up tilt to improve venous drainage
- Head in neutral position
- Avoid undue flexion/turning of head to avoid IJV compression
- Avoid undue abdominal pressure to avoid increasing IAP.

Maintenance

- O_2 + air + isoflurane/seroflurane (0.5–1 MAC) + fentanyl boluses + NDMR
- Avoid nitrous oxide as it increases ICP
- TIVA is a good alternative which allows good ICP control
- Enflurane contraindicated in neurosurgery as it causes seizures especially with hypocapnea
- Mannitol can be used before craniotomy—facilitates brain retraction without causing contusion in deep seated tissues.

Hemodynamics

- Aim for CPP around 60–70 mm Hg
- Maintain MAP > 80 mm Hg
- Failure of cerebral autoregulation occurs if CPP < 50 mm Hg
- Thus, patient is more susceptible to cerebral ischemia during hypotension
- Maintain BP around 10% of preop values
- Hypotonic solutions avoided to prevent fluid flux across blood brain barrier–RL avoided
- Maintain high plasma osmolality
- Control BP with fluids and vasopressors
- Moderate hypothermia (around 35 ºC) beneficial.

Extubation

- Fully reverse neuromuscular blockade
- Assess neurological status before extubation
- Extubate fully awake
- Hypertension at extubation increases risk of postoperative hematoma.

Postoperative

Monitoring

- *Pulse oximetry;* Temperature
- *NIBP/IBP;* ECG
- Urine output.

Care

- Continue to maintain patients airway
- Adequate sedation and analgesia
- Assess and document size and reactivity of pupils
- Deep vein thrombosis prophylaxis.

Complications

- *Delayed awakening:* Shivering
- *Seizures:* PONV
- *HTN/hypotension:* Cerebral edema
- *Pain:* Postoperative hematoma.

MYASTHENIA GRAVIS (MG)[1,2,3,6]

Introduction

Myasthemia gravis is a chronic autoimmune disorder of neuromuscular junction characterized by weakness and fatigueability of voluntary muscles with improvement following rest.

Incidence

- 1: 20,000 to 30,000
- More common in females than males with a 6:4 ratio
- Peaks of incidence 3rd decade in females and 5th decade for men.

Associated Autoimmune Disorders

- Rheumatoid Arthritis
- SLE
- Diabetes mellitus
- Autoimmune thyroid disease
- SIADH
- Cushings syndrome
- Hypogammaglobulinemia
- RBC Aplasia.

Etiopathogenesis

- Autoimmune disorder
- Autoantibodies to:
  - n-ACH receptors (n-ACHR)
  - Muscle membrane proteins:
    - Tyrosine kinase
    - Rapsyn
    - Agrin.
- These autoantibodies damage neuromuscular junction by:
  - Complement activation and damage to muscle membrane
  - Degradation of n-ACHR
  - Blockade of n-ACHR.

Clinical Classification

Myasthenia Gravis in Pediatric Age

- Neonatal transient MG:
  - In babies born to mothers with myasthenia gravis
  - Seen in 15–20% babies to myasthenic mothers
  - Circulating anti-ACHR antibodies are passively transferred
  - Present in 12–48 hrs of birth and lasts for 2–4 weeks
    - Feeble cry
    - Poor feeding effort
    - Respiratory difficulty
    - Ptosis and facial weakness.
- Neonatal persistent MG:
  - Very rare
  - No detectable antibodies to ACHR
  - Onset at 2–3 months of age.
- Juvenile myasthenia: Similar to adult MG.

Myasthenia Gravis in Adults: *Osserman and Genkins Classification*[3]

Class	Name	Description
I	Ocular myasthesia	Involves ocular muscles only
		Ptosis and diplopia
		Electrophysiologic tests of other muscles is negative
Ia	Ocular myasthemia with peripheral involvement	Ocular muscles involved
		Ptosis and diplopia
		Peripheral muscles show no symptoms
		Positive electromyogram for MG
II. Generalized myasthenia		
IIa	Mild	Slow onset
		Usually ocular
		Spreading to bulbar and skeletal muscles
		Good response to drug therapy
		No respiratory muscle involvement
		Low mortality rate
IIb	Moderate	Slow onset
		Ocular with more severe involvement of peripheral muscles
		Dysarthria, dysphagia, etc
		Fair response to drug therapy
		No respiratory muscle involvement
		Patients activities limited
		Low mortality rate

Contd...

Contd...

Class	Name	Description
III	Acute Fulminating Myasthenia	Rapid onset
		Progresses within 6 months
		Severe bulbar and skeletal muscle involvement
		Poor response to treatment
		Involves respiratory muscles
		Patients activities limited
		Low mortality rate
IV	Late severe myasthenia	Develops 2 yrs after onset of group I or II symptoms
		Progression may be gradual or rapid
		Severe bulbar and skeletal involvement
		Poor response to treatment
		Involves respiratory muscles
		Patients activities limited
		High mortality

Clinical Features

Muscle Weakness

- Fluctuating muscle weakness
- Worsens with exertion, improves on rest-*Hallmark*
- Patients feel energized after waking from sleep
- Weakness worsens as the day progresses.

Ocular

- Occurs as first manifestation usually
- Ptosis and diplopia
- Ptosis:
  - Symmetrical/asymmetric
  - Unilateral/bilateral
  - Typically alternates between eyes.
- Extraocular muscle involvement:
  - Varies from single muscle involvement to total opthalmoplegia
  - Muscle fatigue can cause nystagmus.
- Pupil usually spared
- Progress to more generalized weakness in 80–85% patients
- If it remains ocular for 2 yrs, chances of generalizing are rare.

Bulbar Muscles

- Dyarthria, dysphagia, weight loss
- Difficulty in chewing
- Nasal regurgitation and nasal twang in voice due to palatal involvement
- Involvement of facial muscles:
  - Especially elevators of angles of mouth
  - Levator angulii oris and levator labii superioris
  - Produces ***Myasthenic snarl.***

Limb Muscles

- In 15–20% patients with myathesia gravis
- Proximal muscles more involved:
  - Difficulty in climbing stairs
  - Difficulty in lifting hands.
- Weakness of neck extensors:
  - Rectus capitis posterior major and minor
  - Unable to keep head upright.
- Respiratory muscle involvement: dyspnea, especially in supine position
- Diaphragmatic involvement:
  - Reduced forcefulness of cough
  - Inability to project voice.

Mass Effect

- Cough, dyspnea
- SVC syndrome.

Cardiovascular

- Focal myocarditis
- LV diastolic dysfunction
- Atrial fibrillation
- AV conduction delay.

Factors Aggravating Myasthenic Crisis

- Physical and emotional stress
- Infections—especially pulmonary and viral
- Pregnancy
- Surgery
- Heat and exposure to bright sunlight
- Drugs:
  - Quinidine, procainamide, penicillamine
  - Calcium channel blockers, β blockers
  - Aminoglycosides, erythromycin, clindamycin, ciprofloxacin
  - Phenytoin.

Diagnosis

Clinical Examination

- Monitor prolonged upward gaze
- Holding outstretched hand in abduction
- Determine vital capacity.

Electrophysiological Testing

- Stimulation of peripheral nerves
- Supra maximal stimulus of 2 Hz, 4 times over 2 seconds in TOF patterns
- Decrease in twitch response of 10% between 4th and 1st twitch is diagnostic of myasthenia gravis.

Tensilon Test

- Patient is fatigued by a simple task which can be easily assessed, like slurred speech
- IV edrophonium 2–8 mg is then given and response seen
- MG patients show dramatic improvement which lasts 10 mins.

Curare Test

Rarely used nowadays.

Regional Test

- Tourniquet applied to both arms
- 0.2 mg of d-tubocurarine (d-tc) diluted to 20 cc given in one arm
- 20 cc normal saline given in the other arm
- Markedly reduced twitch response in d-tc arm within 6 mins suggestive of MG
- Up to 70% of ACHRs are blocked in MG
- Thus even a small curarizing dose as used in the test is enough for paralysis.

Systemic Test

- 0.5–1 mg increments of d-tubocurarine given
- Up to a maximum dose of 0.03 mg/kg IV to elicit exaggerated symptoms
- Increased chances of respiratory failure during the test—not preferred.

ICE Pack Test

- Based on fact that cooling improves neuromuscular transmission
- Placing ice packs for 2 minutes over eyelids causes cooling of lid
- Positive test when clear resolution of ptosis occurs.

Serological Tests

- Anti-ACHR antibodies:
  - Found in 80% patients with generalized MG
  - Found in 50% patients with only ocular MG
- ***MUSK*** antibodies (muscle specific kinase).

Other Tests

- Single fiber electromyography:
  - More sensitive
  - Evaluates time interval between 2 muscle fiber APs in same motor unit
- Nystagraphy
- Stapedius reflexometry.

Treatment

Anticholinesterases

- Prolong duration of ACH at post-synaptic membranes
- Pyridostigmine 30–120 mg per day PO in 3–6 divided doses
- Side effects:
  - Cholinergic crisis
  - Occurs due to excessive ACH at NMJ
  - Weakness occurs due to persistent depolarization of muscle membranes.

Corticosteroids

- Reduces amount of ACHR antibodies
- Also reduces anti-ACHR reactivity of peripheral blood lymphocytes
- 1 mg/kg or 40–60 mg prednisolone PO on alternate days.

Immunosuppressants

- Azathioprine and cyclosporine used most commonly
- 50–100 mg/day PO Azathioprine
- Slowly increased till WBC count is 3000–4000 cells/cc
- Many months may be required before maximal therapeutic effect
- Cyclosporine takes only 1–2 mths to show maximal therapeutic effect
- Causes nephrotoxicity and hepatotoxicity
- Cyclophosphamide, tacrolimus, rituximab and mycophenolate mofetil also used.

Plasmapheresis

- Removes circulating antibodies from plasma and returns blood cells back to circulation
- Patients condition improves rapidly but effect is short lived.
- Used along with IV immunoglobulins for myasthenic crisis
- Five exchanges are done over 2 wks (2–3 L per exchange)
- May cause reduction in pseudocholinesterase which increases DOA of scholine.

Intravenous Immunoglobulins

- 400 mg/day for 5 days given IV
- Rapid improvement which can last several weeks
- Used for treatment of myasthenic crisis.

Thymectomy

- Approaches:
  - Sternal splitting
  - Transcervical
  - Video assisted thoracoscopy (VATS)
  - Robotic surgery.
- < 10% pts have thymoma in MG
- < 25% undergo resolution of symptoms after thymecotomy
- If thymectomy is done in patients with no thymoma, 50% patients have complete resolution while 90% improve
- Contraindications:
  - Prepubertal children
  - Those patients with only ocular symptoms.

Preoperative Assessment

History

- Muscles involved
- Duration and severity of disease
- Total daily requirement of pyridostigmine
- Evaluate severity of myaesthenia, involvement of respiratory and bulbar muscles.

Lab Investigations

- Complete blood count – especially if cyclosporine used
- Thyroid function tests
- Serum electrolytes as hypokalemia increases muscle weakness
- Blood glucose level as steroid use
- LFTs and RFTs—especially if cyclosporine used
- Preop ABG and PFTs as baseline to help extubation
- Serial FVC measurement for respiratory reserve
- Flow volume loop
- CT/MRI of thymus
- Tests for lupus erythematosus, Antinuclear antibodies, Rheumatoid factor
- Chest X-ray
- Bone densitometry in older patients
- ECG as pyridostogmine may cause bradycardia.

Preoperative Preparation and Premedication

- Patients should be admitted while in remission 24 hrs before surgery
- Preoperative physiotherapy and incentive spirometry
- Discuss need for postoperative ventilation
- To be scheduled as first case of the day in OT
- Anticholinesterase therapy: Controversial
  - If only mild symptoms, discontinue anticholinesterase therapy
  - Continuing therapy in mild cases can:
    - Increase susceptibility to vagal arrhythmias
    - Inhibit metabolism of ester LA, scholine and mivacurium
  - If patient is pyridostigmine dependant/has severe disease, continue therapy
- Antiaspiration prophylaxis if bulbar involvement
- Glycopyrrolate/IM Atropine to reduce secretions from anticholinesterase therapy
- Premedicate with small dose BZDs if only ocular symptoms present
- Avoid opoids as respiratory depression possible
- Stress dose steroids if patient is on steroid therapy.

Anesthetic Considerations

- To be scheduled as first case in the day
- Use of regional anesthesia/local anesthetic techniques where possible
- Increased risk of aspiration if bulbar involvement
- Reduced doseage of ester local anesthetics which inhibit plasma cholinesterase
- Reduced respiratory reserve:
  - Avoid premedication with opioids
  - Postoperative ventilation may be required.

Considerations for Neuromuscular Blockade

Succinylcholine

- Variable response to SCH
- In patients not receiving anticholinesterase therapy:
  - Succinylcholine resistance occurs
  - Resistance due to reduced number of functional ACHR at NM junction.
- In patients receiving anticholinesterase therapy:
  - Plasma cholinesterase activity is reduced
  - Thus, more scholine reaches motor end plate
  - Succinylcholine metabolism also is reduced.
  - Thus, duration of action of scholine increases to ≃ 87 mins.
- In patients who have received plasmapheresis also:
  - Plasma cholinesterase levels reduce
  - Duration of action of succinylcholine is prolonged.

- Formation of phase II block occurs with normal doses.

Nondepolarizing Muscle Relaxants

- Extremely sensitive to NDMR as ACHRs are reduced by 70%
- Profound weakness to precurarizing dose of muscle relaxants
- Avoid long acting NDMR
- Atracurium, vecuronium, cisatracurium and rocuronium safe
- Mivacurium not used as it is metabolised by pseudo cholinesterase
- Cisatracurium is preferable as:
  - Short $T_{½}$
  - Small V_d
  - Lack of cumulative effect
  - High clearance
  - Spontaneous reversal.
- Initial doses of NDMR reduced to 10–20% of normal dose
- Corticosteriods may block effects of steroidal relaxants like vecuronium.

Monitoring

- *Pulse oximetry;* Temperature
- *E_TCO_2;* CVP if significant fluid shifts
- *BP-IBP if cardiovascular instability;* Baseline ABG
- *Urine output;* Frequent blood sugars
- Neuromuscular monitoring with:
  - Mechanomyogram
  - Twitch monitor
  - Integrated electromyographic monitor
  - Accelograph monitor.
- Response to orbicularis oculi is reduced more than adductor pollicis due to ocular involvement.

Induction and Intubation[1]

- Neuromuscular blockade avoided as much as possible
- Thiopental/propofol + remifentanil + O_2 + N_2O
- Volatile agents like isoflurane/sevoflurane provide muscle relaxation for intubation
- NDMRS used if patient does not tolerate cardiovascular depressant effects of VA
- Initial dose of NDMR reduced to 10–20% of normal dose
- LA sprayed on vocal cords to reduce intubation response (4% lidocaine)
- If rapid sequence induction, 1.5 mg/kg SCH can be used safely
- Insert orogastric tube if early return to oral intake not predicted.

Maintenance

- Cisatracurium preferred in reduced doses
- 10–25% of ED_{95} of intermediate acting muscle relaxants sufficient for most cases
- If SCH is used, avoid other MR till muscle function has returned and no fade is present
- Controlled ventilation to ensure adequate gas exchange
- Maintainance with O_2 + N_2O + Isoflurane + Remifentanil infusion
- Use of dexmedetomidine for transternal thymectomy associated with asystole
- Dexmedetomidine accentuates centrally mediated increase in vagal activity due to pyridostigmine.

Extubation

- Extubation criteria:
  - Patient can generate negative inspiratory pressure > –20 cm H_2O
  - Peak occlusion pressure > 30 cm H_2O
  - FVC >15 ml/kg with sustained head lift ≥ 5 seconds
  - Able to maintain normocapnea and adequate oxygenation.
- Continue mechanical ventilation until spontaneous recovery present rather than using reversal
- Patient may be reversed if preoperative symptom control is good
- Avoid reversal otherwise as it increases risk of cholinergic crisis
- Edrophonium good for reversal as onset is rapid and high dose prolongs DOA.

Postoperative

Monitoring

- *Pulse oximetry;* Neuromuscular monitoring
- *ECG;* Urine output
- *BP;* Temperature
- *CVP;* ABG and Glucose

Pain Control

- Adequate pain control is necessary
- Use lower doses of opioids to avoid respiratory depression
- Epidural opioids decreases opioid requirements
- RA supplementation where possible
- NSAIDs, PCA
- Multimodal analgesia.

Ventilation

Leventhal Orkin and Hirsch scoring:[3]

S. No.	Category	Points
1	Duration of more than 6 years	12
2	History of COPD	10
3	Pyridostigmine dose > 750 mg/day	8
4	Vital capacity < 2.9 L	4

- Score > 12 points indicates need for postoperative ventilation
- Not very useful score
- Even patients with < 12 score may require ventilation in the event of transternal thymectomy or upper abdominal surgery.

Complications

Cholinergic Crisis

- Due to overdoseage of ACHE inhibitors
- Salivation, bradycardia, weakness respiratory secretion, bronchospasm
- ACH induced pupillary contriction (miosis) occurs
- No improvement/worsening of symptoms with 10 mg tensilon
- Keep pacing instrument ready.

Myasthenic Crisis

- Delayed extubation for > 24 hrs postsurgery due to myaesthenic weakness
- Due to underdoseage of ACHE inhibitors
- Similar symptoms profile to cholinergic crisis
- Hypercarbia induced pupillary dilatation (mydriasis)
- Improvement in symptoms with 10 mg tensilon
- Keep instrument for pacing ready.

Management

- Physiotherapy and incentive spirometry
- Resume pyridostigmine therapy as soon as possible
- Repeated PEFR and FVC measurement to monitor impending respiratory failure
- ABG changes occur very late
- Anticholine esterase therapy:
  - Doseage of neostigmine based on neuromuscular monitoring results
  - Start with 2.5–5 mg IV boluses
  - Increase by 1 mg boluses every 2–3 minutes
  - Dose increased upto a maximal equivalent dose of oral pyridostigmine
  - One mg neostigmine = 30 mg pyridostigmine
  - Resume oral anticholinesterase therapy as soon as possible.

Differential Diagnosis

- Botulism
- Lambert Eaton syndrome
- Thyrotoxicosis
- Muscular dystrophy
- Amyotrophic lateral sclerosis
- Progressive external ophthalmoplegia
- Drugs:
  - Quinidine, d-penicillamine, procainamide
  - Diuretics by causing hypokalemia
  - Erythromycin, clindamycin, aminoglycosides, ciprofloxacin
  - Phenytoin
  - Calcium channel blockers, beta blockers.

EATON LAMBERT/MYASTHENIC SYNDROME

S. No.	Feature	Myasthenia gravis	Lambert Eaton syndrome
1	Gender	Female > Male	Male > Female
2	Age at onset	20–40 yrs	50–70 yrs
3	Presentation	Weakness of ocular, bulbar, facial	Weakness of proximal muscles
		Fatigue with activity	Increased strength on activity
		Muscle pain uncommon	Muscle pain common
		Normal deep tendon reflexes	Reduced or absent deep tendon reflexes
4	Pathology	15–20% patients have thymoma	Small cell carcinoma of lung
5	Electromyography	Voltage decreases to repeated stimulus	Voltage increases to repeated stimulus
6	Response to MR	Increased sensitivity to NDMR	Increased sensitivity to NDMR
		Resistance to scholine	Increased sensitivity to NDMR

Contd...

Contd...

S. No.	Feature	Myasthenia gravis	Lambert Eaton syndrome
7	Antibodies	Anti ACHR	Ca^{2+} channel associated synaptogamin
		MUSK antibodies	
8	Dysautonomia	Absent	Present
9	Treatment	Anticholinesterase	3, 4 diaminopyridine
		Plasmapheresis	Less responsive plasmapheresis
		IV immunoglobulins	
10	Response to ACHE	Good response	Poor response

HYPERTHERMIA AND NEUROLEPTIC MALIGNANT SYNDROME[10]

Introduction

- Hyperthermia is an elevation in body temperature (37.5–38.3 ºC or 100–101 ºF) characterized by an unchanged setting of thermoregulatory center
- Fever is an elevation of body temperature which occurs in conjunction with an increase in hypothalamic set point
- Normal body temperature = 36.8 + 0.4 ºC
- Fever: (Harrison)
  - AM temperature > 37.2 or 98.9 ºC
  - PM temperature > 37.7 or 99.9 ºC.

Etiology

- Heat stroke:
  - Exertional
  - Non-exertional:
    - Anticholinergics
    - Antihistaminics
    - Antiparkinsonian
    - Diuretics
    - Phenothiazines.
- Drug induced:
  - Amphetamine, cocaine, phencyclidine
  - MDMA (ecstasy), LSD
  - Salicylates, lithium, anticholinergics
  - Sympathomimetics.
- Neuroleptic malignant syndrome:
  - Phenothiazines, butyrophenones, metaclopramide, domperidone
  - Fluoxetine, loxapine, thiothixene, molindone
  - Withdrawal of dopaminergic agents.
- Serotonin syndrome:
  - Selective serotonin reuptake inhibitors
  - MAO inhibitors
  - Tricyclic antidepressants.
- Malignant Hyperthermia:
  - Volatile anesthetics
  - Succinylcholine.
- Endocrinopathy:
  - Thyrotoxicosis
  - Pheochromocytoma
  - Diabetic ketoacidosis.
- CNS Disorders:
  - Cerebral hemorrhage
  - Status epilepticus
  - Hypothalamic injury
  - Meningitis, encephalitis, brain abscess.
- Generalized infection:
  - Sepsis
  - Malaria
  - Typhoid
  - Tetanus.

Complications of Hyperthermia

S. No	System	Initial	Delayed
1	Vital signs	Hypotension	
		Hyperthermic rebound	
		Hypothermic overshoot	
2	Muscular	Shivering	
		Rhabdomyolysis	
3	Neurological	Delirium	Cerebral edema

Contd...

Contd...

S. No	System	Initial	Delayed
		Seizures	
		Coma	
4	Cardiac	Heart failure	
5	Pulmonary	Pulmonary edema	ARDS
6	Renal	Oliguria	Renal failure
7	Gastrointestinal	Diarrhea	Hepatocellular necrosis
			Mucosal GI hemorrhage
8	Metabolic	Hypokalemia	Hyperkalemia
		Hypernatremia	Hypocalcemia
			Hyperuricemia

Neuroleptic Malignant Syndrome

Introduction

Combination of hyperthermia, rigidity and autonomic dysfunction occurring as an idiosyncratic reaction to administration of neuroleptics.

Etiology

- Phenothiazines, butyrophenones, metaclopramide, domperidone
- Fluoxetine, loxapine, thiothixene, molindone
- Withdrawal of dopaminergic agents.

Pathophysiology

- Due to dopamine D_2 receptor antagonism
- D_2 receptor blockade in hypothalamus causes elevated temperature setpoint
- This causes impairment of heat dissipating mechanisms
- Peripherally antipsychotics cause increased calcium release from sarcoplasmic reticulum
- This causes hyperthermia, rigidity and increased muscle breakdown.

Clinical Features

- Fever, diaphoresis
- Autonomic instability, labile blood pressure
- Rigidity, dysphagia, tremors
- Confusion, psychomotor agitation, delirium
- Hyperthermia, tachycardia, shuffling gait.

Investigations

- Raised CPK, LDH, AST, ALT, alkaline phosphatase
- Leucocytosis, thrombocytosis
- Hyperuricemia, hyperphosphatemia, myoglobinemia
- Proteinuria, myoglobinuria.

Treatment

- Discontinue antipsychotic immediately
- Hydration, alkalinization of urine to prevent ATN due to rhabdomyolysis
- Cooling and supportive measures
- Circulatory and ventilatory support as required
- Dantrolene:
  - Maybe useful in the treatment of rigidity
  - Less well defined role in NMS as compared to MH
  - Initially 2 mg/kg IV
  - Repeated every 10 minutes upto maximum dose of 10 mg/kg/day.
- Bromocriptine:
  - For treatment of muscular rigidity
  - 2.5–4 mg PO Q6H.
- Levodopa/carbidopa, amanditine and diazepam are useful
- NTG/SNP if vasoconstricted state
- Electroconvulsive therapy if refractory NMS
- Resumption of antipsychotics:
  - Waiting period of 2 weeks following complete resolution for oral medication
  - Waiting period of 6 weeks for parenteral therapy
  - Use of different neuroleptic than the offending agent.

HYDROCEPHALUS[1,2,3]

Introduction

- Congenital/acquired disease causing increase in the amount of CSF resulting in enlarged cerebral ventricles and a raised ICP
- Ideally ICP maintained < 20 mm Hg
- Normal CSF volume = 150 ml, around 500 ml produced per day.

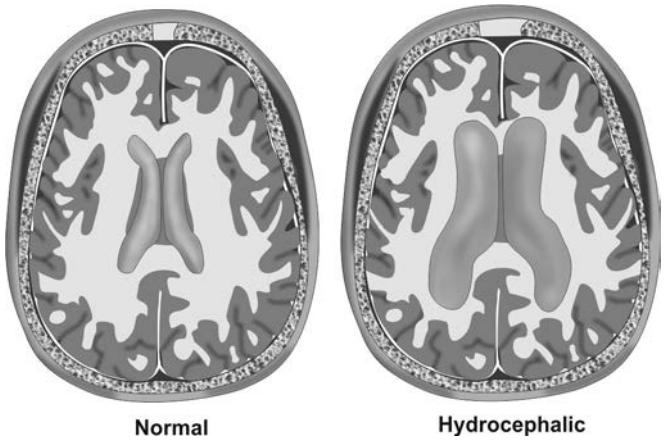


Fig. 1.10: Changes in hydrocephalus

Etiology

Excessive Production

- Choroid plexus papilloma.

Obstruction of CSF Pathways

- Within ventricular system
  - Lateral ventricle (atrium/body/foramen of *Monro*)
  - Third ventricle
  - Acqueductal stenosis
  - Fourth ventricle ***(Dandy-Walker).***
- Within subarachnoid space
  - Basal cisterns (Chiari, postinfectious)
  - Convexity.

Decreased Absorption

- Obstruction at arachnoid villi:
  - Plugging by tumor cells
  - Protein
  - Blood
  - Bacteria.
- Obstruction of dural venous sinuses:
  - Thrombus
  - Hematological malignancies
  - Infections.
- Obstruction of extracranial venous sinuses:
  - Achondroplasia.

Classification

Communicating

- CSF escapes from ventricular system but not absorbed by arachnoid villi
- Causes:
  - *Infections:* Blood in CSF due to SAH
  - *Bacteria:* Proteins
  - Tumor cells.

Noncommunicating

- Infections:
  - Abscess
  - Meningitis: TB/pyogenic
  - Encephalitis.
- Neoplastic
  - Astrocytoma
  - Ependymoma
  - Choroid plexus papilloma
  - Oligodendroglioma
  - Medulloblastoma
  - Meningioma.
- Vascular:
  - AV malformation
  - Aneurysm.
- Congenital:
  - Arachnoid cyst
  - Colloid cyst
  - Chiari malformation
  - **Dandy-Walker** malformation
  - Atresia of outlet formen.

Clinical Features

- In preterm infants hydrocephalus due to intraventricular hemorrhage
- In neonates raised ICP is blunted/minimized as sutures are open
- In infants:
  - Symptoms
    - Increased irritability
    - Decreased level of consciousness, lethargy, poor feeding, drowsiness
    - Vomiting, dysphagia
    - Headache on awakening, diplopia
    - Gait disturbances, head banging, apathy
    - Enlarged head.
- Signs
  - Cranium
    - Thin shiny skin
    - Dilated scalp veins
    - Bulging anterior fontanelle
    - Cranial enlargement/deformity.
  - Eyes
    - *Sunset sign:* inferiorly deviated eyes where sclera above cornea is visible

- Strabismus, ptosis
- Papilledema with absent pulsations in retinal blood vessels
- Loss of corneal reflex.

– *Cardiovascular:* ***Cushings triad:***
- Hypertension
- Bradycardia
- Altered respiratory rate
- Due to distortion of brain stem.

– Extremities
- Spastic palsy of lower extermities due to stretching of cortical fibers.

Variations

- Normal Pressure Hydrocephalus: Triad of:
  – Abnormal gait
  – Dementia
  – Urinary incontinence.
- Hydrocephalus –Ex-vacuo:
  – Ventricular dilatation with normal ICP.

Differential Diagnosis

- Megalencephaly:
  – Hurlers syndrome,Tay Sachs disease
  – No increase in ICP or ventricular size.
- Chronic subdural hematoma
  – Large head
  – Located in parietal region
  – No sunset sign/scalp vein prominence.
- Hydrencephaly
- Rickets, achondroplasia
- Hemolytic anemia.

Diagnosis

- Serial head circumference measurement
- > 2 cm every month during first 3 months of life
- Normal head circumference measurements:
  – At birth: 35 cms
  – 3 months: 41 cms
  – 6 months: 43 cms
  – 2 year: 49 cms.
- Skull radiographs:
- Persistent widening of sagittal and coronal suture > 0.5 cm after 2 wks of life
- CT Scan/MRI for confirmation and etiology
- Cranial USG for ventricular size
- Shunt scan for site of malfunction if pre-existing shunt present.

Surgical Management

- Surgical excision of obstructive lesion
- Extracranial shunts:
  – Ventriculoperitoneal shunt (*most common*)
  – Ventriculoatrial shunt
  – Ventriculopleural shunt
  – Lumboperitoneal shunt.
- External ventricular drain (EVD)
- Endoscopic ventriculostony
- Ventriculoperitoneal shunt:
  – Catheter inserted via occipital burrhole into frontal horn of lateral ventricle
  – Catheter inserted on nondominant side (right side)
  – Reservior placed subcutaneously adjacent to burrhole
  – Drain passes through subcutaneous tunnel to a point near epigastrum
  – Inserted into peritoneal space through small laparotomy
  – Flushing device present in burrhole to keep system clear
  – *Valve system:* Prevents CSF draining too rapidly with changes in posture
  – Inadvertent gastrotomy can occur if stomach is inflated.
- Double barrelled shunt:
  – Done if obstruction at more than one level in ventricular system
  – 2 proximal ends, one is lateral ventricle and other in IV ventricle
  – Done in prone position.
- Lumboperitoneal shunt:
  – Done in lateral position
  – Catheter positioned is lumbar CSF space via Tuohy needle
  – Catheter tunnelled subcutaneously to anterior abdominal wall
  – Inserted into peritoneal space via small laparotomy.
- Endoscopic ventriculostomy:
  – Burrhole in skull
  – Percutaneous flexible neurendoscope passed through burrhole
  – Ventriculostomy done to bypass obstruction
  – Damage to basilar artery/branches and nerve injury possible.
- External ventricular drain:
  – Emergency procedure
  – Decreases ICP till infection is controlled with antibiotics

  - EVD clamped during transfer of patient and level of drainage bag kept constant
  - Sudden decompression can cause rupture of cortical veins.

Anesthetic Considerations

- Maintain normal blood pressure
- Maintain normothermia
- Dyselectrolytemia due to vomiting/hormonal alterations
- Avoid increase in ICP:
  - Hypoxia
  - Hypercapnea
  - Succinylcholine
  - Ketamine.
- Difficult airway.

Preanesthetic Assessment

History

- *Vomiting:* Suggests increase ICP and delayed gastric emptying
- Drug history:
  - Steroids-glucose intolerance
  - Anticonvulsants-enzyme induction.
- Immunization history for congenital rubella.

Examination

- Airway assessment: Difficult airway due to enlarged head
- Pulmonary compliance and renal function assessed
- Neurological status and gag reflex to assess ability to protect airway
- Level of consciousness which is an indicator of raised ICP.

Investigations

- *Complete blood count;* Electrolytes
- *ECG;* Blood glucose
- *Renal function tests;* Arterial blood gas
- *Liver function test;* Skull X-ray
- CT scan
- *Ultrasonography;* For size site and vascularity of lesions.

Preoperative Optimization and Premedication

- NPO orders:
  - 6 hrs solids, milk
  - 4 hrs breast milk
  - 2 hrs water, clear fluids.
- Informed consent
- Correct dehydration/electrolyte imbalance due to vomiting and diuretics
- Restrict IV fluids to 30 ml/kg/day if cerebral edema present
- Avoid glucose containing IV fluids as:
  - It decreases osmolality
  - Increases cerebral edema
  - Also has poor postoperative neurological outcome.
- Avoid routine use of sedation if raised ICP/altered sensorium
- Avoid atropine and if sympathetic nervous system immaturity
- Prophylactic phenytoin required:
  - 15 mg/kg IV loading dose
  - Followed by single daily dose of 3–4 mg/kg.
- Antibiotic prophylaxis as per hospital protocol
- Emotional preparation in older children
- Compression stocking for DVT prophylaxis.

Monitoring

- *ECG;* Temperature as exposure of large surface area of body
- *Pulse oximetry;* E_TCO_2
- *Urine output;* Precordial stethoscope
- NIBP/IBP if hemodynamically unstable
- Fontanelle palpation for online trend monitoring of ICP.

Induction

Inhalational

- Used when IV access unavailable
- Avoided when child is stuporus
- Sevoflurane is *agent of choice* as:
  - Minimal effect on cerebral hemodynamics
  - Cardiac stability
  - Absence of airway irritation.

Intravenous

- *Rapid sequence induction*
- Raised ICP with delayed gastric emptying increase chances of vomiting and aspiration
- Succinylcholine 1–1.5 mg/kg, fentanyl 2–3 µg/kg, thiopentone 3–4 mg/kg
- Deep intubation to avoid coughing which increases ICP
- IV lidocaine avoided as it may cause sudden cardiac arrest
- RAE tube may be used as airway is remote
- Ketamine does not increase ICP in neonates as it does in adults as open sutured cranium has increased compliance.[3]

Position
- Supine with head turned to opposite direction
- If raised ICP occurs 30° head-up position with minimal neck rotation/flexion
- If shunt tubing is placed posteriorly-lateral position.

Maintenance
- Isoflurance/sevoflurance and fentanyl boluses
- Remifentanil infusion 0.5 µg/kg/min
- Nitrous oxide avoided as:
  - Increases cerebral blood flow
  - Increases cerebral blood volume
  - Gastric distension which may cause inadvertent gastrostomy during laparotomy
  - Postoperative nausea and vomiting causing raised ICP.
- Additional muscle relaxation provided before laparotomy
- Opioid boluses during burrowing of subcutaneous tunnel.

Ventilation
- Spontaneous ventilation not preferred as increased risk of venous air embolism
- Spontaneous ventilation also increases chances of pneumothorax
- Hyperventilation with moderated $PaCO_2$ between 25–30 mm Hg
- Maintain normocapnea if ICP is normal.

Hemodynamics
- No significant blood loss/third space loss
- Avoid hypothermia from cooling and evaporation:
  - Overhead warmer
  - Drape limbs
  - Use warm IV solutions.
- Sudden hypotension due to reduction of ICP during cannulation of ventricle
- Blood loss may occur from burrhole if dural veins are enlarged
- Bradycardia/arrhythmias may occur due to shift in intracranial content.

Emergence
- Adequate reversal of neuromuscular blockade
- Extubate fully awake after full recovery of protective reflexes
- Avoid coughing/straining during extubation
- Keep intubated if apnea/bradycardia before surgery due to intracranial abnormalities.

Postoperative
Pain

Only minor postoperative discomfort:
- Paracetamol
- Low dose morphine in first 24 hrs
- LA infilteration over abdominal incision at end of surgery.

Management
- Continue IV fluids till adequate oral intake
- Maintain normothermia
- If focal neurological signs present, urgent CT scan for intracranial hematoma.

Monitoring
- *Pulse oximetry;* Urine output
- *Blood pressure;* CNS status
- *ECG;* Temperature.

Complications
- Nausea, vomiting
- Seizures
- *Shunt infection/obstruction:* Acute hydrocephalus
- Pneumothorax/hemothorax if subcutaneous trocar penetrates pleura
- Venous air embolism especially if ventriculoatrial shunt
- Blood loss if dural veins are breached
- Intracranial hemorrhage if CSF is drained too rapidly
- Subdural hematoma due to tearing of bridging veins.

MENINGOMYELOCELE[1,2,3,6]

Introduction
- Hernial protrusion of a part of meninges and spinal cord through a defect in vertebral column
- Most common congenital primary neural tube defect
- Results from failure of neural tube closure during the 4th week of gestation
- Neural tube defects or myelodysplasia refers to abnormality in fusion of embryological neural groove that normally closes in first month of gestation.

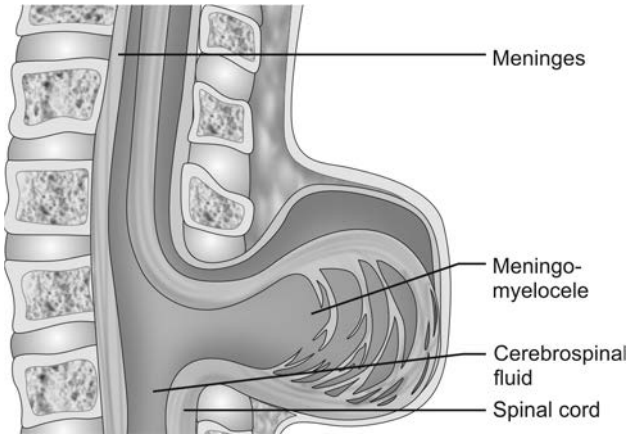


Fig. 1.11: Meningomyelocele

Clinical Features

- Most common in lumbosacral or sacral region
- Can extend to thoracic region
  - Presents as cystic mass on back containing
  - Neural placode
  - Arachnoid
  - Dura
  - Nerve tissue and roots
  - CSF.

Motor Problems

- Meningocele patients are usually born without CNS deficits
- Motor deficits occur if spinal cord is tethered caudally by sacral roots
- Flaccid/spastic paraplegia, loss of sensation to pinprick
- Hydrocephalus rarely seen at presentation but occurs postsurgery
- Varying degree of scoliosis requiring posterior spinal fusion.

Urological Complications

- Loss of anal urethral and bladder sphincter tone
- Bowl and bladder dysfunction
- Recurrent UTI complicated by gram-negative sepsis
- Sever dilatation of upper urinary tract
- Dilatation necessitates urinary diversion procedures like:
  - Vesicostomy
  - Cutaneous urethrostomy
  - Ileal/colonic conduit construction.
- Bladder exstrophy and prolapsed uterus.

Associated Abnormalities

- Latex allergy
  - Due to:
    - Impaired immune system
    - Repeated exposure to latex products from frequent hospitalization
    - Daily bladder catheterization for those with neurogenic bladder
  - Limit latex exposure especially
  - ***Latex free surgical environment.***
- Brainstem Anomaly: ***Arnold Chiari II malformation Consists of:***
  - Caudal displacement of cerebellar vermis through formen magnum
  - Caudal displacement of medulla oblongata
  - Cervical spine kinking of medulla
  - Obliteration of cisterna magna.
- Brainstem Dysfunction:
  - Occur in 20% patients
  - Vocal cord and other cranial nerve palsy due to:
    - Pressure on brainstem
    - Focal infarcts of brainstem
  - Stridor, apnea
  - Aspiration pneumonia, sleep disordered breathing pattern
  - Lack of coordination and spasticity
  - Bradycardia, hypertension.
- Hydrocephalus: In 80–90% patients
- Other associated conditions:
  - ***Klippel Feil syndrome***
  - Congenital cardiac defects
  - Clubfoot
  - Dislocation of hips
  - Scoliosis.

Investigations

General

- Complete blood count, electrolytes, blood glucose, RFTS
- Blood for grouping and cross matching
- Ultrasonography of head, menigomyelocele sac and kidney if possible
- Chest X-ray, X-ray spine
- Cultures from lesion and draining CSF.

Diagnostic

- *Prenatal ultrasound:* Pick-up rate of 100%
- Elevated maternal serum α feto protein: 50–90% pick-up

- Amniotic fluid α feto protein is more reliable and done between 14–16 wks gestation
- Amniotic fluid acetylcholine esterase
- CT and MRI confirms anomaly, Neural tube defects and spinal cord anomalies.

Management

Lorber's criteria for selective surgery:

- Surgery not done if:
  - Severe paraplegia at or below L_3
  - Kyphosis/scoliosis/gross hydrocephalus
  - Other associated gross congenital anomalies
  - Intracerebral birth injury
  - Neonatal ventriculitis before closure of back.
- Most centers close defect and place shunt for hydrocephalus at same time
- Repaired within 24–48 hr of birth
- If infected surgery is done only when three 24 hour CSF cultures are sterile
- Open neural tube defects require skin flaps to close defects
- Early repair advantageous as:
  - Decreases risk of ventriculitis
  - Decreases progression of neurological deficits
  - Restores normal configuration of spine.

Preop Assessment

History

- Drug history
- Folic acid supplementation during pregnancy
- Recurrent UTI
- History of itching/rashes/wheezing on exposure to latex.

Examination

- Neurological examination, hydrocephalus
- Vocal cord mobility and ventilatory response to hypoxia and hypercarbia
- Gastro-esophageal reflux and aspiration
- Other life threatening congenital anomalies.

Investigations

General and diagnostic.

Anesthetic Considerations

- *Prevent infection:* Antibiotics in preoperative period
- Preoperative nursing in prone position to avoid cyst rupture
- Difficult airway if large cervical meningomyelocele
- *Care during positioning to avoid cyst rupture:* Prone position
- Avoid high oxygen concentrations to prevent *retinopathy of prematurity*
- Avoid hypothermia due to exposure of large surface area
- Maintain ECF volume by replacing third space losses
- *Latex free surgical environment.*

Preoperative Preparation and Premedication

- NPO guidelines
- Informed consent
- Nurse in prone position
- Cover placode with saline soaked gauze to prevent dessication
- Antibiotic therapy in preoperative period according to hospital protocol.

Anesthetic Management

Done in latex free surgical environment.

Monitoring

- Pulse oximetry
- ET CO_2
- NIBP
- ECG
- Precordial stethoscope
- Invasive monitoring if:
  - Large size defects
  - Multilevel meningomyelocele where significant cutaneous undermining is needed.

Induction

Inhalational Induction

- Done if no intravenous access
- Sevoflurane *agent of choice.*

Intravenous Induction

- Thiopentone 3–4 mg/kg + NDMR + fentanyl 2 µg/kg
- RAE tube may be used
- *Rapid sequence induction* if large hydrocephalus/ large cervical meningomyelocele
- If large cervical meningomyelocele awake intubation in lateral/supine position.

Position

During Induction

- Supine position
- Towels under head
- Defect rests in *doughnut* to minimize trauma
- Lateral position tried if defect is large.

During Surgery

- Prone position
- Abdomen and chest to be free to avoid pressure on epidural veins and prevent bleeding
- Rolls placed under chest and hips
- Prevent injury to exposed neural tissue
- Extremities in relaxed position and padded
- Avoid excess rotation of neck.

Maintenance

- O_2, + N_2O + Isoflurane + titrated fentanyl + atracurium
- High O_2 concentrations avoided to prevent *retinopathy of prematurity* (88–92%)
- Avoid NMBAs if nerve stimulator used for identification of neural structures.

Hemodynamics

- Large third space losses to be replaced with normal saline
- Possibility of underestimating fluid and blood loss from deficit
- Increased blood loss when large amount of skin required to cover defect
- Rupture of cyst with CSF leakage replaced with full strength balanced salt solution
- Avoid hypothermia:
  - Radiant heat warmers
  - Prevent drying/thermal injury to neural tissues.

Extubation

- Adequate reversal of neuromuscular blockade to be ensured
- Assess airway patency carefully before extubation
- Fully awake extubation in those with central neurodeficits
- Postoperative ventilation done if nasal encephalocele present.

Postoperative

Management

- Nurse in prone position
- Prevent hypothermia
- Humidified gases to be used.

Monitoring

- *ECG;* NIBP
- *Pulse oximetry;* Urine output
- Temperature
- Neurological status for hydrocephalus.

Pain

- NSAIDs
- Low dose morphine
- LA infilteration around wound site
- *Multimodal analgesia.*

Complications

- *Respiratory:* Especially in those with brainstem abnormalities
  - Stridor
  - Apnea post extubation
  - Respiratory arrest, cyanosis
  - Bradycardia.
- Cranial nerve palsy causing inspiratory strisor
- Brainstem herniation
- Hydrocephalus:
  - Lethargy, vomiting, seizures
  - Apnea, bradycardia.

Regional Anesthesia

- Spinal anesthesia with tetracaine has been tried
- 2 out of 14 infants had adverse postoperative respiratory events
- One had transient apnea with bradycardia
- The other child had brief desaturation and bradycardia
- This was seen when subarachnoid block was supplimented with midazolam sedation
- No evidence of anesthesia induced CNS depression was seen.

Prevention

Folate Supplementation

- Decreases risk of neural tube defects by 70%
- 0.4 mg/day of folic acid for primary prevention
- If previously delivered child with NTD, 5 mg/day for subsequent prevention
- Prophylaxis given for 2 months before and 3 months after conception.

POSTERIOR FOSSA SURGERY[1,2,3]

Introduction

- Components:
  - Cerebellum
  - Pons
  - Medulla
  - Fourth ventricle.
- Boundaries:
  - *Superiorly:* Tentorium
  - *Inferiorly:* Foramen magnum

  - *Posteriorly:* Occiput
  - *Anteriorly:* Clivus.
- Importance
  - Pons and medulla contain major sensory and motor pathways:
    - Cardiovascular and respiratory centers
    - Lower cranial nerve nuclei
    - Reticular Activating System (RAS)
    - Networks for protective reflexes like gag, cough, eye blink.
  - CSF flows out from third ventricle to fourth ventricle and out on surface of brain through ***foramen of Magendie and Luschka***. Any obstruction here will cause hydrocephalus.

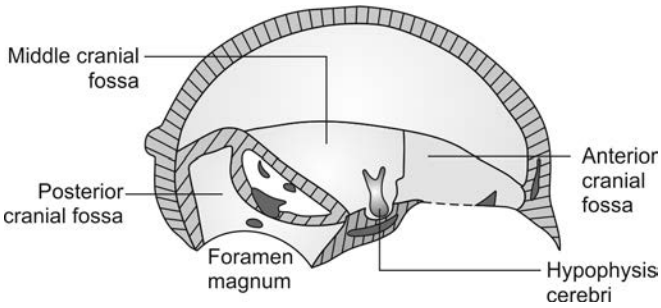


Fig. 1.12: Posterior cranial fossa

Posterior Fossa Surgeries

- Tumor excision/debulking
- Foramen magnum decompression
- Vascular procedures
- Decompression of cranial nerve V (***Tic Douloureaux***):
  - Dissection along intracranial portion of nerves
  - Identification of offending blood vessel which encroaches on nerve
  - Placement of insulating Teflon pad between blood vessel and nerve.
- Decompression of CN VII (Hemifacial spasm) and CN IX (Glossopharyngeal Neuralgia)
- Balloon compression of trigeminal ganglion:
  - Rapid inflation of Fogarty type balloon within ***Meckels cave***
  - Balloon introduced percutaneously through cheek and beneath maxilla
  - General anesthesia preferred as very painful procedure
  - Profound bradycardia is sign of adequate compression.

Posterior Fossa Lesions

- Malignant tumors:
  - Primary:
    - Astrocytoma in children
    - Ependymoma from Fourth ventricle
  - Secondary: Metastasis to cerebellum.
- Benign tumors:
  - Acoustic neuromas in cerebellopontine angle from CN VIII
  - Hemangioblastoma
  - Medulloblastoma from vermis of cerebellum in children
  - Meningiomas.
- Vascular:
  - Aneurysm of superior cerebellar, posterior inferior cerebellar and vertebral artery
  - AV malformation
  - *Hematomas:* Spontaneous and traumatic
  - Hemangiomas.
- Others:
  - Abscesses
  - Arnold-Chiari malformation.

Anesthetic Considerations

- Sitting position:
  - *Hemodynamic alterations:* Hypotension
  - Venous air embolism, paradoxical air embolism
  - Macroglossia and airway obstruction.
- Brain stem and cranial nerve manipulation:
  - Hemodynamic alterations
  - Vital center dysfunction
  - Cranial nerve injury causing poor gag reflex
  - Vocal cord palsy and stridor
  - *Delayed awakening:* Reticular Activating System.
- Pneumocephalus
- Poor nutrition and dehydration d/t dysphagia.

Preoperative Considerations

History

- Nausea, vomiting
- Aspiration
- Hoarseness, dysphagia.

Examination

- Assess intracranial pressure status:
  - Consciousness, headache, vomiting
  - Assess response to steroids
  - If hydrocephalus present, EVD may be required.

- Cardiovascular system:
  - Tolerance of sitting and prone position
  - *Echo for cardiac septal defect:* Predispose to PAE in sitting position
  - *Preoperative uncontrolled hypertension:* Prone for hypotension and cerebral ischemia in sitting position.
- Respiratory system:
  - Indirect laryngoscopy for vocal cord palsy and Mallampatti grade
  - Have reduced levels of consciousness and impaired airway reflexes
  - Increased chances of silent aspiration if bulbar palsy.

Special Investigations

- Echocardiography, pulmonary function tests
- Auditory function for schwanomma surgery
- Scans examined for size of lesions, degree of edema and presence of hydrocephalus
- Fluid and electrolyte status for dehydration and electrolyte abnormalities due to vomiting/diuretics
- Blood glucose in patients on chronic steroids.

Position

Prone

- Allows good access to midline structures
- Increased bleeding is seen
- Avoid abdominal compression as it increases cerebral venous pressure
- Adequately support chest and pelvis.

Lateral/Park Bench

- For laterally placed lesions (CP angle):
  - Acoustic neuroma
  - Cerebellar hemisphere.
- Neck flexed and head rotated towards floor
- Avoid nerve damage: Pad shoulder, greater trochanter and paroneal nerve
- Avoid jugular vein compression due to excess flexion/rotation of neck
- Damage to eyes possible.

Supine: For trigeminal neuralagia, acoustic neuroma

Sitting position: Use is declining

- Using standard OT table, remove head portion
- Place back vertically to 60°
- Legs slightly flexed to ensure buttocks are firm against vertical portion
- Head is held by Mayfield pin fixator mounted on frame across table
- Minimum of 2 finger gap between chin and suprasternal notch
- *Maintain head up tilt:* Prevents venous congestion
- Forehead rests on horshoe ring mounted on frame
- Padding of elbows, ischial spines, heels, forehead
- All catheters and endotracheal tube secured well
- Advantages: (all surgical)
  - Better spatial orientation
  - Reduces ICT
  - Easy access to midline lesions
  - Less bleeding
  - Good venous and CSF drainage.
- Disadvantages: (all anesthetic)
  - Postural hypotension
  - Hemodynamic instability
  - Venous air embolism, paradoxical air embolism
  - Pneumocephalus, quadriplegia
  - Excessive neck flexion:
    - Jugular compression
    - Tongue swelling
    - Cervical cord ischemia.
- Relative contraindications:
  - Extremes of age
  - Uncontrolled hypertension
  - COPD.

Anesthetic Technique

Induction

- Thiopentone 3–5 mg/kg + vecuronium 0.15 mg/kg + remifentany l 0.2–0.5 µg/kg/min
- Propofol 2–3 mg/kg and fentanyl 3 µg/kg are alternatives
- Induction agents given slowly to avoid hypotension and reduction in cerebral perfusion pressure
- Lidocaine 1.5 mg/kg or labetolol 5 mg increments to reduce BP response to intubation
- Armoured endotracheal tube used to prevent kinking
- Insert NGT if patient has/is at increased risk for postoperative bulbar dysfunction
- Protect eyes.

Monitoring

- *Pulse oximetry;* ETCO2
- *ECG;* Temperature
- *Urine output;* NIBP/IBP
- Neuromuscular monitoring
- Central venous pressure
- SSEP, spontaneous/evoked electromyographic activity

- Brainstem/auditory evoked potential
- Cranial N function through electromyography:
  - *CN VII for acoustic neuroma:* As it is stretched across capsule of tumor
  - From tongue for hypoglossal N
  - From glottis through electrodes in specialized ETT to monitor CN X.
- *Coagulation studies:* For vascular tumors (meningiomas) as intraop coagulopathy is possible
- Monitor for venous air embolism: Transesophageal echocardiography.

Maintenance

- O_2 + isoflurane/sevoflurane < 1MAC+ Remifentanil 0.15–0.25 µg/kg/min
- Alternatively TCI/propofol 3–6 µg/ml + remifentanyl 0.15–0.25 µg/kg/min
- Alfentanyl 25–50 µg/kg/hr or fentanyl top-ups as alternative
- Avoid nitrous oxide as:
  - Increases cerebral metabolic rate and worsens outcome of VAE
  - Increases chances of postoperative pneumocephalus.
- NMBAS avoided after intubating dose to allow assessment of cranial N function
- Lumbar CSF drainage done sometimes:
  - Improves surgical conditions
  - Reduces incidence of postoperative CSF leaks.
- Measures to reduce tumor edema:
  - Mannitol to reduce edema and attain adequate brain relaxation
  - 3% saline better than mannitol if anuric renal failure present
  - Infilterate pin sites of *Mayfield* with local anesthetic
  - Further remifenta 0.5 µg/kg or propofol 0.5 mg/kg may be required
  - Fixator application may cause marked hypertensive response.
- Intermittent pneumatic compression devices to calves and feet
- IV morphine during skull closure for postoperative analgesia when remifentanil is stopped.

Ventilation

- Traditionally spontaneous ventilation to allow detection of change in respiratory patterns which would indicate surgical interference with respiratory center
- Not used now as proximity of cardiovascular and respiratory centers permits cardiovascular signs to serve as indicator of injury to respiratory center
- Controlled ventilation with mild hypocapnea: 30 to 35 mm Hg.

Hemodynamics

- Surgical intervention/retraction of brainstem may alter vitals
- Inform surgeon to retract or dissect more gently
- Modest hypotension to improve surgical field
- BP brought close to normal prior to closure to assess adequacy of hemostasis
- Avoid atropine and β blockers unless absolutely necessary
- Inform surgeon if atropine used to modify surgical technique
- Maintain normothermia
- Normal saline used as maintenance fluid
- Blood/colloid to replace blood loss
- FFP and platelets given if coagulopathy as in vascular tumors
- Sudden changes in BP and HR increases chances of damage to respiratory center
- Cardiovascular responses intraop:
  - Bradycardia and hypotension
  - Tachycardia and hypertension
  - Bradycardia and hypertension
  - Ventricular arrhythmias.

Extubation

- After adequate neuromuscular reversal
- Fully awake extubation
- Avoid coughing and struggling at extubation
- Airway obstruction due to airway edema and macroglossia possible postextubation.

Postoperative

Management

- Elective postoperative ventilation if:
  - Poor preoperative neurological status
  - Occurrence of adverse intraoperative event
  - Prolonged surgery with significant tissue retraction
  - Lesion > 30 mm diameter with mass effect
  - Cerebral edema.

Monitor

- *Pulse oximetry:* Urine output
- *NIBP/IBP:* Temperature
- *ECG:* Neurological status.

Pain

- NSAIDs avoided
- Low dose morphine: Only if no respiratory depression
- Multimodal analgesia.

Complications

- Venous air embolism
- Hydrocephalus
- Postoperative nausea and vomiting especially after CP angle surgeries
- Airway obstruction due to:
  - Macroglossia caused by:
    - Prolonged surgery
    - Increased neck flexion
    - Use of oropharyngeal airways.
  - Partial damage to vagus nerve
  - Increased flexion of cervical spine.
- Brainstem damage:
  - Due to postoperative posterior fossa swelling
  - Can occur some hours after good recovery
  - Detected by deterioration in CNS status after surgery
  - Posterior fossa swelling due to:
    - Tendency of cerebellum to swell after prolonged retraction
    - Bleeding and hematoma
    - Reduced respiration may result from and may increase swelling.
- Can cause cranial nerve damage:
  - During dissection on floor of fourth ventricle
  - CN IX, X and XII, VII and VIII may get injured
  - Loss of patency of upper airway and decreased gag reflex
  - Insert NGT and maintain NPO status till gag reflex returns.
- Reduced respiratory drive and apnea
- CN VII damage is indicated by prolongation of interpeak latency between peaks I and V of BAEP waveform.

CIRCLE OF WILLIS

Introduction

- This represents a free anastomosis between blood vessels supplying the brain
- Equalizes pressure in arteries of the two sides: Also called ***circulus arteriosus.***

Situation

Located in interpeduncular subarachnoid cistern.

Formation

- *Anteriorly:* Anterior communicating artery
- *Posteriorly:* Basilar artery as it divides into right and left posterior cerebral artery
- Each side:
  - Anterior cerebral artery
  - Internal carotid artery
  - Posterior communicating artery
  - Posterior cerebral artery.

Branches of Internal Carotid Artery

- Ophthalmic artery
- *Anterior cerebral artery:* Larger branches
- Middle cerebral artery
- *Posterior communicating artery:* Smaller branches
- Anterior choroidal artery.

Branches of Cranial Part of Vertebral Artery

- Meningeal artery
- Anterior spinal artery
- Posterior spinal artery
- Posterior inferior cerebellar artery
- Medullary artery.

Branches of Basillar Artery

- Pontine artery
- Labyrinthine artery
- Anterior inferior cerebellar artery
- Superior cerebellar artery
- Posterior cerebral artery.

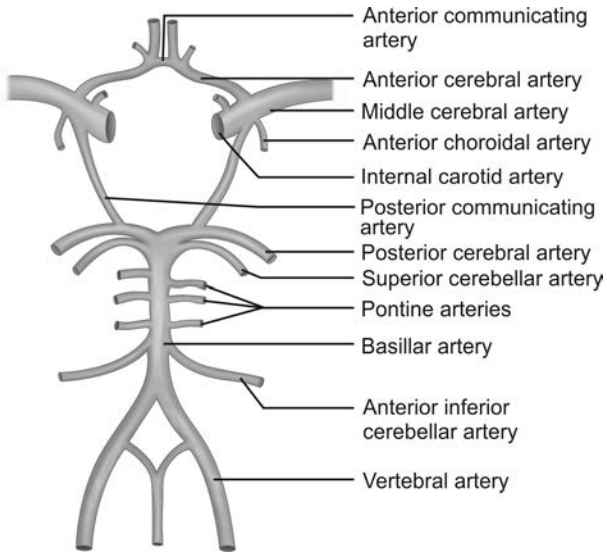


Fig. 1.13: Circle of Willis

CAROTID ENDARTERECTOMY (CEA)[1,2,3]

Introduction

- Prophylactic surgery done in patients with thromboembolic/obstructive atherosclerotic lesions in area of carotid bifurcation to prevent stroke
- *Carries high morbidity and mortality:* Risk-benefit analysis important for patient selection.

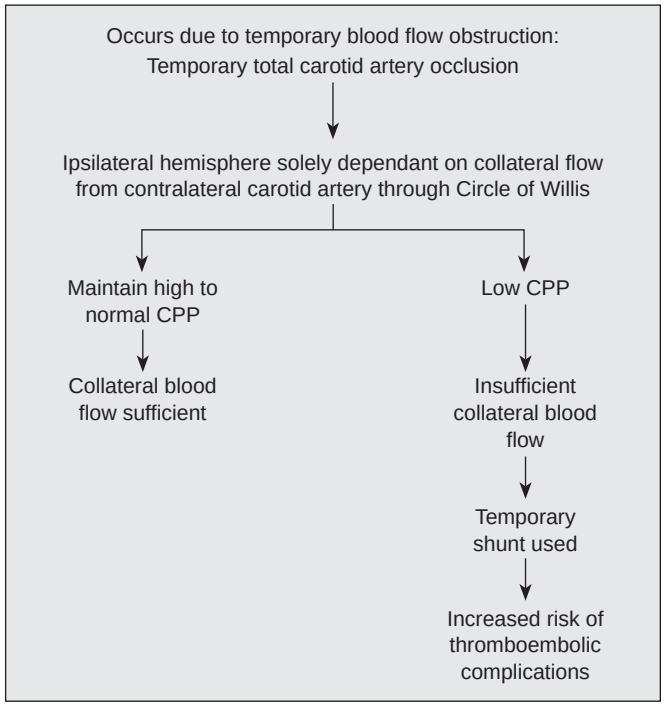
Incidence

- Stroke is third leading cause of death
- 83% strokes are ischemic
- 7.6% of ischemic strokes cause death within 30 days.

Etiology

- Atheromatous plaque most common at bifurcation of common carotid artery
- Clot embolism into distal cerebral blood vessels may cause reduced blood flow
- Cerebrovascular sequelae occur due to:
  - Embolization of thrombus
  - Atheromatous debris
  - Hypoperfusion secondary to stenosis.

Physiological Effects



Presentation

- Wide range of presentation based on severity
- Incidental: Asymptomatic finding during investigation of arterial disease
- Asymptomatic bruit
- ***Amaurosis fugax:***
  - Transient attacks of monocular blindness
  - Due to embolus into ophthalmic artery.
- ***Transient ischemic attacks:***
  - Last less than 24 hours
  - Paresthesias, clumsiness, speech impediment.
- ***Reversible ischemic neuro-deficit (RIND):***
  - Lasts less than 3 weeks
  - Stroke/CVA
  - 30% one-year mortality rate.

Treatment

- Medical therapy:
  - Only approved therapy is with recombinant TPA
  - To be given within 3 hours of onset of symptoms
  - *Risk factor control:* HTN, diabetes, hyperlipidemia, cardiac disease.
- Carotid end arterectomy:
  - Controversial role
  - Currently it is the *gold standard.*
- Endovascular therapy:
  - Emergency angioplasty and stenting
  - Mechanical disruption of arterial clot
  - Mechanical extraction of thrombi.

Indications of CEA

- Symptomatic stenosis more than 70% with RIND
- Stenosis 50–69%, age 75 years, male sex, recent stroke (within 3 months)
- Hemispheric symptoms and concomitant intracranial stenosis
- TIA with angiographic stenosis
- Unstable CNS status which persists despite anticoagulation.

Patient Selection

- Age less than 80 years
- Symptomatic patients:
  - ***NASCET Trial:***
    - North American Symptomatic Carotid Endarterectomy Trial
    - Concluded that patients with 70% stenosis and TIA have clear benefits from surgery
  - ***ECST trial:***
    - European Carotid Surgery Trial (ECST)
    - Conclusions:
      - No benefit if < 30% stenosis present, even with symptoms

- Unclear benefit if 30–69% stenosis
- Significantly reduced stroke incidence in patients with 70% stenosis.

– ***Asymptomatic patients:***
- *CASANOVA trial:* CEA not indicated in asymptomatic patients with 50–90% stenosis
- *MACE study:* Terminated early due to increased risk of MI and TIA
- *ACA study:* Patients treated with CEA and aspirin therapy have reduced 5 years risk of ipsilateral stroke compared with patients treated with aspirin alone
- *ACS trial:* Asymptomatic carotid stenosis around 70% with carotid end arterectomy and medical therapy have reduced 5 year risk of stroke compared with patients treated by medical therapy alone.

Procedure

- Incision along anterior border of SCM between ear and sternal notch
- Carotid and IJV dissected
- Heparin 5000 IU after exposure of common carotid artery bifurcation
- Cross clamp common carotid artery (CCA), internal (ICA) and external (ECA) carotid artery sequentially
- Shunt (from CCA to ICA) inserted based on:
  – Surgical preference
  – Estimated magnitude of cerebral perfusion.
- Artery repaired directly or with patch angioplasty
- Remove clamp sequentially from ECA, CCA and then ICA
- Sequence used to prevent any debris from entering cerebral circulation
- Problems of shunting:
  – Air embolism
  – Kinking of shunt
  – Shunt occlusion against side of blood vessel wall
  – Injury/disruption of distal ICA
  – *May impair surgical access to artery:* Increases cross-clamp time.

Preoperative Assessment

- History:
  – 60% patients have asymptomatic CAD
  – Asses severity of preoperative symptoms of CVA
  – *Age and female sex:* Increased incidence of CVS and CNS complications
  – HTN: SBP 180 mm Hg increases risk of stroke and postoperative death
  – Diabetes and renal failure common
  – History to rule out peripheral vascular disease, COPD.
- Investigations:
  – Hb, hematocrit, urinalysis, BUN, serum creatinine
  – *ECG:* Arrhythmias, MI, LVH
  – *Chest X-ray:* Cardiomegaly, pulmonary edema, COPD
  – Doppler angiography and oculoplethysmography
  – Duplex scan combines B-mode anatomic imaging and pulse Doppler spectral analysis of blood flow velocity
  – MR angiography.
- Examination:
  – Head and neck, potential airway problems evidence of positional ischemia
  – Blood pressure:
    - Determine BP and HR from time of preoperative clinic to perioperative period
    - Helps determine range of patients acceptable values of BP
    - Intraoperatively, maintain hemodynamics within this range.

Anesthetic Technique[1]

Choice of technique controversial (GA vs RA):

- General anesthesia:
  – Advantages:
    - Reduces cerebral oxygen consumption the most
    - Reduces stress response to surgery
    - Secure airway present
    - Reduces patient discomfort
    - Easier control of blood pressure.
  – Disadvantages:
    - Volatile anesthetics impair cerebral autoregulation
    - Protects from cardiac ischemia
    - Requires special cerebral function monitors
    - More labile BP: BP fluctuations common
    - Increased incidence of MI
    - Increased requirement of vasoactive drugs.
- Local anesthesia:
  – Advantages:
    - Allows monitoring of cerebral function continuously
    - *Provides awake patient:* Gold standard of cerebral function monitoring

- *BP and cerebral perfusion unaltered:* More stable BP
- Better postoperative recovery
- Reduced incidence of MI
- Reduced requirement of vasoactive drugs
- Avoids use of drugs with negative inotropic activity in patients with low cardiac reserve
- Reduced hospital costs, inexpensive monitoring.

– Disadvantages:
- Patient has to lie still with neck turned for more than 90 minutes
- Cannot use volatile anesthetic induced neuroprotection
- Patient and surgeon cooperation required
- *Discomfort during surgery:* May require additional IV sedation
- Increases perioperative blood pressure
- Loss of control if seizures or sudden LOC
- *Remote airway:* Difficult to control airway in emergency
- *Awake patient may panic and become combative:* Loss of control of surgical field.

- Combined GA with LA:
  – Superficial cervical plexus block with light GA
  – Dexmedetomidine used for sedation
  – Reduced need of shunt and no stroke
  – Clonidine 1 µg/kg/hr better
  – Clonidine also gives more hemodynamic stability postoperaitvely.

Anesthetic Goals

- Maintain adequate cerebral blood flow
- Maintain normal BP, PaO_2 and $PaCO_2$ throughout the procedure
- Avoid cardiac ischemia and infarction
- Ablation of surgical pain and stress responses
- To have awake patient at the end of surgery for CNS examination.

Premedication

- Avoid long acting agents like lorazepam
- *Short acting benzodiazepines preferred:* Midazolam 0.05 mg/kg IV
- Continue aspirin and clopidogrel in perioperative period
- Discontinuing aspirin therapy may cause increased risk of MI and TIA
- Continue antianginal and antihypertensives on day of surgery.

Local Anesthesia

- Techniques: C_2 to C_4 segment blockade by:
  – Deep cervical block
  – Superficial cervical block
  – Deep and superficial cervical block
  – Cervical epidural block.
- Deep cervical plexus block:
  – Head turned away, neck extended
  – Palpate C_2 transverse process below mastoid process, C_6 at the level of cricoid cartilage
  – C_3 and C_4 are at 2 cm intervals along a line joining C2 to C6
  – 5–8 ml LA injected at each of C_2, C_3 and C_4
  – Complications:
    - Phrenic nerve block
    - Vertebral artery injection
    - Injection into CSF
    - *Laryngeal nerve palsy:* Respiratory distress.
  – Contraindicated in anticoagulated patients.
- Superficial cervical plexus block:
  – Infilterate along posterior border of SCM
  – Usually, this is sufficient
  – Additional analgesia by local injection by surgeon
  – More preferred than deep block.
- Cervical epidural:
  – Provides good operating conditions
  – Major complications:
    Dural puncture
    - Total spinal
    - Puncture
    - Respiratory paralysis.

General Anesthesia Position

- Reverse Trendelenburg with head up and feet up to reduce venous pooling
- Head turned away from operating side
- Shoulders raised with support placed between shoulder blades
- Head kept in position with head ring
- Drapes heaped up like tent away from patients face to prevent claustrophobia.

Induction

- Thiopentone/propofol/etomidate useful + rocuronium 0.9–1.2 mg/kg for induction
- Avoid hypotension/HTN
- Etomidate useful in patients with low cardiac reserve

- Blunt laryngoscopy and intubation responses with xylocard
- Normal/flexometallic ETT may be used
- Esmolol 0.5 mg/kg IV or NTG 5–25 µg for intubation responses
- Phenylephrine 50–100 µg IV for hypotension at induction.

Ventilation

- Maintain normocarbia/moderate hypocarbia (30–35 mm Hg)
- *Hypercarbia dilates blood vessels in normal areas:* Causes ***cerebral steal phenomenon.***

Monitors

- Non-specific monitors:
  - ECG, pulse oximetry
  - NIBP in both arms as PVD causes differences between the two arms
  - E_TCO_2, VA concentration
  - Airway pressure, FiO_2
  - Arterial line for IBP and blood gases
  - PA catheter/CVP via subclavian/femoval vein if decompensated CCF
  - TEE in very high risk patients.
- Cerebral function monitors:
  - Awake patient:
    - *Gold standard* of monitoring cerebral function during LA
    - Contralateral hand grip with squeaky toy which the patient squeezes
    - Observe for loss of consciousness and speech assessment
    - No new neurological symptoms after a test clamp of 1 minute indicates adequate collateral flow
    - Orientation in time and place, mental tasks like counting to 100 can be done.
  - Carotid artery stump pressure:
    - Stump pressure and waveform measured
    - Measures pressure in ICA once CCA and ECA are clamped
    - Closely resembles perfusion pressure in Circle of Willis
    - Stump pressure less than 50 mm Hg associated with hypoperfusion
    - Not reliable, no longer widely used.
  - Transcranial Doppler:
    - Probe placed on petrous temporal bone
    - Measures MCA blood flow velocity
    - Detects and quantifies embolic signals.
  - Regional cerebral blood flow:
    - Direct Xe^{133} cerebral blood flow measurement
    - Calculated by measuring washout of radioisotopes from MCA territory
    - Determines critical cerebral blood flow which is flow below which 50% patients show signs of ischemia on EEG
    - Measures around 20 ml/kg/min with halothane and 10 ml/kg/min with isoflurane.
  - Somatosensory evoked potentials:
    - Also evaluates deep brain structures
    - Not essential for CEA
    - May be superior in patients whose baseline EEG is not easily interpretable because of previous stroke
    - VA can reduce amplitude of SSEP.
  - EEG/processed EEG:
    - Both raw and processed EEG have been used
    - Does not monitor deep brain structures
    - Only cerebral cortex is monitored
    - Not ischemia specific
    - It is affected by changes in temperature, $PaCO_2$, depth of anesthesia, noise in OT
    - *Gold standard* in anesthetized patients
    - Consider shunt placement if EEG changes occurs
    - Maybe false negative in patients with preexisting neurodeficits
    - Deterioration in EEG begins when CBF ≤ 15 ml/100 g/min
    - Cellular metabolic failure occurs when CBF ≤ 12 ml/100 g/min
    - Most common EEG changes of ischemia:
      - Ipsilateral attenuation
      - Ipsilateral attenuation with slowing
      - Ipsilateral slowing without attenuation
      - Difficult to interpret and requires skill and experience.

Cerebral Protection

- Thiopentone/propofol/etomidate used along with volatile anesthetics
- Mild hypocarbia beneficial
- Maintain mild hypothermia.

Maintenance

- Maintain light planes of anesthesia:
  - Permits EEG monitoring
  - Maintains BP in high normal range.
- 50% N_2O + O_2 + isoflurane/sevoflurane 1 MAC
- Avoid N_2O if possible as it increases $CMRO_2$ and increases MCA flow velocity
- Intermediate action NDMR used to avoid high dose of VA
- Small doses of opioids to avoid postoperative respiratory depression and sedation:
  - Fentanyl ≤ 3 µg/kg
  - Sufentanil 0.5–1 µg/kg
  - Remifentanil infusion ideal
  - Alfentanyl 10–25 µg/kg.
- Continuous thiopentone infusion or TIVA with remifentanil and propofol are other options
- Sometimes thiopentone 4–6 mg/kg bolus given just before carotid occlusion: No proven benefit
- Spray trachea with 100 mg lidocaine to reduce ETT stimulation during surgery
- Heparin 75–100 IU/kg IV given before cross clamping.

Hemodynamics

- *1 medium bore IV catheter enough:* Major blood loss is rare
- Patients who are HTNsive preinduction have hypotension postinduction
- Vasoactive agents like ephedrine/adrenaline used to increase BP during GA
- Bradycardia and hypotension (rarely asystole) common during stimulation of carotid sinus:
  - Treat with anticholinergics
  - Ask surgeon to stop manipulation
  - 1% lidocaine infilteration around carotid sinus prevents bradycardia.
- Cross clamping requires 10–20% rise in MAP to preserve CPP
- Use nonglucose containing IV fluids: Lactated Ringers is ideal
- Total IV fluids ≤ 10 ml/kg/2 hrs as fluid overload may cause postoperative HTN
- Isovolemic hemodilution with dextran/hestarch to reduce viscosity
- *Hyperglycemia increases ischemic injury:* Maintain blood sugar less than 200 mg%
- Warming equipment for OT, IV fluids and hot air blanket for patient.

Extubation

- Confirm neurological integrity before extubation
- Extubate in deep planes to limit hypertensive response
- Tight hemodynamic control at emergence
- Patient to be wide awake after extubation to allow CNS examination
- Heparin not reversed after arteriotomy closure
- If hemostasis is inadequate small dose protamine can be given IV (2 mg/kg).

POSTOPERATIVE CARE

Management

- Supplemental oxygen mandatory as reduced ventilatory response to PaO_2 in case of bilateral loss of carotid body function
- Blood pressure:
  - Control BP to within range of patients preoperative value
  - Treat pain, bladder distension, hypoxia and hypercarbia
  - If HTN persists, 5 mg labetolol increments given
  - Usually HTN peaks 2–3 hours postoperatively and persists for 24 hours.
- Admit in ICU if ≥ 4 of following:
  - Stroke, CCF
  - HTN, MI
  - Arrhythmias
  - Chronic kidney disease.

Monitors

- ECG, pulse oximetry
- IBP, temperature
- Urine output, CNS status.

Analgesia

- Reduced incidence of postoperative pain as CEA is only superficial surgery
- Reduced opioids dose
- Paracetamol with LA block usually effective.

Complications

- Stroke/neurodeficits:
  - 3% incidence
  - Predictors of stroke
  - Emboli during wound closure
  - 90% reduction of MCA peak systolic velocity at cross clamping

  - More than 100% increase of pulsatility index of Doppler signal at clamp release.
- Cranial nerve damage:
  - Vagus nerve
  - Hypoglossal nerve
  - Marginal mandibular nerve
  - Posterior auricular nerve.
- Hyperperfusion syndrome: HTN and headache
- Myocardial infarction
- Altered BP regulation: HTN/hypotension (HTN more common)
- Carotid body dysfunction:
  - This abolishes cardiorespiratory response to hypoxemia
  - Respiratory regulation becomes totally dependant on changes in $PaCO_2$.
- Impaired baroreceptor function
- Respiratory insufficient due to:
  - RLN/hypoglossal nerve injury
  - Neck hematoma
  - Deficient carotid body function.
- Wound hematoma
- Tracheal compression and deviation.

Nascet Risk Stratification (*See Table*)

- Medical risk:
  - Age > 70 years, morbid obesity
  - Severe HTN (180/110 mm Hg), COPD
  - Angina, myocardial infarction (less than 6 months prior to surgery)
  - Congestive cardiac failure.
- Neurological risk:
  - Progressing deficit
  - New deficit (< 24 hours)
  - Frequent daily TIAs
  - Multiple cerebral infarcts.
- Angiographic risk:
  - Presence of soft thrombus
  - Proximal/distal plaque extension
  - ICA siphon stenosis
  - High carotid bifurcation
  - Contralateral carotid occlusion.

INTRACRANIAL ANEURYSMS[1,2,3,6]

Introduction

Intracranial saccular aneurysm result from progressive degeneration of blood vessel wall.

Incidence

- Most common in women
- Incidence increases with age
- 0.2 to 9.9% in general population.

Anatomy

- 90% in Anterior Cerebral circulation
- 10% in Posterior Cerebral circulation
- ***Most common*** in Anterior Communicating artery Complex (ACOM)
- Also common in middle cerebral artery
- Usually occurs at junctions of blood vessels in *Circle of Willis*
- Multiple aneurysms in 20% cases
- Small aneurysms (< 10 mm diameter) have rupture rate = 0.05% per year
- Large aneurysms (> 10 mm diameter) have rupture rate = 0.5% per year.

Pathogenesis

- Smoking, hypertension and genetic predisposition
- Myotic aneurysms occur due to septic focus.

Factors Affecting Rupture

- Size of aneurysm
- Strength of aneurysm wall
- History of previous rupture
- Transmural pressure gradient (only factor under anesthetist control).

Clinical Features

- Peak age of rupture with SAH = 55–60 yrs (6th decade)
- After with rupture SAH:
  - Rarely, warning signs such as headache, dizziness, orbital pain
  - Slight motor/sensory disturbance

Group	Medical risk	Neurological risk	Angiographic risk	Outcome
I	No	Neurologically stable	No	1% morbidity and mortality
II	No	Neurologically stable	Significant	2% morbidity and mortality
III	Major	Neurologically stable	Major	7 % morbidity and mortality
IV	Major	Neurologically unstable	Major	10% morbidity and mortality

  - Sudden onset of severe headache
  - *Transient loss of consciousness:* Acutely increased ICP causing global cerebral hypoperfusion
  - Neck stiffness, diplopia, photophobia, nausea and vomiting
  - Systemic hypertension, cardiac arrhythmias.
- Aneurysmal rupture can occur earlier in cocaine abuse patients
- Aneurysmal rupture during pregnancy occurs most commonly between 30–40 wks of gestation or in postpartum period and only rarely at time of labor
- AV malformation commonly bleed at time of labor.

Grading of Severity of SAH

World Federation of Neurosurgeons Grade (WFNS grade):

Grade	GCS score	Motor deficit
I	15	Absent
II	14–13	Absent
III	14–13	Present
IV	7–12	Present/absent
V	3–6	Present/absent

Hunt-Hess Modification of Botterell Classification

Grade	Description
I	Asymptomatic
	Mild headache
	Nuchal rigidity
II	Moderate – severe headache
	Nuchal rigidity
	No focal deficits
III	Mild focal deficits
	Drowsiness, confusion
IV	Hemiparesis/early decerebrate rigidity
	Stupor
	Vegetative disturbances
V	Decerebrate rigidity
	Deep coma
	Moribund

Complications of Rupture

- Subarachnoid hemorrhage
- Intracerebral/subdural hematoma
- Hydrocephalus
- Mass effect causing:
  - Cranial nerve palsies
  - Raised ICP
  - Focal neurodeficits
  - Seizures.
- ***Cerebral salt wasting syndrome*** due to:
  - Release of Brain Natriuretic Peptide (BNP)
  - Supine diuresis secondary to raised thoracic blood volume
  - Negative nitrogen balance
  - Reduced erythropoiesis
  - Increased catecholamine levels
  - Iatrogenic blood loss.
- SIADH

Conditions Associated with Aneurysms

- Fibromuscular dysplasia
- Adult polycystic kidney disease
- Marfans syndrome
- Coarctation of aorta
- Hereditary hemorrhagic telangiectasia.

Investigations

- Routine blood chemistry and hematology
- Blood grouping, typing and screening
- Platelet count and coagulation profile
- ECG changes
  - ST elevation/depression
  - *T-wave flattening/inversion:* ***Canyon T-waves***
  - U-waves, prolonged QT interval (> 55 msec)
  - Rhythm disturbances usually resolve within 10 days following SAH
  - Susceptible to Torsades de pointes due to increased QT_c.
- CT brain shows high density (white) blood clot in basal subarachnoid cisterns.

Treatment

- Modes of Treatment
  - Endovascular coil placement under fluoroscopic guidance to pack aneurysmal sac which then undergoes thrombosis
  - Placement of clip across neck of sac under direct vision if:
    - Aneurysm with wide neck
    - Difficult anatomy
    - Too distal for coiling
    - Pregnant patients
    - Contrast allergy.
- Timing of obliteration of Sac:
  - May be early 24–96 hrs or late ≥ 10–14 days following SAH
  - Elective if it presents as mass effect
  - Contemporary approach is to treat aneurysm within 24 hrs.

EARLY SURGERY

Indications
- Patients with unstable hemodynamics
- Seizures/mass effect from thrombus
- Large bleed/evidence of bleeding/aneurysmal growth.

Advantages
- Reduced incidence of re-bleeding which is prime cause of death
- Subsequent vasospasm can be aggressively treated with volume loading and HTN
- Reduced hospital stay
- Reduced medical complications (DVT, pneumonia, atelectasis).

Disadvantages
- Technically difficult as brain is edematous and clot is friable
- Increased risk of intraoperative aneurysmal rupture.

DELAYED SURGERY

Done if stable hemodynamics/advanced age.

Preoperative Evaluation
- Evaluate associated medical conditions
- WFNS grading before and after surgery to assess progress after surgery
- Counselling required for grade I and II patients who are anxious
- ECG and ECHO essential as cardiopulmonary dysfunction maybe present
- Optimize cardiac and pulmonary function.

Preoperative Preparation
- Premedication only in anxious patients as it may reduce consciousness levels
- Continue anticoagulants, and calcium channel blockers before surgery
- Fluid resuscitation required if cerebral salt wasting syndrome
- Fluid restriction if SIADH present.

Anesthetic Considerations
- Avoid acute HTN with attendant risk of rupture
- Maintain CPP and intramural aneurysmal pressure
- Maintain high normal MAP to prevent critical reduction of cerebral blood flow
- Preparedness to perform precise manipulations of MAP during clipping/hemostasis
- Provide adequate brain relaxation to facilitate brain access and minimize retraction
- Enzyme induction in those patients on anticonvulsants preoperatively.

Induction
- Thiopentone 3–5 mg/kg + fentanyl 2–3 µg/kg + vecuronium 0.1 mg/kg
- Any anesthetic technique which allows good hemodynamic control can be used
- Careful and slow induction to minimize changes in transmural pressure
- Rupture during induction occurs in 1% patients with 75% mortality
- Deep plane especially during:
  - Intubation
  - Insertion of pins
  - Scalp incision
  - Turning bone flap
  - Opening dura.
- IV lidocaine/esmolol/labetalol to reduce sympathetic response
- Lumbar CSF drain may be required
- IV Mannitol 0.5–1 gm/kg just before opening dura mater
- Mannitol is repeated 15 minutes after opening dura.

Position
- Anterior circulation and Basilar artery aneurysms:
  - Frontal/frontoparietal craniotomy
  - Patient supine and head slightly turned.
- Aneurysm in vertebral system:
  - Posterior fossa craniotomy
  - Lateral park bench position.

Monitoring
- *Pulse oximetry;* Transcranial Doppler
- *E_TCO_2;* Intraoperative angiography
- *ECG;* Jugular venous oximetry
- IBP mandatory
- Core temperature
- CVP especially if prophylactic fluid loading to treat vasospasm
- Urine output
- EEG and SSEP: To monitor cerebral perfusion during induced hypotension or aneurysmal clip application.

Ventilation
- ETT with IPPV
- *Moderate hyperventilation:* Maintain E_TCO_2 between 30–35 mm Hg.

Maintenance

- Any technique which allows adequate brain relaxation
- TIVA with propofol or balanced anesthesia with isoflurane/sevoflurane (< 1 MAC)
- Opioid infusion and atracurium/vecuronium for muscle relaxation
- Nitrous oxide avoided as it reduces intracranial compliance
- Continuous administration of propofol to control blood pressure
- $T_{½}$ of NDMR may be reduced in patients on anticonvulsants
- Total dose of fentanyl to be < 10–12 µg/kg unless postoperative ventilation planned
- Thiopentone 3–5 mg/kg before temporary aneurysm clipping
- If temporary occlusion lasts > 10 min recirculation established
- Additional thiopentone administered before applying temporary clip.

Lumbar CSF Drain

- Kept closed till surgeon opens dura mater, after which CSF is drained
- Drain is closed again after removal of retractors to allow CSF to accumulate and reduce the size of postoperative pneumocephalus
- *Use is declining:* CSF release from basal cisterns used for brain relaxation.

HEMODYNAMICS

Normotension

- Maintain normotension to maximize cerebral perfusion
- Important during temporary occlusion to maximize collateral circulation.

Normovolemia

- Maintain normovolemia to maximize cerebral perfusion
- After securing aneurysmal clipping, CVP and PCWP are raised to 10–12 mm Hg with crystalloid/colloid/blood
- Postoperative hematocrit of 30–35 desirable-hemodilution reduces risk of vasospasm and improves perfusion.

Deliberate Hypotension

- Usually avoided
- MAP of 40–50 mm Hg may be required if active arterial bleeding
- Avoided in patients with:
  - Cardiovascular disease
  - Cerebrovascular disease
  - Intracerebral hematoma
  - Fever/anemia/renal disease.
- Largely replaced by temporary clipping of feeding blood vessels.

Induced Hypertension

- Maybe required during temporary clipping to maintain collateral circulation
- After clipping aneursym, some surgeons puncture dome of aneurysm to confirm adequate clip placement
- Increase SBP to 150 mm Hg with phenylephrine.

Fluids

- *Potential for massive blood loss:* Adequate blood should be available
- Crystalloid isotonic solutions without glucose used before clipping to replace deficits and maintains fluid balance.

Intraop Cerebral Protection

- Moderate hypothermia (not beneficial–***IHAST II trial***) 33–35 ºC if used
- Preoperative hyperbaric oxygen
- Maintain mean arterial pressure
- Efficient brain relaxation
- Reduce retractor pressure
- Limit duration of temporary occlusion to < 10 minutes
- Pharmacological agents:
  - *Thiopentone:* Not ideal due to hemodynamic effects
  - Thiopentone may be used if prolonged occlusion (*Miller*)
  - *Propofol and etomidate are alternatives:* No validating studies
  - Volatile anesthetic preconditioning
  - Statins
  - Diazoxide
  - Prophylactic use of nimodipine
  - Magnesium prevents *Delayed Ischemic Neuro Deficits (DINDS)*
  - Antihypertensives.

Extubation

- Rapid emergence to allow neurological assessment
- Rapid and smooth extubation to prevent coughing, straining, hypercarbia and HTN

- Prevent HTN with labetalol/esmolol/hydralazine/SNP
- *Patients with intraop complications/reduced consciousness:* Postoperative mechanical ventilation.

Intraop Aneurysmal Rupture

- Occurs most commonly as neck of aneurysm is dissected
- Temporary clip used to stop hemorrhage from main blood vessel
- *Uncontrolled bleeding:* Use deliberate hypotension to allow surgical access and control bleeding
- Deliberate hypotension with:
  - Fentanyl boluses
  - Thiopentone 3–5 mg/kg
  - Labetolol 5–10 mg increments
  - Sodium nitroprusside increments.
- Normotension restored following control of bleeding.

POSTOPERATIVE

Management

- Hypertension due to:
  - Pain
  - Hypercarbia
  - Pre-existing hypertension.
- Treated by treating cause/using antihypertensives
- Hypotension avoided by using intravascular volume resuscitation.

Pain

- *NSAIDS:* Avoid
- Low dose opioids
- *Multimodal analgesia.*

Complications

- Vasospasm:
  - Occurs in 70–90% patients after SAH
  - Peak incidence between 4–10 days after initial SAH
  - Causes delayed cerebral ischemia.

Etiology

- Due to BOXES (bilirubin oxidation products) which accumulate around blood vessels following metabolism of oxyhemoglobin in accumulated blood
- 5 HT, catecholamines, histamines, angiotensin, lipid peroxidase and endothelin: Unclear role
- Mainly occurs due to presence of blood in basal cisterns, in the vicinity of Circle of Willis.

Diagnosis

- Cerebral angiography is ***gold standard***
- Transcervical Doppler USG showing flow velocity > 120 cms/sec in MCA suggests vasospasm
- Presents as focal and fluctuant neurodeficits.

Treatment

- Calcium Channel Blockers:
  - Patients with SAH coming to OT must receive nimodipine
  - Nicardipine is IV alternative
  - Minimal effects on hemodynamics during anesthetic induction
  - No reduction in vasospasm on angiography but reduction in morbidity
  - Reduces incidence of cerebral infarction by 34%
  - Reduces incidence of poor outcome post SAH by 40%.
- Triple H Therapy:[1]
  - Hypertension, hypervolemia and hemodilution to optimize cerebral perfusion
  - Induced HTN with dopamine/phenylephrine
  - Raise MAP to 20–30 mm Hg above baseline systolic BP
  - Hypovolemia to reduce HCT to low 30s
  - Complications:
    - Pulmonary edema
    - Cardiac failure
    - Myocardial infarction
    - Hypertensive intracranial hemorrhage.
- Angioplasty:
  - Reduces severity of vasospasm
  - Increases risk of blood vessel dissection and rupture.
- Endovascular Infusion of Vasodilators:
  - Papavarine, verapamil and nicardipine used
  - Papaverine being neurotoxic is less favored
  - Intraarterial verapamil is better alternative.
- Intracisternal Fibinolytic Therapy:
  - Urokinase/r-TPA used to remove vasospastic agents from subarachnoid space
  - Removal of subarachnoid blood done at the same time following exposure of the brain.
- Endothelin A Antagonist:
  - *Clazosentan* undergoing phase III trials
  - Magnesium and simvastatin too undergoing trials.

2. Rebleeding:
   - Most often within first 48 hrs following initial SAH
   - Chance of rebleeding in first 24 hrs is 4%

- Chance of rebleeding after 1 year is 11%
- Mortality rate in rebleeds is 42%.

3. Intracranial HTN:
   - Usually requires no treatment as ICP becomes normal by end of first week
   - Emergency ventriculostomy if:
     - Severe intracranial HTN
     - Intracerebral/Intraventricular hemorrhage
     - Vasospasm
     - Hydrocephalus.
4. Hyperemic Complications:
   - Comprise cerebral edema/hemorrhage occurring during endovascular embolization/surgical resection
   - Theories to explain it:
     - *Normal Perfusion Pressure Breakthrough theory (NPPB)*
     - *Occlusive hyperemia theory*
   - SPECT imaging identifies patients at risk of developing NPPB
   - NIRS (near infrared spectroscopy) detects hyperemic status after AVM resection by measuring cortical O_2 saturation.
5. Siadh
6. Cerebral Salt Wasting Syndrome:
   Triad of:
   - Hyponatremia
   - Volume contraction
   - High urinary sodium ≥ 50 mmol/L.
7. SAH associated myocardial dysfunction:
   - Reversible stunning like injury
   - Associated with high troponin levels
   - ECG changes as described in investigations.

ANESTHESIA FOR PARKINSONS DISEASE (PD)[1,2,3,11]

Introduction

- Name given to clinical syndrome with:
  - Impairment of voluntary movement (bradykinesia)
  - Rigidity
  - Tremors.
- Also called '***shaking palsy***' or '***the happy disease***'.

Etiology

- *Idiopathic:* Accounts for almost 75% cases
- Positive family history
- Male gender, rural living
- Genetic factors:
  - Autosomal dominant inheritance with poor penetrance
  - Mutations in *synuclein* gene (SNCA).
- *Infections:* Postencephalitic Parkinsons disease, AIDS
- Environmental factors:
  - MPTP-induced Parkinsons
  - Herbicides and insecticides may increase risk of Parkinsons
  - Cigarette smoking reduces risk of developing Parkinsons.
- Multifactorial etiology.

Parkinsons Syndrome

- Caused by conditions which affect brainstem/disrupt dopaminergic pathway
- Clinical features are that of Parkinsons disease but etiology is different
- Causes:
  - Cerebrovascular disease: atherosclerosis, multi-infarct disease
  - Repeated head trauma
  - Intracranial neoplasms
  - Toxins:
    - ***Wilsons disease***
    - Carbon monoxide poisoning
    - Heavy metal poisoning.
  - Drugs
    - Phenothiazines
    - Butyrophenones
    - Metoclopramide
    - Reserpine
    - *Chronic trichloroethylene exposure.*

Parkinson Plus Syndromes

- Refers to neurodegenerative conditions associated with features of Parkinsons
- These are associated with more extensive pathologies in brain and brainstem
- They have multiple clinical features in addition to Parkinsonian features
- Therefore they are called Parkinson plus syndromes
- Causes:
  - Progressive supranuclear palsy
  - Cortico-basal degeneration
  - Multiple system atrophy
  - Striatonigral degeneration
  - ***Shy-Drager syndrome***
  - Diffuse Lewy body disease.

Pathogenesis

- Characterized by death of dopaminergic neurons in substantia nigra of basal ganglia

- Mechanisms of cell death:
  - Mitochondrial dysfunction
  - Oxidative stress
  - Excess nitric oxide formation
  - Deficient neurotrophic support
  - Immune mechanisms.
- Cell death in substantia nigra causes a decrease in dopamine production
- Dopamine deficiency causes increased activity of inhibitory nuclei in basal ganglia
- This causes inhibition of thalamic nuclei receiving outflow from basal ganglia
- Excessive thalamic inhibition causes suppression of cortical motor system
- This causes akinesia, rigidity and tremors
- Inhibition of brainstem locomotor areas cause abnormalities of posture and gait.

Clinical Features

- Classical triad:
  - Tremors
  - Muscle rigidity
  - Bradykinesia
- Tremors:
  - Resting tremors oscillating at 4–6 Hz
  - Characteristic ***pill rolling*** quality
  - Ceases at the onset of movement.
- Muscle rigidity:
  - Rigidity along with tremors causes ***cog wheeling*** nature of rigidity.
- Bradykinesia:
  - Paucity of movements
  - Slow movements with reduction in amplitude of finger excursions characteristic
  - May cause disturbed sleep patterns
  - Handwriting becomes micrographic.
- Posture and gait:
  - Slightly flexed posture
  - Loss of postural reflexes is a commonly associated feature
  - Retropulsion (several steps backwards) or propulsion (several steps forward) on losing balance
  - Lack of arm swing, with small rapid steps causes ***festinant gait***
  - Gait initiation failure, gait hypokinesia and ***freezing gait*** at later stages.
- Others:
  - Expressionless facial features: ***mask like facies***
  - Primitive reflexes like glabellar tap sign can be elicited.
- Autonomic dysfunction:
  - Orthostatic hypotension
  - Seborrhea, sialorrhea
  - Urinary and bowel disturbances
  - Sleep disorders, depression, anxiety.

Investigations

- Predominantly clinical diagnosis
- MRI:
  - Usually normal
  - Can detect cerebrovascular etiology or neurodegenerative etiology.
- Sphincter electromyography:
  - Reflects degeneration of ***Onuf's*** nucleus
  - Useful to distinguish Parkinsons disease from multiple system atrophy.

ANESTHETIC CONSIDERATIONS

Respiratory

- Upper airway dysfunction:
  - *Difficult airway*: Flexion deformity of neck, risk of aspiration
  - *Retained secretions:* Antisialogogue mandatory
  - *Pharyngeal dysfunction:* Causes dysphagia, prone for aspiration pneumonia
  - *Intrinsic laryngeal muscle dysfunction:* Prone for postoperative laryngospasm
  - *Sleep apnea:* In postencephalitic Parkinsons.
- Lower airway dysfunction:
  - *COPD:* Abnormal function of upper airway causes obstructive ventilatory pattern
  - May have coexisting COPD.

Autonomic Nervous System

- *Orthostatic hypotension:* Gradual change in posture recommended
- *Defective temperature regulation:* Prone for hypothermia.

Cardiovascular

- *Cardiac arrhythmias common:* Watch for intraoperative arrhythmias
- *Hypertension:* Intubation response should be blunted
- Hypovolemia.

Gastrointestinal

- *Poor nutrition:* Dyselectrolytemia
- *Susceptible to reflux:* Postextubation aspiration possible
- Abnormal glucose metabolism.

Urological
- Difficulty in micturition.

Central Nervous System
- Muscle rigidity
- *Tremors:* Difficult ECG interpretation
- *Confusion, hallucinations:* Postoperative delirium, cognitive dysfunction.

Pharmacological Considerations
- Avoid drugs precipitating Parkinsons:
  - *Phenothiazines:* Metoclopramide
  - *Butyrophenones:* Droperidol.
- Anesthetic agents:
  - Halothane avoided as it sensitizes heart to catecholamines
  - Ketamine avoided as it causes exaggerated sympathetic response
  - Fentanyl (even at normal doses) may exacerbate muscle rigidity
  - Alfentanil may cause dystonic reactions
  - Succinylcholine may cause hyperkalemia.
- Drug interactions:
  - *Avoid meperidine with selegiline:* Causes ***Serotonin syndrome.***

PREOPERATIVE ASSESSMENT

History and Examination
- Dose of medicines, timing, control of symptoms
- Side effects of anti-PD drugs
- Associated systemic features:
  - Pharyngeal muscle dysfunction:
    - Dysphagia
    - Sialorrhea.
  - Respiratory impairment
  - Orthostatic hypotension, hypertension
  - Difficulty in micturition, bowel disturbances
  - Akinesia, tremors, muscle rigidity
  - Confusion, hallucinations
  - Speech impairment.

Investigations
- *Complete blood count:* Respiratory infections
- *Blood glucose estimation:* Altered glucose metabolism
- Renal function tests
- *Serum albumin/transferring:* For nutritional status
- *Electrocardiography:* Pre-existing arrythmias
- *Chest X-ray:* Aspiration pneumonia
- *Pulmonary function tests:* Obstructive ventilatory pattern
- Arterial blood gas
- MRI.

Preoperative Preparation
- NPO orders:
  - 6 hrs for solids
  - 2 hrs for clear liquids.
- Informed consent
- Assess and discuss need for possible postoperative ICU/HDU stay
- Anti-aspiration prophylaxis:
  - IV ranitidine 1 mg/Kg
  - 30 ml sodium citrate given preoperatively.
- Continue Parkinsons medication on the day of surgery
- Glycopyrrolate 0.2 mg IV antisialogogue
- Midazolam 0.03 mg/kg IV for anxiolysis and sedation.

Choice of Anesthetic Technique
- Regional anesthesia preferred over general anesthesia
- Regional anesthesia can be technically difficult as:
  - Tremors
  - Rigidity can make positioning difficult
  - Twitches from peripheral nerve stimulator hard to discern
  - Poor cooperation if patient has dementia.
- Advantages of regional anesthesia:
  - Patient remains conscious
  - Avoids effects of general anesthesia and muscle relaxants which mask tremors
  - Reduced risk of respiratory complications
  - *Prevents PONV:* Can resume anti-PD medications in immediate postoperative period.

Monitors
- *Pulse oximetry;* ECG may show artefacts due to tremors
- *NIBP;* Unreliable due to tremors
- *Capnography;* Temperature
- *Urine output;* Neuromuscular monitoring
- Invasive hemodynamic monitoring for those with severe PD or cardiac comorbidities.

Induction
- Thiopentone decreases dopamine release from striatal neurons: *Avoided*
- Propofol may be anesthetic of choice as it reduces tremors

- Propofol 2 mg/kg + fentanyl 2 µg/kg + vecuronium 0.1 mg/kg IV
- Rapid sequence induction for severe PD causing respiratory compromise/esophageal spasm
- High dose opioids as in opioid induction may cause *wooden chest*
- Nasogastric tube inserted after intubation.

Maintenance

- O_2 + air + isoflurane (1 MAC) + fentanyl boluses
- *Halothane avoided* as it sensitizes the heart to catecholamines
- Isoflurane and sevoflurane are less arrythmogenic.

Positioning

- Difficult positioning due to muscle rigidity
- Gradual change of position due to autonomic instability
- Adequate padding at pressure points essential.

Hemodynamics

- *Adequate fluid resuscitation:* Dehydration due to vomiting associated with anti-PD drugs
- Autonomic insufficiency alters response to hypovolemia
- Vasodilatation associated with anesthetic induction may cause severe hypotension
- Sudden, exaggerated hypotension possible with central neuraxial blockade
- Directly acting vasopressors (phenylephrine, epinephrine) to treat hypotension.

Extubation

- Fully reversed, awake extubation
- Adequacy of ventilation and recovery from NMDR established before extubation
- Assess:
  - Spontaneous breathing pattern
  - Presence of gag reflex
  - Ability of patient to focus
  - Presence of 4 twitches/sustained tetanus.
- Adequate suction to remove excessive secretions before extubation.

POSTOPERATIVE

Management

- Anti-PD drugs to be started as soon as possible after surgery
- L-Dopa can be administered via nasogastric tube if required
- Good physiotherapy and early ambulation to aid postoperative recovery
- Breathing exercises and spirometry to prevent chest infections
- Diphenhydramine 25 mg IV can be used to reduce postoperative tremors.

Pain

- Opioids may be used but have to be replaced with NSAIDs as soon as possible
- PCA may be difficult to operate
- NSAIDs (ketorolac) useful as they do not interfere with respiratory function
- Local anesthetic infilteration useful
- Multimodal analgesia best.

Complications

- Pathological reflexes at emergence:
  - Babinskis reflex
  - Hyper-reactive stretch reflexes
  - Ankle clonus
  - Decerebrate posturing
- Aggravated rigidity
- Postoperative laryngospasm, respiratory failure
- Aspiration pneumonia: *Most common*
- PONV: Domperidone *Antiemetic of choice*
- Postoperative confusion, hallucinations.

ANESTHESIA FOR GUILLAIN BARRÉ SYNDROME[1,2,3,11]

Introduction

Guillain Barré syndrome is an acute demyelinating polyneuropathy characterized by an ascending motor weakness, sensory and autonomic dysfunction following a prodromal illness.

ETIOLOGY

Precipitating Events

- Triggering infection:
  - Campylobacter jejuni
  - Cytomegalovirus
  - Epstein Barr virus
  - Mycoplasma pneumonia.
- Immunizations:
  - Rabies vaccine
  - Swine flu.
- Lymphomas/Hodgkins disease
- Traumatic events
- Surgery.

Pathogenesis

- Precipitating events trigger autoimmune response
- Auto-antibodies formed against glycolipids and gangliosides
- This causes multifocal demyelination and secondary axonal degeneration
- Demyelination causes conduction blockade resulting in motor paralysis.

CLINICAL FEATURES

Symptoms

Motor weakness:

- Rapidly evolving progressive ascending motor paralysis
- Starts in lower limbs and ascends cranially
- Weakness may involve respiratory muscles and cause respiratory failure
- Deep aching pain in muscles and back
- *Lower cranial nerve involvement:* Difficulty in swallowing, maintaining airway
- Bulbar weakness: facial nerve palsy
- Ophthalmoplegia.

Sensory disturbances:

- Pain: Severe lower back pain
- *Numbness and paraesthesias:* Starts distally and ascends upwards
- Sensory ataxia and dysarthria.

Signs:

- *Flaccid areflexic paralysis:* Diminishes DTR with absent proprioception
- Muscle wasting within 2 weeks of onset of symptoms
- Autonomic dysfunction:
  - Labile blood pressure
  - Orthostatic hypotension
  - Resting tachycardia
  - Arrhythmias
  - Urinary retention
  - Paralytic ileus
  - Hyperhydrosis.
- *Metabolic derangements:* Hyponatremia due to SIADH.

TYPES[8]

Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP)

- *Most common* form
- Due to inflammation of myelin sheaths of peripheral nerve axons
- Causes slowing and blockage of conduction through peripheral nerves
- Secondary axonal damage occurs in severe cases
- *Symmetrical ascending motor weakness:* Hypo/areflexia.

Acute Motor Axonal Neuropathy (AMAN)

- Associated with precedent Campylobacter jejuni infection
- Selective motor nerve and axonal involvement
- Antibodies bind to ganglioside antigens on axonal cell membrane
- Macrophage invasion, inflammation and axonal damage follows
- Clinical features similar to AIDP but tendon reflexes preserved.

Acute Motor and Sensory Axonal Neuropathy (AMSAN)

- Both motor and sensory fibers involved
- Antibody mediated motor and sensory axonal damage
- Clinical features similar to AMAN but involves sensory symptoms
- More severe and associated with prolonged/partial recovery.

Miller Fisher Syndrome

- Antiganglioside antibodies to GQ1b causes ophthalmoplegia
- Causes demyelination of nerve roots
- Ataxia, areflexia and ophthalmoplegia characteristic
- 25% patients develop limb weakness.

Chronic Inflammatory Demyelinating Polyradiculoneuropathy

- Slowly progressive with relapsing course
- Clinical features similar to AIDP.

INVESTIGATIONS

Diagnostic

- Raised ESR, CRP
- Anti-GM 1, anti-GD 1a, anti-GQ 1b antibodies
- Serology:
  - Campylobacter jejuni
  - Mycoplasma pneumonia
  - Cytomegalovirus
  - Epstein-Barr virus.
- *Stool culture:* Campylobacter jejuni
- *CT scan:* To rule out other causes, raised ICP
- *MRI:* Excludes cervical nerve involvement

- *Lumbar puncture:* Raised protein with normal cell count and glucose
- *Nerve conduction studies:* Demyelinating pattern with axonal loss.

To Rule Out Complications

- Complete blood count
- *Liver function tests:* Raised ALT and AST, gamma GT, creatine kinase
- Renal function tests
- *Chest X-ray:* Aspiration pneumonia
- Features of SIADH
- Autonomic function tests
- *PFTs:* Reduced vital capacity, maximal inspiratory and expiratory pressures
- *Arterial blood gases:* Progressive respiratory failure.

DIFFERENTIAL DIAGNOSIS

Neurological

- Myasthenia gravis
- Eaton Lambert syndrome
- Multiple sclerosis
- Transverse myelitis.

Metabolic

- Hypokalemic periodic paralysis
- Hypermagnesemia
- Hypophosphatemia
- Acute intermittent porphyria.

Infective

- Postdiphtheria neuropathy
- Polio
- Botulism
- Tick paralysis.

Toxins

- *Heavy metal poisoning:* Lead
- *Biological toxins:* Snake, scorpion
- *Drugs:* Nitrofurantoin, aminoglycosides.

Others

- Acute polymyositis
- Critical illness myopathy.

Diagnostic Criteria

Essential Criteria

- Progressive weakness of more than one limb
- Areflexia
- Duration of progression < 4 weeks.

Supportive Criteria

- Relative symmetry
- Mild sensory signs/symptoms
- Cranial nerve involvement, especially bilateral CN VII involvement
- Recovery beginning 2–4 weeks after progression ceases
- Autonomic dysfunction
- Absence of fever at onset
- Typical CSF, EMG and nerve conduction studies.

MANAGEMENT

Monitor

- *Pulse oximetry:* Desaturation is late sign
- *Blood pressure:* Invasive monitoring as autonomic instability
- ECG
- *Arterial blood gases:* Evidence of respiratory failure
- Others:
  - Head lift
  - Upper limb weakness
  - Respiratory rate
  - Vital capacity measured thrice daily
  - Maximal inspiratory and expiratory pressures.

Airway

- 30% patients require ventilation
- Indications for intubation:
  - Vital capacity < 15 ml/kg or < 1L
  - Maximum inspiratory pressure < 30 cm H_2O
  - Maximum expiratory pressure < 40 cm H_2O
  - Bulbar involvement with weak cough and dysphagia
  - Evidence of respiratory failure
  - Autonomic instability.
- Tracheostomy if prolonged respiratory support needed.

Deep Vein Thromboprophylaxis

- Subcutaneous low molecular weight heparin
- Pneumatic compression devices
- Early physiotherapy and ambulation.

Nutrition

- Early resumption of enteral nutrition via nasogastric tube
- *Paralytic ileus common:* Treat with metaclopramide/domperidone
- Total parenteral nutrition when enteral measures are inadequate.

Immunomodulatory

- Intravenous immunoglobulins:
  - Most effective if administered within 2 weeks of onset
  - 400 mg/kg IV for 5 days
  - Indications:
    - Muscle weakness
    - Respiratory depression.
  - Contraindications:
    - Previous anaphylaxis to IV Ig
    - IgA deficiency.
  - Side effects:
    - Nausea, headache
    - Erythroderma
    - Fluid overload
    - Acute renal failure.
- Plasma exchange:
  - Best if commenced within one week of onset of symptoms
  - Beneficial upto 30 days after onset of symptoms
  - Involves passage of blood through cell separator
  - Plasma fraction is removed and replaced with FFP or human albumin
  - Thus, antibodies associated with autoimmune response are removed
  - 40–50 ml/kg plasma exchange for 4–5 days
  - Indications:
    - Muscle weakness
    - Respiratory weakness.
  - Contraindications:
    - Coagulopathy
    - Sepsis
    - Hemodynamic instability.
  - Side effects:
    - Nausea, vomiting
    - Coagulopathy
    - Immunosupression
    - Hypocalcemia.

Others

- Frequent turning to avoid pressure sores
- Prompt correction of dyselectrolytemias
- *Physiotherapy:* For clearance of secretions, prevention of sequelae of limb disuse
- Suction clearance of secretions.

Corticosteroids

- Of historical significance to suppress immune response
- No longer used as no evidence of improving long term prognosis.

ANESTHETIC CONSIDERATIONS

Neurological

- *Careful limb positioning:* Compression nerve palsies common
- Neuropathic pain common in postoperative period
- Higher incidence of postoperative cognitive decline and depression.

Respiratory

- *Cranial nerve involvement:* Upper airway obstruction causing postoperative respiratory failure
- Susceptible to aspiration pneumonia due to:
  - Bulbar palsy causing difficulty in swallowing
  - Laryngeal paralysis.
- Perioperative respiratory dysfunction: intercostal and diaphragmatic weakness
- Possibility of prolonged postoperative ventilation.

Cardiovascular

- Arrhythmias common:
  - Atrial fibrillation
  - Paroxysmal atrial tachycardia
  - Ventricular tachyarrhythmias
  - Prolonged QT interval
  - Atrioventricular blocks
  - Asystole.
- Autonomic dysfunction:
  - Labile blood pressure, orthostatic hypotension
  - Avoid drugs with negative impact on cardiovascular function
  - Exaggerated response to endotracheal intubation, surgical incision
  - Arrhythmias common during endotracheal suction
  - Gradual change of posture to avoid hemodynamic disturbances
  - Treat hypotension with:
    - Volume expansion
    - Direct acting adrenergic agents
    - Sensitive to vasoactive drugs due to denervation supersensitivity.
- Deep vein thrombosis: High risk due to immobility.

Gastrointestinal

- Poor oral intake due to bulbar weakness: dyselectrolytemias
- Early institution of enteral/parenteral feeding
- Susceptible to paralytic ileus in postoperative period: treat with prokinetic agents.

Pharmacological

- Succinyl choline absolute contraindication as it causes:
  - Severe hyperkalemia
  - Life-threatening arrhythmias
  - Sudden hyperkalemic cardiac arrest
  - Rhabdomyolysis.
- More sensitive to non-depolarizing muscle relaxants: avoid NMBAs
- Use intermediate acting NMBAs with neuromuscular monitoring when indicated
- Avoid drugs which prolong action of NMBAs:
  - Aminoglycosides
  - Calcium channel blockers
  - Ranitidine
  - Anticonvulsants.
- Use short-acting anesthetic agents: to prevent postoperative respiratory failure
- Sensitive to local anesthetics: profound hypotension and bradycardia possible.

Preoperative Assessment and Preoperative Preparation

- Assess airway, mouth, dentition and neck
- Assess bulbar function to prevent aspiration during induction
- Assess respiratory muscle function: vital capacity, mouth occlusion pressures, cough
- Assess autonomic function: ECG, postural hypotension, excessive sweating
- Correct electrolyte imbalance/hyponatremia
- NPO orders:
  - 6 hrs solids
  - 2 hrs clear fluids.
- Informed consent
- Anti-aspiration prophylaxis
  - Metaclopramide 10 mg IV
  - 30 ml of nonparticulate 0.3M sodium citrate.

Monitor

- *Pulse oximetry;* Blood pressure
- *ECG;* $ETCO_2$
- *Temperature;* Urine output
- Neuromuscular monitoring mandatory
- Invasive pressure monitoring: for autonomic instability, blood loss anticipated.

Position

- Careful positioning to avoid compression palsy
- Gradual change of posture to avoid hypotension.

Induction

- *Rapid sequence induction*
- Propofol 2 mg/kg + fentanyl 1–2 µg/kg + rocuronium 0.1 mg/kg
- Profound hypotension with induction of anesthesia
- Prevent intubation response: IV xylocard 1.5–2 mg/kg 90 seconds before intubation
- Ryles tube inserted.

Maintenance

- O_2 + air + isoflurane + fentanyl boluses + vecuronium boluses
- Reduced requirement of NDMRs: reduce doseage
- Pneumatic compression devices applied.

Ventilation

- Controlled ventilation preferred
- Profound hypotension may occur at the initiation of positive pressure ventilation.

Hemodynamics

- Profound hypotension during:
  - Induction of anesthesia
  - Change in posture
  - Blood loss.
- Exaggerated HTN with intubation/surgical incision
- Treat hypotension with:
  - Volume expansion
  - Direct acting adrenergic agents
  - Exaggerated response to direct acting adrenergic agents.
- Normal temperature maintained to prevent hypothermia-induced delayed awakening.

EXTUBATION

Fully reversed and extubated when fully awake

Indications for postoperative ventilation:

- Vital capacity < 15 ml/kg or < 1L
- Maximum inspiratory pressure < 30 cm H_2O
- Maximum expiratory pressure < 40 cm H_2O
- Bulbar involvement with weak cough and dysphagia
- Evidence of respiratory failure
- Autonomic instability.

POSTOPERATIVE MANAGEMENT

Management

- Care of skin, bladder and bowel
- Vigorous chest physiotherapy to prevent hospital-acquired pneumonia

- DVT prophylaxis instituted as soon as possible after surgery.

Monitors
- *Pulse oximetry;* Blood pressure
- *ECG;* Temperature
- Arterial blood gas
- Muscle strength: head lift, vital capacity.

Analgesia
- Multimodal analgesia useful
- *Analgesic adjuncts:* Useful for opioid sparing properties
  - *Anticonvulsants:* gabapentin better than cabamezepine
  - Tricyclic antidepressants.

ANESTHESIA FOR EPILEPSY PATIENTS[1,2,3,11]

Introduction
- Seizures are episodes of abnormal and excessive synchronized electrical brain activity
- Epilepsy is defined as recurrent (two or more) epileptic seizures unprovoked by any immediate identifiable cause.

Classification
International League Against Epilepsy
- Partial seizures
  - Simple partial seizure
  - Complex partial seizure
  - Partial onset seizure with generalization.
- Generalized seizures
  - Typical absence seizures
  - Atypical absence seizures
  - Myoclonic seizures
  - Tonic-clonic seizures
  - Clonic seizures
  - Tonic seizures
  - Atonic seizures.
- Status epilepticus.

ETIOLOGY

Genetic
- Epilepsy syndromes
- Juvenile myoclonic epilepsy
- Benign rolandic epilepsy.

Trauma
- Depressed skull fractures
- Intracranial hemorrhages.

Tumor
- *More common* with anterior hemisphere tumors.

Infections
- Meningitis
- Encephalitis.

Cerebrovascular Diseases
- Hemorrhage
- Infarction.

Cerebral Degenerative Diseases
- Alzheimers disease
- Multi-infarct dementia
- Multiple sclerosis.

Metabolic Disorders
- Hypo/hypercalcemia
- Hypoglycemia
- Hypo/hypernatremia
- Hypomagnesemia.

Differential Diagnosis
- Syncope:
  - Micturition syncope
  - Cough syncope
  - Cardiac syncope
  - Carotid sinus syncope.
- Transient ischemic attack (TIA): Carotid occlusion or stenosis
- Basilar migraine: loss of consciousness common
- Hyperventilation syndromes
- Narcolepsy and cataplexy.

Anesthetic Considerations
- Maintenance of intracranial hemodynamics
- To provide brain protection to achieve good neurological recovery
- To ensure rapid recovery for postoperative neurological assessment
- Management of refractory status epilepticus
- Anesthetic potentiation of seizure activity: Avoid these drugs:
  - Enflurane
  - Sevoflurane (especially > 1 MAC)
  - Methohexital
  - Etomidate, ketamine
  - Alfentanil, pethidine, tramadol.
- Enzyme induction:
  - Carbamazepine
  - Phenytoin

  - Phenobarbital
  - Primidone.
- Enzyme inhibition: Sodium valproate.

Choice of Anesthetic Technique

- Regional anesthesia safe technique
- Factors known to precipitate seizures have to be avoided
- Sedation and anxiolysis mandatory to prevent hyperventilation which reduces seizure threshold.

PREOPERATIVE ASSESSMENT HISTORY

Epilepsy

- Etiology of seizures
- Type and pattern of seizures
- Frequency and control of seizures
- Triggers for seizures:
  - Fasting
  - Stress
  - Sleep deprivation
  - Alcohol, drugs.
- Antiepileptic therapy.

Examination

- Difficult airway:
  - Craniosynostosis
  - Gingival overgrowth from AED therapy.
- Complications of antiepileptic therapy:
  - Acidosis
  - Renal, liver damage
  - Coagulopathies.

Investigations

- Complete blood count
- Liver function tests: especially those on ethosuximide, valproate, carbamazepine
- Coagulation abnormalities
- ECG and echocardiography: especially if tuberous sclerosis/murmurs
- Plasma levels of antiepileptic therapy for poorly controlled epilepsy
- EEG
- CT scan: for detecting structural abnormalities
- *MRI:* For detecting small brain lesions
- *SPECT:* Single photon emission tomography for cerebral blood flow
- *PET:* Positron emission tomography for cerebral blood flow and glucose metabolism.

Preoperative Preparation and Premedication

- Neurologist review if recent change in nature of seizures
- Informed consent to be taken
- NPO orders:
  - 6 hrs for solids
  - 2 hrs for clear fluids.
- Avoid prolonged preoperative starvation to prevent metabolic disturbances
- Continue antiepileptic therapy on the morning of surgery
- Re-establish antiepileptic medication as soon as practical after surgery
- Need for possible prolonged postoperative ventilation to be explained
- Sedation beneficial as hyperventilation reduces seizure threshold
- Midazolam 0.03 mg/kg IV useful for anxiolytic and anticonvulsant properties.

Monitoring

- *Pulse oximetry;* Electrocardiography
- *Noninvasive blood pressure;* $ETCO_2$
- *Neuromuscular monitoring;* Urine output
- Temperature
- Invasive hemodynamic monitoring in ASA III, IV patients
- Repeated ABG, blood glucose estimation if prolonged surgery.

Induction

- Thiopentone 4–5 mg/kg + fentanyl 2 µg/kg + vecuronium 0.1 mg/kg IV
- Rapid sequence induction for status epilepticus/prolonged seizures
- Avoid:
  - Ketamine and etomidate for induction
  - High induction dose (> 0.5 mg/kg) or prolonged infusion of atracurium
  - Succinylcholine for RSI (as epileptogenic) – rocuronium preferred.

Maintenance

- O_2 + Air + isoflurane (1 MAC) + fentanyl boluses used
- Isoflurane is *volatile anesthetic of choice*
- Halothane and desflurane also may be used
- Nitrous oxide use is controversial
- Increased requirements of opioids and NMBAs due to enzyme induction by AEDs

- Avoid:
  - Enflurane (any concentration) and sevoflurane (> 1.5 MAC) contraindicated
  - Alfentanil and pethidine.

Ventilation

- Avoid hypoxia, maintain normocapnea
- Avoid hyperventilation as hypocapnea reduces seizure threshold.

Hemodynamics

- Avoid hypotension, maintain MAP to around 20% of preoperative values
- Avoid hypoglycemia, hyponatremia during prolonged surgery
- Avoid Ringers lactate and glucose-containing fluids: may contribute to metabolic acidosis
- Normal saline is preferred fluid.

POSTOPERATIVE

Management

- Restart AED therapy as soon as possible after surgery:
  - *If NPO for 12–24 hrs postoperative:* Restart oral AEDs once oral feeding established
  - If NPO for > 24 hrs postoperative:
    - Replace oral AEDs by parenteral AEDs 2–3 times a day
    - Restart oral AEDs once oral feeding is established.

Monitoring

- *Pulse oximetry;* Electrocardiogram
- *Blood pressure;* Urine output
- Plasma levels of AEDs for 48 hrs postoperatively.

Pain

- Avoid pethidine and tramadol for postoperative analgesia
- Regional blocks safe
- Multimodal analgesia preferred.

Complications

- Status epilepticus
- Infections: neutropenia, aplastic anemia due to AED
- Halothane hepatitis.

STATUS EPILEPTICUS[1,2,3,8,10]

Introduction

Status defined as continuous seizure activity of atleast 30 min duration or intermittent seizure activity of atleast 30 min duration during which consciousness is not regained.

Classification

- Generalized status: *most common*
- Partial status
- Convulsive status
- Non-convulsive status.

Clinical Features

- Generalized tonic clonic seizures
- Loss of consciousness
- Urinary incontinence
- Tongue-biting.

Differential Diagnosis

- Myoclonic jerks
- Septic rigors
- Dystonia
- Pseudostatus epilepticus.

MANAGEMENT

Airway

- Ensure patent airway
- Endotracheal intubation if required: ***rapid sequence induction***
- Prevent aspiration of gastric contents
- Prevent tongue bite if possible
- Protect patient from injuries resulting from seizures.

Breathing

- Ensure adequate ventilation and oxygenation
- 100% oxygen.

Circulation

- Establish large bore IV access
- Fluid resuscitation to maintain adequate blood pressure and cerebral perfusion pressure
- IV vasopressors started if required
- Check and correct hypoglycemia:
  - 100 mg thiamine IV followed by 50 ml of 50% glucose
  - 2 ml/kg of 25% glucose.

Monitoring

- *Electrocardiography;* Pulse oximetry
- *Arterial pressure;* Blood glucose
- Temperature
- Continuous EEG monitoring for seizure activity if NMBA used.

Investigations

- Complete blood count
- Blood urea, serum creatinine
- Serum electrolytes: sodium, calcium, magnesium
- Blood glucose, arterial blood gases
- Liver function tests, coagulation profile
- Lumbar puncture
- Drug toxicology, blood concentrations of AEDs
- Chest X-ray for aspiration pneumonia
- Brain imaging.

Antiepileptic Therapy[8]

Status Epilepticus
↓
Lorazepam 0.1 mg/kg (4 mg)
↓
Continuing seizures
↓
Phenytoin 15 mg/kg at < 50 mg/min
OR
Fosphenytoin 15 mg/kg at 100–150 mg/min
↓
Continuing seizures
↓
Phenobarbital 15 mg/kg at < 50 mg/min
↓
Continuing seizures
↓
Intensive care management
↓
Continuing seizures
↓
General anesthesia with:
Thiopentone 5 mg/kg followed
by 3–5 mg/kg/hr infusion
Midazolam 0.1 mg/kg followed by 2–20 μg/kg/min

Treatment of Cause

- *Alcohol withdrawal:* High-dose thiamine (250 mg) with glucose
- *Drug withdrawal:* Noncompliance with AED therapy
- Dyselectrolytemia
- Hypoglycemia: 50 ml of 50% glucose.

COMPLICATIONS

Central Nervous System

- Cerebral hypoxia
- Cerebral edema
- Cerebral hemorrhage
- Cerebral venous thrombosis.

Cardiovascular System

- Myocardial infarction
- Hyper/hypotension
- Arrhythmias
- Cardiac arrest
- Cardiogenic shock.

Respiratory System

- Apnea
- Respiratory failure
- Pneumonia
- Pulmonary edema.

Metabolic

- Hyponatremia
- Hypoglycemia
- Hyperkalemia
- Metabolic acidosis
- Acute tubular necrosis
- Acute hepatic necrosis
- Acute pancreatitis.

Miscellaneous

- Disseminated intravascular coagulation
- Rhabdomyolysis
- Fractures.

CAUSES OF PERIOPERATIVE SEIZURES

Central Nervous System

- Pre-existing epilepsy
- Previous history of traumatic brain injury (TBI)
- ***Breakthrough seizures***: Due to missed dose of anticonvulsants
- Trauma
- Intracranial hemorrhage
- Cerebral venous thrombosis
- Intracranial Space Occupying Lesions (ICSOL):
  - Tumors
  - Abscesses.

Metabolic Disturbances

- Hypoxia
- Hypercarbia/Hypocarbia
- Hyponatremia
- Hypocalcemia
- Hypomagnesemia

- Hypoglycemia: ***Neuroglycopenia***
- Hypothermia.

Infections

- Febrile seizures
- Toxemias:
  - Encephalitis
  - Meningitis
  - Parasitemias: Schistosomiasis/tapeworm
  - Sepsis.

Peripartum

- Ecclampsia
- Amniotic fluid embolism
- Magnesium sulfate toxicity.

Drugs

Proconvulsant Drugs

- Dopaminergic antagonists: Metaclopramide
- Tricyclic antidepressants
- Antipsychotics: clozapine, olanzapine
- Antiepileptics: Phenytoin/carbamazepine at supratherapeutic range
- Methylxanthines: theophylline/aminophylline
- Prostaglandins
- Beta blocker toxicity
- Beta lactam antibiotics: infants/history of meningitis/supratentorial craniotomy.

Anesthetic Agents

- Volatile anesthetics:
  - Enflurane: Especially at > 2 MAC
  - Sevoflurane: Proconvulsant at > 1.5 MAC when associated with hyperventilation.
- Induction agents:
  - Etomidate:
    - Dose dependent action: proconvulsant action at smaller induction doses
    - Burst suppression at higher doses.
  - Methohexitone
  - Ketamine: Proconvulsant with subcortical electrical activation
  - Propofol:
    - *Dose dependent action:* Proconvulsant action at smaller induction doses
    - Burst suppression at higher doses.
- Atracurium/cisatracurium:
  - Occurs due to laudanosine formation
  - Accumulation at high doses/repeated prolonged dosing
  - Laudanosine levels > 17 µg/ml is epileptogenic.
- Meperidine: in renal failure/at high doses
- Tramadol in renal failure patients
- Pentazocine.

Medication Errors

- Local anesthetic systemic toxicity (LAST)
- Intrathecal tranexemic acid/repeat doses of tetracaine.

Drug Withdrawal

- Alcohol withdrawal
- Sedative drug withdrawal: Diazepam withdrawal
- Antiepileptic withdrawal: Phenobarbital, carbamazepine.

ANESTHESIA FOR AWAKE CRANIOTOMY[1,2,3,6]

Introduction

Comprises entire spectrum of techniques which allow intraoperative brain mapping during surgery in and around eloquent brain areas, in order to minimize risk of postoperative functional sequelae.

INDICATIONS

Anatomical

- Resection of tumors in eloquent cortex:
  - Frontal lobe:
    - Motor area
    - ***Brocas*** speech area
  - Temporal lobe: ***Wernicke's*** speech area
- Arteriovenous malformations
- Aneurysms.

Physiological

- Deep brain stimulation:
  - Parkinson's disease
  - Dystonias.

Pharmacological

Primarily intractable epilepsy surgery.

CONTRAINDICATIONS

Absolute

- Uncooperative patient.

Relative

- Confused patient
- Extreme anxiety

- Obstructive sleep apnea
- Morbidly obese
- Vascular tumors
- *Tumor with dural involvement:* Painful
- *Low occipital tumors:* Prone position
- Inexperienced surgeon.

Anesthetic Goals

- Maintain patient cooperation:
  - Optimal analgesia
  - Adequate sedation and anxiolysis
  - Comfortable positioning
  - Prevent nausea, vomiting and seizures.
- Smooth transition between anesthesia and consciousness:
  - *Asleep:* Sufficient depth of anesthesia during opening/closing of bone flap
  - *Awake:* Full consciousness during brain mapping.
- Homeostasis:
  - Safe airway and adequate ventilation
  - Hemodynamic stability
  - Normal ICP.
- Facilitate excision of maximum amount of lesion without neurological impairment
- Minimal interference with electrophysiological recordings.

Preoperative Assessment

- Evaluate seizure history:
  - Type and pattern of seizures
  - Frequency of seizures
  - Previous and current anticonvulsant therapy
  - Complications of anticonvulsant therapy
  - Plasma concentrations of drugs.
- Airway assessment:
  - Ease of mask ventilation
  - Mallampati score, predictors of difficult laryngoscopy
  - *Obstructive apnea risk:* Obesity, sleep apnea, retrognathia
  - Important as anesthetist should be prepared for emergency intubation, in lateral position.
- Evaluate nausea and vomiting risk:
  - Past anesthesia exposure
  - Kinetosis
  - Evaluate hemorrhagic risk:
  - Type of lesion
  - Antiplatelet therapy
  - Medical history.
- Evaluate intracranial pressure:
  - Type of lesion
  - Radiological and clinical signs.
- Evaluate patient cooperation:
  - Anxiety
  - Pain tolerance
  - Neurological deficits
  - Psychological status.

Preoperative Preparation

- Informed consent
- NPO orders:
  - 6 hrs for solids
  - 2 hrs for clear fluids.
- Psychological preparation of patient for awake surgery:
  - Explain procedure
  - Reassure that procedure will be entirely painless
  - Possibility of nausea on traction of temporal lobe explained.
- Good IV line is secured, arterial line may be inserted under LA
- Benzodiazepines avoided in epilepsy surgery to minimize effect on ECoG
- Clonidine 2–3 µg/kg PO may be given one hour before surgery
- Preoperative antibiotics as per hospital protocol
- Antiemetic prophylaxis:
  - Metoclopramide 10 mg IV
  - Ondansetron 4–8 mg IV.
- IV dexamethasone 8 mg before surgery:
  - Reduces ICP
  - Reduces incidence of PONV.

OT Preparation (SOAP-ME)

- Suction apparatus (S)
- *Oxygenation:* airway devices (O)
- Anesthetic drugs: local anesthetics, sedatives (A)
- *Pharmacy:* other medications (antiemetics, vasopressors, anticonvulsants) (P)
- Monitors (M)
- *Emergency drugs:* atropine, adrenaline (E)
- OT temperature to be suitable
- Surgical table covered with soft, thick dressing
- Position all instruments in order to minimize movement of objects and personnel
- Patient's face exposed to allow him to:
  - Look and communicate with anesthetist and surgeon

  - Look at brain-mapping pictures
  - Airway treatment during emergencies.
- Audio-video recorder system to allow recording of patient's responses during cortical mapping.

Monitors

- *Pulse oximetry;* ECG
- *NIBP;* $ETCO_2$
- *Respiratory rate;* Temperature
- *Continuous IBP:* For recording BP and periodic ABGs
- *Urine output;* BIS monitoring
- Central venous catheter placement if large blood loss anticipated
- Ramsay sedation score/VAS score for adequacy of sedation/analgesia.

Position

- Patient allowed to position themselves in the most comfortable position
- Draped to allow constant, unimpeded access to airway
- Clear drapes used to prevent claustrophobia.

TECHNIQUES

Local Anesthesia

- Infiltration of local anesthetic into relevant areas of scalp, pericranium and dura
- Scalp block is used for craniotomy
- Nerves blocked with scalp block:
  - Supraorbital N
  - Zygomatico-temporal N
  - Auriculotemporal N
  - Lesser occipital N
  - Greater occipital N.
- Local anesthetic infiltration of pin sites and incision line also used
- Local anesthetic infiltration of Trigeminal nerve trunk for analgesia of dura
- IV sedation required until dural opening as patient might be distressed.

Monitored Anesthesia Care

- Introduction:
  - Sedation and analgesia, carefully titrated to different surgical planes
  - Used in conjunction with LA infiltration
  - Requires good regional anesthesia of scalp with carefully titrated anesthetics for success.
- Drugs used:
  - Fentanyl + droperidol in incremental doses: ***neuroleptanalgesia*** (used earlier)
  - Propofol infusion + fentanyl boluses
  - Propofol + remifentanil infusion as Target Controlled Infusion
  - Dexmedetomidine infusion.
- Technique:
  - Radial arterial line, Foley's catheter inserted under LA
  - Patient's position adjusted on surgical table to be comfortable
  - Scalp block is performed with ropivacaine/levobupivacaine
  - This is reinforced with infilteration of pin-sites and surgical incision line
  - Analgesia and sedation co-administered with short-acting agents:
    - Propofol 100 µg/kg/min IV
    - Remifentanil 0.05 µg/kg/min added 5 mins before pin placement
    - Remifentanil reduced to 0.01 µg/kg/min after placement of pins
    - Ramsay score of 3–4 is goal during pin-fixation and craniotomy.
  - Nasal airway used with supplemental oxygen to maintain airway patency
  - Mannitol 0.25 g/kg administered at the time of skull opening
  - Labetalol 5–10 mg IV boluses to keep SBP < 150 mm Hg with heart rate > 50 bpm
  - Hydralazine 5 mg IV boluses when SBP > 150 mm Hg with heart rate < 50 bpm
  - Sedation terminated 15 minutes prior to intraoperative monitoring
  - Patient is maintained fully awake till end of brain-mapping/tumor removal.
  - In case of pain arising during resection/dural opening:
    - Paracetamol 1 g IV
    - Remifentanil 0.025–0.05 µg/kg/min.
  - Sedation recommended at the end of tumor resection when dural closure initiated:
    - Propofol 15 µg/kg/min IV and titrated to sedative effect
    - Remifentanil 0.01 µg/kg/min IV
    - Ramsay score of 2–4 maintained until removal of Mayfield fixators.
  - IM diclofenac 1 mg/kg half-an-hour before end of surgery
  - Repetition of scalp block done for postoperative analgesia.

- Advantages:
  - Full cooperation of patient if successful
  - Does not require ETT/LMA insertion
  - Accurate monitoring of brain function.
- Disadvantages:
  - Maintaining optimal sedation with adequate intraoperative control of airway difficult
  - Oversedation causes respiratory depression
  - Undersedation makes the patient uncooperative
  - Emergency airway intervention risky in time of intraoperative seizures.

Asleep-Awake-Asleep (AAA) Technique[1,3]

- Introduction: Technique involves general anesthesia with intraoperative wake-up.
- Phases:
  - Phase 1: Induction of GA with ETT/LMA until brain is exposed
  - Phase 2: Patient is gradually awakened and extubated to allow brain-mapping
  - Phase 3: GA is induced after resection of tumor and ETT/LMA reinserted.
- Technique:
  - First part of procedure is done under general anesthesia
  - Propofol with remifentanil infusion is *technique of choice*
  - BIS monitoring used to guide target-controlled infusions
  - ProSeal LMA can be used during first phase for airway control
  - Mannitol 0.25 g/kg administered at the time of skull opening.
  - Labetolol 5–10 mg IV boluses to keep SBP < 150 mm Hg with heart rate > 50 bpm
  - Hydralazine 5 mg IV boluses when SBP > 150 mm Hg with heart rate < 50 bpm
  - Dose of remifentanil reduced after dural opening to allow spontaneous ventilation
  - Propofol infusion rate is then reduced and stopped to awaken patient
  - LMA/ETT is then removed when patient is fully awake
  - Patient is maintained awake till completion of resection
  - After resection of lesion, propofol and remifentanil are restarted and LMA reinserted
  - This technique carries minimal risk of coughing, straining and vomiting.
- Alternate techniques:
  - Alternatively, LMA is kept in-situ during awake phase
  - This can cause coughing and straining when the patient awakens
  - ETT with catheter attached spirally to ETT is used as an alternative to LMA
  - Local anesthetic is injected into catheter to provide for airway anesthesia during awake phase
  - This allows tube tolerance during the awake phase with ETT in-situ.
- Advantages:
  - Allows titratable levels of anesthesia
  - Guarantees patient immobility and maximum patient comfort
  - Allows adequate oxygenation and ventilation
  - Fast and reliable wake-up
  - Patient feels less psychological stress and discomfort.
- Disadvantages:
  - Physical stress associated with intubation
  - Awake phase may cause airway irritation, coughing and raised ICP
  - Patient movement possible during awake phase with rigid Mayfield head fixation
  - Reinsertion of airway devices maybe difficult at end of surgery
  - Residual anesthetic effect during awake phase affects evaluation of cortical function
  - Longer hospital stays.

Asleep-Awake (AA) Technique[1,3]

- Done in two phases:
  - Phase 1: Patient is induced and ETT/LMA is inserted
  - Phase 2: After exposure of brain, patient is awakened and ETT/LMA is removed.
- Patient is left awake or lightly sedated thereafter till the end of surgery.
- Advantages:
  - Avoids re-induction of GA at the end of surgery
  - Avoids problems relating to reinsertion of airway device.
- Disadvantages:
  - Awake phase may cause airway irritation, coughing and raised ICP
  - Patient movement possible during awake phase with rigid Mayfield head fixation
  - Last part of surgery involves administering sedation without securing airway.

Postoperative Analgesia

- Opioids increase risk of sedation, PONV
- NSAIDs may cause postoperative intracranial hemorrhage
- Scalp infiltration along with paracetamol effective and reduces need for opioids.

COMPLICATIONS

Anesthesia-related

- Airway obstruction
- Desaturation/hypoxia
- Raised ICP
- Hypertension/hypotension
- Tachycardia/bradycardia
- Nausea/vomit
- Shivering
- LA systemic toxicity
- Pain
- Poor cooperation—conversion to general anesthesia.

Surgery-related

- Focal seizures
- Generalized seizures
- Aphasia
- Bleeding
- Raised ICP
- Venous air embolism.

HYPOPHYSECTOMY[1,2,3]

Introduction

Refers to excision/destruction of pituitary gland.

Anatomy

- Pituitary gland lies within pituitary fossa (***Sella turcica***) of skull base.
- Boundaries are:
  - *Floor:* Roof of sphenoid sinus
  - *Lateral walls:* Cavernous sinus (with carotid artery and CN III, IV and VI)
  - *Roof:* Diaphragm sella with pituitary stalk.
- Hormones secreted:
  - Anterior lobe (adenohypophyses)
    - Luteinizing hormone (LH)
    - Follicle-stimulating hormone (FSH)
    - Growth hormone (GH)
    - ACTH
    - Thyroid-stimulating hormone (TSH)
    - Prolactin
    - Melanocyte-stimulating hormone.
  - Posterior lobe:
    - Oxytocin—formed in hypothalamus
    - Vasopressin.

Pathology

- Most commonly adenomas—prolactinoma and nonsecreting adenomas
- Nonpituitary tumors—craniopharyngiomas
- *Rathke's pouch cysts*
- Hyposecretion of hormones:
  - Due to:
    - Tumor compression
    - Necrosis after postpartum hemorrhagic shock (***Sheehans syndrome)***
    - Head injury
    - Radiation/surgical/chemical hypophysectomy.
  - Order in which endocrine function lost (GnRH > GH > ACTH > TSH)
  - Endoscopicc endonasal approach has fewer nasal dental and cosmetic problems and postoperative diabetes insipidus incidence.
- Hypersecretion of hormones: (*See table on next page*)

CLINICAL PRESENTATION

Hypersecretion of pituitary hormones:

- *GH:* gigantism in prepubertal age, acromegaly in adults
- *ACTH:* Cushing's syndrome
- *Prolactin:* galactorrhea, infertility, secondary amenorrhea.

Mass effect if large (> 1 cm diameter) tumor:

- Headache
- Hydrocephalus (rare) – if suprasellar extension
- Visual field defects due to optic chiasm compression
- ***Bitemporal hemianopia*** *classical*
- Hypopituitarism if hemorrhage into tumor
- Cranial nerve palsies – CN III, IV, VI.

PREOPERATIVE ANESTHETIC CONSIDERATIONS

General

- Remote airway
- Raised ICP
- Oropharyngeal packing
- Use of submucosal epinephrine to decrease bleeding.

Acromegaly

- OSAS
- Hypertension

Location	Hormone	Type	Clinical presentation
Anterior pituitary	Prolactin	Prolactinoma	Galactorrhea
			Amenorrhea
			Infertility, hypogonadism
	ACTH	Basophilic adenoma	Cushing's syndrome
			Centripetal obesity
			Diabetes mellitus
			HTN
			Difficult airway
Suprasellar	Nonsecretory	Craniopharyngioma	SIADH
		Rathke's cleft cyst	Panhypopituitarism
		Suprasellar extension	Visual symptoms
		of pituitary lesion	Hydrocephalus

- Diabetes mellitus and glucose intolerance
- Increased ventilation-perfusion mismatch
- Peripheral neuropathy
- Skeletal muscle weakness
- Osteoporosis
- Poor ulnar collateral blood flow
- Difficult airway due to:
  - Dental malocclusion
  - Enlarged tongue and epiglottis
  - Thich pharyngeal and laryngeal soft tissues
  - Enlarged jaw
  - Thick vocal cords
  - Subglottic narrowing
  - Thyroid enlargement
  - Rarely RLN palsy.

Cushing's

- *HTN;* Fragile skin
- *OSAS;* Perioperative steroid cover
- *DM;* Osteoporosis
- Obesity and GERD
- Raised intravascular volume state
- Increased infection
- Muscle weakness
- Electrolyte imbalance.

PROLACTIN-SECRETING TUMORS

No anesthetically important endocrinopathy.

TSH

Correct hypothyroidism preoperatively.

Surgical Procedure

- Under radiological control, surgeon enters sphenoid sinus
- Reaches pituitary fossa by removing bony floor
- After incising dura, tumor is removed and nasal packs inserted.

Preoperative Preparation

- Make note of visual disturbances and cranial nerve palsies preoperatively
- Prophylactic antibiotic cefuroxime 1.5 g IV
- Bruising may occur on IV access
- Avoid sedation if difficult airway anticipated
- Antiaspiration prophylaxis:
  - IV metaclopramide 10 mg
  - IV ranitidine 1 mg/kg.
- Standard NPO guidelines and consent
- Train patient to breathe via mouth preoperatively.

Induction

- Thiopentone 3–5 mg/kg or propofol 1–2 mg/kg with fentanyl 1–2 µg/kg and vecuronium 0.1 mg/kg
- Smaller size RAE tube used to minimize chances of airway trauma
- RAE tube secured to lower jaw at corner of mouth opposite surgeon's dominant hand
- ETT fixed at left corner of mouth for right-handed surgeons
- Small esophageal stethoscope and temperature probe can lie with ETT
- Cover entire bundle with towel clipped below lower lip to protect it from preparation solutions
- Fiberoptic intubation if difficult airway anticipated
- Throat pack placed to prevent blood accumulation in stomach (vomiting) and glottis (coughing at extubation)

- Vasoconstrictor (***Moffett's solution***/Xylometazoline) into each nostril to improve surgical access
- Lumbar drain placed if suprasellar extension
- Proper eye cover as exophthalmos increases chances of corneal abrasion.

Monitoring

- *SpO_2:* Nerve stimulator at lower extremity
- *$ETCO_2$*: Temperature
- *ECG:* Urine output
- NIBP
- IBP—check status of collateral circulation
- Intraoperative visual evolved potential in surgeries near visual pathway.

Ventilation

- IPPV with ETT
- If no suprasellar extension:
  - Modest hyperventilation to $PaCO_2$ 30–35 mm Hg
  - Decreases brain volume
  - Minimizes degree to which arachnoid bulges into sella.
- If supassellar extension present:
  - Normocapnea/hypercarbia which helps to deliver lesion into sella for excision.

Position

- Supine
- Slight head up tilt to avoid venous engorgement and venous air embolism.

Maintenance

- Valsalva maneuver after resection to check for CSF leak
- O_2 + Air + Isoflurane + Remifentanil 0.05–2 µg/kg/min
- If suprasellar extension present, 10–40 ml saline/air injected via lumbar drain to increase intraventricular pressure and prolapse suprasellar part of tumor into surgical field
- Also air delineates brainstem from pituitary gland on fluoroscopy
- Mucosal surface of nose infiltrated with LA + epinephrine
- Watch during infiltration for arrhythmias
- Deep planes at time of incision, made under lower lip
- Deliberate hypotension facilitates repair.

Hemodynamics

- Blood loss less unless carotid artery/cavernous sinus ruptures
- If intraoperative diabetes insipidus occurs, fluid management is hourly maintenance fluid plus 2/3rd of previous hour urine output (*1/2 NS or 5% Dextrose fluid of choice*)
- If hourly fluid requirement > 350–400 ml, use desmopressin.

Extubation

- Fully awake extubation after full reversal
- Remove throat pack and thorough suctioning
- Extubate after return of spontaneous respiration and airway reflexes
- Smooth emergence especially if CSF space has been opened
- Avoid repeated Valsalva maneuvers (coughing, vomiting) which reopens CSF leak and increases risk of meningitis.

POSTOPERATIVE

Management

- CSF drainage via lumbar drain or 24–48 hrs if CSF leak occurs during surgery
- IV fluid maintenance
- Avoid vomiting—antiemetics.

Monitor

- SpO_2, NIBP, ECG, Temperature
- Foley's catheter and urine output
- Electrolytes and serum osmolarity.

Analgesia

- Morphine 0.1–0.2 mg/kg is *Analgesic of choice*
- Avoid high-dose opioids—sedation causes airway obstruction.

Complications

- Hemorrhage from cavernous sinus/carotid artery
- Postoperative hematoma:
  - Presents as postoperative visual defects/changes in mental status
  - Tight surgical packing of sella causes backward pressure on brainstem and optic nerve.
- Diabetes insipidus:
  - If damage occurs to posterior lobe of pituitary
  - Usually occurs within 4–12 hrs postoperatively and is transient
  - Suspect if > 1 L dilute urine (Specific Gravity < 1.005) within 12 hrs
  - Associated with plasma sodium concentration > 143 mEq/L

  - Plasma osmolarity >295 mosm/kg with urine osmolarity < 300 mosm/kg with high urine output ≥ 2 ml/kg/hr confirms diagnosis.
- Venous air embolism
- Cranial nerve palsies
- Aiway obstruction:
  - Especially if preoperative OSAS
  - Occurs due to nasal pack which usually stays for 24–48 hrs
  - Obligate oral breathing required which may not be adequate if patient has upper airway obstruction due to large tongue/increased pharyngeal soft tissues
- SIADH, hypopituitarism
- CSF leak, meningitis, headache, PONV.

ANESTHESIA FOR MRI[1,2,3]

Introduction

MRI is a diagnostic technique which uses electromagnetic fields to perform noninvasive imaging.

Principle

- Based on principle that atomic nuclei with odd number of protons or neutrons have potential to act as magnetic dipoles
- Since biological tissues have high water content, H1 detection is the basis of MRI
- Patients are placed within strong magnetic field
- Pulses of radiofrequency (RF) energy are applied
- This results in intermittent release of RF energy from H1 nuclei which is detected by a series of close fitting receiving antennae known as coils
- The RF signals are collected and interpreted by computer to produce images
- Strength of magnetic field during MRI measured in Tesla
- One Tesla is equal to 10,000 Gauss (G)
- The magnetic field of earth is ≃ 0.5–1.5 G
- Most common strength of scanners is 0.5 and 1.5 T
- Increased strength is associated with better spatial resolution.

USES OF MRI

Central Nervous System

- *Posterior fossa tumors:* Head trauma
- *Cerebral infarcts:* Dementia
- Intracranial infections.

Others

- Spinal cord
- Cardiac chambers
- Musculoskeletal system—tendon/muscle/ligament injuries
- Intrathoracic disorders
- Intraabdominal disorders.

ADVANTAGES OF MRI

- Provides multiplane images
- Obtains images in any plane—transverse, sagittal, coronal/oblique
- Excellent spatial resolution and soft tissue contrast
- Not affected by bony artefacts
- Does not employ ionizing radiation
- Requires little patient preparation
- May provide intravascular contrast without IV contrast media
- Noninvasive
- Does not in itself produce biologically deleterious effects.

PROBLEMS OF MRI

- Remoteness of location
- Lack of trained personnel to assist in the event of emergency
- Minimum consideration given to anesthetic requirements in design of area like:
  - Lack of pipeline gases and suction
  - Lack of waste gas exhaust capabilities.
- Limitations from magnetic field of imager.

SAFETY ISSUES

Implanted Ferromagnetic Objects

- Includes intraocular foreign bodies, scissors, O_2 cylinders, laryngoscopes and stylets
- These may move in the magnetic field
- Have potential to become dangerous projectiles
- Implanted pacemakers, AEDs, cochlear implants and cerebrovascular clips may be inactivated/dislodged
- These may cause hemorrhage/motile injury to adjacent structures.

Metal Objects/Electronic Monitors

- May produce RF waves which interfere with images generated by MRI/scanner causing degraded images

- Alternately, specially adapted monitors and equipment required which are positioned as far away from magnet as possible.

Thermal Injury

- RF energy may be absorbed by tissues/other objects and produces localized heating
- Unlikely that body temperature increases by > 1 ºC
- Thermal effects may not be great enough to cause tissue damage.

Noise

- Noise generated by scanner in range of 65–95 dB
- This may cause temporary/permanent hearing loss
- Difficult to monitor heart sounds via esophageal/precordial stethoscope
- Wear ear protection, like ear plugs.

Pregnancy

Pregnant patients in first trimester should not enter scanner.

Zones of MR Suite[1]

American College of Radiologists Classification

ZONE I	Public free access
ZONE II	Interface between public zone and MR suite
	All movements by nonMRI personnel supervised
ZONE III	Area where introduction of ferromagnetic objects forms a hazard
	Separated from Zone II by physical restriction (locked doors)
ZONE IV	Scanner room
	Marked lighted signs

Indications for Anesthesia in MRI

- Trauma and shock
- Children
- Ventilated/other ITU patients
- Intraoperative MRI—stereotactic neurosurgery
- Mental illness
- Patients with severe movement disorders
- Patients whose position is limited by pain
- Patients with learning difficulties
- Claustrophobic patients.

Aims of Anesthesia for MRI

- Absolute immobility to obtain best possible images
- Not painful—hypnosis, amnesia and immobility are aims
- Maintain patient safety and comfort throughout MRI
- Rapid recovery
- Equipment used should be:
  - MRI safe—can be used with no additional risk to patient
  - MRI-compatible—as well as being MR safe, it does not degrade images produced and its function is not altered by the scanner.

Anesthetic Problems in MRI

- Remote airway
- Limited patient access and visibility
- Need to exclude ferromagnetic components
- Interference/malfunctioning of monitoring equipment due to magnetic field
- Potential degradation of images by RF currents from leads/monitoring equipment
- Necessity to not move anesthetic/monitoring equipment once examination has started to prevent degradation of magnetic field homogeneity
- Limited access to MR suite for emergency personnel.

Preoperative Assessment

- All female patients to have pregnancy test
- Assess all implanted devices:
  - Type of orthopedic implant
  - Pacemaker and internal defibrillators—*MRI contraindicated*
  - Aneurysms clips, cochlear implants, prosthetic heart valves, may get dislodged/heat up/cause induction of electric currents
  - Metal workers may have intraocular foreign bodies—screen by plain radiography before MRI.
- Tattoos may heat up in magnetic field due to presence of FeO.

Contraindications of MRI

- Obese patients may not fit into bore of magnet
- Cardiac pacemakers and ICDS as the following may occur:
  - Heating of leads
  - Inhibiting of pacemaker output of rapid pacing
  - *Reed* switch malfunction
  - ICD malfunction
  - Torque on pacemaker pack.
- Pregnancy in first trimester
- Suspected ferromagnetic intraocular foreign bodies
- Ferromagnetic vascular clip patients

- Titanium clips are an exception as they are non-ferromagnetic
- Hemodynamically unstable patients on infusion pumps as pumps cannot be taken inside.

MONITORING IN MRI SUITE

General Principles

- Must conform to same ASA standards
- Important as direct patient visualization difficult
- MR-compatible monitors used
- If non-MR-compatible, place monitors outside scan room and pass long cables through specially shielded holes in walls
- If within room, monitors are modified to make them MR-compatible and placed atleast 6–8 feet from magnet bore
- MR-compatible anesthesia machine with piped anesthetic gases to be available
- Non-MR-compatible machines kept outside 50 G line and bolted onto floor
- All gas cylinders to be MR-compatible.

Specific Monitors

- Pulse oximeters to use fiberoptic cables to avoid burns
- Capnograph—delay in obtaining signal as sampling tube will be longer
- NIBP safe provided connections of cuff and hose are plastic
- Precordial and esophageal stethoscopes useless
- Temperature monitoring is difficult unless probes with RF filters are used.
- ECG:
  - Cables to be shielded and use specific electrodes
  - May have ST-T changes similar to pericarditis due to magnetic field in MR
  - ECG may be completely distorted due to RF energy and static magnetic field.
- Padding to be placed between patients skin and monitor cables to prevent burns
- Avoid loops in cable and check for exposed segments.

ANESTHETIC MANAGEMENT

Choice of Anesthesia

- GA with ETT/LMA commonly used
- Children from 3–7 yrs may require sedation
- Older children are often compliant without sedation
- Younger children sleep deeply enough after feeds.

Site of Induction

- On tipping trolley in anesthesia room
- Best induced outside MRI room, where effects of magnet on laryngoscope and equipment are not a problem
- Patient transferred to docking table and shifted on non-ferromagnetic trolley.

Airway Management

- Remote airway
- Mostly LMA suffices. Pilot balloon taped away from scan site as spring inside may cause artefact
- MR-compatible LMAs available
- Those with poor gag/pregnant patients require intubation
- Preformed ETT with pilot balloon taped away from scan site
- Flexometallic tube not used as they degrade images
- Laryngoscope to be plastic with lithium battery and aluminium spares
- Airway to be clear as partial airway obstruction may cause increased respiratory movement and image artefact.

Maintenance

- Easier with sevoflurane/isoflurane, as this avoids need for MR-compatible infusion pumps
- TIVA with propofol and remifentanil infusion is alternative
- Circuits have to be very long to go into chamber
- Use long extension lines for IV lines
- Contrast used is Gadolium DTPA which has very low incidence of anaphylaxis.

Cardiac Arrest

- For most MR scanners, time to reduce magnetic field to neutral is 3–20 mins
- It then takes 3–4 days to restore the field to superconductive levels with high costs to replenish liquid nitrogen and helium
- Thus, magnetic field deactivated only in dire situations
- If cardiac arrest occurs, patient is quickly moved from MR room and resuscitation initiated.

Awakening

Awaken patient once shifted back to induction area where conventional monitoring can be resumed.

SEDATION IN MRI

Adults

- Oral benzodiazepines most commonly used
- IV sedation bolus midazolam/low-dose propofol with remifentanil infusion
- Monitor pulse oximetry, $ETCO_2$ if possible
- Short MR sequences improve patient compliance.

Children

- Children < 3 yrs sleep deeply after feed
- Children > 7 yrs are often compliant without sedation
- Chloral hydrate, benzodiazepines and low-dose propofol infusions used
- Conscious sedation does not ensure compliance due to noise
- Supplemental O_2 and adequate monitoring mandatory.

BRAIN DEATH[1,2,3,10]

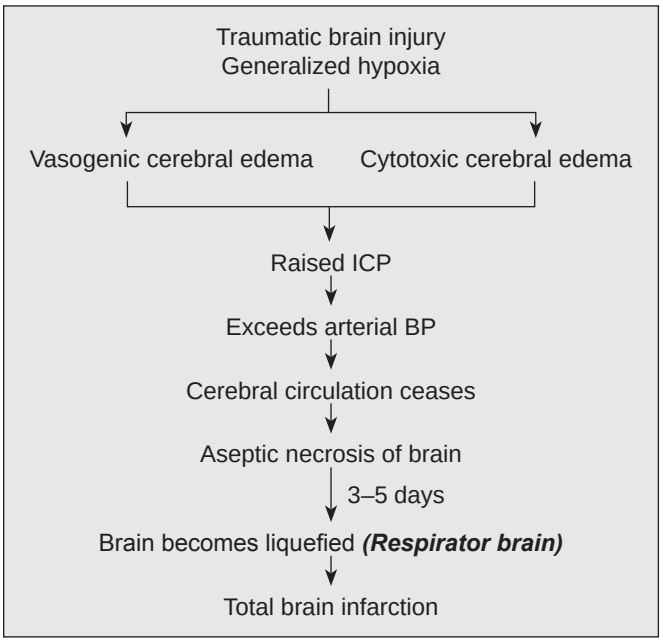
Introduction

- Brain death is the absence of clinical brain function when the proximate cause is known and demonstrably irreversible
- Death is irreversible loss of capacity for consciousness, combined with irreversible loss of capacity to breathe
- Cerebral death/persistent vegetative state is cessation of function of cerebral cortices. Brainstem function controlling respiratory centers ANS and endocrine and immune systems are preserved with a flat cortical EEG
- Brainstem death:
  - Concept first developed in UK
  - Involvement of bilateral cerebral cortices not required
  - Does not require EEG for confirmation
  - Based on rationale that brainstem and not cortices control respiration, circulation homeostasis and reticular formation for consciousness.

MECHANISM OF BRAIN DEATH

Areas of Brain Involved

- Ascending Reticular Activating System (ARAS)
- Primary respiratory center in reticular core of medulla
- Circulatory center (nucleus tractus solitarius)
- Thermoregulatory centers in hypothalamus
- Pituitary gland
- CNS control over immune system:
  - Increased cytokines (IL-1β, TNFα) seen
  - Increased ICAM and VCAM
- Braindeath does not include lower portion of spinal cord caudal to C_2.



Diagnostic Criteria[1]

American Academy of Neurology 1995

- Two examinations required, separated by atleast 6 hours
- Diagnosis done by 2 or 3 physicians who are independent of transplant team
- Atleast one physician should be a specialist in neurology/neurosurgery/anesthesia.

1. Prerequisites

- Clinical/neuroimaging evidence of acute CNS catastrophe
- Exclusion of complicating causes:
  - Severe electrolyte imbalance
  - Acid-base disoders
  - Endocrine disturbance.
- No dug intoxication/poisoning
- Core temperature > 32 ºC (90 ºF).

Lazarus sign: Spontaneous/reflex movements due to intact spinal cord at time of skin incision or in synchrony with respiration produced by mechanical ventilation

Arm flexion, shoulder adduction, hands crossed and opposed just below chin.

2. Clinical Findings

- Coma:
  - GCS 3
  - No motor response to pain in all extremities
  - Nailbed and supraorbital pressure included.
- Absent brainstem reflexes:
  - Pupils
    - No responses to bright light
    - Size mid-position (4 mm) to dilated (9 mm).
  - Ocular movement:
    - No oculocephalic reflex (valid only if no cervical spine injury)
    - No deviation of eyes to irrigation of ear with 50 ml cold water.
  - Facial senses and facial motor responses:
    - No corneal reflex with throat swab
    - No jaw reflex
    - No grimacing on nailbed/TM joint/supraorbital ridge pressure.
  - Pharyngeal/tracheal reflexes:
    - No response to stimulation of posterior pharynx
    - No cough response to bronchial suctioning.
- Apnea testing: most important and mandatory
  - Prerequisites:
    - Core temperature > 36.5 ºC or 97 ºF
    - Systolic BP > 90 mm Hg
    - Euvolemia/positive fluid balance in last 6 hrs
    - $PaCO_2$ normal/$PaCO_2$ = 40 mm Hg
    - Preoxygenate to make $PaO_2 \geq 200$.
  - Connect pulse oximeter and disconnect ventilator
  - Deliver 100% O_2 at 6L/min into trachea
  - Look for respiratory movements (abdomen/chest excursions)
  - Measure PaO_2, $PaCO_2$ and pH 8 minutes after and reconnect ventilator
  - Absent respiratory movements with $PaCO_2$ > 60 mm Hg or 20 mm Hg increase over baseline. $PaCO_2$ levels indicate brain death
  - If respiratory movements present: Not brain death, repeat test for confirmation
  - After connecting ventilator, draw ABG if:
    - SBP < 90 mm Hg
    - Pulse oximeter shows desaturation
    - Cardiac arrhythmias present
    - If $PaCO_2$ > 60 mm Hg or > 20 mm Hg increase over baseline $PaCO_2$, it indicates brain death.

Brain Death Guidelines in Children[1]

Differences from adult guidelines:

- 3 separate longer observation periods required
- 2 corroborating EEGS and 1 EEG with radionucleide angiography required.

History

- Determine cause of coma
- Exclude remediable/reversible causes.

Clinical Examination

- Coma and apnea
- Absent brainstem function
  - Midposition/fully dilated pupils
  - Absent spontaneous eye movements
  - Absent bulbar muscle movements
  - Absent corneal, gag, cough, rooting and sucking reflexes.
- Absent respiratory movements on apnea test
- Patient not hypothermic/hypotensive for age
- Flaccid tone
- Absent spontaneous/induced movements excluding spinal cord events.

Observation Period

- *7 days to 2 months:* 2 examination and EEG separated by > 48 hrs
- *2 months to 1 year:* 2 examinations and EEG separated by > 24 hrs
- *Older than 1 year:* Atleast 12 hour observation.

Laboratory Testing

- EEG–through 30 minute period
- Angiography—lack of visualization of cerebral circulation
- Other techniques:
  - Xenon CT
  - Digital subtraction Angigraphy (DSA)
  - Transcranial Doppler
  - Evoked potentials.

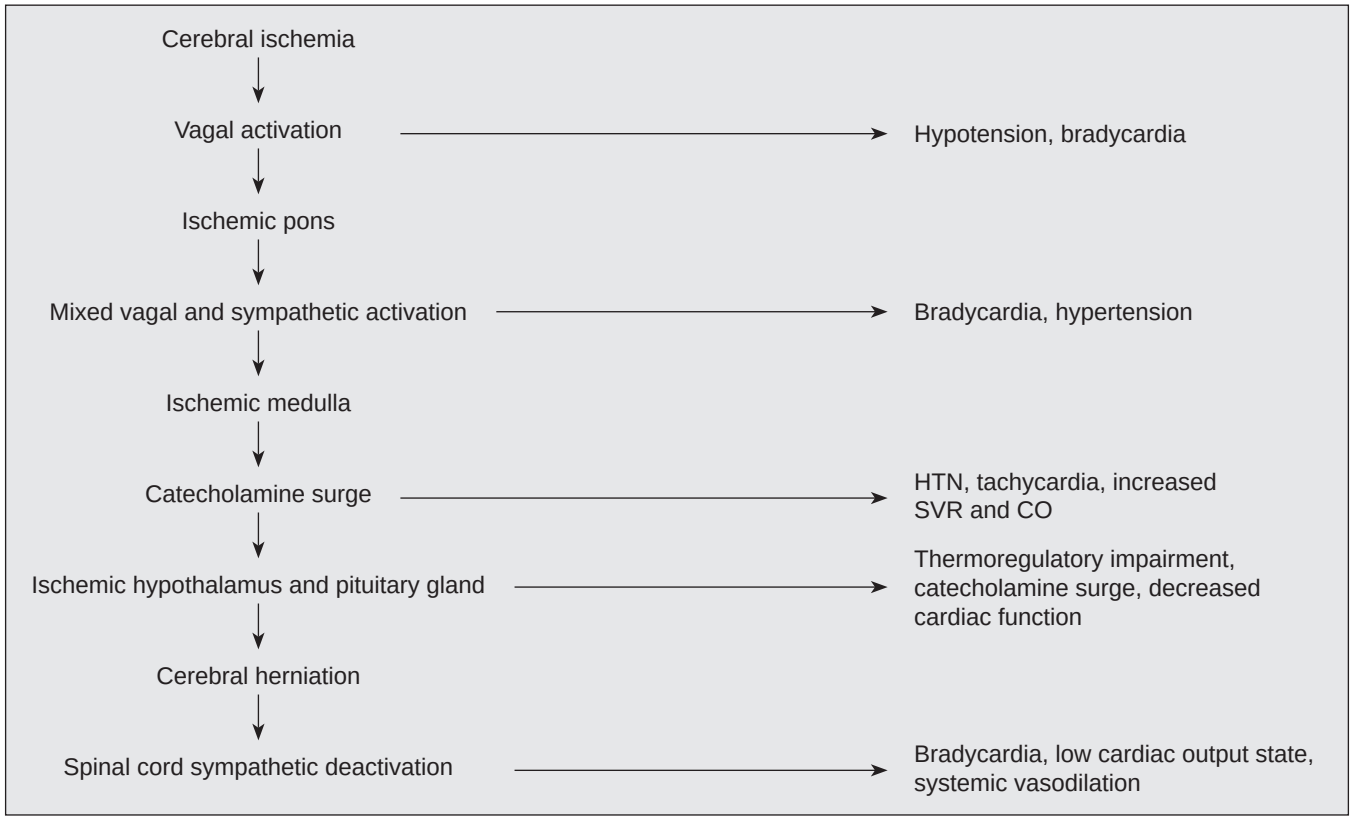
Confirmatory Tests

- Mandatory in children < 1 year
- Strongly recommended in children
- Not mandatory in adults.
- **Cerebral Angiography:**
  - Contrast injected under high pressure in anterior/posterior circulation
  - No intracerebral filling to be detected at level of entry of carotid artery/vertebral artery into skull

  - External carotid artery should be patent
  - Filling of superior longitudinal sinus may be delayed.
- **EEG:**
  - Minimum of 8 scalp electroles to be used
  - Interelectrode impedance to be from 100–10000 ohms
  - Distance between electrodes to be atleast 10 cms
  - Sensitivity should be increased to atleast 2 μv for 30 minutes
  - EEG should show lack of reactivity to intense somatosensory/audiovisual stimuli.
- **Transcranial Doppler USG:**
  - Probe at temporal bone above zygomatic arch
  - Alternative is suboccipital transcranial window for vertebrobasilar artery
  - Should show lack of diastolic/reverberatic flow and small systolic peaks in early systole.
- **Cerebral Scintigraphy:**
  - $Tc^{99}m$ used
  - Isotope to be injected within 30 minutes after reconstitution
  - Static images immediately at 30 min, 60 min and 2 hrs later.
- **Evoked Potentials:**
  - BAEP and SSEP of median nerve used
  - Loss of waves II, III, IV and V regarded as brain death
  - Bilateral absence of N20–P22 responses with median N stimulation is confirmatory.
- **CT Angiography**
  - Noninvasive
  - Average global flow < 5 ml/dl/min confirms brain death.
- **MRI**
- **PET SCAN**

ORGAN HARVEST IN BRAIN DEATH

Pathophysiology of Brain Death *(See Flow chart)*[1,3,10]



PHASES OF BRAIN DEATH

Hyperdynamic Phase

- Not seen in all patients
- Sympathetic overactivity
- Catecholamine surge (epinephrine and norepinephrine):
  - Increased HR, BP, cardiac output
  - Increased systemic vascular resistance
  - Altered myocardial O_2 demand-supply balance.

Cardiovascular Collapse Phase

- Loss of sympathetic tone
- Profound vasodilation
- Myocardial depression
- Aggravated by hypovolemia secondary to diabetes insipidus.

Patient Selection

- Ideally donor < 60 yrs
- No end-organ damage from systemic disease
- Proper intrinsic function of organ to be harvested
- Requires cessation of both cerebral and brainstem function
- Rule out reversible causes of coma:
  - Hypothermia
  - Hypotension
  - Drugs
  - Toxins.

CONTRAINDICATIONS

Absolute

- Uncontrolled sepsis
- Active viral infection
  - *HIV:* CMV
  - *Hepatitis B and C:* Herpes simplex
- Malignancies except:
  - Primary intracranial tumor
  - Non-melanotic skin cancer
  - Ca cervix in situ.

Relative

- *Chest trauma:* Active infection
- *Prolonged cardiac arrest:* Major cardiac disease
- Those who have recieved intracardiac injections (for heart transplants).

Care of Patient before Harvest

- Frequent turning to avoid decubitus ulcers
- Skin care and dressing changes
- Urinary and intravascular catheter care
- Nasogastric tube for gastric decompression and prevention of aspiration
- Arterial line in upper limbs as femoral line may be inaccurate during surgery.

MAINTENANCE THERAPY END POINTS

Hemodynamics

- SBP from 100–120 mm Hg
- MAP around 60 mm Hg
- Urine output > 100–300 ml/hr
- Core temperature > 35 ºC.

Ventilation

- PaO_2 > 80–100 mm Hg
- SPO_2 > 95%
- pH from 7.35–7.45
- Hematocrit around 30–35%
- Hemoglobin around 10–12 gm%.

Investigations

- Hb, hematocrit, complete blood count, blood glucose
- Urinanalysis, serum electrolytes, BUN, serum creatinine
- LFT, coagulation profile
- Serology for Hepatitis B, C and HIV
- Blood and urine culture if:
  - Evidence of infection
  - Duration of hospitalization > 72 hrs
- Incase of multiorgan donors
  - ECHO for heart transplant
  - Bronchoscopy for lung transplant.

ANESTHETIC GOALS

General

Preservation of:

- Tissue perfusion
- Tissue oxygenation
- Mileu preservation
- Organ viability.

Hemodynamics

- Maintain euvolemia
- CVP from 6–12 mm Hg
- PCWP < 12 mm Hg
- Minimize use of vasopressors (associated with renal graft failure)

- Urine output > 100 ml/hr
- Maintain hematocrit of around 30%
- Maintain INR < 1.5 using FFP
- Serum sodium < 155 mmol/L (increase associated with liver graft failure).

Ventilation

- PaO_2/FiO_2 > 300 mm Hg
- $PaCO_2$ 30–35 mm Hg
- Peak airway pressure < 30 mm Hg
- PEEP < 5 cm H_2O during organ transport.

Monitoring

- *ECG:* Core temperature
- *BP:* Urine output
- *Pulse oximetry:* CVP
- PAC for PCWP and pulmonary venous oximetry for unstable donors with persistent acidosis.

HEMODYNAMIC SUPPORT

Factors Affecting Hemodynamics

- Hypovolemia secondary to ICP therapy
- Diabetes insipidus
- Hyperglycemia-induced osmotic diuresis
- Coincident cardiac dysfunction
- Vasodilation secondary to brain death.

Principles

- Bradycardia not treated unless symptomatic as it is seen due to *Cushing's reflex*
- Regardless of hypotension/hypertension, patient is usually hypovolemic
- Maintain adequate filling pressure – CVP 6–12 mm Hg and PCW < 12 mm Hg
- Low filling pressure for lung transplant
- Higher filling pressure for renal transplant.

Fluid Resuscitation

- Choice of fluids according to electrolyte status
- Maintian hematocrit around 30% and hemoglobin of 10 gm%.

Drug Therapy

- **Vasoactive agents:**
  - Dopamine 1–10 µg/kg/min—higher doses increase chances of ATN (***first choice***)
  - Dobutamine 5–15 µg/kg/min (***second choice***)
  - Norepinephrine 0.05–0.1 µg/kg/min
  - Epinephrine 2–4 µg/min
  - Phenylephrine 100–150 µg/min loading dose followed by 40–60 µg/min
  - Vasopressin 0.01–0.04 IU/min.
- **Chronotropic agents:**
  - *Atropine has no chronotropic effects after brain death*
  - Isoproterenol 0.05–0.1 µg/kg/min
  - Epinephrine 0.05–0.5 µg/kg/min.

Hypotensive agents:

- Sodium nitroprusside 0.5–5 µg/kg/min
- Nitroglycerine 0.5 µg/kg/min
- Esmolol 0.05 mg/kg/min
- Avoid calcium channel blockers and long-acting beta blockers due to negative inotropic action.

VENTILATORY SUPPORT

Factors Affecting Ventilation

- Aspiration
- Pulmonary contusion/effects of CPR and shock
- Pneumonia and pulmonary edema
- Atelectasis/volutrauma/barotrauma due to ventilation.

Principles

- Pressure control/volume control mode depending on airway pressure
- Tidal vdume 8–12 ml/kg if no lung injury
- Tidal volume 6–8 ml/kg if lung injury present
- PaO_2 from 70–100 mm Hg, SpO_2 > 95%
- FiO_2 < 60%
- If FiO_2 > 40%, it contraindicates lung transplantation
- PaO_2/FiO_2 > 300
- PEEP < 5 cm H_2O
- $PaCO_2$ 35–45 mm Hg
- Plateau pressure ≤ 30 cm H_2O.

METABOLIC SUPPORT

Most commonly metabolic alkalosis due to mechanical hyperventilation to treat raised ICP.

Others

- Contraction alkalosis
- Hypo/hypokalemia
- Hypophosphatemia
- Hypernatremia
- Metabolic acidosis.

Treatment

- Treat correctable causes
- Change ventilatory parameters
- Drugs to correct acid-base deficits.

ENDOCRINE SUPPORT

Diabetes Insipidus

- Most common endocrine disorder
- Suspect if polyuria with hypernatremia (> 150 m Eq/L) with hyperosmolarity (< 310 mosm/L) with dilute urine (osmolarity < 300 mosm/L)
- 5% Dextrose used to treat free water deficit
- Once urine output > 4 ml/kg/hr, desmopressin 1–4 µg IV QID
- Vasopressin 1 IU IV bolus followed by infusion 0.5–4 IU/hr alternative.

Hormonal Cocktail

- Methylprednisolone 15 mg/kg $Q_2$4H
- T_3 4 µg IV followed by 3 µg/hr
- Desmopressin IU then 0.5–4 U/hr to maintain SVR at 800–1200 dyne/s/cm^5
- Insulin infusion to maintain 120–180 mg%
- T_4 20 µg/kg bolus followed by 10 µg/kg/hr infusion.

Renal Support

- Maintain adequate systemic perfusion pressure and brisk urine output > 1–2 ml/kg/hr
- Decreased use of vasopressor
- Volume loading to increase urine output
- Loop diuretics (furosemide)/osmotic diuretics (mannitol)
- Avoid nephrotoxic agents—aminoglycoside and NSAIDs.

Temperature Regulation

- Patient becomes poikilothermic after brain death
- Aggravating factors:
  - Systemic vasodilation
  - Administration of cold IVF and blood products
- Maintain core temperature > 35° C
- Humidified and heated ventilator gases, warm IV fluids and warming blankets.

COAGULATION ABNORMALITIES

Causes

- DIC and coagulopathy
- Dilutional coagulopathy due to fluid resuscitation
- Release of thromboplastin from injured brain
- Massive blood transfusion
- Hypothermia.

FFP transfusion to maintain INR < 1.5.

Fibrinolytics like EACA avoided as increased microvascular thrombosis rendering organ unsuitable for transplant.

Reperfusion Injury

Cytoprotective strategies:

- High-dose steroids
- N-acetylcysteine
- P-selectine inhibitors.

Other Drugs

- PGE_1 to improve circulation of lung preservation solution
- Glucocorticoids
- Systemic heparinization just before exsanguination and excision
- Broad spectrum antibiotics
- Mannitol.

ANESTHESIA FOR ECT[1,2,3,6]

Introduction

- Consists of programmed electrical stimulation of CNS to initiate seizure activity
- Used since 1934.

Mechanism of Action

- Changes in blood-brain barrier permeability
- Regional cerebral blood flow changes and electrolyte changes
- Changes in neuro-endocrine activity
- Acute discharge of neuro-endocrine units (ACTH, prolactin)
- Changes in ion transport, neurotransmitters and biogenic amines.

Indications

- **Severe endogenous depression:**
  - Not responding to medical therapy
  - Associated with suicidal tendencies.
- Catatonia, mania
- Bipolar mood disorders
- Schizophrenia, severe melancholia.

Contraindications

- **Absolute contraindications:**
  - Myocardial infarction in last 3 months
  - Cerebrovascular accident in last 3 months
  - Raised ICP, pheochromocytoma.
- **Relative contraindications:**
  - Recent intracranial surgery, intracranial mass lesion
  - Untreated cerebral aneurysm
  - Retinal detachment, glaucoma

  - Cochlear implants, cardiac conduction defects
  - Aortic aneurysm, uncontrolled angina
  - Major bone fractures, severe osteoporosis
  - DVT (not anticoagulated), high-risk pregnancy.

Physics

- Electric current applied transcutaneously
- Two electrodes positioned unilaterally/bilaterally
- Phases of GTCS induced:
  - Latent phase: for 2–3 seconds
  - Tonic phase: for 10–12 seconds
  - Clonic phase: for 30–50 seconds.
- Optimal seizure duration more than 25 seconds and less than 120 seconds
- Typical setting during ECT:
  - Pulse 60 Hz
  - Duration 0.75 msec
  - Total stimulus duration 1.25 seconds.
- If seizure lasts more than 150–180 seconds, it should be terminated
- Done 3 times a week for 6–12 treatments, followed by weekly/monthly maintenance therapy
- Done till improvement is seen or treatment is deemed unsuccessfully
- Bilateral ECT more commonly performed
- Unilateral ECT performed on non-dominant hemisphere and has advantage of reducing cognitive side effects.

Physiological Changes

- Cardiovascular system:
  - Initial parasympathetic activity (lasts 10–15 seconds):
    - Bradycardia, hypotension
    - Rarely asystole
    - Premature atrial/ventricular complexes, VT
  - Later sustained increased in sympathetic activity:
    - ≥ 20% increase in heart rate
    - 30–40% increase in systolic BP, increased myocardial O_2 consumption
    - Reduced myocardial oxygen supply
    - Oxygen demand-supply imbalance
    - LV systolic and diastolic dysfunction
    - Cardiac arrhythmias:
      - Sinus tachycardia
      - PVCs, bigeminy, trigeminy, VT.
  - ECG changes:
    - ST depression, T wave inversion
    - No changes in myocardial enzyme levels.
- Central nervous system:
  - Increased $CMRO_2$
  - Increased cerebral blood flow (1.5–7 times baseline)
  - Increased intracranial pressure
  - Cerebral vasoconstriction initially which can increase chances of cerebral hypoxic events.
- Other changes:
  - Increased intraocular pressure
  - Increased intragastric pressure
  - Reflux esophagitis.

Complications

- **Neurological:**
  - Short-term memory loss, headache
  - Cerebrovascular accidents
  - Status epilepticus
  - Emergence agitation
  - Drowsiness, confusion, disorientation
  - Attention deficit.
- **Cardiovascular:**
  - MI, CCF
  - Sudden death
  - Pulmonary edema
  - Transient arrhythmias.
- **Others:**
  - Myalgia, weakness
  - Nausea, anorexia
  - Fractures, dislocation
  - Amenorrhea, pulmonary aspiration.

Anesthetic Goals

- Rapid and smooth induction
- Amnesia
- Muscle relaxation
- Airway protection
- Control of hemodynamics
- Prevention of complications and bodily injuries
- Rapid and smooth emergence.

Anesthetic Considerations

- Difficult history taking
- Drug interactions
- Short duration of procedure
- Antiaspiration prophylaxis
- Hemodynamic alterations
- Use anesthetic drugs which do not alter seizure activity
- Complications.

Preoperative Evaluation

- **History and examination:**
  - Difficult history taking, may be unreliable
  - Evaluate coexisting CNS, CVS disease, osteoporosis and fragile bones
  - Rule out contraindications for ECT
  - Consider other cardiac, respiratory and musculoskeletal medicine
- Investigations: Routine blood investigations, ECG, CXR, RFT
- Preoperative drug administration:
  - **MAO inhibitors:**
    - Moclobemide stopped 24 hours preoperatively
    - Tranylcypromine, phenelzine and isocarboxacid stopped more than 2 weeks before surgery
    - Selegiline: not necessary to stop if dose is less than 10 mg/day. (*See table above*)

Drug	Effect	Recommendations
SSRIs	SIADH	Continue till ECT
	Causes serotonin syndrome with meperidine and tramadol	
TCAS	Anticholinergic, antihistaminic, sedative	Continue till ECT
	Increases central sympathetic tone	
Lithium	Nephrogenic DI, delayed awakening, postictal confusion	Discontinue before ECT
	Prolongs NMBA, BZD action	
MAOI	Cheese reaction, serotonin syndrome	Continue till ECT
	Hypertensive crises with sympathomimetics	

PREMEDICATION

- NPO for 6–8 hours
- Informed consent
- Glycopyrollate: anti-sialogogue, parasympatholytic: 0.01 mg/kg IV
- Atropine not indicated as it causes tachycardia
- Sedatives avoided as they delay emergence and increase seizure threshold
- Antiaspiration prophylaxis:
  - 0.3 M sodium citrate 15 ml
  - H_2 antagonist: ranitidine 1 mg/kg IV
  - Metoclopramide 10 mg IV.
- Blunting sympathetic response (not routinely used):
  - Atenolol 25–50 mg PO
  - Sublingual nifedipine 10 mg.

OT PREPARATION

- Skilled assistant
- Emergency drugs:
  - β blockers: atenolol/labetolol/esmolol
  - Nicardipine IV
  - IV NTG/hydralazine.
- Airway equipment:
  - Ambu bag, airways, face mask
  - Laryngoscope, ETT, stylet, LMA.
- Defibrillator.

CHOICE OF DRUGS

Induction Agents

Drug	Dose	Advantage	Disadvantage
Methohexital	0.75–1 mg/kg	Gold standard Minimal anticonvulsant effect	Reduced availability, myoclonus, reduces seizure duration
Etomidate	0.15–3 mg/kg	Reduces seizures threshold Prolongs seizure duration	Hyperdynamic response, causes pain on injection, longer emergence time increases muscle tone, PONV
Propofol	0.75 mg/kg	Better cardiovascular stability, reduced PONV, faster emergence, as good as methohexital	Pain on injection Short-acting Reduces seizure duration
Thiopentone	2–5 mg/kg	Resistant cases Longer DOA compared to propofol	Reduces cardiovascular stability Causes raised ICT Emergence agitation
Ketamine	Not used due to adverse cardiovascular actions		

Muscle Relaxants

Drug	Dose	Advantage	Disadvantage
Succinyl-choline	0.5 mg/kg	Drug of choice	Raises ICP, IOP, IGP
		Partial block reduces ECT seizures	
Mivacu-rium	0.15 mg/kg		May need reversal

Other Agents

- Remifentanil
  - Used in patients in whom seizures are difficult to elicit
  - To prevent fractures
  - Reduces dose of induction agent
  - Increases seizure duration.
- Caffeine/theophylline:
  - Reduces seizure threshold
  - Prolongs seizures
  - Used for seizure augmentation.

Procedure

- ETT if increased risk of aspiration (pregnancy, GERD, hiatus hernia)
- Anesthesia is induced, NMBA given
- Patient ventilated with oral airway and self-inflating bag and mask with 100% oxygen
- LMA may be useful
- Moderate hyperventilation beneficial to improve quality and duration of seizures
- Bite block inserted to protect teeth
- Stimulus applied through two electrodes placed on patient's scalp
- If seizure lasts more than 150–180 seconds, it is terminated with 5 mg diazepam IV
- 15–30 mg ketorolac IV to reduce myalgia
- Aspirin and paracetamol used if ketorolac is contraindicated
- Labetolol 0.3 mg/kg or esmolol 1 mg/kg to reduce hypertensive response
- SNP and hydralazine are alternatives
- CCB (nifedipine/nicardipine) and diltiazem also reduce HTN
- α2 agonists clonidine/dexmedetomidine (1 µg/kg over 10 minutes) before induction reduces hypertension without affecting seizure duration.

Monitors

- ECG, NIBP
- Pulse oximetry
- Visual observation of limb for duration of seizure
- EEG for central seizure
- EMG for peripheral seizure.

POSTICTAL CARE

- Oxygen supplementation till fully awake
- Midazolam 0.05 mg/kg IV to reduce emergence agitation
- Record anesthetics and NMBAs as treatment is repeated over weeks and consistent patient condition must be provided
- Complications:
  - Postictal confusion, agitation
  - Aggression: treated with midazolam
  - Headache: treated with NSAIDs
  - Reversible memory loss and cognitive impairment
  - Nausea, fractures and dislocation
  - Dental and oral injury
  - Laryngospasm, exacerbation of IHD.

CHAPTER

2

Anesthesia for Respiratory Disease

ANATOMY OF LARYNX[1,2,3]

Introduction

- Larynx is the organ for voice production and phonation
- It is a sphincter at the inlet of lower respiratory passage.

Situation and Extent

- Extends from root of tongue to trachea
- In adult males, it lies in front of C_5-C_6
- Lies higher in children and infants:
  - In infants: Level of C_3 vertebra
  - In children at 6 years age: Level of C_4-C_5 vertebrae.

Size

- Length is 44 mm in males
- Length is 36 mm in females
- At puberty, male larynx grows rapidly, while female grows little.

Constitution

Cartilages

- Unpaired cartilages:
  - Thyroid
  - Cricoid
  - Epiglottis.
- Paired cartilages:
  - Arytenoid
  - Corniculate
  - Cuneiform.

Thyroid Cartilage

- Largest laryngeal cartilage
- Alae meet anteriorly forming 90° angle in males and 120° in females
- Vocal cords attached to middle of thyroid cartilage.

Cricoid Cartilage

- Only cartilage which forms a complete ring
- Posterior part: Expanded laminae
- Anterior part: Narrow arch.

Epiglottis

- Leaf like elastic cartilage
- Forms anterior wall of laryngeal inlet.

Arytenoid Cartilage

- Pyramidal shaped
- Has following parts:
  - *Base*: Articulates with cricoid
  - *Muscular process:* Attached to intrinsic laryngeal muscle
  - *Vocal process:* Vocal cord
  - *Apex:* Supports corniculate cartilage.

Corniculate Cartilage of Santorini

Articulates with apex of arytenoids.

Cuneiform Cartilage of Wrisberg

- Situated in front of corniculate cartilage
- Provides passive support to folds.

Laryngeal Joints

- Cricoarytenoid joint:
  - Synovial joint

  - Two types of movements:
    - *Rotatory*: Abduction and adduction of vocal cords
    - *Gliding*: Closing and opening of posterior part of glottis
- Cricothyroid joint: Synovial joint.

Laryngeal Membranes

- Extrinsic membranes:
  - Thyrohyoid membrane: Pierced by:
    - Superior laryngeal blood vessels
    - Internal laryngeal nerve.
  - Cricothyroid membrane
  - Cricotracheal membrane.
- Intrinsic membranes:
  - Cricovocal membrane:
    - True vocal cord
    - Extends from midthyroid level to vocal process of arytenoids
    - Forms vocal ligament.
  - Quadrangular membrane:
    - False vocal cord
    - Present between epiglottis and arytenoid
    - Lower border forms the vestibular ligament.

Muscles of Larynx

- Intrinsic muscles:
  - Attach laryngeal cartilages to one another
  - Those acting on vocal cords:
    - Abductors: Posterior cricoarytenoid
    - Adductors:
      - Lateral cricoarytenoid
      - Interarytenoid (also called transverse arytenoid)
      - Thyroarytenoid (external part).
    - Tensors: Cricothyroid
    - Vocalis: Internal part of thyroarytenoid
    - Relaxors: Thyroarytenoid.
  - Those acting on laryngeal inlet:
    - Openers: Thyroepiglottis (part of thyroarytenoid)
    - Closers:
      - Interarytenoid (oblique part)
      - Aryepiglottic (posterior oblique part of interarytenoid).
- Extrinsic muscles:
  - Attach larynx to surrounding structures
  - Move larynx as a whole
  - Elevators:
    - Primary elevators:
      - Stylopharyngeus
      - Salpingopharyngeus
      - Palatopharyngeus
      - Thyrohyoid
    - Secondary elevators:
      - Mylohyoid
      - Digastric
      - Stylohyoid
      - Geniohyoid
  - Depressors:
    - Sternohyoid
    - Sternothyroid
    - Omohyoid

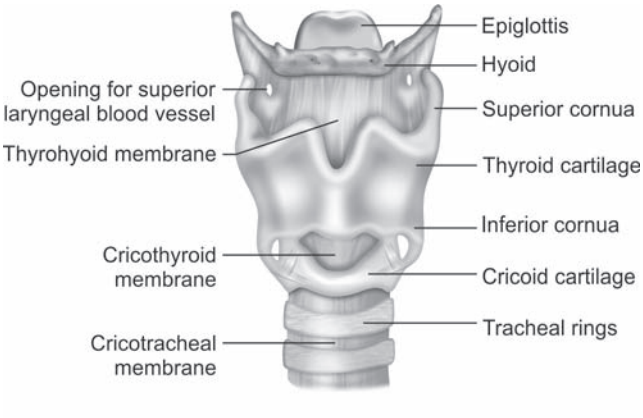


Fig. 2.1: Anterior view of larynx

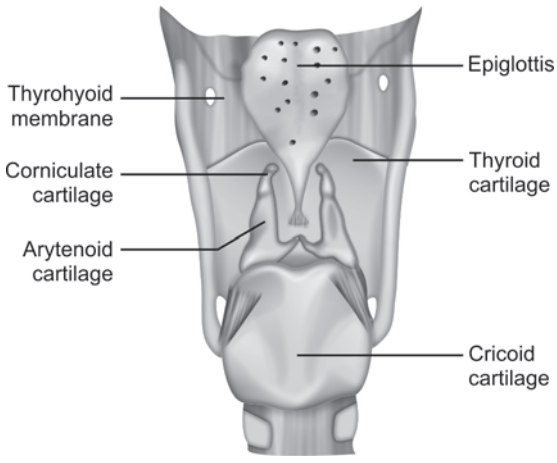


Fig. 2.2: Posterior view of larynx

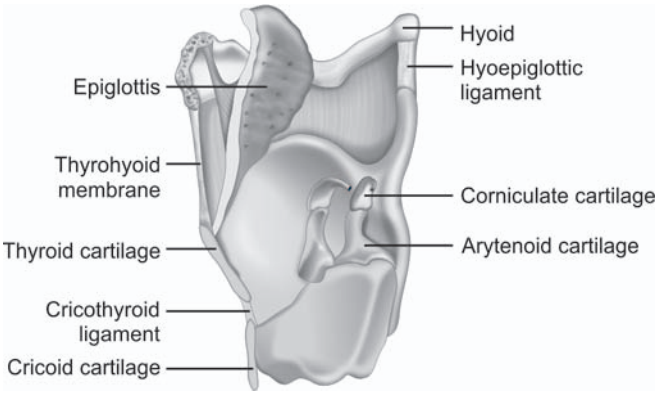


Fig. 2.3: Lateral view of larynx

Blood Supply

- Up to vocal cords:
  - Superior laryngeal artery: Branch of superior thyroid artery (from external carotid artery)
  - Superior laryngeal vein: Drains to superior thyroid vein.
- Below vocal cords:
  - Inferior laryngeal artery: Branch of inferior thyroid artery
  - Inferior laryngeal vein: Drains into inferior thyroid vein.

Lymphatic Drainage

- Above vocal cords: Anterosuperior group of deep cervical nodes
- Below vocal cords:
  - Posteroinferior group of deep cervical lymph nodes
  - Few into prelaryngeal lymph nodes.

Nerve Supply

- Motor nerve supply:
  - All intrinsic muscles supplied by recurrent laryngeal nerve
  - Except cricothyroid which is supplied by external laryngeal nerve (branch of superior laryngeal nerve).
- Sensory nerve supply:
  - Above vocal cords: Internal laryngeal branch of superior laryngeal nerve
  - Below vocal cords: Recurrent laryngeal nerve.

Mucus Membrane of Larynx

- Lines larynx
- Loosely attached at most places
- Mucous glands distributed all over membrane except vocal folds
- Epithelium:
  - Ciliated columnar epithelium
  - Exception: Over vocal cords and upper vestibule where stratified squamous epithelium.

Laryngeal Cavity

Divided into 3 parts by vestibular and vocal folds:

- Vestibule
- Ventricle
- Subglottic space.

Spaces of Larynx

- ***Pre-epiglottic space of Boyer***:
  - Filled with fat, areolar tissue, lymphatics
  - Common site for laryngeal carcinoma.
- Paraglottic space: Continuous with pre-epiglottic space
- ***Reinke's space:***
  - Potential space
  - Scanty connective tissue
  - Present under epithelium of vocal cords.

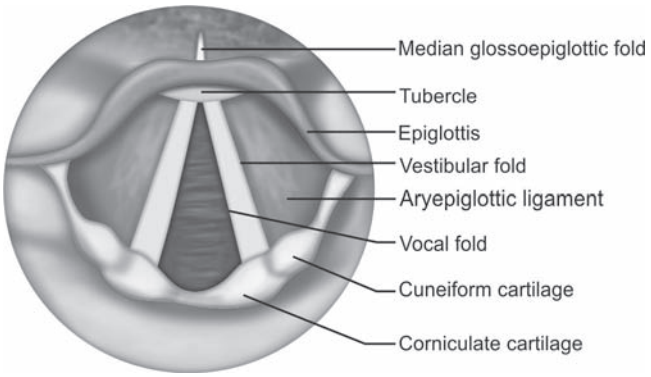


Fig. 2.4: Cross section of glottis

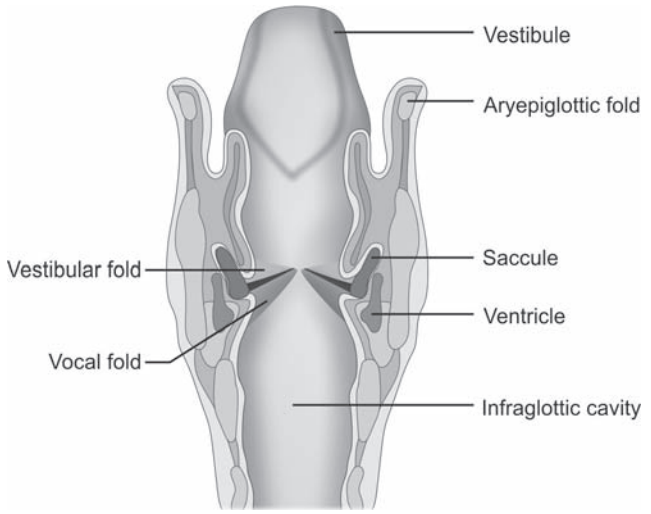


Fig. 2.5: Spaces of larynx

VOCAL CORD PARALYSIS[1,2,3]

Etiology

- In topographical manner:
  - Supranuclear palsy: Rare
  - Nuclear palsy:
    - Involves ***nucleus ambiguus*** in medulla
    - Vascular causes
    - Motor neuron disease
    - Neoplastic causes
    - Polio myelitis
    - Syringobulbia.
  - High vagal lesions:
    - Intracranial lesions:
      - Meningitis
      - Posterior fossa tumors.
    - At jugular foramen:
      - Fractures
      - Nasopharyngeal carcinoma
      - Glomus tumors.
    - At parapharyngeal space in neck:
      - Parapharyngeal tumors
      - Lymphomas
      - Penetrating injuries.
  - Low vagal/recurrent laryngeal nerve lesions:
    - Right sided palsy:
      - Neck trauma, thyroid diseases or surgery
      - Esophageal carcinoma, cervical lymphadenopathy
      - Subclavian artery aneurysms
      - Carcinoma of right lung apex (Pancoasts tumor)
      - Tuberculosis of cervical pleura
      - Idiopathic causes.
    - Left sided palsy:
      - Neck trauma, thyroid disease or surgery
      - Bronchogenic carcinoma
      - Esophageal carcinoma
      - Aortic aneurysm
      - Mediastinal lymphoma
      - Intrathoracic surgery
      - Idiopathic causes
      - ***Ortner's syndrome.***
    - Bilateral palsy:
      - Thyroid surgery
      - Thyroid carcinoma
      - Carcinoma of cervical esophagus
      - Cervical lymphadenopathy.
  - Systemic causes:
    - Diabetes, leprosy
    - Syphilis, lead poisoning
    - Diphtheria, mumps, typhoid.
  - Idiopathic in 30% cases
- Congenital causes:
  - Birth trauma
  - Congenital anomaly of great vessels/heart (great vein malformation of Galen).

Classification

- Recurrent laryngeal nerve palsy:
  - Unilateral RLN palsy:
    - Partial RLN palsy
    - Complete RLN palsy.
  - Bilateral RLN palsy:
    - Partial RLN palsy
    - Complete RLN palsy.
- Superior laryngeal nerve palsy:
  - Unilateral palsy
  - Bilateral palsy.
- Combined palsies:
  - Unilateral palsy
  - Bilateral palsy.
- Vagal nerve palsy.

Recurrent Laryngeal Nerve Palsy

Unilateral RLN Palsy

- Ipsilateral paralysis of all intrinsic muscles occurs, except cricothyroid
- ***Semon's law***: In progressive lesions of RLN, only abductors of vocal cords (posterior cricoarytenoids) are first to be paralyzed and last to recover, compared to adductors
- ***Wagner-Grossman hypothesis***: Cricothyroid muscle, which receives innervation from SLN keeps cord in paramedian position due to its adductor function
- Clinical features:
  - One third of patients are asymptomatic
  - Vocal cord:
    - Takes median/paramedian position
    - Does not move laterally on deep inspiration.
  - Changes in voice:
    - Gradually improves overtime
    - This is due to compensation by healthy vocal cord, which crosses midline.
  - No treatment is required.
- Partial unilateral RLN palsy:
  - Only abductor fibers are impaired

- Adductor fibers are intact
- Vocal cord in midline on affected side
- During inspiration, unaffected side fully abducts to compensate
- During phonation, unaffected side is adducted.

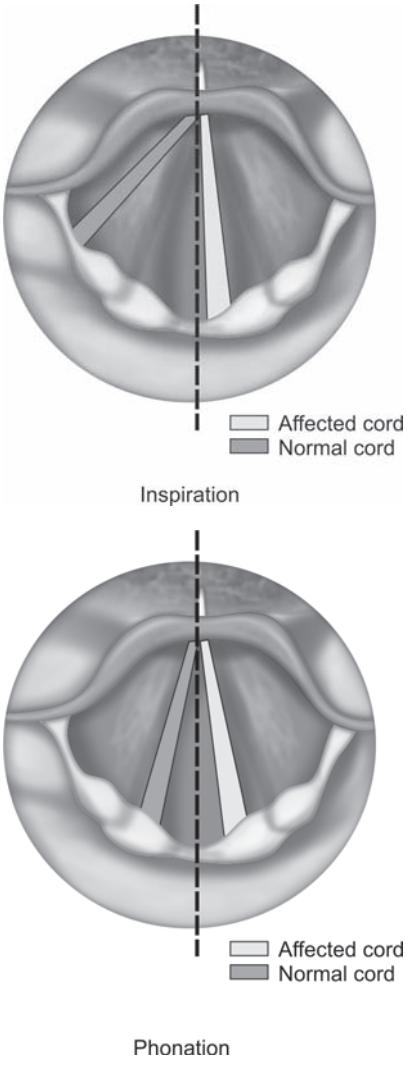


Fig. 2.6: Partial unilateral recurrent laryngeal nerve palsy

- Complete unilateral RLN palsy:
  - Both adductor and abductor affected
  - Vocal cord in paramedian position on affected side
  - During inspiration, unaffected vocal cord fully abducted and respiration not effected
  - During phonation, unaffected vocal cord crosses midline and comes in opposition with affected side.

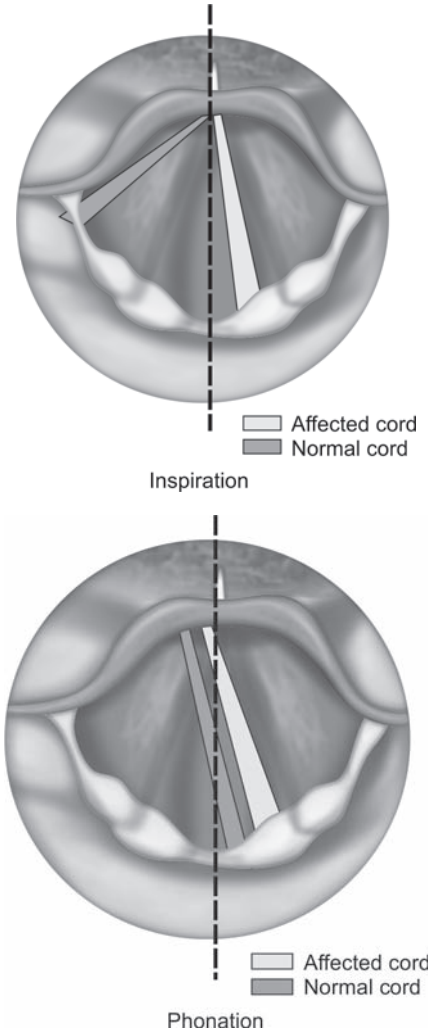


Fig. 2.7: Complete unilateral recurrent laryngeal nerve palsy

Bilateral RLN Palsy

- Acute condition
- Position of vocal cord is median/paramedian due to unopposed cricothyroid action
- Clinical features:
  - Dyspnea and stridor which worsen on exertion
  - Voice is good.
- Treatment:
  - Emergency tracheostomy
  - Lateralization of vocal cords:
    - Arytenoidectomy
    - Endoscopic lateralization
    - Type II thyroplasty
    - Cordectomy
    - Nerve muscle implant.

- Partial bilateral RLN palsy:
  - Only abductor fibers on both vocal cords are affected
  - Vocal cords remain in midline position as adductors take upper hand
  - Narrowing of glottis with severe impairment of respiration
  - Voice is good
  - Requires immediate tracheostomy
  - Lateralize vocal cords with surgery
  - More dangerous than complete bilateral RLN palsy.

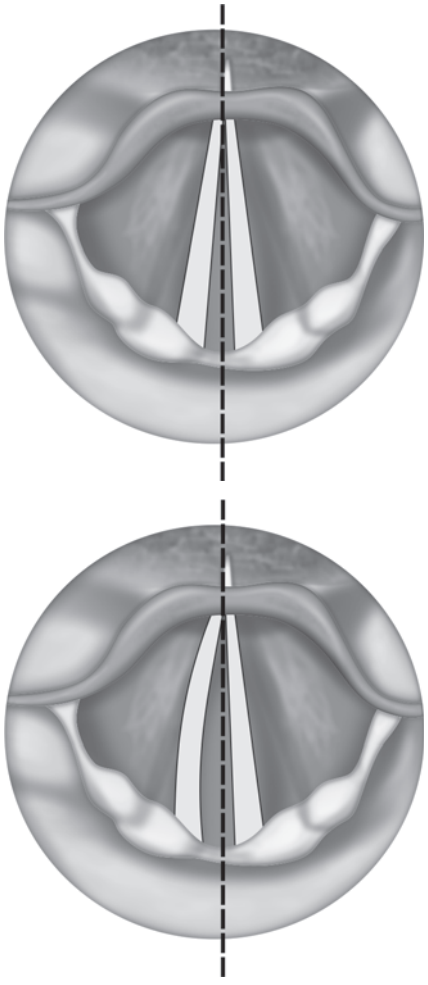


Fig. 2.8: Partial bilateral recurrent laryngeal nerve palsy

- Complete bilateral RLN palsy:
  - Bilateral abductor and adductor fibers affected
  - Both sides vocal cords remain in paramedian position
  - Respiration not affected as much as bilateral partial RLNP.

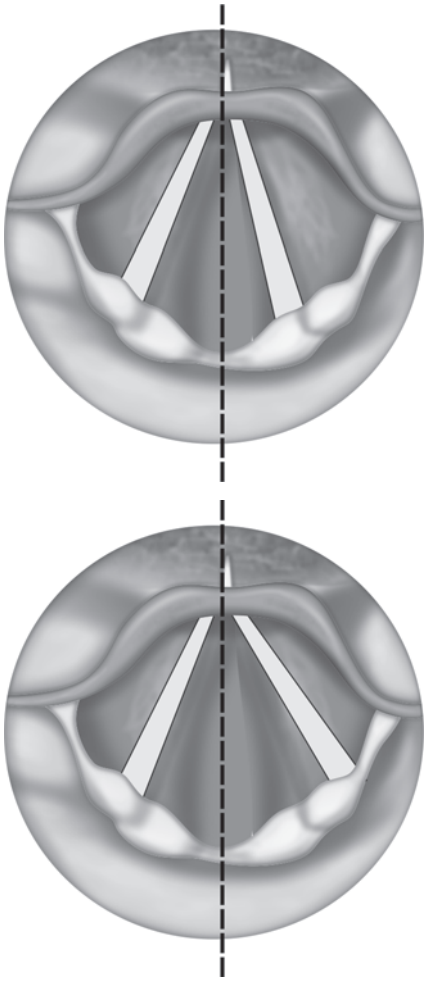


Fig. 2.9: Complete bilateral recurrent laryngeal nerve palsy

Superior Laryngeal Nerve Palsy

Unilateral SLN Palsy

- SLN supplies cricothyroid which is tensor of vocal cord
- Palsy occurs in:
  - Thyroid surgery
  - Neuritis
  - Tumors, diphtheria.
- Clinical features:
  - Weak voice
  - Increased risk of aspiration
  - Pitch cannot be raised
  - Vocal cords:
    - Askew position of glottis
    - Shortening of cord with loss of tension
    - Flapping of paralysed cord
    - *Cadaveric position*

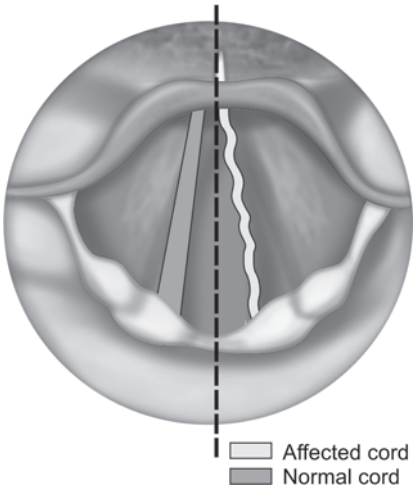


Fig. 2.10: Unilateral superior laryngeal nerve palsy

Bilateral SLN Palsy

- Occurs in:
  - Trauma, cervical lymphadenopathy
  - Neuritis, neoplasia.
- Clinical features:
  - Aspiration of food: Coughing and choking fits
  - Voice is weak and husky.
- Treatment:
  - Neuritis cases recover spontaneously
  - Epiglottopexy may be required to close inlet and protect lungs.

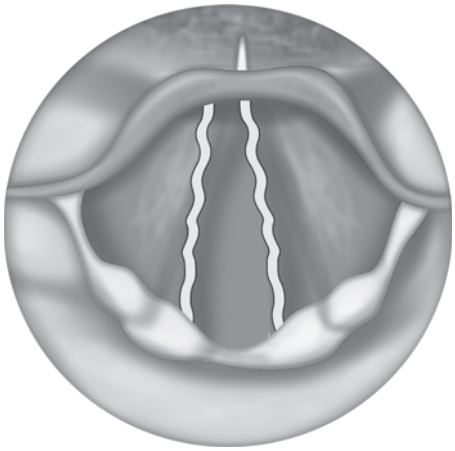


Fig. 2.11: Bilateral superior laryngeal nerve palsy

Combined Paralysis

Unilateral Combined Paralysis

- Paralysis of all muscles in ipsilateral side except interarytenoid (as it receives bilateral innervation)
- Causes:
  - Thyroid surgeries
  - Lesions of ***nucleus ambiguus***/vagus nerve.
- Clinical features:
  - Vocal cord in cadaveric position, 3.5 mm from midline
  - Healthy vocal cord unable to approximate paralyzed cord
  - Hoarseness of voice, aspiration
  - Ineffective cough.
- Treatment:
  - Speech therapy
  - Medialization of vocal cords:
    - Teflon paste injection
    - Type I thyroplasty
    - Muscle/cartilage implant
    - Cricoarytenoid joint arthrodesis.

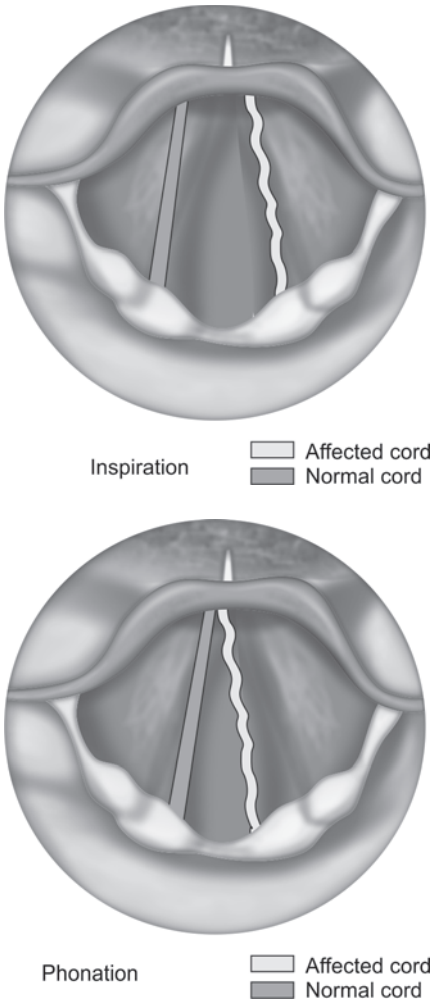


Fig. 2.12: Unilateral combined palsy

Bilateral Combined Paralysis

- Occurs rarely
- Total anesthesia of larynx with both vocal cords in cadaveric position
- Clinical features:
  - Aphonia
  - Inability to cough
  - Aspiration.
- Treatment:
  - Tracheostomy
  - Vocal cord plication
  - Epiglottopexy
  - Total laryngectomy.

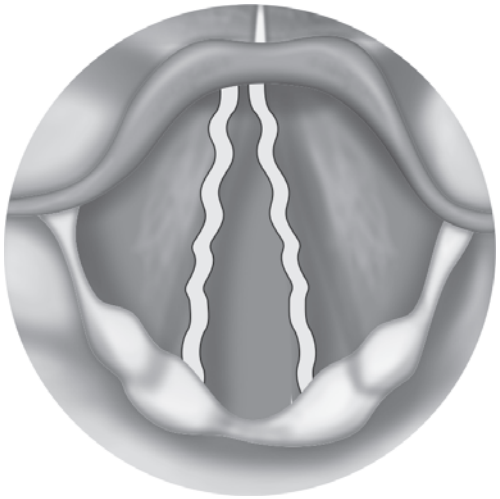


Fig. 2.13: Bilateral combined palsy

Congenital Vocal Cord Palsy

- Unilateral palsy:
  - Occurs more commonly
  - Causes:
    - Birth trauma
    - Congenital anomalies of heart/blood vessels.
- Bilateral palsy:
  - Less common
  - Causes:
    - Hydrocephalus
    - ***Arnold-Chiari malformation***
    - Intracranial hemorrhage
    - Meningocele
    - Cerebral/nucleus ambignus agenesis.
- Treatment: tracheostomy.

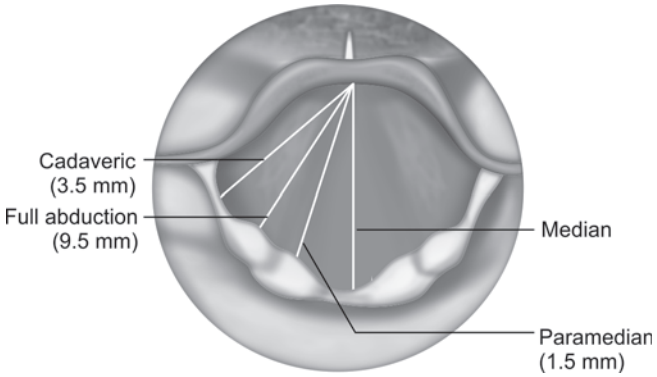


Fig. 2.14: Vocal cord positions

AIRWAY ASSESSMENT[1,2,3]

Definition[3]

- Difficult intubation defined by need for more than 3 intubation attempts or attempts which last more than 10 minutes
- Difficult airway defined as the situation in which a conventionally trained anesthetist experiences difficulty with mask ventilation (unassisted anesthetist unable to maintain SpO_2 more than 90% using 100% oxygen) or inability to place endotracheal tube with conventional laryngoscopy after three attempts or attempts lasting more than 10 minutes.

Objectives

- To provide safe anesthesia
- To facilitate successful management of difficult airway
- To reduce risk and likelihood of complications:
  - Airway trauma
  - CNS damage
  - Cardiopulmonary arrest.

Airway Assessment

History

- Medical history:
  - Congenital/acquired facial (oropharyngeal) anomalies
  - Acromegaly, obstructive sleep apnea syndrome
  - Supraglottic tumors, laryngeal edema, radiotherapy, croup, epiglottitis, ***Ludwig's angina.***
- Surgical history:
  - Unstable cervical spine
  - Faciomaxillary surgery
  - Vertebrobasillar insufficiency
  - Rheumatoid arthritis, ankylosing spondylitis.

- Anesthetic history:
  - Previous difficult intubation
  - Pneumothorax, aspiration of gastric contents.

General Examination

- Morbid obesity:
  - BMI more than 30 kg/m^2 suggests difficult intubation: use HELP position
  - Neck circumference > 40 cms suggests difficult intubation
  - Causes of difficult intubation in obesity:
    - Short and thick neck
    - Limited atlantoaxial joint movement
    - Low cervical fat pads: Reduced thyromental distance
    - Thick suprasternal, presternal fat pads
    - Excess soft tissue in pharynx and mouth.
- Pregnancy, women with large breasts
- Abnormal posture
- Congenital anomalies:
  - Meningomyelocele
  - Faciomaxillary anomalies
  - Cystic hygroma.
- Acromegaly:
  - Large jaw, tongue, lips, head
  - Generalized soft tissue swelling
  - Vocal cord thickening
  - Chondrocalcinosis of larynx
  - Subglottic narrowing
  - Enlarged thyroid gland.

Local Examination

- Face:
  - ***Pierre-Robins syndrome***
  - ***Treacher-Collins syndrome***
  - ***Klippel-Feil syndrome***
  - ***Goldenhaar syndrome***
  - ***Down's syndrome***
  - Burns contractures.
- Nose:
  - Deformities
  - Potency of nostril.
- Teeth:
  - Dentures/edentulous
  - Long, loose/bucked teeth.
- Oral cavity:
  - Macroglossia/glossoptosis
  - High arched palate/cleft palate
  - Limited mouth opening (less than 4 cms)
  - Micrognathia/retrognathia
  - Protruding/receding mandible.
- Neck and cervical spine:
  - Neck: Increased thickness, abnormally long/short neck
  - Reduced range of movement, neck circumference more than 40 cms.
- Distances:
  - Interincisor distance more than 4 cms
  - Mentohyoid distance
  - Thyromental distance: Tip of jaw to superior border of thyroid cartilage: More than 6.5 cms
  - Sternomental distance: More than 12.5 cms
  - Horizontal length of mandible (9 cms).
- Temporomandibular joint:
  - Temporomandibular joint ankylosis
  - Masseteric spasm.

Specific Tests

Mallampati Score

- Evaluates degree of laryngeal exposure which would be possible on laryngoscopy
- Ratio of size of tongue to oropharynx
  - Class I: Faucial pillar and uvula seen completely
  - Class II: Only base of uvula seen
  - Class III: Soft palate seen
  - Class IV: Only hard palate seen *(see fig. next page)*.

Atlanto-Occipital Joint Extension

- Evaluates ability to make sniffing/Magills position
- Normal is 35° with head held erect and facing directly to the front
- Measures angle traversed by occlusal surface of upper teeth on maximal extension.

Mandibular Space

- ***Patil's test***:
  - Measures thyromental distance
  - Interpretation:
    - Less than 6 cms suggests difficult airway
    - Between 6–6.5 cms suggests less difficult airway
    - More than 6.5 cms is normal.
- ***Savva D test***: Measures sternomental distance: more than 12.5 cms is normal
- ***Delilkan test***:
  - Index finger of left hand placed under jaw tip
  - Index finger of right hand placed on occipital tuberosity

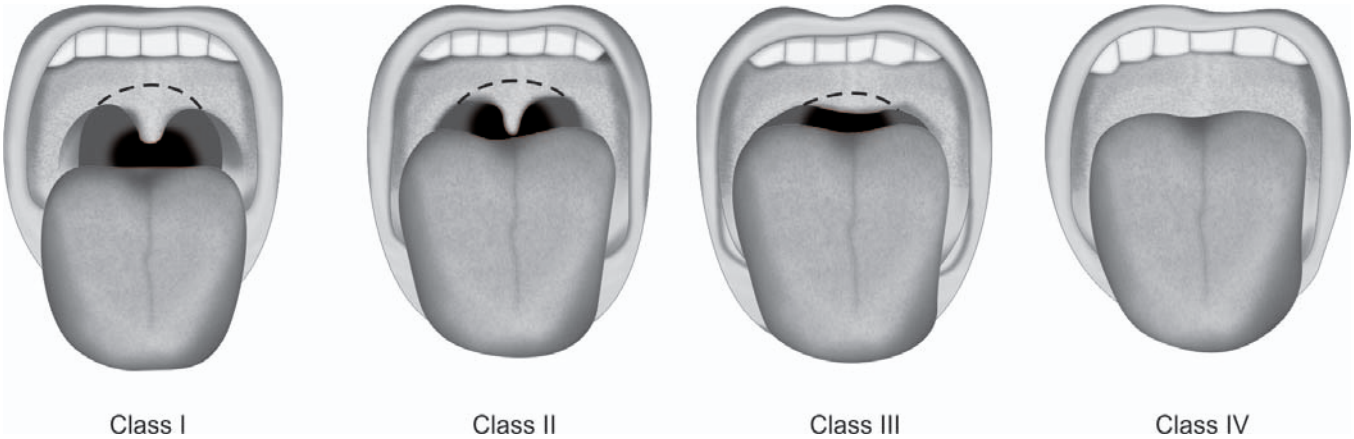


Fig. 2.15: Mallampatti scoring[3]

- Patient asked to look at the ceiling
- Interpretation:
  - If left finger higher than right: normal neck extension
  - If left finger is at same height or lower than right finger: abnormal extension.

Cormack and Lehanes Degree of Laryngeal Exposure

- Class I: full exposure of vocal cord
- Class II: partial exposure with posterior commissure seen
- Class III: only epiglottis seen
- Class IV: not even epiglottis seen
- Classes I and II: adequate exposure
- Class III and IV: inadequate exposure.

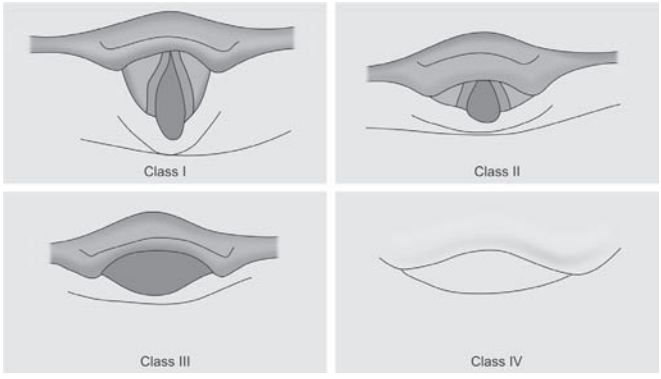


Fig. 2.16: Cormack and Lehanes classification[3]

Investigations

- Plain X-ray: Neck and chest
- Radiological assessment:
  - Posterior mandibular depth (PMD): Distance between alveolus immediately behind third molar to lower border of mandible
  - Effective mandibular length (EML):
    - Distance between tip of lower incisor to TMJ
    - Direct laryngoscopy is difficult if EML is less than 3-6 times PMD.
  - Reduced gap between occiput and C_1 vertebra.
- Fluoroscopy for vocal cord mobility and emphysema
- Esophagogram for extrinsic mass/vascular ring
- Ultrasound for cellulitis, lymphadenopathy
- CT/MRI for congenital anomalies, mass, stenosis
- Pulmonary function tests: spirometry, pressure volume loops
- Indirect laryngoscopy
- Fibreoptic laryngoscopy.

Difficult Mask Ventilation

Inability of trained anesthetist to maintain SpO_2 more than 90% using face mask for ventilation and 100% FiO_2, provided the preventilation SpO_2 was within normal range.

- Predictors:
  - Mallampati class IV
  - History of snoring, obesity
  - Male sex
  - Old age.
- OBESE score for predicting difficult mask ventilation:

  O: obese (BMI > 30)

  B: bearded

  E: elderly (> 55 years)

  S: snorers

  E: edentulous.

Scoring Systems for Difficult Airway

Wilsons Score

Risk factor	Score
Weight	
Less than 90 kgs	0
90-110 kgs	1
More than 110 kgs	2
Head and Neck Movement	
More than 90°	0
Around 90°	1
Less than 90°	2
Protruding Anterior Maxillary Teeth	
Normal	0
Moderate	1
Severe	2
Jaw Movement (Interincisor Gap and Subluxation)	
IG > 5 cms or subluxation > 0	0
IG < 5 cms or subluxation = 0	1
IG < 5 cms or subluxation < 0	2
Receding Mandible	
Normal	0
Moderate	1
Severe	2

- Wilson's score less than 2 predicts normal intubation
- Wilson's score 3 predicts 75% difficult intubation cases
- Wilson's score 4 predicts 90% difficult intubation cases
- Best predictor of difficult airway in a recent study was Wilson score.

Lemon Score

Physical signs	Less difficult airway	More difficult airway
Look externally	Normal face and neck	Abnormal face shape
	No face or neck pathology	Sunken cheeks
		Edentulous/bucked teeth
		Receding mandible
		Narrow mouth
		Bull neck, obesity
Evaluate 3-3-2-1	Mouth opening > 3 fingers	Less than 3 fingers
	Hyoid-chin distance > 3 fingers	Less than 3 fingers
	Thyromental distance > 2 fingers	Less than 2 fingers
	Lower jaw anterior subluxation > 1 finger	Less than 1 finger
Mallampati score	Mallampati I and II	Mallampati II and III
Obstruction	None	Peritonsillar abscess
		Epiglottitis
		Retropharyngeal abscess
Neck mobility	Normal flexion and extension	Limited range of movement

LM-MAP Score

- L: Look for external face deformities
- M: Mallampati score
- M: Measurements 3-3-2-1
- A: Atlanto-occipital extension
- P: Pathological obstruction – edema, tumors.

Four Ds

- D_1-dentition: Prominent upper teeth, receding chin
- D_2-distortion: Edema/blood/vomitus/tumor/infection
- D_3-disproportion: Short chin/bull neck/large tongue
- D_4-dysmobility: Temporomandibular joints and cervical spine.

Magboul 4Ms with Stop Sign

4Ms: Mallampati, measurement, movement, malformation

S: Skull (hydrocephalus/microcephalus)

T: Teeth (bucked, protruded, loose, macro/micrognathia)

O: Obstruction (obesity, short, bull neck, swelling in head/neck)

P: Pathology: craniofacial anomalies, Treacher-Collins, Goldenhar, Pierre-Robins syndromes.

EXTUBATION OF DIFFICULT AIRWAY[1,2,3]

Preparation of Extubation

- Fully awake extubation
- Sniffing/lateral/sitting position can be used
- Bite block should be in place to prevent biting the tube
- Remove throat pack if any

- Preoxygenate, fully reverse the patient
- Suction pharynx (trachea also if indicated)
- Extubate over guiding stylet:
  - ***Cooks airway exchange catheter***
  - ***Cardiomed endotracheal ventilation catheter.***

Extubation Risk Assessment Tests

- ***Leak test***
- Visualization of airway swelling
- Flexible fibreoptic scope visualization
- Neurological status assessment.

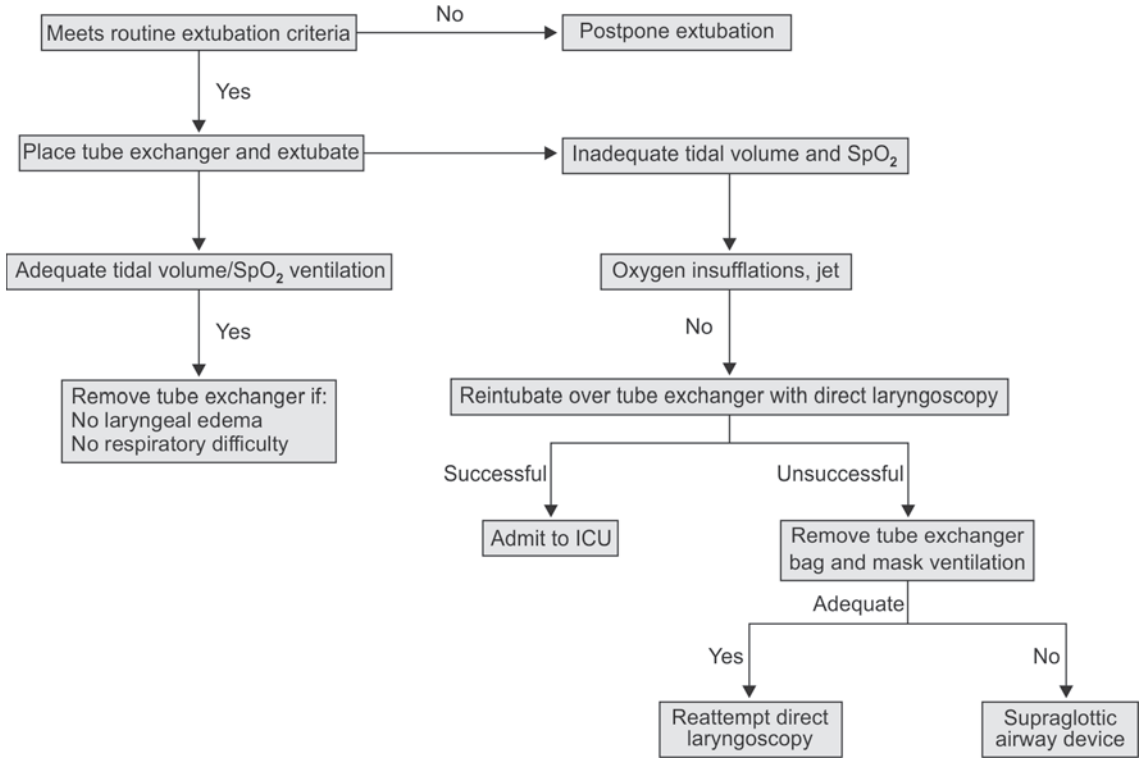
Equipment Preparation

- Airways
- Ambubag, T-piece
- Laryngoscope blade
- ETT tube, LMAs
- Cricothyrotomy set.

Routine Extubation Criteria

- Awake, alert, able to follow commands:
  - Sustained eye opening for pediatrics
  - Patient is able to understand commands for adults.
- Protective reflexes returned:
  - Gag reflex
  - Swallow reflex
  - Cough reflex.
- Adequate reversal of neuromuscular blockade:
  - Train of Four 4/4
  - Sustained tetany at 50 Hz
  - Strong hand grip
  - Sustained head lift (more than 5 seconds).
- ABG reasonable with FiO_2 40%:
  - pH > 7.30
  - $PaO_2 \geq 60$ mm Hg
  - $PaCO_2 < 50$ mm Hg.
- Respiratory mechanics adequate:
  - Respiratory rate 25–35/min
  - Tidal volume > 5 cc/kg
  - Vital capacity ≥ 10–15 ml/kg
  - Negative inspiratory force ≥ – 20 cm H_2O
  - Maximum Voluntary Ventilation > twice the minute volume.
- For patients at risk of laryngeal edema:
  - Cuff leak test
  - Direct laryngoscopy and airway inspection
  - Fibreoptic bronchoscopic evaluation.

Extubation of Patient with Difficult Airway



NONRESPIRATORY FUNCTIONS OF LUNGS[1,2,3]

Nonrespiratory Functions of Lungs

Acid Base Balance

- Alters pH of blood by altering $PaCO_2$
- May cause respiratory acidosis/alkalosis.

Heat Exchange

- More in upper respiratory tract
- Significant role of lungs in extreme cold and dry conditions and during hyperventilation.

Gas Reservoir

- Helps in voice production and phonation
- Helps in coughing, sneezing and hiccoughs.

Immunological

- Pulmonary alveolar macrophages
- Mucociliary escalator
- IgA production.

Metabolic Functions of Lungs

- Uptake and conversion of chemicals in blood
- Synthesis of:
  - Pulmonary surfactant
  - Proteins.
- Activation: Converts ATI to ATII
- Inactivation of:
  - Nor adrenaline
  - Serotonin
  - Bradykinin
  - Prostaglandins.
- Drug metabolism.

Endocrine Functions of Lungs

- Formation of local hormones:
  - Histamine from mast cells
  - Serotonin from mast cells .
- Release of hormones:
  - Histamine
  - Serotonin
  - Bradykinin
  - Prostaglandins PGE_2, PGF_2.

Nonrespiratory Functions of Pulmonary Circulation

- Reservoir of blood:
  - Stores around 450 ml of blood
  - Valsalva manoeuvre reduces store to around 250 ml.
- Filter:
  - Acts as vascular filter
  - Emboli, fat cells, cancer cells, bone marrow, particles in IV fluids.
- Fluid exchange and drug absorption.

FACTORS AFFECTING TISSUE OXYGENATION[1,2,3]

Introduction

- Aerobic cellular respiration depends on efficient supply of oxygen and substrate to the mitochondria
- Normally oxygen content in mitochondria is 10 mm Hg
- Critical value of PO_2 in mitochondria is 1–2 mm Hg (Pasteur point) below which anaerobic respiration sets in.

Physiology

- ***Oxygen flux***:
  - This is the amount of oxygen which leaves the left ventricle per minute (DO_2)
  - The normal delivery of oxygen to tissues is 1000 ml/min
  - DO_2 = cardiac output (Q) × arterial O_2 content
  - $DO_2 = Q \times Hb\% \times SaO_2 \times 1.39$ ***(Huffner's constant)***
  - Since there are three variables which are multiplied to derive the DO_2, a small change in one variable may cause a large change in DO_2
  - Huffner's constant is the amount of O_2 (in ml), in 1 gm of Hb at sea level.
- ***Supply independent oxygen consumption***:
  - The normal delivery of oxygen to tissues is 1000 ml/min
  - The normal consumption of O_2 at the tissue level is 250 ml/min (VO_2)
  - Thus, oxygen is delivered in excess to the tissues
  - This enables body to cope with a reduction in DO_2 without initially compromising aerobic respiration and oxygen consumption.
- ***Supply dependent oxygen consumption***:
  - When VO_2 falls with a reduction in DO_2, it is called supply dependent O_2 consumption
  - Tissues are in dysoxia below this point.
- Thus factors which decrease tissue oxygenation are:
  - Reduced delivery (DO_2)
  - Increased consumption (VO_2)
  - Histotoxic hypoxia.

Factors Causing Reduced Delivery (DO_2)

Macrovascular Level

- Factors affecting cardiac output:
  - Hypovolemia
  - Hemorrhage
  - Congestive cardiac failure.
- Factors affecting hemoglobin concentration (Hb%):
  - Anemia:
    - Causes reduction in diffusive oxygen conductance
    - Causes reduction in number of binding sites for oxygen
    - Reduces surface area of RBC for effective oxygen diffusion.
  - Oxyhemoglobin dissociation curve:
    - Factors causing shift to right:
      - Acidosis (Bohr effect)
      - Hyperthermia
      - Hypercapnea
      - Increased 2,3-DPG
      - High altitude
      - Propranolol
      - Isoflurane.
    - Factors causing shift to left:
      - Alkalosis
      - Hypothermia
      - Hypocapnea
      - Reduced 2,3-DPG
      - Fetal hemoglobin (HbF)
      - Carboxyhemoglobin
      - Methemoglobin
      - Carbon monoxide inhalation.
- Factors affecting arterial oxygen saturation (SaO_2):
  - Ventilation perfusion mismatch: Lung collapse, chronic lung diseases
  - Diffusion limitation: Intestitial fibrosis
  - Right to left shunting: Acute lung diseases (through inadequately oxygenated alveoli).

Microvascular Level

- Factors affecting microvascular tone:
  - Central factors: Sympathetic vasoconstrictor tone reduces blood flow
  - Local factors: Vasodilator tone:
    - Subject to autoregulation
    - Hypoxia causes vasodilation and increased blood flow by:
      - Increasing production of:
        - Nitric oxide (NO)
        - PGI_2
        - Endothelial derived humoral factor (EDHF)
      - Stimulation of ATP sensitive potassium channels.
- Factors affecting oxygen diffusion from microvasculature to mitochondria:
  - Capillary surface area
  - Oxygen content
  - Myoglobin facilitated diffusion of oxygen.

Factors Affecting Oxygen Consumption

- Severe exercise
- Fever
- Thyrotoxicosis
- ***Halothane shakes***
- Pain
- Shivering.

Histotoxic Hypoxia

- Oxygen delivery to mitochondria may be normal
- But mitochondria may be unable to utilize the oxygen due to some defect in the electron transport chain
- This can be due to:
  - Carbon monoxide/cyanide poisoning
  - Narcotics, alcohol poisoning
  - Hydrogen sulfide poisoning (sewage by product used in leather tanning).

Oxygen Cascade

- Oxygen content of air (at sea level) is 160 mm Hg and falls to 10–15 mm Hg at the mitochondrial level. The transport of oxygen down this gradient is described as oxygen cascade
- Normally oxygen content in mitochondria is 10 mm Hg
- Critical value of PO_2 in mitochondria is 1-2 mm Hg (Pasteur point) below which anaerobic respiration sets in.

OXYGEN FLUX[1,2,3]

Introduction

- Refers to amount of oxygen leaving left ventricle per minute in arterial blood
- Also is the amount of oxygen delivered to peripheral tissues per minute.

Measurement

- Oxygen flux = (O_2 bound to hemoglobin) + (dissolved O_2)

O_2 bound to Hb = cardiac output × Hb × SaO_2 × K
Dissolved O_2 = cardiac output × pO_2 × 0.03
K = Huffner's constant which is amount of O_2 carried by 1 gm of Hb (around 1.31 ml)

- The amount of O_2 dissolved in plasma is negligible and hence is ignored (0.003 ml of O_2/mm Hg/0.1 L of plasma)
- Dissolved O_2 = 0.003 × 100 mm Hg × 100 ml = (0.3 ml/100 ml plasma)
- Thus oxygen flux = CO × Hb × SaO_2 × 1.31.

Normal Values

- O_2 flux assuming CO of 5 liter and Hb of 15.6 with SaO_2 98% = 1000 ml O_2/min
- Normally 250 ml/min of O_2 is taken up in tissues
- Thus, remaining 750 ml/min (or 75%) is returned to lung in mixed venous blood (M_vO_2 = 75%).

Oxygen	Mixed venous	Arterial
Dissolved in plasma	0.13 ml/100 ml plasma	0.3 ml/100 ml plasma
Tension (PaO_2)	40 mm Hg	100 mm Hg
Amount combined with Hb (oxyhemoglobin)	14 ml/100 ml blood	19 ml/100 ml plasma
Saturation	75%	100%

Factors Affecting Oxygen Flux

Factors Affecting O_2 Carrying Capacity

- Anemia
- Congestive cardiac failure
- Metabolic/respiratory acidosis
- Reduced alveolar ventilation.

Factors Increasing Demand

- Exercise
- Pain
- Shivering
- Halothane shakes
- Thyrotoxicosis
- Metabolic acidosis.

Clinical Relevance

- Maximal PaO_2 which can be achieved is 400–500 mm Hg
- For every 1% increase in SaO_2, PaO_2 increases by 40–50 mm Hg
- PaO_2 of 100 mm Hg indicates SaO_2 of 98%.

OXYGEN CASCADE[1,2,3]

Introduction

Steps by which partial pressure of O_2 decreases from a higher level in inspired gas to a lower level in mitochondria is called O_2 cascade.

Steps

- Uptake in lungs
- Transport in blood
- Global delivery to tissues
- Regional distribution of O_2 delivery
- Diffusion from capillary to cell
- Cellular utilization of O_2.

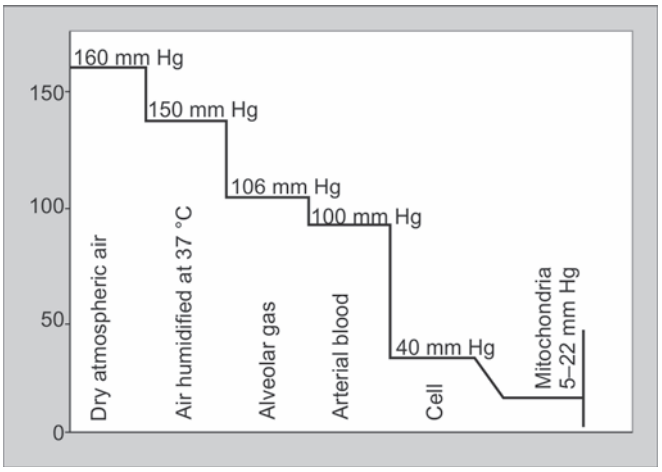


Fig. 2.17: Oxygen cascade

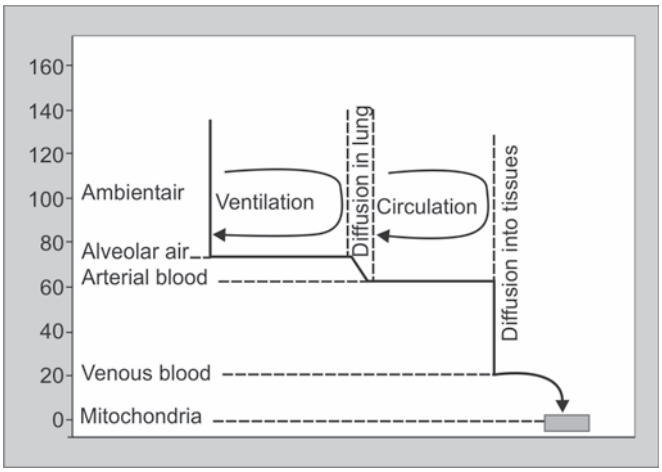


Fig. 2.18: Oxygen cascade

Factors Affecting Cascade

- Dry atmospheric air:
  - Barometric pressure
  - FiO_2

  - Partial pressure of O_2 (PiO_2) = barometric pressure × FiO_2 = 760 × 0.21 = 160 mm Hg.
- Humidification at 37 °C:
  - Depends on saturated vapor pressure of water at body temperature
  - PO_2 = (atmospheric pressure – SVP) × FiO_2
  - PO_2 = (760-47) × 0.21=150 mm Hg.
- Alveolar gas:
  - Dilution of atmosphere air by arterial air
  - Constant uptake of O_2
  - Diffusion defects.
- Arterial O_2 tension:
  - V-P mismatch
  - True shunt of pulmonary arterial blood
  - Cardiac output.
- Cellular PO_2:
  - Blood flow
  - Hb%
  - Cardiac output.
- Mitochondria: ***Pasteur point:***
  - If DO_2 falls below 1–2 mm Hg (0.2 kpa), aerobic metabolism stops
  - This point is called Pasteur point.

Causes of Failure of Cascade

- Stagnant hypoxia:
  - Low cardiac output
  - Peripheral vascular disease
  - Mechanical vascular occlusion.
- Anemic hypoxia:
  - Anemia
  - Acute blood loss
  - Hemoglobinopathy.
- Hypoxic hypoxia:
  - Inadequate ventilation
  - V-Q mismatch
  - Low FiO_2.
- Shunt hypoxia:
  - Arteriovenous shunt
  - Congenital cardiac diseases.

Oxygen Transport in Blood

Transported in two forms:

- Combination with hemoglobin: Each gram of Hb carries 1.31 ml of O_2
- Dissolved in plasma: 100 ml plasma carries 0.3 ml O_2.

Clinical Implications

- When FiO_2 increased to 100%
  - Small amount of O_2 dissolves in plasma at rate 0.3 ml O_2/100 ml plasma
  - But no significant increase in amount of oxygen carried by hemoglobin
  - This is because it is already 95% saturated with oxygen.
- Any interference at any point of O_2 cascade causes significant changes downstream
- High altitude:
  - On ascent to higher attitude, barometric pressure reduces
  - Thus even if FiO_2 is 21%, PiO_2 is only 70 mm Hg.

OXYGEN DISSOCIATION CURVE[1,2,3]

Introduction

- Curve which mathematically equates percentage saturation of hemoglobin with partial pressure of oxygen in blood
- It describes nonlinear tendency of oxygen to bind to hemoglobin.

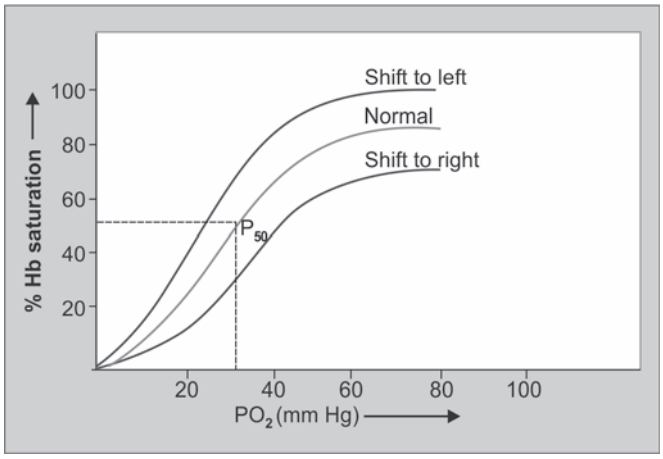


Fig. 2.19: Oxygen dissociation curve

Rationale

- ***Cooperativity***: Binding of oxygen to one site on hemoglobin molecule facilitates binding of oxygen at other sites
- This causes sigmoid shape of curve
- As one molecule of oxygen becomes unbound, affinity for others also falls.

Clinical Importance

- Role of hemoglobin: Reduction of Hb% from 15 to 10g% reduces PaO_2 from 100 to 40 mm Hg

- Role of Hb saturation: Small fall in SaO_2 may cause large drop in PaO_2
- Role of cardiac output:

Moderate hypoxemia increases CO and reduces PVR

Compensation for fall in CO is slow as hemoglobin production is slow and ODC is flat (it cannot be come more saturated).

- ***Bohr effect:*** Affinity of hemoglobin to oxygen reduces due to increase in $PaCO_2$ or H^+ ion concentration. Thus, at tissue level, where $PaCO_2$ concentration is high, unloading of O_2 occurs easily
- ***Haldane effect***: Deoxygenation of hemoglobin increases its ability to carry CO_2 and oxygenation of Hb reduces it. Thus, in lungs oxygenation causes unloading of CO_2.

Implications of Shape of Curve

- Allows hemoglobin to load and unload O_2 efficiently as condition dictates
- After hemoglobin saturation 90% curve is flat
- Reflects 4 stage loading of O_2: Each Hb molecule binds four O_2 molecules
- O_2 unloading in tissues occurs over steep portion of curve.

SpO_2	PaO_2
98%	100 mm Hg
90%	60 mm Hg
75%	47 mm Hg
50%	26.6 mm Hg
25%	15 mm Hg

Causes of Shift in ODC Curve

Shift to left	Shift to right
Alkalosis	Acidosis
Hypothermia	Hyperthermia
Hypocarbia	Hypercarbia
Reduced 2,3 – DPG	Increased 2,3-DPG
Fetal hemoglobin	High altitude
Carboxyhemoglobin	Isoflurane
Methhemoglobin	Propranolol
CO inhalation	
Causes reduced O_2 delivery to tissues	Causes increased O_2 delivery to tissues

Myoglobin Dissociation Curve

- Myoglobin is important oxygen source for muscle
- Curve has hyperbolic shape
- Reflects one stage loading of O_2
- Each myoglobin molecule has one site for O_2 binding
- P_{50} is 5 mm Hg implies a high oxygen affinity at low PO_2.

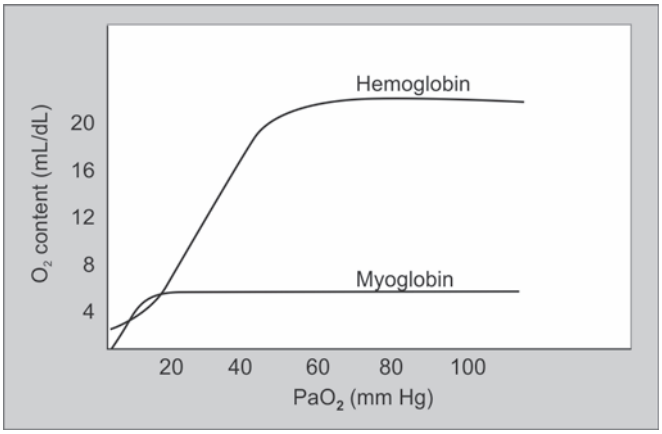


Fig. 2.20: Myoglobin dissociation curve

PULMONARY FUNCTION TESTS[1,2,3]

Goals

- Screen for obstructive/restrictive lung diseases
- Quantify severity of disease if present
- Follow progression of disease
- Observe response to therapy
- Predict probability of postoperative complications.

Preoperative Indications

- Age > 60 yrs
- Known history of pulmonary disease
- History of chronic cough/wheeze
- History of smoking
- Obesity
- Prolonged duration of anesthesia
- Abdominal/thoracic surgery
- Severe neuromuscular disease.

Types of Pulmonary Function Tests

- Distribution of ventilation
- Regulation of ventilation
- Ventilation perfusion relationships
- Arterial blood gases
- Spirometry.

SPIROMETRY

Introduction

Spirometry is the measurement of air moving in and out of the lungs during various respiratory maneuvers.

Static Lung Tests

Tidal Volume

- Volume of air moving in and out of lungs during quiet respiration
- 6-8 ml/kg
- Reduces with:
  - Decrease in lung compliance
  - Reduced respiratory muscle strength.

Inspiratory Reserve Volume

- Maximum volume of air inhaled from end inspiratory tidal position
- 3.2 – 3.6 L.

Expiratory Tidal Volume

- Maximum volume of air exhaled out from resting end expiratory tidal position
- Normally around 1.2 L.

Residual Volume

- Volume of air remaining in lungs after maximal exhalation
- Not measured by spirometry
- Indirectly measured (FRC-ERV).

Vital Capacity

- Usually 60 ml/kg.

Inspiratory Capacity

- Largest volume of gas that can be inspired from resting expiratory level
- Decreased in the presence of significant extrathoracic airway obstruction
- Correlates well with effective coughing.

Functional Residual Capacity

- Volume of gas remaining in lung at the end of passive expiration
- Influences ventilation perfusion relationships in lung.

Dynamic Lung Tests

Forced Vital Capacity

- Volume of gas expired as forcefully and rapidly as possible after maximal inspiration
- Measurement depends on patient effort and cooperation
- Normally FVC = VC
- Decreased FVC increases risk of postoperative pulmonary complications
- FVC decreased in restrictive diseases, COPD.

Forced Expiratory Volume

- Forced expiratory volume of gas flowing over a given time interval is FEV_T
- T is the time in seconds from onset of expiration
- Decreased values common in obstructive and restrictive diseases
- Normal patients exhale at least 83% of FVC in first second of exhalation
- $FEV_1/FVC > 0.83$
- $FEV_2/FVC > 0.94$.

Forced Expiratory Flow

- Measure of how much volume can be expired from lungs as a flow rate
- Measured from FVC curve
- Each quartile of FVC curve expressed as FEF value
- $FEF_{25\%}$: Amount of air forcefully expelled out in first 25% of FVC test
- $FEF_{50\%}$: Amount of air expelled out from lungs during first half of FVC test
- Useful when detecting obstructive disease
- $FEF_{50\%}$ lesser in obstructive airway disease.

$FEF_{25-75\%}$

- Amount of air expelled out during middle half of FVC test
- It is an indicator of obstructive disease.

Peak Expiratory Flow Rate

- Maximum flow rate achieved during FVC maneuver beginning with full inspiration and ending with maximal expiration
- Useful measure of response to bronchodilator therapy.

Maximum Voluntary Ventilation

- Patient breathes in and out as maximally and rapidly for 10–15 seconds
- Total volume of air breathed is measured
- Reflects status of respiratory muscles, thoracic compliance and airway resistance
- Easy way to assess respiratory muscle strength before surgery
- Test is effort dependent
- Poor predictor of true pulmonary compliance and strength.

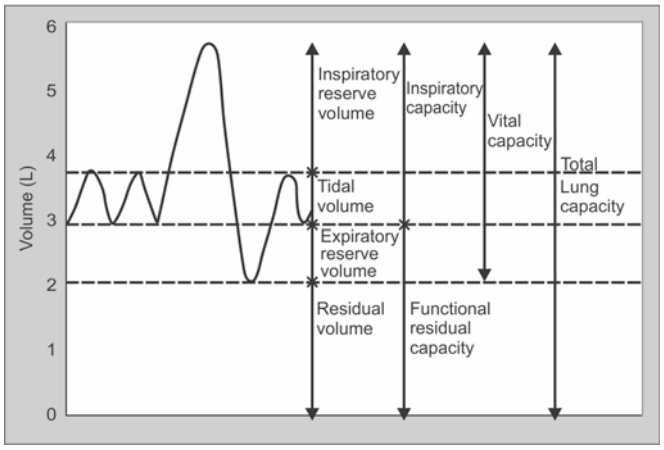


Fig. 2.21: Pulmonary function tests[2]

Limitations

- Not disease specific
- Cannot be used as sole screening tool
- Variable values depending upon age, sex, gender
- Effort dependent results
- Specific measurements do not predict postoperative pulmonary complications.

FUNCTIONAL RESIDUAL CAPACITY[1,2,3]

Introduction

- It is the amount of air remaining in the lungs after normal expiration
- FRC = Residual Volume + Expiratory Reserve Volume (RV + ERV).

Normal Values

- 2400 ml for a 70 kg adult
- Ranges from 1.8 to 3.4 Litres
- Amounts to around 40% of Total Lung Capacity.

Measurement[2]

Helium Dilution Technique

- Measures dilution of inhaled helium by air already present in lungs at end of normal expiration
- Spirometer is filled with oxygen and helium
- The amount of helium is known at beginning of test (C_1)
- Patient is asked to breathe normally, starting from FRC
- The helium enters lungs and spreads to a new concentration C_2
- Helium dilution is calculated by using $C_1V_1 = C_2V_2 = C_2(V_1 + FRC)$
- Older and simpler method, but less accurate
- FRC by this technique measures volume of gas in lungs which is in communication with airways.

Body Plethysmography

- ***Gold standard*** for measuring FRC
- Patient is placed in a ***body box or pneumotachometer*** which is used to measure FRC
- Changes in volume of body determined as a change in pressure within the body box
- FRC by this technique measures total volume of gas at end expiration including air which is trapped behind closed airways
- Requires sophisticated and expensive equipment.

Nitrogen Washout Method

- Also called ***Fowlers method***
- Total quantity of N_2 washed out of lungs by breathing in oxygen is measured
- More commonly used for anatomical dead space calculationSubject inhales 100% O_2 and exhales through a one way valve measuring N_2 content
- FRC is then determined by plotting N_2 concentration vs expired volume.

CT Scan

Multiple Breath SF_6 Procedure

Physiology

- At FRC, the force which retracts the lungs inwards is exactly equal and opposite to the force which expands the chest wall outwards.

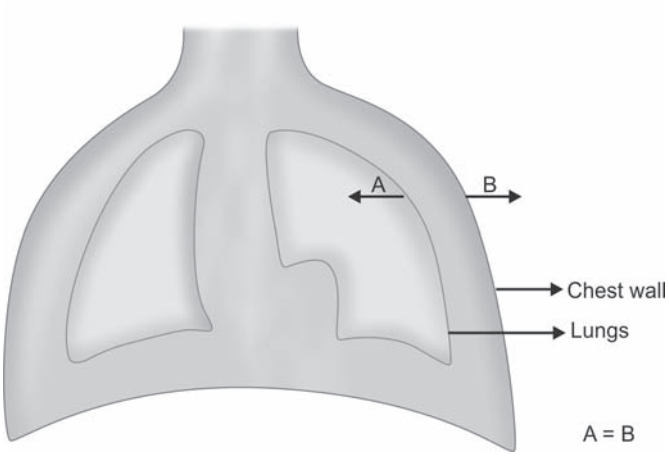


Fig. 2.22: FRC physiology

- This creates a negative intrapleural pressure
- In erect position, lung tissue gravitates towards the base

- This creates a vertical gradient of intrapleural pressure
- Intrapleural pressure at the apex = – 10 cm H_2O (erect)
- Intrapleural pressure at the base = – 2.5 cm H_2O (erect)
- Thus, alveoli are more distended at apex than at base.

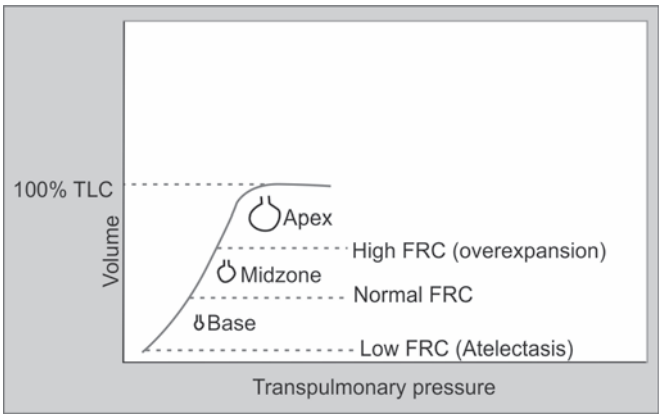


Fig. 2.23: FRC physiology[3]

Factors Affecting Functional Residual Capacity

- Increased functional residual capacity:
  - Ageing
  - Positive end expiratory pressure PEEP, CPAP
  - Emphysema, bronchitis, asthma
  - Peribronchial fibrosis
  - Bronchiolar obstruction
  - Erect/propped up position.
- Decreased functional residual capacity:
  - Ageing
  - Obesity, supine position, Trendelenburg position
  - Pregnancy, sedation
  - Neuromuscular disease:
    - Myasthenia gravis
    - Poliomyelitis.
  - Ascites, hepatosplenomegaly
  - Bilateral diaphragmatic palsy
  - Upper abdominal and thoracic surgery/wound
  - Restrictive pulmonary disease, tuberculosis, sarcoidosis, pneumothorax.

Significance of Functional Residual Capacity

- Gas exchange
  - Allows continuous exchange of gases
  - Some air is always present in lungs due to FRC
  - Therefore, O_2 and CO_2 concentrations are constant.
- Dilutes inhaled toxic gases
- Load on right ventricle is reduced as collapsed lung increases PVR
- Preoxygenation:
  - Fills FRC (prior to induction) with oxygen
  - This increases oxygen reserve from 500 ml to 2400 ml
  - Thus, apneic periods are tolerated better.
- Closing capacity (CC):
  - If CC = FRC, some airways remain closed, even with normal tidal volume breathing
  - If CC > FRC, airway closure causing V/Q mismatch.
- Position: FRC reduces with:
  - Supine position
  - Trendelenburg position.

Effects of Anesthesia

- Reduced FRC:
  - FRC reduced by around 20% (0.5–0.7 litres) post-induction
  - FRC can be reduced by up to 50% in obese patients
- Mechanism: Reduced FRC occurs due to:
  - Loss of inspiratory muscle tone:
    - This causes loss of outward recoil of chest wall
    - Thus, chest is drawn inwards
    - This reduces FRC.
  - Loss of tone of scalene, sternocleidomastoid, intercostal muscles
  - Loss of tone of diaphragm: Cephalad displacement
  - Supine/Trendelenburg position.
- Consequences:
  - Areas of low V/Q ratio
  - Atelectasis
  - Altered pulmonary mechanics
  - Airway closure
  - Postoperative hypoxemia.
- Causes of postoperative reduction in FRC:
  - Incisional pain
  - Reflex diaphragmatic dysfunction: Main cause
  - Absence of spontaneous sighs
  - Mechanical disruption of thorax and abdomen
  - Stimulation of splanchnic and visceral afferents due to:

- Bowel distention
- Local irritation
- Pneumoperitoneum.

- Prevention:
  - 30° head up tilt
  - Positive end expiratory pressure
  - CPAP.
- Restoration of FRC by:
  - Early and active lung expansion maneuvers:
    - Deep breathing and coughing
    - Incentive spirometry
    - CPAP
    - Recruitment maneuvers
    - Sighs: can generate up to 40 cm H_2O pressure.
  - Adequate postoperative analgesia:
    - Epidural: Very effective
    - Systemic opioids
    - Restoration of FRC by analgesia alone is limited and never complete.

LUNG COMPLIANCE[1,2,3]

Introduction

Lung compliance is the change in lung volume (lung expansion) per unit pressure change

Normal compliance of intact lung: 100 mL/cmH_2O.

Measurement

- Compliance C: $C = \Delta V/\Delta P$

  Where C is compliance
  ΔV is change in lung volume
  ΔP is change in pressure.
- Total compliance $(C_T) = 1/C_T = 1/C_L + 1/C_{CW}$

  Where total compliance = C_T
  Lung compliance = C_L
  Chest wall compliance = C_{CW}.

Types

- Static compliance
- Dynamic compliance
- Specific compliance.

Static Compliance

- Measured when there is no airflow
- Reflects elastic resistance of lung and chest wall
- Measures from 40–60 ml/cm H_2O in critically ill patients
- Plateau pressure:
  - Obtained by applying inspiratory hold/ occluding port at end inspiration
  - It is the pressure needed to maintain lung inflation in the absence of air flow.

$$\text{Static compliance } (C_{ST}) = \frac{\text{Corrected tidal volume}}{(\text{Plateau pressure} - \text{PEEP})}$$

Dynamic Compliance

- Measured when airflow is present
- Airway resistance is critical factor in measuring compliance
- Reflects condition of airway resistance and elastic properties of lung and chest wall
- Measures from 30-40 ml/cm H_2O in critically ill patients
- Peak inspiratory pressure is pressure used to deliver tidal volume by overcoming nonelastic (airways) and elastic (lung parenchyma) resistance.

$$\text{Dynamic compliance } (C_{DYN}) = \frac{\text{Corrected tidal volume}}{(\text{Peak inspiratory pressure} - \text{PEEP})}$$

Specific Compliance

- Normally measures 0.05/cm H_2O
- Similar value in both sexes and all ages including neonates
- Measures intrinsic elastic property of lung tissue.

$$\text{Specific compliance} = \frac{\text{Compliance}}{\text{FRC (in ml)}}$$

Factors Affecting Compliance

- Lung elastic recoil
  - Surface tension in alveoli
  - Stretched elastic fibres in lung parenchyma
- Lung volume
- Diseased states.

Variations in Compliance

- High compliance:
  - Emphysema
  - Asthma
  - Ageing.
- Low compliance:
  - Low static compliance
    - ARDS, Fibrosis
    - Tension pneumothorax
    - Pulmonary hypertension
    - Atelectasis
    - Retained Secretions
    - Obesity.

- Low dynamic compliance:
  - Bronchospasm
  - Kinking of ETT
  - Airway obstruction.

High Compliance

- Change in lung volume is large per unit change in pressure
- Exhalation is often inadequate due to lack of elastic recoil of lungs
- Related to conditions which increase patient's FRC
- Characteristics:
  - Obstructive lung defect
  - Chronic air trapping
  - Destruction of lung tissue
  - Enlargement of terminal and respiratory bronchioles
  - Reduced minute ventilation.

Low Compliance

- Change in volume is small per unit pressure change
- Work of breathing is high as lungs are stiff
- Low compliance causes refractory hypoxemia
- Condition compensated for by an increase in respiratory rate
- Characteristics:
  - Restrictive lung defect
  - Reduced lung volume
  - Reduced minute ventilation.

Compliance Curves

- Apices are well-inflated
- Midzone and base less inflated.

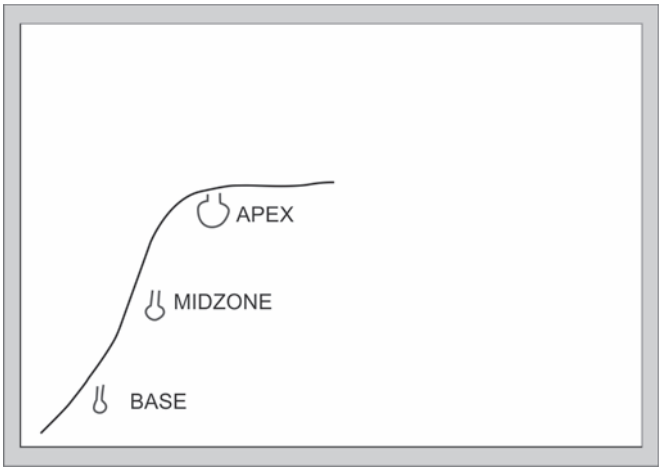


Fig. 2.24: Compliance curve[2]

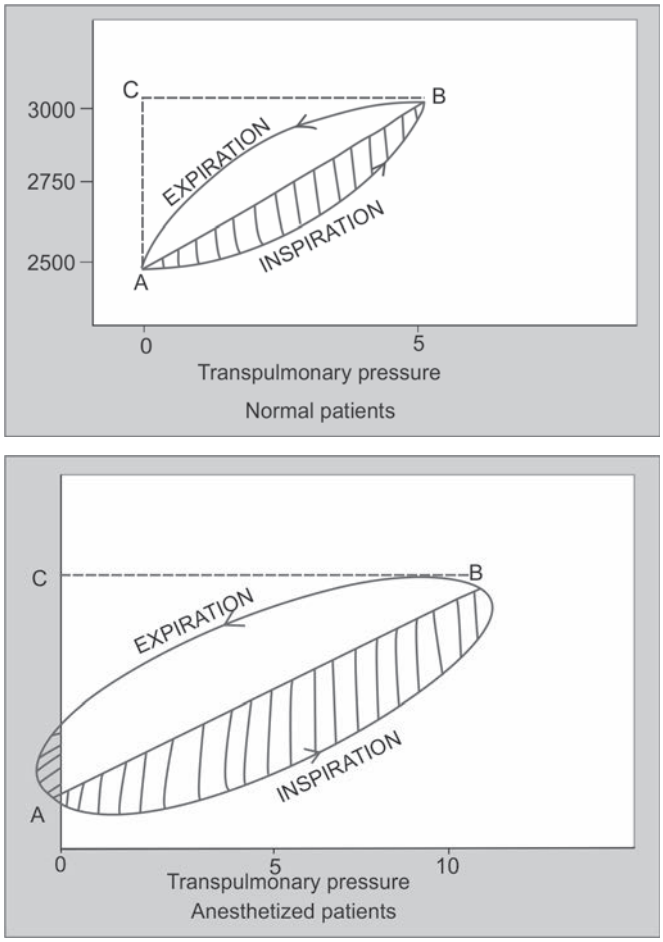


Fig. 2.25: Compliance curve in normal and anesthetized patients[3]

Clinical Implications

Work of Breathing

- Decrease in compliance indicates increase in Work Of Breathing (WOB)
- If P_{PEAK} and P_{PLAT} are constant, a decrease in compliance will cause reduction in tidal volume
- Thus, if patient cannot compensate for reduced compliance by increasing WOB, a reduction in tidal volume and hypoventilation results
- Thus, in low compliance states, a reduced tidal volume and fast respiratory rate occur.

Effects of Ventilation and Oxygenation

- Abnormal compliance may cause muscle fatigue, ventilatory and oxygenation failure
- Oxygenation failure occurs if lungs cannot supply oxygen needed for metabolism
- Ventilatory failure occurs when patient's minute volume cannot keep up CO_2 production.

Indicators of Compliance

Pressure-Volume Loop

- Line drawn from beginning point, dividing inspiratory and expiratory limb serves as the slope
- Shift in slope towards volume axis indicates increase in compliance
- Shift in slope towards pressure axis indicates low compliance
- Increased pressure (ΔP) is required to deliver the same tidal volume (ΔV).

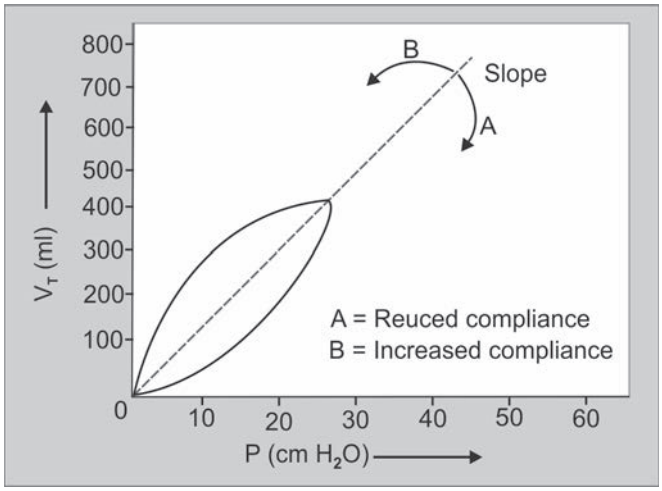


Fig. 2.26: Pressure-volume loop

Plateau and Peak Inspiratory Pressure

- Changes in plateau pressure:
  - Conditions which cause changes in plateau pressure cause similar changes in peak inspiratory pressure
  - For example, atelectasis causes increased P_{PLAT} and PIP
  - As P_{PLAT} and PIP are increased, static and dynamic compliance reduces
  - When atelectasis resolves, P_{PLAT} and PIP return to normal.
- Changes in peak inspiratory pressure:
  - In conditions where airway resistance is increased, PIP increases while P_{PLAT} remains unchanged
  - As PIP increases, dynamic compliance reduces
  - As P_{PLAT} remains unchanged, static compliance remains the same
  - When bronchospasm resolves, PIP and CDYN return to normal.

FLOW-VOLUME LOOPS[1,2,3]

Introduction

- Graphic analysis of gas flow rates at different lung volumes
- Lung volume plotted on X axis and flow rate on Y axis.

Procedure

Involves 4 phases of breathing into spirometer:

- Tidal breathing for several breaths
- Maximum inspiratory effort to TLC
- Maximum expiration to residual volume as forcefully and as quickly as possible
- Maximum inspiration to TLC.

Normal Curve

Ratio of inspiratory and expiratory flow rates at 50% Vital Capacity (V_{50}) = 1.

Parts of Curve

Effort Dependent: (Start of curve to V_{75})

- Ist part of expiration
- After approximately one-third of vital capacity
- Primarily due to subject's muscle effort rather than lung characteristics.

Effort Independent: (V_{75}–V_{25})

- Linear part of curve after one-third of expiration
- Increasing effort above certain flow will not cause further increase in flow
- Occurs due to dynamic compression of large airways.

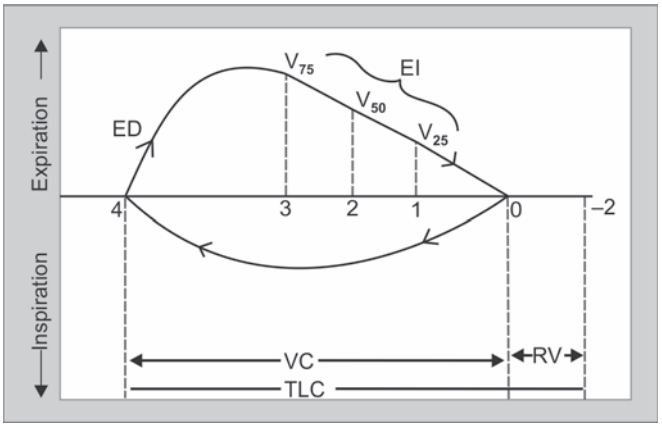


Fig. 2.27: Normal flow-volume loop[3]

Large Airway Obstruction

Fixed Obstruction[3]

- Can be intrathoracic or extrathoracic
- Examples:
  - Goitre
  - Tracheal stricture following tracheostomy
  - Tumors.
- No significant change in obstruction during inspiration/expiration
- Mid-VC ratio is 1 as both flow rates are reduced to same extent
- Curve is flattened during both inspiration and expiration
- E/I = 1.

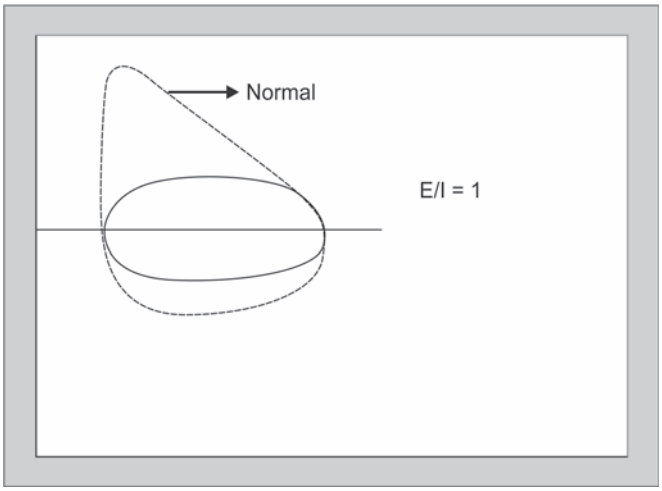


Fig. 2.28: Flow-volume loop in fixed large airway obstruction

Variable Extrathoracic[3]

- ***E***xpiratory flow ***N***ormal in ***E***xtrathoracic
- Examples:
  - Vocal cord palsies
  - OSAS
  - Pharyngeal muscle weakness
  - Neuromuscular disorders
- Expiratory flow is normal while inspiratory flow reduces
- Expiration normal as obstruction is pushed out by force of expiration
- During inspiration, obstruction is sucked into trachea
- Partial obstruction occurs causing flattening of inspiratory limb
- E/I >1.

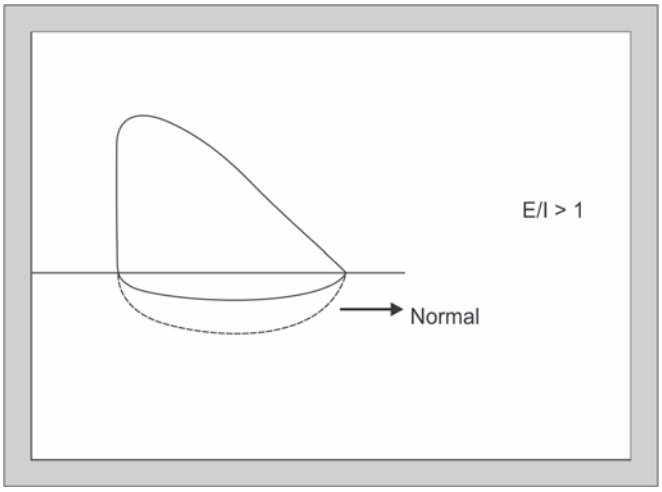


Fig. 2.29: Flow-volume loop in variable extrathoracic obstruction

Variable Intrathoracic[3]

- ***I***nspiratory limb is ***N***ormal in ***I***ntrathoracic
- Examples:
  - Tumors of trachea and bronchii during forced expiration.
- Tumor sucked outwards during inspiration
- Normal morphology of inspiratory limb of loop
- During expiration, tumor pushed into trachea causing partial obstruction
- Flattening of expiratory part of limb
- E/I <1.

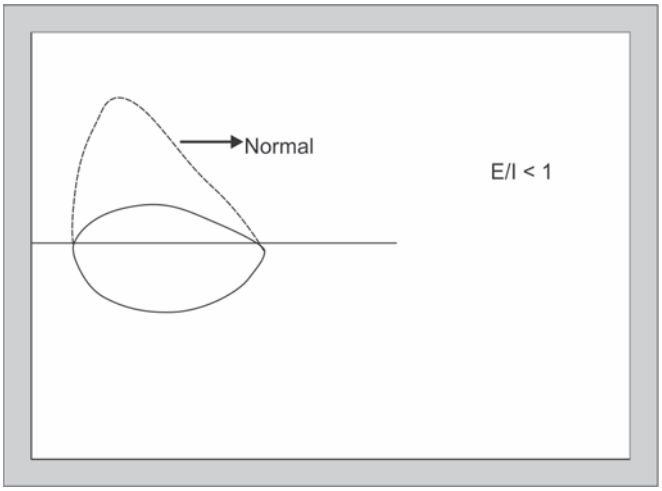


Fig. 2.30: Flow-volume loop in variable intrathoracic obstruction

Pulmonary Disease[3]

Obstructive Lung Disease

- Increased TLC
- Reduced peak expiratory flow rate

- Scalloping of expiratory limb of loop
- Curvilinear shape of expiratory limb with upward concavity
- Scalloping occurs when small airways start to close
- Flow rate reduced due to small airway obstruction
- Initial part of expiratory curve represents large airways which empty quicly without much obstruction.

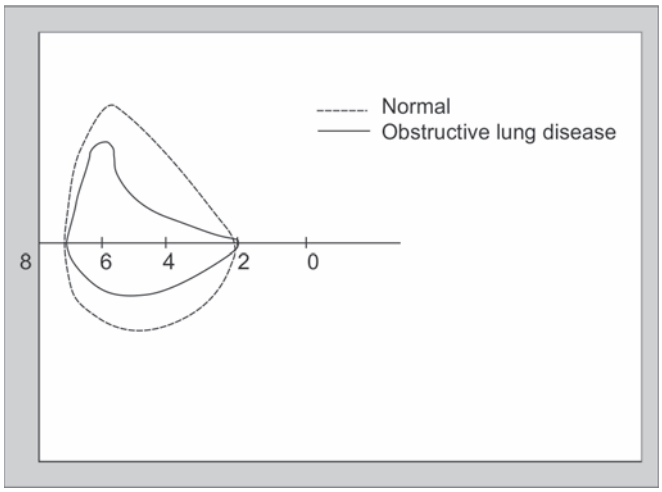


Fig. 2.31: Flow-volume loop in obstructive lung disease

Restrictive Lung Disease

- Reduced TLC
- $FEF_{25-75\%}$ is normal as no obstruction
- Flow volume loop is normal
- Reduced lung volume and peak flow rate.

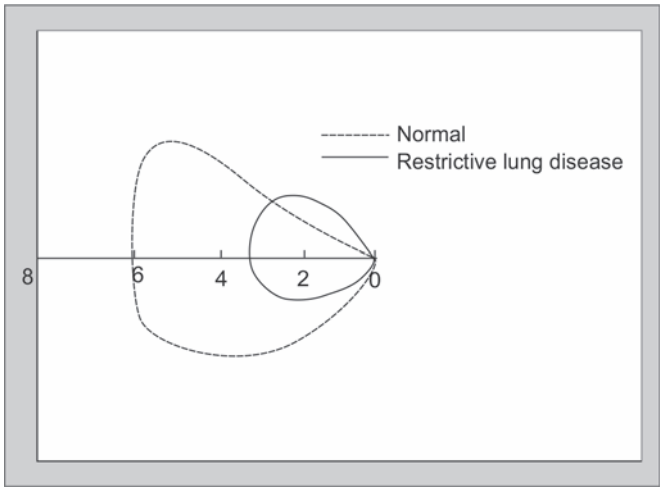


Fig. 2.32: Flow-volume loop in restrictive lung disease

Mixed Lung Disease

- Features of both OLD and RLD

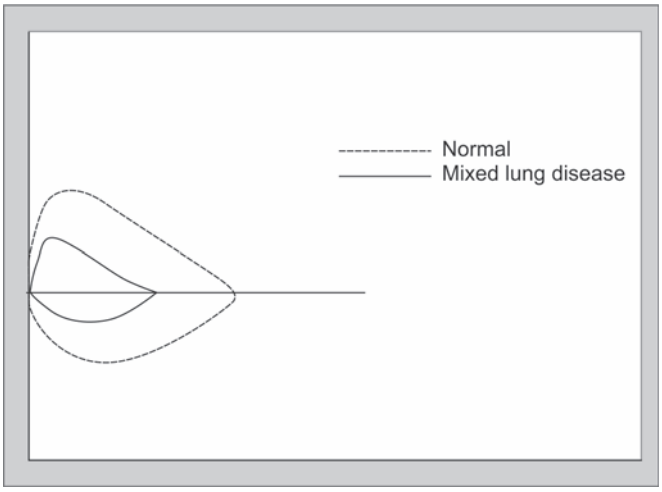


Fig. 2.33: Flow-volume loop in mixed lung disease

HYPOXIC PULMONARY VASOCONSTRICTION (HPV)[1,2,3,11]

Introductions

Auto-regulatory mechanism which aims at reducing blood flow in hypoxic lung regions.

Stimulus

- Partial pressure of oxygen in alveoli:
  - Partial pressure of O_2 in alveoli is the strongest stimulus
  - Reduction in P_AO_2 stimulates precapillary vasoconstriction
  - Partial pressure of O_2 at hypoxic site {$PSO_2 = P_AO_2 - P_vO_2$} triggers HPV
  - This occurs when $P_AO_2 < 100$ mm Hg.
- P_vO_2: Stimulus for HPV in areas of atelectasis
- Size of hypoxic segment: Smaller the hypoxic region, stronger the HPV.

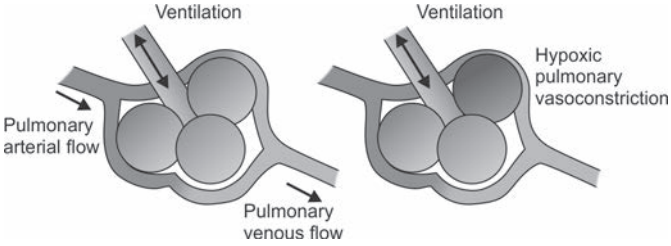


Fig. 2.34: Hypoxic pulmonary vasoconstriction

Mechanisms of Hypoxic Pulmonary Vasoconstriction

- Vasoconstrictor substances:
  - Released on occurrence of hypoxia
  - Leukotrienes are most probable mechanism

  - Others are:
    - Prostaglandins
    - Histamine
    - Catecholamines
    - Angiotensin
    - Serotonin
    - Bradykinin.
- Direct action: Direct vasoconstrictor action of hypoxia on pulmonary vascular smooth muscle
- Nitric oxide:
  - Hypoxia inhibits NO release from endothelium
  - This inhibits cycloxygenase synthesis causing vasoconstriction.

Characteristics

- Occurs when $P_AO_2 \leq 100$ mm Hg
- Maximal at $P_AO_2 \leq 30$ mm Hg
- Reduces blood flow to nonventilated lung by around 50%
- Rapid onset over first 30 minutes
- Slowly increases to maximum response at around 2 hrs
- Response to second hypoxic challenge will be greater than the first challenge: preconditioning occurs.

Determinants of Hypoxic Pulmonary Vasoconstriction[1]

- Distribution of hypoxia: Hypoxia at sublobular level may induce collateral ventilation initially and HPV later on
- V/Q ratio: HPV reduces blood flow in low V/Q areas
- Mixed venous oxygen tension: high or low M_vO_2 inhibits HPV
- FiO_2: Low FiO_2 causes HPV in normal lung
- Alveolar CO_2 (P_ACO_2):
  - Hypocapnea inhibits HPV
  - Hypercapnea stimulates HPV.
- Acidosis increases HPV
- PEEP increases pulmonary vascular resistance and shunts blood to hypoxic lung
- High-frequency ventilation increases HPV in collapsed lung
- Vasodilators (NTG and SNP) inhibit HPV
- Vasoconstrictors (adrenaline, phenylephrine) inhibit HPV
- Volatile anesthetics: inhibit HPV
- Pulmonary vascular pressure:
  - HPV occurs only if PVR is normal
  - HPV inhibited if low/high PVR
- Infection: Pneumococcus inhibits HPV by causing atelectasis.

Effects of Hypoxic Pulmonary Vasoconstriction

- Redistributes pulmonary blood flow from hypoxic to ventilated lung
- Maintains PaO_2 by reducing shunt flow through hypoxic lung
- Reduces shunt flow by almost 10–20%.

DEADSPACE/WASTED VENTILATION[1,2,3,9]

Introduction

- Deadspace is the amount of air inhaled by the patient which does not take part in gaseous exchange
- Dead space ventilation is the condition when ventilation is in excess of perfusion.

Types

- Anatomic dead space
- Alveolar dead space
- Physiological dead space.

Anatomical Dead Space[9]

Introduction

It is the volume of air present in conducting airways, which does not take part in gaseous exchange.

Normal Value

- Around 1 ml/lb or 2 ml/kg of ideal body weight
- For a tidal volume of 500 ml, around 150 ml volume is anatomical dead space.

Example

- Reduction in V_T causes a higher anatomic dead space to V_T percent
- If V_T is reduced from 500 to 300 ml, Dead Space (DS) to TV percent would increase from 30% (150/500) to 50% (150/300).

Alveolar Dead Space[9]

Introduction

Normal lung volume which is unable to take part in gaseous exchange due to reduction or lack of pulmonary perfusion (e.g. pulmonary embolism).

Explanation

- Occurs when ventilated alveoli are not perfused by pulmonary circulation

- Occurs due to:
  - Reduced perfusion: Low cardiac output:
    - Congestive cardiac failure
    - Blood loss.
  - Obstruction of pulmonary blood vessels:
    - Vasoconstriction
    - Embolism.

Physiological Dead Space[9]

Introduction

This is sum of anatomical and alveolar dead space.

Measurement

Physiological DS to TV ratio (V_D/V_T) is calculated as:

$$\frac{V_D}{V_T} = \frac{PaCO_2 - P_ECO_2}{PaCO_2}$$

- Where $PaCO_2$ is arterial CO_2 and P_ECO_2 is PCO_2 of mixed expired gas sample collected simultaneously
- V_D/V_T less than 60% predicts weaning success.

Explanation

- Normally, physiological dead space approximates anatomic dead space
- In diseased state, when anatomical/alveolar DS is increased, physiological DS is always higher than anatomical DS.

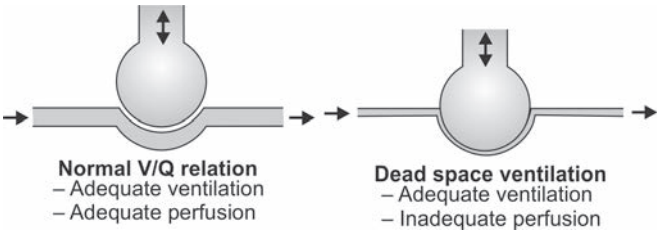


Fig. 2.35: Dead space ventilation[9]

Factors Increasing Physiological Dead Space

Type of change	Clinical condition
Low tidal volume	Relative increase in V_D/V_T : • Drug overdose • Neuromuscular disease
Increased alveolar dead space	Low cardiac output: 1. Congestive cardiac failure 2. Blood loss
	Obstruction of pulmonary blood vessels: 1. Pulmonary vasoconstriction 2. Pulmonary embolism

Causes of Wasted Ventilation

- Insufficient ventilation
- Muscle fatigue
- Ventilatory failure
- Oxygenation failure.

Measurement

- By N_2 washout or Fowler's method
- Total quantity of N_2 washed out of lungs by breathing in O_2 is measured
- Can be measured with single breath/multiple breaths
- Subject inhales 100% O_2 and exhales through one way valve measuring N_2 content
- Anatomical dead space first fills up with 100% oxygen
- On expiration, N_2 concentration starts at 0% and increases slowly.

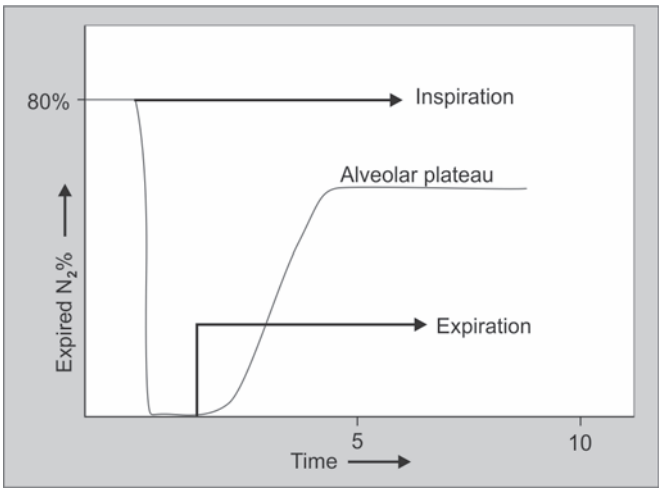


Fig. 2.36: Nitrogen washout technique

ALVEOLAR-ARTERIAL O_2 TENSION GRADIENT[9]

Introduction

It is the difference between measured pressure of O_2 in blood and calculated pressure of O_2 in alveolar sacs.

Calculation

I. $P(A–a)\ O_2$ = (calculated P_AO_2)–(measured PaO_2) = $P_AO_2 – PaO_2$

- $P(A–a)\ O_2$ = alveolar arterial O_2 tension gradient in mm Hg
- PAO_2 = alveolar O_2 tension in mm Hg
- PaO_2 = arterial oxygen tension in mm Hg

II. ***Alveolar gas equation:*** calculation of P_AO_2:

$$P_AO_2 = [P_B - P_{H_2O}\ FiO_2] - \frac{[PaCO_2]}{RQ}$$

P_B = Barometric pressure (760 mm Hg)

- P_{H_2O} = water vapour pressure (47 mm Hg)
- P_aCO_2 = arterial CO_2 tension
- RQ = respiratory quotient = 0.8.

Values

- Normal P(A–a) O_2 should be ≤ 10 mm Hg, but can range from 5–20 mm Hg
- Normal P(A–a) O_2 should be less than

$$\frac{[\text{patient's age}]}{4} + 4$$

- P(A–a) O_2 increases by 1 mm Hg every decade
- On IPPV, on 100% FiO_2, P(A–a)O_2 ≤ 350 mm Hg suggests strong likelihood of weaning success
- P(A–a) O_2 ≥ 350 mm Hg should be corrected prior to weaning trial
- On 100% O_2, every 50 mm Hg difference in P(A–a)O_2 approximates 2% physiological shunt.

Importance

- Used to estimate degree of hypoxemia:
  - P(A–a) O_2 ≤ 10 mm Hg = Normal
  - P(A–a) O_2 10–30 mm Hg = mild impairment of gas exchange
  - P(A–a) O_2 20–30 mm Hg = moderate impairment of gas exchange
  - P(A–a) O_2 ≥ 30 mm Hg = severe impairment of gas exchange
- Used to locate source of hypoxemia
- To estimate degree of physiological and right-left shunt
- To predict success of weaning.

Alterations in Alveolar-Arterial Gradient

- Physiological increase in P(A–a) O_2:
  - Old age
  - Obesity
  - Fasting
  - Supine patient
  - Heavy exercise.
- Hypoxemia with increase in P(A–a) O_2:
  - Arises from impaired gas exchange across alveolar membrane
  - Diffusion defects
  - V/Q mismatch
  - Shunting.
- Hypoxemia with normal P(A–a) O_2:
  - Occurs when gas exchange across alveolar membrane is normal, i.e. due to extrapulmonary causes
  - Alveolar hypoventilation
  - Low FiO_2 < 21%.

INTRAOPERATIVE BRONCHOSPASM[1,2,3]

Introduction

Bronchospasm is an abnormal contraction of the smooth muscle of bronchi, resulting in acute narrowing and obstruction of the respiratory airway.

Etiology: According to cause:

Respiratory Causes

- Upper airway:
  - Tumors of pharynx and larynx
  - Tracheomalacia
  - Laryngeal edema/infection
  - Foreign body.
- Lower airway:
  - COPD
  - Bronchial asthma
  - Bronchitis
  - Bronchiectasis
  - Cystic fibrosis.
- Pulmonary:
  - Infection
  - Pulmonary edema
  - Pneumonia.

Mechanical Irritation

- Airway manipulation
- Endotracheal intubation
- Endobronchial intubation
- Secretions in large airway
- Aspiration of gastric contents.

Drugs

- Anesthetics:
  - Desflurane in smokers
  - Isoflurane inhalation induction.
- Others:
  - Morphine
  - Mivacurium, atracurium, rapacuronium, doxacurium
  - Beta blockers
  - Aspirin, NSAIDs

- Cholinesterase inhibitors: neostigmine
- Atropine > 1 mg
- Glycopyrrolate > 0.5 mg.

Allergy

- Allergens, latex allergy, anaphylaxis
- Drugs:
  - Antibiotics
  - IV contrast
  - Transfusion reactions.

Others

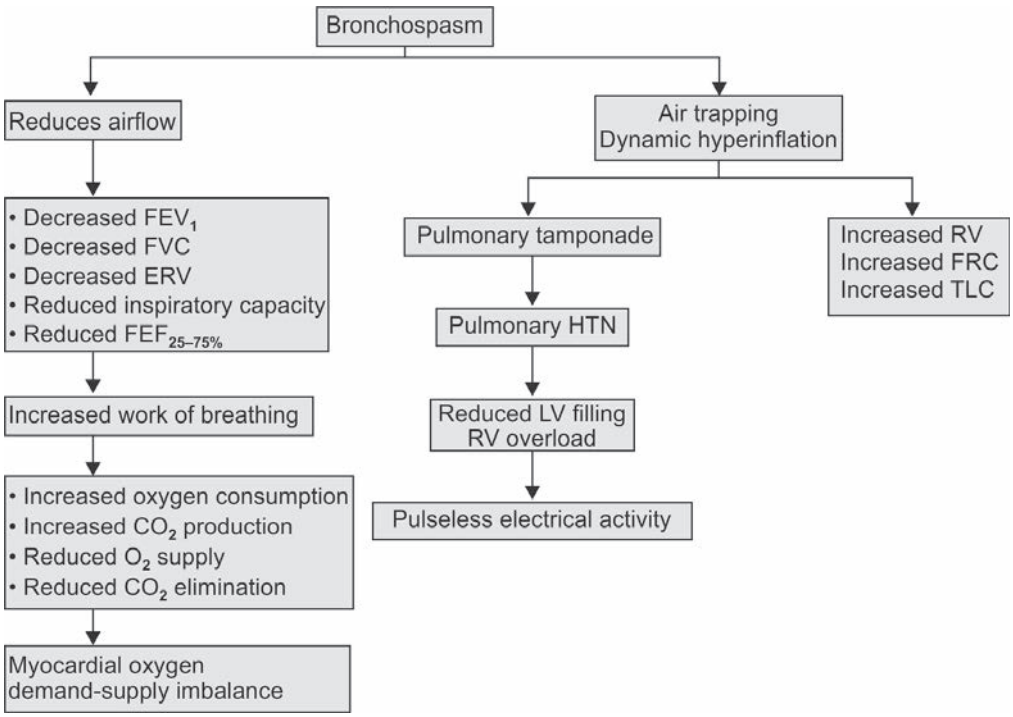
- Light anesthetic plane
- Distended urinary bladder
- Peritoneal retractions
- Smoke inhalation
- Carcinoid tumor.

Etiology

As per anesthetic stages:

- Causes during induction:
  - Airway irritation
  - Aspiration
  - Anaphylaxis
  - Pulmonary edema
  - Displaced ETT
  - Unknown.
- Causes during maintenance: *most common:*
  - Anaphylaxis
  - Aspiration
  - Airway irritation
  - Pneumothorax
  - Endobronchial intubation
  - Pulmonary edema
  - Drug-induced:
    - Vancomycin
    - Protamine.
- Causes at extubation:
  - Airway irritation
  - Extubation spasm
  - Pulmonary edema
  - Aspiration
  - Anaphylaxis/allergy
  - Accidental extubation.

Pathophysiology[3]



Clinical Features

- Signs and symptoms:
  - Reduced chest excursion
  - Coughing
  - Reduced breath sounds
  - Prolonged expiratory phase
  - Wheezing/rhonchi
  - ***Silent chest***: critically reduced air entry.
- Monitors:
  - Hypoxia, hypercarbia
  - Reduced phase II slope on capnograph
  - Reduced compliance of reservoir bag
  - Reduced tidal volume
  - Increased peak inspiratory pressure.

Differential Diagnosis

- Causes of unilateral rhonchi:
  - Endobronchial intubation
  - Foreign body: dislodged tooth
  - Tension pneumothorax
  - Kinked endotracheal tube
  - Obstructed endotracheal tube (ETT)
  - Interstitial pulmonary edema.
- Causes of raised peak airway pressure:
  - Increased inspiratory flow rate
  - Excessive tidal volume
  - Increased intrapleural pressure
  - Coughing/bucking
  - Steep Trendelenburg position
  - Pleural effusion
  - Tension pneumothorax
  - Ascites
  - Abdominal gas insufflation/packs
  - Increased resistance in ETT: narrowing/kinking/secretions.

Prevention

- Bronchodilators and steroids before induction in susceptible patients
- Prefer LMAs over ETT
- Neostigmine for reversal of NMB may precipitate spasm
- Careful suctioning at emergence in deep planes
- Adequate analgesia at emergence
- Deep extubation preferred
- Postoperative period:
  - Adequate analgesia
  - Bronchodilator therapy
  - Incentive spirometry
  - Deep breathing exercises
  - Early mobilization

Treatment

- Monitors:
  - Pulse oximetry
  - E_TCO_2, ECG
  - NIBP, ABG
  - Peak inspiratory pressure
  - Frequent auscultation
  - Auscultate chest and respiratory limb of anesthesia circuit to confirm wheeze.
- Ventilation:
  - Turn to manual bag ventilation
  - Switch to 100% FiO_2
  - Heliox mixture with 21–30% O_2 (low viscocity of 0.52 kg/m^3).
- Deepen anesthetic plane:
  - Increase concentration of isoflurane/sevoflurane
  - Ketamine agent of choice for asthmatics
  - Propofol can also be used.
- β_2 agonists:
  - Through nebulization/MDI via airway adaptor
  - Salbutamol:
    - 2.5 mg via nebulisation
    - Repeated every 20 minutes for 3 times
    - Then given 2–4 hourly.
  - Terbutaline 0.25 mg S/C every 20 minutes for 3 doses
  - Albuterol, levalbuterol and pirbuterol are others.
- High-dose steroids:
  - IV methyl-prednisolone 125 mg bolus followed by 40–60 mg IV Q6H
  - IV hydrocortisone 200 mg Q4–6H
  - IV dexamethasone.
- Others:
  - Ipratropium bromide:
    - 0.5 mg through nebulization every 30 mins for 3 times
    - Followed by 2–4 hourly thereafter.
  - Epinephrine 0.3 ml of 1:1000 solution bolus followed by 0.5–2 mg/min infusion
  - $MgSO_4$ 1–2 gms IV
  - Aminophylline:
    - 5 mg/kg slow IV bolus
    - Followed by 5 mg/kg/hr infusion.
  - Racemic epinephrine nebulization.

INTRAOPERATIVE HYPERCARBIA[1,2,3]

Introduction

Hypercarbia exists when $PaCO_2 \geq 45$ mm Hg.

Etiology

Increased CO_2 Production

- Fever
- Sepsis
- Thyrotoxicosis
- Pheochromocytoma
- Malignant hyperthermia
- IV infusion of dextrose-containing solutions
- Total parenteral nutrition.

Impaired CO_2 Transport

- Reduced cardiac output
- Hypotension
- Hypovolemia
- Pulmonary embolism
- Occlusion of blood vessels: V/Q mismatch.

Impaired Ventilation

- Anesthesia-related: Respiratory muscle weakness due to:
  - Muscle relaxants
  - High spinal
  - Epidural
  - Phrenic nerve palsy due to peripheral nerve block
  - Depressants—Volatile agents/sedatives.
- Ventilator-related:
  - Disconnection/kinked ETT
  - Faulty inspiratory/expiratory valves
  - Exhausted soda-lime
  - Low tidal volume/respiratory rate
  - Spontaneous ventilation with low flow of gases
  - Leaks in breathing circuit.
- Pulmonary causes:
  - Atelectasis
  - Pulmonary embolism
  - Bronchospasm
  - Pneumothorax.
- Surgery-related:
  - Laparoscopic surgery with CO_2 insufflation
  - Upper abdominal surgeries: pain and reduced FRC
  - One lung ventilation associated surgeries.
- Respiratory tract infections:
  - Pneumonia
  - COPD
  - Pleural effusion.

Effects of Hypercarbia

Central Nervous System

- For each 1 mm Hg rise in $PaCO_2$, CBF increases by 1.8 ml/100 g/min
- Increased CO_2 crosses BBB causing:
  - Reduced pH of CSF
  - Vasodilation of cerebral blood vessels
  - Raised ICP
- $PaCO_2 \geq 90$ mm Hg reduces seizure threshold (***CO_2 narcosis***).

Respiratory System

- Hypercarbia increases pulmonary vascular resistance
- Potentiates hypoxic pulmonary vasoconstriction
- Maximal stimulation occurs at $PaCO_2$ around 100 mm Hg.

Cardiovascular

- Increases plasma epinephrine and norepinephrine
- Increases heart rate and BP
- Very high level causes hypotension and bradycardia.

Git and Renals

- Increases hepatic and portal venous blood flow
- Causes retention of HCO_{3-} in renal tubules
- Metabolic alkalosis: compensatory.

Metabolic Effects

Increases potassium leakage from cells into plasma.

Treatment

- Supportive:
  - Antibiotics for any pathological states/infections preoperatively
  - Avoid dextrose solutions if increased chances of hypercarbia
  - Treat hypotension and hypovolemia promptly.
- Anesthesia-related:
  - Titrate volatile anesthetics, NMBA and sedatives
  - Avoid high spinal/epidural
  - Caution during nerve block: ultrasound-guided blocks better
  - Use NM monitoring to avoid excess muscle relaxation
  - Give adequate dose of reversal
  - Adequate intraoperative analgesia to reduce BMR
  - Insufflation pressure kept at ≤ 20 mm Hg in laparoscopic surgeries.

- Ventilator-related:
  - Thorough machine check preoperatively
  - Correct kink/disconnection in ETT
  - Leaks in breathing circuit corrected
  - Increase FGF during spontaneous ventilation according to minimum volume needed
  - Adjust tidal volume and respiratory rate according to $PaCO_2/ETCO_2$
  - If soda lime exhausted, increase FGF and change to open circuit.
- Treat cause:
  - Pheochromocytoma: SNP/NTG/$MgSO_4$
  - Thyroid storm: Maintain HR < 90 bpm, esmolol, antithyroid medications
  - Malignant hyperthermia: Dantrolene
  - Pulmonary edema:
    - Diuretics
    - Positive pressure ventilation with PEEP.
  - Pneumothorax:
    - 14 gauge needle inserted in 2nd ICS, midclavicular line
    - ICD in 4th ICS, midaxillary line.
  - Air embolism:
    - 100% oxygen
    - Inotropes
    - Trendelenburg or Durant's position
    - Hyperbaric oxygen therapy.
  - Bronchospasm:
    - 100% oxygen
    - Deepen anesthetic plane
    - Salbutamol inhaled
    - IV aminophylline and hydrocortisone.

SURFACTANT THERAPY[9,10]

Introdcution

These are lipoprotein molecules secreted by the lungs which contain a polar and nonpolar portion, and maintain the stability of pulmonary tissue by reducing the surface tension of fluids lining the lung, thereby preventing atelectasis.

Structure

Has ***amphipathic*** structure with:

- Tail/hydrophobic group:
  - Can be linear/branched
  - Has little affinity for bulk solvent.
- Head/hydrophilic group:
  - Strong affinity for bulk solvent
  - Can be neutral/charged.

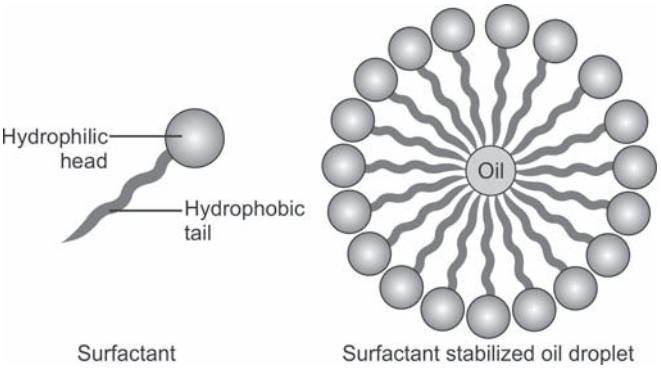


Fig. 2.37: Surfactant structure

Components

Naturally occurring surfactant contains:

- Phospholipid:
  - Makes up 90% of surfactant
  - Phosphatidyl-choline 85%
  - Remaining 15% contains:
    - Phosphatidyl-inositol
    - Phosphatidyl-glycerol.
  - 60% of phosphatidylcholine is dipalmitolyl-phosphatidyl-choline.
- Neutral lipids: Predominantly cholesterol
- Four types of proteins:
  - SP-A
  - SP-B
  - SP-C
  - SP-D.

Metabolism

- Synthesized by:
  - Type II alveolar epithelial cells
  - Airway epithelial cells
  - ***Clara cells.***
- Stored in lamellar bodies as closely packed bilayers which serve as intracellular store of surfactant
- Secreted into alveoli by exocytosis.

Functions

- Prevents end expiratory collapse of alveoli
- Regulates size of alveoli
- Increases pulmonary compliance
- Keeps alveoli dry
- Plays role in pulmonary host defence mechanisms.

Indications

AARC Clinical Practice Guidelines, 2013

Prophylactic Use

Infants at high risk for Respiratory Distress Syndrome (RDS) like:

- Gestational age ≤ 26 weeks
- Birth weight < 1250 grams
- Micropreemies:
  - < 30 weeks gestation
  - 500 gms–1 kg weight
- Congenital surfactant deficiency
- Pulmonary alveolar proteinosis
- $PaO_2/P_AO_2 < 0.22$.

Therapeutic Use

- Signs of RDS:
  - Grunting
  - Nasal flaring
  - Chest retraction
  - Cyanosis
- Positive chest X-ray for RDS (***bilateral ground glass appearance***)
- Increased oxygen requirements
- Increasing ventilatory requirements (from CPAP to invasive mechanical ventilation)
- Meconium aspiration syndrome
- Gestational age usually < 34 weeks
- $PaO_2/P_AO_2 < 0.22$.

Contraindications

AARC Clinical Practice Guidelines, 2013

- Congenital anomalies incompatible with life beyond the neonatal period
- Respiratory distress in infants with laboratory evidence of lung maturity
- Diagnosis of congenital diaphragmatic hernia: administration of surfactant may cause a clinical deterioration in infants with substantial pulmonary hypoplasia
- Hemodynamically unstable patient
- Active pulmonary hemorrhage.

Classification

Class	Origin	Example
Natural	Amniotic	• Human amniotic fluid • Surfactant
Modified natural	Bovine	• BLESS • Infasurf • Survanta • Alveofact
	Porcine	• Curosurf
Synthetic	Synthetic	• KL_4 surfactant
		• ALEC
		• Venticute
		• Exosurf

Dosage

Name	Feature	Doseage
Synthetic surfactants		
KL4 surfactant	With proteins	Not yet available
ALEC	With proteins	Not yet available
Venticute	With proteins	Not yet available
Exosurf	Without proteins	Prophylactic dose:
	Colfosceril palmitate	5 ml/kg Q12H for upto 3 total doses
		First dose within 15 mins of birth
		Rescue dose:
		5 ml/kg Q12H upto 2 total doses
Modified natural surfactants		
Infasurf	Bovine	3 ml/kg Q12H upto 3 doses
Survanta	Bovine	4 ml/kg Q6H upto 4 doses in first 48 hrs
	Beractant	
Curosurf	Porcine	Initial dose 2.5 ml/kg
		Up to two additional doses 1.25 ml/kg Q12H can be given

Complications

- Procedural complications resulting from the administration of surfactant:
  - Plugging of ETT by surfactant
  - Hemoglobin desaturation and increased need for supplemental O_2
  - Bradycardia due to hypoxia
  - Tachycardia due to agitation, with reflux of surfactant into the ETT
  - Pharyngeal deposition of surfactant
  - Administration of surfactant to only one lung (For example, with right mainstem intubation)
  - Administration of suboptimal dose.
- Physiologic complications of surfactant replacement therapy:
  - Apnea
  - Pulmonary hemorrhage
  - Marginal increase in retinopathy of prematurity
  - Volutrauma resulting from increase in lung compliance following surfactant replacement
  - Nosocomial infections.

Monitoring During Therapy

- Position of patient
- Oxygen saturation by pulse oximetry
- Blood pressure, heart rate, ECG

- FiO_2 and ventilator settings
- Breath sounds, chest-wall movement
- Proper placement and position of delivery device and ETT
- Pulmonary mechanics and tidal volumes
- Following administration, monitor:
  - Reflux of surfactant into ETT
  - Invasive and/or noninvasive measurements of arterial blood gases
  - Chest radiograph.

Modes of Administration

AARC Clinical Practice Guidelines, 2013

- Insure (Intubation, Surfactant, Extubation)
  - Early surfactant replacement therapy through ETT
  - Prompt extubation to nasal CPAP
  - Associated with:
    - Less need for mechanical ventilation
    - Lower incidence of bronchopulmonary dysplasia
    - Lesser air leak syndromes
    - Lesser mechanical ventilation
    - Extubation from lower ventilator settings.
- Selective surfactant replacement therapy:
  - Surfactant replaced through ETT
  - Patient is ventilated following replacement
  - Subsequently extubated from lower ventilator settings
  - This technique is initiated upon clinical evidence of RDS, such as:
    - Radiological findings
    - Increased FiO_2 requirement
    - Increased work of breathing.
- Pharyngeal instillation before first breath:
  - Done as soon as the infant's head appears on the perineum or at operative incision
  - The mother stops pushing
  - The pharynx and stomach are suctioned with a catheter
  - Surfactant solution is instilled into the posterior pharynx through a catheter
  - This is done without direct laryngoscopy
  - Infant is then stimulated to breathe as soon as the shoulders and rest of the body are delivered.
- Laryngeal mask airway (LMA) administration:
  - LMA requires less skill to place than traditional intubation with an ETT
  - Surfactant delivery can be accomplished sooner with LMA.
- Bronchoalveolar lavage:
  - Bronchoalveolar lavage with surfactant is another alternative
  - Surfactant lavage is a safe and effective alternative treatment for MAS
  - Synthetic surfactant lucinactant is used due to its properties to resist inactivation by plasma proteins and oxidants present in inflamed lungs.
- Aerosolized surfactant:
  - Aerosolized surfactant and nasal CPAP theoretically allow administration of surfactant without intubation
  - Ideal preparation, dose and route of delivery are still being researched
  - Distribution of intratracheally instilled surfactant has been largely determined by gravity and unaffected by the position of the chest
  - Therefore, leaving the chest in a horizontal position results in the most even distribution of surfactant to the lungs.

Outcome

- Surfactant replacement therapy helps to:
  - Reduce severity of RDS
  - Reduce pulmonary intestitial emphysema (PIE)
  - Improves lung function
  - Has beneficial long-term effects on airway resistance
  - Reduce pulmonary vascular resistance
  - Reduce severity of epithelial necrosis
  - Reduce incidence of bronchopulmonary dysplasia
  - Reduce incidence of intraventricular hemorrhage.
- Surfactant does not work on all patients though
- It dramatically reduces mortality rate in RDS
- No benefit, however, in adult ARDS
- Randomized trials failed to show any advantages between synthetic or natural surfactant
- Both have been found effective for treatment of RDS.

OXYGEN THERAPY[1,2,3,4,9,10]

Introduction

- Refers to the administration of oxygen as a therapeutic modality.

Physical Properties

- Colorless, odorless and tasteless
- Molecular weight 32

- Specific gravity 1.105
- Boiling point at 760 mm Hg = –183 °C
- Melting point – 218 °C
- Solubility in plasma @ 37 °C = 0.003 ml/100 ml blood/mm Hg PaO_2
- Solubility in water @ 37 °C = 2.4 ml/100 ml water
- Cannot be ignited but supports combustion
- Below –183 °C, it is transparent blue liquid and slightly heavier than water
- Critical temperature = –118 °C.

Preparation and Storage

- By fractional distillation of liquid air
- CO_2-removed air is used
- O_2 and N_2 separated using their boiling points
- Stored in liquid form in 1500 kg-capacity tanks
- Tanks insulated by vacuum shell
- Temperature maintained between –175 and 150 °C.

Cylinders

- Black with white shoulders in India
- Green in USA
- Pin index = 2, 5
- Capacity:
  - E cylinder = 660 L/1900 PSI
  - M cylinder = 3450 L/2200 PSI
  - H cylinder = 6900 L/2200 PSI
- Pressure at pipeline/circuit = 4 bar/60 PSI
- Pressure at pressure regulator = 400 KPa/60 PSI.

Indications

Hypoventilation

- Reduced central drive:
  - Anesthesia drug overdose
  - Inadequate NMBA reversal
  - Chest injuries
  - Cerebral injury.
- Peripheral causes:
  - Reduced diaphragmatic movement
  - Postoperative pain
  - Pulmonary embolism
  - Upper airway obstruction.

Intrapulmonary Shunt

- Pulmonary arteriovenous communication
- Congenital heart disease
- Endobronchial intubation
- COPD
- Atelectasis
- Airway obstruction
- Pneumothorax/hemothorax
- Secretions.

Wasted Ventilation

- Pulmonary embolism
- Pulmonary obstruction
- Pulmonary HTN
- Cardiac failure
- Shock.

Diffusion Defects

- Pulmonary edema
- Retained secretions.

Increased Demand

- Convulsions
- Postoperative shivering
- Hyperthermia.

Goals

- Increase oxygen content of blood
- Increase oxygen delivery to tissues
- Achieve $PaO_2 > 60$ mm Hg with $FiO_2 < 0.5$
- Achieve $SpO_2 > 90\%$ with $FiO_2 < 0.5$
- Decrease myocardial and respiratory workload.

Methods[4]

Low Flow/Variable Performance Equipment

- Nasal cannula
- Nasal catheter
- Facemask:
  - Simple facemask
  - Facemask with reservoir bag
  - Partial rebreathing
  - Non rebreathing.

High Flow/Fixed Performance Equipment

- Venturi mask
- Nebulizers
- Oxygen hood
- Hyperbaric oxygen.

Intravenous Oxygen Therapy

ECMO

S. No.	Low flow system	High flow system
1.	FiO_2 for given flow rate varies with RR and TV	Not influenced by tidal volume/resp rate
2.	Variable performance	Fixed performance

Contd..

Contd..

S. No.	Low flow system	High flow system
3.	FiO_2 not predictable	FiO_2 fixed and accurate
4.	FiO_2 depends on capacity of anatomical reservoir	Does not depend on capacity of reservoir
5.	FGF inadequate to meet total inspiratory flow	FGF is adequate
6.	Rebreathing occurs	No rebreathing
7.	Temperature of gas not controlled	Can be controlled
8.	Humidity of gas not controlled	Can be controlled
9.	Used in patients with stable breathing patterns:	In dyspneic patients :
	• Postoperative ward	• Postoperative ward
	• Anemic patients	• Anemic patients
10.	Examples:	Examples:
	• Nasal cannula	• Venturi mask
	• Nasal catheter	• Anesthetic bag and mask
	• Face mask	• Hyperbaric oxygen

Nasal Cannula[4]

Introduction

- Most widely used device.

Usage

- Prongs inserted 1 cm inside nares
- Continuous O_2 flow fills anatomical reservoir (50 ml)
- Reservoir empties into lungs with each inspiration
- Recommended flow rate = 1–6 L/min.

Delivered FiO_2

- Calculated using ***Sharpies and Harrisons*** formula:
- Reservoir O_2 + Nasal O_2 + Room air O_2 = Final O_2
- Precise FiO_2 cannot be calculated as air mixes with 100% O_2.

S. No	Flow rate	FiO_2
1.	1 liter	24%
2.	2 liters	28%
3.	3 liters	32%
4.	4 liters	36%
5.	5 liters	40%
6.	6 liters	44%

Indications

- Patients with low O_2 requirement
- Stable breathing pattern
- Home oxygen therapy.

Advantages

- Simple and cheap
- Comfortable for patients
- Well tolerated
- Can be worn during eating, drinking, etc.

Disadvantages

- Irritates nasal mucosa
- Drying of nasal cavity
- Unpredictable FiO_2.

Nasal Catheters[4]

Design

- Appears like suction catheter with multiple openings at distal end
- Sizes 8–14 Fr.

Use

- Tip of catheter to be inserted upto fold of soft palate
- Catheter slowly pulled back so that tip lies beyond posterior nares above uvula
- Has to be changed from 1 nostril to the other every 8 hrs
- Flow rates upto 3 L/min in conscious patients
- Flow rates upto 6L/min in unconscious patients
- Upto 40% FiO_2 delivered.

Advantages

- Gas flow does not impinge on one area of nostril due to multiple openings.

Disadvantages

- FiO_2 unpredictable
- Nasal irritation.

Nasal Mask[4]

Design

- Combination of nasal cannula and face mask
- Lower edge of masks flanges rest on upper lip, surrounding external nose
- FiO_2 similar to that obtained by nasal cannula.

Advantages

- Comfortable
- O_2 not jetted into nose like with nasal cannula
- No risk of sores on external nares on long-term use.

Simple Face Mask[4]

Introduction

- Simple transparent device
- ***Marcy Catteral*** mask.

Design

- O_2 flows into mask through tubing
- Exhaled gas leaves through holes on side of mask
- Minimum flow rate of 4L/min to avoid rebreathing
- Usually flow rate of 6–10 L/min.

FiO_2 : 35–65% depending on flow rate, ventilator pattern and mask size.

Disadvantages

- Has to be removed during eating, drinking, etc
- CO_2 can collect in mask and add to dead space if flow rate < 5L/min
- Flow rate > 10L/min vented out through openings and does not increase FiO_2.

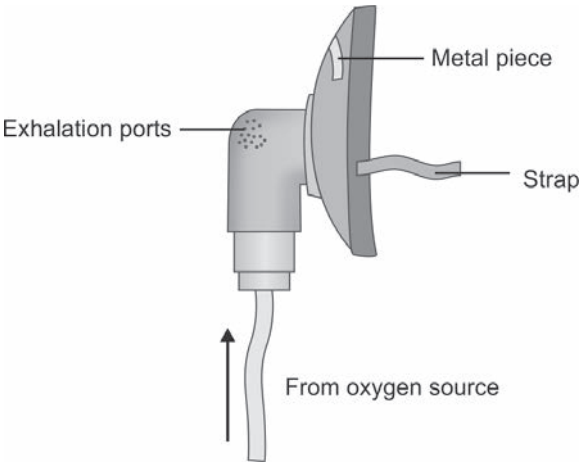


Fig. 2.38: Simple face mask

Partial Rebreathing Mask[4]

Design

- Combines facemask and collapsible O_2 reservoir bag
- O_2 flows continuously to the bag
- Inspired O_2 contains:
  - O_2 from reservoir bag
  - Air entrained through sideports
  - Air from space between mask and skin of face
- If O_2 flow rate adjusted to prevent collapse of the bag, minimal rebreathing occurs
- FiO_2 attained: 35–75% with flow rates 5–7 L/min.

Disadvantages

- Some amount of rebreathing still possible.

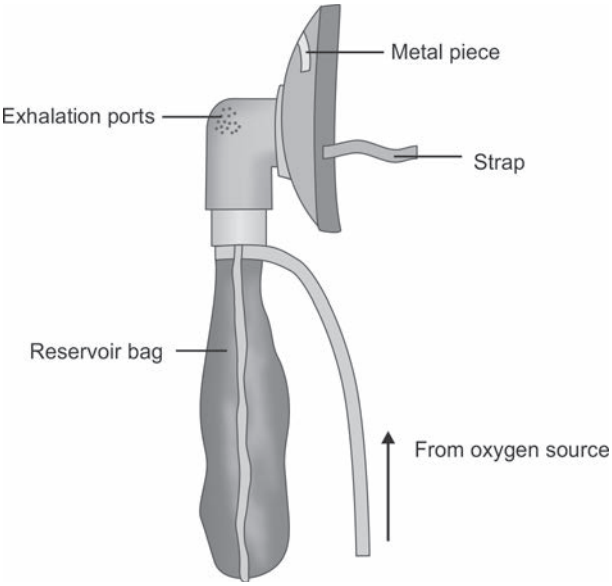


Fig. 2.39: Partial rebreathing mask

Nonrebreathing Mask[4]

Design

- Combines facemask with reservoir bag and unidirectional valve
- Valve prevents rebreathing
- Second valve seals side holes of mask during inhalation
- Flow rates of up to 6–10 L/min
- Reservoir bag volume = 750–1250 ml.

FiO_2: 60–80% but up to 95–100% achievable.

Indications

- When FiO_2 > 60% needed at low flows
- When patient needs NPPV but does not tolerate it
- Failed NPPV
- Patients with hypoxemia and spontaneous ventilation
  - Trauma
  - Poisoning
  - Myocardial infarction.

Advantages

- Higher FiO_2
- Low flow rates
- No rebreathing.

Disadvantages

- Needs airtight fitting
- To be removed during feeding
- Needs close observation.

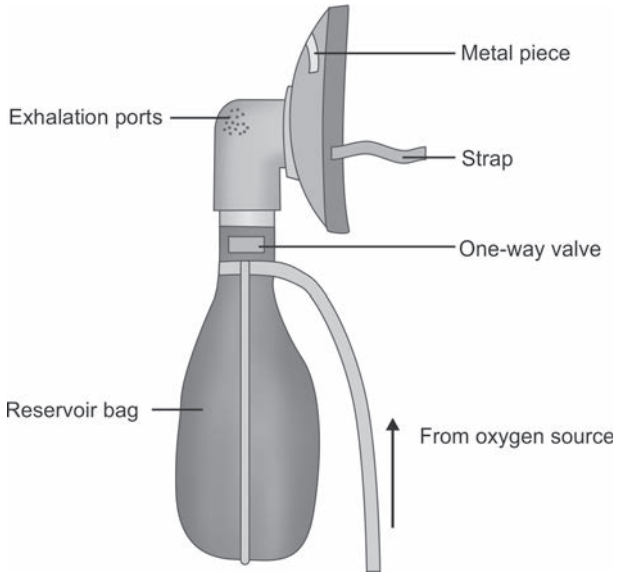


Fig. 2.40: Nonrebreathing mask

VENTURI MASK[1,3,4]

Introduction

- High airflow fixed performance oxygen enrichment device.

Principle

Venturi Principle

- Pressure of gas/liquid is inversely proportional to velocity in laminar flow
- If velocity of gas increases due to narrowing of tube diameter, pressure at narrow point must decrease
- If constriction is designed properly, gas from side branch can be entrained by mainstream.

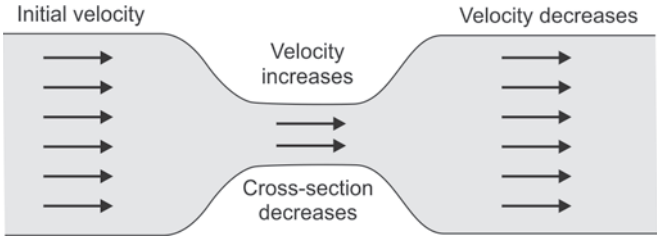


Fig 2.41: Venturi principle

Bernoullis Principle

- When stream of gas is pushed through narrow orifice, pressure on outside of stream falls

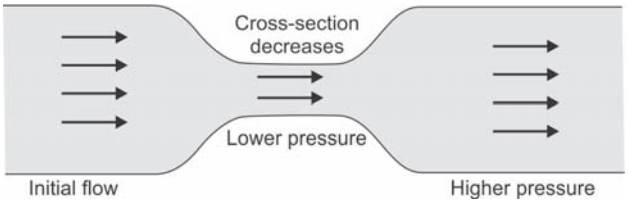


Fig. 2.42: Bernoullis principle[3]

Venturi Tube

- Has a constriction of suitable shape
- Distal limb has gradually increasing diameter
- Linear velocity of gas is same, proximal and distal to the constriction.

Design

- Specified flow of pure oxygen enters mask through narrow orifice
- Just past this orifice are openings for room air to enter and mix with oxygen
- Critical feature is size of opening through which oxygen enters base of mask
- At point A, 100% oxygen flows into wider point B through a narrowed orifice
- Oxygen velocity increases at the narrowing and hence, pressure drops
- Thus, room air is drawn through entrainment port, diluting oxygen
- FiO_2 can be calibrated by varying aperture controlled by colored nozzle.

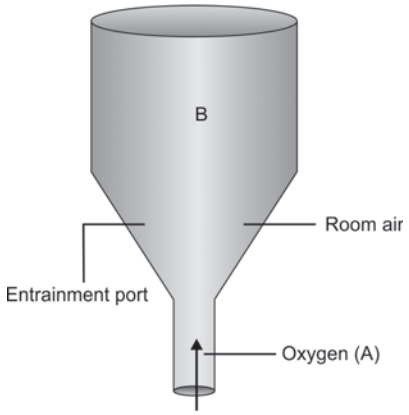


Fig. 2.43: Venturi mask principle

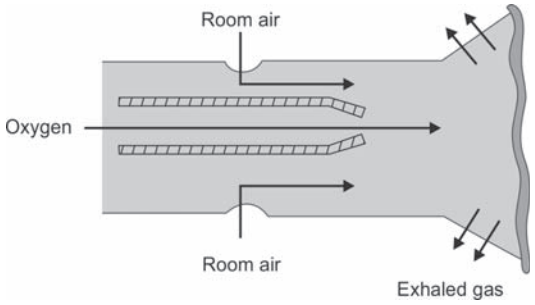


Fig. 2.44: Venturi mask design[9]

Indications
- Unstable respiratory pattern
- Inadequate ventilator efforts
- Increased pulmonary shunt—COPD, asthma
- Pulmonary edema
- Pulmonary consolidation
- ARDS.

Advantages
- No need of airtight fit
- FiO_2 predictable and accurate
- Fixed enrichment ratio independent of patient's ventilator pattern
- No apparatus dead space
- No rebreathing
- Easy to use
- Economical due to low oxygen flows.

Disadvantages
- Facial discomfort
- Cannot be worn during feeding, drinking, coughing, etc.
- FiO_2 can be increased if enrichment ports are obstructed by patient's hands or bedsheets.

FiO_2 Delivered[4]

S. No	O_2 flow rate	Total flow to patient	Color	FiO_2
1.	4 L/min	104 L/min	Blue	0.24
2.	4–6 L/min	44–66 L/min	White	0.28
3.	6–8 L/min	48–64 L/min		0.31
4.	8–10 L/min	48–60 L/min	Yellow	0.35
5.	10–12 L/min	32–48 L/min	Red	0.40
6.	12 L/min	33 L/min	Green	0.50

INTRAVENOUS OXYGEN THERAPY (IVOX)

Introduction
IVOX introduced by ***Regelsberger.***

Design
- Available in sizes 7–10 mm outer diameter
- Basic functional component is hollow fibers furled into a bundle
- Houses around 1000 fibers with numerous pores of 0.3 mm diameter
- 6 FDA–6 FAP membrane selectively permeable to gases covers the pores
- Lies freely inside the lumen of SVC/IVC without impairing the blood flow
- Pulsating balloon within the bundle directs the blood flow within
- Size selected by calculating venous size using Doppler USG.

Indications
- ARDS/ALI
- Acute respiratory failure
- Acute exacerbation of lung disease
- Patients awaiting lung transplants
- Lung surgery.

Contraindications
- Narrow vein size
- Left-sided SVC
- Absent/duplicate/hypoplastic IVC
- Peripheral vein thrombosis/infection
- Refractory cardiac failure
- Coagulopathies
- MODS.

Method of Insertion
- Obturator with J-tipped wire introduced into right femoral v/IJV
- Position checked with C-arm
- Device advanced to occupy the entire length of IVC and lower portion of SVC
- Device unfurled to lie within the lumen
- Blood shunts between the hollow fibers
- Bacterial filter connected to oxygen inlet
- Venotomy repaired
- 100% oxygen introduced through central conduit of coaxial tube
- Gases drawn along the length of fiber under subatmospheric pressure
- This negative pressure prevents gas embolization in the event fiber ruptures
- Can be used for upto 28 days without complications.

Complications
- Thrombocytopenia
- Blood loss
- Ipsilateral pedal edema
- Femoral vein thrombosis
- Limb ischemia.

Factors Affecting Performance
- Device surface area for gas exchange
- PaO_2
- PvO_2

- $PvCO_2$
- Cardiac output
- Duration of implantation.

Advantages
- Reduces pulmonary workload
- Permits reduction in ventilatory support
- Reduces airway pressure
- Prevents ventilator-induced cardiac derangements.

Disadvantages
- Supplies only 30–40% of total metabolic requirement of oxygen
- Limited gas transfer capability
- IVOX removed under propofol sedation under sterile conditions.

COMPLICATIONS OF OXYGEN THERAPY

Pulmonary

Progressive Hypercapnea

- Occurs if respiratory drive is dependent on hypoxic stimulus
- Inhaling high FiO_2 causes hypoventilation and hypercarbia
- Common in COPD patient (respiratory center insensitive to hypercarbic drive)
- Prevented by controlling FiO_2 to 24–30% in COPD patients.

Absorption Atelectasis

- Occurs when 100% oxygen administered in COPD
- O_2 displaces all the N_2 in airway
- O_2 has high solubility and thus gets absorbed
- O_2 remaining in airway gets fully absorbed causing alveolar collapse
- Changes occur within 6 minutes of 100% O_2.

Drying and Crusting of Secretions: Dry O_2 administration.

Nitrogen Narcosis: Hyperbaric O_2 therapy.

Cardiovascular
- Rare complication of cardiovascular depression
- Hyperbaric oxygen has direct myocardial depressant actions
- Especially in patients with increased sympathetic activity
- Sudden relief of hypoxia abolishes sympathetic overactivity
- Causes hypotension and circulatory collapse.

Others
- Fire hazard
- Depression of hematopoiesis
- Oxygen toxicity—free radical-mediated injury.

OXYGEN TOXICITY[1,3,10]

Introduction
- Results from overproduction of free radicals from oxygen molecule.

Molecules Formed
- Superoxide ions
- Hydrogen peroxide
- Singlet oxygen.

Structures Damaged
- DNA
- Lipids
- –SH-containing proteins.

Protective Enzymes
- Superoxide dismutase
- Catalase
- Antioxidants
- Free radical scavengers:
  - Glutathione peroxidase
  - Vitamins C and E
  - Acetyl cysteine
  - Mannitol.

Factors Affecting Toxicity
- Inspired oxygen concentration
- Time of exposure
- Humidity
- Circulating catecholamine levels
- Circulating corticosteroid levels
- Circulating endotoxins
- Leucocyte accumulation in lungs
- Drugs:
  - Bleomycin
  - Mitomycin C.

Measurement of Toxicity

Measured in Unit Pulmonary Toxic Dose (UPTD)

S. No.	UPTD	Change
1.	< 1425	10% fall in vital capacity
2.	> 2190	20% fall in vital capacity

Manifestations

- Pulmonary toxicity: ***Lorren-Smith*** effect
- CNS toxicity: ***Paul-Bert*** effect
- Retrolental fibroplasia in neonates (RFN)
- Retinopathy of prematurity (ROP).

Paul-Bert Effect

Mechanism

- Inactivation of –SH containing enzymes controlling GABA levels
- Occurs on exposure to oxygen at 2 ATM pressure
- Increased incidence with:
  - Acute hyperbaric oxygen administration
  - High-dose penicillin
  - Hypoglycemia and sepsis.

Clinical Features

- Twitching of periocular and perioral muscles
- Pupillary dilatation
- Visual dazzle
- Vertigo/nausea
- Numbness, seizures.

Treatment

- Gradual withdrawal of high-pressure oxygen
- Inhalation of room air
- Anticonvulsants: Phenytoin phenobarbitone barbiturates.

Lorren-Smith Effect

Mechanism

- P_AO_2 more important than P_aO_2
- Occurs when oxygen administration at pressures between 0.7 and 3 ATM
- Occurs after 30 hrs exposure to PiO_2 of 100 kPa
- Patient can tolerate 100% oxygen up to 10-12 hrs.

Pathophysiology

- Due to peroxidation of lipids-resulting lipid peroxides inhibit cell function
- Oxidation of –SH groups in essential enzymes
- Reversal and inhibition of electron transport chain
- Loss of pulmonary surfactant
- Absorption, collapse and alveolar edema.

Pathology

Exudative Phase

- Interstitial edema
- Destruction of type I pneumocytes.

Proliferative Phase

- Proliferation of type II pneumocytes
- Thickened blood air barrier
- Hyaline membrane formation.

Clinical Features

- Substernal discomfort
- Chest pain, cough—earliest signs
- Reduced vital capacity most sensitive indicator
- Respiratory rate, minute volume and compliance falls
- Frank ARDS.

Retrolental Fibroplasia

Etiology

- Due to oxygen-induced retinal vasoconstriction
- Occurs in premature infants with:
  - < 30 wks gestation
  - < 1200 gms birthweight
  - Exposure to high oxygen concentration, eg, 150mm Hg > 2 hrs
- PaO_2 < 140 mm Hg is safe.

Staging

S. No.	Stage	Changes
1.	I	Thin white line separates anterior avascular and posterior avascular parts of retina
2.	II	White line increases in volume and called Ridge
		5–10% progress to stage III
		80% regress to normal
3.	III	Tissue proliferates posteriorly from ridge
		Can be mild/moderate/severe
		Can regress by 6 months
4.	IVa	Partial retinal detachment with macula attached
		Macula gets detached
5.	V	Total retinal detachment

Prevention of Oxygen Toxicity

- Use lowest FiO_2 for shortest time
- Reduction of oxygen consumption
- Air breaks—intermittent air-breathing periods
- Early use of PEEP to reduce shunt
- –SH compounds, glutathione and cysteine
- Antioxidants—Vitamins C and E
- Maintain acid-base balance.

LARYNGOSPASM[1,2,3,10]

Introduction

It is an exaggerated glottic closure reflex which persists long after the removal of the stimulus.

Etiology

- More common after upper airway procedures, especially ENT surgeries
- More common in pediatric age group
- Intraoperative causes:
  - Respiratory tract infections, chronic smokers
  - Drugs: morphine, barbiturates: increase parasympathetic activity
  - Volatile anesthetics: ether > isoflurane > halothane > enflurane
  - Procedures:
    - Endoscopy
    - Esophagoscopy, upper abdominal manipulation.
  - Lighter planes with stimulation of visceral nerve endings in pelvis, abdomen, thorax, larynx
  - Presence of nasogastric tube
  - Local airway irritation, nasal irritation.
- Postoperative causes:
  - Immediate postoperative causes: extubation, especially after halothane anesthesia
  - Delayed postoperative causes:
    - Local airway irritation by:
      - Collected secretions, regurgitated gastric contents after bout of coughing
      - Silent regurgitation by the sides of nasogastric tube
      - Presence of oropharyngeal or nasopharyngeal airway.
    - Hypoxia producing vomiting and regurgitation
    - Epiglottitis.

Pathophysiology

Flow Chart (*see next page*).

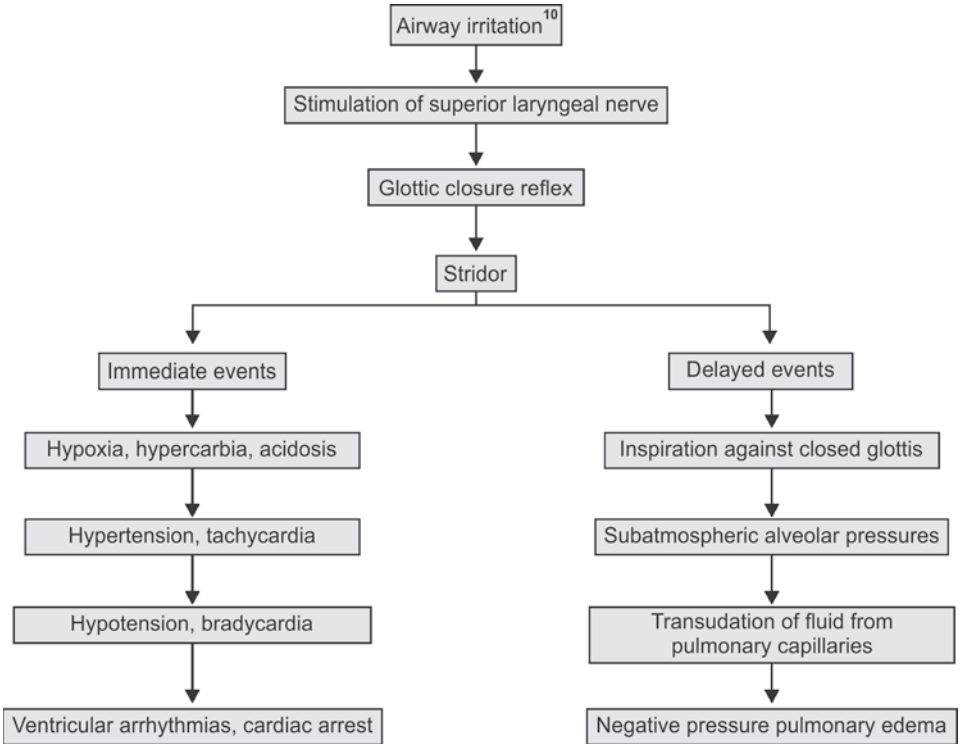
Clinical Features

- More common in children, especially after ENT surgeries
- Acutely dyspneic and tachypneic
- Intercostal and suprasternal notch indrawing
- Abdominal wall rises but chest sinks during inspiration and vice versa
- Stridor, tracheal tug and paradoxical respiratory movements as obstruction worsens
- On auscultation, inspiratory and expiratory sounds best heard with precordial stethoscope in children which ceases on complete obstruction (***silent chest***).

Management

Intraoperative Management

- Remove noxious and irritant stimulant:
  - Stop surgical stimulation of visceral nerve endings
  - Suctioning of larynx
  - Removal of artificial airway.
- Deepen anesthetic plane:
  - Intravenous propofol or other IV drugs preferred
  - 1–2 mg/kg propofol IV may be given
  - Caution while using volatile anesthetics as they may increase laryngospasm
  - Sevoflurane may be used: least irritant.
- Facilitate ventilation:
  - Gentle positive end expiratory pressure
  - Continuous positive airway pressure (CPAP) of 40 cm H_2O with 100% O_2 via tightly sealed face mask
  - Acts as pneumatic splint to break the spasm
  - Forcible jaw thrust with bilateral digital pressure on body of mandible just anterior to mastoid process: ***Laryngospasm point: Larson's maneuver***
  - If complete obstruction, avoid CPAP as stomach distension occurs.
- Heliox mixture:
  - Mixture of 70% helium and 30% oxygen
  - Turbulent airflow depends on gas density
  - Since helium makes gas mixture less dense, air flow is improved
  - Concentration of helium titrated according to hypoxia
  - Improved tidal volume and reduced airway resistance occurs.
- Racemic epinephrine:
  - 1 mg of 1:1000 solution in 5 ml of normal saline nebulized every 30 minutes
  - Droplet deposition on inflamed swollen mucosa causes intense vasoconstriction
  - This reduces cord edema.
- Steroids:
  - Dexamethasone 0.1 mg/kg IV Q6H
  - Takes 4–6 hrs to act.



- Succinylcholine:
  - If all maneuvers fail succinylcholine in a dose of 0.1–0.5 mg/kg IV used
  - IM dose: 4–5mg/kg
  - Intralingual/intraosseus routes also can be used.
- Deepen plane of anesthesia before resuming noxious stimulus
- If all these methods fail to relieve spasm, percutaneous airway should be considered
- Management of complications: Negative pressure pulmonary edema
  - 100% oxygen
  - Head end elevation
  - Positive airway pressure
  - Diuretics.

Postoperative Management

- Remove noxious stimuli:
  - Thorough oropharyngeal and nasopharyngeal suctioning before shifting to ward
  - Nasogastric tube aspiration at 1-hour intervals
  - Removal of airway.
- Facilitate ventilation:
  - Ensure proper oxygenation after extubation
  - Good topical anesthesia for larynx
  - Anesthetic plane cannot be deepened as it will delay extubation
  - Facilitate ventilation with CPAP and Larsons maneuver.
- Drugs:
  - Racemic epinephrine, steroids, heliox mixture
  - Succinylcholine if all other measures fail.
- Securing airway:
  - Reintubate patient if desaturation continues with standby expert
  - Forceful intubation against closed glottis not advised
  - Percutaneous airway preferred in such cases.

Prevention of Postextubation Laryngospasm

- IV lidocaine 1 mg/kg
- Topical lidocaine
- IV magnesium sulfate
- Deep extubation, lateral position
- Adequate suctioning before extubation.

Differential Diagnosis

If laryngospasm fails to resolve with all these maneuvers, think of other causes of postextubation stridor like:

- Laryngomalacia
- Tracheomalacia

- Vocal cord palsy
- Airway edema
- Hematoma
- Soft tissue obstruction
- Presence of foreign materials like packs.

INTERCOSTAL DRAIN[1,9,10]

Introduction

Thoracostomy tube connects intercostal space with drainage system for removal of air and fluid

Indicatons

- Large pneumothorax > 25%
  - Positive pressure ventilation
  - Ruptured bleb
  - Chest trauma
  - Bronchopleural fistula
  - Iatrogenic:
    - Thoracocentesis
    - Bronchoscopy
    - Transbronchial biopsy
    - CVP catheterization.
- Large pleural effusion
- Hemothorax
- Empyema thoracis
- Chylothorax.

Contraindications

No absolute contraindications

Relative contraindications:

- Insertion site infection
- Bleeding diathesis.

Complications

- Subcutaneous emphysema
- Hemorrhage
- Hematoma
- Blood clot inside ICD
- Infection
- Kinking of ICD preventing lung re-expansion
- Laceration of lung parenchyma
- Laceration of abdominal organs.

Chest Tube Size

- Neonates: 12–14 Fr
- Children: 18 Fr
- Small adults: 28–32 Fr
- Large adults: 36–40 Fr
- Large size tubes for hemothorax/chylothorax/empyema (28–40 Fr)
- Smaller size adequate for adult pneumothorax (16–20 Fr).

Site of Insertion

- Pneumothorax: II or III intercostal space anteriorly along MCL or MAL
- Pleural effusion: IV to VI ICS along MAL (usually a line lateral to nipple)
- Point of entry directly over body of rib to avoid injury to neurovascular bundle.

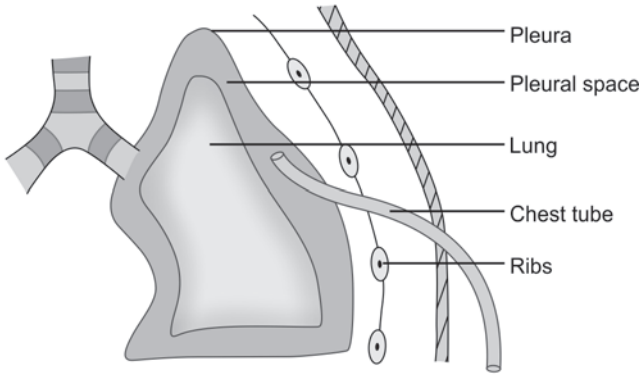


Fig. 2.45: ICD site of insertion[9]

Method of Placement

Operative Tube Thoracostomy

- Under strict asepsis
- Adequate LA infiloteration
- Incision above and parallel to rib
- Blunt dissection into pleura
- Finger inspection of pleural space
- Chest tube guided into space with finger and hemostat
- Safer than trocar method
- Finger inspection prevents placement of tube between parietal pleura and chest wall.

Trocar Tube Thoracostomy

- Under strict asepsis
- Adequate LA infilteration
- Incision above and parallel to rib
- Chest tube with trocar inside inserted into incision
- Inserted upto 1–2 cm to avoid puncture of lung
- Once inside space tube advanced over trocar
- ICD clamped before complete withdrawal of trocar
- Requires smaller incision
- Causes less pain and patient discomfort.

Drainage Systems

One-chamber System

- Chamber initially contains 100 ml sterile water
- Short air vent tube prevents pressure build-up inside chamber
- ***CREECH*** tubing submerged 2 cm inside water
- This acts as water seal
- Allows air to escape and prevents return.

Disadvantages

- Fluid accumulation causes more of Creech tubing to be submerged causing labored breathing
- Work of breathing proportional to depth of submersion of tube
- Kinking/obstruction of tube causes absence of bubbling (confused with clearance of pneumothorax).

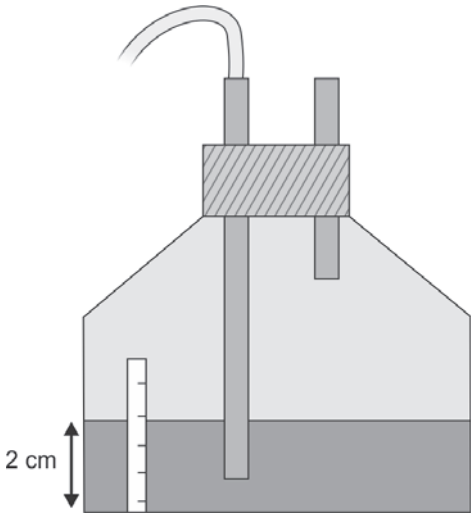


Fig. 2.46: One-chamber system[9]

Two-chamber System

Chamber 1:

- Collects pleural fluid/evacuates pleural air
- Amount of drainage measured from 1st bottle.

Chamber 2:

- Short tube allows air to escape and prevents pressure build-up
- Long tube submerged in 2 cm water.

Advantages

- Submersion depth of chamber 2 unchanged
- Work of breathing unaffected by volume of fluid collected in chamber 1.

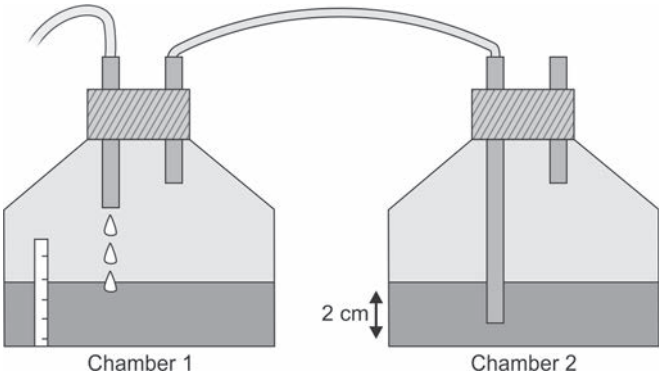


Fig. 2.47: Two-chamber system[9]

Three-chamber System

- Most commonly used
- Most versatile.

Chamber 1

- Collection chamber
- Collects pleural fluid from patient.

Chamber 2

- Water seal chamber
- Has 2 cm depth water in it
- Functions as water seal.

Chamber 3

- Suction chamber
- Regulates amount of suction in the system
- Water level in chamber regulates amount of suction
- Water level of 15 cm height attains suction of –15 cm H_2O
- –10 to –20 cm H_2O recommended
- Overfilling of water increases suction
- Underfilling reduces suction.

Working Principle

- Vacuum draws air into fluid through venting tube
- Causes constant bubbling effect
- Too much bubbling indicates high vacuum level
- Keep water in chamber 3 at appropriate level
- Evaporation lowers submersion depth.

Care of ICD

- Water level in chamber 2 and creech tube to vary with respiration
- If drainage holes on ICD become visible, reposition or reinsert immediately
- If ICD disconnected from patient:
  - Apply occlusive vaseline gauze over incision
  - Monitor for respiratory distress.

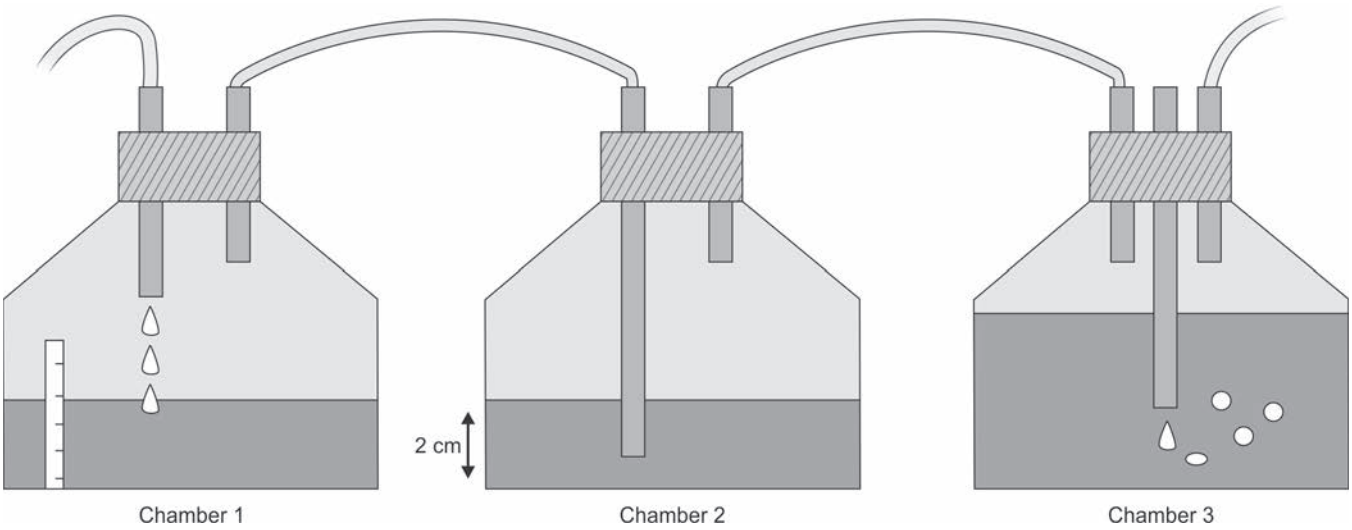


Fig. 2.48: Three-chamber system[9]

- If ICD disconnected from drain:
  - Clamp ICD for not more than 1 min
  - Reconnect to new drainage system.
- If excessive bubbling through chamber 2:
  - Maybe air leak in drainage system
  - Large pneumothorax.

Transport with ICD

- Oxygen source, emergency drugs and airway equipment to be ready
- Chest tube must be functional
- Ensure stable vital signs prior to transport
- Drainage system not to be dropped/tipped
- Drainage system to be lower than patient's chest at all times (else fluid may flow back into pleural cavity and cause infection)
- ICD not to be clamped at any time (may cause tension pneumothorax)
- ICD to be connected to water seal system during transport.

Removal of ICD

- Removed when:
  - Drainage has stopped
  - < 100 ml drain in 24 hrs
  - Pneumothorax has resolved with no air leak (bubbling in chamber)
  - No air leak on Valsalva/forceful cough.
- Procedure:
  - Suture removed
  - Valsalva maneuvre before pulling out ICD
  - Petroleum gauze and pressure dressing to opening immediately
  - Follow-up chest X-ray after 4 hrs.

CIGARETTE SMOKING[1,2,3]

Introduction

Smoking history is reported by the number of pack-years defined as average number of packs per day times the number of years smoked.

Effects of Smoking

Preoperative Effects

- Acute effects:
  - Carbon monoxide effects:
    - Normal COHb levels = 1%, 8–10% in smokers
    - Effects of carboxyhemoglobin:
      - Causes absolute reduction in blood oxygen content
      - Shift of oxyhemoglobin dissociation curve to left
      - Reduced delivery of oxygen to tissues.
  - Nicotinic effects:
    - Blood levels of nicotine ranges between 15–50 mg/ml
    - Induces hepatic enzymes
    - Stimulates sympathoadrenal system causing:
      - Raised epinephrine, norepinephrine levels
      - Raised cortisol levels.
- Chronic effects:
  - Respiratory system:

- Increased sputum production with reduced ciliary motility: Increased volume of sputum
- Increased synthesis of elastolytic enzymes from macrophages: COPD
- Increased airway reactivity: COPD
- Increased reactive oxygen metabolites: OH^-, peroxide radicals
- Immunoregulatory changes: Altered antigen presentation
- Increased epithelial permeability, changed pulmonary surfactant
- V/Q mismatch, gas trapping, increased dead space ventilation
- Inefficient carbon dioxide elimination, arterial hypoxemia
- Flattened diaphragmatic configuration and increased lung compliance: Limited elastic recoil

– Changes in pulmonary function:
- Increased minute ventilation: 1.5–2 times normal
- FEV_1 and VC may be normal
- FEV_1/VC and RV/TLC may be reduced
- Impaired diffusion capacity (due to CO).

– Cardiovascular system:
- Increased SBP and DBP
- Increased heart rate
- Increased myocardial oxygen demand
- Coronary vasospasm, variant angina and MI.

– Gastrointestinal system:
- Increased gastric volume
- Lax LES tone
- Increased chances of preoperative acid peptic disease
- Increased risk of aspiration.

Postoperative Effects

- Postoperative pulmonary function:
  – Primarily restrictive changes:
    - Proportional reduction in all lung volumes
    - No change in airway resistance
    - Severity is gauged by reduction in FRC
    - Reduced FRC due to abdominal contents impinging on and preventing movement of diaphragm
    - Rapid and shallow respiration occurs.
  – Operative site is *single most important determinant:*
    - Upper abdominal surgeries: 40–50% reduction in FRC
    - Lower abdominal and thoracic surgeries: 30% reduction in FRC
    - Intracranial, vascular ENT surgeries: 15–20% reduction in FRC.
  – After median sternotomy for cardiac surgery, low FRC for several weeks due to:
    - Widened mediastinum
    - Intrapleural fluid
    - Altered chest wall compliance.
- Postoperative pulmonary complications (PPC):
  – Mainly pneumonia and segmental atelectasis occurs
  – Sometimes ventilatory failure can occur
  – Most important postoperative pulmonary care is to ambulate the patient
  – Predictors of postoperative pulmonary complications:
    - Operative site
    - Operative duration: PPC increases for lasting more than 3 hours
    - Analgesic technique: PPC reduced by postoperative epidural analgesia
    - Associated comorbidities.
  – Operative site is important predictor of PPC:
    - Nonlaparoscopic upper abdominal surgeries increase risk of PPC at least 2 fold
    - Lesser risk for lower abdominal, thoracic and ENT surgeries.
  – Associated comorbidities:
    - Patients with COPD are at increased risk for PPC
    - Asthma does not increase risk of postoperative pneumonia and atelectasis but can be exacerbated.
- Postoperative Nausea and Vomiting (PONV):
  – Smokers have reduced risk of PONV
  – This is due to desensitization to nausea by low postoperative cerebral dopamine levels
  – This causes reduced stimulation of CTZ
  – Perioperative cessation of smoking thus causes reduced dopamine levels.

Preoperative Strategies

- Cessation of smoking:
  – Cessation ≥ 6 months prior to surgery equalizes risk for PPC to non-smokers
  – Cessation ≥ 8 weeks before surgery implies 4 times lesser risk of PPC because:
    - Normalization of mucociliary function occurs within 2–3 weeks of quitting smoking

- Normalization of carboxyhemoglobin levels occurs within 8–24 hours of quitting smoking.

– Smokers who reduce number of cigarettes but do not stop may still be taking same amount of nicotine through modifying smoking techniques: So no use.
– Effects of preoperative smoking cessation:
  - Reduced CO levels
  - Increased oxygen delivery
  - Reduced myocardial work
  - Reduced coronary vasoconstrictors
  - Improved exercise capacity
  - Improved mucociliary activity
  - Reduced airway reactivity
  - Improved pulmonary immune function
  - Better wound healing.

- Pharmacological adjuncts:
  – Adjuncts increase success of cessation of smoking
  – Adjuncts may increase risk of graft rejection
  – Various adjuncts available:
    - Nicotine chewing gum: 22 mg/day for person who smokes 1 pack/day
    - Nicotine nasal spray
    - Transdermal patch
    - Buproprion hydrochloride SR 100 mg Q12H started 1-2 weeks before cessation trial
    - Second line adjuncts: clonidine, nortriptiline, ***varenicline***.
- Other strategies:
  – Bronchodilation, chest physiotherapy, forced oral fluids
  – Deep breathing exercises, incentive spirometry
  – Stirup regimes are as effective as incentive spirometry
  – Intermittent CPAP mask:
    - Normally, FRC return to normal after upper abdominal surgery in 3–7 days
    - Use of CPAP mask reduces this duration to 72 hours.

S. No.	Time of cessation	Benefits
1	12–24 hrs before surgery	Reduced CO, nicotine levels
2	48–72 hrs before surgery	COHb levels normalized
		Improved ciliary function
3	1–2 weeks before surgery	Decreased sputum production
4	4–6 weeks before surgery	Improved PFTs
5	6–8 weeks before surgery	Immune function, metabolism normalizes
6	8–12 weeks before surgery	Reduced postoperative morbidity and mortality
		4 times reduced risk of PPC
7	> 6 months before surgery	Equal risk of PPC as non-smokers

CHRONIC OBSTRUCTIVE PULMONARY DISEASE[1,2,3,10]

Introduction

- COPD is a disease characterized by airflow limitations which is not fully reversible (less than 12% reversibility postbronchodilator therapy: ***GOLD definition***
- COPD includes 3 components:
  – *Chronic bronchitis:* Defined as productive cough on most days for 3 months duration for 2 consecutive years or recurrent excessive sputum which severely impairs expiratory flow
  – *Emphysema*: Anatomically defined as condition characterized by destruction and enlargement of airways distal to respiratory bronchioles (including respiratory bronchioles, alveolar ducts and alveoli)
  – *Small airway disease:* Chronic airflow obstruction within small bronchioles.

Etiology

- Smoking > 60 pack years associated with COPD, passive smoking
- Occupational exposure: Coal mining, cotton, textiles, dust
- Ambient air pollution:
  – M allele: Normal α_1 antitrypsin (AT) levels
  – S allele: Slightly reduced 1 antitrypsin levels
  – Z allele: Severely reduced 1 antitrypsin levels.
- Childhood respiratory tract infection
- Previous history of tuberculosis
- Poor socioeconomic status
- Malnutrition.

Pathophysiology

- Increased residual volume
- Reduced inspiratory capacity due to respiratory muscle shortening

- Flattened diaphragmatic configuration (which reduces efficiency with which diaphragm function)
- Barrel chest deformity
- Gas trapping.
- Increased lung compliance:
  - Causes limited elastic recoil
  - This prevents complete passive emptying
  - Thus patients forcefully exhale to reduce gas trapping.
- Chronic bronchitis:
  - Have increased $PaCO_2$
  - This causes raised bicarbonate levels in CSF
  - Medullary chemoreceptors become reset to higher blood levels of CO_2
  - Chemoreceptor sensitivity to CO_2 is reduced in such patients
  - Thus, they hypoventilate when given high oxygen concentration due to reduced hypoxic drive.

Clinical Features

Symptoms

- Episodic dyspnea/dyspnea on exertion (emphysema)
- Chronic, productive cough (chronic bronchitis)
- Orthopnea, wheezing
- Personal history of smoking and atopy
- Family history of allergies
- Past history of respiratory illness
- Sleep induced hypoxemia due to hypoventilation during REM sleep.

Signs

- Nasal polyps
- Rhonchi on auscultation
- Prolonged expiration lasting more than 6 seconds
- Early inspiratory/end inspiratory/expiratory crackles
- Reduced or absent breath sounds
- ***Barrel shaped chest***
- ***Tripod sign***:
  - Patient sits in tripod position
  - Done to facilitate use of sternocleidomastoid, scalenei and intercostal muscles.
- ***Hoovers sign***: paradoxical inward movement of ribcage with inspiration
- Signs of right heart failure:
  - Raised CVP
  - Hepatic congestion
  - Peripheral edema.

Collateral Ventilation in COPD[1]

- Refers to ventilation of alveolar structures through passages or channels which bypass normal airways
- Pathways for collateral ventilation are:
  - Interalveolar pores: ***Pores of Kahn***
  - Accessory bronchioles:
    - ***Channels of Lambert***
    - Alveolar passage.
  - Accessory respiratory bronchioles connecting bronchiole to bronchiole
  - Across fissures.
- In normal lungs, resistance to collateral flow is 50 times greater than resistance to flow in normal airways
- This resistance is markedly reduced in emphysema with low resistance collateral channels with pressure gradients across them
- This is proven by the fact that selective lobar intubation and ventilation does not lead to collapse of other lobes.

Investigations

- Bedside pulmonary function tests:
  - ***Sucrose breath holding*** more than 30 seconds
  - ***Match blowing test***
  - Limitation indicates limited cardiorespiratory reserve
- Complete blood count:
  - Leucocytosis due to infection
  - Polycythemia
  - Raised serum α_1–AT levels
  - COHb levels ≥ 8–10%.
- ECG:
  - RV strain pattern
  - R:S ratio > 1 in lead V1
  - Low voltage QRS
  - Poor R wave progression
  - P pulmonale in lead II: Indicates right atrial hypertrophy.
- Chest X-ray:
  - Normal lung fields in early COPD
  - Hyperinflation, increased vascular markings: chronic bronchitis
  - Hyperinflation, reduced vascular markings especially at lung base: Emphysema
  - Emphysematous bullae
  - Retrosternal air space more than 2 cm diameter in lateral chest X-ray
  - Consolidation if LRTI.

Characteristic	Cardiac dyspnea	Respiratory dyspnea
Onset	Dyspnea followed by cough	Cough followed by dyspnea
Predominant symptom	Dyspnea	Cough
Cardiac symptoms	Chest pain, palpitations, syncope	Rare
PND, orthopnea	*Pathognomonic*	Orthopnea may be present
		PND absent
Relieving factors	Diuretics and inotropes	Rest and bronchodilators

Feature[3]	Chronic bronchitis	Emphysema
Also called	Blue bloaters	Pink puffers
Characteristic	Combination of cyanosis and edema	Lack of cyanosis with pursed lip breathing
Pathophysiology	Mucus and inflammation	Loss of elastic recoil
	Thickening of bronchial wall	Destruction of lung parenchyma
Elastic recoil	Normal	Reduced
Airway resistance	Increased	Normal or slightly increased
Built	Often obese	Thin built, cachexic
Consciousness	Drowsy	Alert
Respiratory drive	Poor	Good
Dyspnea	Moderate	Severe
Cough	Frequent	With exertion
Sputum	Copious	Scanty
Respiratory failure	Early onset, Type II failure	Late onset, usually Type I failure
Hematocrit	Increased, polycythemia	Normal, normocythemia
PaO_2	Reduced	Reduced
$PaCO_2$	More than 40 mmHg	Usually normal, < 40 mm Hg
Spirometry	Moderate airway obstruction	Severe airway obstruction
Total lung capacity	Normal	Reduced
DLCO	Normal	Reduced
FEV_1	Reduced	Reduced
Cor pulmonale	Marked and early	Mild and late
Chest X-ray	Increased vascular markings	Hyperinflation
		Reduced pulmonary markings
CT scan	Normal	Emphysematous changes
Prognosis	Poor	Good
Anesthetic management	More complications	Less complications

- CT scan for emphysema
- ABG:
  - Hypoxemia with (A-a) O_2 gradient 10 mm Hg
  - Awake hypercapnea more than 45 mm Hg indicates increased risk of POPC.
- Spirometry:
  - If abnormal, indicates a 20–40% risk of POPC
  - No threshold value beyond which risk of surgery is prohibitive

- FVC: normal or slightly elevated
- FEV1: normal or slightly reduced
- FEV1/FVC reduced
- $FEF_{25–75\%}$:
  - Reduced to less than 70%
  - May be first and only abnormality.
- FRC: Normal or increased if gas trapping
- TLV: Normal or increased if gas trapping
- MV: 1.5–2.5 times normal.

  - Exercise testing $VO_{2(max)}$ < 1 Liter indicates 75% mortality risk
  - Bronchodilator therapy:
    - 15% improvement in PFT following bronchodilator therapy indicates positive response
    - Improvement indicates that this therapy should be started before surgery.
- Flow volume loops
- Echocardiography if pulmonary HTN or cor pulmonale
- Overnight oximetry/formal sleep studies if central apnea present.

Gold Classification of Severity: *Global initiative for COPD 2003 criteria*[1]

Severity	Clinical	FEV_1/FVC	FEV_1
At risk	Chronic cough	Normal	Normal
	Sputum production		
Mild	Chronic cough	< 0.7	> 80% predicted
	Sputum production		
Moderate	Chronic cough	< 0.7	50–80% predicted
	Sputum production		
Severe	Chronic respiratory failure	< 0.7	30–50% predicted
Very severe	PaO_2 < 60 mm Hg	< 0.7	< 30% predicted
	$PaCO_2$ > 50 mm Hg		< 50% predicted with respiratory failure

American Thoracic Society Classification of Severity

- Stage I:
  - FEV_1 more than 50% predicted (includes mild and moderate COPD)
  - No significant dyspnea, hypoxia or hypercarbia
- Stage II: FEV_1 between 35–50%
- Stage III: $FEV_1 \leq 35\%$
- Life expectancy ≤ 3 years in patients ≥ 60 years age with stage III COPD.

Predictive Factors for Perioperative Mortality and Morbidity

- Advanced age more than 60 years
- Inability to walk 500 feet in 6 minutes
- Inability to ascend 2 flights of stairs (12 steps per flight of stairs)
- Smoked > 40 pack years
- Morbid obesity
- Current respiratory symptoms
- PaO_2 < 50 mm Hg on room air
- $PaCO_2$ > 45 mm Hg
- Postoperative FEV1 < 40% of predicted normal
- FEV1 < 800 ml or $PaCO_2$ > 45 mm Hg indicates very high-risk of POPC
- Less than 15 ml/kg/min oxygen consumption on exercise testing (VO_{2max})
- Combined predicted FEV_1 and DLCO postoperatively < 35% of normal
- Serum albumin < 3.5 g/dl
- BUN > 0.3 mg/dl
- Emergency surgery
- Thoracic/upper abdominal surgery: 20–70% rate of occurrence of POPC
- Anesthetic/surgery duration > 3 hours
- General anesthesia > spinal anesthesia > epidural anesthesia.

POPC Risk Reduction Strategy[1,3]

Preoperative Strategies

- Smoking cessation atleast 8 weeks prior to surgery
- Treat evidence of expiratory airflow obstruction
- Treat RTI with antibiotics
- Lung volume expansion maneuvers
- Deep breathing exercises
- Incentive spirometry
- Chest physiotherapy
- Intermittent CPAP.

Intraoperative Strategies

- Minimal invasive techniques for surgery: Laparoscopy preferred
- Use regional anesthesia where possible
- Avoid long acting neuromuscular blockers
- Avoid prolonged surgery lasting more than 3 hrs.

Postoperative Strategies

- Lung expansion maneuvers
- Optimal analgesia
- Patient controlled analgesia
- Neuraxial opioids
- Regional techniques for analgesia
- Nerve blocks.

Choice of Anesthetic Technique

- Regional anesthesia preferred over general anesthesia

- Level restricted to T6 sensory level only as respiratory muscle dysfunction occurs above this
- Regional anesthesia preferred over GA as:
  - Avoids airway instrumentation
  - Better pain control which improves pulmonary function
  - Eliminates need for opioids
  - Reduces risk of DVT
  - Allows early mobilization: Reduces risk of POPC.
- Avoid use of histamine releasing agents:
  - Ester group of local anesthetics
  - Drugs with preservatives of amide group
- LMA preferred over ETT as it produces lesser degree of airway resistance.

Preoperative Patient Preparation and Premedication[1,2,3]

- Smoking cessation:
  - Cessation for more than 8 weeks reduces risk of POPC
  - Cessation for more than 4–8 weeks improves mucociliary clearance.
- Optimize dosage and continue use of bronchodilators:
  - Increase frequency of inhalers/nebulization to Q4H
  - β_2 agonists are ***drugs of choice***
  - Ipratropium bromide reported to produce more bronchodilation than β_2 agonists.
- Addition of bronchodilator therapy:
  - Added if 15% improvement in PFT after bronchodilator trial
  - Nebulization:
    - Salbutamol:
      - 0.5% respirator solution used
      - 0.5 ml salbutamol + 1.5 ml saline nebulized Q6H
      - Dose can be increased to 1 ml of salbutamol
      - Salbutamol respule 2.5 mg Q4–6H.
    - Ipratropium bromide:
      - Respirator solution used
      - 0.5 ml ipratropium + 1.5 ml saline Q4–6H
      - Ipravent respule 500 µg Q4–6H.
  - Inhalers:
    - Budesonide respule 0.5 mg or 1 mg Q12H
    - Salbutamol inhaler 2 puffs QID
    - Tiotropium bromide inhaler 2 puffs OD
    - Ipratropium bromide 2 puffs QID.
- Steroids:
  - Cause only 15–20% reduction in inflammation in COPD patients
  - Steroids given only if adequate response to bronchodilator therapy is not seen
  - Inhalational agents: Fluticasone/beclomethasone dipropionate/budesonide/mometasone
  - Short course of oral prednisolone 30–40 mg/day to be reduced in 7–10 days.
- Aminophylline:
  - 5–7 mg/kg IV over 20 minutes loading dose
  - Followed by 0.5–0.7 mg/kg/hr to maintain serum aminophylline levels of 5–20 µg/ml.
- Antibiotics:
  - Given preoperatively if active infection: amoxicillin with clavuronic acid 625 mg TID
  - Sepsis prophylaxis with appropriate antibiotics.
- Other drugs:
  - Acetylcysteine (mucolytic) and oral expectorants to patients with viscous secretions
  - Cromolyn sodium/nedocromil/roflumilast as oral anti-inflammatory agents
  - Caution with sedative drugs in patients with severe obstruction/hypercapnea
  - DVT prophylaxis (as polycythemia usually present).
- Lung expansion strategies:
  - Cough and deep breathing exercises
  - Incentive spirometry, stir up regimens
  - Intermittent CPAP
  - Postural drainage and chest percussion if secretory chest.
- Pulmonary rehabilitation:
  - Comprises of education in breathing exercises and nutrition
  - Done for 2–4 wks prior to surgery
  - Helps to reduce risk of POPC
  - Used for nonmalignant resection in patients with severe COPD.
- Adequate hydration:
  - Forced oral fluids more than 3 L/day
  - Prevents dehydration and drying up of secretions
- Correct conditions which contribute to respiratory muscle weakness:
  - Malnutrition
  - Electrolyte imbalance
  - Metabolic and endocrine disorders
- If COPD with cor pulmonale:

  - Inhaled NO with O_2 1 L/min can be used for 3 months
  - Portable inspiratory pulsing device used
  - This causes greater increase in pulmonary hemodynamics than oxygen alone
  - NO relieves pulmonary vasoconstriction and also increases blood supply to poorly ventilated areas
  - This causes reduction in PaO_2
  - Thus, NO should always be combined with low O_2 flows.
- Premedication:
  - Benzodiazepines
  - Antisialogogues:
  - Glycopyrrolate and ipratropium bromide used
  - Use is controversial as it may dry up secretions.

Induction

- Adequate preoxygenation as FRC may be increased
- Propofol (2 mg/kg), ketamine (1.5 mg/kg), etomidate or midazolam may be used
- Avoid long acting muscle relaxants: Vecuronium/rocuronium
- Avoid long acting opioids and NMB to prevent prolonged respiratory depression
- Opioids like fentanyl/pethidine/alfentanyl/remifentanyl preferred
- Avoid histamine releasers:
  - Morphine, pancuronium
  - Atracurium and cisatracurium, mivacurium.
- Prevent bronchospasm at intubation:
  - Deep planes at intubation
  - IV lidocaine 1.5–2 mg/kg 90 seconds prior to intubation
  - Local anesthetic spray on vocal cords may help.

Monitors

- Pulse oximetry:
  - Detects significant desaturation
  - PaO_2 is important to detect subtle changes in intrapulmonary shunting
- E_TCO_2, NIBP
- ECG: For arrhythmias/MI (due to hypercapnea)
- Baseline ABG:
  - Important as postoperative ventilation aims at keeping $PaCO_2$ at baseline levels
  - Increased $PaCO_2$-$ETCO_2$ gradient may be present.
- CVP may be used if RVF present but will not indicate intravascular volume in such cases
- Urine output, neuromuscular monitoring
- Temperature monitoring
- Precordial stethoscope.

Hemodynamics

- Adequate hydration important to prevent drying up of secretion.
- Judicious fluid therapy in patients with cor pulmonale
- Titrated to maintain urine output more than 0.5 ml/kg/hr.

Ventilation

- Avoid spontaneous ventilation as hypercapnea results
- Avoid hyperventilation:
  - Can cause prolonged apnea
  - CO_2 production reduces under GA due to low BMR
  - $PaCO_2$ levels as it is will be low under GA
  - Thus, CO_2 levels have to build up considerably before baseline $PaCO_2$ levels are reached to trigger ventilation
- Ventilatory settings:
  - $FiO_2 \geq 50\%$
  - Tidal volume 8–10 ml/kg
  - Respiratory rate 8–10/min: Allows enough time for expiration and also for venous return
  - Increased expiratory time
  - Avoid PEEP/sighs:
    - Adverse cardiovascular effects
    - Also, increased risk of bulla rupture.
  - Slow inspiratory flow rate preferred
  - Inspiratory flow rate and tidal volume adjusted to keep peak airway pressure < 40 cm H_2O
- Humidification of gases:
  - Important to prevent drying up of secretions
  - Especially useful if duration of surgery more than 2 hours
  - Done with HME filter.
- Goals of mechanical ventilation:
  - PaO_2: 60–100 mm Hg
  - $PaCO_2$ maintained at preoperative levels
  - pH 7.35–7.45.

Maintenance

- Nitrous oxide avoided as it may cause:
  - Expansion and rupture of bullae
  - Tension pneumothorax
  - Also aggravates pulmonary hypertension.

- Maintain with volatile anesthetics (isoflurane and sevoflurane preferred)
- Halothane sensitizes patients to catecholamines and is avoided in:
  - Patients with hypercarbia
  - Preoperative β_2 agonist and aminophylline therapy.
- Propofol based GA may be used
- Avoid long acting opioids and NMB (alfentanil/remifentanyl/vecuronium preferred).

Extubation

- Deep and early extubation after thorough suctioning as ET tube:
  - Increases airway resistance
  - Causes reflex bronchoconstriction
  - Reduced ability to clear secretions
  - Increases risk of iatrogenic infections.
- Reversal of NMB controversial as neostigmine may cause bronchoconstriction
- Recovery in sitting position improves FRC.

Intraoperative Complications

- Bronchospasm
- Deepen anesthetic plane and increase FiO_2:
  - Increase MAC of volatile anesthetic
  - IV ketamine supplementation
  - ETT suction, check for kinking/obstruction
  - Stop surgical stimulation
  - Nebulized β_2 agonists
  - Use ICU ventilators to control airway pressure.
- Rupture of bulla
- Pneumothorax: Needle in IInd ICS in mid-clavicular line
- Myocardial infarction: Due to comorbidities
- Arrhythmias: Due to hypercarbia
- Laryngospasm.

Postoperative Care

Complications

- Pneumonia
- Atelectasis
- Bronchospasm
- Prolonged mechanical ventilation
- Pneumothorax
- Prolonged bronchopleural fistula.

Postoperative Management

- Propped up recovery position: Improves FRC
- Oxygen to prevent postoperative hypoxia associated with reduction in FRC but $PaCO_2$ should be monitored
- Early mobilization is single most important aspect of pulmonary care
- Antibiotic prophylaxis
  - Salbutamol 2.5 mg nebulization QID
  - Ipratropuim 500 µg nebulization QID
  - Convert to inhalers atleast 24 hrs prior to discharge.
- Avoid smoking as it causes delayed wound healing and reduces resistance to infection
- Chest physiotherapy:
  - Lung expansion maneuvers
  - Stir up regimens
  - Incentive spirometry
  - Use of intermittent CPAP returns FRC to normal within 72 hrs
  - FRC returns to normal after 3–7 days if CPAP is not used.
- Administration of steroids after 3rd postoperative day does not delay wound healing.

Postoperative Ventilation

- May require postoperative ventilation especially in patients with $FEV_1 < 50\%$
- Mechanical ventilation in postoperative period on routine basis seldom beneficial
- Ventilatory goals:
  - Maintain preoperative $PaCO_2$ levels
  - Maintain normal pH
  - Gradual weaning of ventilator
  - T-piece trial beneficial prior to extubation
  - Use of bilevel nasal ventilation and BIPAP as weaning mode after extubation.

Monitors

- Pulse oximetry, NIBP
- Periodic ABGs especially in stage II and III patients
- Urine output, ECG.

Postoperative Analgesia

- Epidural/regional nerve blocks
- Morphine avoided
- Fentanyl, pethidine and tramadol can be used
- Avoid aspirin in asthmatic bronchitis.

ONE LUNG VENTILATION[1,2,3,11]

Introduction

First done in 1936 by ***Magill*** using a double lumen tube.

Goals of OLV

- Provide quiet field for performance of surgery
- Maintains adequate gas exchange:
  - Hemoglobin saturation ≥ 90%
  - $PaO_2 \geq 60$ mm Hg.
- Maximize pulmonary vascular resistance in non-ventilated lung
- Minimize pulmonary vascular resistance in ventilated lung
- Protect ventilated lung from over-distension injury:
  - Protective lung ventilation
  - Plateau airway pressure ≤ 25 cm H_2O
  - $PaCO_2$ around 35 ± 3 mm Hg
  - Tidal volume 6–8 ml/kg.

Indications: *Benumof Thoracic Anesthesia 1983*

Absolute Indications

- Isolation of lungs to prevent spillage/contamination:
  - Infection, abscess
  - Massive hemorrhage
  - Unilateral infected cyst/bulla.
- Surgical opening of major conductive airway
- Control of distribution of ventilation to one lung:
  - Bronchopleural Fistula (BPF)
  - Bronchopleuralcutaneous fistula
  - Unilateral cyst/bulla
  - Major disruption/trauma to bronchus
  - Unilateral bronchoalveolar lavage
  - Video assisted thoracoscopic surgery (VATS).

Relative Indications

- Surgical exposure: High priority:
  - Upper lobectomy
  - Pneumonectomy
  - Lung volume reduction surgery
  - Mimimally invasive cardiac surgery
  - Thoracic aortic aneurysm.
- Surgical exposure: Low priority:
  - Middle/lower lobe lobectomy
  - Thoracoscopy
  - Esophageal resection
  - Mediastinal mass resection
  - Thymectomy
  - Bilateral sympathectomy
  - Thoracic spine surgery.
- ***Differential lung ventilation*** in reperfusion injury:
  - After lung transplant
  - After unilateral pulmonary thromboembolectomy
  - Unilateral lung trauma.

Techniques of Lung Separation

Double Lumen Tube

- ***Carlens*** left sided DLT
- ***Whites*** right sided DLT
- ***Robertshaws*** left/right sided DLT
- ***Brice Smith*** left/right sided endobronchial tube
- Bronchocath-portex type DLT.

Single Lumen Tube with Endobronchial Blocker

- Modified SLT with enclosed BB:
  - Integrated Torque Control Blocker (***Univent)***
  - ***Fogarty*** arterial embolectomy catheter.
- Conventional SLT with enclosed BB:
  - Hybrid wire-guided BB (***Arndt Endobronchial System***)
  - ***Cohens*** tip deflecting endobronchial blocker
  - ***Fuji uniblocker.***

Single Lumen Endobronchial Tubes

- ***Gordon-Green*** (right side) with carinal hook
- ***Macintosh-Lothersdale*** (left side)
- ***Pallistor-Brompton*** triple cuff tube: Two bronchial and one tracheal cuff.

ETT Advanced into Bronchus

Anesthetic Management

Monitors

- Pulse oximetry: after initiation of OLV, PaO_2 falls for up to 45 minutes
- $ETCO_2$, shape of capnogram, differential capnography
- Peak airway pressure
- Pressure volume loop
- Actual tidal volume (VT) delivered: Measured with spirometer
- Frequent ABGs
- Ausculate dependent lung frequently
- DLT position checked once lateral position assumed.

Position

- Mostly lateral position
- In lateral position:
  - PaO_2 levels are better than supine position
  - Dead space and arterial $ETCO_2$ gradient increases
  - This requires a 20% increase in minute volume to maintain same $PaCO_2$.

Maintenance

- TIVA technique preferable to volatile anesthetics
- When MAC ≤ 1, volatile anesthetics inhibit hypoxic pulmonary vasoconstriction.

Techniques[3]

Technique	Advantages	Disadvantages
Double Lumen Tubes:		
Direct laryngoscopy	Quickest technique	Size selection difficult
Via tube exchanger	Placement possible without bronchoscopy	Difficult to use if difficult airway
Fibreoptically	Repositioning rarely required	Potential laryngeal trauma
	Bronchoscopy to isolated lung possible	Potential bronchial trauma
	Suction to isolated lung possible	Not optimal for postoperative ventilation
	CPAP can be easily added	
	Can alternate OLV to either lung easily	
Bronchial Blocker(BB):		
Arndts system	Size selection not an issue	More time required for positioning
Cohen blocker	Easily added to regular ETT	Repositioning required more often
Fuji uniblocker	Allows ventilation during placement	Bronchoscopy required for positioning
	Easier in difficult airway and children	Right lung isolation suboptimal
	Postoperative ventilation by removing BB	Bronchoscopy to isolated lung impossible
	Selective lobar isolation possible	Minimal suction to isolated lung
	CPAP to isolated lung possible	Difficult to alternate OLV to either lung
Univent	Same as bronchial blocker	Same as for BB
	Less repositioning compared to BB	
Endobronchial tube	Like regular ETT	Bronchoscopy necessary for placement
	Easier use in difficult airway	Does not allow suction to isolated lung
	Longer than regular ETT	Difficult right lung OLV
	Short cuff for lung isolation	
	Indicated in difficult airway	
ETT in bronchus	Easier in difficult airway	Does not allow suction to isolated lung
		Cuff not designed for lung isolation
		Difficult right lung OLV

Hemodynamics

- Limit fluid administration
- Avoid fluid overload
- Resume two lung ventilation if:
  - Hypotension
  - Tachycardia
  - Dusky complexion.
- Arrhythmias and hypotension common during left thoracotomy due to pericardial manipulation
- Keep cardiotonic drugs ready.

Ventilation

- Mode of ventilation:
  - Volume controlled/pressure controlled ventilation recommended
  - Pressure controlled ventilation indicated in:
    - Patients at high-risk of Acute Lung Injury (ALI)
    - Bullae, pneumonectomy
    - Post lung transplantation.
- Fraction of inspired oxygen:
  - FiO_2 of 0.95-1 recommended
  - FiO_2 of 0.95 reduces incidence of absorption atelectasis.
- Tidal volume:
  - 5–8 ml/kg recommended
  - Adjust tidal volume to maintain:
    - Peak airway pressure ≤ 35 cm H_2O
    - Plateau airway pressure ≤ 25 cm H_2O
- Respiratory rate:
  - Maintain rate of 12–20 breaths/minute
  - Adjust rate to maintain E_TCO_2 between 32–38 mm Hg
  - $PaCO_2$-E_TCO_2 is usually ≥ 1–3 mm Hg during OLV.

- Positive end expiratory pressure:
  - Maintain PEEP of 5 cm H_2O
  - Avoid PEEP in patients with COPD.
- Continue two lung ventilation for as long as possible
- Continuous Positive Airway Pressure (CPAP):
  - Applied to non-ventilated, non-dependent upper lung
  - 1–2 cm H_2O CPAP to fully inflated lung enough
  - Even 5-10 cm H_2O CPAP may increase volume of lung and impede surgery
  - Considered as most effective and first line therapy to treat hypoxia
  - Mechanism of action:
    - Reduces shunt flow through collapsed lung
    - Diverts blood to ventilated lung due to increase in vascular resistance in non-ventilated lung
    - Improves V/Q ratio.
  - Applied after delivering an inspiratory VT to non-dependent lung to keep it slightly expanded
  - Disadvantages:
    - Reduces surgeons view
    - Increases chance of air leak if stapler placed on partially deflated lungs
    - Hemodynamic changes and over-distension if CPAP ≥ 15 cm H_2O.
  - Apply frequent recruitment manoeuvres.
- Positive end expiratory pressure:
  - Applied to dependant lung
  - Useful in patients with low dependant lung volume
  - Mechanism of action:
    - Restores alveoli
    - Recruits alveoli
    - Improves gas exchange.
  - If PEEP applied along with large V_T
    - Over-distension of alveoli occurs
    - Compression of intra-alvelolar blood vessels
    - May worsen V/Q mismatch.
  - Reduce intrinsic/auto PEEP by:
    - Reducing V_T, RR and I : E time ratio
    - Treat bronchospasm
    - Clear secretions
    - Applying extrinsic PEEP.

Hypoxia During OLV[1]

Prediction of Hypoxia During OLV

- Side of surgery: common during right thoracotomy as:
  - Right lung is larger and 10% better perfused than left
  - Increased shunt and reduced $PaCO_2$ during right side thoracotomy.
- Two lung oxygenation:
  - If PaO_2 levels are good during TLV in lateral position, they will be better during OLV
  - Thus, chances of hypoxia is less if PaO_2 is good with two lung ventilation.
- Preoperative ventilation-perfusion scan: To study shunting and PaO_2.

Treament of Hypoxia During OLV[1,3]

- Severe/precipitous desaturation: Resume two lung ventilation
- Gradual desaturation:
  - Ensure delivered FiO_2 is 1
  - Ensure cardiac output is optimal
  - Reduce volatile anesthetics to ≤ 1 MAC
  - Check position of DLT/BB with fibreoptic bronchoscopy
  - Hand ventilate to check for lung compliance
  - Recruitment to ventilated lung may worsen hypoxia initially
  - PEEP of 5 cm H_2O to ventilated lung (except emphysema)
  - CPAP of 1-2 cm H_2O to non-ventilated lung (recruitment of this lung done immediately before CPAP)
  - Intermittent reinflation of non-ventilated lung
  - Partial ventilation techniques to non-ventilated lung
    - Oxygen insufflation
    - High frequency ventilation
    - Lobar collapse with bronchial blocker.
  - Mechanical restriction of blood flow to non-ventilated lung (ligation of PA).
- Other manoeuvers:
  - Pressure controlled ventilation instead of volume control in patients with significant restrictive lung disease (preoperative FVC < 77% of predicted value)
  - Deepen anesthetic plane if light
  - Bronchodilator therapy if bronchospasm
  - Suction secretions with bronchoscope and check position of tube
  - Do not hyperventilate dependant lung as hypocapnea causes:
    - Increased shunt fraction and decreased $PaCO_2$
    - Increased vascular resistance in dependant lung.

- Newer interventions:
  - Eliminate vasodilators: NTG, halothane
  - Selective administration of PGE1 to ventilated lung
  - Nitric oxide synthetase inhibitor (***L-Name***) to hypoxic lobe
  - Almitrine with nitric oxide 20 ppm to non-ventilated lung.
- If all the manoeuvres fail, institute two lung ventilation.

Postoperative

Ventilation

- Indications:
  - Facial edema
  - Secretions
  - Laryngeal trauma
  - Hypothermia
  - Inadequate NMJ reversal
  - Unexpected blood loss/fluid shift.
- Management of individual tubes:
  - Univent tube: Withdraw blocker and use as SLT
  - Bronchial blocker:
    - Remove blocker
    - Leave single lumen tube in place.
  - Double lumen tube:
    - Leave DLT in place if difficult airway/facial edema
    - In such cases, withdraw DLT to place the 19–20 cm mark at teeth
    - Change to single lumen tube in other cases
    - Change to SLT with tube exchanger/***Bullard/Wu*** laryngoscope
    - Extubate after diuresis and steroid therapy to reduce facial and airway edema.

Postoperative Analgesia

- Cryoanalgesia
- Thoracic epidural
- Intercostal nerve block.

PHYSIOLOGY OF ONE LUNG VENTILATION[1,3]

Introduction

Significant changes occurs in an anesthetized patient on turning from supine to lateral decubitus.

Physiology of OLV in Lateral Decubitus Position

Spontaneous Breathing, Closed Chest

Ventilation

Increased ventilation to dependant lungs as:

- Gravity causes vertical gradient in pleural pressure
- Alveoli in dependant lung are compressed.
- Lower diaphragm is pushed higher inside chest than upper diaphragm by abdominal contents
- Thus, lower diaphragm overlying dependant lung contracts better
- This results in better ventilation.

Perfusion

Increased perfusion to dependant lung due to gravity.

V/Q Ratio

- Not greatly altered
- V/Q ratio decreases from nondependent to dependant lung
- This occurs as perfusion increases more than ventilation in lateral decubitus position.

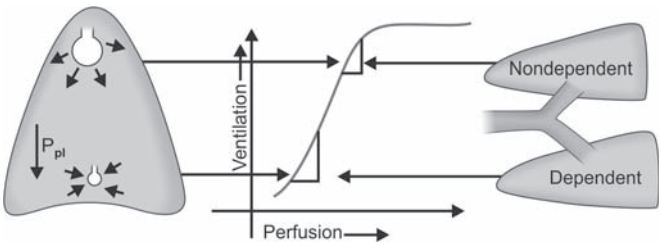


Fig. 2.49: OLV: Spontaneous breathing, closed chest

Spontaneous Breathing, Open Chest

Ventilation

- Complications due to mediastinal shift and paradoxical breathing
- Dependent lung is poorly ventilated as FRC is decreased by mediastinal weight
- Nondependent lung has no restriction to movement by chest wall, which is open
- Therefore, it is better ventilated.

Perfusion

Dependent lung is better perfused.

V/Q Ratio

- Dependent lung is poorly ventilated and over-perfused
- Nondependent lung is over inflated and under-perfused
- Therefore, V/Q mismatch occurs.

Anesthetized, Closed Chest

Ventilation

- Most of the tidal volume delivered (55%) goes to non-dependent lung

- Increased compliance of nondependent lung as:
  - Compression of dependent lung and loss of FRC
  - Excursion of dependent lung is limited by mediastinum
  - Cephalic movement of abdominal organs via flaccid diaphragm prevents lower diaphragm movement.
- FRC of nondependent lung becomes 15 times that of dependent lung.

Perfusion

Dependent lung gets more perfusion.

V/Q Ratio

- Nondependent lung moves from initial flat portion to steep portion of P-V curve
- Dependent lung moves from steep portion to lower flat portion of P-V curve.

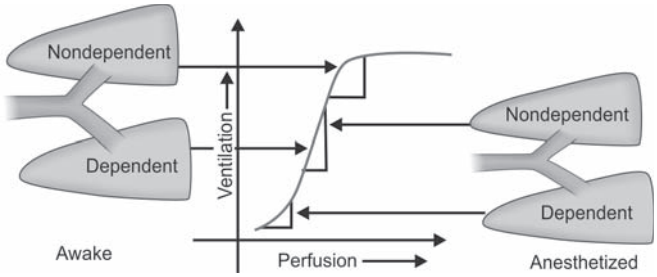


Fig. 2.50: OLV: Anesthetized, closed chest

Anesthetized, Open Chest

Ventilaton

- More ventilation to nondependent lung as:
- Decreased resistance to diaphragmatic movements by abdominal contents in nondependent lung
- Decreased resistance to nondependent lung movement due to open chest wall
- Poor ventilation of dependent lung as resistance to movement by abdominal contents is maximum here.

Perfusion: Dependent lung is better perfused

V/Q Ratio: Increased V/Q mismatch

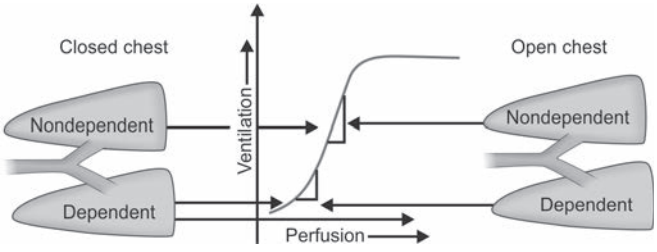


Fig. 2.51: OLV: Anesthetized, open chest

Physiology of One Lung Ventilation

- Since nondependent lung is not ventilated, blood flow through that lung becomes a shunt
- Thus massive right-left stunt occurs with huge V/Q mismatch and PaO_2 reduces
- $PaCO_2$ remains the same provided minute ventilation is maintained
- Perfusion to non-dependent lungs reduces due to:
  - Passive mechanisms:
    - Gravity
    - Surgical retraction
    - Pre-esxisting disease
  - Active mechanism: Hypoxic pulmonary vaso-constriction
- Perfusion to dependent lung increases due to:
  - Gravity
  - Hypoxic pulmonary vasoconstriction.

Factors Which Counter Effects of Lateral Decubitus Position

- Kinking of pulmonary artery in operated lung
- Gravity dependent reduction in dependent lung perfusion
- Progressive atelectasis due to mechanical compression
- Reduces perfusion of nondependent lung
- Obligatory right-left transpulmonary shunt due to increased A-aDO_2
- Hypoxic pulmonary vasoconstriction
- Surgical retraction and mechanical compression of nondependent lung.

DOUBLE LUMEN TUBES[1,3,4]

Introduction

- DLT is a bifurcated tube with both an endotracheal and endobronchial lumen which is used to achieve isolation of either lung during OLV
- Most widely used technique for lung isolation
- First used by ***Carlens*** in 1950.

Indications: *Benumof Thoracic Anesthesia 1983*

Absolute Indications

- Isolation of lungs to prevent spillage/contamination:
  - Infection, abscess
  - Massive hemorrhage
  - Unilateral infected cyst/bulla
- Surgical opening of major conductive airway
- Control of distribution of ventilation to one lung:
  - Bronchopleuralfistula (BPF)
  - Bronchopleuralcutaneous fistula

  - Unilateral cyst/bulla
  - Major disruption/trauma to bronchus
  - Unilateral bronchoalveolar lavage
  - Video assisted thoracoscopic surgery (VATS).

Relative Indications

- Surgical exposure: High priority:
  - Upper lobectomy
  - Pneumonectomy
  - Lung volume reduction surgery
  - Mimimally invasive cardiac surgery
  - Thoracic aortic aneurysm.
- Surgical exposure: Low priority:
  - Middle/lower lobe lobectomy
  - Thoracoscopy
  - Esophageal resection
  - Mediastinal mass resection
  - Thymectomy
  - Bilateral sympathectomy
  - Thoracic spine surgery.
- ***Differential lung ventilation*** in reperfusion injury:
  - After lung transplant
  - After unilateral pulmonary thromboembolectomy
  - Unilateral lung trauma.

Contraindications

- Difficult upper airway anatomy
- Small patients
- Full stomach
- Traumatic laryngitis
- Tracheobronchial tree disruption
- Carinal/proximal mainstem bronchial lesions
- Critically ill patients.

Types

- Carlens left sided DLT
- Whites right sided DLT
- Robertshaw right/left sided DLT
- Bronchocath-Portex type DLT
- Silibroncho DLT
- Brice-Smith left/right sided endobronchial tube.

Advantages

- Quickest technique
- Placement possible without bronchoscopy
- Requires lesser degree of skill
- Repositioning rarely required
- Suction to isolated lung possible
- Bronchoscopy to isolated lung possible
- CPAP can be easily added
- Can alternate OLV to either lung easily
- Allows conversion to two lung ventilation.

Disadvantages

- Expensive
- Size selection difficult
- Difficult to use in difficult airway/abnormal trachea
- Not optimal for postoperative ventilation
- Potential laryngeal trauma
- Potential bronchial trauma
- Trauma to vocal cord, larynx and arytenoids
- Difficult to place as larger cross sectional area.

Selection of DLT Size[3]

- Chest X-ray, CT scan useful to select appropriate size
- Formula for selection of size: Left bronchial diameter = 0.68 × tracheal diameter
- Properly sized left sided DLT should have bronchial tip 1–2 mm smaller than patients left bronchus diameter to allow for space occupied by deflated bronchial cuff.

Sex	Height	ID	Size (Fr)
Female	< 160 cms/ 63 inches	5 mm	35 Fr
Female	>160 cms	5.5 mm	37 Fr (most common)
Male	< 170 cms/ 67 inches	6 mm	39 Fr (most common)
Male	> 170 cms	6.5 mm	41 Fr

Depth of Insertion

Formula for depth of

$$\text{insertion} = \frac{12 + [\text{patient height}]\ \text{cms}}{10}$$

- In patients with height ≤ 155 cms, height is not good predictor of adequate depth
- Between 170–180 cms, average depth for DLT insertion = 29 cms
- For every 1 cm increase/decrease in height, DLT is advanced/withdrawn by 1 cm.

Complications

- Traumatic laryngitis
- Tracheobronchial tree disruption:
  - Oversized DLT
  - DLT migration into bronchus
  - Presents as:

- Unexpected air leak
- Subcutaneous emphysema
- Airway bleeding
- Protrusion of cuff into surgical field.

- Tension pneumothorax of dependent lung
- Malposition of DLT and occlusion of right upper lobe (RUL):
  - Fails to collapse dependent lung: Gas trapping
  - Partial collapse of lung: hypoxemia
  - Insertion into wrong side
  - Inadequate depth of insertion.

Techniques of Insertion

- Blind technique with direct laryngoscopy
- Direct vision technique with bronchoscopic guidance
- Via tube exchanger.

Blind Technique with Direct Laryngoscopy

- Pass DLT beyond glottis with direct laryngoscopy
- Turn DLT 90° counter-clockwise (for left sided DLT) after endobronchial cuff has passed vocal cords
- DLT should pass glottis without any resistance
- Advance DLT to correct depth
- Too deep insertion may cause left mainstem bronchial rupture
- Inflate tracheal cuff with 20 cc of air and bronchial cuff with upto 2 cc air.

Confirmation of DLT Position

- Auscultation
- Fibreoptic bronchoscope:
  - Through tracheal lumen
  - Through endobronchial lumen.
- Chest X-ray
- Fluoroscopy
- Radiopaque marker
- Water seal test
- Selective capnography.

Confirmation by Auscultation[1]

- 3 step method followed
- Not reliable
- Step 1:
  - During bilateral ventilation, tracheal cuff inflated to seal air leak at glottis
  - Auscultate to confirm bilateral ventilation.

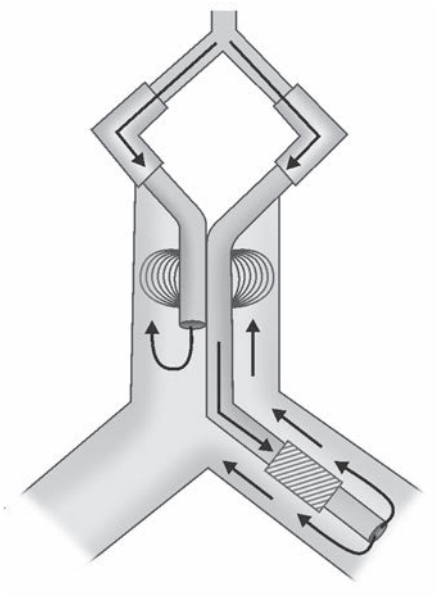


Fig. 2.52: DLT confirmation step 1[1]

- Step 2:
  - Tracheal lumen of DLT clamped proximally
  - Port distal to clamp is opened
  - During ventilation via bronchial lumen, bronchial cuff inflated to minimum volume
  - This seals air leak from open tracheal lumen port
  - Auscultate to confirm correct unilateral ventilation.

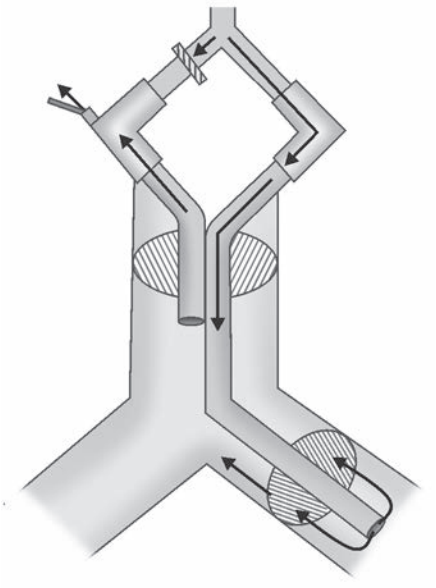


Fig. 2.53: DLT confirmation step 2[1]

- Step 3:
  - Tracheal lumen clamp released and port closed
  - Auscultate to confirm resumption of bilateral breath sounds.

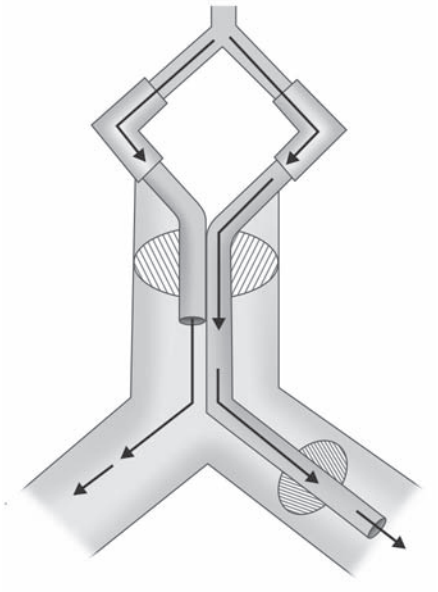


Fig. 2.54: DLT confirmation step 3[1]

- Step 4:
  - Clamp each side selectively
  - Check for absent sounds on unilateral side
  - Contralateral side should have clear breath sounds.

Confirmation by Fibreoptic Bronchoscope

- Through tracheal lumen:
  - Identify takeoff of right upper lobe (RUL) bronchus
  - Ensure endobronchial cuff is around 5 mm below carina in left bronchus
  - This prevents bronchial cuff herniation over the carina after inflation.
- Through endobronchial lumen:
  - Check tube patency
  - Identify both LUL and LLL orifices
  - Determine margin of safety.

Confirmation with Radio-Opaque Marker

- Radio-opaque line surrounds ***Mallinckrodt's Bronchocath tube***
- Line is proximal to bronchial cuff
- Marker is 4 cm from distal tip of endobronchial lumen
- Marker reflects white during fibreoptic visualization.

CARLENS TUBE[1,3,4]

Introduction

Originally used for differential bronchospirometry and selective PEEP.

Features

- Sizes 35, 37, 39, 41 French
- With tracheal and bronchial cuffs
- With two separate pilot balloons to inflate cuffs
- Two ETT connections for two channels
- Oval shaped lumen
- Tip at 45 angle to shaft.

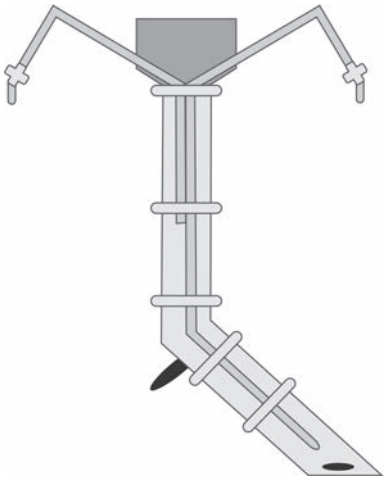


Fig. 2.55: Carlens tube

Advantages

- Helps in OLV
- Helps to isolate and collapse operative lung
- Prevents spillage of secretions into normal lung
- Suction can be done at any time.

Procedure

- Carinal hook is initially tied with a knot which is relased after positioning, for easy intubation
- Under direct laryngoscopy, endobronchial tip is passed through cords
- Tube is rotated 180 to left
- Allow carinal hook to pass anterior commissure of vocal cords
- Once hook enters trachea, tube rotated 90 back to right
- Now, endobronchial tip is positioned to left and hook to right
- Advance tube till resistance felt at carina
- Inflate bronchial cuff first and then tracheal cuff.

Robertshaw DLT

Features

- Sizes no. 8 (small), medium no. 10 and large no. 12
- 35, 37, 39, 41 Fr available
- 32 Fr used for small adults and 28 Fr used for pediatrics
- No carinal hook present
- Right sided tube has slit over bronchial cuff for RUL
- Has a D-shaped lumen and is bigger compared to other tubes
- Left sided angle of 45° at the tip and right sided angle of 20 at tip.

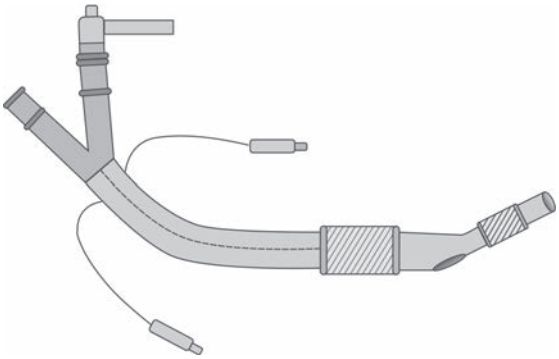


Fig. 2.56: Robertshaw double lumen tube

Procedure

- Tube inserted between vocal cords with concavity facing upwards
- Rotate the tube through 90°
- Once tube passes vocal cords, remove laryngoscope
- Support the jaw and advance tube
- Endobronchial portion directed towards the bronchus which has to be intubated.

Advantages

- Absence of carinal hook
- Left and right sided tubes are available
- Larger diameter and D-shaped lumen:
  - Allows easy passage of suction catheter
  - Low resistance to gas flow.
- Has fixed curvature which facilitates easy positioning
- Decreased chances of kinking.

Whites DLT

- Sizes 37, 39, 41 Fr available
- Has both tracheal and bronchial cuffs
- Two separate pilot balloons are present to inflate cuffs
- Slit is present to ventilate RUL
- For right lung anesthesia, clamp left side to allow left lung surgery.

Silibroncho DLT

- D-shaped wire reinforces lumen to maintain tip at 45°
- Reinforcement prevents kinking of lumen but maintains flexibility at same time
- Especially useful if left mainstem bronchus is perpendicular to trachea:
  - Occurs if patient has already undergone left upper lobectomy
  - Expansion of LLL, in this case displaces left mainstem bronchus upwards.

BRONCHIAL BLOCKERS[1,3,4]

Introduction

- A blocker is a balloon on a suction catheter which is placed under direct vision/bronchoscopic vision into the bronchus, following endotracheal intubation to allow OLV
- First used by ***Sir Ivan Magill.***

Characteristics of Ideal Blockers[4]

- Balloon shaped to stabilize it in bronchus
- Low pressure and high volume characteristics of balloon preferred
- Flexible and easy to manipulate into mainstem/lobar branches
- Balloon to have channel for deflation and suction distal to it
- Be adaptable to use internal and external to standard ETT
- Wide variety of sizes.

Indications

- Difficult DLT insertion (pediatric/difficult intubation)
- Airway anatomy unsuitable for DLT
- Patients with cancer who have undergone previous pulmonary resection
- Rarely used at present as displacement of BB causes spread of spilled contents.

Technique

- Trachea intubated with SLT
- BB may pass within/outside the ETT
- When BB is inflated, that lung will not be ventilated
- Suction catheter element which passes to the tip allows the isolated lung to be deflated and suctioned
- Blocker therefore allows continued inflation of one lobe of operated lung

- For example, if placed in right bronchus intermedius, it will allow RUL ventilation when surgery is on RLL.

Types of Bronchial Blockers

- ***Thomsons***
- ***Magills***
- ***Macintosh-Lothersdale.***

Use of Bronchial Blockers

- Modified SLT with enclosed BB:
  - ***Integrated Torque Control Blocker: Univent***
  - ***Fogarty Arterial Embolectomy catheter.***
- Conventional SLT with enclosed BB:
  - ***Hybrid Wire Guided BB***
  - ***Cohens Tip deflecting endobronchial blocker***
  - ***Fuji Uniblocker.***

Advantages

- Size selection is not an issue
- Easily added to regular ETT
- Allows ventilation during placement
- Easier to place in difficult airway
- Postoperative two lung ventilation (TLV) is possible by removing BB
- Selective lobar lung isolation possible
- CPAP to isolated lung possible.

Disadvantages

- More time for positioning and repositioning is often required
- Bronchoscope is essential for positioning
- Right lung isolation is suboptimal due to RUL anatomy
- Bronchoscopy to isolated lung is impossible
- Minimal suction is possible to isolated lung
- Difficult to alternate OLV to either lung

Size Selection

- Most commonly used intraluminally (coaxially) with SLT
- Maybe used separately through glottis/tracheostomy, external to SLT
- For 9 Fr BB, ETT ≥ 7 mm ID used with FOB ≤ 4 mm diameter
- Larger bronchoscopes require ETT ≥ 7.5 mm ID.

Complications

- Failure to achieve lung separation
- Inclusion of distal wire loop to stapling line during right upper lobectomy
- Displacement of BB with lodgement above carina
- Shearing of balloon.

Comparison

Feature	DLT	Univent	Arndt
Time to position	2 minutes	2 minutes	3 minutes
Time for lung collapse	17 minutes	19 minutes	26 minutes
Suction	±	±	Majority require
Surgical exposure	Excellent	Excellent	Excellent

UNIVENT[3]

Introduction

- Single lumen ETT with moveable endobronchial blocker
- ***Torque Control Blocker Univent*** (TCBU) is latest version of Univent.

Design

- Has two compartments:
  - Large lumen for oxygen/air passage
  - Small lumen in the middle of enclosed BB.
- BB has high pressure and low volume cuff
- BB is made of flexible non-latex material
- It has a flexible shaft which is easy to guide into a bronchus
- Has a shape similar to standard ETT
- Channel present within the Univent, encloses a moveable BB which can be used to block left/right/any secondary bronchi
- First generation Univent tube was difficult to direct into selected bronchus, as the BB would spin on its long axis
- Second generation TCBU contains a high friction coefficient which facilitates direction of BB into target main stem bronchus.

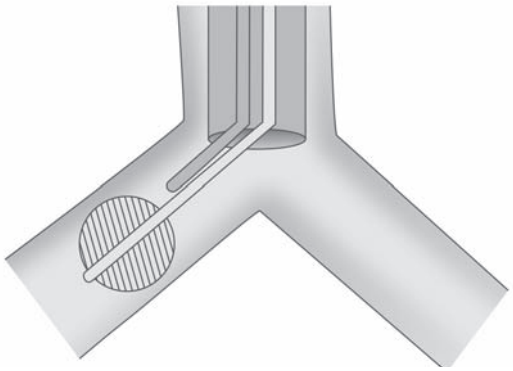


Fig. 2.57: Univent bronchial blocker

Technique
- Enclosed BB fully retracted into lumen of tube
- Conventional ETT intubation technique used
- FOB passed into main lumen through the bronchoscope adaptor
- Under direct vision, BB is advanced into targeted bronchus.

Advantages
- Useful in patients with:
  - Difficult airway
  - Planned postoperative ventilation
  - Following mediastinoscopy/thoracotomy when tube exchange is difficult
  - Following bilateral lung transplant.
- During OLV in tracheostomy patients, as a selective lobar blocker to improve oxygenation
- Effective with different ventilation modalities like HFJV during sleeve pneumonectomy
- Can be converted to SLT by deflating and withdrawing.

Complications
- Failure to achieve lung separation
- Inclusion of BB into stapling line
- Inflation of BB cuff near tracheal lumen causing respiratory arrest
- Risk of negative pressure pulmonary edema
- Malpositioning during patient positioning
- Slow deflation of lung.

ARNDT BLOCKER[3]

Introduction
It is a wire guided endobronchial blocker.

Structure
- Available in 5 and 7 Fr pediatric size with 65 and 78 cm lengths
- It is an independent BB which is attached to a 7 or 9 Fr catheter
- Inner lumen of catheter measures 1.4 mm diameter
- Murphys eye present at distal end of catheter to facilitate lung deflation
- Has high volume and low pressure cuff which is elliptical/spherical shape
- Inner lumen has flexible nylon wire which exists as a small and flexible wire loop
- Wire loop is coupled with FOB and serves as a guide wire.

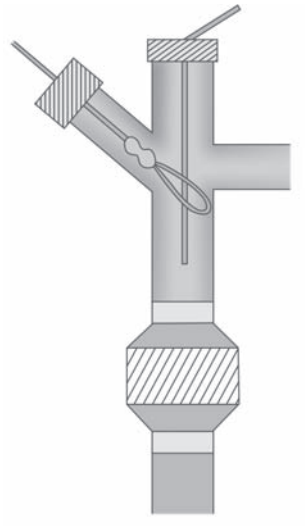


Fig. 2.58: Arndt blocker

Technique
- FOB advanced distally enough so that BB enters bronchus
- When deflated, cuff is approximately 2 cm inside bronchus, withdraw FOB
- Once patient is turned lateral, cuff of BB fully inflated with 4–6 ml air to obtain total bronchial blockade
- 2–3 ml air is enough to inflate cuff if selective lobar blockade is attempted
- For right mainstem bronchus blockade, Arndt blocker is advanced independent of wire loop by observing its entrance into bronchus under FOB visualization
- Wire loop is withdrawn to convert 1.4 mm channel into suction port to expediate lung collapse.

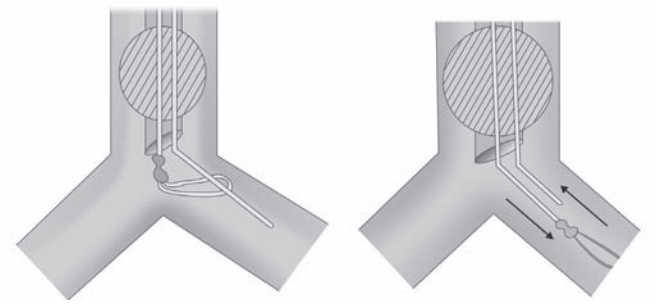


Fig. 2.59: Arndt blocker use

Complications
- Shearing of balloon on blocker removal
- More prone to dislodgement during positioning
- Inclusion of loop in suture line.

FOGARTY ARTERIAL EMBOLIZATION CATHETER

Introduction

- Designed specifically as vascular tool, but can be used for lung isolation
- Can be used as rescue device (when DLT is difficult to position) by advancing it through SLT.

Disadvantages

- Made of natural rubber latex: *Contraindicated in latex allergy*
- Has no communicating channel: No suction/oxygen insufflation
- Lack of guide wire device
- Air leak from breathing circuit common: prevented by placing Fogarty catheter external to ETT
- Balloon is high pressure and low volume.

Complications

- Airway rupture by forceful introduction
- Can be included in stapling line

Cohens Bronchial Blocker

- Uses a wheel located in most proximal part of unit which deflects tip of distal part of BB into desired bronchus
- Preangled at the distal tip to facilitate insertion
- Arrow is present on distal shaft, above the balloon, which when seen with FOB indicates the direction in which tip will deflect
- Inserted through SLT with the aid of FOB
- Arrow aligned with bronchus to be intubated and proximal wheel turned towards desired side and then BB advanced with FOB guidance
- Blue color cuff, can be used with 7 mm ETT
- High volume and low pressure cuff
- 6–8 ml air seals bronchus with cuff.

Fuji Uniblocker

- 9 French, balloon tipped
- Made of silicon
- Has fixed distal angulation to aid insertion
- Does not have wheel device
- Same device as univent but can be used as an independent BB though a standard ETT.

PREOPERATIVE EVALUATION FOR THORACOTOMY[1,3]

Goals

- To recognize patients ability to tolerate procedure
- To identify high risk patients
- To stratify perioperative management
- To focus resources on high-risk patients to improve outcome.

Initial Assessment

- All patients:
  - Cardiopulmonary tests
  - Concomitant illnesses.
- Cancer patients:
  - Mass effect
  - Metastasis effect
  - Metabolic effect
  - Medication effect.
- COPD patients:
  - Baseline ABG
  - History of bronchodilator, steroid and physiotherapy
- Renal dysfunction:
  - Blood urea nitrogen
  - Serum creatinine

History

- Dyspnea: onset, severity, positional variation
- Orthopnea which relieves on upright position
- Cough, hemoptysis, wheeze
- Exercise tolerance
- History of cigarette smoking: ≥ 20 pack-years increases risk of Post Operative Pulmonary Complications (POPC)
- History of bronchodilator and steroid therapy for perioperative supplementation.

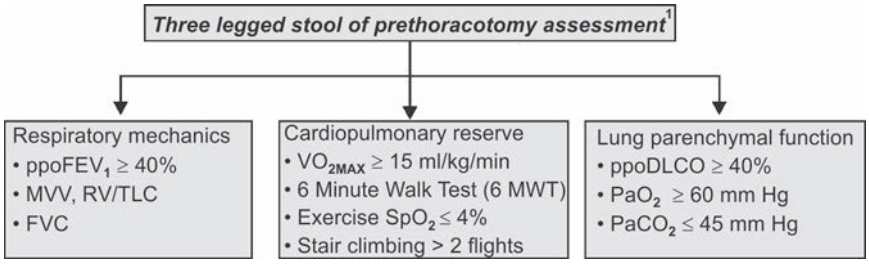
Examination

- Cyanosis, clubbing, osteoarthropathy
- Respiratory rate and pattern
- ***Hoovers sign, Tripod sign***
- Tracheal deviation, wheeze, crackles, decreased or absent sounds
- Signs of right ventricular failure:
  - Split S_2 with increased P_2
  - Edema
  - Raised JVP
  - Congestive hepatomegaly.

Investigations

Routine Investigations

- Complete blood count, BUN, serum, creatinine, electrolytes
- ABG on room air, coagulation profile
- Chest X-ray, CT/MRI to localize lesion
- ECG: Signs RV overload



Assessment of Respiratory Function[1,3]

Respiratory Mechanics

- Baseline FEV_1, FVC, MVV, RV/TLC ratio
- Predicted postoperative FEV_1, ($ppoFEV_1$): Most valuable
  - Interpretation:
    - $PpoFEV_1$ > 40% indicates low-risk of POPC
    - $PpoFEV_1$ 30–40% indicates moderate risk of POPC
    - $PpoFEV_1$ < 30% indicates high-risk of POPC.
  - Calculation: Percentage of functional tissue removed is based on functional segments of lung removed
    $ppoFEV_1$ = Preoperative FEV_1 × [1 – (per cent age of functional tissue removed)]/100

Parenchymal Function

- PaO_2 < 60 mm Hg and $PaCO_2$ > 45 mm Hg contraindicates patient for resection
- ppoDLCO: ***NETT trial***:
  - ppoDLCO < 40% predicts increased risk of POPC
  - ppoDLCO < 20% predicts increased mortality rate.

Cardiopulmonary Interactions

Gold standard for assessment of cardiopulmonary function:

- VO_{2MAX}:
  - Most useful predictor of outcome
  - VO_{2MAX} > 20 ml/kg/min implies low-risk of POPC
  - VO_{2MAX} < 15 ml/kg/min implies high-risk of POPC
  - VO_{2MAX} < 10 ml/kg/min is an absolute contraindication for lung resection.
- ***Brunellis*** stair climbing test:
  - 20 steps to be present per flight
  - Done at patients own pace but without stopping
  - Ability to climb 5 flights of stairs implies VO_{2MAX} is more than 20 ml/kg/min
  - Ability to climb 2 flights implies VO_{2MAX} of around 12 ml/kg/min
  - Inability to climb 2 flights predicts high-risk of POPC.
- 6 minute walk test (6 MWT):
  - 6 MWT < 2000 feet or 610 mts implies VO_{2MAX} < 15 ml/kg/min
  - Exercise oximetry ≥ 4% during 6 MWT or stair climbing predicts high-risk of POPC.

Others

- Ventilation-perfusion scintigraphy: Done if preoperative FEV_1 or DLCO < 80% predicted
- Split lung function tests:
  - Test simulates postoperative respiratory situation
  - Done using BB/endobronchial tube.

Assessment for Malignancies[1,3]

Mass effect:

- Tracheal distortion
- RLN/phrenic nerve palsy
- Pancoasts tumor
- Obstructive pneumonia
- Lung abscess.

Metastasis:

- Brain
- Bone
- Liver
- Adrenals.

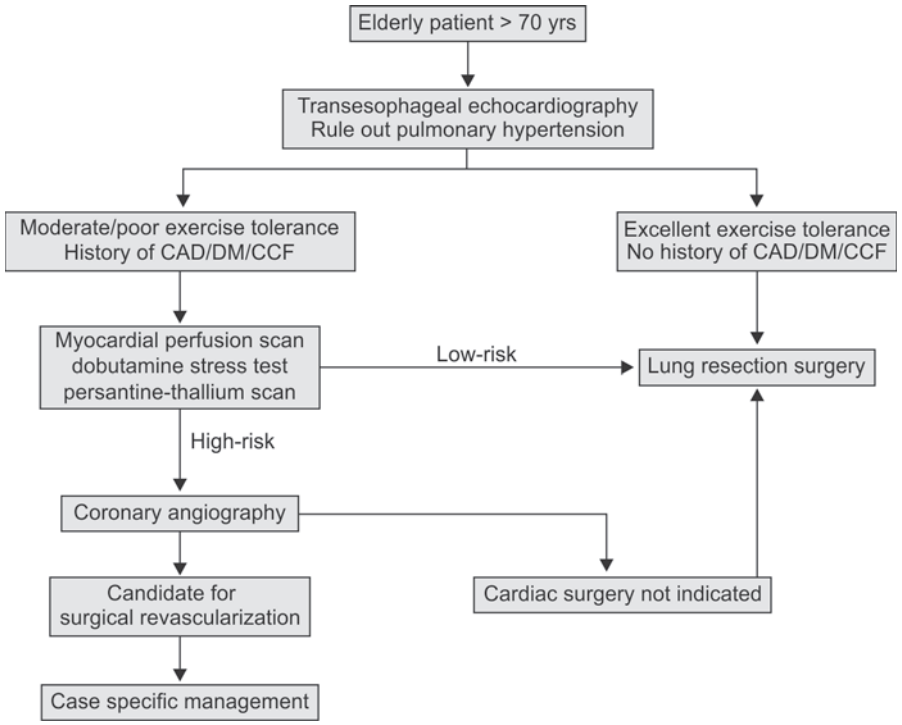
Medications:

- Pulmonary toxicity:
  - Bleomycin
  - Mitomycin.
- Cardiotoxicity: Doxorubicin
- Nephrotoxicity: Cisplatin.

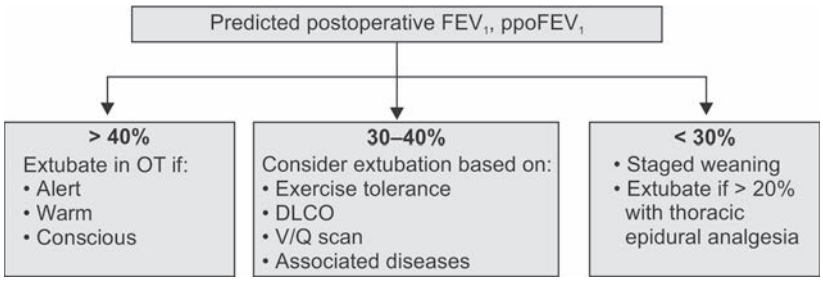
Metabolic:

- Hypercalcemia due to hyperparathyroidism
- Cushing syndrome: ACTH
- SIADH, GH
- Lambert Eaton syndrome
- Hypertrophic pulmonary osteoarthropathy.

Assessment of Cardiac Function[1]



Implications of Preoperative Assessment[1]



LUNG VOLUME REDUCTION SURGERY[1,3,11]

Introduction

Multiple wedge resections of hyperinflated and poorly functioning lung tissue is done, to reduce lung volume and improve symptoms in severe emphysema.

Definition

- Blebs are subpleural collection of air under visceral pleura generated due to a ruptured alveolus
- Bullae are thin walled air filled intraparenchymal lung spaces which are generated by the loss of alveolar structural tissue
- Pneumatoceles are thin walled air filled spaces which are generated by pulmonary infection/trauma.

Indications

- Severe heterogenerous emphysema
- Blebs/bullae causing:
  - Symptomatic dyspnea
  - Giant bulla occupying > 30% of hemithorax
  - Rapidly expanding bullae/blebs
  - Recurrent pneumothorax
  - Bilateral pneumothorax
  - Prolonged ICD drainage

- Single pneumothorax if patient is exposed to rapid atmospheric pressure changes:
  - Pilots
  - Scuba divers.

Patient Selection

National Emphysema Treatment Trial (NETT)

- Severe respiratory failure
- Heterogenous emphysema for most affected areas
- FEV_1 or DLCO ≥ 20% predicted
- Best for upper lobe disease and low base line exercise capacity
- For patients with homogenous emphysema (α_1 antitrypsin deficiency), pneumonectomy or lung transplant preferred.

Preoperative Preparation and Premedication

- Perioperative steroid supplementation given as patient is often on steroids
- DVT prophylaxis necessary as increased risk of DVT due to polycythemia
- Chest physiotherapy for secretions
- Antibiotic therapy to be given for infections
- Airway blocks given if awake intubation is planned
- Continue cardiac and respiratory medicines
- IV midazolam 0.03 mg/kg given if patient is not symptomatic
- IV glycopyrrolate 0.01 mg/kg as an antisialogogue
- Place thoracic epidural for postoperative pain management.

Monitors

- Pulse oximetry, E_TCO_2
- ECG, NIBP/IBP
- Urine output, temperature
- CVP essential as large fluid shifts occurs
- Continuous spirometry
- Bilateral precordial stethoscope
- Monitor airway pressure and tidal volume.

Induction

- GA with DLT and OLV is preferred
- Prolonged preoxygenation:
  - Necessary in these patients as they have:
    - Poor alveolar ventilation
    - Increased airflow resistance
    - Increased FRC.
  - Preoxygenation is done for 10–12 minutes.
- IV induction done with thiopentone or propofol
- Slow induction occurs due to high preoperative sympathetic tone
- Profound hypotension can occur at the time of induction
- DLT inserted following NMB with fibreoptic bronchoscopic (FOB) guidance.

Maintenance

- TIVA is *preferred technique*
- N_2O contraindicated if balanced anesthesia is used
- Volatile anaesthetics have increased alveolar-arterial gradient
- If balanced anesthesia used, isoflurane 0.5–1 MAC can be used
- Prophylactic ICD insertion is not recommended as it may rupture bulla.

Ventilation

- If bulla or bleb is present, maintain spontaneous ventilation till surgical isolation of the same
- If IPPV given prior to bulla isolation:
  - Increased anatomical deadspace occurs due to increased size of bulla
  - Air leak, bulla rupture and tension pneumothorax possible.
- Ventilatory strategy:
  - Deliberate hypoventilation and permissive hypercapnea
  - One lung ventilation
  - Tidal volume 6–7 ml/kg
  - Respiratory rate 10–12/min
  - I : E ratio 1 : 4
  - Peak airway pressure ≤ 20 cm H_2O
- Reduce auto-PEEP:
  - Intermittently disconnect from ventilator to allow lungs to empty
  - Manual compression of chest to empty auto-PEEP.

Hemodynamics

- Precipitous hypotension occurs on induction due to auto-PEEP
- Large fluid shifts occur intraoperatively:
  - Judicious use of IV fluids as pulmonary HTN and RV dysfunction
  - Use colloids to reduce the risk of pulmonary edema
  - Inotropic support to reduce fluid administration, if RV dysfunction.
- Watch for hypothermia:
  - Warm IV fluids
  - Warm blankets.

Extubation

Extubate as soon as possible if AWaC (Alert, warm, comfortable).

Postoperative Care

Management

- Minimize airway pressure if postoperative ventilation required
- Adjust FiO_2 to maintain SpO_2 between 90–92%
- Accept $PaCO_2$ up to 50 mm Hg
- Watch closely for air leaks from ICD: Maximum suction 10 cm H_2O
- Pulmonary rehabilitation postextubation:
  - Chest physiotherapy
  - Incentive spirometry
  - Early mobilization.

Analgesia

- Multimodal analgesia
- Opioids: Systemic/neuraxial/PCA
- Intercostal, intrapleural, paravertebral, epidural blocks
- NSAIDs.

Complications

- 5–10% mortality rates
- Airleak and pneumothorax most common
- Bronchopleural fistula
- Retained secretions, infections
- Bronchospasm
- Pain.

Prognosis

- Intermediate postoperative improvement occurs in symptoms and PFTs
- Occurs due to:
  - Decompression of airways
  - Reduction in airway resistance
  - Reduction in work of breathing
  - Reduction in auto-PEEP
  - Increase in dynamic compliance.
- Used as an alternative to lung transplant.

PNEUMONECTOMY[1,3,11]

Introduction

Pneumonectomy refers to complete removal of the lung.

Indication

Done when lobectomy is inadequate to remove local disease or ipsilateral lymph node metastasis.

Procedure

Pneumonectomy

- Surgery is done through posterolateral incision
- Mediastinal pleura is incised
- Pulmonary artery, superior and inferior pulmonary veins, and mainstem bronchus stapled
- Entire lung is taken out of chest
- Tests are done for any air-leaks
- Reconstruction of bronchial stump is completed.

Extrapleural Pneumonectomy

- Done for patients with malignant pleural mesotheliomas
- Extensive resection of liver, pericardium, diaphragm, parietal pleura and chest wall is done
- Increased blood loss occurs due to involvement of chest wall blood vessels.

Sleeve Pneumonectomy

- Mostly done for right sided tumors via right thoracotomy
- For tumors of most proximal parts of mainstream bronchus and carina
- Left thoracotomy done in two stages:
  - First stage: Left thoracotomy and pneumonectomy
  - Second stage: Right thoracotomy and carinal excision.
- High complications and mortality.

High-Risk Patients

- Age > 70 yrs
- FVC < 50% predicted
- FEV_1 < 50% predicted or < 2 liters
- MVV < 50% predicted
- DLCO < 50% predicted
- $PaCO_2$ > 45 mm Hg on room air
- Abnormal ECG.

Premedication

- Continue all cardiovascular and respiratory drugs
- IV midazolam 0.03–0.15 mg for anxiolysis
- IV glycopyrrolate 10 µg/kg
- DVT prophylaxis with LMWH
- Antibiotic prophylaxis
- Blood should be kept cross matched and ready.

Monitor

- Pulse oximetry, E_TCO_2
- NIBP, ECG

- Urine output, temperature
- Tidal volume, airway pressure
- Continuous display of airway pressure volume loops
- Arterial cannulation:
  - For taking ABG samples
  - Monitoring IBP.
- CVP:
  - Used for fluid access
  - Unreliable as a monitor of intravascular fluid status due to:
    - Lateral position of patient
    - Open chest.

Induction

- GA with OLV and DLT is *technique of choice*
- Large bore IV access is necessary
- Prolonged preoxygenation is required
- IV induction is done with thiopentone or propofol
- Slow induction occurs due to high preoperative sympathetic tone
- Profound hypotension can occur at the time of induction
- DLT/BB/SLT used: Choose one which does not interfere with ipsilateral airway
- DLT inserted following NMB with fibreoptic bronchoscopic (FOB).

Maintenance

- TIVA or balanced anesthesia can be used
- TIVA is the preferred technique
- Use 0.5–1 MAC isoflurane if balanced anesthesia is used
- Avoid N_2O and halothane if balanced anesthesia is used
- Avoid neuromuscular blockers if Eaton–Lambert syndrome.

Ventilation

- Lung protective OLV/HFPPV with DLT useful:
  - Tidal volume 5–6 ml/kg ideal
  - Limit peak airway pressure to < 35 cm H_2O
  - Limit plateau airway pressure to < 25 cm H_2O
- Suction airway to collapse the lung before reinflation
- Withdraw DLT/BB before stapling bronchus to avoid accidental inclusion
- *Leak-test* of suture line is performed:
  - Release clamp on DLT to the operated side
  - Slowly increase inflation pressure to 25–30 cm H_2O with stump under water
  - Check for any air-leaks.
- Replace DLT with SLT at the end of surgery.

Hemodynamics

- Rarely massive blood loss occurs
- Judicious fluid administration:
  - Reduces risk of postoperative Acute Lung Injury (ALI)
  - Administration of less than 3 L in first 24 hrs is associated with reduced risk
  - Use inotropes/vasopressors instead of fluids for hemodynamic instability
- Surgical manipulation can cause cardiac compression and hypotension
- Significant blood loss possible in extrapleural pneumonectomy.

Extubation

- May require postoperative ventilation if long duration surgery and large fluid shifts
- Extubate when patient is AWaC.

Postoperative Care

Management

- Nurse in sitting up position to allow expansion of remaining lung
- Humidified oxygen via face mask
- Judicious fluid administration
- Chest X-ray for pneumothorax.

Analgesia

- Multimodal analgesia
- Opioids: Systemic/neuraxial/PCA
- Thoracic epidural
- Paravertebral/intercostal/intrapleural blocks.

Complications

- Hemorrhage
- Retention of secretions
- Infection
- Atelectasis
- Respiratory failure
- *Acute Lung Injury (ALI):* Increased risk if:
  - Preoperative alcohol abuse
  - Right sided pneumonectomy
  - Increased ventilatory pressure intraoperatively
  - Increased perioperative IV fluid administration
  - Increased urine output in postoperative period
- Arrhythmias: usually atrial arrhythmias
- Pulmonary HTN and RV dysfunction due to

increased afterload from increase in PVR occurring postoperatively
- Cardiac herniation if right sided pericardial resection is done
- Postpneumonectomy pulmonary edema especially in sleeve pneumonectomy.

Management of ICD

- Single basal ICD is used
- ICD is left clamped but connected to underwater seal
- Unclamped for 1–2 minutes every hour to drain blood and release air
- This centralizes mediastinum
- Suction is a contraindication as it can pull mediastinum
- If ICD is not placed intraoperatively:
  - Air is aspirated from postpneumonectomy space at the end of surgery
  - Cannula is placed through chest wall in supine position
  - Aspirate air till there is negative pressure in the space
  - This will centralize mediastinum.
- Remove ICD after 12–24 hours if no drain.

BRONCHOPLEURAL FISTULA (BPF)[1,3,11]

Introduction

- A communication between tracheabronchial tree and pleural space
- If there is additional communication to the surface of chest, it is called cutaneous bronchopleural fistula.

Incidence

- 2–11% after pulmonary resection
- Mortality of 5–70%.

Etiology

- Most commonly occurs due to giving away of bronchial suture after pneumonectomy
- Erosion of bronchus by carcinoma or chronic inflammation
- Spontaneous drainage of lung abscess/empyema cavity into bronchial tree
- Traumatic rupture of bronchus/bulla/cyst (by barotrauma/PEEP)
- Penetrating chest wound.

Diagnosis

- Clinical features:
  - Sudden onset dyspnea, severe in nature
  - Cough with hemoptysis or brownish sputum
  - Fever
  - Subcutaneous emphysema
  - Contralateral deviation of trachea
  - Sepsis, ARDS
  - Persistent airleak, empyema
  - In lobectomy patients, persistent air leak, purulent sputum and drainage are diagnostic.
- Investigations:
  - Preoperative BT, CT, creatinine, urea, LFTs, ECG
  - Neutrophilia, raised total counts
  - ABG: hypoxia, hypercarbia, metabolic acidosis
  - Chest X-ray:
    - Air filled pleural space, new air-fluid level
    - Shifting of trachea, collapse of lung
    - Reducing fluid level on serial chest X-ray following pneumonectomy.
  - Bronchography, sinogram: *Confirmatory test*
  - Bronchoscopy
  - Accumulation of radionucleide in pleural space after inhalation of xenon or O_2–N_2O mixture.
- Methylene blue injection into pleural space and recovering it in sputum.

Predisposing Factors

- Perioperative radiation therapy
- Residual neoplasm
- Infection at resection site
- Long avascular bronchial stump.

Anesthetic Considerations

- Inability to effectively ventilate these patients may be encountered due to large air leak
- Also positive pressure ventilation might increase air leak across BPF causing tension pneumothorax and delayed healing of fistula
- Reduced alveolar ventilation on the other hand causes carbon dioxide retention and increased acidosis
- Reducing risk of contaminating healthy lung is important if empyema is present.

Preoperative Preparation and Premedication

Drainage of Empyema

- Empyema if present, should be drained before any surgery is done, to close the BPF
- This is done to avoid risk of tension pneumothorax during positive pressure ventilation
- Drainage is done with person sitting up and leaning towards affected side

- A drain to underwater seal system is left in the pleural cavity before anesthesia
- Chest X-ray should be taken to determine efficacy of procedure.

Estimation of Size of BPF

- Important as it determines the amount of air leak from the tidal volume administered
- Two methods:
  - Amount of ICD drain:
    - After pneumonectomy if continuous drainage occurs, it implies that BPF is large
    - If drainage is intermittent, it implies small size of BPF.
  - Loss of tidal volume:
    - Estimate loss of tidal volume between inspired and expired tidal volume
    - Smaller difference between inspired and expired tidal volume implies smaller sized BPF
    - This is done by connecting spirometer to:
      - A tightly fitting face mask in non-intubated patients
      - To ETT in intubated patients.

Premedication

- NPO orders
- Informed consent
- Premedication is not required in case of emergency surgery
- Diazepam 5 mg PO/midazolam can be used
- Glycopyrrolate 10 µg/kg IV as antisialogogue
- Antiaspiration prophylaxis if awake intubation planned.

Monitors

- Pulse oximetry, capnography, ECG
- Blood pressure: IBP preferred
- CVP, urine output
- Temperature

Position

- Lateral decubitis position
- Lung with BPF placed in nondependent position (on the upper side).

Induction and Intubation

- 100% oxygen with face mask of appropriate size
- Sitting up position preferred preinduction to prevent spill over
- Priority is to isolate affected side in terms of contamination and ventilation
- Endobronchial tube placed before positive pressure ventilation initiated
- Care of ICD:
  - Chest tube position in infected area confirmed
  - Chest tube has to be left unclamped to:
    - Avoid any bouts of coughing
    - Prevent build up of a tension pneumothorax in case a pre-existing valve mechanism exists.
  - During induction, suction from chest tube is avoided to prevent loss of tidal volume.
- Choice of ETT:
  - Single lumen ET tube can be used for small sized BPF
  - Double lumen tube for larger sized BPF
  - Largest possible tube selected so that it provides a close fit in trachea
  - Endobronchial tube selected such that bronchial lumen is on side opposite to BPF.
- Intubation techniques:
  - Awake intubation of an anesthetized airway:
    - Done with the help of fibreoptic bronchoscopy and double lumen tube
    - Is the safest and most ideal technique
    - Neuroleptanalgesia with topical airway anesthesia may be required
  - Intubation after deep anesthetic plane:
    - Done with patient breathing spontaneously
    - Using IV propofol 2 mg/kg or thiopentone 5 mg/kg.
  - Rapid sequence induction:
    - Done with IV ketamine/thiopentone and succinylcholine
    - Has increased risk of tension pneumothorax and contamination.
- Once tube is adequately positioned in trachea, there may be outpouring of pus from tracheal lumen
- Thus, this lumen should be immediately suctioned with a large bore catheter
- Fibreoptic intubation of DLT/SLT is preferred in postpneumonectomy patients, with tip of endobronchial lumen placed in existing lung.

Maintenance

- Nitrous oxide avoided
- Oxygen + air + isoflurane/sevoflurane used
- Fentanyl + vecuronium intermittant boluses
- High frequency oscillatory ventilation:
  - May be used along with permissive hypercapnea
  - Minimizes air leak and also stabilizes hemodynamics
  - Especially useful in patients with multiple BPF

- After chest is opened, if excessive air leak is encountered, when using SLT, ventilation can be improved by lung packing and manual control of air leak.

Extubation

- Early extubation preferred
- Thus is to avoid barotrauma to surgical stump from positive pressure ventilation
- Extubated fully awake, warm and fully reversed.

Postoperative Management

- Change double lumen tube to SLT
- Shifted to ICU in sitting position after establishment of adequate spontaneous ventilation
- Respiratory failure is common postoperatively, in these patients.

Conservative Management of BPF

- Bronchopleural fistulas can be conservatively managed if small, by adequately ventilating them and giving antibiotics.
- Ventilatory strategies:
  - One lung ventilation:
    - Bronchus of normal lung intubated and ventilated
    - This allows BPF to rest and heal with help of antibiotics
    - This may lead to an intolerable intrapulmonary shunt
    - PEEP may be needed to maintain PO_2.
  - Differential lung ventilation:
    - Each lung is managed with different types of ventilation
    - Done through DLT and two synchronized ventilators
    - Healthy lung is ventilated with normal ventilator
    - Affected lung is exposed to smaller tidal volume or HFJV
    - CPAP with oxygen at pressures below the *critical opening pressure* of the BPF can be used
    - Critical opening pressure is determined by assessing lowest level of CPAP which must be applied to the bronchus on affected side to produce continuous bubbling through the underwater seal.
  - High-frequency jet ventilation:
    - Used for larger BPF or multiple BPFs
    - This causes minimal gas loss through fistula as VT is low
    - Thus, BPF may heal more quickly
    - Also, hemodynamic effects are usually minimal.
  - Unidirectional chest tube valve:
    - Usually, inspiratory cycle of ventilator triggers closure of chest tube valve
    - Valve again opens during expiration
    - This reduces gas flows across BPF during positive pressure ventilation
    - Flow across fistula is reduced by increasing pleural pressure during positive pressure breaths
    - This reduces the pressure gradient across the BPF.
  - Other strategies:
    - PEEP to pleural cavity equalizing with intrathoracic PEEP
    - If disruption occurs early in post-pneumonectomy patients, resuture stump
    - Small fistula can be closed by bronchoscopy or with fibrin glue.

PLEURECTOMY[1,3,11]

Introduction

Pleurectomy refers to the procedure where parietal pleura is stripped overall but diaphragmatic and mediastinal surface of lung.

Indications

- Spontaneous pneumothorax:
  - Treatment of choice for patients with recurrent spontaneous pneumothorax
  - Young, tall and thin patients
  - Males, smokers.
- Secondary pneumothorax:
  - Chronic bronchitis, emphysema
  - Tuberculosis
  - Cystic fibrosis
  - Bronchogenic carcinoma

Procedure

- Using VATS/lateral/anterolateral thoracotomy
- Patient placed in lateral/semilateral position
- In debilitated patients/malignancy, pleurodesis is done using VATS.

Preoperative Assessment

- Same as prethoracotomy evaluation
- Also estimate size of existing pneumothorax and presence of functioning drain.

Premedications
- NPO orders
- Informed consent
- IV midazolam 0.03–0.15 mg/kg
- IV glycopyrollate 10 µg/kg
- Antibiotic prophylaxis
- DVT prophylaxis with LMWH
- ICD placement:
  - ICD placed preoperatively 12 hrs before surgery if:
    - Large pleural effusion > 2/3rd of hemithorax
    - 200 ml pleural collection.
  - Drain pleural fluid slowly as rapid reinflation of collapsed lung can precipitate ipsilateral ***re-expansion pulmonary edema.***

Monitor
- SpO_2, E_TCO_2
- NIBP, ECG
- Temperature, urine output
- Tidal volume, airway pressure
- IBP/CVP depending on patients condition.

Anesthetic Technique
- Open surgery or VATS: GA with OLV and DLT
- Talcum pleurodesis: GA with SLT and IPPV.

Induction
- Large bore IV access is necessary
- IV induction is done with thiopentone or propofol
- Slow induction as profound hypotension can occur at the time of induction
- DLT inserted following NMB with fiberoptic bronchoscopic (FOB)
- Intubate only once ICD is in place or if patient has no pneumothorax.

Maintenance
- TIVA is preferred if OLV as volatile anesthetics inhibits HPV
- Balanced anesthesia for small procedures with SLT
- If used, 0.5–1 MAC isoflurane is used
- Halothane and N_2O avoided.

Ventilation
- Collapse of lung may be necessary to aid surgical exposure
- Maintain minimal airway pressure
- Test for air-leaks by inflation of lungs to 25–30 cm H_2O and placing in water seal
- Aim for full expansion of lung at the end of surgery using CPAP, to oppose parietal and visceral pleura
- Potential for pneumothorax on nonoperative side.

Hemodynamics
- Precipitous hypotension occurs on induction
- Significant blood loss possible if pleura is diseased
- Circulatory collapse:
  - Possible when turned effusion side up
  - Occurs due to mediastinal shift which reduces venous return
  - Turn patient supine and drain effusion if this happens.

Extubation
- Extubated when patient is AWaC
- Postoperative ventilation required if:
  - Bilateral pleurectomy
  - Generalized lung disease
  - Large fluid shifts.

Postoperative Care
Management
- Nurse in sitting up position
- Humidified oxygen via face mask
- Drain pleural space
- Chest X-ray to confirm full lung expansion
- Suction on ICD aids lung expansion
- Lung volume replacement therapy:
  - Deep breathing
  - Incentive spirometry
  - Intermittent CPAP.

Analgesia
- Very painful surgery, especially if bilateral pleurectomy
- Multimodal analgesia:
  - Thoracic epidural
  - Paravertebral/intercostal/intrapleural blocks
  - Opioids: systemic/neuraxial/PCA
  - NSAIDs.

Complications
- Pneumothorax
- Atelectasis
- Empyema
- Trauma to vital structures.

POSTOPERATIVE ANALGESIA FOR THORACIC SURGERY[1,3,11]

Introduction
- No single technique is preferred and sufficient
- Multimodal analgesia is used.

AIIMS

- To reduce distress of patient
- To make early mobilization possible
- To improve lung function
- Reduce postoperative complications
- Reduce mortality and morbidity
- Reduce length of hospital stay.

Causes of Pain

Acute Pain

- Incision pain: caused by intercostal nerve (T_4–T_6)
- Chest drain: pain caused by intercostal nerves (T_7– T_8)
- Diaphragm pleural pain caused by phrenic nerve (C_3– C_5)
- Mediastinal pleural pain caused by vagus nerve (CNX)
- Shoulder joint pain caused by brachial plexus (C_5– C_7).

Chronic Pain

- Chronic incisional pain
- Chronic post-thoracotomy neuralgia.

Ipsilateral Shoulder Pain

- Position during surgery
- Exacerbation of chronic arthralgia due to position
- ICD in lung apex causing irritation of parietal pleura
- Referred pain from diaphragmatic irritation
- Transection of major bronchus
- Posterior end of posterolateral thoracotomy incision is not blocked by thoracic epidural. This can be described as shoulder pain.

Analgesic Alternatives

Regional Blocks

- Intercostal neve block
- Extrapleural nerve block
- Intrapleural nerve block
- Paravertebral block
- Thoracic epidural.

Opioids

- Parenteral
- Intrathecal
- Epidural
- Patient-controlled analgesia.

Others

- Cryoanalgesia
- Ketamine
- Dexmedetomidine
- NSAIDs
- TENS.

Regional Blocks

Intercostal Nerve Block

- Useful for incisional pain
- Block given at lower border of rib at lateral edge of sacrospinalis muscle
- Total bupivacaine dose per session to be less than 1 mg/kg
- Simple to perform
- Short duration of action of bupivacaine necessitates indwelling catheter
- Indwelling catheters are difficult to position percutaneously
- Does not act on diaphragmatic/mediastinal pleura.

Extrapleural Block

- Indwelling catheter is placed in pocket of retracted pleura
- Tip of catheter lies at the costovertebral joint
- Good analgesia
- LA may spread to paravertebral space.

Intrapleural Block

- Catheter placed between parietal and visceral pleura
- Causes widespread intercostal nerve block
- Does not spread to paravertebral space
- Unpredictable action as local anesthetic may be drained through ICD
- Causes rapid systemic absorption of local anesthetic.

Paravertebral Block

- Good analgesia of anterior and posterior primary ramii
- Allows local anesthetic spread to multiple levels from the insertion site
- Indwelling catheter is difficult to place and frequent dislodgment of catheter possible
- Causes fewer side effects than thoracic epidural.

Thoracic Epidural

- Given at T_3 – T_8 level with bupivacaine + fentanyl/ hydromorphone infusion
- Gold standard of analgesia for thoracic surgeries
- Provides for excellent analgesia with raised FRC
- Causes extensive sympathetic block and motor weakness

- Respiratory depression and hypotension may occur if bolus injections used
- Foley's catheter mandatory to differentiate urinary retention from oliguria.

Opioids

- Generally poor analgesia even with PCA, as MEAC produces sedation and hypoventilation
- Can be used as adjuvant to reduce local anesthetic dose.

Others

Cryoanalgesia

- Implies the application of extreme cold –60 °C to intercostal nerve
- Produces disruption of nerve impulse transmission for upto 6 months
- Associated with:
  - ***Chronic post-thoracotomy pain syndrome***
  - Higher failure rates.

NSAIDs

- Inadequate when used alone
- Synergistic action with regional anesthesia and opioids
- Reduces opioid consumption by 30%
- Good for shoulder pain
- Paracetamol upto 4g/day PO or PR
- COX-II inhibitors are better.

Ketamine

- Low-dose ketamine effective at doses of 1 mg/kg IM
- Continuous low-dose infusion can be given for refractory pain

Dexmedetomidine

- Reduces opioid consumption
- 0.3–0.4 µg/kg/hr IV infusion.

Transcutaneous Electrical Nerve Stimulation (TENS)

- Useful for mild to moderate pain
- Insufficient pain relief if used alone.

VIDEO-ASSISTED THORACOSCOPIC SURGERY (VATS)[1,2,3,11]

Introduction

It is a minimally invasive (key-hole) surgical procedure allowing direct vision into thoracic cavity without a big incision.

Indications[1]

General Intrathoracic Cavity

- Diagnosis/biopsy of any intrathoracic structure
- Lazer application for treatment of tumors
- Diagnosis and drainage of pleural effusion
- Treatment of chylothorax
- Debridement of empyema
- Retrieval of foreign body.

Lungs

- Wedge resection, segmentectomy, lobectomy
- Closure of persistent/recurrent pneumothorax
- Identification and closure of bronchopleural fistula (BPF)
- Removal of bronchogenic cysts
- Lung Volume Reduction Surgery (LVRS).

Pleura

- Adhesiolysis
- Pleurodesis
- Decortication.

Mediastinum

- Removal of mediastinal cysts
- Thymectomy
- Resection of tumors.

Esophagus and Diaphragm

- Tumor staging and resection
- Repair of diaphragm
- Antireflux surgery
- ***Heller's*** cardiomyotomy, CDH repair.

Heart

- Pericardiectomy
- Diagnosis of cardiac herniation post-pneumonectomy
- MIDCAB
- Minimally invasive valve procedures
- PDA ligation.

Spine and Nerves

- Dorsal thoracic sympathectomy
- Splanchnicolysis
- Drainage of spinal abscess
- Discectomy
- Fusion and correction of spinal deformity.

Trauma

- Assessment of injury
- Treatment of haemorrhage
- Evacuation of clot.

Advantages
- Small and cosmetic incision
- Less postoperative pain
- Earlier mobilization
- Faster postoperative recovery
- Lesser overall morbidity
- Better PFTs compared with open thoracotomy
- Lesser blood loss
- Reduced OT time for some procedures
- Reduced hospital stay and costs.

Procedure
- Lateral decubitus position
- Small incision made in lateral chest wall
- 2–3 additional incisions made for larger surgeries to allow application of surgical instruments and stapling devices
- Trocar is introduced into chest after ipsilateral lung has been collapsed
- Thoracoscope is placed through trocar into chest
- At the end of surgery, chest drain is inserted and lung re-expanded.

Anesthetic Considerations
- CO_2 insufflation done during VATS causes:
  - Raised airway pressure
  - Increased E_TCO_2
  - Mediastinal shift with hypotension
  - Reduced SpO_2.
- One-lung ventilation
- Potential for massive, sudden hemorrhage
- Sudden mediastinal shift and hypotension possible
- Lateral position surgery.

Choice of Anesthetic Technique
Local Anesthesia
- LA infiltrated into lateral thoracic wall and parietal pleura
- Topical local anesthetic applied on visceral pleura
- Stellate ganglion block given concomitantly to inhibit cough reflex from hilar manipulation
- Partial collapse of lung on ipsilateral side occurs when air enters pleural cavity
- Give high FiO_2 via facemask to overcome shunt due to loss of lung volume.

Regional Anesthesia
- Intercostal N block at the level of incision and two spaces above and below
- Thoracic epidural, paravertebral, intrapleural blocks
- Technique reserved for brief procedures
- Spontaneously breathing patient may not tolerate long surgeries as loss of lung volume due to collapse occurs
- IV stellate ganglion block accompanies RA always.

GA with OLV
- Technique of choice
- DLT/BB used to collapse lung
- DLT is better as it allows selective ventilation of contralateral lung
- DLT allows rapid collapse of lung: CO_2 insufflation is not required

GA with TLV
- GA with two-lung ventilation
- Require CO_2 insufflation
- Useful in small children where lung isolation not possible as even smallest size DLT will obstruct RUL bronchus.

ANESTHETIC MANAGEMENT
Preoperative Evaluation
- Same as for thoracotomy
- Also evaluate for congenital heart disease and airway compression
- 50% compression of trachea indicates increased perioperative risk

Preoperative Preparation and Optimization
- Intranasal (0.3 mg/kg) or IV midazolam (0.03–0.15 mg/kg)
- Adequate blood kept ready as potential for bleeding
- Continue bronchodilator and steroid therapy
- Antibiotic prophylaxis, chest physiotherapy given preoperatively.

Monitors
- Pulse oximetry, E_TCO_2
- NIBP, ECG
- Neuromuscular monitor
- Temperature, urine output
- Precordial stethoscope, airway pressure
- ***Differential capnography***
- IBP in radial artery of dependent arm
- CVP placement on the side of thoracoscopy recommended to avoid bilateral pneumothorax
- CVP is required for vascular access especially in children.

Induction
- Two venous ports necessary as torrential bleeding possible
- IV or inhalational induction can be used
- Short-acting agents used to allow rapid emergence and recovery
- Intermediate-acting NMBAs used depending on duration of surgery
- Rigid bronchoscope is used to stent obstruction, if airway compression present.

Position
- Supine/slight lateral (15–30) position for anterior mediastinal surgeries
- 90 lateral position for hilar masses and lobectomy
- Nearly prone position for posterior mediastinal masses.

Maintenance
- TIVA-preferred technique as volatile anesthetics inhibit HPV
- If balanced anesthesia is used, 0.5–1 MAC isoflurane is used
- Halothane and N_2O avoided.

Ventilation
- Ventilatory goals:
  - FiO_2 0.95
  - Tidal volume 5–6 ml/kg
  - Respiratory rate 12–20 cycles/min
  - E_TCO_2 32–38 mm Hg
- OLV started before introduction of trocar
- Increase minute ventilation if hypercarbia occurs
- CPAP cannot be used for upper lung as distended lung will interfere with surgical exposure
- Almitrene with NO can be used to prevent hypoxemia.

Hemodynamics
- Ringer's lactate is *fluid of choice*
- Minimal blood loss occurs usually
- Judicious fluid therapy as excessive IV fluids can cause:
  - Increased intrapulmonary shunting
  - Pulmonary edema of dependent lung
  - Occurs especially if prolonged surgery
- Give fluids for replacing deficits
- Maintenance and third space fluid replacement is avoided.

Extubation
- Functional ICD with under water seal inserted prior to extubation
- Check bilateral air entry at the time of extubation
- Extubate when AWaC
- Avoid coughing/straining at extubation.

Postoperative Care
Management
- Nursed in sitting up position
- Encourage early mobilization of patient
- Avoid high airway pressures, to prevent rupture, if postoperatively ventilated.

Analgesia
- Multimodal analgesia
- Less pain after VATS
- LA infiltration at the incision site
- Intrapleural block, paravertebral, thoracic epidural
- Opioids: systemic/neuraxial/PCA
- NSAIDs.

Complications
- Hemorrhage
- Subcutaneous emphysema, empyema, recurrent pneumothorax
- Infection, pneumonia, empyema, abscess
- Pulmonary edema
- Visceral damage: RL nerve, aorta, SVC, trachea
- Lung herniation through chest wall
- Air embolism
- Persistent air-leaks
- Dissemination of mets to thoracostomy tube site
- Atrial arrhythmias: AF, SVT
- ***Down lung syndrome***
- ***Horner's syndrome.***

LUNG TRANSPLANT[1,2,3,11]

Indications
- COPD
- Cystic fibrosis and bronchiectasis
- Pulmonary fibrosis:
  - Idiopathic
  - Associated with connective tissue disorders
- Primary pulmonary HTN
- Bronchoalveolar lung cancer
- Lymphangioleiomyomatosis.

Inclusion Criteria
- Untreatable parenchymal/vascular disease
- Absence of other major medical illnesses
- Substantial limitation of daily activity
- NYHA III or IV patients

- Rehabilitation potential
- Acceptable nutritional status
- Disease-specific mortality > transplant-specific mortality for 1–2 years.

Contraindications

Absolute Contraindications

- Untreatable disease of other organ systems
- Active malignancy within the last 2 years
- Noncurable chronic pulmonary infection
- Chronic active hepatitis B, C or HIV
- Significant chest wall/spinal deformity
- Untreatable psychiatric condition
- Documented noncompliance with therapy
- Substance addiction:
  - Either active or in the last 6 months
  - Alcohol
  - Smoking
  - Narcotics.

Relative Contraindications

- Age > 65 yrs
- Critical/unstable: shock, mechanical ventilation, ECMO
- Severely impaired functional status
- Poor rehabilitation potential
- Highly resistant infections
- BMI ≥ 30 kg/m^2
- Severe osteoporosis
- Illnesses causing end-organ damage:
  - Diabetes
  - Hypertension
  - Peripheral Vascular Disease (PVD)
  - CAD poststenting/PTCA.

Types

- Single lung transplant
- Bilateral sequential transplant
- En-bloc double lung transplant
- Heart lung transplant
- Riving related lobar transplant.

Single lung transplant	Double lung transplant
Technically easier	More difficult
Not done in infections as native lung can infect new lung	Can be done
Useful for difficult recipients (prior thoracic surgery)	Not done for difficult recipients
Bad functional improvement	Good improvement

Contd...

Contd...

Single lung transplant	Double lung transplant
Increased VP mismatch postoperatively	No such increase
Better survival	No such increase
CPB used if severe pulmonary HTN	CPB used routinely

Procedure

- For single lung transplant:
  - Lateral decubitus position
  - Via thoracotomy
  - Pelvis is angled to allow femoral cannulation for CPB
  - OLV during resection and removal of lung
  - Once OLV is stabilized, lung is dissected and PA isolated
  - Progressive temporary clamping of PA done
  - If temporary clamping is well-tolerated, PA is clamped and stapled
  - Pneumonectomy is completed
  - Implant graft beginning with airway anastomosis
  - Anastomosis completed with telescoping bronchial anastomoses or use of omental wrap
  - PA branches attached to graft
  - Cuff of left atrium anastomosed to pulmonary vein
  - Partially inflate implanted lung, de-air LA cuff and pulmonary veins
  - Restore circulation of organ.
- For double lung transplant:
  - Supine position
  - ***Clamshell incision***
  - Bilateral anterior thoracotomy with or without transverse sternotomy
  - Double in-bloc transplant uses hypothermic CPB and cardioplegia
  - OLV during dissection and removal of lung
  - Sequential transplant does not require CPB routinely and done in 2 phases:
  - First phase:
    - Most severely compromised lung (as by V-P scan) removed by ventilation of contralateral lung
    - Bronchial anastomosis with new lung.
  - Second phase: other lung removed during ventilation of transplanted lung.

Preoperative Evaluation

- Same as for thoracotomy
- History of exercise tolerance and use of continuous pulmonary vasodilator (prostacycline).

Preoperative Preparation and Premedication

- NPO orders
- Informed consent
- IV midazolam 0.03 mg/kg IV, especially if pulmonary HTN
- Avoid sedation if:
  - Tachypnea
  - Functional limitation
  - Significant right-left shunt.
- Diphenhydramine to protect against histamine release
- Thoracic epidural catheter (even if CPB and anti-coagulation planned)
- Large bore IV access and central venous access for PAC
- Additional central venous access with multi-lumen catheter for IV fluids
- Meticulous removal of air from tubing, especially if right-left shunt
- Cannulate femoral artery for CPB.

OT Preparation

- Anesthesia machine should have:
  - Wide range of I : E ratio
  - Different ventilator modes
  - Efficacy at high airway pressures
- Apparatus to deliver CPAP
- Fiberoptic bronchoscope to confirm DLT position
- CPB on standby
- Suction apparatus
- Nitric oxide delivery system desirable.

Monitors

- Pulse oximetry, E_TCO_2
- NIBP, ECG
- Neuromuscular monitoring
- Urine output, temperature
- Serial ABGs, blood glucose
- PAC:
  - May migrate to surgical field on positioning laterally
  - Surgeon should palpate and withdraw before clamping PA
- IBP through femoral A as radial A may be clamped after position
- TEE for RV function, intracardiac shunts and evaluation of vascular anastomosis.

Induction

- Prolonged preoxygenation required as:
  - Patients generally have increased FRC
  - Increased airway pressures
  - Reduced alveolar ventilation
  - Preoxygenation done for 15–20 minutes
- Thiopentone/etomidate/propofol/ketamine used depending on disease
- Gradual induction as high preoperative sympathetic tone will be lost on induction
- Precipitous hypotension on induction possible
- Fentanyl 10–15 µg/kg or sufentanyl 1–2 µg/kg with succinylcholine/NDMR.

Position

- Supine if double lung transplant
- Lateral decubitus for single lung transplant.

Maintenance

- TIVA preferred as:
  - Frequent need for airway access during surgery for:
    - Suction
    - Bronchoscopy.
  - This may lighten patient if VA used
- Also VA contraindicated in end stage lung disease as it inhibits HPV
- If necessary 0.5–1 MAC isoflurane used
- Halothane and N_2O contraindicated.

Ventilation

- De-airing of LA cuff and pulmonary veins to be done before anastomoses
- Left-sided DLT preferred
- If cystic fibrosis with thick secretions:
  - Single lumen ETT inserted first
  - This is followed by FOB-guided bronchial lavage
  - This is followed by DLT insertion.
- Watch for pulmonary tamponade during IPPV
- Ventilatory goals:
  - Permissive hypercapnea with lung-protective ventilation
  - Tidal volume 6–7 ml/kg
  - 100% FiO_2 used intraoperatively as it:
    - Causes pulmonary vasodilatation
    - Reduces RV afterload.
  - I : E ratio = 1 : 4 or 1 : 5.
- Intermittent apnea with open ventilator circuit to allow venting of lungs if pulmonary tamponade occurs
- Prevent hypoxia/hypercarbia/hyperinflation if pulmonary hypertension
- Consider ECMO if refractory hypoxemia.

Hemodynamics

- Large volume shifts occur during surgery
- Minimize IV fluid administration (around 10–20 ml/kg/hr)
- Monitor RV function during conversion to OLV as RV afterload increases
- TEE for RV dysfunction during PA clamping
- If PA clamping is not tolerated, treat with:
  - PGE_1
  - Nitric oxide
  - Inotropes
  - CPB if RV dysfunction persists.
- During bronchial anastomosis watch for:
  - Low cardiac output
  - Arrhythmias
  - Systemic hypotension and pulmonary HTN.
- Increased chances of hypothermia:
  - Warm IV fluids used
  - Warm blankets
  - Forced air warmers.

Role of CPB

- Electively indicated for:
  - Severe pulmonary HTN
  - Children in whom DLT may cause RUL obstruction.
- Emergent indication in:
  - RV dysfunction
  - Early graft dysfunction during second lung transplant
  - Surgical mishaps.
- CPB not preferred as it:
  - Increases lung dysfunction
  - Increases bleeding and blood product use
  - Associated with increased duration of ventilation.
- Replace DLT with SLT at the end of surgery.

Extubation

- Generally postoperatively ventilated
- FO bronchoscopy done to:
  - Examine bronchial anastomosis
  - Suction blood and secretions.
- Inspect upper airway for edema before DLT removal
- Reduce FiO_2 and start weaning when AwaC
- Differential lung ventilation of native and transplanted lungs is also rarely done.

Postoperative Care

Management

- Nurse with transplant side up for obstructive lung disease and pulmonary HTN patients
- Nurse with transplant side down for restrictive lung disease patients
- Induction phase of immunosuppression started for 5–10 days
- Antibiotic therapy to be continued.

Complications

- Pulmonary HTN and RV failure during PA clamping
- Systemic hypotension following transplantation as new lung has vasodilator preservatives
- Air embolism due to incomplete de-airing of LA cuff
- Anastomotic leaks at LA cuff or PA
- Early graft rejection
- Fulminant pulmonary edema
- Hypoxemia due to:
  - OLV
  - Graft rejection
  - Secretions in cystic fibrosis.
- Pneumothorax
- Infections: CMV, pneumocystis carinii.

Considerations in Previous Lung Transplant

- Immunocompromised status of patient
- Chemotherapy causing:
  - Tumors
  - Cardiac failure
  - Renal failure.
- Cough reflex present only in native airway as transplanted lung is denervated
- Bronchiolitis obliterans common
- Capnography:
  - Differences in compliance between native and new lung present
  - This causes biphasic pattern of capnograph with two peaks.
- DLT with differential lung ventilation if single lung transplant as difference in compliance and blood flow of the two lungs.

BRONCHOALVEOLAR LAVAGE (BAL)[1,2,3,9]

Introduction

This is a treatment modality during which 10–20 L of NS is instilled and then drained in 500-1000 ml aliquots through one side of DLT under GA.

Indications

- Symptomatic pulmonary alveolar proteinosis: BAL is *treatment of choice*
- Can be used as an alternative therapy but with no convincing results in:

- Cystic fibrosis
- Asthmatic bronchitis
- Lipid pneumonitis
- Radioactive dust inhalation
- Silicosis.

Preoperative Investigations

- Routine blood investigations
- Chest X-ray, CT scan, V-P scan to determine most impaired lung
- If recent lung biopsy done, ICD placed as BPF maybe present.

Monitors

- SpO_2, E_TCO_2
- NIBP, ECG
- Precordial stethoscope on ventilated lung to check fluid leak
- Tidal volume, pulmonary compliance
- CVP, PAC/TEE
- In and out fluid with each cycle
- ABG: terminate if increase in (A-a) DO_2.

Induction

- Adequate preoxygenation done before induction
- IV induction done with thiopentone/propofol/etomidate
- Atracurium used for muscle relaxation
- Left-sided DLT with FOB confirmation
- Secure DLT and maintain hand on DLT throughout procedure
- This is necessary to prevent tube dislodgement under pressure of saline during BAL
- Check cuff seal at 50 cmH_2O for perfect lung separation.

Position

- Supine
- Head down during drainage to aid drainage.

Ventilation

- OLV with highest possible FiO_2
- Oxygenation increases during filling and reduces during drainage phase as transmitted hydrostatic pressure from lavage lung acts like HPV
- If severely hypoxemic:
  - Nitric oxide administration to ventilated lung
  - ECMO
  - Inflation of PAC balloon in PA of lavage lung.
- In very small children where DLT cannot be used, CPB done.

Procedure

- Supine position
- If both lungs equally involved, left lung lavaged first as gas exchange better with larger right lung
- GA induced, OLV instituted to nonlavage lung
- Irrigation system connected to nonventilated tube of DLT
- Irrigation:
  - 1 liter NS (37 °C) introduced in nonlavage lung
  - Irrigating fluid placed 30 cm above midaxillary line
  - Collection container placed 60 cm below the patient
  - Small level suction is also used (< 20 cm H_2O)
  - Cycle repeated till effluents are clear.
- Usually 10–20 L instilled and more than 90% is recovered
- If cumulative dose of in-fluid exceeds out-fluid by more than 1000 ml:
  - Suspect hydrothorax
  - Immediate chest X-ray taken
- Vibration and percussion applied as physiotherapy during filling and drainage phase
- Lavage lung suctioned at the end of procedure
- 10 mg furosemide IV given to increase diuresis
- Replace DLT with SLT at the end of procedure
- Inspect FOB and suction if required
- If bilateral BAL, 1 hr of two-lung ventilation done, to allow recovery of lavaged lung as this will be used for gas exchange.

Postoperative Care

- Conventional ventilation with PEEP (usually for < 2 hours)
- Extubate when AWaC
- Alveolar infiltrates on chest X-ray clear within 24 hours
- Cough and lung volume expansion strategies.

Complications

- Spillage of fluid
- Hydrothorax
- Pulmonary edema
- Severe hypoxemia
- Iatrogenic infections.

MEDIASTINAL MASS[1,2,3,11]

Anatomy

- Parts of mediastinum:
  - Superior mediastinum
  - Inferior mediastinum:

- Anterior mediastinum
- Posterior mediastinum
- Middle mediastinum.

- Boundaries:
  - Transthoracic plane:
    - Extends from sternal angle to lower border of T_4 at upper level of pericardium
    - Divides into superior and inferior mediastinum.
  - Inferior mediastinum is divided into anterior, middle and posterior mediastinum by heart and pericardial sac.

Contents

- Anterior mediastinum:
  - Extends between anterior pericardial reflection and sternum
  - Contains:
    - Thymus
    - Aortic arch
    - Superior vena cava
    - Areolar tissue
    - Lymph nodes.
- Middle mediastinum contains:
  - Heart and pericardium
  - Tracheal bifurcation
  - Main bronchi
  - Hila of lung
  - Phrenic nerve
  - Lymphatics
  - Lymph nodes.
- Posterior mediastinum:
  - Extends between posterior pericardial reflection and vertebral column
  - Contains:
    - Esophagus, thoracic duct
    - Descending aorta
    - Azygous and hemiazygous vein
    - Vagus nerve
    - Sympathetic chain
    - Paravertebral lymph nodes.

Mediastinal Masses

- Tumors:
  - Anterior mediastinum:
    - Thymic tumors
    - Thyroid and parathyroid tumors
    - Lymphomas
    - Germ cell tumors.
  - Middle mediastinum
    - Lymphoma
    - Mesenchymal tumors.
  - Posterior mediastinum:
    - Esophageal carcinoma
    - Neurogenic tumors.
- Benign conditions:
  - Development cysts:
    - Pericardial cysts
    - Esophageal cysts.
  - Granulomatous lymphadenopathy:
    - Tuberculosis
    - Sarcoidosis.
  - Vascular:
    - Aneurysms:
      - Thoracic aorta
      - Innominate vein.
    - Aberrant blood vessels:
      - Persistent LSVC
      - Anomalous left pulmonary artery.

MEDIASTINOSCOPY[3]

Introduction

Diagnostic procedure introduced by ***Carlens.***

Indications

- Staging of bronchogenic carcinoma: high sensitivity > 80% and specificity 100%
- Mediastinal mass biopsy
- Diagnosis of mediastinal lymphadenopathy:
  - Sarcoidosis
  - Lymphomas.

Contraindications

Absolute Contraindication

Previous mediastinoscopy as adhesions may make dissection impossible

Relative Contraindications

- Cerebrovascular disease
- Severe cervical spine disease
- Superior vena caval obstruction
- Thoracic aortic aneurysm
- Tracheal deviation
- Previous chest radiotherapy.

Procedure

- Cervical mediastinoscopy:
  - Via small transverse 3 cm incision above suprasternal notch

  - Patient placed in reverse Trendelenburg position
  - Scope is passed into pretracheal area
  - It is advanced along anterior aspect of trachea
  - Scope passes behind aortic arch, innominate vein and left recurrent laryngeal nerve
  - Biopsy taken and lymph nodes are palpated digitally.
- ***Chamberlain procedure:***
  - Anterior mediastinoscopy
  - Done via II or III ICS
  - Incision through bed of II or III costal cartilage
  - Incision made lateral to sternal border
  - Used to inspect lower mediastinum
  - Position of patient is supine with head on ring, neck extended and sandbag under shoulders.

Preoperative Assessment

- Clinical assessment:
  - Mostly smokers with pulmonary disease
  - Associated history of HTN, coronary disease, PVD
  - History of stroke or TIA and signs of reduced cerebral circulation
  - Airway obstruction history:
    - Unilateral wheeze
    - Dyspnea, stridor
    - Cough, cyanosis.
  - Recurrent RTI if tracheobronchial compression
  - Eaton Lambert's syndrome with proximal myopathy
  - Syncope on Valsalva suggestive of cardiac compression
  - Positional variation: orthopnea reduces on sitting up.
- Investigations:
  - Complete blood count
  - Blood urea, serum creatinine, electrolytes
  - Baseline ABG on room air
  - Chest X-ray and ECG: Mediastinal widening due to SVC syndrome
  - Pulmonary function tests:
    - Done in upright and supine position
    - Disproportionate reduction in MEFR: Increased chances of tracheomalacia
    - Combined OLD and RLD pattern suggests increased incidence complications
    - If cyanosis occurs with good PFTs:
      - Indicates PA occlusion
      - Pulmonary angiography should be done.
  - Flow Volume Loop in supine and upright position
  - CT scan/MRI of airway:
    - Extent of tumour
    - Effect on surrounding structures
    - General anesthesia is safe if:
      - Tracheal cross-sectional area ≥ 50%
      - PEFR ≥ 50% of predicted.
  - ECHO: Supine and upright for cardiac compression.

Factors Predicting Postoperative Pulmonary Complications

- Cardiopulmonary signs and symptoms at presentation
- Combined obstructive and restrictive picture
- PEFR < 40%
- Tracheal diameter < 50% on CT scan.

Anesthetic Considerations

- Tracheobronchial tree compression:
  - Airway obstruction
  - Persistent LRTI.
- Persistent tracheobronchial obstruction postoperatively:
  - If diagnostic procedure, compression is not relieved
  - May be aggravated due to injury.
- Compression of intrathoracic superior vena cava:
  - Tongue and orofacial swelling
  - Laryngeal edema
  - Distension of veins:
    - Increased chances of bleeding at intubation
    - Altered consciousness
    - Raised ICP.
- Cardiac Compression:
  - Cardiac tamponade
  - Arrhythmias
  - Cardiac arrest postinduction.
- Eaton Lambert's syndrome: Sensitive to NDMR and DMR
- Systemic coexisting diseases:
  - Usually advanced ASA grade
  - Paraneoplastic syndromes:
    - ACTH
    - ADH
    - Parathyroid hormone.
- Preoperative chemotherapy and radiotherapy complications:

  - Bleomycin lung
  - Cisplatin: renal complications
  - Anthracycline, doxorubicin: Cardiac complications.
- Intraoperative vital organs damage: Left RLN or bilateral RLN injury:
  - Postoperative stridor
  - Phrenic nerve injury
  - Torrential bleeding: SVC, aorta.

Anesthetic Goals

Prevent partial obstruction being made complete by:
- Passing ETT/bronchoscope/stent past the obstruction
- Securing airway in awake, spontaneously breathing patient
- Maintain spontaneous ventilation after induction
- Avoid NMBA
- Lateral/semi-Fowler's position if extreme airway compromise.

Preoperative Assessment

Grading of symptoms:
- Asymptomatic
- Mildly symptomatic: Can lie supine with some cough or pressure sensation
- Moderately symptomatic: Can lie supine for short periods but not indefinitely
- Severely symptomatic: Cannot tolerate supine position.

Preoperative Preparation and Premedication

- Consider preoperative chemotherapy or radiotherapy to shrink tumor
- Head-end elevation, steroids and diuretics if SVC obstruction
- Cross-matched blood to be kept readily available
- Adequate local anaesthetic if fibreoptic planned
- Antisialogogues: To reduce secretions
- Sedation:
  - Avoid sedatives if airway obstruction
  - IV midazolam 0.05 mg/kg if no airway obstruction.
- Shift in head up position if significant dyspnea is present
- If severely symptomatic, stenting is performed prior to surgery.

Choice of Anesthetic Technique

- Local anesthesia preferred if minor procedure
- GA with ETT and spontaneous ventilation if obstruction is technique of choice:
  - GA with inhalational induction if no airway obstruction
  - GA with IV induction preferred if:
    - Tracheal diameter ≥ 50%
    - PEFR ≥ 50% predicted.

Risk Stratification for General Anesthesia[1]

Stage	Risk class	Description
A	Safe	Asymptomatic adult
		Tracheobronchial (TB) diameter > 50% of normal
B	Unsafe	Severely symptomatic
		Child with TB < 50% of normal regardless of symptoms
C	Uncertain	Mild to moderate symptoms in child with TB diameter > 50% of normal
		Mild to moderate symptoms in adult with TB diameter < 50% of normal
		Adult or child unable to give history

Monitors

- SpO_2 on right hand as decrease in amplitude of signal indicates innominate artery compression
- $ETCO_2$, ECG
- NIBP on left hand as innominate A compression by mediastinoscope can give low readings
- IBP on right hand necessary to check for:
  - Reflex arrhythmias
  - Compression of innominate artery
- Neuromuscular monitoring especially, if Eaton-Lambert's syndrome
- Airway pressure for tracheal/bronchial compression by mediastinoscope
- PA catheter, cardiac output monitor if cardiac/PA compression.

Induction

- IV access secured in lower limb in case SVC tear occurs during surgery
- Avoid drug administration in upper limb in SVC syndrome as action is unpredictable
- Induce in sitting or leaning forward position if PA or cardiac compression
- Awake intubation with fiberoptic bronchoscopy
- Reinforced tube is preferred to reduce risk of kinking
- ETT is used to stent obstruction if obstruction is proximal
- Rigid bronchoscope or anode tube if obstruction is at carinal level.

Maintenance

- Balanced anesthesia with volatile anesthetics, opioid boluses or infusion-preferred method
- IV ketamine with N_2O and O_2 in children
- Maintain deep planes to avoid coughing/bucking as:
  - Increased risk of trauma by mediastinoscope
  - Can cause venous engorgment in chest.
- Neuromuscular Blocking Agents (NMBAs):
  - Avoid NMBAs in Lambert's-Eaton syndrome
  - Maintenance on spontaneous ventilation preferred
  - If obstruction is already stented, NMBAs may be used.

Ventilation

- Spontaneous ventilation critical to avoid precipitating complete obstruction
- If mechanically ventilated:
  - Pressure-controlled ventilation used to detect early increase in airway pressure
  - Sanders injector/jet ventilator used if rigid bronchoscope
  - Lowest FiO_2 which is compatible with adequate SpO_2 used, if patient has had recent bleomycin therapy.
- Pleura may be breached:
  - Drained by wide bore nasogastric tube
  - This is removed as positive pressure is applied to lungs
  - Suture line is completed simultaneously to prevent pneumothorax.

Hemodynamics

- Cardiac compression:
  - Commonly occurs during the procedure
  - Watch for arrhythmias, factitious cardiac arrest
  - Vasopressors/inotropes used if hypotension occurs due to compression
- Hemorrhage:
  - Hemorrhage is the *most common* complication
  - Blood loss may be substantial
  - If venous bleeding occurs, induce hypotension to decrease the size of tear
  - Fluids, if given in upper limb, may enter mediastinum
  - Therefore, if venous bleeding occurs, use lower limb large bore angiocatheter.

Extubation

- Perform fiberoptic bronchoscopy prior to extubation to rule out tracheomalacia in long standing cases
- Extubate only after:
  - Full recovery of reflexes
  - Full recovery of neuromuscular function.
- Consider postoperative ventilation if:
  - Long duration of surgery
  - Accidental resection of major nerves
  - Airway patency absent.

Postoperative Care

Management

- Nursing in sitting up position
- Check X-ray for pneumothorax is mandatory
- Watch for stridor due to RLN injury or paratracheal hematoma.

Analgesia

- Multimodal analgesia
- LA infilteration of wound
- Regional blocks:
  - Intercostal N block
  - Paravertebral block
  - Superior cervical plexus block.
- Paracetamol and NSAIDs
- Patient-controlled anesthesia.

Complications

- Hemorrhage:
  - *Most common complication*
  - Stopped by tamponade or hemostasis following thoracotomy or median sternotomy.
- Airway obstruction post-induction due to:
  - Loss of lung volume with a constant mediastinal mass size causing compression
  - Increased central blood volume with a constant mediastinal mass size
  - Obstructed tip of ETT by wall of tracheobronchial tree
  - Loss of pleural pressure and transmural pressure gradient
  - Tracheomalacia, RLN injury
  - Increased mass size due to surgical manipulation causing edema and hematoma
  - Creation of turbulent gas flow by PPV.
- Air leak syndromes:
  - Pneumothorax
  - Hemothorax
  - Chylothorax
  - Pneumomediastinum.
- Nerve injury:
  - RLN injury, phrenic N, injury

  - Initiation of autonomic reflexes by:
    - Stimulation of tracheal/aortic arch receptors
    - Vagal reflexes.
- Factitious cardiac arrest:
  - Absent right radial pulse but present on left side
  - Occurs due to compression of innominate A by mediastinoscope
  - Important to recognize if carotid bruit/TIA/stroke
  - Transient left hemiparesis possible postoperatively.
- Others:
  - Acute tracheal collapse
  - Esophageal tear, thoracic duct injury
  - Mediastinitis
  - Air embolism in spontaneously breathing patient with venous rent in sitting position.

Recent Advances

Video-assisted mediastinoscopy:
- Increases visual field and image magnification
- Reduces complications
- Video-assisted mediastinal lymphadenectomy (VAMLA)
- Video-assisted lobectonmy (VATS-lobectomy).

RIGID BRONCHOSCOPY[1,2,3]

Introduction

It is essentially a hollow tube with blunted and bevelled edges and sidearm for providing anesthesia.

Indications for Bronchoscopy[3]

Diagnostic

- Cough, hemoptysis, wheeze
- Unresolved pneumonia, atelectasis
- Diffuse lung disease, trachea-esophageal fistula
- To rule out metastasis
- Assessment of local recurrence
- RLN palsy, diaphragmatic palsy
- Acute inhalational injury
- Preoperative evaluation
- During mechanical ventilation.

Therapeutic

- Foreign body
- Retained secretions
- Atelectasis, lung abscess
- Repositioning of endotracheal tubes
- Placement of endobronchial tubes
- Laser surgeries of airway
- Stent insertion, splinting airway.

Indications for Rigid Bronchoscopy

- Foreign body
- Massive hemoptysis
- Vascular tumors
- Endobronchial resection, diathermy
- Surgical assessment before mediastinoscopy
- Prior to thoracotomy
- Stent insertion.

Complications

- Trauma to teeth, bronchial/tracheal perforation
- Hemorrhage, bronchospasm
- Subglottic edema
- Barotrauma, especially if HFJV
- Blood clots causing airway obstruction
- Aspiration:
  - As airway is never completely secured
  - Defer bronchoscopy in patients at risk for aspiration.

Preoperative Assessment

- Similar to thoracotomy
- Look for clinical signs of airway obstruction.

Premedication

- Antiaspiration prophylaxis: Night before and day of surgery as airway is not secure
- Pulmonary therapy if possible:
  - Cool saline mist
  - Racemic epinephrine nebulization
  - Systemic steroids.
- Continue all cardiac and respiratory drugs
- No sedation if significant airway obstruction
- IV glycopyrrolate 10 µg/kg
- IV midazolam 0.03-0.15 mg/kg.

Monitors

- Pulse oximetry, precordial stethoscope
- No way to measure E_TCO_2/VA concentration as airway is open to atmosphere
- NIBP, ECG
- Airway pressures
- CVP/PAC/IBP according to patient condition
- ABGs if prolonged procedure.

Induction

- Adequate preoxygenation
- IV induction:
  - Preferred in elderly
  - Propofol/short acting IV agents till airway is secured

  - Short acting MR (succinylcholine/mivacurium) for intubation if not contraindicated.
- Inhalation induction:
  - For children/upper airway obstruction
  - Place mouth guard to protect gums and teeth.

Maintenance

- Deep anesthetic planes with prompt return of respiration as very painful
- TIVA with propofol and remifentanyl preferred
- Balanced anesthesia with VA used in children
- If balanced anesthesia used, loss of VA occurs
- Use vecuronium/atracurium if prolonged surgery
- Use lowest possible FiO_2 (< 40% if possible) if Nd-YAG lazer used, to reduce risk of airway fire
- Place throat packs if increased leak of tidal volume during PPV
- If desaturation occurs, stop surgery and ventilate with bronchoscope/ETT/mask.

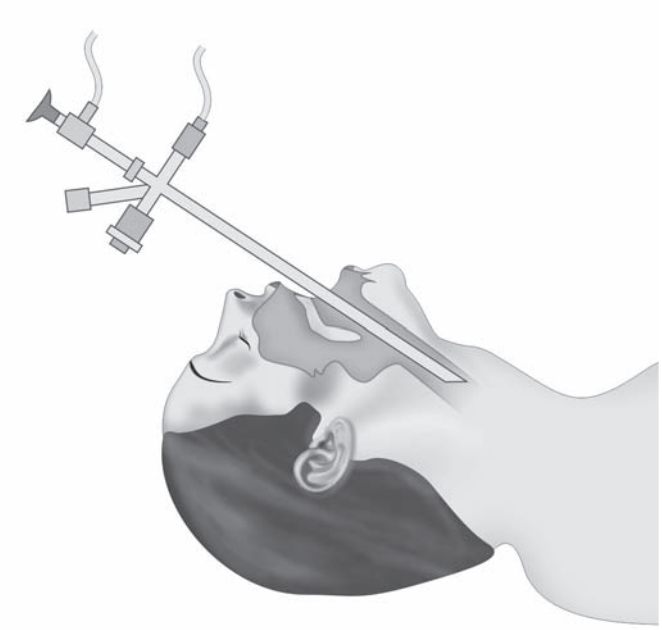


Fig. 2.60: Rigid bronchoscopy

Postoperative Care

- Postoperative ventilation if edematous airway
- Extubate when AWaC
- O_2 by mask in sitting position
- Suctioning done with diseased side up
- Racemic epinephrine nebulization or steroids if airway edema.

Ventilation

Challenging as shared airway:

Spontenous Ventilation

Topical anesthesia/nerve blocks to reduce coughing.

Apneic Ventilation

- After preoxygenation induction and NMB cessation of IPPV
- $PaCO_2$ increases 6 mm Hg during first minute and at 3 mm Hg/min thereafter
- O_2 insufflated via catheter placed above carina at 10–15 L/min
- Limits duration of surgical exposure to 5 min intervals.

Ventilating Bronchoscope

- Ideal for infants and children
- Mechanical ventilator connected to side of arm bronchoscope
- Has glass slide device at the proximal end of bronchoscope
- T-piece can be attached to side port and intermittent ventilation done to reservoir bag.
- Advantages:
  - Requires lighter planes
  - Better immobilization of airway and better exposure
  - Lung compliance and tidal volume monitored constantly
  - Avoids barotrauma seen with HFJV.
- Disadvantages:
  - Limits period of instrumentation as ventilation possible only when eyepiece is in place
  - Causes hypoxia and hypercarbia if leaks are present around bronchoscope
  - Leak of VA and light anaesthetic plane possible if discrepancy between size of bronchoscope and airway.

High-frequency Positive Pressure Ventilation

- Upto 150 breaths/min
- Tracheobronchial wall immobilized during ventilation and thus better surgical conditions.

Sanders Venturi Injector

- Technique:
  - High-pressure O_2 (50 PSIG) injected intermittently
  - This is done through needle at proximal end of bronchoscope
  - Needle is 16–18 G, 2.5–3.5 cm, placed parallel to long axis of bronchoscope
  - Match injector needle size with type of bronchoscope and O_2 pressure used

  - O_2 delivered using controllable pressure relief value and toggle switch
  - When toggle switch is depressed, room air is entrained along with O_2
  - Ensure proximal end of bronchoscope is open to allow gas exchange.
- Physiology:
  - Uses Venturi principle to entrain air
  - System is pressure limited as long as proximal end is open
  - Insertion of suction catheter/forceps into lumen of bronchoscope may increase luminal pressure.
- Advantages:
  - Allows continuous ventilation as the presence of eye-piece is not necessary for ventilation
  - Duration of bronchoscopy is minimized
  - Permits extended bronchoscopy.
- Disadvantages:
  - Entrainment of air causes variable FiO_2 at the distal end
  - Poor ventilation if compliance of lungs is poor
  - Difficult to assess adequacy of ventilation
  - Uncertain FiO_2 and volatile anesthetic dose
  - Barotrauma.

CHAPTER

3

Obstetric Anesthesia

PHYSIOLOGICAL CHANGES OF PREGNANCY[3,16]

Introduction

- Physiological changes occur during pregnancy in major systems due to:
  - Hormones secreted by corpus luteum and placenta in first trimester
  - Mechanical effects and compression by enlarging uterus in second and third trimester.

Central Nervous System

- Increased sensitivity to GA and RA
- Increased susceptibility to sedatives as progesterone has sedative effects
- Reduced MAC of halothane and isoflurane by 25% and 40%
- Altered pain threshold
- Epidural venous engorgement:
  - Raised peak local anesthetic concentration
  - Increased incidence of bloody tap.
- Reduced volume of CSF due to:
  - Swelling of epidural veins
  - Increased CSF pressure due to raised intra-abdominal pressure.
- Increased lumbar lordosis causing more cephalad spread of local anesthetic
- 30% reduction in LA dose to produce same level of block as non-parturient.

Cardiovascular System

- Increased heart rate 20–30%
- Increased stroke volume 20–50%
- Increased cardiac output 30–50%:
  - Cardiac output increases from 5th wk
  - Cardiac output reaches maximum by 32 wks.
- Contractility (variable) $\pm$ 10%
- Systemic vascular resistance reduced by 20%
- Systemic BP unchanged or slight decrease in mid-trimester by 10–15 mm Hg
- Supine hypotension syndrome
  - IVC compression occurs by 13–16 wks
  - Aortic compression occurs by 28–30 wks.
- Central venous pressure unchanged
- PCWP unchanged
- PAP and PVR slightly decreased by 30%
- Wide, loud and split S_1, S_3 and soft ejection systolic murmur
- Left axis deviation, due to upward displacement of heart by uterus on ECG
- Arrhythmias:
  - Sinus tachycardia
  - Ventricular ectopics
  - Paroxysmal supraventricular tachycardia
  - Paroxysmal atrial complexes
  - Ventricular arrhythmias.

Respiratory System

- Friable mucosa of nasopharynx
- Capillary engorgement of mucosa, edema of oro-pharynx, larynx and trachea
- Reduced airway resistance due to bronchiolar dilatation by progesterone
- Increased oxygen demand
- Increased requirement for CO_2 elimination
- Increased work of breathing
- Mostly diaphragmatic pattern of breathing due to:
  - Limited thoracic cage movement
  - Pressure of gravid uterus.
- Changes in pulmonary function tests:
  - Increased tidal volume, unchanged respiratory rate

  - Increased minute volume by 45%
  - Reduced FRC by 20%
  - Closing capacity unchanged
  - Reduced Total Lung Capacity
  - Reduced Expiratory Reserve Volume
  - Reduced Residual Volume.
- Rightward shift of oxygen dissociation curve
- PaO_2 increases to 106 mm Hg due to increased minute ventilation
- $PaCO_2$ falls to 30 mm Hg by 12 wks and remains at this level.

Gastrointestinal System

- Impaired esophageal and intestinal motility due to progesterone
- Increased risk of aspiration and GERD due to:
  - Raised intragastric pressures up to 40 cm H_2O
  - *Relaxation of lower esophageal sphinter:* Reduced LES tone
  - Delayed gastric emptying
  - Shift in stomach position with change in angle of gastroesophageal junction.
- *Rapid sequence induction* with cricoid pressure for ***parturient ≥ 12 wks*** gestation
- Increased cortisol and human placental lactogen:
  - This causes reduced glucose tolerance
  - This causes hyperglycemia and ketosis.

Renals

- Increased renal blood flow and GFR due to raised cardiac output
- Increased GFR by 50%
- Increased creatinine clearance, low BUN, serum creatinine and uric acid levels
- Glycosuria due to high GFR (up to 1–10 gms/day)
- Proteinuria up to 300 mg/day
- *Dilatation of calyces, pelvis and ureters:* Urinary stasis causing frequent UTIs.

Hematological

- Na^+ and water retention due to RAS stimulation and increased mineralocorticoid activity
- Blood volume increases by 45% while RBC volume increases only 30% causing anemia
- Average Hb 11.6g% and average HCT 35.5%
- Increased PaO_2, rightward shift of ODC and increased cardiac output to maintain O_2 transport
- Raised levels of factors VII, VIII, IX, X, XII, and fibrinogen: Hypercoagulability
- Reduced anticoagulant activity: Reduced protein C and S, impaired fibrinolysis
- Platelet count unchanged may be increased with increased activity in third trimester
- Increased total protein levels, reduced albumin: globulin ratio
- Relative reduction in protein levels due to increased plasma volume: Raised free drug fraction
- Reduced serum cholinesterase levels to 20% below normal at term.

SUPINE HYPOTENSION SYNDROME[1,2,3,16]

Introduction

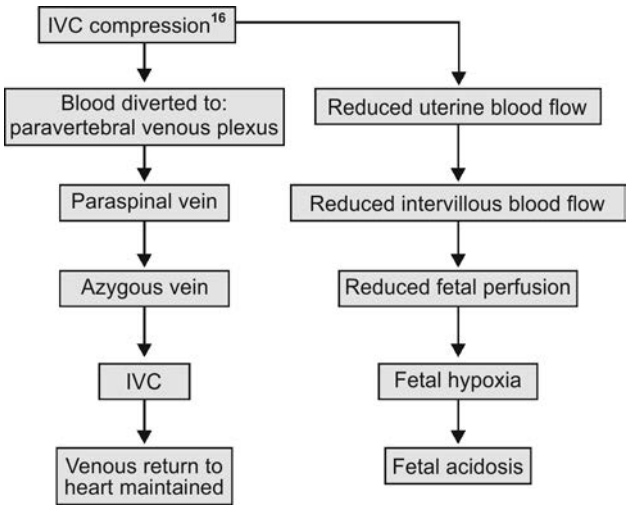
Hypotension occurring when parturient adopts supine position due to compression of abdominal aorta and IVC by the enlarging uteroplacental mass

Risk Factors

- Primigravida with tight skin around abdomen
- Obesity
- Multiple pregnancy
- Polyhydramnios
- Pregnancy-induced hypertension
- Dehydration, bleeding, hypovolemia.

Pathogenesis[1]

- IVC compression occurs at 13–16 weeks
- Aortic compression occurs at 28–30 weeks
- Compensatory mechanisms:



Types

Concealed Caval Compression

- When compensatory mechanisms act
- No clinical symptoms.

Revealed Caval Compression

- When compensatory mechanisms insufficient
- Clinical symptoms present.

Clinical Features

- Hypotension, bradycardia/tachycardia
- Narrow pulse pressure
- Reduced femoral artery pressures: ***Poseiro sign***
- Nausea, vomiting
- Pallor, giddiness, sweating
- On long standing:
  - Pooling of venous blood
  - Edema, varicose veins, thrombophlebitis.
- Aggravated by:
  - Spinal anesthesia
  - Epidural anesthesia
  - Thiopentone
  - Halothane.

Treatment

Position

- Avoid supine position ***after 28 wks***
- Left lateral tilt of table to 15° by:
  - Tipping table
  - ***Crawford wedge***
  - Stationary ***Colon Morales left uterine displacers*** under right hip
  - Foam wedge
  - Folded sheets.
- Left lateral tilt to 30° if polyhydramnios/twins
- Inflatable bag to elevate right buttock and back by 10–15 cms.

Fluid Therapy

- 10–20 ml/kg IV fluids bolus before spinal anesthesia
- Preloading done 15–20 mins before giving spinal
- Large bore IV cannula preferred.

Vasopressors

- Five mg ephedrine/phenylephrine 25–50 µg IV bolus
- Epinephrine if hypotension associated with bradycardia.

Supplement Oxygen

4 L/min by face mask.

Severe Hypotension

- Manual left uterine displacement (LUD)
- Trendelenburg position if severe
- Immediate Cesarean section if patient is in shock.

FETAL EVALUATION[1,2,3,16]

Tests

First and Second Trimester Evaluation

- Aneuploidy and Neural Tube Defects (NTD) genetic screening
- Maternal serum triple marker screening:
  - Alpha fetoprotein
  - Human chorionic gonadotropin
  - Estriol.
- Nuchal thickness and translucency: Increased nuchal thickness implies risk of NTD
- Aneuploidy testing:
  - Amniocentesis
  - Chorionic villus sampling
  - Cordocentesis
- Ultrasonography.

Third Trimester Evaluation

- Determination of lung maturity:
  - Lecithin—sphingomyelin ratio ≥ 2 indicates pulmonary maturity
  - Fetal lung maturity index
  - Surfactant albumin ratio ≥ 50 indicates pulmonary maturity.

Antepartum Surveillance

- Nonstress test
- Contraction stress test
- Biophysical profile
- Doppler velocimetry
- Fetal scalp sampling
- Fetal scalp stimulation
- Fetal pulse oximetry.

Triple Marker Testing

- Useful only when performed between 15–20 wks gestational age
- Detects NTD, trisomy 18 and 21
- Maternal Serum Alpha Feto Protein (MSAFP):
  - MSAFP ≥ 2.5 MOM (multiples of median) is abnormally high
  - MSAFP ≤ 0.5 MOM is abnormally low (risk of trisomy 18 and 21)
- *Maternal serum estriol:* Decreased estriol implies risk of trisomy 18 and 21.
- Human Chorionic Gonadotropin (HCG):
  - *Decreased HCG:* Risk of trisomy 18
  - *Increased HCG:* Risk of trisomy 21.

CONTRACTION STRESS TEST (CST)[16]

- Considered as stress test as it evaluates FHR response to uterine contractions. Contractions are generated either:
  - Spontaneously with oxytocin (***Oxytocin Challenge Test***) or
  - By breast stimulation
- In normal placental unit → Uterine contraction → Decreased uterine blood flow
  ↓
  Increased FHR or no deceleration ← Fetal compensation ← Decreased fetal O_2 delivery.
- In placental insufficiency → Uterine contraction → Decreased uterine blood flow
  ↓
  Repetitive late deceleration ← No compensation ← Reduced O_2 delivery to fetus
- Implications of CST:
  - CST must have at least 3 uterine contractions felt by mother in 10 mins
  - Negative CST ensures fetal well-being for at least next 7 days
  - Positive CST warrants:
    - Continuous monitoring or
    - Immediate delivery via vaginal/Cesarean section.

Biophysical Profile

- Indications for antepartum testing:
  - Post dates (≥ 42 weeks)
  - Cyanotic heart disease
  - Hypertensive disease
  - Hypothyroidism
  - Gestational DM
  - IUGR
  - Reduced fetal movements
  - Twins with discordant IUGR
  - History of previous still birth
  - Unexplained increase in MSAFP.
- Variables assessed:
  - Fetal movements
  - Amniotic fluid volume
  - Fetal tone
  - Nonstress test
  - Fetal breathing movement.
- Interpretation
  - *8–10:* Normal
  - *4–6:* Suspect, to be repeated within 24 hrs
  - *0–2:* Severe fetal distress, to be delivered immediately.

Scoring System of Biophysical Profile[16]

No	Variable	Normal (score 2)	Abnormal (score 0)
1	Fetal movements	≥ 3 discrete limb movements in 30 min	< 3 discrete limb movements in 30 min
2	Fetal tone	≥ 1 episode of return to flexion from extension opening and closing of hand	Slow extension with return to partial flexion
			Movement of limb in full extension
			Absent fetal movements
3	Breathing	≥ 1 episode of ≥ 30 sec duration in 30 min	No episode of > 30 sec duration in 30 min
4	AF volume	≥ 1 pocket of AF measuring ≥ 1 cm in two perpendicular planes	No AF pocket
			Pocket < 1 cm in 2 perpendicular planes
5	NST	≥ 2 episodes of acceleration of ≥15 bpm and duration associated with fetal movements	Acceleration < 15 bpm in 30 min
			< 2 accelerations

Doppler Velocimetry

- USG to measure maternal and fetal blood flow
- Variables determined:
  - Systolic-diastolic ratio (S/D ratio)
  - ***Pourcelot ratio***
  - Pulsatile index.
- Carotid artery and umbilical artery used
- Poorest sensitivity, lowest positive predictive value: Not useful
- May be useful in fetuses with IUGR where absence, or reversal of umbilical artery blood flow during diastole suggests fetal distress.

Nonstress Test

Introduction: Constitutes the study of fetal heart rate and its changes without the requirement of uterine contraction.

Method

- Fetal heart rate and variation studied over 20 mins
- Nonreactive NST after 20 min mandates fetal stimulation by:
  - Oral/IV fluids to mother

– Vibroacoustic stimulations (VAS):
  - Uses electric artificial larynx
  - Generate sound levels averaging 82 db
  - Stimulus applied for 1 sec every min for 3 times
  - ≥ 2 acceleration of ≥ 15 bpm lasting ≥ 15 sec in 10 min period: *Reactive VAS-NST.*

Monitors

FHR Monitors

- Noninvasive Doppler USG probe applied on maternal abdomen over fetal back/chest
- Direct invasive fetal scalp electrode (requires 3–4 cm dilation of cervix and membrane rupture)
- Cardiotachometer which measures R–R interval of FHR.

Uterine Activity Monitors

- Noninvasive tocodynamometer placed over abdomen
- Invasive intrauterine amniotic fluid pressure (transducer tipped) catheter
- Manual palpation
- Adequate uterine activity when contractions occur every 2–3 mins of about 50–70 mm Hg peak height intensity.

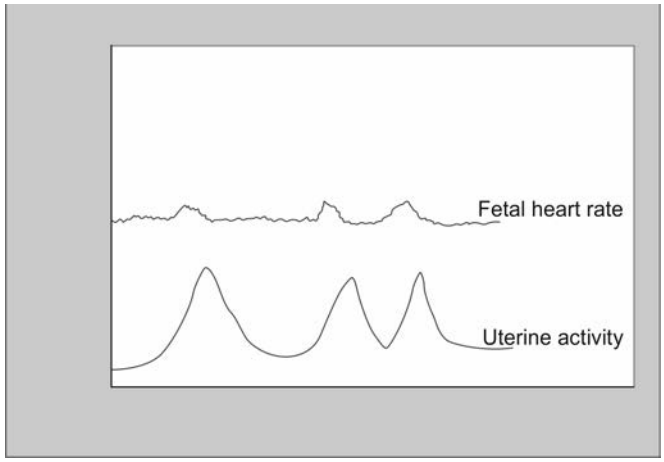


Fig. 3.1: Nonstress test

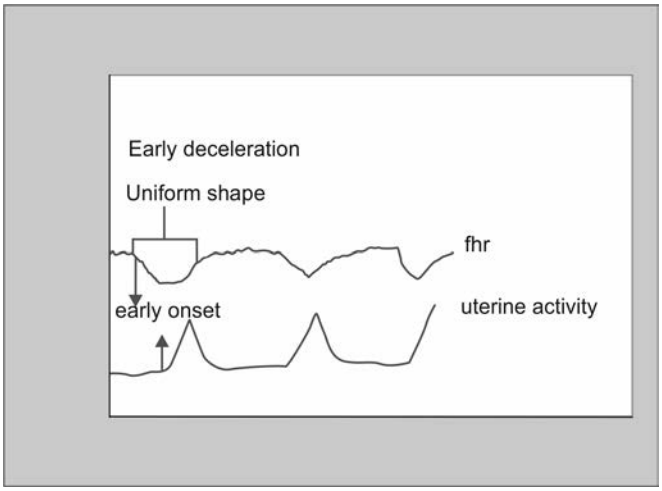
FHR Characteristics

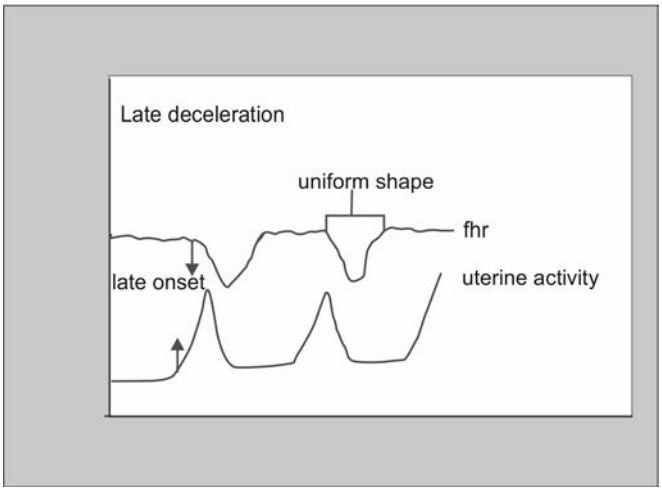
No	Term	Definition
1	Baseline FHR	110–160 bpm, measured over ≥ 2 min
2	Bradycardia	Baseline rate < 110 bpm for ≥ 10 min
3	Tachycardia	Baseline rate > 160 bpm for ≥ 10 min
4	Variability	Fluctuations in baseline FHR of ≥ 2 cycles/min
5	Acceleration	Abrupt increase in FHR ≥ 15 bpm above Baseline lasting ≥ 15 sec and ≥ 2 min
6	Prolonged acceleration	Acceleration > 2 min and < 10 min duration
7	Early deceleration	Gradual decrease in FHR below baseline, uniform shape, early onset
		Return to baseline associated with uterine contraction
		Nadir of deceleration at same time as peak of contraction
8	Late deceleration	Gradual decrease in FHR below baseline, uniform shape, early onset
		Return to baseline associated with uterine contraction
		Nadir of deceleration occurs after peak of contraction
9	Variable deceleration	Abrupt decrease in FHR below baseline
		Decrease is ≥ 15 bpm, duration ≥ 15 sec and ≥ 2 min
		Variable shape
10	Prolonged deceleration	Abrupt decrease in FHR below baseline
		Decrease is ≥ 15 bpm
		Duration ≥ 2 min but < 10 min

Significance

- **Bradycardia:**
  – Fetal hypoxia
  – Brady arrhythmias (complete heart block)
  – β blockers
  – Hypothermia
- **Tachycardia:**
  – Hypoxemia
  – Anemia, prematurity (fetal)
  – Cardiac arrythmias
  – Congenital anomalies
  – Maternal fever, dehydration, thyrotoxicosis, sympathomimetics
- **Early and Late Deceleration:**
  – Reduced placental reserve (PIH, IUGR)
  – Following asphyxia

- **Variable deceleration:**
  - Umbilical cord compression
  - Substantial head compression during 2nd stage.





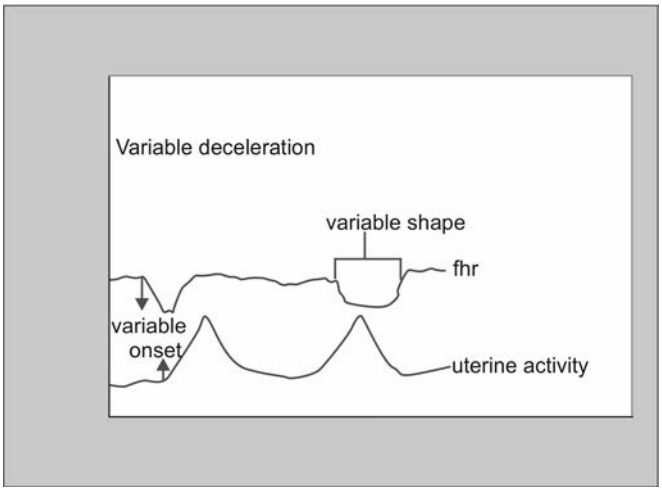


Fig. 3.2: Nonstress test interpretation

Unusual FHR Patterns

Sinusoidal Pattern

- Regular smooth sine wavelike baseline
- Frequency 3-6/min, amplitude range 30 bpm
- Seen in RH isoimmunization, following opioid administration.

Saltatory Pattern

- Rapid variation in FHR
- Frequency 3–6 bpm, amplitude > 25 bpm
- Usually not associated with fetal decompensation.

Dysrhythmias

- Complete Heart Block
- Paroxysmal Atrial Complexes
- Paroxysmal Ventricular Complexes
- Supraventricular Tachycardia
- Paroxysmal Atrial Tachycardia
- Atrial flutter, bigeminy, asytole.

Interpretation of NST

Relative NST

- ≥ 2 FHR accelerations, ≥ 15 bpm above baseline lasting ≥ 15 sec in 20 mins
- ≥ 2 FHR accelerations, ≥ 15 bpm above baseline lasting ≥ 15 sec in a 10 min period following VAS stimulation
- Seen in normal fetus.

NST Patterns Associated with Risk of Fetal Acidosis

- Absent variability with:
  - Persistent tachycardia
  - Persistent bradycardia (< 80 bpm).
- Absent or minimal variability with:
  - Recurrent late deceleration
  - Recurrent mod—severe variable deceleration
  - Sinusoidal pattern.

APGAR SCORE[1,2,3,16]

Introduction

- Score to evaluate newborn immediately after birth to identify depressed infants requiring resuscitation
- Useful in predicting short-term mortality for groups of infants, especially those of low birth weight
- Designed by ***Virginia APGAR*** in 1953.

Score

		0	1	2
Appear-ance	Color	Blue, pale	Pink body, blue limbs	Complete-ly pink
Pulse	Heart rate	Absent	< 100	> 100
Grimace	Reflex irritability	No res-ponse	Grimace	Cough, sneeze, cry
Activity	Muscle tone	Limp	Some flexion	Active motion
Respira-tion	Resp. effort	Absent	Slow, irregular	Good, crying

Performance

- Performed by pediatrician/individual not directly involved in care of mother
- Taken at 1 and 5 minutes after birth
- Repeated at 10 and 20 minutes if condition changes in response to resuscitative efforts
- Heart rate and respiratory effort are *most important* in identifying distressed newborn
- Color is of *least value*.

Uses

- *Resuscitation:* Based on 1 minute score

Score	Category	Intervention
≥ 7	Normal	No ventilatory assistance
	Mild respiratory acidosis	
4–6	Moderately depressed	Oxygen via mask
	Respiratory acidosis	
0–3	Severe depression	Endotracheal intuba-tion
	Combined resp. and met acids	Cardiac massage

Prognostic Value

- Low 1 min score inversely proportional to mortality at 28 days
- Low 5 min score inversely proportional to mortality at 1 year.

Limitations

- Subjective score
- Crude measurements: Only looks at vital signs
- Observation only for very brief period
- Subtle effects of perinatal asphyxia/maternal medication may be missed
- Little value when used to predict survival in any individual case.

INNERVATION OF FEMALE GENITAL TRACT[1,2,3,16]

External Genitalia

- Anterosuperior part:
  - Ilioinguinal N (L_1 L_2)
  - Genital branch of genitofemoral N (L_1L_2).
- Posterior inferior part:
  - Pudendal branch from posterior cutaneous N of thigh (S_1–S_3).
- *Vulva:* Labia and perineal branch of pudendal N (S_{234}).

Internal Genitalia

- Vagina:
  - Sympathetic and parasympathetic from pelvic plexus
  - Lower part by pudendal N.
- Uterus:
  - *Sympathetic:* $T_{5\text{-}6}$ motor, T_{10} to L_1 sensory
  - Parasympathetic S_{234} by pelvic N.
- *Fallopian tubes:* Uterine and ovarian N
- *Ovary:* Sympathetic via Ovarian N (T_{10}).

Pelvic Floor

- Inferior rectal N
- Perineal branch of pudendal N (S_{234})
- 4th sacral nerve.

Urinary Bladder

- Sympathetic:
  - Pelvic plexus
  - Conveys pain of over distension.
- Parasympathetic:
  - Pelvic plexus form ***Nervi Erigentes*** (S_{234})
  - For bladder evacuation.
- *Urethra:* pudendal N.

Pelvic Ureter

- Sympathetic: Hypogastric and pelvic plexus
- Parasympathetic: Sacral plexus

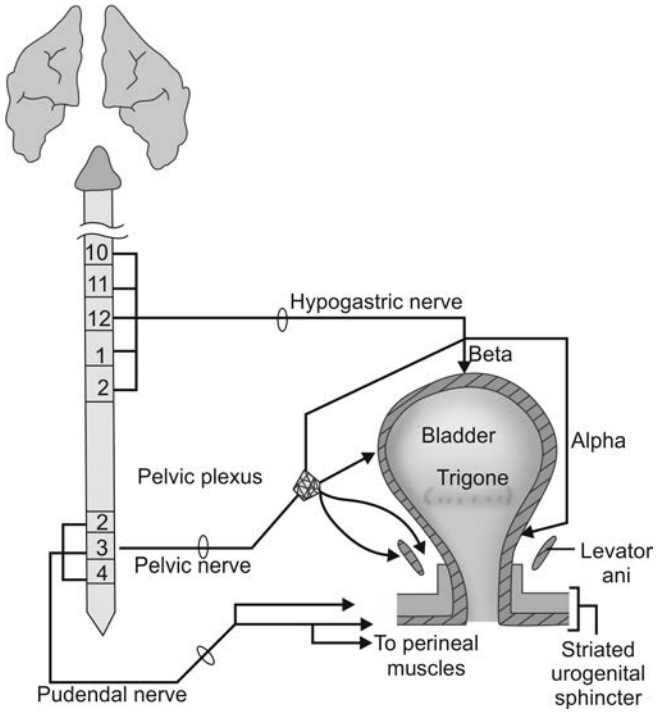


Fig. 3.3: Innervation of female genital tract[2]

Pain Pathway During Labor

- Source of pain:
  - Contraction of myometrium against cervical resistance
  - Progressive dilation of cervix and lower uterine segment
  - Stretching and compression of pelvic and perineal structures.
- First stage of labor:
  - Visceral pain due to uterine contraction and cervical dilatation
  - Involves up to $T_{10} - L_1$ dermatomes
  - Primarily in lower abdomen, referred to lumbosacral/gluteal or thighs
  - Visceral afferents → Sympathetic N → Uterine and cervical plexus
    ↓
    Spinal cord (T_{10}–L_1) ← hypogastric and aortic plexus.
- Second stage of labor:
  - Perineal pain, due to compression of pelvic and perineal structures
  - Involves T_{10}–S_4 segments
  - Carried via pudendal N to spinal cord T_{10}–S_4 segments.

LABOR ANALGESIA[1,2,3,16]

Techniques

Nonpharmacological

- Psychoprophylaxis (***Dick Read***)
  - Education program
  - Strong focus of attention
  - Human support
  - Relaxation techniques of voluntary muscles
  - Breathing techniques
  - Specific activities to concentrate on.
- Water bath
- Touch and massage
- Intradermal sterile water injection
- Acupuncture
- Hypnosis
- TENS
- Biofeedback
- ***Bradley Leboyers technique***
- ***Lamaze technique***:
  - Deep breath taken at the beginning of contraction
  - This is followed by rapid, shallow breathing for duration of contraction.

Pharmacological

- Opioids:
  - *Meperidine:* Fentanyl
  - *Remifentanil:* Nalbuphine
  - *Butorphanol:* Tramadol.
- Sedative tranquilizers:
  - *Benzodiazepines:* Barbiturates
  - *Hydroxyzine:* Phenothiazines.
- *Others:* Ketamine.

Inhalational Analgesia

- Entonox
- Sevoflurane (0.8%)
- Isoflurane
- Enflurane (0.25%)
- Desflurane.

Regional Analgesia

- Epidural analgesia
- Subarachnoid block
- Combined spinal epidural analgesia
- Paracervical block
- Pudendal block
- Lumbar sympathetic block
- Caudal block.

Newer Advances

- Patient controlled analgesia:
  - *PCIVA:* Patient Controlled IV Analgesia with remifentanil
  - *PCIA:* Patient Controlled Inhalation Analgesia with sevoflurane
  - *PCEA:* Patient Controlled Epidural Analgesia
  - *CI-PCEA:* Computer Integrated PCEA
  - *CI-AMB:* Computer Integrated Automated Mandatory Boluses.
- Acoustic Puncture Assisted Devices for identifying epidural space
- Ultrasound guided epidural anesthesia
- Transverse abdomen plane block (TAP block)
- *EREM:* Extended Release Epidural Morphine.

Transcutaneous Electrical Nerve Stimulation

- Reduces pain by nociceptive inhibition at presynaptic level in dorsal horn
- Inhibits propagation of nociception along unmyelinated small fibers
- Blocks impulses to target cells in substantia gelatinosa
- May provide analgesia during 1st stage of labor
- Pads applied over lower back region between T_{10}–L_1
- Usually as adjuvant, not as sole analgesic.

Pharmacological Analgesia

- Meperidine:
  - Most commonly used parenteral opioid
  - 50–100 mg IM: Peak onset of action 40–50 mins
  - 25–50 mg IV: Onset of action 5–10 mins, duration of action 3–4 hrs
  - Lesser respiratory depression
  - Loss of beat-to-beat variability in FHR tracings.
- Fentanyl:
  - *25–30 µg IV:* Onset 3–5 mins, duration 30–60 mins
  - Can be given S/C, orally or transdermally
  - Reasonable analgesia with minimal neonatal depression
  - Mild maternal sedation at 50–100 µg.
- Remifentanil:
  - Mostly as PCIVA
  - Bolus of 0.4 µg/kg with lockout time of 1 min
  - Continuous infusion of 0.05 µg/kg/min with 25 µg bolus, lockout time of 5 mins
  - No adverse effects, but crosses fetomaternal barrier
  - Rapid metabolism by maternal nonspecific esterases.
- Butorphanol:
- *Agonist-antagonist:* κ agonist, µ antagonist, minimal affinity
- 1–2 mg IM/IV: Duration of action 4 hours
- Causes sedation and respiratory depression: Not routinely used
- *Ceiling effect* for respiratory depression: Increasing doses do not produce further respiratory depression.
- Nalbuphine:
  - *Agonist-antagonist:* Partial κ agonist, potent µ antagonist, minimal affinity
  - *10 mg IV/IM:* 2–3 mins onset of action, duration of action up to 6 hrs
- Promethazine:
  - Most commonly used phenothiazine
  - 25–50 mg IV to prevent emesis
  - Potentiates analgesic effects of opioids.
- Ketamine:
  - 0.5–1 mg/kg every 2–5 mins to total of 1 mg/kg in 30 mins
  - Supplements incomplete neuraxial block
  - *Hypertension, psychomimetic effects:* Not routinely used.
- Tramadol:
  - *1–2 mg/kg IV/IM:* Duration of action 2–3 hrs
  - *Weak µ agonist:* 10% as potent as morphine
  - *Less respiratory depression:* not seen at 1–2 mg/kg doses.
- Benzodiazepines:
  - Causes sedation, hypnosis, cyanosis and amnesia
  - Not routinely used.
- *Hydroxyzine:* 50–100 mg IM.

Inhalational Analgesia

- Entonox:
  - *50% N_2O:* O_2 mixture
  - Was used both as sole analgesic and as adjuvant earlier
  - Maximal effect after 45–60 mins
  - Important to use entonox at early onset of contraction
  - Use discontinued after peak of contraction
  - Causes nausea, dizziness, dysphorea, lack of cooperation
  - OT pollution
  - Not routinely used
  - Used now as adjunct or when regional analgesia not possible.

- Volatile anesthetics:
  - Not routinely used
  - Sevoflurane 0.8% most commonly used
  - Isoflurane and enflurane (0.2–0.25%) and desflurane (0.2%)
  - Causes more intense sedation, unpleasant smell, OT pollution
  - Unconsciousness and loss of airway reflexes occur if accidental overdose
  - PCIA uses sevoflurane and special vaporizes.

Regional Anesthesia

Epidural Analgesia

- Indicated when patient is in active labor:
  - Cervix 5–6 cm dilated in primigravida
  - Cervix 3–4 cms in multigravida.
- T_{10}–L_1 level required for 1st stage of labor
- S_2–S_3 level required in 2nd stage of labor
- Good analgesia, minimal motor block, reduced stress response.
- Epidural analgesia regimen:

No	Drug	Bolus	Infusion
1	Bupivacaine	10–15 ml of 0.25–0.125 % solution	8–15 ml/hr of 0.0625–0.125% solution
2	Ropivacaine	10–15 ml of 0.1–0.2 % solution	8–15 ml/hr of 0.5–0.2% solution
3	Fentanyl	50–100 µg in 10 ml solution	1–4 µg/ml
4	Sufentanyl	10–25 µg in 10 ml solution	0.03–0.05 µg/ml

- Patient Controlled Epidural Analgesia (PCEA) regimen:

Mode	Basal Infusion			Lockout	
	Drug	Rate (ml/hr)	Bolus (ml)	Interval (min)	Hourly maximum (ml)
Demand only	Bupivacaine	0	4	10–20	15–20 ml, 0.125%
Continuous infusion + demand	Bupivacaine	4–8	2–4	10–20	15–20 ml, 0.0625%

Subarachnoid Block

- Used for:
  - Multiparous women in active labor (6–9 cm dilated)
  - Primipara fully dilated and significant pain
  - Patients in early labor, 2–4 cm dilated, prior to active phase
- Saddle block used if:
  - Forceps delivery
  - Repair of vaginal/rectal tears postpartum
  - Removal of placenta.
- Continuous spinal analgesia with microcatheters if accidental dural puncture occurs during epidural: good analgesia, prevents PDPH

No	Drug	Dose
1	Bupivacaine	1.25–2.5 mg
2	Hyperbaric lignocaine	40–50 mg
3	Meperidine	10–20 mg
4	Fentanyl	12.5–25 µg
5	Sufentanyl	3–10 µg
6	Neostigmine	0.3 mg with bupivacaine
7	Clonidine	50 µg with bupivacaine

Combined Spinal Epidural: OAA 2005 guidelines

- Restricts routine use of combined spinal epidural
- 5 µg sufentanyl or 15 µg fentanyl for initial subarachnoid block
- This is followed by epidural continuous infusion of 0.125% bupivacaine at 8–15 ml/hr
- Indicated in:
  - Very early stage of labor when local anesthetics are avoided
  - Advanced stage when rapid analgesia required
  - Difficult epidural as it reduces failure rate of epidural.
- Methods of CSE:
  - Epidural catheter followed by SAB at lower interspace
  - Epidural needle besides spinal needle at same interspace
  - Needle through needle technique at same interspace.
- Advantages:
  - Makes ambulation possible: ***Walking epidural***
  - Reduces epidural complications:
    - Patchy block
    - Poor sacral spread.

- Reduces duration of 1st stage of labor
- Onset of subarachnoid block immediate
- Duration of action of subarachnoid block 2–3 hrs
- Same catheter can be used for operative anesthesia if required
- Reduced motor block.

Paracervical Block

- Alternative where neuraxial blockade contraindicated
- Simple to perform, does not affect progress of labor
- Local anesthetic injected submucosally into fornix for vagina, lateral to cervix
- Close proximity of injection site to uterine artery makes it technically difficult
- Blocks transmission through paracervical ganglion
- Good for 1st stage of labor
- No pain relief offered during 2nd stage of labor
- Complications:
  - Profound fetal tachycardia
  - Local Anesthetic Systemic Toxicity (LAST)
  - Postpartum neuropathy
  - Infection.

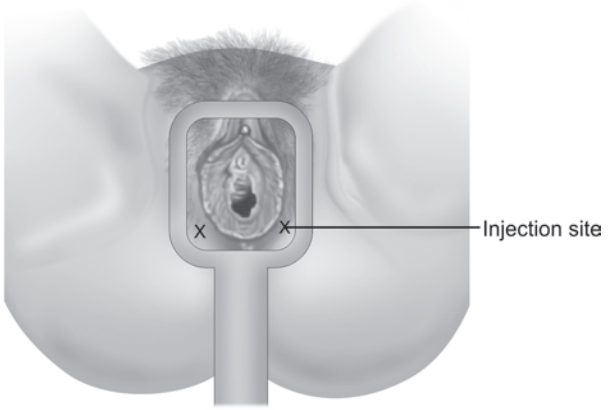


Fig 3.4: Paracervical block[2]

Pudendal Nerve Block

- Through transvaginal approach in lithotomy position
- Ischial spine palpated transvaginally/transrectally
- Needle placed transvaginally under ischial spine on each side
- Advanced 1–1.5 cm through sacrospinous ligament
- 10 ml of 1% lidocaine injected
- Local anesthetic deposited behind sacrospinous ligament
- Satisfactory for vaginal delivery and outlet forceps delivery
- Not useful for:
  - Mid forceps delivery
  - Repair of vaginal laceration
  - Uterine cavity exploration.
- Complications:
  - LAST
  - Infection
  - Hematoma
  - Sciatic nerve block.



Fig. 3.5: Pudendal nerve block[2]

Lumbar Sympathetic Block

- Paravertebral lumbar sympathetic block
- Technically difficult
- Fewer complications than paracervical block.

WALKING EPIDURAL[1,2,3,16]

Introduction

- Combined spinal epidural technique, used for labor analgesia which allows maternal ambulation
- Also called ***minimal motor block epidural***.

Indications: *OAA 2005 guidelines*

- Does not advocate routine use of combined spinal epidural
- Early in labor when local anesthetics are not preferred
- Late in labor when immediate analgesia required
- Difficult epidural as it reduces failure rate of epidural
- Initial profound analgesia required but ongoing analgesia not required for sometime, e.g. Artificial Rupture of Membranes in anxious mother).
- Where rapid analgesia required and epidural catheter may be useful for later intervention (trial for forceps extraction where cesarean section may follow).

Techniques
- Epidural catheter at higher space, SAB at one interspace lower
- Epidural catheter besides spinal needle in same space
- Needle through needle technique in same space.

Dosages
- For initial subarachnoid block:
  - *Fentanyl:* 10–15 µg
  - *Sufentanyl:* 5–10 µg
  - *Bupivacaine:* 1.25–2.5 mg.
- For later epidural block:
  - 0.625–0.125% bupivacaine at 8–15 ml/hr
  - 1–2 µg/ml fentanyl or 0.03–0.05 µg/ml sufentanyl used as additives.

Criteria for Ambulation
- No obstetric or medical contraindications
- Maternal desire to ambulate
- Presence of second person to walk with patient
- Ambulate only when spinal anesthesia with opioids
- Avoid when spinal anesthesia with local anesthetics
- Ability to perform sustained straight leg raising test ≥ 10 sec
- Ability to perform partial knee bends at bedside
- < 10% change in BP from supine to sitting position.

Advantages
Maternal
- Rapid onset of analgesia
- Reduces chances of patchy/unilateral block as with plain epidural
- Lesser amount of local anesthetic in systemic circulation
- Reduced motor block
- Better hemodynamic stability
- Ability to ambulate
- Analgesia can be prolonged using epidural catheter
- Same catheter can be used for operative analgesia
- Greater maternal satisfaction
- Feeling of self-control.

Obstetric
- Reduced duration of 1st stage of labor
- Enhanced rate of cervical dilation due to gravity
- Correct positioning of fetal head due to gravity
- Lesser need for augmentation
- Reduced need for assisted deliveries
- Improved APGAR scores

Side Effects
- Pruritus, nausea and vomiting, respiratory depression
- Urinary retention
- Hypotension, PDPH
- FHR abnormalities and fetal bradycardia
- Costly kits
- Epidural hematoma
- Broken catheter.

Contraindications
- Coagulopathy
- Abruptio placentae
- Platelet count ≤ 1,00,000/mm^3
- Hemodynamically unstable patient
- Non-reassuring fetal heart rate
- Patient refusal
- Medical/obstetric contraindications to ambulation
- **Technique:** As for epidural
- **Monitoring:** As for epidural

PLACENTAL TRANSFER OF DRUGS[1,2,3,16]

Introduction
Medications administered to pregnant women may cross placenta and have harmful effects on the fetus.

Mechanisms of Transfer
- Simple diffusion:
  - *Along* concentration gradient
  - Requires no carrier molecule/energy
  - Governed by ***Fick's principle***
  - Formula:

$$Q/t = \frac{KA\,(C_m - C_f)}{D}$$

  - Q/t = Rate of diffusion
  - K = Diffusion coefficient
  - A = Surface area of membrane available for exchange
  - C_m–C_f = Concentration gradient between maternal and fetal circulation
  - D = Thickness of membrane.
- Facilitated diffusion:
  - Occurs *along* concentration gradient
  - Requires carrier molecule.
- Active transport:
  - Occurs *against* concentration gradient
  - Requires carrier molecules and energy.

- Pinocytosis:
  - Molecules engulfed by invagination of placental membrane
  - Molecules are then transferred to fetal circulation.
- Breaks/Leakages.

Factors Governing Transfer

Drug Factors

- *Molecular weight:* Low molecular weight (< 500 D) cross placenta
- Lipid stability:
  - Lipid soluble drugs cross placenta
  - Thiopentone, local anesthesia, benzodiazepines.
- Protein binding:
  - Highly protein bound drugs do not cross placenta
  - Bupivacaine, succinylcholine are highly protein-bound.
- Degree of ionization:
  - Ionized drugs do not cross placenta
  - Glycopyrollate, succinylcholine, neostigmine, NDMR ionized.
- *pKa:* If pKa of drugs is close to physiological pH, more drug will be ionized and wont cross placenta.

Maternal Factors

- Total dose
- Addition of adjuvants like adrenaline reduces peak LA level
- *Route of administration:* Injection into high vascular epidural space increases peak concentration of drug
- Maternal metabolism and excretion: Hepatic/renal dysfunction increases toxicity
- *Maternal protein binding:* Increased protein binding reduces transfer
- Maternal pH alters extent of ionization and transfer.

Placental Factors

- Placental blood flow
- Placental ageing.

Fetal Factors

- Solubility of drug in fetal blood
- Concentration of drug in fetal blood returning to placenta
- Uptake by fetal tissues
- Fetal hepatic metabolism and renal excretion
- Nonplacental routes of fetal drug exertion
- Fetal protein binding
- Fetal pH and adequacy of fetal circulation.

Specific Drugs

- At present, no anesthesia drug (premedication, IV induction agent, volatile agents or local anesthetics) has been proven to be teratogenic in humans
- Drugs which do not cross placenta:
  - NDMR
  - SCH
  - Neostigmine
  - Glycopyrrolate
  - Insulin, heparin.
- Drugs which cross placenta
  - Potentially dangerous:
    - Opioids (morphine > remifentanil > sufentanyl > pethidine> fentanyl)
    - Benzodiazepines
    - Local anesthetics
    - Atropine, ephedrine
    - α_2 agonists
    - β blockers.
  - Safe:
    - Thiopentone
    - Propofol
    - Ketamine
    - Volatile anesthetics.

FDA Categories of Drugs

Category A

- Controlled studies show no fetal risk
- *Risk is remote*
- For example: Water

Category B

- No risk in animal studies reported
- No controlled human studies
- *No risk after 1st trimester:*
- *For example:*
  - Propofol
  - Methohexital
  - Fentanyl
  - Demerol
  - Enflurane
  - Isoflurane
  - Sevoflurane
  - Desflurane
  - Lidocaine
  - Ropivacaine.

Category C

- Fetal risk present in animals

- But no human studies available
- *To be given only if benefits outweighs risks*
- *For example:*
  - Thiopentone
  - Ketamine
  - Etomidate
  - Morphine
  - Sufentanyl
  - Halothane
  - Bupivacaine
  - Chloroprocaine.

Category D

- Confirmed evidence for human risks
- *But benefits acceptable despite known risk*
- *For example:* Diazepam.

Category E

- Confirmed evidence of teratogenicity
- Human/animal studies show teratogenicity
- Fetal risk clearly outweighs any benefits of use in pregnancy
- *Contraindicated*
- *For example:* Thalidomide, antimetabolites.

Teratogenecity

Opioids

- Increased incidence of neonatal jaundice
- Neonatal depression if used during labor
- Withdrawal syndrome with chronic abuse.

Nonopioids

- Parcetamol safe
- Aspirin: IUGR, stillbirth
- Ibuprofen and ketorolac:
  - Increased maternal hemorrhage
  - Premature PDA closure
  - Prolonged labor.

Warfarin

- ***Contradi syndrome***
- Stippled epiphysis, nasal and limb hypoplasia
- CNS effects
- Increased fetal hemorrhage
- Heparin and LMWH is safe during pregnancy.

Anticonvulsants

- Phenytoin:
  - Fetal hydantoin syndrome
  - Growth and performance delays.
- Carbamazepine:
  - Craniofacial defects
  - Developmental delay.

Antiemetics

- *Prochlorperazine:* Extrapyramidal effects
- *Promethazine:* Fetal platelet aggregation
- *Droperidol, metaclopramide, ondansetron:* No risks
- *Omeprazole and ranitidine:* No risks.

Antihypertensives

- *ACE inhibitors:* IUGR, neonatal renal failure
- *β blockers:* IUGR, fetal bradycardia and hypoglycemia
- Calcium channel blockers, α_2 agonsists, methyldopa: no adverse effects.

Benzodiazepines

- Cleft lip and palate
- ***Floppy infant syndrome***: Hypotonia, lethargy, cyanosis, hypothermia.

Hormones

- Antithyroid: Fetal hypothyroidism and goiter
- Steroids:
  - Low birth weight
  - Congenital cataract
  - Cleft lip and palate.

Antibiotics

- Aminoglycosides: Ototoxicity, potentiate NMBAs
- Sulfonamides:
  - Hyperbilirubinemia
  - Anemia if maternal G6PD deficiency.
- Tetracycline:
  - Teeth discoloration and hypoplasia
  - Skeletal growth restriction.
- *Bronchodilators:* No effects.

TOCOLYTICS[1,16]

Introduction

- Drugs which prevent preterm labor and immature birth by suppressing uterine contraction
- Preterm labor is defined as:
  - Labor between 20–37 completed wks from 1st day of last menstrual period with:
    - Regular uterine contraction at least 30 seconds duration every 10 min
    - Cervical effacement/dilation.
- Low Birth Weight (LBW) if birth weight < 2500 gms

- Very Low Birth Weight (VLBW) if birth weight ≤ 1500 gms.

Risk Factors for Preterm

- History of previous preterm delivery
- Smoking, low socioeconomic status
- Subclinical chorioaminotis, genital infection, pyelonephritis
- Infection/thrombosis of placenta
- Placenta praevia/abruption
- Pregnancy induced hypertension
- Antepartum hemorrhage
- Cervical incompetence.

Indications for Tocolytics

Prolonged Tocolysis

- Fetus < 2500 gm
- 20–30 wks gestational age
- Intact membrane
- Documented contraction
- Cervical effacement ≥ 80%
- Cervical dilation 2–4 cms.

Short-term Tocolysis

- *Fetal distress:* To prepare for immediate delivery
- In utero fetal surgery
- Exit procedures
- Patient transfer to better setup
- Postoperative tocolysis.

Contraindications

- Fetal anomalies incompatible with life
- Ruptured amniotic membrane (long-term)
- Severe hemorrhage
- Maternal cardiac disease
- Fever of unknown origin
- Amnionitis.

Choice of Anesthesia

- Safest method of delivery is controversial
- Cesarean section done mostly
- Indications for cesarean section:
  - Very low birth weight
  - Intra uterine growth retardation
  - Fetal distress
  - Breech presentation
  - Antepartum hemorrhage.
- Continuous lumbar epidural is *technique of choice*
- Extensive neonatal resuscitation is required postpartum.

Drugs Used

- β_2 adrenergic agonists:
  - Ritodrine 0.05–0.1 mg/min
  - Terbutaline 0.01 mg/min
  - Salbutamol.
- Calcium channel blockers:
  - Nifedipine 20 mg bolus dose
  - This is followed by 10–20 mg Q4H till contraction decreases.
- Oxytocin Antagonists: Atosiban
- Prostaglandin synthesis inhibitors:
  - Indomethacin (per rectal)
  - Sulindac
  - Aspirin
  - Ketorolac.
- Nitric oxide donors: Nitroglycerine IV 30–200 μg bolus 4 rapid tocolysis
- Magnesium sulfate:
  - Tocolytic *agent of choice*
  - 4 gm IV over 20 min followed by 2 g/hr.

Screening

- Repeated vaginal examinations
- Bishop's score ≤ 4
- Fetal fibronectin in vaginal fluid
- Transvaginal USG:
  - Cervical length < 3 cm at 24–28 weeks
  - Cervical funnelling/dilatation of internal but not external os.

Anesthetic Considerations

- β_2 agonists:
  - Delay GA/NAB for 10 mins after discontinuation of infusion to decrease tachycardia
  - Avoid aggressive hydration preoperatively (250–500 ml preload adequate)
  - Tachycardia:
    - Difficult to assess depth of anesthesia which causes sedative overdose
    - May be taken as hypovolemia and therapy can cause fluid overload.
  - Avoid drugs which cause tachycardia (atropine, pancuronium)
  - Ectopics and atrial fibrillation possible with β_2 agonists
  - Risk of fluid overload due to increased ADH activity
  - Avoid halothane as it sensitizes myocardium to catecholamines
  - Ephedrine to treat hypotension.

- Calcium channel blockers:
  - Increases myocardial depression, conduction defects and vasodilation when used with VA
  - Increased postpartum hemorrhage due to uterine atony
  - Potentiates NMBAs.
- Atosiban:
  - Can cause chest pain, tachycardia, palpitation, hypotension
  - Nausea, vomiting and headache
  - High cost.
- Cox inhibitors:
  - Increased bleeding time: Epidural hematoma
  - Increased chances of postpartum hemorrhage.
- Magnesium sulphate:
  - Increased hypotension following SAB
  - Increased sensitivity to NMBAs (both DMR and NDMR)
  - Reduced postoperative analgesic requirement
  - Intraoperative bleeding due to platelet aggregation
  - Reduced intraoperative and postoperative analgesic requirements
  - Increased postpartum hemorrhage due to uterine blood flow.

ANTICOAGULATION IN PREGNANCY[1,16]

Indications (ACCP 2012)

- Recent history of DVT/pulmonary embolism
- Treatment of DVT/pulmonary embolism
- Mechanical prosthetic heart valves
- Atrial fibrillation in patient with structural heart disease
- History of SLE
- To prevent recurrent miscarriage in APLA syndrome
- Antithrombin deficiency
- Combined thrombophilias.

Choice of Anticoagulants

Warfarin

- Warfarin crosses placenta
- Associated with ***Conradi syndrome/Warfarin Embryopathy***
- Contraindicated during first trimester
- Safe to use during 2nd and 3rd trimesters
- Can be started from 12 weeks of pregnancy
- Does not cross over into breast milk
- Not contraindicated during postpartum
- Can be restarted 7 days after delivery.
- Warfarin indicated throughout pregnancy only for patients with: *(**ACCP 2012***)
  - Mechanical valve with past history of clot
  - Older generation prosthetic valve.

Heparin

- Does not cross placenta
- Can cause maternal hemorrhage/osteoporosis/HIT
- Relative heparin resistance occurs in pregnancy
- Reversal of anticoagulation before delivery makes it preferred choice
- Given in pregnant women with prosthetic valves from conception to delivery
- Heparin discontinued once active labor begins
- UH and LMWH do not cross into breast milk and are safe during breastfeeding.

Monitoring

- Baseline PT taken at a time when heparin will not affect measurement
- Between 4–6 hrs after IV bolus dose
- Subsequent daily measurements done under similar conditions
- After discharge from hospital weekly/biweekly PT measurements to ensure 2–2.5 fold prolongation of baseline PT
- PT measured monthly once dosage is established
- Anti factor Xa activity more reliable for monitoring LMWH action.

Dosage (ACCP 2012)

Unfractionated Heparin

- 80 IU/kg bolus followed by 18 IU/kg/hour for therapeutic indications
- 5000 IU/7500 IU/10000 IU Q12H in 1st, 2nd and 3rd trimesters respectively for prophylactic indications
- Titrate to achieve aPTT of 1.5 to 2 times control, 6 hrs after last injection of heparin.

LMWH

- Enoxaparin 1 mg/kg Q12H therapeutic dose
- Enoxaparin 0.5 mg/kg Q12H prophylactic dose.

Warfarin

- Warfarin 5–10 mg Q24H adjusted to INR of 2–3.

Surgery/Delivery During Anticogulation

- Oral anticoagulants:
  - Withstand minor surgery if PT < 35 sec
  - Withstand major surgery if PT < 18 se or INR < 1.7

  - If hemostasis becomes a problem:
    - Withold drug
    - Vitamin K 5–50 mg IV
    - FFP 5–8 ml/kg.
- Heparin:
  - Can be fully anticoagulated during delivery or surgery
  - If hemostasis becomes a problem protamine given in 50 mg IV boluses.

ACCP 2012 Guidelines

Regimen I

- Switch to LMWH on confirmation of pregnancy if patient on warfarin
- Continue LMWH throughout pregnancy to achieve peak anti Xa levels
- Stop LMWH 24 hrs prior to induction of labor
- Continue LMWH for 6 wks postpartum if acute DVT/PE.

Regimen II

- UFH alternatively can be used throughout pregnancy.

Regimen III

- Heparin used till 12th week
- Warfarin then continued from 12th week till near time of delivery
- Heparin restarted during time of delivery.

Newer Drugs (ACCP 2012)

- Danaparoid (Heparinoid) is most preferred newer drug in pregnancy in patiens with HIT
- Fondaparinux best alternative to danaparoid in HIT
- Lepirudin (Recombinant Hirudin) approved for treatment of HIT
- Bivalirudin approved only for those patients with unstable angina undergoing angioplasty
- Avoid DTIs (Dabigatran) and Factor Xa inhibitors (Fondaparinux/Rivaroxaban) unless severe HIT.

LAPAROSCOPY IN PREGNANCY[16]

Introduction: Pregnancy is no longer considered a contraindication to laparoscopic surgery.

Advantages

- Earlier ambulation and return to routine activity reduces chances of DVT
- Earlier return of GI function
- Reduced hospital stay duration
- Reduced infection and reduced postoperative incisional hernia
- Lesser bleeding
- Lesser pain: Reduces narcotic use
- Lesser manipulation of uterus while obtaining adequate exposure:
  - Reduces chances of preterm labor
  - Reduces premature delivery
  - Reduced likelihood of spontaneous abortion.
- Better osmosis.

Disadvantages

- Increases chances of hypoxia, hypercapnea and hypotension
- Increased postoperative nausea and vomiting (PONV)
- Narrow field of vision during surgery
- Harmful effects of CO_2:
  - Fetal tachycardia and HTN
  - Severe maternal acidosis
  - Severe fetal acidosis.

Indications

- Diagnostic:
  - For acute abdomen in pregnancy
  - Diagnosis of ectopic pregnancy.
- Therapeutic:
  - Laparoscopic appendicectomy
  - Laparoscopic cholecystectomy
  - Linear salpingotomy for unruptured ectopic pregnancy
  - Laparoscopic fundoplication and hernia repair.

Timing of Surgery

- Ist trimester:
  - Risk of teratogenecity
  - 12% miscarriage rate.
- IIIrd trimester:
  - 30% risk of preterm labor which increases with gestational age
  - Gravid uterus prevents proper visualization of surgical field.
- IInd trimester:
  - 0% miscarriage rate, 8% preterm labor
  - No risk of teratogenicity
  - Gravid uterus does not cause obstruction
  - ***Safest*** according to ***ASGES (American Society for Gastro Endoscopic Surgery)***
  - Ideally done at < 23 wks gestational age.

Guidelines for Laparoscopic Surgery During Pregnancy: ASGES[1]

- DVT prophylaxis using intermittent pneumatic compression device
- Use of prophylactic antibiotic recommended
- Minimize operative time
- Left lateral position used as in open surgery to prevent IVC compression
- Minimize reverse Trendelenburg position as:
  - Venous stasis causes increased risk of DVT
  - Reverse Trendelenburg position reduces cardiac a output.
- Use open technique to enter abdomen rather than trocar
- ***Hassen's*** technique is safer option
- Insertion of Verres needle in subcostal region is less likely to produce uterine injury
- Risk of bowel injury is high as gravid uterus pushes bowel into upper abdomen
- Alternative techniques to lift abdominal wall are:
  - Use of abdominal wall lifting devices
  - Optical trocar which allows visualization at the time of trocar insertion
- Maintain IAP between 6–15 mm Hg[1]
- E_TCO_2 should be kept between 25–32 mm Hg.[1]

Anesthetic Technique

- Regional anesthesia:
  - May cause precipitous hypotension and fetal distress
  - High block can cause paralysis and hypotension
  - Difficulty in controlling ventilation and maintaining $PaCO_2$
  - Inadvertent intrathecal/intravascular injection of local anesthetic
  - Increased incidence of shoulder tip pain
  - Nasogastric tube not well tolerated
  - Advantageous as awake mother prevents aspiration
  - Epidural anesthesia preferred over spinal anesthesia.
- General anesthesia: ***Technique of choice*** as:
  - Patient may be anxious
  - Respiratory compromise and dyspnea possible in awake patient
  - Nasogastric tube may be uncomfortable in awake patient
  - Allows control of ventilation to adjust hyperapnea.

Preoperative Management

- NPO for 6 hrs solids, 4 hrs liquids and 2 hrs clear fluids
- Preoperative antibiotics
- Premedication: Diazepam 0.05 mg/kg or midazolam 0.05 mg/kg IV
- Antiaspiration prophylaxis:
  - 30 ml of non-particulate sodium citrate
  - 50 mg ranitidine IV
  - 10 mg metoclopramide or 8 mg ondansetron IV
- Antisialogogue:
  - 0.01 mg/kg glycopyrrolate IV
  - Also combats reflex vagal activity from peritoneal stretching.
- DVT prophylaxis
- Preoperative fetal heart rate monitoring
- Shift to OT in left lateral position.

Intraoperative Management

Induction and Intubation

- Adequate preoxygenation with 100% oxygen as patient rapidly desaturates
- Thiopentone 3 mg/kg + SCH 1 mg/kg + O_2 + Isoflurane 1%
- ***Rapid sequence induction*** with cricoid pressure is ***technique of choice***
- Smaller sized ETT (7)
- Insert nasogastric tube and Foleys catheter.

Monitoring

Maternal Monitors

- Monitors:
  - Pulse oximetry
  - NIBP/IBP
  - ECG
  - E_TCO_2
  - Temperature
  - Nerve stimulator
  - Peak airway pressure
  - Minute ventilator
  - Serial ABG for $PaCO_2 – E_TCO_2$ difference.
- Clinical assessment:
  - Skin color, turgor, capillary refill
  - Cornea and conjunctiva for edema in Trendelenburg position
  - Pulse rate and rhythm
  - Upper chest for subcutaneous emphysema
  - Urine output as oliguria occurs despite adequate hydration especially when IAP > 15 mm Hg.

Fetal Monitors:

- FHR: Cardiotachometer
- Uterine activity: Tocodynamometer
- Transvaginal ultrasonography.

Maintenance

- Propofol when used for maintenance (in TIVA) reduces PONV incidence
- Fentanyl 1 µg/kg and vecuronium 0.1 mg/kg IV boluses for maintenance
- O_2 + 1% isoflurane used to maintain balanced anesthesia
- Halothane avoided as it can cause arrhythmias in the presence of CO_2
- N_2O avoided as:
  - It prevents bowel distention
  - It reduces incidence of PONV
  - Avoiding nitrous oxide also increases the delivered FiO_2.
- E_TCO_2 maintained between 25–32 mm Hg (maternal physiological alkalosis)
- Intermittent NGT suctioning required as CO_2 diffuses into stomach and distends it
- Table is tilted to left and Trendelenburg restricted to 10.

Hemodynamics

- Strict maintenance of BP with fluid boluses and vasopressors
- 2.5 – 4 ml/kg/hr of Ringers Lactate through 16-18G IV cannula
- Third space and insensible fluid loss is lesser
- Volume of retained intraperitoneal saline to be added to total fluid infuses
- Volume of retained intraperitoneal saline = (Volume of fluid used for irrigation) – (Volume of fluid in suction container).

Extubation

- Fully awake in lateral and head down position to reduce risk of aspiration
- Shift to PACU in left lateral position.

Postoperative Management

- Remove Foleys catheter and NGT if patient is fully awake, stable and voiding adequately
- Supplemental O_2 mandatory as O_2 demand increases following laparoscopic surgery
- Ondansetron or metoclopramide to reduce PONV incidence.

Complications

- Air leak syndromes:
  - Subcutaneous emphysema
  - Pneumothorax
  - Pneumopericardium
  - Pneumomediastinum.
- Gas embolism usually when laparoscopy is associated with hysteroscopy
- PONV:
  - Main complication postlaparoscopic surgery
  - May be severe
  - Steps to reduce PONV:
    - Preoperative nasogastric tube drainage
    - Propofol based anesthesia
    - Intraoperative administration of ondansetron/metaclopramide.
- Aspiration pneumonia
- Postoperative pulmonary dysfunction:
  - Lesser in pelvic surgery compared with upper abdominal surgery
  - FRC returns to baseline values within 72 hrs.
- *Pulmonary edema:* As fluid may be increased due to low urine output intraoperatively
- Pain:
  - More of visceral nature
  - Lesser compared with open laparotomy.

Monitoring

- Pulse oximetry
- ECG
- BP as hemodynamic changes outlast duration of pneumoperitoneum
- Urine output
- ABG.

Postoperative Analgesia

- Topical anesthesia and infiltration reduces postoperative
- Intraperitoneal instillation of 0.5% lidocaine 80 ml or 0.125% bupivacaine with epinephrine in right subdiaphragmatic area reduces shoulder tip pain
- NSAIDs for shoulder tip pain
- Opioids, clonidine also helpful.

MITRAL STENOSIS IN PREGNANCY[1,5,16]

Introduction

- Most common lesion associated with Rheumatic Heart Disease (RHD)
- 90% of pregnant women with RHD have mitral stenosis.

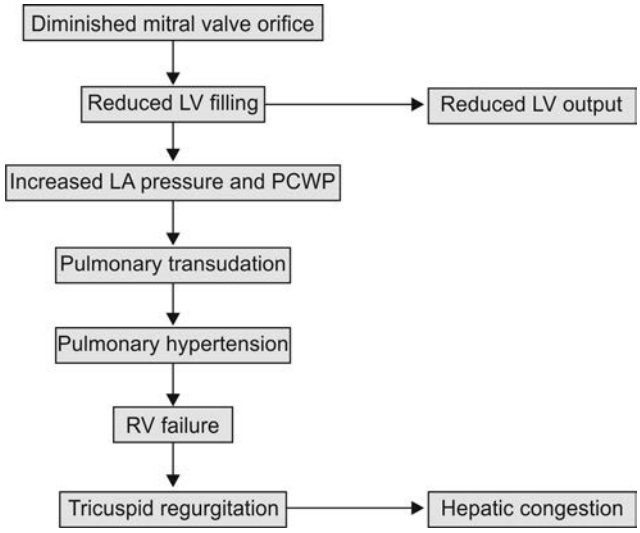
Grading of Severity

- *Normal:* 4–6 cm^2
- *Mild MS:* 1.5–2.5 cm^2
- *Moderate MS:* 1–1.5 cm^2
- *Severe MS:* 0.6–1 cm^2.

Pathology

- Disease is characterized by thickening and commissural fusion of valve leaflets
- With increased rigidity, fusion and contracture of chordae tendinae and papillary muscle heads occurs
- The valve eventually becomes ***fish mouthed*** and may calcify on long standing.

Pathophysiology



Pregnancy Induced Changes on MS[16]

- Moderate stenosis may become severe
- Larger atrioventricular gradient develops which increases progressively
- Increased heart rate of pregnancy reduces diastolic filling time:
  - This can increase left atrial pressures and PCWP
  - Therefore there is increased likelihood of pulmonary edema
  - Women with asymptomatic MS before pregnancy tolerate pregnancy well
  - Those with previous pulmonary congestion have increased incidence of pulmonary edema and mortality during pregnancy
  - Morbidity and mortality is greatest during labor and immediate postpartum period.
- Rapid right ventricular decompensation occurs in severe MS due to limited ability to increase cardiac output
- Increased incidence of complications:
  - Pulmonary edema (25%)
  - Atrial fibrillation (7%)
  - Paroxysmal atrial tachycardia (3%).
- After delivery:
  - Sudden increase in preload occurs following umbilical cord clamping
  - This may flood pulmonary circulation causing severe pulmonary edema.

Clinical Features

- Symptoms of MS usually occur 10–20 years after acute rheumatic fever
- Symptoms first occur on an average at 31 yrs age
- They proceed in 7 years to total incapacity without surgical correction
- 50% patients die in 5 years span
- Symptoms can be precipitated by pregnancy
- 25% women with MS become symptomatic during pregnancy.

Symptoms

- Fatigue, dyspnea on exertion, PND, orthopnea
- Hemoptysis due to rupture of bronchopulmonary varices
- Systemic/pulmonary arterial embolization
- Rapid decompensation occurs if:
  - *Infection:* Pregnancy
  - *Atrial fibrillation:* Pulmonary edema.
- *Recurrent pulmonary infection:* Bronchitis, pneumonias.

Signs

- Malar flush with pinched and blue facies: ***mitral facies***
- Small volume pulse, cold extremities with peripheral cyanosis in severe MS
- Irregularly irregular pulse ***(delirium cordis)***: If atrial fibrillation present
- Increased respiratory rate and crackles due to pulmonary congestion
- Engorged neck veins with prominent 'a' wave
- Tender liver (with systolic pulsation if tricuspid regurgitation), ***ascites precox***
- Ascites, anasarca and pleural effusion indicative of right ventricular failure
- Auscultation:
  - Loud S_1
  - Accentuated P_2 component of second heart sound

- Pulmonary ejection systolic click if pulmonary HTN is present
- Mitral stenosis murmur:
  - Low pitched rumbling mid-diastolic murmur (MDM)
  - Best heart with bell of stethoscope
  - With patient in left lateral position
  - Breath heard in expiration
  - Radiating towards axilla
  - Accentuated by squatting/handgrip/exercise at apex.
- Opening snap along left sternal border/just medial to apex.

Clinical Assessment of Severity

- S_2–OS gap:
  - Normal is 0.05 – 0.12 sec
  - If OS closer to S_2, MS is more severe
- Severity of MS increases as duration of MDM increases
- Can be assessed indirectly by assessing severity of pulmonary HTN
- Higher the RVSP, more severe is MS (Normal < 25 mm Hg).

Investigation

- Chest X-ray:
  - Normal in early stages, avoided in 1st trimester
  - LA and RV enlargement later on and right ventricular apex
  - ***Mitralisation of left heart border***
  - Pulmonary edema
  - Calcified valve, splaying of carina.
- ECG:
  - Broad P-wave in V_1 (LA enlargement) – ***P mitrale***
  - Right axis deviation, RBBB: RVF
  - Atrial fibrillation.
- ECHO/TEE (intraoperative):
  - Diagnostic and for monitoring purposes
  - Detecting LA thrombus
  - Increased LA size, pulmonary HTN.
- Serial vital capacities
- Holter monitoring
- Cardiac catherization:
  - Capillary wedge pressures 25–30 mm Hg (normal = 0–12 mm Hg), when mitral valve area ≤ 2 cm^2
  - Increased pulmonary vascular resistance
  - Valvular diastolic pressure gradients > 25 mm Hg, if severe MS
  - For calculation of MVA using ***Gorlin's equation***
- Pressure volume loop in MS:

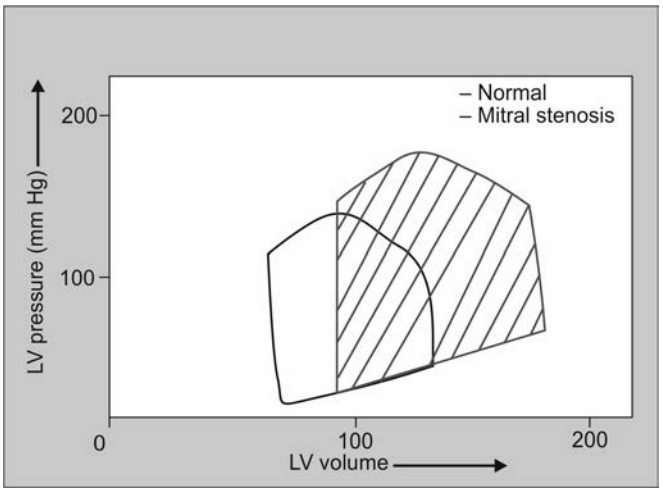


Fig. 3.6: Pressure–volume loop in mitral stenosis[3]

Medical Management

- β blockade to prevent tachycardia with propranolol/atenolol
- Beta blockade reduces chances of maternal pulmonary edema
- Esmolol avoided as it is teratogenic
- Atrial fibrillation requires aggressive treatment with digoxin and β blockade
- Treat pulmonary edema with bed rest in lateral decubitus position and administration of diuretics
- Salt and water restriction.

Surgical Management

- Surgery advised if:
  - Moderate to severe MS is recognized before pregnancy
  - If medical treatment is unsatisfactory during pregnancy
  - Closed mitral valvotomy preferred to mitral valve replacement.
- Closed mitral valvotomy:
  - Can be either surgical or balloon valvulotomy
  - Can be done at any stage of gestation if symptoms are severe
  - Best done during IInd trimester
  - Balloon valvulotomy with radiation shielding of fetus preferred
  - Done with ***Inoue*** ballon if:
    - Valve has no calcification
    - Without extensive subvalvular thickening
    - Mild or no MR

- Symptomatic patients with isolated MS with MVA < 1.7 cm^2.
  - Maternal mortality after closed surgical valvulotomy is 2–3%.
- Mitral valve replacement:
  - Bioprosthetic heterogenous porcine valve preferred
  - Bioprosthetic valve avoids risk of warfarin related complications
  - Best done in IInd trimester
  - Indicated if:
    - MS is associated with significant MR
    - Where valve is distorted by previous transcatheter manipulation
    - Done only if critical MS with MVA < 1cm^2 and NYHA class > III.

Anesthetic Considerations[16]

- Maintain sinus rhythm
- Prevent rapid ventricular rates
- Minimize increases in central blood volume
- Avoid marked decrease in SVR
- Prevent increase in pulmonary arterial pressures.

Prevent Rapid Ventricular Rates

- Sinus tachycardia and AF with FVR most common
- Digoxin therapy started prior to pregnancy
- Should be continued to maintain ventricular rate ≤ 110 bpm
- AF with FVR markedly decreases cardiac output and cause pulmonary edema
- Selective cardioversion (25 J) may be used
- Propranolol 0.2–0.5 mg IV every 3 mins used to decrease ventricular rate
- Discontinue propranolol when:
  - Total propranolol dose is 0.1 mg/kg
  - When heart failure ensues.
- Avoid esmolol
- Digitalization used when prolonged but not immediate rate control is required:
  - Digoxin 0.5 mg IV over 10 min
  - Followed by 0.25 mg IV Q2H till full digitalizing dose is achieved
  - Each dose has an effect in 15 min with full effect in 1–2 hrs
- Sinus tachycardia > 140 bpm or resulting in decreased CO/increased PCWP:
  - Reverse precipitating event
    - Pain
    - Light GA
    - Hypercapnea
    - Acidosis.
  - Administer propranolol.

Minimize Increases in Central Blood Volume

- Avoid:
  - Over transfusion
  - Trendelenburg position
  - Autologous transfusion via uterine contraction
- Increase in central blood volume can precipitate RVF, pulmonary edema
- CVP and PAP used to assess increase in central blood volume.

Avoid Decreases in SVR

- Decrease in SVR is compensated by increase in HR as the stroke volume is fixed
- Marked increase in HR may cause decompensation
- SVR may be maintained with phenylephrine infusion
- Ephedrine ***not recommended*** as it may increase HR.

Prevent Increases in Pulmonary Arterial Pressure

- Avoid hypercarbia, hypoxia, acidosis, lung, hyperinflation and increased lung water
- Prostaglandins, oxytocin and methylergometrine boluses used to treat uterine atony
- Should be used with caution as they may increase PAP
- If pulmonary HTN and RVF occurs:
  - IV dopamine (3–8 µg/kg/min) inotropic support
  - Pulmonary vasodilation with SNP (0.1–0.5 µg/kg/min)
  - Avoid higher doses of SNP to avoid generalized vasodilation and cyanide toxicity.

Anesthetic Management

- Labor Analgesia:
  - Segmental lumbar epidural anesthesia preferred as:
    - Eliminates pain and tachycardia accompanying uterine contraction
    - Perineal analgesia blocks urge to push
    - Prevents fatigue and deleterious effect of Valsalva maneuver.
  - Fetal descent occurs by uterine contraction per se
  - Delivery is facilitated by outlet forceps or vacuum extraction

  - Left uterine displacement and IV fluids to treat hypotension
  - Phenylephrine is preferred vasopressor.
- *LSCS:* ***SAB Contraindicated***
  - Regional Anesthesia:
    - For NYHA I and II
    - Preferred over GA as:
      - Induced sympathectomy decreases both preload and afterload
      - This relieves pulmonary congestion
      - In some cases increases cardiac output.
    - Continuous Epidural preferred over SAB as controlled hypotension
    - Anesthetic levels established by slowly tirating LA through catheter
    - Epinephrine omitted from LA solution as it causes tachycardia and peripheral vasodilation
    - Hypotension with decreased PCWP: Fluids to restore normal filling pressure
    - Hypotension with normal PCWP: Phenylephrine infusion
    - Combined spiral epidural may be used.
  - General Anesthesia: Used in emergency situation and NYHA III and IV patients.

Conduct of General Anesthesia

Premedication

- Avoid oversedation to avoid hypoxia, hypercarbia and pulmonary hypertension
- Diazepam 0.1 mg/kg PO
- Antibiotic prophylaxis – no longer recommended
  - Ampicillin 2 g (50 mg/kg) IV
  - Gentamicin 1.5 mg/kg IV 30 mins before surgery
  - 1 gm ampicillin IV 6 hrs after surgery
  - Continued for 2 days after surgery
  - Vancomycin with gentamicin in penicillin allergic patients.
- Antiaspiration prophylaxis:
  - 15–30 ml of 0.3 M sodium citrate PO
  - 1 mg/kg Ranitidine IV
  - 10 mg metoclopramide IV.
- Anticoagulation 100 IU/kg heparin if patient is in AF
- Drugs producing tachycardia to be avoided:
  - Atropine
  - Pancuronium
  - Pethidine
  - Ketamine.
- Continue morning dose of digoxin
- IV crystalloid preloading via 18G cannula.

Position

- Supine with left lateral tilt to avoid hypotension
- *Avoid steep Trendelenburg:* Increases venous return and precipitates pulmonary edema.

Induction and Intubation

- Preoxygenate with 100% O_2 for 3–5 minutes or for 4 maximal capacity breaths.
- Mild stenosis:
  - After abdominal preparation and draping ***Rapid Sequence Induction***
  - 4 mg/kg thiopentone and 1 mg/kg succinylcholine
  - Rocuronium 1.2 mg/kg may be used as alternative
  - Defasciculating dose of NDMR not required.
- Moderate to severe stenosis:
  - Inhalational induction with halothane
  - Halothane causes decrease in HR
  - Halothane may also precipitate junctional rhythm
  - IV fentanyl 2–4 µg/kg or morphine 0.1 mg/kg
  - May cause fetal depression but benefits outweigh risks
  - Opioid induction useful if frank pulmonary edema.
- Xylocard used to decrease intubation response
- Deep planes for intubation to avoid detrimental tachycardia
- Cricoid pressure which is released only after is inflated and tube position checked
- Tachycardia due to intubation/incision treated by deepening anesthetic plane
- Propranolol may be used to treat tachycardia.

Hemodynamics

- Avoid ephedrine as it causes tachycardia
- IV fluids through large 16/18G cannula
- Phenylephrine is preferred vasopressor agent
- RV dysfunction if present is managed by:
  - Optimizing acid base balance
  - Maintaining hypocapnea and hyperoxia
  - Using vasodilators (NTG 0.1–0.5 µg/kg/min) to decrease PVR.
- IV bolus dose of oxytoxin and ergometrine ***contraindicated.***

Maintenance

- Before delivery of fetus:
  - 100% O_2 + 0.5% halothane
  - Vecuronium 0.1 mg/kg or cisatracurium
  - Isoflurane avoided as it decreases SVR
  - N_2O avoided as it increases PVR
- After delivery of fetus:
  - 100% O_2 + 0.5% halothane
  - 1 µg/kg fentanyl + 0.05 mg/kg midazolam + 0.1 mg/kg vecuronium.

Extubation

- Follow same hemodynamic goals at extubation
- Avoid tachycardia
- Fully awake in left lateral position with head down: decreases aspiration chances
- Neostigmine and glycopyrrolate not used regularly due to tachycardia by glycopyrrolate.

Intraoperative Problems

- Hypotension : Dobutamine
- Atrial fibrillation : Cardioversion
- Pulmonary edema : Diuretics, PEEP
- Cardiac arrest.

Postoperative

Complications

- Pulmonary edema
- Atrial fibrillation
- Aspiration
- Prolonged mechanical ventilation
- Respiratory depression.

Monitoring

- Pulse oximetry; BP
- ECG; Urine output
- Temperature; ABG
- Chest X-ray; Fetal activity, APGAR score.

Analgesia

- Opioids—fentanyl 1 µg/kg/min infusion
- NSAIDs—Diclofenac 50 mg IV
- Continuation of anticoagulation as per ACCP guidelines
- Epidural analgesia if valve area > 1.5 cm^2.

PERIPARTUM CARDIOMYOPATHY[1,2,3,16]

Introduction

- Dilated cardiomyopathy occurring between 36 weeks of gestation and 5 months postpartum
- Also called ***Cardiomyopathy of pregnancy, Puerperal cardiomyopathy, Postpartum heart disease.***

Incidence

- 1 in 3000 to 1 in 1500 pregnancies worldwide
- High in Nigeria:
  - Due to the tradition of ingesting ***Kanwa*** (dried lake salt)
  - Ingested while lying on heated mud beds twice a day for 40 days postpartum
  - High salt intake causes volume overload
- Mortality ranges from 18–56%
- 82% occur in 1st 3 months post partum
- Only 7% develop in last months of pregnancy.

Etiology

Various theories to explain occurrence:

- Accelerated HTN reported in 30% cases
- Maternal immunological response to fetal antigen:
  - Fetal cells escaping into maternal circulation are not rejected due to:
    - Suppressed immune system in pregnancy
    - Weak immunogenicity of fetal antigen.
  - Fetal cells lodge into the cardiac tissue during pregnancy
  - After delivery, immune competency is regained
  - Fetal cells are recognized as nonself
  - Thus an autoimmune response may be triggered
- Fragmentation of tropocollagen:
  - Fast involution of uterus after delivery causes fragmentation of tropocollagen
  - This causes release of actin, myosin and metabolites
  - Antibodies against actin cross react with myocardial tissue
  - Patient acquires cardiomyopathy.
- Beriberi:
  - Onset of lactation associated with increased BP and nutritional requirements
  - This may reduce vitamin B_1 levels: Wet beriberi and CCF.

Predisposing Factors

- Black race:
  - High BP and increase in incidence of sickle cell anemia
  - This can cause CCF due to longstanding anemia
- Old age > 30 years old
- Obese > 30 BMI
- Multiparous women.

- Twin pregnancies due to increased demands on existing maternal physiological changes
- Preeclampsia
- Chronic HTN > 140/90 mm Hg
- Prolonged tocolytic therapy with β agonists:
  - Terbutaline and ritodrine
  - β agonist activity: tachycardia, arrhythmias, MI, sodium retention, hypertension.
- Malnutrition:
  - Reduced selenium levels
  - Wet beriberi
  - Nutritional anemia
  - Hypoproteinemia: causes edema.

Pathology

- Dilatation of heart
- Increased weight of heart (double the normal weight of 300–350 gms)
- Hypertrophy and mural thrombi on LV
- Loss of myocardial fibers with intestitial edema.

Pathophysiology

- Patients with significant myocardial damage remain asymptomatic when at rest
- Physiological stress like pregnancy increases cardiac work
- Pregnancy causes:
  - Increase in preload associated with uterine contraction or surgery
  - Increase in cardiac demand:
    - Heart rate
    - Stroke volume
    - Increased contractility.
  - This causes increased stress on myocardial function.
- With progressive ventricular failure:
  - End diastolic volume increases, reducing subendocardial blood flow
  - Cardiac output reduces, reducing coronary perfusion further
  - Myocardial O_2 demand–supply imbalance ensues
  - This causes further ventricular compromise.

Clinical Features

Symptoms

- Gradual/insidious onset/sometimes acute onset dyspnea and pulmonary edema
- Edema, dyspnea on exertion, orthopnea, fatigue, PND, cough hemoptysis.

Signs

- Signs of LVF:
  - Crackles cyanosis
  - Tachycardia cold extremities
  - Diaphoresis LV thrust
  - Narrow pulse pressure
  - S_3 gallops at apex and radiating to axilla
  - Audible S_4.
- Signs of RVF:
  - Raised JVP
  - Hepatojugular reflex
  - Anasarca
  - Hepatomegaly
  - RV heave.
- Systemic embolization of mural thrombi:
  - Especially to kidneys causing pyelonephritis
  - Cerebral embolization, pulmonary embolization and infarction.
- Signs of valve regurgitation:
  - Mitral regurgitation
  - Tricuspid regurgitation (functional).
- Arrhythmias:
  - Supraventricular tachycardia
  - Atrial fibrillation
  - Ventricular tachycardia/fibrillation.

Investigations

- Chest X-ray:
  - After 1st trimester
  - Cardiomegaly, pulmonary vascular congestion
  - Patchy infiltrates and intestitial congestion in lower lung fields: CCF
  - Pleural effusion.
- CT scan lungs for pulmonary emboli
- ECG:
  - ST-T changes
  - Ectopics, sinus tachycardia
  - Rarely atrial fibrillation
  - LV hypertrophy: High voltage complexes
  - P pulmonale in lead V1
  - First degree heart block, bundle branch block patterns.
- ECHO:
  - LV enlargement
  - Global systolic dysfunction with or without LVH
  - Elevated filling pressures
  - Stress ECHO
  - Intracardiac thrombi.
- Cardiac catheterization

- Endomyocardial biopsy if condition does not improve after 2 weeks therapy for CCF
- *Routine blood with:* D-dimers, factor V, anticardiolipin Abs for differentiating DIC
- Viral serological tests:
  - Viral HIV; Rickettsial
  - Toxoplasmosis; Syphilis
  - Chagas disease (trypanosomiasis)
  - Diphtheria
- Nuclear study/angiography with fetal shield after 1st trimester.

Diagnostic Criteria: *NIH/NHLBI Guidelines*

- Onset of heart failure between 37 weeks of pregnancy to 5 months postpartum
- LVEF < 45% or LV diastolic diameter > 2.7 cm/m^2
- No evidence of heart disease prepartum
- No other causes of heart failure
- LV fractional shortening < 30%.

Differential Diagnosis

- *Toxic:* Cocaine, alcoholic cardiomyopathy
- Infective:
  - HIV; Rickettsial
  - Toxoplasmosis; Syphilis
  - Chagas disease (trypanosomiasis)
  - Diphtheria
- Collagen vascular disease: Sarcoidosis
- Endocrine: Thyrotoxicosis, pheochromocytoma
- *Previous heart ailment:* Valvular, ischemic, myopathic.

Choice of Anesthesia Technique

- Regional anesthesia:
  - Used for labor and vaginal delivery and non-emergent Cesarean section
  - Advantages
    - Early administration of labor analgesia reduces cardiac stress
    - Continuous epidural offers better hemodynamic control
    - RA causes sympathectomy induced reduction in afterload
    - This improves myocardial performance
    - If fixed low cardiac output state exists, RA with only opioids may offer more hemodynamic stability
  - Guidelines for regional anesthesia:
    - Continuous FHR monitoring required
    - Preloading and prophylactic ephedrine not used.
- General anesthesia:
  - Used if fetal distress/acute maternal decompensation
  - Complications:
    - *Hypotension:* Pulmonary edema
    - *Hypoxemia:* MI and dysrrhythmias.
- Slow maternal circulating time causes:
  - Late onset of action of drugs
  - This may be presumed to be insufficient dosage
  - This may lead to additional dosage administration and overdosage.

Technique of General Anesthesia

Premedication

- Supplemental oxygen administration
- Low sodium diet (< 2g/day of NaCl)
- Bed rest not recommended due to increased risk of DVT
- Left uterine displacement to avoid supine hypotension syndrome
- Antiaspiration prophylaxis
- IE prophylaxis based on individual patient
- Anticoagulation if indicated:
  - Markedly enlarged heart
  - History of embolization
  - History of atrial fibrillation
  - Significantly reduced cardiac output
- Stop ACE inhibitors and angiotensin II antagonists on day of surgery
- Diuretics and digoxin continued on morning of surgery.

Monitoring

- *BP:* Invasive BP monitoring
- Pulse oximetry
- ECG
- Urine output
- Pulmonary artery catheter for management of hemodynamic status
- Cardiac output monitoring
- FHR monitoring.

Induction

- Preoxygenation important as maternal oxygen demand increases by 20% at birth
- Opioid induction preferred with neonatologist to manage neonatal depression
- Propofol + sufentanil + vecuronium can be used alternatively for induction
- Deep intubation as tachycardia can precipitate heart failure.

Maintenance

- O_2 + N_2O + isoflurane
- Avoid anesthetics associated with myocardial depressant effects like halothane
- N_2O relaxant technique can be used if marked LV failure
- Graded doses to avoid postoperative depression
- N_2O avoided if pulmonary hypertension
- Prevent tachycardia at the time of incision
- PEEP to reduce pulmonary congestion and increase forward output.

Hemodynamics

- Avoid fluid overload: judicious use of colloids
- Avoid blockers and calcium channel blockers
- NTG/SNP for preload and afterload reduction if cardiac decompensation occurs
- Dopamine/dobutamine/milrinone for inotropic support
- If condition does not improve with standard medical therapy, consider:
  - Pacemaker placement
  - Intra Aortic Balloon Pump (IABP)
  - Left Ventricular Assist Devices (LVAD)
  - Cardiac transplantation
- CO increases 65% after delivery due to:
  - Release of IVC compression
  - Autotransfusion of blood back into maternal circulation.

Extubation

Fully awake extubation in left lateral position to avoid aspiration.

Intraoperative Complications

- Hypotension
- Pulmonary edema
- Hypoxemia
- MI
- Arrhythmias
- Delayed awakening.

Postoperative

- ACE inhibitor and angiotensin II inhibitor in postpartum period (not during pregnancy)
- Avoid captopril as it crosses placenta and causes renal failure in neonate
- Hydralazine with NTG/amlodipine are alternatives to decrease preload and afterload.

Future Pregnancies

- Controversy as to whether patient can safely undergo another pregnancy
- If woman conceives, serial ECHO monitoring, recommended
- These patients decompensate earlier with more severe symptoms
- Dobutamine challenge test used to predict cardiac performance in future pregnancy
- If heart of patient with PPCM returns to normal size, subsequent pregnancies may be tolerated
- If heart remains enlarged, future pregnancies can cause intractable CCF and death.

Prognosis

- Mortality 25–50% with 25–50% of these patients dying in 1st 3 months postpartum
- Most common cause of death CCF, SVT (AF and atrial flutter)
- Prognosis related to LV size and severity of LV dysfunction at the time of presentation
- In 50% patients, heart size returns to normal in 6–12 months after the onset of disease
- Infants whose mothers present with PPCM after delivery had good outcome
- Infants whose mothers presented with PPCM before delivery had a less favourable outcome.

GESTATIONAL DIABETES MELLITUS[1,2,3,16]

Definition: Abnormal carbohydrate tolerance with onset or first detected during pregnancy after a 75 gm oral glucose load.

American Diabetic Association Criteria

Time	Normal tolerance mg%	Impaired tolerance mg%	Diabetes mg%
Fasting	< 110	110–126	> 126
2 hr postprandial	< 140	140–200	> 200

Classification[16]

Priscilla White's Classification

Class	Onset	Fasting glucose	2-hr post-prandial	Therapy
A_1	Gestational	< 105 mg%	< 120 mg%	Diet
A_2	Gestational	> 105 mg%	> 120 mg%	Insulin

Class	Age of Onset	Duration (Yrs)	Vascular Disease	Therapy
B	> 20	< 10	None	Insulin
C	10–19	10–19	None	Insulin
D	< 10	> 20	Benign retinopathy	Insulin
F	Any	Any	Nephropathy	Insulin
R	Any	Any	Proliferative retinopathy	Insulin
H	Any	Any	Heart	Insulin

Risk Factors

- Age > 30 yrs
- Obesity, Asian race
- Family history of diabetes mellitus
- Previous birth of overweight baby > 4 kgs
- Previous still birth with pancreatic islet hyperplasia on fetal autopsy
- Unexplained perinatal loss
- Polyhydramnios
- Recurrent vaginal candidiasis
- Persistent glucosuria.

Maternal Hazards

- Infection
- Preeclampsia
- Polyhydramnios
- Diabetic retinopathy, nephropathy
- Diabetic ketoacidosis
- Abortion, preterm labor
- Prolonged labor, PPH, perineal injuries due to large baby
- Puerperal sepsis
- Lactation failure.

Fetal Hazards

- Macrosomia, birth injuries, IUD
- IUGR
- Neonatal complications:
  - Hypoglycaemia; Hyperbilirubinemia
  - RDS; Hypo Ca^{2+}, Mg^{2+}
  - Acidosis; Cardiomyopathy.
- Birth defects:
  - NTD, anencephaly, microcephaly
  - VSD, ASD, COA, TGA
  - Renal agenesis, hydronephrosis
  - Duodenal/anorectal atresia
  - Single umbilical artery
  - Impaired O_2 transport due to lower 2, 3 DPG concentration
  - Decreased buffering capacity to acid load.

Glycemic Control

Tight Perioperative Glycemic Control Regimen:[1]

- Maintain blood sugar between 79 and 120 mg%
- Determine preprandial blood sugar on evening before surgery
- IV infusion of 5% Dextrose at 50 ml/hr/70 kg
- Piggyback regular insulin infusion at (Blood gucose/150) IU/hr
- Repeat blood glucose Q4H
- Adjust infusion rate to maintain blood glucose between 80 and 120 mg%
- On day of surgery, start nondextrose containing fluids
- Insulin infusion at (Blood Glucose/150) IU/hr
- Determine Blood Glucose:
  - Once at start of surgery
  - Every two hours for rest of 24 hr period.
- Treat hypoglycaemia (blood glucose < 50 mg%):
  - 15 ml 50% Dextrose
  - Termination of insulin infusion.

Anesthetic Considerations

- Difficult intubation due to:
  - ***Stiff joint syndrome***
  - Pregnancy induced changes.
- Risk of aspiration due to:
  - Diabetic gastroparesis
  - Pregnancy-induced changes
- In the presence of autonomic neuropathy:
  - Increased risk of hypothermia
  - Poor response to atropine/catecholamines
  - Precipitous hypotension on neuraxial blockade
  - Increased risk of nerve injury
  - Increased risk of silent MI.
- Reduced O_2 saturation and transport
- Reduced sympathetic response to hypoglycemia under GA
- Perioperative complications:
  - Congestive cardiac failure
  - Renal failure
  - Infections.

Choice of Technique

- For labor analgesia, small dose opioids for moderate pain
- For Cesarean section, epidural/SAB safe

- For labor analgesia with severe pain: epidural analgesia.

Anesthetic Technique

- Valsalva maneuvers during 2nd stage contraindicated if retinopathy present
- Vitreous hemorrhage occurs with Valsalva maneuver in the presence of retinopathy
- Routine left uterine displacement
- Acute hydration with dextrose-free fluids before induction
- Hypotension promptly treated with IV ephedrine to prevent fetal acidosis
- *Rapid sequence induction* with cricoid pressure for GA
- Difficult airway cart with *polio blade* and short handle
- Gradual positional changes to avoid hypotension
- Anti-aspiration prophylaxis.

ANEMIA IN PREGNANCY[1,16]

Introduction: *WHO 1993 Guidelines*

- Hb concentration of < 11g% or HCT < 33% in 1st and 3rd trimester
- Hb concentration < 10.5 g% in 2nd trimester
- Hb concentration < 10g% at any time in pregnancy.

Classification

Physiological Anemia in Pregnancy

- Hb < 10 gm%
- RBC count 3.2 million/mm^3
- PCV 30%
- Normal RBC morphology with central pallor on peripheral smear.

Pathological Anemia in Pregnancy

- Nutritional: Iron, Vitamin B_{12}, Folate, Proteins.
- Hemorrhagic:
  - *Acute:* Antepartum hemorrhage
  - *Chronic:* Hookworm, hemorrhoids
- Bone marrow insufficiency:
  - Aplastic anemia
  - Radiation
  - Infection with parvovirus B_{12}
  - Drugs (aspirin, indomethacin).
- Anemia of chronic disease:
  - Chronic renal failure
  - Neoplasms
- Infections:
  - Malaria
  - Hookworm
  - Tuberculosis.

Hereditary Anemia

- Sickle-cell disease
- Thalassemia
- Other hemoglobinopathies
- Hereditary hemolytic anemia: Spherocytosis.

Compensatory Mechanisms

- Increased cardiac output
- Reduced blood viscosity
- Increased 2,3 DPG in RBC
- Rightward shift of Oxygen Dissociation Curve (ODC)
- Increased production of erythropoietin.

Severity of Anemia

- *Mild anemia:* 10–10.9 g/dl
- Moderate anemia: 7–9.9 g/dl
- *Severe anemia:* < 7g/dl.

Complications

Maternal Complications

- Heart failure at 30–32 wks
- Uterine atony, APH
- PPH
- Preeclampsia
- Preterm labor
- Infection
- Puerperal sepsis
- Uterine subinvolution
- Pulmonary embolism
- Puerperal venous thrombosis.

Fetal Complications

- Low birthweight
- Intrauterine death
- Fetal acidosis.

Preoperative Assessement

- History of tiredness, fatiguability, breathlessness, palpitation, angina
- Tachycardia, wide pulse pressure, ejection systolic murmur, pallor, crepts
- Investigations:
  - Complete hemogram, reticulocyte count
  - Stool and urine analysis, ESR, serum creatinine, BUN, bilirubin

- Serum proteins, iron, B_{12} and folate levels, TIBC, Hb electrophoresis
- ECG for evidence of MI
- MCHC, MCV, MCH.

Goals of Anesthesia

- Minimize factors affecting O_2 delivery
- Prevent increase in O_2 consumption
- Optimize PaO_2 in arterial blood.

Choice of Anesthesia

- Regional anesthesia preferred (SAB/CSE) as:
  - Good analgesia
  - Ability to provide supplemental O_2
  - Reduce blood loss
  - Reduce DVT.
- Disadvantages of regional anesthesia:
  - Hypotension and hemodilution
  - Chance of pulmonary edema due to overload
- Avoided in B_{12} deficiency with CNS symptoms as it worsens subacute degeneration of cord.

Monitoring

- ECG, SpO_2, NIBP, E_TCO_2, temperature, urine output
- IBP, CVP in unstable patients
- PA catheter and mixed venous oxygen saturation helpful
- Serial Hb and HCT when major blood loss anticipated.

Anesthetic Considerations

- Avoidance of hypoxia:
  - Preoxygenate with 100% O_2 for 3–5 mins or 4 vital capacity breaths
  - High FiO_2 (40–50%) intraoperatively
  - Spontaneous ventilation used only for short surgeries
  - Difficult airway anticipation
  - Avoid conditions increasing O_2 consumption:
    - Shivering
    - Fever
    - Acute blood loss
    - Pain
    - Light planes.
- Minimize anesthesia induced oxygenation changes:
  - N_2O used cautiously in B_{12} and folate deficiency
  - Avoid hypoventilation to minimize alkalosis
  - Avoid hypoventilation to avoid acidosis
  - Titrate induction agents to prevent hypotension
  - Careful and slow positioning to avoid hypotension
  - Left lateral tilt beyond 28 wks
  - Avoid hypothermia.
- Blood transfusion:
  - *Hb ≥10 g%:* Rarely indicated
  - *Hb ≤ 6 gm%:* Always indicated
  - *Hb 7–9 gm%:* Decision based on:
    - Ongoing blood loss
    - Coexisting disease
    - Threat of bleeding.

Sickle-cell Disease

- Complications:
  - Increased preterm labor
  - Abruption, placenta previa
  - Pregnancy-induced hypertension.
- GA/RA acceptable
- Avoid factors predisposing sickling
  - Hypoxemia
  - Hypovolemia
  - Hypotension
  - Acidosis
  - Hypoventilation
  - Hypothermia
  - Light planes.

Thalassemia

- Chronic anemia causes tissue hypoxia
- Multiple transfusion: Hemosiderosis and heart failure
- Concomitant difficult airway due to abnormal facies.

AMNIOTIC FLUID EMBOLISM[1,3,10,16]

Introduction

- AF embolism, though rare, is a condition with a mortality rate of 80–100%
- 1st reported by Meyer in 1926
- Also called ***Obstetric shock*** or ***Anaphylactic syndrome of pregnancy.***

Incidence

- 1 : 8000 to 1 : 80000
- Responsible for 10% of all maternal deaths
- Mortality rate up to 86%
- 25% of patients die within 1 hr of initial symptoms.

Components of Amniotic Fluid

- Volume of amniotic fluid increases from 50 ml at 12 wks to 1000 ml at term

- It is hypotonic due to dilution with fetal urine
- The damage to the lungs is irreversible because of contents of amniotic fluid
  - pH = 6.9–7.15
  - Suspended particles:
    - Lanugo, fetal squames, fetal gut mucin
    - Hair, meconium, trophoblasts
    - Vernix caseosa
  - Nitrogenous products:
    - Amino acids, uric acid, proteins
    - Urea, creatinine
  - Others:
    - Glucose, enzymes, hormones
    - Vitamins, steroids, lipids
  - Electrolytes:
    - Na, Mg, Fe, Cl, Mn
    - K, Ca, PO_4, S, Zn
  - Biochemical mediators:
    - Surfactant, IL_1, prostaglandin E_1, E_2, F_{1x}, F_{2z}
    - Endothelin, TNF , arachidonic acid
    - Leukotriene $C_4$and D_4, TxA_2, thromboplastin
    - Collagen, TF3, phospholipase A_2
    - PF3 (TF = Tissue factor, PF = Platelet factor)
    - PG F2 is the *most significant* for causing syndrome.

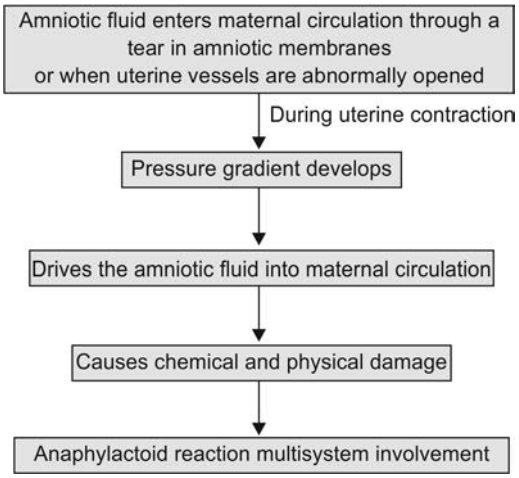
Predisposing Factors

- Elderly and multiparous
- Multiple pregnancy
- Commoner with male fetus
- Polyhydramnios
- Intrauterine death
- Term pregnancy in the presence of IUCD.

Precipitating Factors

- Artificial rupture of membranes, use of oxytocics, tumultuous labor
- 1st trimester curettage abortion
- 2nd trimester abortion using saline, glucose, PG, urea, hysterotomy
- Abdominal trauma, placenta rupture, uterine rupture
- Amniocentesis, intrauterine fetal monitoring
- During LSCS
- When uterine/decidual blood vessels are abnormally opened:
  - Placenta accreta
  - Ruptured uterus
  - Retained placenta.
  - Trauma from intrauterine manipulation:
    - Rupturing membrane
    - Inserting catheter for pressure recording.
  - Endocervical venous laceration/lower uterine tear during normal labor.

Pathogenesis



Pathogenetic Theories of AFE[16]

Anaphylactic Shock Theory

- Fetal contents of amniotic fluid produce a reaction similar to anaphylactic shock
- Hallmark symptoms of cutaneous flare, bronchospasm and airway edema.
- Controversial as:
  - Symptoms not due to histamine: Histamine usually absent in amniotic fluid
  - Symptoms not due to antigenic reexposure: AFE seen in both prime and multigravida.

Pulmonary Vascular Obstruction Theory

- Physical plugging of pulmonary capillaries due to:
  - Abnormal volume of amniotic fluid entering maternal circulation
  - Abnormal substances present in amniotic fluid like lanugo.

Alveolar Capillary Leak Theory

- Alveolar capillary leak occurs secondary to acute microvascular emboli
- ARDS and pulmonary edema due to alveolar capillary leakage
- Increase in ECF volume and decreased colloid osmotic pressure.

LV Dysfunction Theory

- Biphasic pattern of hemodynamic disturbances seen in AFE
- Initially pulmonary vasospasm due to amniotic fluid present in pulmonary vasculature
- This causes pulmonary hypertension and hypoxia
- Secondary phase of LVF with secondary elevation of pulmonary arterial pressure
- LV dysfunction may be due to:
  - Hypoxic LV injury
  - Direct depressant effect of amniotic fluid on myocardium
  - Myocardial ischemia due to coronary vasospasm: by endothelin present in AF.

Bleeding Diathesis Theory

- Amniotic fluid assists in post partum hemostasis
- Entry into maternal circulation produces intravascular clotting
- This consumes fibrinogen producing increased bleeding
- AF also has thromboplastin like effect and contains plasmin proactivator and factor X activator
- This causes intravascular coagulation and multisystem damage

Pathophysiology

- *Phase I:* Hypoxia, hypotension, pulmonary hypertension, corpulmonale, LV dysfunction
- *Phase II:* LV failure, ARDS, consumptive coagulopathy. **(See below Flow Chart)**

Clinical Features

- Can occur during:
  - Labor — Normal delivery
  - Cesarean section — Postpartum period.
- Prodromal symptoms: Chills and vomiting (rare)
- Patient usually goes into cardiac arrest soon after prodromal symtoms.

Phase I

- Classical presentation of:
  - Sudden onset dyspnea and hypotension
  - Hypoxia with altered mental state
  - Followed soon by cardiorespiratory arrest
- Shock is 1st clinical presentation in 10–15% cases
- GTCS in 10–20% cases
- Isolated coagulopathy as initial presentation in 10–15% cases
- Isolated coagulopathy presents as bleeding from
  - Per vagina
  - From incision site
  - IV catheter site
  - Epidural catheter site
  - Mouth and gums.
- If meconium-stained AF, shorter time from initial symptoms to arrest
- Cardiac arrest and DIC may occur simultaneously.

Phase II

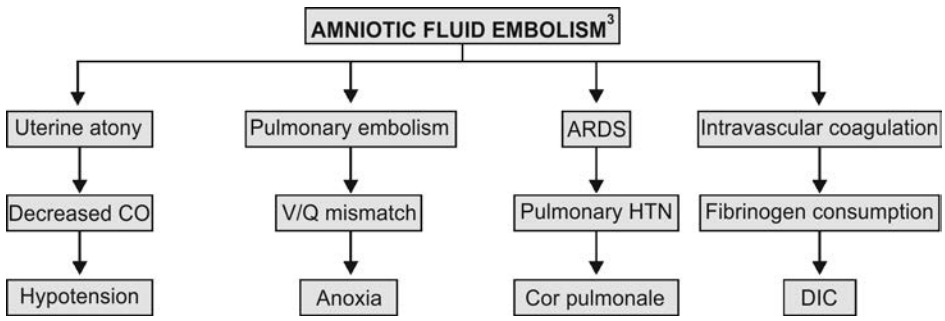
- Noncardiogenic pulmonary edema in 70% patients with bilateral crepts and wheeze
- ARF due to prolonged hypotension
- Multiorgan failure due to hypoperfusion of heart, brain, kidneys
- Exsanguination.

Clinical Features Under GA

- Hypotension : Arrhythmias
- Pulmonary edema : Generalized bleeding

Neonatal Features

- Respiratory acidosis at birth, umbilical cord pH < 7
- Good prognosis generally with no neurological deficit
- Survival rate as high as 70%
- 50% of the surviors have normal CNS outcome.



Long-term Prognosis

- Hemiplegia/permanent CNS deficits due to AF in cerebral blood vessels
- Bilateral Central Retinal Artery Occlusion (CRAO)
- Field defects if ocular occlusion.

Diagnosis

Clinical Tests

- Decreased O_2 saturation in pulse oximetry
- Decreased E_TCO_2 with increased [$PaCO_2$–E_TCO_2] gradient
- ECG: Arrhythmias, MI, asystole
- *Chest X-ray:* Normal/effusion/cardiomegaly/pulmonary edema
- *ABG:* Reduced PO_2 and SO_2, reduced gradient between alveolar and arterial PO_2
- *TEE:* Long axis 4-chamber view:
  - Acute RVF
  - Suprasystemic right sided pressures
  - Bulging of interatrial septum
  - LV dysfunction.
- PA catheter:
  - Increased PCWP
  - Reduced LV stroke work index
  - Reduced SVR
  - Increased PA pressure
  - Increased pulmonary vascular resistance.

Confirmatory Tests

- Pulmonary artery catheter/CVP aspirate:
  - For pulmonary microvascular cytology
  - Only used for confirmation, not for early diagnosis and treatment
  - PAC/CVP blood used:
    - Blood is stained for fetal squames/mucin with:
      - *Nile Blue A*
      - *Papanicola Oil Red O*
      - *Acid mucopolysaccharides.*
    - Fetal squames: Not sensitive/specific (not confirmatory)
    - Fetal mucin: More sensitive indicator
  - Newer technique using monoclonal antibodies:
    - Uses TKH 2 antibodies
    - Measures maternal serum zinc coproporphyrin I
    - This is characteristic of meconium.
- Autopsy:
  - Section from all parts of lungs are examined for:
    - Squames (fetal skin)
    - Bile containing meconium
    - Lanugo
    - Fat from vermix caseosa
    - Mucin from fetal gut.
  - Finding AF elements in lungs is confirmatory.

Differential Diagnosis

- Acid aspiration
- Pulmonary thromboembolism
- Air embolism
- Acute LV failure
- Hemorrhagic/septic shock/anaphylactic shock
- Abruptio placentae/uterine/hepatic rupture
- Acute MI/peripartum cardiomyopathy
- Ecclampsia (if convulsion present)
- Local anesthetic drug reaction
- Total spinal anesthesia
- Cerebrovascular accident.

Management

Objectives

- Maintain oxygenation
- Restore normal BP and cardiac output for vital organ perfusion
- Correct coagulopathy.

Cardiopulmonary Resuscitation: In case of cardiac arrest:

- In left lateral position
- Continuous cricoid pressure during positive pressure ventilation
- Higher level of DC shock (above midpoint of sternum)
- Removal fetal and maternal monitors before shocking
- Reduced tidal volume breaths.

Airway and Breathing

- 100% oxygen
- If unconscious intubate with 0.5–1 mm smaller ETT
- Prevent traumatic intubation
- High FiO_2 to maintain $SpO_2 > 90\%$
- PEEP may help to improve oxygenation.

Circulation

- IV access, prevent bleeding from IV site
- Fluid administration guided by CVP monitoring
- Rapid volume infusion to optimize preload
- After correction of hypotension, fluid therapy at maintenance levels to avoid pulmonary edema

- Inotropes: Dopamine, dobutamine or norepinephrine
- Foleys catheter with urine output > 0.5 ml/kg/hr
- Diuretics only to mobilize excess fluids
- Relieve uterine compression of IVC in left lateral position.

Coagulopathy

- FFP, fresh blood, platelet concentrate and cryoprecipitate
- Cryoprecipitate helpful as it is rich in both fibrinogen and fibronectin.

Uterine Atony

- Oxytocin, methylergometrine, PGF_2 α and manual massage
- Oxytocics may cause increased pulmonary vascular resistance
- If persistent bleeding, uterine exploration for tears and retained placenta.

Prophylatic Antibiotics

Steroids:

- 500 mg (high dose) hydrocortisone IV Q 6H
- May be helpful but not tested.

Cardiopulmonary Bypass

Open pulmonary artery thromboembolectomy in moribund patients with AFE.

Care of Fetus

- Fetal monitoring
- Delivery to be done within 5 mins of maternal cardiac arrest
- This gives best chance of fetal survival at > 24 wks gestational age
- Delivery may increase likelihood of success of CPR in cardiac arrest.

Treatment of Complications

- Hemodialysis for acute renal failure
- Anticonvulsants for seizures
- Industrial surfactant: ***Pluronic F68***, antiprostaglandins.

Prevention

- Prophylactic measures difficult
- Avoid uterine trauma during amniotomy
- Placental incision during Cesarean section avoided
- Avoid trauma at IV catheter insertion site during labor
- Do not strip membranes from cervix in labor
- Avoid intrauterine death
- Care with syntocinon in prolonged labor
- Do early termination with curettage.

Prognosis

- Neurological morbidity rates are high and few patients are without consequences
- If amniotic fluid is meconium-stained, no mother survives without neurodeficits
- Rapid death within 1 hour of onset of symptoms common.

St George's Hospital Recommendations

- Blood-grouping, cross-matching and screening for antibodies in all patients at ANC
- Anticipate those at risk: Previous PPH
- Ergometrine to be avoided, prefer oxytocin
- Control source of bleeding
- IV fluids–RL, hestarch, gelatin, albumin, dextran
- FFP/cryoprecipitate/platelet concentrate
- 2 large bore IV lines
- Monitoring: BP, SPO_2, ECG
- Assess blood loss
- Maintain input/output
- Prompt surgical intervention
- Warming of blood
- Inotropic support
- Consult hematologist, anesthetist.

PULMONARY ASPIRATION[1,3,10,16]

Introduction

- Leading cause of maternal anesthetic deaths
- All pregnant patients to be considered full stomach regardless of NPO status.

Incidence

- One of the leading causes of maternal anesthetic deaths
- Approximately 33% of fatalities due to aspiration
- Mortality following aspiration around 4–5%.

Predisposing Factors[16]

Physiological Changes During Pregnancy

- Slowed GIT transit due to:
  - Increased progesterone and gastrin
  - Reduced motilin
  - Mechanical displacement of pylorus by gravid uterus.
- Increased gastric volume

- Increased gastric acidity due to gastrin
- Decreased gastroesophageal sphincter tone:
  - Decreases from 35 to 24 cm H_2O
  - Increased risk of aspiration if patient has GERD in supine position.
- Gastroesphageal reflux:
  - Twin pregnancy
  - Hydramnios
  - Gross obesity can increase intragastric pressure to 40 cm H_2O.

Combined Risk of Volume and pH:

- 0.4 ml/kg (25 ml) of gastric fluid is threshold
- pH < 2.5 causes aspiration pneumonitis
- 70% patients who were fasted for surgery are at high risk for aspiration.

Loss of Airway Reflexes

- Increased aspiration during failed intubation
- More common during emergency induction of general anesthesia.

Choice of Anesthetic Technique

- Deep sedation > GA > RA
- *Deep sedation:* Obtunded reflexes along with increased nausea due to opioids
- RA may cause aspiration due to:
  - *LA toxicity:* Convulsions, CNS depression
  - Supine hypotension-induced nausea and vomiting
  - *Abdomen muscle weakness:* Reduced ability to cough and clear airway.

Other Factors

- Labor-related nausea
- Pain, fear, ketosis
- Obesity, polyhydramnios, twin pregnancy
- Recent food ingestion
- Drugs:
  - Opioids, benzodiazepines
  - Sedatives
  - Ritodrine, β agonists
  - Magnesium sulfate.

Types of Pulmonary Aspiration

- Chemical pneumonitis/acid aspiration syndrome
  - Materials with pH < 2.5.
- Solid/particulate matter
- Fecal/bacterial contaminated material (rare):
  - Intestinal obstruction
  - Perforation
  - Bowel infarct.

Prevention of Aspiration[16]

Avoid Loss of Consciousness

- Avoid GA when alternatives are present
- Avoid oversedation
- Avoid hypotension of regional anesthesia + aorto-caval compression
- Avoid LA toxicity.

Appropriate GA Techniques

- Assume all second trimester patients are at increased risk of aspiration
- Intubate all second trimester patients receiving GA
- *Rapid sequence induction* with succinylcholine 1.5 mg/kg
- Trained assistant for induction *mandatory*
- Defasciculation with NDMR unnecessary
- Cricoid pressure from before loss of consciousness, to cuff inflation
- Use of cuffed ETT
- Extubate only when fully awake
- Inflate lungs and during inflation, cuff of ETT deflated
- Positive pressure is maintained as ETT is removed.

Appropriate Position

- During induction:
  - Head up position causes increased chances of aspiration if vomiting occurs
  - Head up position also makes laryngoscopy difficult
  - Supine with right hip elevation by 10–15 ideal
  - Support head on small pillow in sniffing position.
- During extubation: Lateral head down position.

ANTIASPIRATION PROPHYLAXIS[1,16]

- *Fasting guidelines:* ***ASA 1999 guidelines for obstetrics***
  - Clear fluids:
    - Uncomplicated labor: 100–200 ml/hr of oral liquids with ice chips
    - Patients with additional risk: Further oral restriction on case-by-case basis
      - Obesity
      - Difficult airway
      - Increased risk of Cesarean section
      - Nonreassuring fetal heart rate pattern on NST.
  - Solids:
    - NPO for 6–8 hrs
    - Avoid solid foods in labouring patients

- Oral antacid therapy:
  - Sodium citrate:
    - 0.3 M nonparticulate sodium citrate
    - 15–30 ml dose to those scheduled for Cesarean section
    - Action lasts for 40 min–1 hr
    - Less pulmonary damage if aspiration occurs
    - Side effects: Metabolic alkalosis, laxative effect, bad taste.
  - Sodium bicarbonate:
    - 8.4% dilute $NaHCO_3$ 20 ml
    - Not very effective
    - Can release about 0.4 L of intragastric gas.
- H_2 antagonists, proton pump inhibitors:
  - H_2 antagonists:
    - 150 mg Ranitine or 300 mg cimetidine PO on night before surgery
    - Dose repeated 1–2 hrs before induction
    - 50 mg ranitidine IV 30 mins before emergency Cesarean section
    - Rapid administration causes cardiovascular depressions and arrhythmias
    - Increases gastric pH
    - *Inhibits cytochrome* $P_{450:}$ Prolongs drug action.
  - Proton pump inhibitors:
    - Omeprazole 20–40 mg PO
    - Lanzoprazole 15–30 mg PO
    - Inhibits proton pump of oxyntic cells
    - Longer duration of action and reduced incidence of adverse reactions.
- Prokinetics:
  - Metaclopramide 10 mg PO/IM/IV:
    - One hour before surgery for oral and IM dose
    - 1–3 mins before induction for IV dose.
  - Increased gastric emptying over 40–60 min period
  - Reduces gastric volume below 25 ml
- Anticholinergic therapy:
  - Glycopyrollate/atropine/scopolamine
  - Reduces volume of gastric secretions and amount of acid secreted
  - May reduce lower esophageal sphincter tone and increase GERD risk
  - Not routinely recommended during pregnancy
  - Reserved for specific medical/anesthetic indications.
- *Nasogastric tube:* Decompress stomach if distended, before extubation
- Routine antiaspiration prophylaxis:
  - Antiaspiration prophylaxis not recommended routinely as:
    - Most patients will not require GA
    - 0.3 M sodium citrate and IV metoclopramide adequate for most GA patients
    - Costly if used on routine basis
    - Routine prophylaxis causes:
      - Increased pH of stomach
      - This increases intragastric bacterial growth
      - If aspiration occurs, aspiration of colonized gastric content occurs.

Clinical Presentation

- Usually present within first 2 hrs of aspiration
- Latency period of 6–8 hrs.

Clinical Staging

Stage I	Profound dyspnea
	Tachycardia
	Bronchospasm with normal X-ray
Stage II	Increasing cyanosis and hypoxemia
	Minor X-ray findings
Stage III	Profound hypoxemia with wide (A–a) DO_2
	Reduced compliance
	Diffuse bilateral infiltrates on X-ray
Stage IV	ARDS

Investigations

- Gastric aspirate analysis
- ABG for PaO_2, alveolar-arterial gradient, hypercarbia
- CVP and urine output for fluid therapy
- Chest X-ray:
  - Soft, mottled densities in peripheral and dependent lung areas
  - Occurs 12–24 hrs after aspiration.
  - ***Snowstorm*** appearance.

Treatment

- Airway:
  - Turn patient to side and head-down position
  - Suction mouth and posterior pharynx
  - Intubate with cuffed ETT
  - Suction ETT several times after intubation.
- Ventilation:
  - Ventilate with 100% O_2 between suctioning

  - Use minimum required FiO_2, as high FiO_2 increases lung injury
  - Positive pressure ventilation markedly reduces mortality.
- Saline/$NaHCO_3$ lavage:
  - Avoid except if aspiration of particulate matter
  - Lavage spreads material and extends lung damage.
- Fiberoptic bronchoscopy:
  - Fiberoptic bronchoscopy through ETT to remove smaller particulate matter
  - Bronchoscopy to remove solid material and re-expand atelectotic segments
  - Send gastric aspirate for culture, pH.
- Others:
  - Steroid therapy not recommended now
  - Antibiotic therapy according to culture and sensitivity reports.
- *Experimental therapies:* Not very successful:
  - Anti-TNFx, interleukin antibodies
  - Prostacycline, PGF2, NSAIDs, surfactant.

HYPERTENSIVE DISORDERS OF PREGNANCY[1,2,3,10,16]

Classification[16]

- Pregnancy-induced HTN:
  - *Hypertension which occurs as a consequence of pregnancy which regresses after delivery*.
    - *Preeclampsia:* HTN with renal involvement
    - *Ecclampsia:* HTN with renal and CNS involvement
    - *HELLP syndrome:* HTN with hepatic and hematological involvement
    - *Gestational HTN:* HTN without proteinuria/pathological edema or any other manifestations of end-organ disease.
- Chronic HTN:
  - *Hypertension which antecedes pregnancy and persists after delivery (< 20 wks gestation and > 3 months postpartum)*
- Pregnancy-aggravated HTN:
  - HTN which is aggravated by pregnancy due to:
    - Superimposed preeclampsia
    - Superimposed ecclampsia.
- Transient HTN:
  - *Hypertension which occurs after mid trimester of pregnancy with mild elevation of BP and regresses after delivery.*

Diagnostic Criteria

Preclampsia

- Gestation:
  - Occurs after 20 weeks of gestation
  - Regresses within 3 months postpartum.
- Hypertension:
  - Sustained elevation of SBP > 140 mm Hg
  - DBP > 110 mm Hg on one occasion
  - DBP > 90 mm Hg on 2 separate occasions measure at least 4 hrs apart.
- Proteinuria:
  - > 300 mg in 24 hrs
  - Two clear catch midstream urine samples 4 hours apart with:
    - +2 or +3 on dipstick assay
    - > 1g/L
- *Edema:* Not essential for diagnosis.

Severe preeclampsia: ACOG 1996 Criteria

- Sustained SBP > 160 mm Hg–180 mm Hg
- Sustained DBP> 110 mm Hg
- Grandmal seizures (ecclampsia)
- Pulmonary edema
- Hepatocellular dysfunction:
  - Raised ALT
  - Raised AST.
- Thrombocytopenia
- Microangiopathic hemolysis
- Oliguria < 500 ml in 24 hrs
- Raised serum creatinine (serum: plasma creatinine > 0.09 mmol/L)
- Proteinuria > 5 gm in 24 hrs or +3 or +4 on dipstick
- Intrauterine growth retardation
- Evidence of end-organ damage:
  - Headache
  - Visual disturbances
  - Epigastric pain
  - Right upper quadrant pain.

S. No.	Features[1,3,16]	Mild	Severe
1	Systolic BP	< 160 mm Hg	> 160 mm Hg
2	Diastolic BP	< 110 mm Hg	> 110 mm Hg
3	Grandmal seizures	Absent	Present
4	Headache	Absent	Present
5	Visual disturbances	Absent	Present
6	Pulmonary edema	Absent	Present

Contd...

Contd...

S. No.	Features[1,3,16]	Mild	Severe
7	Liver enzymes	Normal	Raised
8	Epigastric pain	Absent	Present
9	Right upper quadrant pain	Absent	Present
10	Urine output	> 500 ml/24 hrs	< 500 ml/24 hrs
11	Urine proteins	+1 to +2 dipstick	+3 or +4 dip-stick
12	Thrombocytope-nia	> 1,00,000/ mm^3	< 1,00,000/mm^3
13	Hemolysis	Absent	Present
14	HELLP syndrome	Absent	Present
15	Cyanosis	Absent	Present
16	IUGR	Absent	Present

Risk Factors for Preeclampsia

Hypertensive Disease

- Family history of HTN during pregnancy
- History of chronic HTN
- History of chronic preeclampsia
- History of systolic HTN during early pregnancy
- Increased pulse pressure during 1st trimester.

Associated Diseases

- Chronic kidney disease
- Systemic lupus erythematosus
- Circulating anticardiolipin antibodies
- Protein S deficiency
- Protein C resistance
- APLA syndrome.

Obstetric Factors

- Afro-American race
- Young age or age > 40 years
- Obesity
- No smoking
- Poor socioeconomic status
- Nulliparity
- Multiple gestation, twin pregnancy
- Large for gestational age baby
- Polyhydramnios
- DM, erythroblastocis fetalis
- Molar pregnancy.

Pathophysiology[16]

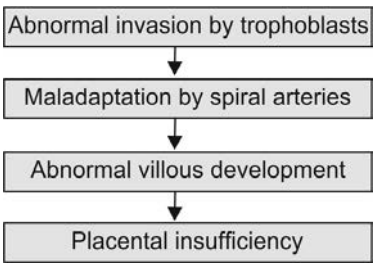
- Genetic factors:
  - Altered expression of angiotensinogen T235
  - Decrease in calcitonin gene-related peptide
- Immunological factors:
  - Reduced TH_1 subset cells (T-helper)

    ↓

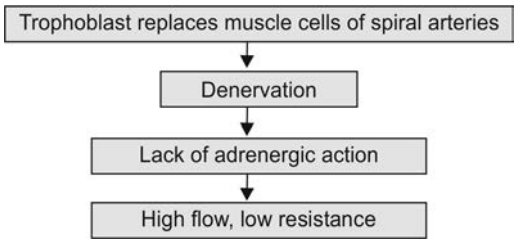
    TH_1–TH_2 imbalance

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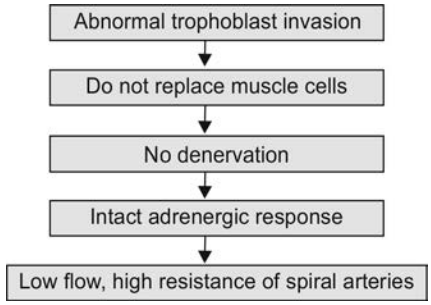
    Increased production of cytokines which favor preeclampsia
  - Digoxin like immune-reactive substances formed
- Metabolic factors:
  - Altered nitric oxide activity
  - Altered xanthine oxidase activity
  - Altered serotonin activity
  - Raised intracellular calcium levels.
- *Calcium metabolism:* Increased intracellular calcium levels
- Free fatty acid metabolism:
  - Increased uptake of FFA by liver
  - This causes hypertriglyceridemia
- Free radical injury:
  - Abnormal trophoblast invasion occurs
  - This causes free radical and lipid eroxidise expression by decidual tissue
  - This causes endothelial injury.
- *Coagulation factors:* Altered vWF: Factor VIII ratio causing hypercoagulability.
- Platelet factors:
  - Reduced 5 HT_1 receptors in preeclampsia
  - Serotonin released from platelets stimulates 5 HT_2 only
  - This cause vasoconstriction and increased platelet aggregation.
- Abnormal placentation:



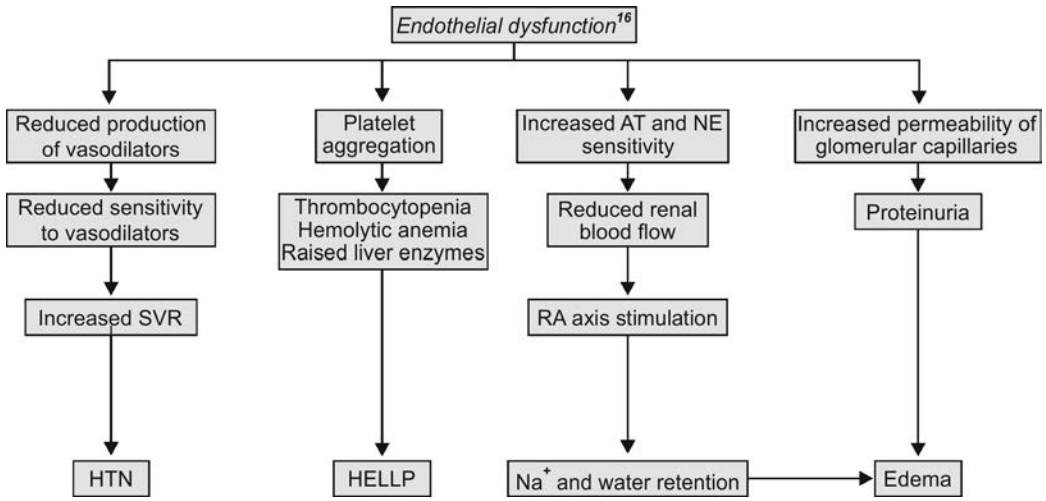
- Vasospasm:[16]
  - Normally:



  - In preeclampsia:



- Endothelial dysfunction:



Pathology[16]

Central Nervous System

- Cerebral edema
- Microinfarcts, punctate hemorrhage, thrombosis
- Hyperreflexia, hyperreactivity
- Headache, visual disturbances, vertigo, convulsions.

Cardiovascular

- Renin angiotensin axis stimulation
- Increased systolic BP
- Increased cardiac output
- Reduced intravascular volume—sensitive to fluid overload
- Reduced colloid osmotic pressure
- Reduced blood volume: Hemoconcentration.

Respiratory

- Edema of upper airways due to:
  - Increased capillary permeability
  - Reduced colloid osmotic pressure
- Mild ventilation perfusion mismatch
- Increased chances of pulmonary edema

Hepatic

- Periportal necrosis
- Subcapsular hemorrhage
- Fibrin deposits in sinusoids
- Impairment in function
- Hepatomegaly, fatty liver, rupture of liver

Coagulation

- Thrombocytopenia
- Consumption, increased platelet activation
- DIC
- Altered factor VIII: vWF levels.

Renals

- Reduced GFR
- Decreased renal flow, vasospasm
- Increased BUN, serum creatinine and uric acid levels
- Acute renal failure, oliguria, azotemia.

Uteroplacental

- Placental modular infarcts
- Reduced intervillous blood flow

- Hyperactive uterus
- Increased sensitivity to oxytocin
- IUGR.

Complications

Maternal

- Convulsions, ecclampsia
- Cerebrovascular accidents
- Cerebral edema
- Intracranial hemorrhage
- Congestive cardiac failure
- Pulmonary edema
- Fatty liver
- Liver rupture
- Acute renal failure
- DIC, post partum hemorrhage, abruption
- Septic shock.

Fetal

- Preterm labor
- IUGR, small for gestational age
- Respiratory distress syndrome
- Meconium aspiration
- Intracranial/intraventricular hemorrhage
- Chorioaminionitis.

Early Predictors

- Rollover test: HTN on turning patient from left lateral to supine position
- Angiotensin II infusion test
- Raised plasma fibronectin
- Raised uric acid levels > 5.9 mg/dl
- Hypocalciuria
- Raised placental peptides:
  - CRH
  - Activin A
  - Inhibin B.

Prevention

- Dietary modification:
  - Calcium supplementation
  - Low-salt diet
  - Fish oil supplements
- Antioxidants: Vitamin C and E
- Low dose aspirin prophylaxis (60–100 mg/day).

Obstetric Management of Severe PE

- Expedited delivery if:
  - Maternal indicators:
    - Severe uncontrolled HTN
    - Persistent CNS symptoms, ecclampsia
    - Pulmonary edema
    - AST or ALT > twice normal range with abdominal tenderness
    - Thrombocytopenia < 1,00,000/mm^3
    - Acute renal failure.
  - Fetal indicators:
    - Fetal distress in NST
    - Amniotic fluid index < 2
    - USG-determined fetal weight < 5th percentile
    - Retrograde umbilical artery end-diastolic flow.
- Conservative management if:
  - Maternal indicators:
    - Controlled HTN
    - AST and ALT increased but no abdominal tenderness
    - Oliguria < 0.5 ml/kg/hr which improves with rest/fluids
    - Proteinuria < 5 gm/day.
  - Fetal indicators:
    - BPP > 6
    - Amniotic Fluid Index > 2
    - USG estimated fetal weight > 5th percentile.

Preoperative Evaluation

Clinical

- Duration and severity of preeclampsia
- Compliance with therapy
- Time and dose of last drug intake: $MgSO_4$/β-blockers
- Assessment of other organ involvement
- Coexistent diseases
- History of last food intake
- Airway assessment
- Intravascular volume status assessment.

Investigations

- Complete blood count: Hemoconcentration
- Peripheral blood smear: schistocytes, Burr cells, Mexican hat cells
- Blood urea, serum creatinine, uric acid
- Liver function tests: AST, ALT, LDH, serum albumin
- Coagulation studies: BT, CT, PT, INR, FDP, D-dimer, TEG
- Urine analysis:
  - Microscopy
  - 24 hrs sample for albuminuria.
- Baseline ultrasound for fetal growth
- NST weekly from the time of diagnosis

Choice of Anesthetic Technique[41]

Labor Analgesia

- Epidural analgesia:
  - Continuous epidural is *technique of choice*
  - 0.125% bupivacaine and 2 μg/ml fentanyl infused at 10 ml/hr at L_2L_3 space.
  - Advantages:
    - Analgesia provided for both 1st and 2nd stage of labor
    - T_{10}–L_1 level required for 1st stage of labor
    - S_2–S_3 level required for 2nd stage of labor
    - Able to produce relaxation if forceps delivery/vacuum
    - Can be converted to surgical anesthesia if Cesarean section
    - Increases intervillous blood flow.
  - Disadvantages:
    - Hypotension, infection, catheter breakage
    - Hematoma if coagulopathy present
    - Time-consuming, onset of action > 20–30 min
    - Nerve injury due to fat needle
    - Increased risk of bloody tap due to fat needle

Other Alternatives for Regional Anesthesia

- Continuous spinal epidural anesthesia
  - Paracervical block
  - Pudendal nerve block with entonox and local perineal infiltration if forceps application or vacuum extraction
  - Patient-controlled analgesia
  - Patient-controlled epidural analgesia.
- General anesthesia:
  - If refusal of RA by patient
  - Semiconscious patient where airway control required
  - Nonreassuring fetal heart rate pattern
  - Hemodynamically unstable mother
  - Contraindication to RA: coagulopathy, abruptio
  - Pulmonary edema, APH, abruptio, ecclampsia.

Anesthesia for Cesarean Section

- Epidural anesthesia:
  - Advantages:
    - Avoidance of GA:
      - No intubation and extubation response
      - Reduced risk of aspiration
      - Reduced risk of failed intubation
      - Awake patient: Easy assessment of CNS status
    - Epidural advantages:
      - Maintains uteroplacental perfusion
      - Improves intervillous blood flow
      - Complete pain relief
      - Good for postoperative analgesia
      - Reduces stress response to surgery and catecholamine levels
      - Stable cardiac output.
  - Disadvantages:
    - No airway control
    - Risk of total spinal/high spinal
    - Risk of hypotension
    - Risk of IV infusion of LA if bloody tap-LAST
    - Hematoma, if associated coagulopathy
    - Slow onset of action > 20–30 mins
    - Time-consuming procedure: not useful if fetal distress
- Spinal anesthesia:
  - Advantages:
    - Causes quick onset of anesthesia
    - Avoids risks associated with GA:
      - No intubation and extubation response
      - Reduced risk of aspiration
      - Reduced risk of failed intubation
      - Awake patient: Easy assessment of CNS status.
  - Disadvantages:
    - Profound hypotension due to:
      - Intravascular volume depletion
      - Concomitant $MgSO_4$ and β-blockers therapy.
- General anesthesia:
  - Advantages:
    - Controlled airway
    - Faster onset < 5 mins
    - Better hemodynamic stability
    - Avoids spinal hematoma.
  - Disadvantages:
    - Difficult airway
    - Increased risk of airway trauma and bleeding
    - Intubation response
    - Interaction between $MgSO_4$ and NDMR: delayed awakening
    - Increased chances of aspiration.

Preoperative Optimization

Goals

- To minimize vasospasm
- Improve intravascular volume

- Improve circulation, especially to uterus, placenta and kidneys
- To correct fluid and electrolyte imbalance
- Seizures prophylaxis
- Prevention and treatment of coagulation abnormalities
- Terminate pregnancy when most feasible.

Optimization

- General:
  - Bed rest
  - Nurse in left lateral position
  - Diuretics if pulmonary edema
  - Keep grouped and cross-matched blood ready
  - Continuous fetal monitoring
  - Secure two IV lines (large bore).
- IV fluids at 60–125 ml/hr of RL/NS to maintain:
  - Urine output > 1 ml/kg/hr
  - CVP around 4–5 mm Hg
  - 5–10 mm Hg of PCWP
  - 10 ml /kg loading dose if RA planned.
- Antihypertensives:
  - Labetalol 10–20 mg IV increments till maximum 1 mg/kg
  - Hydralazine 5–10 mg IV increments till maximum 20 mg
  - Sodium nitroprusside 0.5–5 µg/kg/min IV
  - NTG—0.5–5 µg/kg/min IV or 50–100 µg/min or 400 µg sublingual
  - Methyldopa: 250 mg TID upto maximum 3 g/day PO
  - Nifedipine 10–20 mg sublingual followed by 10 mg TID
  - *Trimethaphan:* 1–4 mg IV bolus followed by 1 mg/ml infusion
  - *Clonidine:* 4 µg/kg PO
  - Prazosin.
- Seizures prophylaxis:
  - $MgSO_4$ IV regimen:
    - 4 gm IV over 20 min
    - This is followed by 1–4 gm/hr infusion.
  - $MgSO_4$ IM regimen:
    - 5 gm IM in both buttocks
    - This is followed by 5 gm IM in alternate buttock Q4H.
  - Diazepam 5–10 mg followed by 30 mg in 500 ml NS titrated to effect.
  - Phenytoin:
    - 10 mg/kg loading dose
    - This is followed by 5 mg/kg at 2 hrs
    - This is followed by 200 mg TID for 5 days
  - Thiopentone 75–100 mg IV for immediate control.
- Antiaspiration prophylaxis:
  - 15 ml of 0.3 M sodium citrate
  - 1 mg/kg IV ranitidine
  - 0.15 mg/kg IV metoclopramide.
- Prevention and treatment of coagulopathy:
  - Maintain platelet count > 1,00,000/mm^3
  - Use whole blood, FFP, platelet concentrates and cryoprecipitate.

Monitoring

- SpO_2, NIBP, ECG
- Foleys catheter, hourly intake – output chart
- Hourly deep tendon reflexes
- Maternal muscle strength and $MgSO_4$ levels
- Uterine contraction monitor – tocodynamometer
- Fetal heart rate monitoring
- Invasive BP if:
  - Refractory severe HTN
  - Rapid acting vasodilator therapy.
- CVP/PA catheter if:
  - Pulmonary edema
  - Refractory oliguria
  - Difficulties in fluid therapy anticipated.
- Capnography and neuromuscular monitoring if GA planned.

Conduct of Epidural Analgesia/Anesthesia

- Antiaspiration prophylaxis
- Large-bore IV cannula (16 G) to give preloading with IV fluids
- O_2 administered by mask
- Attach monitor
- Epidural catheter under strict asepsis in L_2–L_3 or L_3–L_4 levels
- Test dose with 3 ml 0.25% bupivacaine and 1:2,00,000 adrenaline
- If no significant changes in 5 mins:
  - 3 ml 0.25% bupivacaine
  - Followed by 0.125% bupivacaine and 2 µg/ml fentanyl at 10 ml/hr
  - Rate adjusted to maintain analgesic level at T_{10}– L_1 dermatome
  - If additional perineal relaxation required, 1–2% lidocaine 5–10 ml given
  - 0.5% bupivacaine in incremental doses till T_4 level for Cesarean section
  - Treat hypotension with:
    - IV ephedrine 2–5–10 mg
    - Left uterine displacement
    - Additional IV fluids.

Conduct of General Anesthesia

Preoperative Preparation

- 2 large-bore IV cannula
- IV fluids at 60–125 ml/hr NS/RL
- Informed consent taken
- Antiaspiration prophylaxis
- Antihypertensive therapy
- Seizure prophylaxis
- Keep adequate blood ready.

Anesthestic Considerations

- Difficult airway due to edema
- Exaggerated hypertensive response to intubation and extubation
- Increased risk of aspiration
- Drug interaction with $MgSO_4$:
  - Increased sensitivity to NDMR
  - Increased duration of action of NDMR
  - Reduced BP: Profound hypotension with RA
  - Hypotension refractory to therapy
  - Platelet aggregation: Increased bleeding
  - Neonatal hyporeflexia and respiratory depression
  - Reduced beat-to-beat variability in FHR
  - Increased Postpartum Hemorrhage (PPH) due to:
    - Tocolysis
    - Increased uterine blood flow.

OT Preparation

- Emergency drugs
- Facemask (transparent), airways
- ETT–7, 6.5, 6 and 5.5 size
- Different laryngoscopy blade sizes, gum elastic bougie
- Anesthetic drugs
- Skilled assistant for rapid sequence induction
- Working suction kept ready.

Induction

- Preoxygenation with 100% O_2 for 5 mins
- Thiopentone (2.5%) 4 mg/kg IV
- Apply cricoid pressure
- Succinylcholine IV 1 mg/kg
- Intubate with small-sized ETT
- Check bilateral air entry
- Inflate ETT cuff and release cricoid pressure
- Reduce intubation response with:
  - IV $MgSO_4$, labetalol, esmolol
  - IV NTG, SNP, lidocaine
- If dyspnea/stridor/dysphonia, awake intubation/tracheostomy preferred.

Maintenance

- O_2 + N_2O (50%) + 0.5 MAC isoflurane
- 2/3rd MAC of volatile anesthetics used
- Give titrated small doses of vecuronium/atracurium
- Neuromuscular monitoring mandatory
- IV fentanyl 2 µg/kg after delivery of fetus
- Continue $MgSO_4$ intraoperatively
- Judicious IV fluids, prevent overloading
- If uterine atony unresponsive to oxygtocin, 15 methyl PGF_2 α is given
- Otherwise avoid ergot alkaloids due to hypertensive crisis.

Extubation

- Fully awake, fully reversed
- IV xylocard/esmolol to decrease extubation response.

Postoperative

Monitors

- Urine output and intake output chart hourly till postpartum diuresis occurs
- Monitor for CNS status, convulsions
- Monitor for neuromuscular weakness
- Monitor for 12–24 hrs.

Analgesia

- COX-2 inhibitors
- NSAIDS
- IV/IM/neuraxial opioids /PCA/PCEA
- Epidural/CSE.

Management

- Fluids at < 80 ml/hr
- $MgSO_4$ continued for 24 hrs after last seizure episode
- Change from IV to oral antihypertensives
- May require antihypertensives for 3 months
- Advise about risk of preeclampsia in later pregnancies.

ECCLAMPSIA[1,2,3,10,16]

Introduction

Occurrence of seizures in preeclampsia patient with no other known cause of seizures.

Clinical Features

- Can occur before, during or after labor
- Preceded by:
  - Visual disturbances, headache, vertigo, vomiting
  - Epigastric pain
  - Sudden onset severe edema with oliguria
  - Hyperreflexia with clonus
- Onset of twitching around mouth followed by GTCS of variable duration
- Associated with:
  - Respiratory arrest and cyanosis during convulsions
  - Postictal hemiparesis due to intracranial hemorrhage.

Complications

- Cerebral edema
- Raised ICP
- Status epilepticus
- Cerebral hemorrhage
- Pulmonary edema due to:
  - Aspiration
  - Cardiac failure.
- Acute renal failure
- Liver rupture
- Placental abruption
- Respiratory failure
- Death.

Differential Diagnosis

- Epilepsy
- Meningitis
- Encephalitis
- Rupture of aneurysm
- Tumors
- Cysticercosis.

Treatment

Symptomatic Therapy

- Nurse in ecclampsia unit
- Left lateral position
- Reduce light and sound stimulation
- Suction airway, jaw thrust and head tilt
- Supplemental O_2/ETT with IPPV
- Keep mouth open with soft mouth gag to prevent tongue bite
- Foley's catheter with intake output monitor
- CVP, PA catheter and IBP placement
- Secure two large-bore IV lines
- IV fluids at 60–125 ml/hr (RL/NS).

Definitive Therapy

Only definitive therapy is immediate Cesarean section under GA.

Antihypertensive Therapy

- Labetalol 10–20 mg IV increments till maximum 1 mg/kg
- Hydralazine 5–10 mg IV increments till maximum 20 mg
- Sodium nitroprusside 0.5–5 µg/kg/min IV
- NTG—0.5–5 µg/kg/min IV or 50–100 µg/min
- Trimethaphan: 1–4 mg IV bolus followed by 1 mg/ml infusion.

Anticonvulsant Therapy

- ***Pritchard's*** regimen:
  - Loading dose 4 gms $MgSO_4$ IV over 5 mins
  - Alternatively, loading dose 5 gm $MgSO_4$ IM in each buttock (10 ml of 50%)
  - Followed by 5 gm IM alternate buttock Q4H for 24 hrs postpartum.
- *University of Tenessee regimen:* 2–6 gm $MgSO_4$ (20%) IV over 10 min followed by 1–3 gm/hr
- ***Zuspan*** regimen: 4 gm $MgSO_4$ IV followed by 1–2 gm/hr infusion
- ***Sibai*** regimen: 6 gm $MgSO_4$ IV followed by 2 gm/hr infusion.
- ***Lytic cocktail*** regimen/***Menon*** regimen:
  - 25 mg chlorpromazine + 100 mg pethidine IM
  - 50 mg chlorpromazine + 25 mg promethazine IM at 4 hr intervals upto 24 hrs
  - 100 mg pethidine in 500 ml 10% dextrose at 20–30 drops per minute
- ***Lean*** regimen:
  - Diazepam 4 mg IV
  - Followed by 40 mg in 500 ml 5% Dextrose at 30 drops/minute
- *Others:* Thiopentone, phenytoin.

Complications

- *Cerebral edema:* Mannitol/hypertonic saline, hyperventilation
- *Pulmonary edema:* Diuretics, IPPV
- *Acute renal failure:* Diuretics, RRT
- *Liver rupture:* IV fluids, surgical repair
- *DIC:* FFP, cryoprecipitate

HELLP SYNDROME[1,2,3,10,16]

Introduction

- First suggested by ***Weinstein*** in 1982
- Consists of:
  - Hemolysis
  - Elevated liver enzymes
  - Low platelet count in women with ecclampsia or preeclampsia.

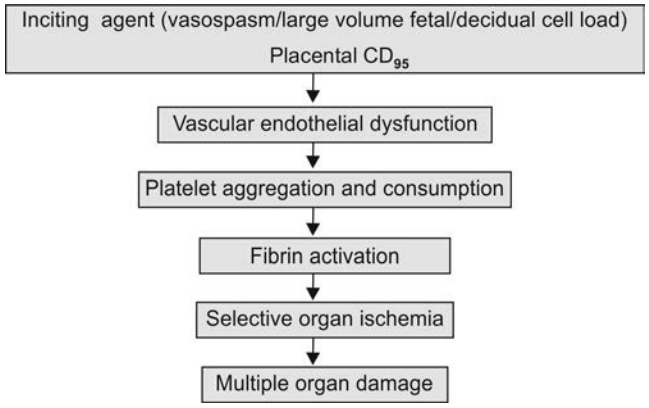
Incidence

4–12% of preeclampsia.

Diagnostic Criteria

- Hemolyis:
  - Bilirubin > 1.2 mg/dl
  - Abnormal peripheral smear.
- Elevated liver enzymes:
  - SGOT > 70 IU/L
  - LDH > 600 IU/L.
- Low platelets (< 1,00,000/mm^3).

Pathophysiology



Clinical Features

- Occurs before 36 weeks of gestation
- Headache, nausea and vomiting, visual disturbances
- Epigastric/right upper quadrant pain
- Shoulder pain on deep breathing: ***Kehr's sign***
- Bleeding:
  - Gut hemorrhage
  - Retinal hemorrhage
- Edema, mild proteinuria
- Mild hypertension
- Acute renal failure with oliguria.

Risk Factors Increasing Morbidity

Clinical Factors

- Epigastric pain
- Nausea, vomiting
- Ecclampsia
- Severe HTN
- Abruption.

Laboratory Factors

- Platelet count < 50,000/mm^3
- LDH > 1400 IU/L
- AST > 150 IU/L
- ALT > 100 IU/L
- Uric acid > 7.8 mg/dL
- CPK > 200 IU/L
- Creatinine > 1 mg/dL.

Classification

- ***Mississippi*** classification: Based on platelet count
  - *Class I:* Platelet count < 50,000/mm^3
  - *Class II:* Platelet count 50,000–1,00,000/mm^3
  - *Class III:*
    - Platelet count 1,00,000 – 1,50,000/mm^3
    - Hemolyis + hepatic dysfunction
    - LDH > 600 IU/L, AST >70 IU/L, ALT > 40 IU/L.
- ***Tennessee*** classification:
  - Complete HELLP:
    - Platelet count < 1,00,000/mm^3
    - LDH > 600 IU/L
    - AST > 70 IU/L
    - Hemolysis.
  - Incomplete HELLP: Only 1 or 2 of the above
- ***Martins*** classification:
  - *Class I:* Platelet count < 50,000/mm^3
  - *Class II:* Platelet count 50000–1,00,000/mm^3
  - Class III: Platelet count > 1,00,000/mm^3.

Management

Early diagnosis important.

Symptomatic Therapy

- Optimize fluid therapy
- *Optimize blood therapy:* Platelets if PC < 50,000 with severe preeclampsia
- IV fluids with large-bore cannula
- Nurse in left lateral position
- O_2 supplementation/ETT with IPPV
- Soft mouth gag to prevent tongue bite
- Foley's catheter with intake-output monitoring.

Antihypertensive Therapy

To keep BP< 160/110 mm Hg

- Labetalol 10–20 mg IV increments till maximum 1 mg/kg
- Hydralazine 5–10 mg IV increments till maximum 20 mg
- Sodium nitroprusside 0.5–5 µg/kg/min IV
- NTG- 0.5–5 µg/kg/min IV or 50–100 µg/min
- *Trimethaphan:* 1–4 mg IV bolus followed by 1 mg/ml infusion.

Anticonvulsant Therapy

As in ecclampsia.

Definitive Therapy

- Only definitive therapy is immediate delivery via Cesarean section under GA
- If immature fetus, give glucocorticoids and delivery within 48 hrs
- Plasmapheresis done for refractory cases.

Dexamethasone Rescue Therapy

- Antipartum therapy:
  - Indications:
    - If platelet count < 1,00,000/mm^3 or
    - Platelet count between 1–1.5 lac/mm^3 with:
    - Severe HTN
      - Ecclampsia
      - Epigastric pain
      - Fulminant disease.
  - 10 mg IV Q12H
- Postpartum therapy: 10 mg IV Q12H followed by 5 mg IV Q12H for 2 days.

Complications

- Liver hematoma and infarction, liver failure
- Pulmonary edema, embolism
- DIC, abruption, GI bleed, retinal detachment
- Acute renal failure, ARDS, sepsis, stroke.

Anesthetic Implications

- Impaired drug metabolism due to hepatic involvement
- Hepatic rupture possible
- Invasive hemodynamic monitoring
- Large-bore IV cannula with readily available blood
- Epidural is safe if:
  - Platelet count > 1,00,000 cells/mm^3
  - Normal bleeding time
  - Normal coagulation profile.
- GA preferred if:
  - RA unsafe
  - Abruption, coagulopathy
  - Hemodynamically unstable
  - Non reassuring FHR.
- Avoid IM injections.

Investigations

- Peripheral smear:
  - Schistocytes
  - Burr cells
  - Spherocytes, Mexican hat cells.
- Raised LDH and haptoglobin: Early markers
- Raised indirect bilirubin, reduced Hb
- FDP and antithrombin III activity if platelet count < 50,000 cells/mm^3
- Raised AST, ALT levels.

Differential Diagnosis

- Fatty liver of pregnancy
- Hepatitis
- Cholecystitis
- Appendicitis
- Hemolytic uremic syndrome (HUS)
- Lupus flare.

ANTEPARTUM HEMORRHAGE[1,2,3,16]

Introduction

- Hemorrhage which occurs after 24 wks gestational age (GA) and before delivery
- Obstetric hemorrhage defined a blood loss > 500 ml after completion of 3rd stage of labour
- Massive obstetric hemorrhage when:
  - Blood loss > 1500 ml
  - Reduction in Hb > 4 g%
  - Acute transfusion requirement > 4 units.

Etiology

- Abnormal placentation:
  - *Placenta previa:* Vasa previa
  - *Placenta accreta:* Hydatiform mole
  - *Abruption:* Circumvallate placenta.
- Uterine atony:
  - *Overdistended uterus:* Halogenated anesthetics
  - *Polyhydramnios:* Previous uterine atony
  - Multiple gestation
- Trauma during labor:
  - Uterine rupture
  - Cesarean section

  - Complicated vaginal delivery
  - Hysterectomy
- Coagulopathies:
  - Abruption
  - Massive transfusion
  - Amniotic fluid embolism
  - Congenital/acquired coagulopathy
  - Severe preeclampsia, HELLP syndrome: Sepsis
  - Retention of dead fetus.
- Others:
  - Vaginal/vulvar varicosities
  - Ectopic pregnancy
  - Cervical polyp/malignancy.

Placenta Previa

Introduction

Abnormal implantation of placenta in lower uterine segment.

Risk Factors

- Previous history of Cesarean section
- Advanced age
- Prior uterine scar
- Multiparity
- Prior placenta previa.

Types

- Complete: Completely covers cervical os
- Marginal: Lies close to, but not covering cervical os
- Partial: Covers part, but not whole os.

Classification

- *Placenta accreta:* Placenta attached onto myometrium
- *Placenta increta:* Placenta attached into myometrium
- Placenta percreta:
  - Penetration through full thickness of myometrium
  - Implanted on bowel/bladder/pelvic organs.

Abruptio Placenta

Introduction

- Separation of normally implanted placenta from decidua basalis before delivery of fetus
- Occurs anytime between 20 wks and term.

Risk Factors

- Advanced age
- High parity
- Multiple gestation
- Pregnancy-induced hypertension
- Uterine abnormality
- Premature rupture of membrane
- Tobacco/cocaine use.

Types

- Complete
- Partial
- Concealed
- Revealed.

Uterine Rupture

Risk Factors

- History of previous scar
- Weak myometrium due to multiple gestation
- Polyhydramnios
- Trauma
- History of prolonged labor under influence of oxytocin.

Presentation of APH

- Profuse vaginal bleeding
- Hypovolemic shock with no bleeding if concealed hemorrhage
- Abnormal uterine tone
- Pain and uterine tenderness in abruptio
- Painless bleeding in placenta previa
- Retroplacental hematoma in USG

Stage[16]	Blood loss	% Loss	Signs	Degree of shock
I	< 1000 ml	10–15%	Normal BP	Compensated
			Palpitation, tachycardia, dizziness	
II	1000–1500 ml	15–25%	Orthostatic hypotension	Mild
			Pulse pressure < 30 mm Hg	
			Weakness, tachycardia, sweating	
III	1500–2000 ml	25–35%	Hypotension	Moderate
			Oliguria, pallor, restlessness	

Contd...

Contd...

Stage[16]	Blood loss	% Loss	Signs	Degree of shock
			Cold clammy skin, tachypnea	
IV	> 2000 ml	> 35%	Unrecordable BP	Severe
			Respiratory/ cardiac arrest	
			Anuria, altered sensorium	

Anesthetic Considerations

- Profuse bleeding:
  - Preop hypotension and fetal distress
  - Requirement of large amount of blood
  - Gross underestimation of blood loss if concealed hemorrhage
  - Inadequate preoperative preparation due to emergency surgery
  - Increased chances of postpartum hemorrhage.
- Possibility of extended surgery for:
  - Emergency hysterectomy
  - Uterine/internal iliac artery ligation.

OT Preparation

- Small-sized ETT (upto 6 size)
- Laryngoscope blade: Polio blade with short handle
- Airways, facemask, bougie, LMA, cricothyrotomy set
- Anesthetic drugs preloaded, emergency drugs, atropine, adrenaline
- Suction apparatus
- CVP and IBP transducer systems
- Fluid warmer, rapid fluid infusion devices, hand-inflated pressure bags
- Adequate amount of crystalloids and colloids
- Cross matched blood (atleast 2 units).

Patient Preparation

- Two large bore 14–16 G IV access
- Oxygen via face mask 6–8 L/min
- Arrange for fluids and cross matched blood ASAP
- CVP and IBP access for monitoring and fluid transfusion, Foley's catheter
- Correct hypovolemia:
  - Crystalloid 2 liters RL
  - Colloids upto 1.5 liters in 24 hrs
  - Cross-matched blood if Hb < 7 g%
  - O –ve blood if cross-matched blood unavailable.
- Correct coagulopathy:
  - FFP/cryoprecipitate
  - Platelet concentrate
  - Factor VII 60–120 µg/kg if no DIC.
- Coagulation profile with TEG, Hb%, HCT, cross-matching
- Emergency coagulation profile with ***Clot Coagulation Test***:
  - 5 ml blood drawn in clean glass tube
  - Suspect coagulation factor deficiency if:
    - No clot within 6 mins
    - Clot lysis begins within 1 hr
  - Suspect hypofibrinogenemia if no clot forms in 30 mins.
- Anti-aspiration prophylaxis:
  - 0.3 M sodium citrate 30 ml
  - IV ranitidine 1 mg/kg
  - IV metoclopramide 0.15 mg/kg.
- Stop $MgSO_4$and $CaCl_2$ therapy
- ***Double setup examination*** done with full preparation for Cesarean section if placenta previa suspected.

Choice of Anesthetic Technique

- Regional anesthesia preferred if:
  - Mild-to-moderate abruption
  - Minimal bleeding
  - No hypovolemia
  - No coagulopathy
  - No uteroplacental insufficiency
- Saddle block for dilation and curettage
- General anesthesia preferred if:
  - Uncontrolled hemorrhage
  - Coagulopathy
  - Fetal distress
  - Patient refusal.

Induction

- Ketamine 1–2 mg/kg, etomidate 0.3 mg/kg: *Agents of choice*
- Thiopentone and propofol less preferred as cardiovascular collapse possible
- *Rapid sequence induction* with cricoid pressure.

Maintenance

- Balanced anesthesia with volatile agents if controlled bleeding
- TIVA with IV infusion of ketamine if uncontrolled
- Initially 100% O_2 followed by N_2O + 0.5–1% Iso/enflurane depending on maternal tolerance.

- NDMR:
  - Pancuronium used if shock
  - Atracurium if acute renal failure
  - Vecuronium for uncomplicated cases.
- IV fentanyl 5–10 µg/kg
- IV NTG 50–100 µg bolus or volatile anesthetic used if uterine relaxation required during dilatation and curettage.

Monitors

- *SpO_2;* IBP, CVP
- *ECG;* Temperature
- *NIBP;* Urine output
- *E_TCO_2;* NM monitoring.

Control of Bleeding

Uterotonic Therapy

- Oxytocin 20–40 IU in 1000 ml RL over 4–8 hrs
- Methergine 0.2 mg IM Q2–4 H as required
- Carboprost 0.25 mg IM Q 15–60 mins as required
- Misoprostolol 800–1000 mg PO/PR/PV Q2H
- Dinoprostone 20 mg PO Q2H
- Intramyometrial PGE2 0.5 mg or PGF2 α 0.2 mg.

Medical Management

- FFP: RBC = 1:1
- Platelets transfused to maintain counts > 50,000/mm^3
- *Novoseven* 60–120 µg/kg IV
- Fibrinogen concentrates if fibrinogen < 100 mg%
- Prothrombin concentrates: Needs further clinical trials
- Tranexemic acid:
  - 1 gm slow IV bolus over 5 min
  - Repeated once within 30–60 mins if bleeding continues
- Aprotimin/methotrexate
- Uterine massage.

Surgical Management

- Uterine tamponade with ***Sengstaken-Blackmore esophageal catheter***/bimanual compression/packing
- Compression sutures ***(B-Lynch***)
- Selective radiological embolization with:
  - Gelatin sponge
  - Polyurethane foam
  - Polyvinyl methyl alcohol particle.
- Arterial ligation:
  - U/L or B/L uterine artery
  - U/L internal iliac artery
  - U/L or B/L ovarian artery.
- Emergency hysterectomy
- Exploration and repair if trauma/retained products.

Extubation

- Fully conscious, awake, reversed
- Hemodynamically stable with controlled bleeding
- Extubated in lateral position.

Complications

- Hemorrhagic shock
- Postpartum hemorrhage
- Coagulopathy, DIC
- ***Couvelaire uterus:*** Extravasated blood dissects between myometrial fibers
- ***Sheehan's syndrome***: Anterior pituitary necrosis
- Intrauterine death of fetus
- Acute renal failure.

POSTPARTUM HEMORRHAGE[1,3,16]

Introduction

- Blood loss > 500 ml after delivery causing:
  - Symptoms of hypovolemia
  - 10% reduction in hematocrit after delivery
  - Requirement of blood product transfusion.

Etiology

Primary Causes

- Uterine atony
- Uterine inversion
- Genital laceration
- Retained products
- Abnormal placentation
- Coagulopathies
- Amniotic fluid embolism.

Secondary Causes

- Retained products
- Subinvolution
- Uterine infection
- Anticoagulation.

Risk Factors

- Previous history of PPH
- Advanced age — Prolonged use of oxytocin
- Multiparity — Prolonged labor

- Multiple gestation
- Polyhydramnios
- Placental abruption
- Chorioamminotis
- IUD of fetus
- Fibroids.

- Cesarean section
- General anesthesia
- Instrumental delivery
- Anticoagulation

Types

- *Primary PPH:* Occurring within 1st 24 hrs of delivery
- *Secondary PPH:* Occurring between 24 hrs and 6 wks of delivery.

Prevention

- Active management of Third Stage Labor (AMTSL)
- Administration of oxytocin within 1 min of birth of baby
- Controlled cord traction by skilled assistant
- Uterine massage after delivery of placenta
- Misoprostol 600 µg PO/SL if oxytocin unavailable.

Clinical Features

Table of shock in APH.

Management

Uterotonic Therapy

- Oxytocin 20–40 IU in 1000 ml RL over 4–8 hrs
- Methergine 0.2 mg IM Q2–4H as required
- Carboprost 0.25 mg IM Q 15–60 mins as required
- Misoprostolol 800–1000 mg PO/PR/PV Q2H
- Dinoprostone 20 mg PO Q2H
- Intra-myometrial PGE2 0.5 mg or PGF2α 0.2 mg

Medical Management

- FFP: RBC = 1 : 1
- Platelets transfused to maintain counts > 50,000/mm^3
- *Novoseven* 60–120 µg/kg IV
- Fibrinogen concentrates if fibrinogen < 100 mg%
- Prothrombin concentrates: Needs further clinical trials
- Tranexemic acid:
  - 1 gm slow IV bolus over 5 min
  - Repeated once within 30–60 mins if bleeding continues
- Aprotimin/methotrexate
- Uterine massage.

Surgical Management

- Uterine tamponade with ***Sengstaken-Blackmore esophageal catheter***/bimanual compression/packing
- Compression sutures ***(B-Lynch)***
- Selective radiological embolization with:
  - Gelatin sponge
  - Polyurethane foam
  - Polyvinyl methyl alcohol particle.
- Arterial ligation:
  - U/L or B/L uterine artery
  - U/L internal iliac artery
  - U/L or B/L ovarian artery.
- Emergency hysterectomy
- Exploration and repair if trauma/retained products.

Multidisciplinary Approach

- Obstetrician
- Anaesthetist
- Blood bank
- Hematologist
- ICU physician.

Special Situations

- $MgSO_4$ therapy: stop $MgSO_4$ infusion and IV Ca gluconate given
- Uterine inversion:
  - Manual replacement
  - Hydrostatic pressure to revert uterus.
- Placental adherence:
  - Hysterectomy
  - Embolization if massive hemorrhage.

Complications

- DIC, TRALI, ARDS, MODS
- Acute tubular necrosis, ARF
- Venous thromboembolism
- ***Sheehan's syndrome***
- Surgical complications:
  - Urinary tract/bowel/vascular injury
  - Genitourinary fistula, genitointestinal fistula
  - Uterine synechiae: ***Asherman's syndrome***
  - Pelvic hematoma and sepsis.

POSTPARTUM STERILIZATION[1,2,16]

Types

Postpartum Sterilization

- Done at the time of child birth
- Advantages.
  - Fallopian tubes easily accessible
  - Simpler surgical procedure
  - Reduced incidence of bowel vessel injury

- Reduced incidence of bowel laceration
- Eliminates use for rehospitalization
- Reduced length of hospital stay.

Interval Sterilization

- Done when complete involution of uterus occurs: 6 months after delivery
- Done laparoscopically usually
- *Indications:* Complicated pregnancy/associated medical conditions.

Methods

- Tubal Ligation:
  - ***Madlener's technique***
  - ***Kroener's technique***
  - ***Pomeroy's technique***
  - ***Uchida's technique.***
- Laparoscopic coagulation.

Anesthetic Techniques

Local Anesthesia with IV Sedation

- Rapid onset and recovery
- Ease of administration
- No nausea and vomiting
- Reduced postoperative complications
- Done for tubal ligation.

Regional Anesthesia

- Spinal/epidural anesthesia
- Sensory level of T_4 required
- Sometimes if no excessive stimulation, T_{10} level may be adequate
- 6 mg hyperbaric tetracaine, 75 mg 5% lidocaine in 10% dextrose for SAB
- 1 mg/kg preservative-free pethidine in 10% dextrose for SAB
- 10–15 ml 0.5% bupivacaine for epidural.

General Anesthesia with ETT

- For immediate postpartum laparoscopy
- Rapid sequence induction with succinylcholine and cricoid pressure
- Short-acting mivacurium for subsequent doses
- Trendelenburg's position
- Prevent light anesthesia during coagulation of fallopian tube
- Postoperative analgesia:
  - Skin infiltration with local anesthetic
  - Per rectal diclofenac 1–2 mg/kg.
- Bradycardia common due to vagal stimulation:
  - Glycopyrollate administered preoperatively
  - Atropine kept ready.

General Anesthesia with LMA

- For internal laparoscopic sterilization
- Antiaspiration prophylaxis important.

ECTOPIC PREGNANCY[1,2,16]

Introduction

Pregnancy in which fertilized ovum is implanted and develops outside uterine cavity.

Sites of Ectopic Pregnancy

- Tubal pregnancy (most common—95%):
  - Ampulla (55%)
  - Infundibulum (18%)
  - Isthmus (25%)
  - Intestitial (20%).
- Ovarian
- Abdominal:
  - Intraperitoneal
  - Extraperitoneal (broad ligament).
- Uterine:
  - Cervical
  - Angular
  - Cornual.

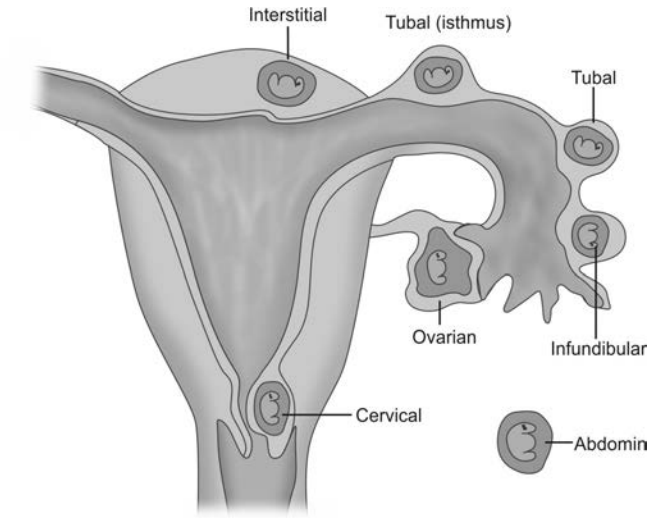


Fig 3.7: Sites of ectopic pregnancy[16]

Types

Acute Ectopic

- Associated with tubal rupture/abortion
- Massive intraperitoneal hemorrhage/peritubal hematocele

- Classical triad of amenorrhea, pervaginal bleeding, abdominal pain
- Pelvic hematocele/broad ligament hematoma
- Nausea, vomiting, syncope, features of shock, tender abdomen.

Subacute/Chronic Ectopic

- *Most common type*
- Associated with pelvic hematocele
- Insidious onset, history of previous abdominal pain, and scanty per vaginal bleeds
- Dysuria, frequency due to urinary bladder irritation, rectal tenesmus, fever.

Risk Factors

- History of PID/tubal ligation/previous ectopic pregnancy
- Contraception failure
- Tubal reconstruction
- History of infertility
- Prior history of IUCD use
- Previous induced abortion.

Diagnosis

- Amenorrhea with abdominal distension
- Empty uterus with gestational sac present on transvaginal ultrasound
- Endometrial thickness < 8 mm, blood progesterone < 17.5 ng/ml
- Laparoscopy/laparotomy.

Preoperative Assessment and Preparation

- Assess volume status and airway
- Hb, TC, DC, cross matching, coagulation test
- 2 large bore 14–16 G IV cannula
- Crystalloid/colloid/blood
- Arrange for blood, auto transfusion and cell salvage
- Midazolam 0.05–0.15 mg/kg IV for anxiolysis
- Antiaspiration prophylaxis.

Choice of Anesthesia

- GA with RSI and IPPV is *method of choice*
- Laparoscopic salpingectomy/salpingotomy/injection of cytotoxic drugs preferred.

Anesthetic Considerations

- Profuse bleeding:
  - Preoperative hypotension and fetal distress
  - Requirement of large amount of blood
  - Gross underestimation of blood loss if concealed hemorrhage
  - Inadequate preoperative preparation due to emergency surgery
  - Increased chances of post partum hemorrhage
- Possibility of extended surgery.

Anesthetic Technique

Induction

- 3 minutes preoxygenation
- Left lateral tilt maintained
- Ketamine/etomidate *agents of choice*
- *Rapid sequence induction* with succinylcholine and cricoid pressure
- Fentanyl 1–2 µg/kg
- Induce after patient is draped as sudden hypotension possible on induction.

Maintenance

- 0.5–1 MAC volatile anesthetics depending on hemodynamics
- Avoid N_2O if laparoscopy planned
- Ketamine infusion in unstable patients
- Short acting opioids with titrated NDMRs
- Blood replacement as per requirement
- Patients respond well after clamping of bleeding vessel
- Auto transfusion and cell salvage beneficial.

Extubation

- Fully reversed and awake
- Postoperative analgesia and PONV prophylaxis.

ANESTHESIA FOR FETAL SURGERY[1,3,16]

Introduction

- Advanced diagnostic modalities, like amniocentesis, fetoscopy, dynamic image USG, fetal MRI, percutaneous fetal sampling have permitted early treatment of fetal malformations before they cause fetal demise
- ***Fetal sentinence*** refers to the capacity of the fetus to experience painful/unpleasant sensation.

Advantages

- *In utero* environment supports rapid postoperative healing
- Umbilical circulation meets nutritional and respiratory needs without outside assistance.

Prerequisites

- Fetal surgery should be performed only for:
  - Fetal anomalies which progress *in utero*

- Cause harm to fetus before fetal lungs are mature
- Anomalies for which surgical success postnatally is less likely.

Indications[3]

- Absolute indications:
  - Repair of meningomyelocele
  - Ablation of anastomotic vessels in acardiac twins
  - Insertion of pleura amniotic shunt for fetal pleural effusion
  - Resection of malformed pulmonary tissue:
    - Congenital cystic adenomatoid malformation
    - Extralobar pulmonary sequestration.
  - Laser ablation of anastomotic vessels in Twin-Twin Transfusion Syndrome (TTS)
  - Twin Reverse Arterial Perfusion (TRAP)
  - Vesicoamniotic shunting for urinary tract obstruction
  - Removal of sacrococcygeal teratoma.
- Experimental indications:
  - Fetal tracheal occlusion for CDH
  - Treatment of amniotic band syndrome
  - Treatment of acqueductal stenosis
  - Treatment of cleft lip or palate
  - Treatment of congenital heart disease
  - Treatment of fetal hydronephrosis
  - Treatment of gastrochisis.
- Twin-Twin Transfusion Syndrome (TTS)
  - Unbalanced intertwin transfusion between monochorionic twins
  - Leads to a recipient who develops polyhydramnios and hydrops
  - The donor develops oligohydramnios, IUGR, death.
- Twin Reverse Arterial Perfusion (TRAP)
  - One twin is a acardiac/anencephalic and non viable
  - Nonviable twin has vascular anastomosis to a normal twin
  - Normal twin develops heart failure because of providing cardiac output to two fetuses.

Percutaneous Interventions

- Percutaneous umbilical vein sampling for direct fetal transfusion
- Aspiration of:
  - Thoracic cysts
  - Pleural effusions
  - Ascites
- Biopsy of fetal skin/muscle/liver.

Timing of Surgery

Between 24–29 weeks of gestation.

Anesthetic Considerations

- Avoid maternal hypotension as it causes fetal acidosis and asphyxia
- Avoid fetal hypoxia:
  - Avoid maternal hypoxia (hyperoxia is not a problem)
  - Avoid maternal hyperventilation:
    - Alkalosis shifts oxyhemoglobin dissociation curve to left
    - Reduces delivery to fetus.
  - Hypoventilation as it causes fetal acidosis.
- Reduce material anxiety: Can be due to:
  - Concerns about fetal safety
  - Fear of pain and complication due to procedure.
- Analgesic considerations:
  - Pain may cause uterine contraction which may lead to preterm labor
  - Pain in fetus due to fetal sentinence to be avoided
- Risk of preterm labour:
  - Uterine stimulation during fetal interventions may cause uterine contraction
  - This can lead to preterm labor
  - Uterine stimulation reduces uterine blood flow and causes placental separation
  - This is more likely when gestational age > 27 weeks as uterus is more irritable
  - Less likely when gestational age < 20 weeks.

Anesthetic Techniques[3]

- Maternal sedation and local anesthesia:
  - For percutaneous needle aspiration/catheter insertions
  - Local anesthesia with 0.5 ml of 1% lidocaine as field block
  - *Drug of choice* for sedation is benzodiazepines:
    - Midazolam 0.05 mg/kg IV
    - Diazepam 0.05 mg/kg IV.
- Narcotics like fentanyl are alternatives
- Disadvantages:
  - Increased chances of hypoxia
  - Unprotected airway: Increased risk of aspiration
  - Persistence of fetal movements
  - Does not block peritoneal/uterine pain
  - Monitoring required for 3–4 hrs for ventilation and hemodynamics.

- Local anesthesia with fetal paralysis:
  - For fetal umbilical vein sampling
  - Maternal local anesthesia with 0.5 ml of 1% lidocaine as field block
  - Pancuronium IV through umbilical vein or IM into fetal thigh or shoulder
  - Pancuronium 0.01 mg/kg IV or 0.5 mg/kg IM
  - Advantages:
  - Minimal parenteral analgesia to mother
  - Minimal risk to maternal-airway
  - No risk of maternal neuromuscular blockade: Drugs do not cross placental barrier
  - Loss of fetal movements for 2–4 hrs.
- Disadvantages:
  - No fetal analgesia/anesthesia
  - If emergency delivery is required, fetus would be paralysed
  - Fetus would require respiratory assistance after delivery.
- Regional anesthesia:
  - Used for major procedures
  - Advantages:
    - Excellent analgesia and good relaxation of abdomen
    - Excess fetal movements can be reduced by fetal injection of pancuronium 0.2 mg/kg and fentanyl 25–50 µg/kg
    - Fentanyl is safe in preterm infants
    - Pancuronium: Vagolytic effect increases heart rate and maintains cardiac output
    - Avoids problems associated with intubation, keeps mother awake: safe airway.
  - Disadvantages:
    - Can cause maternal hypotension
    - Avoided when fetal status is compromised.
- General anesthesia:
  - Useful for major procedures to reduce material anxiety
  - Advantages:
    - Excellent analgesia
    - Excess fetal movements reduced with direct muscle-relaxant injection
    - Safe airway and reduces risk of Mendelson syndrome.
  - Disadvantages:
    - Problems associated with intubation
    - Halogenated agents may cause fetal hypotension and acidosis.

Preoperative Evaluation and Preparation

- Only healthy parturients to be approved (between 24 and 29 wks)
- Family counselling about fetal benefits, maternal risks and alternatives
- Family to be warned that current and all subsequent pregnancies will be C-section
- Consent taken for rectal suppository
- O negative, CMV negative blood irradiated and cross-matched to be kept ready in the event of fetal transfusion in intraoperative period
- Maternal sedation with 0.05 mg/kg midazolam IV
- Avoid heavy sedation to prevent aspiration and maternal hypoxia
- Parturient nursed in quiet environment without cold as fetal stress causes increased catecholamines and growth hormones
- Antiaspiration prophylaxis with:
  - 30 ml of nonparticulate antacid, like sodium citrate
  - *H2 receptor antagonist:* 50 mg ranitidine IV
  - *Antiemetics:* 8 mg ondansetron IV/10 mg metaclopramide IV.
- Shift to operation theater in left lateral position: Avoid supine hypotension syndrome.

Monitoring

- Maternal monitoring:
  - BP
  - Pulse oximetry
  - E_TCO_2
  - ECG
  - Temperature
  - Urine output
  - Tocodynamometer for uterine activity.
- Fetal monitoring:
  - Important to monitor fetal asphyxia/distress
  - Blood gas: pH and electrolytes
  - Blood glucose
  - FHR:
    - Electronic monitors
    - Pulseoximeter
    - Cardiotachometer
    - Plethysmography with spectrophotometric oximetry.
  - Fetal ECG
  - Fetal BP and umbilical blood flow
  - Transvaginal ultrasonography for fetal cardiac contractility.

Induction and Intubation

- 100% oxygen used to adequately preoxygenate patient
- Thiopentone 3 mg/kg, succinylcholine 1 mg/kg IV
- ***Rapid sequence induction*** with cricoid pressure.

Maintenance

- 100% O_2 or 50% O_2 + 50% N_2O with 0.7% halothane/1% isoflurane
- 0.7% halothane/1% Isoflurane (≤ 1 MAC) causes mild reduction in fetal BP with no change in FHR/acid-base status
- 1.5% halo (≥ 1 MAC) causes fetal hypotension, reduces FHR and acidosis
- IV vecuronium 0.1 mg/kg for maternal muscle relaxation
- Additional fetal injection of 0.1 mg/kg pancuronium and 25 µg/kg fentanyl to prevent fetal movements
- No danger of teratogenicity as these procedures are done after 1st trimester
- In asphyxiated fetuses, use of inhalation agents is controversial.

Hemodynamics

- Maintenance of BP is important as fetal distress can occur
- IV fluid boluses and vasopressors like ephedrine to counter hypotension
- Patient in lateral position or tilting table to the left to avoid supine hypotension syndrome
- Special staplers available for vascular hemostasis to reduce hemorrhage.

Extubation

- Awake extubation to reduce risk of aspiration
- Avoid coughing/straining as it can jeopardize integrity of uterine closure.

Intraoperative Tocolysis

- Magnesium sulfate:
  - 4 g IV over 20 minutes at the time of uterine closure
  - Continuous infusion 2 g/hr for postoperative tocolysis.
- Nitroglycerine:
  - For immediate tocolysis when uterus is refilled with saline to replace drained amniotic fluid
  - 50–200 µg NTG IV bolus
  - High dose avoided as fetal liver has limited ability to metabolize cyanide breakdown product.
- β adrenergic agonists:
  - Salbutamol/terbutaline/ritodrine
  - Continued through infusion pump for some days for postoperative tocolysis
- Rectal indomethacin: Can be continued for some days for postoperative tocolysis
- Halogenated agents: Halothane/isoflurane/sevoflurane.

Postoperative

Monitoring

- SpO_2 ABG
- BP FHR
- HR
- Urine output and temperature.

Complications

- Pain
- Pulmonary edema due to fluid loading when tocolytic therapy is used
- Aspiration
- Preterm labor
- Respiratory depression: Fetal distress.

Analgesia

- Indomethacin suppository
- Fentanyl 1 µg/kg
- Epidural analgesia.

Minimal Access Fetal Surgery (MAFS)

- Ammo endoscopy done by distension of uterus with Hartmann's solution
- Avoids maternal hysterotomy: Reduces incidence of bleeding, preterm labor and uterine rupture
- Uterine irritability is low and, hence, epidural anesthesia with conscious sedation is used.

EXIT PROCEDURE[3,16]

Introduction

- ***Exutero Intrapartum Treatment***
- Approach to fetus with critical airway obstruction which maintains interoplacental support for a period of time after partial delivery of fetus

Indications

- Large fetal neck masses
- Reversal of tracheal occlusion from clips used for congenital diaphragmatic hernia
- Other congenital airway occlusion identified perinatally.

Principle

- Experimental occlusion of trachea inutero causes pulmonary hyperplasia
- In foetuses with CDH, fetal tracheal occlusion may cause increased lung growth
- Tracheal plugs and surgical clips used to occlude trachea
- These are placed directly into fetal trachea endoscopically
- Exit procedure is used to remove these tracheal occlusion at the time of birth.

Anesthetic Considerations

- Maintenance of uterine relaxation during fetal manipulation
- Administration of fetal anesthesia
- Ensuring adequate fetal oxygenation and fetal monitoring
- Rapid reversal of uterine relaxation following umbilical cord clamping to reduce maternal blood loss.

Procedure

- Procedure involves:
  - Partial delivery of fetus
  - Surgical treatment of fetal pathology (attaining patent fetal airway)
  - Delivery of fetus
  - Clamping umbilical cord.
- Usually requires 2 anesthetic teams: 1 for mother and the other for fetus or newborn
- Modified LSCS with GA and volatile anesthetic (MAC < 2 and FiO_2 of 1) induced uterine relaxation is performed
- Surgeon removes the occlusive device
- Anesthetist performs laryngoscopy, ET intubation of fetus while it is still maintained on placental circulation.
- Lungs are expanded and surfactant administered
- Umbilical cord is clamped and neonate removed from placental support.

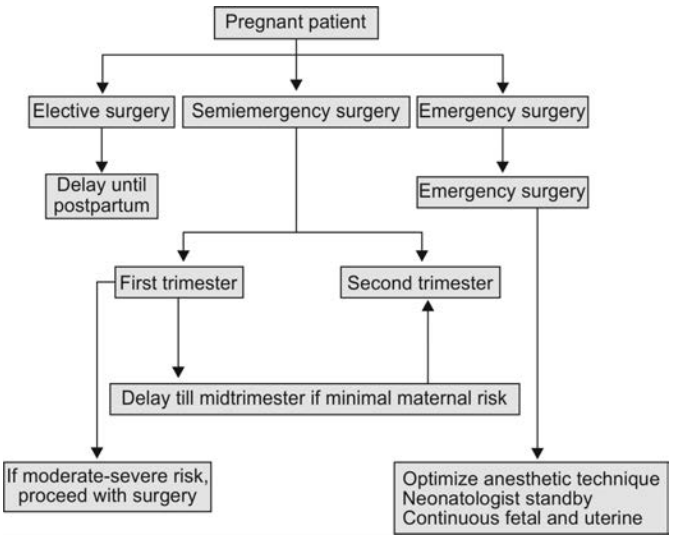
Monitoring

- Sterile USG for FHR monitoring during fetal manipulation
- Sterile pulse oximetry sensors for fetal oxygenation
- Fetal temperature.

Anesthetic Sequence

- *Rapid sequence induction*
- IV opioids to mother can also produce fetal anesthesia
- IM fentamyl 25 µg/kg, NMB and atropine 0.1 mg/kg after partial delivery, to fetus
- IV NTG and halogenated anesthetics (< 2 MAC) for short-acting tocolysis.
- IV vasopressors to ensure adequate uteroplacental blood flow as NTG and volatile anesthetics cause hypotension
- Reverse uterine relaxation rapidly by:
  - Reducing inhalational agents
  - Uterotonic agents like oxytocin to reduce maternal bleeding.

NONOBSTETRIC SURGERY IN PREGNANCY[16]



APPENDICITIS IN PREGNANCY[1,3,16]

Introduction

Most common nonobstetric surgical emergency in pregnancy.

Clinical Features

Most common in 1st and 2nd trimester.

Symptoms

- Abdominal pain variable in position due to growing uterus
- Anorexia, nausea, vomiting
- Diarrhea/constipation, dysuria.

Signs

- Fever 37–38 °C
- Tachycardia > 100 bpm
- Abdominal guarding and rigidity

- Tenderness:
  - Right iliac fossa
  - Right upper quadrant
  - Mid epigastric
  - Diffuse.
- Rectal tenderness
- ***Rebound pain***
- Reduced bowel sounds
- ***Psoas test:***
  - Indicates inflammation of iliopsoas group of muscles
  - Occurs in retrocecal appendicitis
  - Actively flex thigh at hip joint
  - Alternately passive extension of thigh with patient lying on the side
  - Abdominal pain indicates positive psoas test.
- ***Obdurator test:***
  - Indicates inflammation of obdurator internus
  - Patient lies on back
  - Knees and hips flexed to 90°
  - Flexion and internal rotation of hip causes pain.
- ***Rovsing's sign:***
  - Palpation of left lower quadrant increases pain in right lower quadrant of abdomen
  - Not useful in pregnancy.
- ***Alder's sign:***
  - To differentiate uterine and appendiceal pain
  - Pain localized with patient supine
  - Patient turned to her left side
  - If pain shifts to the left, it is assumed to be uterine.

Differential Diagnosis

Obstetric

- Preterm labor
- Abruption
- Chorioamnionitis
- Ovarian cyst tortion
- Threatened abortion.
- Salpingitis
- Degenerating myoma
- Tubo-ovarian abscess

Nonobstetric

- Glomerulonephritis
- Pyelonephritis
- Cholecystitis
- Pancreatitis
- Renal calculus
- Sickle-cell crisis
- Porphyria
- Pneumonia
- Intestinal obstruction
- Mesenteric adenitis.

Anesthetic Goals

- Delay elective surgery till second trimester if possible
- Preserve maternal life in emergency surgery
- Optimize maternal physiological function
- Avoid teratogenicity
- Avoid oxytocic effects on myometrium
- Optimize uteroplacental blood flow
- Use regional anesthesia where possible
- Avoid awareness under general anesthesia.

Anesthetic Considerations

- Avoidance of teratogenic agents:
  - *Category D*: diazepam
  - *Category C*:
    - Thiopentone
    - Etomidate
    - Sufentanyl
    - Chloroprocaine
    - ketamine
    - morphine
    - bupivacaine
    - halothane
- Prevention of supine hypotension syndrome
- Maintenance of fetal oxygenation:
  - Maintain PaO_2, $PaCO_2$, BP
  - Avoid hyperventilation – alkalotic shift of ODC
  - Avoid high MAC of volatile anesthetics
  - Avoid excess airway pressures – hypotension
  - Use regional anesthesia where possible.
- Prevention of preterm labor:
  - β2 agonists
  - Magnesium
  - Indomethacin
  - atosiban
  - sulphate NTG
  - nifedipine.

Preoperative Preparation

- Large-bore IV access
- Preload with 10–20 ml/kg crystalloid
- Nurse in 15 left lateral tilted position if > 16–20 weeks gestation
- Premedication avoided
- Avoid NSAIDs to avoid premature closure of ductus arteriosus
- Benzodiazepines for sedation if required
- IV glycopyrrolate 10μ/kg
- Antiaspiration prophylaxis after 16 weeks gestation
  - Nonparticulate 0.3 M sodium citrate 30 ml 30 min before surgery
  - IV ranitidine 1 mg/kg
  - IV metaclopramide 0.15 mg/kg
- Prophylactic tocolysis if indicated

Choice of Anesthesia

- Regional anesthesia is *technique of choice*
- Spinal preferred as:
  - Lower doses of LA reduce chances of fetal LA toxicity
  - Accidental injection of LA intravascularly avoided.
- Epidural anesthesia with graded doses alternative
- GA with ETT and IPPV if patient hemodynamically unstable.

Advantages of Regional Anesthesia

- Minimizes fetal drug expoure
- Airway management simplified
- Decreased blood loss.

Effects of Surgery on Fetus

- Hypovolemia
- Hypotension
- Hypoxemia
- Intrauterine fetal asphyxia
- Fetal acidosis
- Preterm labor
- Teratogenicity.

General Anesthesia

Monitors

- Pulse oximetry temperature
- NIBP IBP/CVP if hemodynamically unstable
- ECG cardiotocometer
- End tidal CO_2 tocodynamometer
- Urine output entropy
- FHR monitoring feasible after 18 weeks when fetus becomes viable.

Induction

- 3–5 mins preoxygenation with 100% oxygen
- ***Rapid sequence induction*** with ***Sellick's maneuver***
- Thiopentone succinycholine for induction
- Avoid ketamine in early pregnancy as it increases uterine tone
- Intubation with 6.5 or 7 mm ETT
- Left lateral position tilt.

Maintenance

- O_2 air (50 : 50) morphine/pethidine NDMR isoflurane 0.5–1 MAC
- Avoid teratogenic agents
- Avoid N_2O in early pregnancy as:
  - It inhibits methionine synthetase
  - Inhibits DNA synthesis
  - Reduces placental blood flow.

Ventilation

- Maintain E_TCO_2 within normal limits of pregnancy
- Avoid maternal hypercarbia as it causes fetal acidosis
- Avoid PEEP as it may aggravate hypotension.

Hemodynamics

- Hypotension aggressively treated to avoid uteroplacental insufficiency
- Judicious fluid boluses as increased chances of pulmonary edema
- Ephedrine used to treat hypotension unresponsive to fluid boluses
- Phenylephrine and metaraminol alternatives.

Extubation

- Fully awake and fully reversed
- Return of protective airway reflexes
- Extubate in left lateral position.

Postoperative

- Routine administration of tocolytics controversial
- Thromboprophylaxis with heparin essential to avoid risk of DVT
- Multimodal analgesia essential
- Pain increases risk of preterm labor
- Regional analgesia techniques important to reduce dosage of opioids
- Avoid NSAIDs to reduce risk of premature closure of ductus arteriosus
- Postoperative analgesia may mask awareness of early contractions
- Tocometry important monitor for preterm labor
- Monitor tocodynamometer and fetal heart rate.

Complications

- Preterm labor perforation of viscera
- Abortion peritonitis
- Maternal and fetal mortality epidural hematoma
- Pulmonary edema (very common).

CHAPTER

4

Pediatric Anesthesia

DIFFERENCES IN ADULT AND PEDIATRIC AIRWAY

Feature	Pediatric	Adult
Supraglottic		
Nares	Narrow	Wide
Angle of jaw	Obtuse	Acute
Tongue size	Larger	Smaller
Palate	Nonossified	Ossified
Epiglottis	Large, floppy, Ω shaped, more cephalad	Thinner
Position of larynx	Newborn—C3	C5–6
	At 6 years—C4–5	
Description of larynx	More anterior and cephalad	Lower
Vocal cords	Anterior slanting	Not so
Aryepiglottic folds	Thicker – difficult to fix laryngoscope blade	Thinner
Submucosal tissue	More—increased chance of edema	Less
Subglottic		
Cartilages	Soft,collapse easily—reduce cricoid pressure	Harder, stable
Lumen	Narrow, circular—uncuffed tube	Wide, elliptical
Subglottis	Funneled	No funneling
Cricoid	Narrow before puberty	Wide
Narrowest part	Subglottis	Vocal cord
Tracheal length	Reduced (4 cm)	More
Angulation of bronchi	More horizontal	Less
Diaphragm	Higher	Lower
Ribs	Horizontal	Slanted
Alveoli	Lesser (20–50 million)	More (300 million)

PHYSIOLOGICAL DIFFERENCES IN NEONATE

System	Features	Anesthetic implications
CNS	Small brain (10% of body weight)	Lowers MAC values by 25%
	Poorly developed blood brain barrier	Increased drug toxicity
	Immature neuromuscular junction	Increased sensitivity to d-TC
	Spinal cord ends at L2L3	SAB given at lower level
	Increased CSF volume (4 ml/kg)	Increased drug dose in SAB
	Thin unmyelinated neurons	Faster onset of neuraxial blocks
	Increased body surface area: weight ratio	More hypothermia
	Less insulating tissue	More hypothermia
	Shivering nonexistent	Nonshivering thermogenesis for temperature regulation
	Increased chances of intraventricular hemorrhage	Avoid drastic BP changes
Cardiovascular	Myocardium has 30% less contractile tissue	Fixed stroke volume Cardiac output depends more on HR
	Rt ventricular muscle thicker than Lt ventricle till 3–6 months	ECG axis + 180º Normalizes to + 90º at 3–6 months
	Patent shunts – PDA, PFO	Avoid air bubbles in IV lines
	BP lower (50–65 mm Hg at birth)	Systolic BP good indicator of blood volume
	Higher heart rate 100–170 bpm	< 80 bpm indicates cardiac arrest
	Higher cardiac output (350–400 ml/kg @ birth)	70 ml/kg in adults
	Volume dependant but volume intolerant	Avoid fluid overload
	Blood volume more:	
	100 ml/kg preterm	
	90 ml/kg term	
	75 ml/kg school age	
	Hemoglobin drops during first 3 months	Physiological anemia
	Inactive baroreceptor reflexes	Difficult to maintain if hypovolemic Replace fluid deficits promptly
	Immature sympathetic nervous system	Vagal predominance Bradycardia common
Respiratory	Obligate nose breathers	Care while passing nasogastric tube
	Increased airway resistance	Position head carefully
		Minimize apparatus resistance
	Increased dead space	Use circuits with low dead space
		Rendall-Baker-Soucek mask
	Surfactant appears at 28 weeks	RDS babies < 28 weeks
	Lecithin-sphingomyelin ratio	> 2 is normal
	Narrow caliber of airway	Increased work of breathing
	Narrowest area is subglottis	Increased subglottic area
	Cartilages are soft	Gentle cricoid pressure
	Thick aryepiglottic folds	Laryngoscope blade difficult to fix
	Circular cricoid cartilage	No need of cuffed ETT
	Reduced FRC and lung volumes	Accelerated desaturation

Contd...

Contd...

	Increased basal metabolic rate	Mandatory adequate preoxygenation
	Poorly developed lung elastic tissue	Airway closure during tidal ventilation due to low compliance
	Less compliance	High respiratory rate to maintain
	Lesser number of alveoli	ventilation as fixed tidal volume
	Poor respiratory mechanics	Small tidal volume
	More horizontal ribs	No bucket handle movement
		Only piston movement
	Increased basal metabolic rate	Alveolar ventilation 100 ml/kg/min
	Increased alveolar ventilation	Rapid emergence from volatile anesthetics
	Increased closing volume	Air trapping more common
	O_2 and N_2O almost completely absorbed	Air O_2 mixture below 3 months age to prevent absorption atelectasis
	Immature respiratory center	Very sensitive to depressants
	CO_2 dissociation curve shifts to left	Hyperventilation at lower CO_2 levels
	Lower PO_2	50 mm Hg term neonate
		75 mm Hg after 1 week
Renals	Reduced GFR and tubular reabsorption	Judicious fluid therapy
	Obligatory salt losers	Hyponatremia in postoperative period
	Reduced drug elimination	Increased drug toxicity and DOA
Liver	Immature enzyme systems	Increased duration of action of drugs
	Lack of fats and proteins	Reduced gluconeogenesis
		Increased hypoglycemia
Blood	Fetal Hb normalizes by 3-6 mths	Shift of ODC to left
	Reduced 2,3-DPG	Shift of ODC to left
	Parenchymal shunt due to atelectasis	Low PO_2
	Cardiac shunts-PFO and PDA	
	Anatomical AV shunts	
	Increased chances of hypocalcemia in 1st 48 hrs	Supplement after birth
	Increased hypoglycemia chances in LBW babies	Supplement after birth
	Water retention postoperatively	Reduce maintenance fluids by 1/3rd in postoperative period
	Hyperglycemia causes osmotic diuresis and IVH	Use dextrose containing fluids only in VLBW and endocrinopathies

PEDIATRIC DAY CARE SURGERY[15]

Indications

General Surgery

- Hernia
- Cyst excision
- Abscess
- Dressing
- Endoscopy.

ENT

- Adenoidectomy
- Tonsillectomy
- Myringotomy.

Ophthalmology

- Examination under anesthesia
- Strabismus
- Chalazion.

Orthopedics

- Closed reduction
- Cast change.

Urology

- Circumcision
- Meatotomy
- Cystoscopy
- Hypospadiasis.

Selection Criteria
- ASA I–II
- ASA III if well controlled
- Good preoperative evaluation
- Mild URTI can be taken up.

Preoperative Preparation
- Informed consent
- NPO status
- Anxiolysis:
  - Midazolam 0.5 mg/kg PO, 0.2 mg/kg nasal
  - Ketamine 2–5 mg/kg IM
  - Fentanyl PO or transmucosal 15 µ/kg
  - Sufentanyl 1.5–3 µ/kg intranasal.
- Continue other medications
- Parental presence preferable.

Anesthetic Goals
- Rapid induction
- Prompt recovery
- Early discharge
- Minimal side effects.

Induction
- IV Agents:
  - Thiopentone 5–6 mg/kg
  - Ketamine 2 mg/kg
  - Propofol 2–2.5 mg/kg.
- IM Induction:
  - Ketamine 5 mg/kg.
- Inhalational induction:
  - Sevoflurane
  - Halothane.
- Rectal:
  - Ketamine 6 mg/kg
  - Midazolam 0.4 mg/kg.
- Muscle relaxants:
  - Atracurium 0.5 mg/kg
  - Vecuronium 0.1 mg/kg
  - Rocuronium 0.6–0.9 mg/kg.

Airway Management
- Facemask; LMA; COPA preferred
- ETT avoided.

Maintenance
- Fluids according to type of surgery and weight.
- Avoid if brief procedures.
- Short acting narcotics:
  - Fentanyl
  - Remifentanyl
  - Sufentanyl.

Postoperative
- Analgesia:
  - Ketorolac
  - Paracetamol
  - Diclofenac.
- Treat PONV.

Complications
- Pain
- PONV
- Sore throat (LMA)
- Croup (ETT)
- Fever
- Headache.

Advantages
- Reduces separation anxiety
- Increased parental involvement
- Reduces risk of nosocomial infections
- Reduced morbidity and mortality
- Greater efficiency
- Reduced waiting list
- Reduced hospital stay.

Disadvantages
- Multiple trips for preparation
- Skilled anesthetist required
- Good postoperative care mandatory.

Regional Anesthesia
- Caudal anesthesia most popular
- Spinal less popular.

Discharge Criteria
Steward recovery scale:

Sign	Criterion	Score
Consciousness	Awake	2
	Responds to stimuli	1
	Not responding	0
Airway	Coughing/Crying	2
	Maintaining good airway	1
	Airway requiring maintenance	0
Movement	Purposeful movement	2
	Non-purposeful movement	1
	Not moving	0

FLUID THERAPY IN PEDIATRICS[1,15]

Goals

- Correction of fluid deficits
- Ensure adequate intravascular volume
- Ensure good cardiac output
- Prevent electrolyte disturbances
- Prevent hypoglycemia
- Replace ongoing losses
- Compensate for autonomic changes under anesthesia
- Prevent volume overload.

Pediatric Challenges

- Small size
- Small surface area—volume ratio
- Immature homeostasis
- Immature renals
  - Reduced GFR
  - Reduced glomerular surface area.
- Increased basal metabolic rate
- Differences in total body water
  - Preterm infants: 90% of body weight
  - Term infants: 75% of body weight
  - Adults: 60% of body weight.
- Increased circulating blood volume:
  - Preterm neonate: 100 ml/kg
  - Term neonate: 90 ml/kg
  - Infants: 80 ml/kg
  - School age: 75 ml/kg
  - Adults: 70 ml/kg.

Effects of Anesthesia

- Preoperative fasting increases deficit
- Reduced BMR under GA
- Reduced sympathetic tone
- Increased venous capacitance and peripheral pooling
- Blunted baroreceptor reflexes
- Reduced cardiac output with
  - Halothane
  - Sevoflurane
  - Thiopentone
  - Propofol.
- Reduced venous return by IPPV and CPAP
- Surgery induced third spacing due to capillary leak and tissue edema.

Fluid Requirements

Fluid Deficits

- Increased fluid losses:
  - Diarrhea
  - Hemorrhage
  - Vomiting
  - Burns
  - Polyuria
  - Fever.
- Maldistribution
  - Third space loss
  - Sepsis
  - Hypoalbuminemia—cirrhosis, CCF.
- Reduced oral intake
  - Fasting
  - Other illnesses.

Maintenance Fluids

- Insensible losses:
  - Sweating
  - Respiratory tract.
- Sensible:
  - Urine
  - Feces.

Ongoing Losses

- Ongoing illness
- Anesthetic vasodilation
- Surgical
  - Bleeding
  - Third spacing
  - Evaporation.

Calculation of Requirements

*Maintenance: **Holliday and Segar***

- Hourly maintenance fluid:
  - 0–10 kgs: 4 ml/kg/hr
  - 10–20 kgs: 2 ml/kg/hr
  - > 20 kgs: 1 ml/kg/hr.

Deficit

- Number of NPO hours x maintenance requirements per hour
- 50% deficit during 1st hour
- Remaining 50% over next 2 hours
- Consider fever, prematurity and renal concentrating ability.

Third Space Losses

- 1 ml/kg/hr for minor surgeries like hernia repair
- 15–20 ml/kg/hr for major abdominal and thoracic surgeries
- 50 ml/kg/hr for necrotizing enterocolitis surgery.

Blood Loss

- Using gravimetric method.

Choice of Fluids: NPSA guidelines

Maintenance

- Isotonic crystalloids
- 0.9% NS or RL.

Third Space

- Isotonic crystalloids
- 0.9% NS or RL.

Deficit

- Isotonic crystalloids
- 0.9% NS or RL.

Blood Loss

- 1 ml blood with 1 ml blood
- 1 ml blood with 1 ml colloid
- 1 ml blood with 3 ml crystalloid
- Routine dextrose administration not recommended.

Postoperative

Choice of Fluids: NPSA guidelines:

- 0.9% NS or RL
- 0.9% NS with 5% dextrose
- 4.5% albumin
- 5% dextrose increases chances of hypoglycemia as in:
  - Neonates
  - Child receiving hyperalimentation
  - Endocrinopathies
  - @ 125–250 ml/kg/hr.

NPO Status Postoperatively

- Usually 1st 3 postoperative hrs
- If intake delayed for > 3 hrs, administer fluids
- Consider:
  - Maintenance requirements
  - GI losses
  - Additional losses (fever)
  - Fluid for drug dilution.

Maintenance fluids reduced to 1/3rd calculated dose as:

- ADH secretion and
- Free water retention occurs postoperatively.

Complications of Fluid Therapy

- Anasarca
- Pulmonary edema
- Bowel swelling
- Laryngeal edema
- Hyperchloremic metabolic acidosis from excess NS
- Hyponatremia if large amounts of RL
- Coagulopathy if colloids like dextran.

NPO GUIDELINES

For Pediatric Age[15]

Age	Fasting time	
	Milk and solids (hrs)	Clear fluids (hrs)
< 6 months	4	2
6 months–3 years	6	3
> 3 years	8	3

For All Ages: ASA 1999 Task Force:[1]

Ingested material	Fasting time
Clear fluids	2 hrs
Breast milk	4 hrs
Infant formula	6 hrs
Non human milk	6 hrs
Light meal (toast with clear fluids)	6 hrs

Clear Fluids

- Water
- Clear tea
- Fruit juice without pulp
- Carbonated beverages
- Black coffee.

Advantages of Liberal NPO Guidelines

- Improved patient comfort
- Reduced dehydration
- Reduced hypovolemia at induction
- Reduced chances of hypoglycemia
- Clear fluids 2 hrs preoperative stimulates peristalsis, reduces gastric volume and pH.

Administration of Drugs

- To be given 60–90 minutes before arrival to OT
- Can be ingested with up to 150 ml water.

CHILD WITH URTI[15]

Introduction

Important cause of anesthetic morbidity and mortality.

Etiology

Gram-positive

- Staphylococcus
- Pneumococcus
- Streptococci
- Hemophilus.

Gram-negative

- Pseudomonas
- E. coli
- Klebsiella.

Virus

- Myxovirus
- Picorna
- Paramyxo
- Corona
- Adeno
- Rhino

Types

URTI

- Pharyngitis
- Laryngitis
- Croup
- Epiglottitis
- Otitis media
- Tonsillitis
- Sinusitis.

LRTI

- Pneumonia
- Bronchiolitis
- Bronchiectasis
- Cystic fibrosis.

Implications

- Increased secretions
- Breath holding
- Increased apnea, stridor, coughing
- Increased laryngospasm
- Increased bronchospasm
- Increased episodes of desaturation
- Seeding of LRT—nosocomial pneumonia.

Recommendations

Preoperative

- Child with active RTI for elective procedures: Postpone for 4–6 wks
- Child with active RTI for emergency procedures: Take adequate precautions and continue
- Corticosteroids if taken should be continued
- If on 2 agonists, monitor theophylline levels between 10–20 µgs/ml
- Preoperative nebulization if bronchospasm/bronchial asthma.

Intraoperative

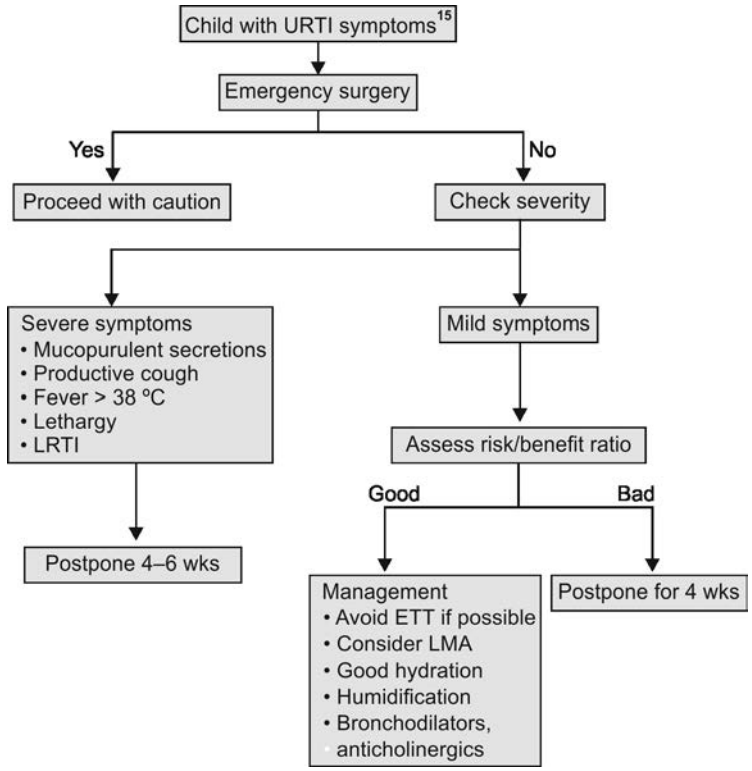
- Preoxygenate for 3–5 mins
- Use transparent facemask for induction
- IV induction preferred
- LMA preferred over ETT as reduced risk of laryngospasm
- Suction following ETT placement
- Halothane avoided in children on 2 agonists
- Maintain deep anesthetic planes
- Thorough suction in deep planes
- IV xylocard 1.5 mg/kg to reduce spasm
- Avoid extubation in light planes
- Extubate fully awake or in deep planes
- Nebulization with ipratropium or humidified air
- Humidification of gases to reduce inspissation of secretions.

Risk Predictors

- Active URTI
- Nasal congestion
- Productive cough
- Parental smoking
- ETT in child< 5 years
- History of reactive airway disease
- Surgery involving airway
- Surgery involving airway
- History of prematurity
- ETT > LMA > MASK
- History of snoring.

Risk Factors for Nosocomial Pneumonia

- Presence of tracheostomy tube
- Increased duration of intubation
- Existence of active URTI
- Preoperative antibiotic therapy
- Presence of azotemia
- Increased gastric pH.



PEDIATRIC SPINAL[15]

Introduction

- Increasingly used in children.

Anatomical Differences

- Spinal cord ends at L2–L3 (L1–L2 in adults)
- Dura ends at S3 (S2 in adults)
- ***Tuffiers*** line at L4 spinous process
- CSF volume is more—4 ml/kg (2 ml/kg in adults)
- Smaller pelvis and sacrum
- Thinner ligaments:
  - Easy to penetrate
  - Difficult to feel fascial planes
  - Vascular response less marked
  - Less hypotension.

Indications

General Surgery

- Hernia
- Lower abdomen surgery
- Colostomy
- Anoplasty
- Rectal biopsy
- Perineoplasty
- Appendicectomy.

Orthopedic Surgery

- Clubfoot tendon lengthening
- Fracture reduction
- Incision drainage abscess.

Urological Surgery

- Circumcision
- Vesicostomy
- Orchidotomy
- Orchiopexy
- Varicocelectomy
- Hydrocelectomy
- Hypospadiasis repair
- Meatoplasty.

Advantages

- Patient awake and breathing spontaneously
- Complete analgesia
- Minimal physiological alterations
- Avoids general anesthesia complications:
  - Respiratory depression

  - Postoperative apnea
  - Cardiovascular instability
  - Airway manipulation
  - Reduced total anesthetic requirements
  - Hastens wake up time
  - Smooth recovery
  - Reduced PONV as no opioids.
- Reduced postoperative pulmonary complication
- Excellent postoperative analgesia
- Reduced stress response to surgery
- Reduced bleeding intraoperatively
- Facilitates limb immobilization after N.repair/skin graft.

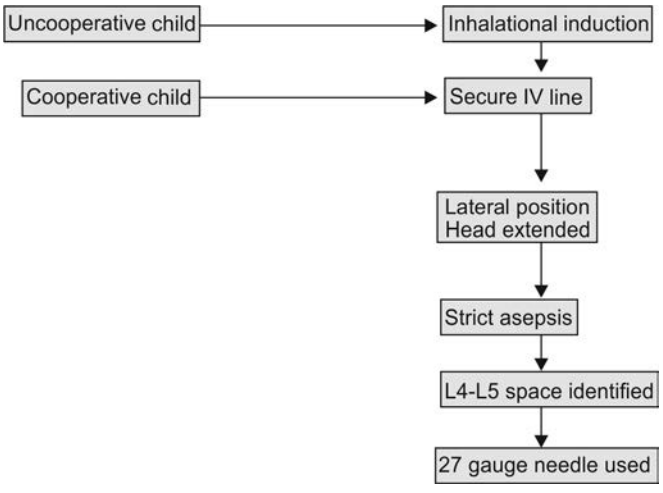
Disadvantages

- Requires expertise
- Requires GA/sedation
- Limited duration of action—unsuitable for long surgeries
- Increased risk of inadvertent complications.

Differences in Technique

- Test dose of local anesthetic essential for allergy
- Performed at lower level as spinal cord reaches L3 in infants
- Requires sedation/GA
- Rarely causes hypotension in child < 10 years
- Crystalloid preloading not required
- Dose of Local anesthetic higher as CSF volume is twice that in adults (4 ml/kg vs 2 ml/kg)
- In infants < 2 months LA dose reduced by 50% as protein binding by 1 glycoprotein is lesser
- Block duration shorter than in adults.

Technique[15]



Dosage[15]

Bupivacaine (0.5%)	0–5 kgs	5–15 kgs	> 15 kgs
Amount (mg/kg)	0.5	0.4	0.3
Volume (ml/kg)	0.1	0.08	0.06
Duration (min)	65–75	70–80	75–85

Complications

- Bradycardia
- High spinal
- Respiratory obstruction
- Backache
- Meningitis
- Infection
- Shivering
- Hematoma.

Contraindications

- Local site infection
- Sepsis
- Meningomyelocele
- Spina bifida
- Hydrocephalus
- Coagulopathy
- Convulsive disorder
- VP shunt
- Vertebral implants
- Progressive neuromuscular disorders.

PEDIATRIC EPIDURAL[15]

Introduction

Less commonly performed cue to technical difficulties.

Anatomical Differences

- Shallower epidural space-spread of local anesthetic is more even
- Shorter skin—epidural distance:
  - 1.5 mm/kg till 1 year
  - 1 mm/kg thereafter.
- Thinner ligaments
  - Easy to penetrate
  - Difficult to feel fascial planes.
- Nerves are thinner—more rapid onset of action
- Incomplete myelination—block achieved at lower LA concentration
- Vascular response less marked
- Less hypotension.

Technical Differences

- Test dose local anesthetic essential for LA allergy
- Hanging drop method not done due to short skin-space distance
- Needle continuously advanced with continuous loss of resistance monitoring
- Saline preferred for LOR as air can cause air embolism
- Catheter passes easily in space; can even reach cervical cord level.

Determination of Catheter Position

- Measurement of distance to be travelled
- N.stimulator connected with metal needle attached to saline filled catheter and stimulated Muscular jerk indicates position of cathter tip stimulating that particular segment
- Radiopaque dyes like IOHEXOL for epidurography.

Dosages

- 0.05–0.1% bupivacaine 0.1–0.2 ml/kg/segment
- Additives:
  - Ketamine 0.25–0.5 mg/kg
  - Buprenorphine 1–2 µ/kg
  - Midazolam 25 µ/kg
  - Fentanyl 0.5–1 µ/kg or 0.3–1 µ/kg/hr infusion
  - Morphine 15–50 µ/kg or 0.2 µ/kg/hr infusion
  - Clonidine 1–2 µ/kg or 0.08–0.2 µ/kg/hr infusion
  - Tramadol 0.5–2 mg/kg
    - Ketamine has unpredictable duration of action and hallucination
    - Buprenorphine
      - Acts for 24–30 hrs
      - Less respiratory depression
      - Causes nausea and vomiting.

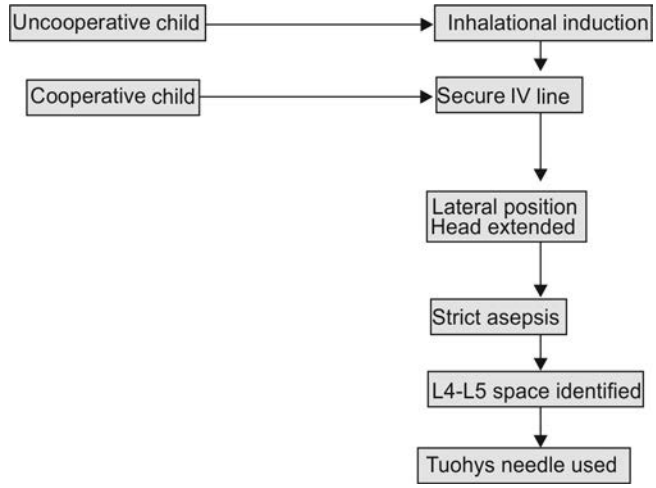
Advantages

- Patient awake and breathing spontaneously
- Complete analgesia
- Minimal physiological alterations
- Avoids general anesthesia complications:
  - Respiratory depression
  - Postoperative apnea
  - Cardiovascular instability
  - Airway manipulation
  - Reduced total anesthetic requirements
  - Hastens wake up time
  - Smooth recovery
  - Reduced PONV as no opioids.
- Reduced postoperative pulmonary complication
- Excellent postoperative analgesia
- Reduced stress response to surgery
- Reduced bleeding intraoperatively.

Disadvantages

- Uncertain depth of space
- Risk of dural puncture as epidural space is narrow
- Difficult to feel LOR as under GA, ligaments are lax.

Technique[15]



Modified Bromage Scale: > 2 Years Age

Score	Description
1	Complete motor block
2	Patient able to move feet, Almost complete motor block
3	Partial motor block, Patient able to move knees
4	Weakness of hip flexion, Able to raise leg but unable to keep it raised
5	No detectable weakness of hip flexion, Able to keep leg raised >10 sec
6	No weakness at all, Able to perform partial knee bend when supine

Complications

- Total spinal
- Backache
- Infections
- Meningitis
- Epidural abscess
- Hematoma
- Intravascular injection—LAST.

Contraindications
- Local site infection
- Sepsis
- Meningomyelocele
- Spina bifida
- Hydrocephalus
- Coagulopathy
- Convulsive disorder
- VP shunt (Ventriculo-Peritoneal shunt)
- Vertebral implants
- Progressive neuromuscular disorders.

Considerations for Last in Pediatrics
- Signs masked due to GA
- Immature blood brain barrier
- Lower blood levels of LA cause toxicity.

CAUDAL ANESTHESIA[15]

Introduction
Local anesthetic injection into epidural space via sacral canal through sacral hiatus.

Anatomy
- Sacral hiatus is formed by failure of union of S4 and S5 vertebra in the midline
- Bony defect is covered by posterior sacrococcygeal ligament
- Remnants of S5 articular process is called sacral cornua
- Contains:
  - Terminal part of dural sac terminating at S3
  - Cauda equina formed by S1-S5 and coccygeal N
  - Valveless venous plexus
  - Areolar tissue
  - Lymphatics.

Indications[15]
- Pediatric Anesthesia
  - General Surgery:
    - Rectal
    - Inguinal
    - Urogenital
    - Circumcision
    - Orchidectomy
    - Orchidotomy.
  - Orthopedic surgery:
    - Clubfoot
    - Fracture reduction
    - I and D of abscess.
- Adult Anesthesia
  - Vaginal hysterectomy
  - Inguinal herniorrhaphy
  - Hemorrhoidectomy
  - Anal dilation
  - Lower limb surgeries.
- Obstretric Analgesia
- Postoperative Analgesia
  - Circumcision
  - Hemorrhoidectomy
  - Anal dilation.
- Chronic Pain: Lower Back Pain

Technique
- Under sedation
- Lateral Sims position
- Strict asepsis
- Identify posterior superior iliac spine
- Identify midline
- Palpate tip of coccyx
- Palpate sacral hiatus proximally
- Needle inserted perpendicular to skin
- Once sacral surface is hit, needle slightly withdrawn redirected and advanced at 45° angle
- Advance till sudden 'POP' felt
- Aspirate for blood or CSF
- Inject the local anesthetic in graded aliquots.

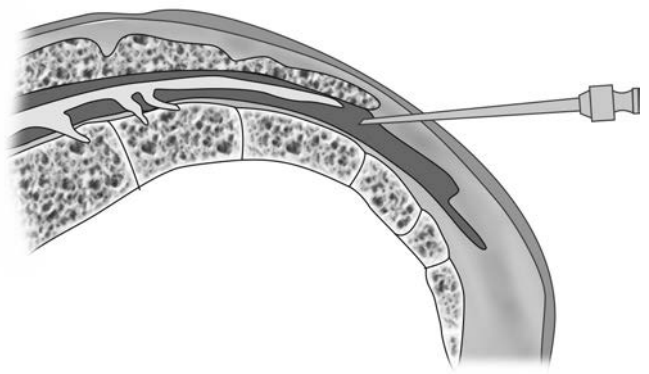


Fig. 4.1: Caudal anesthesia

Dose of Local Anesthetic
Armitage formula
- 0.5 ml/kg of 0.25% bupivacaine—anal surgery, circumcision
- 1 ml/kg of 0.25% bupivacaine—lower thoracic level
- 1.25 ml/kg of 0.25% bupivacaine—mid thoracic level (herniorrhaphy, orchidectomy).

Additives

- Morphine 50–70 mics/kg
- Clonidine 1 mic/kg
- Butadol 5–25 mics/kg.

Continuous Caudal Epidural

- Using catheter threaded into caudal space
- Position of catheter tip confirmed with fluoroscopy/nerve stimulator
- Catheter up to thoracic epidural to achieve T_2–T_4 block possible
- Dose same as bolus dose with frequent top ups.

Complications

- Absent/patchy block
- IV or IO placement: LAST
- Dural puncture
- Injection into fetal scalp
- Excessive spread
- Pain at injection site
- Periosteal hematoma
- Urinary retention
- Infection
- Permanent neurodeficits.

Contraindications

- Local pathology:
  - Pilonidal sinus
  - Sacrococcygeal teratomas
  - Sepsis.
- Fixed cardiac output state:
  - Aortic stenosis
  - Mitral stenosis.

PEDIATRIC POSTOPERATIVE ANALGESIA[15]

Introduction

Pain often undertreated due to difficulty in assessment and fear of side effects of medications.

Assessment of Pain

- Self-Report Measures
  - **Faces** Pain Scale
  - **Oucher** Scale
  - **Manchester** Pain Scale
  - **Visual Analogue Scale.**
- Observational—Behavioral Measures
  - **Cheops** Scale
  - **Flacc** Scale
  - **Comfort** Scale.
- Physiological Measures
  - University of Wisconsin scale
  - Noncommunicating Childrens pain scale
  - Pain Indicator for Communicatively Impaired Children (PICIC)
  - Revised FLACC scale.
- Neonatal Pain Assessment
  - Premature Infant Pain Profile (PIPP)
  - **Cries** Scale
  - **Comfort** Scale.

Methods

- Behavioral Methods
  - Hypnosis
  - Biofeedback
  - Relaxation
  - Behavioral pain therapy.
- Physical Methods
  - Rest and limb elevation
  - Cold application
  - TENS.
- Pharmacological Methods
  - NSAIDs
  - Opioids
  - Local anesthetics.
- Regional Blocks
- Recent Advances
  - EMLA cream
  - Ethylchloride vapocoolant spray
  - Iontophoresis with fentanyl
  - Liposomal lidocaine.

Level of action	Drug
Peripheral	Local anesthetics, Peripheral blocks
	Opioids
	NSAIDs
Spinal	Local anesthetics
	Opioids
	α_2 agonists
Cortical	Opioids

Rationale

- Multimodal analgesia used
- Target multiple sites along pain pathway
- Choose drugs with synergistic effect and different side effect profile
- Most severe in first 24–72 hrs
- Round the clock coverage for first 24 hrs and then as required

- If cognitive impairment, diazepam used if clonus/spasms along with multimodal approach.

Drug Dosages

Paracetamol

- 7.5 mg/kg IV for neonates
- 15 mg/kg IV older children
- 30 mg/kg PR followed by 20 mg/kg TID
- Total daily dose:
  - < 100 mg/kg in children
  - < 75 mg/kg in infants
  - < 50 mg/kg neonates.

NSAIDs

- Diclofenac 1 mg/kg IM q8h
- Ibuprofen 6–10 mg/kg q6h
- Ketorolac 0.5 mg/kg q8h.

Opioids

- Tramadol 1–2 mg/kg q6h
- Morphine 50–100 µ/kg or 10–40 µ/kg/hr infusion
- Fentanyl 0.5–1 µ/kg or 0.1–0.2 µ/kg/min infusion
- Remifentanyl 0.1–0.5 µ/kg or 0.05–5 µ/kg/min infusion
- Alfentanyl 5–10 µ/kg or 1–4 µ/kg/min infusion
- Sufentanyl 0.5–5 µ/kg or 0.01–0.05 µ/kg/min infusion.

Local Anesthetics

- Ropivacaine/bupivacaine
  - 2 mg/kg bolus
  - 0.4 mg/kg/hr is maximum allowable dose.

Others

- Ketamine 0.5 mg/kg followed by 10–20 µ/kg/min infusion
- Dexmedetomidine 0.5 µ/kg followed by 0.15–0.25 µ/kg/min infusion.

Regional Blocks

- Local infilteration
- Ilioinguinal—iliohypogastric block for herniorraphy
- Penile block for circumcision
- Fascia iliaca block for lower limb
- Intercostal block for thoracic/upper abdominal surgeries
- Subarachnoid, caudal, epidural-perineal and lower limb surgeries.

GASTROCHISIS AND OMPHALOCELE[15]

Introduction

Failure of gut to return to abdominal cavity during fetal development causing persistent herniation of abdominal contents without a covering sac.

Omphalocele

- Occurs in 10th week of life
- Due to non return of bowel from extraembryonic coelom
- Covered by outer membrane called amnion and inner layer of peritoneum
- Umbilical cord at the apex of sac.

Gastrochisis

- Occurs later in fetal life
- Due to occlusion of omphalomesenteric artery
- Ischemia and atrophy of anterior abdominal wall
- Bowel uncovered and exposed
- Defect in lateral abdominal wall
- Umbilical cord in one side.

Treatment

Primary Closure

- If defect is small
- Criteria for safe primary closure:
  - Intragastric pressure < 20 cm H_2O
  - Intravesical pressure < 20 cm H_2O
  - $ETCO_2$ < 50 mm Hg
  - Maximum ventilator pressure < 35 cm H_2O.

Staged Closure

- For larger defects
- Using Dacron reinforced silo
- Silo acts as temporary housing for bowel
- Silo secured at the edge of the defect
- Size gradually reduced over 3–7 days
- Allows abdominal cavity to accommodate contents gradually without compromising perfusion or ventilation.

Anesthetic Considerations

- Infection, sepsis preoperatively
- Electrolyte imbalance preoperatively
- Massive fluid losses intraoperatively
- Massive heat loss intraoperatively
- Full stomach
- Reduced ventilation postoperatively due to reduced FRC.

Preoperative Preparation

- Informed consent
- NPO 6 hrs solids
  - 4 hrs milk
  - 2 hrs clear fluids.
- IV line in arms as postoperative venous congestion of lower limbs
- Antibiotic prophylaxis especially if gastrochisis
- Insert NGT and aspirate stomach contents
- 2 IV cannulae.

Monitors

- Pulse oximetry
- Capnography
- ECG
- NIBP
- Temperature
- Urine output
- Invasive BP
- Precordial stethoscope.

Pulse oximeter and NIBP of lower limb to check for reduced venous return following abdominal closure.

Induction

- Awake intubation if difficult airway
- Rapid sequence induction with gentle cricoid pressure
- Epidural via thoracic or caudal, tip at T4–T8
- Central line if postoperative parenteral feeding.

Maintenance

- Avoid nitrous oxide
- Increased dose of relaxants to facilitate primary closure
- 5–10 µ/kg fenta or epidural infusion for analgesia.

Hemodynamics

- Massive fluid losses
- Exposed visceral surfaces
- Third space losses due to partial bowel obstruction
- 20 ml/kg RL, 5% albumin
- Prevent hypothermia
  - Cover head of baby
  - Warm IV fluids
  - Warm theater
  - Adequate blankets.

Watch for aortocaval compression and hypotension if tight primary closure reduced venous return and lower limb edema.

If hypotension following wound closure:
- Reopen wound
- Aggressive hydration
- Inotropic support.

Complications

- Obstruction
- Aortocaval compression
- Reduced organ perfusion
- Sepsis
- Lower lobe atelectasis due to splinting of diaphragm.

Postoperative

- Ventilation if large defect
- Reduced opioid dose as reduced hepatic function
- Head up position nursing.

TRACHEOESOPHAGEAL FISTULA[6,15]

Introduction

- Abnormal connection between esophagus and trachea
- Can occur congenitally or as a complication of surgery (tracheostomy).

Classification

GROSS' Classification

Five types:

Type	Description	Incidence
A	Blind esophageal pouch proximally	87%
	TEF between distal esophagus and membranous portion of trachea	
B	Pure esophageal atresia without TEF	5%
C	H type fistula, TEF without atresia	4%
D	Esophageal atresia with proximal TEF	1%
E	Esophageal atresia with double TEF	1%

VOGT classification

Type	Description
I	Esophageal agenesis, very rare
II	Blind esophageal pouch proximally
	TEF between distal esophagus and membranous portion of trachea
IIIA	Pure esophageal atresia without TEF
IIIB	H type fistula, TEF without atresia
IIIC	Esophageal atresia with proximal TEF

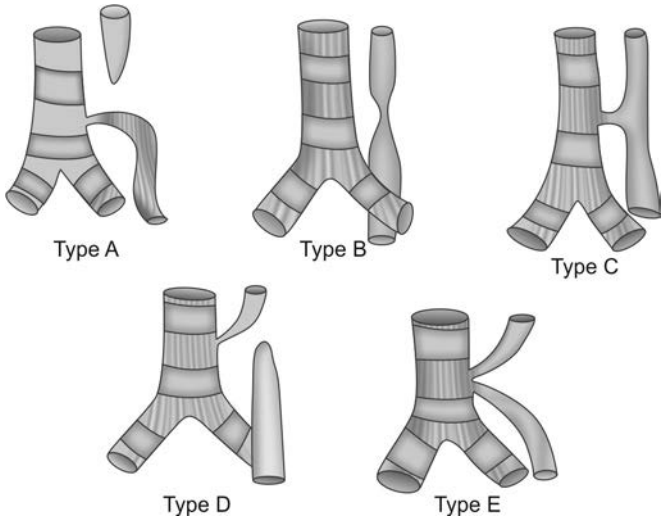


Fig. 4.2: Gross classification of tracheoesophageal fistula[6]

Associated Anomalies[6]

Vater

- Vertebral defects/VSD
- Anal atresia
- Tracheoesophageal fistula
- Esophageal atresia
- Radial aplasia
- Renal anomalies.

Vacterl

- Vertebral defect
- Anal malformation
- Cardiac defects
- Tracheoesophageal fistula
- Esophageal anomalies
- Radial aplasia
- Renal anomalies
- Limb defects.

Musculosketetal

- Hemivertebrae
- Syndactyly
- Radial aplasia
- Rib anomalies
- Polydactyly
- Scoliosis.

Cardiac

- VSD
- TOF
- COA
- PDA
- Rt aortic arch
- ASD.

Gastrointestinal

- Imperforate anus
- Meckel's diverticulum
- Duodenal atresia
- Annular pancreas
- Malrotation.

Genitourinary

- Renal agenesis
- Hypospadiasis
- Horseshoe kidney
- Polycystic kidney disease.

Embryology

- 4th to 5th week of intrauterine life
- Imperfect division of foregut into anteriorly positioned larynx and posterior esophagus.

Clinical Features

History

- H type fistulas present later in life
- Polyhydramnios in mother
- Classically copious fine white frothy mucus in mouth
- Choking coughing and cyanosis with first feed
- Aspiration of saliva with first feed
- Frequent LRTI.

On Examination

- Signs of dehydration
- Scaphoid abdomen if no fistula
- If fistula present, abdominal distension due to build up of air in stomach
- Inability to pass 8–10 fr NGT beyond 10–12 cms (normal distance to infants gastric cardia is 17 cms).

Investigations

- Chest X-ray:
  - Pulmonary infilterates
  - Coiled NGT in proximal esophageal pouch
  - Right aortic arch
  - Rib anomalies.
- Abdomen X-ray:
  - Skeletal anomalies

  - Intestinal malrotation
  - Intestinal obstruction.
- Contrast upper GI X-ray:
  - Not required
  - Increases risk of aspiration.
- Echocardiography
- Renal USG
- Prenatal USG:
  - Polyhydramnios
  - Air in stomach confirms presence of fistula.

Procedure

- Always emergency
- Full body assessment if condition allows 24–48 hr wait
- In left lateral position through right thoracotomy, extrapleurally
- Fistula usually present where azygous vein crosses trachea to enter SVC
- Azygous vein divided
- Fistula isolated
- Tracheal end sutured
- Esophageal end identified, dissected to asses length for primary anastomosis
- Anastomosis completed if length inadequate; gastrostomy for feeding and esophagostomy for drainage of saliva
- Gastrostomy feeding, upper pouch suction done till 1 year age
- Colonic interposition for esophagus or gastric pull up done at 1 year.

Waterston Classification[15]

- Group A:
  - > 2.5 kg
  - No other problems
  - Lowest mortality.
- Group B:
  - 1.8–2.5 kgs
  - Moderate pneumonia
  - Moderate congenital problems
  - 32% mortality.
- Group C:
  - < 1.8 kgs
  - Higher birth weight with severe problems
  - Severe pneumonia
  - Severe congenital problems
  - 94% mortality.

Anesthetic Considerations

- Pediatric patients
- Difficult IV access
- Shared airway
- Difficult airway
- Preoperative dehydration
- Hypothermia
- Associated anomalies.

Preoperative Preparation

- Nurse in semiupright position with head end up
- Observe for apneic spells
- Prevent aspiration
- Optimize respiratory system
- Oral feeding contraindicated
- Low pressure suction to upper esophageal pouch through 8 fr Replogle sump tube
- Antibiotic therapy with chest physiotherapy
- Supplemental O_2 therapy
- ETT with IPPV depending on severity
- $D\frac{1}{2}$ NS at 4 ml/kg/hr
- Cover extremities, head with gamgee pads/ aluminium foil
- Shift with thermal protection.

OT Preparation

- Switch off air conditioner
- OT table prewarmed with heating mattress
- Warmed fluids and blood ready
- Warmed gases
- Include manometer in circuit
- Suction
- Oxygen source
- Airway equipment
- Pharmacy: Anesthetic drugs
- Monitors checked and calibrated
- Emergency drugs.

Monitors

- Pulse oximetry
- End tidal carbon dioxide
- ECG
- Temperature
- Urine output
- Precordial stethoscope
- Airway pressure.

Induction

- Awake intubation:
  - *Technique of choice* but traumatic
  - Done rarely nowadays if:
    - Severe airway problems
    - Sick gasping infant
    - In emergencies.
- Disadvantages:
  - Technically difficult
  - Increases arterial and venous pressure
  - Increased ICP
  - Increased intracranial hemorrhage chances
  - Increased hypoxemia chances.
- Intravenous induction:
  - Preferred over awake
  - 22/24G cannula with EMLA cream
  - Thiopentone 3–4 mg/kg or ketamine 2 mg/kg
  - No muscle relaxant till ventilation assured
  - Avoid positive pressure ventilation to avoid stomach distension.
- Inhalational induction:
  - With sevoflurane/halothane, O_2 and air
  - Done if no IV access
  - Watch for apnea, breath holding and bradycardia.

Intubation

- Position:
  - Sniffing position
  - No pillow
  - Flat shoulders
  - Head in doughnut to stabilize.
- Straight/curved blade
- 2.5–3.5 mm ID ETT
- Correct ETT size is that which has leak at 30 cmH_2O airway pressure
- 2 techniques of intubation:
  - Routine intubation with tip of ETT above carina.
  - Intentional intubation of right bronchus → withdraw tube gently → tip of tube lies just above carina → fix ETT.
- Ideal ETT position between carina and TEF, just above carina
- Confirmation of ETT Position:
  - Feel for ETT tip at suprasternal notch
  - Flex head and auscultate breath sounds. If at carina, tube slips into right bronchus and
  - breath sounds reduce on left side.
- Auscultate stomach to ensure no distension occurs through TEF.

Maintenance

- O_2 + air + halothane/isoflurane
- Atracurium is drug of choice
- Epidural via thoracic/caudal
  - Tip of catheter @ T5–6
  - 0.1–0.2 ml/kg/hr 0.125% bupivacaine.

Ventilation

- Tidal volume 7–10 ml/kg
- Respiratory rate 35–40/min
- Titrate FiO_2 to maintain SpO_2 between 95–98%
- Hand ventilate during lung retraction
- Intraoperative desaturation due to right lung migration during retraction
- Increase FiO_2 if hypoxemia during lung retraction
- Suction blood and secretions from ETT intermittently.
- If ETT blocked by blood clot, emergency ETT exchange
- Watch for ETT kinking and accidental extubation intraoperative.

Hemodynamics

- Maintain hematocrit > 35%
- 5% albumin and PRBCS
- D 1/2 NS as replacement fluid
- Maintenance with RL/NS
- Third space losses 8 ml/kg/hr
- Warming blanket, warm IV fluids.

Postoperative

- Usually extubated at the end of surgery
- Postoperative ventilation if:
  - Chest contaminated
  - Associated anomalies
  - Premature infant
  - Respiratory distress syndrome.
- IMV/PEEP/supplemental O_2 depending on severity
- Nurse in lateral and supine position
- Percussion and vibration of chest only after third day
- Prolonged intubation if tracheomalacia/bronchomalacia.

CONGENITAL DIAPHRAGMATIC HERNIA[15]

Introduction

Failure of closure of diaphragm allowing abdominal contents to herniate into the thorax.

Classification

- Absent diaphragm
- Diaphragmatic hernia
  - Bochdaleks posterolateral hernia (80%)
  - Morgagnis anterior hernia (2%)
  - Paraesophageal hernia (15–20%).
- Eventration.

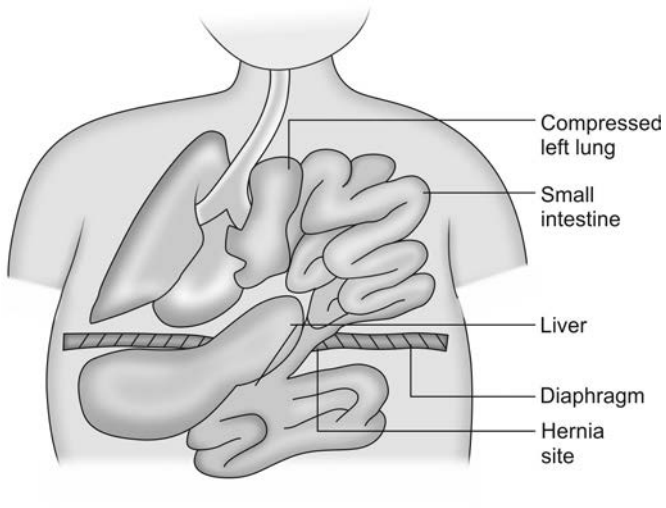


Fig. 4.3: Congenital diaphragmatic hernia[15]

Clinical Features

- Classical *triad*-dyspnea
  - Cyanosis
  - Apparent dextrocardia.
- Scaphoid abdomen with barrel shaped chest
- Bowel sounds in chest, reduced air entry in chest
- Displaced heart sounds
- Hypoxia, acidosis.

Investigations

- Antenatal ultrasonography
- Complete blood count
- Serum electrolytes, Calcium, Glucose.
- Arterial blood gas
- Chest X-ray:
  - Bowel loops in chest
  - Mediastinal shift
  - Absent lung markings.

Pathophysiology

- Pulmonary dysplasia due to:
  - Compression by bowel
  - Global embryopathy.
- Pulmonary hypertension
- Reduced preload due to IVC obstruction
- Reduced cardiac output.

Treatment

- Severe pulmonary HTN—delay surgery
- Mild to moderate pulmonary HTN—wait for 48–72 hrs
- Mild pulmonary HTN—take for surgery
- Moderate—severe pulmonary HTN—plan for HFOV till pulmonary pressures controlled, then shift to conventional ventilation and surgical correction.

Techniques of Repair

- Primary closure
- Staged procedure
- VATS
- FETO (fetoscopic tracheal occlusion).

Procedure

- Via transabdominal left subcostal incision
- Bowel contents replaced into abdomen
- Right thoracotomy done with abdominal incision
- Diaphragmatic defect is closed
- Muscle flap or synthetic mesh closure if large defect.

Modes of Ventilation

- Conventional ventilation:
  - Gentle ventilation
  - With low peak inspiratory pressures
  - Prevent over distension
  - Maintain preductal SpO_2 > 90%
  - Prevent hypoxia, hypercarbia and acidosis
  - Ideally not to involve use of paralysis, hyperventilation or alkalosis
  - Permissive hypercapnea
  - Dobutamine or tolazoline tried if persistent hypoxemia.
- Surfactant therapy:
  - Has poor results unless given prophylatically before first breath
  - Exosurf 5 ml/kg q12h 3 doses.
- Inhaled nitric oxide therapy:
  - Reduces need for ECMO

  - Causes significant improvement.
- High frequency oscillatory ventilation
  - Reduces need for ECMO
  - Yet to be proven to have positive impact on survival.
- ECMO
  - For CDH with severe hypoxemia
  - Mainstay of therapy
  - Useful for severe pulmonary HTN and hyperplasia.
- Newer techniques:
  - PCV with permissive hyper apnea < 60 mm Hg
  - Maintain preductal SpO_2 between 85–95%.

Preoperative Preparation

- Informed consent
- Nasogastric tube to reduce abdominal distension
- venous access in upper limbs
- Prevent hypothermia
- Lateral nursing of neonate with hernia side down.

Anesthetic Considerations

- Full stomach
- Potential hypoxia and hypotension
- Difficult IV access
- Difficult intubation
- Primary pulmonary HTN and right ventricular failure
- Avoid hypoxia, hypercarbia and acidosis
- Hypothermia.

OT Preparation: (SOAPME)

- **S**uction
- **O**xygen source
- **A**irway equipment
- **P**harmacy:anesthetic drugs
- **M**onitors calibrated and ready
- **E**mergency drugs.

Anesthetic Management

Monitors

- Pulse oximeter
- End tidal carbon dioxide
- ECG
- Temperature
- Airway pressure
- Esophageal stethoscope
- Urine output
- Invasive BP
- Precordial stethoscope right axilla
- 2 Pulse oximeters used for preductal and postductal measurements.

Induction

- Preoxygenation
- Rapid sequence induction
- High dose fentanyl 2–5 mics/kg to reduce pulmonary HTN
- Avoid positive pressure ventilation or mask ventilation
- Nasogastric tube to decompress stomach
- Avoid lower limb IV access as raised intra-abdominal pressure reduces venous return
- If umbilical v and a are cathterized by neonatologist, maintain both during surgery.

Maintenance

- Balanced anesthesia with O_2 + air + isoflurane + fentanyl boluses + NDMR
- Avoid N_2O to avoid abdominal distension (difficult closure)
- Maintain deep planes to reduce PVR
- Vasopressors required to increase SVR and reduce shunt fraction
- Avoid increasing R – > L shunt
  - Hypoxia
  - Acidosis
  - Hypercarbia
  - Hypothermia.
- Single dose caudal or catheter can be threaded to thoracic level
- Replace significant blood loss.

Ventilation

- Adjust FiO_2 to keep:
  - PaO_2 80–100 mm Hg
  - SpO_2 95–98%.
- Small tidal volume to keep:
  - Airway pressure < 20–30 cm H_2O
  - $PaCO_2$ > 25–30 mm Hg.

Complications

- 'Honeymoon phenomenon'[15]
  - Smooth early recovery followed by sudden pulmonary HTNsive crisis.
  - Postoperative ventilation beneficial
  - Wean slowly over 48–72 hrs

  - Occurs due to:
    - Impaired visceral perfusion
    - Reduced diaphragmatic excursion
    - Worsened pulmonary compliance
    - Raised intra-abdominal pressure.
- Hypoxia
- Distension of stomach
- Persistant pulmonary hypoplasia
- Contralateral pneumothorax
- IVC compression, Hypotension
- Cardiac arrest.

Management of Pulmonary Hypertensive Crisis

- Maintain systemic blood pressure
- Reduce pulmonary vascular resistance
- Reverse R→ L shunt
- Reduce barotrauma
- Improve SpO_2 and O_2 delivery to tissues
- Avoid polycythemia, alkalosis, sedation and NMBAS
- Pulmonary vasodilators
- ECMO.

Postoperative Management

- Maintain PaO_2 > 150 mm Hg
- Close fluid management
- Hemodynamic monitors.

HERNIA REPAIR[15]

Introduction

Protrusion of part or whole of a viscus from its normal position through an opening in the wall of its containing cavity.

Types

- Inguinal
- Femoral
- Epigastric
- Umbilical
- Paraumbilical
- Obdurator
- Spigelian
- Lumbar
- Gluteal
- Perineal
- Sciatic
- Diaphragmatic
- Incisional
- Hiatus
- Femoral hernia more common in multiparous.

Preoperative Assessment

- Mostly daycare surgery
- History:
  - Chronic cough
  - Constipation
  - Obesity with concurrent diseases
  - Pregnancy.
- If bowel obstruction:
  - Vomiting
  - Dehydration
  - Fluid and electrolyte balance
  - Hypovolemia.
- Investigations:
  - Complete blood count
  - ECG
  - Chest X-ray
  - Arterial blood gases
  - Pulmonary function tests.

Anesthetic Techniques

GA with ETT

- For large abdominal wall hernias which need muscle relaxation
- Hernias with increased aspiration risk
- Obstructed/strangulated hernias
- Hemodynamically unstable patients.

GA with LMA

- Anxious patients
- Children
- Obese patients
- Inguinal/femoral hernia (minimal risk of aspiration).

Regional Anesthesia

- For elective hernia repair
- High risk patients
  - Spinal
  - Epidural
  - Caudal
  - Inguinal field block
  - Ilioinguinal/iliohypogastric N block.

Local Anesthesia

- For those unfit for other techniques

- Not suitable for anxious/obese/uncooperative patients.

Choice of Technique

- If > 5 kgs, GA with LMA
- If < 5 kgs, ETT with IPPV
- Avoid ilioinguinal block in neonates as LA spread reduces surgical field
- Caudal block if bilateral hernia
- Spinal anesthesia usually inadequate if bilateral hernia.

Premedication

- Informed consent
- NPO guidelines
- Antiaspiration prophylaxis:
  - Ranitidine 1 mg/kg IV
  - Metaclopramide 0.15 mg/kg.
- IV fluids if vomiting/dehydration
- Midazolam 0.05–0.15 mg/kg IV for anxiolysis
- Glycopyrrolate 10 µ/kg IV
- Oral analgesics
- No sedation if increased risk of aspiration
- Antibiotic prophylaxis.

Monitor

- Pulse oximetry
- NIBP
- ECG
- End tidal CO_2
- Invasive BP if sick infant.

Induction

- NGT if strangulated
- *Rapid sequence induction* with gentle cricoid pressure if strangulated/obstructed
- Epidural insertion if large laparotomy wound.

Maintenance

- O_2 + air + Isoflurane
- Avoid N_2O
- Adequate muscle relaxation if large abdominal hernias
- Multimodal intraoperative analgesia
- Extubate with minimal coughing to protect hernia repair
- Prevent hypothermia if large wound
- Up to 15 ml/kg third space losses if large wound.

Postoperative

- Multimodal analgesia with opioids, NSAIDs/wound infilteration with LA
- Chest physiotherapy for patients with respiratory disease
- Consider DVT prophylaxis
- Diclofenac/paracetamol PR or PO.

INGUINAL FIELD BLOCK

Introduction

Blocks ilioinguinal, iliohypogastric, genitofemoral N and branches from intercostal N.

Technique

- 2.5 cm medial to anterior superior iliac spine
- Needle inserted perpendicular to skin
  - One LOR as it passes external oblique aponeurosis inject 10 ml LA to block iliohypogastric N
  - 10 ml injected between internal oblique and transverse abdominis to block ilioinguinal N
  - Withdraw needle to plane superficial to external oblique
  - Inject subcutaneously in fanwise fashion to block subcostal and lower intercostal N
  - Palpate deep inguinal ring (1.5 cm above midpoint of inguinal ligament). Insert needle into canal and inject 5 ml to block genital branch of genitofemoral N
  - Subcutaneous infilteration at medial end of incision or fanwise from pubic tubercle blocks contralateral innervation.

Complications

- Intravascular injection: LAST
- Intraperitoneal injection
- Femoral N block—I/L weakness of legs.

ILIOINGUINAL/ILIOHYPOGASTRIC BLOCKS[2]

Anatomy

- Arise from T12–L1
- Pass over quadratus lumborum
- Pierce internal oblique muscle just medial to anterior superior iliac spine
- Becomes subcutaneous by piercing external oblique aponeurosis 2–3 cm superior to superficial inguinal ring
- Sensory and motor supply to inguinal region and perineum

- Needle to lie between internal oblique muscle and external oblique aponeurosis.

Indications
- Inguinal herniorrhaphy
- Orchiopexy.

Drugs
- 0.25% bupivacaine
- 2–10 ml depending on size of patient.

Technique
- Draw line from ASIS to umbilicus
- Point at one fourth this line from ASIS
- 24–26 number needle at this point perpendicular to skin
- Advance till LOR as it pierces external oblique aponeurosis
- 0.3 ml/kg LA injected
- Advance further till it pierces internal oblique muscle and LOR felt
- 0.1–0.2 ml/kg LA injected between internal oblique muscle and transverse abdominis muscle
- Gently massage the area to spread the LA
- Block genital branch of genitofemoral N if required with 1–2 ml LA.

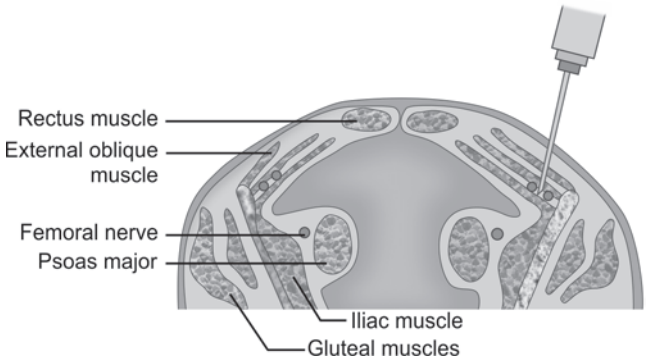


Fig. 4.4: Ilioinguinal/iliohypogastric nerve block[2]

Complications
- Intravascular injection
- Intraperitoneal injection
- Femoral N block.

ANESTHESIA FOR STRABISMUS SURGERY[15]

Introduction
Deviation of visual axis of one eye with respect to the other.

Types
- Comitant Strabismus:
  - Esotropia/Convergent
  - Exotropia/Divergent.
- Incomitant Strabismus:
  - Paralytic
  - Restrictive.

Comitant Strabismus
- Abnormal relation of eyes retained in all directions of gaze
- Abnormal afferent pathways/central mechanism
- Normal efferent pathway
- Esotropia common in hypermetropes
- Exotropia common in myopes.

Incomitant Strabismus
- Abnormal efferent pathways
- Normal afferent pathway and central pathways
- Paralytic due to CN III trauma
- Restrictive due to muscular fibrosis/local space occupying lesions of orbit.

Time of Surgery
- Visual maturation occurs by 5 years
- Thus has to be corrected by 4–5 years age
- Preferably at 18 months
- In older children done mostly for cosmesis.

Anesthetic Considerations
- Remote airway
- Forced duction test
- Profound analgesia with minimal muscle relaxation
- Risk of malignant hyperthermia
- Risk of PONV—Oculogastric reflex
- Oculocardiac reflex
- Quiet emergence without coughing.

Preoperative Assessment
- URTI
- Other myopathies
- History of drug intake/eye drops, especially echothiophate as it reduces plasma cholinesterase
- Levels increased duration of action of succinylcholine
- Avoid excess preoperative sedation
- IV glycopyrrolate 10 µ/kg
- PO midazolam 0.5 mg/kg half hour before surgery.

Monitors
- Pulse oximetry
- End tidal carbon dioxide

- ECG
- NIBP
- Temperature
- Precordial stethoscope.

Induction

- Inhalational induction with halothane/sevoflurane if no IV line
- IV induction with thiopentone 3–4 mg/kg + atracurium
- Ketamine avoided due to nystagmus and blepharospasm
- Droperidol 75 µ/kg 15 min before manipulation of extraocular of EOM
- 0.25 mg/kg metaclopramide or ondansetron 0.15 mg/kg after induction
- Dexamethasone 0.15 mg/kg IV after induction
- Minimize opioid use.

Maintenance

- O_2 + N_2O + Halothane/sevoflurane
- Controlled ventilation
- If oculocardiac reflex develops:
  - Stop stimulus
  - Increase anesthetic depth
  - Assess ventilation
  - IV atropine if persistant.
- Warming blankets.

Extubation

- Smooth emergence mandatory
- Neostigmine 0.05–0.06 mg/kg with glyco 0.01 mg/kg
- Extubate lateral position before fully awake.

Postoperative

- Correct fluid deficits
- Delay ingestion of fluids to reduce chances of PONV
- Thin juice once fully awake
- Pain:
  - Paracetamol 30 mg/kg PR at induction
  - Ketorolac 0.75 mg/kg IV.
- Do not arouse forcefully.

LMA FOR STRABISMUS SURGERY

Advantages

- No need for muscle relaxants
- Lighter planes for tube tolerance
- Reduced hemodynamic changes
- Reduced straining/coughing on extubation
- Armoured LMA preferred.

Disadvantages

- Increased risk of aspiration
- LMA displacement intraoperatively
- Increased risk of oculocardiac reflex due to:
  - Lighter planes
  - Spontaneously breathing patient.

Forced Duction Test

- Done in incomitant strabismus
- To differentiate paretic muscle and restrictive force preventing ocular motion
- Surgeon grasps sclera near corneal limbus
- Moves eye in each field of gaze
- Assesses tissue and elastic properties
- Gives clues about site of mechanical restriction of EOM
- Valuable for:
  - Paralysis of EOM
  - Previous orbital trauma
  - Previous strabismus surgery.

Anesthetic Significance

- Cannot be performed for 20 minutes after succinylcholine as:
  - Skeletal muscle paralysis lasts only < 5 minutes
  - Force required to rotate globe remains high for 15–20 mins
  - Increased chances of oculocardiac reflex during test.
- Can be performed after intubation with non depolarising agents
- Can be done under deep inhalational anesthesia.

FOREIGN BODY ASPIRATION[15]

Introduction

A leading cause of death between 1–3 years age.

Types of Foreign Body

- Organic:
  - Peanuts
  - Custard apple
  - Tamarind seeds
  - Popcorn
  - Jelly beans.

- Inorganic:
  - Beads
  - Buttons
  - Coins
  - Small toys
  - Pins.

Phases of Aspiration

Immediate

- Choking
- Gagging
- Coughing
- Wheezing
- Stridor.

Asymptomatic Second Phase

- Few minutes to months after first phase
- Depends on location, degree of obstruction and type of foreign body.

Renewed Symptomatic Phase

- Airway infection and inflammation
- Repeated coughing bouts, sputum, wheezing, fever, hemoptysis.

Clinical Features

- History:
  - Foreign body aspiration
  - Coughing, choking, stridor on feeding
  - Voice changes, barking cough—laryngeal edema
  - Stridor, aphonia, hoarseness—foreign body in trachea/larynx.
- Examination:
  - Chest retraction—upper airway obstruction
  - Unilateral diminished breath sounds
  - Bilateral reduced breath sounds: Tracheal foreign body.
- Investigations:
  - Chest X-ray:
    - > 90% radiolucent
    - Mediastinal shift
    - Ipsilateral atelectasis
    - Contralateral hyperinflation
    - Absence of mediastinal shift on lateral decubitus film.

Differential Diagnosis

- Asthma
- Croup
- Pneumonia
- Bronchitis
- Tracheomalacia
- Bronchomalacia
- Vocal cord dysfunction
- Psychogenic cough.

Complications

- Acute:
  - Organic foreign body—swell up and cause airway edema
  - Oil containing seeds—chemical inflammation
  - Vegetable seeds swell and fragment—distal airway obstruction.
- Chronic:
  - Tracheal/bronchial stenosis
  - Bronchiectasis
  - Lung abscess
  - Tissue erosion
  - Pneumomediastinum
  - Pneumothorax.

Management

Emergency

Out of Hospital Management

- If complete obstruction:
  - Back blows, Chest thrust—infants
  - HEIMLEICHS maneuvre, abdominal thrust in children
  - Never use blind finger sweeps
  - CPR if collapse.
- If incomplete obstruction:
  - Encourage coughing and spontaneous respiration
  - Shift to hospital.

In Hospital Management

- Phase I presentation:
  - Rigid bronchoscopy is *treatment of choice.*
- Phase II presentation:
  - Bronchodilators
  - Antibiotics
  - Steroids
  - Chest physiotherapy
  - Rigid bronchoscopy.

Preoperative Preparation

- Informed consent
- No preoperative sedation
- NPO guidelines if not emergency as airway not secure during rigid bronchoscopy

  - 6 hrs solids
  - 2 hrs clear fluids.
- Antibiotics coverage
- Steroids and bronchodilator therapy
- Antiaspiration prophylaxis:
  - Metaclopramide 0.15 mg/kg IV
  - Ranitidine 1 mg/kg IV.

OT Preparation

- Suction
- Oxygen source: Pipeline/cylinder
- Airway equipment
- Pharmacy: Anesthetic drugs preloaded
- Monitors: Calibrated
- Emergency drugs—especially atropine.

Monitors

- Pulse oximetry
- NIBP
- ECG
- End tidal CO_2 not reliable as most expired gases escape around the bronchoscope
- Pulse oximetry—lag phase before showing desaturation.

Induction

IV Induction

- *Rapid sequence induction* with gentle cricoid pressure
- IV line with EMLA cream
- Propofol/thiopentone used
- Propofol better as it is stable in reactive airway
- Early cricoid pressure can cause coughing and laryngospasm
- Forceful cricoid pressure causes airway obstruction
- ETT may dislodge highly placed foreign body
- High complete obstruction—dislodge foreign body with ETT into right
- Mainstem bronchus to allow some ventilation
- Large/swollen foreign body—tracheostomy
- Avoid muscle relaxants till location of foreign body is determined.

Inhalational Induction

- Less preferred
- Maybe delayed if foreign body is highly placed
- With sevoflurane/halothane
- N_2O avoided as it may cause distal lung expansion
- Topical LA spray with 10% lidocaine to reduce coughing on laryngoscopy
- Dose up to 4 mg/kg lidocaine.

Technique

- Using ventilating bronchoscope
- Visualizes airway and ventilates simultaneously
- 2.5–6 mm ID sizes
- ED is 2 mm larger
- Whole airway and subglottic area visualized first
- Forign body removed
- Tracheobronchial tree visualised for any remnants and airway inflammation
- Vigorous irrigation and suction to remove secretions.

Postoperative

Ventilation

- Intubate if atelectasis/airway edema
- Use O2 – Air mixture for ventilation
- Nitrogen helps to keep distal alveoli distended.

Management

- Steroids, bronchodilators and antibiotics
- Nebulized racemic epinephrine
- Humidified O2
- Monitor for airway obstruction.

Complications

- Trauma to airway and teeth
- Dislodgement of foreign body
- Complete airway obstruction
- Barotrauma
- Hypoxia and hypercarbia:
  - Frequently remove telescope
  - Withdraw bronchoscope to midtrachea and ventilate.
- Bronchospasm—bronchodilators, albuterol nebulization
- Pneumothorax
- Iatrogenic tracheoesophageal fistula.

Modes of Ventilation

Spontaneous Ventilation

- Advantages:
  - Reduced risk of foreign body dislodgement
  - Continuous ventilation during bronchoscopy
  - Depth of anesthesia can be increased by increasing volatile anesthetic concentration
  - Rapid airway assessment possible once foreign body is removed.
- Disadvantages:
  - Requires deep planes at scopy
  - May cause hypoventilation

- May cause arrhythmias
- Requires assistance.

Controlled Ventilation

- Advantages:
  - Airway immobilized
  - Good exposure
  - Less volatile anesthetic doses required
  - Reduced atelectasis
  - Better oxygenation.
- Disadvantages:
  - Maybe difficult if not airtight
  - Maybe impossible during suction/instrumentation
  - May dislodge foreign body distally.

Jet Ventilation

- Causes barotrauma
- Dislodges foreign body distally.

CIRCUMCISION[15]

Introduction

Excision of prepuce or foreskin around the penis.

Indications

- Phimosis is only absolute indication
- Cultural and religious reasons.

Preoperative Assessment and Preparation

- Rule out active URTI
- Rule out bleeding diathesis/previous anesthesia
- No investigations required unless clinically indicated
- NPO orders
- Informed consent for local anesthesia and rectal suppository
- Topical EMLA @ IV site 60–90 mins before surgery.

Premedication

- If < 2 years:
  - Paracetamol 15 mg/kg PO
  - Paracetamol 30 mg/kg PR.
- If > 2 years:
  - Diclofenac 1 mg/kg PO
  - Diclofenac 1 mg/kg PR
  - Midazolam 0.5 mg/kg 45 min before
  - IV glycopyrrolate 10 µ/kg.

Anesthetic Technique

- GA with LMA and regional block:
  - Caudal if < 5 kgs
  - Penile block if > 10 kgs
  - Ring block if > 5 kgs.

Monitoring

- Pulse oximetry
- NIBP
- ECG
- Precordial stethoscope.

Induction

- IV/inhalational depending on presence of IV line
- Spontaneous ventilation
- Low opioid requirement as regional anesthetic supplementation.

Extubation

- Thorough suction
- Deep extubation to reduce laryngospasm.

Postoperative

- Very painful procedure
- Good postoperative analgesia required
- Topical lidocaine gel applied frequently
- Gel should contact suture lines
- Oral PCT 15 mg/kg TID.

Complications

- Urinary retention
  - Inadequate analgesia
  - Persistant caudal block.
- Bleeding
- Nausea and vomiting.

PENILE BLOCK[2,15]

Anatomy

- Distal two thirds of penis supplied by:
  - Dorsal N of penis (branch of pudendal N)
  - N passes under pubic bone and crosses subpubic space from back to front
  - Enters suspensory ligament and then penis
  - Runs along inner side of BUCKS fascia accompanied by artery and vein.
- Proximal one third supplied by branches from:
  - Perineal N
  - Ilioinguinal N
  - Genitofemoral N.

- Suspensory ligament divides subpubic space into 2 separate compartments
- Subpubic space filled with areolar tissue
- Covered with membranous layer of superficial fascia or ***Scarpas*** fascia which continues as ***Bucks*** fascia.

Indications

- Circumcision
- Hypospadiasis
- Preputioplasty
- Retraction of prepuce.

Drugs

- Bupivacaine 0.25%
- Ropivacaine 0.25%
- Lidocaine 1%
- 2 ml for infants
- Up to 10 ml for adolescent
- *Do not* use adrenaline as arteries are end arteries.

Technique

- Complete asepsis
- 21 # regional block needle
- Palpate lower border of pubic symphysis with index finger and retract penis
- Insert needle perpendicular to skin between fingers and pubic arch
- Advance till bone is struck or slight loss of resistance felt
- If bone is struck, walk needle inferiorly until free
- Once LOR felt, inject:
  - Half LA @ 11 o'clock position
  - Remaining half LA @ 1 o'clock position
  - Final 1 ml on underside of penis.
- Repeat on the other side.

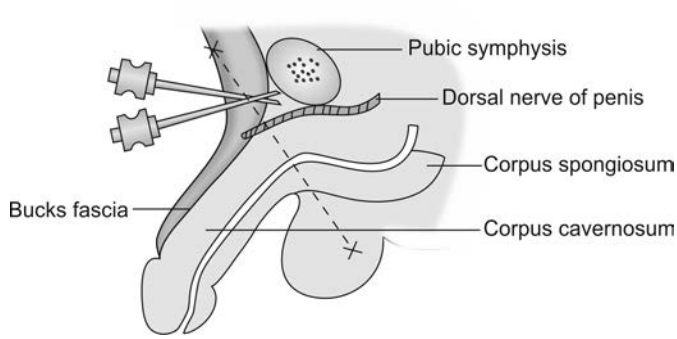


Fig. 4.5: Penile block[2]

Complications

- IV injection—LAST
- Damage to dorsal N of penis—glans necrosis
- Compressive hematomas
- Penile necrosis if adrenaline used.

CHAPTER

5

Blood and Blood Products

COLLOID VS CRYSTALLOID

Property	Crystalloid	Colloid
Molecular weight	Low molecular weight	High molecular weight
Tonicity	Iso/hypo/hypertonic	Hypertonic
Starling forces	Increases hydrostatic pressure	Increases oncotic pressure
Permeability	Pass through semipermeable membrane	Does not pass
Vol expansion	Expands intestitial volume	Expands plasma volume
Duration of action	Lesser	Longer
Half life	30 minutes	2 hours
Replacement ratio	Replaced in 3:1 ratio	Replaced in 1:1 ratio
Allergic reaction	Rare	Common
Edema	Precipitates intestitial edema	Reduces cerebral and pulmonary edema
Blood grouping	Does not interfere	Dextrans interfere by causing Rouleax formation
Clotting	Does not interfere	Interferes with clotting
Acute renal failure	Does not cause	Contributes to ARF
Cost	Cheap	Expensive
Example	RL, NS, DNS	3% hetastaren alb doctrine

HYDROXYETHYL STARCH

Introduction

- Complex polysaccharide which is used for intravenous volume expansion in the perioperative period
- Colloid solution.

Clinical Pharmacology

- Artificial colloid obtained from starch
- Contains amylopectin (highly branched and more stable component of starch)
- Average molecular weight 450,000 Da
- Available as 10%, 6%, and 3% solution.

Pharmacokinetics

- Degraded in serum and tissues by amylase
- Excreted mainly in kidneys with long elimination $T_{1/2}$
- Initial volume expansion of 62% of infused volume is obtained
- 100% of influenced volume volume expansion occurs over.

Strength	Plasma volume expansion period
Hestar 3%	1–2.5 hours
Hestar 6%	3–4 hours
Hestar 10%	4–8 hours

- Duration of volume expansion lasts around 24 hours
- 50% of influenced volume detected after 3 hours
- 9% can be detected after 24 hours in case of 3 % HES.

Indications

- Prophylaxis and treatment of hypovolemia and shock due to:
  - Surgery
  - Trauma
  - Infection
  - Burns:
    - If burns > 30% of body surface area
    - If ≥ 3–4 lts of crystalloids has been given over 18–24 hours post burns
- Therapeutic hemodilution to improve blood rheology
- Therapeutic plasma exchange
- Preloading for spinal anesthesia
- Acute normovolemic hemodilution (autologous blood transfusion)
- Cardiac priming: not recommended as bleeding occurs in post bypass period.

Dosage and Administration

- Hematocrit of 30% is taken as threshold for use of colloidal volume substitute
- Due to possibility of anaphylactic reaction:
  - Initially 10–20 ml hestarch is to be infused slowly
  - Only then should the actual rate of infusion start
- Rapid infusion of hestarch may cause circulatory overload and tissue damage. Thus recommended dose per hour:
  - In hemorrhagic shock up to 20 ml/kg/hour or 0.33 ml/kg/min
  - Septic shock and burns: lower rates of infusion
  - Children < 10 years: not to exceed 15 ml/kg/hour
  - Hemodilution: 500 ml in 4–6 hours, 1000 ml in 8–12 hours
- Recommended maximum daily dosage:
  - Hestar 3%: up to 66 ml/kg/day
  - Hestar 6%: up to 33 ml/kg/day
  - Hestar 10%: up to 20 ml/kg/day

Contraindications

- Severe hemorrhagic defects
- Severe congestive cardiac failure
- Renal failure with oliguria/anuria
- Chronic hepatic disease
- Patients allergic to starch
- Hyperhydration states
- Early pregnancy use is contraindicated unless benefits overweigh hazards to fetus.

Adverse Reactions

- Hypersensitivity
  - Rare as hestarch is nonantigenic
  - Rash/pruritis/anaphylaxis: Stop administration
- Serum macroamylasemia may occur: Serum amylase as a marker of pancreatic disease not reliable for 3 to 5 days after HES infusion
- Nausea and vomiting rarely
- Pruritus due to deposition of HES in skin: Treated with capsaicin
- Hematological:
  - May interfere with clotting time as it decrease levels of FVIII and vWF
  - It also coats platelet surface and causes platelet dysfunction
  - APTT prolongation occurs: Not used in neurosurgery patients
  - Can compromise hemostasis after cardiac surgery
- Does not interfere with blood grouping, typing or cross matching
- Circulatory overload
- Hyperchloremic metabolic acidosis.

Interactions

- May increase renal toxicity of amino sugar like kanamycin, gentamicin and paramomycin: Concomitant use avoided
- Not to be mixed with citrated blood/oily suspensions for injection.

Advantages

- Added oncotic properties
- Increase duration of hemodynamic effects due to long elimination $T_{1/2}$
- Low antigenicity: Infrequent anaphylaxis
- Absent disease transmission
- Low cost compared with albumin.

Composition

Each 100 ml	HES 3%	HES 6%	HES 10%
HES	3 g	6 g	10 g
NaCl	0.9 g	0.9 g	0.9 g
Water	Gs	Gs	Gs
Avg. molecular weight	200000D	200000D	200000D
mOsm/L	308	308	308
mEq/L	Na-154, Cl-154	Na-154, Cl -154	Na – 154, Cl - 154
pH	3.5–7	3.5–7	3.5–7

MEASUREMENT OF SURGICAL BLOOD LOSS[1,3,4]

Introduction

- Amount of blood lost during surgery can be measured by:
  - Assessing the amount of blood lost from the patient
  - Assessing the amount remaining in the patient.

Methods

- Visual observation of degree of bleeding:
  - Measure of blood in surgical container
  - Estimating blood on surgical sponges and laparotomy pads
  - Fully soaked 4 × 4 sponge contains approximately 10 ml of blood
  - Soaked laparotomy pads contain 100–150 ml of blood
  - 1 ml blood is taken to be equal to 1 gm blood.
- Clinical estimation:
  - Serial haematocrit/Hb concentration reflects ratio of blood loss to plasma
  - This does not necessarily reflect blood loss
  - Serial Hb measurement is especially useful during long procedures.
  - Clinical signs:
    - Hypotension, low CVP, tachycardia
    - Palor, diaphoresis, reduced urine output
- Gravimetric method:
  - Simplest and most commonly used method
  - Blood loss estimated by measurements of gain in weight of swabs and towels
  - This is taken together with measurements of contents of suction bottle
  - 1 ml blood assumed to weigh 1 gm
  - Disadvantages:
    - Weighing of swabs underestimates blood loss by 25%
    - This is because it does not take into account:
      - Evaporation
      - Blood lost in floor, drapes and body cavities
  - Overestimating of blood loss may occur if the swabs also measure urine, pus and other fluids during mopping.
- Dilution Methods:
  - Colorimetric method:
    - Swabs and towels are mixed thoroughly with known volume of fluid
    - Change in optical density of water is measured
    - This is done at the isobestic absorption wavelength of Hb
    - This is related with Hb concentration of patients blood

      Blood loss = $\frac{\text{colorimeter reading} \times \text{volume of solution}}{200 \times \text{patients Hb (gm\%)}}$
    - Alternatively, change in electrical resistance due to blood electrolytes in the bath can be measured
      - Uses:
        - In operations involving complex exchanges of blood
        - Extracorporeal circulation
        - Useful to wash out bladder in TURP
      - Disadvantages: Errors due to:
        - Incomplete extraction
        - Contamination with bile
- Use of radioactive tracer dilution methods:
  - Method:
  - Tracers used:
    - Patients RBCs labelled with Cr^{51} following incubation with the isotope
    - Pooled human albumin labelled with 1^{125} or I^{131}
  - I^{125} is the *isotope of choice* as it emit less energy
  - Tracer should remain in the compartment whose volume is being measured
  - The activity of the tracer is first measured and then injected IV
  - The activity remaining in the empty syringe is measured
  - This is deducted from the amount of isotope injected

- After 10–15 mins, a sample of blood is withdrawn from the opposite arm
- This is to ensure that there is no contamination from isotope remaining at the injection site
- The activity of this sample is then measured and the dilution volume calculated from the result
- Repeated measurements can be made to estimate the change in blood volume
- Allowance is made for residual radioactivity from previous measurements.
- Errors:
  - In a shocked patient, the time taken for mixing throughout the blood volume may be more
  - So, measurement is a better indicator of effective circulating volume than the total volume
  - Also, loss of injected isotope by vigorous hemorrhage (before mixing) may happen.

American College of Surgeons Classes of Acute Hemorrhage

Factors	Class I	Class II	Class III	Class IV
Blood loss (ml)	< 750	750–1500	1500-2000	≥ 2000
Blood loss (% blood volume)	15	15–30	30–40	≥ 40%
Pulse (bpm)	100	100	120	≥ 140
Blood pressure	Normal	Normal	Reduced	Reduced
Pulse pressure	Normal or ↑	Decreased	Decreased	Decreased
Capillary refill test	Normal	Positive	Positive	Positive
Urine output (ml/hr)	30	20–30	5–10	Negligible
CNS mental status	Sligjhtly anxious	Mildly anxious	Anxious, confused	Confused, lethargic
Respiratory rate (/min)	14–20	20–30	30–40	35
Fluid replacement (3:1 rule)	Crystalloid	Crystalloid	Crystalloid + blood	Crystalloid+ blood

TRANSFUSION TRIGGER[1,3]

Introduction

Transfusion trigger refers to the hemoglobin level below which transfusion of RBCs is indicated.

Considerations for Transfusion

- Age
- Blood volume
- Cardiovascular status
- Cardiac output
- Blood loss
- Intramucosal pH
- Oxygen extraction ratio.

ASA 1996 Guidelines[1]

- Transfusion rarely required if Hb >10 gm%
- Transfusion always indicated if Hb < 6 gm%
- Hb between 6 and 10 g% transfusion depends on complications of inadequate oxygenation and cardiovascular status
- Use of blood just based on Hb, not considering other conditions is not indicated
- Whenever possible use:
  - Acute normovolemic hemodilution
  - Preoperative autologous blood donation
  - Postoperative modifications to reduce blood loss
- Indication for autologous blood transfusion more liberal.

Habibi Recommendations[1]

Transfusion indicated if:

- Hb ≤ 8 g% in all patients
- Hb ≤ 10 g% in ischemis heart disease and emphysema
- Hb ≤ 10 g% if autologous blood transfusion
- Hb ≤ 12 g% in ventilator dependant patient

- If blood loss ≥ 20% blood volume
- Blood loss ≥ 100 ml in pediatric patients.

Herbert Recommendations

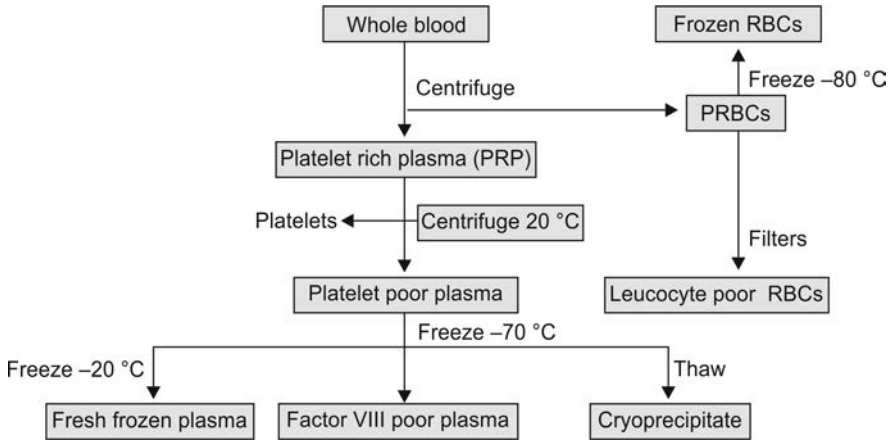
- If Hb ≤ 10 g% in unstable angina and anterior wall MI
- Hb between 10 and 12 g% in critically ill patients.

BLOOD COMPONENT THERAPY[1,2,3]

Introduction

Transfusion therapy which is aimed at the need to correct deficiency of specific component of whole blood by administration of that specific fraction instead of giving whole blood.

Separation of Whole Blood



Blood Components

- Erythrocyte preparations:
  - PRBCs
  - Washed RBCs
  - Leukocyte poor RBCs
  - Frozen RBCs
- Leukocyte preparations:
  - Granulocytes
  - Mononuclear cells
- Platelets
- Plasma fractions:
  - FFP
  - Cryoprecipitate
  - Platelet rich plasma
  - Fractionated plasma:
    - Factor VIII concentrate, factor IX concentrate
    - Autothrombin III concentrate
    - Prothrombin complex
    - Albumin
    - Intravenous immunoglobins.

Hazards of Blood Component Therapy

Immediate Reactions

- Febrile reactions
- Allergic reactions
- Acute hemolytic reaction
- Sensitivity to leukocytes and platelets
- Noncardiogenic pulmonary edema
- Bacterial contamination
- Circulatory overload
- Dilutional coagulopathy
- Air embolism.

Delayed Reactions

- Delayed hemolytic reaction
- Post-transfusion purpura
- TA- GVHD
- Transmission of hepatitis B, C, CMV, HIV, HTLV 2, WNV.

ERYTHROCYTE PREPARATIONS[1,3,13,14]

Packed Red Blood Cells

Manufacture

- Obtained by apheresis collection or prepared from anticoagulated whole blood.
- Following centrifugation, plasma is removed and 100 ml of additive solution is added.
- Each unit contains:
  - 200 ml RBCs

  - Plasma < 50 ml
  - Hematocrit of 55–60%
- Thus, it contains same amount of Hb as whole blood but much of plasma is removed.

Indications

ASA 1996 Guidelines

- Anemia:
  - Rarely required when Hb > 10 gm%
  - Almost always indicated when Hb < 6 gm%
  - The decision to transfuse between 6 and 10 g% depends on:
    - Cardiopulmonary risk factors
    - Ongoing blood loss
    - Clinical judgment
  - Usually, transfusion trigger = 7g%
  - Transfusion trigger of 10 gm% if MI/emphysema (***Habibi,*** *et al.)*
  - Transfuse when Hb < 12 gm% if mechanically ventilated (***Habibi,*** *et al.)*
- For anemic patients, CCF or RBC exchange in thalassemias
- Acute blood loss: If blood loss < 1500–2500 ml in adults
- Pediatric patients.

Shelf Life

21–42 days (at 1–6 °C)

Dosage

Each 2 units or 15 ml/Kg increases Hb by 2 g/dl.

Administration

- Administered after reconstitution with crystalloid/colloid which:
  - Does not contain calcium: Causes clotting
  - It is not hypotonic: Causes hemolysis
- Solutions recommended are:
  - 5% Dextrose in 0.4% saline
  - 5% Dextrose in 0.9% saline
  - 0.9% saline
  - Normosol R with pH of 7.4.

Leukocyte Poor Red Cells

Manufacture

- Prepared during procuring blood or at the time of transfusion by:
  - Using specially designed filters
  - Sedimentation
  - Inverted centrifugation
  - Filtration through nylon/cotton fibers
  - Saline batch washing
  - Frozen thawed red cells/blood through micro-aggregate filters
- 99.9% WBCs and residual WBC count < 5000 WBCs.

Indications

- Patients with recurrent febrile reactions to prevent nonhemolytic febrile reactions
- Frequently transfused patients to reduce HLA antigen alloimmunization
- Prevent transmission of CMV and TA-GVHD.

Washed Red Cells

Manufacture

- Packed red cells obtained by centrifugation are washed with saline by:
  - Manual batch centrifugation
  - Continuous flow separation
- Removes ≥ 98% plasma patients, electrolyte and antibodies
- Should be used within 24 hours after processing due to risk of bacterial contamination.

Indications

- Hypersensitivity to plasma/allergy to whole blood
- Patients with recurrent allergic/febrile reactions
- Patients with IgA/haptoglobin deficiency
- Neonatal transfusion to reduce quantity of metabolic breakdown products, extracellular potassium and risk of CMV transmission
- To avoid TA-GVHD
- Patients at risk for hyperkalemia
- Multiple transfusion patients.

Frozen Red Cells

Manufacture

After addition of cryoprotective agent (10% glycol), RBC may be stored continually below freezing temperature – 80 °C.

Shelf Life

3–5 years.

Advantages

- Ready supply of metabolically superior RBCs
- Freezing arrests biochemical changes which occur during liquid storage

- Reduced incidence of:
  - Nonhemolytic reactions
  - Sensitization to HLA antigen
  - Transfusion hepatitis
- Availability of inventory of rare blood.

Irradiated RBCs

Manufacture

Gamma irradiation with 25 Gv prevents lymphocyte proliferation and thus prevents TA-GVHD.

Indications

- Congenital/acquired immunodeficiency
- Stem cell transplant recipients
- HLA matched products, transfusion from relatives, granulocyte production
- Fetal/neonatal transfusion.

LEUKOCYTE PREPARATIONS[1,3,13,14]

Granulocyte Preparations

- Collection of granulocytes requires processing between 5–10 liters of blood
- Indications:
  - Absolute granulocyte count < 500 cells/ml
  - Fever, unidentified mircroorganisms
  - No reduction in fever after 48 hours of antibiotic therapy.

Mononuclear Cells

Manufacture

- Factors which stimulate stem cell release into circulation:
  - Human growth factor (best)
  - Glucocorticoids
  - Folinic acid
  - Endotoxins
- Cell separator techniques facilitate processing large quantities of blood to collect stem cells.

Indications

Therapeutically used for bone marrow transplantation for:

- AML
- Hodgkins
- Multiple myeloma
- CA breast, ovary
- Neuroblastomas.

PLATELET PREPARATIONS[1,3,13,14]

Types

- Apheresis platelets (collecting more platelets from 1 donor to avoid multiple donors)
- Platelet concentrates (from multiple donors)
- Lymphocyte depleted platelets
- Ultraviolet B irradiated platelets.

Manufacture

- Platelet concentrates:
  - Manufactured from whole blood by centrifugation
  - Contains 5.5×10^{10} platelets suspended in 50 ml of plasma
  - Stored at 20–32 °C under constant agitation for 5 days
  - Only blood product to be stored at room temperature
  - It is lymphocyte contaminated
  - 5–6 platelet concentrates pooled to obtain adult dose
  - 1 unit of platelet concentrate increases platelet count by 7000–10000 cells/mm^3 one hour after transfusion in a 70 kg adult.
- Apheresis platelets:
  - From single donor by apheresis
  - Single Donor Platelets (SDP)
  - Contains 3×10^{11} platelets in 200 to 400 ml plasma
  - Stored at 20–22 °C under constant agitation for 5 days
  - 1 unit SDP increases platelet count by 30,000 to 60, 000 cells/mm^3
  - Each SDP unit is equivalent to '6 pack' platelet concentrate.

Indications

ASA 2006 Guidelines

- Platelet count < 10, 000/mm^3 in non-bleeding patients without other abnormalities of hemostasis
- Platelet count 10,000 to 50,000/mm^3 for:
  - Lumbar puncture/epidural anesthesia
  - Central venous access
  - Endoscopy with biopsy
  - Liver biopsy
  - Vaginal delivery
  - Laparotomy
  - To maintain same platelet count or ≥ 50,000/mm^3 during DIC with ongoing blood loss.

- Platelet count 75,000/mm^3: To maintain > 75, 000/mm^3 during management of massive blood loss
- Platelet count 1,00, 000/mm^3: Intended procedures where closed cavity bleed may be especially hazardous (neurosurgery)
- Microvascular bleeds due to platelet dysfunction in:
  - Uremia
  - Cardiopulmonary bypass
  - Massive blood transfusion.

Shelf Life

5 days.

Contraindications

- Diseases associated with platelet activation:
  - Thrombotic thrombocytopenic purpura
  - Heparin induced thrombocytopenia
  - Administration of platelet concentrates may increase thrombosis
- Idiopathic Thrombocytopenic Purpura: Unless life threatening bleeding
- Prophylactic administration:
  - Massive blood transfusion
  - After cardiopulmonary bypass.

Dosage

- 5 ml/kg or 6 units of platelet concentrates increases count by 50,000 cells/mm^3
- 1 unit of apheresis platelets increases count by 40 to 60,000 cells/mm^3
- Use ABO compatible platelet concentrates where possible
- *Platelet concentrates/RDP need not be group specific*
- ABO incompatible platelet concentrates also produce effective hemostasis
- If the volume of incompatible plasma is large as in SDP transfusion:
  - Use plasma reduced SDP
  - Replace plasma with compatible plasma.

Side Effects

- Infection:
  - Especially if stored for ≥ 5 days
  - Also as it is stored at room temperature, increased chances of infection
  - Suspect sepsis from platelet concentrates if fever within 6 hours of transfusion
- Platelet refractoriness:
  - Suspected if poor increment in platelet count 30 to 60 minutes after transfusion
  - Clinical causes:
    - Hypersplenism
    - Fever
    - Medication
    - Disseminated intravascular coagulation
  - Immunological causes:
    - Antibodies to HLA
    - Antibodies to platelet specific antigens.

PLASMA FRACTIONS[1,3,13,14]

Fresh Frozen Plasma

Types

- FFP: When fluid position of centrifuge is thawed within 6 to 8 hours
- $FP_{24:}$
  - Plasma frozen 24 hours after phlebotomy
  - Comparable to FFP except a 25% reduction in factor VIII and V levels.

Manufacture

- Obtained by apheresis/separation of plasma from centrifuged whole blood
- Plasma is frozen at –20 °C within 6 and 8 hours of collection (FFP) or within 24 hours (FP_{24})
- Each unit of FFP prepared from 1 unit of blood will have 200 to 250 ml.

Shelf Life

1 year frozen and 24 hours thawed.

Contents

- Factors IV, V, VII, VIII, IX
- Especially rich in factors V and VIII (contains 1 IU/ml of each factor)
- Protein C, S and antithrombin III
- Electrolytes, albumin, immunoglobulins and complement.

Indications

ASA Task Force Recommendations

- Urgent reversal of warfarin therapy
- Heparin resistance:
  - Antithrombin III deficiency

  - In patients requiring heparin when antithrombin III concentrates are not available.
- Replacement of isolated factor deficiencies:
  - Used when the specific concentrates are unavailable
  - Factor II, V, VII, VIII, IX, X
  - Protein C and S
  - C_1 esterase inhibitors
  - Antithrombin III deficiency.
- Treatment of:
  - Hemolytic Uremic Syndrome (HUS)
  - Disseminated Intravascular Coagulation (DIC)
  - Thrombotic Thrombocytopenic Purpura (TTP).
- Massive blood transfusion, if PT/APTT $\geq$ 1.5 times the control, i.e. $\geq$ 17 seconds.

Dosage

- 10–15 ml/kg FFP to achieve minimum of 30% coagulation factor concentration: If clotting factor deficiency therapy
- 5–8 ml/kg of FFP for warfarin therapy reversal
- 1 unit of FFP provides coagulation factors equivalent to:
  - 4–5 units of platelet concentrates
  - 1 unit of apheretic platelets
  - 1 unit of whole blood
- Fresh Frozen Plasma need not be of the same Rh type
- For example, A +ve FFP can be given to A –ve patient.

Side Effects

- Risk of transmission of hepatitis B and C, HIV
- Sensitization to foreign proteins may occur.

Contraindications

Not to be used

- For augmentation of plasma volume
- For augmenting albumin concentration
- Avoid administrating PRBCs and FFP to same patient as it increases risk of infections
- In such cases give whole blood if required.

Cryoprecipitate

Manufacture

- Prepared as cold insoluble precipitate by thawing FFP at 4 °C and removing supernatant
- 1 unit of cryoprecipitate will have volume of 10 and 20 ml only.

Contents

- Principally factor VIII, XIII (80 IU of VIII and 40–60 IU of XIII)
- VWF 80 IU
- 100–250 mg of fibrinogen, fibronectin
- Trace of other plasma protein
- Antibodies in cryoprecipitate is very low.

Shelf Life

1 year frozen.

Indications

- Treatment of hemophilia A, has been replaced now by F VIII concentrates
- Treatment of fibrinogen deficiency:
  - Congenital deficiency
  - Acquired deficiency:
    - DIC
    - Massive blood transfusion when fibrinogen levels < 80–100 mg/dl
    - Cryoprecipitate preferred to fibrinogen preparation due to high hepatitis rates
- von Willebrand disease
- Factor XIII replacement in:
  - Sepsis
  - Trauma
  - Burns
- Bleeding due to uremia unresponsive to DDAVP
- ***Coagulum pyelotomy***:
  - Coagulum formed by addition of thrombin and calcium to cryoprecipitate
  - Used to trap calculi in renal pelvis to facilitate pyelotomy removal
- Fibrin sealant if virus inactivated concentrate is unavailable.

Side Effects

- Preparations may contain RBC fragments with RhO antigen
- This may sensitize RH –ve individuals to RhO antigen.

Dosage

- 1 dose or 10 U or 1 U/5 kgs increases fibrinogen by 50 mg/dl
- Units are usually pooled in order to facilitate transfusion (5–10 U/pool)
- ABO compatible units preferred but it is not very important as concentration of antibodies in cryoprecipitate is very low

- *Cryoprecipitate need not be group specific*
- Should be administered through a filter as rapidly as possible at at least 200 ml/hour
- Infusion should be completed within 6 hours of thawing.

Fibrin Glue

- When FFP is thawed, supernatant forms cryoprecipitate
- The precipitate contains large amounts of fibrinogen
- When centrifuged, about 4 ml of concentrated precipitate results
- With added thrombin, this is locally applied as fibrin glue.

Albumin

Manufacture

- Source is whole blood/serum/placenta
- Contains 96% albumin and 4% other proteins
- Available in 5% and 25% solution in isotonic saline.

Usage

- Can be used without regard to ABO type and cross match
- Should be administered within 4 hours of starting infusion.

Indications

- Hypoproteinemia, burns and peritonitis
- For volume expansion acutely.

Side Effects

- Very costly and in short supply
- Risk of bacterial sepsis and *Creutzfeldt-Jakob disease.*

Antithrombin III Concentrates

Dosage

- Infusion of 50 U/kg will increase AT III levels to 120% of normal
- 1 Unit = amount of AT III in 1 ml of pooled plasma
- The AT III levels in plasma should be kept at levels ≥ 80%.

Indications

- Congenital/acquired AT III deficiency:
  - For AT III deficiency related thrombosis and thrombosis propylaxis
  - Use is considered when:
    - Inadequate heparinization despite adequate dosing
    - Recurrent thrombosis is observed despite adequate anticoagulation
- In shock and DIC.

Prothrombin Concentrates

Manufacture

- Factor IX recovered from plasma by absorption with ion exchange
- These are complexes of vitamin K dependent II, VII, IX, and X
- Commercially available as ***Konyne and Proplex.***

Indications

- Hemophilia B/factor IX deficiency (***Christmas disease***)
- Acquired hypoprothrombinemic bleeding disorders like warfarin overdose.

Side Effects

Risk of hepatitis.

Intravenous Immunoglobulin

Manufacture

Pools of plasma fractionated to create concentrated immunoglobulin product (mainly IgG) which is virally inactivated.

Indications

- Hematological conditions:
  - Acquired hypogammaglobulinemias
  - Acquired RBC aplasia
  - HIV associated thrombocytopenia
  - Idiopathic thrombocytopenic purpura (ITP)
  - Post-transfusion pupura (PTP)
- Neurological conditions:
  - Acute disseminated encephalomyelitis
  - Dermatomyositis
  - ***Guillaine-Barre syndrome***
  - ***Eaton-Lambert syndrome***
  - Myaesthenia gravis
- Viral infections:
  - Cytomegalovirus
  - Pediatric HIV.

Adverse Reactions

- Anaphylaxis, especially in IgA deficiency
- Headache, febrile reaction
- Renal failure.

LEUCOREDUCTION[1,2,3]

Introduction

Involves the removal of leucocytes from blood or blood components which are used for transfusion.

Indications

- Prevention of febrile nonhemolytic reaction
- Prevention of infection with leucocyte borne viruses:
  - New variant Creutzfeldt–Jakob Virus (NVCJS)
  - Ebstein-Barr Virus
  - Cytomegalovirus
  - Human T-cell Lymphotrophic Virus
- NVCJD especially common in posttonsillectomy patients
- Prevention of bacterial infection
- For improved survival of grafts
- Prevention of TRALI and non-Hodgkins lymphoma.

Methods

- Prestorage leukoreduction:
  - Three generations of filters used
  - Remove 99.9% leucocytes after which it is stored.
- Poststorage leukoreduction: Done after storage, once blood is ordered.

Complications

- ***Red Eye Syndrome***: Occurs within 24 hrs of transfusion when cellulose acetate filter is used
- Cost outweighs benefits.

TRANSFUSION-RELATED IMMUNOMODULATION[1,3]

Introduction

Transfusion related immunomodulation refers to the transient depression of immune system which occurs following transfusion of blood products.

Benefits

Allogenic survival: Increased chances of graft survival in renal transplant if recipient is transfused with donors blood for 1 week prior to surgery.

Hazards

- Increased postoperative infections like NVCJD, HIV
- Increased chances of cancer recurrence
- Increased transmission of non-Hodgkins lymphoma
- Increased chances of TRALI
- It is a mechanism of nonhemolytic febrile reaction
- Platelet refractoriness may occur
- Increased chances of SIRS and MODS.

Mechanisms of Trim

- Natural killer cell activity
- Cytokine production
- Monocyte function
- Interleukin production
- CD4/CD8 count
- Production of anti-idiotype antibodies
- Cell mediated toxicity against certain target cells
- Response to mitogens.

Types of Trim

- Antigen of specific: Occurs in renal transplant cases repeated transfusion
  - Repeated exposure to B- and T-cell antigens
  - Increased FaS receptors
  - T-cell apoptosis
  - Reduced graft rejection
- Anti-idiotype antibodies
- Bystander suppression.

Prevention of Trim

- Avoid blood products
- Use blood substitutes
- Gamma irradiation of blood
- Leucoreduction.

Indications for Gamma Irradiation of Blood

Absolute Indications

- Bone marrow transplant recipients
- Intrauterine transfusion
- Congenital cell-mediated immunodeficiency diseases
- Acute lymphoid leukemia, Hodgkin's lymphoma
- Immunocompromised organ transplant recipient.

Relative Indications

- Neonate < 1200 gms
- HIV with opportunistic infection
- Patients on immunosuppressive therapy for cancer.

MASSIVE BLOOD TRANSFUSION[1,2,3]

Introduction

Massive blood transfusion is defined as:

- Replacement of 1 circulating blood volume (around 10–12 units of PRBCS) within 24 hrs
- Loss of 50% of circulating blood volume within 3 hrs
- Loss of 10% of circulating blood volume within 10 mins
- Transfusion of 10 units of blood within 6 hrs
- Transfusion of 4 units of blood within 1 hour with continuing blood loss
- Transfusion of 1 unit of blood within 5 minutes.

Preparation for Massive Blood Transfusion

- Two large gauge venous cannula (14 G)
- Triple lumen central venous catheter via:
  - Internal jugular vein
  - Subclavian vein
  - Femoral vein.
- Use of three way taps reduces the need to use needles for drug administration
- Wear gloves to prevent contamination of hands with spilled blood
- Monitors:
  - Triple lumen central venous catheter used for:
    - Rapid blood sampling
    - Measurement of CVP.
  - Foleys catheter to measure urine output
  - Central and peripheral temperature should be measured
  - Pulse oximetry, arterial pressure and ECG should be monitored.

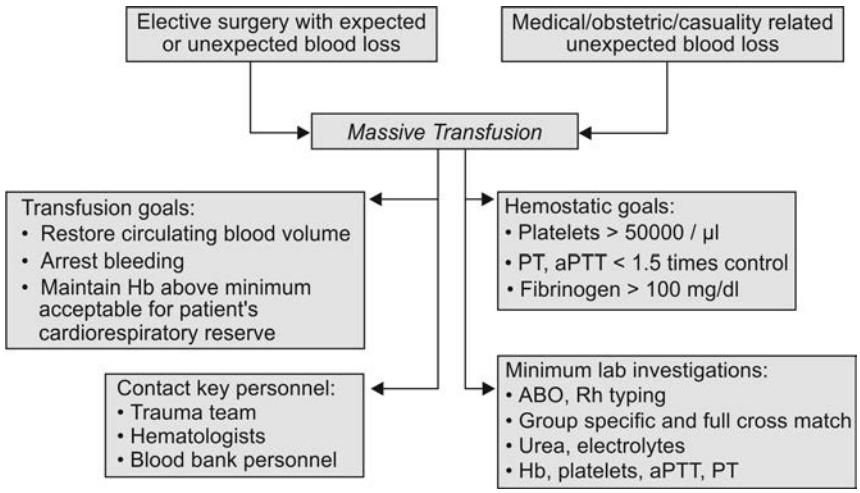
Method of Administration

- Constant pressure infusion device
- Do not prime the system with fluids containing Ca^{2+} like:
  - Lactated Ringers
  - Hemaccel.
- Hematomic Rapid Infuser Device with a 3 liter reservoir:
  - Cell saved or banked blood and FFP can be stored in the reservoir
  - This blood is warmed and infused at rates of 21/min.
- For faster rates of transfusion:
  - Increase height of fluid above patient
  - Manual compression of bag
  - Using syringe and three way tap to aspirate and push volume.

Warming of Stored Blood

- Double length blood warming coil
- Counter current aluminium heat exchangers
- Plastic coils/plastics cassettes in warm water bath (37–38 °C)
- Warming plates which have an upper (43 °C) and lower limits (33 °C) is *safest*.

Management of Massive Transfusion



Complications of Massive Transfusion

Coagulopathy

- Occurs due to the following reasons:
  - Reduced synthesis and release of clotting factors (hepatic ischemia)
  - Dilution of endogenous clotting factors with colloids/RL
  - Thrombocytopenia and DIC
  - Chelation of calcium by citrate (least important)
  - Hypothermia.
- Clotting factor deficiency occurs before thrombocytopenia
- Concentration of II, V and VIII are reduced in stored blood
- *Transfusion guidelines*:
  - If platelet count < 50000/µl, platelet transfusion
  - If INR > 1.5, transfuse FFP
  - If fibrinogen < 100 mg/dl, transfuse cryoprecipitate.

Citrate Toxicity

- Not caused by citrate ion per se, but because citrate binds to Ca^{2+}
- Each unit of blood contains 3 gms of citrate
- Increased chances of citrate toxicity possible when:
  - Pediatric patients
  - Cardiac disease and low cardiac output states
  - Hypotension and hypovolemia
  - Hepatic disease
  - Liver transplantation
  - Hyperventilation
  - Alkalosis
  - Hypothermia
  - Hyperkalemia
- Factors precipitating toxicity:
  - Rate of blood transfusion more important than total volume of blood transfused
  - Hypocalcemia occurs only when:
    - Rates of transfusion > 1 ml/kg/min
    - 1 unit blood transfused in 5 min.
  - Rate of citrate metabolism reduces by 50% when body temperature reduces from 37 °C to 31 °C.
- Clinical features:
  - Reduced myocardial function
  - Hypotension, narrow pulse press, increased diastolic pressure and CVP
  - Increased QTc, widened QRS and flattened T-waves.
- Treatment:
  - 1 gm calcium gluconate (10%) given IV for every 5 units blood/FPP
  - 13.4% calcium chloride contains 0.192 mmol/ml of Ca^{2+}
  - 10% calcium gluconate contains only 0.22 mmol/ml of Ca^{2+}
  - $CaCl_2$ is not used much even though it contains more Ca^{2+} as it very irritant to veins.

Hyperkalemia

- Serum K^+ is as high as 19–30 mEq/l in stored blood after 21 days
- This is because RBCs exchange K^+ ions to uptake H^+ ions generated by metabolism
- Precipitating factors:
  - Large amounts of blood must be given for hyper K^+ to occur
  - Rate of blood infusion ≥ 120 ml/min
  - Premature infants are especially susceptible
- Transfuse only fresh (< 8 days old) plasma reduced or washed PRBCs if rapid transfusion is required (≥ 10–15 ml/kg/2 hours) in premature infants
- Hypokalemia occurs 24 hrs after transfusion as the transfused cells correct their electrolyte composition and K^+ enters cells.
- Thus, metabolic acidosis and hyper K^+ occur first but net result is hypokalemia and alkalosis.

Hypernatremia

- Serum Na^+ of whole blood and FFP > normal blood levels due to sodium citrate
- Hypernatremia occurs when large volume of plasma is given to patients with disordered salt and water handling: Liver disease, cardiac and renal disease
- Na^+ increases to 150–160 mm/l after 3 weeks of storage of plasma.

Acid Base Abnormalities

- Causes of acidosis of bank blood:
  - pH of storage media like CPDA is very low (5.5). When blood is added, its pH reduces to 7.0
  - Accumulation of lactic acid and pyruvate by RBC metabolism reduces pH further to 6.9 after 21 days storage
  - PCO_2 increases to 150–220 mm Hg as the plastic container does not provide air escape mechanisms for CO_2.
- On blood transfusion, the citrate present in stored blood is metabolized in liver

- This generates large amounts of bicarbonate which may neutralize metabolic acidosis initially
- Thus, prophylactic sodium bicarbonate administration is not recommended
- Thus, initially, metabolic acidosis and hyperkalemia occur while later alkalosis and hypokalemia occur.

Hypothermia

- One unit of PRBCs at 40 °C will reduce core temperature of 70 kg patient by 0.25 °C
- Blood warming device must be used for any transfusion requiring > 2 U blood
- If < 30 °C ventricular irritability and cardiac arrest occurs
- Safest method is passing blood through plastic coils or plastic cassettes in warm water bath (37–38 °C)
- Harmful effects of hypothermia:
  - Shifts ODC curve to left
  - Reduces metabolism of citrate, lactate and other drugs
  - Increased incidence of arrhythmias
  - Impairs hemostasis
  - Increases oxygen consumption
  - Increased postoperative infection
  - Masks clinical signs
  - Shivering increases O_2 consumption by 400%.

Tissue Oxygenation

- Depletion of 2, 3-DPG shifts ODC curve to left
- Tissue oxygen delivery is reduced
- Transfusion of 2,3-DPG depleted blood while increasing Hb, results in less efficient oxygen delivery
- After transfusion, 2,3-DPG returns to normal in 12–24 hrs.

Hyperbilirubinemia

- Jaundice as significant amounts of transfused blood may not survive
- Also, liver function may be impaired, particularly in the presence of sepsis or multi organ failure, *paradoxical conjugated hyper bilirubinemia* occurs
  - Increased load of bilirubin from destroyed RBCs occurs which is conjugated
  - There may be delayed excretion which causes conjugated hyperbilirubinemia.

Multiorgan Dysfunction

- Due to lysis of RBCs during storage causing free Hb release
- This causes oxidant mediated injury causing MODS.

Microaggregates

- Platelet aggregates form during 2nd–5th day
- From 10 days onwards, larger aggregates form with:
  - Fibrin
  - Degenerated WBCs
  - Platelets
  - Size of 100–200 µm which can cause:
    - Acute lung injury
    - Hypoxemia
    - DIC and tissue ischemia
    - Complement activation.
- Use filter when > 1 L of blood is transfused.

TRANSFUSION-RELATED ACUTE LUNG INJURY[1,3,10,13,14]

Introduction

- Non cardiogenic form of pulmonary edema occurring after blood product administration
- New acute lung injury occurring within 6 hrs of a completed transfusion with ratio of PaO_2/FiO_2< 300 mm Hg or O_2 saturation as measured by pulse oximetry of less than 90% when the patient is breathing room air: ***NHBLI definition.***

Incidence

- 1 : 5000 units transfused
- Mortality of at least 5%
- Associated with transfusion of all products:
  - Whole blood
  - PRBCs
  - FFP, platelets, cryoprecipitate
  - Intravenous immunoglobulin therapy (IVIg therapy)
  - Granulocytes, stem cell preparation.

Risk Factors

- Multiparous donors:
  - Percentage of antileukocyte antibodies after 1st pregnancy is 9%
  - Percentage of antileukocyte antibodies after 2nd pregnancy is 18%
  - Percentage of antileukocyte antibodies after 3rd pregnancy is 23%.
- Underlying clinical conditions: ***Two hit hypothesis***
  - Trauma
  - Surgery

  - Sepsis
  - Systemic Inflammatory Response Syndrome (SIRS)
- Blood components: FFP, cryoprecipitate and platelet concentrates have higher incidence of antileukocyte antibodies than PRBCs
- Storage of blood products causes:
  - Accumulation of cytokines which injuries alveolar capillary membrane
  - Depletion of nitric oxide causing pulmonary vasoconstriction
  - Depletion of nitric oxide also causes increase in hydrostatic pressure and TRALI
- Massive transfusion: strong association between exposure to multiple transfusions and development of TRALI.

Pathogenesis

Controversial 3 theories to explain the mechanisms.

Antigranulocyte Antibody Theory

- Donor blood contains antibodies against recipient WBC antigen
- Antigen-antibody binding occurs causing cellular activation
- The activated neutrophils lodge in pulmonary capillaries
- Reactive oxygen metabolites released which cause pulmonary endothelial leakage.

Granulocyte Priming Theory

- Biologically active substances (such as lipids and cytokines) are present within the transfusion
- These substances are called Biological Response Modifiers or BRM
- Examples of BRM are lysophosphatidyl choline
- These have the ability to prune the activity of granulocytes in pulmonary vasculature
- This causes increased vascular permeability leading to TRALI.

Two Event Hypothesis

- TRALI occurs due to a combination of both theories
- The first event is caused by the recipients underlying clinical conditions like:
  - Surgery
  - Infection
  - Inflammation.
- This primes circulating neutrophils and sequesters them in pulmonary circulation
- The second event involves transfusion of anti-leukocyte antibodies or BRMs in stored blood component
- These in turn activate the primed neutrophils causing endothelial damage and capillary leak.

Other Possible Mechanisms

- Direct injury to pulmonary endothelium
- Immune complex formation with complement activation
- Cytokine network activation
- BRM like ILs causing direct injury
- Monocyte activation.

Clinical Features

- Acute onset dyspnea, severe hypoxemia
- Fever, chills, rigors
- Noncardiogenic pulmonary edema, hypotension/hypertension
- Fluid in ET tube within 1–2 hrs after transfusion but in full force within 6 hrs
- If undiluted edema fluid obtained from ETT, edema fluid protein: plasma protein ratio $\geq$ 0.6 suggests TRALI rather than TACO
- Chest X-ray shows bilateral chest infiltrates
- PO_2 levels return to normal within 48–96 hrs
- Hypoxia and chest X-ray infilterates may persists for 7 days.

Investigations

- Hemoconcentration, peripheral neutrophilia after initial neutropenia as all WBCs will leak into alveoli
- Sudden reduction in serum albumin
- Leucocyte antibodies to recipient antigen and increased neutrophil priming activity in lipid fraction of plasma in stored blood products
- Bilateral chest infiltrates
- Edema fluid: plasma protein ratio $\geq$ 6.

Differential Diagnosis

- ***Transfusion associated circulatory overload*** (TACO):
  - Raised JVP
  - Increased systolic BP at the time dyspnea develops
  - Widened pulmonary vascular pedicle on chest X-ray
  - Increased BNP shortly after transfusion
- Hemolytic transfusion reaction
- Anaphylaxis due to transfusion of IgA containing products to a recipient with IgA deficiency.

Diagnostic Criteria

AECC Conference Recommendations

- No pre-existing acute lung injury before transfusion
- Onset of lung dysfunction within 6 hrs of transfusion
- Acute lung injury as evidenced by:
  - Acute onset of signs and symptoms
  - Hypoxemia:
    - $PaO_2/FiO_2 < 300$ or
    - Room air $SpO_2 < 90\%$ or
    - Other clinical evidence of hypoxemia
  - Bilateral infiltrates on chest X-ray without cardiomegaly
  - No clinical evidence of left atrial HTN (Pulmonary Artery Occlusion Pressure (PAOP) < 18 mm Hg)
- No temporal association of onset to alternative causes of ALI.

Prevention

- Avoid multiparous donors
- ***Prestorage leucoreduction*** is useful
- Limit preparation of high plasma volume components like FFP, TPF, P_{24}, plasma frozen within 24 hrs after phlebotomy, apheresis platelets, whole blood) from donors known to be leukocyte alloimmunized
- HLA antibody testing and screening.

Treatment

- *Immediately stop blood transfusion*
- Mainly supportive hemodynamic and ventilatory support
- Supplemental O_2 if mild manifestations
- Mechanical ventilation with low tidal volume and plateau pressures if moderate-severe manifestations
- High FiO_2, PEEP may be required (similar to ARDS)
- Diuretics have no role in TRALI can be tried if TRALI cannot be differentiated from TACO
- IV corticosteroids have been tried to reduce complement mediated granulocyte activation
- Efficacy of corticosteroids however, has not been tested
- Prostaglandin E_1 has also been tried
- Rapid resolution usually occurs in 96 hrs.

JEHOVAH'S WITNESS[1,3]

Introduction

Christian movement with following beliefs:

- Prohibits consumption of blood
- Belief prevents them from accepting whole blood and its primary components
- Belief that blood which is removed from body is unclean and should be disposed
- Believe procedures with removal and storage of their own blood is unacceptable.

Legal Issues

Consent

- Procurement of informed consent before any medical intervention
- Special consent forms with section for specific exclusion from consent
- Patient interviewed in the presence of independent witness while obtaining consent.

Children

- Full and frank discussion between anesthetist, surgeon and parents
- Children under 16 yrs can give consent themselves if they understand the issues involved (***Gillicks competence***)
- If consent for transfusion is refused:
  - An application is made to high court
  - Application for specific issue order which allows transfusion without removing parental authority.
- In emergencies, blood should be given.

Emergencies

- Perform blood transfusion if Jehovahs witness status unknown
- If relatives suggest patients may not accept blood transfusion, documentation of same to be done
- If refusal of transfusion consent is retracted, make a witnessed entry in patients notes.

Anesthetic Considerations

- Preoperative planning, preparation essential for successful outcome
- Unlawful to administer blood to a Jehovahs Witness patient who has expressly forbidden it

- Acute Normovolemic Hemodilution often unacceptable to JW patient as it involves removal and storage of blood before transfusion
- Intraoperative blood salvage may be acceptable to some if:
  - Blood is not stored
  - Circuitry is designed so that it remains in continuity with patients own circulation.
- Patients may refuse blood component therapy too
- ***Bloodless medicine***: Team which reduces blood loss and uses best available alternatives to allogenic transfusion therapy.

Preoperative Preparation

- Optimize Hb%, treat anemia
- Optimize nutritional feeding: Enteral supplementation or TPN
- Drugs:
  - To increase RBC production: iron, folate, Vitamin B_{12}, Erythropoeitin
  - To promote clotting: Vitamin K.
- Management of anticoagulant therapy and congenital/drug induced coagulopathies
- Restricted diagnostic phlebotomy
- Prophylactic embolization:
  - Pelvic tumors
  - Vascular tumor like metastasis
  - Aneurysmal bone cyst.
- Prescribe for cell salvage apparatus.

Intraoperative Management

- Choice of technique:
  - Prefer laproscopic surgery
  - Prefer regional anesthetic technique
  - Invasive monitoring with IBP and CVP
  - Hypotensive anesthesia techniques.
- Physiology:
  - Proper positioning: Lateral position for THR
  - Maintain normothermia
  - Avoid hypoventilation and hypercarbia
  - Avoid high intrathoracic pressures.
- Recent advances:
  - Intraoperative blood salvage
  - Acute normovolemic hemodilution (ANH)
  - Acute hypervolemic hemodilution (AHH)
  - Use of blood substitutes
- Drugs to enhance hemostasis:
  - Factor VII a
  - Tranexemic acid: 10 mg/kg IV up to 30 mg/kg/day
  - Aprotinin
  - Ethamsylate
  - Desmopression.
- Adequate topical hemostatasis:
  - Argon lazer beam cautery (diathermy)
  - Spray coagulation
  - Use of arterial tourniquet
  - Avoid large abdominal packs
  - Hemostats:
    - Collagen and cellulose pads (***Kaltostat***)
    - Fibrin glue (***Tisseal***).

Postoperative Management

- Good compressive padded dressing
- Limb elevation in TKR
- Maintain normothermia
- Adequate analgesia
- Stop bleeding sources
- Maintain hypotension/prevent normotension till bleeding stops
- Oral/parental iron therapy
- Erythropoietin therapy
- Appropriate fluid and volume management
- Reduce transfusion trigger
- Postoperative blood salvage
- Restricted diagnostic phlebotomies
- Prevent and treat coagulation disorders promptly.

Hematology and Oncology

- Individualized chemotherapy regimens to reduce hematotoxicity
- Embolization of vascular tumors
- Restricted diagnostic phlebotomy
- Tolerance of anemia
- Pharmacological prophylaxis of bleeding.

BLOODLESS MEDICINE[1,3]

Introduction

- Bloodless medicine is defined as a team approach that reduces blood loss and uses the best available alternatives to allogenic transfusion therapy, while focusing on the provision of the best possible medical care to all patients
- Mainly started for Jehowahs Witnesses who refuse transfusion based on interpretation of Old and New testament tests.

Principles of Bloodless Medicine[1,3]

Preoperative Assessment and Planning

- Management of anemia, optimize preoperative Hb
- Management of anticoagulation, congenital and drug induced coagulopathies
- Prophylactic interventional radiology and embolization
- Restricted diagnostic phlebotomy
- Prescribing and scheduling of cell salvage apparatus
- Optimize nutritional status:
  - Total parenteral nutrition
  - Supplemental enteral feeds
- Drugs to increase RBC production:
  - Iron
  - Vitamin B_{12} and folate
  - Erythropoetin
  - Drugs to promote clotting: Vitamin K.

Intraoperative Blood Conservation

- Argon beam diathermy
- Use of tourniquet
- Avoid large surgical packs
- Meticulous surgical hemostasis
- Pharmaceutical enhancement of hemostasis: Fibrin glue
- Hypotensive anesthesia
- Regional anesthetic technique
- Reduce transfusion trigger
- Surgical positioning to minimize blood loss
- Intraoperative blood salvage
- Hypotensive anesthesia
- Recombinant factor VII, tranexamic acid, aprotinin, desmopressin.

Postoperative Blood Conservation

- Adequate analgesia
- Good padded compressive dressing
- Maintenance of normothermia
- Maintain limb elevation post TKR
- Stop bleeding if active bleed present
- Avoid attempts to normalize BP until bleeding has stopped
- Oral/parenteral iron to improve iron stores.
- Exogenous erythropoietin therapy effectively increases RBC mass.

Hematology and Oncology

- Aggressive exogenous erythropoietin and iron therapy for prophylaxis of anemia
- Individualized chemotherapy protocols to minimize hematologic toxicity
- Tolerance of anemia
- Pharmacological prophylaxis and treatment of bleeding
- Restricted diagnostic phlebotomy.

Advantages

- Eliminates risk of transfusion reactions
- Eliminates risk of disease transmission
- Eliminates risk of alloimmunization to RBCs, WBCs
- Reduces demand on blood supply
- Eliminates risk of TA-GVHD.

PERIOPERATIVE BLOOD CONSERVATION STRATEGY[1,2,3]

Preoperative Strategies

- Preoperative Autologous Blood Donation (PABD)
- Preoperative arterial embolization.

Intraoperative Strategies

- Anesthetic modifications:
  - Regional anesthetic technique
  - Proper positioning
  - Normothermia
  - Pharmacological agents:
    - Erythropoeitin
    - Blood substitutes
    - DDAVP
    - Antifibrinolytics.
  - Hypotensive anesthesia
  - Acute Normovolemic Hemodilution (ANH)
  - Intraoperative blood salvage.
- Surgical modification:
  - Topical hemostasis with fibrin glue
  - Tourniquet.

Postoperative Strategies

- Postoperative blood salvage
- Good padded compressive dressing
- Limb elevation post-TKR.

Autologous Blood Transfusion

Definition

One in which donor and the recipient are the same.

Types

- Preoperative Autologous Blood Donation (PABD)

- Intraoperative blood salvage
- Postoperative blood salvage
- Acute normovolemic hemodilution.

Advantages

- Eliminates risk of transfusion reactions
- Eliminates risk of disease transmission
- Eliminates risk of allo-immunization to RBC, WBC, platelets
- Eliminates risk of Transfusion Associated-GVH disease
- Safe and acceptable blood cover in ***Jehovahs witness*** patients
- Safe transfusion in patients with multiple allo-antibodies and rare blood group
- Readily available blood in major hemorrhage
- Reduced demand on homologous blood supply
- Hemodilution improves tissue perfusion by reducing blood viscocity
- Preoperative donation stimulates erythropoiesis prior to surgery.

Disadvantages

- Expensive equipment and trained staff required: not cost effective
- Complex logistics required for collection, storage, and transfusion
- Bacterial contamination still possible
- Tendency to over-transfuse patient
- Patient may become grossly anemic and develop coagulation defects during collection
- Suitable for certain operative procedures only
- If surgery delayed blood becomes outdated and may cause wastage.

PREOPERATIVE AUTOLOGOUS DONATION[1,2,3,14]

Introduction

- Procedure in which patients own blood is collected, through repeated phlebotomies over a span of 4–5 weeks to be transfused during the surgery.

Patient Selection

AABS Recommendations

- Patients in whom elective surgery can be scheduled several weeks in future
- Surgical procedure for which blood is usually cross matched
- Hb ≥ 11 g% or HCT > 33%
- May donate up to 10.5 ml/kg excluding samples for testing
- No weight/age bar
- No medical contraindication for donation of blood.

Advantages

- Low K^+ compared to stored blood
- Relatively normal pH, normothermic
- Functionally superior cells
- High levels of 2,3-DPG.

Disadvantages

- Expensive
- Blood may have to be discarded if not transfused
- Can administer wrong unit of blood to patients.

Indications

- Cardiac surgery
- Major vascular surgery
- Liver transplantation
- Prostatectomy
- Major orthopedic surgeries: Spine, THR, TKR, etc.

Contraindications

- Active bacterial infection
- History of indwelling urinary catheter/device penetrating skin
- Cardiac disease:
  - Significant AS
  - Cyanotic heart disease
  - Uncontrolled HTN
  - Frequent unstable angina
  - Significant LMCA narrowing
  - History of MI/CVA within 6 months of the planned donation.
- Active seizure disorder
- Hb < 11 gm%
- Hemorrhagic shock.

Complications

- Risk of contracting infection during phlebotomy
- Vasovagal attack during blood donation
- Human errors in transfusing blood like transfusing wrong unit of blood
- Iatrogenic anemia, MI/cerebral hypoxia.

Special Considerations

- Elderly patients can donate blood if:
  - Physiological conditions permit
  - No major underlying disease
  - Age alone is not criteria.

- Pediatric patients:
  - Generally children > 33 kgs preferred
  - Has been done in children 8 years old also
  - Venous access and emotional tolerance of venepuncture limits collection.
- Obstretic patients:
  - Generally not required in obstetric patients
  - Can be considered in:
    - Patients with autoantibodies to multiple antigens
    - Placenta previa.

Crossover Usage

- If the amount of blood collected preoperatively exceeds the actual usage subsequently, the remaining blood may be used for homologous transfusion to other patients
- Called ***crossover usage***
- No longer permitted by AABB as autologous donors are not voluntary donors.

Techniques

- Blood is collected at the nearest blood collection facility
- Optimal donating period begins 4-6 weeks before surgery in order to:
  - Allow sufficient number of units to be collected
  - Also to enable more complete RBC regeneration before surgery.
- Blood donated at weekly intervals or once in 3 days depending on the physical status of the patient
- Upto a maximum of 4 units of blood can be collected or 10.5 ml/kg
- Last blood donation not be collected later than 72 hrs before surgery to allow for restoration of intravascular volume
- Patient receives supplemental iron 2 mg/kg/day × 3 weeks in the form of:
  - Ferrous sulphate 325 mg PO TID
  - Ferrous gluconate 325 mg five times a day.
- Iron supplementation increases RBC expansion from 14 to 19%
- Blood drawn last is usually given first in PABD
- Erythropoietin given to anemic patients (HCF < 39%) scheduled for noncardiac, nonvascular surgery can cause up to 50% RBC volume expansion
- Collected blood has shelf life of 35–42 days
- Collected blood is stored till patients are discharged/ till unit become outdated.

INTRAOPERATIVE BLOOD SALVAGE[1,2,3,14]

Introduction

Collection and reinfusion of blood lost during surgery.

Indications

- Cardiac surgery, aortic reconstruction surgery
- Orthopedic surgery:
  - Spine instrumentation
  - Joint arthroplasty.
- Liver transplant
- Splenectomy
- Trauma patients
- Ruptured ectopic pregnancy.

Characteristics of Salvaged Blood

- Free Hb levels of 200–500 mg% is common
- 2,3-DPG levels are high
- FDP and complement activation is present
- Platelets and coagulation factors are deficient
- Salvaged blood is more alkaline.

Methods of Collection

- Semicontinuous flow devices
- Canister collection
- Single use reservoir.

Contraindications

- Sickle cell disease
- Contaminated surgical field with:
  - Malignant cells: Risk of metastasis
  - Bowel contents
  - Amniotic fluid: Risk of amniotic fluid embolism
- Presence of pro-coagulant material like topical collagen in surgical field.

Complications

- Hemolysis
- Renal failure due to free Hb
- Air embolism, amniotic fluid embolism
- Reinfusion of debris from surgical field:
  - Fat, air
  - Platelets, lymphocytes, free Hb, RBC stroma
  - Heparin, bacteria
  - Debris like PMMA/bone cement.
- Dilutional coagulopathy as all clotting factors and platelets are removed by washing.

Technique

- Cell salvage device used to salvage blood from operative field
- Recommended maximum vacuum setting is not more than 150 mmHg
- Suction should be done from within the blood pool and not at the blood-air interface.
- Anticoagulate the salvaged blood
- RBCs separated by centrifugation
- They are washed with saline and filtered through 40 µm filters
- Washed RBCs suspended in saline in aliquots of 125/225 cc with hematocrit of 45–65
- Blood can be stored:
  - At room temperature for up to 4 hrs
  - At 1–6 °C for 24 hrs provided storage at 1–6 °C is begun within 4 hrs of ending collection.
- Storage at room temperature for recovered blood: 4 hrs (washed/unwashed)
- Storage at room temperature for ANH blood: 8 hrs.

POSTOPERATIVE BLOOD SALVAGE[1,2,3,14]

Introduction

- Postoperative recovery of defibrinogenated blood from mediastinal chest tubes and wound drains after TKR or THR with immediate reinfusion of unwashed blood.

Indications

- Cardiac surgery:
  - Reinfusion of blood from mediastinal tubes
  - This may affect lab tests like creatinine kinase
  - Increased CK may be present even though no preoperative MI has occurred
  - Blood collected from heart lung machine can be transfused back after processing.
- Orthopedic surgery: TKR/THR/spinal fusion instrumentation
- Post-traumatic salvage:
  - Following chest/abdominal trauma
  - Blood from hemothorax/hemoperitoneum.

Technique

- Blood salvaged postoperatively is collected from mediastinal/chest/joint drains and transfused back without washing
- Being defibrinogenated, it does not require anti-coagulation prior to transfusion
- Up to 1400 ml of unprocessed blood can be reinfused as it has high concentration of cytokines
- If transfusion of blood has not begun within 6 hrs of initiating collection, the blood must be discarded
- Shelf life of 6 hrs.

Complications

- Theoretical risk of reinfusion of:
  - Free Hb, RBC stroma
  - Marrow fat, tissue debris
  - Toxic irritants/methacrylate debris
  - FDPs and complement.
- Risk of bacterial contamination if storage time > 6 hrs
- Mild coagulopathy develops as:
  - Platelets are deranged: Prolonged bleeding time
  - No clotting factors are present: Prolonged PT, aPTT
- Renal insufficiency if large amounts of free Hb present
- Air embolism
- Complement activation causing:
  - Noncardiogenic pulmonary edema
  - Upper airway edema.

ACUTE NORMOVOLEMIC HEMODILUTION[1,2,3]

Introduction

- Entails withdrawal of patients blood early in the intraoperative period with simultaneous administration of crystalloid or colloids to maintain normovolemia
- When replacement of ANH collected in part by synthetic oxygen carriers, it is called ***Augmented Hemodilution***
- Blood is collected on the day of surgery rather than over several weeks as in PABD
- Also in PABD, no crystalloids are given to increase the blood volume.

Usefulness

- Reduces amount of allogenic blood transfusion to 1-2 units/patient
- Provides fresh supply of coagulation factors and platelets
- Improved tissue perfusion with hemodilution as blood viscosity is reduced
- Patients loses blood of low HCT intraoperatively
- Withdrawn blood is reinfused at the end of surgery: Less Hb is lost in blood

- Blood component sequestration:
  - Blood is collected intraoperatively
  - It is subjected to various procedures like apheresis and centrifugation
  - Individual blood components are separated.
- Acute hypervolemic hemodilution:
  - Involves rapid infusion of fluid to achieve hemodilution without prior withdrawal of blood
  - Associated changes:
    - Decrease in PCV and SVRI by around 30%
    - Increase in CI and LVEDP
    - Increase in PAP and PCWP which normalize on stoppage of surgery
    - Slight increase in MAP and decrease in HR,
    - Low chance of pulmonary edema.

Patient Selection Criteria

- For surgeries where likelihood of transfusion exceeds 10%
- Preoperative Hb level is atleast 12 g%
- Absence of clinically significant coronary pulmonary, renal/liver disease
- Absence of severe HTN
- Absence of infection and risk of bacteremia.

Contraindications

Absolute

- Severe anemia with HCT < 24%
- Hemorrhagic shock
- Myocardial pump failure
- Hemostatic disorders
- Limited ability to increase cardiac output like AS, LV dysfunction
- Respiratory failure
- End stage renal disease
- Severe sepsis.

Relative

- Less severe anemia
- Severe respiratory distress
- CCF/LV dysfunction
- History of stroke
- CAD/carotid artery disease
- ESRD.

Compensatory Mechanisms in ANH

- Blood:
  - Reduced blood viscosity
  - Reduced RBC aggregation
  - Shift of ODC to right
  - Reduced oxygen carrying capacity (below 30%).
- Oxygen utilization: Increased blood flow to tissues with increased O_2 extraction
- Cardiac:
  - Increased cardiac output
  - Coronary vasodilatation
- Cerebral: Increased cerebral blood flow: hyperventilation avoided
- GIT:
  - Increased HbF
  - Increased O_2 extraction in liver
  - Centrilobular hepatic necrosis
- Renal: Renal vasoconstriction causing decrease in fraction of CO to kidneys
- Pregnancy: ANH done with caution as reduction in material HCT reduces placental perfusion.

Technique

- Informed consent
- Timing: Prior to induction of anesthesia with awake patient is better
- Blood collection:
  - Site of collection:
    - Peripheral line not preferred as tube resistance and sludging occurs
    - Arterial line not used as we cannot monitor IBP during procedure
    - Central venous line is *best* and IJV/subclavian vein used.
  - Calculation of volume to be collected:
    - Calculates estimated blood volume (EBV)
    - EBV = 70 ml/kg in females and 75 ml/kg in males
    - Baseline HCT noted
    - Target HCT:
      - 7g/dl in healthy patients
      - 10g if CVS/RS/CNS disease
    - Calculate average HCT =
      $$\frac{\text{Baseline HCT + Target HCT}}{2}$$
    - Volume of blood collectable =
      $$\frac{\text{Baseline HCT – Target HCT}}{\text{Average HCT}} \times \text{EBV}$$
- Anticoagulation of specimen:
  - CPD anticoagulant added to blood collection bag
  - This is then attached to a port in the IV line.

- Sample collection:
  - 450 ml of blood is collected per bag
  - Collect whole blood and mix blood in bag with CPD
  - Bag is agitated using an agitator/by manually kneading the bag every minute.
- Asanguinous fluid administration:
  - 3 ml crystalloid replaced for every 1 ml blood collected
  - 1 ml colloid replaced for every 1 ml blood collected
  - Ensure that blood collection and fluid infusion do not mix if 3 port CV line is used.
- Storage:
  - Can be stored at room temperature for up to 8 hrs
  - After 6 hrs refrigerate at 0 °C
  - Intermittent agitation done to ensure that sludging does not occur.
- Reinfusion of whole blood:
  - Given according to surgical condition
  - Any remaining blood given in operating theater or refrigerated
  - Diuretic given if risk of hypervolemia
  - Last collected blood infused first as when whole blood is collected with ANH, each subsequent unit becomes more dilute.
- Monitoring during ANH:
  - Heart rate, BP
  - Capnography
  - ECG
  - Pulse oximetry
  - If more advanced cases, with large volume of blood sequestered:
  - CVP/PAP
  - Cardiac output
  - Transesophageal Echocardiography.

Complications

- Iatrogenic anemia may not be safe
- MI/cerebral hypoxia possible if severe hemodilution
- Bleeding diathesis during surgery due to:
  - Dilutional thrombocytopenia
  - Hypofibrinogenemia as coagulation factors are being sequestered.
- Volume overload.

FIBRIN GEL

- Blood derivatives derived from a source of fibrin and factor XIII (fibrin stabilizing factor) in which a solution of fibrinogen is mixed with a solution of thrombin and applied to surgical field
- Applied directly to wounds which display diffuse microvascular bleeding.
- Risk of anaphylaxis and HIV transmission present
- Also topical use of fibrin sprays, bone wax/surgical/platelet gel.

DRUGS

Erythropoietin

- Indications:
  - If patient cannot undergo PABD due to anemia/limited time to donate blood
  - Now used in PABD to reduce blood transfusion in major surgeries, Jehowahs witness
  - Used for in anemic patients undergoing renal dialysis.
- Efficacy:
  - Erythropoiesis is seen in 3 days
  - Equivalent of 1 unit of blood produced in 70 days
  - Always administered with iron supplementation (IV iron saccharate).
- Dosage:
  - 300 U/kg for 15 days beginning 10 days before surgery
  - 600 U/kg weekly once starting 3 wks before surgery
  - One more 600. U/kg dose administered on the day of surgery.
- HTN and seizures occur in patients with CRF and rare thrombotic events.

Desmopressin

Synthetic vasopressin analogue.

Aprotinin

- Fibrinolytic inhibitor
- Reduces blood loss in TKR, THR and spinal fusion
- High cost and allergic reactions, risk of ARF limits use.

Tranexamic Acid

- 10 mg/kg bolus up to a maximum of 30 mg/kg/day

- T ½ = 3 hrs
- Reduces total blood loss by 50%.

OTHER MEASURES

- Position of patient:
  - Bleeding during THR is less with patient in lateral position than in supine
  - Elevation of lower limb after TKR reduces postoperative blood loss.
- Maintain normothermia
- Controlled hypotensive spinal/epidural/general anesthesia with additives like clonidine
- Preoperative arterial embolization for:
  - Pelvic fractures
  - Surgery on vascular tumors like:
    - Metastasis
    - Aneurysmal bone cysts.
- Efficient padded compressive dressing for tamponade effect.

RECOMBINANT FACTOR SEVEN[1,2,3]

Introduction

Recombinant factor VIIa (RF-VIIa) or novoseven was developed for the treatment of patients with hemophilia A or B and inhibitors to exogenouos factor VIII or IX preparations.

Chemistry and Preparation

- It is a vitamin-K dependant glycoprotein
- Contains 406 amino acid residues with molecular weight 50 kDa
- Is structurally similar to human plasma derived factor VIIa
- Supplied as a sterile white lyophilized powder of factor VIIa in single use vial
- Diluent is a 10 mmol solution of histidine in water, for injection
- After reconstitution:
  - Each vial contains 1 mg/ml of novoseven
  - Should be administered within 3 hours of reconstitution
- In pregnancy/lactating mothers:
  - *Category C drug*
  - Should be used during pregnancy only if potential benefits justifies potential risks to fetus
  - Still not known if it is excreted in human milk.

Mechanism of Action

- Activates *extrinsic pathway* of the coagulation cascade:
  - Recombinant VIIa complexes with tissue factor
  - This can activate factor X to factor Xa as well as factor IX to IXa
  - Factor Xa then complexes with other factors and converts prothrombin to thrombin
  - This results in occurrence of a ***Thrombin burst***
  - This leads to the formation of a hemostatic plug by converting fibrinogen to fibrin
  - This causes local hemostasis.
- This process may also occur on the surface of activated platelets as factor VIIa has affinity for activated platelets.

Indications[3]

- On-label indications:
  - Hemophilia A or B with inhibitors to exogenous factor VIII or IX preparations
  - Congenital factor VII deficiency
  - ***Glanzmanns thrombasthenia***
- Off-label indications:
  - To reverse anticoagulant effects of:
    - Warfarin, LMWH
    - Selective Xa inhibitors: fondaparinux
  - Trauma with excess bleeding
  - Intracerebral hemorrhage
  - Cardiac surgery
  - Orthotopic liver transplantation, liver biopsy
  - Gastrointestinal bleeding
  - Retropubic prostatectomy
  - Obstetrical hemorrhage.

Dosage

FDA Guidelines

- For hemophilia A/B with inhibitors: For bleeding episodes:
  - 90 µg/kg bolus Q2H until hemostasis is achieved
  - Posthemostatic dosing: Q3-6H for severe bleeds.
- Hemophilia A/B with inhibitors: For surgery:
  - 90 µg/kg immediately before surgery and every second hourly during surgery
  - Postsurgical dosing:
    - Minor surgeries:
      - 90 µg/kg IV Q2H for first 48 hours
      - Then Q2-6H until healing is achieved.
    - Major surgeries:
      - 90 µg/kg IV Q2H for first 5 days
      - Then Q4H till hemostasis is achieved.
- Trauma patients: 75–200 µg/kg
- Bleeding unresponsive to conventional therapy: 60 µg/kg

- Factor VII deficiency: 15–30 µg/kg Q4-6H until hemostasis is achieved
- Acquired hemophilia: 70–90 µg/kg Q2-3H until hemostasis is achieved.

Monitoring During Therapy

- PT/INR, aPTT and factor VII levels may be useful
- Factor VII has the ability to normalize INR and shorten prolonged aPTT in hemophilia.

Contraindications

- Clinical states where in tissue factor is widely exposed:
  - If administered, thrombosis occurs at locations distant from the site of bleeding
  - Examples:
    - DIC, crush injury, septicemia
    - Postcardiac surgery
    - Patients on ECMO or ventricular assist devices.
- Patients with known hypercoagulability:
  - History of thrombotic complications like MI, liver disease, DIC
  - Elderly patients, postoperative immobilization
  - ***Factor-V Leiden deficiency***
  - Antiphospholipid antibody syndrome.
- Acidosis:
  - Acidosis decreases the efficacy of recombinant factor VIIa
  - Administration avoided when pH is less than 7.2
  - Thus pH should be maintained above 7.2 before instituting therapy.
- Hypothermia (less than 33 °C):
  - Hypothermia decreases the efficacy of recombinant factor VIIa
  - Hence, temperature should be maintained above 33 °C before instituting therapy.
- Hypersensitivity: Avoided when hypersensitivity to:
  - Novoseven
  - Mouse/hamster/bovine proteins.

Benefits

- Anticoagulant therapy:
  - Used to reverse effect of warfarin
  - Useful when vitamin K supplementation is insufficient
  - However, fibrin burst occurs in response to factor VIIa therapy
  - This requires availability of factor X
  - Thus, in severe overdose, factor VIIa alone might be ineffective.
- Hemorrhagic stroke:
  - Useful in patients with intracranial hemorrhage
  - Factor VIIa use showed a reduction in expansion of the hemorrhage
  - This resulted in a reduction in mortality.
- Cardiac surgery:
  - Has been used to control bleeding in cardiac surgery
  - Prophylactic administration, however, is not recommended.
- Orthotopic liver transplant/liver biopsy:
  - Prophylactic administration recommended in:
  - Patients with a poor MELD score
  - Patients with prolonged prothrombin
  - Reduces intraoperative bleeding.
- Trauma: Owing to the high cost, use is restricted to:
  - Patients with survivable injury/medical disease
  - Patients not in terminal shock (pH less than 7, K^+ more than 6 meq/l)
  - Not in cardiac arrest
  - Not requiring vasoactive support.

Side Effects

- Pyrexia, headache, pruritus
- Injection site reaction, hypertension, urticaria
- Arthralgia, hypotension, hypersensitivity
- Thrombotic events:
  - Occur at sites distant from the site of bleeding
  - Majority of these events produce arterial thrombi resulting in:
    - CVA, MI
    - Pulmonary emboli
    - Clotted devices
    - Deep veins thrombosis/superficial thrombophlebitis.
- Antibody formation: should be suspected if:
  - Factor VIIa activity fails to reach expected levels
  - Prothrombin time is not corrected
  - Bleeding not controlled after treatment with recommended dose.
- High cost limits its routine use in clinical situations.

Drug Interactions

- Avoid simultaneous use of activated prothrombin complex/prothrombin complex concentrates
- Novoseven should not be mixed with infusion solutions.

ARTIFICIAL BLOOD[1,2,3]

Introduction

- The term artificial blood is applied to substitutes designed to replace oxygen carrying capacity of human RBCs
- The term oxygen therapeutics more accurately describes these substitutes, as blood performs other functions besides carrying oxygen
- Also called ***synthetic oxygen carrying substances/ synthetic blood.***

Types

- Oxygen carriers can be divided into two main groups:
  - Perfluorocarbons (PFCs) emulsion
  - Modified hemoglobin solutions.
- Perfluorocarbons:
  - Chemically inert synthetic molecules which consist primarily of carbon and fluorine atoms
  - Oxygen has 100 times greater affinity for PFC solutions than in plasma
  - PFCs therefore increase dissolved O_2 in fluid phase of blood without binding to O_2 molecule
  - PFCs can dissolve many other gases like CO_2 also
  - PFCs molecules are very small (< 0.2 μm)
  - They measure about one-fourth the diameter of an RBC
  - This small size enables them to traverse capillaries through which RBCs cannot flow
  - This can benefit damaged tissue where RBCs cannot flow through
  - PFCs will not mix with blood and thus emulsions are made by dispersing small drops of PFCs in water
  - This liquid is then mixed with antibiotics, vitamins, nutrients and salt
  - PFCs can carry O_2 so well that humans can survive breathing liquid PFC solution: Called liquid breathing.
- Hemoglobin based oxygen carriers (HBOCs):
  - The Hb molecule in HBOCs needs to be stabilized to prevent the dissociation of $\alpha_2\beta_2$ tetramers into $\alpha\beta$ dimers
  - Formation of dimers renders the hemoglobin nonfunctional
  - Also, formation of dimers is toxic to kidneys as:
    - Dimers get filtered by the kidney
    - They interact with minute amounts of cell wall pieces in renal glomeruli
    - This results in ATN and ARF.
  - Development of a suitable stroma free Hb molecule thus depends on the development of a stable functional tetramer of Hb which would not dissociate into dimmers
  - This problem has been overcome by chemical binding causing polymerization (using dia-spirin) and cross linking and encapsulating these molecules.
- First approved HBOC:
  - Was PFC based
  - Called ***Fluosol DA 20***
  - Manufactured by Green Cross
  - Approved for use in 1989
  - Withdrawn in 1994 due to side effects and complexity of use.

Advantages of Blood Substitutes

- Unlimited source:
  - Donor blood is a limited source
  - Since oxygen therapeutics are synthetic, their supply is unlimited.
- Avoids blood transfusion associated diseases:
  - HIV
  - Hepatitis B
  - ***Creutzfeld-Jakob disease***
  - Mad cow disease
- Blood substitutes do not contain any antigens:
  - Can be used across all blood types without immunological reactions
  - Useful in emergency scenarios where rapid blood transfusion would be impossible.
- Long shelf-life:
  - Can be stored at room temperature for much longer time
  - Most HBOCs have shelf-life of 1–3 years
  - Donated blood has shelf-life of 42 days
- Oxygen carrying capacity:
  - Blood substitutes allow for immediate full capacity oxygen transport
  - Transfused blood requires 24 hours to reach full oxygen transport capacity
  - This is due to 2,3-DPG depletion in stored blood.

Parameter	Synthetic blood	Allogenic blood
Oxygen delivery	Rapid and consistent	Dependant on 2,3-DPG
Risk of disease transmission	None	Present
Storage	Room temperature	Stored refridgerated
	Stable efficacy	Loss of efficacy
Shelf-life	1–3 years	42 days
Preparation	Ready to use	Cross match required
Compatibility	Universal	Type specific
Duration of action	1–3 days	60–90 days

Perfluorocarbons

Examples

- Oxygent:
  - PFCs are surrounded by lecithin surfactant
  - These are suspended in water based solution
  - Lecithin is digested intracellularly
  - Have slightly increased risk of stroke.
- Oxycyte: Undergoing phase II trials
- PHER–O_2: Still in research phase
- Perfluoran: Being used in Russia and Mexico
- Perflubron:
  - Newer emulsion in which emulsifying agents are similar to primary compound
  - Perflubron (perfluorooctyl-bromide) has been developed as a stable emulsion by addition of perfluorodecyl bromide as emulsifying agent
  - The emulsion is then buffered with egg yolk phospholipids
  - The resulting solution has an oxygen carrying capacity which is almost 3 fold that of earlier fluosol solutions
  - Solution also has a longer half life.

Physiology

- Perfluobron oxygen carrying capacity is directly related to the oxygen partial pressure
- Direct diffusion of oxygen is the mechanism by which oxygen is delivered to the tissues
- Thus, oxygen delivered to the tissues may be more available and more readily off loaded from the blood stream than Hb delivered oxygen
- The oxygen content of PFC obeys ***Henry's laws of partial pressures***:
  - The amount of oxygen dissolved in a PFC solution is directly related to the partial pressure of oxygen, to which the solution is exposed
  - This fact limits use of PFCs to situations where partial pressures of oxygen are supranormal, i.e. when alveolar oxygen tension (PaO_2) reaches 400 mm Hg
  - This is impossible to attain without supplemental oxygen administration
  - Such high PaO_2 may be impossible at high altitudes with any maneuver.

Advantages of PFCs

- The amount of oxygen dissolved in plasma is only less than 1% of total oxygen content in arterial blood
- By contrast, administration of perfluobron can increase dissolved oxygen to 10–15% of total arterial oxygen content.

Disadvantages of PFCs

- Long half life:
  - PFC molecules are sequestered in reticulo-endothelial system particularly in Kupffer cells of liver and macrophages
  - These are subsequently released into the plasma as dissolved gas
  - The PFC gas is then exhaled unchanged and unmetabolized via the lungs
  - Current generation PFCs have a retention time of around 1 week in the RES
  - Thus, PFCs have a retention time of nearly 1 week in the RES
  - This poses a problem with respect to dosage
  - Although PFC gas has a half life of 3-4 hours in plasma phase, the longer T ½ in RES
  - Limits additional dosing of PFCs for 1–2 weeks
  - Thus, PFCs are essentially single dose drugs
- Also, effective oxygen delivery occurs at supra-normal alveolar oxygen tension (400 mm Hg).

Hemoglobin-based Oxygen Carriers (HBOC)

Examples

- Hemopure:
  - Ultrapurified bovine RBCs which have been glutaraldehyde polymerized
  - They are then suspended in balanced salt solution.
- Oxyglobin:
  - Stabilized bovine hemoglobin in balanced salt solution with no RBCs
  - Approved for veterinary use.
- Polyheme:
  - Uses human hemoglobin polymerized and incorporated into electrolyte solution
  - If hemoglobin gets disassociated, it takes up nitric oxide, causing vasoconstriction.
- Hemospan:
  - Available in powder form which is then mixed and transfused
  - Polyethylene (PEG) glycol is used to eliminate Hb toxicity
  - It can be stored for many years.
- Dextran hemoglobin
- Hemotech: Half life of 180 days compared to 41 days for donated blood
- Hemassist: Diaspirin crosslinked hemoglobin
- Recombinant hemoglobin (rHb 1.1 and rHb 2.0)
- Maleimide activated PEG modified Hb (MP_4).

Physiology

- HBOCs cause shift of oxygen-hemoglobin dissociation curve to left
- Lack of 2,3-DPG associated with stroma free hemoglobin causes the hemoglobin to be non functional at physiological levels of tissue oxygenation
- The P_{50} of native *stroma free hemoglobin (SFH)* is around 17 mm Hg
- This problem has been overcome by binding pyridoxal phosphate to the hemoglobin molecule.
- The resulting SFH has a P_{50} of 32 mm Hg as compared to native RBC associated Hb with P_{50} of 27 mm Hg.

Advantages of HBOCs

- Do not require supranormal oxygen tension to be effective in delivering oxygen
- Lack of isoagglutinating antigens due to absence of RBC membrane obviates blood typing and screening
- Does not transmit HIV or hepatitis B/C.

Disadvantages of HBOCs

- Plasma hemoglobin is not a true blood substitute:
  - Hemoglobin can replace only the oxygen transport capacity of blood
  - Lacks the coagulation/immunological aspects of blood.
- Free hemoglobin avidly binds nitric oxide, causing HTN due to vasoconstriction
- Metabolism of free hemoglobin:
  - Identical to natural hemoglobin released from RBC destruction
  - This can cause increase in bilirubin levels
  - Amylase levels also increase (from pancreas).
- Consequences of HBOC metabolism may be similar to multiple blood transfusions:
  - Hemosiderosis
  - Chronic iron overload.
- Decrease in cardiac index (may be due to nitric oxide).

Recombinant Human Hemoglobin

- Produced using E.coli expression system
- α-subunits are covalently bound by addition of a single amino acid to the genetic structure of native hemoglobin, thus preventing dissociation of hemoglobin tetramer
- This produces hemoglobin with P_{50} of 32 mm Hg
- Advantages:
  - Does not require cross matching
  - Does not transmit disease
  - Maximum tolerable dose of rHb is unknown
- rHb 1.1 is produced from E. coli and causes arterial vasoconstriction
- rHb 2.0 does not cause vasoconstriction.

Newer Technologies

- Hemoglobin containing vesicles (nano-dimension artificial RBCs)
- Allosteric modifier (RSR13)
- Stem cells: Hematopoietic stem cells used to produce RBCs
- Dendrimers: Used as substitute oxygen carriers
- Biodegradable micelles:
  - Recombinant hemoglobin is encapsulated within micelle forming amphiphillic block copolymers
  - These are between 30–100 nm in diameter
  - The hydrophobic core of polymer micelle solubilizes the similarly hydrophobic Hb protein
  - The water soluble corona (usually polyethyleneglycol/PEG) provides barrier to protein

absorption and provides protection from clearance by RES.
- Placental umbilical cord blood:
  - Cord blood collected aseptically from placenta after birth can be used as blood substitute
  - It has a higher hemoglobin content and growth factors than normal blood.

SICKLE-CELL ANEMIA[1,3,8,16]

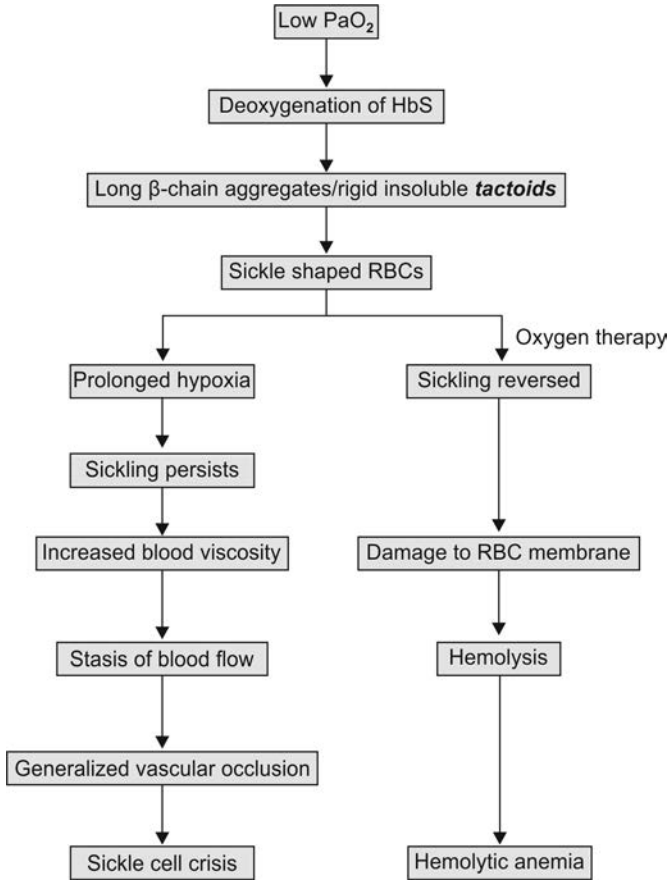
Introduction
- Sickle cell anemia is a hemoglobinopathy in which the dominant Hb is unstable HbS instead of HbA
- Sickle cell syndrome includes:
  - Sickle cell anemia (HbSS)
  - Double heterozygote condtions like
    - Sickle cell C (HbSC)
    - Sickle thalassemia (HbSThal).

Genetics
- HbS occurs due to a mutation in chromosome 11
- Glutamic acid is replaced by valine at 6th position from N-terminus of β chain
- Sickle cell trail refers to heterozygotes who have one βA and one βS chain (HbSA)
- Sickle cell disease refers to homozygotes who have both βS genes.

Incidence
- Endemic in Africa, Meditteranean, Middle east and India
- Sickle cell trait occurs in 8-10% African-Americans
- 0.2% homozygotes with sickle cell disease amongst African–Americans.

Types
- Sickle cell trait: (SCT)
  - Heterozygous for sickle gene (HbSA)
  - Asymptomatic carrier state for HbS
  - RBCs have HbS concentration < 50% (38–45%)
  - Have normal blood film and Hb level
  - Are asymptomatic but have positive sickling test
  - HbAs begins to sickle only when oxygen saturation of Hb is less than 20%
  - No special treatment is required, except to avoid:
    - Hypoxia
    - Dehydration
    - Infection
    - Acidosis
    - Hypothermia.
- Sickle cell disease: (SCD)
  - Homozygous for sickle gene (HbSS)
  - RBCs have HbS concentration between 70–98%
  - RBC lifespan reduced to 12–17 days in contrast to normal of 120 days
  - Characterized by chronic hemolysis, acute episodic vaso-occlusive crisis.

Pathophysiology



Mechanisms of Cellular Injury in SCD
- Erythrocyte and platelet adhesion to endothelium
- Endothelial dysfunction secondary to inflammation and reduction of NO
- Reduced NO due to leukocyte superoxide release
- Leucocytosis and complement system activation
- Activation of coagulation cascade with thrombosis and ischemia
- Activation of cytokine and inflammatory mediators
- Free radical injury due to leukocyte superoxide release
- Free radical injury secondary to free Hb

- Reperfusion injury
- Excessive iron stores secondary to repeated erythrocyte transfusion.

Clinical Features

- Clinical features manifest at 3–4 months of age when switch from HbF to HbA occurs
- Episodic painful crisis bone and joint pains common where pain is poorly localized
- Central nervous system:
  - Stroke
  - Aneurysms
  - Meningitis.
- Psychological:
  - Depression, anxiety
  - Substance abuse, Narcotic dependence
- Eye:
  - ***Proliferative sickle retinopathy***
  - Hemorrhage, visual loss
- Cardiovascular system:
  - Cardiomegaly, cardiomyopathy
  - Pulmonary HTN, cor pulmonale
  - Diastolic dysfunction.
- Respiratory system:
  - ***Acute chest syndrome***
  - Hypoxemia, pulmonary infarcts, fibrosis
  - Asthma, sleep apnea
  - Thromboembolism
  - Pneumonia.
- Hematological:
  - ***Hemolytic anemia***
  - Aplastic anemia
  - Shift to left of oxyhemoglobin dissociation curve (ODC).
- Immune system:
  - Immunosuppression, increased infections and sepsis due to:
    - Reduced IgM levels
    - Reduced capacity for phagocytosis
    - Reduced capacity for opsonization.
  - Leucocytosis.
- Musculoskeletal:
  - ***Painful crisis***
  - Bone marrow hyperplasia
  - Avascular necrosis
  - Osteomyelitis
  - Bone infarcts
  - Skeletal deformities, growth retardation
  - Cutaneous ulcers.
- Spleen:
  - ***Autoinfarction***
  - Hyposplenism
  - ***Splenic sequestration.***
- Liver:
  - Jaundice
  - Hepatitis
  - Cirrhosis
  - Gallstones, cholestasis.
- Genitourinary:
  - Priapism
  - Polyuria due to impaired concentrating ability of kidney
  - Chronic renal failure
  - Papillary necrosis, glomerular necrosis.

Predictors for Increased Risk of Complications

- Age > 30 years
- Previous history of stroke/acute coronary syndrome
- Asthma, resting hypoxemia
- Frequent painful crises
- Pulmonary HTN
- Thoracic, cardiac and intracranial surgeries: high risk
- Abdominal and orthopedic surgeries: moderate risk
- Tonsillectomy, adenoidectomy, myringotomy: mild risk.

Life-threatening Complications

- Sepsis
- Aplastic crisis
- Splenic sequestration
- Acute chest syndrome.

Causes of End Organ Damage

- Sickling and adhesion of cells in blood vessels secondary to tissue ischemia
- Hemolytic crisis/aplastic crisis.

Sickle-cell Crisis

- Vascular occlusion with organ infarction and pain
  - Acute chest syndrome
  - Infarctive crisis.
- Hemolytic crisis with features of sudden hemolysis
- Sequestration syndrome with RBCs sequestration in liver and spleen
- Aplastic crisis with bone marrow suppression.

Acute Chest Syndrome

- Precipitated by:
  - Pulmonary infection
  - Fat embolism from bone marrow necrosis
  - Worsening of asthma
  - Perioperative respiratory dysfunction.
- Clinical features:
  - Fever, cough
  - Dyspnea, tachypnea, wheezing
  - Chest pain, hypoxemia
  - Pleural effusion and pulmonary infilterates on chest X-ray
  - Progresses to ARDS, respiratory failure, pneumonia
- Treatment:
  - Bronchodilators
  - Mechanical ventilation
  - Antibiotics
  - Steroids
  - Exchange transfusion to reduce HbS concentration.

Infarctive Crises

- Precipitated by:
  - Infection
  - Trauma
  - High temperature.
- Clinical features:
  - Acute onset pain
  - Usually abdominal pain, fever, vomiting.
- Treatment:
  - Adequate hydration
  - Partial alkalinization of blood
  - Partial exchange transfusion with HbA containing RBCs
  - Antibiotics
  - Oral bicarbonate upto 20g/day to produce alkalinisation
  - Treatment of pain with opioids/epidural local anesthetics + opioids.

Hemolytic Crises

- Drop in Hb, increase in reticulocytes and bilirubin
- Usually accompanies vaso-occlusive crisis.

Splenic Sequestration Crises

- Occurs mainly in children
- Treatment:
  - Volume resuscitation
  - RBC transfusion
  - Splenectomy after resolution of crisis.

Aplastic Crises

- Temporary bone marrow shut down manifested by:
  - Precipitous fall in Hb
  - Absence of reticulocytes.
- RBC transfusion given till normal marrow function is re-established.

Factors Causing Increased Sickling

- HbS concentration $\geq 50\%$
- Low PO_2: $PaO_2 \leq 40$ mm Hg causes sickling in SCD
- $PaO_2 \leq 20$ mm Hg causes sickling in SC trait
- Reduced body temperature causes vasoconstriction causing stasis and sickling
- Increased body temperature casues increasing metabolic requirements precipitating sickling
- Dehydration
- Acidosis favors sickling which is more in veins than arteries.

Investigations

- Complete blood count
  - Hb usually between 6–9 gm% in SC trait
  - Leucocytosis and thrombocytosis occur as reactive features.
- Peripheral blood smear:
  - Normal in SC trait
  - Normocytic normochromic anemia
  - Increased reticulocytes, sickled cells and target cells
  - ***Howell–Jolly*** bodies if atrophied spleen.
- Sickling test with sodium metabisulfate
- Screening for HbS with quick solubility test, e.g. ***Sickledex***
- Hb electrophoresis:
  - Definitive and confirmatory
  - HbS level aimed at < 30% in crisis.
- BUN, serum creatinine, urinanalysis
- Chest X-ray, ECG, ECHO
- Liver function tests, electrolytes, PT/PTT, INR
- ABG in patients with cardiac disease.

Treatment

- Mainly supportive
- Early treatment of complication
- Hydroxyurea used to increase circulating levels of HbF

- Only *curative therapy is bone marrow transplant* reserved for young patients having severe presentation
- Hyperbaric O_2 therapy used in SC crises due to:
  - Reduction in rate of sickling
  - Improved tissue oxygenation by direct diffusion.
- Splenic autoinfarcts require lifelong therapy with:
  - Penicillin
  - Aggressive immunization programme against pneumococcus.

Preoperative Preparation

- Assessment of existing organ dysfunction
- Preoperative hydration aggressively is necessary
- Prophylactic antibiotic cover with correction of coexisting infection
- Preoperative alkalinization has antisickling effect but shifts ODC to left
- Preoperative transfusion:
  - Hematologist advice before surgery
  - Transfusion goals:
    - To increase HbA to 40–50%
    - To decrease HbS < 30%
    - Hematocrit of 30–35%
    - Hematocrit to be kept < 35% as:
    - Increased HCT will cause increase in blood viscosity
    - This precludes stasis in circulation
    - This can cause vascular occlusion.
  - If exchange transfusion needed, use only buffy coat poor, HbS free, washed RBCs
  - Compatible blood difficult to find as RBC antibodies common due to multiple transfusions
  - Sample blood for grouping and antibody screening as previous transfusion common
  - Patient selection for exchange transfusion:
    - Minor surgery: Not required unless severe SCD
    - Moderate to high risk surgery: Transfusion required.

Anesthetic Goals

Maintain

- Good oxygenation
- Good hydration
- Normothermia
- Normal acid base balance
- Avoid tourniquets/limb circulation stasis.

Intraoperative Management

Preoperative Preparation and Premedication

- NPO orders
- Informed consent
- Avoid drugs causing respiratory depression: Opioids avoided.

Monitoring

- Pulse oximetry in multiple areas including ear and toe especially in pregnant patients
- NIBP
- Urine output
- ECG
- Capnography
- If pulmonary HTN or cardiac dysfunction, IBP and CVP monitoring
- Serial arterial blood gases to ensure adequate oxygenation.

Induction

- Adequate preoxygenation with high FiO_2
- Induction with thiopentone and succinylcholine followed by tracheal intubation
- Avoid endobronchial intubation as one lung ventilation precipitates acute chest syndrome.

Maintenance

- Moderate hyperventilation maintained with N_2O + O_2 + isoflurane
- Opioids + NDMR + Volatile anesthetics
- Opioids carefully titrated to prevent postoperative respiratory depression
- Guidelines for tourniquet use:
  - It should be applied as distally as possible
  - Limb should be thoroughly exsanguinated before application
  - Ischemic time should be minimized
  - Prevent respiratory and metabolic acidosis at the time of tourniquet release
- Avoid conditions which increase sickling:
  - Adequate oxygenation necessary
  - Prevent vascular stasis
  - Avoid increases in oxygen consumption: Maintain deep planes of anesthesia
  - Avoid hypothermia.

Ventilation

- Titrate FiO_2 to maintain normal or increased PaO_2
- Avoid hypoventilation and hypoxia
- Prevent respiratory/metabolic acidosis.

Hemodynamics

- Rapid correction of hypotension and maintenance of intravascular fluid volume
- Maintain blood visocity at low level:
  - Limit maximum hematocrit to 35%
  - Avoid overtransfusion.
- Avoid hypothermia using body warming and IV fluid warming devices
- Avoid shivering.

Role of Regional Anesthesia

- Regional anesthesia is better avoided
- Administer supplemental O_2
- Compensatory vasoconstriction, stasis and reduced PaO_2 may occur in areas which are not blocked and may result in infarction.

Postoperative

Complications

- Increased respiratory infections
- Acute chest syndrome in SCD patients undergoing surgery under GA
- Sequestration syndrome: Lethal in obstetric patients immediately postpartum
- CCF in patients with cardiomegaly and pulmonary HTN.

Management

- Supplemental O_2
- Chest physiotherapy
- Adequate antibiotic cover to control chest infection
- Maintain intravascular volume, HCT between 30–35%
- Early mobilization
- Respiratory depression, acidosis and hypoxia, may occur with opioids
- Avoid shivering as it increases O_2 consumption.

Pain

- Carefully titrated opioids for pain relief
- Tolerance to opioids possible due to frequent opioid based analgesia for sickle crises
- NSAIDs only as adjuvant therapy
- Local infilteration techniques useful-multimodal analgesia.

DISSEMINATED INTRAVASCULAR COAGULATION[1,3,10,16]

Introduction

An acquired condition characterized by intravascular activation of coagulation with loss of localization causing widespread coagulation.

Causes

Obstetric Causes

- Amniotic fluid embolism
- Intrauterine fetal death
- Abruptio placentae
- Septic abortion
- Preeclampsia, HELLP syndrome.

Extensive Tissue Damage

- Trauma, crush injury
- Burns
- Rhabomyolysis
- Hypo/hyperthermia
- Hemolytic transfusion reactions, multiple transfusions.

Infections

- Bacteremias: *most common*
- Gram negative toxemia
- Rocky mountain spotted fever
- Fungemias
- Viremias.

Malignancies

- Adenocarcinomas
- Prostatic carcinoma
- Promyelocytic leukemia
- Metastatic malignancies
- ***Trousseau's syndrome.***

Vascular Abnormalities

- Abdominal aortic aneurysm
- Giant hemangiomas
- Vasculitis
- Multiple telangiectasias.

Fat Embolism

- Long bone fractures
- Sickle cell crisis.

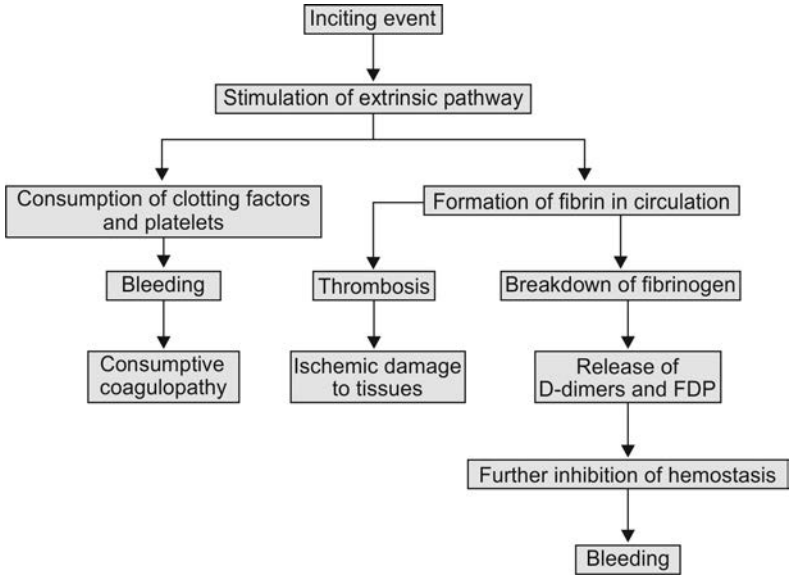
Toxic Procoagulant Molecules

- Rattle snake venom
- Viper venom.

Organ Damage

- Liver failure
- Stroke
- Head injury.

Pathophysiology[1,10]



Clinical Features

Signs of DIC

- Bleeding from at least 3 unrelated sites suggests DIC
- Bleeding more common in acute fulminant DIC
- Thrombotic manifestations seen in chronic DIC
- Thrombotic manifestations occur first in malignancy associated DIC
- In others, hemorrhagic diathesis occurs first
- Organs with greatest blood supply like kidney and brain suffer maximum damage
- Pulmonary function may be impaired due to microthrombus formation
- Signs of bleeding:
  - Petechiae, purpura, subcutaneous hematomas
  - Ecchymosis, hemorrhagic bullae, jaundice
  - Bleeding from GIT, GUT, mucosal and venepuncture sites.
- Signs of thrombosis:
  - Acral cyanosis
  - Skin necrosis of lower limbs: Purpura fulminans
  - Localized infarction and gangrene.

Signs of Multiorgan Failure

- CNS: Altered consciousness, stupor
- CVS: Hypotension, tachycardia, circulatory collapse
- RS: Pleuritis, ARDS
- GIT: Hematemesis, hematochezia
- GUT: Renal failure, renal cortical necrosis, metrorhaggia.

Complications

- Purpura fulminans
- Multiorgan failure.

Differential Diagnosis

- Acute/chronic liver failure
- Hemolytic uremic syndrome
- Thrombolic thrombocytopenic purpura
- Heparin induced thrombocytopenia
- Other consumptive coagulopathies.

Components of DIC

- Exposure of blood to procoagulant substances
- Fibrin deposition in microvasculature
- Impaired fibrinolysis
- Depletion of coagulation factors and platelets (***Consumptive Coagulopathy***)
- Multiple organ damage and failure.

Investigations[3]

No	Test	Normal	DIC
		Most useful	
1	Platelet count	2.5–4 lacs/µL	< 50,000/µL
2	Fibrinogen level	400–650 mg/dL	< 150 mg/dL
3	Prothrombin time	10–12 seconds	> 100 seconds
		Helpful	
1	aPTT	35–50 seconds	> 100 seconds
2	Thrombin time	15–20 seconds	> 100 seconds
3	Fragmented RBCs/schistocytes	Absent	Present
4	FDP and d-Dimers	< 16 µ/ml	> 200 µg/ml
5	Specific factors:		
	II		Reduced
	V		Reduced
	VII		Reduced
	VIII		Reduced/normal/high
	IX, X		Reduced

Other Investigations

- ***3P test (plasma-protamine-paracoagulation) test:***
  - Can be used to confirm diagnosis sometimes
  - Tests for presence of soluble complexes composed of fibrin monomers (generated by excess thrombosis) and FDPS
  - The addition of protamine destabilizes these complexes forming a precipitate.
- Levels of prothrombin fragments F1+ F2
- Levels of thrombin-antithrombin complexes
- α_2 antiplasmin levels reduced by binding to excess plasmin
- Reduced plasminogen
- Reduced protein C-levels
- Thromboelastography.

DIC Score

Scoring	0	1	2	3
Platelet count	> 100000	< 100000	< 50000	
Fibrin marker	No elevation	Moderate elevation	Strong increase	Strong increase
Prolonged INR	< 3 seconds	3–6 seconds	> 6 seconds	
Fibrinogen levels	> 1 g/L	< 1 g/L		

- Score > 5 compatible with overt DIC and scoring has to be repeated daily
- Score < 5 suggestive of now overt DIC.

Treatment

Treatment Goals

- To increase fibrinogen levels to 100–150 mg/dL
- Supportive therapy for circulatory compromise
- Treatment of cause.

Treatment of underlying cause

- Antibiotics for septicemia
- Uterine evacuation/hysterectomy for obstetric cause
- Antisnake venom.

Supportive Therapy

- Correction of:
  - Hypovolemia
  - Acidosis
  - Hypothermia.

- Fluids, RBCs/inotropes to support CVS
- Mechanical ventilation if respiratory complications.

Hemostatic Therapy

- Indications:
  - Platelets if platelet count < 50,000/µl with bleeding or if platelet count < 20, 000/µl
  - Cryoprecipitate when fibrinogen level < 50 mg/dl
  - Fresh frozen plasma to replace clotting factors.

Component	Dose	Lab parameter	Target lab parameter	
			No clinically significant bleeding	Clinically significant bleeding
Platelets	1 dose	Platelet count	> 100000/µl	20–50000/µl
FFP	10–15 ml/kg Usually 3–5 units	aPTT/PT		< 1.5 times upper limit of normal reference range
Cryoprecipitate	10 units	Fibrinogen	>80-100 mg/dl	> 80–100 mg/dl

- 1 dose of platelets is equal to:
  - 1 unit of single donor platelets
  - Or a 4 pack or 6 pack of pooled random donor platelets.

Heparin

- Use restricted to conditions where thrombosis is clinically problematic
- Also useful in chronic DIC
- 5–10 IU/Kg/hr as infusion without any bolus dose
- Avoid if intracranial/GI bleed/abruption/imminent surgery
- For refractory bleeding, heparin use is controversial.

Antifibrinolytics

- Used only if all other modalities are unsuccessful
- Used only if documented hypofibrinogenemia and fibrinolysis
- Disastrous if administered in the presence of widespread thrombosis as it can cause disseminated thromboembolism.

Other Therapies

- Recombinant activated protein:
  - Especially useful in patients with sepsis
  - Reduces mortality and organ failure.
- Antithrombin III concentrates (ATC)
- Tumor factor inhibitors.

Anesthetic Management

Preoperative Preparation

- Manage underlying cause:
  - Antibotics
  - Correct hypovolemia
  - Fluids and blood products warmed to avoid hypothermia
  - Surgery to remove cause as soon as coagulopathy corrected to acceptable level.
- Correct coagulopathy: PC and FFP, cryoprecipitate if fibrinogen < 1g/dl
- Heparin is best avoided before surgery
- Premedication avoided in critically ill
- IM injections are avoided.

Perioperative Management

- Regional anesthesia contraindicated in coagulopathy
- Controlled ventilation and invasive monitoring preferred in critically ill patients
- Nasotracheal intubation avoided
- Insert NGT carefully to prevent trauma
- Large bore IV cannula with infusion of warmed IV fluids
- Replace blood loss promptly
- Measure platelet count and clotting function regularly and replace promptly.

Postoperative Management

- May require mechanical ventilation, intensive cardiovascular monitoring and support
- Frequent measurement of hematological parameters.

THROMBOELASTOGRAPHY[1,3,10]

Introduction

- Viscoelastic technique which measures the entire spectrum of clot formation from early fibrin strands, then clot retraction and eventually fibrinolysis

- Developed by Harter in 1948
- Provides a measure of the mechanical properties of evolving clot as a function of time
- It evaluates clot formation as a dynamic process unlike standard coagulation tests which measure isolated end points.

Method of Recording

- 0.35 ml of blood is placed in a prewarmed cuvette containing:
  - Calcium
  - Contact activator
  - The metal piston is attached by a torsion wire to an electronic needle recorder
  - The piston is lowered into the blood in the cuvette
  - Cuvette continuously rotates around an axis of 5° arc forwards and backwards
- As clot formation occurs, the piston becomes enmeshed within the clot
- Rotation of the cuvette is then transferred to the piston and to an electronic recorder
- The amplitude of excursion of the recorder is proportional to the speed of piston rotation
- Interpretations:
  - A weak clot stretches and thus delays the arc movement of the piston which is expressed as a narrow TEG
  - A strong clot will move the piston simultaneously and proportionally to the cuvette movements forming a thick thromboelastogram.

Disadvantages

- Lack of specificity associated with abnormal findings
- Qualitative assessment is not possible.

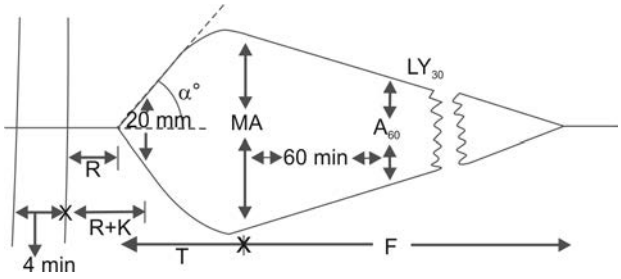


Fig. 5.1: Normal thromboelastogram[3]

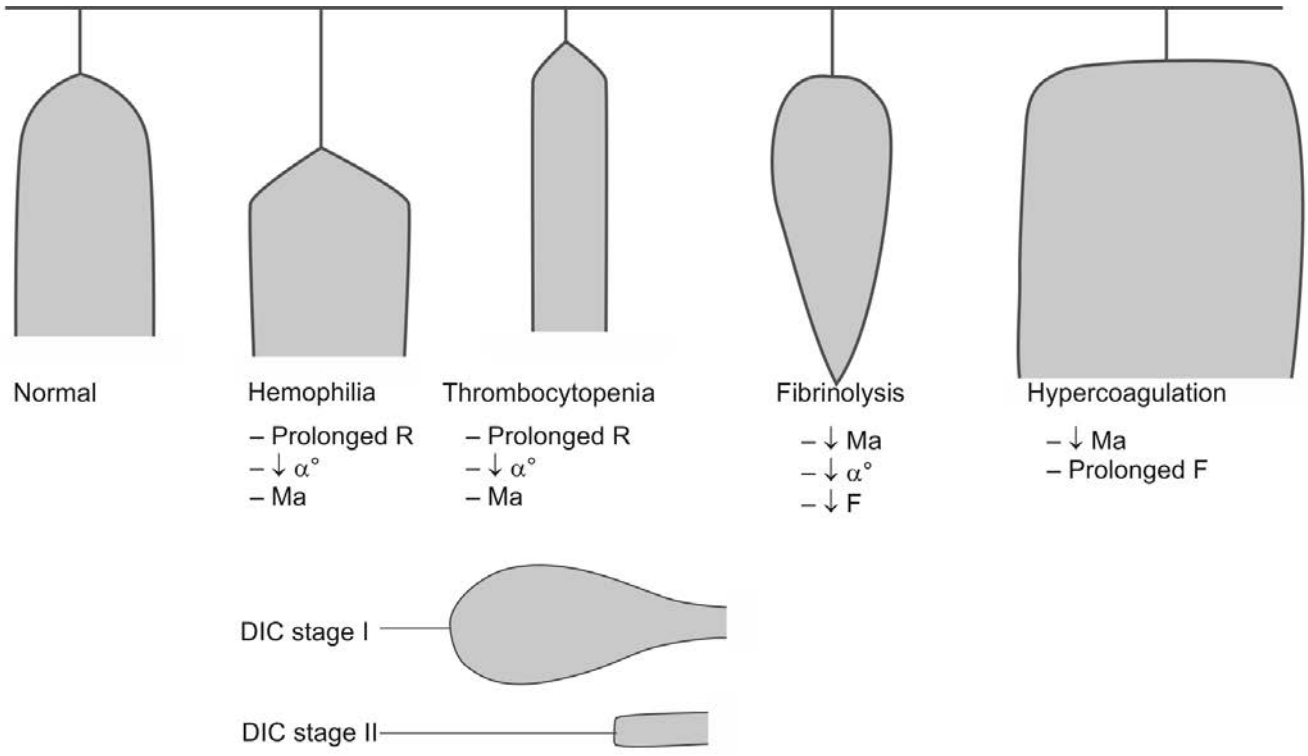


Fig. 5.2: Thromboelastogram patterns[3]

Parameters Measured by TEG[1,3]

Parameter	Description	Normal	Increased	Decreased
R	Period of time from initiation of test to formation of initial clot	7.5-15 mins 5-7 mins Kaolin activated	• Factor deficiency • Intrinsic pathway defects • Anticoagulation • Heparin • Hypofibrinogenemia • Thrombocytopenia	Hypercoagulable states
K	From beginning of clot formation till amplitude of clot formation reaches 20 mm, Represents dynamics of clot formation	5–10 mins 1–3 mins Kaolin	• Factor deficiency • Thrombocytopenia • Thrombocytopathy • Hypofibrinogenemia	Hypercoagulable states
α angle Represents rate of clot formation and acceleration kinetics of fibrin build up and cross linking	Angle between line in the middle of TEG tracing and line tangential to the developing body of tracing	20–40° 53–67° Kaolin	Hypercoaguable state	• Hypofibrinogenemia • Thrombocytopenia
MA Maximum amplitude	Maximum amplitude reflects strength of a clot which is dependent on number and function of platelets (80%) and its interaction with fibrin (20%)	47–58 mm 59–68 mm Kaolin	Hypercoaguable state	• Fibrinolysis • Thrombocytopenia • Thrombocytopathy • Hypofibrinogenemia
MA60	Measures rate of amplitude reduction 60 mins after MA Represents clot stability			Fibrinolysis
$\frac{MA + x}{MA}$	Ratio of amplitude at specific time interval (x) after MA, divided by MA Used as a measure of rate of fibrinolysis $\frac{MA + 60}{MA}$ is most widely used	Ratio < 0.85 represents abnormal fibrinolysis		
A_{60}	Amplitude 60 minutes after MA			
F	Whole blood clot lysis time			
LY_{30}	Measures % decrease in amplitude post MA Measures degree of fibrinolysis	< 7.5% < 7.5% with Kaolin	Fibrinolysis	
EPL	Computer prediction of 30 mins lysis based on clot diminution of trace commencing 30 sec post MA, earliest indicator of abnormal lysis	< 15%		

Uses of TEG

- Coagulation monitoring during:
  - Cardiac surgery
  - Obstetric anesthesia
  - Liver transplantation
  - Trauma anesthesia
- Differentiates surgical bleeding from coagulopathy in cardiac surgery
- Real time detection of excessive fibrinolysis in liver transplant and CPB
- Diagnosis of precoagulant defects:
  - Platelet dysfunction
  - DIC
  - Hemophilia
  - Fibrinolysis
  - Hypercoagulability.
- Detects characteristic abnormalities in clot formation and fibrinolysis.

TEG Treatment Algorithm for Bleeding

TEG finding	Interpretation	Treatment
R (plain) > R (heparinise)	Inadequate heparin reversal	Protamine
R between 11–14 mins	Reduced clotting factors	2 units FFP
R > 14 mins	Severe clotting factor deficiency	2 units FFP

Contd...

Contd...

TEG finding	Interpretation	Treatment
40 < MA > 48	Reduced platelet number and function	1 unit platelet
MA < 40	Severe thrombocytopenia	2 units platelets
LY30 > 7.5%, EPL > 15%	Hyperfibrinolysis	Anti-fibrinolytics

Recent Additions to Thromboelastography

- Use of TEG activators or accelerants:
  - Celite
  - Kaolin
  - Tissue factor.
- Use of abciximab to block platelet component of clot formation
- Heparinise cups to make TEG more sensitive to monitor the function and reversal of heparin.

SONOCLOT[1,3]

Introduction

Alternative viscoelastic monitor of coagulation.

Method

- In contrast to TEG, sonoclot immerses a rapidly vibrating probe into a 0.4 ml sample of blood
- As clot formation occurs, impedance to probe movement through the blood increases
- This generates an electrical signal with a characteristic ***clot signature.***

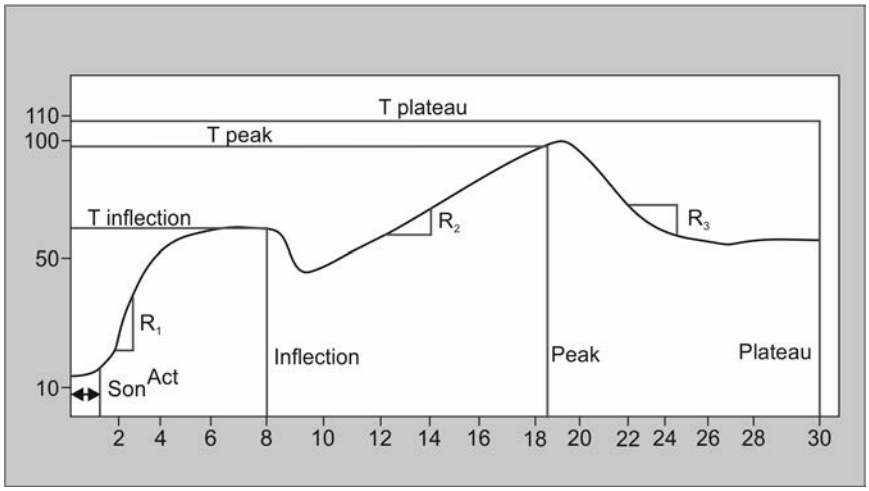


Fig. 5.3: Sonograph

Parameters

Sonact

- The onset time which is the time in seconds from the immersion until the beginning of fibrin formation
- Represented by initial flat portion of graph
- Similar to activated clotting time (ACT).

Initial Upslope R_1

- Indicates rapid increase in viscosity of clot due to conversion of fibrinogen to fibrin
- Reflects speed at which clot is being formed.

Time to Inflection (T-inflection)

- Inflection in graph produced by platelets getting incorporated in fibrin mesh
- Indirect measure of R_1.

R_2

- Represents continuation of clot formation
- Represents strengthening with further fibrinogenesis and platelet fibrin interaction.

T Peak

Represents completion of fibrin formation.

R_3

Downslope represents rate of clot retraction.

Interpretation

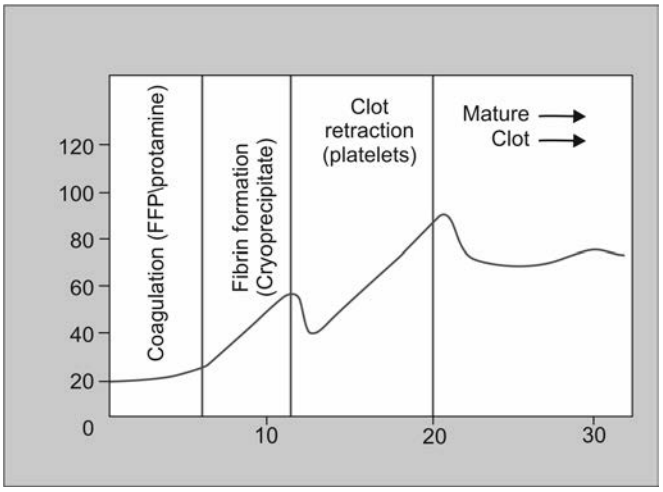


Fig. 5.4: Sonoclot interpretation

- Initial clot formation time: Son ACT
- Fibrin gel formation phase: T inflection
- Fibrin gel formation rate: R_1
- Clot retraction: T peak
- Rate of clot retraction: R_3
- Fibrinolysis.

Uses of Sonoclot

- Used to derive ACT
- Provides information regarding clot strength and fibrinolysis
- Helps to manage anticoagulation
- Manage blood product usage
- Identify hypercoagulable patients.

ACTIVATED PARTIAL THROMBOPLASTIN TIME

Introduction

APTT is a test which measures the time taken for clot formation in recalcified blood plasma following addition of contact activators which measures the activity of intrinsic and common pathways of coagulation.

Specimen

- Citrated anticoagulated whole blood
- Kept refridgerated and transported as soon as possible.

Procedure

- Around 30% of normal concentration of clotting factors can produce normal aPTT
- aPTT reagent should be able to detect factor levels of 30% or less
- Contact activators used are:
  - Celite
  - Kaolin
  - Microsilicate
  - Elagic acid
  - Diatomaceous earth.
- Contact activator avoids prolonged time of natural contact activation
- Plasma sample (platelet poor plasma) added to activator
- This is incubated at 37 °C for 5 mins
- Thromboplastin preparation added, mixed with $CaCl_2$ and timer started
- Time to fibrin clot formation recorded.

Range

- 25–35 second
- Panic range > 70 seconds

- Healthy premature babies have prolonged aPTT which returns to normal at 6 months
- APTT adjusted to 1 ½ to 2 times normal in heparin therapy
- Normal PTT value 120 seconds.

Pathway Tested

Intrinsic and final common pathway.

Factors Tested

- High Molecular Weight Kininogens (HMWK)
- Prekallikrein
- Factors I, II, V, VIII, IX, X, XI, XII.

Uses

- Evaluation of intrinsic pathway
- Heparin therapy: Response to heparin measured with PTT, aPTT, whole blood CT
- Screening for hemophilia A and B (Factor VIII)
- Dysfibrinogenemia
- DIC
- Liver failure
- Vitamin K deficiency.

Prolonged in

- Deficiency of Factors II, V, VIII, IX, X, XI, XII
- Fibrinogen < 100 mg/dL
- Antifactor VIII
- Fibrin degradation products (FDP)
- DIC, Vitamin K deficiency
- Heparin therapy
- Lupus anticoagulant antibodies.

Contraindications

Specimen obtained < 3 hrs after heparin doses.

Additives

- Reaction initiated by kaolin, Ca^{2+} and phospholipids is called aPTT
- Addition of negatively charged phospholipids shortens clotting time
- Phospholipids are platelet substitutes (hence sample is platelet poor)
- Sources of phospholipids:
  - Rabbit brain
  - Cephalin (dehydrated rabbit brain)
  - Bovine brain
  - Soya bean.

PROTHROMBIN TIME

Introduction

- Measures activity of extrinsic pathway (I, II, V, VII, X) and common pathway
- Reaction time which is initiated by addition of thromboplastin and Ca^{2+} to form a clot in whole blood is called prothrombin time.

Specimen

- Sodium citrate anticoagulated whole blood
- Calcium is added to reagent just prior to test.

Procedure

- Clotting time of blood determined after addition of calcium and excess of thromboplastin (0.2 ml) to 0.1 ml plasma at 37 °C
- Clot detection is either by observation/by automated device
- Addition of thromboplastin shortens clotting time of plasma to 11-12 sec
- Result depends on:
  - Concentration and source of thromboplastin
  - Calcium concentration
  - Method used to detect clot formation.
- Results vary from lab to lab.

Normal Range

- 10–14 seconds
- Panic range > 20 sec for nonanticoagulated specimens
- Panic range > 3 times control for anticoagulated specimen
- Healthy premature babies have normally prolonged PT which normalizes by 6 months
- If APTT is normal, prolonged prothrombin time represents F VIII deficiency.

Pathway Tested

Extrinsic coagulation pathway.

Coagulation Factors Tested

Tissue factor, factors I, II, V, X, VII.

Uses

Screening for:

- Deficiency of prothrombin
- Dysfibrinogenemia
- Afibrinogenemia
- Liver failure

- DIC
- Heparin effects
- Coumarin/warfarin effects
- Screening for vitamin K deficiency: (factor V < VII and X)
  - Raised PT reflects severe liver disease unless vitamin K deficiency is present as only 20–30% of normal factor activity is required for clotting
  - Failure of PT to correct following vitamin K administration implies severe liver disease and correction normally requires 24 hrs.

Additives

- Sources of thromboplastin
- Human brain/lung
- Rabbit brain/lung
- Placenta
- Recombinant thromboplastin.

Limitations

- Not a very sensitive test
- Does not identify the cause of hemostatic defect
- PT gets prolonged only when clotting factor activity is < 30%
- Thus, PT increases only marginally even if prothrombin reduces to as low as 10%
- PT is unaffected until fibrinogen < 100 mg/dL
- Thus fall PT identifies the defect very late in course of disease
- More sensitive to fall in factor VII than in factor II (prothrombin)
- Results vary from lab to lab.

INTERNATIONAL NORMALIZED RATIO

Introduction

INR is a mathematical calculation developed to standardize PT values and negate differences in sensitivity between reagents in calculating PT.

Definition

- It is ratio of patient PT time to a control sample raised to the power of ISI value of the control sample used
- ISI = international sensitivity index.

Formula

$$\text{INR} = \frac{\text{PT of patient (seconds)}}{\text{Mean of normal range}} \times \text{ISI}$$

Normal Value

- INR of 1.3–1.5 (15–18 sec) recommended
- INR of 1.5–2 recommended in patients with prosthetic valves and recurrent emboli.

Derivation

- Each thromboplastin reagent has an international sensitivity index (ISI) value
- ISI value shows how sensitive it is compared with the international reference thromboplastin
- ISI is usually between 1 and 1.4
- ISI of 1 $\rightarrow$ TP specimen has same sensitivity as reference TP
- ISI > 1 $\rightarrow$ TP specimen less sensitive than reference TP
- ISI < 1 $\rightarrow$ TP more sensitive than reference TP.

Factors Increasing INR

Associated with increased risk of bleeding.

- Alcoholism with concomitant liver disease
- Drugs:
  - Amiodarone
  - Anabolic steroids
  - Cimetidine
  - Clofibrate
  - INH
  - Omeprazole
  - Piroxicam
  - Cotrimoxazole
  - Erythromycin
  - Fluconazole
  - Fluroquinolones
  - Metronidazole
  - Phenylbutazone
  - Propranolol

Factors Reducing INR

Associated with increased risk of thrombosis

- Enteral feeds with high vitamin K levels
- Drugs:
  - Avocado
  - Barbiturates
  - Carbamazepine
  - Griseofulvin
  - Rifampicin
  - Sucralfate

ACTIVATED CLOTTING TIME[1,3,5,17]

Specimen

Fresh whole blood free of venepuncture derived thromboplastin.

Procedure

- Mixing minimum of 2 ml whole blood with an activator like celite or kaolin
- Tubes of freshly drawn blood incubated at 37 °C
- These are tilted at 30 second intervals until flow of blood stops
- Tilting and recording done manually or by automated machine
- Contact of blood with activator initiates clotting cascade
- Commercially available devices detect onset of clot formation
- In patients receiving aprotinin, kaolin is used to measure ACT as it will bind aprotinin and remove it from plasma.

Types

Hemochron

- Most commonly used device
- Has a test tube with a small magnet at the bottom
- Magnet is in contact with proximity detection switch
- Blood sample and analyser added to test tube and incubated at 31 °C
- Tube is rotated gently
- As fibrin clot forms, magnet gets enmeshed in it
- Magnet gets pulled from switch which triggers an alarm and records end timer.

Hepcon Act II

- Has plunger-bob-flag assembly
- Assembly is repeatedly raised and dropped into sample
- As clot forms, rate of descent is slowed
- This triggers an optical detector which records time.

Normal Range

- 9–12 seconds
- Reflects activity of classical intrinsic pathway.

Uses

- Monitoring heparin therapy during cardiac surgery:
  - Baseline ACT determined before IV heparin
  - Approximately 3 min after administration ACT sample taken
  - Done at 30 minute intervals thereafter
  - During CPB,
    - ACT > 300 sec: Effect of heparin adequate
    - ACT 180–300 sec: Questionable effect
    - ACT < 180 sec: Inadequate effect.

Limitations

- Insensitive to low dose heparin
- Insensitive to factor VII deficiency (gets prolonged only if factor level < 5%)
- Hypothermia and hemodilution prolong ACT
- Assays overall coagulation activity
- Prolonged values may not be exclusively due to heparin therapy
- Abnormal values may be due to platelet abnormality.

Prolonged Act

- Heparin therapy
- Impaired ability of blood to generate clot (very rare)
  - Severe thrombocytopenia
  - Platelet inhibitors:
    - Prostacyclin
    - Monoclonal antibodies against GP II b/IIIa.

Artefactual Prolongation

- Aprotinin
- Hemodilution
- Hypothermia.

CHAPTER

6

Machine and Monitors

MINIMUM MONITORING STANDARDS-ASA 1986[1,2,3]

Introduction

- Emphasizes importance of regular and frequent measures and integration of clinical judgement with experience and the potential for extenuating circumstances which can influence accuracy of monitoring systems
- Emphasizes melding of physical signs with instrumentation.

Objectives

- Intended to encourage quality patient care
- Applied to all GA, RA and MAC
- Standards may be exceeded at any time based on judgement of anesthetist.

Standard I

Objective

- Emphasizes importance of clinical observation
- To modify anesthesia care based on clinical observations.

Requirement

- Qualified personnel to be in OT during GA/RA/MAC to monitor patient continuously
- If known direct hazard to anesthetist, e.g. radiation, some provision for remote observation to be made
- If emergency requires temporary absence of anesthetist, judgement exercised to compare emergency with anesthetized patients condition and in selection of substitute during temporary absence.

Standard II

- Constitutes standards for evaluation of patients oxygenation ventilator, circulation and temperature
- Mandates the following:

Oxygenation

Objective

- To ensure adequate O_2 concentration in inspired gas and blood during all anesthetics.

Methods

- Use of O_2 analyzer with low concentration alarm limit during GA
- Assess blood oxygenation using pulse oximetry
- Adequate illumination and exposure of patient to assess color.

Ventilation

Objective

- To ensure adequate ventilation of patient during all anesthetics.

Methods

- Clinical signs:
  - Chest excursion
  - Movement of reservoir breathing bag
  - Auscultation of breath sounds.
- Sufficient ventilation assessed by clinical signs and exhaled CO_2
- Ensure correct placement of ETT/LMA with clinical assessment and identification of CO_2 is expired gas
- Continuous E_TCO_2 monitored from time of ETT/LMA placement till extubation
- Monitor tidal volume and E_TCO_2

- When using mechanical ventilator, use a device which is able to detect disconnection of circuits
- Device to give audible alarm on disconnection.

Circulation

Objective

- To ensure adequacy of patients circulatory function during all anesthetics.

Methods

- Continuous display of ECG
- Determine BP and HR at least at 5 min interval
- In addition to these, at least one of:
  - Palpation of peripheral pulse
  - Evaluation of quality of pulse
  - Auscultation of heart sounds
  - Pulse plethysmography/oximetry
  - Monitoring IBP trace
  - Ultrasound peripheral pulse monitoring.

Temperature

Objective

- To aid in maintenance of appropriate body temperature during all anesthetics.

Methods

- Continuously monitor patients temperature and record on anesthesia record.

PULSE OXIMETRY[1,2,3,4]

Introduction

- Non-invasive method of measuring hemoglobin saturation with oxygen using a light signal transmitted through tissue
- ***Fifth vital sign.***

Principle

- Estimates SpO_2 from differential absorption of red and infrared light in tissues
- ***Beer Lambert law:*** Relates concentration of solute to intensity of light transmitted through the solution
- Oxyhemoglobin absorbs more infrared light (940 nm)
- Deoxyhemoglobin absorbs more red light (660 nm)
- Ratio of absorption of red and infrared wavelength analyzed by microprocessor.

Physics

- Combines two technologies:
  - *Spectrophotometer:* Measures oxyhemoglobin saturation
  - *Optical plethysmography:* Measures pulsatile changes in arterial blood volume at sensor site.
- Differentiation between arterial blood and other components by determining change in transmitted light caused by pulsatile flow of arterial blood.

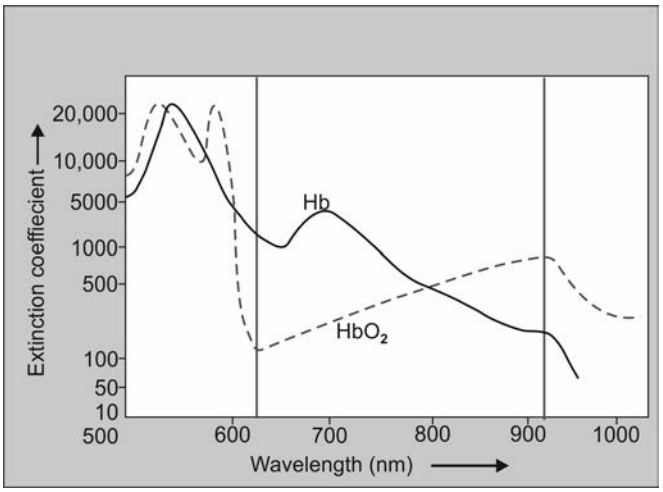


Fig. 6.1: Pulse oximetry[4]

Types of Pulse Oximetry[4]

- Transmission pulse oximetry:
  - Most common type
  - Light beam transmitted through a vascular bed and detected on the opposite side of that bed.
- Reflectance pulse oximetry:
  - Relies on light reflected back from blood
  - Probe has both the LED and photodiode on same side
  - Disadvantages:
    - Can be errors due to light reflected from skin
    - Signal weaker than that in transmission pulse oximetry
    - Vasoconstriction may overestimate SpO_2.
- Co-oximetry:
  - ***Gold standard*** for measuring SaO_2
  - Traditional blood gas analyzer capable of measuring:
    - Concentration of oxyhemoglobin
    - Reduced hemoglobin
    - Carboxyhemoglobin
    - Methemoglobin
- Transcutaneous oximetry:
  - Two wavelengths of light used to measure quantity of oxygenated and deoxygenated blood
  - Measures SaO_2 instead of PO_2.

Results Displayed

- Percentage saturation of hemoglobin
- Arterial pulse waveform
- Heart rate.

Other Variables

- Fractional O_2 saturation (% HbO_2) is ratio of oxyhemoglobin to sum of all hemoglobin species present
- Functional O_2 saturation (SaO_2) is ratio of oxyhemoglobin to all functional hemoglobin.

Sites of Application

- Finger, toe
- Ear
- Cheek, forehead
- Tongue, pharynx, esophagus
- Thenar, hypothenar eminence, palm, wrist
- Lower calf, ankle, foot
- Penis.

Uses of Pulse Oximetry

Anesthetic Procedures

- Mandatory for any anesthetic procedure including moderate sedation cases
- Particularly useful in:
  - Pre-existing lung diseases
  - Special anesthetic techniques (one lung ventilation)
  - OSAS and polysomnography.

Controlling Oxygen Administration

- Allows lowest safe oxygen flow
- Prevents development of retinopathy in premature infants by setting high SpO_2 alarms at 95% (avoids hyperoxia).

Monitoring Vascular Volume and Peripheral Circulation

- Skipped beats/waxing and waning pattern indicates hypovolemia
- Reduction in plethysmographic amplitude indicates hypovolemia
- Dicrotic notch descends to baseline with increasing vasodilation and gets higher with vasoconstriction
- Can detect arm positions which compromise circulation (during shoulder surgery)
- Patients with limb fractures may have compromised circulation distal to fracture
- Evaluating effectiveness of palmar collateral circulation.

Determining SBP: By placing pulse oximeter on same side as BP cuff.

Locating Artery

- When axillary artery not palpable, place pulse oximeter on a ipsilateral finger
- Apply pressure on axilla till pulse wave disappears.

Evaluate Epidural: Increase in amplitude of pulse oximeter waveform by 10% indicates successful block.

Adequacy of CPR: Amplitude of pulse oximetry waveform indicates adequacy of CPR.

Complications

- *Corneal abrasions:* On recovery from GA, if patient rubs eye with finger having probe
- Pressure and ischemic injury:
  - On prolonged application
  - Ranging from persistent numbness to ischemic injury.
- Burns:
  - Due to incompatibility between probe of one manufacturer and pulse oximeter of another
  - During MRI.
- Electrical shock:
  - Rare
  - Due to diathermy.

Advantages

- Light weight and compact
- Accurate, noninvasive fast response time
- Not affected by other gases/vapors
- Tone modulation with change in saturation
- Continuous measurement displayed
- Determines respiratory and circulatory variables:
  - If BP low and pulse signal good, patient is vasodilated with good CO
  - If BP and pulse signal low, patient has low CO.

Recent Advances

- Error correction of inaccuracies due to motion sensitivity and hypoperfusion
- *Multiwavelength pulse oximeters:* 8 wavelength pulse oximeters capable of measuring several species of Hb
- *Reflectance pulse oximetry:* Useful if poor signal transmission during hypoperfusion.

Contraindications

Limitations/Disadvantages

- Failure to detect:
  - *External pressure:* CPB
  - *Hypotension, hypovolemia:* Hypothermia
  - *Raynauds phenomenon:* Improper position
  - Low cardiac output.
- Inaccurate:
  - *Sickle cell anemia:* Onychomycosis
  - *High amounts of fetal Hb:* Too large/too small a probe
  - *Low saturation levels:* Long finger nails
  - *Dark skinned people:* Dyes: methylene blue, indocyanin green
  - *Nail polish:* Poor peripheral pulsations.
- Methemoglobinemia:
  - Methemoglobin absorbs light equally at both red and infrared wavelengths
  - As a result of this, the 1:1 absorption ratio corresponds to saturation reading of 85%
  - Thus, metHb causes falsely high reading of SpO_2 if $SaO_2 < 85\%$
  - *Drugs causing metHb:* Nitrobenzene, benzocaine, dapsone
  - CarboxyHb and HbO_2 absorb light at 660 nm identically
  - Thus false readings are recorded in carbon monoxide poisoning (100%).
- Interference:
  - *Optical interference*: Due to stray light like sunlight/fluorescent light/OR light/IR radiant warmers causing inaccurate readings
  - *Electrical interference*: Due to electrocautery
  - *Motion artefacts*: In shivering/Parkinsons
  - Erractic performance in dysrrhythmias
  - May not function in IABP patients.
- Delayed hypoxic event detection:
  - Does not detect hypoventilation and hypercarbia with reduction in SpO_2
  - Especially if patient is receiving supplemental O_2.

CAPNOGRAPHY[1,2,3,4]

Definitions

- Capnography is defined as continuous monitoring of CO_2 concentrations versus time in a gas mixture
- Capnogram is the tracings of waveforms obtained on the monitor
- Capnography is the machine that generates the wave form
- Capnometer is the device that performs the measurement and displays the readings in numerical form.

Types of Capnographs

Side Stream Analyzer

Technique

- Sample is removed from circuit to be evaluated
- Withdraws gas 50–150 ml/min via sampling tube near ETT
- Sample transported to a distant device for evaluation
- Sampled gas is then released into atmosphere/returned to circuit through a second tube.

Sites of sampling

- Endotracheal tube
- Facemask (placed in patients nears/attached to upper lip)
- LMA (can be inserted through elbow connector)
- Mask outlet in non-intubated patients
- Jet ventilator (connected to sampling lumen).

Advantages

- Allows for unobstructive sampling near patient
- Calibration usually automatic
- Patient interface is light
- Sampling port can be used to administer bronchodilators.

Disadvantages

- Prone to gas leak, sample tube obstruction and moisture problems
- Hypoventilation if sampling rate > fresh gas flow rate
- Error if sampling rate > expiratory flow rate: Causes inspired gas to be sampled

Sources of error

- Water vapor condensation in sample tubing
- Liquids and particulate matter entering cell
- Delayed response time
- Multiple sites for damage/gas leakage
- CO_2 can diffuse out of sample tube
- Longer tubing increases chances of error.

Main Stream/Direct Flow Through

Technique

- Total volume of inspired and expired gas passes through sensing device
- Sensing device located at endotracheal tube (sensor)
- Measuring chamber warmed to 40 ºC to prevent condensation of water vapor on sensor window, e.g. *Siemens Sirecrust 300* and *FEF* E_TCO_2 detector.

Advantage
- Allows for analysis of multiple gases
- Very accurate and stable
- Avoids sampling system
- No delay in response time
- Reduces sample tubing dead space.

Disadvantages
- Large and bulky
- Adds more dead space in pediatric patients
- Can cause kinking of ETT due to weight
- Requires frequent calibration
- Prone to soiling with mucus/saliva due to proximity to patient
- Leak/circuit disconnection can occur
- Can measure only O_2 and N_2O
- Difficult to use in intubated patients
- *Siemens 300 Sirecrust* uses a heated sensor which may cause thermal burns

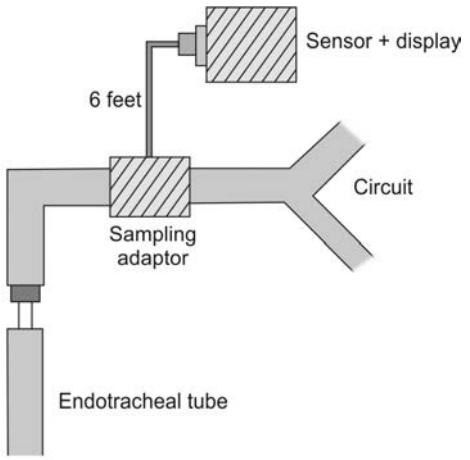


Fig. 6.2: Side stream capnograph[4]

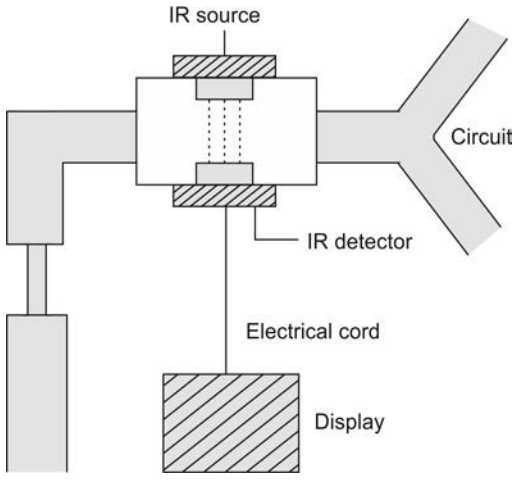


Fig. 6.3: Main stream capnograph[4]

Side Stream vs Mainstream Capnography[4]

No	Main stream/non-diverting	Side stream/diverting
1	Sensor located between breathing circuit and ETT	Sensor located in main vent
2	No sampling required	Sample tubing aspirates gas
3	Have fast response time	Slow response time
4	Standard gas not required for calibration	Supply of calibration gas is needed
5	Frequent calibration required	Automatically calibrated
6	Increased dead space due to use of adaptor	No such problem
7	Patient interface heavy due to weight of adaptor	Patient interface is light
8	Adaptor causes kink in ETT/ disconnection of circuit	No such problem
9	Difficult to use in unintubated patients	Relatively easy
10	Cannot be used for this	Sampling port: to administer bronchodilator
11	Water and secretions are seldom a problem	Secretions can occlude sample tubing
12	Damaged by inhaled drugs like inhaled β blockers	Not so
13	May cause thermal burns	Not so
14	Not possible	Hyperventilation: if sampling rate > FGF

Principles

Three methods available:
1. *Infrared analysis:* Quantitative
   - Blackbody radiation technology
   - Microstream technology.
2. *Chemical colorimetric analysis:* Semiquantitative
   - Hygroscopic
   - Hydrophobic.
3. Mass spectroscopy.

INFRARED ANALYSIS

Introduction

- Most common technology
- Used most commonly with side stream sampling.

Principle

- Gases with 2 or more dissimilar atoms in a molecule have specific IR light absorption spectra (e.g: CO_2, N_2O)
- Amount of IR absorbed proportional to concentration of absorbing molecules

- Concentration determined by comparing IR light absorbance in sample with known standard.

Technologies

Blackbody Radiation Technology

- Most commonly used
- Heated element called blackbody emitter is source of IR
- Filter present to block radiation which is outside the desired range
- Analyzer selects appropriate IR wave length to maximize absorption by selected gas
- Sensor detects transmitted IR light and converts it to electrical signals
- Electrical signal amplified and concentration is displayed.

Microstream Technology

- Laser based technology to generate IR light
- Uses smaller sample cell and low flow rates (50 ml/min)
- IR light precisely matches absorption spectrum of CO_2
- Emitted electrons excite nitrogen molecules
- These molecules collide with CO_2 molecules and excite them
- IR light of signature wavelength of CO_2 emitted as excited CO_2 molecules drop back to ground state
- Amplitude of signal depends on amount of IR radiation absorbed which is proportional to CO_2 concentration.

Advantages

- Rapid response time
- Require low sample flow
- Not affected by pressure of other gases
- Small sample cell required which is useful in:
  - Small patient
  - High respiratory rates
  - Low flow applications
  - Nonintubated patient.

Disadvantages

- Continuous withdrawal of gas from RS (if used with side stream)
- Propensity to leak/occlude
- Sensitive to water accumulation.

CHEMICAL COLORIMETRIC ANALYSIS

Principles

- Consists of a pH sensitive indicator enclosed in a housing
- When indicator is exposed to carbonic acid (formed by reaction CO_2 and H_2O), it becomes acidic.

Technologies

Hygroscopic

- Can detect CO_2 concentration in range 0.25–0.6%
- Minimum CO_2 concentration to produce color change is 0.54%
- Life span of detector depends on humidity of expired gas
- Reduced humidity prolongs detectors life
- Color changes are:
  - *Purple:* Low CO_2 ($< 0.5\%$ or < 2.3 mm Hg)
  - *Biege:* Moderate CO_2 (0.5–2% or 3.7–7.6 mm Hg)
  - *Yellow:* High CO_2 ($> 2\%$ or ≥ 15.2 mm Hg)
  - Changes color back to purple after removal of CO_2.

Hydrophobic

- Color changes from blue to green to yellow as CO_2 concentration increases
- Faster response time
- Less affected by humidity
- Performs better at higher respiratory rate.

Advantages

- Cheaper, easy to use, disposable
- Small in size, portable
- Useful in remote site resuscitative evaluation
- Not affected by N_2O or anesthetic vapor
- Require no other equipment.

Disadvantages

- May be several breaths before conclusion is drawn
- Wait for six breaths with colorimetric methods
- False positive results in:
  - Ingested carbonated drinks/antacids
  - Mask ventilation.
- False negative results in:
  - Low tidal volume
  - Low E_TCO_2 concentration
  - Compromized lung perfusion.

MASS SPECTROMETRY

- Gas withdrawn continuously through capillary lines
- Sample directed into mass spectrometer
- Sample is ionized and then exposed to magnetic field in a vacuum chamber
- Ionized molecules separated by mass–charge ratio

- Collectors in vacuum chamber determine concentration of each gas component.

CAPNOGRAPH[1,2,3,4]

Types of Capnographs

- Time volume capnograph
- Volume capnograph.

Description

- Height depends on E_TCO_2 concentration
- Frequency depends on respiratory rate
- Rhythm shows regularity of breathing
- Normal shape is ***Top Hat/Sine Wave***
- Baseline is normally zero (EA).

Phases of Capnograph

Phase I: EA

- *Inspiratory Baseline*
- Usually is zero
- Reflects inspired gas devoid of CO_2.

Phase II: BC

- *Expiratory upstroke*
- Rapid S-shaped upswing
- Represents transition gas from anatomical dead space
- Prolonged in:
  - Partial endotracheal tube obstruction
  - COPD, bronchospasm
  - Upper airway obstruction.

Phase III: CD

- *Plateau phase*
- Represents gas coming from alveoli
- End of phase III at point D is *End tidal point.*

Phase IV: DE

- *Inspiratory downstroke*
- Represents patient inhalation
- CO_2 levels abruptly falls to zero.

Angles of Capnograph

α Angle

- *Take off/elevation angle*
- Angle between phase II and phase III
- Normally between 100–110°.
- Decreased in obstructive lung diseases
- Increased in:
  - Airway obstruction
  - PEEP.

β Angle

- Angle between phase III and descending limb of capnogram
- Normally around 90°
- Decreased in airway obstruction and PEEP
- Increased in rebreathing.

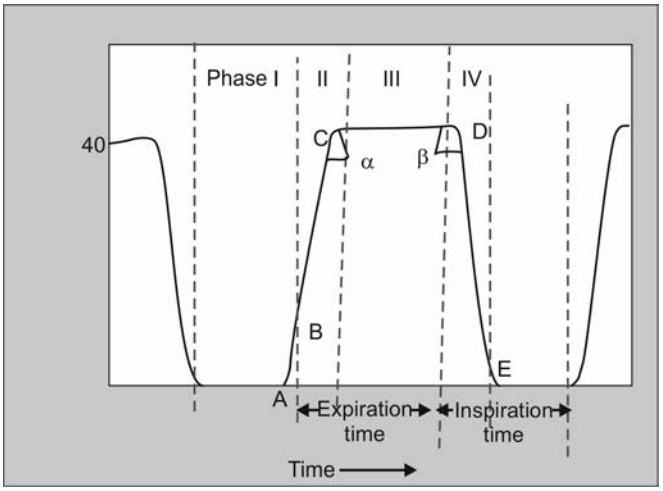


Fig. 6.4: Time-volume capnograph[4]

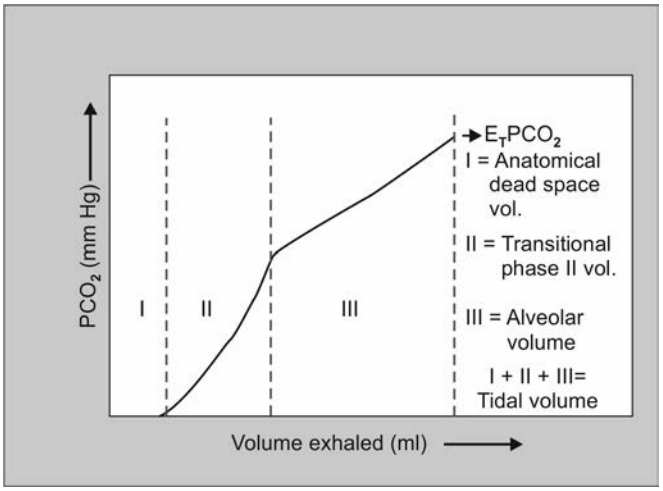


Fig. 6.5: Volume capnograph: single breath carbon dioxide curve[4]

Variation in Shape of Waveform

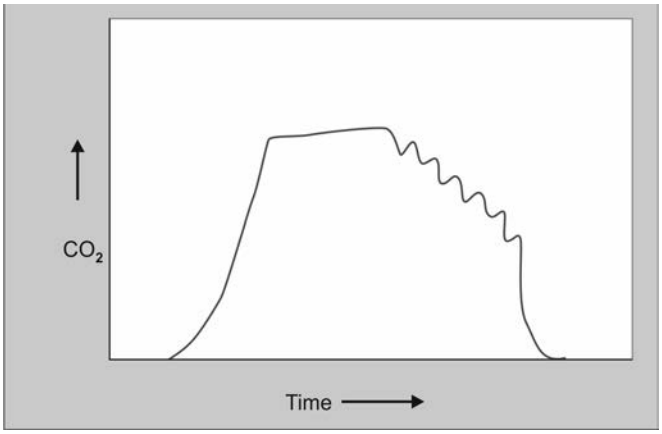


Fig. 6.6: Cardiogenic oscillations on capnograph[4]

- *Cardiogenic oscillations*
- Due to heart beating against lungs.

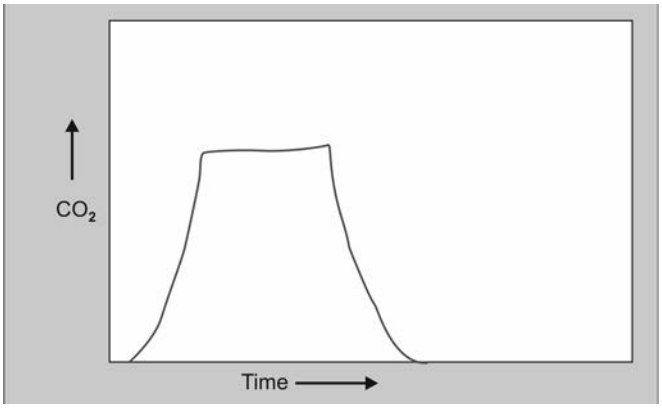


Fig. 6.7: Incompetent inspiratory unidirectional valve on capnograph[4]

- Incompetent inspiratory unidirectional valve
- Prolonged plateau with slanting inspiratory down-stroke.

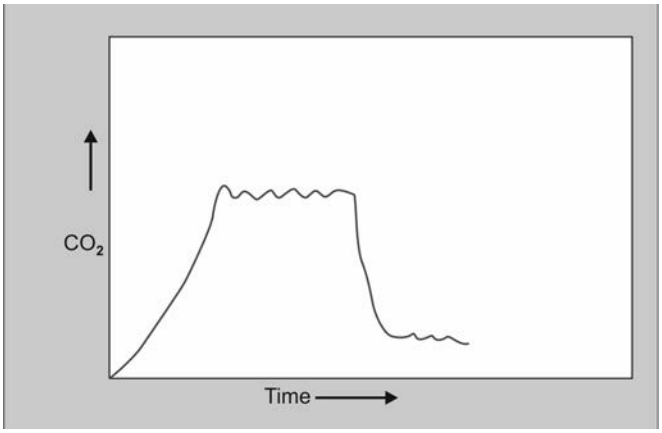


Fig. 6.8: Irregular plateau/baseline[4]

- Irregular plateau/baseline
- Displacement of ETT into upper larynx/lower pharynx with intermittent ventilation of stomach and lungs
- Pressure on chest.

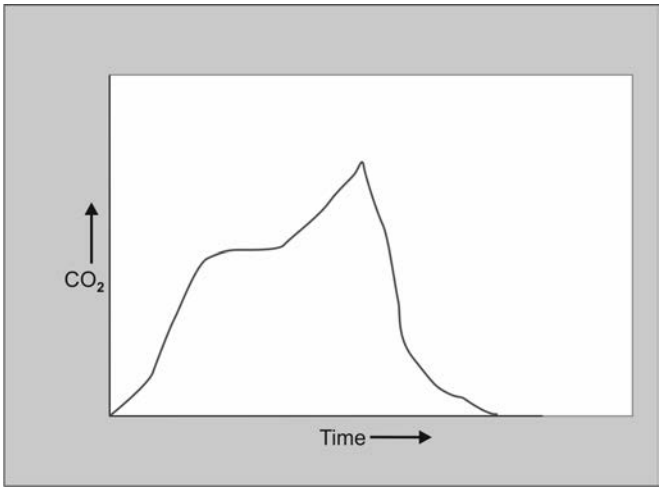


Fig. 6.9: Leak in sample line[4]

- Leak in sample line during IPPV
- Also in obese and pregnant patients.

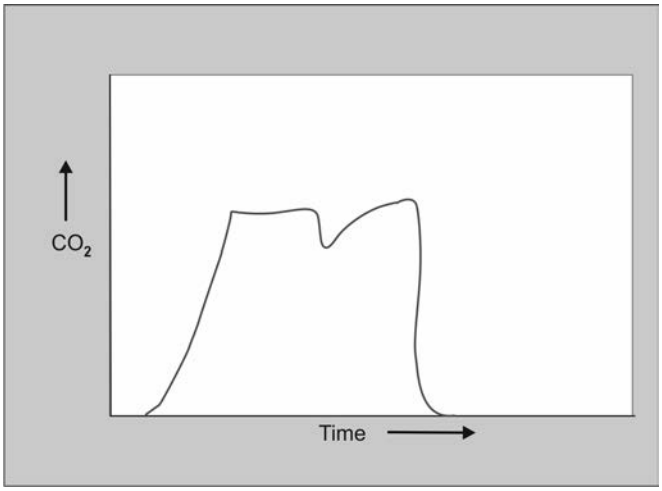


Fig. 6.10: Biphasic expiratory plateau[4]

- Biphasic expiratory plateau
- Severe kyphoscoliosis
- One lung ventilation
- Single lung transplantation
- Very high airway resistance.

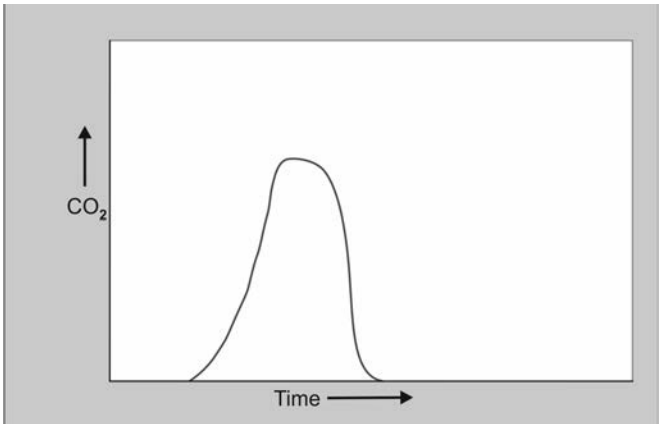


Fig. 6.11: Obstruction[4]

Obstruction /sample contamination

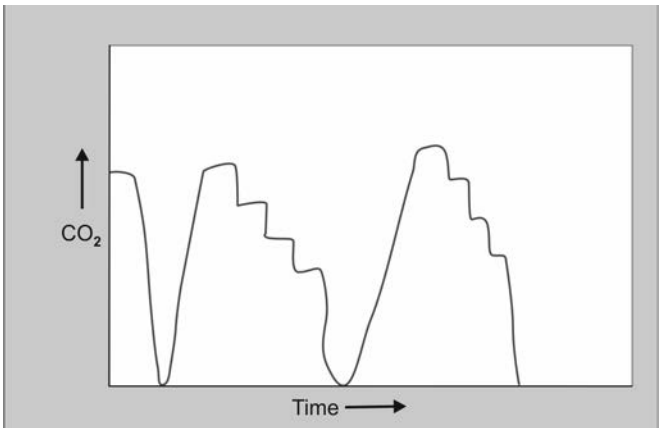


Fig. 6.12: Sample contamination[4]

- Contamination of sample with fresh gas or ambient air
- Occurs due to sampling site being too close to fresh gas flow inlet
- Leak in sample tube.

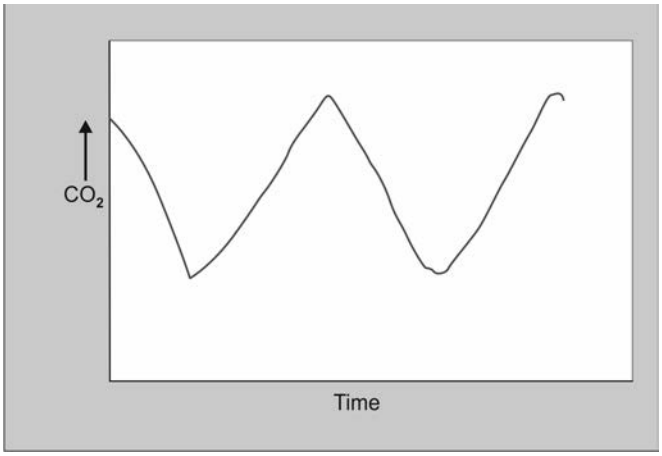


Fig. 6.13: Low sampling rate[4]

Too low sampling rate in side stream analyzer.

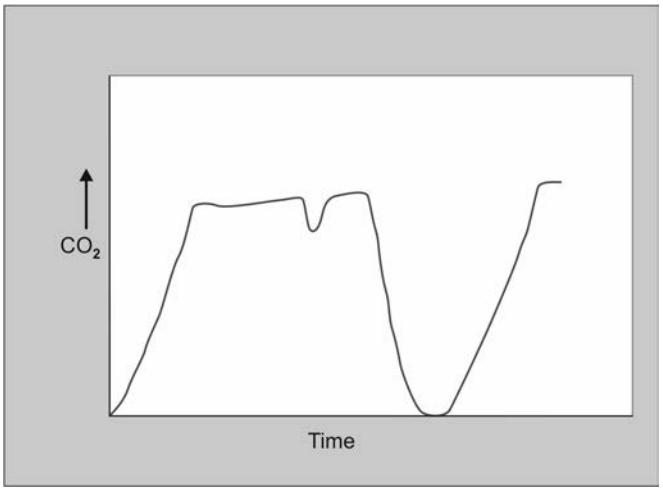


Fig. 6.14: Curare cleft[4]

- Curare cleft/notch
- Depression is last third of plateau
- Occurs if patient is spontaneously breathing
- Due to lack of synchronous action between intercostal muscles and diaphragm
- Also seen in:
  - Flail chest
  - Hiccough
  - Pneumothorax
  - Spontaneous breaths in a patient on ventilator.

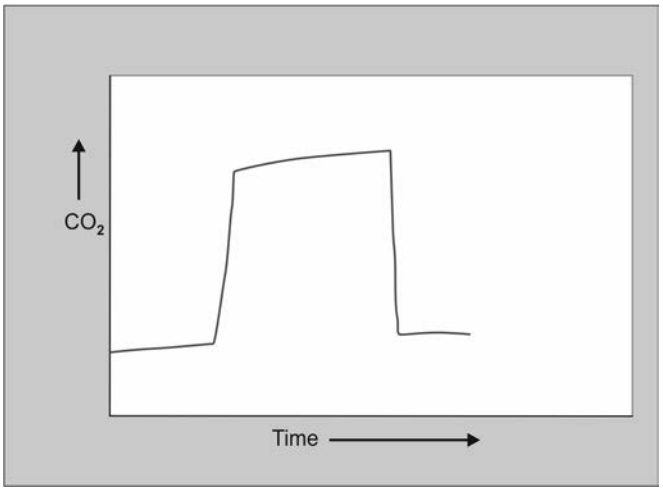


Fig. 6.15: Rebreathing[4]

Rebreathing with elevated base line.

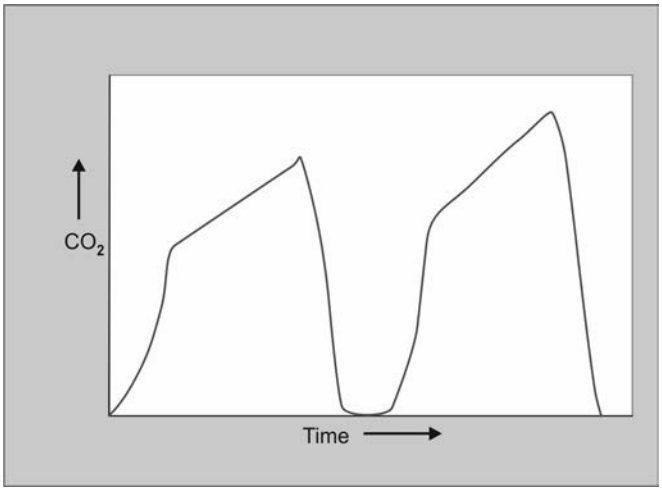


Fig. 6.16: Prolonged expiratory upstroke[4]

- Prolonged expiratory upstroke
- COPD
- Bronchospasm
- Upper airway obstruction.

CAPNOMETRY

Normal Values

- *E_TCO_2:* 35–45 mm Hg
- *$PaCO_2$-E_TCO_2 gradient:* 1–5 mm Hg ($PaCO_2 > E_TCO_2$)
- *$PaCO_2$-E_TCO_2 gradient during general anesthesia:* 5–10 mm Hg.

Elevated E_TCO_2 with Normal Waveform[4]

- Hypoventilation
- Hyperthermia
- Malignant hyperthermia
- Sepsis
- Hyperthyroidism
- Pain, anxiety, shivering
- Increased skeletal muscle tone, convulsion
- Sodium bicarbonate injection
- Reperfusion:
  - Tourniquet release
  - Aortic cross clamp release.
- During laparoscopic surgery with CO_2.

Decreased E_TCO_2 with Normal Waveform[4]

- Hyperventilation
- Hypothermia, shock
- Hypothyroidism
- Increased depth of anesthesia, use of muscle relaxants
- Increase anatomical dead space
- Pulmonary embolism
- Surgeries on heart lung and dissecting aneurysm (where pulmonary BF is reduced)
- Wedging of PA catheter
- Leakage in sample line.

Zero E_TCO_2 with Absent Waveform[4]

- Disconnection
- Apnea
- Ventilator malfunction
- Blockage of sample line.

Elevated E_TCO_2 with Elevated Baseline[4]

- Rebreathing
- Exhausted absorbent, bypassed absorbent
- Malfunction of nonrebreathing valve
- Inadequate fresh gas flow rates, misassembly
- Problem with inner tubing in Bain circuit
- Increased apparatus dead space.

Elevated E_TCO_2 with Abnormal Waveform[4]

- Prolonged expiratory upstroke seen
- Upper airway obstruction
- COPD
- Bronchospasm.

Causes of Increased $PaCO_2$-E_TCO_2 Gradient[4]

- Right-left cardiac shunt
- Endobronchial/esophageal intubation
- Decreased cardiac output states
- Increased dead space ventilation:
  - Air/amniotic fluid/fat pulmonary embolism
  - Bronchospasm.
- Hypoperfusion states with decreased pulmonary blood flow
- Sample contamination:
  - Disconnection
  - Cuff leaks
  - Sample tube leaks.
- Shallow tidal breaths
- Uneven alveolar emptying
- COPD
- Smoking
- Advanced age.

Uses of Capnography[4]

Respiration

- *To confirm correct placement of ETT:* Presence of stable E_TCO_2 for > 3 successive breaths (*Barash*)

- Determines if tip of fiberscope is in trachea
- Determines position of double lumen tube.

Metabolism

- Diagnosis of malignant hyperthermia
- Rise is E_TCO_2 occurs before rise of body temperature in malignant hyperthermia.

Circulation

- Assessment of Effectiveness of CPR-better than ECG, pulse and BP (DORSH)
- Detects pulmonary embolism.

Equipment Function

- Indicates:
  - Apnea/extubation
  - Disconnection of circuit
  - Ventilator malfunction
  - Leaking ETT cuff/circuit.
- Incompetent inspiratory/expiratory valve
- Assessment of functioning of soda lime canister.

Others

- Detection of tracheo-esophageal/broncho-esophageal fistula
- Guides blind intubation
- Detects tracheo-bronchial injury during thoracoscopy
- Confirm placement of needle in cricothyroidotomy
- Correct positioning of Ryles tube.

TEMPERATURE MONITORING[1,2,3,4]

Introduction

Objective of temperature monitoring and perioperative thermal management is to detect normal disturbances and maintain appropriate body temperature during anesthesia.

Uses

- Monitor intraoperative hypothermia
- To estimate mean body temperature and total body heat content
- Prevent overheating (as during rewarming)
- Facilitates detection of malignant hyperthermia
- Rough measure of peripheral perfusion and cardiac output (peripheral temperature)
- To evaluate vasomotion and adequary of neuromuscular monitoring through muscle/skin surface monitoring.

Types

- Mercury thermometer
- Electrical thermometers:
  - Thermistor
  - Thermocouple
- Deep tissue thermometers
- Infrared monitors
- Liquid crystal thermometry.

Indications: Miller

- When duration of surgery ≥ 1 hr.
- For office-based sedation, RA/GA in pediatric patients (ASA)
- During regional anesthesia when changes in body temperature are intended/anticipated/suspected
- Core temperature when duration of GA ≥ 30 mins
- When ambient OT temp ≥ 21 ºC
- In PACU when intraoperative hypothermia occurs.

Mechanism

- Mercury thermometers:
  - Slow, cumbersome
  - Largely obsolete, used only in calibration laboratories.
- Thermocouple:
  - Two dissimilar metals contact each other at one or more points
  - Produces voltage when temperature of one metal differs from other parts of circuit
  - Two junctions are created in the circuit
  - First junction is maintained at a known temperature
  - Second junction is placed on temperature probe tip
  - The temperature difference produces a current
  - Voltage of the current depends on temperature difference across the junctions
  - The voltage of current is then recorded as temperature.
- Thermistor:
  - Type of resistor whose resistance varies significantly with temperature
  - Change in resistance of thermistor is recorded as a temperature.
- Infrared monitors:
  - Evaluate IR energy emitted from surfaces above absolute zero degrees
  - Too large to fit onto tympanic membrane
  - Extrapolate tympanic membrane temperature from outer ear temperature
  - Unreliable.

- Deep tissue thermometers:
  - Creates a region of zero heat flow under the probe
  - Based on actively reducing cutaneous heat flux to zero
  - Newly developed system: *CTM-205*
  - Derives core temperature from temperature of forehead and sole of foot.
- Liquid crystal thermometry:
  - Organic crystals existing in a state between solid and liquid- *Liquid Crystal*
  - Suspension of microencapsulated liquid crystals used
  - Suspensions are set into thin polymer sheets with black substrate, usually adhesive
  - This is placed on skin surface to monitor temperature.

Sites

Core Temperature

- Tympanic membrane:
  - Difficult to position due to curvature of aural canal
  - Occlude canal with wool after positioning to avoid cooling by ambient wind
  - Good reflection of core temperature
  - Theoretically measures brain temperature as TM is close to ICA
  - Risk of TM perforation
  - Minimal lag time.
- Nasopharynx:
  - Accurate if placed adjacent to nasopharyngeal mucosa
  - Causes epistaxis
  - Altered by respiratory gases, but close to ICA.
- Oral and axillary temperature:
  - Axillary 0.5–1 ºC lesser than oral temperature
  - Oral 0.5–1 ºC lesser than rectal temperature.
- Esophageal:
  - Incorporated into esophageal stethoscope
  - Placed at point of maximal heart sounds/even more distally
  - Positioned behind heart in lower third of esophagus
  - 24 cms below larynx
  - Position avoids measuring temperature of tracheal gases
  - Reliable even during rapid temperature changes.
- Tracheal temperature:
  - Thermistor placed within anterior surface of specially designed tracheal tube
  - Inaccurate even at fresh gas flows < 1L/min.
- PA blood temperature:
  - Accurate core temperature
  - ***Gold standard*** for core temperature monitoring
  - Approximates jugular bulb temperature.
- Urinary bladder:
  - Difficult to probe
  - Temperature influenced by urinary flow
  - Considered as *intermediate temperature.*
- Rectal temperature:
  - Affected by cystoscopy, lavage, stools
  - Considerably lags behind core temperature
  - Considered an '*intermediate temperature*'
  - Slow responses to change in core temperature.

Peripheral Temperature

- Considerably lower than core temperature
- Forehead temperature 2 ºC lower than core temperature
- Does not increase rapidly during malignant hyperthermia
- Indicates cardiac output.

NONINVASIVE BLOOD PRESSURE MONITORING[1,2,3,4,5]

Indications

- Use of any anesthetic no matter how trivial, is absolute indication
- As an indicator of organ perfusion.

Contraindications

- Extremities with vascular abnormalities
- On limbs with AV shunts created for dialysis
- On limbs with IV line.

Techniques

Palpation

- Riva-Rocci method/Return to flow method
  - Locate palpable peripheral pulse
  - Inflate BP cuff proximal to pulse until flow is occluded
  - Release cuff by 2–3 mm Hg per heart beat
  - Measure cuff pressure at which pulsations are again palpable
  - Disadvantages:
    - Underestimates SBP due to:

- ° Insensitivity of touch
- ° Delay between flow under cuff and distal pulsations
- Does not provide DBP/MAP.

Doppler Probe

- Indicated in:
  - Obese patients
  - Pediatric patients
  - Shock.
- Doppler probe transmits ultrasound signals which is reflected by tissues
- As RBC move through artery, Doppler frequency shift is detected by the probe
- Difference between transmitted and recorded frequency creates swishing sound
- Probe to be positioned directly above an artery
- Interference from probe movement/electrocautery
- Shift in frequency of sound waves when their source moves relative to the observer: ***Doppler effect.***

Piezo Electric Crystal

- Variation of Doppler technology
- Detects lateral arterial wall movement
- Detects both SBP and DBP.

Auscultation

- Inflate cuff to pressure between SBP and DBP
- Partially collapses artery and produces turbulent flow with ***Korotkoff sounds***
- Stethoscope placed under/distal to distal third of BP cuff
- Appearance of first sound taken as SBP
- Disappearance of sound/muffled sound: DBP
  - Phase I:
    - Snapping sound
    - Clear tapping sounds for at least 2 consecutive beats is the systolic BP
  - *Phase II:* Murmurs heard between systolic and diastolic BP
  - *Phase III:* Loud, crisp tapping sound
  - *Phase IV:* Thumping sounds heard within 10 mm Hg of diastolic BP.
  - *Phase V:* Disappearance of sound considered as diastolic BP.
- Disadvantages:
  - ***Auscultatory gap***:
    - When sounds not heard between SBP and DBP
    - Common in hypertensive patients
    - Underestimation of diastolic BP
  - Difficult to auscultate sounds during hypotension/vasoconstriction
  - Motion artefacts and electrocautery interferes with measurement
  - Quick deflation underestimates BP
  - Unreliable in low flow states as flow will be non-pulsatile.

Oscillometry

- Types:
  - Automated intermittent
  - Automated continuous
- Variations in cuff pressure due to arterial pulsations during cuff deflation used
- Arterial pulsations cause oscillations in cuff pressure
- Oscillations are small if cuff is inflated above systolic BP
- Oscillation are maximal at mean arterial pressure, after which they decrease
- Pressure at which oscillation amplitude changes is taken as SBP
- Pressure at which peak amplitude of pulsations occurs corresponds to MAP
- SBP and DBP derived from formula which examine rate of change of pressure pulsations
- Disadvantages:
  - Unreliable during arrhythmias (AF)
  - Not used on patients on CPB
  - May underestimate systolic BP
  - Shivering, motion artefacts may overestimate BP.

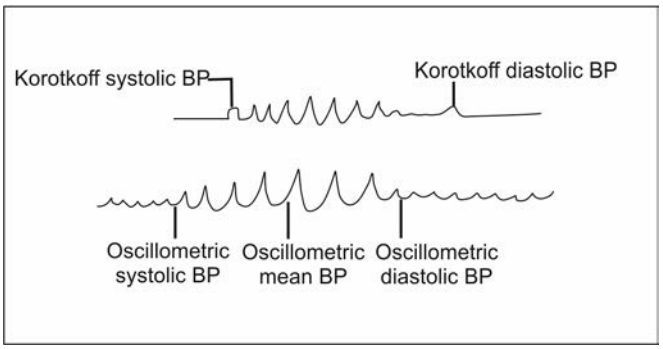


Fig. 6.17: Oscillometry[4]

Arterial Tonometry

- Measures beat to beat BP
- Senses pressure required to partially flatten superficial artery against a bony structure
- Contains several pressure transducers applied to skin over artery

- Contact stress between transducers and skin reflects intraluminal pressure
- Produces tracing similar to invasive BP waveform
- Sensitive to movement artefact and frequent calibration required.

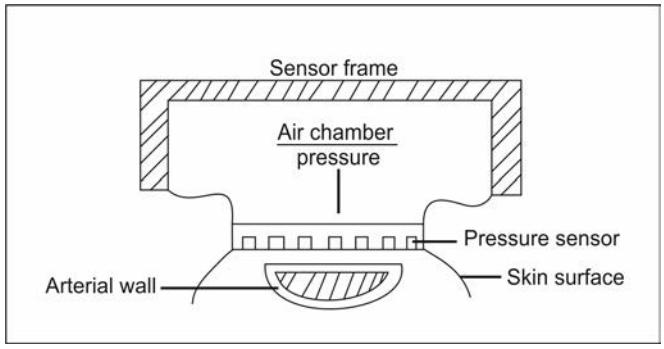


Fig. 6.18: Arterial tonometry[4]

Other Methods

- Photo oscillometry
- Motion of arterial wall.

Prerequisites

- Cuff bladder should extend at least half way around extremity
- Width of cuff should be 40% of circumference of extremity
- Bladder length should encircle at least 80% of extremity.

Complications

- Pain
- Petechiae and ecchymoses
- Hematomas beneath and distal to cuff
- Venous stasis and thrombophlebitis
- Extravasation of intravenous fluids
- Nerve palsies on frequent use:
  - *Ulnar neuropathy*
  - Avoided by applying cuff proximal to ulnar groove
- Compartment syndrome due to prolonged inflation cycle.

Sources of Error

- Equipment failure in obese patients
- False high readings in:
  - Small cuffs
  - Cuff applied too loose
  - Extremity below heart level.
- False low readings in:
  - Large cuffs
  - Extremity above heart level
  - Quick deflation.
- Hydrostatic error:
  - When cuff is placed on extremity above/below level of RA
  - Corrected by adding/subtracting 0.7 mm Hg for every centimeter that the cuff is off the horizontal plane of heart.

Automated Continous Techniques

- Allow continuous assessment of BP without arterial cannulation
- Techniques:
  - Arterial volume clamp method for finger BP
  - Using pulse transit time
  - Arterial tonometry
  - ***Finapres:***
    - Based on oscillometry and plethysmography
    - Cuff tied around middle phalanx/base of thumb.

INVASIVE BLOOD PRESSURE MONITORING[1,2,3,4,5]

Indications

During Surgery

- Cardiac/vascular/chest/brain/spine surgeries
- Unstable patients undergoing surgery
- Induced hypotension/hypotensive anesthesia
- Anticipation of wide blood pressure swings
- Planned mechanical/pharmacological cardiovascular manipulation
- Failure of NIBP.

Others

- Need for multiple arterial blood gas analysis
- Supplementary diagnostic information from waveform
- Determination of volume responsiveness from systolic BP and pulse pressure variations
- End organ disease necessitating precise BP regulation.

Contraindications

- Arteries without documented collateral blood flow
- Extremities with PVD (***Raynauds phenomenon***).

Sites of Cannulation

Radial Artery

- Preferred site as superficial collateral flow

- Collateral flow verified by:
  - ***Allens test***
  - Doppler probe
  - Plethysmography
  - Pulse oximetry.
- Disadvantage includes a large difference between aortic root and radial artery pressure after separation from CPB.

Allens Test

- Unreliable
- Exsanginate hand by making a fist while occluding radial and ulnar A with fingertips
- Patient relaxes blanched hand
- Flushing of thumb:
  - *Within 5 sec:* Good collateral flow
  - *5–10 sec:* Equivocal
  - *> 10 sec:* Insufficient collateral.

Ulnar Artery

- More difficult as deeper and more tortuous course
- Prime source of blood flow to hand.

Brachial Artery

- Insertion site medial to biceps tendon
- Predisposed to kinking
- Large and easily identifiable
- Close to aorta: Less waveform distortion
- Damage to median nerve, can accommodate 18 G needle.

Axillary Artery

- Can cause nerve damage from hematoma/traumatic cannulation
- Insertion site at junction of pectoralis and deltoids
- Air and thrombi can embolize to brain during flushing.

Femoral Artery

- Prone to:
  - *Pseudoaneurysm:* Retroperitoneal hemorrhage
  - Atheroma
  - Increased incidence of infection and arterial thrombosis.
- Aseptic necrosis of head of femur in children
- Easy access possible in low flow states
- Longer catheters preferred.

Dorsalis Pedis and Post Tibial Artery

- Have most distorted waveforms as farthest from aorta
- Higher systolic BP estimates
- Modified Allens test for collateral flows.

Complications

- *Hematoma:* Bleeding
- *Vasospasm:* Arterial thrombosis
- *Air embolism:* Skin necrosis
- Abnormal blood flow which normalizes in 3–70 days
- *Nerve damage:* Axillary N/ulnar N/median N
- Infection
- Unintentional intraarterial drug injection
- Potential for thromboembolism during catheter placement
  - Reduced by compressing proximal and distal arterial segment
  - Aspirate cannula during withdrawing.
- Loss of digits
- Volume overload due to continuous flush system in pediatrics.

Increased Risk of Complication in

- *Prolonged cannulation:* Female gender
- *Hyperlipidemia:* Use of vasopressor
- *Repeated insertion attempts:* Extra corporeal circulation.

Reduced Risk of Complications in

- Small sized catheter used
- Heparinized saline continuously infused at 2–3 ml/hr
- Flushing of catheter is limited
- Meticulous attention to asepsis.

Technique of Radial Artery Cannulation

- Direct arterial puncture
- *Seldinger technique:* Guide wire assisted cannulation
- *Transfixation:* Withdrawal method.

Direct Arterial Puncture

- Supinate hand, extend wrist
- Pressure-tubing-transducer system to be ready nearby
- System flushed with heparinized saline (0.5–2 IU/ml of saline)
- Palpate radial pulse
- Tip of index middle finger identifies area of maximal impulse
- Prepare skin with bactericidal agent
- 0.5 ml lidocaine infilterated directly above artery with 27 G needle

- 18 G needle used as skin punch
- 20/22 G IV catheter through skin at 45° angle directed toward point of palpation
- Upon blood flashback, lower needle to 30°
- Advance catheter 1–2 mm to make sure tip of catheter is in lumen of artery
- *Spin* catheter to advance it off the needle which is withdrawn
- Connect pressure tubing
- Water proof tape/suture to hold catheter in place.

Prerequisites

- *Tubing of catheter to be stiff:* Remove air bubbles
- *Limit number of stop cocks:* Connecting tube not very long
- Mass of fluid is small.

Position of Transducer

- Diaphragm at the level of mid-axillary line/right atrium in supine position
- In sitting position craniotomies, transducer placed at level of ear
- This approximates BP in *Circle of Willis* as arterial BP in brain is different from left ventricular pressure.

Components of System

Mechanical Coupling

- Achieved by connecting fluid filled tubing to intravascular space
- Mechanical motion of fluid in tubing converted to electrical signals by mechanoelectrical transducer.

Pressure Transducer

- Converts mechanical energy to electrical signals
- Contains diaphragm which forms base of fluid filled dome
- Pressure of fluid on tubing moves diaphragm
- Sensing elements in diaphragm converts movement into electrical signal
- Based on ***Strain Gauge principle*** where stretching a wire/silicon crystal changes its electrical resistance
- Sensing elements arranged as a ***Wheatstone bridge circuit*** so that voltage output is proportional to pressure on diaphragm
- When pressure applied on diaphragm, strain on number 2 and 3 resistor is increased while that on number 1 and 4 is reduced
- Change in resistance across the bridge was proportional to change in BP.

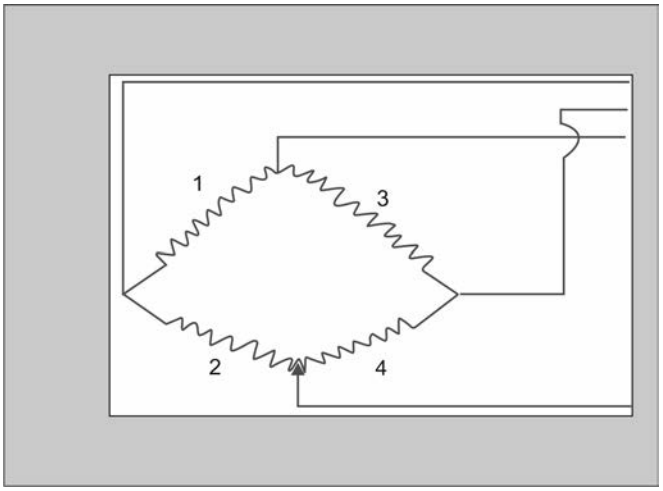


Fig. 6.19: Wheatstone bridge circuit[4]

Amplifier and Processing Unit

- Amplifies small electrical signals
- Processes waveforms and derives ABP using ***Fourier analysis.***

Display: Can be via:

- Oscilloscope
- Digital read out
- Galvanometer.

Waveform Analysis

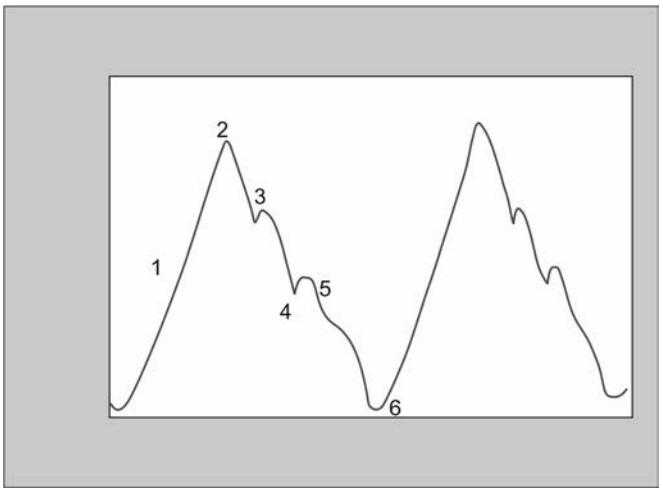


Fig. 6.20: Arterial pressure waveform[4]

- Systolic upstroke
- Systolic peak pressure
- Systolic decline
- Dicrotic notch
- Diastolic runoff
- End diastolic pressure.

- Rate of upstroke indicates contractility
- Rate of down stroke indicates peripheral vascular resistance
- Variations in size during respiratory cycle indicates hypovolemia
- Area under pressure curve equals mean arterial pressure.

Physics of IBP

Accuracy of transducing system affected by two properties:

- DAMPING (ζ): *Zeta*
  - Represents tendency of fluid in measuring system to extinguish motion
  - Damping coefficient of 0.6–0.7 optimal
  - Under damping falsely overestimates systolic BP and vice versa.

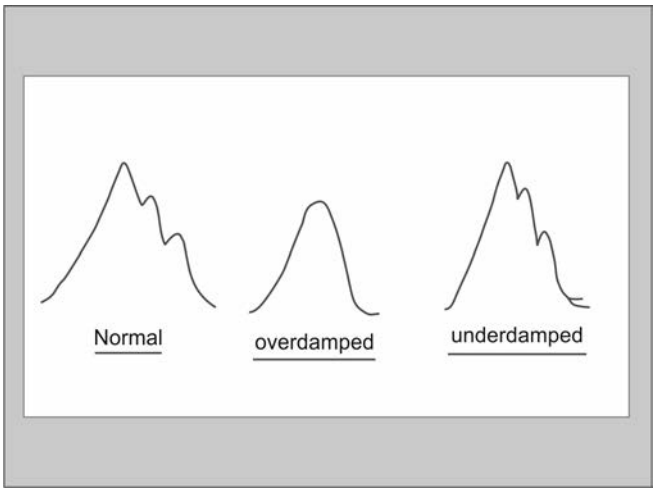


Fig. 6.21: Damping

- Natural frequency: (*Fn*)
  - Represents tendency of measuring system to resonate
  - *Fn* of transducer (usually > 200 Hz) must exceed *Fn* of arterial pulse (16–30 Hz)
  - Addition of tubing, stopcocks and air bubbles reduces *Fn* of system
  - If *Fn* is very low, system will be over-damped and SBP will be underestimated
  - Optimize ζ and *Fn.*
- Fast flush test:
  - Bedside method to determine ζ and *Fn* of transducing system
  - Examine characteristics of resonant waves recorded after release of a flush
  - Damping estimated by amplitude ratio of first pair of resonant waves
- *Fn* estimated by dividing paper speed by interval cycle.

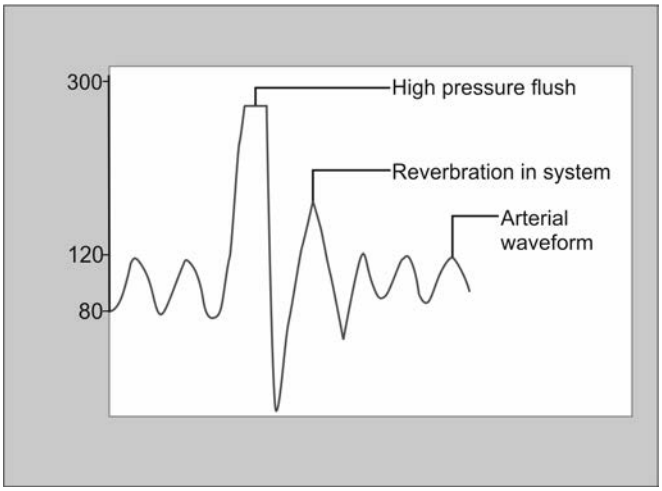


Fig. 6.22: Fast flush test[5]

Sources of Error

- Hydrostatic error:
  - Sudden increase in BP as position of transducer not adjusted
  - Commonly occurs after change in OT table height.
- Transducer system to be rezeroed multiple times
- ***Whip effect***:
  - Especially seen in intracardiac catheters
  - Due to oscillation of free tip of catheter in whip like fashion
  - Column of fluid in measuring system also oscillates.
- Overdamping/underdamping
- Thrombi/air in tubing.

CENTRAL VENOUS PRESSURE[1,2,3,4,5]

Introduction

Important procedure for intravascular volume status monitoring and also administration of drugs in presence of poor peripheral line.

Uses

- Gives estimate of intravascular volume status
- Assesses venous tone
- Assess right ventricular function and right ventricular filling pressure
- Useful in diagnosing pathological cardiac conditions like constrictive pericarditis
- Approximates LV filling pressure in healthy heart.

Indications[2]

- Assessment of volume status:
  - For major surgeries involving:
    - Large fluid shifts
    - Blood loss in patients with good heart function
    - Major trauma.
  - IV volume assessment when urine output is unreliable or unavailable:
    - Chronic renal failure
    - Radical cystectomy.
- Frequent venous blood sampling
- Drug/fluid infusions:
  - Inadequate peripheral IV access
  - Chronic drug administration/administration of vasoactive and irritant drugs
  - Rapid infusion of IV fluids
  - Total parenteral nutrition.
- Hemodialysis
- Placement of temporary transvenous pacing wire
- Surgeries with high risk of air embolism like sitting position posterior fossa craniotomies.

Contraindications[2]

Absolute Contraindications

- ***SVC syndrome***:
  - Venous cannula not to be put in neck/subclavian area/upper extremity
  - Venous pressures of SVC does not reflect RA pressure in SVC syndrome
  - Medications administered through IJV will reach central circulation through collaterals in a delayed fashion
  - Rapid fluid administration trough IJV will:
    - Increase venous pressure even more
    - Cause pronounced edema.
- Infection at site of cannulation
- Renal cell carcinoma extending into RA
- Fungating tricuspid valvular vegetation.

Relative Contraindications

- Coagulopathies: Can cause:
  - Hemorrhage
  - Hematoma and infection
  - Hemothorax
  - Airway obstruction.
- Newly inserted pacemaker:
  - Pacemaker wires may get dislodged during insertion of CVP catheter
  - A wait of 4–6 wks in patients with newly inserted pacemaker wires is required
- Ipsilateral carobid endarterectomy due to possibility of carotid artery puncture.

Sites of Cannulation

- Depends of skill of operator
- Avoid sites involving:
  - Infection
  - Burns
  - Other dermatological processes.
- Preferred sites:
  - Internal jugular vein
  - Subclavian vein
  - External jugular vein
  - Antecubital vein
  - Femoral vein.
- Risk of infection: femoral v. > internal jugular v. > subclavian v.
- IJV better in patients with:
  - *Coagulopathies:* Bleeding at subclavian artery if punctured is difficult to control
  - Acute lung injury where risk of pneumothorax is high.

Methods to Reduce Risk of Infection

- Education program with safety checklist
- Chlorhexidine preparatory solution
- Use subclavian vein site
- Avoid femoral puncture site
- Use maximal barrier precautions:
  - Cap
  - Mask
  - Sterile gloves
  - Gown
  - Sterile drape.
- Avoid guide wire exchanges as much as possible
- Use antimicrobial impregnated catheters if infection rates remain high
- Fluid administration sets changed every 72 hrs
- Remove catheters when no longer needed.

Use of Ultrasound Guidance

Advantages

- Allows better visualization of anatomy and exact vessel location
- Avoids preexisting thrombus
- Reduces failure rates and multiple attempts at catheterization
- Reduces infection rates.

Indications of USG Guided Access

- Anatomically difficult:
  - Morbid obesity, short and thick neck
  - Local scarring
  - Radiation therapy
  - Transplant patients
  - Edema.
- Associated comorbidities:
  - Coagulopathies
  - Bullons emphysema
  - Maximal ventilatory support.

Techniques of Cannulation

Three techniques of cannulation:

- Catheter over needle
- Catheter through needle
- Catheter over guide wire (***Seldingers technique***).

IJV Cannulation[2]

Central/Middle Approach:

- Positioned at 15° Trendelenburg position, head turned to contralateral side
- Using maximal barrier precautions after LA infilteration, operator punctures skin with 22 G finder needle with a syringe attached at apex of triangle formed by:
  - Two bellies of sternocleidomastoid muscle
  - Clavicle
- Internal Carotid Artery pulsations are felt 1–2 cms medial to this point
- Finder needle directed at 45° angle towards ipsilateral nipple with constant aspiration
- After successful puncture, large bore needle is introduced in identical place
- After cannulation, guidewire is introduced
- Depth of guidewire insertion limited to 15–20 cms to avoid arrhythmias
- Scalpel used to enlarge skin invision
- A dilator is advanced over guide wire to dilate the tract and is removed
- The central venous catheter is then threaded over the guidewire
- Dressing catheter with chlorhexidine impregnated sponge reduces infection.

Anterior Approach

- Needle inserted 0.5 to 1 cm lateral to carotid artery pulsations at level of cricoid/midpoint of sternal head of sternocleidomastoid directed at ipsilateral toe.

Posterior Approach

- Needle inserted 1 cm dorsal to point where external jugular vein crosses posterior border of sternocleidomastoid and directed caudally and ventrally towards suprasternal notch
- Incidence of carotid artery puncture is high as needle is aimed in the direction of the carotid artery.

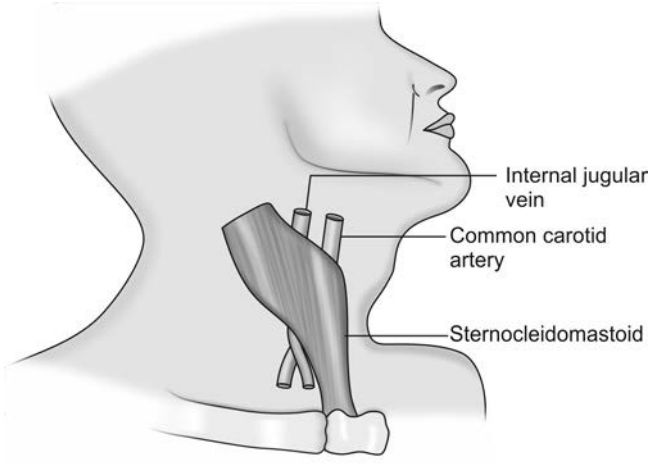


Fig. 6.23: Internal jugular vein cannulation

Subclavian Vein Cannulation

Position

- Patient is 15–30° Trendelenburg with bedroll between scapulae
- Patients head turned to contralateral side, arms are by the side.

Infraclavicular Approach

- Skin puncture with 18 G needle, attached to syringe
- Puncture done 2–3 cm caudal to midpoint of clavicle
- Direction of insertion towards suprasternal notch until it abuts the clavicle
- The needle is walked down the clavicle until inferior edge is cleared
- As needle is advanced, it is kept as close to inferior edge of clavicle as possible, to avoid puncturing dome of pleura
- When blood return is established:
  - Needle bevel is turned 90° towards heart
  - Syringe is removed and guidewire inserted
  - Needle is removed and dilator is advanced over guide wire
- The central venous catheter is advanced over guidewire to appropriate depth.

Supraclavicular Approach

- Skin puncture just superior to clavicle and lateral to insertion of clavicular head of SCM
- Needle advanced towards contralateral nipple just under
- It should enter subclavian vein at depth of 1–4 cms
- Approach has 90–95% success rate.

Confirmation of Proper Position of Cannula

- Comparison of color/PaO_2 of blood sample and arterial sample drawn simultaneously
- Attach cannula to transducer via sterile tubing to observe pressure waveform
- Retrograde flow:
  - Attach cannula to sterile tubing and allow retrograde flow into upright tubing
  - If in vein, blood level in tubing will stop rising at level consistent with CVP
  - Also, the blood level will demonstrate respiratory variation
- Ultrasonography
- Chest X-ray is *confirmatory.*

Complications[1,2,3,5]

- Complications during central venous cannulation:
  - Arterial puncture with hematoma and infection/airway obstruction
  - Arteriovenous fistula
  - Air emboli if negative pressure within venous system
  - Nerve injury:
    - Phrenic nerve
    - Brachial plexus
    - Stellate ganglion
  - Hemothorax if subclavian artery lacerated
  - Chylothorax if injury to thoracic duct
  - Pneumothorax which is most common with subclavian artery cannulation
  - Catheter/wire shearing: may require:
    - Removal with surgery
    - Removal through percutaneous transvenous technique
- Complications of catheter presence:
  - Thrombosis, thromboembolism
  - Infection, sepsis, endocarditis
  - Arrhythmias:
    - Extrasystoles
    - Ventricular fibrillation
    - Transient atrial/ventricular arrhythmias
    - Complete heart block
    - Prevented by limiting guide wire insertion to 22 cms.
  - Hydrothorax:
    - Due to erosion of catheter into pleural cavity
    - Fluid infused via catheter will then accumulate in pleural cavity
  - RA/RV perforation and tamponade:
    - Increased incidence with long dilators/catheters and inflexible guidewire
    - Reduced incidence by reducing angle of puncture to 40°
    - Use single orifice polyurethane/silicon catheters/pigtail tip catheters.

Normal CVP Waveform

Wave form component	Phase of cardiac cycle	Mechanical event
Upstrokes		
a wave	Atrial systole	Atrial contraction
c wave	Isovolumetric contraction	Tricuspid valve "doming" into RA
	Carotid impact wave	Due to early systolic pressure transmission from adjacent carotid artery
v wave	Last part of isovolumetric relaxation	Systolic filling of RA
Downstrokes		
x descent		Atrial relaxation, descent of base, systolic collapse
x' descent		
y descent		Early ventricular filling diastolic collapse
		TV opens and blood from RA enters RV

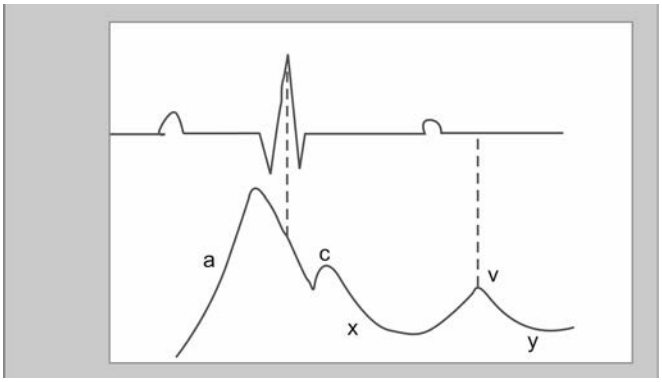


Fig. 6.24: Normal CVP waveform

Waveform Abnormalities

- Loss of A wave: Atrial flutter/fibrillation
- ***Canon A waves:*** Occurs when:
  - RA contracts against closed tricuspid valve as in:
    - Junctional rhythm
    - Complete heart block
    - Ventricular arrhythmias.
  - Increased resistance to RA emptying:
    - Tricuspid stenosis
    - Right ventricular hypertrophy
    - Pulmonary stenosis
    - Pulmonary arterial HTN.
- ***Canon V waves***/C-V waves:
  - Tricuspid regurgitation
  - Right ventricular failure
  - RV papillary muscle ischemia
  - Constrictive pericarditis/tamponade.
- *Constrictive pericarditis:* M configuration with:
  - Prominent A and V waves
  - Steep X and Y descents
- Atrial fibrillation:
  - Loss of a wave
  - Prominent c wave.
- Tricuspid regurgitation:
  - Tall systolic c-v wave
  - Loss of x descent.
- Tricuspid stenosis:
  - Tall a wave
  - Attenuation of y descent.
- Right ventricular ischemia:
  - Tall a and v waves
  - Steep x and y descents
  - M/W configuration.
- Constrictive tamponade:
  - Dominant x descent
  - Attenuated y descent.

PULMONARY ARTERY PRESSURE MONITORING[1,2,3,4,5]

Introduction

- PAC catheters is a very useful monitor of:
  - LV and RV function
  - Hemodynamic status
  - Guides therapy with pharmacological and non-pharmacological agents.

Uses

- Guides fluid therapy and inotropic/vasopressor therapy
- Measures hemodynamic indices like:
  - CVP, PA Occlusion Pressure (PAOP)
  - PA pressure, PVR
  - PCWP, MVO_2
  - Intracardiac ECG
  - Right and left ventricular stroke work index.
- Oxygenation variables like:
  - O_2 delivery
  - O_2 consumption
  - O_2 extraction
  - Mixed venous oxygen saturation (MvO_2).
- Used for intracardiac ECG monitoring
- Helps to measure thermodilution cardiac output
- Used to calculate lung water
- Helps to differentiate:
  - Cardiogenic and noncardiogenic pulmonary edema
  - Circulatory and respiratory failure.

Types of PA Catheter

- Standard PA catheter
- Pacing PA catheter
- Continuous cardiac output PA catheter
- Continuous MvO_2 PAC
- RVEF PA catheter.

Indications

Complex Fluid Management

- Shock
- Multiple organ failure
- Acute renal failure
- Massive trauma, acute burns
- Hemorrhagic pancreatitis.

Specific Surgical Procedure

- Pericardiectomy
- Aortic cross-clamping (thoracic aortic aneurysm surgery)
- Sitting craniotomy
- Liver transplants, porto-systemic shunts.

Cardiac Disease

- CAD with LV dysfunction/recent infarction
- Valvular heart disease/pulmonary HTN/pulmonary embolus
- Heart failure:
  - Cardiomyopathy
  - Cardiac tamponade
  - Cor pulmonale.
- Those surgeries requiring CPB.

Pulmonary Diseases

- Acute respiratory failure, ARDS
- Severe COPD
- Those requiring high levels of PEEP
- Differentiation of cardiogenic and noncardiogenic PE
- Aspiration of air emboli.

High Risk Obstetrics

- Severe toxemia
- Placental abruption.

Contraindications

Absolute Contraindications

- Tricuspid/pulmonary valve prosthesis
- Tricuspid/pulmonary endocarditis
- Right heart mass (thrombus/tumor).

Relative Contraindications

- Complete LBBB (due to risk of complete heart block)
- ***Wolff-Parkinson-White syndrome:***
  - Due to possibility of tachyarrhythmias
  - PAC with pacing capacity is better in WPW patients.
- Ebsteins anomaly
- Septicemias as PAC may serve as nidus for injection
- Hypercoagulable states as thrombus may form.

Description

- Typically multiple lumen catheter
- 5–7.5 French diameter
- 110 cms long with PVC body
- Extra connecting tubes for attachment to the pressure transducer
- Ports:
  - Tip: PA lumen/distal lumen
  - Port A:
    - Air channel for inflation of ballon
    - 1.5 cc balloon is located just proximal to tip.
  - Port B:
    - Used to measure temperature for calculation of cardiac output
    - Approximately 4 cm proximal to balloon is the thermistor.
  - Port C:
    - Two additional lumens at 19 cms and 30 cms from tip
    - Proximal lumen at 30 cms from tip for:
      - Drug infusion
      - Cardiac output injection
      - Measurement of PA pressure
    - Distal lumen is ventricular port at 19 cms from tip for infusion of drugs
  - *Port D:* Some PACs have connections for temporary pacing
  - *Port E:* Some PACs are coated with heparin.

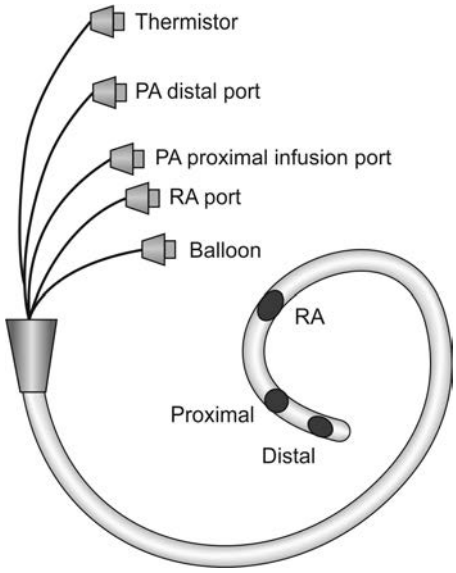


Fig. 6.25: PA catheter

PAC Insertion Technique: *Seldinger technique:*

- After identifying major vein, instead of CV catheter, a dilator and sheets are threaded over guide wire
- Catheter placement is most commonly performed by observing the pressure waves as catheter is floated from CVP position through right heart chambers into PA
- Preparation of PA catheter:
  - PA catheter is first checked by inflating and deflating balloon
  - Irrigate all 3 intravascular lumens with heparinized saline.
- Catheter is then threaded through the PA sheath
- Distal port connected to transducer and zeroed to patients midaxillary line
- At approximately 15 cms distal tip enters RA
- CVP tracing varying with respiration confirms an intrathoracic position
- Balloon is then inflated with 1.5 cc air to:
  - Protect endocardium from catheter tip
  - Allow right ventricles cardiac output to direct catheter forwards.
- Balloon is always deflated during withdrawal

- ECG monitoring done continuously at this stage
- A sudden increase in systolic pressure on distal tracing indicates RV location of catheter
- Sudden increase in diastolic pressure indicates PA entry which normally occurs at 40 cms
- Maneuvres to enhance catheter floation in difficult cases:
  - Deep inhalation
  - Slight head up position
  - Right lateral tilt
  - Injecting iced saline through proximal lumen to stiffen catheter increases risk of RV perforation
  - Administer small dose of inotrope to increase CO.

Access site	Distance to RV in cms
Right internal jugular vein	35
Right superior vena cava (subclavian vein)	35
Left internal jugular vein	45
Femoral vein	50
Right antecubital vein	60
Left antecubital vein	70

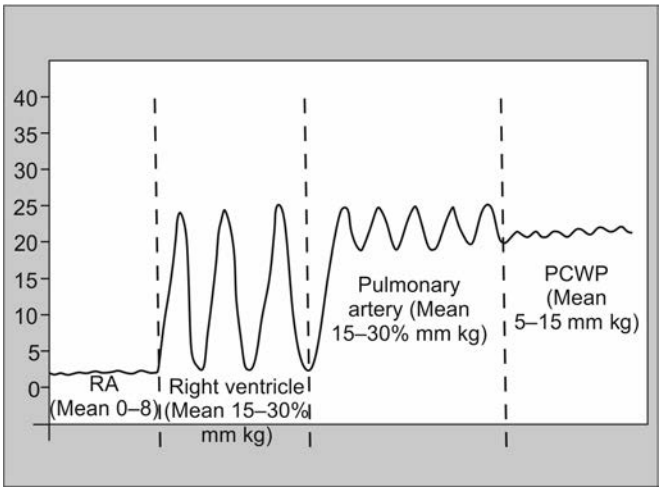


Fig. 6.26: PAC catheter insertion[3]

Prevention of PAC Infection

- Educate clinicians
- Use of maximal sterile barrier precautions:
  - Mask and cap
  - Sterile gloves and gown
  - Large steri-drapes.
- 2% chlorhexidine skin preparation
- Avoid routine change of CVP/PAC solely for reducing risk of injection.

Factors Affecting Accuracy of PAC Monitoring

Pulmonary Vascular Resistance

- Increased PVR causes reduced pulmonary blood flow
- Causes of increased PVR:
  - Acute/chronic lung diseases
  - Pulmonary emboli
  - Alveolar hypoxia
  - Acidosis
  - Hypoxemia
  - Tachycardia
  - Vasoactive drugs.

Alveolar Pulmonary Arterial Pressure Relationship

- Due to gravity dependent variation in pulmonary venous flow, directed PA catheter usually advances to gravity dependent areas of highest blood flow
- In zone III, $P_A > P_V > P_{ALV}$ meets the criteria for interrupted blood flow and continuous communication intracardiac pressure.
- If PCOP > PAEDP:
  - Non-phasic PCOP tracing
  - Unable to aspirate blood from tip
  - Implies PAC is not in Zone III.

Respiratory Pattern/Airway Pressures

- Changes in intrathoracic/intrapleural pressures affect transmural pressure, relation between PCOP and LVEDP
- Changes in PEEP changes intravascular and intrapleural pressures:
  - PEEP increases alveolar pressure: zone III converted to zone II
  - Alters ventricular distensibility and reduces venous return.
- If PEEP ≤ 10 cm H_2O, no effect in PCOP of PAC located in Zone III
- Higher PEEP changes PCOP-LVEDP relationship
- When PEEP > 10 cm H_2O, subtract 1–2 mm Hg from displayed wedge pressure for every 5 cm H_2O PEEP

Intracardiac Shunts: PAWP waveform abnormalities:

Condition	Characteristics
Mitral regurgitation	Tall regurgitant C-V waveform
	Obliteration of X descent
Mitral stenosis	Tall a waves
	Attenuation of Y descent
Ventricular septal defect	Tall anterograde v waves
Myocardial infarction	Tall a waves
	Tall v waves

Reduced Ventricular Compliance

- Relationship between pressure and volume is not linear
- LV compliance is a dynamic factor
- Causes of reduced ventricular compliance:
  - MI, HTN
  - Restrictive myopathies
  - Right-left shunts
  - Aortic stenosis
  - Cardiac tamponade (***square pattern***)
  - Inotropic drugs.

PAC Pressures[3,5]

Pressures	Mean (mm Hg)	Range (mm Hg)
Right atrial pressure	5	1–10
RVESP/RVEDP	25/5	15–30/0–8
PA systolic/PA diastolic	23/9	15–30/5–15
Mean PA pressure	15	10–20
PCWP	10	5–15
LAP	8	4–12
LVEDP	8	4–12
LV systolic pressure	130	90–140

Derived Hemodynamic Parameters[1,3,5]

Parameter	Normal value
Cardiac index (CI)	2.8–4.2 L/min/m^2
Stroke volume (SV)	50–110 ml/beat
Stroke index (SI)	30–65 ml/beat/m^2
Left ventricular stroke work index (LVSWI)	45–60 g.m/m^2
Right ventricular stroke work index (RVSWI)	5–10 g.m/m^2
Systemic vascular resistance (SVR)	900–1400 dyne sec cm^{-5}
Systemic vascular resistance index (SVRI)	1500–2400 dyne sec cm^{-5}/m^2
Pulmonary vascular resistance (PVR)	80–120 dyne sec cm^{-5}
Pulmonary vascular resistance index (PVRI)	250–400 dyne sec cm^{-5}/m^2

Oxygen Delivery Parameters[1,3,5]

Parameter	Normal value
Arterial oxygen content	18–20 mL/dL
M_vO_2	13–16 mL/dL
Arteriovenous oxygen difference	4–5.5 mL/dL
Pulmonary capillary oxygen content	19–21 mL/dL
Pulmonary shunt fraction	2–8%

Contd...

Contd...

Parameter	Normal value
Oxygen delivery	800–1100 mL/min
Oxygen consumption	150–300 mL/min

Complications[1,2,3,5]

- Complication of central venous access:
  - Arterial puncture
  - Bleeding
  - Pneumothorax
  - Air embolism.
- Complication of central venous catheterization:
  - Catheter shearing
  - Guidewire embolization
  - Arrhythmias:
    - Supraventricular tachycardia
    - Atrial fibrillation
    - Ventricular tachycardia/fibrillation
    - Right bundle branch block
    - Complete heart block.
  - Air embolism
  - Arterial puncture
  - Postoperative pneumothorax
  - Minor increase in tricuspid regurgitation
  - RA rupture.
- *Complication of catheter residence:* Late complication:
  - Mechanical problems:
    - Catheter entrapment
    - Catheter coiling/knotting/tip migration
    - Balloon rupture
    - Infection: risk increases if catheter in situ for > 72 hours
    - Sepsis, endocarditis
    - Thrombosis, embolism
    - Pulmonary infarction
    - Valvular damage.
  - Structural damage:
    - Delayed vascular injury/fistula
    - Cardiac perforation
    - TV/PV/endocardial damage
    - PA rupture/PA aneurysm:
      - More common in patients with:
        - Pulmonary HTN
        - Coagulopathy
        - Heparinization
        - Overwedging.
      - Even trace hemoptysis not to be ignored as it heralds PA rupture
      - If suspected, place double lumen tube to maintain oxygenation of unaffected lung.

PAC Modifications[1,3,4,5]

- Mixed venous oxygen saturation:
  - Oximetric PAC uses *reflectance spectrophotometry*
  - Several wave lengths are transmitted through optical fibers embedded in PAC
  - The reflected intensity of light identifies saturation of blood surrounding tip of PAC.
- Intermittant cardiac output monitoring:
  - Ice cold NS or 5% dextrose used for cardiac output measurement
  - Bolus of cooled fluid is injected into the PA
  - Thermistor at the tip of PAC records the reduction in temperature as bolus passes through PA
  - Factors which determine cardiac output:
    - Specific heat of blood and indicator
    - Volume of injectate
    - Catheter size
    - Specific gravity of blood and injectate
    - Area of blood-temperature curve.
- Continuous cardiac output monitoring:
  - Pulsed thermodilution:
    - Uses coiled RV filament
    - Filament applies low power heating signal to RA and RV in cyclical manner
    - Thermistor at PAC tip detects changes in blood temperature
    - It sends major information to a computer
    - Computer uses stochastic analysis to create thermodilution curve
    - Cardiac output is calculated from thermodilution curve based on conservation of heat equation.
  - Another technique:
    - Applies heat to a thermistor at PAC tip
    - RV out flow then cools the tip
    - The temperature changes registered are proportional to RV outflow
    - This determines the cardiac output.
- RV ejection fraction:
  - Performed with special PA catheter which has a rapid response thermistor
  - Analyzes exponential decay of PA temperature over several cardiac cycles
  - Cardiac output calculated from the data
  - Ejection fraction = CO – mean residual fraction
  - RVEF useful in:
    - RV dysfunction
    - For assessment of RV preload
    - During liver transplantation.
- Intracardiac pacing:
  - For bipolar ventricular/atrial/atrioventricular intracardiac pacing
  - PA catheter has 5 lumen
  - 2.4 French bipolar pacing electrode passed through additional lumen for pacing.

Controversy of PAC Monitoring

- Perioperative outcomes reported as improved/worsened/unchanged by using PAC
- Errors in diagnosis and treatment are common as values are interpreted by health staff
- At present preponderance of studies have had difficulties in demonstrating outcome benefits.

ICP MONITORING[1,2,3]

Introduction

Normal ICP:

- 10–15 mm Hg in adults and young children
- 3–7 mm Hg for young children
- 1.5–6 mm Hg for preterm infants
- ≥ 20 mm Hg: Raised ICP.

Lundberg's Classification

- 0–10 mm Hg : Normal
- 15–20 mm Hg : Mildly increased
- 20–40 mm Hg : Moderately increased
- ≥ 40 mm Hg : Severely increased.

Indications for ICP Monitoring

- Benign intracranial HTN
- Meningitis/encephalitis
- Encephalopathy:
  - Lead ingestion
  - Hypertensive crisis
  - Hepatic encephalopathy.
- Postcraniotomy cerebral edema
- Intracranial space occupying lesions
- Severe traumatic brain injury (GCS 3–8 with abnormal CT scan)
- Intracranial hemorrhage
- Post subarachnoid hemorrhage associated with hydrocephalus/coma
- Intracranial space occupying lesions (ICSOL):
  - Tumor, hematoma, abscess
  - AV malformation/aneurysm obstructing CSF.
- Decompensated/normal pressure hydrocephaline
- Others:
  - Reyes syndrome
  - Venous sinus thrombosis.

Contraindications

- Coagulopathy, anticoagulant therapy
- Prothrombin time > 13 seconds/INR > 1.3
- Scalp infection
- Severe midline shift causing ventricular displacement
- Cerebral edema causing ventricular collapse.

Sites of Monitoring

- Ventricular:
  - ***Gold standard***
  - Most reliable.
- Subdural:
  - Hollow bolt inserted via burrhole
  - Fiberoptic device/pressure transducer passed into subdural space by incising dura
  - Hemorrhage and infection possible
  - Underestimates ICP.
- Intraparenchymal:
  - Using silicone strain gauge monitor
  - More accurate
  - Can be inserted by non-neurosurgery staff.
- Extradural:
  - Using catheters in extradural space
  - Not reliable and rarely used.

Types of Monitoring Devices

- Fluid filled transduced ventriculostomy
- Fiberoptic sensors
- Microchips (internal strain gauge devices)
- Air pouch technologies.

Locations of Monitoring Devices

- Ventricular
- Parenchymal
- Subdural.

ICP Techniques

Invasive

- Ventricular catheter:
  - ***Gold standard***
  - Most reliable, inexpensive, accurate and can be re-zeroed
  - Consists of a catheter placed at level of foramen of Monroe/lateral ventricle
  - Catheter attached to pressure resistant tubing filled with preservative free saline
  - This catheter is attached to a non-flush strain gauge transducer
  - Transducer is zeroed at external auditory meatus
  - Maybe difficult if ventricles are narrow due to edema/ventriculitis
  - Injury to basal ganglia, infection and blocked catheter can occur
  - Antibiotic coated drains prevent infections.
- Fiberoptic transducers:
  - Using fiberoptic catheter with flexible diaphragm
  - Have fiberoptic probe which has a transducer at the tip which is inserted into brain
  - Placed intraventricular/intraparenchymal
  - Changes in light intensity reflected from diaphragm is calibrated as ICP
  - Disadvantages:
    - High cost
    - Inability to zero device insitu
    - Can be broken if patient is restless
    - Has to replaced every 5 days to prevent infection.
- Implanted microchip Transducer:
  - Solid state pressure transducer with piezo-resistive strain gauze implanted at tip of nylon fiber (***Codman microsensor***)
  - Pressure applied at the sensor tip generates electrical voltages
  - Intraventricular/intraparenchymal/subdural/epidural
  - Low infection and hemorrhage rates.
- Subarachnoid bolts:
  - Metallic cylindrical instruments inserted such that their tip protrudes into subarachnoid space
  - Most common device used: ***Richmond screw/ Becker bolt***
  - Easier to install but are less accurate.
- Continous monitoring of intracranial compliance:
  - ***Spiegelberg air pouch*** ICP/compliance monitor
  - Balloon surrounding the end of a catheter is called airpouch
  - Airpouch gets repeated inflated and deflated with 0.05–0.1 cc of air
  - Pressure exerted on the balloon pouch is the pressure of the surrounding tissue
  - Resultant pressure and volume changes calculates compliance and ICP
  - ICP calculated in terms of PVI/VPR on a continuous basis
  - PVI/VPR = Pressure volume index/volume pressure ratio).

Noninvasive

- Transcranial doppler flow velocity to derive estimated CPP

- ***Rotterdam transfontanelle ICP transducer***
- USG guided Optic Nerve Sheath Diameter (ONSD)
- ONSD 5 mm = ICP > 20 mm Hg.

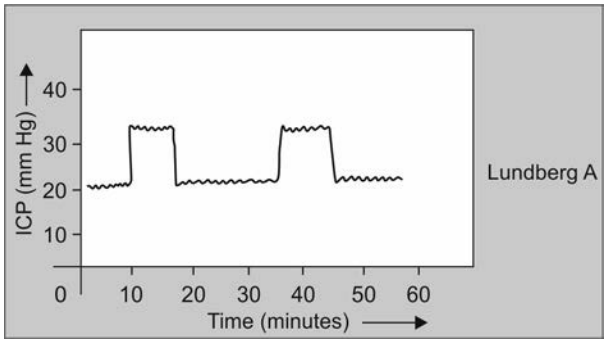
ICP Waveforms

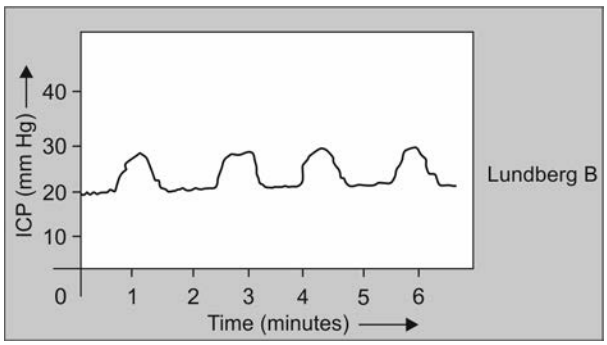
Normal Waveform

- Has two components
  - Baseline pressure
  - Variation of pressure (i.e. pressure waves).
- Variations due to small pulsations transmitted from systolic BP to intracranial cavity
- Blood pressure pulsations are superimposed on slower oscillations due to respiratory cycle.

Pathological Waveforms

- Arterial pulses on ICP waveform become more prominent
- Three types of pathological waveforms
  - Lundberg A:
    - *Plateau waves*
    - ICP elevation ≥ 50 mm Hg lasting 5–20 mins.
  - Lundberg B:
    - *Pressure pulses*
    - ICP elevations upto 50 mm Hg occurring every 30 sec–2 mins.
  - Lundberg C
    - Amplitude of 20 mm Hg
    - Frequency of 4–8/min.





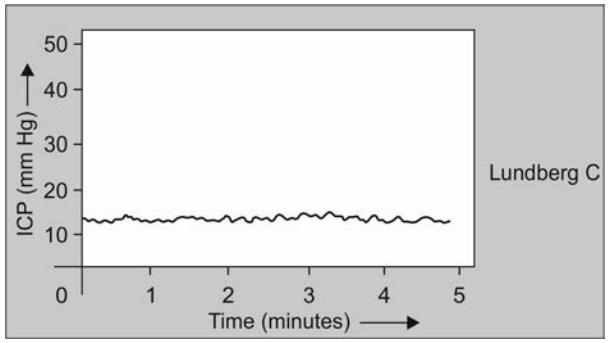


Fig. 6.27: Lundbergs waves

Complications

- Intraparenchymal/Intraventricular/Subdural hemorrhage
- Bacterial ventriculitis/meningitis
- CSF leakage
- Overdrainage causing ventricular collapse
- *System malfunction:* Occlusion/opposition of catheter tip against ventricular wall.

EVOKED POTENTIAL

Introduction

They are the electrophysiological responses of nervous system to sensory/motor/auditory/visual stimulation.

Uses

- To evaluate spinal cord function during surgery on or near spinal cord
- Auditory nerve and brain stem function during surgery on pituitary tumors/optic N/optic chiasm.

SOMATOSENSORY EVOKED POTENTIALS[1,2,3]

Introduction

SSEP is a signal which is detectable on EEG, generated in response to a specific applied sensory input, by stimulating a peripheral sensory nerve.

Method

- Stimulus applied maybe electrical/mechanical/thermal/magnetic
- Stimulus is applied over:
  - Tibial N
  - Paroneal N
  - Median N
  - Ulnar N
  - Sometimes cranial nerves with sensory pathways.
- Evoked potentials are recorded over sensory cortex.

Indications

- During spine surgery when dorsal column is at risk
- During carotid surgery like:
  - Carotid endarterectomy
  - Aneurysm surgery
  - Embolization of AVM.
- During streptokinase dissolution of occluding blood clot and to detect cerebral ischemia in SAH
- In comatose patients, the extent of CCT prolongation correlates with extent of injury. Assymetry between the 2 hemispheres is the most important criterion for recognizing the onset of cerebral ischemia.

Disadvantages

- Detects dysfunction only in posterior part of spinal cord
- Cannot exclude anterior cord dysfunction as somatosensory stimulation follows dorsal column pathways of vibration and proprioception which are supplied by postspinal artery, while motor pathway is supplied by anterior spinal artery
- Volatile anesthetics produce depression of SSEP
- Opioids produce depression of SSEP, but to a lesser extent that volatile anesthetics
- Ketamine and etomidate increase amplitude of SSEP.

Principle

- Low voltage electrical current which stimulates a peripheral nerve, is applied
- Resulting evoked potentials reflect integrity of sensory neural pathways from peripheral N to somatosensory cortex
- Due to presence of spontaneous EEG activity, a single peripheral stimulus which generates cortical activity of low amplitude would not be detectable amidst background noise
- Thus, summation followed by signal averaging of repetitive stimuli is necessary for meaningful signals.

Results

- *Post stimulus latency:* Time from application of stimulus to occurrence of a peak/complex in evoked potential waveform
- *Peak amplitude:* Size of waveform is the peak amplitude
- *Polarity:* Direction of wave deflection (positive P or negative N)
- *Central conduction time and conduction velocity (CCT and CV):* Derived from post stimulus latency.

SSEPs are described in terms of polarity and latency.

For example, N 20 is SSEP generated by stimulation of median N which has a latency of 20 msec and a negative deflection.

Interpretation

Short Latency SSEPs

- < 10–15 msec for BAEP
- < 40 msec for SSEP
- Subcortical in origin and represent initial cortical activity
- Not affected by volatile anesthetics.

Intermediate Latency SSEPs

- 40–120 msec
- They are near field potentials when recorded from scalp
- Have greater amplitude than short latency SSEPs
- Arise from primary sensory area of cerebral cortex
- Affected by volatile anesthetics but to a lesser extent than long latency SSEPs.

Long Latency SSEPs

- 120–500 msec
- Depressed by volatile anesthetics.

Ischemia/mechanical disruption of nerve suggested by:

- 50% reduction in signal amplitude
- 10% increase in latency.

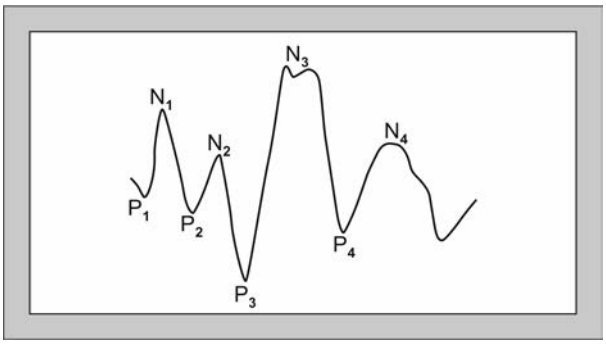


Fig. 6.28: Somatosensory evoked potential

MOTOR EVOKED POTENTIALS[1,2,3]

Introduction

Evoked potentials generated in response to stimulus applied over *motor cortex.*

Method

- Stimulus applied in a transcranial fashion over motor cortex
- Electromyographic deflection is detected by electrodes embedded in muscle belly

- Transcranial signal is applied as a rapid train of four or more stimuli
- Voltage of signal is adjusted to achieve adequate signals in upper and lower extremities
- Evoked potentials are detected at thenar eminence and abductor hallucis muscle
- Stimulus can also be applied to peripheral/cranial N/nerve roots/spinal cord.

Disadvantages

- Recording MEPs require direct (epidural) or indirect (transosseus) stimulation of brain/spinal cord
- Extremely sensitive to volatile anesthetic: Use only TIVA
- Not possible to monitor MEPs if significant neuromuscular blockade present
- Stimulus can cause patient movement
- Obtain MEP only when slight patient movement is not problematic
- Bite block mandatory to prevent tongue injury.

Uses

- Used during any spine/intracranial/cervical spine surgery
- Reflects integrity of motor pathway from peripheral to motor cortex
- Used to monitor anterior segment of spinal cord
- Obviates need for wakeup test during spine surgery.

Interpretation

- Latency of signal is unreliable and not used to make clinical decisions
- Only amplitude is considered important
- 50% reduction in amplitude is considered significant.

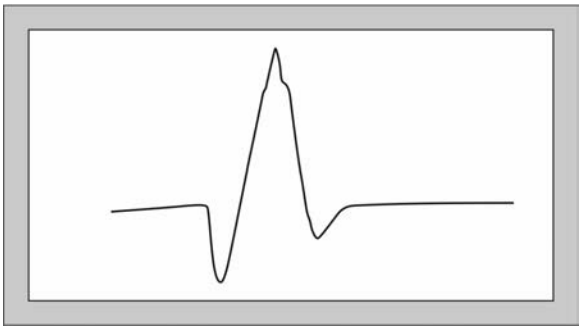


Fig. 6.29: Motor evoked potentials

BRAINSTEM AUDITORY EVOKED POTENTIALS[1,2,3]

Introduction

Instead of electrical stimulus applied to somatosensory nerve, a standardized sound (click) is applied to eighth cranial nerve via auditory apparatus.

Uses

- In comatose patients
- During surgery of cerebropontine angle and floor of IV ventricle
- During procedures close to CN V, VII or VIII
- Alternative to clinical assessment of sedation
- During acoustic neuroma surgery and any surgery around brainstem.

Basis

- Arise from brainstem auditory pathways
- First 10–15 msec of AEPs is subcortical in origin and referred to as BAEP
- Volatile anesthetics produce depression of AEPs
- *Resistant to effects of anesthesia.*

Interpretation

- Consists of series of positive and negative waves
- Latency of each peak has a significance with respect to integrity of various parts of auditory pathway
- Waves can be recorded in field far from vertex and ear or from vertex and noncephalic reference.

Peak	Generator
I	Acoustic N
II	Intracranial acoustic N/cochlear nucleus
III	Superior olive (pons)
IV	Lateral lemniscus (pons)
V	Inferior colliculus (midbrain)
VI	Medial geniculate body (thalamus)
VII	Thalamocortical radiation

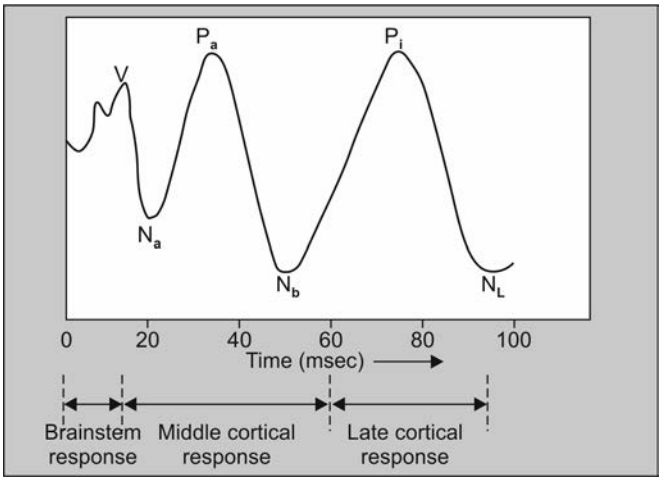


Fig. 6.30: Auditory evoked potentials

VISUAL EVOKED POTENTIALS

- Produced by flashes from light emitting diodes which are mounted on goggles placed on patients closed eyes
- Evoked potentials over occipital cortex recorded
- Used during surgeries involving visual pathways
  - Transphenoidal surgery
  - Anterior fossa surgery
- Volatile anesthetics depress VEP, especially if MAC ≥ 0.8
- Thus, signals are difficult to record during anesthesia
- Generated by light stimulation of retina.

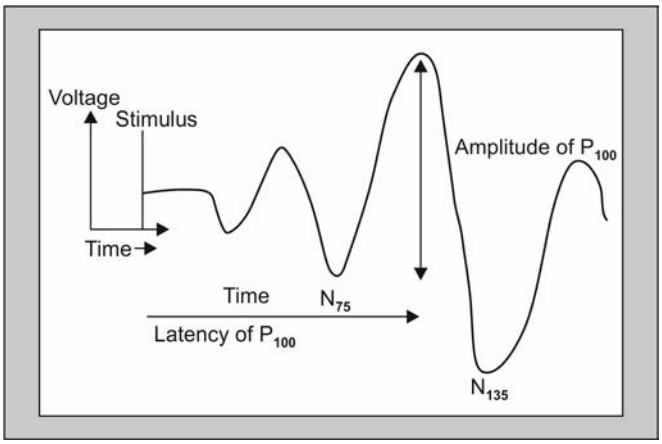


Fig. 6.31: Visual evoked potentials

BISPECTRAL INDEX[1,2,3]

Introduction

- Measure of level of consciousness by algorithmic analysis of patients EEG during general anesthesia
- Developed be ***Aspect Medical Systems.***

Indications

- Patient factors:
  - Obesity
  - Geriatric
  - Pregnant
  - Critically ill
  - Opioid abuse
  - Previous history of awareness under GA.
- Anesthetic technique:
  - TIVA
  - Low flow
  - Induced hypotension
  - Rapid sequence induction.
- Surgery:
  - Cardiac surgery
  - Neurosurgery
  - Obstetric surgery.

Working Principle

- 4 EEG electrodes are placed:
  - 2 inches above nose
  - Next to eyebrow
  - 2 electrodes in temple region.
- Analysis of EEG data by 3 different approaches:
  - ***Fourier*** analysis
  - Bispectral analysis
  - Time - domain analysis.
- Compares patients EEG data with that of EEG database
- Database has values of patients under GA since 1995
- BIS index displayed after analysis
- BIS index is a combination of 3 parameters derived from EEG analysis:
  - Burst Suppression Ratio
  - Relative β ratio
  - Sync Fast Slow.
- BIS index is a dimensionless number on a scale from 0–100
- 0 represents cortical electrical silence
- 100 represents normal cortical activity.

Interpretation[3]

No	BIS value	Correlation
1	> 93	Awake
		Intact memory
		Premedicated patient
2	75–80	< 10% event recall
3	40–60	Recommended for GA maintenance
4	65–85	Recommended for sedation
5	< 40	Deep sedation
		Burst suppression

Advantages

- Reduced risk of awareness
- Reduced use of narcotics and sedatives
- Reduced use of costly drugs like propofol
- Faster wake up time
- Shorter PACU stay
- Easy to use
- Inexpensive and noninvasive.

Disadvantages

- Falsely elevated BIS index with:
  - Errors in electrode placement
  - EMG activity
  - Pacemakers
  - Patient warmers.
- Does not predict movement in response to surgical stimulus as this occurs due to spinal reflexes
- BIS scores vary with type of BIS monitor
- Score based on adult population and cannot be extrapolated to children
- Poor correlation with sedation scores (***Ramsay*** scale) when used for ICU sedation
- Latency of 14–155 seconds
- Explicit recall occurred even with BIS value of 47.

Clinical Applications

- Monitoring sedation and hypnosis
- Monitors awareness and recall during general anesthesia
- Guides optimal titration of anesthetics
- Predicts level of sedation in ICU.

BIS Interactions

- Anesthetic doses of ketamine do not alter BIS values
- BIS not affected by even 75% N_2O producing unconsciousness
- Beta blockers may alter EEG response to stimuli and reduce BIS values
- Changes in body temperature can alter EEG signal and affect BIS index
- Greater with halothane than equipotent doses of isoflurane.

Current Status

- ***Myle***s in a RCT of 2500 patients at high risk for intraoperative awareness found only 2 patients with *explicit recall* with use of BIS monitor
- Yet to be validated adequately by clinical trials.

Recent Advances

- BIS-Vista monitor
- Bilateral BIS monitor with:
  - 4 channel EEG
  - Asymmetry indicator (ASYM)
  - Density Spectral Array.
- Synch-fast slow subvariables:
  - Indicates quality of EEG overall
  - Determines effects of artifacts like EMG on BIS

DEPTH OF ANESTHESIA[1,2,3]

Introduction

Measured indirectly as response to some form of stimulation.

Methods

Clinical Signs

- Blood pressure
- Heart rate
- Respiratory rate
- Pupillary response
- Perspiration
- Tearing
- Eyelash reflex
- Movement
- Response to command.

Clinical Scores

- ***EVANS*** or ***PRST*** score
- ***Modified Observer Assessment of Alertness and Sedation Score*** (MOAASS).

Clinical Techniques

- Skin conductance
- Isolated forearm technique
- Surface electromyogram
- Facial electromyogram
- Lower esophageal contractility
- Heart rate variability.

Brain Electrical Activity Monitoring

- EEG
- Compressed Spectral Analysis (CSA)
- Cerebral Function Monitor (CFM)
- Bispectral index
- Entropy
- Narcotrend
- Patient state analyzer
- **SNAP** index.

Evoked Potential Monitors

- Motor evoked potentials
- Somatosensory evoked potentials
- Auditory evoked potentials
- Visual evoked potentials.

Clinical Scores

PRST Score/Evans Score[1,3]

Introduction: Most commonly used system for depth of anesthesia monitoring.

No	Index	Condition	Score
1	Systolic BP	< Control +15	0
		< Control + 30	1
		> Control + 30	2
2	Heart rate	< Control + 15	0
		< Control + 30	1
		> Control +30	2
3	Sweating	Nil	0
		Moist skin	1
		Visible sweat beads	2
4	Tears	No excess tears in open eyes	0
		Excess tears in open eyes	1
		Tears overflowing in closed eyes	2

Advantages

- Simple
- Does not require special instruments.

Disadvantages

- Parameters nonspecific about anesthetic agents
- Tachycardia due to anticholinergic drugs may affect score
- Beta blockers opioids and regional anesthesia affect score
- Values widely variable among individuals.

Modified Observer Assessment of Alertness and Sedation Score

Score	Description
5	Responds readily to name spoken in normal tone
4	Lethargic response to name spoken in normal tone
3	Responds only after name called loudly/repeatedly
2	Responds only after mild prodding/shaking
1	Responds only after painful trapezius squeeze
0	No response to painful trapezius squeeze

Isolated Forearm Technique

Technique

- Tourniquet applied to upper arm
- Tourniquet inflated to level above systolic BP before giving muscle relaxant
- Patient asked to move his hand
- Movement of arm either spontaneously or in response to command indicates awareness.

Limitations

- Nonspecific response considered as awareness
- Level of anesthesia to prevent movement is higher than routinely used
- Tourniquet induced ischemia/complications possible.

Spontaneous Surface Electromyogram

Introduction

Electrical activity measured from the surface of various muscle groups in patients who are not completely paralyzed.

Rationale

- Frontalis muscle
- Less affected by neuromuscular blockade
- Innervated by facial N
- Stick acts as electrode and placed on frontalis muscle
- Levels falls during anesthesia
- Rises during awakening.

Lower Esophageal Contractility

Rationale

Nonstriated fibers of lower half of esophagus retain activity even after complete skeletal muscle paralysis.

Types

- Spontaneous lower esophageal contractions:
  - Nonresponsive spontaneous contractions
  - Detected by pressure transducers
  - Under control of central esophageal contractility center
  - Increased frequency of contractions occurs when:
    - Lightening of plane of anesthesia
    - Emotion and stress in awake patient.
- Provoked lower esophageal contractions:
  - Due to sudden distention of esophagus by event such as arrival of bolus of food
  - Induced by rapid inflation of balloon catheter in lower esophagus
  - Smooth muscle contractions detected by distally placed pressure transducers.

Interpretation

Esophageal contractility index = 70 × (SLOC rate + PLOC amplitude).

Current Status

- Limited role in measuring depth of anesthesia
- Easy to interprete
- Can be used with muscle relaxants
- Not a reliable method.

Heart Rate Variability

Rationale

- Anesthetic agents first act on brainstem and then on cerebral cortex
- Measures brainstem mediated autonomic tone
- Not affected by any factor other than anesthetic depth.

Components

- *Low Frequency Fluctuations*: Believed to be due to circadian rhythm
- *Medium Frequency Fluctuations*: Due to baroreceptor reflexes
- *High Frequency Fluctuations*: Coincides with frequency of ventilation
- Characterized by >10% variation in P waves of ECG over 5 mins.

Limitations

- Depends on intact autonomic nervous system
- Depends on healthy myocardial conducting system
- Interference when:
  - Autonomic neuropathy
  - Beta blocker therapy
  - Sepsis
  - Conduction defects.

Compressed Spectral Analysis

Technique

- Superimposes linear plots of successive epochs of time on each other
- Generates 3 dimensional display of:
  - Amplitude: Y axis
  - Frequency: X axis
  - Time: Z axis.

Limitations

- Patient variability
- Agent variability
- Confounded by hypoxia hypercarbia and hypotension
- Not reliable
- Can only provide a trend in conjunction with others.

Parameters

- Total power
- ***Spectral Edge Frequency***
- ***Peak Power Frequency.***

Cerebral Function Monitor

Technique

- Uses single biparietal/bitemporal lead to obtain EEG signal
- Output is no longer a regular EEG signal
- It represents overall cortical background activity of brain
- Unreliable when using inhalational agents.

Entropy

Introduction: Defined as amount of disorder in a system.

Rationale

- Describes irregularity complexity and unpredictability of a signal
- EEG signal most complex in awake patient
- Becomes more regular as anesthetic depth increases
- Entropy is high during awake state
- Entropy approaches zero (isoelectric EEG) with increasing anesthetic depth.

Technique

- Based on processed EEG and frontalis muscle EMG signals
- Entropy algorithm used.

Parameters

- **State entropy:**
  - Index from 0–97 (awake)
  - Computed over frequency range 0.8–32 Hz
  - Consists mostly of EEG activity
- **Response entropy:**
  - Index from 0–100 (awake)
  - Computed over frequency range 0.8–47 Hz
  - Consists mostly of EMG frontalis activity.
- **Burst suppression ratio/index:**
  - Ratio of suppressed activity to total activity period in EEG in 1 minute
- **Reproducible hypnosis index:**
  - Used in neurosurgery for supratentorial lesions.

Interpretation

- Target range for entropy – 40 to 60
- RE and SE around 40 indicate low probability of awareness

- Increasing EMG activity indicates impending arousal
- If SE is low and RE is high, consider:
  - Further analgesia
  - Further muscle relaxants.

Current Status

- Correlates with BIS monitoring.

Narcotrend

Technique

- 2 electrodes placed on patients forehead
- 3rd electrode serves as reference
- Multivariate statistical algorithm transforms EEG data into 6 letter calculation of depth of anesthesia.

Parameters

- *Narcotrend Index*
- *Signal Quality Index*
- EMG activity
- *Burst Suppression Ratio*
- *Narcotrend Stage Classification.*

Narcotrend Stage:

- A = Awake
- B = Sedated
- C = Light anesthesia
- D = General anesthesia
- E = Deep hypnosis + general anesthesia
- F = GA + burst suppression.

Narcotrend Index:

- Similar to BIS score:
  - 0 = Deeply anesthetized
  - 100 = Fully awake.

Current Status

- Reduces propofol consumption
- Reduces end tidal concentration of sevoflurane.

Patient State Index

Rationale

- EEG in awake patient has occipital dominance
- EEG changes to frontal dominance on induction
- Returns to occipital dominance on awakening.

Principle

- Uses 5 leads in frontotemporal region
- Uses time frequency and spatial information
- Uses collection of EEG databases for comparison and analysis
- Initially called ***PSA-400*** or ***Sedline monitor***
- Quantifies propofol/sufentanyl in ICU
- Patient State Index varies from 0–100.

Snap Index

Introduction

Single channel device to monitor EEG.

Technique

- Uses 3 SNAP electrodes
  1. Center of forehead
  2. Arch of eyebrow
  3. End of eyebrow line above temple.

Current Status/Implications

- SNAP returns to baseline before awakening
- BIS remains below baseline after awakening
- SNAP more sensitive to unintentional awareness.

MONITORS OF TISSUE OXYGENATION[1,2,3]

Factors Affecting Tissue Oxygenation

- Hemoglobin concentration
- Percentage saturation of oxygen
- Oxygen consumption
- Hemoglobin affinity for oxygen (P_{50})
- Cardiac output.

Methods

- **Clinical signs:**
  - Tachycardia
  - Hypotension
  - Oliguria
  - Hypothermia.
- **Surrogate markers of hypoperfusion:**
  - pH
  - Anion gap
  - Base excess
  - Serum lactate.
- **Global measures:**
  - DO_2 and VO_2
  - Blood lactate
  - Mixed venous oxygen saturation
  - Central venous oxygen saturation.
- **Regional measures:**
  - Brain tissue oxygen monitoring
  - Jugular bulb oximetry
  - Sublingual capnometry

- Gastric tonometry
  - Saline
  - Air.
- Near infrared spectroscopy
  - Venous occlusion
  - Arterial occlusion.
- Transcutaneous PO_2 and PCO_2.

DO_2 and VO_2

Introduction

Most commonly used methods of assessing global oxygen delivery.

Measurement

- DO_2:
  - Global measure of oxygen delivery
  - DO_2 = Cardiac output × arterial oxygen content
  - $DO_2 = CO \times [SaO_2 \times Hb \times 1.39 + (0.003 \times PaO_2)]$.
- VO_2:
  - $VO_2 = 10 \times CO \times (CaO_2\text{-}CvO_2)$
  - CaO_2 = Arterial oxygen content
  - CvO_2 = Venous oxygen content.
- OER:
  - Oxygen Extraction Ratio
  - VO_2/DO_2.

Normal Values

- VO_2 = 250 ml/min if cardiac output = 5L/min (O_2 consumption)
- DO_2 = 1000 ml/min if cardiac output = 5L/min (O_2 delivery)
- OER = 25%.

Significance

- Level of oxygen transport at which VO_2 begins to fall = ***Critical DO***$_2$
- Below critical DO_2, tissues start anaerobic glycolysis and cause lactic acidosis.

SERUM LACTATE LEVELS[1,2,3]

Introduction

Conventional measure of global oxygen demand supply balance.

Normal Values

- *Normal value:* 1 mmol/l
- *In tissue hypoxia:* > 1.5–2 mmol/l

Physiology

- During shock, primary energy source is anerobic glycolysis
- Pyruvate converted to lactate instead of entering Tricarboxylic Acid cycle
- Pyruvate $\xrightarrow{\text{Lactate dehydrogenase}}$ Lactic acid + 2 ATP

Factors Affecting Lactate Levels

- **Elimination of lactate:**
  - Increased levels in liver dysfunction
- **Regional blood flow:**
  - Complete obstruction to blood flow to limb/organ
- **Rate of glucose metabolism:**
  - If glucose metabolism > oxidative capacity of mitochondria, lactate increases
  - Inborn errors of metabolism
  - Catecholamine administration.

Clinical Implications

- Follow changes in lactate levels rather than absolute values:
  - Continuous fall in level associated with survival
  - Persistent rise associated with continued ischemia
- Poor outcome levels if lactate levels do not reduce within 24 hours.

GASTRIC TONOMETRY[1,2,3]

Introduction

Mostly widely studied technique of tissue capnometry

Rationale

- Reduction in cardiac output elicits strong vasoconstriction response
- Also, during hypoperfusion, gut permeability increases
- Endotoxins and microorganisms enter systemic circulation
- Anerobic metabolism occurs in the gastric villi
- This increases gastric mucosal PCO_2 which is used as indicator.

Physiology

- Vulnerability to hypoxia due to *countercurrent* mechanism of villi
- Most of oxygen diffuses directly out of arterioles into adjacent villi

- Tips of villi therefore have lower oxygen and higher CO_2 concentration
- Thus tips of villi are vulnerable to hypoxia.

Indications

- Cardiac surgery
- Major vascular surgery
- Severe sepsis
- Trauma and burns patients
- Acute pancreatitis
- High-risk surgical patients.

Techniques

Saline Tonometry

- Gastric tube with gas permeable silicon balloon at tip placed in stomach
- Balloon filled with saline and left *in situ* for 60 to 90 minutes
- After 60 to 90 minutes saline aspirated and PCO_2 analyzed
- Intraluminal PCO_2 assumed to be equal to gastric Mucosal PCO_2
- Initial 1.2 ml saline discarded to avoid dead space sampling.

Disadvantages

- Errors while sampling
- Loss of CO_2 during transport
- Underestimation by blood gas analyzer
- *Long equilibration time:* Rapid changes not detected
- Only intermittent measurements possible.

Air Tonometry

- Automated gas analyzer connected with gastric tonometer catheter
- 6 ml air pumped into balloon of catheter
- After predetermined time, monitor draws air from balloon
- Initial 1.2 ml discarded to avoid dead space sampling
- PCO_2 of rest of sample measured with infrared sensor
- Shorter equilibration time-can detect rapid changes in PCO_2.

Variables Determined

- **Gastric mucosal PCO_2 ($PgCO_2$):**
  - Three variables determine $PgCO_2$:
    a. Arterial oxygen content
    b. Local blood flow
    c. Tissue CO_2 production.
  - If $PaCO_2$ constant, $PgCO_2$ determines local blood flow.
- **Gastric intramucosal pH:**
  - Calculated using ***Henderson Hasselbach*** equation
  - Assumes arterial HCO_3 to be equal to mucosal HCO_3
  - Assumes that pH of fluid in hollow viscus equals that of surrounding tissue.
- **CO_2-GAP**
  - CO_2-GAP = $PgCO_2 - PaCO_2$
  - Eliminates influence of ventilation on $PgCO_2$
  - Increased CO_2-GAP due to poor perfusion or increased demand.

Current Status

- Most widely used technique of regional perfusion monitoring
- Useful to predict outcome in critically ill patients.

Limitations

- Assumes gastric mucosal HCO_3 equals arterial HCO_3
- Respiratory acid base abnormality will affect pH calculation
- Enteral feeding can increase intraluminal CO_2 production.

NEAR INFRARED SPECTROSCOPY[1,2,3,4]

Introduction

Method of continuous noninvasive bedside monitoring of global tissue oxygenation.

Principle

- Uses principle of light absorption and transmission
- Measures noninvasively:
  - Hb concentration
  - Percentage saturation of oxygen
  - Cytochrome aa_3.
- Has greater tissue penetration than pulse oximetry
- 25 mm spacing between emission and detection probe
- 95% of detected signal is from depth of 23 mm tissue penetration.

Techniques

- **Venous occlusion method:**
  - Pneumatic cuff inflated to 50 mm Hg
  - Pressure blocks venous return but not arterial flow

  - Venous blood volume and pressure increases
  - This causes increase in total Hb and HbO_2
  - This reflects change in regional blood flow and oxygen consumption.
- **Arterial occlusion method:**
  - Pneumatic cuff inflated to 30 mm Hg above SBP
  - Pressure blocks venous and arterial flow
  - Local available O_2 depleted
  - This causes reduced HbO_2, increased Hb with constant total Hb
  - After release of cuff, hyperemic response with increase in HbO_2 occurs.

Parameters

- Fraction of oxyhemoglobin (HbO_2)
- Fraction of deoxyhemoglobin (Hb)
- Tissue Hb saturation (S_tO_2)
- Total tissue Hb (HbT)
- Absolute tissue Hb index (THI)
- Cytochrome aa_3 redox state:
  - Monitors changes in cytochrome aa_3 redox state
  - Measures adequacy of tissue oxidation
  - In reduced state, cyt aa_3 shows weak peak at 70 nm.

Muscle Oxygen Tension

- NIRS measures muscle oxygenation
- Applied in superficial muscles like:
  - Brachioradialis
  - Tibialis anterior
  - Deltoids
- S_tO_2 maybe similar in severe sepsis/in normal volunteer.

Limitations

- Represents average HbO_2 saturation in arterioles, venule and capillaries
- Relative contribution of arteriole/venule cannot be measured
- Does not measure microcirculatory blood flow
- Interpretation of StO_2 in terms of tissue oxygenation difficult
- Measurements influenced by adipose tissue thickness
- Thenar eminence most commonly used as adipose tissue is minimal
- No gold standard to which NIRS can be compared.

TRANSCUTANEOUS PO_2 AND PCO_2[1,2,3,4]

Principle

- Based on ***Polarography***
- Principle that at higher temperature, ability of skin to transport gases is increased
- Amperometric transducer used
- Rate of chemical reaction is detected by current drained through an electrode
- Sensor heats skin 43–45 °C.

Factors Affecting Transcutaneous Measurement

- **Skin thickness:**
  - Good in newborns due to thin epidermal layer
  - Thick skin causes $PtCO_2$ to be lower than $PaCO_2$.
- **Tissue perfusion:**
  - Low tissue perfusion causes reduced $PtCO_2$
  - $PtCO_2$ does not reflect $PaCO_2$ in shock.
- **Temperature:**
  - Heating stratum corneum to > 40 °C causes:
    - Change in structure causing faster oxygen diffusion
    - Shift of ODC in heated dermal capillary bed
    - Dermal capillary hyperemia.

Parameters

- **Trancutaneous O_2 index (tc-index):**
  - Measures changes in $PtCO_2$ relative to changes in PaO_2
  - With adequate blood flow, $PtCO_2 = PaO_2$ and tc-index = 1
  - In shock, $PtCO_2$ drops and tc index falls
  - Tc-index > 0.7 associated with hemodynamic stability
  - Normally $PtCO_2$ is 70–80% of PaO_2 when circulation is normal.
- **Transcutaneous CO_2 partial pressure**:
  - Used as index of cutaneous blood flow
  - Difference between $PaCO_2$ and $PtcCO_2$ occurs due to accumulation of CO_2 in skin due to hypoperfusion
  - $PtcCO_2$ is less sensitive to changes in hemodynamics than $PtCO_2$.

SUBLINGUAL CAPNOMETRY[1,2,3,4]

Principle

- Sublingual mucosal PCO_2 used as a measure of tissue perfusion

- High $PsICO_2$ associated with impaired microcirculation.

Method

- Uses ***Capnoprobe***
- Consists disposable $PsICO_2$ sensor which is CO_2 sensing optode
- Optode contains CO_2 permeable silicon capsule filled with fluorescent dye in a buffer solution at distal end of optical fiber
- Indicator excited by light travelling through optical fiber
- Changes in fluorescence causing changes in projected light is monitored by optical fiber
- Changes are due to formation of CO_2 and H_2CO_3 causing parallel changes in pH of solution
- Light signals are transferred via optical fiber and converted to numerical PCO_2 value.

Current Status

- Reliable marker of tissue hypoperfusion
- $PsICO_2$ > 70 mm Hg predictive of circulatory failure
- Ps (I-a) CO_2 > 25 mm Hg indicates poor prognosis
- Capnoprobe not used anymore due to presence of bacteria in buffer solution.

BRAIN TISSUE OXYGEN MONITORING[1,2,3,4]

Introduction

- Allows continuous monitoring of cerebral oxygenation
- Oxygen sensor placed on white matter of brain
- Normal $PbrO_2$ = 25–35 mm Hg

Indications

- **Traumatic brain injury:**
  - Low $PbrO_2$ during first 24 hours after injury
  - Increased mortality associated with long duration of values < 15 mm Hg
  - Currently $PbrO_2$ of 15 mm Hg is critical limit in TBI.
- **Subarachnoid hemorrhage:**
  - Low $PbrO_2$ values
  - Depth of tissue hypoxia related to severity of hemorhage
- **Ischemic stroke**
- **Selection of critical perfusion pressure.**

Principle

- Based on ***Polarography principle***
- Employs ***Clark cell*** method to measure tissue oxygenation
- Clark cell is semipermeable membrane embracing set of bipolar electrodes
- One end has silver and other end has gold electrodes
- Dissolved oxygen permeates membrane into electrolyte solution
- Depolarization occurs at cathode which generates current
- Electrical current generated, is delivered to brain tissue O_2 monitor.

Technique

- Small O_2 sensitive catheter introduced into white matter
- Position catheter in ischemic penumbra for information about parts of brain at risk
- Oxygenation measured by polarography technique
- Values reflect balance between O_2 demand and supply
- Catheter inserted through bolt inserted into skull.

Types of Electrodes

- **Neurotrend:**
  - Requires larger burr hole
  - Measures $PbrO_2$, PCO_2 and pH.
- **Licox:**
  - Measures only $PbrO_2$
  - 0.5 mm diameter and 5 mm long area.

Factors Affecting $PbrO_2$

- **PO_2 values:**
  - $PbrO_2$ increases with increasing PaO_2 or FiO_2 values
- **PCO_2 values:**
  - $PbrO_2$ decreases on hyperventilation
- **Peep:**
  - Causes reduced ICP with no influence on oxygen delivery/consumption
- **Cerebral perfusion pressure:**
  - When CPP < 60 mm Hg, $PbrO_2$ decreases by 6 mm Hg
  - When CPP > 60 mm Hg, effecton $PbrO_2$ is less significant
  - Thus, maintain CPP > 60 mm Hg.
- **$SjvO_2$:**
  - If $SjvO_2$ < 55% it reflects drop in CPP and increased risk of ischemia
- **Brain metabolic waste:**
  - When $PbtO_2$ < 10 it causes reduction in glutamate and aspartate
  - When glucose reduces, $PbtO_2$ also reduces

– When glucose reduces, anerobic respiration causes increased lactate.

Complications
- Infection
- Cerebral hemorrhage
- Parenchymal laceration.

Current Status
- Used in TBI to prevent *Secondary brain injury.*

MIXED VENOUS OXYGEN TENSION[1,2,3,4,5]

Introduction
- Direct measurement of reduced Hb percentage of blood in right ventricle, i.e. mixture of blood from SVC, IVC and coronary sinus
- Represents end result of both oxygen delivery and consumption at the tissue level.

Procedure
- Continuous monitoring based on *Reflectance spectrometry*
- Light of selected wavelength transmitted down one fiberoptic filament to blood flowing past catheter tip
- Reflected light transmitted back via second filament to photodetector.

Formula
- $SvO_2 = \frac{SaO_2 - VO_2\ (mlO_2/min)}{Q \times 13.9 \times Hb\ (g/dL)}$

SvO_2 = MvO_2 saturation
SaO_2 = Arterial O_2 saturation
VO_2 = O_2 consumed
CO = Cardiac output
Hb = Hemoglobin.

Normal Values
- SvO_2 normally > 75 %
- SvO_2 < 60 %: Imbalance between O_2 demand and supply causing the use of venous O_2 reservoir due to:
  - Hypoxemia
  - Low cardiac output
  - High O_2 consumption.

No	SvO_2 Levels	Consequences
1	> 75%	Normal extraction
		O_2 supply > O_2 demand
2	50–75 %	Compensatory extraction

Contd...

Contd...

No	SvO_2 Levels	Consequences
		Increasing O_2 demand/reducing O_2 supply
3	30–50 %	Exhaustion of extraction
		Beginning of lactic acidosis
		O_2 supply < O_2 demand
4	25–30 %	Severe lactic acidosis
5	< 25 %	Cellular death

Conditions Affecting SvO_2[1,3,5]

No	SvO_2	Conditions	Examples
1	Increased > 75 %	Increased O_2 delivery	Increased FiO_2
		Reduced O_2 demand	Sepsis
			Paralyzed patient
			Postanesthesia
			Hypothermia
		Impaired O_2 utilization	Sepsis
			Cyanide poisoning
		Technical problems	Improper catheter wedging
2	Decreased < 60%	Increased O_2 demand	Shivering
			Increased physical activity
			Seizures
			Pain
			Fever
			Raised BMR
		Poor O_2 supply	Hypoxic hypoxia (low FiO_2)
			Anemia
			Low cardiac output states
			Shock
			Hypovolemia
			Arrhythmias
			During suctioning
		Depletion of venous reservoir	Prolonged hypoxia

False Increase in SvO_2
- Wedging of catheter
- Improper PAC tip positioning
- Inaccurate calibration
- L to R shunting
- Sepsis
- Mitral regurgitation.

Uses

- Reflects cardiac output and cardiac index status (normal value indicates adequate tissue perfusion)
- Reflects O_2 delivery and consumption
- To calculate ***oxygen extraction ratio*** **(OER)**

$$= \frac{SaO_2 - SvO_2}{SaO_2} \text{ (Normal 24–28)}$$

- To determine optimum PEEP (that which increases SaO_2 without causing drop in SvO_2).

JUGULAR VENOUS OXIMETRY[1,3,5]

Introduction

- Provides information about balance between global cerebral O_2 delivery and metabolic demand
- For nonquantitative assessment of adequacy of cerebral blood flow
- Normal value 55–75%.

Principle

- $SjvO_2$ catheter:
  - Based on unique light absorption spectrum of Hb
  - Uses 2–3 wavelengths of light for ***Reflectance photospectrometry***
  - Light directed into blood by one optical fiber and reflected back to a photosensor
  - Sensor measures absorption of reflected light at various wavelengths
  - Final $SjvO_2$ displayed as percentage of oxyHb to total Hb
- Methods of monitoring:
  - Intermittent measurements with serial samples
  - Continuous monitoring with fiberoptic catheter.

Procedure

Two methods:

- Direct puncture:
  - Direct puncture of jugular bulb
  - 1 cm below and 1 cm anterior to mastoid process.
- Retrograde IJV catheterization:
  - IJV cannulation similar to Central venous cannulation procedure
  - Needle guidewire and catheter advanced in cephalad direction
  - J shaped guidewire to avoid injury to jugular bulb
  - Guidewire advanced only 2–3 cm beyond needle insertion
  - Position confirmed by lateral skull X-ray
  - Tip to be at level of and just medial to mastoid process.

Site of Insertion

- Bilateral brain injury: In IJV on side of dominant drainage (usually right)
- Focal brain injury: In IJV ipsilateral to side of brain injury.

Indications

- Head injury:
  - Provides early diagnosis of ischemia
  - Useful guide for hyperventilation therapy and fluid management
- Following SAH
- To diagnose cerebral vasospasm
- During AVM embolization (to determine adequacy of embolization)
- During aneurysmal surgery
- During cardiac surgery.

Interpretation

- **$SjvO_2$**:
  - Percentage saturation of oxyhemoglobin
    - *< 50%:* Pathological
    - *50–55%:* Critical
    - *55–75%:* Normal
    - *> 75%:* Hyperemic
- **$AjvDO_2$**:
  - Difference in O_2 content between arterial and jugular venous blood (SaO_2–$SjvO_2$)
    - 4–8 ml O_2/100 ml blood = > normal
    - < 4 ml O_2/100 ml blood = > O_2 supply > demand (excess)
    - > 8 ml O_2/100 ml blood = > O_2 demand > supply (ischemia).
- **OER**:
  - Oxygen extraction ratio
  - Normal 24–28 %
  - $\frac{SaO_2 - SjvO_2}{SaO_2}$
- **CEO_2**:
  - *Normal:* 24–40%
  - *Hyperemia:* < 24%
  - *Ischemia:* > 40%

Factors Affecting $SjvO_2$

- Factors causing fall in $SjvO_2$:
  - Fall in DO_2:
    - Hypocapnea

- Hypotension
- Vasospasm
- Hypoxia
- Anemia
- Hemorrhage
- Sepsis
- Cardiorespiratory insufficiency.

– Raise in VO_2:
- Raised BMR
- Seizures
- Shivering
- Pain
- Light anesthesia.

• Factors causing raised $SjvO_{2:}$
– Raise in DO_2:
- Hypercarbia
- Drug induced vasodilation
- Arterial HTN
- AV malformation

– Fall in VO_2:
- Coma
- Hypothermia
- Sedatives
- Cerebral infarcts
- Brain death.

Complications

• Infection
• Raised ICP
• Pneumothorax
• Arterial puncture
• Thrombosis.

Limitations

• Poor correlation of $SjvO_2$ with cerebral oximeter
• Extracerebral contamination with blood from scalp/meninges possible
• False low reading if catheter tip abuts vessel wall
• Not sensitive to focal ischemia–measure of global cerebral oxygenation
• Hemodilution can alter $SjvO_2$
• Side of cannulation unclear in focal brain injury: ipsilateral/contralateral
• Frequent calibration required.

Current Status

• Recommended in patients with head injury on hyperventilation therapy
• Benefits of $SjvO_2$ on long-term cerebral function yet to be proven
• ***Best monitor*** at present for continuous monitoring of cerebral oxygenation.

ANESTHESIA MACHINE CHECKLIST[1,2,3,4]

• AIMS
– To ensure that the machine delivers the set percentage of oxygen
– To rule out leaks in the system
– To rule out obstructions
– Called ***Cock Pit Drill.***

1993 FDA Recommendations

Check Emergency Ventilation Equipment

• Verify back-up ventilation equipment available and functioning.

Check High Pressure System

• Check O_2 cylinder supply:
– Cylinder should be shut off
– Check cylinder by color coding and label
– Ensure cylinder is connected to correct yoke
– Verify O_2 cylinder is at least half full, i.e. 1000 PSIG
– Open O_2 flow control valve, register flow of 4–5 l/min
– Open N_2O flow control valve and note that no flow
– Close flowmeter and note bobbins fall to zero
– Listen to O_2 pressure failure alarm if present.

• Check pipeline supply:
– Pipelines should be disconnected
– Pipeline pressure should be between 50–60 PSIG
– Check initial status of low pressure system (flow control knob to common gas outlet)
– Close flow control valve and turn vaporizer off
– Check fill level and tighten filler caps.

• Check O_2 pressure fail safe mechanism:
– Open N_2O cylinder, note pressure gauge shows any flow
– Open N_2O flowmeter should register no flow as O_2 line is not pressurized
– Open O_2 cylinder and register flow in both O_2 and N_2O flowmeters
– Close O_2 cylinder and note flowmeter bobbins fall to zero and O_2 fail safe alarm is activated
– Close both flow control valves.

Check Low Pressure System

- Check initial status:
  - Close flow control valves and turn off vaporizer
  - Check fill level of vaporizer and tighten filler caps.
- Perform *Leak test of machine low pressure system*:
  - Verify flow control valves are closed and master switch off
  - Attach suction bulb to common gas outlet
  - Squeeze bulb repeatedly till fully collapsed
  - Verify it stays collapsed for at least 10 seconds
  - Open vaporizer one at a time and repeat suction test
  - Remove suction bulb and reconnect breathing system.
- Test flowmeter:
  - Perform test flow of all gases through full range
  - Check smooth operation of floats
  - Check if proportionating device is working by creating hypoxic mixture and verifying correct changes in flow.

Check Breathing System

- Calibrate oxygen analyzer:
  - Turn on master switch and all monitors
  - Remove analyzer and calibrate to read 21% at room air
  - Verify low O_2 alarm is enabled and functioning
  - Connect to common gas outlet
  - Flush with 100% oxygen
  - Verify that it reads > 90%.
- Check initial status of breathing system:
  - Set selector switch to bag mode
  - Circuit should be complete, undamaged and unobstructed
  - Verify CO_2 absorbent is adequate
  - Install breathing circuit accessory equipment
    - Humidifier
    - Positive end respiratory pressure valve.
- Perform *Leak test of breathing system*:
  - Check integrity of inner and outer tube of Bains circuit
  - Set all gas flows to zero or minimum
  - Close APL valve and occlude Y piece
  - Pressurize breathing system to 30 cm H_2O with O_2 flush
  - Ensure pressure remains fixed for at least 10 seconds
  - Open APL valve, ensure pressure decreases.
- *Flow test*:
  - Checks integrity of unidirectional valves
  - Detects obstruction in circle system
  - Remove Y piece from circle system
  - Breathe through the two corrugated tubes individually
  - Valves should be present and move appropriately
  - Operator should be able to inhale but not exhale through inspiratory limb
  - Should be able to exhale but not inhale through expiratory limb.

Check Manual and Automatic Ventilation Systems

Test ventilation system and unidirectional valves:

- Place second breathing bag on Y piece
- Set appropriate ventilatory parameters for next patient
- Switch to ventilator mode
- Turn ventilator on
- Fill bellows and breathing bag with O_2 flush
- Set O_2 flows to minimum, other gas flows to zero
- Verify during inspiration that bellows deliver appropriate tidal volume
- Verify during expiration that bellows fill completely.
- Set gas flows at 5 L/min
- Verify bellows and simulated lungs fill and empty appropriately
- Check for proper action of unidirectional valves
- Exercise breathing circuit accessories and ensure proper function
- Turn ventilator to bag mode
- Ventilate manually and ensure inflation and deflation of artificial lungs
- Remove second breathing bag from Y piece.

Scavenging System

- Ensure proper connection between scavenging system, APL and ventilator relief valve
- Adjust waste gas vacuum (if possible)
- Fully open APL valve and occlude Y piece
- With minimal O_2 flow, allow scavenger bag to distend fully
- Verify absorber pressure gauge reads < 10 cm H_2O.

Monitors

- Check, calibrate and set alarm limits of all monitors:
  - Pulse oximeter
  - Capnometer
  - Oxygen anlayzer
  - Respiratory volume monitor (spirometer)

  - Pressure monitor with high and low airway pressure alarm.
- Others:
  - Laryngoscope
  - Blades
  - Ambu bag
  - Suction
  - Airways, masks
  - Other accessories for intubation.

Final Positon: Check Final Status of Machine

- Vaporizers off
- APL valve open
- Selector switch to bag
- All flowmeters to zero/minimum
- Suction level adequate
- Breathing system ready to use.

Work Station Self-tests

- Present in many new anesthesia machines
- Comprehensiveness of these tests varies from model to another
- Checks for functioning of:
  - Electronic components
  - Mechanical components
  - Pneumatic components.
- Tested components are:
  - Gas supply system
  - Flow control valve
  - Circle system
  - Ventilator
  - Integrated vaporizers.

Modifications in Boyle Mark IIIs

Gross

- Extra shelf on top of machine
- Bigger size and facility for extracylinder.

Circuits

- Simple lever movement changes open and close circuits
- Change of circuits at platform level
- Connections for jet ventilator
  - With preset valve pressure reduced to 60 PSIG
  - In older machines: 15–20 PSIG.

Vaporizers

- Space present for another vaporizer
- No trilene lock.

Flowmeters

- O_2 is made downstream
- O_2 flow control valve is touch and color coded
- *Master and slave regulator system, Link 25 system*
- Emergency O_2 button type
- Pressure gauge for N_2O
- Only 2 flow tubes with the flow:
  - Boyle mark IIIs: O_2 8 L and N_2O 12 L
  - Others: O_2 5 L and N_2O 10 L.

SAFETY FEATURES OF ANESTHESIA MACHINE[1,2,3,4]

AIMS

- Aims at avoiding:
  - Delivery of hypoxic mixtures
  - Delivery of excessive anesthetic concentrations
  - Development of excessive machine pressures
  - Administration of wrong agent
  - ***Tipping***: High concentrating of volatile anesthetics delivered
  - ***Overfilling:*** High, sometimes lethal concentrations delivered.

SAFETY FEATURES

- **To the OT personnel:**
  - Antistatic rubber in anesthesia machine tubing, wheels and reservoir bags
  - Prevents generation of static electricity which can lead to fires.
- **To the patient:**
  - To prevent delivery of hypoxic mixtures:
    - Before flow control valves:
      - Pipelines
        - Non interchangeable quick couplers
        - Flexible pipelines
        - Color coding
        - ***Diameter index safety system (DISS)***
      - Cylinders
        - Color coding
        - Cracking of cylinders
        - ***Pin index safety system (PISS)***
      - Master switch
        - All alarms activated on turning on switch
  - Pressure regulators
  - Oxygen pressure failure safety devices
    - Pressure sensor shutoff valve
    - Gas loaded regulator.

- At flow control valve level:
  - Oxygen ratio control devices
    - Oxygen ratio monitor
    - Oxygen ratio monitor
    - ***Link 25 system***
- Beyond flow control valves:
  - Flowmeter:
    - Touch and color coded knobs
    - Calibration
    - Flowmeter sequence
      - Oxygen analyzer
      - Vaporizer: Use of only one vaporizer.

- **To prevent delivery of excess anesthetic:**
  - Vaporizers constructed with back flow compensation
  - Locking device: Prevents use of more than 1 vaporizer simultaneously
  - Back flow check valve to prevent pumping effect
  - Trilene interlock (in older machines)
    - Prevents use of trilene vaporizer and closed circuit at same time
    - This prevents phosgene formation.
- **To prevent excess pressure on machine:**
  - Reservoir bag
  - Adjustable pressure limiting (APL) valve
  - Pressure relief valve before common gas outlet
  - Pressure relief valve after pressure regulator.

TO PREVENT DELIVERY OF HYPOXIC MIXTURE

Before Flow Control Valves: Pipelines

- Noninterchangeable quick couplers:
  - To tap gases at wall outlets
  - Each coupler contains pair of nonthreading, gas specific, male and female component
  - Insertion into incorrect outlet prevented by using different shapes, space/combination of both for mating portions
  - Wall outlet and connector should be from same manufacturer.
- ***Diameter index safety system (DISS):***
  - Developed to provide noninterchangeable connections for pipelines
  - Consists of a body, nipple and nut combination
  - There are two concentric and specific shoulders on the nipple
  - Small bore mates small shoulder
  - Large bore mates large shoulder
  - Diameter of each port varies for specific gases
  - Color coding of outlets, noses and couplers are additional features
  - *Not followed in India.*

Cylinders

- **Color coding:**
  - Different color of cylinders to help identify gas
  - Top and shoulder of each cylinder painted with color assigned to the contained gas
  - Coding also used on pipelines, connectors, knobs and gauges.

Gas	Color[4]
Oxygen	Black with white shoulder
Nitrous oxide	Blue
Nitrogen	Grey
Air	Grey body, white and black shoulder
Cyclopropane	Orange
Ethylene	Red
O_2-CO_2 (CO_2 > 7.5%)	Predominant green
O_2-CO_2 (CO_2 < 75)	Predominant green, rest grey
O_2- He (He < 80.5%)	Predominant brown
O_2- He (He > 80.5%)	Predominant brown, rest green
Entonox (N_2O 7.5%, O_2 52.5%)	Blue body, white shoulder

- **Cracking of cylinders:**
  - Cylinder valve to be opened slightly for a moment to clear outlet of dust which might enter the regulator
  - Also helps to know if cylinder is full/empty
  - Outlet to be painted away from operator and other personnel
  - Performed before attaching cylinder to yoke.
- ***Pin index safety system***:

  Introduction
  - Consists of holes on cylinder valves positioned in an arc below the outlet port
  - Pins on yoke/pressure regulator positioned to fit into these holes.

  Uses
  - Prevents connection of wrong gas cylinder to machine
  - Used in small cylinders (E type) to fit directly to machines.

  Components
  - Contains two pins projecting from inner surface of yoke

- Two corresponding holes present in cylinder valve
- Seven hole locations present
- Holes are on circumference of a circle of 9/16 inch radius, centered in the port
- Two pins are assigned to each gas, one on either side of midline
- Pin are 4 mm in diameter and 6 mm long
- Except pin 7 which is slightly thicker.

Disadvantages

- Problems arise when special gas mixtures used
- For example, 5% CO_2 mixture with O_2 has different pin index from 100% CO_2
- CO_2 mixtures of 7% or greater would be fitted with pin index for 100% CO_2.

Gas[4]	Piss score
Air	1–5
O_2	2–5
N_2O	3–5
O_2- CO_2 (CO_2 > 7.5%)	1–6
O_2- CO_2 (CO_2 < 7.5%)	2–6
O_2-He (He > 80.5%)	4–6
O_2-He (He < 80.5%)	2–4
Cyclopropane	3–6
Ethylene	1–3
Nitrogen	1–4
Entonox (N_2O 7.5%, O_2 52.5%)	7

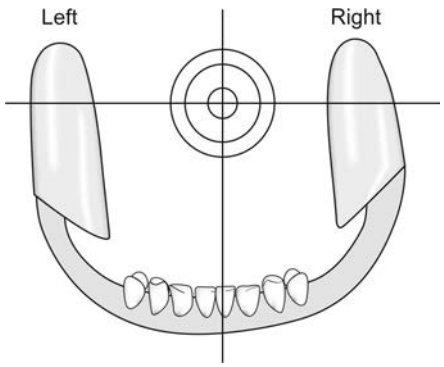


Fig. 6.32: Pin index safety system[4]

- **Master switch:**
  - Turning on master switch causes both pneumatic and electric functions to be activated
  - All alarms and safety devices automatically activated before machine can be used
  - There should be batteries for backup should main power fail.
- Pressure regulators:
  - Reduces pressure and keeps it constant till the end
  - Prevents damage to flowmeters, vaporizers and ventilators.
- Oxygen pressure fail safe precautions:
  - Prevents delivery of 100% anesthetic when O_2 depletion goes unnoticed:
    - Cuts off supply of gases other than O_2
    - Gives audible/visible alarms.
  - Shuts off/proportionately reduces supply of N_2O and other gases
  - Activated when O_2 pressure falls below critical level
  - These devices are:
    - Pressure sensor shut off valve: interrupts N_2O supply if O_2 pressure falls below threshold
    - Gas loaded regulator:
      - Where O_2 pressure regulator (primary regulator) controls secondary/slave regulators in N_2O line
      - If primary regulator fails, slave valve ensures only O_2 is delivered.

At Flow Control Valves: Proportionating Systems

- Oxygen ratio monitor (ORM)
  - Present in Drager machines
  - Contains linear resistors inserted between O_2 and N_2O flow control valves
  - Pressure drop across resistors monitored
  - These are transmitted via pilot line to an arrangement of opposing diaphragms
  - Diaphragms are linked together with a capacity of closing a leaf spring contact
  - Alarm activated if O_2% drops in a mixture of O_2 and N_2O below predetermined level
  - Drawbacks:
    - Gives alarm but does not control gas flow
    - No alarm activated when piping system contains gas other than O_2.
- Oxygen ratio monitor controller (ORMC)
  - Present in Drager machine
  - Design same as ORM
  - Salve regulator additionally present
  - This is controlled by a mechanism of opposing diaphragms which controls N_2O delivery pressure to N_2O control valve and thus N_2O flow
  - Monitors ratio of O_2 flow and gives alarm when it falls < 30%

- Also reduces N_2O flow proportionally to maintain ratio
- Disadvantages:
  - Operator cannot override function of device when desired
  - Limits N_2O flow when O_2 falls only, unlike Link 25 also increases O_2 flow as N_2O flow is increased.

- ***Link 25 control***

Introduction

- *Hypoxic safe guard/proportionating system* which links N_2O flow control valve to O_2 flow control valve in order to maintain a minimum O_2 concentration of 25%.

Mechanism

- Present in Ohmeda and Boyle Ultima machines
- There is mechanical integration of N_2O and O_2 flow control valves
- Integration allows independent adjustment of either valve to maintain minimum O_2 concentration of 25%
- N_2O has a gear with 14 teeth fixed to the spindle
- O_2 has a gear with 29 teeth which is mounted on O_2 spindle which threads so that it can float over the spindle
- For every 2.07 rotation of N_2O spindle, O_2 gear will rotate once
- N_2O gear will engage O_2 spindle only when proportion of N_2O in mixture exceeds 75%
- Thread mounting of O_2 gear is such that it allows independent rotation of O_2 flow control valve
- Flows in flowmeter are linked to rotation by regulating supply pressure of gases with secondary regulators situated just before flowmeters, i.e. N_2O is supplied at 26 PSIG and O_2 at 14 PSIG
- Ratio of O_2 to N_2O flow can never be < 1:3
- When N_2O flow valve is turned through two revolutions/28 teeth, O_2 flow valve revolves once due to 2:1 gear ratio
- The final 3:1 flow ratio is because N_2O is supplied at 26 PSIG and O_2 is supplied at 14 PSIG
- Thus, combination of mechanical and pneumatic aspects of system yields final O_2 concentration.

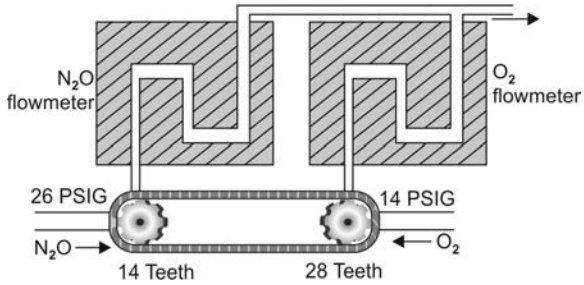


Fig. 6.33: Link 25 system[4]

Advantages

- Prevents administration of FGF with $FiO_2 < 0.25$
- N_2O flow automatically lowered when O_2 flow decreased too much.

Disadvantages

- 97% N_2O concentration can be delivered if chain is cut/broken
- Ratio of N_2O:O_2 other than 3:1 occurs if regulators are not precise
- Malfunctioning of spindle and gear if not properly aligned
- Malfunctioning possible if threads in spindle undergo wear and tear
- Leaks downstream like a broken O_2 flow tube can cause delivery of hypoxic mixture
- Device links only N_2O and O_2. So if third gas like air is induced in flowmeter assembly, there is no assurance of 25% O_2 delivery in the mixture
- When using air and desflurane, it is possible to deliver < 21% O_2
- Does not detect if correct gas is actually flowing through its flowmeters (whether gas is actually flowing in flowmeter is really O_2).

Beyond Flow Control Valves

- **Flowmeters and control knobs:**
  - Touch and color coded knobs
    - O_2: White, fluted, larger and more projected
    - N_2O: Blue, not fluted and smaller
    - Bar placed in front of knobs in some machines to prevent alteration in setting
    - Float has radiolucent material, so it can be seen in dark
    - Glass behind flowmeter bank is radiolucent
    - Use flowmeters only to calibration: Not possible to give less than calculated flows
    - Flowmeter sequence:
      - O_2 flowmeter always downstream

    - If O_2 is upstream and leak occurs through the flowmeter not in use:
        - O_2 escapes through leak
        - N_2O is directed towards common gas outlet
        - This leads to delivery of hypoxic mixture.
- Oxygen analyzer:
  - ***Only*** safety device which detects hypoxic mixture delivery
  - Measures O_2 % using fuel cell/by polarographic method
  - Calibration done daily at room air to read 21%.

FEATURES TO PREVENT EXCESS ANESTHETIC

- Back flow check valve at common gas outlet to prevent pumping effect
- Vaporizers constructed with back flow compensation
- Use of only one vaporizer at a time with locking device- ensures that only one vaporizer turned on at a time
- ***Keyed Index Safety System (KISS)*** to prevent filling of vaporizer different agent
- Trilene interlock as reaction of trilene and sodalime in closed circuit forms phosgene.

FEATURES TO PREVENT EXCESS PRESSURE

- Safety blow off valves downstream of regulator to allow escape of gas if by accident, the regulators fail and allow high output pressures
- Pressure relief valve fitted to protect back bar which opens at 3–5 PSIG
- Barotrauma may occur if gases are flowing but breathing circuit is obstructed
- Whole back bar would be subjected to pressure of 60 PSIG and patient may be exposed to that pressure
- APL which opens at > 60 cm H_2O
- Reservoir bag: Made of compliant material but gives way when pressure > 50 cm H_2O.

LEAK TEST[1,4]

Introduction

- Checks integrity of machine from flow control valve to common gas outlet
- Evaluates machine which is downstream of all safety devices, except O_2 analyzer.

Sites of Leaks

- Flow tube cracks/breaks
- Interface between flow tubes and manifold
- O ring junction between vaporizer and its manifold
- Loose filler caps on vaporizers.

Complications of Leaks

- Hypoxia
- Patient awareness.

Types of Leak Tests

- Oxygen flush test
- Common gas outlet occlusion test
- Traditional positive pressure leak test
- North American Drager positive pressure leak test
- Ohmeda 8000 interval positive pressure leak test
- Ohmeda negative pressure leak test
- 1993 FDA Universal negative pressure leak test.

Prerequisites

- To be done daily/whenever vaporizer is changed
- Should be performed with machine switched off as minimum mandatory flow may reduce ability to detect small leaks
- Test repeated with each vaporizer turned on
- If this is not done, leaks associated with vaporizer or its mounting may not be found.

Negative Pressure Leak Test

- Also called ***Universal leak test***
- Used for machines with check valves but also for those without valves
- Uses suction bulb attached to a tubing with 15 mm adaptor
- Suction bulb is fitted to the common gas outlet
- When leak is present in circuit, room air is entrained through the leak and suction bulb inflates
- In the absence of leak, suction bulb remains deflated
- Many newer machines not compatible with universal leak test.

Procedure

- Verify flow control valve and master switch is off
- Attach suction bulb to common gas outlet
- Squeeze bulb repeatedly till fully collapsed
- Verify bulb stays collapsed for at least 10 sec
- Open vaporizer one at a time and repeat suction test
- Remove suction bulb and connect breathing system.

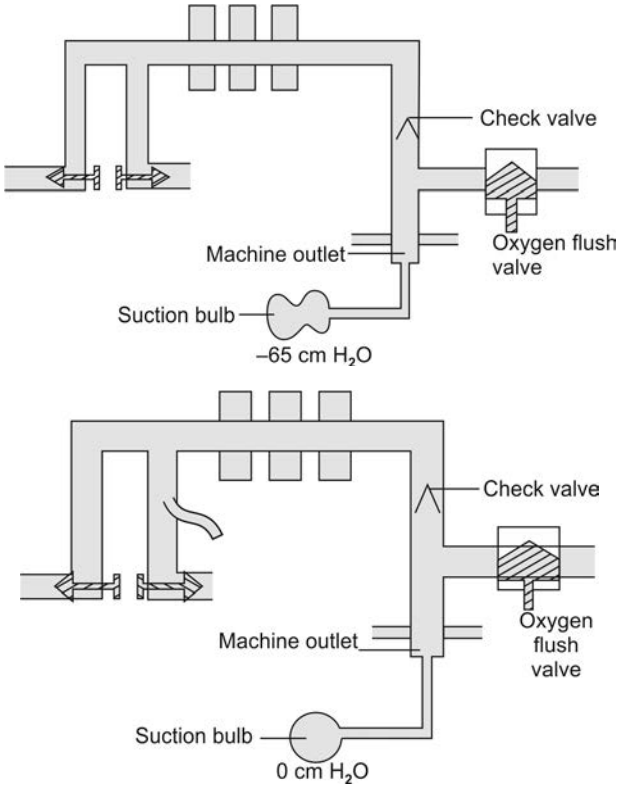


Fig. 6.34: Universal leak test[4]

Positive Pressure Leak Test

- Used for machines without an outlet check valve
- Detection of leak by pressurizing breathing circuit with O_2 flush valve.

Disadvantages

- Dangerous if used in Ohmeda machines with check valves
- Inappropriate evaluation if leaking flush valve is present
- Positive pressure from breathing circuit results in closure of outlet check valve
- Valve on airway pressure gauge fails to decline
- System appears tight with the test but only circuit downstream of check valve is leak free
- Thus, vulnerable area exists from check valve back to flow control valves which is not tested by positive pressure test.

Types of Positive Pressure Leak Test

- Pressure gauge test:
  - Pressure gauge attached to common gas outlet (CGO)
  - Flow control valve slowly opened till pressure on gauge reaches 30 cm H_2O (22 mm Hg)

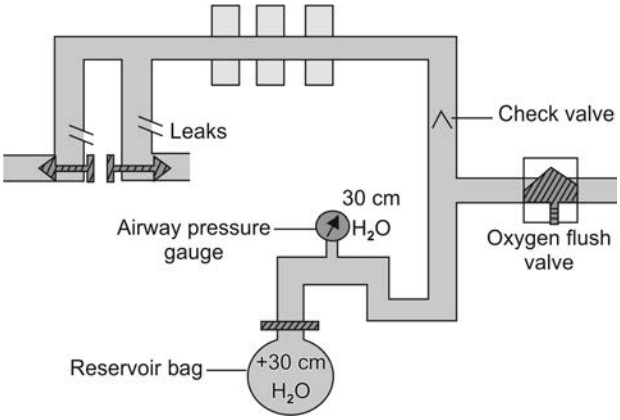


Fig. 6.35: Positive pressure leak test[4]

  - Flow is lowered till that pressure is steady
  - Flow rate then is equal to leak rate in machine
  - Leak rate should be ≤ 50 ml/min
  - Cannot be performed if minimum mandatory flow present as this is around 200 ml/min.
- Fresh gas line occlusion test:
  - Flow of 50 ml/min set on flowmeter
  - Fresh gas line is kinked
  - Indicator on flowmeter should more downwards
  - Can be used during case
  - Cannot be used if minimum mandatory flow present.

Combination Breathing System and Machine Leak Tests

Retrograde Fill Test

Procedure

- APL valve closed, patient port closed
- Master switch turned on
- O_2 flush used to fill reservoir bag
- As pressure on manometer rises, flow on flowmeter adjusted to maintain 30 cm H_2O pressure in breathing system
- Flow to maintain steady flow should be < 350 ml/min.

Advantages

- Checks breathing system and low pressure parts of machines
- Can be performed quickly
- Allows continuous airway pressure alarms to be checked.

Disadvantages

- Insensitive to small leaks
- Does not localize leak.

Squeeze Bulb Test

- Master switch and flow control valves switched off
- Occlude Y piece and close APL valve
- Suction bulb with 22 mm connector attached to reservoir bag mount
- Bulb squeezed till breathing system pressure gauge is > 50 cm H_2O
- If drop in pressure from 50 to 30 cm H_2O takes > 30 sec, leak rate is acceptable.

In Use Test

- During machine use, leak can be quantified
- Lower fresh gas flows to as low as possible
- If ventilator bellows/reservoir bag continues to fill, leak rate is less than fresh gas flow.

Identifying Site of Leak

- Systematic check of machine/breathing system
- Follow route of gas travel
- Apply alcohol on hands and move hands over components.

OXYGEN FAILURE DEVICES[1,3,4]

Introduction

On delivery of hypoxic mixture Oxygen Failure Devices:

- Cuts off supply of gases other than O_2
- Gives an audible/visible alarm when O_2 pressure falls to a dangerous level.

Types

- Oxygen failure safety device (OFSD)
- Oxygen failure alarm.

Oxygen Failure Safety Devices

Introduction

Safety devices which shuts off/proportionately reduces and ultimately stops supply of N_2O and other gases if O_2 supply pressure decreases.

Mechanism

- Machine designed such that when O_2 supply pressure is reduced below normal, set O_2 concentration at common gas outlet does not fall below 19%
- Incorporated at level of pressure regulator
- O_2 pressure regulator works as primary regulator
- Output from this regulator controls secondary regulator located in N_2O line
- If O_2 pressure falls, N_2O flow will be automatically stopped
- O_2 failure safety valve closes the line at pressure between 15 and 30 PSIG.

Types

- In Ohmeda machine:
  - N_2O regulator totally out off when O_2 pressure falls below critical level (20–25 PSIG)
- In Drager Narcomed:
  - N_2O outlet pressure falls proportionate to fall is O_2 pressure
  - But further decrease in O_2 pressure causes N_2O to fall and finally stop.

Example

- When O_2 pressure is normal, diaphragm and stem pushed downwards, opening the valve
- The anesthetic gas flows is at A, around the stem and out at C
- When pressure falls, stem move upwards, closing the valve
- Middle chamber is vented to atmosphere to prevent mixing of anesthetic gas and O_2 if diaphragm ruptures or packing leaks.

Checking OFSD

- Flows of O_2 and other gas (usually N_2O) are turned on
- Source of O_2 pressure is then removed
- Fall is O_2 pressure noted on cylinder/pipeline pressure gauge
- If OFSD is functioning properly, flowmeter for other gas will fall to bottom of tube just before O_2 indicator falls to bottom of its tube.

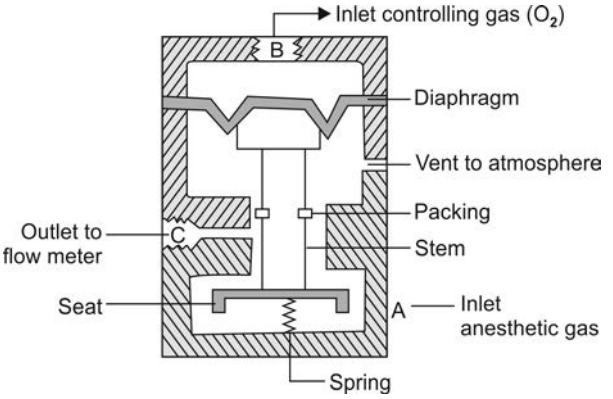


Fig. 6.36: Oxygen failure safety device

Oxygen Failure Alarms

Introduction

When O_2 pressure falls below 30 PSIG, at least a medium priority alarm to be enunciated within 5 seconds and it shall not be possible to disable this alarm.

Mechanism

- Pressurized canister is filled with O_2 during normal use
- When O_2 pressure falls, O_2 flows out from this canister through a whistle giving an audible alarm of 60 dB for 7 to 10 seconds
- End of whistle does not mean low pressure conditioner has been activated.

Limitations

- Can permit hypoxic mixtures if:
  - Crossover in pipeline system cylinder with wrong gas
  - Accidentally closed/partially closed O_2 flow control
  - *Low O_2 flow:* Depleted cylinder/disconnected pipeline
- Does not offer total protection against hypoxic mixture as it does not prevent anesthetic gas from flowing if there is no O_2 flow
- Equipment problems like leaks/operator errors are not prevented.

OXYGEN FLUSH VALVE[1,3,4]

Introduction

Receives O_2 from pipeline inlet/cylinder and directs it to common gas outlet at high unmetered flows.

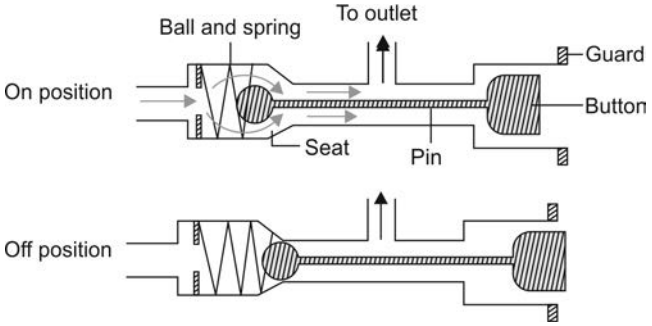


Fig. 6.37: Oxygen flush valve[4]

Mechanisms

- Flow rates will be 35–75 L /min
- Only O_2 flushed through this valve
- Consists of button and stem connected to a ball which is in contact with seat
- When button is depressed ball is forced away from seat and O_2 flows to common gas outlet
- Spring forces ball to close seat when button is not pressed
- Activation of flush may produce positive/negative pressure in machine which can be transmitted back to flowmeter and vaporizer, causing reading to change.

Hazards

- *Barotrauma:* Due to use during inspiration delivered by anesthesia ventilator
- *Internal leakage:*
  - O_2 enriched mixture delivery
  - Dilution of anesthetics in low flow (closed circuit)
- *Sticking of flush valve:* Obstruction of O_2 flow and anesthetic gas
- *Accidental activation:* Prevented by placing it in a collar.

LOW FLOW ANESTHESIA[1,2,3,4]

Definition

- Technique which uses fresh gas flows less than minute ventilation
- Technique in which at least 50% expired gases have been returned to lung after CO_2 absorption
- For most practical considerations FGF of 2 L/min is called low flow anesthesia.

BAKERS CLASSIFICATION

- *Metabolic flow:* 250 ml/min
- *Minimal flow:* 250–500 ml/min
- *Low flow:* 500–1000 ml/min
- *Medium flow:* 1–2 L/min.

Equipment

- Circuit with CO_2 absorber to reutilize expired gases required
- Two circuits commonly used are:
  - To and fro circuit by ***Walters***
  - Closed circuit by ***Brain Sword***
- To and Fro Circuit:
  - Consists of a single channel for inspiration and expiration
  - Advantages:
    - Simple and requires minimum breathing components
    - Resistance to spontaneous breathing is minimal
    - Easy to clean and sterilize.

– Disadvantages:
  - Cumbersome and heavy near patients head end
  - Difficult to manage, especially the CO_2 absorber
  - Possibility of inhaling soda time dust
  - Increase in dead space of apparatus as soda lime is exhausted.

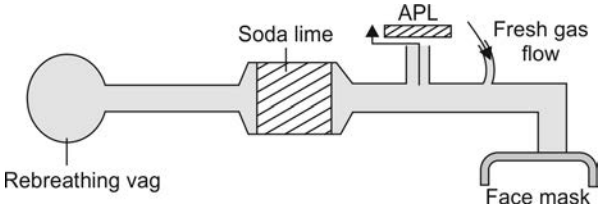


Fig. 6.38: To and fro circuit[4]

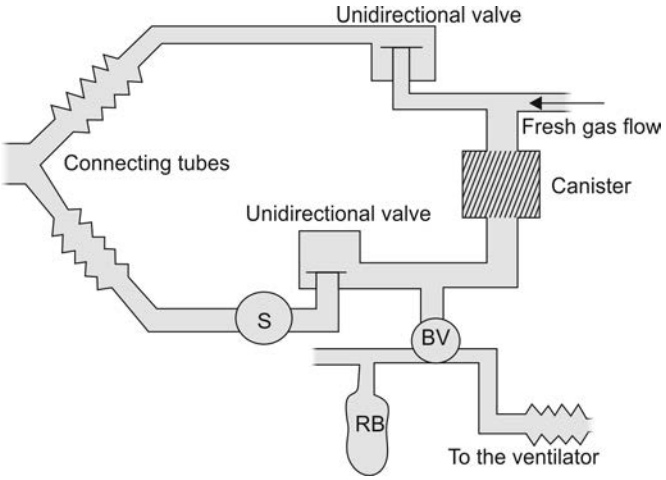


Fig. 6.39: Closed circuit[4]

Monitoring

- Inspired O_2 analyzer (when N_2O is being used)
- Monitoring of end tidal anesthtic concentration by:
  – Mass spectrometry
  – *Raman spectrometry*
  – *Riken gas indicator*
  – Photo acoustic surface absorption
  – Infrared absorption.

Techniques of Low Flow Anesthesia

Loading

- Use of high flows for a short time
- 10 L/min flows with up to 2 MAC concentration
- At the end of 3 minutes/3 time constants circuit is brought to the desired concentration
- Commonest and most effective technique
- Disadvantages of high flows and OT pollution.

Prefilled Circuit[4]

- Use of 2 circuits
- Magills circuit used for preoxygenation
- Circle is fitted with test lung and entire circuit filled with gas mixture of desired concentration
- Following intubation circuit is connected to patient.

Using Large Dose of Anesthetics[4]

- Fresh gas flow started with metabolic flow of O_2 and large amount of N_2O (3–5 L/min)
- O_2 concentration which falls is continuously monitored and N_2O flow reduced once desired O_2 concentration is achieved (33–40%)
- Seldom used as increased chances of hypoxia
- Setting in vaporizer brought to 0.5–0.8% after 10 min.

Injection Technique[4]

- Extremely reliable method
- Injection of agent directly into circuit
- 1 ml halothane gives 226 ml vapor at 20 °C
- 1 ml isoflurane gives 196 ml vapor at 20 °C
- Around 2 ml agent injected in graded aliquots into circuit
- Injection through self sealing rubber diaphragm covering one limb of metal T piece into either inspiratory/expiratory limb
- Wire mesh/gauze piece inside T-piece helps in vaporization of the liquid.

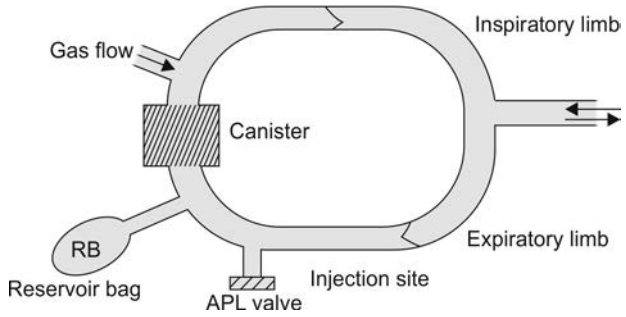


Fig. 6.40: Injection technique of low flow anesthesia[4]

Maintenance of Low Flow Anesthesia[4]

Gothenburg Technique

- Initially high flows:
  – O_2 1.5 L/min and N_2O 3.5 L/min for 6 min after induction
  – Called *loading phase.*
- Followed by O_2 4 ml/kg/min
- N_2O adjusted to maintain O_2 concentration around 40% in circuit

- This is detected by O_2 analyzer which is thus very important
- In the absence of O_2 analyzer:
  - Use 10 L/min for 3 minutes
  - Followed by 400 ml/min O_2 and 600 ml/min N_2O for 20 mins
  - 500 ml O_2 and 500 ml N_2O thereafter
  - This maintains O_2 concentration between 33–40% at all times.

Injection Methods of Kennedy and Lowe

For halothane in a 50 kg patient:
- 0–5 min : 27 ml /hr
- 5–30 min : 5.5 ml/hr
- 30–60 min : 3.5 ml/hr
- 60–120 min : 2.5 ml/hr

Termination of Low Flow Anesthesia

High Flows

- At the end of surgery, open circuit
- Use high flows and let out agent
- Causes wastage of gas and OT pollution.

Activated Charcoal

- Activated charcoal heated to 220 °C adsorbs volatile anesthetics
- Charcoal containing canister with a bypass placed in circuit at the end of surgery
- Gas is directed through this canister.

Advantages of Low Flow Anesthesia

- Economical
- Humidified gases are provided
- Maintains body temperature in long surgeries
- Less OT pollution.

Disadvantages of Low Flow Anesthesia

- Accurate adjustment of fresh gas flows required
- Accumulation of trace gases
- Oxygen analyzer required
- Expired gas mixture analysis
- Risk of hypoxia if leaks/O_2 supply failure.

Precautions

- Leaks should be sought during maintenance phase
- Most gas monitors sample gas at rate of 200 ml/min which may be more than half fresh gas flow
- Thus sample to be returned back to the circuit to maximize FGF utilization.

Factors Affecting Low Flow Anesthesia

During Initiation

- Factors governing inhaled tension of anesthetic:
  - Volume of circle system (usually 6–7 L)
  - FRC of lung to be denitrogenated (around 3 L)
  - Diffusion of anesthetic through rubber tubes.
- Factors responsible for increase in alveolar tension of volatile anesthetics::
  - Concentration effect
  - Minute ventilation.
- Factors responsible for uptake from lungs
  - Blood solubility of volatile agents (Blood-Gas Partition Coefficient)
  - Cardiac output
  - Alveolar-venous partial pressure gradient.

During Maintenance

- Delivery of hypoxic mixture
- Steady alveolar anesthetic concentration to be maintained
- Two theories to explain volatile anesthetic uptake:
  - Exponential theory by ***Lowe***
  - Linear theory by ***C.Y Lin***

STERILIZATION AND DISINFECTION[1,2,3,4]

Definition

- *Sterilization:* Process capable of removing/destroying all viable forms of microbial life, including bacterial spores, to an acceptable sterility assurance level (usually 10^{-6} implying that possibility of microorganism surviving on item is less than 1 in 1,000,000 or 1×10^{-6})
- *Disinfection:* Process capable of destroying most microorganisms but as ordinarily used, not bacterial spores.

Levels of Disinfection

Centre for Disease Control
- High Level:
  - Kills all organisms
  - Except spores and species such as *Creutzfeldt - Jakob* Disease
  - Most high level disinfectants produce sterilization with sufficient contact time.
- Intermediate level:
  - Kills vegetative bacteria; mycobacterium tuberculosis, fungi and viruses
  - Does not kill spores.

- Low level:
  - Kills most vegetative bacteria but not mycobacterium TB
  - Kills some fungi and viruses, but not spores.

Methods of Sterilization

- Physical Methods
  - Moist Heat:
    - *Around 100 C:*
      - Boiling (100 °C for 15 min)
      - Tyndallization.
    - *Below 100 C:* Pasteurization, low pressure autoclaving
    - *Above 100 C:* autoclaving.
  - Dry heat:
    - Hot air oven
    - Flames.

Organisms[1,3,4]		Germicidal level	
Bacterial spores • B. subtilis • Cl. sporogenes	High level D1		
Mycobacteria • M. bovis • M. tuberculosis		Intermediate	
Nonlipid/small viruses • Polio virus • Rhino virus		Level D1	Low level
Fungi • Cryptococcus • Candida Vegetative bacteria • Pseudomonas • Salmonella Lipid of medium sized viruses • Herpes simplex • Hepatitis B, HIV			disinfection

- Chemical Methods
  - Glutaraldehyde
  - Orthophthaldehyde
  - Quaternary Ammonium compounds
  - Phenolic compounds
  - Alcohols
  - Chlorhexidene
  - Iodine
  - Chlorine compounds
  - Hydrogen peroxide
  - Formaldehyde
  - Ozone
  - Peracetic acid.
- Gas Sterilization
  - Ethylene oxide
  - Propylene oxide.
- Radiation
  - Gamma rays
  - Ultraviolet rays.
- Filteration.

CLEANING

Introduction: First and most important step in decontamination.

Method

- Prevent drying of blood/body fluids as devices
- Enzymatic foam sprays breakdown proteins and blood
- Stainless steel and other metals are not soaked in saline/sodium hypochlorite to prevent erosion
- Item is soaked in water and enzyme pre-soak, with or without detergent for ≥ 3 mins
- Consult manufacturer instructors for each device.

Steps

- Remove tape and adhesive residue with solvent
- Disassemble and water rinse with water temperature ≤ 45 °C for 15 mins
- Thoroughly scrub with attention to corners, crevices and lumens
  - Immersible devices cleaned under water to prevent aerosolization of microorganisms
  - Nonimmersible items cleaned with cloth soaked in detergent
  - Cleaning accomplished by:
    - Manually
    - Washer-sterilizer
    - Ultrasonic cleaner.
- Rinsing to remove soil/residual detergent
- Dry thoroughly as:
  - Humid environment increases growth of microorganisms
  - Water on item may dilute chemical agent
  - Ethylene oxide may form ethylene glycol with water which is toxic
  - Towel/air dried.
- Inspect for cleanliness and functionality.

Area for Cleaning

- Designated location
- Separate from other parts of facility
- Entry only for authorized personnel

- Away from traffic, patients and clean storage
- Floor, wall, ceiling and work surface made of nonporous materials
- Air pressure to be negative relative to surrounding space
- This prevents air flowing out of space
- Minimum of 6–10 total air exchanges per hour with 100% fresh air
- Air to be exhausted outside without recirculation.

PASTEURIZATION[1,4]

Introduction

- Equipment immersed in water at elevated temperature (but < 100 °C) for a specific time
- ***Tyndallization***: Steaming of object at around 100 °C for 30 mins on consecutive days, only for heat sensitive culture media.

Techniques:

- 70 °C for 30 minutes
- 80 °C for 40 minutes
- ***Holder method***: 60°C for 30 mins
- ***Flash*** modification: 71.1°C for 15 seconds.

Mechanism of Action

- Moisture increases cellular permeability
- Heating coagulates proteins.

Applications

- Breathing tubes, reservoir bags
- ETT, face mask, airway
- Laryngoscope blade, stylet, bite-blocks
- Elbows, adaptors, Y- connectors
- Ventilator bellows.

Advantages

- Low temperature is less damaging to equipment
- No toxic fumes/residues
- Simple, inexpensive, reliable.

Disadvantages

- Treated equipment is wet
- Should be dried and packaged
- May get recontaminated during packing
- Heat may damage some materials.

AUTOCLAVING[1,4]

Introduction: Utilizes saturated steam under pressure for sterilization.

Principle

- At sea level, water at 100 °C
- When boiled in closed vessel and higher pressure, temperature at which it boils and that of the steam it forms, exceeds 100 °C
- Increase in temperature depends on pressure within chamber
- Steams transfers heat to materials rapidly, on contact
- Moisture increases all permeability
- Heating coagulates proteins.

Techniques

- 121°C for 15 mins
- 126°C for 10 mins
- 134°C for 3–5 mins at 32 PSIG pressure
- 150°C for few seconds
- *Flash sterilization*:
  - Items steam sterilized for immediate use
  - Usually items sterilized unwrapped.
- Design: Parts of autoclave machine:
- Chamber/Pressure vessel:
  - Items to be sterilized placed here
  - Can withstand high pressure
  - Safety valve prevents excess pressure.
- Jacket:
  - Portion surrounding chamber
  - Maintains temperature of chamber.
- Doors:
  - 1 or 2 doors
  - Hinged/sliding.
- Shelf:
  - Items placed on shelf in chamber
  - Door closed and secured.

Functioning: Phases of autoclaving:

- Conditioning/heatup phase:
  - Air displaced from chamber
  - Incoming steam displaces air through port/drain at bottom of chamber
  - Chamber drain remains open till temperature in drain is same as temperature of steam entering chamber
  - This indicates that air has been removed.
- Sterilization/exposure phase:
  - Steam enters load to be sterilized and gives up latent heat
  - Sterilization time at intended temperature is set
  - Lowest temperature in sterilizer is 121°C
  - Cycles may be programmed at 134°C and 145°C
  - Wrapped items sterilized for 30 mins at 121°C
  - Unwrapped items for 20 mins at 121°C

- Post-exposure/exhaust phase:
  - Items dried before being removed
  - Chamber exhausted to atmosphere
  - Filtered air circulated through chamber or deep vacuum is created within chamber.

Monitors of Autoclaving

- Mechanical indicators
  - Indicates and records time, temperature and pressure
- Biological indicators:
  - Standardized preparation of *Basillus subtilis*
  - Spores packed in strips/ampules
  - Placed in most difficult to sterilize location in load
  - Exposed to sterilization, retrieved, incubated and examined for growth
  - Rapid detection system gives fluroscence when it is exposed to UV light.
- Chemcial indicators:
  - 5 classes of chemical indicators
  - Higher classes are more sensitive
    - Internal and External indicators
      - Indicates that item has been exposed to sterilization, e.g. autoclave tape/signaloc tape
      - Exhibit color change from white to black.
    - ***Bowie Dick vacuum test***
      - Only assesses vacuum pump efficiency
    - Single parameter indicator
      - Test tube containing a chemical
      - Chemical melts on exposure to correct combination of sterilization parameters.
    - Respond to one or more sterilization parameters
      - Contains ink which changes color on exposure to correct combination of sterilization parameters.
    - Integrating indicators/integrators
      - Responds to all parameters of sterilization over a specified range of temperature.

Sources of Error

- Problems with steam:
  - Steam quality/saturation = Percentage of liquid in steam
  - Steam quality to be ≥ 97% (< 3% liquid water)
  - Low pressure:
    - Implies steam will be super heated
    - Steam is less able to transfer heat energy
  - High pressure:
    - Implies steam will change to liquid
    - Pack becomes wet.
- Air in chamber:
  - Impairs sterilization
  - Reduces steam penetration as poor conductor of heat.
- Equipment malfunction:
  - Out of calibration temperature/pressure gauges
  - Incorrect steam supply pressure
  - Faulty pressure control valves, vacuum pumps.
- Personnel errors:
  - Inadequate cleaning/packing
  - Poor loading techniques, overcrowding of items.

Advantages

- Kills viruses and spores
- Economical, fast and good penetration
- Easy to use, reliable
- Absence of toxic products and residues
- Material pre-packaged and sterile until use
- Linen and rubber not destroyed.

Disadvantages

- Equipment damage
- Metal corrosion, blunts, cutting edges
- Shortened life of electronic components
- Reduces light transmission in fiberoptic laryngoscope blades
- Inequality in level of disinfection at different sites.

Low Pressure Autoclaving

- 73°C at 290 mm Hg for 2 hrs
- Pressure is subatmospheric (1/3rd atomospheric press)
- Steam is formed at 73 °C
- Good for heat sensitive objects
- Also called *Low Temperature Steam (LTS)*
- If formaldehyde is added, spores are also killed (LTS-F).

DRY HEAT STERILIZATION[1,4]

Hot Air Oven

Uses

- For items damaged by moist heat
- Talc, glycerine, oils, petroleum jelly, waxes, powders.

Advantages

- Technique penetrates well
- Does not corrode metal
- **Disadvantages:** Slow.

Techniques

- 170 ºC for 60 mins
- 160 ºC for 120 min
- 150 ºC for 150 min.

Flames

- Ophthalmic instrument heated directly on flames (1000 °C).

CHEMICAL DISINFECTION[1,4]

Introduction

- Involves immersing an item in a solution containing a disinfectant
- Also called ***Cold Sterilization.***

Factors Influencing Chemical Disinfection

- Concentration of chemical:
  - Higher concentration increases bactericidal activity (except alcohol)
  - Very high concentration damages item and skin of personnel
  - Water left on item dilutes active chemical
  - Equipment to be dried before chemical disinfection.
- Temperature: Higher temperature increases effectiveness of agent
- Evaporation and light deactivation:
  - Evaporation occurs in uncovered container
  - If active agent more volatile than diluent, dilution occurs
  - Chlorine products are susceptible to evaporation.
- *Bioburden*: Higher the microbial load, longer the exposure time required
- pH:
  - Increase in pH decreases the efficiency of phenols, iodine and hypochlorites
  - Increase in pH increases the efficacy of glutaraldehyde and quarternary ammonium compounds.
- Time:
  - For high level disinfection, minimum contact time of 20–30 min is recommended
- Use pattern and Use life:
  - Use pattern refers to how many times a solution can be used
  - Use life is time during which activated solution may be used once disinfectant solution is mixed.

Area for Disinfection

- Designated areas
- Cleaning area separate to be from chemical storage area
- Area to be large enough to ensure vapor dilution
- Air exchange rate not less than 10 per hour
- Local exhaust ventilation to be installed
- Training to be given to each employee
- Personnel to wear protective gear for skin, eyes, clothing and gloves
- Minimize splashing, spilling and personnel exposure
- Chemical kept in closed container with tight fitting lid
- Small spills absorbed and neutralized with special mats
- Large spills treated with chemical spill kits with neutralizer/deactivator.

Monitoring

- Standard biological preparations available only for sterilization
- Only way to assess is direct assay sterility test which is difficult and time consuming
- Physical monitors:
  - Exposure time
  - Temperature
  - Pressure.

Advantages

- Economical, easy and fast
- Suitable for heat sensitive equipment.

Disadvantages

- Equipment will be wet
- Pre-packaging not possible
- Risk of recontamination during drying/wrapping
- Cannot be used for all types of equipment
- More prone for error
- Impregnates rubber and plastic
- Irritating to skin, unpleasant odor
- Maybe harmful to patient
- Difficult to monitor efficacy
- Instruments have to be disassembled.

Glutaraldehyde (2% solution with 0.3% Na_2CO_3)

Advantages

- Excellent germicidal property
- Acts in the presence of organic matter
- Noncorrosive equipment
- Long shelf life, around 30 days.

Uses

- Endoscopes
- ETT, breathing, equipment.

Disadvantages

- Dilution during use (≥ 1–1.5% recommended)
- Evaporates at room temperature
- Needs activation (made alkaline with Na_2CO_3) to become sporicidal
- pH kept between 7.5–8.5 to be sporicidal.

Side Effects

- Headache, skin, eyes and mucous membrane irritation
- Asthma like symptoms
- Salivary gland enlargement in contaminated oral airways.

Spectrum

- Bacteria, fungi, viruses at room temperature within 15 mins
- High level disinfection requires 20–30 mins
- Sporicidal if between 3–10 hrs exposure.

Orthophthaldehyde (OPA/Cidex OPA)

Spectrum

- High level disinfection at room temperature after 12 mins
- Sporicidal with prolonged exposure.

Advantages

- Noncorrosive, faster disinfection
- Minimal odour
- No need of activation/mixing
- Effective in presence of organic soil
- Can be discarded through drain.

Disadvantages: Stains proteins.

Side Effects

- Stinging, tearing and redness of eyes
- Dermatitis on repeated contact
- Lesions of skin, lip, mouth and esophagus if residues present.

Quaternary Ammonium Compounds

Spectrum

- Low level disinfectant
- No sporicidal effects
- Bacteria, viruses and fungi at room temperature in 10 mins
- More active against gram-positive than gram-negative bacteria
- Inactivates HIV but some do not inactivate hepatitis
- Ineffective against mycobacterium TB
- Only chemical agent ineffective against TB.

Advantages

- Quick to act, nontoxic, noncaustic
- No noxious fumes.

Disadvantages

- Early generation Quats affected by hard water, soap and preterm
- Inactivated by organic materials
- Deteriorates with age.

Chlorhexidine

- 0.1% aqueous solution for 20 min for ETT decontamination
- 0.5% in 50% ethyl alcohol for skin sterilization in 30 sec
- Ideal hand scrub
- Residual effect ensures prolonged disinfection.

Alcohols

Ethyl/isopropyl alcohol (70–90% by volume).

Spectrum

- Intermediate: Low level disinfectants
- Effective against most viruses including HIV, Hepatitis B, bacteria, fungi and mycobacterium TB
- Inactive against spores.

Advantages: Reduces bacterial count in hand rubs.

Disadvantages:

- May not maintain contact time: Evaporates rapidly
- Inactivated by proteins
- Incorrect results while measuring anesthetic agents if it gets into gas sampling lines
- Hardens rubber and plastics on repeated use
- Inflammable: Fire hazard.

Phenols

1.5% to clean surface of equipment.

Spectrum

- Bacteria, fungi, mycobacterium TB, most viruses
- Common respiratory viruses resistant to phenols
- Not sporicidal except at ≥ 100 °C
- Intermediate: Low level disinfectant
- ***Disinfectant of choice*** for gross organic contamination.

Advantages

- Activate in presence of organic matter
- Active after mild heating, very stable

- Used mainly on environmental surfaces and non critical devices.

Disadvantages

- Bad odor
- Irritating to skin
- Absorbed by rubber
- Damage to skin and mucous membrane
- Difficult to rinse off most materials.

Iodine

- 0.5–2% in alcohol used
- *Iodophore* is combination of iodine and a solubilizing agent.

Spectrum

- Bacterial, virucidal, tuberculocidal
- Prolonged contact for fungi and spores
- Intermediate: Low level disinfectant.

Advantages: Principally used as antiseptic.

Disadvantages:

- Unstable in presence of hard water, heat and organic soil
- Corrosion of metals
- Staining of nonmetallic objects
- Tincture iodine irritates skin.

Chlorine Compounds

- Sodium and calcium hypochlorite (household bleach)
- Chlorine dioxide and chloramine.

Spectrum

- 50–100 ppm for vegetative bacteria and fungi
- 200 ppm for virus, Hepatitis B at 500 ppm
- 1000 ppm for high level disinfection, NOT SPORICIDAL.

Advantages: Inexpensive and fast acting.

Disadvantages:

- Corrosive, irritating to personnel
- Irritates eye and mucus membranes
- Inactivated by organic matter
- Not used for instruments, environmental disinfection agent.

Hydrogen Peroxide

Spectrum

- Bacteria, viruses, fungi and spores
- 3% hydrogen peroxide for work surfaces
- 7.5% solution for 30 mins for high level disinfection.

Advantages: Not inactivated by organic matter

Disadvantages:

- Reduced effectiveness on exposure to heat and light
- Damages rubber and plastic
- Corrodes metal
- Irritant to skin and eye.

Formaldehyde

Spectrum

- High level disinfectant
- Bacteria, viruses, fungi, TB
- Ineffective against spores.

Advantages

- Not corrosive
- Not inactivated by organic matter.

Disadvantages

- Highly toxic, flammable gas
- Pungent odour, irritates eyes and skin
- Potential carcinogen.

Ozone

Advantages

- Compatible with plastic
- Environment friendly, non-toxic residues
- No exhaust ventilation required
- Treated objects are dry
- Less expensive compared gas plasma.

Disadvantages

- Corrodes metal
- Unsuitable for natural rubber
- Unsuitable for some metals (brass and copper).

Peracetic Acid/*Steris 20*

Introduction

It is 36% peracetic acid with corrosion and degradation inhibitors contained in a single use container.

Spectrum

- Bacteria, fungi, viruses
- Spores at low temperature itself
- Maybe effective against *prions.*

Advantages

- Effective in the presence of organic matter
- Decomposition products not harmful (acetic acid, O_2, H_2O and H_2O_2)

- Useful for heat sensitive items like endoscopes
- Less damaging than autoclaving
- Quick method, wrapping not necessary
- Can be used on wet/dry items
- Personnel are not exposed to toxins
- No sterilant dilution necessary
- Can be located in OT itself
- Leaves no residues.

Disadvantages

- Can corrode metals
- Can cause skin and eye damage
- Can oxidize untreated metals
- More costly
- Only small number of items sterilized per cycle.

Procedure

- Equipment must be clean, need not be dry
- Placed in special tray which is placed in processor
- Each tray has holes for fluid entry and drainage
- Continuous flow of sterilant on exposed surfaces occurs
- Sealed package of sterilant concentrate placed in sterilizer
- Lid closed and cycle is started.

Sterilization Cycle

- Sterilized concentrate mixed with filtered sterile water
- Mixture heated to between 50–55 °C
- Diluted sterilant enters trays and covers instruments
- Circulation of sterilant continues for 12 minutes
- Sterilant is drained
- Instruments and chamber rinsed 4 times with sterile water
- Sterile air is pumped into chamber to displace water
- Cycle takes 20–45 minutes
- Printout confirming parameters were met is handed out at the end of cycle.

GAS STERILIZATION[1,4]

Chemistry

- Ethylene oxide is colorless, poisonous gas with sweet odour
- Inflammable in concentrations ≥ 3%.

Preparation

- Available in high pressure tanks, ampoules and cartridges
- Mixed with CO_2 or CFCS or freon to reduce flammability
- 10% gas in CO_2 with humidity of 30–50% used
- Cylinder has aluminium color body with red shoulders
- Circular yellow band present below shoulders.

Spectrum: Bacteria, fungi, viruses and spores.

Physical Parameter of EOS

- *Gas concentration:* EOS between 450–750 mg/L recommended
- *Temperature:* Between 38–60 °C
- *Relative humidity:* Between 40–80%
- *Exposure time:* Between 1.5–6 hrs, upto 12 hrs.

Design of Machine

- Pressure rated vessel with port for admitting air
- Vacuum pump for evacuating chamber gas components
- Jacket to heat vessel
- Steam source to humidify chamber and contents
- A means to inject sterilant
- Computer and monitors to document process.

Uses

- Pump oxygenator
- ***Ruben valve***, plastic pump tubing
- Teflon prosthesis
- Grafts
- Catheters.

Preparation of Instrument

- Item should be suitable for EOS
- Items disassembled, cleaned, dried and wrapped
- Caps, plugs, valves and stylets removed
- Equipment thoroughly cleaned and rinsed, dried with towel/air
- Wrap item in material permeable to EO gas and water vapor
- Devices sorted according to sterilization time
- Devices placed in wire baskets/metal carts which do not absorb EO
- Items loosely loaded to allow gas penetration
- Items not to be in contact with chamber walls.

Sterilization Cycle

- Warming of chamber
- Evacuation of air
- Introduction of moisture and maintaining it for dwell period
- Introduction for ethylene oxide

- Raising of chamber pressure and temperature
- Exposure to EO for required time
- Releasing pressure in chamber
- Removal of EO mixture (***Purge cycle***)
- Introducing filtered air in chamber which re-establishes atmospheric pressure.

Aeration Cycle

- Reduces retained EO on items to safe level
- Done by ambient aeration/mechanical aeration
- Takes long time.

Indication of Gas Sterilization

- *Physical:* Measures exposure time, temperature, humidity and pressure
- Chemical:
  - Tapes/strips/cards/sheets
  - Changes color when sterilization parameters are met.
- Biological:
  - Used at least once a week
  - Placed in most inaccessible region of load.

Complications

- To patient:
  - Skin reaction
  - Respiratory tract inflammation
  - Hemolysis if blood is exposed to item
  - Sensitization and anaphylaxis
  - Increases risk of latex sensitization.
- Equipment alteration:
  - Leaches plastics, weakens integrity
  - ETT becomes soft and kinks easily.
- Personnel:
  - Acute exposure:
    - Headache, eye irritation, coughing, metallic taste
    - Nausea, vomiting, diarrhea, fatigue ability
    - Memory loss, drowsiness, weakness, dizziness, CNS symptoms
    - Lack of coordination, convulsions
    - Upper respiratory tract irritation, dyspnea, respiratory paralysis.
  - Chronic exposure:
    - Corneal burns, cataract, keratitis
    - Skin reaction, respiratory infection
    - Affects CNS and PNS: Reduces cognition
    - Anaemia
    - Mutagenic, carcinogenic
    - Affects reproductive system.

Advantages

- *Reliable:* Gas permeates crevices and narrow lumens
- Use on heat/moisture labile materials
- Minimal damage to equipment
- Items can be prepackaged
- Can be stored sterile for long periods
- Eliminates risk of recontamination
- Large load can be sterilized at a time.

Disadvantages

- Fires and explosion hazard
- Long total processing time
- Costly and needs trained personnel
- Monitoring is required to reduce personnel exposure
- Some materials deteriorate after repeated EOS
- Petroleum based lubricants cannot be EO sterilized.

GAS PLASMA STERILIZATION[1,4]

Introduction

Called ***fourth state of matter.***

Physics

- Contains cloud of reactive ions, electrons and neutral atomic and molecular particles
- Produced by applying energy to hydrogen peroxide
- Reactive species interact with intracellular molecules required for metabolism and reproduction.

Advantages

- Effective, simple to operate
- Temperature during cycle does not exceed 50°C
- Useful for heat and moisture labile items
- Less corrosive than steam
- Used for hinged and nonhinged items
- Uses low concentration of agent
- *No toxic residues:* Only O_2 and water, lack of personnel exposure
- Short processing time
- Sterilized product is dry and ready to use.

Disadvantages

- Small size of sterilization chamber
- Cellulose, paper, linen, powders and implants cannot be processed
- Penetration not as good as EOS
- Items with collapsible surfaces like bags need a block to keep surfaces apart
- May require modification of wrapping and stacking techniques.

Procedure

It has 5 phases.

1. Prepacking phase:
   - Item cleaned and dried
   - Can be unwrapped/kept in nonwoven wrap
   - Hydrogen peroxide cassette placed inside sterilizer along with items.
2. Preconditioning/Vacuum phase:
   - Door closed, chamber is evacuated
   - Vacuum is created in gas chamber
   - Filtered air reintroduced to restore atmosphere pressure.
3. Diffusion phase:
   - Chamber evacuated again
   - Small volume of H_2O_2 is injected from cassette
   - H_2O_2 vaporizes and diffuses around items for a fixed time.
4. Plasma phase:
   - Low temperature plasma is formed using radiofrequency energy
   - Temperature increases by around 5 °C during this phase.
5. Vent phase:
   - Filtered air is introduced into chamber
   - Air displaces vapor from chamber
   - H_2O_2 vapor passes through device which decomposes it.

RADIATION STERILIZATION[1,4]

Principle

Uses electromagnetic waves produced during disintegration of radioactive elements.

Spectrum

Bacteria, viruses, spores, fungi.

Advantages

- Items can be prepackaged
- Item remains sterile until use
- Heat labile substances can be sterilized
- No risk from retained radioactivity.

Disadvantages

Expensive, not practical for everyday use.

Gamma Rays

- Derived from Co^{60} source
- Lethal dose for bacteria is 2.5 megarads
- ETT, catheters, plastic equipment can be sterilized
- Highly expensive
- Used for sterilizing disposable equipment after manufacturing.

Ultraviolet Rays

- Special lights emitting UV rays fixed on roof at appropriate angles
- Whole OT and equipment to be exposed for 6 hrs or more
- Patients and personnel to be protected (especially skin and eyes).

CLASSIFICATION OF INSTRUMENTS[1,3,4]

Introduction

- *Centre for Disease Control*
- Instruments and other items classified by risk of infection involved to prevent nosocomial infection.

Critical Items

- Must be sterile
- Present high risk of infection if contaminated
- Vascular, regional block needles and catheters.

Semicritical Items

- Do not pierce mucus membrane
- Should be sterile/at least high level disinfected
- Example:
  - *Endoscope;* Oral/nasal airways
  - *Laryngoscope blades;* Resuscitation bags
  - *Temperature probes;* Breathing tubes and connectors
  - *Temperature probes;* Breathing tubes and connectors
  - *Facemask;* Oxygen mask
  - *Esophageal stethoscope;* ETT.

Noncritical Items

- Come in contact with intact skin
- Require only cleaning followed by intermediate disinfection
- Example:
  - *Stethoscope;* Head straps
  - *BP cuff;* Blood warmers
  - *Pulse oximeter;* CO_2 absorber assemblies
  - *Arm board;* Adaptors for O_2 sensors
  - *ECG cable and electrode;* Exterior of machine, ventilator
  - *Humidifier;* Scavenging system
  - *IV fluid pump;* Monitors
  - Equipment carts.

Environmental Surfaces

- Do not ordinarily come into direct contact with patient
- If they do, it is only with intact skin
- Can cause secondary cross contamination by health care workers
- Adjustment knobs/handles, floors, walls, window sills.

Sterilization of Individual Instruments

ET Tube, Airways, Suction Catheter

- Wash with soap and water, rinse
- Brush clean inner aspect of ETT and airway
- Soak for 30–60 mins in 0.1% chlorhexidine for sterilization
- Autoclaving is effective but must be replaced after six uses
- Gamma radiation effective
- Boiling effective but softens tubes.

Facemask

- Wash with soap and water
- Do not boil
- Soak in water at 60–70 ºC for 20 minutes.

Laryngoscope Blade

- Clean, wipe with 70% alcohol
- 0.1% chlorhexidine in 70% alcohol is alternative
- Boil/autoclave after cleaning (remove bulb).

Humidifier

- 60 ºC when in use keeps it pasteurized
- Pasteurization, Cu sponges
- Frequent and thorough washes.

Syringes and Needles

- Gamma radiation ideal for disposable syringes and needles
- Glass syringes autoclaved
- If emergency, boil in distilled water for 5 mins.

Ventilator

- Use bacterial filters at the time of usage
- Ethylene oxide/ultrasonic nebulization with H_2O_2. alcohol
- Internal irrigation with antiseptic
- Breathing units autoclaved/disposable breathing units used
- Formalin chambers
- Immerse breathing circuits in Cidex for 1 hour and then rinse.

Machine Ventilator

- Outside of ventilator cleaned and disinfected with germicide
- Bellows and tubings sterilized with EOS
- Most parts of newer ventilators can be autoclaved
- Follow manufacturer recommendation.

Machine

- Top surface supplied with clean cover for every case
- Cleaned between cases and end of day, then sprayed with germicide
- Do not get liquid in vaporizer filling tunnels
- Attention to frequently used knobs
- Drawers cleaned regularly after removing contents.

Gas cylinder: Wash with soap, water, wipe and spray germicide.

Absorbers

- Effective filter, rarely contaminated
- Follow manufacturer instruction
- Autoclaving possible with newer absorbers
- Canister cleaned when absorbent is changed
- EOS/glutaraldehyde/gamma radiation.

Mapleson's Systems

- Disassembled and components cleaned
- Metal components are autoclaved
- Rubber and plastic sterilized with gas/plasma/glutaraldehyde
- Use disposable tubing
- Bain and Lack circuit sterilization difficult as central tubing is present.

Pulse Oximeter Probe and Cable

- Cleaned with alcohol/recommended cleaning solution
- Cables sterilized by gas plasma
- Usually done at end of day/when visibly contaminated.

BP Cuff, Tubing, Stethoscope

- Spray cuff with topical disinfectant
- Clean with detergent at end of day/when contaminated
- Gas sterilization/chemical/plasma sterilization (only for nonfabric cuffs)
- Stethoscope washed with water and wiped with alcohol
- Earplugs cleaned with alcohol applicator.

Resuscitation Bags

- Valve disassembled and cleaned
- Disinfected after each use if possible
- Follow manufacturer instructions.

Transesophageal Echo Probes

- Clean carefully, soak in disinfectant
- Automated reprocessor for ultrasound probes available
- Glutaraldehyde used.

Reservoir Bag

- High level disinfection required
- Cleaned manually/washing machine
- EOS/pasteurization are preferred sterilization methods
- May result in gradual deterioration
- *Chemical disinfection:* Care to empty air pockets with disinfectants.

Breathing Tubing

- Corrugated tubes to be periodically drained during use
- Water which has condensed may run into patient/absorber
- Subject to high level disinfection
- Soak in container with water and detergent to clean
- Remove Y tubing and pasteurize (intact Y tube loosens fit)
- Chemical disinfection, with care to exclude air pockets.

STERILIZATION OF LARYNGEAL MASK AIRWAYS[1,4]

Introduction

- 76% LMAS have occult blood
- Consult manufacturer recommendations
- Disposable device economical
- Class: Semicritical device
- Warrants high level disinfection/sterilization.

Cleaning

- Soak in 8–10% $NaHCO_3$ solution before cleaning to remove secretion
- Inflation valve not to be exposed to any fluid
- Clean with diluted (8–10%) $NaHCO_3$/detergent solution
- Pipe cleaner type brush inserted through distal aperture
- Ultrasonic cleaning more effective for proteinaceous material
- Supplementary potassium permanganate cleaning reduces protein content
- Rinsed with water and dried
- Packaged in cover.

Sterilization Methods

- Autoclaving is the ***only recommended*** method
- Up to 134 ºC used: Higher temperature makes tube brittle
- Remove as much air as possible from cuff before autoclaving
- Residual air will expand in heat and damage cuff/valve/pilot balloon
- Use sterilizer without vacuum phase
- After sterilization, LMA left in package until prior to use
- Chemical/gas not used as pharyngitis and laryngitis possible
- Radiation sterilization for disposable LMAS.

STERILIZATION OF FIBEROPTIC ENDOSCOPES[1,4]

Introduction

- Semicritical device
- Fragile, complex and heat sensitive
- Difficult to sterilize
- High level disinfection/sterilization recommended.

Preparation

- Store in clean area with distal tip protected
- Best decontaminated in endoscopy unit
- Leak test performed before immersion to avoid damage which occurs during cleaning
- If leak occurs, remove unit from service and consult manufacturer.

Cleaning

- Follow manufacturer recommendations as each solution is toxic to FOB
- Remove from patient and wipe exterior with disinfectant
- Flush all channels with water/enzymatic solution (diluted)
- Place FOB in enzymatic detergent solution
- Place water resistant cap over video connector before submersion
- All channels filled with solution and allowed to soak for 2–5 mins

- Clean fiberscope with special cleaning devices for channels
- Short strokes used to introduce the brush
- If resistance felt, proceed from other direction
- Solution suctioned from all channels until free of debris
- Rinse with sterile water
- FOB hung vertically to drain any residual fluid
- Brush is inserted into suction port in anterograde fashion
- Retrograde introduction increases damage to internal lining of suction port.

Methods of Sterilization

Chemical

- All lumens/channels to be filled with disinfectant
- After disinfection, wash with sterile water then 70% alcohol
- Agents used:
  - Glutaraldehyde (2% for 10 mins)
  - Hydrogen peroxide (for 20 mins)
  - Orthophthaldehyde
  - Steris-20.

Gas/EO Sterilization

Automated endoscope reprocessors:

- Have been implicated in infection
- Have filteration systems
- Change filters regularly
- FOB cooled for 5–7 mins after processing.

HOSPITAL WASTE MANAGEMENT

Cat.	Name	Content	Disposal
I	Human anatomical waste	Human tissues, Organs	Incineration
		Body parts	Deep burial
II	Animal waste	Animal tissues, organs	Incineration
		Waste of veterinary hospital	Deep burial
III	Microbiology waste	From lab culture	Autoclaving
		Stocks/ specimens	Microwaving
		Live/attenuated vaccines	Incineration
IV	Waste sharps	Needles	Disinfection (chemical)
		Syringes	Autoclaving, Microwave
		Scalpels/ blades	Mutilation, Shredding

Contd...

Cat.	Name	Content	Disposal
V	Discarded medicine	Outdated medicines	Incineration
			Drug disposal-secured landfills
VI	Solid waste	Blood contaminated items	Incineration
			Autoclaving
			Microwave
VII	Solid waste	Items other than waste sharps	Chemical treatment
		Tubings, catheter, IV sets	Autoclave, Microwave
IX	Incineration ash	Ash from incineration	Municipal landfill
X		Chemicals in disinfectants	Chemical treatment
			Discharge in drainage for liquids
			Secure landfills for solids

Color Coding of Hospital Waste

Color	Container	Category	Treatment
Yellow	Plastic bag	I, II, III. VI	Incineration
			Deep burial
Red	Plastic bag Disinfected container	III, VI, VII	Autoclaving/ Microwave
			Chemical treatment
Blue/ White translucent	Plastic bag Puncture proof container	IV, VII	Autoclave/Microwave
			Chemical treatment
			Shredding/Mutilation
Black	Plastic bag	V, IX, X (solids)	Secured landfill

ANESTHESIA CIRCUITS[1,2,3,4]

Introduction

Breathing circuit is an interface which connects patients airway to anesthetic machine creating an artificial atmosphere from which the patient breathes.

Components

- Fresh gas entry port
- Reservoir for gas:
  - Bag
  - Corrugated tube.
- Expiratory valve (APL), unidirectional valve, nonrebreathing valve

- CO_2 absorber
- Patient connections port
- Corrugated tubes connecting these components
- *Filters:* Bacterial HME filters.

Requirements

Essential

- Deliver gases to alveoli in same concentration as set concentration
- Effectively eliminates CO_2
- Have minimal apparatus dead space
- Low resistance.

Desirable

- Economy of fresh gas
- Conservation of heat
- Humidification of inspired gases
- Light weight
- Convenient
- Efficient during controlled and spontaneous ventilation
  - Efficient CO_2 elimination
  - Efficient fresh gas utilization.
- Adaptable for adults/children and ventilators
- Provision to reduce OT pollution.

Classification Systems

- ***McMahon's*** classification
- ***Dripps*** classification
- ***Miller's*** classification
- ***Moyers*** classification
- ***Collins*** classification
- ***Conway*** classification
- ISO classification.

McMahon's *Classification*[4]

Open circuit	No rebreathing
Semiclosed circuit	Partial rebreathing
Closed circuit	Total rebreathing

Dripps *Classification*[4]

Open	Inhales air + agent
	Exhales to atmosphere
	No reservoir bag
	No rebreathing
	Open drop, T piece
Semi-open	Inhales air + agent from machine
	Exhales to atmosphere
	Small reservoir
	Minimal rebreathing
	T piece with small reservoir (***Jackson-Rees***)
Semi-closed	Inhales from machine
	Exhales to atmosphere and machine
	Large reservoir bag
	Rebreathing possible
	Maplesons systems
Closed	Inhales from machine
	Exhales to machine
	Large reservoir bag
	Rebreathing present with CO_2 absorbent
	Brian-Swords Circle system

Miller's *Classification*[4]

Systems without CO_2 absorbent	Systems with CO_2 absorbent
Unidirectional flow	
• Non-rebreathing system • Circle system	• Circle systems with absorber • Brian-Sword
Bidirectional flow	
• Afferent reservoir system: – Mapleson A – Mapleson B – Mapleson C – Lacks system	***Ralf Waters*** To and Fro system
• Efferent reservoir system: – Mapleson D – Mapleson E – Mapleson F – Bains system	
• Enclosed afferent reservoir system: – Millers	
• Combined system: – Humphrey ADE	

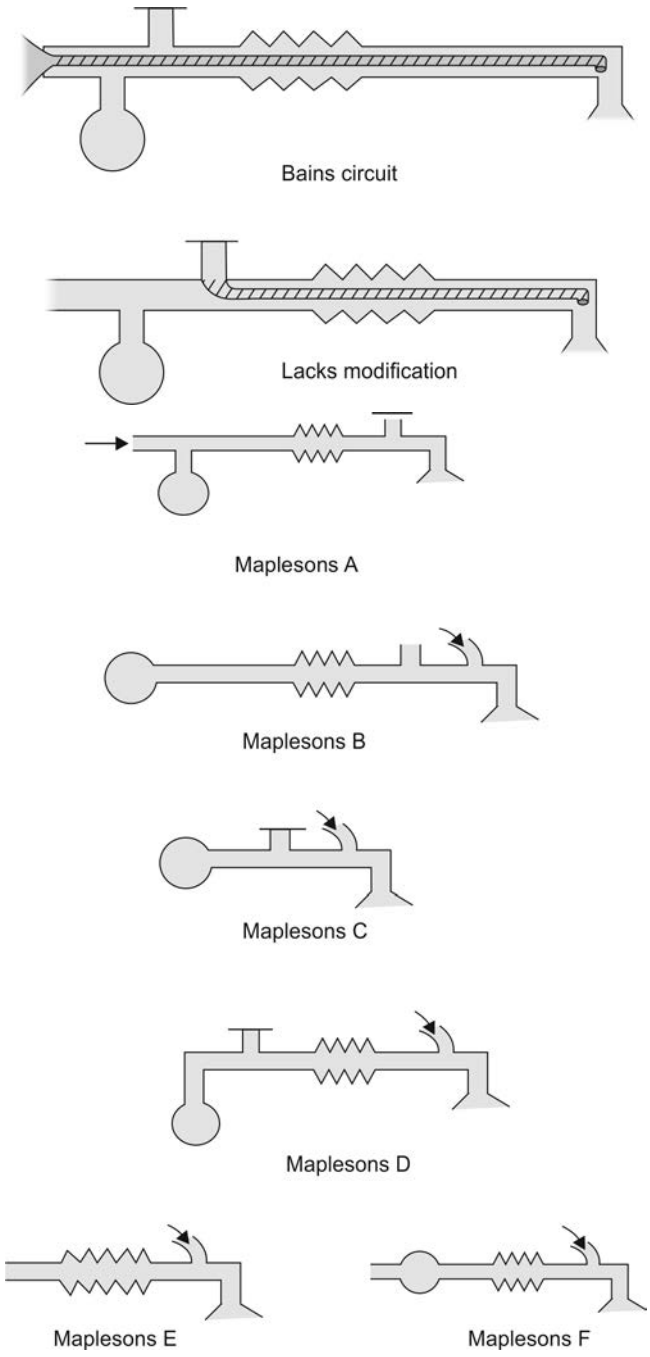


Fig. 6.41: Anesthesia circuits classification[4]

Advantages

- Simple inexpensive and rugged
- Variation in minute volume does not affect E_TCO_2 much
- In coaxial systems inspiratory limb is warmed by expiratory gases
- Low circuit resistance
- Easy to position conveniently
- Light weight and not bulky
- Compression and compliance volume losses from circuit is less
- No toxic compounds like compound A/Carbon monoxide.

Disadvantages

- Requires high gas flows
- Inspired heat and humidity low due to high fresh gas flows
- Optimal FGF difficult to determine
- Difficult to scavenge Maplesons E and F
- Not suitable for patients with malignant hyperthermia as it is not possible to increase FGF enough to remove increased CO_2 load
- APL valve close to patients and inaccessible in Maplesons A, B and C.

MAPLESON A/MAGILLS[1,4]

Description

- ***Most efficient*** system for *spontaneous ventilation*
- ***Least efficient*** system for *controlled ventilation*
- FGF from machine end, near reservoir bag
- APL valve present near patient end
- Corrugated tube connecting bag and APL valve
- Sensor/E_TCO_2 monitor between APL valve and patient in adults
- Sensor present between APL valve and corrugated tube in pediatrics to decrease dead space
- Dead space at patient end and upto APL valve.

Technique of Use

- For spontaneous ventilation, APL valve kept fully open
- For controlled ventilation, APL valve partially closed
- APL valve opens during expiration in spontaneous and inspiration during controlled ventilation
- Ideally FGF rates around 60–80 ml/kg/min.

Functional Analysis

Spontaneous Respiration

Inspiration (1st): Fresh gas from prefilled circuit enters lung.

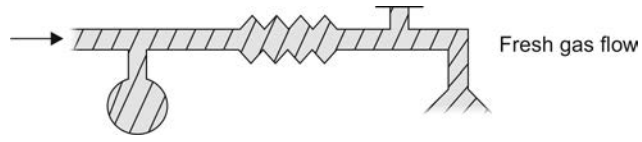


Fig. 6.42: Maplesons A during first spontaneous inspiration effort[3,4]

- Expiration
  - Dead space (first) and then alveolar gas flows into corrugated tube and bag
  - Fresh gas from inlet flows into reservoir bag
  - When reservoir bag fills, APL valve opens up
  - First, alveolar gas is vented out followed by alveolar gas in corrugated tube
  - During expiratory pause:
    - If FGF > MV, dead space gas pushed out
    - If FGF = MV, some dead space gas remains
    - If FGF < MV, more alveolar gas retained.

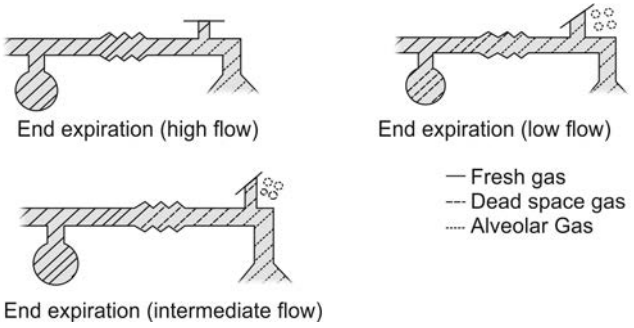


Fig. 6.43: Maplesons A during first spontaneous expiration effort[3,4]

- Inspiration (2nd)
  - First gas inhaled is that present between patient and APL valve
  - Next gas will be alveolar gas/dead space gas/ fresh gas depending on FGF rates.

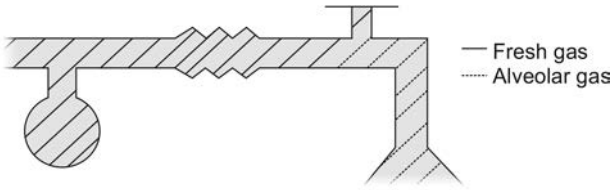


Fig. 6.44: Maplesons A during second spontaneous inspiration effort [3,4]

Controlled Ventilation

- Inspiration (First inspiration)
  - Fresh gas from prefilled circuit alone is inhaled
  - APL valve opens during inspiration.

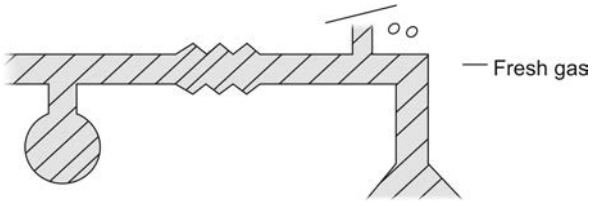


Fig. 6.45: Maplesons A during first controlled inspiration[3,4]

- Expiration
  - No gas escapes APL valve unless bag fills
  - Thus all exhaled gases remain within circuit
  - Alveolar and dead space gas enters corrugated tube
  - If tidal volume is large, alveolar gas may enter bag.

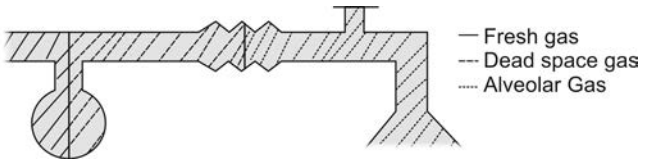


Fig. 6.46: Maplesons A during first controlled expiration[3,4]

- Inspiration (Second inspiration)
  - Alveolar gas inhaled first
  - APL valve opens when pressure in the circuit increases
  - Gas flows to patient and exits APL valve too
  - When all exhaled gas is driven out of tube, fresh gas fills tubing
  - Some fresh gas enter patient while some is vented out
  - Rebreathing of alveolar gas and wastage of fresh gas occurs
  - ***Least efficient*** for controlled ventilation.

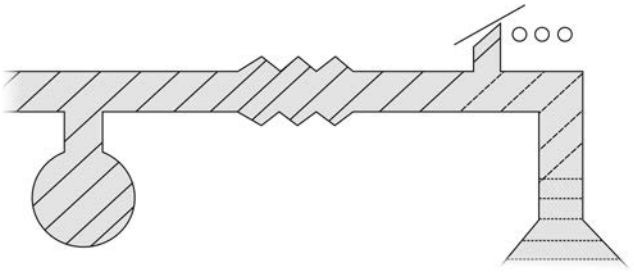


Fig. 6.47: Maplesons A during second controlled expiration[3,4]

Lacks Modification of Mapleson A

- Added expiratory limbs, running from patient to APL valve
- APL valve at the machine end of system
- Easier to adjust APL valve
- Facilitates scavenging of excess gases
- Increased resistance and work of breathing due to coaxial tube
- Available as dual/parallel tube and coaxial configuration.

Preuse Check

- Positive pressure check by closing APL valve and patient port

- If coaxial system:
  - Attach tracheal tube to inner tube
  - Blow with APL valve closed
  - Reservoir bag will move if leak is present
  - Occlude both tubes at patient end
  - Open APL valve and pressure reservoir bag
  - If leak in inner tube is present, gas escapes APL valve.

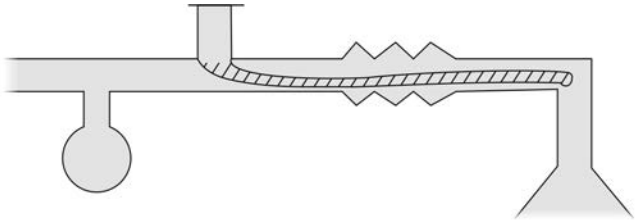


Fig. 6.48: Lacks modification of Maplesons A system[3,4]

MAPLESON D[1,2,3,4]

Description

- Has T-piece near patient end
- T-piece is 3 way tubular connector:
  - Patient connection port
  - Fresh gas port
  - Port with connected corrugated tubing.
- Fresh gas flow (FGF) near patient end
- APL valve present near machine end, between reservoir and corrugated tube.

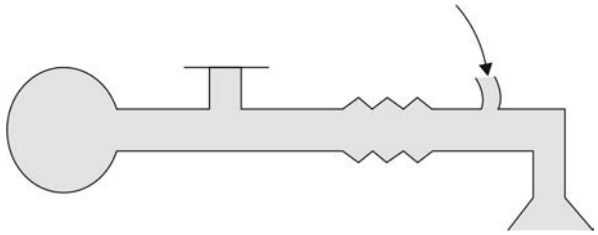


Fig. 6.49: Maplesons D system[4]

Technique of Use

- ***Most efficient*** of Mapleson circuits for controlled ventilation
- For spontaneous ventilation, APL valve kept fully open
- Excess gas vented through APL during expiration in spontaneous ventilation
- Excess gas vented through APL during inspiration in controlled ventilation
- FGF at 150–200 ml/kg/min (2–4 times minute volume).

Functional Analysis

Spontaneous Respiration

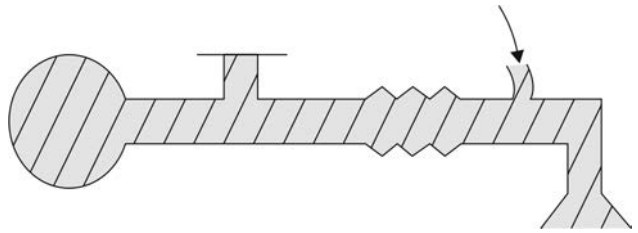


Fig. 6.50: Maplesons D during first spontaneous inspiration[3,4]

- During Inspiration (First inspiration): FGF enters lungs.

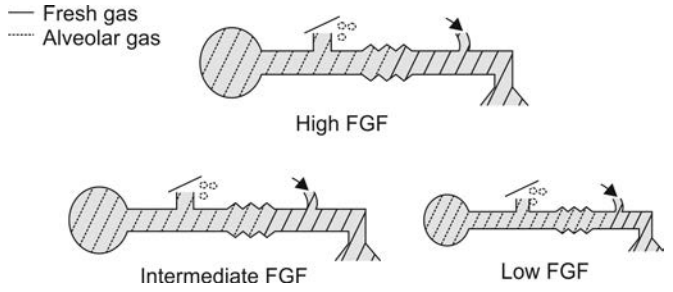


Fig. 6.51: Maplesons D during first spontaneous expiration[3,4]

- During Expiration:
  - Alveolar gas and dead space gas enters tube
  - FGF keeps mixing with alveolar gas
  - When reservoir bag fills, APL valve opens
  - During expiratory pause
    - If FGF > MV, corrugated tube filled with fresh gas
    - If FGF = MV, corrugated tube fills with some alveolar gas
    - If FGF < MV, most of corrugated tube fills with alveolar gas.

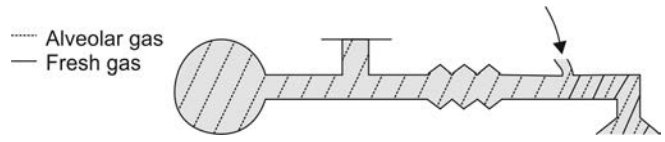


Fig. 6.52: Maplesons D during second spontaneous inspiration[3,4]

- During inspiration (Second inspiration):
  - If FGF is high, all the gas drawn from corrugated tube will be FG
  - If FGF is low, some exhaled gas with CO_2 will be inhaled
  - E_TCO_2 increases and thus respiratory rate of patient will increase to compensate.

Controlled Ventilation

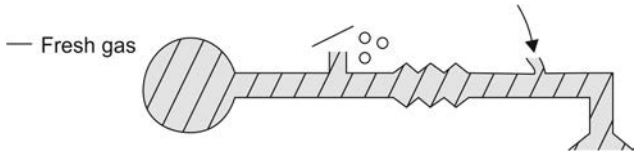


Fig. 6.53: Maplesons D during first controlled inspiration[3,4]

- Inspiration (First inspiration):
  - FGF flows into lung from prefilled circuit
  - APL valve opens.

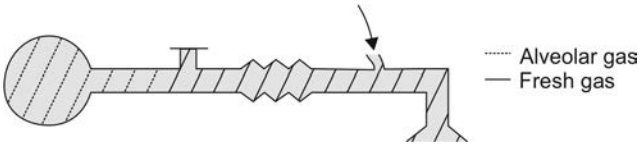


Fig. 6.54: Maplesons D during first controlled expiration[3,4]

- Expiration:
  - Gas exhaled, flows down corrugated tubing
  - Fresh gas enters at the same time
  - During expiratory pause, fresh gas pushes exhaled gas down the tubing.

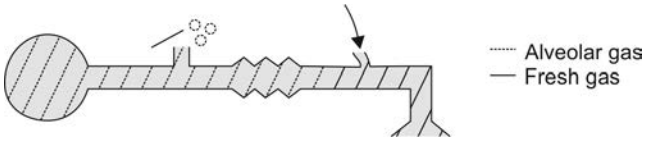


Fig. 6.55: Maplesons D during second controlled inspiration[3,4]

- Inspiration (Second inspiration)
  - FGF and gas from tubing enters patient
  - If FGF is low, some exhaled gas is inhaled
  - If FGF is high, little rebreathing occurs.

Preuse Check

- Occlude patient end, close APL valve and pressurize systems
- Coaxial systems:
  - Flowmeter test
  - Pethicks test.

BAINS SYSTEM[1,2,3,4]

Description

- Coaxial modification of Mapleson D
- FGF tube runs coaxially inside corrugated tubing
- FGF tube ends at point where FGF enters Mapleson D
- Traditionally, 1.8 metres long
- Length can be increased by adding additionally corrugated tube at machine end
- Outer tube is transparent to allow inner tube inspection.

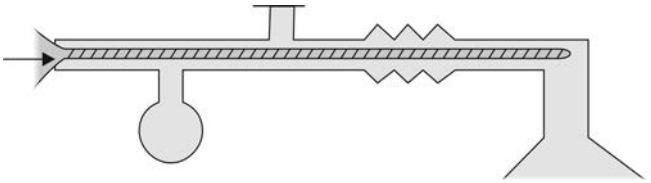


Fig. 6.56: Bains coaxial system[4]

Advantages

- Light weight, convenient
- Easily sterilized
- Reusable
- Facilitates scavenging from APL valve
- Exhaled gases in outer tube warms fresh gas
- Useful in remote location (MRI suite) by adding corrugated tube to machine end
- Can be connected to ventilator by removing reservoir bag.

Disadvantages

- Kinking/leakage/disconnection of inner tube causing severe hypercarbia
- Incorrect system assembly is hazardous.

Technique of Use

- APL valve closed partially in controlled ventilation
- Valve opened fully for spontaneous ventilation
- Excess gas escapes at exhalation in spontaneous ventilation
- Excess gas escapes at inhalation in controlled ventilation
- FGF should be 2 times the minute volume.

Functional Analysis (Same as Mapleson D)

Spontaneous Ventilation

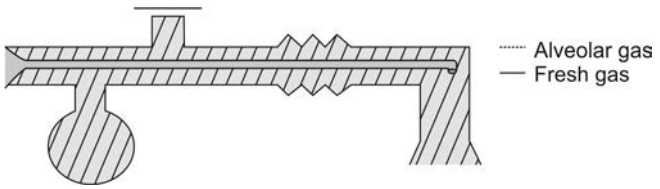


Fig. 6.57: Bains system during first spontaneous inspiration[3,4]

- Inspiration (First inspiration): FG from machine flows into patient

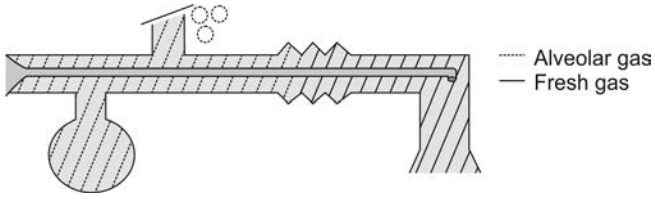


Fig. 6.58: Bains system during first spontaneous expiration[3,4]

- Expiration:
  - Continuous FGF at patient end
  - Expired gas continuously mixed with FG at patient end
  - Expired gas flows back to corrugated tube and bag
  - APL valve opens when bag is full
  - During expiratory pause, FGF pushes exhaled gases more into reservation bag.

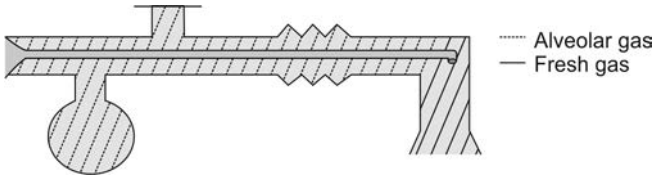


Fig. 6.59: Bains system during second spontaneous inspiration[3,4]

- Inspiration (Second inspiration):
  - Patient inhales FG as well as mixed gas from tube
  - Amount of mixed gas depends on FGF.

Controlled Ventilation

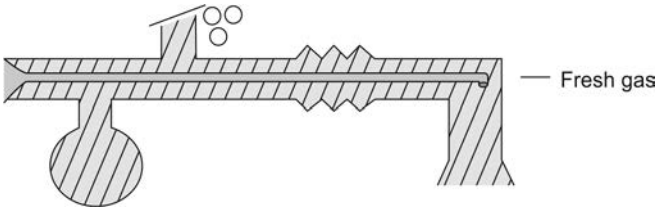


Fig. 6.60: Bains system during first controlled inspiration[3,4]

- Inspiration (First inspiration):
  - FG flows from prefilled circuit to patient
  - APL valve opens to allow FG escape.

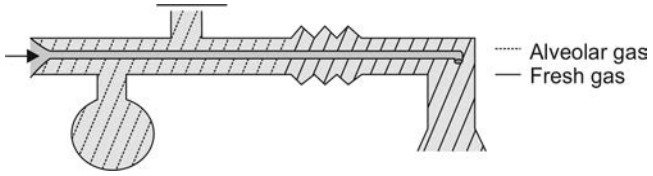


Fig. 6.61: Bains system during first controlled expiration[3,4]

- Expiration:
  - Continuous mixing of FG with expired gas
  - During expiratory pause FG pushes MG into reservoir bag

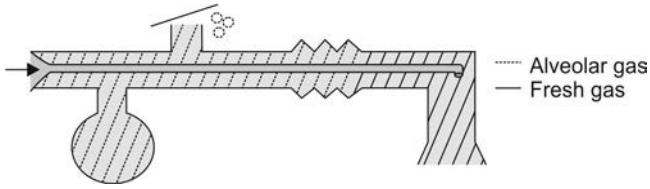


Fig. 6.62: Bains system during second controlled inspiration[3,4]

- Inspiration (Second inspiration):
  - Patient ventilated with a mixture of gases
  - Mostly fresh gas if FGF is high
  - Some rebreathing occurs if FGF is low
  - APL valve opens and some mixed gas vented out.

Preuse Test

- Outer tube:
  - Pressurize system with closed APL valve and patient end
  - Bag inflates.
- Inner tube:
  - Set low flow on flowmeter
    - Occlude inner tube at patient end with finger
    - If flowmeter indicator falls, inner tube is intact.
  - ***Pethicks test***
    - Activate O_2 flush and observe bag
    - High flow at patient end creates negative pressure in outer tube
    - Bag will collapse if inner tube is intact
    - Bag will inflate if inner tube not intact.

MAPLESON E[1,2,3,4]

Design

- Length of tubing may be attached to T-piece to form a reservoir
- Does not have a bag
- Expiratory port may be enclosed in a chamber from which excess gas is evacuated
- E_TCO_2 placed between expiratory port and expiratory tubing
- Difficulty is scavenging: Rarely used
- Used for providing O_2 to spontaneously breathing patients.

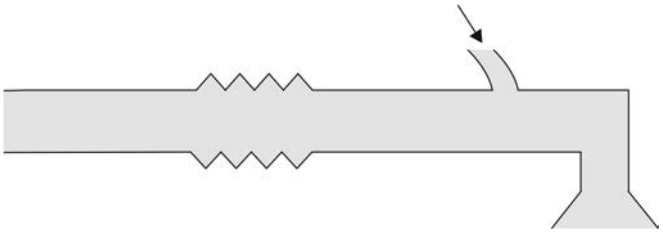


Fig. 6.63: Maplesons E system[4]

Technique of Use

- Expiratory limb open to atmosphere for spontaneous ventilation
- Controlled ventilation by occluding expiratory limb and allowing FG to inflate lung.

Functional Analysis

- Similar to Mapleson D
- Rebreathing depends on:
  - FGF
  - Patients minute volume
  - Volume of exhalation limb
  - Respiratory pattern
  - Type of ventilation.

Rebreathing

- If no expiratory limb is present, no rebreathing is possible
- If expiratory limb is present, FGF kept at twice the MV to prevent rebreathing
- During controlled ventilation, no rebreathing as only FG inflates lung.

Air Dilution

- Not possible during controlled ventilation
- During spontaneous ventilation, if no expiratory limb is present or volume of limb is less than patients tidal volume, air dilution prevented by providing FGF > PIFR (3–4 times MV)
- FGF of twice MV with reservoir of 1/3rd tidal volume prevents air dilution.

Disadvantages

- Barotrauma during controlled ventilation
- Cannot assess lung compliance
- No APL valve to buffer pressure.

Modifications

- FGF inlet extending inside T-piece body towards patient connection
- Pressure limiting device addition.

MAPLESON F[1,2,3,4]

Description

- ***Jackson Rees modification of T-piece***
- Hole in tail/side of bag to vent gases
- Ventilator may be used instead of bag
- APL valve may be placed at patient end to protect against high pressure
- Scavenging by enclosing bag in chamber which is suctioned.

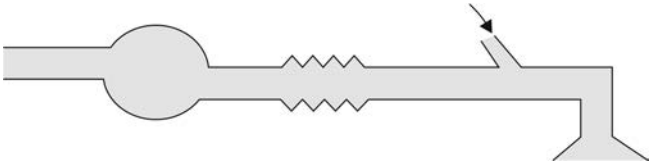


Fig. 6.64: Maplesons F system[4]

Technique of Use

- Relief mechanism, i.e. the hole in tail, is left fully open during spontaneous ventilation
- Relief mechanism is occluded during controlled ventilation
- HME not preferred with spontaneous ventilation
- FGF to be more than twice the minute volume.

Functional Analysis

- Similar to Mapleson D
- Decreased work of breathing than pediatric circle system
- If HME is added between patient and T-piece during inhalational induction, more of FGF will enter expiratory limb delaying induction as HME increase resistance.

Hazards

- No APL valve present to buffer pressure
- If ventilators are used, disconnection at common gas outlet may not be detected by airway pressure monitor due to high resistance of FG tubing.

CHAPTER

7

Cardiac Anesthesia

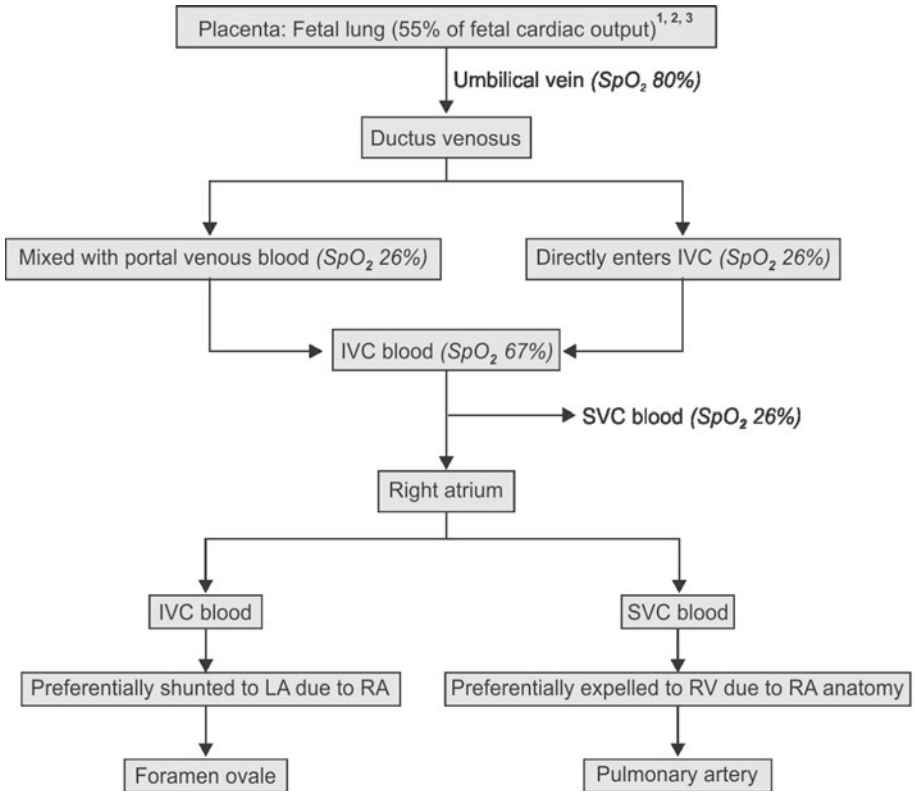
PHYSIOLOGY OF FETAL CIRCULATION[1,2,3,7]

Introduction

Fetal pulmonary and systemic circulation are essentially in parallel instead of in series as in adults due to two anatomical shunts, the ductus arteriosus and foramen ovale.

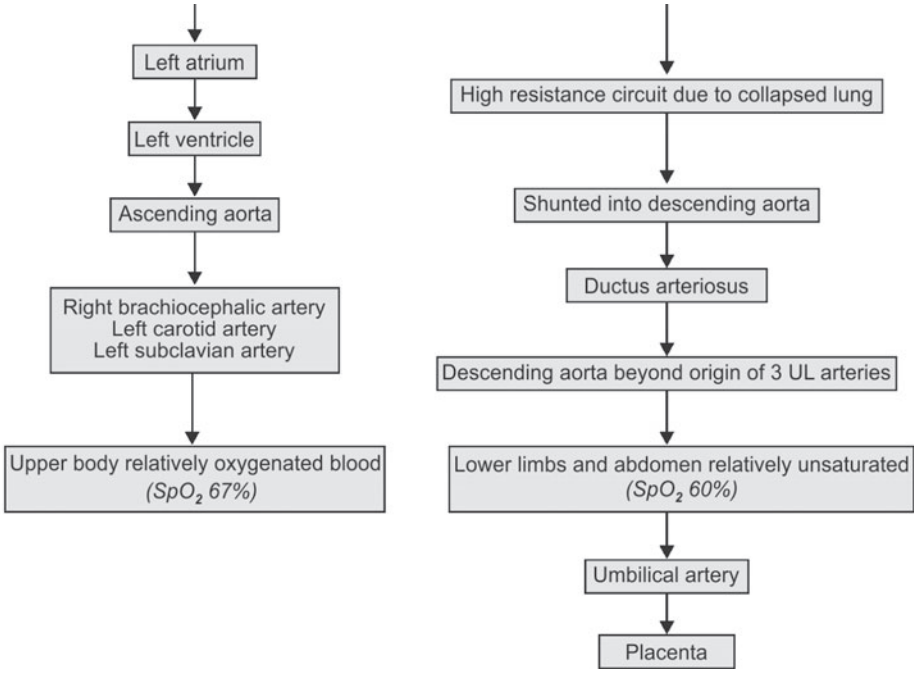
Fetal Circulation

- Fetal pulmonary circulation is essentially a high resistance circuit
- This is due to collapsed nature of the lungs in-utero
- Pulmonary capillaries are formed only after 24–25 weeks of gestation
- These later come to lie close to an immature alveolar epithelium.



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Changes Occurring at Birth

- The major cardiopulmonary adaptations at birth are:
  - Recovery from births asphyxia
  - Reflex initiation of breathing and expansion of lungs
  - Establishment and maintenance of adequate spontaneous ventilation
  - Conversion of fetal parallel circulation into series adult circulation.
- Closure of ductus arteriosus:
  - Occurs mainly due to reduction in pulmonary vascular resistance
  - This causes pulmonary vascular resistance to equalize SVR
  - Thus, blood flow decreases through ductus arteriosus
  - Eventually, ductus arteriosus closes
  - Physiological closure occurs at 10–15 hrs of life
  - Anatomical closure occurs at 2–4 weeks of life
  - Chemical mediators which aid in DA closure:
    - Prostaglandins
    - Bradykinin
    - Acetylcholine.
  - Factors causing reduced pulmonary vascular resistance:
    - Clamping of umbilical cord:
      - This separates fetus from placenta (fetal lung)
      - Thus, source of oxygenated blood is removed
      - This causes fetus to become increasingly asphyxia
      - Finally fetus gasps several times
      - Respiratory efforts initiated at 30 seconds
      - Efforts become sustained at 90 seconds.
    - ***Vaginal squeeze***:
      - Outward recoil of chest occurs as it passes through narrow vaginal vault
      - This makes intrapleural pressure negative (–30 to –50 mm Hg)
      - This causes expansion of lung
      - This factor is absent in cesarean section causing TTN.
- Closure of foramen ovale:
  - At birth, systemic vascular resistance increases
  - This causes an increase in LA pressure which causes closure of foramen ovale
  - Functional closure of foramen ovale occurs soon after birth
  - Anatomical closure occurs between 3 months to 1 year of life
  - Factors causing raised SVR:
    - Clamping of cord:
      - Causes increased umbilical artery pressure which raises SVR

    - Pushes around 100 ml of blood from placental circulation into systemic circulation (placental transfusion).
  - Increased LA pressure:
    - Increased pulmonary blood flow occurs due to reduction in PVR
    - This increases pulmonary venous return into left heart
    - Thus LA pressure increases, closing foramen ovale .
  - Vaginal squeeze:
    - Around 20–30 ml/kg of plasma ultrafilterate is present in fetal lungs
    - At birth, chest wall is squeezed as it passes through vaginal vault
    - Thus, ultrafilterate gets pushed into systemic circulation due to vaginal squeeze (90 ml).
- Fate of ductus venosus:
  - Ductus venosus atrophies as no blood flows from umbilical vein once it is clamped
  - It then forms *ligamentum venosum* of the liver.
- Thus the two sites of right to left shunting are closed at birth
- This converts fetal parallel circulation into adult circulation in series.

Applied Physiology

- Failure to establish adequate alveolar ventilation at birth will cause failure to recover from birth asphyxia.
- Conditions causing this are:
  - Congenital diaphragmatic hernia
  - Meconium aspiration
  - Congenital heart diseases
  - Polycythemia, infections
  - Hypoxia, hypercarbia, acidosis, prolonged stress
  - Raised PVR:
    - Truncus arteriosus
    - Pulmonary atresia.
- Persistent pulmonary HTN of newborn (PPHN):
  - Oxygen demand of fetus is 7 ml/kg/min
  - This increases to 18 ml/kg/min at birth before settling to 6 ml/kg/min
  - This is double the oxygen demand of adults (3 ml/kg/min)
  - This can cause rapid desaturation and further pulmonary vasoconstriction
  - This may lead to failure of closure of DA
  - Also reduced pulmonary venous return can cause persistent FO
  - Thus right to left shunting persists
  - This can worsen hypoxemia, leading to PPHN.

CLASSIFICATION OF CHD[1,2,3,5]

- Lesions causing outflow tract obstruction:
  - LVOT obstruction:
    - Coarctation of aorta
    - Aortic stenosis.
  - *RVOT obstruction:* Pulmonary valve stenosis
- Lesions causing left-right shunting:
  - Ventricular septal defects (VSD)
  - Atrial septal defects (ASD)
  - Patent ductus arteriosus (PDA)
  - Endocardial cushion defects
  - Partial anomalous pulmonary venous return (PAPVR).
- Lesions causing right-left shunting:
  - With decreased pulmonary blood flow
    - Tetralogy of Fallot (TOF)
    - Pulmonary atresia
    - Tricuspid atresia.
  - With increased pulmonary blood flow:
    - Transposition of great arteries (TGA)
    - Truncus arteriosus
    - Total anomalous pulmonary venous return (TAPVR)
    - Single ventricle
    - Double outlet right ventricle (DORV)
    - Hypoplastic left heart syndrome.

CORONARY CIRCULATION[1,2,3,5]

Introduction

- The coronary arteries encircle the heart like a crown and hence it is called coronary circulation.
- Averages around 250 ml/min at rest (5% of cardiac output).

Components

- Main components of coronary circulation are:
  - Right coronary artery
  - Left coronary artery
- Origin of coronary arteries:
  - Originate from the coronary sinuses present on the proximal aorta
  - Arise from just beyond the cusps of aortic semilunar valves
  - These are the first branches of proximal aorta
- Branches of right coronary artery:
  - Right marginal artery
  - Posterior descending artery

- Branches of left coronary artery:
  - Left circumflex artery
  - Left anterior descending artery.
- *Left coronary artery* is called ***widow artery*** as blockade of this artery results in sudden death.

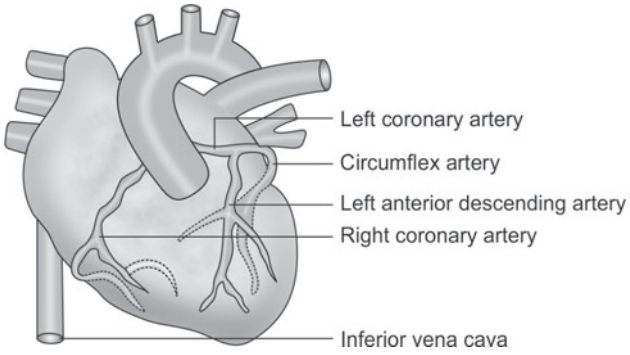


Fig. 7.1: Coronary circulation[2]

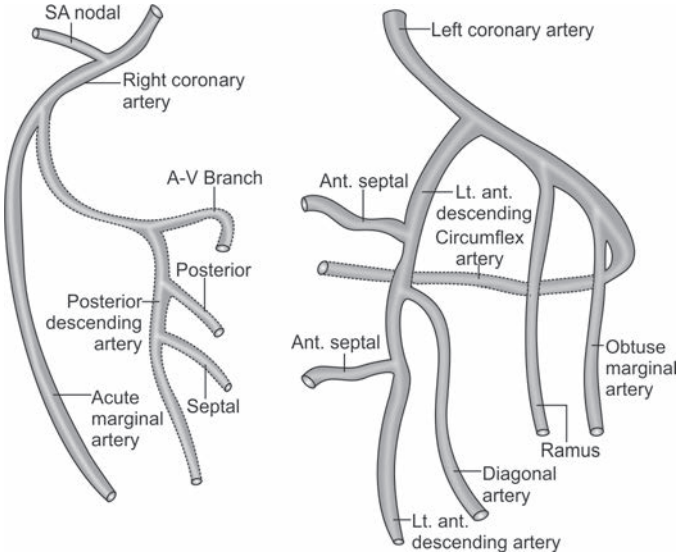


Fig. 7.2: Coronary circulation schematic[2]

Microcirculation

- The main coronary artery lies on the epicardial surface
- Branches of this penetrate the myocardium and supply the subendocardium with blood
- The diameter of these feeder branches is narrower and these are essentially end arteries.

Coronary artery	Part of myocardium supplied	Part of conduction system supplied
Right coronary artery		
Posterior descending artery	Right atrium	Sinoatrial node (60%)

Contd...

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Coronary artery	Part of myocardium supplied	Part of conduction system supplied
Right marginal artery	Right ventricle	Atrioventricular node (85–90 %)
	Inferior LV surface (85%)	Proximal part of bundle of His
	Posterior LV surface (85%)	Part of posterior fascicle of LBB
Left coronary artery		
Left anterior descending artery	Anterior surface of LV	Most of RBB
	Part of lateral surface of LV	Anterior fascicle of LBB
	Most of interventricular septum	Part of posterior fascicle of LBB
Left circumflex artery	Left atrium	Sinoatrial node (40%)
	Part of lateral surface of LV	Atrioventricular node (10–15 %)
	Inferior surface of LV (15%)	
	Posterior surface of LV (15%)	

Cardiac Dominance

- The artery giving rise to posterior descending artery is called the dominant artery
- Most often, PDA arises from right coronary artery
- Therefore, most often coronary circulation is right dominant circulation
- In about 10% of hearts, RCA is small and does not give rise to PDA
- In these cases, LCX continues as PDA
- Such cases are called left dominant coronary circulation.

Coronary Veins

- Coronary veins travel alongside arteries
- They drain into coronary sinus or directly into right atrium via ***Thebasian veins***
- Coronary sinus:
  - This is largest vein draining the heart
  - Receives 85% of coronary blood flow
  - Opens into posterior wall of right atrium
  - Lies in the atrioventricular groove
  - Veins draining into coronary sinus:
    - *Great cardiac vein:* Lies along anterior interventricular groove
    - *Anterior cardiac vein:* Lies along RCA
    - *Middle cardiac vein:* Along posterior interventricular groove.

- Anterior cardiac veins also empty directly into RA via Thebasian veins which receive remaining 15% of coronary blood.

PHYSIOLOGY OF CORONARY CIRCULATION[1,2,3,5]

Introduction

- Unique as it is intermittent rather than continuous as in other organs
- During contraction, intramyocardial pressure in LV approaches systemic arterial pressure, almost completely occluding intramyocardial part of coronary artery.

Normal Perfusion Curves

- Left ventricle is perfused during diastole
- Right ventricle is perfused during systole and diastole
- Normal coronary flow = 250 ml/min at rest
- Coronary autoregulation occurs between perfusion pressures of 50–120 mm Hg.

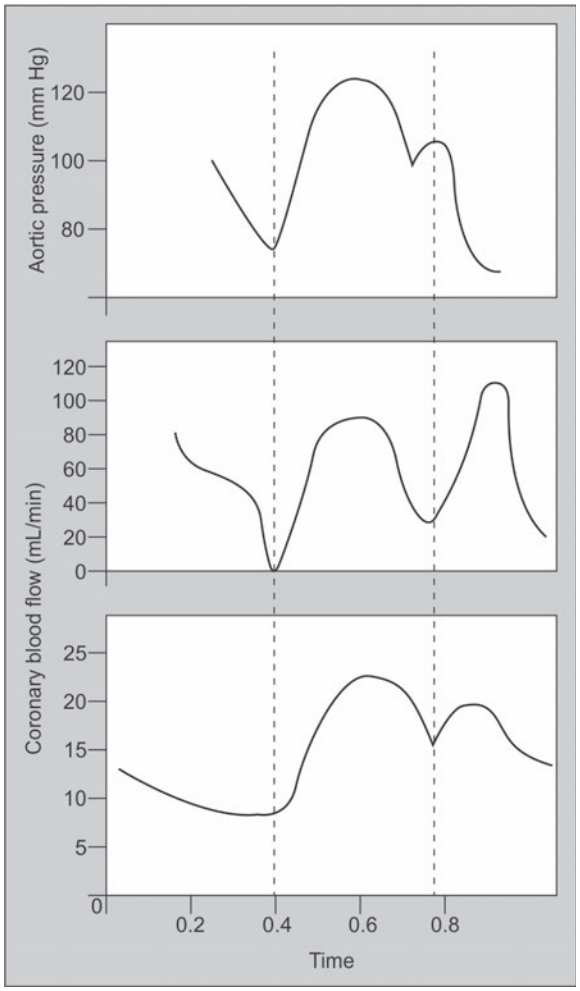


Fig. 7.3: Normal perfusion curves[2]

Determinants of Coronary Blood Flow

- Coronary perfusion pressure, coronary steal
- Myocardial metabolism, heart rate
- Myocardial extravascular compression
- Neurohumoral control:
  - Autonomic innervation
  - Coronary blood vessel diameter
  - Autoregulation.

Perfusion Pressure

- Coronary perfusion pressure = (Arterial diastolic BP) – (LVEDP)
- Arterial diastolic pressure is more important determinant of CBF than MAP.

Myocardial Metabolism

- Normal cardiac oxygen consumption = 80 – 100 ml/100 gm myocardium
- Flow-metabolism coupling
- Refers to link between myocardial metabolism and blood flow
- Factors which cause coupling:
  - Oxygen
  - Carbon dioxide
  - Nitric oxide
  - Adenosine
  - K_{ATP} channels.

Neural and Humoral Control

- Coronary innervation:
  - Sympathetic innervation:
    - From superior, middle and inferior cervical ganglia: Mainly stellate ganglion
    - Also from first four thoracic ganglia
  - Parasympathetic innervation by vagus nerve.
- β-adrenergic coronary dilation
- α-adrenergic coronary constriction
- Parasympathetic control of vagus.

Control of Coronary Blood Flow

- Autoregulation:
  - Refers to the tendency for organ blood flow to remain constant despite changes in arterial perfusion pressure
  - Occurs between MAP of 60–140 mm Hg
  - Occurs by metabolic coupling in blood vessels less than 150 μm
  - Critical mediator for autoregulation is oxygen, acting via adenosine.

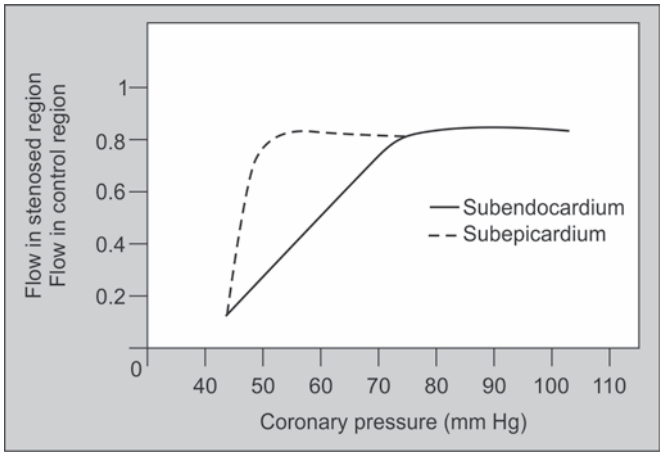


Fig. 7.4: Coronary autoregulation curve[2]

- Coronary reserve:
  - Intense vasodilatation occurs during MI, causing a large increase in blood flow
  - This is called reactive hyperemia
- Transmural blood flow.

Effects of Anesthetic Agents

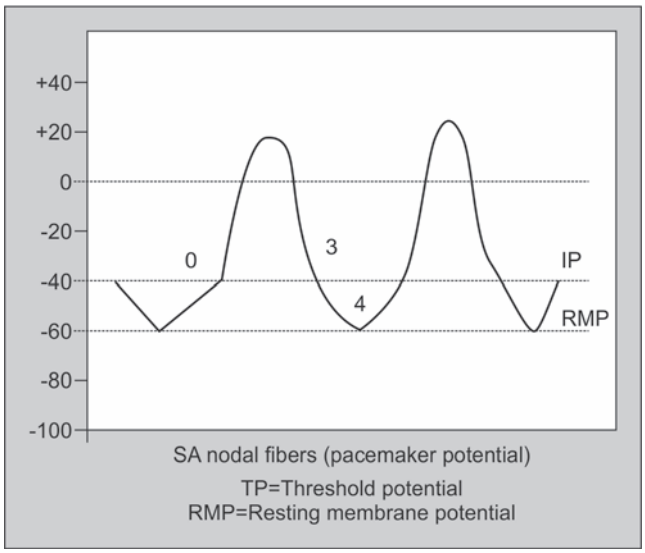
- Most volatile agents are coronary dilators through:
  - Action on ATP sensitive K^+ channels
  - Stimulation of adenosine A_1 receptors
- Halothane > isoflurane > desflurane > sevoflurane (negligible)
- Volatile agents protect against reperfusion injury
- They also reduce myocardial O_2 requirements during ischemia and infarction.

CARDIAC ACTION POTENTIAL[1,2,3,5]

Introduction

While action potential for skeletal muscle and nerve is due to abrupt opening of fast Na^+ channels, in cardiac muscle, it is due to opening of both fast Na^+ (spike) and slower Ca^{2+} channels (plateau).

Normal Action Potential



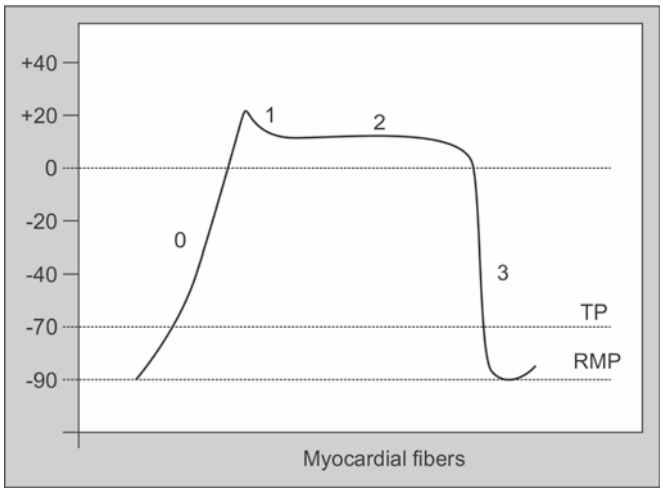


Fig. 7.5: Cardiac action potential[2]

Phase	Name	Event	Ion Movement
0	Upstroke	Opening of fast Na^+ channels	Na^+ comes into cell
1	Early rapid repolarization	Closure of Na^+ channels	K^+ goes out of cell
		Transient increase in K^+ permeability	
2	Plateau phase	Activation of slow Ca^{2+} channels	Ca^{2+} comes into cell
3	Final repolarization	Closure of Ca^{2+} channels	K^+ goes out of cell
		Increase permeability to K^+	
4	Resting potential	Normal permeability restored	K^+ goes out of cell
		Intrinsic slow leakage of Ca^{2+} into cells	Na^+ and Ca^{2+} enter cells

Events in Action Potential

Myocardial cells

↓

Normal ventricular resting membrane potential (–80 to –90 mV)

↓

Cell membrane potential is less negative

↓

Threshold potential reached (–70 mV)

↓

Action potential fired

↓

K^+ efflux once Ca^{2+} channels close

↓

Cell membrane potential becomes more negative

↓

Resting membrane potential

Pacemaker cells

↓

Normal sinoatrial resting membrane potential (–50 to –60 mV)

↓

Cell membrane potential less negative due to constant intracellular Na+ leakage

↓

Threshold potential reached (–40 mV)

↓

Action potential fired

↓

K^+ efflux, state of hyperpolarization

↓

Resting membrane potential

CARDIAC CYCLE[1,2,3,5]

Introduction

Sequence of electrical and mechanical events which occurs during course of a single heart beat.

Phases of Cardiac Cycle

- Atrial systole
- Ventricular systole:
  - Isovolumetric contraction
  - Rapid ejection phase
  - Slow ejection phase.

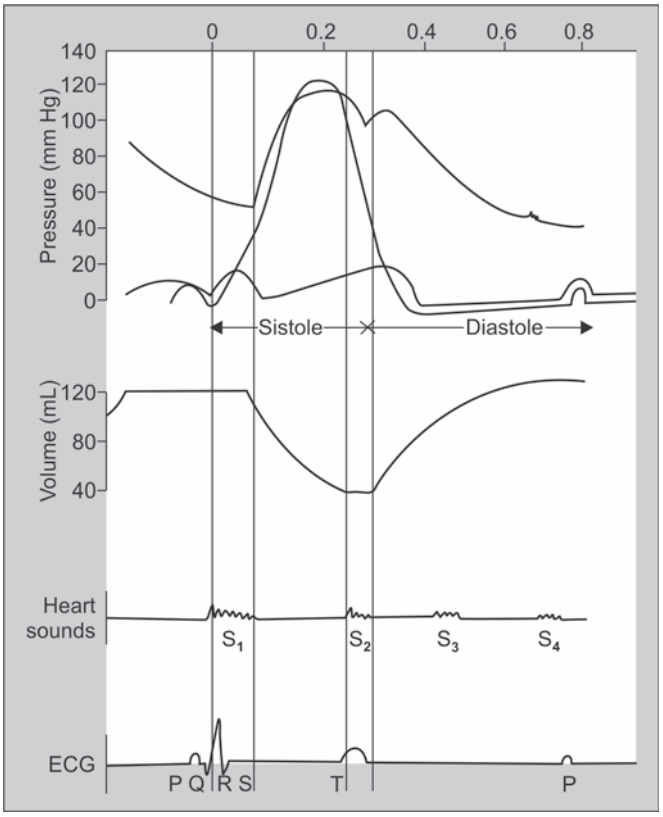


Fig. 7.6: Cardiac cycle[2]

- Ventricular diastole:
  - Isovolumetric relaxation
  - First rapid filling phase
  - Diastasis/slow filling phase
  - Second rapid filling phase.

Events in Cardiac Cycle

Atrial Systole

- Electrical event: P wave, PR interval
- Mechanical event:
  - Atrial systole/atrial kick
  - 25–30% cardiac output ejected
  - Fully completed before ventricle begins to contract.
- Pressure-volume event:
  - *a* waves in JVP
  - Atrial pressure increases.
- Heart sound event: S_4 produced, which is abnormal and seen in:
  - Massive pulmonary embolism
  - Cor pulmonale
  - Hypertrophic obstructive cardiomyopathy
  - Tricuspid regurgitation.

Isovolumetric Contraction

- Electrical event: QRS complex formed
- Mechanical event:
  - Atrioventricular valves close
  - Represents interval between closure of AV valves and opening of semilunar valves.
- Pressure volume event:
  - *c* wave in JVP
  - Contraction is isovolumetric, while intraventricular pressure increases.
- Heart sound event: S_1 produced due to closure of atrioventricular valves.

Rapid Ejection Phase

- Electrical event: Falls on QT segment
- Mechanical event: Semilunar valves open at the beginning of this phase
- Pressure volume event:
  - Opens up semilunar valve
  - Ejects blood, causing a sudden reduction in ventricular pressure
- *Heart sound event:* No event.

Slow Ventricular Ejection

- *Electrical event:* T wave due to repolarization
- *Mechanical event:* Aortic and pulmonary valves close at the end of this phase
- Pressure volume event:
  - Blood flow out of the ventricle reduces
  - Ventricular volume reduces more slowly
  - When ventricular pressure reduces below that in artery, semilunar valves open
- Heart sound event:
  - S_2 produced when semilunar valves close
  - Usually split S_2 as aortic valve closes before pulmonary valve.

Isovolumetric Relaxation

- *Electrical event:* No electrical deflection
- *Mechanical event:* Atrioventricular valves are closed, with closed semilunar valves
- Pressure volume event:
  - Atrial pressure increases, as blood collects passively
  - v waves occur in JVP
  - Ventricular pressure continues to fall
  - Ventricular volume is minimal.
- *Heart sound event:* S_2 occurs when semilunar valves close.

Rapid Filling Phase

- *Electrical event:* No events
- *Mechanical event:* Atrioventricular valves open
- Pressure volume event:
  - Blood from atria enters ventricles
  - Ventricular volume increases rapidly
- Heart sound event:
  - S_3 produced due to rapid passive filling of blood
  - Causes of S_3 gallop:
    - Myocardial infarction
    - Congestive cardiac failure
    - Hypertension.

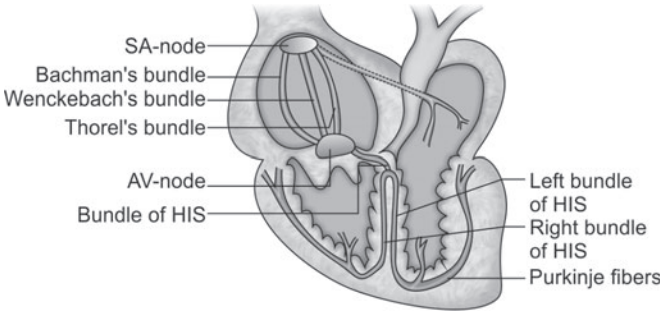
Diastasis

- *Electrical event:* No events
- *Mechanical event:* Rest of blood which has accumulated slowly flows into ventricles
- *Pressure volume event:* Ventricular volume increases more slowly
- *Heart sound event:* No events.

Second Rapid Filling Phase

- *Electrical event:* P wave, PR interval
- *Mechanical event:* Atrial systole/atrial kick
- Pressure-volume event:
  - *a* waves in JVP
  - Atrial pressure increases
- *Heart sound event:* S_4 produced.

CONDUCTION SYSTEM OF HEART[1,2,3,5]



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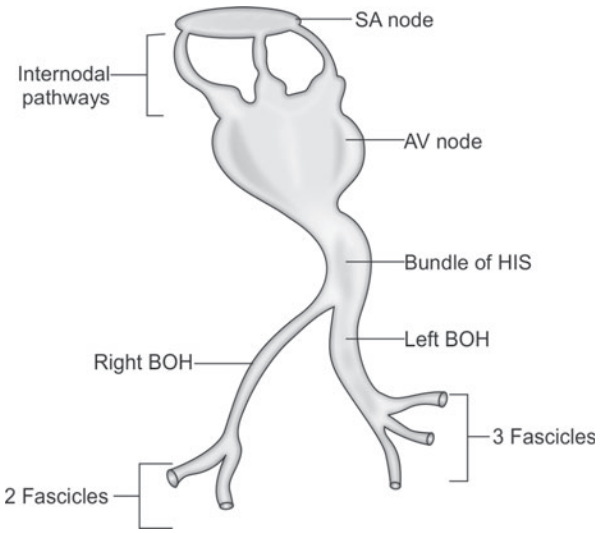


Fig. 7.7: Conduction system of heart[2]

Sinoatrial Node

- Location:
  - RA wall at SVC-RA junction
  - Located 1 mm below epicardial surface
  - ***Crista terminalis***
  - 50% cells have pacemakes activity
- Blood supply:
  - 60% RCA via SA nodal artery
  - 40% LCA
- Function:
  - Primary pacemaker of heart as it has fastest heart rate
  - Conduction to RA, interatrial septum, LA
- Intrinsic pacemaker activity:
  - 60–100 bpm
  - Called *sinus rhythm.*

Internodal Pathways

- Three pathways exist:
  - ***Bachmanns*** anterior bundle
  - ***Wenckebachs*** middle bundle
  - ***Thorels*** posterior bundle
- *Function:* Conducts impulses between SA node and AV node.

Atrioventricular Node

- Location:
  - Floor of RA
  - Situated just behind septal leaflet of tricuspid valve
  - Present near opening of coronary sinus.
- Anatomy:
  - Fibres are smaller with lesser gap junctions: Permits for AV nodal delay
  - Three functional regions:
    - Atrionodal region
    - Nodal region
    - Nodal-HIS regions.
  - AV delay occurs at Atrionodal and Nodal regions.
- Blood supply:
  - 90% RCA
  - 10% left circumflex artery.
- Function:
  - Receives impulses from SA node
  - Delays relay allowing atria to empty before ventricles contract.
- Intrinsic pacemaker activity:
  - 40–60 bpm
  - Called *junctional rhythm.*

Bundle of HIS

- *Location:* Upper part of interventricular septum
- Anatomy:
  - Divides into right and left Bundle of HIS
  - Right BOH has 3 fascicles
  - Left BOH has 3 fascicles:
    - Anterior fasciculus
    - Septal fasciculus
    - Posterior fasciculus
- *Blood supply:* Dual blood supply to left posterior fasciculus via LAD and PDA
- Function:
  - Receives impulses from AV node
  - Conducts them to Purkinje fibers
- *Intrinsic pacemaker activity:* 40–60 bpm.

Purkinje Fibers

- Location:
  - In ventricular myocardium
  - Penetrates one-third of ventricular myocardium.
- Function:
  - Fastest speed of conduction
  - Receives impulses from Bundle of HIS
  - Conducts them to ventricular myocardium.
- *Intrinsic pacemaker activity:* 20–40 bpm.

Variations

Pre-excitation Syndromes

- Terms used to describe rhythm that originate from above the ventricles but in which impulse travels via a pathway other than AVN and BOH.

- Types:
  - ***Wolff-Parkinson: White syndrome*** via ***bundle of Kent***
  - ***Lown-Ganong: Levine syndrome*** via ***James bundle***
  - ***Mahaim fibers.***

PRE-EXCITATION SYNDROME[1,2,3,5]

Introduction

Pre-excitation is a term used to describe rhythms that originate from above the ventricle but in which the impulse travels via a pathway other than the AV node and BOH.

Embryology

- During fetal life, strands of myocardial tissue form connection between the atria and ventricles, outside the normal conduction system
- These strands normally become nonfunctional soon after birth
- In patients with pre-excitation syndrome, these connections persist
- These strands form congenital malformations of working myocardial tissue.

Types of Malformations

- *Accessory pathways*: Bypass part or whole of the normal conduction system
- *Bypass tracts*: When one of the accessory pathway is attached to normal conductive tissue.

Examples: There are 3 major forms of pre-excitation syndromes:

- ***Wolff-Parkinson-White (WPW) syndrome***:

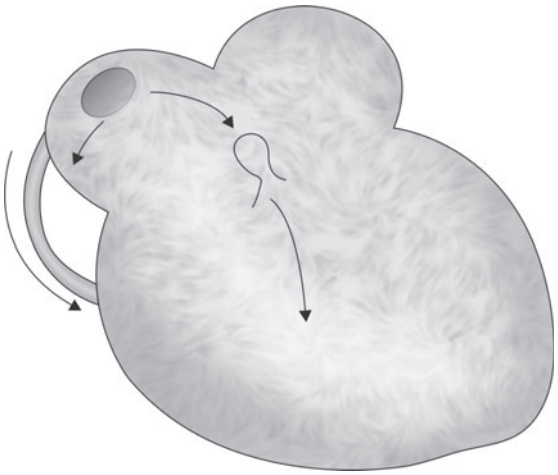


Fig. 7.8: WPW syndrome

  - The accessory pathway is called *Bundle of Kent*
  - This connects atria directly to ventricles, by passing the normal conduction system
  - Thus, the AV node is bypassed
  - Hence, AV nodal delay does not occur.
- ***Lown-Ganong–Levine syndrome:***
  - The accessory pathway is called *James bundle*
  - This connects atria directly to lower part of AV junction
  - Thus, it partially bypasses AV node.

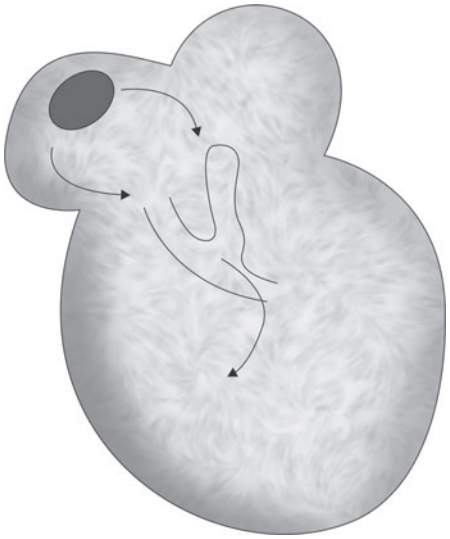


Fig. 7.9: LGL syndrome

- ***Mahaim fibers***:
  - These cause an unnamed pre-excitation syndrome
  - Fibers originate below AV node and insert into ventricular wall
  - This bypasses the ventricular conducting system.

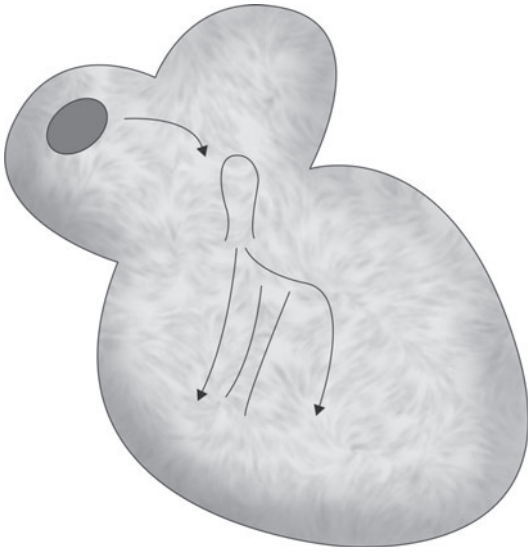


Fig. 7.10: Mahaim fibers

Incidence
- 1.5–3.1 per 1000 individuals
- More commonly occurs in men
- WPW syndrome is *most common* type of pre-excitation syndrome.

Description
- WPW syndrome
  - Delta waves
  - Short PR interval
  - Wide QRS duration (> 0.12 seconds)
- LGL syndrome:
  - No delta waves
  - Short PR interval
  - Normal QRS duration
- Mahaim fibers
  - Delta wave present
  - Normal PR interval
  - Widened QRS complexes.

Pathophysiology
- Patients with WPW are predisposed to tachyarrhythmias because of:
  - Accessory pathway bypassing the AV nodal delay
  - Pathway also provides a mechanism of re-entry
- Two types of re-entry are seen in WPW syndrome:
  - *Antidromic conduction*:
    - Rare variety
    - Occurs in an impulse generated from SAN
    - This travels via to ventricles via accessory pathway
    - Bypasses AV node on the way to ventricles
    - Impulse re-enters atria via AV node
  - *Orthodromic conduction*:
    - More common
    - Occurs in an impulse generated from SAN
    - This enters ventricles via AV node
    - Impulse re-enters atria via accessory pathway of Kent.

Clinical Features
- Palpitations, anxiety
- Light headedness, dizziness, weakness
- Chest discomfort, dyspnea, signs of shock
- *Complications:* Three main types of dysrrhythmias:
  - *AV nodal re-entrant tachycardia:* Most common
  - Atrial fibrillation
  - *Atrial flutter:* Least common.

Treatment
- Stable, symptomatic patient with orthodromic AVRT (narrow QRS):
  - Oxygen administration, IV access secured
  - Vagal maneuvers to convert rhythm
  - IV adenosine: May transiently increase risk of atrial fibrillation
  - IV calcium channel blockers/β blockers: Cause transient AV block
  - Avoid digoxin and verapamil as:
    - Conduction through AVN is slowed
    - This may speed up conduction through accessory pathway
- Stable, symptomatic patient with antidromic AVRT (wide QRS):
  - Oxygen administration
  - IV access secured
  - IV procainamide/amiodarone
  - Amiodarone preferred in CHF patients
- Unstable patients: Synchronized cardioversion.

CARDIAC OUTPUT[1,2,3,5]

Definition
Volume of blood ejected per minute from LV to aorta to support the metabolic demands of peripheral tissues.

Normal Values
- *Males:* 5–6 L/min
- *Females:* 10–20% less than males
- Children:
  - 350–400 ml/kg/min at birth
  - 150–200 ml/kg/min after first week of life
- *Cardiac index:* 3.2 L/min/m^2 (2.5–4.2 L/min/m^2)
- Body surface area calculated from nomogram based on weight and height.

Formula
- Cardiac output = stroke volume × heart rate
- Cardiac index = cardiac output/body surface area
- Stroke volume = (End diastolic volume) – (End systolic volume).

Factors Affecting Cardiac Output
- Factors increasing cardiac output:
  - Fever, raised BMR, exercise, pregnancy
  - Posture: Supine, lithotomy, trendelenburg
  - Anemia, beri-beri, hyperthyroidism
  - Arteriovenous fistula.

- Factors decreasing cardiac output:
  - Sleep, heart rate more than 120 bpm
  - Posture: Standing up, sitting
  - Reduced ventricular compliance due to:
    - Myocardial infarction
    - Valvular heart disease
    - Cardiac tamponade
    - Left ventricular hypertrophy
  - Reduced venous return due to:
    - Hemorrhage
    - Acute venodilatation, spinal anesthesia
    - Venous obstruction
    - Intermittent positive pressure ventilation.

Factors Affecting Stroke Volume

Preload

Definition

- Represents filling of heart chamber with blood during diastole
- Represents the muscle length prior to contraction or end diastolic fiber length
- Venous return is the amount of blood flowing from veins into RA each minute.

Formula

$$\text{Venous return} = \frac{\text{(Arterial pressure) – (RA pressure)}}{\text{Total peripheral resistance}}$$

- 55 to 60% of blood in body is in systemic veins
- Equivalent of EDV of LV in intact heart (normal around 120 ml).

Determinants of Preload

- Determinants of ventricular filling
- Venous return, blood volume
- Rhythm (artrial contraction)
- Heart rate
- Distribution of blood volume:
  - Posture
  - Intrathoracic pressure
  - Pericardial pressure
  - Venous tone (major determinant).
- Determinants of ventricular compliance:
  - Hypertrophy, asynchrony
  - Ischemia, fibrosis
  - Pericardial disease
  - Overdistension of contralateral ventricle
  - Increased pleural/airway pressure
  - Tumors, surgical compression.

Measurement of Preload

- Pulmonary artery pressure, PCWP
- CVP is poorest estimate of LV preload
- LVEDV via echocardiography
- LVEDP via cardiac catheterization.

Afterload

Definition

- Force which the heart must pump against, in ejecting blood from the heart
- SVR accounts for 95% of resistance to ejection.

Formula

$$\text{SVR} = \frac{\text{(MAP – RAP)}}{\text{CO}} \times 80$$

$$\text{PVR} = \frac{\text{(PAP – LAP)}}{\text{CO}} \times 80$$

- Normal SVR = 900–1500 dynes seconds/cm^{-5}
- Normal PVR = 150–250 dynes seconds/cm^{-5}
- SVR represents ratio of pressure to cardiac output.

Factors Affecting Afterload

- Viscosity and density of blood
- Aortic pressure, SVR
- Aortic valve area, vascular distensibility
- Volume and thickness of LV
- Systolic intraventricular pressure.

Contractility

Definition

- Myocardiums intrinsic ability to generate work from a given end diastolic fiber length
- Intrinsic force of myocardial contraction in inotropic state.

Factors Affecting

- Increased by:
  - Sympathetic activity
  - Calcium
  - Noradrenaline
  - Digoxin.
- Decreased by:
  - Parasympathetic activity:
  - Increased K^+ levels
  - Magnesium ions
  - Acidosis, hypoxia
  - β blockers, calcium channel blockers.

Measurement of Contractility

- Ejection fraction
- Isovolumetric contraction phase indices (d_p/d_t)
- Load dependent indices (slope of end systolic – pressure volume relation)
- Preload recruitable stroke work
- LV systolic wall thickening.

Heart Rate

- *Normal:* 60–80 bpm
- Formula:
  - Maximum heart rate = (220 – age in years)
  - Normal intrinsic heart rate = 118 bpm – (0.57 × age)
- *Factors increasing heart rate:* Exercise, fever, stress, high BMR
- *Factors decreasing heart rate:* Sleep, hypothermia, low BMR
- CO decreases progressively when heart rate ≥ 120 bpm, as diastolic filling time reduces.

Frank Starling's Law

Introduction

- Force of contraction of muscle is directly proportional to initial length of muscle fiber
- Represents the ability of heart to change its force of contraction and therefore stroke volume in response to changes in venous return.

Uses

- Illustrates relationship between CO and LVEDV
- Illustrates relationship between SV and RAP.

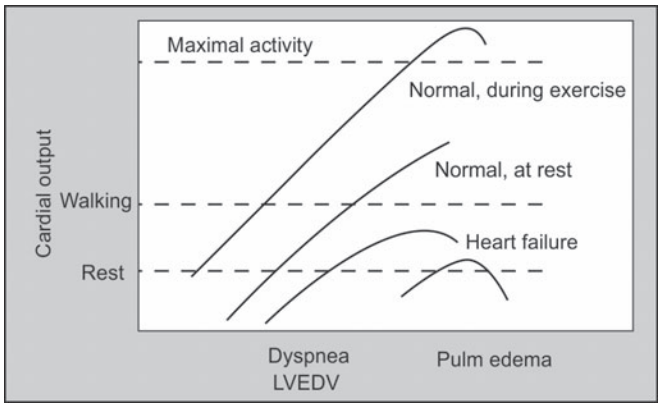


Fig. 7.11: Frank–Starlings law[3]

MYOCARDIAL OXYGEN SUPPLY DEMAND BALANCE[1,2,3,5]

Introduction

- Normal cardiac oxygen consumption = 80–100 ml O_2/100 g myocardium
- Normal oxygen supply = 250 ml/min
- Myocardium usually extracts 75–80% oxygen in arterial blood, compared with 25% in most other tissues
- Thus, it cannot compensate for a decrease in blood flow by extraction of more oxygen from hemoglobin
- This must be met with, by an increase in CBF.

Factors Affecting Supply

- Coronary blood vessel diameter
- Autonomic innervation
- Autoregulation
- Coronary steal
- Coronary perfusion pressure:
  - Aortic diastolic blood pressure
  - LVEDP/RVEDP
- Arterial oxygen content:
  - Arterial oxygen tension
  - Hemoglobin concentration
- *Heart rate:* Diastolic time
- Exogenous substances:
  - Oxygen, carbon dioxide
  - Nitric oxide
  - Adenosine
  - K^+, Ca^{2+}
  - pH, osmolarity.

Factors Affecting Demand

- Basal requirements (20%)
- Heart rate (most important)
- Wall tension:
  - Preload (ventricular radius)
  - Afterload
- Contractility.

Coronary Steal Phenomenon

- Occurs where perfusion pressure for a vasodilated vascular bed (in which flow is pressure dependent), is lowered by vasodilation in a parallel vascular bed; both beds being distal to a stenosis
- There is no evidence of coronary steal due to anesthetic agents in humans.

- Two types of coronary steal:
  a. Collateral steal
  b. Transmural steal.

Collateral Coronary Steal

- If arterioles of R_2 dilate, flow across R_1 to R_2 increases
- However, as R_3 arterioles are maximally dilated at rest, due to autoregulation, R_3 does not dilate anymore
- Hence flow across R_3 reduces.

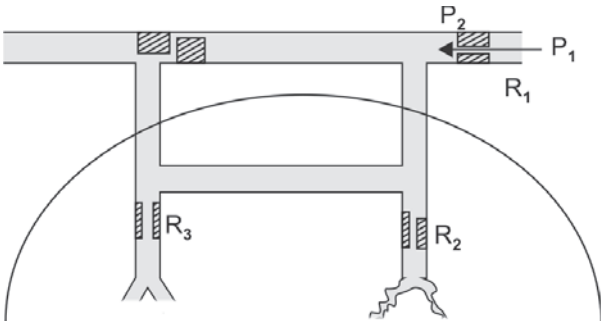


Fig. 7.12: Collateral coronary steal phenomenon

Transmural Coronary Steal

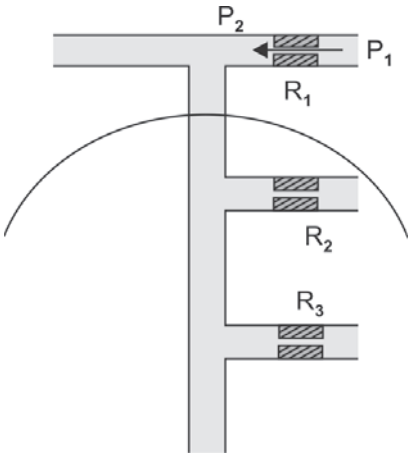


Fig. 7.13: Transmural coronary steal phenomenon

VENTRICULAR PRESSURE-VOLUME LOOPS[1,2,3,5]

Introduction

Aids to visualize changes in ventricular function in response to changes in preload, afterload and inotropy.

Method: LV pressure (LVP) is plotted against LV volume at multiple time points in the cardiac cycle.

Normal P-V Loop

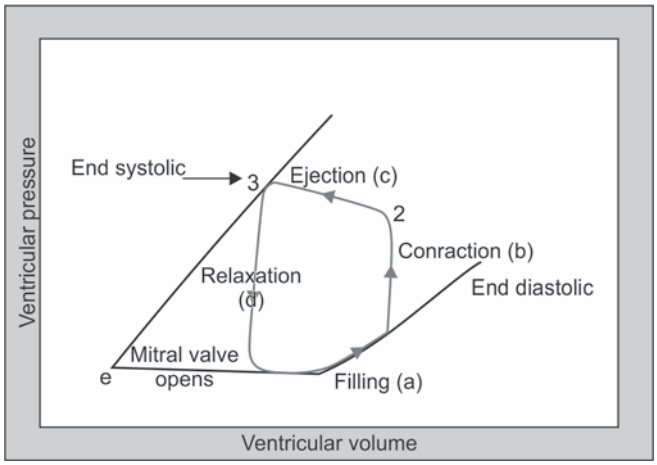


Fig. 7.14: Normal pressure-volume loop[2,3,5]

Point or phase	Event
Point 1	Mitral valve closes
Point 2	Aortic valve opens
Point 3	Aortic valve closes
Point 4	Mitral valve opens
Phase A	*Filling phase*
	Ventricles fill with blood
	LV volume increases
	LV pressure is constant at first and then slowly increases: Almost horizontal line
	Represents LVEDV and LVEDP
Phase B	*Isovolumetric contraction*
	Ventricular pressure increases
	Ventricular volume remains constant: Vertical line
Phase C	*Ejection phase*
	LV volume reduces
	LV pressure increases to a peak value called *peak systolic pressure*
Phase D	*Relaxation phase*
	LV volume remains constant initially due to isovolumetric relaxation
	When passive filling occurs, LV volume slowly increases
	LV pressure decreases during the entire process: Thus vertical line

Pressure Volume Loop in Mitral Stenosis

- Impaired LV filling occurs in mitral stenosis
- This reduces LVEDV which reduces stroke volume and CO
- This causes a low aortic pressure
- This results in a reduced width of curve (i.e. stroke volume) and low LVEDV.

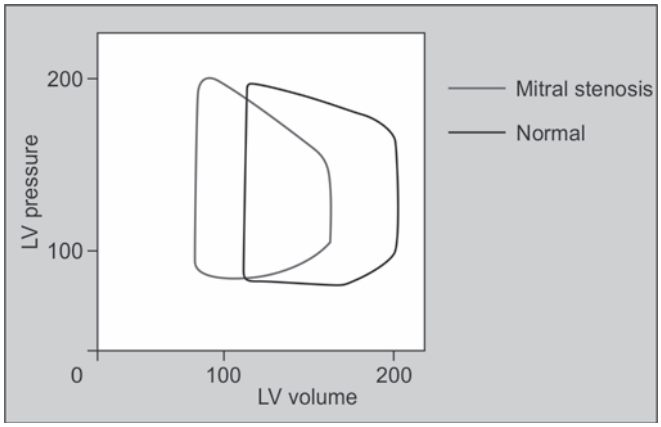


Fig. 7.15: Pressure volume loop in mitral stenosis[5]

Pressure Volume Loop in Mitral Regurgitation

- No true isovolumetric contraction phase present in MR, as blood flows back into LA during this phase
- Width of PV loop is increased (i.e. stroke volume is increased), as blood is ejected into aorta and also back into LA.

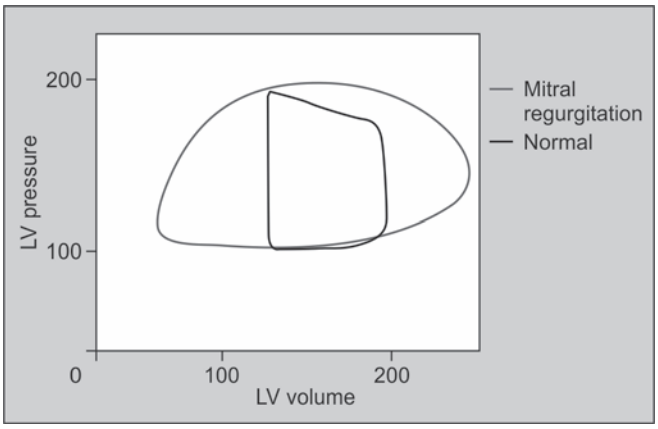


Fig. 7.16: Pressure volume loop in mitral regurgitation[5]

Pressure Volume Loop in Aortic Stenosis

- LV emptying is impaired causing a reduced stroke volume (small width of loop)
- High peak systolic pressures
- Raised end systolic volume and end diastolic volume.

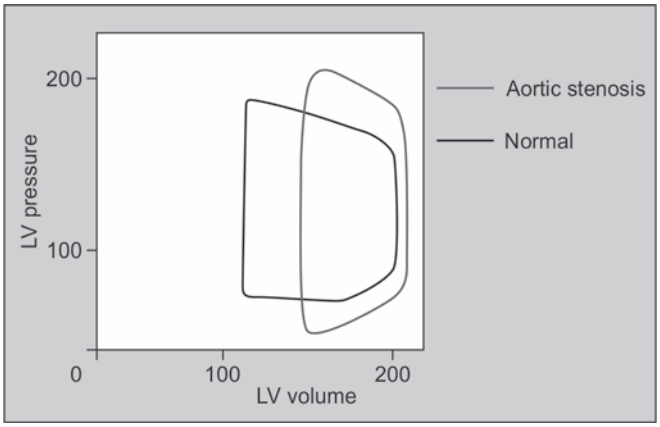


Fig. 7.17: Pressure volume loop in aortic stenosis[5]

Pressure Volume Loop in Aortic Regurgitation

- No true isovolumetric relaxation/contraction
- Greatly increased EDV, as blood flows from aorta and LA into LV
- Raised stroke volume, as volume from LA and aorta is ejected out.

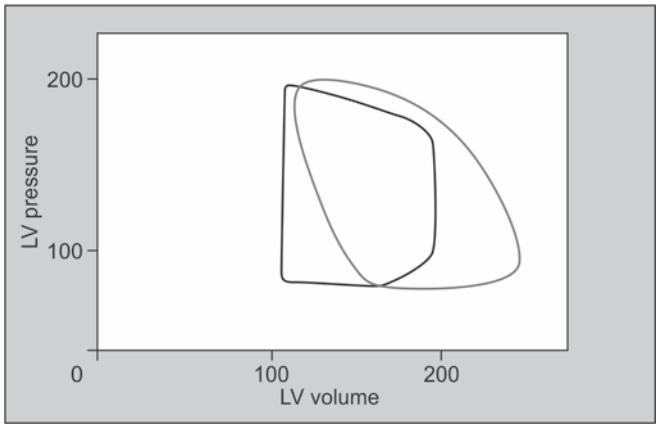


Fig. 7.18: Pressure volume loop in aortic regurgitation[5]

ASSESSMENT OF VENTRICULAR FUNCTION

Assessment of Systolic Function

- Initial rate of rise of arterial pressure tracing
- Change in ventricular pressure overtime during systole (d_p/d_t)
- Ejection fraction
- Ventricular pressure-volume loops
- Preload recruitable stroke work
- LV systolic wall thickening.

Assessment of diastolic function: Using Doppler ECHO via TTE/TEE.

Ejection Fraction

Introduction

- Fraction of end diastolic volume which is ejected from the ventricle
- This measures systolic function of heart.

Calculation

$$\text{Ejection fraction} = \frac{\text{Stroke volume}}{\text{End diastolic volume}} = \frac{(\text{EDV}-\text{ESV})}{\text{EDV}}$$

Normal value: 0.67 ± 0.08

Measurement

- Transthoracic ECHO
- Transesophageal ECHO
- Cardiac catheterization
- Radionucleotide studies.

Grading of LV Dysfunction

Ejection fraction	Grade
• 40–50	• Mild dysfunction
• 25–40	• Moderate dysfunction
• Less than 25	• Severe dysfunction

Factors Reducing Ejection Fraction

- MI/ischemia
- HOCM/DCM
- Myocarditis, amyloid infilterates
- Chronic pressure/volume overload
- HTN, LVF/CCF
- Congenital and valvular heart diseases
- Anemia
- Hypo/hyperthyroidism/pheochromocytoma.

Ventricular Function Curve

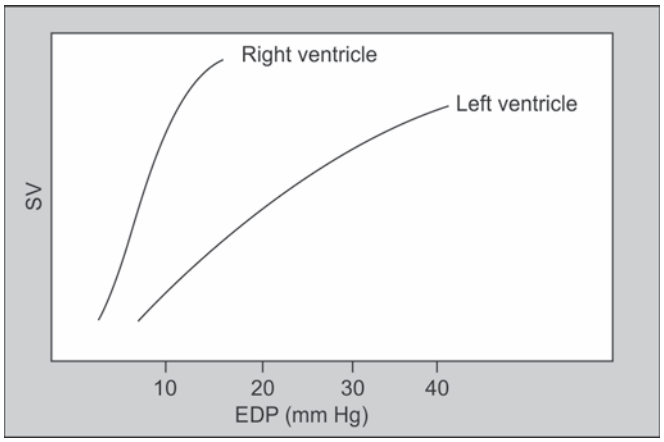
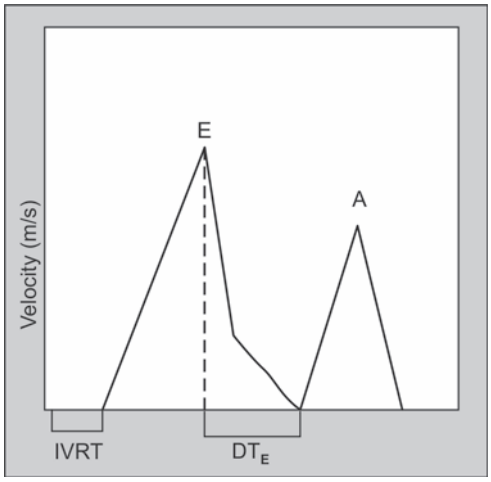
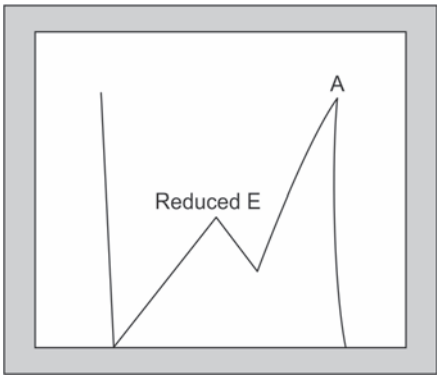


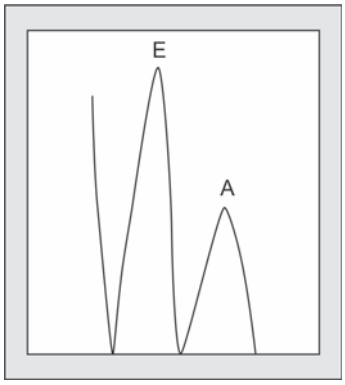
Fig. 7.19: Ventricular function curve

Assessment of Diastolic Function

- Flow velocities across mitral valve measure during diastole
- Three patterns of diastolic dysfunction based on isovolumetric relaxation time, which is the ratio of peak early diastolic flow (E) to peak atrial systolic flow (A)
- Deceleration time (DT) of E (DT_E) also measured and used to categorize diastolic dysfunction.







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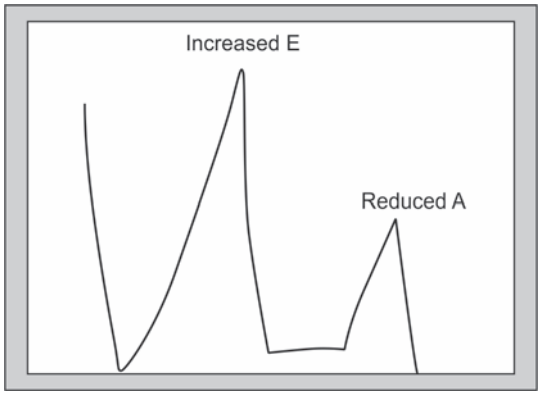


Fig. 7.20: Diastolic dysfunction curves

CAUSES OF INTRAOPERATIVE BRADYCARDIA[1,2,3,5]

Introduction

- Bradycardia is one of the most common arrhythmias that occur during anesthesia
- It may be hemodynamically significant particularly in patients with heart disease.

Causes

Intrinsic

- Systemic causes:
  - Hypoxia
  - Hypercarbia
  - Hypothermia < 34 °C
  - Raised ICT: ***Cushings reflex***
  - Drugs:
    - Opioids, volatile anesthetics, succinylcholine, vecuronium
    - Beta blockers, calcium channel blockers
    - Anticholinesterase inhibitors (neostigmine)
- Cardiac causes:
  - Sick sinus syndrome, sinus bradycardia
  - Junctional rhythm
  - AV nodal blocks
  - Myocardial infarction.

Vagal Response

- Traction on:
  - Extraocular muscles: ***Oculocardiac reflex***
  - Oropharynx (laryngoscopy and intubation, extubation)
  - Bronchus, peritoneum, bowel, rectum
- Right atrial distension
- Bladder distension.

Direct Effect

- Narcotics
- Volatile anesthesia
- Regional anesthesia
- High spinal/spinal shock.

Intrinsic Causes

- Hypoxemia:
  - *Most common* cause
  - Causes cardiovascular and respiratory depression: Bradycardia, hypotension, decreased minute ventilation.
- *Raised ICT:* Causes cushings reflex:
  - Consists of hypertension, bradycardia, irregular respiration.
  - Cushings reflex occurs due to medullary ischemia
- Hypothermia:
  - Causes tachycardia initially due to sympathetic stimulation especially in the presence of shivering
  - Proportionate reduction in heart rate as temperature reduces below 34 ºC
  - Occurs due to direct effect of cold on SA node
  - Bradycardia is not affected by atropine or vagotomy.

Vagal Response

- Occurs due to stimulation of:
  - Oropharynx
  - Bronchus
  - Rectum
  - Peritoneum.
- Stimulation causes bronchospasm, bradycardia and hypotension in lightly anesthetized patient.
- Prevented by:
  - Using atropine IV
  - Topical anesthesia with local anesthetics
  - Adrenergic blocking agents
  - Deep anesthetic planes
  - Vasodilating agents.

Direct Anesthetic Effect

- Volatile anesthetics:
  - Mostly occurs with enflurane, isoflurane, halothane
  - Volatile agents directly depress SA node
  - Occurs after slope of phase II depolarization by affecting calcium flux across membrane.

- Regional block: Mild bradycardia on release of tourniquet may be seen.
- IV local anesthetic:
  - Fetal bradycardia seen when IV local anesthetic is given to mother
  - Paracervical block associated with 20–30% chance of bradycardia.
- Succinylcholine:
  - Bradycardia seen after first dose of SCH in children
  - In adults 80% cases present with bradycardia after second dose of SCH if given within 5 minute after first dose
  - This is due to:
    - Choline molecule from breakdown of SCH may sensitize patient to subsequent SCH
    - SCH may directly stimulate peripheral sensory receptors to produce bradycardia
    - SCH stimulation of parasympathetic NS.
- *Vecuronium:* Lacks vagolytic affect and thus may cause bradycardia.
- *Spinal anesthesia:* Bradycardia following SA is mediated by 3 reflexes:
  - ***Atrial/Bainbridge reflex***:
    - Reduction in venous return occurs following SAB
    - This causes reduced efferent output to cardioaccelerator fibers from the atria
    - This causes bradycardia.
  - ***SA node stretch reflex***:
    - Stretch receptors not stimulated in SAN due to reduced venous return following SAB
    - This causes bradycardia.
  - ***Bezold Jarisch reflex***:
    - Reduced venous return causes increased contractility of ventricle
    - This causes stretching of baroreceptors present in inferoposterior wall of left ventricle
    - This in turn increases vagal output from vasomotor center causing bradycardia.

DIAGNOSIS AND MANAGEMENT OF PERIOPERATIVE ARRHYTHMIAS[1,2,3,5,17]

Introduction

Arrhythmias are the most common perioperative cardiac abnormality in patients undergoing both cardiac and noncardiac surgery.

Etiology

- Patient related
  - *Geriatric age: Old age* increases chances of *atrial fibrillation*
  - *Thrombosis:* Coronary/pulmonary
  - History of coronary artery disease/recent cardiac ischemia
  - Subarachnoid hemorrhage
  - *Toxins:* Digoxin toxicity.
  - Trauma:
    - Cardiac tamponade
    - Tension pneumothorax
- Anesthesia related:
  - Light anesthetic plane/pain
  - Drugs:
    - *Halothane:* Enflurane
    - *Catecholamines:* Aminophylline
  - *Central neuraxial block:* Causes pharmacological sympathetectomy
  - Electrolyte imbalance:
    - Hypo/hyperkalemia
    - Hypo/hypermagnesemia: *Torsades de pointes.*
  - Mechanical irritation:
    - Central venous lines
    - Pulmonary artery catheter
    - Chest tubes
    - Tracheal intubation/extubation.
- Surgery related
  - Noncardiac surgery:
    - Traction on intestines
    - Carotid surgery—direct pressure on carotid body
    - Oculocardiac reflex
    - Neurosurgical causes.
  - Cardiac Surgery:
    - Cardiac compression on beating heart
    - Pericardial traction
    - Atrial sutures
    - Venous cannulation
    - Following release of aortic cross clamp.
- Miscellaneous:
  - Hypovolemia
  - Hypoxia
  - Hypercapnea
  - Hypoglycemia
  - Hypothermia/Fever
  - Acidosis
  - Thyrotoxic crisis.

Classification

- Bradyarrhythmias:
  - Sinus bradycardia
  - Heart block:
    - First degree
    - Second degree
    - Complete heart block.
- Tachyarrhythmias:
  - Narrow QRS (SVT) tachyarrhythmias:
    - Sinus tachycardia
    - Atrial premature complexes
    - Unifocal/multifocal atrial tachycardia
    - Atrial flutter
    - Atrial fibrillation
    - Paroxysmal supraventricular tachycardia (PSVT)
    - AV reciprocating tachycardia (AVRT)
    - AV nodal reentrant tachycardia (AVNRT)
  - Wide QRS tachyarrhythmias:
    - Ventricular premature extrasystole
    - Ventricular tachycardia
    - Ventricular fibrillation
    - Torsades de pointes.

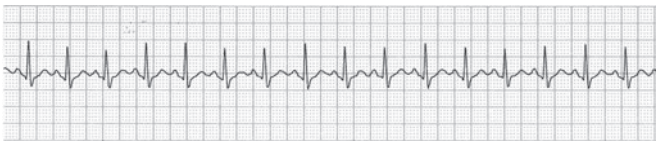
Mechanisms

- Automaticity enhanced:
  - *Normal:* Sinus tachycardia
  - Abnormal:
    - Unifocal atrial tachycardia
    - Accelerated idioventricular rhythms
    - VT post myocardial infarction.
- Triggerred activity:
  - Early after depolarization: Torsades de pointes
  - Late after depolarization:
    - Some VT
    - Digitalis induced arrhythmias.
- *Re-entry:* Sodium channel dependent:
  - Long excitable gap:
    - Atrial flutter
    - Circus movement tachycardia in WPW syndrome
    - Monomorphic VT.
  - Short excitable gap:
    - Atrial flutter
    - Atrial fibrillation
    - Circus movement tachycardia in WPW syndrome
    - Polymorphic VT
    - Monomorphic VT
    - Bundle branch re-entry
    - Ventricular fibrillation.
- *Re-entry:* Calcium channel dependent
  - AV nodal re-entrant tachycardia (AVNRT)
  - Circus movement tachycardia in WPW
  - Ventricular tachycardia.

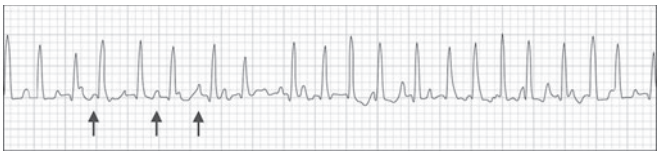
Diagnosis

Tachyarrhythmias

- Sinus tachycardia:
  - Rhythm—Regular
  - Rate—100–180 bpm
  - QRS duration—normal
  - P wave—visible before each QRS complex
  - PR interval—normal.



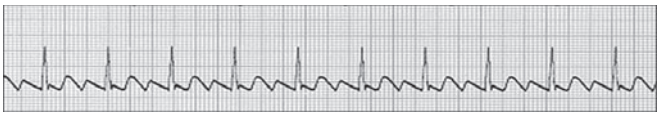
- Unifocal atrial tachycardia:
  - *Rhythm:* Regular
  - *Rate:* 75–200 bpm (ventricular), 120–250 bpm (atrial)
  - *QRS duration:* Normal
  - *P wave:* P wave with consistently abnormal morphology
  - *PR interval:* Usually normal.
- Multifocal atrial tachycardia:
  - *Rhythm:* Irregular
  - *Rate:* 75–200 bpm (ventricular), 120–250 bpm (atrial)
  - *QRS duration:* Normal
  - *P wave:* P waves of atleast 3 different morphologies
  - *PR interval:* Variable.



- Atrial Fibrillation:
  - *Rhythm:* Irregularly irregular
  - *Rate:* 100–160 bpm (ventricular), 400–600 bpm (atrial)
  - *QRS duration:* Usually normal
  - *P wave:* Indistinguishable, ***fibrillatory*** waves
  - *PR interval:* Not measurable.



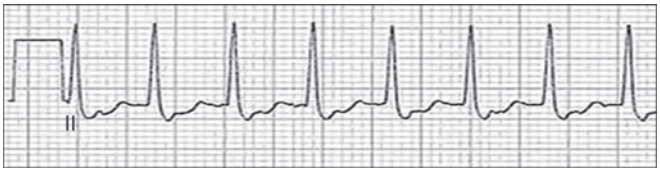
- Atrial flutter:
  - *Rhythm:* Regular
  - *Rate:* Around 110 bpm (ventricular), 250–350 bpm (atrial)
  - *QRS duration:* Usually normal
  - *P wave:* Replaced with multiple ***saw-tooth flutter waves***
  - *P wave rate:* 300 bpm, flutter wave: QRS complexes = 2:1.
  - *PR interval:* Not measurable.



- AV nodal re-entrant tachycardia:
  - *Rhythm:* Regular
  - *Rate:* 180–250 bpm
  - *QRS duration:* Normal, < 120 msec
  - *P wave:* Absent (buried within QRS complex) or occurs immediately after QRS complex
  - *PR interval:* Unmeasurable.



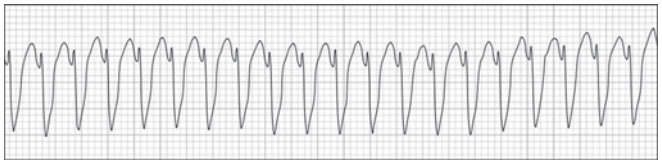
- AV reciprocating tachycardia:
  - *Rhythm:* Regular
  - *Rate:* 150–250 bpm
  - *QRS duration:* Normal in orthodromic, wider in antidromic with ***delta*** waves
  - *P wave:* Follows each narrow QRS complex in orthodromic AVRT
  - *PR interval:* Usually normal
  - *Orthodromic AVRT:* P wave follows each narrow regular QRS complex
  - *Antidromic AVRT:* Wider QRS complexes with ***delta*** waves.



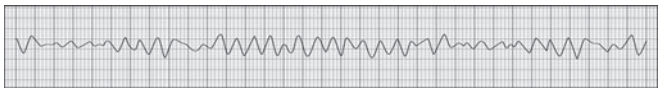
- AV junctional tachycardia:
  - Rhythm: Regular
  - *Rate:* 70–130 bpm (ventricular), 60–100 bpm (atrial)
  - *QRS duration:* Usually normal or widened with aberrant ventricular conduction
  - *P wave:* Inverted/abnormal morphology, irregular relationship with QRS complexes
  - *PR interval:* < 120 msec if present.



- Ventricular tachycardia:
  - *Rhythm:* Regular
  - *Rate:* 180–190 bpm
  - *QRS duration:* Prolonged
  - *P wave:* Not seen
  - *PR interval:* No measurable.



- Ventricular fibrillation:
  - *Rhythm:* Irregular
  - *Rate:* > 300, disorganized
  - *QRS duration:* Not recognizable
  - *P wave:* Not seen
  - *PR interval:* Not measurable.



Bradycardia

- First degree AV block
  - *Rhythm:* Regular
  - *Rate:* Normal
  - *QRS duration:* Normal
  - *P wave:* Ratio 1:1
  - *PR interval:* Prolonged > 20 msec.



- Second degree AV block type I (Wenckebach)
  - *Rhythm:* Regularly irregular

  - *Rate:* Normal or slow
  - *QRS duration:* Normal
  - *P wave:* Ratio 1:1 for 2–4 cycles and then 1:0
  - *P wave rate:* Normal but faster QRS rate
  - *PR interval:* Progressive lengthening of PR interval until a QRS complex is dropped.



- Second degree AV block type II (Mobitz)
  - *Rhythm:* Regular
  - *Rate:* Normal or slow
  - *QRS duration:* Prolonged
  - *P wave:* Ratio 2:1, 3:1
  - *PR interval:* Normal or prolonged but constant.



- Third degree AV block:
  - *Rhythm:* Regular
  - *Rate:* Slow
  - *QRS duration:* Prolonged
  - *P wave:* Unrelated
  - *P wave rate:* Normal but faster than QRS rate
  - *PR interval:* Variation.



Management

General

- Ensure adequate oxygenation and ventilation
- Deepen plane of anesthesia
- Ensure optimum PaO_2, $PaCO_2$
- Correct acid base imbalance and dyselectrolytemias
- Re-evaluate for cardiac pathology
- Prepare:
  - Anti-arrhythmic drugs
  - Anti-ischemic drugs
  - Pacing equipment
  - Defibrillator
- Vagal maneuvers:
  - Carotid massage
  - Ocular massage
  - Valsalva maneuver.

Specific Arrhythmia Treatment

- Supraventricular Tachycardia:
  - Adenosine—***drug of choice*** – 0.1 mg/kg bolus followed by 0.2 mg/kg after 2 minutes if refractory
  - Verapamil—***second drug of choice*** – 0.1–0.2 mg/kg at 1 mg/min
  - Diltiazem—0.25 mg/kg at 2.5 mg/min followed by 0.35 mg/kg if refractory
  - Metoprolol—0.1 mg/kg given every 5 mins to a maximum of 0.3 mg/kg
  - Rapid overdrive pacing
  - Radiofrequency ablation:
    - For AVNRT, focal atrial tachycardia, atrial flutter, atrial fibrillation
    - Ablation around pulmonary veins, coronary sinus, right atrium, SVC
    - Reduces frequency of recurrent atrial fibrillation in 60% patients.
- Atrial fibrillation:
  - Rate control:
    - Diltiazem: (***rule of 15*** in adults)
      - 0.25 mg/kg at 2.5 mg/min
      - Repeat the dose after 15 min if refractory
      - Infusion at 2.5 mg/kg/hr titrated to control ventricular rate.
    - Verapamil:
      - 0.1 mg/kg at 1 mg/min
      - Repeated in 30 mins
      - Watch for prolonged hypotension.
    - Beta blockers:
      - Esmolol 0.25–0.5 mg/kg followed by 0.05 mg/kg/min titrated to a maximum of 0.2 mg/kg/min
      - Propranolol 0.15 mg/kg given over 2 mins.
    - Digoxin:
      - 5–10 µg/kg IV rapid digitalizing dose
      - Half the total calculated dose administered first
      - Remaining dose administered in fractions at 6–8 hour intervals.
  - Anticoagulation:
    - Unfractionated heparin 80 IU/kg followed by 18 IU/kg infusion
    - Maintain aPTT 1.5 to 2 times reference value

- Gradually shift to warfarin therapy
- Maintain INR of 2–3 to prevent thromboembolic sequelae.

– Restore sinus rhythm:
  - DC cardioversion:
    - 200 J with monophasic defibrillator
    - 120–200 J with biphasic defibrillator
    - 0.5–1 J/kg increased to 2 J/kg if ineffective.
  - Chemical cardioversion:
    - Procainamide:
      * 10–15 mg/kg over 30–60 min until one of the four situations arise:
        - Arrhythmia suppression
        - Hypotension develops
        - QRS prolongation > 50% from baseline.
        - Maximum of 17–20 mg/kg has been administered
      * Maintenance dose 1-4 mg/min.
    - Ibutilide:
      * < 60 kg 0.01 mg/kg over 10 min
      * >60 kg 1 mg over 10 min.
    - Dofetilide:
      * Dose adjusted according to creatinine clearance
      * 250–500 mics PO Q12H.
    - Propafenone:
      * 150–300 mg PO Q8H immediate release
      * 225–325 mg PO Q12H extended release.
    - Amiodarone:
      * 5 mg/kg bolus dose over 20 mins
      * 1 mg/min infusion for 6 hrs
      * 0.5 mg/min maintenance for 18 hrs.

- Ventricular tachycardia/ventricular fibrillation:
  – Unsynchronized DC defibrillation
    - 200 J unsynchronized defibrillation with biphasic defibrillator
    - 360 J unsynchronized defibrillation with monophasic defibrillator
    - In children:
      - First shock 2J/kg, second shock 4 J/kg
      - Subsequent shocks > 4 J/kg up to maximum of 10 J/kg.
  – Resistant VT/VF:
    - Lidocaine:
      - 50–100 mg IV over 5 mins
      - Followed by 2–4 mg/min infusion
    - Amiodarone
      - 5 mg/kg bolus dose over 20 mins
      - May repeat twice for refractory cases
    - Bretilium:
      - 5–10 mg/min over 2–5 min
      - Followed by 1–2 mg/min.

MYOCARDIAL PROTECTION[1,2,3,5,17]

Introduction

Myocardial protection refers to the set of pharmacological and physiological strategies aimed at attenuating the intensity of myocardial ischemia-reperfusion injury during cardiac surgery and its consequences on myocardial function.

History

- Early efforts with topical hypothermia:
  – Caused postoperative myocardial depression
  – Also lead to myocardial contracture ***'stone heart'***
- This late led to potassium cardioplegia done by ***Melrose*** in 1955 with:
  – 2.5% solution of potassium citrate and blood
  – High levels of potassium used, produced direct myocardial damage.
- This was replaced in 1970s by cold hyperkalemic blood cardioplegia using lower potassium levels.

Goals of Myocardial Protection

- To provide a quite bloodless field
- Limitation of myocardial damage by reduction of:
  – Intracellular acidosis
  – Edema
  – Depletion of high energy phosphate stores (ATP)
- Preservation of coronary endothelial functions and myocardial flow
- Reduced reperfusion injury.

Principles

- Myocardial vulnerability to injury is a product of:
  – Preoperative functional class of patient
  – Presence of ventricular hypertrophy
  – Coronary artery disease.
- Myocardial protection should begin with preparation of heart prior to surgery
- Metabolic requirements should be reduced during arrest interval
- Favorable metabolic mileu during arrest provides a margin of safety with reduced metabolism
- Measures taken must represent a balance between requirement during aortic cross clamping and reperfusion.

- Reperfusion modification after an ischemic insult can minimize structural and functional damage to myocardium.

Determinants of Oxygen Supply

- Oxygen content of blood
- Aortic root pressure
- Autonomic innervation
- Ventricular pressure
- Local vascular resistance, autoregulation, coronary steal
- Diastolic perfusion time (Heart rate)
- Exogenous drugs.

Determinants of Oxygen Consumption: MvO_2

- Myocardial contractility (inotropy) = velocity of pressure development (dp/dt)
- Wall tension = $\frac{\text{Pressure} \times \text{Radius}}{2 \times \text{Wall thickness}}$
- Heart rate
- Basal oxygen consumption
- Work = Area within systolic pressure – volume loop.

Phases of Myocardial Injury

- Focal ischemia causes irreversible injury, manifested as myocellular necrosis after as little as 30 minutes following coronary occlusion in the intact working heart
- Similar period of global ischemia causes moderate to severe functional depression without obvious necrosis
- Myocardial injury sustained in the surgical setting is divided into 3 phases:
  - Antecedent ischemia:
    - Also called ***Unprotected ischemia***
    - Occurs prior to institution of CPB or delivery of cardioplegia solution.
  - *Protected ischemia:* Occurs during electively initiated chemical cardioplegia
  - Reperfusion injury: Occurs:
    - During intermittent infusion of cardioplegia solution
    - After removal of cross clamping
    - After discontinuing CPB.

Methods of Myocardial Protection

Measures Against Antecedent Ischemia

- Continue all preoperative cardiovascular drugs:
  - Antiarrhythmics
  - β blockers
  - Calcium channel blockers
  - Nitrates, aspirin
  - Digoxin.
- *Premedication:* Sedation for CABG patients
- Conversation to reduce level of anxiety
- Intubation response suppression:
  - *Lignocaine:* 1.5–2 mg/kg IV 90 seconds before intubation
  - *$MgSO_4$:* 20–60 mg/kg IV
  - *Nitroglycerine drip:* 0.5–10 µg/kg/min
  - *Labetolol/esmolol:* 20 mg IV or 300 µg/kg IV respectively
  - Deepen planes of anesthesia: Inhalational or fentanyl 1 µg/kg
  - Brief duration of laryngoscopy: ≤ 10 seconds
- Administration of glucose to increase hearts ability to tolerate ischemic arrest
- Avoid ventricular distension and fibrillatory arrest
- Control of heart rate to < 80 bpm in patients with coronary artery disease
- Adequate hydration to enable heart to tolerate hypotension prior to initiation of CPB
- Anesthetic preconditioning with volatile anesthetics.

Measures Against Protected Ischemia

- These measures are taken during the period of CPB:
  - Asystole with chemical cardioplegia
  - Hypothermia
  - Hypocalcemia
  - Buffering
  - Intermittent cross clamping with brief periods of reperfusion
  - Hypothermic ventricular fibrillation
  - Left ventricular venting.

Measures Against Reperfusion Injury

- Oxygen free radical scavenging
- IV sedation with propofol
- Anti-ischemic agents:
  - ATP sensitive potassium channel openers:
    - Cromokalim
    - Pinacidil
    - Nicorandil
  - Agents which increase intravascular adenosine:
    - 5-amino-4-imidazole carboxamide riboside deaminase inhibitors
    - Transport inhibitors.
- Monoclonal antibodies directed against neutrophil/endothelial components of adhesive glycoprotein complexes.

Asystole

Rationale of Use

- Continued electromechanical activity after cross clamping increases the rate of high energy phosphate depletion
- This causes a more rapid fall in ATP reserves before anoxic arrest ensues
- Intentional chemical induction of diastolic arrest avoids depletion of ATPs
- This conserves myocardial energy reserves
- Reserves can be used during ischemia to maintain ionic and metabolic homeostasis.
- Total electromechanical silence reduces oxygen demand by about 80–90% of which:
  - 30–40% of this reduction is contributed by ventricular decompression
  - The remainder is contributed by asystole accomplished by chemical cardioplegia.

Methods of Inducing Rapid Asystole

- Hyperkalemia
- Hypermagnesemia
- Hypocalcemia
- Calcium channel blockers
- Infusion of local anesthetic agents.

Hypothermia

Benefits

- Hypothermia with sustained myocardial activity reduces myocardial oxygen demand
- Hypothermia in combination with cardiac arrest reduces MVO_2 by 97% if cooling is done to < 22 °C
- Hypothermic cardioplegia increases the duration for which aortic clamping may be safely imposed from < 30 minutes to as much as 4 hours
- Hypothermia enables tissues to withstand complete interruption of blood flow for periods of 20–40 minutes.

Rationale

- Major methods of myocardial protection by hypothermia is:
  - Reduction in myocardial metabolic rate
  - Reduction in oxygen demand of myocardium.
- ***Vant Hoff's law/Q_{10} effect***:
  - MVO_2 in the quiescent heart reduces by 50% for every 10 °C reduction in temperature.
  - Greatest reduction in MVO_2 occurs between 37 °C and 25 °C
  - At 28 °C, a reduction in metabolic rate by 50% occurs
  - Q_{10} is the ratio of metabolic rates at two different temperatures
  - Normally, Q_{10} = 2 to 2.2.
- Greatest protection at 28 °C with little additional protection at temperature < 28 °C.
- Hypothermia is achieved on CPB by two methods:
  - *Passive cooling:* Patients core temperature is allowed to equalize with ambient temperature
  - *Active cooling:* Using heat exchanger.

Advantages of Hypothermia

S. No.	Advantages
1	Reduces myocardial metabolism
2	Reduces oxygen requirement
3	Reduced rate of degradative reactions
4	Reduced progression of ischemic injury
5	Reduced tolerable period of ischemia
6	Reduced potassium needed to accomplish arrest
7	Prolongs cardiac arrest
8	Inhibits intracellular Ca^{2+} gain
9	Reduces excitatory neurotransmitters

Disadvantages of Hypothermia

S. No.	Disadvantages
1	Reduces rate of reparative process
2	Increased myocellular swelling
3	Increases inotropic state and MVO_2 per beat
4	Induces fibrillation
5	Impairs oxygen dissociation
6	Impairs autoregulation
7	Poses threat of phrenic nerve ***freeze injury*** on local application of ice
8	Increases rouleaux formation in RBCs

Hypocalcemia

- Calcium plays a central role in excitation—contraction coupling
- Calcium is needed to transduce electrical signals into a mechanical event
- Removal of calcium from extracellular environment produces a negative inotropic effect
- This causes cessation of contractile activity at very low levels of extracellular ionic calcium.
- ***Calcium paradox***:
  - Can be precipitated in ischemic myocardium by moderate hypocalcemia

  - Hypocalcemic reperfusion causes extended infarct size after reversible coronary occlusion.
- Reduction of extracellular calcium done by direct chelation using:
  - Sodium citrate which may chelate other ions like magnesium
  - Alternative is EGTA.

Oxygen Radical Scavenging

- Hydrogen peroxide is an important transitional molecule in the oxygen radical cascade
- It is involved in ischemic reperfusion injury
- Infusion of cardioplegia is also a form of reperfusion during which injury can occur
- Enzymes and scavengers which inhibit or dismutate free radicals should be administered as a pretreatment therapy
- Free radical scavengers which can be used:
  - Superoxide dismutase
  - Catalase
  - Ibuprofen
  - Indomethacin
  - Nitric oxide.

Anesthetic Preconditioning

- Halothane:
  - Attenuates ST segment changes caused by brief coronary artery occlusion
  - Reduces ST elevation more than sodium nitroprusside and propranolol
- Isoflurane and sevoflurane:
  - Reduce myocardial reperfusion injury
  - Improve functional recovery after global ischemia
- Volatile anesthetics reduce MvO_2 due to:
  - Direct negative inotropic, lusitropic and chronotropic effects
  - Reduction in LV afterload (reduces SVR)
- Volatile anesthetics reduce oxygen free radicals and also cause coronary vasodilatation.

Propofol

- IV sedation with propofol after myocardial revascularization resulted in 17% less frequent incidence of tachycardia and 28% less frequent HTN.
- Infusion of propofol results in significant reduction in myocardial blood flow and myocardial oxygen consumption.
- High dose propofol (120 µg/kg/min) administered for CABG or OPCAB showed improved troponin levels and better hemodynamic function.

CARDIOPLEGIA[1,2,3,5,17]

Introduction

This is the intentional, temporary cessation of the heart for cardiac surgery, by which cardiac standstill is achieved using high potassium concentrations of 12–30 mEq/L within 1–2 minutes.

Mechanism

- Potassium containing cardioplegia solution arrests the heart in diastole
- This causes a diastolic arrest which allows for a longer ischemic time
- This reduces myocardial oxygen demand by ≥ 80%
- Exogenous potassium causes depolarization of myocyte membrane
- This renders the myocardium unexcitable during the time that potassium remains within the tissue
- Wash out of hyperkalemic cardioplegia solution by noncoronary collateral flow causes resumption of electrical and mechanical activity
- This is countered by intermittent (every 20–30 min) replenishment of cardioplegia solution.

Goals

- To provide a quiet and bloodless field.
- Limitations of myocardial damage by reduction of:
  - Intracellular acidosis
  - Edema
  - Depletion of ATP stores
- Preservation of coronary endothelial function and myocardial flow
- Reduce reperfusion injury.

Types

Based on Temperature

- Warm cardioplegia
  - Delivered at 37 °C
  - Mechanisms of action:
    - Reduces reperfusion injury
    - Preserves coronary endothelial function
    - Rapid establishment of myocardial energy stores
    - Reduces calcium influx
    - Causes less activation of lymphocytes
    - Up-regulates protective heat shock proteins
  - Single hot shot warm cardioplegia used for initiation and termination of arrest.
- Cold cardioplegia:
  - Delivered at 10 °C
  - Heat exchanger used
  - Reduces oxygen demand and ischemic damage
  - Ice is used for surface cooling.

Based on Contents

- *Crystalloid cardioplegia:* Using lactated ringers
- Blood cardioplegia:
  - *Using 4:1 or 8:1 concentration of blood:* Crystalloid
  - Blood useful as:
    - Acts as source of oxygen to heart
    - Buffering and antioxidant properties
    - Preferred in anemic and pediatric patients.

Methods of Delivery

- Anterograde:
  - Delivered into coronary arteries via aortic root through a needle placed between aortic cross clamp and aortic valve.
  - Can be delivered through individual grafts in CABG once distal anastomoses has been made
  - Most physiological
- Retrograde:
  - Delivered into coronary sinus through a balloon tipped cannula
  - Better distribution of cardioplegia in:
    - Significant coronary artery disease
    - Aortic regurgitation
    - Aortic valve surgeries
  - Adequate delivery to right ventricular myocardium and posterior one-third of septum is difficult
  - Should be delivered at < 40 mm Hg pressure to limit perivascular edema and hemorrhage.
- *Combined:* Thought to be superior to either of the above.

Timing of Delivery

- Intermittent cardioplegia:
  - Initially 1–1.5 L of *high potassium* cardioplegia (CP) delivered
  - Then 200–500 ml of *low potassium* CP infused at periodic intervals of 20–40 minutes
  - High potassium CP solution contains 20–30 mEq/L of potassium
  - Low potassium CP solution contains 10–20 mEq/L of potassium.
- Continuous cardioplegia:
  - Delivered at low flows
  - Continuous warm cardioplegia advocated for long surgeries
  - Concern about protection of right ventricle and posterior septum in this method.

Composition

- Potassium:
  - *High potassium CP:* 20–30 mEq/L
  - *Low potassium CP:* 10 mEq/L
  - Higher levels cause increased energy requirement and increased potassium load
- Sodium:
  - Concentration lesser than plasma sodium (140 mEq/L)
  - Ischemia increases intracellular sodium.
- Calcium:
  - 0.7–1.2 mmol/L of calcium in CP solution
  - Maintains cellular integrity
  - Hypocalcemic solutions cause massive calcium influx: ***Calcium paradox.***
- Magnesium:
  - 1.5–15 mmol/L of magnesium in CP solution
  - Controls increased influx of calcium.
- Buffers:
  - Bicarbonate prevents increased build up of acid metabolites.
  - *Alternate buffers:* Histidine, THAM (tromethamine)
- Mannitol: To control cellular edema
- Membrane stabilizing agents:
  - Procaine
  - Lidocaine
  - Glucocorticoids.
- Energy substrates:
  - Glucose
  - Glutamate
  - Aspartate
  - Blood/crystalloid.

Strategies to Reduce Ischemic Injury with Cardioplegia[5,17]

No	Principle	Mechanism	Component
1	Reduce O_2 demand	Hypothermia	Blood/crystalloid
			Ice slush/lavage
		Asystole	Potassium chloride, adenosine
			Hyperpolarizing agents
2	Substrate supply and use	Oxygen	Blood, PFC
		Glucose	Blood, glucose, citrate-phosfate-dextrose
		Amino acids	Glutamate, aspartate
		Buffers	Blood, bicarbonate, phosphate, THAM, histidine

Contd…

Contd…

No	Principle	Mechanism	Component
3	Control calcium influx	Hypocalcemia	Citrate
			Calcium channel blockers
			Potassium channel openers
4	Reduce edema	Hyperosmolar solutions	Glucose
			Potassium chloride
			Mannitol
		Moderate infusion pressure	Less than 50 mm Hg

Adverse Effects of Cardioplegia

- Excessive cardioplegia:
  - Absence of electrical activity
  - AV conduction block
- Poorly contractile heart at termination of bypass
- Persistent systemic hyperkalemia.

Cardioplegia Circuits

Two types of circuits:

- Recirculating circuit:
  - For asanguineous delivery
  - Crystalloid CP solution is kept running constantly in the circuit
  - It is delivered to a patient on removing a clamp thus directing flow away from recirculation circuit and to patient
- Non-recirculating circuit:
  - For sanguinous delivery
  - Involves shunting of arterialized blood from oxygenator into the CP circuit
  - Here it is mixed with a crystalloid base solution and delivered
  - Makes only a single pass through heat exchanger.

CARDIOPULMONARY BYPASS-BASIC CIRCUITRY

Introduction

- CPB is a form of extracorporeal circulation in which patients blood is rerouted outside the vascular system and the functions of the heart and lungs is temporarily assumed by surrogate technology
- Almost 25–30% of patients circulating volume is outside the body during CPB.

Goals

- To provide a quiet and bloodless field.
- Limitations of myocardial damage by reduction of:
  - Intracellular acidosis
  - Edema
  - Depletion of ATP stores
- Preservation of coronary endothelial function and myocardial flow
- Reduce reperfusion injury.

Types of Extra Corporeal Circuitry

- Cardiopulmonary bypass (CPB)
- Left heart bypass
- Cardiopulmonary support
- Extra Corporeal Membrane Oxygenation (ECMO).

Components

- Venous line
- Venous reservoir
- Arterial pump
- Heat exchanger
- Oxygenator
- Arterial line filter
- Arterial line
- Accessory pumps:
  - Cardiotomy suction
  - LV vent
  - Cardioplegia pump.
- Accessory devices:
  - Ultrafilter
  - Volatile agent vaporizers
  - In line blood gas monitor.
- Prime.

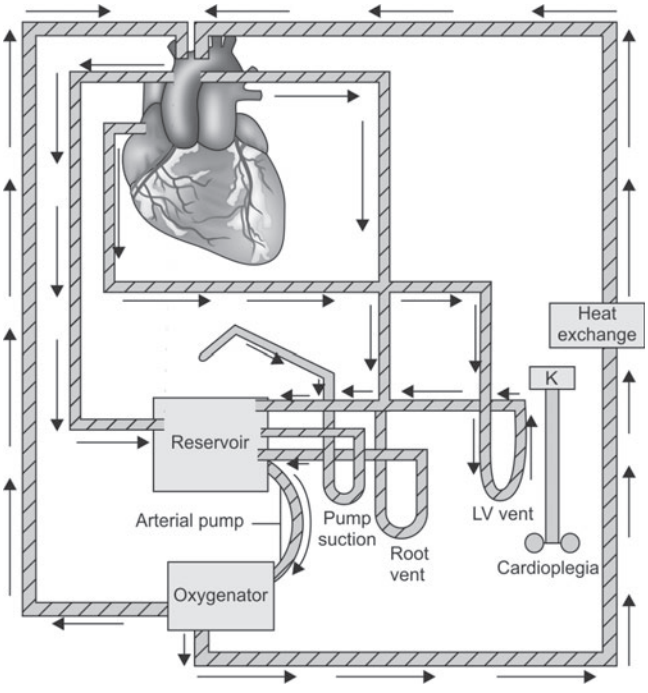


Fig. 7.21: CPB basic circuitry[1]

Venous Line

Description

- Made of medical grade polyvinyl chloride with surface coatings which:
  - Alter bioactivity of surface to reduce markers of subclinical coagulation
  - Attenuate cytokine and other inflammatory markers.

Types of Venous Cannulation

- Single atrial cannulation:
  - Cannula present in RA which drains blood from both RA and IVC
  - It is simpler, faster, less traumatic with one less incision
  - Interferes least with caval return when off bypass.
- Bicaval cannulation/single stage cannula:
  - Placed in SVC and IVC
  - Cannula is snared to prevent systemic venous blood from entering the heart
  - Used anytime when right heart entry is anticipated.
- Cavoatrial cannulation/dual stage cannulation:
  - Superior decompression of right heart
  - Reduced incidence of myocardial ischemia and better protection
  - One cannula is in RA which extends into IVC.
- Femoral venous cannulation done in:
  - In emergent situation
  - Aortic surgery
  - Thoracic surgery.

Venous Reservoir

Description

- Act as buffer for imbalances between venous return and arterial flow
- Postured between venous line and arterial pump
- May be collapsible plastic bags/clear hard shelled plastic containers
- Blood flows in via gravitational drainage
- The amount of venous drainage is proportional to:
  - The pressure in central veins (directly proportional)
  - Height difference between reservoir and patient (directly proportional)
  - Resistance in venous cannula and line (inversely proportional).
- Reservoir has integrated positive and negative pressure release valves which are important for application of suction to the reservoir to augment venous drainage
- If venous reservoir is allowed to empty, air can enter the main pump and cause fatal air embolism
- *Arterial reservoir:* When reservoir is placed beyond oxygenator as in the case of a bubble oxygenator.

Clinical Uses

- Provides time for perfusionist to act if venous drainage is sharply reduced or stopped, in order to avoid pumping air
- Acts as buffer for imbalances between venous return and arterial flow
- Facilitates displacement of large volume of blood out of circulation at strategic times during the operation
- Serves as gross trap for air which enters the venous line
- Serves as a site where blood, fluids and drugs can be added.

Arterial Pumps

- Three types of arterial pumps:
  a. Roller pumps
  b. Centrifugal pumps
  c. Pulsatile assist devices.

Roller Pumps

- Positive displacement pumps which function by occluding a point in a piece of tubing and then rolling the occlusive point of contact along a length of the tubing.
- Can generate extremely high positive and negative pressures and can pump massive quantities of air
- Regulated to automatically reduce their speed when high pressure/air is detected in the path of blood
- If pump inflow is occluded negative pressure will develop in rollerhead causing cavitation
- If pump outflow is occluded, increased pressure may develop proximal to occlusion causing tubing connection to separate or tube to burst
- Subtotal occlusion prevents RBC trauma
- All roller pumps have cranks to allow manual pumping
- Pulsatile flow is possible with some roller pumps
- Pulsations can be produced by instantaneous variations in rate of rotation of roller heads

- Can cause *spallation* which is development of plastic microemboli due to tube compression.
- Advantages of pulsatile flow:
  - *Increased tissue perfusion:* Increases renal and cerebral blood flow
  - Increased O_2 extraction
  - Reduces release of stress hormones
  - Reduces SVR during CPB.

Centrifugal Pumps

- These are non-volatile kinetic energy pumps
- They generate flow by magnetically coupling the high speed revolution of a reusable motor cone to plastic plates inside a disposable cone
- This produces a constrained vortex which propels fluid through the opening on side of cone while drawing fluid into the point of the cone
- In contrast to roller pumps which are placed after the oxygenator, centrifugal pumps are normally between venous reservoir and oxygenator.
- Disadvantages:
  - Unable to generate extremely high/low pressures
  - If bolus of air is introduced, pump will deprime, rendering it unable to pump large volumes of air
  - Lack of point of tubing occlusion allows retrograde flow from patients high pressure arterial system backwards through arterial line, oxygenator, and venous reservoir when revolution of pump goes below a critical threshold
  - Cannot produce pulsatile flow.
- Advantages:
  - Reduced risk of RBC trauma as they are non-occlusive
  - Reduced cavitation
  - Reduces risk of massive air emboli
  - Elimination of tubing wear off and spallation.

Pulsatile Assist Devices

- Examples:
  - Extracorporeal balloon
  - Intra-aortic balloon pump (IABP)
  - Ventricular type pneumatic/hydraulic pumps
  - Modified roller pumps
  - Modified centrifugal pumps
- These pumps may increase the risk of air embolism.

Heat Exchanger

- Facilitates management of patients blood temperature
- Hypothermia common on CPB as up to 25–30% of patients blood is outside the body
- Either cooling and warming of the patient can be achieved by altering temperature of water flowing through the exchanger (4–42 ºC)
- Heat transfer occurs by conduction
- They usually have an inbuilt filter to filter air bubbles which may form during rewarming.
- Counter current device where either heated/cooled water is circulated around a conducting material with good thermal properties which is in contact with patients blood
- The blood is subsequently warmed/cooled and maintained at the desired temperature
- It is located proximal to gas exchange section of circuit to minimize the risk of releasing gas bubbles from blood which can happen if blood is warmed after being saturated with gas.

Oxygenator

- Substitutes for patients lung and performs gas exchange through a blood gas interface
- *Two types of oxygenators:* Membrane/bubble oxygenators
- Membrane oxygenator:
  - Made of microporous polypropylene extruded into thin straws with:
    - Outer diameter of 200–400 µm
    - Wall thickness of 20–50 µm
    - Total surface area of 2–4 m^2
    - Microscopic pores on the sides of fibers (0.5–1 µm)
  - Usually placed after the pump as resistance in most membrane oxygenators requires blood to be pumped through them
  - Has separate gas inlet and outlet ports
  - Ports are small enough to prevent plasma and formed elements from leaving out but still are large enough to allow gas to pass through
  - The venous blood entering the oxygenator is directed across the outside of the fibers: *Blood space*.
  - The gas is concurrently circulated through the inside of the fibers: *gas space*
  - Can arterialize up to 7 L/min of venous blood
  - Arterial oxygenation is inversely proportional to thickness of blood film in contact with the membrane.
  - Arterial CO_2 tension is directly proportional to total gas flow.

- Bubble oxygenators:
  - *Work on principle of direct blood:* Gas contact
  - Positioned proximal to pumps
  - Blood gas interface may cause hemolysis, platelet destruction and microemboli
  - Divided into two sections:
    - Mixing chamber:
      - Fresh gas flows through a perforated plate/screen which forms gas bubbles
      - Diffusion takes place on the bubble surface
      - By using small bubbles a large surface area develops
      - The driving force behind the diffusion of gases is the difference in partial pressures between gases in bubbles and dissolved gases in the blood
      - The oxygenated blood then enters a reservoir/heat exchanger.
    - Reservoir chamber:
      - Blood is allowed to settle and is passed through a defoaming matrix
      - This causes bubbles to destabilize and break down prior to returning to the patient
      - This may cause time dependent destruction of blood elements if CPB time > 90 min.

Arterial Line Filter

- Placed in arterial line as the last component through which blood passes before it returns to patient
- Can be depth filters/screen filters
- Pore sizes of 20–40 µm which removes:
  - Gaseous microemboli
  - Particulate emboli:
    - Thrombi
    - Fat globules
    - Calcium
    - Tissue debris.
- Always has a bypass limb (normally clamped) in case if becomes clogged/develops high resistance.

Arterial Line

- Can be placed in:
  - Ascending aorta
  - Femoral artery
  - Axillary artery
  - Iliac artery which is exposed via retroperitoneal suprainguinal approach.
- Location of cannula determined by:
  - Patient anatomy
  - Surgeon preference
  - Surgical procedure.
- Iliac/femoral artery used when:
  - Aneurysm of ascending aorta
  - When surgery involves multiple procedures involving ascending aorta
  - For peripheral cannulation under local anesthesia in unstable patients
  - When antegrade dissection complicates aortic cannulation.
- Optimal arterial BP required during arterial cannulation as:
  - If too high, increased chances of aortic dissection and tears
  - If too low aorta may collapse
  - Mean blood pressure of 80–100 mm Hg preferred
  - Systolic blood pressure of 100–120 mm Hg preferred.

Cardiotomy Suction

- Aspirates blood from surgical field during CPB and returns it to main pump reservoir
- Excessive suction pressure used may cause RBC trauma due to high negative pressure
- This damage to RBCs precludes blood salvage from cardiotomy
- Disadvantages of cardiotomy suction:
  - Causes:
    - Hemolysis
    - Particulate and gaseous microemboli
    - Fat globule formation
    - Platelet injury
  - This occurs due to amount of air which is aspirated with blood
  - The air blood mixture causes turbulence and high shear stresses which injure both RBCs and platelets.
- Cell saver suction devices:
  - Aspirates blood with controlled vacuum
  - RBCs are automatically washed with saline, separated from the fluid by centrifugation and returned to extracorporeal circuit
  - It removes microaggregates fat, air and tissue debris.

Left Ventricular Vent

- Blood may accumulate in LV due to:
  - Residual pulmonary blood flow

  - From PDA and bronchial arteries
  - Thebesian veins
  - From major aortopulmonary collaterals
  - Due to aortic regurgitation
  - This compromises myocardial protection and thus LV requires regular venting.
- Blood which accumulates is suctioned out using LV vent.
- This is done via catheter passed into:
  - Left ventricular apex directly
  - Left ventricle via right superior pulmonary vein and left atrium
  - Into main pulmonary artery.
- Vented blood passes through a filter and returns to venous reservoir.
- Uses of LV venting:
  - Prevents myocardial distension
  - Reduces myocardial rewarming
  - *Prevents ejection of air:* Used to aspirate air from heart during de-airing procedure
  - Facilitates surgical exposure, e.g. when working on aortic valve.
- Importance:
  - Distension of ventricle causes mechanical damage to muscle from excessive stretching
  - Venting improves preservation by reducing myocardial oxygen demand
  - Venting reduces wall tension due to a reduction in radius of ventricle
  - It facilitates subendocardial perfusion
  - It prevents pulmonary venous hypertension with pulmonary edema.
- *Disadvantage:* May cause systemic air embolism by introducing air into left heart.

Cardioplegia Pump

- Allows optimal control over infusion pressure, rate and temperature of cardioplegia
- Separate heat exchanger ensures accurate control of temperature of cardioplegia solution
- This solution may be infused from a cold IV fluid bag given under pressure or by gravity.

Ultrafilter/Hemofilter/Hemoconcentrator

- Used to increase patients hematocrit without transfusion
- Contains hollow semipermeable fibers which can function as membrane
- Blood is passed through fibers either from arterial side/venous reservoir using an accessory pump
- Hydrostatic pressure forces water and electrolytes across the fiber membrane
- This allows separation of aqueous phase of blood from its cellular and proteinaceous elements
- Effluents of up to 40 ml/min can be removed
- Can be used post bypass to concentrate pump blood before it is given back to patient
- Conserves coagulation factors, platelets and albumins.

In Line Blood Gas Monitors

- Non-invasive flow-through devices to measure blood gases in arterial and venons lines
- Arterial monitor provides continuous assessment of arterial oxygenation like a pulse oximeter
- Venous oximetry provides rapid assessment of balance of oxygen supply and demand.

Automatic Data Collection Systems

- To assist preoperative calculation, processing and storing data during bypass
- This allows perfusionist to attend to more important tasks.

Prime

- Fluid contained within CPB tubing is called prime
- Initially blood was used but practice was stopped due to:
  - Increased demand for blood
  - Scarcity of supply
  - ***Capillary leak syndrome***: Postoperative pulmonary dysfunction due to histamine release
- Crystalloid solutions like RL used now due to similar osmolarity and electrolyte composition
- Average prime volume is 1500–2500 ml
- Minimal volume used based on body weight/BSA
- Other components which are added to make up prime:
  - Mannitol for diuresis
  - Albumin to reduce postoperative edema
  - Electrolytes like calcium to prevent hypocalcemia due to citrate in transfused blood
  - Corticosteroids for anti-inflammatory action
  - Heparin for safe level of anticoagulation
- Blood may be added in:
  - Children

- Small adults
- Patients with preoperative anemia to prevent dilutional anemia

- *Lowest safe hematocrit on CPB is 20%.*

VENTRICULAR SEPTAL DEFECT[1,2,3,5,17]

Introduction

It refers to an abnormal communication between the two ventricles.

Incidence

- Isolated VSDs account for around 25% of all congenital heart defects
- Incidence is higher in premature infants and also slightly higher in males.

Embryology

- Single ventricle divided into two by the union of:
  - Membranous portion of ventricular septum
  - Bulbus cordis
  - Endocardial cushions
- Formation of septum occurs in fifth week of intrauterine life
- Development of VSD due to:
  - *Perimembranous VSD:* Defects in development of membranous septum
  - *Outlet VSD:* Failure of fusion of conus septum
  - *Inlet VSD:* Failure of fusion of endocardial cushion with muscular septum
  - *Muscular VSD:* Inadequate fusion of medial walls of right and left ventricles.

Classification

- *Perimembranous VSD (70%):* May extend into adjacent muscular septum and can be classified based on the direction of extension into:
  - Trabecular extension (typical type)
  - Inlet extension (AV canal type)
  - Outlet extension (TOF type).
- Muscular VSDs (25%):
  - Trabecular extension
  - Inlet extension
  - Outlet extension.
- Subarterial infundibular VSD (5%):
  - Are located just beneath the semilunar valves
  - Thus, aortic regurgitation is commonly associated as aortic valve cusps often protrude into the infundibular VSD.

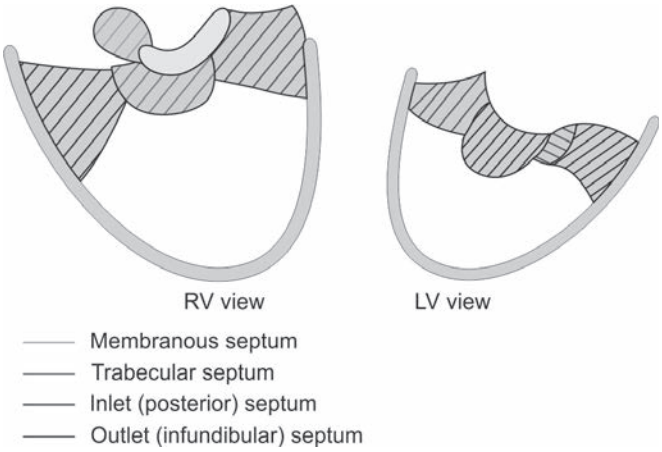
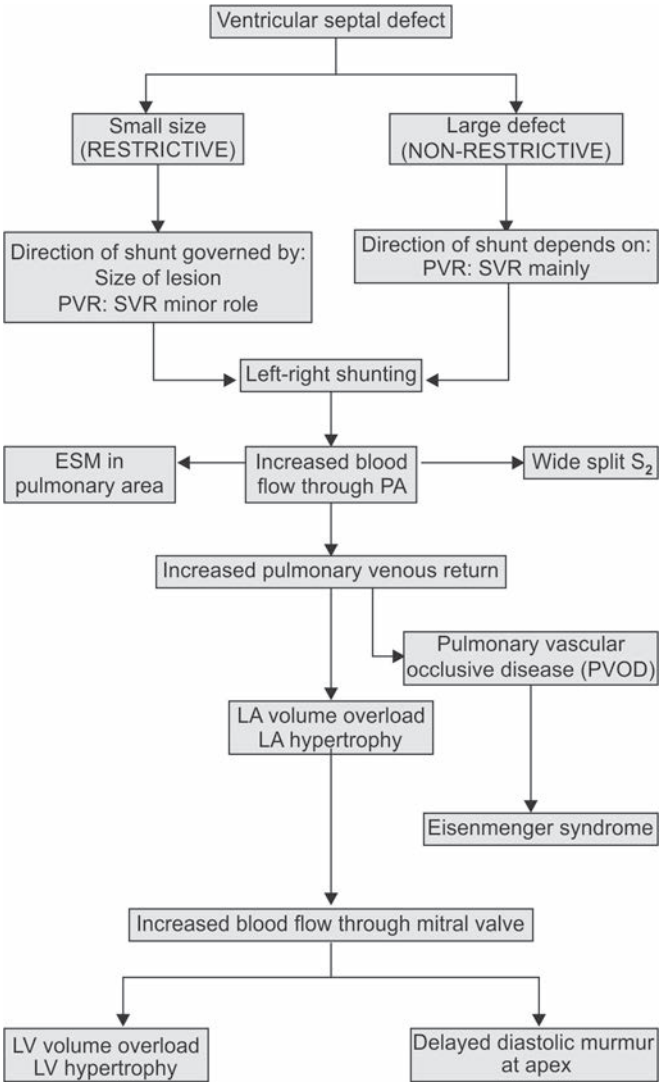


Fig. 7.22: Ventricular septal defects

Pathophysiology



- Only if a large VSD exists, direct transmission of LV pressure to RV causes biventricular hypertrophy
- In small VSDs, since shunting occurs when both ventricles are contracting simultaneously, the shunted blood directly enters pulmonary artery
- Thus, only LV changes are seen and RV is spared in small VSDs.

Clinical Features

- Spontaneous closure:
  - Occurs in 30–40% within first year of life
  - Smaller VSDs have higher chances of spontaneous closure
- Large VSDs:
  - Most patients develop CCF at around 2 months age when PVR reduces to a critical level
  - PVOD may begin at 6–12 months of age
  - The resulting right-left shunt occurs only in teenage years.
- History:
  - Large VSD with or without CCF:
    - Reduced exercise tolerance
    - Recurrent URTI/LRTI
    - Impaired growth and development.
  - Eisenmangers syndrome:
    - Dyspnea on exertion
    - Chest pain, syncope, hemoptysis
    - Cyanosis, clubbing, erythrocytosis.
- Examination:
  - Palpation:
    - Hyperkinetic precordium
    - Systolic thrill at left sternal border
    - LV type of apex.
  - Auscultation:
    - Heart sounds:
      - S_1: Masked by pansystolic murmur
      - S_2: Widely split, increased intensity of P_2
      - S_3: In small left-right shunts.
    - Murmur:
      - *Shunt murmur:* Pansystolic murmur in left third/fourth ICS
      - Flow murmur
      - Pulmonary ejection systolic murmur
      - Mitral delayed diastolic murmur.

Assessment of Severity

- Small VSD:
  - Pansystolic murmur
  - S_2 normally split with normal P_2
  - No delayed diastolic murmur.
- Large VSD:
  - Pansystolic murmur becomes shorter, softer and appears like ESM
  - S_2 widely split, increased intensity of P_2
  - Delayed diastolic murmur present.

Investigations

- Complete blood count:
  - Polycythemia
  - Thrombocytopenia.
- Baseline ABG:
  - For PaO_2 and electrolytes
  - Check K^+ levels if on digoxin therapy
  - Blood glucose for hypoglycemia.
- Renal function tests
- Coagulation profiles:
  - Associated coagulatopathy may be present
  - PT, INR, platelet count, APTT to be checked.
- ECG:
  - *Small VSD:* Normal ECG
  - *Moderate VSD:* LAH, LVH
  - *Large VSD:* LAH, biventricular hypertrophy
  - *Pulmonary vascular occlusive disease:* RVH without LAH/LVH.
- Chest X-ray:
  - *Small VSD:* Normal
  - *Large VSD:* Biventricular enlargement
  - Pulmonary plethora
  - *Moderate VSD:* LA and LV enlargement with pulmonary plethora.
- Echocardiography:
  - Provides definite diagnosis
  - Size and site of VSD identified
  - Direction and magnitude of shunt
  - Color Doppler studies.
- Cardiac catheterization:
  - Location and size of VSD
  - Magnitude of shunt
  - Qp:Qs ratio
  - Pulmonary and systemic vascular resistance
  - Ventricular function.

Treatment

- Medical management:
  - Close follow-up
  - Treat CCF, anemia and recurrent chest infections
  - Congestive cardiac failure (CCF):
    - *Diuretics:* Furosemide 1 mg/kg or 2–3 mg/kg IV or oral.

- *Digoxin:* 20–50 µg/kg PO followed by 8–10 µg/kg maintenance dose
- Reduce by 25% when giving IV therapy.

– Anemia:
- Maintenance of hematocrit is important
- Anemia causes increase in left-right shunt, thereby worsening CCF
- Frequent feeding with high calorie formulas by NGT or oral feeds
- Oral iron therapy can be supplemented.

• Transcatheter closure:
– Indications:
- Mid-muscular/apical VSDs which are difficult to close surgically
- Those which require left ventriculotomy, which is associated with increased chances of LV dysfunction postoperatively.

– Done with *umbrella device*
– Associated with:
- Heart block
- Blood loss
- Hemodynamic instability.

• Surgical correction:
– Usually done between 1–2 years of age
– Increased mortality if done below 6 months of age.
– Indications:
- Significant growth retardation
- CCF unresponsive to medical therapy
- Large VSD with signs of PVOD
- Qp : Qs ≥ 2
- *If associated with CoA or PDA:* Closure of PDA or CoA done first.

– Procedure:
- Approach through RA or RV approach
- Surgical closure done with dacron or pericardial patch repair
- *LV approach seldom used:* LV dysfunction may persist for several years postoperatively
- Distortion of tricuspid valve occurs frequently.

– Contraindications:
- Development of PVOD with right-left shunt
- PVR: SVR ≥ 0.75
- If PVR ≤ one-third of SVR, progression of PVOD in postoperative period is rare.

– PA banding:
- Done very rarely as palliative surgery
- Done if multiple VSDs present (*Swiss cheese* appearance).

Anesthesia for VSD

Anesthetic Goals

- *Rhythm:* Sinus rhythm
- *Rate:* Maintain age appropriate rate
- *Contractility:* Maintain contractility
- *Preload:* Avoid fluid overload, especially if signs of CCF
- *Afterload:* Maintain afterload
- Ventilation:
  – Avoid hypoxia
  – Avoid hypercarbia
  – Avoid hyperventilation and hyperoxemia
  – Avoid hyperinflation and atelectasis
- *Temperature:* Maintain, prevent hypothermia
- *Hematocrit:* Maintain, prevent anemia or polycythemia.

Factors Causing Left-Right Shunt

- Low hematocrit
- Increased SVR, reduced PVR
- Hyperoxemia
- Hyperventilation
- Negative airway pressure.

Factors Causing Right-Left Shunt

- Polycythemia
- Reduced SVR, high PVR
- Hypoxia
- Hypoventilation, hypercarbia
- PEEP.

Preoperative Preparation and Premedication

- Preoperative assessment includes:
  – History of:
    - Symptoms
    - Palliative surgery (PDA/COA)
    - Current medications
    - URTI, immunization
  – Examination should include airway for anticipated difficult intubation
  – Investigation including coagulation profile, ABG and electrolytes.
- *Fasting guidelines:* Avoid hypoglycemia and dehydration
  – 6 hours for solids
  – 4 hours for breast milk
  – 2 hours for clear fluids and water.
- Informed consent
- Treat preoperative URTI/LRTI adequately

- Premedication (in children ≥ 6 months age):
  - *Oral:* Midazolam 0.5 mg/kg with atropine 10 µg/kg
  - *Intramuscular:* Morphine 0.1 mg/kg with atropine 10 µg/kg
  - Avoid premedication in:
    - Children less than 6 months age
    - Those with righ-left shunts.
- Continue all medications except diuretics and anticoagulants
- Infective endocarditis prophylaxis as indicated.

Regional Anesthesia

- Caudal anesthesia:
  - 2 mg/kg bupivacaine + 4 mg/kg lidocaine used
  - Used in noncardiac surgery where applicable
  - Care to prevent reduction in SVR at the time of induction
  - Reduction in SVR causes acute right-left shunting and rapid desaturation
- Contraindicated if coagulation abnormalities present.

OT Preparation

- Anesthesia machine with circuit
- *Airway equipment:* ETT, laryngoscope airways, suction apparatus
- *Anesthetic drugs:* Morphine, fentanyl, NDMR
- Defibrillator, temporary pacemaker
- Equipment for thermal homeostasis
- *Emergency drugs:* Atropine, adrenaline, phenylephrine, dopamine, dobutamine, NTG, isoprenaline.

Monitors

- Pulse oximeter, E_TCO_2
- ECG, NIBP
- Airway pressure monitor
- IBP, CVP, PAC and PCWP as demanded by the procedure
- Left upper extremity not to be used for NIBP/IBP in patients who underwent surgery for CoA
- Foleys catheter, urine output
- Tranesophageal echocardiography
- ABG, electrolytes, blood glucose and hematocrit
- Temperature, precordial stethoscope if noncardiac surgery.

Induction

- Adequate preoxygenation
- Patients with IV line in place:
  - *Good LV function:* Thiopentone 3–4 mg/kg + vecuronium 0.1 mg/kg + fentanyl 2 µg/kg.
  - *Poor LV function:* Ketamine 1–2 mg/kg + vecuronium 0.1 mg/kg.
- Patients with no IV line:
  - Inhalational induction with less than 2% halothane if good LV function
  - IM ketamine 5 mg/kg if poor LV function.
- IV induction is slow in patients with left-right shunt
- Avoid air bubbles in IV line as they will cause paradoxical systemic air embolism in the presence of a right-left shunt.

Maintenance

- If good LV function:
  - O_2 + air + 1% isoflurane
  - Fentanyl 1 µg/kg and vecuronium 0.1 mg/kg intermittent boluses.
- If poor LV function:
  - O_2 + fentanyl 2 µg/kg/hour infusion
  - Vecuronium 0.1 mg/kg and midazolam 0.05 mg/kg intermittent boluses.
- Avoid nitrous oxide as it increases pulmonary HTN and size of air bubbles.

Ventilation

- ET intubation and CMV preferred
- Use low FiO_2 as hyperoxemia increases left-right shunt
- Maintain $PaCO_2$ between 30–40 mm Hg
- Small PEEP preferred as patients have increased pulmonary blood flow
- Avoid:
  - *Hyperventilation and hyperoxemia:* Increases left-right shunt
  - *Hypoxia, hypercarbia and acidosis:* Increases right-left shunt.

Hemodynamics

- Judicious fluids as required if poor LV function
- Avoid anemia as left-right shunt increases (maintain hematocrit ≥ 10 g%)
- Maintain normothermia as hypothermia increases left-right shunt
- Isoprenaline (0.01–0.05 µg/kg/min) or dobutamine (3–5 µg/kg/min) in patients with pulmonary HTN, while coming off bypass
- Pacemaker support if complete heart block post-VSD correction.

Extubation

- Postoperative ventilation required if:
  - Poor preoperative cardiovascular reserve
  - Congestive cardiac failure

- Reversal with neostigmine 0.05 mg/kg and glycopyrollate 0.02 mg/kg
- Extubate when:
  - Patient fully awake
  - Hemodynamically stable
  - Adequately rewarmed
  - Normal acid base status and ABG.

Postoperative Care

Management

- Adequate analgesia to prevent crying
- Avoid factors which precipitate pulmonary hypertension:
  - Crying, stress
  - Hypoxia, hypercarbia
  - Acidosis.

Analgesia

- Titrated opioids to avoid undue sedation
- Patient controlled analgesia
- Ketorolac 0.5 mg/kg or paracetamol 15 mg/kg IV as adjuvants
- Caudal/epidural analgesia where applicable
- Multimodal analgesia preferable.

Monitors

- Pulse oximetry, E_TCO_2
- ECG, NIBP/IBP
- Temperature, urine output
- Echocardiography for LV function and residual VSDs
- CVP, PA pressure.

Complications

- TV regurgitation common, AR rarely
- RVOT obstruction from pericardial patch
- RV/LV dysfunction which persists for years later
- Residual pulmonary HTN/VSD
- Rarely, cerebrovascular accidents and stroke
- Infective endocarditis
- Arrhythmias:
  - Right bundle branch block
  - Right bundle branch block with left anterior hemiblock
  - Complete heart block.

ATRIAL SEPTAL DEFECT[1,2,3,5,17]

Introduction

It is an abnormal communication between the two atria.

Incidence

- OS-ASD accounts for 7–11% of all congenital heart defects
- More commonly seen in girls.

Embryology

- Interatrial septum develops between 4th and 6th weeks of gestation
- A depression is formed in roof of common atrium, which enlarges as a crest
- This forms the *septum primum* (SP)
- SP extends downwards to meet the endocardial (EC) cushions formed in atrioventricular canal
- The opening between the atria formed before the SP meets EC is called ostium primum (OP)
- This is closed when the endocardial cushion fuses with septum primum
- As the septum primum extends downwards, fenestration appear superiorly which ultimately unite together and form the *ostium secundum* (OS)
- At the same time, a thin septum called the septum secundum develops to right of septum primum
- This grows and covers the OS in an incomplete fashion, resulting in the formation of foramen ovale
- After birth, with the increase in SVR and decrease in PVR, foramen ovale usually closes but may persist in 25% causing PFO.

Classification

Sinus Venosus

- ASD situated high in interatrial septum, at the junction of SVC with RA
- Frequently associated with anomalous connection of right pulmonary veins to SVC.

Ostium Secundum Defect

- ASD situated at the center of interatrial septum at the site of foramen ovale
- Situated either at the fossa ovalis, or superior/inferior to fossa ovalis
- OS defect is ten times as common as ostium primum defect
- OS-ASD is the *most common* type of ASD
- When multiple fenestrations of IAS are present in the centered IAS, it is called *Chiari network*
- Occurs due to:
  - Resorption of septum primum
  - Short septum primum
  - Defective septum secundum development.

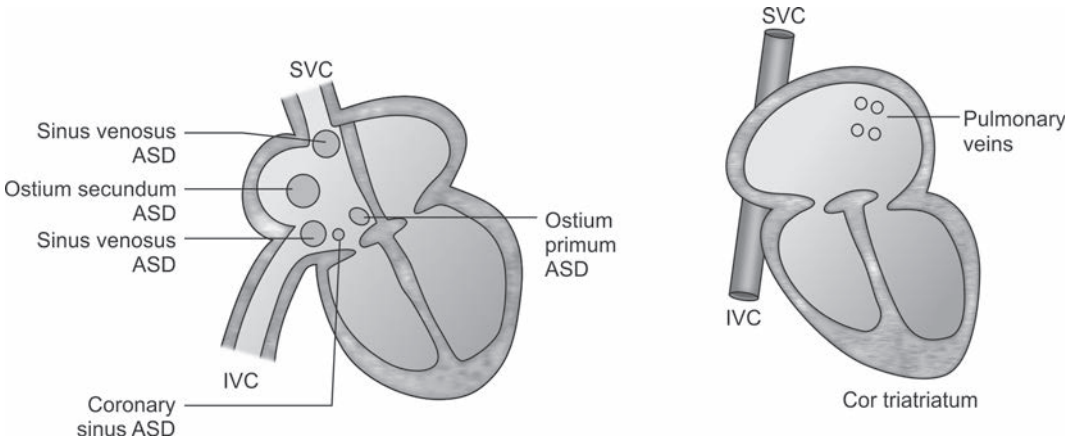


Fig. 7.23: Atrial septal defects

Ostium Primum Defect

- Located at lower end of IAS immediately adjacent to atrioventricular valves
- Due to endocardial cushion defect.
- More common in Down's syndrome
- Associated with cleft in anterior mitral leaflet and mitral incompetence
- Also associated with tricuspid valve incompetence and VSD
- Defect is usually large and manifests early
- Classified as incomplete atrioventricular canal/ partial endocardial cushion defect.

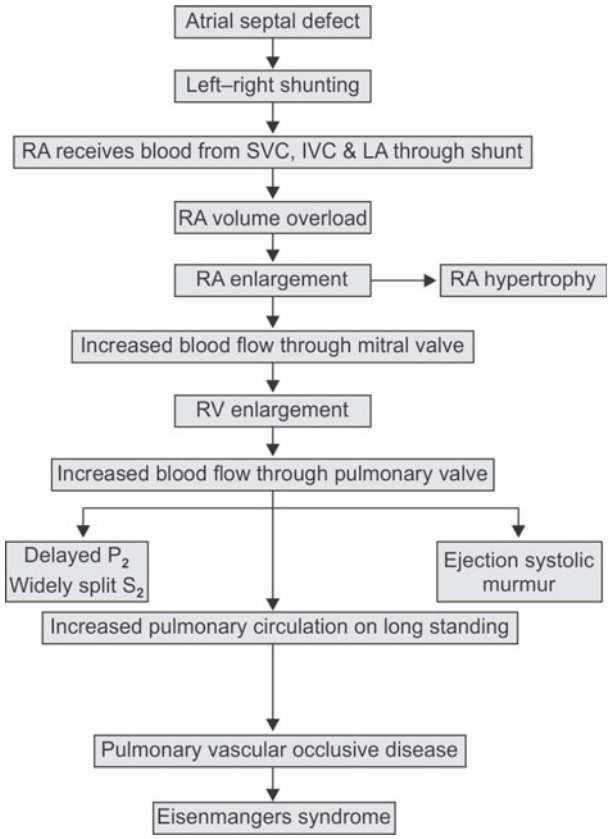
Coronary Sinus Defect

- Defect lies posterior to fossa ovalis, which normally houses the ostium of coronary sinus
- Frequently associated with anomalous connection of right pulmonary veins.

Cor Triloculare Biventriculare

- Called *Common atrium*
- Complete absence of interatrial septum
- Right sided portion of common atrium receives blood from SVC, IVC and coronary sinus
- Left sided portion receives blood from pulmonary veins.
- Commonly associated with:
  - Asplenia and polydactyly
  - ***Ellis-Van Creveld*** syndrome
  - Systemic anomalous venous return
  - Complete or partial anomalous pulmonary venous return.

Pathophysiology



Clinical Features

- History:
  - Majority of patients lead a normal life until adulthood
  - Symptoms of CCF and failure to thrive in 3rd to 4th decades.

- Recurrent chest infections due to increased pulmonary blood flow
- Cyanosis, clubbing, fatigue, dyspnea on exertion
- Precordial pain if pulmonary hypertension and right-left shunt develops
- Mild dyspnea, fatigue are most common early symptoms.

- Examination:
  - Inspection:
    - Skeletal anomalies *(Holt-Oram syndrome)*
    - Facial anomalies (*Down's syndrome*)
    - Visceral anomalies (asplenia)
    - Prominent left costal cartilage from cardiomegaly
    - *Gracile habitus:* Long and narrow bones with poorly developed skeletal muscles.
  - Palpation:
    - Parasternal impulse
    - Systolic thrill in left second ICS
    - Palpable P2.
  - Auscultation:
    - Sounds:
      - S_1: Loud, accentuated
      - S_2: Wide and fixed split, increased P_2 intensity
      - S_3: Inconstant.
    - Murmurs:
      - Shunt murmur absent
      - Flow murmur
      - Delayed diastolic murmur of TR
      - Ejection systolic murmur of PV.
    - S_2 is widely split as increased blood flow through pulmonary valve causes delayed pulmonary valve closure
    - Also, S_2 splitting is fixed and does not vary with inspiration
    - This is because the RV is already fully loaded with shunted blood
    - Thus further inspiration cannot draw more blood into RV.

Complications

- Usually in 3rd to 4th decade
- Congestive cardiac failure
- Eisenmanger syndrome
- Pulmonary vascular occlusive disease.
- Arrhythmias:
  - Atrial flutter
  - Atrial fibrillation, PSVT
  - Atrioventricular conduction abnormalities.

Assessment of severity: If ASD is large:

- Cardiomegaly is more
- Increased intensity of ESM and delayed diastolic murmur.

Investigations

- Complete blood count, renal function tests, coagulation profile
- Baseline ABG and blood glucose
- Chest X-ray:
  - Cardiomegaly: Enlarged RA and RV
  - Pulmonary plethora
  - Localized dilation of SVC at the entrance of anomalous pulmonary veins
- Electrocardiogram:
  - RAD with RVH and RBBB in ostium secundum defects, RVH
  - LAD with RVH in ostium primum defects
- Echocardiogram:
  - Paradoxical anterior ventricular septal motion which contacts with right ventricle rather than LV
  - Location and size of ASD
  - Estimation of left-right shunt
- Catheterization:
  - Not routinely indicated
  - Used only if:
    - Inconsistency in clinical data
    - Significant PAH
    - Associated anomalies
  - Transesophageal echocardiography done if transthoracic echo is ambiguous.

Treatment

- Medical treatment:
  - Consists of treatment of:
    - Recurrent chest infections
    - *Congestive cardiac failure:* Diuretics and digoxin
    - Arrhythmias
  - Spontaneous closure occurs within 25–50% cases within 1st year.
- Surgical treatment:
  - Indications are:
    - Qp:Qs ≥ 2 (ratio of pulmonary to systemic flow)
    - Marked cardiomegaly
    - Marked CCF
    - Retarded growth and development
    - Usually done between 4–6 years of age.

  - Contraindications:
    - Small defect
    - Trivial left-right shunt
    - Severe PAH (as acute RV failure occurs post-operatively).
- Transcatheter closure:
  - Indications:
    - Defects less than 25 mm (8–20 mm)
    - Appropriate sized patients
    - Good interatrial septum length.
  - Devices used are:
    - Clamshell device (Rashkinds double disc device)
    - Angel-Wings ASD device
    - Rashkind umbrella device
    - Sideris buttoned device.
  - Contraindications:
    - Defects more than 25 mm
    - Ostium primum/sinus venous defects
    - Defects associated with anomalous pulmonary venous connection
    - Pulmonary vascular occlusive disease.
  - Complications:
    - Heart block
    - Cardiac erosions
    - Thrombus.

Natural History

- *Small ASDs:* Hemodynamically insignificant, usually symptomless
- Moderate ASDs:
  - May manifest in 3rd–4th decade
  - 14% develop CCF, 20% develop arrhythmias
- *Large ASDs:* Develop PVOD, have reduced life expectancy.

Anesthesia for ASD

Premedication

- Treat preoperative URTI/LRTI adequately
- Informed consent
- Fasting guidelines:
  - *6 hours:* Solids
  - *2 hours:* Clear fluids, water.
- *Premedication:* Morphine 0.1 mg/kg and glycopyrrolate 20 µg/kg IV
- Continue all preoperative medication except diuretics
- Antibiotic prophylaxis as indicated.

Anesthetic Goals

- *Rhythm:* Sinus rhythm
- *Rate:* Maintain age appropriate rate
- *Contractility:* Maintain contractility
- *Preload:* Avoid fluid overload, especially if signs of CCF
- *Afterload:* Maintain afterload
- Ventilation:
  - Avoid hypoxia
  - Avoid hypercarbia
  - Avoid hyperventilation and hyperoxemia
  - Avoid hyperinflation and atelectasis
- *Temperature:* Maintain, prevent hypothermia
- *Hematocrit:* Maintain, prevent anemia or polycythemia.

Factors Causing Left-Right Shunt

- Low hematocrit
- Increased SVR, reduced PVR
- Hyperoxemia
- Hyperventilation
- Negative airway pressure.

Factors Causing Right-Left Shunt

- Polycythemia
- Reduced SVR, high PVR
- Hypoxia
- Hypoventilation, hypercarbia
- PEEP.

OT Preparation

- Anesthesia machine with circuit
- *Airway equipment:* ETT, laryngoscope airways, suction apparatus
- *Anesthetic drugs:* Morphine, fentanyl, NDMR
- Defibrillator, temporary pacemaker
- Equipment for thermal homeostasis
- *Emergency drugs:* Atropine, adrenaline, phenylephrine, dopamine, dobutamine, NTG, isoprenaline.

Monitors

- Pulse oximeter, E_TCO_2
- ECG, NIBP
- Airway pressure monitor
- IBP, CVP, PAC and PCWP as demanded by the procedure
- Foleys catheter, urine output
- Transesophageal echocardiography
- ABG, electrolytes, blood glucose and hematocrit
- Temperature, precordial stethoscope if noncardiac surgery.

Induction

- Adequate preoxygenation
- Patients with IV line in place:
  - *Good LV function:* Thiopentone 3–4 mg/kg + vecuronium 0.1 mg/kg + fentanyl 2 µg/kg
  - *Poor LV function:* Ketamine 1–2 mg/kg + vecuronium 0.1 mg/kg
- Patients with no IV line:
  - Inhalational induction with less than 2% halothane if good LV function
  - IM ketamine 5 mg/kg if poor LV function
- IV induction is slow in patients with left-right shunt
- Avoid air bubbles in IV line as they will cause paradoxical systemic air embolism in the presence of a right-left shunt.

Maintenance

- If good LV function:
  - O_2 + air + 1% isoflurane
  - Fentanyl 1 µg/kg and vecuronium 0.1 mg/kg intermittent boluses
- If poor LV function:
  - O_2 + fentanyl 2 µg/kg/hour infusion
  - Vecuronium 0.1 mg/kg and midazolam 0.05 mg/kg intermittent boluses
- Avoid nitrous oxide as it increases pulmonary HTN and size of air bubbles.

Ventilation

- ET intubation and CMV preferred
- Use low FiO_2 as hyperoxemia increases left-right shunt
- Maintain $PaCO_2$ between 30–40 mmHg
- Small PEEP preferred as patients have increased pulmonary blood flow
- Avoid:
  - *Hyperventilation and hyperoxemia:* Increases left-right shunt
  - *Hypoxia, hypercarbia and acidosis:* Increases right-left shunt.

Hemodynamics

- Judicious fluids as required if poor LV function
- Avoid anemia as left-right shunt increases (maintain hematocrit ≥ 10 g%)
- Maintain normothermia as hypothermia increases left-right shunt.
- Isoprenaline (0.01–0.05 µg/kg/min) or dobutamine (3–5 µg/kg/min) in patients with pulmonary HTN, while coming off bypass
- Pacemaker support especially for ostium primum defects (rare in OS-ASD and SV-ASD).

Extubation

- Early extubation in OT or early postoperative period possible
- Neostigmine 0.05 mg/kg and glycopyrrolate 0.02 mg/kg used for reversal
- Extubate when:
  - Fully awake
  - Hemodynamically stable
  - Adequate rewarmed
  - Normal ABG.

Postoperative Care

Analgesia

- Cautious use of opioids to avoid undue sedation
- Patient controlled analgesia
- Ketorolac 0.5 mg/kg or paracetamol 15 mg/kg IV as adjuvants
- Caudal/epidural analgesia used where applicable
- Multimodal analgesia.

Monitors

- Pulse oximetry, E_TCO_2
- Urine output, NIBP/IBP
- CVP/PAC
- ECG, ABG
- Echocardiography
- Temperature.

Complications

- Postpericardiotomy syndrome (rare)
- Air embolism, cerebrovascular accidents
- SVC obstruction (due to SV-ASD closure)
- Arrhythmias:
  - Transient atrial arrhythmias (Atrila fibrillation and flutter) common
  - Complete heart block occurs in OP-ASD
- Severe brady/tachyarrhythmias rare
- Mitral regurgitation especially in ostium primum.

PATENT DUCTUS ARTERIOSUS[1,2,3,5,17]

Introduction

- The persistence of ductus arteriosus (which is the fetal communication between descending aorta

to pulmonary artery) beyond 3 months after a full term birth is called patent ductus arteriosus.
- Also called *Botallos duct*.

Incidence
- 1 in 2500 full-term normal births
- Premature infants more common, female:male = 3:1
- Incidence increases in congenital rubella syndrome.

Embryology
- Aortic arch develops between 5–6 weeks of gestation from trucus arteriosus as six paired arches
- Pulmonary artery arises from 6th arch
- When pulmonary vascularization is established, the communication with right dorsal aorta completely regresses, while that with left dorsal aorta persists until after birth as ductus arteriosus
- Persistance of this communication beyond 3 months after birth causes PDA.

Anatomy
- PDA has diameter of 5–15 mm and length of 2–15 mm
- Arises from left of PA bifurcation near origin of LPA
- Inserted into lesser curvature of aorta, slightly distal to and opposite to origin of left subclavian artery
- Relations of PDA:
  - *Left main bronclus:* Posteriorly
  - *Vagus nerve:* Anteriorly
  - Recurrent laryngeal nerve encircles ductus and ascends into neck.
- In small children, wall of DA is thick and strong
- In older children, wall is thin and friable especially in those with pulmonary HTN
- Anatomical types of PDA:
  - Cylindrical
  - Window
  - Funnel shaped
  - Aneurysmal which can be spontaneous/acquired from:
    - Mycotic infections
    - Trauma
    - Hypertension.
- Closure of ductus arteriosus:
  - Functional closure of DA begins within 12 hrs after birth
  - Usually is physiologically closed by the second day of life
  - Permanent anatomical closure occurs normally within 1st 2 months of life.

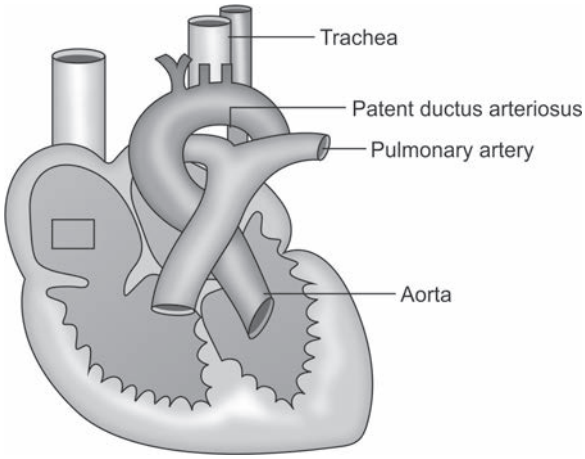
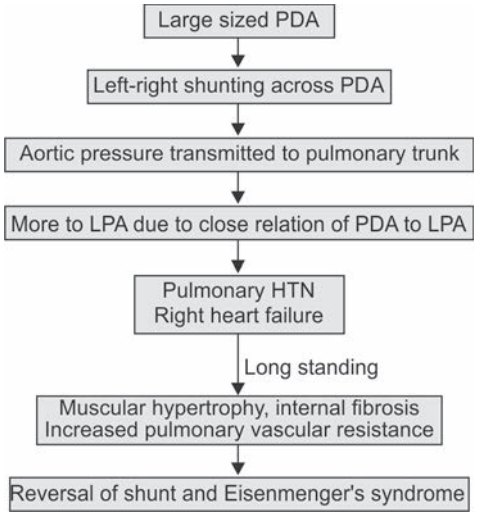


Fig. 7.24: Patent ductus arteriosus

Pathophysiology
- Amount of blood flow through the PDA depends on:
  - Size and shape of communication
  - Difference between SVR and PVR.



Ductus Dependent Cardiac Malformations
- Lesions with restricted pulmonary blood flow:
  - Pulmonary atresia/stenosis associated with:
    - VSD
    - ASD
    - TGA.
  - Tricuspid atresia associated with:
    - ASD
    - VSD.
- Lesions with restricted systemic blood flow:
  - Mitral stenosis with ASD
  - Aortic stenosis with ASD/VSD

- Preductal CoA
- Interrupted aortic arch
- Hypoplastic left heart syndrome.

Clinical Features

Presentation

- Signs of congestive cardiac failure:
  - Failure to thrive
  - Cough, dyspnea, tachypnea
  - Tachycardia
  - Hepatosplenomegaly
- Wide pulse pressure with bounding pulse
- Hyperdynamic precordium
- Systolic and systolic-diastolic murmurs
- *Hallmark:* continuous machinery murmur present in first/second left intercostal space
- *Graham-Steele* murmur:
  - If Eisenmanger syndrome present
  - High pitched diastolic decrescendo murmur
  - Characteristic of pulmonary valvular insufficiency.

Associated Anomalies

- Extracardiac anomalies:
  - Mental retardation
  - Eye defects
  - Deafness
  - Sternal deformities
  - Scoliosis
  - Clubfoot.
- Cardiac anomalies:
  - Lesions with restricted pulmonary blood flow:
    - Pulmonary atresia/stenosis associated with:
      - VSD
      - ASD
      - TGA.
    - Tricuspid atresia associated with:
      - ASD
      - VSD.
    - Lesions with restricted systemic blood flow:
      - Mitral stenosis with ASD
      - Aortic stenosis with ASD/VSD
      - Preductal CoA
      - Interrupted aortic arch
      - Hypoplastic left heart syndrome.
- Syndromes:
  - *Charge syndrome:* Iris coloboma, heart, choanal atresia, micrognathia, difficult airway
  - *Edwards syndrome:* Trisomy 18, micrognathia, small mouth, difficult airway
  - *Goldenhaar syndrome:* CoA, maxillary/mandibular hypoplasia, spine abnormalities
  - *Vater syndrome*
  - *Pataus syndrome:* Trisomy 13.

Differential Diagnosis

- Venous hum
- VSD with aortic regurgitation
- Systemic arterio-venous fistula
- Pulmonary arteriovenous fistula
- Coronary arterial fistula
- Ruptured sinus of Valsalva.

Investigations

- Complete blood count, electrolytes
- Coagulation profile including PT, APTT, platelet count
- Serum protiens, calcium levels
- Arterial blood gas, urine analysis, urine specific gravity
- X-ray chest:
  - Normal or biventricular hypertrophy
  - Enlargement of LA, LV, ascending aorta and aortic arch
  - Enlarged pulmonary vasculature
- *ECG:* Normal or LVH/biventricular hypertrophy
- ECHO:
  - Dilatation of left heart structures
  - Increased LVEF due to arteriovenous shunting
- *Catheterization*: Step up in oxygen saturation at PA level
- Color doppler can viaualize jet of abnormal blood flow.

Medical Management

- Patients with congestive cardiac failure:
- Fluid restriction
- *Furosemide*: May promote patency of DA due to its effects on prostaglandin metabolism
- Digoxin:
  - No benefit in children < 1250g as it does not increase SVR
  - But it may reduce heart rate and thus decrease cardiac output
- Dopamine
- Role of prostaglandins:
  - PGE_1, $PGF_{2\alpha}$ and PGI_2 are used to keep the ductus patent in ductus dependent lesions

- Done in order to promote flow through pulmonary artery
- PGE_1 infused with starting dose of 50–100 ng/kg/min
- Dose adjusted to 10–20 ng/kg/min after favorable effect is seen.
- Side effects of prostaglandins:
  - Fever
  - Hypotension
  - Cutaneous flushing
  - Tachycardia
  - Apneic spells
  - Seizures.

Closure of Ductus Arteriosus

- Indomethacin:
  - Reduces synthesis of prostaglandins by inhibiting cyclooxygenase
  - Indomethacin 0.2 mg/kg IV three times over 24 hours or daily for 72 hours
  - Associated side effects like:
    - Increased bleeding time
    - Renal and hepatic insufficiency
    - Sepsis
    - Necrotizing enterocolitis.
- *Ibuprofen:* Useful and has less effects on organs also
- *Transcatheter closure:* 3 types of occlusion devices:
  - *Porstmann's Ivalon plug*
  - *Rashkinds double disk*
  - *Sideris button device*
  - Close to 90% success rate.
- Surgical closure:
  - Either by division/ligation of PDA
  - *Thoracoscopic technique:* Less pain, can be discharged on same day.

Effects of Various Drugs on Ductus Patency

- Drugs causing PDA contraction:
  - *Increased PaO_2:* Hyperoxia
  - $PGF_{2\alpha}$, Indomethacin, aspirin
  - Acetylcholine, Succinylcholine, histamine
  - NSAIDs
  - Norepinephrine.
- Drugs causing PDA relaxation:
  - PGE_1, PGE_2
  - Hypoxemia, acidosis
  - High altitude
  - Hypothermia.

Anesthetic Considerations

- *Avoid hypothermia*: Causes PDA relaxation and increased left-right shunting
- Avoid hemodilution
- Cross matched blood must be available as blood vessel may be damaged during ligation
- Postoperative ventilation may be required if heart failure is present
- Left lateral thoracotomy approach
- Avoid hypoxia/hyperoxia:
  - *Tidal volume:* Adjusted to keep peak inspiratory pressure between 15–25 cm H_2O
  - *E_TCO_2:* Maintain between 30–35 mm Hg
  - *SpO_2:* Maintained between 87–92%
  - *PaO_2:* Maintained between 50–70 mm Hg.

Preoperative Evaluation

History

- Birth trauma
- Respiratory and cardiovascular status
- History of maternal drug intake
- Fluid status.

Examination

- Airway examination
- Fluid status:
  - Skin turgor
  - Mucous membrane
  - Anterior fontanelle
- Cardiovascular and abdominal examination.

Investigations

- Complete blood count, arterial blood gas
- Electrolytes, coagulation profile
- Urine analysis, urine specific gravity
- X-ray chest and abdomen.

Preoperative Medications

- Informed consent
- Orally hydrated till 2 hrs before surgery
- If this is not possible, IV hydration to be started
- Judicious fluid administration to prevent overload
- Continue inotropic support if present
- Children under 6 months may not require any preoperative sedation
- Midazolam 0.5–0.6 mg/kg PO 30 minutes before surgery.

Induction

- Adequate preoxygenation as apnea and bradycardia can occur
- Prolonged onset time of IV agents with no change if inhalational induction
- *If IV line present:* Ketamine 1 mg/kg + glycopyrrolate 20 µg/kg + vecuronium 0.1 mg/kg IV
- If no IV line present:
  - Halothane/sevoflurane induction
  - Start IV line (largest possible)
  - Fentanyl 1µg/kg+vecuronium 0.1 mg/kg + glycopyrrolate 20 µg/kg
- Avoid succinylcholine as it causes contracture of ductus.

Position

Right lateral decubitus as left posterolateral thoracotomy has to be done

Monitoring

- ECG
- Pulse oximeter in right hand
- Invasive BP monitoring right hand
- End tidal CO_2, inspiratory pressure gauge
- Urinary bag, precordial/esophageal stethoscope
- Esophageal/axillary temperature probe
- Doppler transducer, arterial blood gas monitoring.

Maintenance

- Halothane + NDMR + fentanyl 10 µg/kg or sufentanil 1.5 µg/kg
- N_2O not to be used if pulmonary hypertension is present.

Hemodynamics

- Fluid therapy:
  - Maintenance with 5% dextrose in 1/4th strength NS
  - Maintenance fluids at 4 ml/kg/hr with added 3rd space and blood loss
  - IV tubing to be bubble free to prevent embolization
  - *Maintain hematocrit:* Hemodilution associated with an increase in left-right shunt
  - Replace blood loss with PRBCs or 1:3 crystalloid if hematocrit > 30%.
- Watch for:
  - Bradycardia while handling the ductus
  - Systolic hypotension at the time of ligation of the ductus.
  - Abrupt increase in DBP and mean BP with interruption of DA
  - Increased DBP due to the elimination of low resistance pulmonary circulation.

Ventilation

- Continuous mandatory ventilation (CMV) done with pediatric bellows
- Ventilatory goals:
  - Tidal volume adjusted to keep peak inspiratory pressure between 15–25 cm H_2O
  - FiO_2 adjusted to keep PaO_2 between 50–70 mm Hg
  - Maintain SpO_2 between 87–92%
  - High FiO_2 avoided to prevent retinopathy of prematurity
  - E_TCO_2 to be maintained between 30–35 cm H_2O
- Hypoventilation:
  - Causes hypoxic pulmonary vasoconstriction
  - Reverses shunt to right-left shunt
- Hyperventilation:
  - Reduces pulmonary vascular resistance
  - Causes an increase in left-right shunt
- Lung compliance is reduced by lung retraction and packing during the procedure
- May be hand ventilated with *Jackson-Rees* circuit to:
  - Compensate for changes in pulmonary compliance during thoracotomy
  - Allow adequate field exposure during surgery
  - Deairing pleural cavity before closure.

Intraoperative Complications

- Tear/avulsion of ductus arteriosus with profuse bleeding
- Bradycardia while handling ductus arteriosus
- Inadvertent left pulmonary artery/aortic ligation
- Phrenic nerve/recurrent laryngeal nerve injury
- Trauma to thoracic duct
- Left lung injury from pressure and retraction of lung
- Bacterial endocarditis
- Systemic embolization from calcification of aorta
- Residual shunt with ligation
- Postoperative aneurysm
- *Postoperative hypertension is very common.*

Extubation

- Fully awake extubation in lateral decubitus position
- Majority extubated on table/soon after surgery
- Only sick children require postoperative ventilation
- Done after full reversal with neostigmine and atropine.

Postoperative

Management

- Maybe considered to have normal cardiovascular system postoperatively
- Do not require routine infective endocarditis prophylaxis for subsequent surgeries.

Analgesia

- Local anesthetic infilteration
- Intrapleural block
- Thoracic epidural
- Opioid analgesia
- Paracetamol rectal suppository 30–60 mg/kg.

Complications

- Hypertension related to baroreceptor dysfunction
- Recurrent laryngeal nerve injury
- Phrenic nerve injury
- Systemic thromboembolism
- Reduced systemic blood flow causing:
  - Renal dysfunction
  - Necrotizing enterocolitis due to gastrointestinal hypoperfusion.

COARCTATION OF AORTA[1,2,3,5,17]

Introduction

Congenital constriction of the aorta which impedes the flow of blood below the constriction and increases the blood pressure above the constriction.

Incidence

- Occurs in approximately 7–9% of patients with congenital heart disease
- Most common near ductus arteriosus but also occurs in lower thorax and abdominal aorta.

Embryology

- Aortic arch normally arises from left 4th arch of primitive arches of truncus arteriosus between 5th and 7th weeks of gestation
- Aorta proximal to site of ductal insertion, arising from left 4th arch is the *most common* site of CoA (called preductal CoA)
- Anomalous development occurs from 6th primitive aortic arch to the point of fusion of the two dorsal aortae resulting in post ductal CoA
- Aortic luminal diameter maybe reduced to as little as 1–3 mm.

Etiology

- Intrusion of ductus arteriosus closure into adjacent normal aorta
- Extension of ductal muscle into aortic wall
- Primary aortic malformation/hypoplasia.

Classification

- Thoracic aortic CoA:
  - Preductal/infantile CoA
  - Ductal/juxtaductal CoA
  - Postductal/adult CoA
- Lower thoracic CoA
- Abdominal aortic CoA.

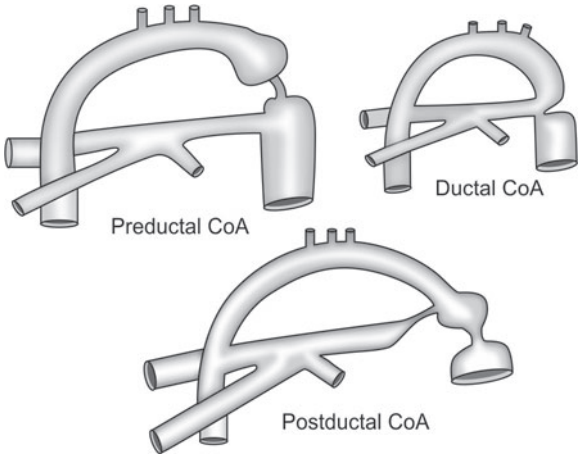


Fig. 7.25: Types of coarctation of aorta

Pathophysiology

Preductal

- Little or no collateral circulation as perfusion of lower body occurs via ductus arteriosus
- Systemic pressures in RV ensures perfusion of ascending aorta and lower body of neonate with preductal CoA, so long as ductus arteriosus remains patent
- Thus, no pressure gradient, upon which development of collateral circulation depends ever occurs
- When the DA closes, these neonates develop CCF, shock, oliguria and CRF.

Postductal

- Pressure gradients between 30–40 mm Hg develop which stimulates collateral circulation development
- Thus, closure of DA has lesser effect on patients with postductal CoA than those with preductal CoA
- Often remains asymptomatic into their teenage/later, in contrast to those with preductal CoA.

Collateral Circulation

- Intercostal artery
- Internal mammary artery
- Internal thoracic artery
- Subdivision of subclavian artery
- Superior intercostal except for first 2 pairs
- Superior epigastric artery
- Perhaps anterior spinal and vertebral artery
- Patients with collaterals are less likely to develop paraplegia following aortic cross clamping.

Clinical Presentation

Symptoms

- Present early if preductal CoA
- Most common cause of CCF between 1–3 weeks age (later in teens if postductal CoA)
- Tachycardia, tachypnea, dyspnea, poor feeding, weight gain, signs of CCF within first 3 months of life.

Signs

Vitals

- Pulses in lower limb is delayed/diminished/absent
- Pulse in upper limb is bounding
- BP decreased in lower limb
- BP abnormally increased in upper limb which may exceed lower limb by ≥ 20 mm Hg
- Localization of lesion:
  - CoA located at aortic isthmus when pulse felt in:
    - Right arm
    - Right carotid artery
    - Left arm but absent on left side
  - CoA is proximal to or adjacent to its subclavian artery take off when pulse is:
    - Present in right arm
    - Absent in left arm and legs
    - Or right arm BP is more than left arm BP
  - If pulse is palpable in left arm but not right upper arm/leg, CoA is distal to left subclavian artery in association with rare anomalous right subclavian artery with original distal to CoA.

Associated Lesions

- More common with preductal CoA
- VSD, PDA, TGA in 40% patients with CoA
- MS, MR, ASD, endocardial fibroelastosis and bicupid aortic valve (very common) may coexist.

Others

- Differential cyanosis of lower half of body:
  - Upper half receives well oxygenated blood from vessels originating from aortic arch above level of CoA
  - But lower half of body is poorly perfused with lower saturation blood from RV via PA and PDA
  - Tissue extraction is high relative to local tissue perfusion and blood oxygen content, from blood in lower half of body, causing cyanosis
- Systolic thrill may be palpable in suprasternal notch area
- Auscultation:
  - S_3 gallop, diffuse ejection systolic murmur
  - Systolic ejection murmur grade 2–3 radiating over right upper sternal border, left sternal border/occasionally posteriorly in interscapular area left of midline
  - Ejection click of bicuspid aortic valve
  - Diastolic murmur of aortic regurgitation
- Metabolic acidosis and oliguria/anuria due to CCF
- *Suzman's sign*:
  - Pulsation in the back due to collateral
  - Most prominent over scapula
  - Best visualized with the patient bending forwards.

Investigations

- ECG:
  - Left Ventricular Hypertrophy with Left Axis Deviation
  - Normal ECG in some patients with postductal CoA
  - Right Ventricular Hypertrophy with Right Bundle Branch Block.
- Chest X-ray:
  - Heart size normal or slightly enlarged with or without ascending aortic dilation
  - In overpenetrated chest films, *3 sign*, representing pre and poststenotic dilation
  - Reverse 3/E sign:
    - On left anterior oblique projection of barium swallow
    - Shows anterior displacement of esophagus
    - Poststenotic aortic dilation will cause an indentation, making it look like E.
  - Pulmonary edema and pulmonary venous congestion

  - Inferior rib notching:
    - Occurs on ribs 4 to 9
    - *Pathognomonic* of collateral circulation
    - Is not seen in infancy and patients < 5 yrs age.
- ECHO:
  - Shelf like membrane in decending aorta from suprasternal notch view
  - Associated defects like VSD/bicuspid aortic valve
- Cardiac catheterization:
  - Indicated when:
    - Information from ECHO is incomplete
    - Concern over collateral flow that may affect the planning of operative repair.
  - Studies pressure differential between ascending and decending aorta with significant pressure drop distal to the site of CoA
  - Confirms VSD, TGA, bicuspid aortic valve.

Treatment

Medical Therapy

- Oxygen therapy, digitalization, diuretics and intropic support for children with CCF
- Prostaglandin E_1 to maintain ductal patency if systemic perfusion depends on right-to-left shunt.

Surgical Therapy

- Usually planned between 4–8 yrs of age
- Resection and anastomosis:
  - *Surgery of choice* when feasible
  - Up to 5 cm can be excised in neonates and infants
  - Only 2.5 cm can be excised in older children and adults as progressive fibrosis reduces elasticity.
- Alternatives:
  - Subclavian artery flap
  - Angioplasty
  - Dacron patch repair
- Prosthetic graft *mandatory* for adult CoA repair.

Anesthetic Management

Preoperative Preparation and Premedication

- Evaluate:
  - Patients physical status
  - Associated cardiac and other medical problems
  - Whether patient has been optimally treated to put patient in best physical condition for surgical stress.
- NPO orders
- Informed consent
- Sedation:
  - Inappropriate as a rule for child < 6–9 months age
  - Sedation for other patients individualized as per needs
  - 0.5–0.7 mg/kg midazolam orally within 15–30 min of induction
  - Better to give sedation in holding area of operating room.
- Temperature:
  - Maintain thermally neutral environment in transfer of patient from hospital room to OR
  - Done so that there is no additional stress on heart due to change in SVR from vasoconstriction/shivering
  - Passive measures like a clear plastic wrap/active methods like warming blankets may be used.
- *Antisialagogue*: Anticholinergic premedication like atropine useful
- Antibiotic chemoprophylaxis:
  - Against gram-positive organisms and common gram-negative organisms
  - Done for:
    - All patients with bicuspid aortic valve
    - Other lesions predisposing to bacterial endocarditis.

Monitoring

- Blood pressure:
  - Left arm cuff not used as left subclavian artery may be clamped/used for surgical repair of CoA
  - Right arm BP cuff can provide valuable information regarding cerebral circulation during periods of left subclavian artery occlusion
  - BP cuff on patients thigh/calf to measure BP gradient between upper and lower limb before and after repair
  - Invasive BP if aorta will be cross clamped at any level - *Right radial artery only*
  - Umbilical artery catheterization may be helpful but it may give very low or no readings at all during aortic cross clamping.
- Pulse oximeter probe on right arm
- ECG lead placement to take into account left lateral thoracotomy approach and right lateral decubitus position
- Central Venous Pressure monitoring.

Induction and Intubation

- Techniques of induction:
- In hemodynamically stable patients with good LV reserve:
  - Thiopentone 3–5 mg/kg with succinylcholine 1.5–2 mg/kg after atropine 5–10 µg/kg
  - Defasciculating dose of NMBA preferred
- In patients with suspected/known reduction in LV function:
  - Rapid IV induction with etomidate 0.15–0.3 mg/kg or ketamine 1–2 mg/kg and vecuronium 0.1 mg/kg
  - Combined benzodiazepine with narcotic induction with midazolam 0.1–0.3 mg/kg and fentanyl 5–20 µg/kg or sufentanil 0.5–1.5 µg/kg with vecuronium 0.1 mg/kg.
- In patients with no intravenous access inhalational induction with halothane to <1.5 MAC as risk of:
  - Bradycardia
  - Severe myocardial depression
  - Complete heart block.
- High arterial oxygen pressures and succinylcholine avoided as if patient has ductus dependent physiology as it may reduce flow through PDA.
- Debubbling is done scrupulously to avoid possibility of right-to-left shunting of air bubbles and peripheral embolization
- Ketamine and other agents which increase SVR to be avoided in patients with bicuspid aortic valve and significant AS/AR
- Left-to-right shunting may cause slight decrease in rate of IV induction
- Right-to-left shunting may increase rate of inhalational induction.

Maintenance

- Primarily narcotic based in patients with depressed myocardial function with:
  - Fentanyl 10–25 µg/kg or sufentanil 1–2.5 µg/kg total dose
  - Low dose inhalational agent used to maintain balanced anesthesia.
- Avoid N_2O due to:
  - Potential for myocardial depression in those getting narcotics
  - Also causes enlargement of air bubbles.
- Neuromuscular blockade with vecuronium/pancuromium.

Hemodynamics

- Ductal manipulation may cause bradycardia:
  - Atropine should be immediately available
  - Manipulation of aorta should be suspended temporarily.
- Avoid left-to-right shunting by preventing:
  - Respiratory alkalosis
  - Hyperoxia
  - Excessive reduction in hematocrit
  - Reduction in pulmonary vascular resistance
  - Increases in systemic vascular resistance.
- In patients with VSD:
  - Avoid hypervolemia to avoid increase in left-to-right shunting
  - Avoid increase in pulmonary artery pressure and pulmonary vascular congestion.
- Dextrose free fluids used except in neonates
- Blood:
  - Given judiciously to avoid reduction in oxygen delivery
  - Administered at rates not likely to provoke MI/cardiac failure.
- Coagulation products generally not required in non-CPB cases.

Postoperative

Postoperative Ventilation

- Healthy older individuals can be extubated early in postoperative period
- Delayed weaning and extubation for:
  - Sicker patients with limited cardiopulmonary reserve
  - Preoperative heart failure.
- Prior to weaning, check:
  - Patient must be rewarmed to a normal body temperature
  - Fluid, electrolytes and coagulation status
  - Hemoglobin levels
  - Recovery of muscle strength and CNS status.

Complications

- Paraplegia:
  - Due to:
    - Ischemia of thoracic spinal cord from prolonged cross clamping
    - Spinal cord HTN below the level of aortic cross clamping causing cord infarction

- Hyperthermia to 38–40 °C during cross clamping.
  - Maintain distal aortic press > 60 mm Hg to reduce incidence of neurological injury
  - Spinal cord infarction is rare if aortic cross clamp time is < 20 mins
  - If cross clamp time > 20 mins, consider placement of a temporary shunt
  - Hypothermia may offer cord protection by reducing spiral cord oxygen requirements and consumption.
- Hypertension:
  - Most patients develop HTN in immediate postoperative period (within 24 hrs)
  - Occurs due to:
    - Increased catecholamine levels, especially norepinephrine
    - Increased plasma renin acitivity
  - β blockers and ACE inhibitors may be used to treat HTN
- Transient renal failure
- Postcoartectomy syndrome:
  - Necrotizing mesenteric arteritis presenting with:
    - Ileus
    - Abdominal pain and distension
    - Melena, vomiting
    - Fecal incontinence and bowel necrosis
  - Less common now due to better control of postoperative HTN.

Natural History

- 50% mortality in first month of life
- ≥ 80% mortality in first 3 months of life
- With surgical correction, mortality reduces to 5%
- For post ductal CoA, average prognosis for survival is about 35 yrs
- Fatality of 60–70% by age 40 yrs due to:
  - Rupture of aorta
  - Congestive cardiac failure
  - Bacterial endocarditis
  - Intracerebral bleed.

MITRAL REGURGITATION[1,2,3,5,17]

Introduction

Mitral regurgitation results from several mechanisms permitting systolic blood flow from left ventricle, back into left atrium.

Causes

No	Cause	Characteristics	Location
Functional mitral regurgitation			
1	Annular dilatation	Dilated cardiomyopathy	Annulus
2	LV ischemia	Ischemic Heart Disease	Tensor apparatus
Organic mitral regurgitation			
Chronic Mitral Regurgitation			
1	Congenital	Cleft mitral valve	Leaflet
		Double orifice mitral valve	
2	Mitral prolase	Myxomatous degeneration	Leaflet
		Redundant tissue	
		Ruptured chordae	
3	Rheumatic	Thickened leaflets	Leaflet
		Calcified leaflets	
		Commissural fusion	
4	Miscellaneous	Fenfluramine	Drug related
Acute mitral regurgitation			
1	Endocarditis	Perforated leaflets	Leaflet
		Vegetations	
2	Post MI	Papillary muscle rupture	Tensor apparatus
3	Post chest trauma	Papillary muscle rupture	Tensor apparatus

Pathophysiology

- Chronic mitral regurgitation:
  - Regurgitation of blood into LA occurs during systole
  - On long standing, the LA dilates, making it more compliant
  - The massively dilated LA, protects the pulmonary capillaries from experiencing significant pressure elevation
  - Thus, pulmonary edema is an uncommon initial presentation in chronic MR.
- Left ventricular ejection fraction in chronic MR:
  - Most often normal or supranormal
  - This is because the LA serves as a low pressure pathway during systolic ejection
  - Thus ejection fraction overestimates the ventricular function
  - Thus, ventricular dysfunction may be unmasked after valve repair/replacement.
  - LVEF becomes low when:
    - LV has decompensated with chronic MR
    - Acute LV ischemia.

- Acute onset mitral regurgitation:
  - LA pressure increased as there is no time for LA compensatory changes to occur
  - *v wave* may be present on LAP/PAP/PCWP recordings
  - In contrast, in chronic MR, the increase in LAP is less dramatic
  - This is due to compliance changes in LA as a function of chamber dilation.
- Determinants of volume of mitral regurgitation:
  - LA–LV pressure differential depends on:
    - Systemic vascular resistance
    - LA compliance
  - Regurgirant volume reduced with:
    - Decrease in systemic vascular resistance
    - Increase in LA pressure.

Clinical Features

- May remain asymptomatic for 20–40 yrs
- If acute MR:
  - Have normal or reduced LA compliance
  - Usually have pulmonary vascular congestion and severe pulmonary edema
  - Congestive heart failure.
- If chronic MR:
  - Have increased LA compliance
  - Usually show signs of low cardiac output and forward LV failure
  - Dyspnea on exertion
  - Paroxysmal nocturnal dyspnea
  - Atrial fibrillation.
- Features of right heart failure:
  - Hepatic congestion and ascites
  - Pedal edema and anasarca
  - Raised JVP (if acute MR).
- Examination:
  - Normal BP, arterial pulse with sharp upstroke
  - Raised JVP with:
    - Prominent *a waves* in patients with sinus rhythm
    - Prominent *v waves* if severe tricuspid regurgitation.
  - Systolic thrill at apex
  - Hyperdynamic LV with brisk systolic impulse
  - Apex beat displaced laterally
  - S_1 absent, wide splitting of S_2.
  - Mitral regurgitation murmur:
    - Holosystolic murmur at apex, radiating to axilla
    - Increased intensity with squatting/hand grip
    - Reduced intensity with valsalva maneuver
    - If acute MR, seagull /cooing quality of murmur.
- Complications:
  - Chest pain due to low diastolic pressure
  - Infective endocarditis
  - Arrhythmias
  - Embolic events.

Investigations

- Complete blood count, BUN, SC, LFT
- Chest X-ray:
  - LA and LV are dominant chambers
  - LA might form right border of cardiac silhouette if massively enlarged
  - Calcification of mitral valve
  - *Kerley A, Kerley B lines, Stag antlers signs* if pulmonary edema.
- ECG:
  - Normal in some
  - Inverted or biphasic T waves
  - ST segment changes in inferior leads
  - Arrhythmias:
    - *Supraventricular tachyarrhythmias most common*
    - Bradyarrhythmias
    - AV bypass tract especially with mitral valve prolapse (*Barlows syndrome*)
  - Biatrial enlargement features.
- Echocardiography:
  - Regurgitant fraction < 30% of total stroke volume: Mild symptoms
  - Regurgitant fraction 30–60% of total stroke volume: Moderate symptoms
  - Regurgitant fraction > 60% of total stroke volume: Severe symptoms.

Carpentier Classification of Mitral Regurgitation

Carpentier type	Leaflet motion	Jet direction
1	Normal	Central
2	Excessive (prolapsed, flail)	Away from lesion
3a	Restricted, structure is abnormal	Variable
3b	Restricted, structure is normal	

- Flow volume curve
- *Transesophageal echocardiography*: Classification of MV leaflet motion.

Treatment

Medical Therapy

- Digoxin
- Diuretics
- Vasodilators which cause reduction in SVR resulting in:
  - Increased forward stroke volume
  - Reduced regurgitant volume
- Afterload reduction maybe life saving in acute MR.

Surgical Therapy

- Considered for patients with moderate to severe symptoms
- Surgical valvuloplasty is preferred, to avoid problems associated with valve replacement like:
  - Thromboembolism
  - Hemorrhage
  - Prosthetic failure.

Anesthetic Goals

- Faster, fuller and vasodilated to maintain forward flow
- *Rate*: maintain slightly higher range (80–100 bpm)
- Rhythm:
  - Maintain sinus rhythm
  - If atrial fibrillation present, control ventricular rate.
- Preload:
  - Maintain preload
  - Increase in preload worsens MR.
- *Afterload*: reduced with anesthetics and vasodilators
- Contractility:
  - May be depressed
  - Titrate myocardial depressants carefully
- M_VO_2: Compromised if MR coexists with IHD.

Rationale for Anesthetic Goals

Heart Rate and Rhythm

- Maintain sinus rhythm in high normal range (80–100 bpm)
- Bradycardia has dual detrimental effects:
  - *Increased duration of systole:* Prolongs regurgitation
  - *Increased diastolic filling interval:* More LV distension.

Preload

- Maintain preload
- Mitral regurgitation is a dynamic condition
- Ventricular distension may cause expansion of an already dilated MV annulus
- This may worsen MR.

Afterload

- Lower SVR so that forward cardiac output is maximum
- Afterload reduction strategies:
  - Maintain adequate anesthetic depth
  - Systemic vasodilators and inodilators
  - Mechanical reduction of afterload with IABP
- Temporary use of ephedrine after which inotropic support needed to augment pressures
- Arteriolar dilators are effective as they reduce LA-LV gradient.

Contractility

- EF indices poorly correlate with LV systolic function
- Manage hypotension by manipulating heart rate and preload
- Persistent hemodynamic instability common inspite of adjusting heart rate and preload
- Consider inotropes for hemodynamic instability:
  - Dobutamine
  - Low dose epinephrine
  - Milrinone
- EF correlates poorly with LV function as it includes both forward systolic flow and regurgitant volume.

Pulmonary Hypertension

- Avoid increases in pulmonary HTN
- Pulmonary artery pressure and pulmonary vascular resistance is already raised
- Avoid hypoxia, hypercarbia and acidosis.

Choice of Anesthetic Technique

- Spinal/epidural anesthesia well tolerated as it reduces the SVR causing reduction in regurgitant fraction
- Bradycardia associated with spinal anesthesia should be avoided as it increases the regurgitant volume.

Preoperative Preparation and Premedication

- Informed consent
- NPO orders

- Premedicate:
  - Premedicate with caution
  - Light premedication advised to prevent airway obstruction
  - Hypoventilation and asphyxia may exacerbate pulmonary HTN
  - Done in high dependency room under supervision
  - 0.5 mg midazolam IV titrated and given in increments
  - Supplemental oxygen can be given at this time
- *Blood loss is usually moderate*: Arrange for 2 units of blood
- Continue antiarrhythmics until day of surgery
- Change warfarin to heparin preoperatively.

Anesthetic Management

Induction

- Opioid based induction:
  - Oxygen + fentanyl 5 µg/kg
  - Pancuronium may be used as muscle relaxant to avoid opiod induced bradycardia
- Acute increases in LV afterload, as after intubation and surgical stimulation to be avoided
- Deep planes during intubation advised
- NTG may be useful to control increases in afterload.

Position

Supine position.

Monitoring

- Pulse oximetry, capnography
- Invasive BP, ECG
- Temperature, urine output
- Transesophageal echocardiography
- Pulmonary artery catheter recording:
  - Very useful, especially for those on vasodilator therapy
  - MR recognized on PA wedge waveform as large *v wave with rapid y descent*
  - Especially prominent in acute MR or chronic MR with acute deterioration
  - Used for:
    - Assessment of intravascular filling
    - Measurement of cardiac output
    - Evaluation of effect of treatment
  - Suspect functional TR if raised PAP occurs.

Maintenance

- Patients with moderate to severe LV dysfunction are very sensitive to the depressant actions of volatile anesthetics
- Opioids + oxygen + isoflurane used
- Isoflurane used though it causes myocardial depression as it also reduces systemic vascular resistance
- Avoid N_2O as it:
  - Increases pulmonary arterial pressure
  - Causes LV dysfunction.

Ventilation

- Avoid factors causing increase in pulmonary arterial pressure:
  - Hypoxia
  - Hypercarbia
  - Acidosis
  - *High airway pressures:* Might constrict pulmonary capillaries and increase PAP
  - Positive end expiratory pressure.

Hemodynamics

Maintain Preload

- Judicious fluid administration
- Avoid fluid overload
- In case of hypotension: (especially acute MR)
  - Administer fluids
  - Inotropic support is rarely required prebypass
  - Avoid vasoconstrictors
  - IABP useful to reduce afterload and increase cardiac output.

Maintain SVR

- NTG especially useful if any increase in SVR/PAP occurs
- Select agents which promote vasodilatation and tachycardia
- Replacement of mitral valve in acute MR is difficult as LA would be small
- Amrinone and milrinone useful as inodilators if RV failure occurs
- *Paradoxical deterioration:*
  - Occurs postmitral valve repair soon after starting inotropes and vasodilators
  - This is due to coexistent HOCM and SAM of mitral valve
  - If this is suspected a trial of volume expansion and vasoconstrictors is given.

Reduce Pulmonary Vascular Resistance

- Avoid hypoxia and hypercarbia
- Check ABGs regularly
- Avoid acidosis
- Pulmonary vasodilatation if PAP > 2/3rd the systemic pressures with:
  - Nitric oxide 40 ppm is the agent of choice
  - Milrinone, amrinone, sildenafil, exoximone are alternatives
  - Inhaled PGE_1:
    - Dilates pulmonary smooth muscle
    - Almost complete first pass metabolism occurs in pulmonary endothelium
    - Therefore it is pulmonary selective vasodilator.

Extubation

- Early extubation avoided to prevent hypoxia and hypercarbia
- Postoperative ventilation may be required
- Extubate if:
  - Spontaneous ventilation with normal ABG
  - No bleeding and hemodynamically stable patient
  - Normothermia.

Postoperative Period

Complications

- Postoperative LV dysfunction, RV dysfunction and biventricular failure
- Paravalvular leaks
- Transverse midventricular disruption
- Posterior wall MI
- Coagulopathy and postoperative bleeding
- Hypothermia from incomplete and non-uniform rewarming
- Pulmonary HTN.

Monitors

- ECG, pulse oximetry
- Invasive BP
- Urine output, CVP
- PA catheter
- ABG, temperature.

Analgesia

- Severe pain common
- *Opioids*: Fentanyl or morphine
- Intercostal nerve block
- Patient controlled analgesia.

HYPERTROPHIC CARDIOMYOPATHY[1,2,3,5,17]

Introduction

- HCM is a genetically determined disease characterized by histologically abnormal myocytes and myocardial hypertrophy developing in the absence of a pressure/volume overload
- Also called:
  - *Idiopathic hypertrophic subaortic stenosis*
  - *Asymmetrical septal hypertrophy*
  - *Hypertrophic obstructive cardiomyopathy*
  - *Muscular subaortic stenosis.*

Etiology

- Autosomal dominant inheritance with variable penetrance
- Mutation of cardiac β myosin chain gene on chromosome 14
- This gene codes for cardiac sarcomere proteins
- Mutation results in hypertrophy of segments.

Pathology

- Bizarre and disorganized arrangement of cardiac muscle cells
- Disorganized myofibrillar architecture
- Myocardial fibrosis and thickening of small intramural coronary arteries
- Systolic compression of intramyocardial segment of coronary artery.

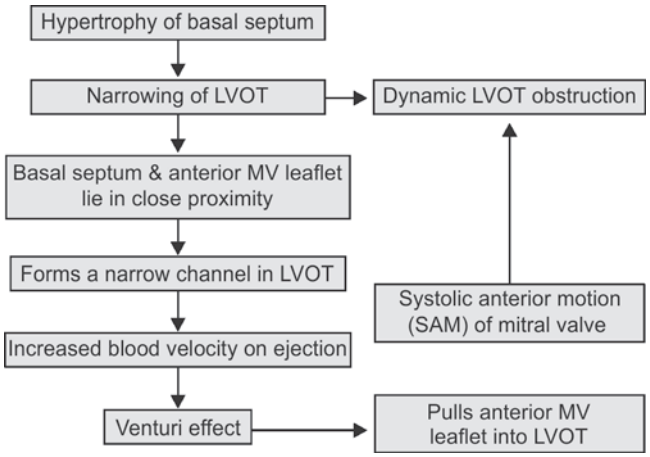
Regions of Hypertrophy

- Septal involvement *most common* (upper interventricular septum just below aortic valve)
- Apex
- Free wall of left ventricle
- *Concentric LVH*: < 10% patients
- Striking regional variations in hypertrophy in contrast to the secondary hypertrophy as in hypertension where it is more uniform.

Pathophysiology

- Characteristically display *diastolic dysfunction* which is reflected by an elevated LVEDP in spite of hyperdynamic ventricular function
- Hypertrophic Obstructive Cardiomyopathy (HOCM):
  - Occurs in 20–30% patients of HCM
  - Called HOCM when HCM patients have subvalvular obstruction

  - In these patients LVOT gradient is formed due to:
    - Systolic septal bulging into LVOT
    - Malposition of anterior papillary muscle
    - Drag forces
    - Hyperdynamic LV contraction causing *Venturi effect*.
  - Obstruction:
    - The obstruction is dynamic and peaks in mid-late systole
    - As opposed to the obstruction in AS which is fixed
    - Beat to beat variability of the degree of obstruction occurs.
- Obstruction is accentuated by any intervention which reduces ventricular size as it facilitates septal-leaflet contact.
- The interventions which increase obstruction are:
  - Increased contractility
  - Increased heart rate
  - Reduced preload/ventricular volume
  - Reduced afterload.



Clinical Features

Symptoms

- Mostly asymptomatic and found as incidental finding on echocardiogram
- Sudden cardiac death (SCD):
  - Most common cause SCD in young people (< 30 yrs)
  - This usually occurs during physical exertion
  - SCD may even be the 1st clinical manifestation.
  - Most common autopsy finding in previously healthy athletes who die suddenly.
- Angina during exercise:
  - Occurs even in the absence of CAD
  - Owing to increased systolic LV pressure, coronary microcirculation is unable to supply hypertrophied myocardium
  - Angina reduces in recumbent posture is very classical as LV size reduces on sitting.
- Others:
  - Dyspnea on exertion
  - Fatigue, syncope
  - Palpitations due to arrhythmias.

Examination

- *Pulses bisferiens*
- Double/triple apical precordial impulse
- Rapidly rising carotid pulse
- SVT/ventricular arrhythmias are common
- 4th heart sound usually audible
- Murmur:
  - Harsh systolic murmur
  - Begins well after 1st heart sound
  - May have holosystolic and blowing quality if associated MR present
  - Best heard at left lower sternal border and apex
  - Reduced by squatting and hand grip
  - Increased by Valsalva maneuver and standing.

Investigations

- Routine blood, BUN, SC, LFT
- ECG:
  - Left ventricular hypertrophy pattern
  - Broad Q waves suggestive of:
    - Old MI
    - Accentuation of normal septal depolarization
- Holter monitoring: For SVT, AF and VT
- Chest X-ray:
  - Maybe normal
  - Mild to moderate increase in cardiac silhouette
- Echocardiogram:
  - Confirmatory
  - LVH with septum ≥ 1.3 times thickness of posterior free wall of LV
  - *Ground glass appearance* of septum
  - LVEF > 80%
- *Doppler echocardiogram:* For peak pressure gradient by determining peak velocity in LVOT
- Thallium 201 scans: Show myocardial perfusion defects even in asymptomatic patients.

- Catheterization studies show:
  - Reduced ventricular compliance
  - Systolic gradient between LV body and subaortic region.

Treatment

Medical Therapy

- β blockers:
  - Reduce inotropy
  - Prevent increases in subaortic pressure gradient.
- Calcium Channel Blockers:
  - Reduce inotropy
  - Improve diastolic compliance by relaxing the heart.
- *Amiodarone*: Used for SVT and ventricular arrhythmias
- Avoid nitrates, digoxin and diuretics
- HOCM with pulmonary edema:
  - Avoid diuretics and digoxin
  - Give volume overload
  - Give β blockers..

Surgical Therapy

- Alcohol ablation of IV Septum, if septal thickness at site of injection ≤ 15 mm
- Pacing:
  - DDD (dual mode, dual chamber, dual sensing)
  - DDD pacing with short AV delay can be useful
  - Cannot be used in patients with atrial fibrillation.
- Septal myectomy (complete):
  - For patients who are symptomatic despite maximal pharmacological therapy
  - For resting gradient ≥ 30 mm Hg and exercise gradient ≥ 50 mm Hg.
- Partial myectomy via aortic approach
- Mitral valve replacement.

Anesthetic Technique

- Regional anesthesia is relatively contraindicated as it reduces SVR and preload
- Continuous spinal/epidural anesthesia may be preferable to bolus dose of LA as it allows better control of LA level
- Ropivacaine is *agent of choice* for Cesarean sections
- Ephedrine and epinephrine contraindicated for hypotension.

Anesthetic Goals

- Rate:
  - Maintain in normal range
  - Avoid tachycardia
  - β blockers used to reduce LVOT gradient and increase LVEDP.
- Rhythm:
  - Maintaining sinus rhythm important
  - Atrial pacing via pulmonary artery catheter maybe useful.
- Preload:
  - Maintain high preload
  - Saturated intravascular space preferred
  - One of the first steps to treat hypotension.
- Afterload:
  - Maintain high systemic vascular resistance
  - Treat hypotension aggressively with α-agonist.
- Contractility:
  - Prefer myocardial depression
  - Avoid inotropic agents.

Rationale for Anesthetic Goals

- Maintain high preload:
  - LV is thick and hypertrophied with a reduced compliance
  - So outflow tract obstruction increases in hypovolemic conditions.
- *Afterload:* Maintain high afterload:
  - Afterload reduction increases the LVOT obstruction
  - Increasing the afterload reduces the outflow gradient
  - This leads to a reduction in SAM and outflow tract obstruction
  - Thus, vasoconstrictors like phenylephrine and vasopressin are used.

Preoperative Evaluation and Premedication

- Evaluate the patient for:
  - Dynamic obstruction
  - Malignant arrhythmias
  - Myocardial infarction.
- NPO orders
- Maintain adequate preload
- Informed consent
- Heavy premedication advised to avoid anxiety induced tachycardia
- Avoid atropine (glycopyrrolate/scopolamine preferred)
- Chronic β blockade and calcium channel blockers continued up to and on the day of surgery
- These are restarted immediately after surgery especially in those undergoing cardiac surgery.

Monitoring

- Pulse oximetry, capnography
- ECG:
  - Leads V5 and lead II used for monitoring
  - Lead II for diagnosing SVT/junctional tachycardia
  - Lead V5 shows abnormal Q waves at times due to accentuation of normal septal depolarization
  - Abnormal Q waves not to be confused for old MI
  - Some patients may have short PR interval.
- Invasive BP monitoring:
  - Arterial waveform shows pulsus bisferiens
  - Initial rapid peak represents early unobstructed ventricular ejection
  - Subsequent downslope and second peak are a result of dynamic obstruction.
- CVP line:
  - Inaccurate guide to changes in LV volume
  - Useful to administer vasoactive drugs.
- PA catheter:
  - Useful for gauging intravascular volume
  - Maintain PCWP in high normal to elevated range
  - PCWP may overestimate patients true volume status
  - PA catheter with pacing potential preferred.
- Urine output
- Temperature.

Position

- Supine position
- Abrupt positioning changes can cause hemodynamic compromise due to changes in preload.

Induction

- *Avoid histamine releasing agents*
- O_2+N_2O+ opioid induction
- Deep planes of intubation preferred to avoid tachycardia
- Thiopentone given in graded doses.

Maintenance

- $O_2 + N_2O$ + volatile anesthetic (halothane/enflurane)
- Opioids and NDMR given as intermittent boluses
- Vecuronium preferred to avoid tachycardia associated with pancuronium
- Halothane and enflurane especially useful as myocardial depression desirable
- Deep level of GA maintained to avoid tachycardia, especially to surgical incision.

Hemodynamics

- Control of atrial rate and rhythm may be beneficial during prebypass period
- Treat hypotension with volume and vasoconstrictors rather than inotropes and vasodilators to preserve adequate cerebral perfusion pressures
- β blockers used as increased heart rate and contractility will increase LVOT obstruction.
- Avoid agents causing increased contractility:
  - Inotropes
  - Calcium
  - β agonists.

Considerations for CPB

- Surgeon should cannulate aorta before atrial manipulation as insertion of venous cannula may precipitate arrhythmias and hypotension
- If junctional tachycardia/SVT while coming off bypass cardioversion to be done
- In cases of junctional rhythm:
  - Patient preload is dependant on atrial contraction
  - Patients will benefit from atrial pacing which is done by:
    - Transesophageal pacing
    - Use of PA catheter with pacing capability.

Ventilation

- Postoperative ventilation may be required
- Extubate if:
  - Spontaneous ventilation with normal ABG
  - No bleeding and hemodynamically stable patient
  - Normothermia.

Postoperative

Monitors

- BP, ECG
- Pulse oximetry
- Temperature
- Urine output
- Arterial blood gas
- Echocardiography.

Analgesia

Opioids/PCA

Complications

- Arrhythmias:
  - Junctional rhythm
  - Supraventricular tachycardia
- Bleeding.

VENOUS AIR EMBOLISM[1,2,3,5,10,17]

Introduction

- Venous air embolism can occur:
  - During any surgical procedure in which operative site is ≥ 5 cms above RA
  - When pressure within an open vein is subatmospheric.

Pathophysiology

- Two preconditions must exist:
  - Direct communication between a source of air and vasculature
  - Pressure gradient to favor passage of air into circulation.
- Small amounts of air:
  - Broken up in capillary bed and absorbed
  - Does not produce symptoms.
- Large amounts of air:
  - 20 ml of air intravenously can produce complications
  - 5 ml/kg of air in intravenous space required for significant injury: Shock/cardiac arrest
  - 2–3 ml of air in cerebral circulation can be fatal
  - 0.5 ml of air is left anterior descending artery can produce VF.
- Transpulmonary passage of air:
  - Air can traverse pulmonary vascular bed to reach systemic circulation when a large volume of air is presented to pulmonary vascular filter
  - Pulmonary vasodilators including volatile anesthetics, reduce the threshold for transpulmonary passage.

Pathogenesis

Can be caused by any open vein/sinus above the level of heart due to:

- Inability of vein to collapse:
  - Intracranial venous sinuses:
    - Transverse sinus
    - Sigmoid sinus
    - Posterior half of sagittal sinus.
  - Diploic spaces
  - Emissary veins
  - Cervical epidural veins
  - Self-retaining surgical retractors
  - Tracks formed around indwelling catheters (like central venous catheter).
- Level of venous pressure at the site:
  - *Posture*: Sitting > supine > prone > lateral
  - Reverse Trendelenburg position:
    - At + 25° intracranial venous sinus pressure 0 cm H_2O
    - At + 90° produces a negative pressure of -12 ± 3 cm H_2O.
  - Spontaneous ventilation:
    - Causes negative intrathoracic pressure
    - This potentiates negative pressure at operative site.
  - In prone position, suction effect of pendulous abdomen can potentiate negative venous pressure within epidural veins.

Etiology

Surgical Procedures

- Neurosurgery and otolaryngological surgery:
  - Most common cause
  - Especially common in *Fowlers sitting position*
  - Also common in posterior fossa surgeries.
- Craniofacial surgery
- Dental implant surgeries
- Liver transplantation
- Genitourinary surgery:
  - Those done in Trendelenburg position
  - Cesarean section
  - Compromised delivery
  - Surgeries involving tumors with high degree of vascularity.
- Orthopedic surgeries:
  - Hip replacement
  - Spine surgery
  - Arthroscopy.
- Vascular surgery:
  - End arterectomies
  - Lateral decubitus thoracotomy.
- *Laparoscopic procedures:* Incidence of VAE > 50%.

Mechanical Insufflation

- Arthroscopic procedures
- Carbon dioxide hysteroscopy
- Laparoscopic surgeries
- Urethral procedures
- Orogenital sexual activity during pregnancy by entering myometrial veins
- Inadvertent infusion of air during IV contrast agent injection for:
  - CT angiography
  - Cardiac catheterization
  - Cardiac ablation procedures.

- Positive pressure ventilation due to barotrauma (VILI) common in:
  - ARDS
  - Hyaline membrane disease
- Ingestion of hydrogen peroxide (rarely).

Iatrogenic Creation of Pressure Gradient

- Procedures causing pressure gradient:
  - During lumbar puncture
  - Insertion of CVP catheters
  - Thoracocentesis
  - Insertion of hemodialysis catheters/Hickmann's catheters.
- Mechanisms of pressure differential:
  - Fracture/detachment of catheter connection
  - Failure to occlude needle hub
  - Presence of persistent catheter tract following removal of CVP catheter
  - Deep inspiration during insertion/removal which causes negative pressure
  - Hypovolemia which reduces CVP
  - Upright position which reduces CVP.

Diving

- Due to pulmonary barotrauma from voluntary breatholding
- *Decompression sickness*: Air bubbles precipitate out into bloodstream if gas dissolved in blood at pressure, is not allowed sufficient time to outgas as ascent
- Rapid rewarming of following CPB.

Clinical Features

Symptoms

In awake patient:
- Dyspnea, nausea, dizziness
- Continuous cough, substernal chest pain
- Gasp reflex:
  - Classic gasp at times
  - Reported when a bolus of air enters pulmonary circulation
- Agitation, disorientation
- Circulatory arrest if large amount of air blocks RVOT/TV/PV or PA (*Saddle embolus*).

Signs

Central Nervous System:
- Altered mental status
- Loss of consciousness
- Seizures, collapse, coma
- Transient focal neurodeficits
- Air bubbles in retinal blood vessels.

Cardiovascular System:
- Raised JVP
- Nonspecific ST and T changes
- Hypotension
- Dysrrhythmias, MI, cardiovascular collapse
- Pulmonary arterial HTN
- Mill wheel murmur:
  - Loud, machinery like churning murmur
  - Occurs due to blood mixing with air in right ventricle
  - Best heard over precordium.

Respiratory System:
- Tachypnea, rales, wheeze
- Cyanosis, hemoptysis
- Reduced E_TCO_2, Low SpO_2
- Raised airway pressure
- Pulmonary edema
- Raised pulmonary vascular resistance.

Skin:
- Crepitus over superficial blood vessels
- *Livedo reticularis*.

Diagnosis

Arterial Blood Gas

- Hypoxia, hypercapnea
- Metabolic acidosis.

Chest X-ray

- May be normal
- Gas in pulmonary arterial system
- Pulmonary arterial dilatation
- *Focal oligemia*: Westermark sign
- Pulmonary edema.

ECG

- Low sensitivity
- Tachycardia, RV strain pattern
- ST depression, transient MI.

CT Scan

- For embolism in central venous system:
  - Axillary and subclavian vein
  - Right ventricle
  - Pulmonary artery.
- CT head for:
  - Intracerebral air
  - Cerebral edema/infarction.

MRI

- Increased water concentration in affected tissues
- Not so reliable.

Transesophageal ECHO

- *Highest sensitivity*, but invasive modality
- More sensitive than precordial Doppler
- Can detect air bubbles as small as 0.25 ml
- Can detect as less as 0.02 ml/kg of air
- Also evaluates cardiac function, right-left shunting of air.

Precordial Dopper

- *Most sensitive non-invasive modality*
- Placed in right parasternal location between 2nd and 3rd or 3rd and 6th ribs
- Interruption of regular swishing of Doppler signal by sporadic roaring sounds indicates VAE
- Precordial Doppler along with E_TCO_2 is the current standard of care
- Transcranial Doppler useful for cerebral microemboli.

End Tidal CO_2

- Sudden reduction in E_TCO_2 occurs
- This is due to sudden increase in pulmonary dead space causing V-Q mismatch
- Reduction of E_TCO_2 by 2 mm Hg is indicative of VAE.

End Tidal Nitrogen

- Most sensitive gas sensing VAE
- Increased ETN_2 occurs if VAE is present
- *Response time is much faster than E_TCO_2*: Changes occur 30–90 seconds earlier.

Pulse Oximetry

Changes in SPO_2 occur very late

Pulmonary Artery Catheter

- Increase in PA pressure can occur
- Relatively insensitive indicator.

Mean Airway Pressure

Increase in MAP is in direct proportion to amount of air entrained.

Prevention of Venous Air Embolism

- Measures to reduce risk during surgery:
  - Nitrous oxide:
    - N_2O can be used provided it is eliminated when VAE occurs
    - If used, better to use 50% N_2O rather than 70%.
  - Positive end expiratory pressure:
    - PEEP no longer used as even 10 cm H_2O PEEP is unlikely to increase CVP
    - PEEP increases chances of pulmonary artery embolism due to barotrauma
    - It also reduces preload, adding to hypotension.
  - Head end elevation:
    - Elevate head end only as much as necessary
    - + 25° Trendelenburg causes 0 cm H_2O pressure in cerebral circulation
    - + 90° Trendelenburg causes +12 cm H_2O pressure in cerebral circulation.
  - Reduce pressure gradient between site of potential entry and RA
  - Surgeons to be meticulous about:
    - Cauterizing
    - Tying blood vessels
    - Applying bone wax.
  - Screening contrast ECHO to detect ASD before sitting position surgeries
- Measures to reduce risk during CVP placement:
  - Avoid and treat hypovolemia before catheter placement
  - During catheter insertion/removal:
    - Patient should be in supine position with head lowered
    - Insertion site should be 5 cms below RA
    - If patient is awake, he can hold breath to increase CVP
    - Doing Valsalva maneuver also increases CVP.
  - Maintain all connections to central line, line closed/docked when not in use
- Measures to reduce risk during IPPV:
  - Prevent barotrauma by minimizing airway pressure during IPPV
  - Avoid PEEP.

Treatment

- Prevent further air entry:
  - Surgeon should flood or pack surgical field with saline

  - Bone wax is applied to skull edges until entry site is identified
  - Intravascular volume infusion to increase CVP to 10–12 cm H_2O
  - Jugular vein compression:
    - Increases cranial venous pressure
    - Also slows air entrainment and cause back bleeding
    - This may help surgeon identify the source of embolus.
  - Lower the head end to prevent cerebral embolization
  - Close wound quickly if none of measures help
  - Inflatable neck tourniquet available in case of VAE
- Treatment of intravascular air:
  - *Aspirate right heart catheter*: RA catheter mandatory in sitting craniotomies
  - Discontinue N_2O immediately
  - FiO_2 100% with inhalational anesthetic
  - Pressors and inotropes
  - *Durant's position*:
    - Lateral position with right side up
    - Allows air to remain in RA, where it will not contribute to airlock in RV
    - Air can then be aspirated from RA.
  - Chest compressions:
    - Maintains cardiac output
    - Helps to break large air bubbles into smaller ones
    - *Forces air out of RV into pulmonary blood vessels*: Improves cardiac output.
  - Hyperbaric oxygen therapy:
    - In case of neurological manifestations/cardiovascular instability
    - Helps by compression of existing bubbles
    - Establishes high diffusion gradient to speed up resolution of existing bubbles
    - Improves oxygenation of ischemic tissue and also reduces intracranial pressure
    - Good prognosis if initiated within 6 hrs.

Paradoxical Air Embolism

- Passage of air across patent foramen ovale which is present in 25% adults
- Necessary gradient to open foramen ovale may be 5 mm Hg
- Significant increase in right heart pressure must occur for PAE to occur
- Even when mean LAP > mean RAP, PAE can occur due to transient reversal of interatrial pressure gradient which occurs during each cardiac cycle
- PEEP and hypovolemia increase risk of PAE
- Avoid even small air bubbles in IV infusion
- *Major cerebral and coronary morbidity*: Causes MI/stroke postoperatively.

TETRALOGY OF FALLOT[1,2,3,5,17]

Introduction

- Tetralogy of Fallots includes:
  - Large subaortic outlet VSD
  - Right ventricular outflow tract obstruction
  - Overriding of aorta
  - Right ventricular hypertrophy.
- Trilogy of Fallots includes:
  - Atrial septal defect
  - Pulmonary stenosis
  - Right ventricular hypertrophy.
- Pentalogy of Fallots includes:
  - Large subaortic outlet VSD
  - Right ventricular outflow tract obstruction
  - Overriding of aorta
  - Right ventricular hypertrophy
  - Atrial septal defect.

Incidence

2 per 10,000 live births

Embryology

- Due to anterior displacement of the conal septum
- This causes large VSD due to malalignment and narrows the RVOT
- Minor anomalies of the anterior leaflet of tricuspid valve also exist as this leaflet is formed by the coral septum.

Anatomy

- VSD is large and unrestrictive and perimembranous
- RVOT obstruction can be at the level of:
  - Infundibulum of RV
  - Pulmonary valve/annulus
  - Main pulmonary artery
  - Peripheral pulmonary arteries
- Infundibular stenosis due to hypertrophy of subpulmonic muscle: *Crista ventricularis*.

Associated Anomalies

- *Patent foramen ovale*: 50–60%
- *Right aortic arch*: 20–25%

- *Multiple muscular VSDs*: 3–15%
- *Left superior venacava*: 8%
- *Abnormalities of origin of LAD*: Arises from RCA and crosses RVOT
- *PDA*: 4%
- *PA stenosis*: 15–30%
- Unilateral absence of PA, usually LPA.

Pathophysiology

- RVOT obstruction:
  - Is dynamic obstruction
  - Can be increased by increases in heart rate and contractility
  - Degree of RVOT obstruction determines the pathophysiological changes.
- Moderately severe RVOT obstruction
  - Predominant shunt is left-right
  - *Acyanotic patient*: Called *Pink tet*:
    - Patient with TOF with source for adequate PA blood flow from:
      - PDA
      - Major aorto-pulmonary collateral arteries: MAPCAs
      - Naturally occurring PA collaterals:
        - Intercostal artery
        - Bronchial arteries
        - Coronary arteries
    - Patient with TOF and insignificant RVOT obstruction.
- Severe RVOT obstruction:
  - Significant right-left shunt
  - Cyanotic patient.
- Acute increase in right-left shunt is due to:
  - *Reduced SVR*: Hypotension
  - *Increased PVR*: Hypoxia, hypercarbia, acidosis
  - *Increased RVOT obstruction*: Tachycardia, increased contractility.
- Congestive cardiac failure in TOF:
  - Since the VSD decompresses RV, CCF is rare in TOF
  - CCF occurs only if TOF is associated with:
    - Anemia
    - Infective endocarditis, myocarditis
    - Systemic HTN
    - Aortic regurgitation/pulmonary regurgitation.

Clinical Features

- Symptoms:
  - Cyanosis
  - Clubbing
  - *Hypercyanotic Tet spells*
  - Failure to thrive, malnourishment.
- Signs:
  - Cyanosis
  - Clubbing, prominent a waves of JVP
  - RV parasternal heave
  - Single audible A_2 as aorta is anterior displaced
  - P_2 is absent as hardly any blood flow occurs through PA
  - Single S_2 helps to differentiate TOF from isolated VSD or PS
  - Systolic murmur along upper left sternal border.
- If VSD with pulmonary atresia, continuous murmur occurs over anterior and posterior chest bilaterally due to aortopulmonary collateral circulation
- Complications:
  - Paradoxical air embolism
  - Polycythemia
  - Coagulation defects
  - *Pulmonary, renal/cerebral thrombosis*: Especially if hematocrit > 65%
  - Cerebral abscess
  - Infective endocarditis
  - *Cardiomyopathy, AR:* Occur late and cause death.
- Without surgical correction:
  - 25% die in 1st year of life
  - 40% die by 4 years
  - 70% die by 10 years
  - 90% die by 40 years.
- *Assessment of severity*: More severe if:
  - Malnourished, inactive
  - Cyanosis is severe due to increased right-left shunt
  - *Shorter and less intense ESM*: Implies PV is more tight.

Hypercyanotic Tet Spells

Introduction

Paroxysmal episodes in which cyanosis acutely worsens.

Precipitating Factors

Increased sympathetic activity due to:

- Crying, fear, anxiety
- Feeding
- Defecation
- Exercise.

Presentation

- Usually does not begin until after 6 months age
- Most common in acyanotic/mildly cyanotic patients
- Occur most commonly in morning and begins with irritability and crying
- Progresses with increasing cyanosis
- May cause seizures if untreated
- Each attack is potentially fatal
- Frequency varies from once in few days to numerous attacks per day.

Mechanism

Due to acute increase in right-left shunt due to:

- Increase in PVR:
  - Hypoxia
  - Negative intrapleural pressure
  - Hypercarbia
  - Acidosis
  - Intermittent positive airway pressure, PEEP.
- Dynamic outflow obstruction:
  - Increased heart rate
  - Increased contractility:
    - Surgical stimulus
    - Inotropes
  - Hypovolemia.
- Decrease in SVR:
  - SBP < 60 mm Hg triggers episodes
  - Drugs:
    - Volatile anesthetics
    - Histamine releasers
    - Ganglionic blockade.

Treatment of TET Spells

- Reduce PVR:
  - Hyperventilate with 100% oxygen
  - Correct acidosis with IV sodium bicarbonate
- Reduce RVOT obstruction:
  - Deepen anesthetic plane with morphine 0.1–0.2 mg/kg IV
  - β blockers:
    - Propranolol 0.1 mg/kg IV
    - Esmolol
  - Volume administration.
- Increase SVR:
  - *Knee chest position*
  - Correct anemia
  - Phenylephrine: 0.25–0.5 µg/kg bolus or 0.025–0.05 µg/kg/min infusion
  - Norepinephrine 0.05 µg/kg/min infusion
  - Intubation and emergent surgery if unresponsive
  - Abdominal aorta/ascending aortic compression.

Investigations

- *Complete blood count*: Polycythemia
- ECG:
  - Right axis deviation
  - Right ventricular hypertrophy.
- Chest X-ray:
  - May be normal
  - Prominent RV, upturned RV apex
  - Concavity of pulmonary conus
  - Oligemic pulmonary fields
  - Right sided aortic arch
  - Boot shaped heart or *Coeur-en-sabot*.
- Echocardiogram:
  - Perimembranous VSD
  - Aortic override
  - Delineates VSD, atrioventricular valve anatomy
  - Used to determine whether there is continuity between MPA and RPA/LPA.
- Doppler ECHO:
  - To estimate gradient between RV and MPA
  - Also diagnose PDA or LSVC.
- Cardiac catheterization studies:
  - Provides information on PVR
  - Ratio of pulmonary to systemic blood flow (Qp: Qs)
  - Degree of valvular PS.
- *Angiocardiography*: Demonstrates:
  - RVOT obstruction
  - Degree of narrowing of pulmonary annulus and MPA
  - *Major Aortopulmonary Collateral Arteries*: MAPCAS.
- *Fundoscopy:* Recognition of papilledema is difficult due to polycythemia with congested retina.

Management

Medical Management

- Treat hypercyanotic spells
- Prevent factors which causes spells like prolonged examination or venipunctures
- Patients with questionable hypercyanotic spells are treated prophylactically with propranolol 0.5–1 mg/kg TID PO.

Surgical Management

Types of Surgeries

- Palliative procedures:
  - Balloon dilation of pulmonary valve
  - Systemic-pulmonary shunts:
    - *Classic BT shunt:* Right subclavian to right pulmonary artery
    - *Modified BT shunt:* Left subclavian to left pulmonary artery with Goretex material
    - *Glenn shunt:* Superior vena cava to right pulmonary artery
    - *Waterstons shunt:* Ascending aorta to right pulmonary artery
    - *Potts shunt:* Descending aorta to left pulmonary artery.
- Definite correction:
  - Right ventriculotomy
  - VSD closure with dacron patch
  - Excision of obstructing RVOT bundles
  - Pulmonary valvotomy
  - Graft for RVOT.
- Rastellis procedure:
  - External conduit placed from body of RV to PA beyond the stenosis
  - This is done if a major coronary artery crosses RVOT
  - Ventriculotomy avoided in this region in such a situation
  - This is the only contraindication to definitive correction after 2 months of age.
- Unifocalization:
  - If TOF with pulmonary atresia, reconstruction of PA with multiple surgeries followed by VSD closure is done
  - Initially RVOT obstruction is relieved and VSD is left open
  - PA is reconstructed via unifocalization procedure
  - The largest of MAPCAS is used to construct RPA and LPA
  - These are than connected to the RV with a homograft
  - This allows flow from RV into PA, thus helping them to grow
  - Eventually VSD is closed and any residual RVOT obstruction is relieved
  - When necessary, a valved homograft is placed between RV and PA.

Indications for Surgery

- Palliative shunts done if:
  - Very small babies (< 2 mths age)
  - Small PA, as it allows PA to enlarge before total repair
- Definitive surgeries:
  - In infants > 2 months age
  - Severe cyanosis/progressive cyanosis.

Timing of Surgery

Elective surgeries usually done between 6–18 months of age.

Anesthetic Management for Definitive Correction

Preoperative Assessment

- *History and clinical examination*: Check for:
  - Upper respiratory infections
  - Ear discharge
  - Loose teeth.
- Investigations:
  - Serum electrolytes, hematocrit
  - Coagulation profile, blood glucose, acid base status
  - Degree of RVOT obstruction and LSVC presence noted.

Preoperative Preparation and Premedication

- NPO guidelines:
  - 6 hours solids, 4 hours breast milk, 2 hours clear fluids
  - Maintain oral feeds/administer IV fluids to avoid dehydration
- Premedicate to avoid sympathetic stimulation:
  - Midazolam 0.5–1 mg/kg 20 minutes before surgery PO
  - Morphine 0.05–0.2 mg/kg IV
  - Avoid sedation in infants < 6 months age
- Anticholinergic to avoid bradycardia associated with anesthetic induction:
  - Atropine 20 µg/kg
  - Glycopyrrolate 10 µg/kg IV as alternative
  - Atropine 10–15 µg/kg PO can be used
  - *Important as patient is already β blocked*: Profound bradycardia can occur.
- Antibiotics:
  - Class IIa recommendations for infective endocarditis prophylaxis
  - Cefazoline 25 mg/kg IV

  - Vancomycin 20 mg/kg IV if penicillin allergy, given over 1 hour
- Continue propranolol up to and on day of surgery
- Continue PGE_1 infusion if already present to keep PDA patent.

OT Preparation

- Suction equipment
- Oxygen source
- *Airway:* ET tube, laryngoscope, blade, airways
- Anesthetic drugs
- Emergency drugs:
  - Epinephrine
  - Atropine
  - Phenylephrine
  - Calcium gluconate
  - Propranolol.

Monitoring

- Pulse oximetry
- Blood pressure:
  - NIBP and IBP used
  - *Location of IBP:* Avoid arteries affected by previous shunts
  - Allows continuous BP assessment and ABG sampling
- ECG, E_TCO_2
- Rectal and esophageal temperature probe
- Urine output
- Central venous catheter:
  - Right IJV/femoral vein
  - Left IJV cannulated if left sided SVC is present.
- Transesophageal echocardiography:
  - For LV and RV function
  - Presence of residual VSD/intracardiac air post correction.
- PA catheter:
  - Not necessary
  - Used to assess PA and LA pressures.

Anesthetic Considerations

- Maintain adequate preoperative hydration and sedation
- Maintain SVR and intravascular volume
- Minimize PVR
- Provide mild myocardial depression
- Relatively slow heart rate desirable
- Deep planes of anesthesia preferable
- Avoid:
  - Histamine releasing agents:
    - Atracurium
    - Morphine
    - Pethidine
  - Excessive PEEP
  - Air bubbles in IV line.

Induction

- Atleast one, but preferably two large bore IV cannulas secured
- Adequate preoxygenation for 5 mins
- *If IV line present:* Induction with ketamine 2 mg/kg and vecuronium 0.1 mg/kg
- If IV line not present:
  - *Inhalational induction:* With oxygen and halothane/sevoflurane
  - IM induction:
    - With ketamine 5 mg/kg IM
    - Obtain IV access
    - Administer IV vecuronium 0.1 mg/kg or pancuronium 0.1 mg/kg.
- IV induction is faster than inhalational induction
- Intubate in deeper planes to prevent intubation response
- Leak above 22–25 cm H_2O preferred if uncuffed ET tube is used
- Fentanyl infusion at 0.1 µg/kg/min causes less hemodynamic changes at the time of intubation and sternotomy
- Correct any acidosis if present
- Cross matched blood to be readily available
- Avoid:
  - Air bubbles in tubing to prevent PAE
  - Histamine releasing drugs as it reduces SVR
  - Excitement/agitation at the time of induction.

Maintenance

- O_2 with halothane/isoflurane
- N_2O avoided
- If used, 50% N_2O with 50% oxygen preferred
- Fentanyl 5–10 µg/kg or sufentanyl 1–2 µg/kg with vecuronium or pancuronium
- Manage tet spells as mentioned earlier.

Ventilation

- Avoid increased airway pressure
- Avoid excessive PEEP
- *Mild hyperventilation*: Maintain $PaCO_2$ around 30 mm Hg

- N_2O does not cause much increase in PVR, but 100% O_2 preferred to avoid hypoxia.

Hemodynamics

- Maintain SVR, and euvolemia
- Avoid increases in PVR
- Slow heart rate preferable
- Provide mild myocardial depression
- Initiation of CPB causes hemodilution
- Hematocrit as low as 20% may be allowed on CPB
- Plasma and platelets may be required in post-bypass period to reduce bleeding secondary to dilutional thrombocytopenia and coagulopathy
- Whole blood may be useful.

Considerations for CPB

- After institution of CPB, administer:
  - Opioids, benzodiazepines and muscle relaxants
  - Repeat antibiotic on CPB.
- Any pre-existing shunt (systemic-pulmonary) is clamped to avoid pulmonary hyperperfusion
- Moderate hypothermia (25 ºC–28 ºC) used for CPB
- Deep hypothermic arrest:
  - 18–20 ºC for deep hypothermic arrest
  - Administer 10 ml/kg dextran 40 in 5% dextrose before cooling is initiated.
- Blood cardioplegia with high dose potassium (30 mEq/L) for cardiac arrest
- Monitor:
  - Blood gases every 20–30 minutes to ensure adequate gas exchange and perfusion
  - Mixed venous O_2 saturation to assess tissue perfusion
  - ACT every 20–30 minutes to ensure adequate anticoagulation
  - ACT maintained ≥480 sec
  - *Urine output*: Maintain urine output at 1–2 ml/kg/hr.
- Heparin reversed with protamine after removal of aortic cannula
- After heart is closed, Trendelenburg position given and deairing to remove air bubbles
- Inotropic support with epinephrine/dopamine/dobutamine/milrinone after declamping
- Weaning from CPB after temperature reaches 36 °C and heart has stable hemodynamics.

Extubation

- Usually mechanically ventilated postoperatively, for 24–72 hours
- Once patient is fully awake, hemodynamically stable and peripherally warm, patient is extubated.

Postoperative

Ventilation

- Avoid increased airway pressure, high FiO_2
- Avoid excessive PEEP
- *Mild hyperventilation*: Maintain $PaCO_2$ around 30 mm Hg.

Complications

- Immediate complications:
  - Left anterior hemiblock/complete heart block/RBBB
  - Residual VSD, residual RVOT obstruction
  - Residual PS
  - Pulmonary regurgitation as valve is frequently excised
  - Low output state
  - Coagulopathies
  - Renal failure
  - Stroke
  - Infection.
- Late complications:
  - RVOT obstruction
  - RVOT aneurysm
  - Residual VSD
  - Valvular insufficiency.

Monitoring

- SpO_2, IBP, ECG
- CVP, ABG
- Urine output, blood glucose
- Peripheral temperature, airway pressure
- Echocardiography.

Pain

- Adequate analgesia important
- Morphine 0.1 mg/kg IV or fentanyl 0.5 µg/kg IV boluses.

Anesthetic Management for Shunt Procedures

Preoperative Assessment

- *History and clinical examination*: Check for:
  - Upper respiratory infections
  - Ear discharge
  - Loose teeth.
- Investigations:
  - Serum electrolytes, hematocrit

  - Coagulation profile, blood glucose, acid base status
  - Degree of RVOT obstruction and LSVC presence noted.

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- Oxygen source
- *Airway*: ET tube, laryngoscope, blade, airways
- Anesthetic drugs
- Emergency drugs:
  - Epinephrine
  - Atropine
  - Phenylephrine
  - Calcium gluconate
  - Propranolol.

Monitoring

- Pulse oximetry:
  - Placed on hand opposite to the side of proposed shunt
  - Occasionally placed on both upper and lower extremity.
- ECG, $ETCO_2$
- BP:
  - NIBP cuff during induction
  - IBP if required after induction
  - Site of IBP should avoid arteries affected by current procedure
  - Same side subclavian artery will be clamped, obliterating radial pulse
- Rectal and esophageal temperature probes
- Precordial stethoscope
- Urine output.

Induction

- Atleast one, but preferably two large bore IV cannulas secured
- Adequate preoxygenation for 5 mins
- *If IV line present*: Induction with ketamine 2 mg/kg and vecuronium 0.1 mg/kg
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- IV induction is faster than inhalational induction
- Intubate in deeper planes to prevent intubation response
- Leak above 22–25 cm H_2O preferred if uncuffed ET tube is used
- Fentanyl infusion at 0.1 µg/kg/min causes less hemodynamic changes at the time of intubation and sternotomy
- Correct any acidosis if present
- Cross matched blood to be readily available
- Avoid:
  - Air bubbles in tubing to prevent PAE
  - Histamine releasing drugs as it reduces SVR
  - Excitement/agitation at the time of induction.

Position

- *Lateral position:* If thoracotomy
- *Supine position:* If midline sternotomy.

Maintenance

- O_2 with halothane/isoflurane
- N_2O avoided

- Fentanyl 5–10 µg/kg or sufentanyl 1–2 µg/kg with vecuronium
- Manage tet spells as mentioned earlier.

Ventilation

- Avoid increased airway pressure
- Avoid excessive PEEP
- *Mild hyperventilation:* Maintain $PaCO_2$ around 30 mm Hg
- Maintain mild alkalosis
- 100% O_2 preferred to avoid hypoxia as:
  - SpO_2 may decrease with one lung ventilation
  - SpO_2 may further decrease with clamping of PA to facilitate anastomosis.

Hemodynamics

- Maintain SVR:
  - Avoid drugs which reduce SVR
  - Promptly treat hypotension with vasoconstrictors
  - Whole blood or PRBCs avoided for volume replacement as preoperative HCT is usually high.
- Decrease PVR:
  - High FiO_2
  - Hypocarbia, mild alkalosis
  - Deep planes of anesthesia
  - NTG, SNP, phentolamine, PGE_1, inhaled nitric oxide if required.
- Favor myocardial depression:
  - Halothane
  - β blockers
  - Fentanyl 0.1 µg/kg/min infusion.
- Careful application of cross-clamp to prevent PA distortion helps to maintain pulmonary blood flow
- Severe desaturation and bradycardia at the time of cross-clamp may necessitate institution of CPB
- *Persistent hemodynamic instability*: Dopamine 5–10 µg/kg/min as it also increases flow through the new shunt
- Once shunt is completed and graft is in place, systemic BP may reduce due to runoff into PA
- Some surgeons may use heparin to maintain graft patency.

Intraoperative Complications

- Hypercyanotic tet spells
- Bleeding
- Severe desaturation during chest closure due to:
  - Change in relation of intrathoracic contents
  - Distortion of PA
  - Kinking of the shunt.

Extubation

- Can be done soon after surgery
- Criteria for extubation:
  - Spontaneous ventilation
  - Normal ABG
  - Normothermia
  - Stable hemodynamics
  - Controlled bleeding.
- Prolonged intubation not advised.

Postoperative

Ventilation

- Extubated soon after surgery
- Prolonged intubation not advised

PAIN: Morphine 0.1 mg/kg or fentanyl 0.1 µg/kg IV.

Monitoring

- SpO_2, BP
- ECG, ABG
- Temperature, urine output
- Echo for RV/LV function.

Complications

- Bleeding
- Pneumothorax
- Pulmonary hyperperfusion and pulmonary edema
- Desaturation due to small shunt size
- Shunt thrombosis
- PA hypoplasia.

Role of RA in Shunting/Definitive Surgery

- More effective in inhibiting stress response associated with surgery than IV narcotics
- Spinal anesthesia:
  - Provides excellent pain relief and allows early extubation
  - Spinal given soon after intubation to maximize time before anticoagulation
  - Given for procedures not involving CPB.
- Epidural (continuous) and caudal anesthesia:
  - Useful and can be used for procedures involving CPB
  - In children, epidural catheter can be threaded through sacrococcygeal membrane for 16–18 cms to reach thoracic epidural space .
  - Complications:
    - Hypotension is very uncommon in children

- Risk of epidural hematoma is small
- Epidural catheter removed after return of normal coagulation parameters postoperatively.

– Continuous epidural doses:
- Initial bolus 0.25% bupivacaine 0.5 ml/kg with hydromorphone 7–8 µg/kg
- *Supplemental doses*: 0.25% bupivacaine 0.3 ml/kg
- *Postoperative period*: 0.1% bupivacaine with hydromorphone 3 µg/kg at 0.3 ml/kg/hr.

INFECTIVE ENDOCARDITIS[1,2,3,5,8]

Introduction

- Proliferation of microorganisms on endothelium of the heart
- Proliferation of microorganisms on arteriovenous shunts, arterioarterial shunts (PDA) or coarctation of aorta is called infective endarteritis.

Pathology

- Vegetations occur at the site of infection
- Vegetation consists of:
  – Platelets
  – Fibrin
  – Microcolonies of microorganisms
  – Scant inflammatory cells.
- Sites of infection:
  – Heart valves (native/prosthetic)
  – On low pressure side of septum in VSD
  – Mural endocardium at sites of damage by aberrant jets of blood or foreign bodies
  – Intracardiac devices.

Classification

- Acute endocarditis:
  – Usually caused by:
    - β hemolytic streptococci
    - Staphylococci
    - Pneumococci
  – *Hectic fever*
  – Rapidly damages cardiac structures
  – Hematogenously seeds extracardiac sites
  – Progresses to death within weeks.
- Subacute endocarditis:
  – Usually caused by:
    - Streptococcus viridians
    - Enterococci
    - Coagulase negative staphylococci
    - HACEK organisms.
  – Indolent course
  – Duration of illness > 3 weeks
  – Structural damage occurs slowly
  – Rarely causes metastatic infection
  – Gradually progressive unless complicated by major embolic event or ruptured mycotic aneurysm.

Etiology

Causative Organisms

- Bacteria:
  – Streptococci, HACEK
  – Pneumococci, enterococci
  – Staphylococcus aureus
  – Coagulase negative staphylococcus
  – HACEK group of organisms
  – Polymicrobial.
- Fungal:
  – Candida
  – Histoplasma
  – Aspergillus
  – Blastomyces
  – Mucormyces.

Predisposing Factors

- Congenital heart disease:
  – Ventricular septal defect
  – Tetralogy of fallot
  – Aortic stenosis
  – Bicuspid aortic valve
  – Tricuspid atresia.
- Surgical/natural shunts:
  – Blalock-Taussig shunt
  – Coarctation of aorta.
- Biprosthetic valves and intracardiac devices:
  – Intercostal drain
  – Transvenous pacemaker.
- Drug addicts: Most commonly, right sided IE involving TV/PV.

Precipitating Factors

- Dental extraction
- Brushing of teeth
- Nasotracheal intubation
- Orotracheal intubation
- Use of oral irrigation devices
- Upper GI endoscopy
- TURP
- Barium enema.

Clinical Features

Features Indicating Infection

- Fever:
- 103–104 °F, acute
- Low grade in subacute infective endocarditis
- Chills, rigors, night sweats
- Arthralgia and diffuse myalgia
- Weakness, malaise, loss of appetite, weight loss
- Amenorrhea in females.

Cardiac Manifestations

- New regurgitant murmur suggests infective endocarditis
- Change in quality of pre-existing murmur
- Perivalvular absesses and fistula
- Embolic events:
  - Stroke
  - Splenic infarct
  - Mesenteric embolism.
- CCF in 30–40% due to:
  - Valvular dysfunction
  - IE associated myocarditis.
- Pericarditis from burrowing of abscess into pericardium
- Heart block due to extension of infection into upper interventricular septum
- MI due to emboli into coronary artery.

Immunological Manifestations

- Arthralgia, myalgia
- Petechiae over skin, mucous membrane and conjunctiva
- *Roth spots:* Petechiac in retina
- *Oslers nodes:* Tender erythematous nodules on pulp of fingertips
- *Janeway lesions:* Non-tender erythematous patches on palms and soles
- *Splinter hemorrhages:* Hemorrhagic spots under nails
- Clubbing, splenomegaly, hematuria.

Other Noncardiac Manifestations

- *CNS:* Stroke, aseptic/purulent meningitis, intracranial hemorrhage due to hemorrhagic infarcts or ruptured mycotic aneurysms, seizures, encephalopathy
- *Mycotic aneurysms:* Focal dilatation of arteries at points in arterial wall weakened by infection in vasa-vasorum where septic emboli have lodged
- Hematogenously seeded infection of skin, spleen, kidney, skeletal system and meninges
- *Embolic events:* Extremities, spleen, kidney, bowel, brain
- Diffuse glomerulonephritis, renal failure/embolic renal infarcts.

Investigations

Identification of Organism

- Blood culture:
  - For diagnosis and detecting antibiotic susceptibility
  - *Sampling*: In the absence of prior antibiotic therapy:
    - Total of three blood culture sets
    - Ideally with first sample separated from the last by atleast 1 hour
    - Obtained from different venipuncture sites over 24 hrs
  - If culture remains negative after 45–72 hrs, two additional cultures obtained to detect fastidious organisms
  - Mainstay of diagnosis.
- Serological tests:
  - Brucella
  - Bartonella
  - Legionella
  - Coxiella burnetti.
- Special stains like periodic acid schiff for tropheryma whippelii
- PCR to recover microbial DNA/RNA.

Echocardiography

- TEE safe and more sensitive compared to transthoracic echocardiography
- Uses:
  - Confirms IE
  - Size of vegetation
  - Detection of intracardiac complications
  - To assess cardiac function.

Other Studies

- Complete blood counts:
  - Normocytic normochromic anemia
  - Leukocytosis
  - Thrombocytopenia.

- Serum creatinine, chest X-ray, ECG
- ESR, CRP levels
- Circulating immune complex titres, RF concentration
- Low complement levels, hypergammaglobulinemia
- *Urine*: Microscopic hematuria and albuminuria
- Cardiac catheterization to check patency of coronary arteries in elderly patients undergoing surgery for endocarditis.

Diagnosis

Dukes criteria

Major Criteria

- Positive blood culture:
  - Recovery of microorganisms consistent with IE from:
    - Blood culture drawn ≥ 12 hrs apart or
    - All of 3 or a majority of 4 or more separate cultures with 1st and last drawn at least 1 hour apart.
  - Single positive culture for C. Burnetti
- Evidence of endocardial involvement:
  - Positive echocardiogram:
    - Oscillating intracardiac mass on valve or
    - Abscess or
    - New partial dehiscence of prosthetic valve.
  - New valvular regurgitation.

Minor Criteria

- Predisposing heart conditions or injection drug abuse
- Fever ≥ 38 °C (≥ 100.4 °F)
- Vascular phenomena:
  - Major arterial emboli
  - Stroke
  - Septic pulmonary infarcts
  - Mycotic aneurysms
  - Janeway lesions.
- Immunological phenomenon:
  - Glomerulonephritis
  - Oslers nodes
  - Roths spots
  - RF factor.
- *Microbiology:* Positive blood culture not meeting major criteria/serology tests.

Interpretation

Diagnosed as infective endocarditis if:

- 2 major criteria or
- 5 minor criteria or
- 1 major with 3 minor criteria.

Treatment

Antimicrobial Therapy

Bacterial endocarditis:

No	Organism	Drug	Duration
1	Streptococcus		
	Penicillin sensitive	Penicillin G	4 weeks
		Penicillin G and gentamicin	2 weeks
		Ceftriaxone	4 weeks
		Vancomycin	4 weeks
	Moderately penicillin resistant	Penicillin G and gentamicin	4–6 weeks
2	Enterococci	Penicillin G and gentamicin	4–6 weeks
		Ampicillin and gentamicin	4–6 weeks
		Vancomycin and gentamicin	4–6 weeks
3	Staphylococcus		
	MSSA with native valve	Nafcillin and gentamicin	4–6 weeks and 3–5 days
		Cefazolin and gentamicin	4–6 weeks and 3–5 days
		Vancomycin	4–6 weeks
	MRSA with native valve	Vancomycin	4–6 weeks
	MSSA with prosthetic valve	Nafcillin and gentamicin and rifampicin	6–8 weeks and 2 weeks and 6–8 weeks
	MRSA with prosthetic valve	Vancomycin and gentamicin and rifampicin	6–8 weeks and 2 weeks and 6–8 weeks
4	HACEK	Ceftriaxone	4 weeks
		Ampicillin and gentamicin	4 weeks

Fungal Endocarditis

- Amphotericin B:
  - Started at 0.25 mg/kg/day
  - Increased by 0.25 mg/kg/day till maximum of 1 mg/kg/day × 2 wks IV.
- 5 fluorocysteine 50–150 mg/kg/day in four divided doses PO
- Both antifungals continued for 2–3 wks
- After this, patient is taken up for surgical removal of vegetation

Drug Doses

No	Drug	Dosage	Frequency
1	Penicillin G	10–20 million units/day	4 doses/day
2	Cefazoline	60 mg/kg/day	3 divided doses
3	Gentamicin	7.5 mg/kg/day	2 divided doses
4	Ampicillin	400 mg/kg/day	4 divided doses
5	Cloxacillin	200 mg/kg/day	3 divided doses
6	Vancomycin	60 mg/kg/day	2–3 divided doses
7	Oxacillin/nafcillin	2 gms	Q4H

Surgical Treatment

- Indications for cardiac surgery:
  - Surgery required for optimal outcome:
    - Moderate to severe CCF
    - Partially dehisced prosthetic valve
    - *Ineffective antimicrobial therapy*: Brucella/fungal infections
    - S. aureus prosthetic valve endocarditis with intracardiac complications.
  - Surgery strongly considered for improved outcome:
    - Perivalvular extension of infection
    - Large (≥ 10 mm diameter), mobile vegetation
    - Persistent unexplained fever (≥ 10 days)
    - Antibiotic resistant enterococci/gram negative bacilli.
- Timing of cardiac surgery:

No	Timing	Indication
1	Emergent (same day)	Acute AR with preclosure of mitral valve
		RSOV into right heart
		Rupture into pericardial sac
2	Urgent (within 1–2 days)	Valve destruction by vegetation
		Unstable (dehisced prosthesis)
		Acute AR/MR with heart failure
		Septal perforation
		Perivalvular extension of infection
3	Elective (usually earlier preferred)	Progressive paravalvular prosthetic regurgitation
		Fungal endocarditis
		Persistent infection after 7–10 days of antibiotic therapy

Infective Endocarditis Prophylaxis[1]

ACC-AHA 2008 guidelines

IE Prophylaxis Recommended for Following Procedures

- Dental procedures involving:
  - Manipulation of gingival tissues
  - Periapical region of teeth
  - Perforation of oral mucosa.
- Respiratory procedures involving incision or biopsy of respiratory muscles
- Infected skin, skin structures or musculoskeletal tissue
- Patients with joint replacement undergoing high risk procedures if:
  - During first 2 yrs after joint replacement
  - Immunocompromised patients
  - Patients with inflammatory arthropathies:
    - Systemic lupus erythematosus
    - Rheumatoid arthritis
  - Comorbid conditions:
    - Previous prosthetic joint infection
    - Malnutrition
    - Hemophilia
    - Insulin dependent diabetes mellitus
    - Malignancy.
- For elective procedures, coexisting enterococcal UTIs should be treated before genitourinary/gastrointestinal procedures
- For emergent procedures, IE prophylaxis considered for patients at highest risk for IE.

IE Prophylaxis no Longer Recommended for Following Procedures

- Gastrointestinal or genitourinary procedures
- For bronchoscopy, unless the procedure involves incision of respiratory mucosa
- For non-dental procedures like:
  - Transesophageal echocardiography
  - Esophagogastroduodenoscopy
  - Colonoscopy
- In patients with screws/pins/plates
- In patients with previous bypass surgeries/stents.

IE Prophylaxis Recommended for Following Cardiac Conditions

- There are no class I recommendations for IE prophylaxis.

- Class IIa recommendations:
  - Prosthetic cardiac valves
  - Patients with unrepaired cyanotic CHD including palliative shunts and conduits
  - Completely repaired CHD with prosthetic material during first 6 months after procedure when endothelialization is taking place
  - Cardiac transplant recipient with valve regurgitation
  - Repaired CHD with residual defects
  - Previous infective endocarditis
  - Patients with congenital heart disease.

IE Prophylaxis Not Recommended for Following Cardiac Conditions

Class III recommendations:

- Patients with isolated secundum ASD
- 6 mths or more after ASD/VSD/PDA repair
- Patients with physiological, functional/innocent heart murmurs, including aortic sclerosis
- Physiological MR without murmur and structurally normal valves
- Physiological TR/PR without murmur and structurally normal valves.

Drugs for Prophylaxis

Single dose given 30–60 mins before surgery

No	Situation	Drug	Adults	Children
1	Oral	Amoxicillin	2 gms PO	50 mg/kg
2	Unable to take orally	Ampicillin	2 gms IV/IM	50 mg/kg
		Cefazoline	1 gms IV/IM	50 mg/kg
		Ceftriaxone	1 gm IV/IM	50 mg/kg
3	Allergic to penicillin, oral	Cephalexin	2 gms PO	50 mg/kg
		Clindamycin	600 mg PO	20 mg/kg
		Azithromycin	500 mg PO	15 mg/kg
		Clarithromycin	500 mg PO	15 mg/kg
4	Allergic to penicillin	Cefazoline	1 gm IV/IM	50 mg/kg
	Unable to take oral	Ceftriaxone	1 gm IV/IM	50 mg/kg
		Clindamycin	600 mg	20 mg/kg
5	Allergic to penicillin, MRSA	Vancomycin	1 gm IV	20 mg/kg

PACEMAKER[1,2,3,5,17]

Classification of Pacemakers

NASPE/BPE 2002 Code

Position I Pacing chamber	Position II Sensing chamber	Position III Response to sensing	Position IV Programmability	Position V Antibradycardia pacing chamber
O = None	O = None	O = None	O = None	O = none
A = Atrium	A = Atrium	I = Inhibited	R = Rate modulation	A = Atrium
V = Ventricle	V = Ventricle	T = Triggerred		V = Ventricle
D = Dual (A+V)	D = Dual (A+V)	D = Dual (T+I)		D= Dual (A+V)

Generic Defibrillator Code

NASPE/BPEG

Position I Shock chamber	Position II Antitachycardia pacing chamber	Position III Tachycardia detection	Position IV Antibradycardia pacing chamber
O = None	O = None	E = Electrogram	O = None
A = Atrium	A = Atrium	H = Hemodynamic	A = Atrium
V = Ventricle	V = Ventricle		V = Ventricle
D = Dual (A+V)	D = Dual (A+V)		D = Dual (A+V)

Indications for AICD

- *Brugadas syndrome*
- Arrhythmogenic RV dysfunction
- Long QT syndrome
- Ventricular fibrillation
- Hypertrophic Obstructive Cardiomyopathy (HOCM).

Preoperative Evaluation

- Focussed history:
  - History of:
    - HTN, DM, MI
    - Previous cardiac surgery
    - Cardiomyopathy
    - Peripheral vascular disease
    - Valvular heart disease
    - Congenital heart disease.
  - *History suggestive of pacemaker dysfunction*: Battery failure:
    - Vertigo
    - Syncopal attacks.
- Focussed examination:
  - Assess previous cardiac disease
  - Assess pacemaker function:
    - Reason for pacemaker insertion
    - Type of pacemaker:
      - *Demand:* Synchronous
      - *Fixed:* Asynchronous
      - AICD.
    - Time of insertion:
      - Electrode displacement possible within 4–6 weeks of insertion
      - Battery failure if long-term.
    - *Irregular heart rate*: Possible competition of pacemaker with intrinsic heart rate
    - Check if pacing pulses are present and create paced beats
- Cardiologists opinion of pacemaker function
- Investigations:
  - ECG:
    - For ischemia/previous MI
    - *Confirm pacing capture:* Pacing rate > intrinsic rate
    - *No intrinsic rhythm:* Patient is pacemaker dependent
    - *Only intrinsic rhythm:* Test pacemaker function by converting to fixed mode with magnet.
  - Chest X-ray:
    - Heart size, lung fields
    - Continuity of pacing leads, distal tip to be within cardiac cavity
    - Location of generator
    - Dual/single chamber
  - *Serum potassium:* Hyperkalemia increases pacing threshold
  - *Acid base balance:* May affect pacing threshold.

Factors Affecting Pacing Function Perioperatively

- *Electrolyte:* Hypo/hyperkalemia
- *Acid base balance:* Acidosis/alkalosis
- *Myocardial:* Ischemia/acute infarction
- *Drugs:* Digoxin toxicity, catecholamines, antiarrhythmics
- *Metabolic:* Hypothermia, thyroid disturbances, hypoxia, hypoglycemia
- Factors which increase the pacing threshold:
  - Hyperkalemia
  - Acidosis, alkalosis
  - Hypoxia, hypoglycemia
  - Hypothermia
  - Antiarrhythmics
  - Thyroid disturbances.

Preoperative Preparation

- Informed consent
- NPO orders
- Premedication with benzodiazepines/opioids
- *Correct associated imbalances*: Potassium and acid base imbalances
- If electromechanical interference (EMI) unlikely, no special precaution needed
- If EMI likely and Cardiac Rhythm Management Device (CRMD) is pacemaker:
  - Reprogram to asynchronous mode when indicated
  - Suspend rate adaptive functions
  - Magnet kept ready to convert to asynchronous mode.
- If EMI likely and CRMD is AICD:
  - Suspend antitachyarrhythmia function
  - Switch off AICD before surgery and attach external pads.

OT Preparation

- Suction apparatus
- Oxygen delivery apparatus
- Anesthetic drugs

- Monitors
- Chronotropic drugs kept ready
  - Atropine: 0.5–3 mg
  - Isoprenaline: 10–100 µg bolus or 1–10 µg/min
  - Ephedrine: 3–30 mg
  - Adrenaline
- Temporary pacing made available
- External cardioverter-defibrillator kept ready.

Monitoring

- Pulse oximetry
- BP, urine output
- *ECG:* Turn off artifact filter
- Peripheral pulse to check cardiac output and pacemaker function
- Invasive monitoring if indicated for surgery
- ABG for electrolytes
- *Nerve stimulator*: May interfere with pacing
- Beat to beat continuous CO monitor in HOCM.

Choice of Anesthetic Technique

- Neuraxial blocks/regional anesthesia:
  - Vasodilation may be poorly tolerated with fixed heart rate
  - Avoid underhydration
  - Caution during nerve blocks as nerve stimulator interferes with pacing
- General anesthesia:
  - *Better preferred*
  - TIVA is preferable.

Considerations for General Anesthesia

Intraoperative

- Ketamine and etomidate cause myofasciculations which may interfere with pacing
- TIVA preferable as volatile anesthetics increase AV delay and pacing threshold
- Halothane is avoided
- N_2O accumulates in pacemaker generator pockets
- Caution with succinylcholine as:
  - Acute increase in potassium causes increase in pacing threshold
  - Myopotentials during fasciculations may be abnormally sensed
- Avoid underhydration
- Considerations for diathermy/electrocautery interference:
  - Use bipolar cantery/ultrasonic scalpel
  - Position of return plate:
    - ICD or pacemaker should not be between the return plate and active electrode
    - Plane described by return plate and active electrode of electrocautery is perpendicular to plane described by pacemaker and pacemaker electrode
  - Use smallest current required to cut/coagulate
  - *Use in short bursts*: One second for every 10 seconds
  - Avoid using electrocautery within 6 inches of the device/leads
  - Activating electrocautery within 15 cms of pacemaker will cause interference, even if not touching the patient.
- Considerations for pacemaker/AICD:
  - Signals from electrocautery maybe misinterpreted as dysrhythmias
  - Convert AICD to no-response either by programming or using magnet
  - Convert pacemaker to asynchronous mode so that it is not inhibited by cautery
  - Once converted, device will not deliver therapy secondary to misinterpretation
  - Do not use electrocautery when AICD is programmed to sense and deliver therapy
  - AICDs must be programmed to respond to a magnet
  - Magnet will not change bradycardia related pacing parameters in the ICD
  - Problems due to electromagnetic interference caused by electrocautery:
    - Reprogramming/inhibition of pacemaker
    - Noise reversion mode/electrical reset
    - Increase in pacemaker threshold
    - Myocardial burns
    - Inappropriate sensing and charging in ICDs.

Postoperative Care

- Immediate postoperative period:
  - Check pacemaker functions, if procedure involved cardioversion and diathermy
  - Monitor cardiac rate and rhythm continuously
  - Back up pacing and cardioversion/defibrillation capability.
- Postoperative restoration of CRMD function:
  - Use cardiologist help
  - Interrogate to assess function
  - Reprogram appropriate setting
  - If CRMD is AICD, restore all antitachycardia therapy.

Treatment of Pacemaker Failure[1,3]

Rate	Response
adequate to maintain BP	Oxygen, airway control
	Place magnet over pacemaker
	Atropine, if sinus bradycardia
Severe bradycardia and hypotension	Oxygen, airway control
	Place magnet over pacemaker
	Transcutaneous/transvenous pacing if magnet fails
	Atropine if sinus bradycardia
	Isoproterenol to increase ventricular rate
No escape rhythm	Cardiopulmonary resuscitation
	Place magnet over pacemaker
	Transcutaneous/transvenous pacing if magnet fails
	Isoproterenol to increase ventricular rate

Emergency Cardioversion/Defibrillation

- Terminate all EMI sources
- Remove magnet to enable defibrillation pads
- Minimize current flow through pulse generator/leads
- Defibrillation pads placed as far away from pulse generator as possible
- Defibrillation pads placed perpendicular to major axis pulse generator/leads
- To extent possible, pads placed in anterior-posterior location
- Use clinically appropriate energies.

Complications

- Failure to fire
- Failure to capture
- *Pacemaker syndrome* seen with VVI mode
- Pacemaker tachycardia.

Patients with AICD

- All ICDs have pacemakers incorporated into circuitry
- Preoperative assessment of cardiac condition
- Cardiology opinion for:
  - ICD interrogation
  - Programming device to no-response mode
- No clear preferences of anesthetic technique between regional/general anesthesia
- Apply patches for external defibrillation when ICD is programmed to no response
- Ensure these pads are as far away as possible from device
- Pads not to be in same plane as device and electrodes
- If PA catheter monitoring is required:
  - Discuss with the cardiologist
  - Document the need for PA catheter and discussion with cardiologist
  - Discuss possibility of dislodgement of ICD electrodes with patient
  - Maintain sterile technique, consider antibiotics before inserting lines.
- Continue antiarrhythmic drugs until time of surgery
- If intraoperative arrhythmias occur:
  - Treat intraoperative causes to prevent recurrence
  - If dysrhythmia continues and *magnet has been used* to create no response mode
  - Remove magnet from ICD
  - Allow ICD to charge and deliver a response
  - If dysrhythmia continues and ICD has been *programmed* to no response mode
  - Reprogram ICD to deliver a response
  - Alternatively, use external defibrillation directly
  - Place external defibrillation paddles in antero-posterior location
  - Deliver sufficient shock
  - External pacing may be required if pacemaker/ICD is damaged with the shock.
- While transporting the patient from OR:
  - Monitor patients ECG
  - Be prepared to deliver external defibrillation
  - Interrogate and reprogram ICD when patient has entered PACU.

Special Considerations

- TURP:
  - Use harmonic scalpel
  - Cutting mode may cause electromagnetic interference
  - Use cautery in short bursts
  - Coagulation mode does not interfere
  - May have to convert to fixed mode if diathermy plate placed around chest
  - Possibility of random reprogramming due to EMI.
- Elective cardioversion:
  - Use lowest possible energy
  - Paddles placed as far away from generator as possible (>10 cm)

  - Paddles placed perpendicular to line between generator and lead tip
  - Follow-up with formal pacemaker interrogation.
- MRI:
  - Contraindicated in pacing dependent patients
  - If required, consult:
    - Physician
    - Cardiologist
    - Radiologist
    - Manufacturer.
- Radiotherapy:
  - ≥ 1000 rads causes pacemakers damage
  - Pulse generator and leads should be outside radiotherapy field
  - Possible surgical relocation of pulse generator
  - Verify pulse generator function before and after therapy.
- Lithotripsy:
  - < 16 KV shock energy to be used
  - Do not focus lithotripsy beam near generator
  - Disable atrial pacing if R waves trigger lithotripsy.
- Radiofrequency catheter ablation:
  - Avoid contact of radiofrequency catheter with generator/leads
  - Radiofrequency current path to be far away from generator or leads
  - Discuss with the surgeon.

PERIOPERATIVE BETA-BLOCKADE[1,2,3,5,17]

Introduction

Beta blockers are amongst the most commonly prescribed drugs and are frequently taken by patients about to undergo surgery.

Classification

- *Nonselective beta blockers*: Act at β_1 and β_2 receptors
  - Propranolol, sotalol, timolol
  - Nadolol, oxprenolol
  - Pindolol, penbutalol
- Cardioselective β_1 blockers:
  - Atenolol, esmolol
  - Betaxolol, metaprolol
  - Bevantolol
- Selective β_2 blockers:
  - Butoxamine
  - ICI-118551.

Intrinsic Sympathomimetic Activity

- Exert partial agonist effect at the receptor while blocking access to more potent agonist
- Thus, may behave like conventional beta blockers when sympathetic activity is high
- This property may protect against harmful effects of β-blockers withdrawal
- β-blockers with Intrinsic Sympathomimetic Activity (ISA):
  - Acebutalol, dilevalol, pindolol
  - Carteolol, oxprenolol
  - Celiprolol, penbutalol.

Reasons for Cardioprotective Effects

- Reduced myocardial oxygen demand and consumption demand in supply ratio
- Less stress on ischemic myocardium due to reduction in heart rate and contractility
- Redistribution of coronary blood flow to ischemic areas
- Increased coronary flow due to increased diastolic time
- Plaque stability due to reduction in shear forces
- Antiarrhythmic effects
- Possible anti-inflammatory effects
- Antiapoptotic.

Indications for Beta Blockade

ACC/AHA 2007 Guidelines

Surgery	No clinical risk factors	≥ 1 clinical risk factor	CHD High risk patients	Currently on β blockade
Vascular	Class IIb, LOE:B	Class IIa, LOE:B	Those found to have ischemia on preop test: Class I, LOE:B	Class I, LOE: B
			Those without ischemia or no previous test: Class IIa, LOE:B	
Intermediate	-	Class IIb, LOE:C	Class IIa, LOE:B	Class I, LOE:C
Low risk	-	-	-	Class I, LOE:C

Current Class I Indications

ACC-AHA 2007 guidelines:

- Should be used in patients previously taking β blockers for all types of surgeries

- Should be used in those with positive stress test undergoing major vascular surgery, although acute administration without titration is associated with harm.

Uses of Beta Blockers

- Treatment of essential HTN
- Treatment of angina pectoris and acute coronary syndromes
- Suppression of cardiac arrhythmias
- Treatment of congestive cardiac failure
- *Prevention of excessive sympathetic nervous system activity*: Intubation, incision
- Preoperative preparation of hyperthyroid and pheochromocytoma patients
- Treatment of migraine, closed angle glaucoma
- Control of *tet spells*.

Beta Blocker Dosages[5]

No	Drug	Oral dose	IV dose
1	Atenolol	50–100 mg QID	
2	Metoprolol	50–100 mg QID	5 mg Q5 min (upto 3 times)
3	Propranolol	60 mg QID	0.1 mg/kg (maximum)
4	Labetolol	100–600 mg QID	1–2 mg/kg
5	Esmolol		50–300 µg/kg/min
6	Carvedilol	25–50 mg BD	15 mg

Adverse Effects of Beta Blockade

- Life threatening bradycardia/asystole
- Congestive cardiac failure
- Glucose intolerance/insulin resistance in diabetes
- Raynauds phenomenon precipitated if pre-existing peripheral vascular disease
- MI on sudden withdrawal
- Uncontrolled HTN if used without prior α-blockade in pheochromocytoma
- Bronchospasm.

Controversy of Perioperative Beta-Blockade

- *Poise trial*:
  - Significant reduction in outcome of cardiovascular events with 30% reduction in MI rate
  - Increased risk of 30-day all cause mortality and stroke
- *MSPIRG trial:*
  - Multicenter Study of Perioperative Ischemic Research Group
  - No improvement in inhospitable outcomes
  - But lower incidence of cardiac events at 6–8 months follow-up
  - Reduction in all-cause mortality at 2 years
- *Pobble study:* No reduction in 30-day cardiovascular mortality in patients undergoing vascular surgery
- *Dipom study:* No benefits in diabetics undergoing major noncardiac surgery
- Conclusion:
  - Thus, early reports showed improved perioperative outcomes
  - Later studies showed no improvement or even worse outcomes in:
    - Low risk patients
    - Those in whom heart rate is not controlled.

Guidelines for Perioperative Beta Blockade

- Uses:
  - Beta blockers should be continued in those already taking them for HTN, angina or arrhythmias
  - β blockers like labetolol and esmolol can be used during intubation and preventing surgical stress response
  - Attempts to discontinue preoperative β blocker therapy causes:
    - Increased risk of rebound tachycardia, with or without AF
    - Myocardial infarction in patients with CAD.
- Dosage:
  - Dosages for all individuals are not the same
  - Dose should be individualized according to patient and surgery
  - *Heart rate control*: Heart rate should be non-ischemia inducing heart rate, 70–80 bpm.
- Administration:
  - Beta blockers should be continued up to time of surgery
  - Should be continued in IV form when GI absorption is in question
  - If β blocker has been omitted in preoperative regimen, use esmolol and labetolol
  - For perioperative MI prophylaxis:
    - Start atenolol 50–100 mg OD 30 days preoperatively
    - Continue in IV form intraoperatively.

ELECTIVE CARDIOVERSION[1,2,3,5]

Introduction

It is the process of conversion of ventricular or supraventricular arrhythmias into normal sinus rhythm using shock delivery which is synchronized with QRS complexes on the ECG.

Indications

- Atrial flutter
- Atrial fibrillation:
  - *Recent onset:* < 12 hours
  - No history of thrombus
- Unstable paroxysmal SVT
- Wolff Parkinson white syndrome
- Unstable monomorphic VT.

Mechanism

- Depolarize entire myocardium
- Prolong refractoriness
- Interrupt re-entrant circuits
- Discharge ectopic foci
- Establishing electrical homogenecity.

Contraindication

- Digitalis induced tachyarrhythmias due to risk of inducing ventricular fibrillation
- Stable atrial flutter with well controlled ventricular rate
- Stable atrial fibrillation with atrial clot.

Complications

- Post shock arrhythmias:
  - Bradycardia, asystole
  - Atrial/ventricular ectopics
  - AV block
  - Ventricular tachyarrhythmias.
- Transient ST elevation with normal cardiac enzymes usually
- Unsuccessful cardioversion due to:
  - Metabolic imbalance
  - Hypovolemia
  - Hypothermia
  - Tension pneumothorax
  - Hemothorax
  - Tamponade
- Myocardial damage
- Systemic/pulmonary embolism in AF.

Preoperative Assessment

- Patient's associated conditions should be stabilized
- Patient should be hemodynamically stable
- Digoxin not to be stopped unless some complication is present
- Serum electrolytes, acid base balance done prior to cardioversion
- ECG taken for detecting new arrhythmias
- Echocardiography to exclude LA clots especially if atrial fibrillation
- Prior anticoagulation for 2–3 weeks duration for AF/flutter ≥ 2–3 days duration
- Anticoagulation continued for 4 weeks after cardioversion
- Antiarrhythmic drugs started prior to procedure reduce incidence of post shock arrhythmias
- Antiarrhythmic drugs used are:
  - Procainamide
  - Amiodarone
  - Quinidine.

Preoperative Preparation

- NPO guidelines:
  - Solids 6 hrs
  - Clear fluids 2 hrs
  - Nonhuman milk 6 hrs
  - Breast milk 4 hrs.
- Sedatives not required
- Antiaspiration prophylaxis:
  - Metaclopranide 0.2 mg/kg IV
  - Ranitidine 1–2 mg/kg IV
- Continue digoxin unless some complications
- *Antiarrhythemic drugs started:* Procainamide, amiodarone
- Continue warfarin therapy.

Dosage

Use only lowest possible energies to avoid myocardial damage:

- *1–3 J/kg or 10–15 J/yr of life*: Pediatric dose
- *Atrial fibrillation:* 100 to 200 J increased in stepwise fashion
- *Atrial flutter and PSVT*: 50–100 J
- *Monomorphic VT*: 100 J → 200 J → 300 J → 360 J (increased in stepwise fashion).

Intraoperative Management

OT Preparation

- All equipment, defibrillator
- *Pacing wires*: Transvenous and transcutaneous

- All intubation equipment
- All emergency drugs.

Monitoring

- Pulse oximetry
- BP
- ECG:
  - Lead which produces large R/S wave and small T wave chosen
  - Obtain 10 lead ECG before and after shocks.

Procedure

- Activate synchronization mode of cardioverter
- Check for proper R-S wave synchronization
- Induction:
  - Preoxygenation for 3–5 minutes
  - Propofol 1–2 mg/kg with fentanyl 10–20 µg IV
  - Etomidate 0.3 mg/kg better choice as induction agent.
- When eyelash reflex lost, apply paddles
- Position of paddles:
  - Anteroposterior position:
    - *Anterior:* Apical area
    - *Posterior:* Interscapular area
  - Anterolateral position:
  - *Lateral:* 5th intercostals space along midclavicular line
  - *Anterior:* Second intercostals space right of sternum.
- Adequate gel applied on paddles to prevent fire hazard
- Remove mask and confirm that no one is touching patient or cart
- Synchronized shock given
- Ventilate patient with 100% O_2 until fully awake/able to maintain patient airway
- Nasopharyngeal airway may be used to maintain airway patency.

Postoperative Management

Monitors

- Pulse oximetry
- *ECG:* Obtain 12 lead ECG
- Noninvasive blood pressure

Complications

- Post-shock arrhythmias
- VF and cardiac arrest
- Thromboembolism to cerebral emboli
- Pulmonary edema
- Aspiration pneumonia.

NEGATIVE PRESSURE PULMONARY EDEMA[1,2,3,5,10,17]

Introduction

- Phenomenon of alveolar capillary membrane injury after exposure of alveoli to subatmospheric pressures leading to abnormal accumulation of fluid in extravascular compartment of lung
- Also called:
  - Postobstructive pulmonary edema
  - Laryngospasm induced pulmonary edema.

Incidence

- 0.05–0.1% incidence
- Mortality as high as 40%
- Occurrence is under-recognized and often misdiagnosed.

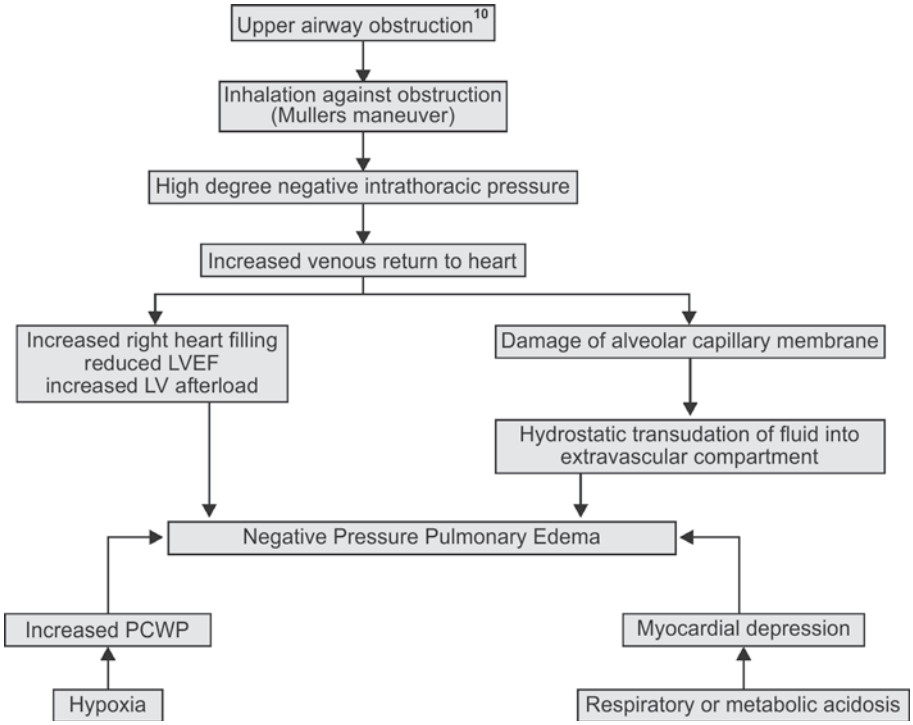
Risk Factors

- Patient related:
  - Male sex, young age
  - Athletes who can generate negative intrathoracic pressures up to –140 cm H_2O
  - Pediatric patients due to complaint chest wall
  - Obstructure sleep apnea, upper airway obstruction, obesity
  - Pharyngeal tumor mass, mediastinal tumor
  - Enlarged tonsils, epiglottitis, croup, Ludwigs angina
  - Vocal cord paralysis
  - Foreign body aspiration
- Surgery related:
  - Nasal, oral or pharyngeal surgeries
  - Chest tube suction
  - Temporomandibular joint arthroscopy
- Anesthesia related:
  - Anatomically difficult intubation
  - Laryngospasm
  - ET tube obstruction
  - ET tube and LMA biting
  - Tongue fall.

Precipating Factors

- Upper airway obstruction
- Laryngospasm
- ***Mullers maneuver:*** Inspiration against closed glottis
- Sudden release of obstruction.

Pathophysiology



Clinical Features

- Usually presents immediately but may occur several hours later
- Rapid onset respiratory distress following occurrence of airway obstruction on emergence from general anesthesia
- Dyspnea and hemoptysis with pink frothy sputum is *hallmark*
- Tachycardia, hypertension and diaphoresis due to sympathetic activation
- Rales and wheeze (due to fluid compressed airway)
- Clinical and X-ray features usually resolve in 24-hours.

Investigations

- Hypoxemia on pulse oximetry
- Hypoxia, metabolic, respiratory or combined acidosis on ABG
- Chest X-ray shows two phases of edema:
  - Intestitial edema
    - *Kerley lines*
    - Peribronchial cuffing
    - Subpleural effusion
    - Occurs with increase in transmural arterial pressure of 15–25 mm Hg .
  - Alveolar flooding:
    - *White-out areas*: Diffuse alveolar and interstitial infiltration
    - Occurs when transmural pressure > 25 mm Hg
    - Nodular opacities which coalesce into frank consolidation
    - Cardiac silhouette usually normal.

Differential Diagnosis

- Aspiration pneumonia
- ALI/ARDS
- Cardiogenic pulmonary edema
- Fluid overload pulmonary edema
- Drug induced noncardiogenic pulmonary edema
- Anaphylaxis
- Pulmonary embolism
- Myocardial infarction
- Pneumothorax.

Prevention

- Prevent laryngeal stimulation and postoperative stridor
- Laryngotracheal topical anesthesia (LTA) before intubation with:

  - 4 % lidocaine solution
  - 10 % lidocaine spray
- IV lidocaine 1–1.5 mg/kg 90 seconds before intubation.

Treatment

- Early diagnosis
- Oxygen supplementation:
  - 100 % oxygen via face mask
  - CPAP/nasal bilevel positive airway pressure (BIPAP)
  - Apply early PEEP to promote alveolar expansion
  - Endotracheal intubation with positive pressure ventilation.
- Diuretics:
  - Role is uncertain yet
  - Furosemide 1 mg/kg IV can be tried.
- Break laryngospasm early:
  - Larsons maneuver
  - Racemic epinephrine nebulization: 1 mg of 1: 1000 solution in 5 ml normal saline
  - Succinylcholine 0.5 mg/kg IV or 0.1–0.2 mg/kg if patient is biting ET tube
  - Dexamethasone/hydrocortisone.

Prognosis

Self limited, with X-ray clearing and normalization of ABG occurring within 24–72 hrs.

ANESTHESIA FOR OPCAB[1,3,5]

Introduction

Bypassing a coronary artery stenosis with an arterial or venous graft without using cardiopulmonary bypass is called Off Pump Coronary Artery Bypass surgery.

Key Surgical Features

- Operation on beating heart
- Absence of cardiopulmonary bypass
- Use of epicardial stabilizer (octopus/vortex stabilizer)
- Multiple vessel grafting
- Temporary interruption of coronary blood flow during anastomosis of distal vessels and intracoronary shunts
- Fast-track extubation either in OT/shortly thereafter.

Advantages of OPCAB[5]

Feature	OPCAB	CABG
Intraoperative		
Ischemia	Transient, coronary	Global myocardial ischemia
Heparin dose	Less	More
Postoperative		
Arrythmias	Rare	Common
Use of antiarrhythmics	Less used	More used
Post-procedure cardiac pacing	Less used	More used
Inotropic support	Fewer required	More required
Perioperative bleeding	Less	More
Perioperative transfusion	Less	More
Metabolic disturbances	Less	More
Cost	Less	More
Side effects of CPB		
Drug pharmacokinetics	More predictable	Less predictable (on CPB)
Intraoperative awareness	Less	More
Hemodilution	Less	More
Complement activation, SIRS	Avoided	Present
Neuropsychiatric impairment	Reduced (< 1%)	More (2–3 %)
Lung injury	Less	More
Troponin I	Less released	More released
Renal function	Better preserved	Impaired
Platelet dysfunction	Less	More

Patient Selection

- Multiple vessel bypass
- Patients at risk for injury with cardiopulmonary bypass like:
  - Advanced age
  - History of CVA/TIA/neuropsychiatric patient
  - Respiratory disease (COPD)
  - Impaired renal function/dialyzed patients
  - Immunosuppression
  - Severe myocardial dysfunction
  - Calcified aorta, aortic disease with increased risk of dissection, rupture
  - Atherosclerotic aorta.

High-risk Patients for OPCAB

- High grade LMCA (left main coronary artery) lesions
- Proximal LAD (left anterior descending artery) lesions
- Triple vessel disease.

Indications to Convert OPCAB To CABG

- *Hemodynamic instability:* Persistence for more than 15 minutes of:
  - Mean arterial pressure less than 50 mm Hg
  - Cardiac index less than 1.5 L/min/m^2
  - ST segment elevation more than 2 μV
  - Malignant arrhythmias
  - Severe LV dysfunction on TEE
  - $MvO_2 \leq 60\%$
- New regional wall motion abnormalities
- Inability to access areas which require revascularization
- Intramyocardial vessels
- Vessel endarterectomy.

Preoperative Assessment

- History:
  - Angina/recent MI
  - Cerebrovascular accident
  - *LV dysfunction:* Orthopnea, paroxysmal nocturnal dyspnea
  - Diabetes mellitus, hypertension, smoking, hyperlipidemia.
- Physical examination:
  - Raised JVP, basal crepitations
  - Pitting edema, S_3 gallop
  - *Airway examination:* Difficult airway anticipated due to DM/obesity.
- Investigations:
  - Routine blood investigations, clotting time, urine, electrolytes, renal function tests
  - ECG, Chest X-ray
  - Echocardiography:
    - 40–50 % EF: Mild LV dysfunction
    - 25–40 % EF: Moderate LV dysfunction
    - Less than 25 % EF: severe LV dysfunction.
  - Angiogram done within last 12 months
  - Depending on patient requirements:
    - Dobutamine stress test
    - Technetium 99 m scan
    - Pulmonary function tests
    - CT brain and chest
    - Endoscopic GI examination.

Preoperative Preparation and Premedication

- Optimize patient's preoperative DM, BP and lipid profile and heart rate
- Good patient communication necessary to avoid anxiety induced tachycardia
- NPO orders
- Informed consent
- Premedication:
  - Diazepam 0.1 mg/kg IV
  - Midazolam 0.03 mg/kg IV
  - Morphine 0.05–0.1 mg/kg IV
  - Ranitidine 1 mg/kg IV or pantoprazole 20 mg IV.
- *Antibiotic prophylaxis:* Cefotaxime 1–2 gms + gentamicin 1.5 mg/kg IV
- Continue morning dose of β-blockers, CCB, and nitrates till day of surgery
- Stop ACE inhibitors to prevent precipitous hypotension intraoperatively
- Oral hypoglycemic to be withheld on the morning of surgery.

OT Preparation

- Anesthetic drugs
- Machine check
- *Emergency medications*: Atropine, adrenaline, phenylephrine, calcium
- *Airway equipment*: ET tube, laryngoscope, airway, LMA, gum elastic bougie
- *CPB machine*: Primed and on stand by
- IABP, if required, in LMCA lesions
- Suction equipment
- External defibrillation pads before preparation and draping, defibrillator.

Procedure

- Sternotomy
- Saphenous vein/radial artery dissection
- Internal mammary artery (IMA) harvesting
- Heparin 2 mg/kg before IMA isolation
- ACT done after 3–5 minutes
- LIMA-LAD anastomosis
- Distal anastomosis with induced bradycardia
- Intracoronary stent applied during anastomosis
- Proximal anastomosis by partial cross clamping
- Heparin reversal with protamine
- Hemostasis
- Closure.

Position

Supine

Monitoring

- ECG:
  - Lead II for rhythm disturbances
  - Lead V_5 with ST segment analysis for ischemia
  - V_4R and V_5R used if right ventricular ischemia

  - May show flatline during circumflex artery anastomosis due retraction of heart.
- Pulse oximetry, capnography
- Invasive blood pressure monitoring
- Bispectral index or entropy monitoring, neuromuscular monitoring
- CVP/PA catheter
- Temperature, urine output
- Periodic ABGs
- Continuous cardiac output monitoring, transcranial *Doppler:* Optional
- Transesophageal echocardiography:
  - Especially in patients with raised LVEDP, to assess LV preload
  - Also for LV function and detecting new RWMA during anastomosis.

Anesthetic Goals

- Cardiac protective anesthetic technique used
- *Rate:* Slow, 70–80 bpm (non-ischemia producing heart rate)
- Rhythm: Sinus rhythm
- *Contractility:* Myocardial depression preferred (if LV function is normal)
- Preload:
  - Judicious preload
  - Reduce wall tension and LVEDP.
- *Afterload:* Maintain afterload (hypertension preferred to hypotension)
- *Temperature:* Keep patient warm
- MvO_2:
  - Maintain myocardial oxygen demand-supply ratio
  - Treat myocardial oxygen supply related disturbances
- *Severe LMCA disease*: Maintain diastolic pressure and heart rate at preoperative values.

Induction

- Adequate preoxygenation for 3–5 minutes
- Induction in calm and relaxed manner
- Two methods of induction:
  - Patients with good LV function:
    - Normal doses of anesthetic agents as sympathetic response usually intact
    - Thiopentone 3–5 mg/kg + vecuronium 0.1 mg/kg + fentanyl 5 µg/kg IV for induction
    - Propofol 2 mg/kg maybe used as alternative
    - Induction agents in titrated doses to prevent hypotension at induction
    - β blockers and vasodilators kept ready to negate intubation response.
  - Patients with poor LV function:
    - Reduced doses of anesthetic as they are unable to produce significant response to stimulation
    - Pancuronium 0.1 mg/kg + fentanyl 10 µg/kg + midazolam 0.15 mg/kg IV for induction
    - Pancuronium is used as muscle relaxant to counter opioid induced bradycardia
    - Etomidate maybe used for induction to maintain hemodynamic stability
    - Vasopressors and inotropes kept ready.
- Deep planes of anesthesia maintained at the time of intubation
- Prevention of intubation response:
  - IV lignocaine 1.5 mg/kg 60–90 seconds prior to intubation
  - Use of NTG/esmolol to blunt intubation response
  - Fentanyl 4–5 µg/kg + vecuronium 0.1 mg/kg IV prior to laryngoscopy.
- Two large (18 G) bore IV cannula inserted
- Ryles tube inserted to deflate stomach and left open
- NTG infusion started and continued throughout procedure.

Maintenance

- Opioid based balanced anesthetic technique used
- Propofol infusion less preferred as inotropic requirements and troponin I increase
- Pure opioid based anesthesia technique preferred if preoperative LV dysfunction is present
- O_2 + N_2O + isoflurane 1 MAC used for balanced anesthesia
- Vecuronium and fentanyl given as intermittent boluses
- Fentanyl bolus given before sternotomy to avoid hypertensive response
- Anticoagulation:
  - Heparin 2 mg/kg IV given before commencing distal anastomosis
  - ACT maintained above 250 seconds.
- Protamine:
  - Given to reverse anticoagulation
  - Dose given once the heart is reperfused with multiple grafts, after proximal anastomosis.

Hemodynamics

- Rigid control of heart rate and blood pressure required
- Heart rate:
  - Maintain heart rate of around 70 bpm (non-ischemia producing heart rate)
  - Esmolol infusion/metaprolol boluses useful.
- Dysrhythmias:
  - Occurs due to manipulation of heart, ischemia or reperfusion injury
  - Keep electrolytes at normal level
  - Infusion of magnesium sulfate or xylocard before manipulation of heart, is useful in preventing arrhythmias
  - Pacemaker to be readily available to treat bradyarrhythmias.
- Hypotension:
  - During distal anastomoses, especially obtuse marginal anastomosis
  - Treatment:
    - Give IV fluids rapidly, 20 Trendelenburg position
    - Phenylephrine 100–200 µg IV bolus or dobutamine infusion
    - Adjust stabilizer and reposition the heart.
- Hypertension:
  - Nitroglycerine 0.5–3 µg/kg/min IV
  - β blockers: Labetalol/esmolol
  - Calcium channel blockers.
- Cardiac output:
  - Maintaining cardiac output more important than BP
  - Maybe reduced due to reduced contractility from ischemia/displacement of heart
  - Dobutamine/dopamine used to maintain cardiac output
  - Insertion of IABP may be necessary, especially in LMCA lesions.
- *Temperature:* Prevent hypothermia:
  - Use warm IV fluids
  - Humidification of air
  - Maintain warm OT temperature
  - Position patient on heating mattress to prevent hypothermia.

Ventilation

- Lungs to be deflated at the time of sternotomy
- Hand ventilation may be required during:
  - Dissection of left internal mammary artery (LIMA)
  - Distal anastomosis to aid surgical exposure, especially for marginal branches of left circumflex artery.
- Hyperventilate (to prevent atelectasis and hypercapnea) subsequently.

Conduct of Anastomosis

Distal Anastomoses

- Most demanding phase of surgery
- Aggressive maintenance of hemodynamic stability required
- LAD-LIMA anastomosis:
  - Intracoronary shunts used to improve coronary blood flow during grafting
  - Prevent hypotension:
    - IV fluids to prevent fall in preload, which occurs when heart is retracted
    - 20° Trendelenburg position helpful to improve preload
    - Avoid steep Trendelenburg to prevent reduction in pulmonary compliance
    - Infusion of dobutamine/dopamine used to maintain BP and CO:
      - If preoperative cardiac function is impaired
      - If cardiac output reduces after application of epicardial stabilizer.
  - Cardiac output improves once anastomosis is complete and stabilizer removed
  - Watch for reperfusion injury when snugger is removed
  - BP and cardiac output should be returned to normal before next anastomosis.
- Obtuse marginal and posterior descending artery anastomosis:
  - Deep pericardial retractors or sling may be used to retract heart
  - This may displace heart with apex pointing anteriorly
  - This may lead to RV dysfunction and biventricular failure
  - This will cause severe reduction in stroke volume as RV cannot expand during diastole
  - Boluses of epinephrine or ephedrine if cardiac index continues to fall during anastomosis (CI < 1.5) to avoid progressive cardiac failure
  - Monitor PA pressure in view of biventricular dysfunction
  - Monitor ABG and maintain pH above 7.3.

Proximal Anastomosis

- Partial cross clamping of aorta done prior to proximal anastomosis
- This requires rapid reduction of blood pressure:
  - Reverse Trendelenburg position beneficial
  - Volatile anesthetics/nitroglycerine useful
- Watch for reperfusion injury on release of snuggers.

Postoperative Management

Ventilation

- *Early extubation*: When extubated less than 10 hours postoperatively
- Extubation if:
  - Awake, normothermic
  - Hemodynamically stable
  - Not bleeding/acidotic
- Early institution of chest physiotherapy.

Postoperative Analgesia

- IV opioids, patient controlled analgesia
- Thoracic epidural
- Ketorolac + small dose opioids
- Multimodal approach.

Monitors

- Pulse oximetry, temperature
- Blood pressure:
  - Maintained at less than 130 mm Hg to protect graft top-ends and reduce bleeding
  - Maintain nitroglycerine infusion to prevent graft spasm.
- *Drains*: Should be less than 100 ml/hr
- ACT, repeated ABG and blood sugar
- Echocardiography for:
  - LV ejection fraction
  - Regional wall motion abnormalities
  - Pericardial effusion and tamponade.

Complications

- Pain, hypertension, tachycardia
- Bleeding, arrhythmias
- Cognitive dysfunction
- LV dysfunction
- Low cardiac output syndrome (LCOS).

Anticipation and Management of Ischemia

- Communication between surgeon and anesthetist
- Observe surgical field, heart size, position and function
- Pharmacological preconditioning
- Maintain adequate coronary perfusion pressures
- Avoid hemodynamic alterations associated with ischemia
- Avoid tachycardia (especially if hypothermia present): Use β-blockers
- Volume loading, trendelenburg, reduction in depth of anesthesia and use of α-agonists may be indicated
- Epicardial pacing may be required for ischemia induced bradycardia.

Regional Anesthesia

- Epidural anesthesia advantages:
  - Reduced stress response
  - Better analgesia
  - Better respiratory function postoperatively
  - *Antianginal:* Reduces dynamic occlusion
  - Better distribution of coronary blood flow
  - Reduced oxygen demand.
- Epidural anesthesia disadvantages:
  - More hypotension
  - Epidural hematoma, infection
  - Dural puncture with post-dural puncture headache
  - Spinal cord injury.

Epicardial Stabilizers

- Allows better access to inferior and posterior surfaces of heart
- Examples:
  - Vortex stabilizer system
  - Octopus stabilizer
  - Cohn stabilizers.

ANESTHESIA FOR ON-PUMP CABG[1,2,3,5]

Introduction

Most commonly performed cardiac surgical procedure where a coronary artery stenosis is bypassed with an arterial/venous graft using cardiopulmonary bypass.

Preoperative Assessment

- History:
  - Angina/recent MI
  - Cerebrovascular accident
  - *LV dysfunction:* Orthopnea, paroxysmal nocturnal dyspnea
  - Diabetes mellitus, hypertension, smoking, hyperlipidemia.

- Physical examination:
  - Raised JVP, basal crepitations
  - Pitting edema, S_3 gallop
  - *Airway examination:* Difficult airway anticipated due to DM/obesity.
- Investigations:
  - Routine blood investigations, clotting time, urine, electrolytes, renal function tests
  - ECG, Chest X-ray
  - Echocardiography:
    - 40–50% EF: Mild LV dysfunction
    - 25–40% EF: Moderate LV dysfunction
    - Less than 25% EF: Severe LV dysfunction
    - Check for MR/AS/AR/VSD/ventricular aneurysm.
  - Angiogram done within last 12 months
  - Depending on patient requirements:
    - Dobutamine stress test
    - Technetium 99 m scan
    - Pulmonary function tests
    - CT brain and chest
    - Endoscopic GI examination.

Preoperative Preparation and Premedication

- Optimize patient's preoperative DM, BP and lipid profile and heart rate
- Good patient communication necessary to avoid anxiety induced tachycardia
- NPO orders
- Informed consent
- Premedication:
  - Diazepam 0.1 mg/kg IV
  - Midazolam 0.03 mg/kg IV
  - Morphine 0.05–0.1 mg/kg IV
  - Ranitidine 1 mg/kg IV or pantoprazole 20 mg IV
- *Antibiotic prophylaxis:* Cefotaxime 1–2 gms + gentamicin 1.5 mg/kg IV
- Continue morning dose of β-blockers, CCB, and nitrates till day of surgery
- Stop ACE inhibitors to prevent precipitous hypotension intraoperatively
- Oral hypoglycemic to be withheld on the morning of surgery.

OT Preparation

- Anesthetic drugs
- Machine check
- *Emergency medications:* Atropine, adrenaline, phenylephrine, calcium
- Airway equipment: ET tube, laryngoscope, airway, LMA, gum elastic bougie
- *CPB machine:* Primed and on stand by
- IABP, if required, in LMCA lesions
- Suction equipment
- External defibrillation pads before preparation and draping, defibrillator.

Position

Supine.

Monitoring

- ECG:
  - Lead II for rhythm disturbances
  - Lead V_5 with ST segment trending for ischemia
  - V_4R and V_5R used if right ventricular ischemia.
- Pulse oximetry, capnography
- Invasive blood pressure monitoring:
  - Preferred on side opposite to IMA dissection
  - This is because sternum will be retracted during dissection of IMA
  - This may cause tenting of subclavian artery and reduce flow through subclavian artery.
- Bispectral index or entropy monitoring, neuromuscular monitoring
- CVP/PA catheter if:
  - Ejection fraction less than 45 %
  - Significant left ventricular RWMA
  - LVEDP more than 18 mm Hg
  - Recent MI or unstable angina
  - Post-MI complications.
- Nasopharyngeal temperature, urine output
- Periodic ABGs
- Continuous cardiac output monitoring, transcranial Doppler: Optional
- Transesophageal echocardiography:
  - Especially useful in patients with raised LVEDP
  - To assess LV preload and LV function
  - Earliest detector of intraoperative MI
  - Also helps in detection of air.

Anesthetic Goals

- Cardiac protective anesthetic technique used
- *Rate:* Slow, 70–80 bpm (nonischemia producing heart rate)
- *Rhythm:* Sinus rhythm
- *Contractility:* Myocardial depression preferred (if LV function is normal).

- Preload:
  - Judicious preload
  - Reduce wall tension and LVEDP
- *Afterload:* Maintain afterload (hypertension preferred to hypotension)
- *Temperature:* Keep patient warm
- MvO_2:
  - Maintain myocardial oxygen demand-supply ratio
  - Treat myocardial oxygen supply related disturbances.
- *Severe LMCA disease:* Maintain diastolic pressure and heart rate at preoperative values.

Induction

- Adequate preoxygenation for 3–5 minutes
- Induction in calm and relaxed manner
- Two methods of induction:
  - Patients with good LV function:
    - Normal doses of anesthetic agents as sympathetic response usually intact
    - Thiopentone 3–5 mg/kg + vecuronium 0.1 mg/kg + fentanyl 5 µg/kg IV for induction
    - Propofol 2 mg/kg maybe used as alternative
    - Induction agents in titrated doses to prevent hypotension at induction
    - β blockers and vasodilators kept ready to negate intubation response
  - Patients with poor LV function:
    - Reduced doses of anesthetic as they are unable to produce significant response to stimulation
    - Pancuronium 0.1 mg/kg + fentanyl 10 µg/kg + midazolam 0.15 mg/kg IV for induction
    - Pancuronium is used as muscle relaxant to counter opioid induced bradycardia
    - Etomidate maybe used for induction to maintain hemodynamic stability
    - Vasopressors and inotropes kept ready.
- Deep planes of anesthesia maintained at the time of intubation
- Prevention of intubation response:
  - IV lignocaine 1.5 mg/kg 60–90 seconds prior to intubation
  - Use of NTG/esmolol to blunt intubation response
  - Fentanyl 4–5 µg/kg + vecuronium 0.1 mg/kg IV prior to laryngoscopy
- Two large (18 G) bore IV cannula inserted
- Ryles tube inserted to deflate stomach and left open
- NTG infusion started and continued throughout procedure.

Ventilation

- Lungs to be deflated at the time of sternotomy to avoid pleural/lung injury
- Hand ventilation may be required during IMA dissection
- Hyperventilate thereafter, if low tidal volume used during dissection, to prevent atelectasis
- Controlled ventilation during de-airing maneuvers while coming off CPB, where positive airway pressure of 30 cm H_2O is given, to empty the heart of air, with Trendelenburg position.

Hemodynamics

- Maintain heart rate around 70 bpm (esmolol/metaprolol useful)
- Maintain systolic BP around 100–120 mm Hg during the procedure
- Maintain systolic BP at around 80–100 mm Hg at the time of aortic cannulation
- Manage hypotension with IV fluids, Trendelenburg position, vasopressors or inotropes
- Hypertension managed with nitroglycerine/β blockers
- Two units of cross matched and grouped PRBCs kept ready in OT
- Blood is especially important in redo cases as RV perforation may occur at the time of sternotomy.

Maintenance

Prebypass

- Isoflurane is safe in patients with CAD, in the absence of hypotension
- Halothane and enflurane also may be used
- Heparin 400 IU/kg given prior to IMA clamping
- Ensure that ACT is more than 480 seconds prebypass
- O_2 + air + isoflurane 0.6–2 MAC used to maintain balanced anesthesia
- Fentanyl 1 µg/kg + pancuronium 0.05 mg/kg intermittent boluses
- Add vecuronium 0.1 mg/kg + morphine 0.1–0.2 mg/kg (fentanyl 250–500 µg) + midaolam 0.05 mg/kg to pump prime
- Make note of urine output once CPB ensues.

During Bypass

- Heparin:
  - Repeated at half the initial dose at 1 hour
  - One-fourth the initial dose at 2 hours and every hour thereafter
- Vecuronium 0.05 mg/kg + morphine 0.1 mg/kg + midazolam 0.03 mg/kg every hour
- Check ABG and ACT every half hour on CPB
- Record temperature, mean arterial pressure, hematocrit, serum potassium and urine output at termination of bypass.

Postbypass

- Deairing maneuvers once heart is being closed
- Defibrillate/cardiovert if VF/SVT
- Inotropes started once aortic cross clamp is removed
- Ventilation is started after:
  - PA perfusion is adequate
  - Last proximal graft is being sutured
  - Prominent pulsations are present on arterial line tracing.
- Discontinue N_2O at this stage to prevent expansion of air bubbles
- Increase inotropes if low BP with rising LA, PCWP and RA pressure at the time of weaning from bypass.
- Protamine (1:1 with heparin) given after venous decannulation
- Last internal suction done after half the protamine dose has been given
- ABG taken 5–10 minutes after protamine completed (for ACT and ABG).

Checklist Prior to CPB Initiation[1,5]

Item	Anesthetic checklist
Anesthetic level	• Narcotics, BZD, additional dose muscle relaxant • Volatile anesthetic availability on pump • Narcotics, benzodiazepines, relaxants added to pump prime
Monitors	• To be visible to anesthetist and perfusionist • Retrograde pressure monitored • Swan-Ganz catheter pulled back 5–10 cms before CPB initiation
Anticoagulation	• Heparin 400 IU/kg given • ACT maintained above 480 seconds
Arterial line	• Check for air
Venous line	• Minimize air to prevent air-lock
Urine output	• Maintained more than 0.5 ml/kg/hour
Retrograde cardioplegia line	• Pressure displayed (usually RV trace) • Position confirmed by TEE if available

Check List Post CPB Initiation[1,5]

Item	Objective	Problems	Solution
Arterial blood flow	Adequate pump flow	Low flow	Check line for kinks
	Normal pump pressure	High pump pressure	Check for aortic dissection
	MAP > 50 mm Hg	Low MAP	Check for innominate A cannulation
Arterial blood color	Bright	Dark color	Check O_2 supply to oxygenator
Venous return	Good return	Poor return	Check line for kinks
	Low venous pressure	High venous pressure	Check line for air Check table height is adequate
Heart filling	Heart to be empty	Distended ventricle	Check venous return Vent the heart If AR present, reduce flow
IV Fluids	Should be off	Still running	Stop IV fluids
Ventilation	Stopped	Ventilation on	Turn off unless partial CPB
	Deflated lungs	Lungs inflated	Check PEEP valve
Anesthesia	Adequate depth	Anesthesia too light	Add vapor to pump gas Repeat IV drugs every hour
Anticoagulation	ACT > 480 sec	Inadequate	Heparin half dose at 1 hour Heparin quarter dose at 2 hours Repeated every hour thereafter
Urine output	More than 2 ml/kg/hr	Inadequate	Diuretics

Check List for Weaning from CPB[1,5]

Item	Objective	Problem	Solution
acid base status	Normal	Base deficit > 5 mmol/L ECF	Correct with bicarbonate
Electrolytes	Normal potassium	Hypo/hyperkalemia	Correct appropriately
	Normal magnesium	Hypo/hypermagnesemia	Use insulin if K^+ very high
	Normal calcium	Hypo/hypercalcemia	
Hematocrit	≥ 7 g/dl	< 6.5 g/dl	Transfusion
			Hemoconcentration
Glucose	< 15 mmol/L	Hyperglycemia	Insulin
Anticoagulation	≤ 120 seconds	≥ 121 seconds	Additional protamine
			FFP/platelet concentrates
Transducer	Zeros correct	Zero drift	Zero again at rewarming
Temperature	36–37 °C	< 36°C	Inadequate rewarming
Blood pressure	between 95–125 mm Hg	Less than 95 mm Hg	Inotropes
Heart rate	≥ 70 bpm	Bradycardia	Treat with anticholinergics
		Tachycardia	Treat hypovolemia/ pain
Rhythm	Sinus rhythm	Heart block	Pacing (DDD is best)
		Atrial fibrillation	Cardioversion
		Ventricular fibrillation	Defibrillation, amiodarone
		Multiple VPCs	Check electrolytes
Cardiac output	Normal	Low	Inotropes ready
SVR	Normal	Inappropriate vasodilation	Vasopressors
		Inappropriate vasoconstriction	Vasodilators
Anesthesia	Adequate depth	Too light	Check infusion
			On vaporizer
IV fluids	Ready to run	Not ready	Prepare IV fluids
Ventilation	Ventilation on	Ventilation off	Switch on ventilation
	FiO_2 > 50%	FiO_2 < 50%	Increase FiO_2 > 50%
	No IMA stretching		
	Check pneumothorax		

FAST TRACK MANAGEMENT OF CABG[1,5]

Introduction

Consists of rapid postoperative extubation (within 4–6 hours), postoperative rehabilitation and discharge from hospital (within postop day 5).

Components of Fast Track CABG

- Patient education
- Same day admission
- Altered anesthetic and surgical management
- Special recovery areas
- Early extubation early mobilization
- Prophylactic/aggressive treatment of complication
- Discharge from ICU on postoperative day number 1
- Discharge from hospital on postoperative day number 5
- Out of hospital follow-up.

Advantages of Early Extubation

- Earlier discharge
- Respiratory benefits:
  - Lesser endotracheal tube related complications
  - Improves mucus transport.
- Cardiovascular benefits:
  - Improved cardiac output
  - Ventricular function returns to baseline within 24 hours after CABG in 90% patients.

Anesthetic Management

- Lower dose of opioids:
  - Fentanyl less than 30 µg/kg
  - Sufentanyl less than 7 µg/kg
  - Remifentanyl less than 3 µg/kg/min.
- Supplementation with:
  - Inhalational agents: Isoflurane 0.6–2 MAC
  - Propofol infusion 25–100 µg/kg/min
  - Midazolam
  - Muscle relaxants
- Postoperative ICU sedation:
  - Propofol infusion continued
  - Midazolam boluses.
- Postoperative analgesia:
  - Morphine, NSAIDs
  - Patient controlled analgesia
  - Neuraxial techniques.

Surgical Approaches to Fast Track Extubation

- Appropriate patient selection
- Rehearsed, efficient surgical team
- Well-planned, expeditious and technically superior surgery
- Meticulous myocardial protection
- Avoid intraoperative complications and residual structural defects
- Appropriate early use of inotropic support
- Management of bleeding
- Avoidance of stroke.

Management in ICU

- Return to ICU:
  - Reverse muscle relaxant as soon as stable to assess level of sedation
  - Start fentanyl infusion at 0.01–0.03 µg/kg/min
  - Continue propofol infusion at 10–30 µg/kg/min
- Awakening:
  - If temperature < 35 °C, maintain propofol infusion
  - If temperature 35–35.5 °C, reduce propofol infusion
  - If core temperature > 35.5 °C:
    - Stop propofol infusion
    - Reduce fentanyl infusion by half
    - Give IV ketorolac 10–20 mg (0.5mg/kg).
- Criteria for weaning:
  - Minimal bleeding (less than 50 ml/hr)
  - Stable hemodynamics
  - No significant arrhythmias
  - Adequate urine output > 0.5 ml/kg/hr
  - Acceptable SpO_2 on 50 % FiO_2
  - Awake enough to follow commands
- Weaning:
  - Wait for 10 minutes after discontinuing propofol infusion to start weaning
  - 10–30 minutes taken to wean ventilatory support
  - Place patient on CPAP when adequate spontaneous efforts
  - Use E_TCO_2 and SpO_2 to assess adequacy of ventilation
  - Maintain:
    - E_TCO_2 < 50 mm Hg
    - SpO_2 > 94%.
- Extubation:
  - Leave fentanyl infusion on as needed
  - Continue monitoring O_2 saturation, ABG, BP, ECG and urine output.

PERIOPERATIVE MYOCARDIAL INFARCTION[1,3,5]

Introduction

- Rise or fall in troponin I levels (215 IU/ml), or other biomarkers with:
  - Cardiac symptoms
  - ECG changes:
    - ST depression more than 1 mm, 60–80 msec after J point in at least 3 consecutive heart beats with stable baseline
    - ST elevation:
      - In men > 40 yrs old, more than 2 mm in V2–V3 or 1 mm in all other leads
      - In men < 40 yrs old, more than 2.5 mm in V2–V3 or 1 mm in other leads
      - In women, more than 1.5 mm in V2–V3 or 1 mm in other leads.
    - T wave inversion with significant ST changes
  - Imaging findings.

Causes

- Tachycardia:
  - More than 110 bpm associated with high risk
  - Most important determinant of myocardial oxygen consumption
  - Heart rate > 80–90 bpm in patients with preoperative resting heart rate 50–60 bpm increases risk.
- Hypotension
- Hypertension
- Anemia with hematocrit < 28%
- Hypoxemia, hypercarbia
- Hypothermia
- Systolic and diastolic myocardial dysfunction.

Differential Diagnosis

- Anxiety
- Esophageal reflux
- Hyperventilation
- Hypo/hyperkalemia.

Types of Perioperative MI

Two types of PMI:

- Type I: Acute coronary syndrome
- Type II: Myocardial oxygen demand-supply imbalance.

Pathophysiology

- Type I Perioperative MI:
  - Occurs in the presence of an unstable coronary plaque
  - Plaque erosion or rupture occurs due to:
    - Sympathetic overactivity
    - Hemodynamic instability with hypotension and tachycardia
    - Coronary vasoconstriction.
  - This leads to acute coronary thrombosis in the setting of:
    - Increased coagulability with decreased fibrinolysis
    - Recent PCI with stent
    - Premature cessation of Dual Antiplatelet Therapy (DAP)
  - This leads to acute coronary syndrome type of perioperative MI.
- Type II Perioperative MI:
  - Occurs in the presence of severe stable coronary artery disease
  - Occurs due to imbalance between myocardial oxygen demand and supply:
    - Increased myocardial oxygen demand may occur due to:
      - Increased heart rate due to:
        - Increased sympathetic activity
        - Withdrawal of β-blocker therapy
        - Arrhythmias.
      - Increased myocardial wall stress due to:
        - Hypertension
        - Increased LVEDP
        - Pulmonary congestion
        - Atelectasis.
    - Reduced subendocardial oxygen supply may occur due to:
      - Hypovolemia with hypotension
      - Systemic vasodilatation
      - Cardiac decompensation
      - Perioperative anemia
      - Hypoxemia.
  - This leads to prolonged ST depression (more than 30 minutes), causing type II perioperative MI.

Diagnosis[3,5]

Method	Information obtained	Problems	Sensitivity
TEE	• New RWMA • Severe hypokinesia • Akinesia/ dyskinesia • Transmural MI	• Only one view at a time	• Highest
Coronary sinus lactate level	• Myocardial lactate production		
PCWP	• Raised PCWP • *a and c* waves	• Poor • sensitivity and specificity	
ST segment monitoring	• ST depression • ST elevation, T wave changes	• Requires V_4R for RCA • V_7,V_9 leads for post. wall ischemia	
Systemic pressures	• Fall in arterial pressure • Increase in CVP	• Low sensitivity and specificity	• Lowest

Cardiac Biomarkers

Biomarkers used:

- Troponin I
- CK-MB
- Lactate dehydrogenase
- Myoglobin
- Glycoprotein-BB
- AST, C-reactive protein, brain natriuretic peptide (BNP), myocardial lactate.

Biomarker[8]	Onset	Peak	Duration
myoglobin	Immediate	2 hrs	24 hrs
GP - BB	1–3 hrs	7 hrs	36 hrs
Troponin	2–4 hrs	12 hrs	7–10 days
CK-MB	4–8 hrs	10–24 hrs	48–72 hrs
LDH	24–48 hrs	72 hrs	10–14 days

Perioperative MI Predictors

- None are reliable predictors
- Rate pressure product (RPP)and triple index (TI):
  - Rate pressure product = heart rate × Systolic blood pressure
  - Triple index = Heart rate × Systolic BP x PCWP.
  - If RPP ≥ 20,000, patient is at increased risk of PMI
  - Both predictor are not reliable
- *Myocardial oxygen supply*: Demand ratio (DPTI: SPTI)
  - DPTI = Diastolic pressure time index = (MDP – LVEDP) × (duration of diastole)
  - SPTI = Systolic pressure time index = MAP × duration of systole
  - MDP = Mean diastolic pressure
  - MAP = Mean arterial pressure
  - If ratio less than 0.5, patient is at increased risk for subendocardial ischemia
  - Index is unreliable as increase in MvO_2 due to contraclility is not reflected.
- Mean arterial BP-heart rate quotient (pressure-rate quotient):
  - Pressure rate quotient = (Mean arterial pressure)/(Heart rate)
  - PRQ less than 1 predicts increased risk of ischemia
  - Heart rate ≥ 110 bpm is most important determinant of PMI.

Prophylaxis

Intervention[1,3,5,8]	Regimen	Recommendation
Perioperative β blockade	• Atenolol 50-100 mg started 30 days before surgery • Therapy continued IV during surgery • Long term β blockers not discontinued	Class I
α_2 agonists	• 300 µg clonidine (2-5 µg/kg) PO 90 min before surgery • Clonidine continued for 72 hrs postop at 200 µg/kg	Class IIa
Statin therapy	• Atorvastatin 20 mg OD started 45 days before surgery • Continued till 2 weeks postoperatively	Class IIa
ACE inhibitors	• Continue preoperative ACE inhibitor therapy • Watch for intraoperative hypotension	Class IIb
Calcium channel blockers	• Not used as individual agents preoperatively • Continue preoperative CCB therapy	Class IIb
Aspirin	• To be stopped 5–7 days before surgery to reduce bleeding • Only exception is CABG where it is continued	
Dual anti-platelet therapy	• Elective surgery discouraged for 4 weeks after BMS • Elective surgery discouraged for 1 year after DES • DAP therapy has to be continued uninterrupted in this time • Restart thienopyridine as soon as possible after surgery • Aspirin to be continued preoperatively	
Other measures	• Use of regional anesthesia where possible • Thoracic epidural reduces incidence of PMI • Use of volatile anesthetics for preconditioning • Maintain hematocrit ≥ 28 % • Maintain normothermia • Use of postoperative sufentanyl 1 µg/kg/hr	
Coronary revascularization	• PCI provides less complete revascularization • PCI associated with more perioperative complications • CABG provides complete revascularization • CABG is associated with less incidence of PMI	DECREASE trial CARP trial Class IIb
NTG	0.5–3 µg/kg/min	Class III

Goals of Perioperative Management

- Careful perioperative monitoring
- Low threshold for treating and preventing tachycardia
- Avoid hypotension, low cardiac output and cardiac decompensation.

Perioperative Management

- Tight perioperative monitoring:
  - ECG
  - Echocardiography
  - Transesophageal echocardiography
  - Invasive blood pressure
  - PA pressure monitoring.
- Additional tests:
  - Arterial blood gas, troponin I levels
  - Treat any acid base disturbances
  - Correct electrolyte imbalance.
- Tachycardia treated aggressively:
  - Tachycardia with hypotension:
    - *Hypovolemia*: IV fluid challenge
    - *Anemia*: Transfuse blood if:
      - Hematocrit less than 25% normally
      - Hematocrit less than 30% in patients with coronary artery disease.
    - Low systemic vascular resistance:
      - Vasopressors added
      - Cut off volatile anesthetics.
    - *Cardiac failure*: Inotropes, IABP
  - Tachycardia with hypertension or normotensive:
    - Beta blocker therapy:
      - Propranolol 0.5 mg boluses up to maximum of 0.1 mg/kg
      - Metaprolol 2.5 mg/kg increments up to maximum of 0.5 mg/kg
      - Esmolol 0.5 mg/kg bolus followed by 50 µg/kg/min.
    - Calcium channel blockers or nitroglycerine
    - Check appropriate pain control, supplement opioids
    - If tachyarrhythmias, treat rate and rhythm.
- Emergency coronary intervention/anticoagulation with GP-IIbIIIa antagonists only if:
  - Persistent ST depression/elevation (lasting more than 30 minutes)
  - Intractable cardiogenic shock.

ISCHEMIC PRECONDITIONING[1,2,3,5,17]

Introduction

- Myocardial ischemic preconditioning refers to the adaptive mechanism by which a brief period of reversible ischemia increases the heart's tolerance to subsequent longer periods of ischemia
- Anesthetic preconditioning refers to administration of volatile anesthetics before prolonged coronary artery occlusion in order to increase the *critical ischemia time* (CIT_{50})
- CIT_{50} is the duration of circulatory disruption, compatible with 50% tissue survival.

Conditions Which Benefit from Preconditioning

- Extreme CAD with poor collaterals
- Severe LVH with reduced subendocardial perfusion
- Anticipated prolonged ischemic time
- Senescent myocardium prone to tissue damage from calcium overload.

Agents used for Preconditioning

- *Volatile anesthetics*: Isoflurane, halothane, sevoflurane, desflurane
- *Adenosine*: Acts through A1, A2 and A3 receptors
- Acadesine
- Acetylcholine
- Carbechol
- *Opioids:* Acts through δ_1 and K receptors.

Beneficial Effects of Volatile Anesthetics

- Altered neutrophil function
- Improves coronary perfusion
- Reduces myocardial oxygen demand
- Preserves energy dependent vital cellular processes
- Negative inotropic effects
- Negative chronotropic effects
- Negative lusitropic effects
- Reduction in LV afterload.

Beneficial Effects of Individual Agents

- Halothane:
  - Attenuates ST changes caused by brief coronary artery occlusion
  - Preserves contractile function and ultrastructural integrity at reperfusion
  - Inhibits platelet thrombus formation by increasing platelet cAMP.

- Isoflurane:
  - Beneficial to LV diastolic function during ischemia
  - Reduces impact of reperfusion injury
  - Increases ratio of myocardial oxygen supply: Demand ratio
  - Reduces troponin I and CK-MB levels after cardiac surgery.
- Sevoflurane:
  - Reduces impact of reperfusion injury
  - Increases blood flow to collateral dependent myocardium via action on calcium activated K^+ channels (BK_{ca})
  - Improves recovery of coronary vascular reactivity
  - Enhances endometrial nitric oxide release.
- Desflurane:
  - Beneficial to LV diastolic function during ischemia
  - Attenuates effects of free radicals on LV function
  - Reduces adhesion of neutrophils and platelets after myocardial ischemia and reperfusion.

Beneficial Effects of Preconditioning

- *CABG:* Better ejection fraction and cardiac index after CABG
- *OPCAB:* Preconditioning less used now due to use of coronary shunts intraoperatively
- *Heart transplant:* Improves contractile function after global myocardial hypothermia, which occurs when donor heart is stored
- *Cardiomyoplasty:* Skeletal muscle preconditioning prior to cardiomyoplasty augments systolic function and limits diastolic dysfunction.

Types of Preconditioning

- *Early preconditioning*: Limited to 1–3 hours after brief ischemic stimulus
- Delayed preconditioning:
  - Occurs after 24 hours of volatile anesthetic exposure
  - Lasts as long as 72 hours
  - Maybe species specific (occurs with sevoflurane but not isoflurane)
  - Late or second window phase.
- Post conditioning:
  - Myocardial protection provided by volatile anesthetics at the time of reperfusion
  - Administered immediately before or during reperfusion
  - 4% sevoflurane during first 10 minutes of CPB reduces postoperative release of BNP (marker of LV dyfunction).

Biochemical Mechanisms of Preconditioning

- Upregulation and activation of mitochondrial and sarcolemmal KATP channel: Acts by reducing coronary vascular tone
- G proteins and coupled receptor ligands:
  - Due to activation of δ_1 opioid receptors
  - These in turn activate G_i and G_s protein.
- *Protein kinases*: PKC, PKG and $P_{13}K$ involved in cardioprotective signal transduction
- Reactive oxygen species:
  - Volatile anesthetics stimulate small bursts of reactive oxygen species (superoxide, H_2O_2 and peroxynitrite)
  - These paradoxically initiate downstream signaling and protect from subsequent ischemic injury.
- Adenosine receptor (especially α_1 and α_2 subtypes)
- Tyrosine kinase
- Na^+: H^+ exchanger
- COX_2, NFKB and NO systems are implicated for delayed preconditioning.

Inhibitors of Preconditioning

- Adenosine antagonists
- δ_1 opioids
- Glibenclamide:
  - As they close K_{ATP} channels
  - Discontinue glibenclamide 24–48 hours preoperatively
- Pertussis toxin
- Hyperglycemia.

ANESTHESIA FOR PATIENTS WITH INTRACORONARY STENTS[1,2,3,5,11,17]

Introduction

Success of stents requires long term antiplatelet therapy and thus, perioperative management of these patients poses special issues.

Types of Stents

- Bare metal stents (BMS):
  - Eliminated acute vessel closure (occurs within 24 hours) which was seen with PTCA

  - However, acute (< 24 hrs) and subacute (24 hrs-30 days) stent thrombosis can still occur
  - Incidence of stent rethrombosis is reduced with dual antiplatelet therapy
  - Restenosis rate is however high
  - This is due to neointimal hyperplasia (medial hyperproliferation) in coronary artery
  - This occurs due to endothelial damage from free ends of the stent.
- Drug eluting stent (DES):
  - Bare metal stent is coated with polymer containing sirolimus/paclitaxel
  - Sirolimus and paclitaxel inhibit neointimal hyperplasia
  - This lowered restenosis rate seen with bare metal stents
  - However, higher incidence of:
    - Late stent thrombosis (> 30 days)
    - Very late stent thrombosis (> 1 year).
  - Risk factors for thrombosis after drug eluting stent:
    - Acute coronary syndrome
    - Diabetes mellitus, old age
    - Renal impairment
    - LVEF ≤ 30%
    - Premature discontinuation of dual antiplatelet therapy (DAP).

Dual Antiplatelet Therapy

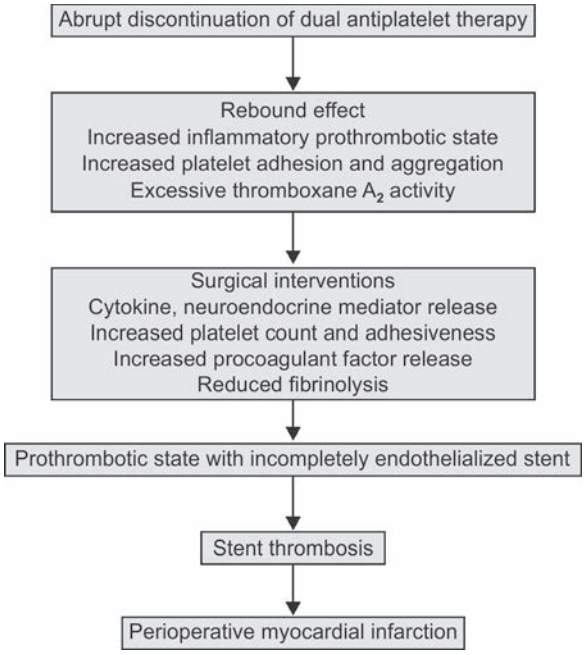
ACC-AHA 2007 recommendations:

- Bare metal stents:
  - Loading dose of 300–600 mg clopidogrel before implantation
  - Aspirin 75–100 mg with clopidogrel 75 mg given for 4–6 weeks postprocedure to allow stent endothelialization
  - Low dose aspirin continued thereafter, for life, as secondary prophylaxis
  - Elective surgery postponed beyond 6 weeks of stent placement (but before 12 weeks when restenosis can occur).
- Drug eluting stent:
  - Loading dose of 300–600 mg clopidogrel given before implantation
  - Aspirin 75–100 mg with clopidogrel 75 mg given for 12 months poststent placement
  - Thereafter, continue low dose aspirin life long, for secondary prophylaxis
  - Postpone elective surgery for more than 12 months after stent placement.
- PTCA alone:
  - Dual antiplatelet therapy given for 2–4 weeks after stent placement
  - Elective surgery postponed for more than 2–4 weeks after stent placement.
- Consider using BMS/PTCA rather than DES in patients due for noncardiac surgery within 12 months
- Discontinue antiplatelet therapy only after discussion with cardiologist.

Perioperative Anesthetic Problems

- *Increased risk of bleeding*: Dangerous in closed compartment surgeries (neurosurgery)
- Acute perioperative stent thrombosis
- Complications arising due to simultaneous neuraxial blockade.

Pathophysiology of Acute Perioperative Stent Thrombosis



Risk Factors for Perioperative Thrombosis with DES

- Factors related to the stent:
  - Stent in LMCA
  - Stent in bifurcation/crossing arterial branch points

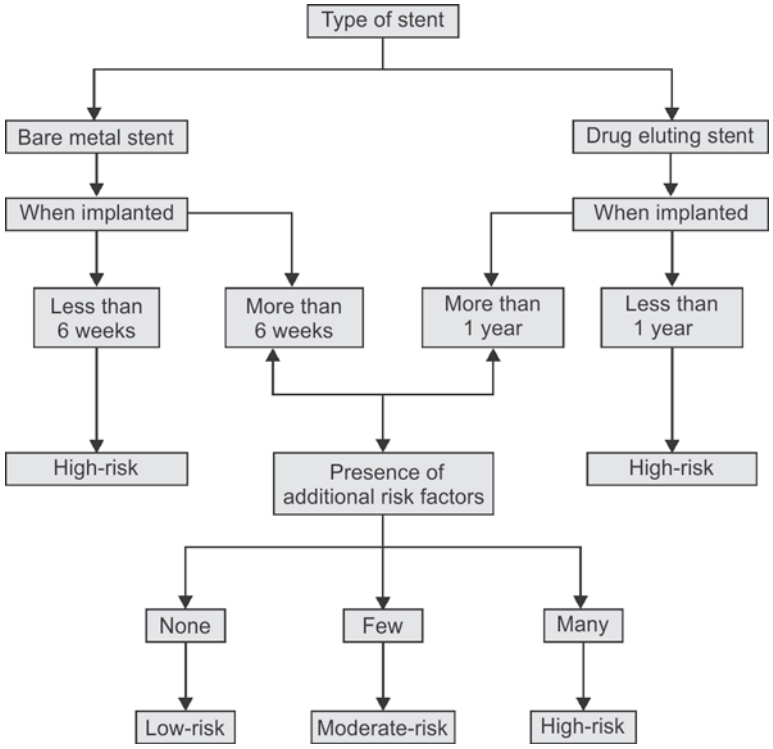
  - In-stent restenosis
  - Greater total stent length, multiple stents
  - Small stent diameter (less than 3 mm).
- Factors relating to patient:
  - Heightened platelet activity (surgery, cancer, diabetes mellitus)
  - Localized hypersensivity vasculitis (due to anti-proliferation drugs)
  - LV dysfunction
  - Diabetes mellitus
  - Plaque disruption into necrotic core
  - Advanced age, prior brachytherapy.
- Factors relating to dual antiplatelet therapy:
  - Resistance to antiplatelet therapy
  - Interruption of DAP therapy within 14 days of stent insertion is the most important factor
  - Inappropriate discontinuation of antiplatelet therapy.

Preanesthetic Evaluation

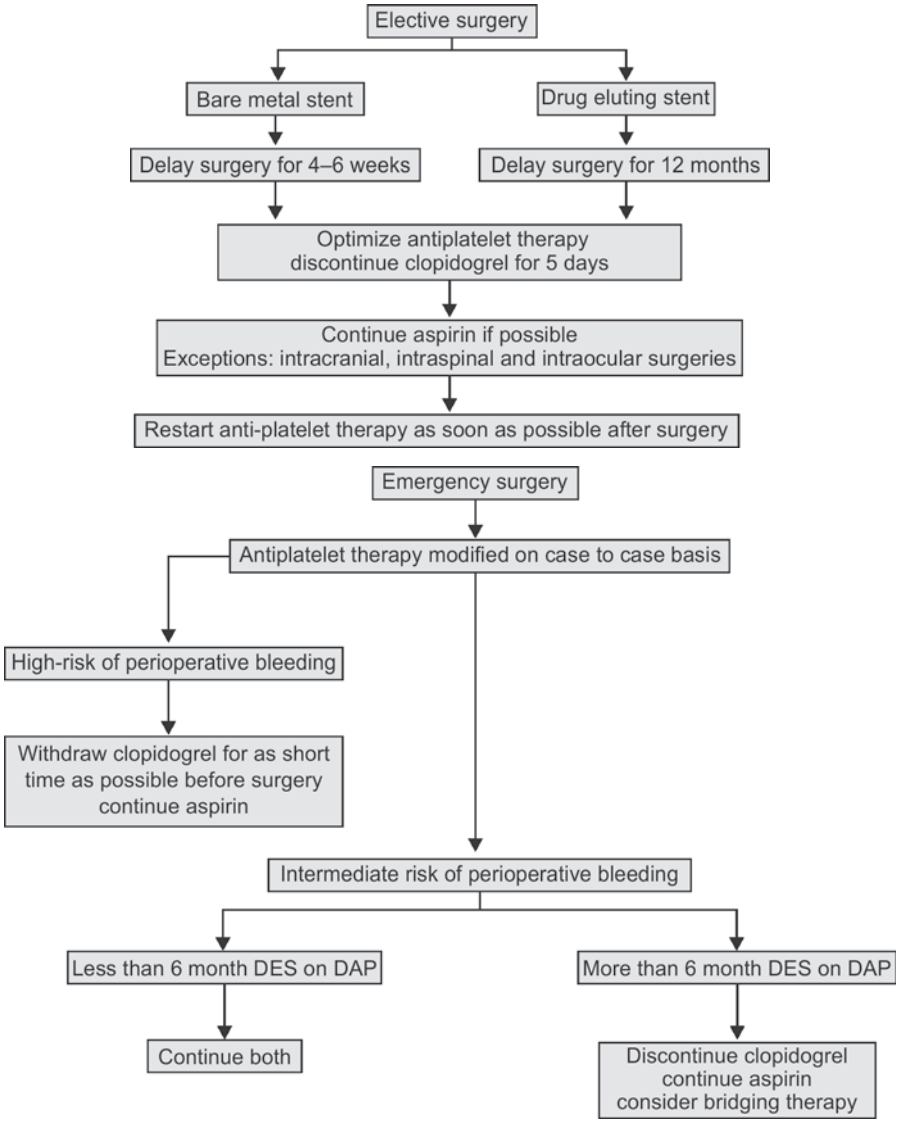
- History:
  - Duration since PCI.
  - Type of stent: BMS/DES
  - Number of stents
  - Location of stents
  - History of adverse cardiac events
  - Previous history of stent thrombosis
  - Drug regimen and any irregularities in the regimen
  - Urgency of surgery
  - *Comorbidities*: DM, CRF, low LVEF
  - History of conditions prone for thrombosis
  - Cardiology consultation.
- Investigations:
  - Routine blood investigations
  - Platelet count and function
  - Bleeding and clotting time
  - Renal function tests
  - Arrange whole blood and platelet concentrates.

Determining Risk of Stent Thrombosis

Circulation 2007



Perioperative Management



Rationale of Continuing Aspirin

- No difference in blood loss between aspirin users and non-users in OPCAB patients
- Protective effects of aspirin provided in vascular surgeries:
  - Improved long term peripheral bypass graft potency
  - Reduced incidence of MI, TIA, stroke, death.
- Increases incidence of bleeding by a factor of 1.5
- Aspirin did not increase severity or perioperative morbidity except in:
  - Intracranial surgeries
  - Spine surgeries
  - Intraocular surgeries
  - TURP (possibly).

Bridging Therapy

- Short acting GP-II_b/III_a antagonists (tirofiban/eptifibatide) is substituted for clopidogrel during perioperative period, if there is high risk of bleeding
- Heparin has no antiplatelet action and is not protective against stent thrombosis
- Use GP-II_b/III_a antagonists in:
  - Patients who have not completed dual anti-platelet therapy
  - Patients whose stent complexities increases risk of developing stent thrombosis.

Dual Antiplatelet Therapy and Neuraxial Blockade

- Neuraxial block not recommended until:
  - Platelet function is within normal limits, or
  - Platelet transfusion is given before surgery.
- If neuraxial blockade is planned:
  - Clopidogrel stopped 7 days before surgery
  - Ticlopidine stopped 14 days before surgery
  - Aspirin alone is not a contraindication for neuraxial blockade
  - Those receiving bridging therapy:
    - Discontinue abxicimab for 48 hrs before NAB
    - Discontinue eptifibatide and tirofiban for 48 hrs before NAB.

PREOPERATIVE ASSESSMENT OF CARDIAC PATIENT FOR NONCARDIAC SURGERY[1,2,3,5,17]

Goals

- To identify risk for heart disease based on risk factors
- To evaluate presence and severity of cardiac disease through symptoms, physical findings and diagnostics tests
- To determine the need for preoperative interventions
- To modify risk factors for perioperative adverse events.

Risk Indices

- Before 1990:
  - NYHA, ASA indices
  - Goldman, Cooperman
  - Detsky, Larsen
  - Penderson, Vanzetto.
- After 1990:
  - ACC/AHA, ACP
  - Lee, ACC updated.

Goldmans Cardiac Risk Index[3]

Characteristic	Score
third heart sound, jugular vein distension	11
Recent MI	10
Nonsinus rhythm, paroxysmal atrial complexes	7
More than 5 ventricular ectopic beats	7
Age more than 70 years	5
Emergency surgery	4
Poor general condition	3
Intrathoracic/intraperitoneal/aortic surgery	3
Aortic stenosis	3

Goldmans score	Cardiac complication rate
0–5 points	1%
6–12 points	7%
13–25 points	14%
More than 26 points	78%

Lee's Revised Cardiac Risk Index (RCRI)

Introduction

It has been validated in several studies as the best scoring system to predict perioperative cardiac risk in patients undergoing cardiac surgery.

Importance

- Traditional risk factors for CAD are:
  - Smoking
  - Male gender
  - Hypercholesterolemia
  - Family history of CAD.
- These are not the same factors which are associated with an increased incidence of perioperative cardiac events
- These are, however, important in assessing significance of chest pain, dyspnea or abnormal ECG.

Components

- High risk surgery:
  - Intraperitoneal surgeries
  - Intrathoracic surgeries
  - Suprainguinal surgeries
  - Vascular surgery.
- Ischemic heart disease by any diagnostic criteria:
  - History of angina
  - Use of sublingual nitroglycerine
  - Positive exercise test
  - Significant Q waves on ECG
  - Patient who has undergone PTCA/CABG.
- Heart failure
- Cerebrovascular disease
- Insulin dependent diabetes mellitus
- Creatinine 2 mg/dl.

Risk of Major Cardiac Events

- 0 risk factors: 0.4 % risk
- 1 risk factor: 0.9 % risk
- 2 risk factors: 7 % risk
- 3 risk factors: 11 % risk

Detsky Modified Multifactorial Index

No.	Characteristic	Score
1	Class IV angina	20
2	Suspected critical aortic stenosis	20
3	History of MI within the last 6 months	10
4	History of pulmonary edema within last 1 week	10
5	Class III angina	10
6	History of unstable angina within the last 3 months	10
7	Emergency surgery	10
8	History of MI more than 6 months back	5
9	History of pulmonary edema more than 1 week back	5
10	Nonsinus rhythm/PAC	5
11	More than 5 ventricular ectopic beats	5
12	Poor medical status	5
13	Age more than 70 years	5
Score more than 15 suggests high risk		

Eagles Criteria for Risk Assessment

Characteristic	Score
age more than 70 years	1
Diabetes mellitus	1
Angina	1
Pathological Q waves	1
Ventricular arrhythmias	1

Score	Significance
Less than 1	No tests indicated
1–2	Noninvasive testing warranted
More than 3	Angiography warranted

Preoperative Evaluation

- History:
  - Presence, severity and reversibility of CAD:
    - Risk factors:
      - Age
      - HTN, DM
      - Cholesterol
      - Smoking
    - Angina pattern:
      - Stable/unstable
      - Medications
      - Aggravating/relieving factors
    - Previous history of MI
  - Myocardial function:
    - Exercise capacity
    - Pulmonary edema
    - Orthopnea, PND, edema
    - NYHA classification:
      - Class 1:
        - No limitations of physical activity
        - On ordinary activity, no fatigue/syncope/palpitations
      - Class II:
        - Slight limitation of physical activity
        - Fatigue/palpitations/syncope on ordinary activity
      - Class III:
        - Marked limitation of activity
        - Fatigue on less than ordinary activity
      - Class IV: Symptoms occurring at rest.
  - Valvular heart disease:
    - Dyspnea, orthopnea, PND
    - History of medications
    - Hemoptysis
    - Embolic events.
  - Associated cerebral, cardiovascular, carotid, aortic vascular disease
  - Prior cardiac evaluation: Noninvasive testing, angiography.
- Physical examination:
  - Vital signs: Pulse, blood pressure, respiratory rate
  - Cardiac examination:
    - JVP, peripheral edema
    - Displaced apical impulse: Cardiomegaly
    - S_3 gallop/S_4 gallop
    - Apical systolic murmur
    - Pulmonary edema.
- Diagnostic tests:
  - Routine blood tests, blood urea, serum creatinine
  - *Serum electrolytes*: Especially in patients on diuretics
  - If Hb 10 g%, transfuse blood in those with low cardiovascular reserve
  - Brain natriuretic peptide ≥ 100 pg/ml indicates high risk of CCF
  - Chest X-ray:
    - Cardiomegaly
    - *Ventricular dysfunction*: Increased vascular markings edema
    - Pleural/pericardial effusion.
  - ECG:
    - Should not be ordered simply because of advanced age
    - Only certain abnormalities are significant in preoperative assessment:

    - Q waves, especially if recent
    - Conduction abnormalities and arrhythmias
  - Establishing baseline for comparison is most important reason to obtain ECG preoperatively
  - If previous ECG available and no change in risk factors/no new physical finding, it is unlikely that repeat ECG will be helpful
  - *ACC-AHA 2007 recommendations*:
    - Class I recommendations:
      - Should be performed
      - For patients with atleast 1 clinical risk factor undergoing vascular surgery
      - Those undergoing intermediate risk surgery with known case of:
        → Congestive cardiac failure
        → Peripheral arterial disease
        → Cerebrovascular accident.
    - Class IIa recommendations:
      - Reasonable to perform
      - For patients with no clinical risk factors undergoing vascular surgery.
    - Class IIb recommendations:
      - Maybe considered
      - For patients with atleast 1 clinical risk factors undergoing vascular surgery
    - Class III recommendations:
      - Should not be performed and not useful
      - Asymptomatic patients undergoing low risk surgeries.
- Stress testing:
  - For patients with normal ECG who can exercise
  - Patients should be likely to achieve adequate heart rate response
  - Test is adequate when patient can achieve 85% of target heart rate
  - Target heart rate = 220 – age in years
  - Positive predictive value of 5–25%
  - Negative predictive value of 100%
  - Thus, it gives more information about patient who will not have an event rather than one who will.
- Dobutamine stress test:
  - Useful for patients with normal ECG but unable to exercise
  - Avoided in:
    - Poorly controlled hypertension
    - Bradycardia.
    - Aortic/cerebral aneurysm
    - Patients with pacemaker.
- Nuclear perfusion imaging:
  - For patients unable to exercise and in whom dobutamine test is contraindicated
  - Myocardium said to have limited blood flow if it is normal at rest but shows reduced isotope uptake with exercise.
- Echocardiography:
  - For evaluating RWMAs and LV ejection fraction
  - Abnormal movement at rest indicates scar tissue
  - Areas which are normal at rest but with abnormality which increases with increasing inotropy and chronotropy indicates stenotic lesions and limited blood flow
  - Classification of LV dysfunction:
    - EF ≥ 50%: Normal
    - EF 41–49%: Mildly LV dysfunction
    - EF 26–40%: Moderate LV dysfunction
    - EF ≤ 25%: Severe LV dysfunction.
- Cardiac catheterization: Does not absolutely risk stratify patients.

Dukes Activity Status Index

1 MET is the oxygen consumption by a resting adult (3.5 ml/kg/min or 250 ml/min).

- Dukes status 1 MET:
  - Able to take care of self
  - Eat, dress, use toilet
  - Walk indoors or on level ground at 3.2–4.8 km/hr
- Dukes status 4 METS:
  - Light housework: Dusting, washing dishes
  - Climbs flight of stairs
  - Walks on level ground at 6.4 km/hr or 4 mph
  - Walks 1–2 blocks
- Dukes status 7 METS: Playing singles tennis, dancing
- Dukes status 10 METS:
  - *Strenous sports:* Swimming, singles tennis, basket ball, football
  - Running rapidly for moderate to long distances
- Significance:
  - *Poor functional capacity:* Less than 4 METS
  - *Moderate functional capacity:* 4 to 7 METS
  - *Good functional capacity:* 7 to 10 METS.

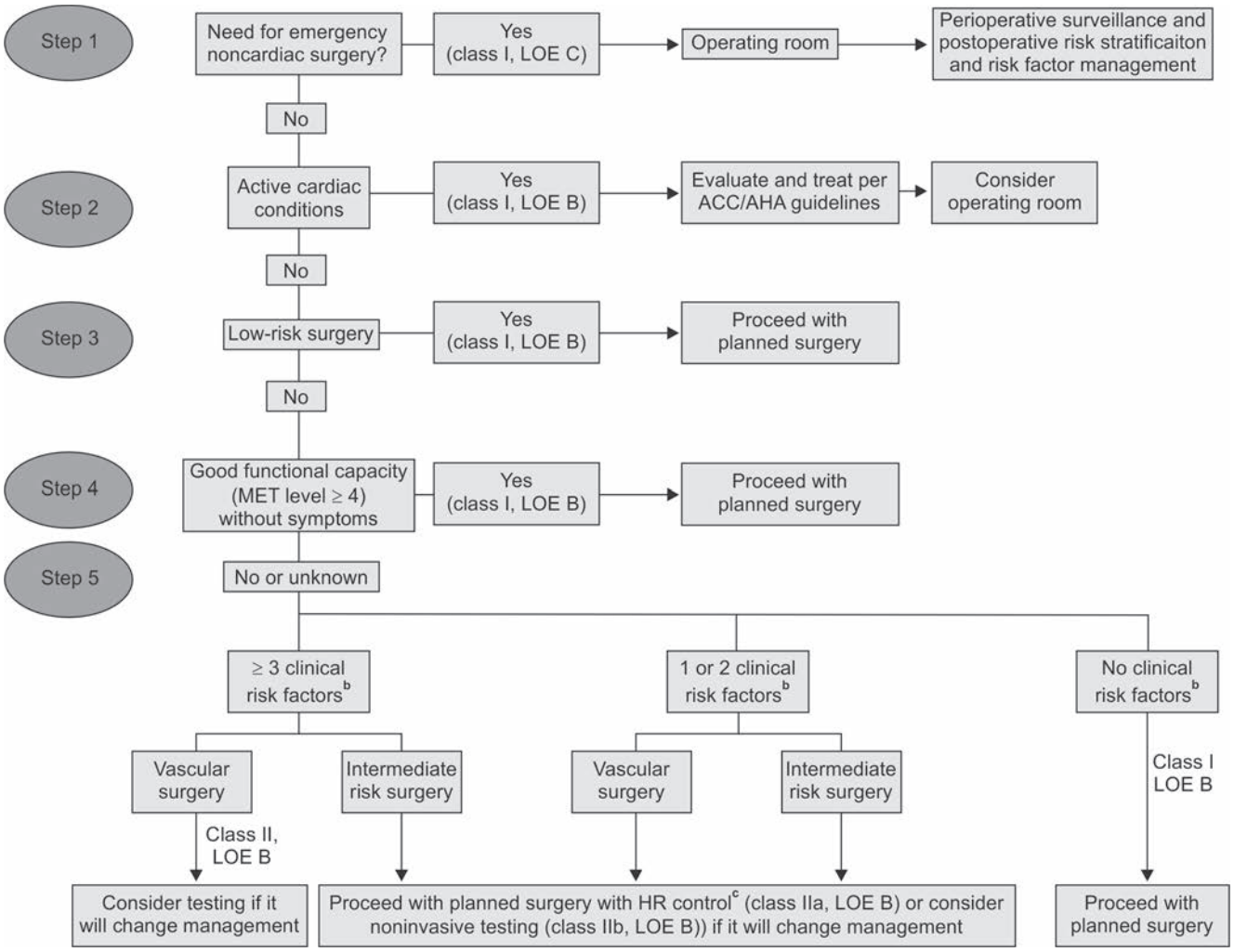
Surgery Specific Risk Factors

- High risk surgery (> 5% risk):
  - Emergency major surgery in elderly
  - Prolonged surgical procedures associated with large fluid shifts/blood loss
  - Aortic/other major vascular surgery
  - Peripheral vascular disease.
- Intermediate risk surgery (< 5% risk)
  - Carotid endarterectomy
  - Head and neck surgery
  - Intrathoracic surgery
  - Intraperitoneal surgery
  - Orthopedic surgery
  - Prostrate surgery.
- Low risk (< 1% risk):
  - Superficial surgeries
  - Endoscopic surgeries
  - Breast, cataract surgery.

ACC-AHA 2007 Perioperative Guidelines *(See Flow Chart)*

Risk factors are:

- Ischemic heart disease
- History of congestive cardiac failure
- History of cerebrovascular accidents
- Diabetes mellitus
- Serum creatinine more than 2 mg/dL.



INTRA-AORTIC BALLOON PUMP[1,2,3,5,17]

Introduction

- Circulatory assist device (CAD) which is designed to augment myocardial perfusion, by increasing coronary blood flow during diastole and unloading left ventricle during systole
- Simplest and most readily available CAD.

Major Types of Circulatory Assist Device

- Counter pulsation devices:
  - IABP
  - Noninvasive counter pulsations.
- Cardiopulmonary assist devices: ECMO
- Ventricular assist devices:
  - LVAD
  - RVAD
  - BiVAD.

Classification of CAD

- By indication:
  - Urgent (unstable angina/uncontrolled CCF):
    - IABP
    - VAD.
  - Emergent (uncontrolled hypotension, inability to wean off CPB):
    - IABP
    - ECMO.
- By duration of therapy:
  - Short term:
    - IABP
    - Abiomed VAD
    - ECMO.
  - Long term:
    - Thoracic VAD
    - Implantable VAD
- By degree of support provided:
  - *Augmentation*: IABP
  - LVAD/RVAD alone
  - Total support (Bivad/ECMO).

Composition of IABP

- 25 mm sausage shaped balloon
- Mode of nonthrombogenic polyurethane
- Mounted on 90 cm long vascular catheter
- Helium/carbon dioxide used as distending gas (helium is preferred)
- Volume of balloon is 30–50 ml.

Insertion of IABP

- Inserted into femoral artery either percutaneously/via surgical exposure
- Length to be inserted calculated by measuring distance between angle of Louis and femoral artery
- Distal tip lies below left subclavian artery (to prevent emboli to brain)
- Proximal tip lies above renal artery
- When peripheral vascular disease present, IABP inserted via ascending aorta after median sternotomy.

Other Approaches

- *Ascending aorta:* If PVD present
- *Iliac artery:* In children where size of femoral artery is small
- Subclavian artery
- Axillary artery.

Indications

- Cardiogenic shock:
  - Postmyocardial infarction
  - Myocarditis
  - Cardiomyopathy
  - Pharmacological.
- Failure to wean from CPB:
  - Right/left ventricular failure
  - Increased inotropic requirements
  - Hemodynamic deterioration.
- Stabilization of cardiac patient for cardiac surgery:
  - MI with VSD
  - MI with mitral regurgitation
  - Unstable, refractory acute coronary syndrome.
- Stabilization of unstable patient for noncardiac surgery:
  - Emergency cholecystectomy
  - Gastrectomy, enterolysis
  - Repair of parastomal hernia
  - Resection of intracranial masses
  - Septic shock.
- Procedure support during coronary angiography
- As a bridge to transplantation
- Trauma/hemorrhagic shock.

Contraindications

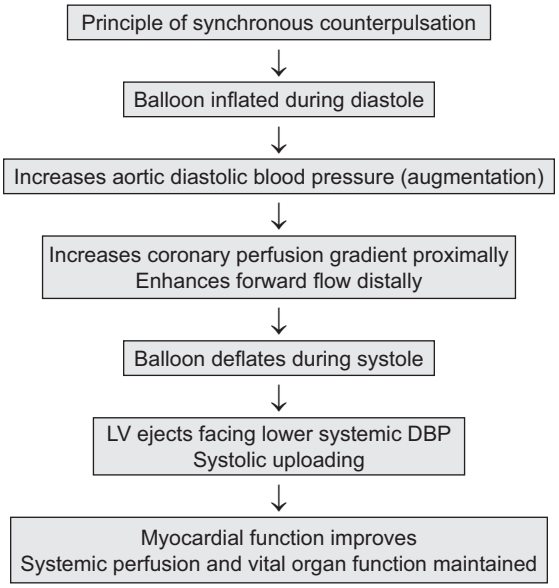
- Absolute contraindications:
  - Abdominal aortic dissection/aneurysm
  - Severe calcific aorta
  - Peripheral vascular disease
- Relative contraindications:
  - Severe AR
  - Irreversible cardiac disease (not a transplant candidate)

- Irregular rhythm
- Irregular pulse pressure
- Irreversible brain damage
- Severe noncardiac systemic disease
- Massive trauma, Do Not Resuscitate (DNR) patients
- Local infection, inability to insert.

Timing and Goal of Inflation and Deflation

- Inflation:
  - Timed to coincide with aortic valve closure
  - Produces rapid rise in diastolic BP
  - Inflated just prior to dicrotic notch
  - Late inflation: Reduces perfusion pressure to coronary artery
  - Early inflation:
    - Called early if inflation occurs more than 40 msec before dicrotic notch
    - Causes aortic regurgitation and LV strain.
- Deflation:
  - Reduces afterload by reducing aortic end-diastolic pressure
  - This reduces myocardial oxygen demand and increases cardiac output
  - *Early deflation*: Causes inappropriate loss of afterload reduction
  - *Late deflation*: Will increase LV work by causing increased afterload
- Factors affecting IABP performance:
  - Position of balloon within the aorta
  - Balloon volume
  - Cardiac rhythm.

Principles[1,5]



IABP Triggers

- *ECG:* More than 120 µV deflation/R wane
- Pacemaker spike
- *Arterial pressure:* More than 15 mm Hg deflation
- Internal trigger.

Associated Therapies

- Heparin to prevent thrombus
- Increased inotropic support while weaning off IABP
- Antibiotic cover
- IV fluids to maintain preload.

Limitations

- Not useful when LV is unable to eject blood into aorta
- Not useful in irregular/fast cardiac rhythms.

Weaning Criteria

- Clinical criteria:
  - Absence of shock syndrome (hypotension, cool extremities)
  - Minimal need for vasopressors (< 5 µg/kg/min dopamine)
  - Cardiac catheterization/major surgery is planned.
- Hemodynamic criteria:
  - Cardiac index more than 2.2 L/min/m^2
  - Wedge pressure < 18 mm Hg
  - Mean BP > 70 mm Hg
  - Less than 10% change in cardiac index, wedge pressure and heart rate during weaning.
- Balloon augmentation is reduced in steps from 1:1 counterpulsation to 1:2, 1:4
- Appropriate intervals required to assess:
  - Hemodynamic and neurological stability
  - Cardiac output and MvO_2
- After appropriate observation at 1:8 counterpulsations, IABP can be removed.

Complications

- Vascular complications:
  - Arterial injury (perforation/dissection)
  - Aortic dissection
  - Femoral artery thrombosis and pseudo-aneurysm
  - Peripheral embolization
  - Lower extremity ischemia (most common)
  - Compartment syndrome
  - Visceral ischemia (mesenteric infarction)
  - Femoral venous catheterization.

- Miscellaneous:
  - Hemolysis, thrombocytopenia
  - Infection, sepsis
  - Claudication pain (after removal)
  - Hemorrhage
  - Paraplegia, spinal cord ischemia
  - Entrapment of balloon
  - Left internal mammary artery occlusion
  - Coagulopathies.
- Complications related to balloon:
  - Perforation of balloon (preinsertion)
  - Balloon tear during insertion
  - Incorrect positioning
  - Gas embolism, cerebrovascular accidents
  - Inadvertent removal.

ENDOVASCULAR AORTIC REPAIR (EVAAR)[1,5,17]

Indications

- Aortic aneurysms
- Aortic dissection
- Aortic tears and rupture.

Surgical Technique

- Arterial access:
  - Most commonly bilateral femoral artery access
  - Depends on size of blood vessel and degree of obstructive arterial disease
  - Balloon dilation and local endarterectomy done if femoral artery is small
  - Adjunctive retroperitoneal procedure done if:
    - Femoral artery is very small
    - Iliac artery aneurysm is present.
- Delivery system:
  - Under fluoroscopic guidance along with stent grafts
  - Stent graft position confirmed by fluoroscopy/TEE.

Preoperative Preparation

- History and examination of patient
- Chest X-ray, CT scan and MRI to delineate aortic anatomy
- NPO guidelines
- Patient reassurance and consent
- Blood grouping and cross matching
- 10–15 units blood kept ready to cope with any emergencies
- Stabilize coexisting diseases and continue preoperative medications.

OT Preparation

SOAP-ME

- Suction apparatus
- Oxygen delivery systems, oxygen cylinders
- *Airway:* Laryngoscope, ET tube, oral airway, LMA
- *Pharmacy:* Thiopentone, propofol, fentanyl
- Monitors
- *Emergency drugs:* Atropine, adrenaline, dopamine, dobutamine, NTG, SNP
- Availability of cardiac surgeon and resuscitation and transport plan if aortic tear/rupture.

Monitors

- Pulse oximetry, E_TCO_2
- ECG, urine output
- Temperature, NIBP, TEE
- Radial arterial IBP:
  - Useful to assess volume, resuscitation and CPR
  - Useful for ABGs
  - Important as hypotensive anesthesia practiced.
- CVP and PA catheter usually not required
- Somatosensory evoked potentials, motor evoked potentials.

Anesthetic Technique

- Local/general anesthesia can be used
- GA is technique of choice as:
  - Procedure may be long
  - TEE may be required throughout the procedure
  - In case of any emergency, airway is already secured.
- If aneurysm is thoracoabdominal, bronchial blockers can be used
- In case of emergencies, blocker can be inflated and left lung can be isolated
- Systemic anticoagulation with heparin done before device placement
- Hypotensive anesthesia is used during placement of stent graft.

Contraindications

- Very short diseased segment
- Increased diameter of diseased segment
- Aortic wall disease of proximal segment.

Complications

- Migration of stent, kinking/leak around stent
- Paraplegia:
  - Common in thoracoabdominal aneurysms
  - Consider CSF drainage to maintain cerebral perfusion pressure.

- Contrast nephropathy:
  - Risk factors:
    - Diabetes, hypertension, old age
    - Renal insufficiency
    - Repeated exposure at short intervals
    - Use of high osmolality nonionic contrast
    - ACE inhibitor therapy.
  - Treatment:
    - Hydration, N-acetyl cysteine
    - Antioxidants, vasodilators
    - Dopamine and phenoldopam tried
    - Dialysis
    - Diuretics not used during first 24 hours.
- Stroke, abdominal pain, mesenteric ischemia
- Endovascular leaks:
  - Type I: Leak occurs between graft and proximal/distal segment
  - Type II: Leak occurring through collateral
  - Type III: Due to problem with in-stent graft.

Advantages

- Reduced mortality and morbidity
- Reduced blood loss
- Reduced postoperative pain
- Reduced ICU stay
- Reduced postoperative pulmonary complications
- Can be done in very old/very sick patients in whom open surgery is contraindicated.

Disadvantages

- Risk of converting to open surgery exists
- Risk of bleeding, stroke, paraplegia, endovascular leaks and contrast nephropathy.

PHYSIOLOGICAL CHANGES DURING AORTIC CROSS CLAMPING[1,2,3,5,17]

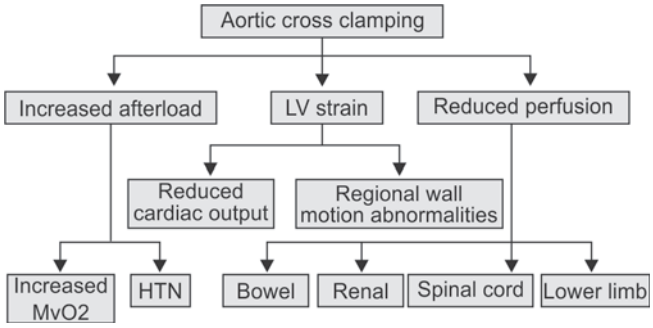
Introduction

Aorta at thoracic/abdominal level, is cross clamped during surgery of abdominal/thoracic/thoracoabdominal aneurysms.

Complications of Cross Clamping

- 30 day mortality: 8–35%
- Complete/partial paraplegia (16–38%)
- Myocardial infarction (11%)
- Respiratory failure (36%)
- Renal failure (18–27%)
- *GI complications*: Mainly hemorrhage: (7%)

Physiological Changes During Clamping



Hemodynamic Changes

- Increased preload
- Increased afterload
- Increased LV wall tension
- Increased regional wall motion abnormalities
- Increased arterial BP, systemic vascular resistance
- Reduced ejection fraction
- Reduced cardiac output
- Reduced renal and splanchnic blood flow
- Increased pulmonary capillary wedge pressure
- Increased central venous pressure
- Increased coronary blood flow.

Metabolic Changes

- Reduced total body oxygen consumption
- Reduced total body oxygen extraction
- Increased mixed venous oxygen saturation
- Reduced total body carbon dioxide production
- Increased epinephrine and norepinephrine levels
- Respiratory alkalosis
- Metabolic acidosis.

Renal Changes

- 80% reduction in renal blood flow with suprarenal clamping
- Redistribution of renal blood flow:
  - Increased blood flow to cortical and juxtamedullary layers
  - Reduced blood flow to ischemia-prone renal medulla.
- Renal hemodynamic changes persists for 30 min after systemic hemodynamics return to baseline
- Increased chances of dialysis dependent ARF:
  - 2–3% incidence regardless of clamp position
  - 13% incidence if post-suprarenal clamping
  - 5% incidence if postrenal clamping.
- Causes of acute renal failure:
  - Reduced glomerular filtration rate

- Reduced renal blood flow
- Ischemia reperfusion injury.

Visceral and Mesenteric Changes

- Reduced blood flow occurs through superior and inferior mesenteric artery
- Ischemia of left colon is more common due to reduced blood supply through inferior mesenteric artery
- Gut ischemia also causes increased gut permeability and bacterial translocation
- High dose methylprednisolone given at induction reduces this response
- Visceral ischemia aggravated by:
  - Preexisting medical conditions
  - Renal dysfunction
  - Stage of aortic disease
  - Level of cross clamping
  - Duration of cross clamping
  - Perioperative hypotension.

CNS and Spinal Cord Changes

- Reduced blood velocity in middle cerebral artery
- Unclamping causes transient dilatation followed by sustained vasoconstriction of pial blood vessels due to:
  - Hemodynamic changes
  - Carbon dioxide accumulation and wash-out
  - Acidosis
  - TXA_2 release
- Supraceliac cross clamping causes:
  - Reduced anterior spinal artery pressure
  - Increased CSF pressure
  - High CVP.

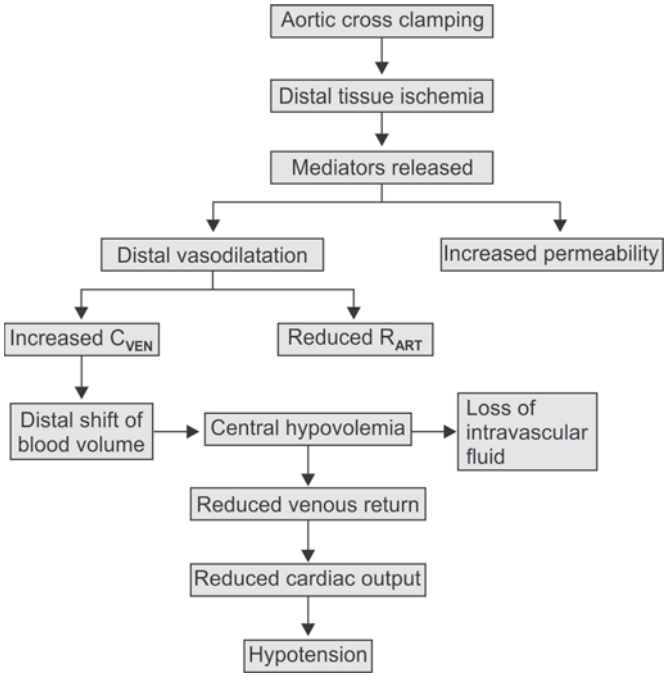
Coagulation Changes

- Increased clotting factor activity occurs during cross clamping
- Reduced speed of clot formation after unclamping.

Therapeutic Interventions

- Afterload reduction:
  - SNP, milrinone
  - Volatile agents
  - Aortofemoral bypass.
- Preload reduction:
  - NTG
  - Controlled phlebotomy
  - Atriofemoral bypass.
- Other changes:
  - Induced hypothermia
  - Reduced minute ventilation
  - Sodium bicarbonate.

Physiological Changes During Unclamping



Hemodynamic Changes

- Reduced afterload
- Distal pooling of blood
- Reduced venous return
- Reduced cardiac output
- Reduced myocardial contractility
- Reduced arterial blood pressure
- Increased pulmonary artery pressure
- Reduced central venous pressure.

Metabolic Changes

- Increased total body oxygen consumption
- Increased total body oxygen extraction
- Reduced mixed venous oxygen saturation
- Increased serum lactate levels
- Reduced activated complement levels
- Increased prostaglandin levels
- Increased myocardial depressant factor levels
- Metabolic acidosis
- Hypothermia.

Therapeutic Interventions

- Reduce volatile agents
- Increased IV fluid administration
- Increased vasoconstrictors
- Reduced vasodilators
- Reapply cross clamp if severe hypotension
- Consider mannitol
- Consider sodium bicarbonate administration.

Humoral Factors Which Cause Organ Dysfunction

- Acidosis
- Activation of RAS
- Activation of sympathetic nervous system
- Oxygen derived free radicals
- Prostaglandins
- Platelet and neutrophil sequestration
- Complement activation
- Cytokine release
- Myocardial depressant factor.

Pulmonary Complications

- Pulmonary edema
- Pulmonary microembolization
- Complications due to one lung ventilation
- Atelectasis due to lung retraction
- Increased ARDS postoperatively due to remote reperfusion injury and capillary leak.

Spinal Cord Protection

- Increase anterior spinal artery pressure:
  - Aortofemoral shunting
  - Maintain proximal hypertension
  - *Gott shunt*: Between proximal thoracic ascending to descending thoracic aorta.
- Reduce CSF pressure:
  - Avoid cerebral vasodilators
  - *CSF drainage*: Role is controversial
  - Corticosteroids, barbiturates.
- Reduce central venous pressure:
  - Controlled phlebotomy
  - NTG, $MgSO_4$, calcium channel blockers
  - Atriofemoral bypass.
- Esoteric measures:
  - Cooling (temperature drift)
  - Oxygen free radical scavengers:
    - N-acetyl cysteine
    - Mannitol
    - Superoxide dismutase
    - Allopurinol.
  - Limit cross clamp time to less than 30 minutes
  - Application of sequential aortic cross clamp
  - Enhanced spiral cord monitoring
    - Somato Sensory Evoked Potentials
    - Motor Evoked Potentials.
  - Use EVAAR where possible
- Avoid postoperative hypotension.

Renal Protection

- Optimize oxygen demand/supply:
  - Reduce tubular reabsorption (loop diuretics)
  - Cooling (temperature drift)
  - Maintain tissue oxygenation (heart, lung, hemostasis)
  - Limit aortic cross clamp time to less than 30 minutes
  - Sequential cross clamping.
- Increase renal tubular flow:
  - Fluid loading (most effective)
  - Loop diuretics
  - Mannitol 0.5–1 gm/kg before reperfusion
  - Dopamine 1–3 µg/kg/min
  - Fenoldopam 0.1–0.3 µg/kg/min
  - Maintain cardiac output.
- Use endovascular techniques where possible (EVAAR)
- Avoid nephrotoxins:
  NSAIDs
  - ACE inhibitors
  - Angiotensin receptor blockers
  - Aminoglycosides.
- Other techniques:
  - Thoracic epidural for sympatholysis
  - Prostaglandins
  - Isovolemic hemodilution
  - Maintain euglycemia
- Renal vasodilators:
  - Prostaglandins
  - Atrial natriuretic peptide
  - Theophylline.

DEEP VEIN THROMBOSIS[1,2,3,5,10,17]

Introduction

- The presence of a thrombus within a deep vein and accompanying inflammatory response in the vessel wall is called venous thrombosis/thrombophlebitis
- Superficial venous system in lower extremity includes greater and lesser saphenous veins and tributaries

- The deep veins are those which accompany major arteries.

Etiology

Conditions associated with increased risk of DVT:

- Surgery:
  - Orthopedic, thoracic surgeries
  - Abdominal, genitourinary surgeries.
- Neoplasms:
  - Pancreas (very common)
  - *Genitourinary*: Ovary, testes
  - Lung carcinoma
  - Breast cancer
  - Stomach tumors.
- Trauma:
  - Fracture spine, hip
  - Fracture of femur, tibia
  - Pelvic fractures
  - Traumatic brain injury:
    - Upto 25% patients with isolated brain injury develop DVT
    - Prophylaxis started 45 hours after injury to prevent increased risk of bleeding.
- Venulitis:
  - *Burgers disease*
  - *Behcets disease*
  - Homocysteinuria.
- *Immobilization*: MI, CCF, stroke, postop convalescence
- Hypercoagulable states:
  - Pregnancy, OCP use
  - Myeloproliferative disorders, APLA syndrome, SLE
  - Multiple myeloma
  - DIC, factor V Leiden deficiency
  - Protein C and S deficiency, dysfibrinogenemia
  - Previous history of DVT.

Pathogenesis

- *Virchows triad* describes factors which predispose to VTE:
  - Stasis of blood
  - Vascular endothelial damage
  - Hypercoagulability.
- Initially, the thrombus contains principally platelets and fibrin
- RBCs then become interspersed with fibrin and thrombus propagates in the direction of blood flow
- Inflammatory response in blood vessel is due to:
  - Granulocyte infiltration
  - Loss of endothelium and edema

Sites of Occurrence

- *Lower extremity:* Femoral vein, popliteal vein, iliac vein
- Pelvic vein
- Superior/inferior vena cava
- Upper extremities:
  - Due to increased use of subclavian or IJV catheters
  - More common in ICU population
  - Can result in pulmonary embolism in up to 2/3rd of cases
  - Also increases risk of post-thrombotic syndrome.

Clinical Features

- 50 % of cases develop within 1 week (usually within 4 days)
- Calf pain is *most common* complaint
- Unilateral leg swelling, warmth, erythema
- Increased tissue turgor, prominent venous collaterals, distended superficial veins
- Tenderness along course of vein, cord may be palpable
- In markedly edematous limb, interstitial tissue pressure exceeds capillary perfusion pressure and causes pallor: *Phlegmasia alba dolens*
- In some patients deoxygenated Hb in stagnant vein imparts cyanotic hue to the limb: *Phlegmasia cerulea dolens*
- Bedside diagnosis may be difficult as only 1 of multiple veins may be involved allowing adequate venous return through remaining patent vessels
- *Homans sign:* Increased resistance or pain during foot dorsiflexion
- *Moses sign:* Pain on squeezing calf muscles.

Complications

- Short-term complications:
  - Prolonged hospitalization
  - Bleeding due to treatment
  - Pulmonary embolism
  - Local extension of DVT
  - Further embolization
  - Pulmonary embolism.
- Long-term complications:
  - Post thrombotic syndrome
  - Pulmonary hypertension
  - Recurrent DVT
  - Embolic stroke through patent foramen ovale.

Investigations

- Investigations to diagnose DVT:
  - D-dimer assay:
    - Sensitive but not specific
    - Increased D-dimer levels in patients with DVT.
  - Duplex venous ultrasonography:
    - Noninvasive test
    - Most often used
    - Low sensitivity in absence of symptoms
    - Thrombus detected by:
      - Direct visualization
      - By inference when vein does not collapse on compression
      - By flow abnormality.
  - MRI: Used for DVT of SVC/IVC/pelvic veins
  - Venography:
    - Confirmatory, *gold standard test*
    - Diagnosed by presence of filling defect
    - Contrast medium injected into superficial veins of foot
    - This is directed to deep venous system by application of tourniquet
- Investigation to rule out pulmonary embolism:
  - Spiral CT/HRCT
  - Pulmonary angiography: *Gold standard*
  - TEE:
    - Demonstrates RV performance, TR
    - May help to see thrombus in PA/right heart
  - *V-Q scan:* Defect in perfusion with normal ventilation.

Differential Diagnosis

- Muscle rupture
- Ruptured popliteal cyst
- Arterial occlusive disease
- Lymphedema
- Trauma/muscle hemorrhage.

Treatment

- Anticoagulation:
  - Prevents thrombus propagation and allows lytic system to act
  - Heparin:
    - UFH 7500–10000 IU IV bolus dose followed by infusion of 1000–1500 IU/hr
    - Rate titrated to keep APTT value twice that of control value
    - Subcutaneous enoxaparin 1 mg/kg BD used as alternative
  - Direct thrombin inhibitors:
    - Lepirudin 0.4 mg/kg followed by 0.15 mg/kg/hr
    - Argatroban 2 µg/kg/min
    - Bivalirudin 0.75 mg/kg followed by 1.75 mg/kg/hr
    - Used in patients with Heparin Induced Thrombocytopenia.
  - Warfarin:
    - Administered during first week of therapy with heparin
    - Started as early as 1st day of heparin therapy if APTT is therapeutic
    - Overlap warfarin with heparin therapy for at least 4–5 days as action of warfarin is delayed
    - Dosage of warfarin adjusted to maintain PT at INR of 2–3.
  - Duration of therapy:
    - Continued for 3–6 months in acute DVT to reduce chance of recurrence
    - Duration of therapy is indefinite for:
      - Recurrent DVT
      - Hypercoagulable states
      - Malignancy.
- IVC filter/IVC plication:
  - Transvenous filter placement done through femoral venous access
  - SVC and IVC filters available
  - Used when anticoagulants are contraindicated to protect from pulmonary embolism
  - Does nothing to already formed thrombus
  - Some filters can be left permanently
  - Removable filters are removed once anticoagulants are started.
- Thrombolytics:
  - Used in:
    - Massive pulmonary embolism
    - Cor pulmonale
    - Hemodynamically compromised patients.
  - Streptokinase/urokinase/t-PA used
  - Early administration of thrombolytics:
    - Accelerates clot lysis
    - Preserves venous valves
    - Reduces chances of developing post thrombotic syndrome.
- Management of pulmonary embolism:
  - Anticoagulation
  - Thrombolytic agents in patients with:
    - Severe hemodynamic compromise

- Cardiac arrest unresponsive to resuscitative measures despite increased risk of hemorrhage.

– Symptomatic patients:
  - Intubate and positive pressure ventilation
  - Fluids and inotropes (amrinone)
  - Continuous IBP, CVP monitor
  - Pulmonary embolectomy with partial CPB .

DVT PROPHYLAXIS[1,2,3,5,17]

Introduction

Venous thromboembolism is a major cause of death after surgery or trauma to lower limbs.

Incidence

- Venous thromboembolism develops in 40–80% of orthopedic patients without prophylaxis
- 1–28 % patients develop pulmonary embolism
- Fatal pulmonary embolism occurs in 0.1–8% patients
- VTE develops in 40–80% orthopedic patients
- Late initiation of prophylaxis (≥ 4 days after trauma) triples the risk of VTE.

Anderson and Spencer's Risk Factors for Development of DVT[3]

Strong Risk Factors

- Fracture of hip/leg/spine injury
- Hip/knee replacement
- Surgeries of hip/pelvis
- Major trauma.

Moderate Risk Factors

- CNS disorders, paralytic stroke
- CVP lines, malignancy
- Thrombophilia, polycythemia
- Malignancy
- CCF, nonvalvular atrial fibrillation with previous cerebral embolus
- Patients with prosthetic valves (Mitral > Aortic)
- Respiratory failure
- Irritable Bowel Disease/DM
- Pregnancy/postpartum
- Knee arthroscopy
- Chemotherapy, hormone replacement therapy, OCP, radiotherapy for pelvic neoplasm.

Weak Risk Factors

- Bed rest more than 4 days
- Immobility due to sitting (car/plane travel)
- Increased age, obesity
- Laparoscopic surgery with duration of surgery more than 30 min
- Pregnancy/antepartum
- Varicose veins
- Trauma, severe infections.

Other Risk Factors

Hypercoagulable states:
- Factor V Leiden deficiency (most common disorder associated with VTE)
- Antithrombin III, protein C and S deficiency
- APLA, lupus anticoagulant, malignancy, OCP therapy.

Preoperative Considerations

- Risk stratification for development of DVT done for patients
- Patients with previous history of DVT:
  – Risk of recurrence:
    - It is 50% within 3 months of previous DVT without anticoagulant therapy
    - If 1 month of warfarin therapy is added, risk reduces to 10%
    - If 3 months therapy is added, risk is reduced to 5%
  – Elective surgery:
    - To be postponed in 1st month after episode of venous/arterial thromboembolism
    - Ideally 3 months of anticoagulation is recommended before surgery
    - If elective surgery cannot be postponed preoperative heparin given while INR < 2
    - Heparin not to be restarted for 12 hours after major surgery
    - Check APTT 12 hrs after restarting therapy
- Patients on anticoagulant therapy:
  – Stop warfarin:
    - INR to be checked during preoperative visit
    - Withhold warfarin for 5 days
    - This allows PT/INR to normalize, if INR was chronically maintained between 2–3
    - Withhold more doses if INR is prolonged
  – Bridging therapy:
    - During the time without warfarin, patients are at increased risk for VTE

- Heparin can be used to bridge anticoagulation therapy in perioperative period
- Use of bridging therapy with heparin, however, is controversial
- LMWH can be used as it can be self administered without need for monitoring
- For patients receiving anticoagulation for 1–3 months after an acute episode of VTE, preoperative IV heparin is not justified
- For those receiving anticoagulation for > 3 months after acute episode of VTE, preoperative heparin is not indicated at all
- However postoperative heparin should be administered until warfarin is resumed and INR is > 2.

Intraoperative Thromboprophylaxis

Risk Stratification[3]

Category	Treatment
low Risk No risk factors Uncomplicated surgery Short duration surgery	Comfortable position Knees flexed at 5° Avoid constriction and external pressure Early mobilization Prefer RA Good postoperative analgesia Good physiotherapy
Moderate Risk Age > 40 years with no other risk factors Procedure lasting > 30 minutes OCP use	Proper positioning *Intermittent pneumatic compression devices* of calf and ankle (applied prior to sedation) and continued till patient is awake and moving Compression stockings Frequent alteration of OT table Early mobilization Aspirin therapy
High Risk Age > 40 years with other risk factor Procedure lasting > 30 minutes under GA OCP use	Treated as per patients with moderate risk Preoperative hematology consultation Consider periop antithrombotic therapy

Thromboprophylactic Regimens

ACCP 2004 guidelines:

- Hip and knee arthroplasty, hip surgeries:
  - LMWH:
    - Enoxaparin 30 mg S/C or IV BD or 40 mg OD
    - Started 12 hours before surgery or 12–24 hours after surgery or 4–6 hours after surgery at half usual dose and then increasing to usual dose the next day
  - *Fondaparinux:* 2.5 mg 6–8 hours before surgery (selective Factor X_a inhibitor)
  - Warfarin started preoperatively or the evening after surgery (INR between 2–3)
  - Intermittent pneumatic compression along with aspirin
  - Sole use of aspirin for prophylaxis not recommended
  - Early mobilization in those at high risk of bleeding.
- Spinal cord injury:
  - LMWH once primary hemostasis achieved
  - Intermittent pneumatic compression devices if anticoagulation is contraindicated
  - During rehabilitation phase, conversion to warfarin therapy via 'bridging'
  - INR maintained between 2 and 3
  - Clotting factor activity maintained at 20–40%.
- *Elective spine surgery:* Routine use of thromboprophylaxis apart from early mobilization not recommended in patients without other risk factors
- *Knee arthroscopy*: Routine use of thromboprophyaxis apart from early mobilization not recommended
- Duration of LMWH therapy:
  - At least 10 days for routine procedures
  - 28–35 days extended prophylaxis in high risk patients.
- *Role of neuraxial anesthesia*: Neuraxial anesthesia reduces incidence of VTE through the following mechanisms:
  - Blood flow changes:
    - Causes rheological changes
    - Results in hyperkinetic lower limb blood flow due to vasodilation
    - This reduces venous stasis.
  - Systemic effects of local anesthetics:
    - Anti-inflammatory property of LA
    - Circulatory effects of adrenaline used as adjuvant.
  - Altered coagulation responses:
    - Prevents increases in Factor VIII and vWF levels
    - Attenuated postop reduction in antithrombin III levels
    - Reduced platelet reactivity.
  - Avoids positive pressure ventilation and its effects on circulation
- Although neuraxial anesthesia reduces risk of VTE, risk of VTE remains significant and warrants pharmacological thromboprophylaxis.

- Continuous psoas compartment/femoral nerve catheters may be alternatives to neuraxial block in these in anticoagulants.

Thromboprophylaxis in ICU

- High index of suspicion if:
  - Unexplained tachycardia, tachypnea, fever
  - Asymmetric limb edema
  - Increased dead space ventilation.
- Anticoagulation:
  - LMWH used in high risk patients
  - UFH (low dose) used in moderate-low risk patients
  - Only TID regimens are effective for UFH
  - Fondaparinux use has not been studied in ICU.
- IVC filters:
  - No evidence supporting preventive placement of filters
  - Can be placed in patients for whom LMWH is contraindicated
  - Removable filters available.
- Other measures:
  - Flush catheter tips with heparin:
    - Heparin concentration should be 1 IU/ml
    - 3–4 ml of heparin added to 500 ml saline
  - Serial compression devices:
    - No evidence of benefit
    - Useful in patients in whom LMWH therapy is contraindicated.

CHAPTER

8

Anesthesia for Endocrine Disorders

ACROMEGALY[1,2,3,6,11]

Introduction

Clinical syndrome which occurs due to overproduction of growth hormone (GH) from anterior pituitary, causing overgrowth of bone, connective tissue and viscera.

Etiology

- Pituitary adenomas (90%)
- Extrapituitary tumors:
  - Hypothalamic hamartoma, choristoma, ganglioneuroma
  - Medullary carcinoma of thyroid
  - Bronchial carcinoid
  - Small cell lung cancer
  - Pancreatic islet cell tumor
  - Adrenal adenoma
  - Pheochromocytoma
- Iatrogenic: Use of recombinant GH to prevent ageing.

Clinical Features

- Neuromuscular:
  - Visual field defects
  - Proximal myopathy
  - Nerve entrapment syndrome (carpal tunnel syndrome, ulnar artery compromise)
  - Kyphoscoliosis.
- Cardiovascular: Major cause of mortality and morbidity:
  - Hypertension
  - Cardiomegaly, LV hypertrophy, diastolic dysfunction
  - CAD, congestive cardiac failure
  - Arrhythmias: SVT/PVCs on stress/exercise
  - Valvular abnormalities
  - Cardiomyopathy.
- Respiratory system:
  - Somnolence, central and obstructive sleep apnea (60% patients)
  - Deep and hollow voice
  - Hoarseness of voice due to:
    - Vocal cord thickening
    - Recurrent laryngeal nerve palsy due to stretching.
  - Dyspnea/stridor due to subglottic narrowing
  - Increased lung volumes
  - Ventilation-perfection mismatch.
- Endocrines:
  - Impaired glucose tolerance
  - Diabetes mellitus (25% patients)
  - Hypo/hyperthyroidism
  - Hypopituitarism (due to tumor-compressing pituitary gland)
  - Hypercalcemia, hypercalciuria
  - Diabetes insipidus.
- Gastrointestinal:
  - Colonic polyps
  - Colon carcinoma.
- Skin:
  - Acanthosis nigricans
  - Hyperhydrosis, oily skin
  - Skin tags.
- Soft tissue:
  - Increased heel pad thickness
  - Coarse facial features
  - Large, fleshy, nose

  - Carpal tunnel syndrome
  - Increased pharyngeal and laryngeal soft tissues, macroglossia, enlarged epiglottis.
- Musculoskeletal:
  - Frontal bossing
  - Increased space between lower incisors
  - Macrognathia, prognathism
  - Increased size of feet and hands
  - Arthropathy.
- Due to parasellar extension:
  - Headache
  - Visual field defects
  - Rhinorrhea.

Pathogenesis

- Hyerptension occurs due to:
  - Prolonged OSAS
  - Antinatriuretic effect of GH: Stimulates renin-angiotensin, and increases blood volume
  - Positive inotropic effect of IGF–I.
- LVH occurs due to interstitial fibrosis.

Investigations

- Complete blood count urea, serum creatinine, thyroid profile, blood sugar
- Electrolytes and serum calcium, baseline ABG
- Preoperative direct laryngoscopy for:
  - Subglottic stenosis
  - Enlarged tongue and mandible
  - Enlarged epiglottis and vocal cords: Reduced laryngeal aperture.
- Indirect laryngoscopy for vocal cord involvement
- Chest X-ray
- ECG: SVT/PVC, bundle branch block, ST-T wave changes, LVH
- Echocardiography:
  - Left ventricular hypertrophy
  - Ejection fraction
  - Regional wall motion abnormalities
  - Diastolic dysfunction.
- Lateral X-ray/CT scan of neck
  - For pharyngeal tissue overgrowth
  - Glottic involvement.
- CT/MRI for suprasellar enlargement and enlarged sella turcica
- Diagnostic:
  - Increased IGF1 levels
  - Random GH level > 5 ng/ml
  - Glucose tolerance test:
    - 75 gms anhydrous glucose given orally
    - Failure of GH level to fall below 1 µg/l within 1–2 hours of glucose challenge is *confirmatory.*

Treatment

- Medical management:
  - Uses:
    - Preoperative shrinkage of large adenomas
    - Relief of symptoms
    - Reduction of GH levels.
  - Indications:
    - Elderly patients with increased morbidity
    - Patients who decline surgery
    - Failure of surgery to achieve biochemical control.
  - Drugs used are:
    - Bromocriptine:
      - Reduces GH levels by decreasing secretion
      - More than 20 mg/day given in 3–4 divided doses
      - Not favorable for long-term use
    - Octreotide:
      - Somatostatin analog
      - 50 mg subcutaneous TID increased up to 1500 µg/day
      - Depot preparation 30 mg IM once a month can be used
      - Provides good palliation in 50% patients.
    - ***Pegvisomant:***
      - Growth hormone analog
      - Binds to GH receptor and prevents GH action
      - Withdraw GH if being used.
  - Symptomatic therapy for carpal tunnel syndrome and other manifestations.
- Radiotherapy:
  - Sterotactic ablation of adenoma by gamma knife radiotherapy useful
  - Can be given if complete removal of tumor by surgery is not possible
  - Disadvantages:
    - High rate of late hypopituitarism
    - Slow rate of biochemical response (5–15 yrs)
    - Ineffective in normalizing IGF levels
    - External pituitary radiation used commonly

- Surgery:
  - Transphenoidal and resection is *treatment of choice*
  - Transfrontal hypophysectomy used if suprasellar extension
  - Advantages:
    - Soft tissue swelling improves immediately
    - GH levels normalize within 1 hour
    - IGF-I levels normalize within 3–4 days
    - LV size usually returns to normal
    - Failure for LV to do so may indicate persistent interstitial fibrosis.

Preoperative Assessment

- History:
  - Chest pain, dyspnea on exertion
  - Numbness, polydipsia, headache/visual disturbances: For spinal anesthesia
  - Hoarseness of voice: Vocal cord palsy thickening/RLN palsy
  - Stridor: Subglottic narrowing.
- Drug history:
  - Octreotide may cause nausea, vomiting and diarrhea
  - Bromocriptine causes severe postural hypotension on induction.
- Examination:
  - Blood pressure, murmurs, edema
  - CNS findings, other systems.
- Airway assessment:
  - Difficult airway common due to:
    - Large jaw, tongue, lips and head
    - Generalized soft tissue swelling of pharynx and larynx
    - Vocal cord thickening, chondrocalcinosis of larynx: Small glottis aperture
    - Subglottic narrowing
    - Enlarged thyroid gland may compress trachea.
  - 30% incidence of difficult airway
  - Difficult airway may be clinically unpredictable.

Preoperative Preparation and Premedication

- Informed consent, discuss possibility of awake fiberoptic intubation
- Discuss need to breathe through mouth post-extubation, if trans-sphenoidal hypophysectomy
- NPO guidelines:
  - 6 hours: Solids
  - 2 hours: Clear fluids and water
- Avoid respiratory depressants
- Glycopyrrolate 20 µg/kg IV especially if awake, fiberoptic intubation is planned
- Somatostatin analogs sometimes used
- Glucose with insulin infusion started if glucose intolerance present
- Continue all medications on the morning of surgery, except insulin.

Role of Regional Anesthesia

- Is the preferred technique where applicable
- May be technically difficult and unreliable due to skeletal changes.

OT Preparation

- Skilled assistant
- Difficult airway Cart:
  - Selection of long armored ET tubes
  - Fiberoptic laryngoscope, tracheostomy tube
  - Large-sized face mask, long-bladed laryngoscope
  - Oral airways.
- Anesthetic drugs thiopentone, fentanyl, vecuronium, succinylcholine
- Suction apparatus
- Monitors
- Emergency drugs:
  - Atropine, adrenaline
  - Phenylephrine, NTG, SNP
  - Dopamine, dobutamine.

Monitors

- Pulse oximeter: Probe may be too small for patients' fingers
- $ETCO_2$, temperature
- ECG, urine output
- Invasive blood pressure monitoring:
  - For prolonged surgery or for repeated ABGs
  - Do Allen's test before inserting radial line, as collateral circulation at wrist may be inadequate
  - Arterial line preferred at brachial/femoral sites.
- CVP/PAC if cardiovascular disease is significant
- Blood glucose at frequent intervals
- Peripheral nerve stimulator:
  - Has altered sensitivity to neuromuscular blockers
  - This is due to hypercalcemia/neuromuscular abnormalities.

Induction

- Adequate preoxygenation for 3–5 minutes
- IV thiopentone (3–4 mg/kg) + fentanyl 1–2 µg/kg + vecuronium 0.1 mg/kg
- Check adequacy of ventilation before administering paralyzing agent
- Anticipate difficult mask ventilation: Use large masks with gauze packing if difficult mask ventilation
- Avoid hypertensive response at intubation: Lidocaine 1.5 mg/kg IV 90 seconds before intubation
- Oral intubation preferred as nasal mucosa may be thickened
- Awake fiberoptic intubation is *technique of choice*
- Use smaller diameter ET tube as vocal cords may be thickened with subglottic stenosis
- Lidocaine 1.5 mg/kg and alfentanyl 10 µg/kg to suppress intubation response
- Elective tracheostomy done if:
  - Awake fiberoptic not possible
  - Those patients with vocal cord involvement
  - History of sleep apnea.

Maintenance

- Avoid nitrous oxide if air pneumoencephalography planned
- O_2 + air + isoflurane 1 MAC used to maintain balanced anesthesia
- Fentanyl and vecuronium given as intermittent boluses
- Hypotensive anesthesia techniques preferred.

Positioning

- Size of patient makes positioning difficult
- Long tables may be required owing to tall stature of patient
- Protect against nerve injuries:
  - Ulnar nerve at elbow
  - Common peroneal nerve below knee
  - Median nerve at wrist.

Hemodynamics

- Judicious fluid therapy in those with poor LV function
- Treat hypertension with antihypertensives
- Hypotensive anesthesia preferred in those undergoing trans-sphenoidal hypophysectomy
- Monitor blood sugar for hyperglycemia.

Extubation

- Fully awake extubation in propped up position when:
  - Conscious and obeys commands
  - Stable hemodynamics
  - Normal temperature
  - TOF ratio 0.7.
- Neostigmine 0.05 mg/kg with glycopyrrolate 0.02 µg/kg to reverse the patient
- Elective postoperative ventilation considered in those with severe airway obstruction.

Postoperative Care

Management

- Propped up position
- Supplemental oxygen therapy
- Encourage oral breathing in case of trans-sphenoidal hypophysectomy
- ACTH and TSH replacement posthypophysectomy.

Monitors

- Pulse oximetry
- $ETCO_2$, NIBP
- ABG, blood glucose
- Urine output, ECG
- Temperature, adequacy of ventilation.

Analgesia

- Caution with the use of opioid analgesics: Respiratory depression
- Patient-controlled analgesia useful
- NSAIDs preferred
- Use regional analgesia where possible
- Multimodal analgesia preferred.

Complications

- Airway obstruction
- Negative pressure pulmonary edema
- Hypoglycemia as insulin requirements reduce postoperatively
- Temporary/permanent diabetes insipidus: treat with DDAVP (especially after hypophysectomy).

HYPERTHYROIDISM[1,2,3,6,8,11]

Introduction

Clinical syndrome resulting from excessive production of thyroid hormones T_3 and T_4.

Incidence

- Most common cause is Graves' disease (60–80% cases)
- Most common between 20 and 50 years and more frequent in women.

Normal Values

Hormone	Conventional units	SI units
TSH	0.5–4.7 µU/ml	0.5–4.7 mU/l
Total T_4	4.5–10.9 µg/dl	58–140 nmol/l
Free T_4	0.8–2.7 ng/dl	10.3–35 pmol/l
Total T_3	60–181 ng/dl	0.92–2.78 nmol/l
Free T_3	1.4–4.4 pg/ml	0.22–6.78 pmol/l

Etiology

- Primary thyrotoxicosis:
  - Graves' disease 90%
  - Toxic multinodular goiter
  - Toxic adenoma
  - ***De-Quervain's thyroiditis***
  - Postpartum thyroiditis: Can persist for 3–6 months postpartum
  - Carcinoma thyroid
  - ***Struma ovarii***
  - ***McCune-Albright syndrome.***
- Secondary thyrotoxicosis:
  - Pituitary adenoma secreting TSH
  - Trophoblastic tumors:
    - Choriocarcinoma
    - Hydatidiform mole
  - Functioning follicular carcinoma
  - Extrathyroidal: Factitious hyperthyroidism (increased iodine intake).
- Iatrogenic causes:
  - Thyroid replacement therapy
  - Iodine therapy: ***Jod-Basedow phenomenon***
  - Amiodarone
  - Radiation therapy.

Clinical Features

- Central nervous system:
  - Insomnia, impaired concentration, nervousness
  - Fine, resting tremors
  - Periodic paralysis and chorea: Rare
  - Depression and withdrawal: *Apathetic thyrotoxicosis*
  - Intolerance to heat, fatigue, apathy
- Ocular signs:
  - ***Von Graefe's***: Upper lid lags as patient looks down
  - ***Joffroy's***: No wrinkling of forehead
  - ***Stellwag's***: Staring look, infrequent blinking
  - ***Moebius***: Inability to converge eyeballs
  - ***Dalrymple:*** Upper sclera visible due to retraction of upper lid.
- Goiter: Diffuse, nodular
- Cardiovascular system:
  - Hypertension:
    - Increased SBP, reduced DBP
    - Widened pulse pressure.
  - Increased stroke volume and cardiac output
  - Reduced SVR and PVR
  - Increased blood volume
  - Bounding pulse, palpitation
  - High output cardiac failure
  - ***Thyrotoxic cardiomyopathy***
  - Mitral valve prolapse, aortic systolic murmur
  - Arrhythmias:
    - Sinus tachycardia
    - Atrial fibrillation, SVT
    - Complete heart block
    - Ventricular arrhythmias.
- Respiratory system:
  - Hypercarbia and increased oxygen consumption due to increased BMR
  - This causes high minute volume: High tidal volume and increased respiratory rate
  - Vital capacity decreases due to respiratory muscle weakness
  - Dyspnea on exertion
  - Exacerbation of asthma.
- Gastrointestinal:
  - Weight loss despite increased appetite
  - Decreased GI transit time
  - Secretory diarrhea
  - Anorexia, vomiting.
- Genitourinary:
  - Amenorrhea/oligomenorrhea
  - Infertility, loss of libido
  - Gynecomastia, spontaneous abortion.
- Hematological:
  - Anemia
  - Neutropenia
  - Thrombocytopenia.
- Dermatological:
  - *Pretibial myxedema*
  - Increased sweating, warm and moist skin

  - Palmar erythema
  - Onycholysis, diffuse alopecia
  - Pruritus and urticaria
  - Clubbing, *thyroid acropachy.*
- Neuromuscular:
  - Muscle weakness
  - Muscle stiffness and wasting
  - *Proximal myopathy*
  - Hyperactive reflexes, osteopenia.

Investigations

- Complete blood count:
  - Anemia
  - Thrombocytopenia
  - Neutropenia.
- Renal function tests, blood glucose, electrolytes (hypercalcemia)
- Increased serum alkaline phosphatase
- Thyroid function tests:
  - Low TSH levels
  - High T_3, T_4 levels
  - Increased uptake of radioactive iodine 24 hours after its administration
  - Tests done within last 6 months are usually adequate if symptoms or therapy have not been changed significantly.
- ECG: LVH, arrhythmias
- ECHO: LVH, RWMA, EF
- *Indirect laryngoscopy*: For preoperative vocal cord movement (medicolegal importance)
- X-ray (AP and lateral): Neck and thoracic inlet
- CT scan for degree of tracheal compression if retrosternal extension
- Pulmonary function tests
- Flow volume loops.

Treatment

- Medical management: Takes 6–8 weeks to make patient pharmacologically euthyroid
  - Antithyroid drugs for 6–8 weeks:
    - Propylthiouracil:
      - 200–300 mg PO Q8–12H
      - Inhibits peripheral T_4 to T_3 conversion.
    - Methimazole:
      - 10–20 mg Q12H
      - Faster response, once daily dosing.
    - Carbimazole 30–45 mg/day
    - Not effective until 6–8 weeks when thyroid stores are depleted and, hence, new thyroid hormones are not synthesized.
  - Saturated solution of potassium iodide (SSKI):
    - Antithyroid drugs should precede SSKI
    - This is because iodide given alone will act as substrate for new thyroid hormone synthesis and worsen thyrotoxicosis
    - 3 drops orally Q8H for 7–14 days
    - Reduces gland vascularity and hormone release (***Wolff-Chaikoff effect***)
    - Continuing SSKI beyond 14 days does not have any beneficial effects
    - Onset of action within 24 hours
    - Contraindications:
      - Children
      - Pregnancy and breastfeeding
    - Safe to become pregnant 4 months or more after iodide therapy
    - Lugols iodine is an effective alternative.
  - Blocker therapy:
    - Nonselective β-blockers better than selective β-blockers
    - Selective β-blockers are good only for treatment of tachycardia
    - Nonselective blockers also block peripheral conversion of T_4 to T_3 via β-action over 1–2 weeks
    - This reduces tachycardia, anxiety, tremors and heat intolerance
    - β-blockers relieve signs and symptoms but do not reduce thyrotoxicosis
    - Propranolol 40–80 mg Q6–8H.
- Radioiodine therapy:
  - Destroys thyroid cell function
  - Used for initial treatment of relapses after trial of antithyroid drugs
  - Antithyroid drugs to be stopped atleast 3 days before radioactive I^{131} therapy to optimize iodine uptake
  - May cause hypothyroidism
  - Not recommended in pregnancy due to risk of fetal hypothyroidism.
- Surgical management:
  - Subtotal thyroidectomy
  - Now less commonly used as alternative
  - Indicated in:
    - Large toxic multinodular goiter
    - Solitary toxic adenoma
    - Failed medical therapy
    - Underlying carcinoma.

ANESTHETIC MANAGEMENT FOR THYROID SURGERY

Preoperative Evaluation

- Elicit history of goiter, history of drugs and anesthetic exposure
- Systemic examination
- Airway assessment: Anticipate difficult intubation if:
  - History of positional dyspnea/dysphagia
  - Infiltrating carcinoma is independent risk factor
  - History of dyspnea/stridor for trachea compression
  - More than 50% tracheal narrowing on chest X-ray.
- Difficult intubation as:
  - Increased chances of cord palsy in malignancy
  - Distortion and rigidity of structures
  - Intraluminal spread of malignancy
  - Displaced larynx.
- SVC syndrome: Venous engorgement of face and arms
- May cause laryngeal edema: Use smaller ET tube
- Preoperative endocrinologist consultation.

Preoperative Preparation for Elective Surgery

- Takes 6–8 weeks to make patient pharmacologically euthyroid:
  - Antithyroid drugs for 6–8 weeks:
    - Propylthiouracil:
      - 200–300 mg PO Q8–12H
      - Inhibits peripheral T_4 to T_3 conversion.
    - Methimazole:
      - 10–20 mg Q12H
      - Faster response, once daily dosing.
    - Carbimazole 30–45 mg/day
    - Not effective until 6–8 weeks when thyroid stores are depleted and, hence, new thyroid hormones are not synthesized.
  - Saturated solution of potassium iodide (SSKI):
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    - Reduces gland vascularity and hormone release (***Wolff-Chaikoff effect***)
    - Continuing SSKI beyond 14 days does not have any beneficial effect
    - Onset of action within 24 hours
    - Contraindication:
      - Children
      - Pregnancy and breastfeeding.
    - Safe to become pregnant 4 months or more after iodide therapy
    - Lugol's iodine is an effective alternative.
  - β-blocker therapy:
    - Nonselective β-blockers better than selective β blockers
    - Selective β-blockers are good only for treatment of tachycardia
    - Nonselective blockers also block peripheral conversion of T_4 to T_3 via β-action over 1–2 weeks
    - This reduces tachycardia, anxiety, tremors and heat intolerance
    - β-blockers relieve signs and symptoms but do not reduce thyrotoxicosis
    - Propranolol 40–80 mg Q6–8H.
- Current trend is:
  - Preoperative preparation with propranolol and NaI alone
  - Advantages:
    - This is a much quicker approach (1–2 weeks vs 6–8 weeks)
    - It shrinks thyroid gland as well as traditional approach
    - It reduces peripheral conversion of T_4 to T_3
    - Also treats symptoms of LVF (but does not correct LVF).

Preoperative Preparation for Emergency Surgery

- Antithyroid drugs:
  - Propylthiouracil 200–400 mg Q6H PO or via NGT
  - Methimazole 20–40 mg Q6H PO/NGT/rectally.
- Saturated solution of potassium iodide:
  - Given after 1 hour of administering antithyroid drugs
  - 5 drops given PO/via NGT Q6H
  - Lugol's iodine 30 drops PO/via NGT Q6H.
- β-blockers:
  - Propranolol 0.5–1 mg/kg IV bolus
  - Esmolol 500 μg/kg IV bolus followed by infusion
  - β-blockers titrated to restore heart rate < 90 bpm.
- Sodium propanoate:
  - 500 mg Q12H
  - Effects similar to iodide therapy

  - Releases iodine which inhibits synthesis and also blocks peripheral conversion of T_4 to T_3
- Steroids:
  - Dexamethasone 2 mg IV Q6H (8–12 mg/day)
  - Reduces hormone release and peripheral conversion of T_4 to T_3
  - Hydrocortisone 40 mg Q6H is an alternative.

Adequacy of Patient Preparation

- Heart rate less than 90 bpm in normal sinus rhythm
- Normal pulse pressure
- Resolution of new cardiac murmur
- Relief of tremors, anxiety, palpitation, dyspnea and heart intolerance.

Role of Regional Anesthesia

- Preferred technique
- Avoid epinephrine containing local anesthetics
- Bilateral superficial cervical plexus block may be used for limited thyroidectomy.

Premedication

- Elective surgery postponed until euthyroid state has been achieved
- Correct preoperative dehydration if diarrhea is severe
- NPO guidelines:
  - 6 hours solids
  - 2 hours clear fluids.
- Informed consent
- Preoperative sedation:
  - Avoid excess sedation
  - Mild sedation with benzodiazepines (0.1 mg/kg diazepam PO)
  - Avoid opioids as muscle fatigue and hypotonicity increases risk of respiratory depression.
- Avoid atropine and scopolamine as:
  - It causes tachycardia
  - Interferes with heat regulation.
- Use glycopyrrolate 0.02 mg/kg IV, if necessary, as antisialagogue
- Continue antithyroid and β-blockers on day of surgery
- PONV and antibiotic prophylaxis.

Anesthetic Goals

- Achieve depth of anesthesia which inhibits sympathetic response to surgical stimuli
- Avoid administration of any drug which stimulates sympathetic nervous system:
  - Ketamine, pancuronium
  - Atropine, ephedrine
  - Epinephrine
- Adequate eye protection.

Monitors

- Pulse oximetry, $ETCO_2$
- NIBP, IBP if LV dysfunction
- CVP/PAC in unstable patients
- ECG, urine output
- Airway pressure if thyroid surgery
- Temperature especially in emergency surgeries
- Esophageal stethoscope
- Neuromuscular monitoring important as increased incidence of myasthenia gravis in thyrotoxic patients.

Induction

- Adequate preoxygenation for 3–5 mins as oxygen requirement is high
- If there is no anticipated airway obstruction:
  - Thiopentone 3–4 mg/kg + vecuronium 0.1 mg/kg + fentanyl 1–2 µg/kg
  - Thiopentone is *agent of choice* as thiourylene nucleus inhibits peripheral T_4 to T_3 conversion
  - Unanticipated airway obstruction may occur after muscle relaxant is administered.
- If airway obstruction is anticipated:
  - Awake fiberoptic intubation/inhalational induction preferred
  - Ask attendant to lift gland upwards and laterally
  - Tip of ETT to be advanced beyond any area of tracheal compression
  - Use armored flexometallic tube to avoid kinking under drapes
  - Tube firmly taped in position and all connection secured as access during surgery is limited
  - Inhalational induction may be delayed if stridor/reduced minute volume preoperatively.
- Ensure adequate anesthetic depth for intubation, rapid lightening of consciousness at intubation may occur
- Also prone for hypotensive response which is exaggerated during induction of anesthesia as they are chronically hypovolemic and vasodilated
- Reduced dosage of initial neuromuscular blocking agent
- Topical local anesthesia of larynx is useful to reduce sympathetic response.

Maintenance

- $N_2O + O_2$ + isoflurane 1 MAC
- Avoid halothane as:
  - Increased chances of hepatic necrosis
  - Adrenaline may be used with LA solution at the time of skin infiltration
- Fentanyl 1 µg/kg and reduced doses of vecuronium given as intermittent boluses
- Reduced fentanyl doses to ensure patient can maintain patent airway postextubation
- Carefully titrate muscle relaxation as thyrotoxicosis patients have increased incidence of myasthenia gravis
- Muscle relaxants cannot be used after intubation if repeat surgery is being performed as surgeon may use nerve stimulator to identify recurrent laryngeal nerve.

Position

- Neck extended fully with head up tilt up to 15–20 to reduce venous bleeding
- Venous air embolism is a complication in this position
- Neck extension may change the ET tube position
- Thus, recheck tube position after final positioning of patient
- Patient prone to corneal abrasion owing to:
  - Exophthalmos
  - Eyelid retraction.

Hemodynamics

- Profound hypotension may occur at the time of induction
- Treat any hypotension with fluids and vasopressors
- Phenylephrine or norepinephrine used commonly
- Avoid sympathomimetics like ephedrine as it may cause exaggerated response
- Carotid sinus manipulation may cause bradycardia and hypotension:
  - Administer atropine
  - Stop stimulating the carotid sinus
  - Administration of lidocaine in that area may prevent recurrence.

Ventilation

- ET intubation with CMV preferred
- Avoid hyperventilation as the resultant alkalosis and hypokalemia may aggravate muscle weakness
- Excess airway pressure may occur during manipulation of trachea
- Head-down tilt and Valsalva maneuver before wound closure helps in identifying bleeding points
- LMA is nowadays being used without the use of neuromuscular blocking agents
- Since patient is spontaneously breathing, it allows real-time recurrent laryngeal nerve function monitoring.

Extubation

- Full reversal with neostigmine 0.05 mg/kg and glycopyrrolate 0.02 mg/kg IV
- Deep planes at extubation is preferred as:
  - It avoids risk of coughing
  - Wound hematoma is avoided which may cause airway obstruction postoperatively.
- Direct laryngoscopy and visualization of vocal cord movement postextubation may be done to check RLN function
- In cases of suspected tracheomalacia:
  - Fiberoptic bronchoscope used to assess for airway collapse as ET tube and bronchoscope are pulled back
  - If tracheal collapse is noted, ET tube and FOB are immediately advanced
  - ET tube is left in place if questionable ability to protect airway
  - Mechanical ventilation is continued postoperatively.

Postoperative Care

Management

- Continue postoperative antithyroid regimen until T_4 levels reduce
- Calcium supplementation if low Ca^{2+} levels due to accidental excision of parathyroid gland
- Check calcium levels at 6 and 24 hours postsurgery
- Nasal fiberoptic laryngoscopy postextubation for documentation of RLN injury
- If hematoma formation occurs:
  - Intubate early before airway edema occurs (due to reduced venous return from cords)
  - 45 head up tilt to increase venous return
  - Remove alternate sutures and inform surgeon
  - Steroids and racemic epinephrine to reduce laryngeal edema.

Complications

- Immediate complications:
  - Airway obstruction due to:
    - Hemorrhage

- RLN injury
- Tracheal collapse
- Tracheomalacia especially if long-standing goiter.

– Thyroid storm.

- Delayed complications:
  – Thyroid storm
  – Recurrent laryngeal nerve injury
  – Hematoma from coughing
  – Bullous glottic edema
  – Tracheoesophageal fistula
  – Pneumothorax if dissection of sternum and mediastinum occurs
  – Phrenic nerve injury
  – Pneumomediastinum
  – Hypocalcemia and parathyroid gland damage: presents within 12–72 hours
  – Superior laryngeal nerve injury: causes increased risk of aspiration.

Pain

- NSAIDs
- Opioids—low dose
- PCA
- Multimodal analgesia
- Superficial cervical plexus block/S/C/LA.

THYROID STORM[1,10,11,12]

Introduction

Life-threatening hypermetabolic state in a patient whose hyperthyroidism has been severely exacerbated by illness/surgery.

Incidence

- Rare but associated with 20–30% mortality
- May occur up to 18 hours after surgery.

Precipitating Factors

- Thyroid-related:
  – Vigorous thyroid manipulation
  – Palpation of thyroid gland, ingestion of thyroid hormone
  – Thyroid surgery
  – Radioactive iodine therapy, iodine therapy
  – Iodinated contrast dyes
  – Withdrawal of antithyroid drug therapy
- Nonthyroid illnesses:
  – Infections
  – Cerebrovascular accidents
  – Congestive cardiac failure, myocardial infarction
  – Bowel infarction, pulmonary embolism
  – Nonthyroid surgery
  – Diabetic ketoacidosis, trauma.
- Most commonly precipitated by operating on an acutely hyperthyroid gland.

Clinical Features

- Can occur intraoperatively, like malignant hyperthermia, or up to 6–24 hours postoperatively
- Presents with:
  – Nausea, vomiting, diarrhea, jaundice
  – Altered consciousness: Agitation, delirium, coma, confusion, seizures
- Sinus tachycardia (> 140 bpm), fever (40 °C), sweating
- Myocardial infarction, cardiac failure and dysrhythmias common
- No muscle rigidity/increase in CPK/metabolic or repiratory acidosis as in malignant hyperthermia.

Differential Diagnosis

- Malignant hyperthermia
- Neuroleptic malignant syndrome
- Pheochromocytoma
- Hypoxic encephalopathy/hypothalamic stroke
- Light anesthesia, sepsis
- Drug overdose: Cosine, amphetamine
- Delirium tremens
- Heat stroke.

Investigations

- Lab analysis usually not useful
- TFTs are not routinely available to emergency physician
- Leukocytosis, hyperglycemia, increased transaminases and bilirubin seen
- ECG, chest X-ray, urinalysis and blood culture used to identify cause.

Treatment

- Treat precipitating cause:
  – Antibiotics for infection
  – Digoxin for CCF, especially if AF with fast ventricular rate
  – Treat diabetic ketoacidosis.
- Nonspecific treatment:
  – Antithyroid drugs:
    - Initiated as first line of therapy

- Propylthiouracil:
  - 1 gm loading dose
  - Followed by 250–500 mg Q6H PO/via NGT
  - Acts within 1 hour.
- Methimazole 40 mg PO followed by 25 mg Q6H PO.

– Iodine therapy:
- Sodium iodide 1 gm IV over 12 hours
- KI 5 drops TID PO/via NGT
- Lugol's iodine 5–10 drops TID PO/NGT
- Start 1 hour after administration of PTU
- Iapanoic acid 1 gm IV Q8H for 24 hours then 500 mg IV BD
- $LiCO_3$ 800–1200 mg PO/day.

– β-blocker therapy:
- IV propranolol:
  - 0.5 mg/kg IV Q 5 min till heart rate is below 90/min
  - Followed by 2 mg IV Q4H.
- IV esmolol:
  - 0.5 mg/kg IV bolus
  - Followed by 50–100 µg/kg/min infusion
- Alternatives:
  - Combined + β-blocker
  - 2 antagonists
  - Reserpine 2.5–5 mg IM Q6H
  - Guanethidine 30–40 mg Q6H PO.

- Steroids:
  – Hydrocortisone 100–200 mg IV Q8H
  – Dexamethasone 2 mg IV Q6H.
- Supportive therapy:
  – Oxygen therapy, Foley's catheter
  – Ventilation if required, NGT inserted as most medications are PO
  – IV saline and glucose to correct electrolytes and blood sugar levels
  – Inotropes, diuretics if CCF present
  – Monitor temperature, IBP and CVP.
- Surface cooling:
  – Cold lavage of body cavity
  – Ice packs, cooling blankets
  – Reduced ambient temperature, tepid sponging
  – Paracetamol preferred: 650 mg PO Q4H
  – Avoid aspirin/NSAIDs as they displace thyroid hormones from serum proteins
  – Pethidine 25–50 mg IV Q4–6H to reduce shivering
  – Hemodialysis and plasmapheresis used if refractory

HYPOTHYROIDISM[1,2,3,6,8,11]

Introduction

Clinical syndrome resulting from deficiency of thyroid hormones T_3 and T_4.

Incidence

- Relatively common
- Incidence 0.5–0.8% of adult population
- More common in females
- Incidence is 4 : 1000 in females and 1 : 1000 in males.

Etiology

- Primary hypothyroidism (95% cases) with increased TSH levels:
  – Iodine deficiency
  – Hashimoto's disease, autoimmune
  – Radiation therapy
  – I^{131} therapy
  – Surgical removal
  – Drugs:
    - Iodine
    - Propylthiouracil, methimazole
    - Lithium, amiodarone.
  – Hereditary defects in biosynthesis
  – Congenital defects in gland development.
- Secondary hypothyroidism with reduced TSH levels:
  – Hypothalamic disease
  – Pituitary disease.

Clinical Features

- Clinical features of hypothyroidism present when TSH > 10 mU/l
- Slow onset, insidious and progressive course
- Central nervous system:
  – Reduced BMR: Lethargy, cold intolerance
  – Slow, dull speech, hoarse voice
  – Slow mental function, slow movements
  – Fatigue, lethargy, listlessness
  – Stiffness, cramps, pain, pseudomyotonia
  – Cerebellar ataxia
  – Depression, apathy, psychosis
  – ***Hashimoto encephalopathy***
  – Slow relaxation of deep tendon reflexes: *Hung up reflexes*
  – Arthralgias.
- Cardiovascular system:
  – Bradycardia
  – Low stroke volume and cardiac output: Hypotension

  - Increased PVR: Hypertension
  - Reduced blood volume: Pale skin
  - Pericardial effusion which is rich in triglycerides and cholesterol
  - Reduced myocardial contractility
  - ***Hypothyroid cardiomyopathy***
  - Cardiac failure (rare in the absence of coexisting cardiac disease)
  - Angina: Rare but may occur at the time of T_4 replacement
  - Predisposed to MI.
  - ECG:
    - Low voltage complexes (due to pericardial effusion)
    - T wave flattening/inversion
    - Ventricular arrhythmias (due to amyloid in conduction system)
    - Predisposed to MI.
  - ***Amyloid cardiomyopathy***
- Respiratory system:
  - Reduced ventilatory response to hypoxia and hypercarbia
  - Pleural effusion
  - Large tongue, sleep apnea
  - Hoarseness of voice, acute respiratory obstruction
  - Maximum breathing capacity, minute volume and CO transfer factor reduced.
- Gastrointestinal:
  - Weight gain with loss of appetite
  - Ileus, constipation
  - Increased gastric emptying time
  - Ascites and peritoneal effusion.
- Genitourinary system:
  - Glomerulonephritis
  - Nephrotic syndrome
  - Amyloid nephropathy
  - Menorrhagia.
- Skin:
  - Myxedema
  - Cool, mottled skin due to peripheral vasoconstriction
  - Dry hair, alopecia, vitiligo
  - Dry, pale and thick skin with reduced sweating
  - ***Carpal tunnel syndrome***
  - *Myxedema:* Non-pitting edema due to mucopolysaccharide (MPS) deposition
  - Periorbital edema
- Hematology:
  - Anemia: Normochromic, normo/macrocytic
  - Associated with pernicious anemia
  - Platelet dysfunction
  - Coagulation factor (VIII) dysfunction
  - Hypercholesterolemia
  - Hypertriglyceridemia.

Investigation

- General investigations:
  - Complete blood count, renal function tests, blood sugar levels (hypoglycemia)
  - Electrolytes: Hyponatremia common
  - Hb, peripheral smear: Anemia
  - Coagulation profile: BT, CT, PT, INR for coagulopathy
  - Increased cholesterol, triglycerides, CPK and LDH
  - ECG:
    - Low voltage QRS complexes
    - Sinus bradycardia
    - Flattened/inverted T waves.
  - Chest X-ray:
    - Cardiomegaly due to pericardial effusion
    - Pleural/pericardial effusion
    - Thoracic inlet X-ray to diagnose tracheal involvement.
  - Indirect laryngoscopy for preoperative vocal cord dysfunction
  - Screen for other autoimmune disorders.
- Thyroid-specific investigations:
  - Thyroid function tests:
    - Reduced FT_4 and FT_3 with raised TSH if primary hypothyroidism
    - Reduced FT_4, FT_3 and TSH if secondary hypothyroidism
    - *Single best predictor* at cellular level is TSH level.
  - Thyroid scan with I^{131}/Tc-99m: cold, hypofunctioning nodule
  - Thyroid USG: Cystic/solid/mixed lesions
  - CT/MRI if tracheal compression
  - TPO antibodies screen.

Classification of Severity

- Subclinical hypothyroidism:
  - Normal T_3 and T_4 levels
  - Raised TSH levels (5–10 mU/l)
  - No clinical features.

- Mild hypothyroidism:
  - Reduced or normal T_3 and T_4
  - Mean TSH of 18 mU/l
  - Some clinical features.
- Severe hypothyroidism:
  - Reduced T_3 and T_4
  - Mean TSH of 90 mU/l
  - Full clinical profile.

Anesthetic Considerations

- Anemia and coagulation abnormalities: Increased blood loss
- Increased sensitivity to sedatives NMBA
- Increased gastric emptying time: Increased chances of aspiration
- Profound hypotension on anesthetic induction
- Prone to hypothermia as BMR is low
- Muscular weakness: Controlled ventilation preferred
- Hypoglycemia and hyponatremia
- Anticipate difficult intubation as:
  - Large tongue
  - Edematous vocal cords
  - Edematous oral cavity
  - Goiter: Tracheal compression, tracheomalacia.

Preoperative Optimization

- Choice of patients:
  - Mild-moderate hypothyroidism: No need to postpone elective surgery
  - Severe hypothyroidism: Postpone surgery when possible till these patients are atleast partially treated
  - Also for pregnant patients and myxedema coma.
- Hypothyroidism with coronary artery disease:
  - Need for thyroid replacement therapy to be weighed against risk of precipitating MI
  - In asymptomatic patients/unstable patients with cardiac ischemia:
    - Delay in T_4 replacement considered
    - Urgent myocardial revascularization—planned
    - Plan to start thyroid replacement therapy in ICU.
- Optimization in elective surgery:
  - Delay surgery if $T_4 < 1$ µg/dl or severe hypothyroidism until patient is euthyroid
  - Start T_4 with 50 µg/day (1.6 µg/kg)
  - Gradually increase to 100 µg/day over weeks through 12.5–25 µg increments
  - In elderly with CAD, start 25 µg/day and increase monthly by 25 µg/day
  - Alternate preparations:
    - Animal thyroid extract
    - L-triiodothyronine
    - Liotrix: Combination of T_4 and T_3 (4:1)
  - Patient may not experience full relief in symptoms until 3–6 months after normal TSH levels are reached.
- Optimization in emergency surgery:
  - IV L-thyroxine 300–500 µg over 1–5 minutes or
  - IV L-triiodothyronine 25–50 µg IV followed by T_3 25 µg IV Q8H
  - Steroid coverage with dexamethasone/cortisol
  - Milrinone:
    - Used in the presence of CCF
    - Phosphodiesterase III inhibitor
    - *Most effective* inotrope in hypothyroidism
    - Does not depend on β-receptors which are low in number and sensitivity in hypothyroidism.

Premedication

- NPO status:
  - 6 hours solids
  - 2 hours clear fluids
- Informed consent
- No preoperative sedation as drug-induced respiratory depression is common
- Adequate IV fluid loading preoperatively as they tolerate hypovolemia poorly
- Antiaspiration prophylaxis:
  - IV ranitidine 1 mg/kg
  - IV metoclopramide 10 mg.
- Continue thyroid hormones on the day of surgery
- Omission of thyroid dose may be tolerated as T_4 has long T ½ of 8 days
- Hydrocortisone 100 mg IV as associated adrenocortical insufficiency present
- Antibiotic prophylaxis as per hospital protocol.

Regional Anesthesia

- RA preferred where possible, if no contraindication
- Adequate intravascular volume to be established to prevent precipitous hypotension
- Difficult landmarks if associated obesity
- Caution exercised if coexistent coagulopathy.

Induction

- Give all anesthetic drugs slowly
- Ketamine is induction *agent of choice* as other drugs associated with hypotension
- Reduced doses of NMBA used as muscle weakness already present
- Rapid sequence induction with ketamine and succinylcholine if full stomach picture
- If airway obstruction is anticipated:
  - Awake fiberoptic intubation
  - Ask attendant to lift gland upwards and laterally
  - Tip of ETT to be advanced beyond any area of tracheal compression
  - Use armored flexometallic tube to avoid kinking under drapes
  - Tube firmly taped in position and all connections secured as access during surgery is limited.

Maintenance

- O_2 + N_2O + isoflurane for balanced anesthesia
- No significant reduction in MAC
- Avoid halothane as it has myocardial depressant action
- Fentanyl 1 µg/kg and small doses of vecuronium given intermittantly
- Ketamine also can be used for maintenance, as an infusion.

Monitors

- Pulse oximetry, $ETCO_2$
- BP: NIBP/IBP based on cardiovascular status
- ECG: MI/arrhythmias
- Urine output, temperature
- Precordial stethoscope if thyroid surgery
- Neuromuscular monitoring: Interference with excitability in hypothyroid patients
- ABG and blood sugar regularly: Hypoglycemia, hyponatremia
- Airway pressure if thyroid surgery.

Ventilation

- ET tube with CMV preferred due to:
  - Preexisting muscular weakness
  - Reduced response to hypoxia and hypercarbia.
- Hypocapnea may be present due to reduce BMR
- Excess airway pressure during manipulation of thyroid gland common.

Hemodynamics

- IV fluids containing dextrose used to prevent hypoglycemia
- Intraoperative hypotension common due to:
  - Reduced cardiac output
  - Blunted baroreceptor reflexes
  - Reduced intravascular volume.
- Hypotension is:
  - Less responsive to catecholamines
  - Ephedrine/dopamine/epinephrine used if severe hypotension
  - *Best inotrope* is milrinone
  - Supplemental steroids given if refractory hypotension.
- Actively warm patient to avoid hypothermia (more common as low BMR present).

Extubation

- Fully awake extubation in semirecumbent position
- Neostigmine 0.05 mg/kg + glycopyrrolate 0.02 mg/kg IV for reversal
- May require prolonged mechanical ventilation as incidence of myasthenia grows in hypothyroidism
- Deep planes at extubation preferred if thyroid surgery has been done, as:
  - It avoids risk of coughing
  - Wound hematoma is avoided which may cause airway obstruction postoperatively.
- Direct laryngoscopy and visualization of vocal cord movement postextubation may be done to check RLN function
- In cases of suspected tracheomalacia:
  - Fiberoptic bronchoscope used to assess for airway collapse as ET tube and bronchoscope are pulled back
  - If tracheal collapse is noted, ET tube and FOB are immediately advanced
  - ET tube is left in place if questionable ability to protect airway
  - Mechanical ventilation is continued postoperatively.

Postoperative Care

Management

- Nurse in propped-up position
- Continue thyroid medications postoperatively
- IV hydrocortisone 100 mg Q6H given
- Calcium supplementation if low Ca^{2+} levels due to accidental excision of parathyroid gland
- Check calcium levels at 6 and 24 hours postsurgery
- Nasal fiberoptic laryngoscopy postextubation for documentation of RLN injury

- If hematoma formation occurs:
  - Intubate early before airway edema occurs
  - 45 head-up tilt to increase venous return
  - Remove alternate sutures and inform surgeon
  - Steroids and racemic epinephrine to reduce laryngeal edema.

Monitors

- Pulse oximetry, BP, ECG
- Temperature, urine output
- Electrolytes and sugar
- ABG.

Analgesia

- Avoid opioids/use low dose to avoid respiratory depression
- Nonopioids: Ketolac as adjuvant
- Regional anesthesia
- Local anesthetic infiltration
- Multimodal analgesia preferred.

Complications

- Myxedema coma
- Delayed recovery owing to:
  - Hypothermia
  - Muscle weakness
  - Slow drug biotransformation
  - Low BMR.
- Respiratory depression/failure
- Sleep apnea
- Reduced free water clearance with dilutional hyponatremia
- Hypothermia
- Prolonged postoperative ileus, bleeding.

MYXEDEMA COMA[1,2,3,6,10,11,12]

Introduction

- Rare and severe form of hypothyroidism in which patients with preexisting long-standing hypothyroidism present with life-threatening decompensation
- It is a medical emergency.

Predisposing Factors

- Infection, trauma, surgery
- Cold exposure, drugs
- CNS depressants/sedatives
- Lithium, amiodarone
- Cerebrovascular accident
- Congestive cardiac failure
- Inadequate thyroid replacement therapy
- Previously undiagnosed hypothyroidism.

Clinical Features

- Mortality rate of 25–30%
- Hypoventilation
- Hypothermia (80% patients) *is cardinal feature*
- Altered sensorium: Delirium, unconsciousness, coma
- Bradycardia with hypotension and cardiovascular collapse
- Severe dilutional hyponatremia due to SIADH
- Hypoglycemia, acidosis, hypercapnea
- Periorbital nonpitting edema, hung-up DTR
- Drug toxicity from medications common due to reduced drug clearance.

Investigations

- Anemia, hyponatremia, hypoglycemia
- Raised serum transaminases, CPK and LDH, hypercholesterolemia
- ABG: hypoxemia, hypercapnea, acidosis
- ECG:
  - Sinus bradycardia
  - Increased corrected QT interval
  - Low-voltage complexes
  - Flat/inverted T waves
- Chest X-ray: Pericardial effusion
- Blood culture and urinanalysis for detecting cause.

Treatment

- ICU admission
- Monitor:
  - ECG, SpO_2, $ETCO_2$
  - BP, drug levels
  - Urine output, electrolytes and sugar
  - Temperature, ABG
- Treat precipitating cause:
  - Empirical antibiotic therapy
  - Only life-saving surgery to be done
- Supportive therapy:
  - ET intubation with CMV may be required for first 48 hours
  - Avoid sedatives/use lower dose
  - Cardiovascular support:
    - Milrinone is *best inotrope*
    - Dopamine/norepinephrine can be tried

- Thyroid replacement therapy:
  - L-thyroxine:
    - 200–300 µg IV loading dose over 5–10 minutes
    - Followed by 50–200 µg/day IV.
  - L-triiodothyronine:
    - 25–50 µg IV loading dose
    - Followed by 25 µg Q8H IV.
  - Combined replacement:
    - 200 µg T_4 + 25 µg T_3 as bolus
    - Followed by 50–100 µg/day T_4 and 10 µg Q8H T_3.
- Steroid replacement therapy:
  - IV hydrocortisone 100 mg QID
  - Continued until normal adrenal function can be confirmed.
- Hypothermia:
  - Prevent additional heat loss
  - Cautious passive external rewarming done
  - Sudden rewarming may cause peripheral vasodilation and cardiovascular collapse
  - External warming done only if temperature < 30 ºC
- Electrolytes and sugar:
  - IV fluid restriction to correct hyponatremia
  - 3% saline used if severe hyponatremia
  - IV glucose containing fluids used for maintenance
  - Avoid hypotonic IV fluids as they cause water retention.

CUSHING'S SYNDROME[1,2,3,6,8,10,11]

Introduction

- It refers to the clinical state of increased free-circulating glucocorticoids
- Cushing's disease refers to only those patients with ACTH secreting pituitary tumors
- Cushing's syndrome refers to patients with all causes of raised cortisol levels.

Incidence

- Most common in third and fourth decades
- 3 times more common in females.

Etiology

- ACTH-dependent disease:
  - Pituitary adenomas
  - Ectopic ACTH-producing tumors:
    - Bronchial adenoma
    - Bronchogenic carcinoma
    - Pancreatic carcinoma
    - Medullary carcinoma thyroid
    - Carcinoid tumor of thymus
    - Carcinoid tumor of ovary.
  - Exogenous ACTH administration
- Non-ACTH-dependent disease:
  - Adrenal adenoma
  - Adrenal carcinoma
  - Adrenal micronodular dysplasia:
    - Sporadic
    - Familial (***Carney's syndrome***)
  - Adrenal macronodular hyperplasia
  - Exogenous glucocorticoid administration: *Most common* cause.
- Others: Pseudo-Cushing's syndrome:
  - Alcoholism
  - Chronic depression
- Cushing's syndrome in patients more than 60 yrs old is most commonly due to adrenal carcinoma/ectopic ACTH production.

Pathogenesis

Main actions of glucocorticoids are:

- Suppression of pituitary ACTH secretion
- Glycogen deposition
- Increased gluconeogenesis
- Fat deposition
- Protein catabolism and reduced protein synthesis
- Immunosuppression
- Mineralocorticoid actions:
  - Sodium retention
  - Potassium loss
  - Increased free water retention.
- Uric acid production.

Clinical Features

- Central nervous system:
  - Labile mood
  - Depression, confusion, psychosis, apathy.
- Cardiovascular:
  - Hypertension
  - Hypervolemia
  - Fluid retention
  - Congestive cardiac failure.
- Genitourinary:
  - Oligomenorrhea/amenorrhea
  - Decreased libido, virilizing signs
  - Hypertrophied clitoris

  - Kidney stones (due to high uric acid)
  - Polyuria
  - Increased reflux esophagitis.
- Metabolic:
  - Glucose intolerance
  - Diabetes mellitus
  - Hypernatremia, increased bicarbonate levels, hypocalcemia
  - Hypokalemic metabolic alkalosis (especially if ectopic ACTH production).
- Skin:
  - Acne, hirsuitism, frontal balding
  - Easy bruising, violaceous striae
  - Hyperpigmentation
  - Thin and fragile skin with poor wound healing
  - Florid complexion (telangiectasis)
  - Plethoric facies
  - Increased chances of infection.
- Subcutaneous tissue:
  - Lemon on matchstick appearance
  - Fat deposition in:
    - Upper face (***moon face***)
    - Interscapular area (***buffalo hump***)
    - Mesenteric bed (***truncal obesity***)
    - Supraclavicular area
    - Mediastinal widening
  - Edema
  - Growth arrest in children.
- Musculoskeletal:
  - Proximal muscle wasting
  - Myopathy, asthenia
  - Proximal weakness.
- Bone:
  - Osteoporosis, osteopenia
  - Pathological rib fractures
  - Vertebral collapse, kyphosis.

Investigations

- General:
  - Complete blood count (leucocytosis)
  - Renal function tests, blood glucose, electrolytes
  - ECG: Ischemia, hypokalemia, LVH
  - Chest X-ray:
    - Kyphoscoliosis, osteoporosis
    - LVH, lower lobe collapse
    - Carcinoma bronchus
  - Lung function tests
  - CT scan/MRI abdomen: Tumor localization
  - Pituitary MRI with gadolinium contrast.
- Confirmatory tests:
  - High plasma cortisol levels with loss of diurnal variation:
    - Absence of normal reduction at 12 AM
    - Absence of peaking at 6 AM
    - Normal value: 165–680 nmol/l.
  - Increased 24 hour urinary cortisol secretion:
    - More than 50 µg/day
    - Failure to fall to less than 10 µg/day.
  - Failure of plasma cortisol to fall less than 5 µg/dl after low dose dexamethasone suppression test (0.5 mg Q6H for 48 hours) is *diagnostic*
  - ACTH levels in plasma:
    - Normal (less than 60 pg/ml) or high levels (30–150 pg/ml) indicates pituitary disease
    - Low levels (less than 10 pg/ml) indicates:
      - Adrenal disease
      - Exogenous cortisol production.
    - Very high levels (more than 200 pg/ml) indicates ectopic ACTH production.

Treatment

- Surgical therapy:
  - Trans-sphenoidal microadenomectomy for pituitary tumors
  - Excision of adrenal tumor by laparoscopy/open excision
  - Adrenelectomy for bilateral hyperplasia has cure rates upto 100%
  - Most patients with carcinoma, however, die within 3 years despite surgery
  - Metastasis to liver and lung most common.
- Medical therapy:
  - Medical adrenelectomy:
    - Done when:
      - Surgery not feasible
      - Severe syndrome prior to surgery.
    - Aim is to produce complete adrenal gland suppression
    - Done with steroid synthesis inhibitors:
      - Ketoconazole 600–1200 mg/day
      - Mitotane 2–3 g/day
      - Aminoglutethimide 1 g/day
      - Metyrapone 2–3 g/day.
  - Mifepristone is a competitive glucocorticoid antagonist and an alternative form of therapy
  - Platinum is an alternative form of therapy.
- Radiation therapy:
  - For osseous mets as these are refractory to drug therapy

  - Pituitary gamma radiation reserved for tumor recurrence
  - Side effects:
    - Ocular motor palsy
    - Hypopituitarism.
  - Remission rate < 50% with long time lag between therapy and remission.
- Treatment modalities for adrenal hyperplasia:
  - Therapy to reduce ACTH production:
    - Transphenoidal resection of microadenoma
    - Radiation therapy.
  - Therapy to reduce adrenocortical cortisol secretion:
    - Bilateral adrenelectomy
    - Chemical adrenelectomy.

Anesthetic Considerations

- OSAS and obesity
- GERD: Aspiration
- Osteoporosis: careful positioning
- Easy skin bruising on IV access: difficult access
- Electrolyte imbalances preoperatively
- Hypertension
- Impaired glucose tolerance
- Increased intravascular volume state
- Muscle weakness: judicious administration of neuromuscular blockers
- Intraoperative steroid replacement therapy
- Postoperative infections common.

Preoperative Assessment

- Routine history, history of drug intake and exercise tolerance
- All investigations, especially electrolytes
- Assess airway for difficult intubation (obese, DM)
- Assess ease of local anesthetic technique
- Check for preoperative weakness: Increased sensitivity to NMB
- Assess ease of IV line placement: Obesity and fragile skin
- Preoperative orthostatic hypotension warns against introperative hypovolemia.

Preoperative Preparation and Premedication

- Optimal control of:
  - DM, hypertension, CCF
  - Electrolyte abnormalities: Postpone surgery if K^+ less than 2.8 mEq/l
  - Restrictive lung disease
- Normalize intravascular volume status and electrolytes preoperatively
- Spironolactone 25–100 mg Q8H (upto 400 mg/day) started preoperatively
- NPO orders:
  - 6 hours for solids
  - 2 hours for clear fluids.
- Informed consent
- Difficult IV access due to obesity and fragile skin: good care of IV lines
- Premedication:
  - Midazolam 0.05–0.15 mg/kg IV
  - Diazepam 0.1 mg/kg PO.
- Continue all medications including inhibitors of cortisol synthesis, steroids and antihypertensives
- Discontinue morning dose of insulin and diuretics
- Start glucose insulin drip if necessary
- Antibiotic and DVT prophylaxis before surgery
- Antiaspiration prophylaxis:
  - Ranitidine 1 mg/kg IV
  - Metoclopramide 10 mg IV.

Monitors

- Pulse oximetry, $ETCO_2$
- NIBP/IBP, ECG
- CVP: Patients tend to have higher CVP
- Peripheral nerve stimulator
- Urine output, temperature
- ABG, blood glucose, hematocrit.

Position

- Careful positioning due to osteoporosis
- Increased risk of corneal abrasion due to exophthalmos: Proper eye cover
- Protect against nerve injury, especially if lateral, position used during adrenalectomy.

Induction

- Adequate preoxygenation for 3–5 minutes
- *Rapid sequence induction* preferred for obese patients
- Etomidate 0.3 mg/kg *induction agent of choice* as it transiently reduces synthesis and release of cortisol
- Reduced dosage of NMB initially if weakness present preoperatively
- Administer anesthetic agents slowly and carefully as patients are sensitive to cardiodepressant effects
- Neuromuscular monitoring before intubation as reduced doses of muscle relaxants administered
- Prepare for difficult intubation
- Avoid laryngoscopic response at induction

Maintenance

- O_2 + N_2O + isoflurane 1 MAC to maintain balanced anesthesia
- Fentanyl 1 µg/kg and vecuronium (low doses) given as intermittent boluses
- Cortisol replacement therapy:
  - Started at the time of starting tumor resection
  - Hydrocortisone 100 mg/day IV for unilateral and bilateral adrenalectomy
- Frequent blood glucose monitoring: Abnormal glucose tolerance intraoperatively.

Ventilation

- ET tube with IPPV preferred as muscle weakness present
- High FiO_2 may be required
- Avoid hyperventilation as it causes alkalosis and hypokalemia.

Hemodynamics

- Avoid IV fluids containing sodium
- Hemodynamic changes not as profound as for pheochromocytoma
- Hypertensive surges at the time of tumor manipulation treated with IV phentolamine 1 mg given every 5 mins
- Major blood loss may occur during resection of highly vascular tumors: keep blood ready.

Extubation

- Extubate when:
  - Fully awake
  - Hemodynamically stable
  - Adequately reversed, TOF ratio > 0.7
  - Good ABG.
- Neostigmine 0.05 mg/kg and glycopyrrolate 0.02 mg/kg IV prior to extubation
- Fully awake extubation in propped up position after TOF ratio ≥ 0.7
- Delayed extubation possible owing to residual neuromuscular weakness.

Postoperative Care

Management

- Avoid excessive administration of Na^+ containing IV fluids as mineralocorticoid action of fludrocortisone will increase Na^+ resorption
- Continuous humidified oxygen therapy
- Physiotherapy, spirometry and early mobilization
- Steroid synthesis inhibitors started if surgery does not reduce effect of carcinoma
- Steroid replacement:
  - Hydrocortisone dose reduced by 50% everyday till 20–30 mg/day on third postoperative day
  - Fludrocortisone 0.05–0.1 mg/day PO started on third postoperative day
  - Fludrocortisone continued lifelong in bilateral adrenalectomy patients
  - If unilateral adrenalectomy, fludrocortisone therapy individualized based on status of contralateral adrenal gland
  - Dosage reduced if HTN/CCF/hypokalemia.
- DVT prophylaxis continued
- Vitamin D (therapy before surgery may cause hypercalcemia and renal stones)
- Insulin infusion and electrolyte correction
- Topical administration of Vitamin A to wound site to increase tensile strength of healing wounds which reduces in the presence of glucocorticoids.

Monitors

- Pulse oximetry, capnography
- NIBP/IBP, CVP
- Temperature, urine output
- Neuromuscular monitoring.

Complications

- Delayed awakening
- Hypoxemia, OSAS
- Adrenal insufficiency
- Transient DI/meningitis if pituitary resection
- Blood loss, pneumothorax
- Persistent hypertension due to permanent changes in vasculature
- ***Nelson's syndrome***: If pituitary tumor not diagnosed preoperatively and only adrenalectomy is done
- Repiratory complications due to:
  - Muscle weakness
  - Obesity
  - Kyphosis and rib fractures.
- Delayed wound healing
- Postoperative stroke, MI, pulmonary thromboembolism
- Electrolyte abnormalities, pancreatitis
- High mortality: 5–10% if bilateral adrenalectomy.

Analgesia

- Opioid infusion: Lower dose to prevent respiratory depression
- Patient-controlled anesthesia
- Epidural analgesia where applicable

- Local anesthesia
- Multimodal analgesia.

Role of Regional Analgesia

- Advantages:
  - Good analgesia
  - Rapid mobilization
  - Reduced DVT incidence
  - Reduced stress response
  - Reduced opioid requirement.
- Disadvantages:
  - Technically difficult due to obesity
  - Consider osteoporosis with vertebral body collapse.

CONN'S SYNDROME[1,2,3,6,11]

Introduction

Syndrome arising due to primary hyperaldosteronism.

Incidence

- Rare occurrence
- Accounts for 1% of patients with hypertension
- More common between 30 and 50 years
- Occurs twice as commonly in females.

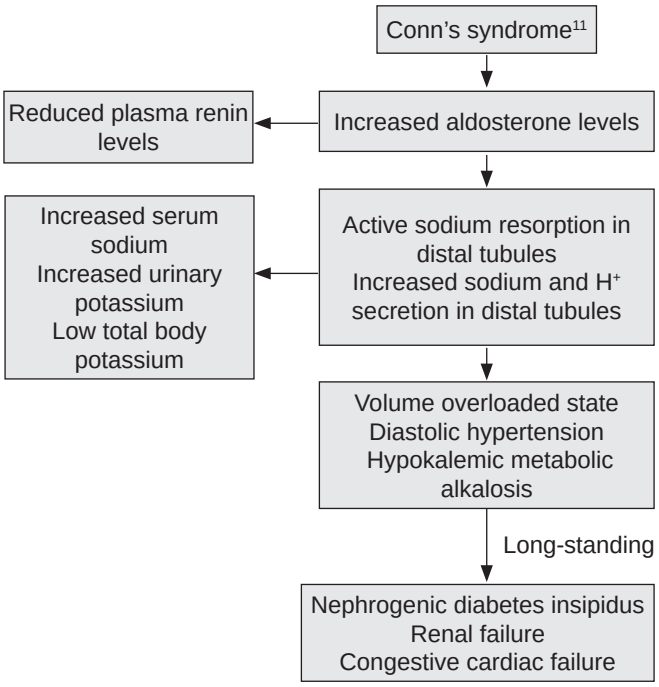
Etiology

- Adrenal adenomas (called aldosteronomas)—60%
- Bilateral adrenal hyperplasia (30%)
- Adrenal carcinoma
- Secondary hyperaldosteronism:
  - Increased aldosterone secretion due to increased renin activity
  - Causes are:
    - Congestive cardiac failure
    - Nephrotic syndrome
    - Cirrhosis
    - Some forms of hypertension (e.g. renal artery stenosis).

Clinical Features

- Cardiovascular:
  - Refractory hypertension: Mainly diastolic HTN (100–125 mm Hg)
  - Renal and retinal damage from hypertension
  - Cardiomyopathy: From chronic potassium depletion
  - Congestive cardiac failure: Due to increased catecholamine levels
  - Arrhythmias, hypervolemia.
- Metabolic:
  - Hypokalemic metabolic alkalosis (usually K^+ 3 mEq/l)
  - Abnormal glucose tolerance (50% patients)
  - Hypocalcemia and tetany due to alkalosis
  - Hypomagnesemia
  - Hypernatremia rarely.
- Renal:
  - Nephropathy, proteinuria
  - Nephrogenic diabetes insipidus due to tubular damage
  - Renal failure due to hypertension
  - Polyuria, nocturia due to impaired renal concentrating ability
  - *Characteristic absence of edema.*
- Neuromuscular:
  - Increased incidence of stroke
  - Skeletal muscle weakness from hypokalemia
  - Skeletal muscle cramps.

Pathophysiology



Diagnostic Criteria

- Severe diastolic hypertension without edema
- Hyposecretion of renin which fails to increase during volume depletion
- Hypersecretion of aldosterone which does not reduce in response to volume expansion.

Investigations

- General:
  - Complete blood count, renal function tests, blood glucose
  - ABG:
    - Hypernatremia
    - Hypokalemic alkalosis
    - Electrolytes (Ca_2^+ and Mg_2^+).
  - ECG:
    - Arrhythmias LVH
    - T wave flattening, U waves suggestive of hypokalemia
  - ECHO for LVH, RWMA, EF
  - Chest X-ray: Cardiomegaly
  - Fundoscopy for retinal hypertensive changes
  - USG, CT, MRI for tumor localization
  - Blood grouping and cross-matching
  - Selective adrenal venous sampling
  - Urinary K^+ levels—raised.
- Diagnostic:
  - Raised plasma aldosterone levels:
    - More than 15 ng/dl when salt intake not restricted
    - More than 9.5 ng/dl after saline infusion is *confirmatory.*
  - Plasma renin activity:
    - If suppressed: Primary aldosteronism
    - If elevated: Secondary aldosteronism.
  - Adrenal venous sampling for aldosterone:
    - High on ipsilateral tumor side
    - Low on contralateral side.
  - Aldosterone-renin ratio:
    - More than 400 in primary aldosteronism
    - Normal in secondary aldosteronism.

Treatment

- Primary aldosteronism due to adenoma:
  - Surgical excision for unilateral adenoma
  - Medical therapy:
    - Used for bilateral adenomas
    - Consists of:
      - Dietary salt restriction
      - Spironolactone 25–100 mg Q8H (up to 400 mg/day)
      - Oral K^+ replacement
      - Antihypertensives: CCB and ACE inhibitors are effective.
- Idiopathic bilateral hyperplasia: Surgery done only when:
  - Significant and symptomatic hypokalemia
  - Not controlled by medical therapy (spironolactone/triamterene/amiloride).

Anesthetic Management Preoperative Optimization and Premedication

- Spironolactone 25–100 mg TID (upto 400 mg/day) started preoperatively
- K^+ infusion (e.g. 6–20 mmol/hr) for atleast 24 hours preoperatively
- Glucose insulin infusion if necessary
- Evaluate volume status: Preoperative orthostatic hypotension may warn against intraoperative hypovolemia
- NPO guidelines:
  - 6 hours: Solids
  - 2 hours: Clear fluids and water.
- Informed consent
- Continue antihypertensives on the day of surgery
- Diazepam 0.1 mg/kg PO for sedation
- Antibiotic prophylaxis as per hospital protocol.

Monitors

- Pulse oximetry, $ETCO_2$
- ECG, NIBP
- IBP useful for ABG, blood glucose and hematocrit
- CVP for guiding fluid therapy
- PAC for intravascular volume status and response to IV fluids
- Temperature and urine output.

Induction

- Adequate preoxygenation for 3–5 minutes
- Thiopentone 3–4 mg/kg + fentanyl 1–2 µg/kg + vecuronium (low dose) for induction
- Slow injection of anesthetic agents to avoid hypotension
- Deep planes of intubation to avoid hypertensive surges

Maintenance

- O_2 + N_2O + isoflurane 1 MAC
- MAC values of inhalational agents increase in the presence of hypernatremia
- Avoid sevoflurane if hypokalemic nephropathy and polyuria present
- Fentanyl 1 µg/kg + vecuronium (low dose) intermittent boluses

- Good muscle relaxation required for surgical exposure
- If bilateral adrenalectomy planned, cortisol infusion at 100 mg/day started
- Monitor acid-base status and electrolytes and glucose frequently
- Abnormal glucose tolerance common intraoperatively as chronic hypokalemia has antagonist action on insulin secretion.

Ventilation

- ET intubation with IPPV preferred
- Avoid hyperventilation to avoid increasing alkalosis and hypokalemia.

Hemodynamics

- Avoid Na^+ containing fluids
- Massive blood loss may occur from injury to the nearby blood vessels
- Treat hypertensive surges with:
  - Phentolamine 2.5–5 mg IV every 5 min
  - Labetolol 10–20 mg IV
- Avoid hypo- and hypertensive episodes.

Extubation

- Neostigmine 0.05 mg/kg + glycopyrrolate 0.02 mg/kg IV
- Watch for residual NMB action potentiated by hypokalemia
- Extubate when:
  - Fully awake
  - Hemodynamically stable
  - Adequately reversed, TOF ratio > 0.7
  - Good ABG.

Postoperative Care

Management

- Respiratory support may be required as:
  - Increased sensitivity to respiratory depressants and NMBS
  - Compensatory respiratory acidosis for metabolic alkalosis.
- Postoperative fludrocortisone as in Cushing's syndrome for bilateral adrenalectomy
- Avoid excessive Na^+ containing fluids
- Insulin infusion for blood sugar control
- Correction of electrolyte abnormalities
- Na^+ and K^+ levels return to normal within a week.

Monitor

- Pulse oximetry, ECG
- NIBP/IBP, CVP
- Urine output, temperature
- ABG, blood glucose, electrolytes
- Chest X-ray.

Complications

- Mineralocorticoid/glucocorticoid deficiency
- Persistent hypertension due to permanent changes in vascular resistance
- Pneumothorax
- Electrolyte abnormalities.

Pain

- Opioids as patient-controlled analgesia
- NSAIDs as adjuvants
- Thoracic epidural: Best pain relief
- Multimodal analgesia.

CARCINOID SYNDROME[1,2,3,6,8,10]

Introduction

- Carcinoid tumor is a slow-growing, benign, small intestinal tumor arising from enterochromaffin cells capable of metastasis but with good prognosis.
- Carcinoid syndrome occurs when a metastatic carcinoid tumor releases vasoactive peptides into systemic circulation which leads to signs and symptoms collectively called 'carcinoid syndrome'.

Apudomas

Tumors of amine precursor uptake and decarboxylation:

- Pheochromocytoma
- Carcinoid tumor
- Gastrinoma
- VIPoma
- Insulinoma.

Sites of Occurrence

- Gastrointestinal tract (75%):
  - Appendix *most common* but rarely metastases to cause syndrome
  - *Ileocecal* region causes *highest incidence of metastasis*
  - Colon, rectum.
- Head and neck
- Lung and bronchus
- Gonads: Testes and ovary
- Thymus, breast
- Pancreas, genitourinary tract.

Substances Secreted

Up to 20 peptides and amines including:

- Serotonin, bradykinin
- Histamine, prostaglandins
- Vasoactive intestinal peptide
- Catecholamines: Dopamine
- Substance P, neurotensin
- Tachykinin, neuropeptide K
- Motilin.

Pathophysiology

- 20% of patients with carcinoid tumor exhibit carcinoid syndrome
- As most tumors are located in GIT, their products are released into portal circulation and destroyed by the liver before they can cause systemic effects
- Carcinoid syndrome, therefore, manifests only in:
  - Patients with hepatic metastasis, who cannot metabolize the products
  - Those in whom products are directly released into systemic circulation like:
    - Carcinoid of thymus
    - Carcinoid of gonads.
- Cardiac disease:
  - Substances which escape hepatic metabolism undergo pulmonary metabolism
  - Thus, right-sided heart disease is more common than left-sided disease.
- Serotonin:
  - Little direct effect on heart
  - Positive inotropic and chronotropic effect
  - Vasoconstriction and vasodilation
  - Increased GI motility
  - Increased net intestinal water, Na^+, Cl^- and K^+ secretion
  - Bronchoconstriction.
- Bradykinin:
  - Vasodilation of small resistance blood vessels
  - Stimulates histamine release from mast cells
  - Increases vascular permeability and causes edema
  - Does not affect myocardium directly.
- Histamine:
  - Vasodilation of small blood vessels
  - Reduces total peripheral resistance
  - Bronchoconstriction.

Clinical Features

- Most commonly asymptomatic
- Most commonly found as incidentaloma during appendicular surgery
- Skin:
  - Flushing:
    - Affects neck and torso
    - Is the *most common* symptom (90%).
  - Venous telangiectasia.
- Gastrointestinal:
  - Diarrhea:
    - Very common
    - Watery diarrhea (upto 30 times/day)
    - Causes malabsorption state and steatorrhea.
  - Chronic abdominal pain, intestinal obstruction
  - Hepatomegaly, hyperglycemia.
- Cardiovascular:
  - Hemodynamic instability
  - Tachycardia
  - Hypotension more common
  - Uncontrolled hypertension
  - ***Carcinoid heart disease***:
    - Components:
      - Right heart lesions: Tricuspid regurgitation, pulmonary stenosis
      - Premature atrial complexes, supraventricular tachycardia.
    - Results in right heart failure with hepatomegaly and edema
    - Occurs due to:
      - Myocardial plaque formation
      - These are deposits of fibrous tissue on endocardium of right-sided valve cusps
      - This is due to action of serotonin and tachykinin on platelets and endocardium.
- Others:
  - Bronchoconstriction (20%), pruritus, lacrimation, facial edema
  - Hypoalbuminemia, hyponatremia, hypokalemia, hypochloremia
  - ***Pellagra:*** Diarrhea, dementia, dermatitis
  - Hemoptysis due to bronchial carcinoid.
- ***Carcinoid triad:***[6]
  - Cardiac involvement (usually tricuspid regurgitation/pulmonary stenosis)
  - Flushing
  - Diarrhea.
- Carcinoid crisis:[6]
  - Clinical features:
    - Intense flushing
    - Diarrhea, abdominal pain
    - Cardiovascular instability.

- Precipitating factors:
  - Stress and anxiety
  - Biopsy
  - Drugs: Catecholamines, pentagastrin, SSRI
  - Tumor debulking surgery
  - Chemotherapy with octreotide
  - Biotherapy
  - Hepatic artery embolization
  - Exercise, alcohol and cheese.

Location[8,10]	Presentation
Small intestine	Abdominal pain
	Intestinal obstruction
	Gastrointestinal bleeding
	Tumor
Rectal	Bleeding
	Constipation/diarrhea
Bronchial	Asymptomatic (31%)
Thymic	Anterior mediastinal mass
Ovarian and testicular	Mass on physical examination
Metastatic	Hepatomegaly

Drugs Associated with Crises

- Succinylcholine, mivacurium
- Atracurium, d-tubocurarine
- Epinephrine, norepinephrine
- Isoprenalin, dopamine
- Thiopentone, morphine.

Diagnosis

- 5–hydroxyl indole acetic acid (5HIAA):
  - Metabolite of serotonin
  - Normally 3–15 mg/24-hour urine sample
  - 30 mg in 24-hour urine sample is diagnostic
  - False positive test: Coffee/chocolate, banana, avocado, walnut, pineapple
  - False negative test: Phenergan, methyldopa, epinephrine and norepinephrine
- Chromograffin levels in plasma.

Preoperative Evaluation

- History and examination:
  - Dyspnea, orthopnea, wheezing
  - Edema, arrhythmia, murmur.
- If diarrhea present:
  - Orthostatic blood pressure
  - Serum electrolytes, BUN, serum creatinine, albumin.
- If cardiac involvement:
  - ECG, echocardiography
  - Electrolytes.
- Others:
  - LFTs and clotting profile if metastatic lesions
  - Chest X-ray and pulmonary function tests.
- Increased perioperative risk with:
  - Increased levels of 5-HIAA
  - Carcinoid heart disease.
- Preoperative endocrinologist consultation.

Treatment

- Medical management:
  - Avoid conditions which precipitate flushing
  - Dietary nicotinamide supplementation
  - Treatment of right heart failure and wheezing
  - H1 + H2 blockers for flushing: Diphenhydramine + ranitidine
  - Antidiarrheals: loperamide/diphenoxylate
  - 5-HT3 blockers for vomiting: Ondansetron
  - Octreotide and lanreotide to reduce tumor size.
- Surgey: Only potentially curative therapy for non-metastatic tumors
- Hepatic artery embolization: Used alone or with chemotherapy *(chemoembolization)*
- Biotherapy: Done with interferons.

Preoperative Optimization

- Octreotide:
  - Synthetic somatostatin analog
  - Somatostatin is a GI regulatory peptide which reduces production and release of gastropancreatic hormones
  - It reduces the amount of serotonin secreted from carcinoid tumor
  - *Drug of choice* for preop, intraop and postoperative management of carcinoid symptoms
  - 50–500 µg (usually 100 µg) S/C Q8H
  - Dose titrated to relief of symptoms and prevention of hypotension
  - Given for 2 weeks preoperatively
  - Half life of 25 hrs, duration of action is 12 hrs
  - IM formulation also available
  - Side effects:
    - Bradycardia and complete heart block following IV bolus
    - Somnolence
    - Hyperglycemia.
- H_1 + H_2 antagonists: H_2 antagonists more important than H_1 antagonists

- Serotonin antagonists:
  - Cyproheptidine and methysergide for GI features
  - Ketanserin for vasoconstriction/bronchospasm, platelet aggregation and hypertension.
- Bradykinin antagonists:
  - Aprotinin and steroids
  - Used for treatment of flushing and hypotension refractory to octreotide
  - Aprotinin inhibits kallikrein cascade
  - Steroids:
    - Reduce synthesis of prostaglandin which mediate actions of bradykinin
    - Effective in bronchial carcinoids.
- Bronchodilators and treatment of right heart failure.

Anesthetic Considerations[11]

- Asymptomatic carcinoid tumor does not present anesthetic difficulties
- Hypovolemia and electrolyte abnormalities
- Use somatostatin analogs to prevent mediator release
- Avoid factors which precipitate crises:
  - Anxiety
  - Hypercarbia, hypoxia
  - Hypothermia, hypotension.
- Prepare for resistant bronchospasm and sudden variation in BP at induction and when tumor is handled
- Avoid histamine-releasing agents.

Preoperative Medication

- Correct fluid and electrolyte abnormalities
- Nutritional support required if severe malabsorption
- NPO orders:
  - 6 hours for solids
  - 2 hours for clear fluids.
- Informed consent
- Continue antagonists of serotonin, bradykinin and histamine preoperatively:
  - Octreotide 10–100 µg IV slowly 1 hour prior to surgery
  - Promethazine, ranitidine
  - Ondansetron is *antiemetic of choice.*
- Anxiolysis with benzodiazepines: Midazolam 0.05–0.15 mg/kg IV.

OT Preparation

- Anesthetic drugs
- Suction apparatus
- Monitors
- Emergency drugs:
  - Atropine, phenylephrine, NTG, SNP
  - Dopamine, dobutamine.
- All antimediator drugs kept ready in OT:
  - Ketanserin
  - Cyproheptidine
  - Somatostatin
  - Aprotinin
  - Antihistaminics.

Monitors

- Pulse oximetry, $ETCO_2$
- NIBP used if short-duration surgery
- IBP/CVP inserted preinduction as induction can cause large BP swings
- ABG and blood sugars
- Temperature, urine output
- Airway pressures
- PA catheter: Caution while floating if right heart valves are damaged
- TEE if right heart is involved.

Induction

- Adequate preoxygenation for 3–5 minutes
- Smooth anesthetic technique with avoidance of major hemodynamic changes
- Etomidate and vecuronium are *drugs of choice*
- Propofol/etomidate used as induction agents
- Vecuronium/rocuronium can be used as muscle relaxants
- Sufentanyl/fentanyl/alfentanyl/remifentanyl can also be used
- Topical laryngeal LA spray and xylocard to avoid pressor response at intubation
- Avoid:
  - Ketamine for induction
  - Succinylcholine as scholine-induced fasciculations can precipitate crisis
  - Histamine releasers, like morphine, pethidine and thiopentone.

Maintenance

- O_2 + air + isoflurane 1 MAC for balanced anesthesia
- Desflurane *is drug of choice* in cases of hepatic metastasis as it is less metabolized
- Vecuronium and fentanyl given as intermittent boluses
- Octreotide infusion at 50–100 µg/hr during surgery with 100–150 µg IV bolus prior to manipulation of tumor

- Fluid resuscitation and electrolyte correction important as carcinoid tumors have high gastric output and gastric fluid losses during surgery.

Intraoperative Complications

- Severe hypo-/hypertension
- Fluid and electrolyte shifts
- Bronchospasm
- Hypo/hyperglycemia
- Hyperglycemia more common as octreotide inhibits insulin secretion.

Hemodynamics

- Hypotension:
  - IV fluid boluses
  - Octreotide 10–20 µg IV bolus dose
  - Aprotinin/vasopressin/angiotensin boluses if refractory hypotension
  - Phenylephrine, calcium chloride, and milrinone relatively safe
  - Avoid vasopressors as they stimulate amine release.
- Hypertension treated with:
  - Ketanserin, octreotide
  - Increased volatile agents
  - Labetolol/clonidine
- Tachycardia: Esmolol/propranolol
- If tricuspid regurgitation present, avoid factors causing pulmonary hypertension:
  - Angiotensin, vasopressin
  - Hypoxia, hypercarbia
  - Acidosis, hypothermia.

Extubation

- Glycopyrollate 0.02 mg/kg + neostigmine 0.05 mg/kg for reversal
- Extubated once patient is:
  - Hemodynamically stable
  - Fully awake
  - TOF $\geq$ 0.7
  - Adequately warmed.

Choice of Regional Anesthesia

- Relatively contraindicated as hypotension can precipitate bradykinergic crisis
- Graded epidural can be used in a patient adequately treated with octreotide
- Avoid hypotension by:
  - Using diluted LA solution
  - Epidural opioids to reduce LA use
  - Graded epidural
  - Adequate preloading with IV fluids.

Postoperative Care

Monitoring

- Pulse oximetry
- Intense hemodynamic monitoring: IBP/CVP/PAC
- ECG, repeated ABG and blood sugar
- Pain scale, urine output and temperature.

Management

- Delayed recovery may occur due to serotonin release
- Octreotide slowly weaned over 7–10 days following resection
- IV octreotide 10–20 µg boluses for hypotension.

Analgesia

- Adequate analgesia to reduce amine release
- Reduce opioid dose as increased somnolence and respiratory depression common
- NSAIDs as adjuvants
- Regional anesthesia, epidural safe
- Local anesthetic infiltration can be used to supplement analgesia
- Multimodal analgesia.

DIABETES MELLITUS[1,2,3,6,8,10,11]

Introduction

American Diabetes Association diagnostic criteria 2004:

- Diabetes mellitus diagnosed if:
  - FBS 126 mg/dl
  - RBS 200 mg/dl with symptoms of diabetes
  - 2 hour PPBS 200 mg/dl
- Called impaired fasting glucose if FBS between 100 and 125 mg/dl
- Called impaired glucose tolerance if 2 hour PPBS is between 140 and 199 mg/dl
- Called critical illness induced hyperglycemia if:
  - Blood glucose 200 mg/dl
  - In the absence of known DM
  - Occurs frequently in elderly.

Classification

ADA 2004 guidelines:

- Primary:
  - Type 1 diabetes mellitus/insulin dependent diabetes mellitus(IDDM)

  - Type IA: immune mediated
  - Type IB: idiopathic
- Type II diabetes mellitus/non-insulin dependent diabetes mellitus (NIDDM)
  - Non-obese NIDDM
  - Obese NIDDM
  - Maturity onset diabetes of young (MODY)
- Gestational diabetes mellitus.

- Secondary:
  - Pancreatic disease:
    - Pancreatitis, pancreatic carcinoma
    - Pancreatectomy, cystic fibrosis.
  - Endocrinological:
    - Acromegaly, Cushing's syndrome
    - Pheochromocytoma, glucagonoma
    - Hyperthyroidism.
  - Genetic syndromes:
    - ***Down's, Klinefelter's syndrome***
    - ***Turner's, Prader-Willi syndrome.***
  - Insulin receptor abnormalities:
    - ***Leprechaunism,*** Type A insulin resistance
    - ***Rabson–Mendelhall syndrome.***
  - Infection: Congenital rubella, CMV
  - Drug-induced:
    - Glucocorticoids, thyroid hormones
    - β-blockers, pentamidine
    - Phenytoin, thiazides.

Incidence

- Most common endocrine disorder
- 8 to 17 per 100,000 per year incidence
- Prevalence 20.1% in patients > 65 years.

Types

Type I diabetes mellitus[8]	Type II diabetes mellitus
IDDM	NIDDM
Absence of insulin in the body	Peripheral insulin resistance
Plasma glucagon is high and suppressible	Plasma glucagon is high and resistant
Age at onset less than 40 years	Age at onset more than 40 years
Chromosome 5	Chromosome 2
Body habitus normal/wasted	Obese

Contd...

Contd...

Type I diabetes mellitus[8]	Type II diabetes mellitus
Susceptible to DKA	Resistant to DKA
Resistant to HONC	Susceptible to HONC
Unresponsive to sulfonylurea therapy	Respond to sulfonylurea therapy
Associated with autoimmune diseases	Not associated with autoimmune diseases

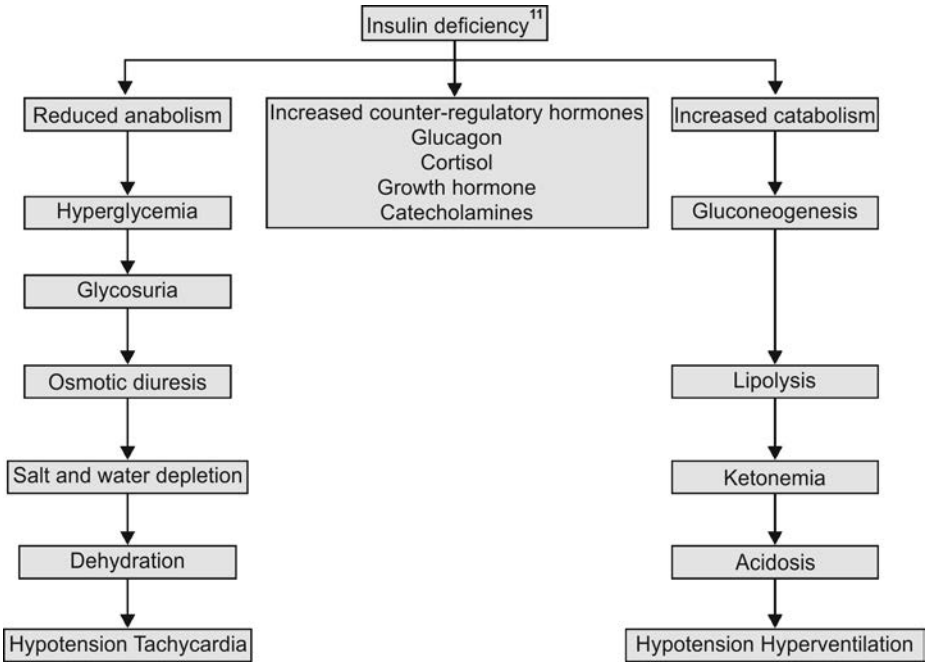
Risk Factors for Type II DM

- Family history of DM
- Overweight, physical inactivity
- Excess abdominal fat (even if BMI is normal)
- Native Americans, Asians, Hispanics
- Female : Male : 2 : 1
- Polycystic ovarian disease, history of vascular disease
- Previous IGT/IFG
- Long-standing HTN 140/90 mm Hg
- Patients on steroids.

Actions of Insulin

Increased anabolism[11]	Decreased catabolism
Carbohydrate metabolism	
Glucose transport	Reduced gluconeogenesis
Glucose phosphorylation	Reduced glycogenolysis
Increased pyruvate dehydrogenase	
Increased pentose phosphate shunt	
Glycogenesis	
Glycolysis	
Fat metabolism	
Triglyceride synthesis	Reduced lipolysis
Fatty acid synthesis	Reduced fatty acid oxidation
Increased lipoprotein lipase	Reduced ketogenesis
Protein metabolism	
Increased amino acid transport	Reduced protein breakdown
Increased protein synthesis	

Pathogenesis



Complications

- Acute complications:
  - Diabetic ketoacidosis (DKA)
  - Hyperosmolar nonketotic coma (HONC)
  - Hypoglycemia (*Blood glucose 50 mg/dl*).
- Chronic complications:
  - Microvascular:
    - Eye disease:
      - Retinopathy
      - Macular edema.
    - Neuropathy:
      - Sensory and motor neuropathy
      - Autonomic neuropathy.
    - Nephropathy.
  - Macrovascular:
    - Coronary artery disease
    - Cerebrovascular accidents
    - Peripheral vascular disease.
  - Others:
    - Cataract, glaucoma
    - Gastrointestinal:
      - Gastroparesis, constipation
      - Diarrhea.
    - Genitourinary:
      - Uropathy
      - Erectile dysfunction.
    - Dermatological
    - Infection
- Complications of therapy:
  - ***Dawn phenomenon:***
    - Occurs in Type 1 DM
    - Due to increased requirement of insulin post midnight
    - This is because of glucagon surge causing hyperglycemia
  - ***Somagyi phenomenon:*** Compensatory hyperglycemia following hypoglycemia.

Preoperative Evaluation

- History:
  - Central nervous system:
    - Peripheral neuropathy (glove and stocking neuropathy)
    - Headache, syncope
    - TIA/stroke
  - Cardiovascular:
    - MI: Increased chances if erectile dysfunction present
    - Silent MI: Increased chances if autonomic neuropathy
    - Hypertension
    - Congestive cardiac failure: Especially if poor glycemic control
    - Dyspnea on exertion/reduced exercise tolerance

  - Respiratory:
    - Frequent infections
    - Reduced VC, FVC, FEV, DLCO.
  - Gastrointestinal:
    - Gastroparesis due to ganglion cell damage
    - Postprandial vomiting, early satiety
    - Delayed gastric emptying.
  - Genitourinary:
    - Erectile dysfunction
    - Renal failure especially if age ≥ 55 years and diabetes and hypertension coexist.
  - Medication history, history of anesthetic exposure
  - Episodes of hypoglycemia/hyperglycemia.
- Examination:
  - Document vitals, orthostatic vital signs and skin breakdown points
  - Sensory examination
  - Airway examination:
    - ***Stiff joint syndrome***:
      - Seen in poorly controlled DM
      - Reduced mobility of cervical, atlanto-occiptal and TM joint occurs.
    - ***Prayer sign***: inability to approximate palmar surface of interphalangeal joints
    - ***Palm print sign***:
      - Alteration in palm print when it is taken on paper
      - Indicates interphalangeal joint stiffness.
- Fundoscopy for retinopathy
- Tests for autonomic dysfunction
- Back for edema and infection: Difficult to perform subarachnoid block.

Investigations

- Routine blood: Hb, TC, DC, ESR
- Renal function tests
- Preoperative FBS ≤ 110 mg% in noncritically ill patients: ***ACE recommendations***
- ECG, treadmill test for silent MI
- Chest X-ray: Cardiomegaly
- Pulmonary function tests
- Glycated hemoglobin:
  - Called HbA1c
  - Best evidence of glucose control over the last 1–2 months
  - Level < 2% recommended by ADA
  - Microalbuminuria 29 mg/day with HbA1c 8.1% predicts 80% risk of CRF
  - HbA1c 8.5–9% predicts increased chances of retinopathy.

Glucotoxicity

- Delayed wound healing:
  - Due to abnormal glycosylation of proteins
  - This causes reduced elastance and tensile wound healing strength
- Intracellular swelling due to macromolecules like sorbitol
- Impaired oxygen transport
- Endothelial dysfunction
- Adverse effect on CNS recovery after ischemia:
  - Common if blood glucose 150–250 mg/dl
  - Blood glucose should be < 200 mg/dl in a diabetic patient about to undergo surgeries in which hypotension or reduced cerebral blood flow may occur.
- Disruption of autoregulation:
  - Causes vasodilation
  - This prevents target organs from protecting against increase in systemic BP.
- Osmotic diuresis: Dehydration and electrolyte imbalance.

Anesthetic Consideration

- Difficult intubation due to stiff joint syndrome
- Increased risk of aspiration due to gastroparesis: Treat all diabetics as full stomach
- Increased risk of hypothermia due to autonomic dysfunction causing vasodilation
- Poor response to atropine/catecholamines if autonomic neuropathy
- Increased risk of nerve injury
- Increased perioperative complications:
  - Perioperative MI in those with erectile dysfunction
  - CCF due to both systolic and diastolic dysfunction
  - Perioperative renal failure
  - Increased risk of wound infections.
- Reduced oxygen saturation and transport in pregnancy due to glycosylation of Hb.

Glycemic Goals

ACE recommendations:

- ICU care: 110–180 mg/dl
- Intraoperative control: Less than 150 mg/dl
- Perioperative control: 90–130 mg/dl

GLYCEMIC REGIMENS[1,3,6,11]

Sliding Sale

- Advantage: Easy to calculate
- Disadvantages:
  - Not used in major surgery
  - Blood glucose not optimally controlled

Blood glucose	Insulin
Less than 150 mg/dl	Nil
150–200 mg/dl	2 IU
200–250 mg/dl	4 IU
250–300 mg/dl	6 IU
300–350 mg/dl	8 IU
More than 350 mg/dl	10 IU + blood sugar monitoring

Modified Sliding Scale

Blood glucose	Insulin
< 60 mg/dl	Selected dose withheld for 1 hour
	IV 50% dextrose at 0.01–0.02 ml/kg/min
	Hourly blood sugar monitoring
≥ 125 mg/dl without supplemental dextrose	Next dose should be 20–40% lesser
≤ 100 mg/dl or < 125 mg/dl and decreasing	Scheduled dose maintained till BS ≥ 125 mg/dl
100–200 mg/dl and stable	Current dose continued
200–350 mg/dl	Increase scheduled dose by 10–20%
≥ 350 mg/dl	Increase dose by 20–40%

Classic Nontight Control Regimen

- NPO from 12 midnight with glass of orange juice kept by the side for emergency
- At 6 AM on the day of surgery, IV 5% dextrose at 125 ml/hr/70 kg body weight
- After starting IV infusion, half the usual morning dose of usual type of insulin given S/C
- Continue 5% dextrose intraoperatively at atleast 125 ml/hr/70 kgs
- Monitor blood glucose postoperatively and treat as per the sliding scale.

Tight Control Regimen

Aim: To maintain blood sugar between 79 and 120 mg/dl.

Indications for Tight Glycemic Control

- Type 1 DM (as they need insulin to avoid DKA)
- Pregnant diabetics
- Major surgery or bowel anastomosis
- Those requiring postprocedure ICU stay
- Diabetics undergoing CPB
- Those with global CNS ischemia (e.g. following cardiac arrest)
- Surgery in those with DKA
- Type II DM does not benefit from tight perioperative control unless ICU stay is required according to current data.

Regimen I

- Determine preprandial blood glucose on the evening before surgery
- IV infusion of 5 and dextrose at 50 ml/hr/70 kg body weight
- *Piggy back* regular insulin:
  - 50 IU added to 250 ml NS
  - Flush infusion line with first 60 ml of infusate.
- Rate of infusion:
  - (Blood glucose)/150 normally
  - (Blood glucose)/100 if:
    - Patient on steroids (except inhaled)
    - Obese with BMI ≥ 35
- Repeat blood glucose Q4H and adjust insulin to obtain blood glucose 100–200 mg/dl.
- On morning of surgery:
  - Administer nondextrose-containing fluids
  - Insulin started with insulin infusion rate (BG/150 or BG/100).
- Determine blood glucose at the start of surgery and Q2H for rest of 24-hour period
- Treat hypoglycemia (< 50 mg/dl) with 15 ml 50% dextrose with termination of infusion.

Regimen II

- Obtain feedback mechanism pancreas and set controls for desired blood glucose levels
- Start 2 IV lines.

Advantages

- Improves CNS outcome after global/focal ischemic event
- Decreased incidence of polyneuropathy
- Improves weaning from CPB
- Decreased renal dysfunction and need for dialysis

- Reduced need for blood transfusion
- Reduces deaths in ICU and duration of ICU stay
- Improved oxygen transport
- Prevents wound infection
- Improves wound healing.

Disadvantages

- Increased incidence of hypoglycemia
- Lack of potassium supplementation.

Gik Regimen

Blood sugar	IV insulin	KCl	IV fluids 100 ml	Subcutaneous
< 100	1 IU	2 mEq	10% D	Nil
101–200	2 IU	2 mEq	10% D	4 IU
201–300	3 IU	2 mEq	10% D	6 IU
301–400	4 IU	2 mEq	5% DNS	8 IU
≥ 400	4 IU	2 mEq	NS	10 IU

Combination of 10% dextrose and insulin is added to 500 ml fluid bag

- This provides 250 gms glucose and 50 U insulin in 24 hours
- Advantage: Prevents hypo/hyperglycemia
- Disadvantage: New bag of fluid is required every time glucose falls outside range.

Vellore Regimen

Advantages: Simple, safe and inexpensive

Disadvantages: Potassium levels are not corrected.

Blood glucose	Insulin	IV Fluid
Less than 70 mg/dl	Nil	D5 100 ml IV rapidly
		Measure blood sugar after 15 min
70–100 mg/dl	Nil	D5 at 100 ml/hr
110–150 mg/dl	1 IU	100 ml D5
150–200 mg/dl	2 IU	100 ml D5
200–250 mg/dl	3 IU	100 ml D5
250–300 mg/dl	4 IU	100 ml D5
More than 300 mg/dl	6 IU	NS

Alberti Regimen

- Initial insulin solution: 500 ml 10% dextrose with 10 mmol KCl and 15 IU insulin
- Infuse at 100 ml/hr (i.e. 3 IU/hr)
- Check blood glucose second hourly
- Adjust infusion rate according to result:

Blood glucose	Infusion
Less than 117 mg/dl	2 IU/hr
117–200 mg/dl	3 IU/hr
More than 200 mg/dl	4 IU/hr

Watt-Hirsch Regimen

- Also called ***variable rate insulin regimen***
- Infuse glucose at 5 gm/hr, K^+ at 2–4 mEq/hr and insulin at 0.5–1 IU/hr
- Measure blood glucose hourly
- Insulin is either piggy backed with glucose or given as separate infusion.

Blood glucose	Action
Less than 80 mg/dl	Stop infusion for 30 minutes
	25 gms glucose given IV
	Restart insulin 0.3–0.6 IU/hr when blood glucose more than 120 mg/dl
80–120 mg/dl	Reduce insulin by 0.3 IU/hr
120–180 mg/dl	No change
180–240 mg/dl	Increase insulin infusion by 0.3 IU/hr
More than 240 mg/dl	Increase insulin infusion by 0.5 IU/hr

Computer Controlled Insulin Infusion

- Computer adjusts rate of infusion according to blood sugar levels
- Baseline blood glucose and initial parameters entered into computer
- Insulin per hour = multiplier × (blood glucose – 60)
- Blood glucose monitored every 20 minutes.

Preoperative Preparation

- Postpone elective surgery if:
  - HbA1c 7–9% for ≤ 5 yrs old
  - HbA1c 6–8% for ≤ 5 yrs old
  - Abnormal electrolytes
  - Ketonuria.
- Posted usually as first case of day to avoid hypoglycemia
- NPO orders:
  - Kept NPO for 12 hours
  - Increased risk of gastroparesis causes delayed emptying
  - Glucose tablet/clear juice kept at bedside in the event of hypoglycemia.
- Correct any fluid deficit/electrolyte disturbances

- VBG/blood sugar and ketones on morning of surgery
- Monitor glucose:
  - Immediately perioperatively
  - Every 3 hours till oral intake has resumed for minor surgery
  - Every 1–2 hour till oral intake has resumed for major surgery.
- Control of blood sugar:
  - Type I DM:
    - Discontinue long acting insulin 1–2 days before surgery
    - Change to subcutaneous short acting insulin Q4-6H according to blood sugar
    - Not necessary to change intermediate acting insulin to short acting insulin preoperatively
    - If insulin pump is present:
      - Continue pump for short surgeries
      - Switch to IV insulin infusions for major surgery
  - Type II DM:
    - Stop long acting OHAs (chlorpropamide) at least 48 hours before surgery
    - Metformin:
      - Stopped 24 hrs before surgery
      - Stopped for 48 hours after any procedure using IV contrast dye.
    - Discontinue morning dose of all other OHAS except thiazolidines which can be taken as they do not predispose to hypoglycemia
  - On the morning of surgery:
    - For type I DM, continue usual insulin as half the usual morning dose
    - 5% dextrose given at 2 mg/kg/min
    - This is followed by insulin at (BG/150 or BG/100) IU/hr
    - Monitor blood glucose hourly intraoperatively
    - Maintain blood sugar with the help of selected protocol.
- Sedation:
  - IV midazolam 0.05–0.15 mg/kg for sedation
  - IV glycopyrollate 0.02 mg/kg.
- Antiaspiration prophylaxis:
  - IV metoclopramide 10 mg
  - IV ranitidine 1 mg/kg.
- Appropriate IV antibiotics as per hospital protocol
- Consider β-blocker therapy on morning of surgery if CAD is present with DM.

Choice of Anesthetic Technique

Regional Anesthesia

Technique of choice where applicable:

- Advantages:
  - Avoids aspiration
  - Better if difficult airway
  - Patient is awake: Easy to recognize hypoglycemia
  - Reduced incidence of DVT
  - Reduced stress response to surgery
  - Good postoperative analgesia
  - Reduced chances of pulmonary infection.
- Disadvantages:
  - Exaggerated hypotension especially if autonomic neuropathy present
  - Increased risk of epidural abscess
  - Caution if pre-existing neuropathy
  - Increased risk of nerve injury.
- Guidelines:
  - Local anesthetic requirement is lower
  - Combination of LA with adrenaline may increase risk of ischemic or edematous nerve injury
  - Bradycardia may be unresponsive to atropine
  - Isoprenaline/1:10,000 adrenaline used in such cases
  - Chart pre-existing nerve damage as increased chance of nerve injury
  - Technique: May be difficult if edema is present.
- Contraindications:
  - Autonomic neuropathy
  - Infections.

General Anesthesia

- Advantages:
  - Better cardiovascular stability
  - Airway is protected from silent aspiration.
- Disadvantages:
  - Difficult intubation
  - Difficult to recognize hypoglycemia
  - Altered elimination of drugs due to renal involvement
  - Increased stress response.

Anesthetic Management

Induction

- Adequate preoxygenation for 3–5 minutes
- Anticipated difficult intubation: Awake intubation preferred
- If not, *rapid sequence induction* used to avoid aspiration

- Etomidate is *drug of choice* as it inhibits adrenal steroidogenesis
- Etomidate, fentanyl and vecuronium used for induction
- Reduce dosage of induction agent and give drugs slowly to avoid hypotension
- Atracurium/cisatracurium if renal fuction tests are altered
- β-blockers and lidocaine used to reduce intubation response as BP is labile.

Monitors

- Pulse oximetry, blood sugar second hourly
- $ETCO_2$, electrolytes and ABG Q4–6H
- BP, ECG
- Urine output, temperature
- IBP/CVP if cardiovascular instability.

Maintenance

- TIVA is good alternative but care to avoid lipid overload
- Avoid volatile anesthetics as it impairs glucose tolerance
- Narcotic based anesthetic techniques best to reduce cardiovascular depression
- Prophylactic NTG used if increased risk of CAD
- Nasogastric tube inserted to empty stomach
- Midazolam in high doses reduces cortisol secretion
- Clonidine and dexmedetomidine give good glycemic control.

Hemodynamics

- Nondextrose containing IV fluids used
- Avoid Ringers lactate as it causes hyperglycemia
- In event of sudden bradycardia and hypotension which is unresponsive to atropine (give up to 40 µg/kg) try adrenaline 1:10,000 or isoprenaline
- If intraoperative hypoglycemia occurs, 20 ml 50% dextrose given and sugars checked after 1 hour
- Bank blood may contain ACD which may aggravate hyperglycemia
- One unit insulin reduces glucose by 25 mg/dl
- 1 ml 25% dextrose increases glucose by 1 mg/dl.

Extubation

- Prolonged duration of action of muscle relaxants and delayed recovery may occur if RFTs are elevated
- Extubate only if:
  - Full neuromuscular recovery
  - Good hemodynamic stability.

Postoperative

- Check blood sugar Q2–6H, serum creatinine and electrolytes Q4–6H
- Continue infusion till oral feeding is established
- If feeding is delayed add glucose to IV fluid as required
- Once patient resumes oral intake and insulin requirement < 20 IU/day treatment is changed to patients chronic regimen
- Metformin is reinstituted only after RFTs found to be normal.

Treatment of Diabetes Mellitus

Exogenous Insulin

Type	Preparation	Onset	Peak	Doa
Fast acting	Insulin-lispro	15 mins	30–90 min	3–4 hrs
	Regular	30–60 mins	2–4 hrs	6–8 hrs
	Semilente	1–3 hrs	5–10 hrs	16 hrs
Intermediate acting	Isophane (NPH)	2–4 hrs	6–12 hrs	18–26 hrs
	Lente	2–4 hrs	6–12 hrs	18–26 hrs
Long acting	Protamine-zinc	4–8 hrs	14–24 hrs	28–36 hrs
	Ultralente	4–8 hrs	14–24 hrs	28–36 hrs

Insulin Analog

Analog	Onset	Peak	Doa
Lispro insulin	5–15 mins	1–2 hrs	2–3 hrs
Glargine insulin	1–3 hrs	No peak	24 hrs
Aspart	5–15 mins	1–2 hrs	2–3 hrs

Oral Hypoglycemic Agents

- Sulfonylureas:
  - Tolbutamide, chlorpropamide
  - Glibenclamide, glipizide, glimepiride, glyburide, glyclazide
  - Insulin secretogogues with increased insulin secretion
  - Duration of action: 12–18 hrs (48 hours for chlorpropamide).
- Biguanides:
  - Metformin mechanism of action:
    - Increases peripheral responsiveness to insulin
    - Reduces hepatic gluconeogenesis
    - Potentiates insulin release.
  - Duration of action of 6–8 hours
  - Can cause lactic acidosis
  - Contraindicated if serum creatinine > 1.5, liver failure, alcoholics, etc.
- Thiazolidinediones:
  - Mechanism of action: releases insulin and increases peripheral responsiveness to insulin
  - Roglitazone, pioglitazone
  - Duration of action: 3–5 hours
- α-glucosidase inhibitors:
  - Acarbose and miglitol
  - Reduces absorption of glucose from GIT
  - Can cause GI flatulence.
- Noninsulin secretogogues: Repaglinide, nateglinide, sitagliptin
- Ingap peptides:
  - Islet neogenesis associated protein (INGAP)
  - Causes regrowth of normally functioning islet cells.
- Inhaled insulin:
  - 1 mg = 3U of subcutaneous insulin
  - Has a rapid onset of action
  - Causes sore throat and dry mouth.

Diabetic Patient for CABG

- Perioperative mortality of 5% vs 1.5% for non-diabetics
- Tight glucose control regimen advocated conventionally
- Recent studies show no difference in mortality and morbidity than those who received conventional glucose management (treatment of blood glucose 200 mg%)
- In fact, statistically insignificant increase in incidence of stroke and death noted with tight control regimen
- Marked hyperglycemia may occur during CPB which may be unresponsive to insulin until rewarming
- Increased inotropic support and IABP may be required postbypass
- Administration of washed cells advocated as ACD or adenine supplemented blood may cause hyperglycemia
- Ill effects during surgery:
  - Reduced vasodilation in response to ischemia
  - Reduced coronary collateral circulation
  - Increased levels of reactive oxygen species, low NO levels
  - Diminished response to ischemic and anesthetic preconditioning.

DIABETIC KETOACIDOSIS[1,3,6,10,11,12]

Introduction

- Acute life threatening complication of diabetes mellitus
- Insulin is the *only anabolic hormone produced by pancreas*.

Incidence

- 15 episodes per 1000 diabetics
- More common in Type I diabetes mellitus
- Can also occur in Type II diabetes mellitus.

Diagnostic Criteria

- Blood glucose ≥ 250 mg/dl
- Osmolality ≥ 300–320 mosm/l
- Arterial pH ≤ 7.3
- Serum bicarbonate 15 mEq/l
- Moderate ketonemia.

Etiology

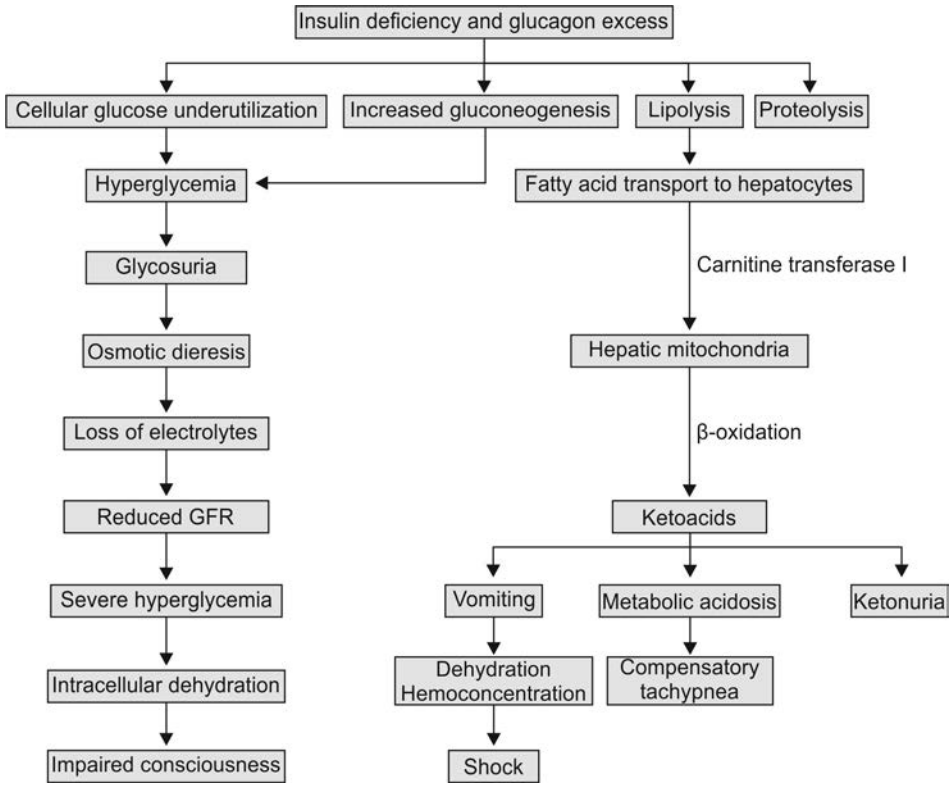
- About 25% patients have no clear precipitating cause
- Omission of daily insulin injection
- Infections:
  - Pneumonia
  - Gastroenteritis
  - Urinary tract infection
  - Pancreatitis
  - Sepsis.
- Infarction:
  - Myocardial infarction
  - Cerebrovascular accident

  - Mesenteric infarcts
  - Peripheral infarct.
- Trauma, surgery
- Hyperthyroidism
- Pregnancy
- Pulmonary embolism
- Drugs:
  - Steroid use
  - Cocaine abuse.

Ketones Produced

- Acetone
- Acetoacetic acid
- β-hydroxybutyric acid.

Pathophysiology[10]



Clinical Features

- Hyperglycemia:
  - Causes increased serum osmolality
  - Osmotic diuresis
  - Hyponatremia, hypokalemia, hypocalcemia, hypomagnesemia
  - Hypochloremia, hypophosphatemia.
- Acidosis:
  - Hyperventilation, shortness of breath
  - ***Kussmaul's breathing if severe*** (fruity odor): *classic presentation*
  - Nausea, vomiting (also caused by raised PGE_2 and PGI_2)
  - Abdominal pain due to ileus, gastric distension/pancreatitis
  - Weakness, lethargy, obtundation, cerebral vasodilatation and edema, coma
  - Hypothermia due to peripheral vasodilatation (even if infection present)
  - Impaired myocardial contractility: Reduced cardiac output.
- Volume contraction:
  - Compensatory polyuria and polydipsia: *earliest symptom*
  - Orthostatic hypotension
  - Hypotension and tachycardia
  - Poor skin turgor, dry mucous membrane
  - Dehydration
  - Frank hypovolemic shock.

Investigations

- Leukocytosis due to hemoconcentration
- ECG: Sinus tachycardia/hypokalemia features
- Blood glucose:
  - Usually 300 mg/dl
  - Lower if impaired gluconeogenesis, as in alcoholics/liver failure.
- Urinary glucose
- Renal function tests:
  - Increased due to fatty acid infiltration of liver
  - Prerenal azotemia
  - Interference from ketone bodies causes spurious elevation
- Liver function tests due to fatty acid infiltration of liver
- Raised serum CPK, amylase, triglycerides, lipoproteins
- ABG/VBG:
  - Wide anion gap metabolic acidosis
  - Compensatory hypocapnea may occur
  - Metabolic alkalosis possible due to vomiting and diuresis
  - Usually venous blood gas suffices for follow-up of therapy
  - ABG required only for follow-up of critically ill patients
  - (ABG pH – VBG pH) = 0.3
  - Anion gap is *most accurate* determinant of recovery.
- *Nitroprusside stick test*:
  - For blood and urine ketone bodies
  - Only detects acetoacetic acid
  - May increase after treating DKA as β-hydroxy butyric acid gets converted to acetoacetic acid
  - Thus only initial ketone detection in urine is necessary as subsequent measurement may yield spurious results.
- Serum electrolytes:
  - Potassium:
    - Initial potassium at presentation maybe normal or high due to:
      - Metabolic acidosis causing extracellular shift of K^+ ions
      - Increased intravascular osmolarity
      - Prerenal azotemia.
    - Initial hypokalemia at presentation indicates severe total body potassium depletion due to osmotic renal losses.
  - Others:
    - Hyponatremia
    - Hypomagnesemia
    - Hypocalcemia
    - Hypochloremia
    - Hypophosphatemia
    - These may be masked due to hemoconcentration
    - Dyselectrolytemias manifest on initiating therapy, usually after 24 hours.

Differential Diagnosis

- Hypoglycemia
- Nonketotic hyperosmolar coma
- High anion gap metabolic acidosis
- Starvation ketoacidosis
- Alcoholic ketoacidosis
- Lactic acidosis
- Uremic ketoacidosis
- Ingestion of salicylates, ethanol, ethylene glycol.

Treatment[1,10]

Surgery is done only if underlying surgical condition will exacerbate acidosis

- Monitors:
  - Blood glucose levels every 1–2 hours
  - Electrolytes, ABG and anion gap every 4 hours
  - Vital signs, respiration, CNS status and intake-output chart every 1–2 hours
  - CVP considered if elderly patient/heart disease present
  - Continuous ECG monitoring.
- General:
  - 1 or 2 large bore IV cannula 16–18 G inserted
  - Nasogastric tube inserted if vomiting/altered mental status
  - ET intubation and CMV if significant respiratory distress present
  - Active warming if hypothermia
  - Foleys catheterization.
- Goals of therapy: DKA has resolved if:
  - pH > 7.3
  - HCO_3 > 18 mEq/l
  - Blood glucose < 200 mg/dl
- Fluids:
  - Average fluid deficit in DKA is 50–100 ml/kg (5–10 L)
  - This is the *first priority in treatment* of DKA

- Choice of fluid:
  - NS recommended for initial resuscitation
  - Hypotonic D½NS:
    - Reduces tendency to develop hyperchloremic MA following treatment with NS
    - Added if blood glucose < 300 mg/dl after initial resuscitation.
  - D5 added when blood glucose is 250 mg/dl to be given at 100 ml/hr.
- Rate of administration:
  - 250–500 ml/hr depending on degree of hypovolemia
  - One third of fluid deficit corrected over first 6–8 hours
  - Remaining two thirds given over next 24 hours
  - Alternative regimen:
    - Two liters over first 2 hours
    - Two liters over next 2–6 hours
    - Two liters over next 6–12 hours
    - Remaining deficit corrected over next 12 hours
    - If volume depletion is not severe, 500 ml/hr given for 4 hours.

- Insulin:
  - Second priority unless K+ < 3.3 meq/l
  - Goal of therapy: Blood glucose 150–200 mg/dl
  - Rate of infusion:
    - Initial bolus of 0.15 IU/kg or 0.4 IU/kg IM
    - Rate of infusion after bolus dose:
      - (Blood glucose)/150 IU/hr
      - (Blood glucose)/100 IU/hr, if:
        - Infection
        - Concurrent steroids
        - BMI 35
  - Duration of infusion: continued until:
    - pH 7.3
    - Anion gap normalized (at least 12 hours usually)
    - Ketonemia resolved (at least 12–48 hours).
  - Method of infusion:
    - Continuous IV infusion of regular insulin
    - Prepared as 100 U insulin in 100 ml of NS
    - Insulin binds to plastic tubing
    - So, first 25 ml of this solution should be discarded
    - Drip is placed at a port closest to skin
    - IM/SC insulin avoided as absorption is erratic due to vasoconstriction in response to hypovolemia.
  - Insulin resistance:
    - Occurs due to infection usually
    - Suspected if blood glucose reduces by 50–70 mg/in first hour
    - Increasing infusion rate, IV bolus of 0.2–0.4 U/kg tried
    - Volume expansion with IVF also makes cells more responsive to insulin.
  - Stopping infusion:
    - Overlap period:
      - When S/C intermediate/long acting insulin given along with infusion of regular insulin
      - Usually started when patient resumes oral feeds.
    - If adequate insulin levels are not reached by S/C route before stopping infusion, DKA relapses.
  - Maximum rate of decline of blood glucose is 75–100 mg/dl/hr
  - Delay insulin therapy by 30 min after K^+ correction if serum K^+ < 3.3 meq/l
- Potassium:
  - Third priority for treatment unless K^+ < 3.3 meq/l
  - Usually K^+ deficit of 3–5 meq/kg is present
  - For each 0.1 change in pH, serum K^+ changes 0.5 meq/l inversely
  - Goal is to maintain K^+ between 4–5 meq/l during acute phase of treatment
  - Intracellular deficit is replaced over many days.

Serum potassium	Rate of administration
More than 5 meq/l	Nil until less than 5 meq/l with good urine output
3.3–5 meq/l, urine > 0.5 ml/kg/hr	10 meq/hr for at least 4 hours
Less than 3.3 meq/l	15–20 meq/hr IV
	Insulin therapy initiated 30 minutes later

  - Potassium phosphate/potassium acetate used to prevent hyperchloremia
  - Oral K^+ supplements started as soon as patient takes oral feeds.
- Phosphate:
  - Monitored on presentation and 24 hours into therapy
  - Corrected only if serum $PO_4^{3-} \leq 1$ mg/dl
  - Usually oral phosphate supplementation is enough

  - No established role of IV phosphate supplementation in emergency department
  - IV dose: 0.2–0.68 mmol/kg IV over 12 hours
  - PO dose: 30 mmol/day (1 g/day)
- Magnesium:
  - Monitored on presentation and 24 hours into treatment
  - Treated only if serum Mg^{2+} < 1.2 meq/l or patient is symptomatic
  - Oral MgO 60–90 meq/day
  - IV $MgSO_4$ (1–2 g over 15 min followed by 250–500 mg/hr).
- Bicarbonate:
  - Routine use in DKA not recommended
  - Indications: ***ADA recommendations***:
    - If pH < 7 after initial resuscitation 50 meq/l in 200 ml ½ NS over 1 hour
    - If pH < 6.9, 100 meq/l in 400 ml ½NS over 2 hours
  - Advantages of bicarbonate:
    - Improved myocardial contractility
    - Elevated VF/VT threshold
    - Improved catecholamine tissue response
    - Reduced work of breathing.
  - Disadvantages of bicarbonate:
    - Worsens hypokalemia
    - *Paradoxical CNS acidosis* due to conversion to CO_2 in CSF
    - Worsening intracellular acidosis
    - Na^+ overload and hypertonicity
    - Shift to left of oxyhemoglobin dissociation curve
    - Impaired tissue oxygenation
    - Delayed recovery from ketosis
    - Increased serum lactate levels
    - Precipitates cerebral edema.
- Others:
  - Treat precipitating cause
  - DVT prophylaxis in high-risk patients.

Prognosis

- Less than 5% mortality
- Increased mortality if:
  - Precipitating cause is MI/infection
  - Increased BUN
  - Increased blood glucose
  - Blood HCO_3^- < 10 meq/l

Complications

- Aspiration in comatose patients
- Vascular stasis, DVT and pulmonary embolism
- ARDS due to fluid therapy
- Cerebral edema (very common) and intracranial hemorrhage
- Sepsis, upper GI bleed
- Complications of therapy:
  - Hypoglycemia
  - Hypokalemia
  - Hypophosphatemia
  - Resistant metabolic acidosis
  - Hyperchloremic nonanion gap metabolic acidosis (common).

Risk of General Anesthesia in Uncorrected DKA

- Increased risk of cardiac arrest due to:
  - Hyperkalemia
  - Severe myocardial depression due to metabolic acidosis
  - Depressant action of anesthetics.
- Increased risk of hypotension and arrest if SAB given due to severe hypovolemia
- Myocardial depression is unresponsive to catecholamine therapy.

HYPEROSMOLAR NONKETOTIC SYNDROME[1,6,10,11,12]

Introduction

- Syndrome of severe hyperglycemia, hyperosmolality and lack of ketonemia in patients with poorly controlled or undiagnosed type II DM
- Also called:
  - Hyperosmolar hyperglycemic state (HHS)
  - Hyperosmolar hyperglycemic nonketotic syndrome (HHN).

Definition

- Serum glucose ≥ 600 mg/dl
- Plasma osmolality ≥ 315 mosm/kg
- Serum bicarbonate ≥ 15 meq/l
- Arterial pH ≥ 7.3
- Serum ketones negative/mildly positive in a 1:2 dilution.

Precipitating Factors

- Central nervous system:
  - Cerebrovascular events
  - Infections.

- Cardiovascular:
  - Myocardial infarction
  - Congestive cardiac failure.
- Respiratory system:
  - Pulmonary emboli
  - Pneumonia.
- Gastrointestinal:
  - GI hemorrhage
  - Parenteral/enteral feeds
  - Pancreatitis
  - Mesenteric ischemia.
- Genitourinary:
  - Renal insufficiency
  - Peritoneal/hemodialysis
  - Urinary tract infections.
- Drugs:
  - Diuretics, lithium
  - β-blockers, mannitol
  - Cimetidine, glucocorticoids.
- Others:
  - Infections, burns
  - Rhabdomyolysis, heat-related illness.

Pathophysiology

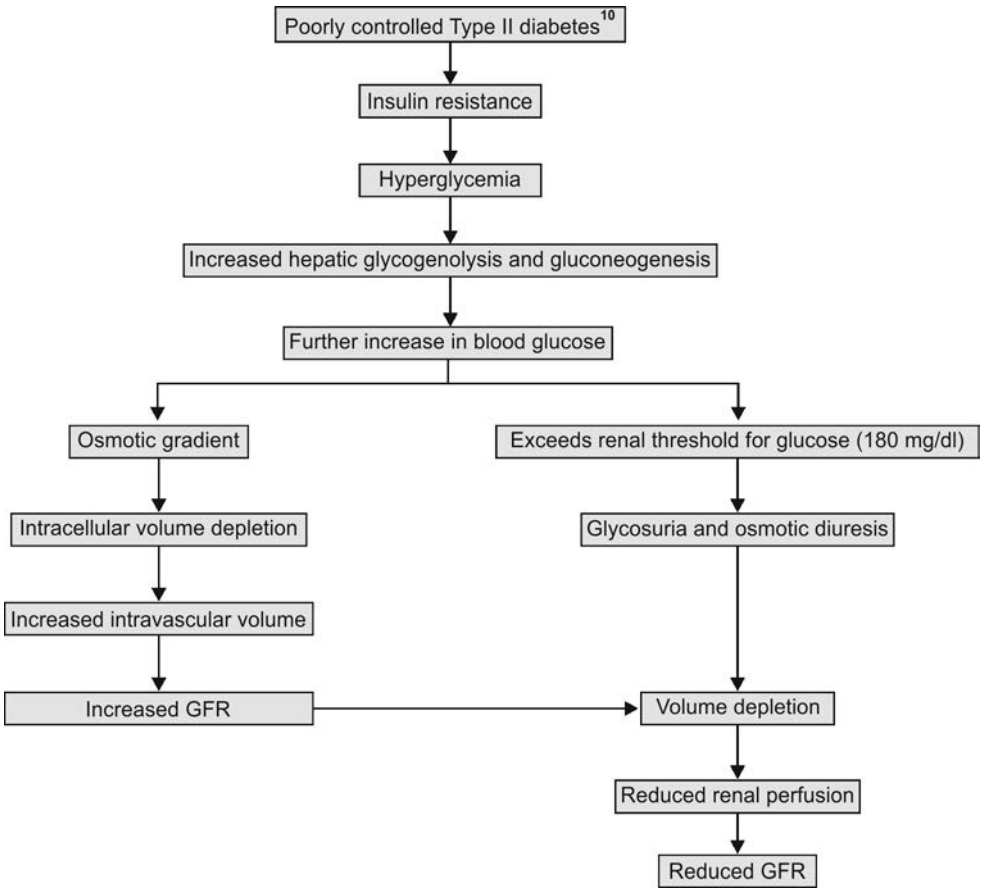
Three main causes of HONC:

- Reduced insulin utilization
- Increased hepatic gluconeogenesis and glycogenolysis
- Impaired renal glucose excretion

Characteristic[10]	DKA	HONC
Plasma glucose	More than 250	More than 600
Arterial pH	Less than 7.3	More than 7.3
Serum bicarbonate	Less than 15	More than 15
Urine ketones	Moderate	Small
Serum ketones	Moderate	Small
Serum osmolarity	300–320	More than 320
Anion gap	More than 10	Less than 12
Alteration in sensorium	Alert to stuporous	Stuporous/comatose

Clinical Features

- Symptoms:
  - Insidious onset of polyuria, weight loss and reduced oral intake



  - Elderly patient with history of poorly controlled type II DM
  - Weakness, anorexia, fatigue, cognitive impairment
  - Dyspnea, cough, pneumonia, UTI
  - History of underdosing/non-compliance with insulin.
- Signs:
  - Poor skin turgor, dry mucous membrane, sunken eyes
  - Hypotension, tachycardia, shock
  - Seizures (focal/generalized) coma, altered mental status
  - Tremors, clonus, hypo/hyperreflexia, positive plantar response
  - Hemiplegia/hemisensory defects
  - Normothermia/hypothermia due to vasodilation.
- Notably absent symptoms:
  - Nausea and vomiting
  - Abdominal pain
  - Kussmaul's respiration.

Investigations

- Definitive investigations:
  - Blood glucose ≥ 600 mg/dl
  - Serum osmolarity ≥ 320 mosm/l with absent ketone bodies
  - Increased BUN and serum creatinine due to prerenal and renal azotemia
  - Electrolytes:
    - Hypo/hyper/normal Na^+
    - Hypokalemia
    - Hypomagnesemia
    - Hypophosphatemia
  - ABG: Anion gap metabolic acidosis in 50% patients
  - Complete blood count
- Ancillary investigations:
  - Blood/sputum/urine culture
  - Liver function tests, pancreatic enzyme determination
  - Cardiac enzymes, ECG
  - Chest X-ray, CT head
  - Thyroid function, coagulation profile
  - Lumbar puncture.

Treatment

- Goals:
  - Treat underlying cause
  - Correct hypovolemia
  - Restore tissue perfusion
  - Correct electrolyte abnormalities
  - Gradual correction of hyperglycemia and osmolarity.
- Monitor:
  - Central venous pressure, urine output
  - BP, ECG, pulse oximetry
  - Serum K^+ every hour until steady state achieved
  - Blood glucose hourly
  - CT brain and mental status assessment for cognitive impairment.
- Fluid resuscitation:
  - Fluid deficits on an average 20–25% of TBW or 8–12 liters
  - Normal saline most appropriate for replacement initially
  - Once hemodynamically stable, use ½NS
  - One half of deficit replaced over 12 hours and balance over next 24 hours
  - Rate of correction according to associated renal and cardiac impairment
  - Rate of correction:
    - 500–1500 ml/hr during first 2 hours followed by 250–500 ml/hr if mild hypotension
    - 4–14 ml/kg/hr if moderate-sever hypotension.
- Electrolytes:
  - K^+ replacement done once urine output is adequate
  - Replaced as potassium phosphate to prevent hypophosphatemia
  - Replace at 10–20 meq/hr, until $K^+ \geq 3.3$ meq/l
  - Phosphate and magnesium usually self-correct and require no treatment.
- Insulin:
  - Volume replacement to precede insulin therapy
  - On administration of insulin, intravascular volume may decrease further
  - Continuous infusion after bolus of 0.1 U/kg at 0.1 U/kg/hr
  - Blood glucose reduces at steady rate of 50–70 mg/dl/hr
  - Once BG < 250 mg%:
    - IV solution changed to D5½NS
    - Insulin infusion reduced to half or 0.05 U/kg/hr.
  - Continue insulin until patient mentally alert and osmolarity < 315 mosm/l
  - Maintain blood glucose between 250–300 mg/dl.

- Postoperative care:
  - If patient is NPO, continue IV insulin
  - Supplement with subcutaneous insulin as needed
  - When patient can eat give SC insulin or shift to previous insulin regimen
  - Look for precipitating causes.

HYPOGLYCEMIA[1,8,10]

Introduction

Diagnosed by ***Whipples triad*** which consists of:
- Symptoms consistent with diagnosis
- Usually occurs at serum glucose < 50 mg/dl
- Resolves following glucose administration.

Etiology

- Fasting hypoglycemia:
  - Critical illness:
    - Hepatic failure, renal failure
    - Cardiac failure, sepsis.
  - Drugs:
    - Insulin, ethanol, quinine
    - Sulfonylureas, salicylates.
  - Hormone deficiencies:
    - Cortisol, glucagon
    - Growth hormone, epinephrine.
  - Endogenous hyperinsulinism:
    - Insulinoma, insulin secretogogue
    - β-cell tumors, autoantibodies to insulin
    - Non β-cell tumors.
  - Disorders of infancy:
    - Transient intolerance of fasting
    - Congenital hyperinsulinism.
- Postprandial (reactive) hypoglycemia:
  - Alimentary/postgastrectomy
  - Noninsulinoma pancreatogenous hypoglycemia syndrome
  - Hereditary fructose intolerance
  - Galactosemia
  - Other causes of endogenous hyperinsulinism
  - Idiopathic.

Clinical Features

- *Hyperepinephrinemic/autonomic/sympathomimetic*:
  - Sympathetic symptoms:
    - Anxiety, irritability, palpitations, nervousness
    - Tremors, nausea and vomiting, tachycardia, HTN.
  - Cholinergic symptoms:
    - Sweating, salivation
    - Bradycardia, paresthesias
    - Changes in pupillary size.
- *Neuroglycopenic*:
  - Altered consciousness, lethargy, unresponsiveness
  - Behavioral changes, confusion, agitation
  - Seizures, focal neurodeficits.

Differential Diagnosis

- Stroke/TIA
- Traumatic brain injury
- Seizure disorder
- Brain tumors
- Psychosis, hysteria
- Sympathomimetic drug ingestion.

Prevention

- Stop/reduce dose of offending drugs
- Treat critical illness
- Replace GH/cortisol if deficient
- Surgery/chemotherapy/radiotherapy for tumors
- Frequent feeding and avoidance of fasting
- Intake of uncooked corn starch at bed time
- Overnight intragastric infusion of glucose in some patients.

Treatment

- Glucose supplementation:
  - Intravenous supplementation:
    - Initially 1 gm/kg body weight dextrose as D50W
    - Followed by D10W infusion to maintain serum glucose > 100 mg/dl
    - Each 50 gm D50W solution increases blood glucose by 60 mg/dl
    - Repeat glucose every 30 minutes for first 2 hours to detect ***rebound hypoglycemia.***
  - Oral supplementation:
    - Useful in conscious and oriented patients
    - 300 gms/1200 Kcal of carbohydrates given as snacks.
- Glucagon:
  - 1 mg given IM/IV
  - Response is slower and short lived (mental status normalizes after 7–10 min)

  - Useful in diabetes/if IV access not available
  - Ineffective in alcoholics, elderly and others with low glycogen stores.
- Steroids:
  - 100–200 mg hydrocortisone IV
  - Especially useful if resistant hypoglycemia/ signs of adrenal insufficiency.
- Octreotide:
  - Somatostatin analog
  - Used for sulfonylurea induced hypoglycemia
  - 50–125 µg SC initially followed by 125 µg/hr infusion
  - Only recommended after glucose therapy has been initiated.
- Thiamine:
  - 100 mg IV thiamine given with glucose in severe nutritional deficiency as it could precipitate ***Wernicke's encephalopathy***
  - Thiamine acts as coenzyme in conversion of pyruvate to α-ketoglutarate which is important to generate ATP (main source of ATP to CNS)
  - Depletion of thiamine causes Wernicke's syndrome.

CHAPTER

9

Pain and Regional Anesthesia

ASSESSMENT OF PAIN[1,2,3]

Introduction

- Pain is what the patient says it is: ***John Bonica***
- Biggest problem in the assessment of pain is that it is subjective
- While patients with postoperative pain may require significantly lesser evaluation, those with chronic pain may require more extensive evaluation
- WHO (1996) stated that upto 80% of patients may be inadequately treated for pain.

History

- History of presenting illness:
  - Onset: Sudden (fracture pain)/insidious (migraine)
  - Duration: Acute or chronic
  - Type of pain:
    - Neuralgic (shooting/stabbing)
    - Deafferentation pain (burning)
    - Malignancy (dull and boring)
  - Site: May be referred pain
  - Radiation of pain
  - Continuous/intermittent/occasional
  - Aggravating/relieving factors
  - Associated bowel and bladder disturbances, numbness and weakness
  - Previous history of interventions and the efficacy of such treatment.
- Personal history:
  - Job satisfaction, work compensation
  - Habits: Tobacco chewing, smoking, alcohol
  - Marital life, family disputes, children, menstrual hisotry.

Physical Examination

- Pallor, icterus, cyanosis, clubbing
- Lymphadenopathy, edema, rashes
- Vital signs
- Central nervous system:
  - Higher mental functions: Sensory and motor system
  - Cranial nerve examination: Reflexes and gait
- Trigger point detection
- Straight leg raising test for back pain with radiculopathy
- Paraspinal tenderness for facetal problems
- Tinels test for nerve compression.

Evaluation of Severity of Pain

Categorical Evaluation

- Pain graded as absent, mild, moderate, severe and excruciating
- Simple but not sensitive test.

Numerical Scale

- 11 point scale where 0 is no pain and 10 represents worst pain
- Unidimensional scale.

Visual Analogue Scale

- Most popular scale as it is easiest and simplest
- Pain assessment done as self report on single dimension
- Consists of a 10 cm scale with digits from 1 to 10
- There are no gradations on the side which the patient sees
- The 100 gradations are only visible to the person evaluating the pain

- Person asked to compare current pain to worst pain he has ever faced in life (like labor pain, surgical pain/fracture pain, etc)
- Useful for pain relief follow up by asking the patient to compare pre-treatment and post-treatment pain.

McGill's Pain Questionnaire

- Assesses pain in a multimodal way
- Measures pain in three ways:
  - Sensory: Discriminative (nociceptive pathway)
  - Motivational: Affective (reticular and limbic pathway)
  - Cognitive: Evaluative (cerebral cortex).
- Contains a checklist of words describing symptoms
- Checklist contains 20 sets of descriptive words:
  - Aspects 1–10 represents sensory aspects of pain
  - Aspects 11–15 represent affective aspects
  - Aspect 16 represents evaluative aspect
  - Aspects 17–20 other miscellaneous aspects.
- Patient selects the sets which apply to his/her pain and circles the words in each set which best describe his pain
- A numerical value is attached to each word
- The sum of all points gives a rank value which is called ***Pain Rating Index (PRI)***
- Each aspect of pain can also be evaluated individually
- Can also be used as a diagnostic tool.

Breakthrough Questionnaire

To assess breakthrough pain in cancer patients.

Body Chart

- Different sites of pain are marked at the time of evaluation
- Marking is done along with the nature of each, so that it is available at the time of review
- Duration, intensity, effect of movement, superficial/deep nature of pain and effect on sleep recorded on chart.

Evaluation of Etiology of Pain

- Plain radiography: Inexpensive, quick and can be done without preparation
- Ultrasonography: Evaluation of abdominal organs
- Doppler: Evaluates arterial and venous systems
- CT scan:
  - Detects acute hemorrhage
  - Gives excellent bony detail
- MRI:
  - Good for soft tissue characterization
  - Useful for diagnosis of nerve entrapment syndromes.
- Scintigraphy: For functional status of an organ
- Epiduroscopy:
  - Fiberoptic camera is inserted through sacral hiatus into lower epidural space
  - Camera guided upwards towards lower lumber discs and nerve roots
  - Allows color visualization of dura, blood vessels, fat, areolar tissue and pathological changes in epidural space.
- Electromyography:
  - Employs needle electrodes to record potentials in individual muscles
  - Muscle potentials are recorded while at rest and then as the patient is asked to move the muscle
  - Triphasic motor unit action potential is usually seen when the patient moves his muscle
  - Abnormal findings, as in denervation, include:
    - Persistent insertion potentials
    - Presence of sharp positive waves
    - Fibrillatory activity
    - Fasciculation potentials.
  - Abnormalities in muscles produces:
    - Changes in amplitude and duration of action potential
    - Polyphasic action potentials.
  - Can be used to:
    - Distinguish between neurogenic and myogenic disorders
    - Confirm diagnosis of entrapment syndrome, neural trauma and polyneuropathies
    - Localize lesion to spinal cord/nerve root/limb plexus/peripheral nerve.
- Nerve conduction studies:
  - Peripheral motor or sensory nerve is supramaximally stimulated
  - Needle electrodes record potentials in the appropriate muscles
  - Characteristics studied:
    - Latency:
      - Time between stimulation and onset of muscle potential
      - Measures fastest conducting motor fibers in the nerve
    - Amplitude: Indicates number of functional motor units
    - Duration: Reflects range of conduction velocities in the nerve.

  - Can distinguish between mononeuropathy and polyneuropathy:
    - Mononeuropathies due to trauma/compression
    - Polyneuropathis can be:
      - Demyelination neuropathies:
        - Due to inherited and autoimmune neuropathies
        - Causes slow nerve conduction with prolonged latency.
      - Axonal neuropathy:
        - Causes reduction in amplitude of action potential with preservation of conduction velocities
        - This neuropathy occurs due to toxic, inherited, traumatic and ischemic diseases.
      - Diabetic neuropathy: It is mixed type.
- Other investigations:
  - Arthrography
  - PET scan
  - Arteriography
  - Myelography.

Psychological Evaluation

- Important as patients with chronic pain often have psychological problems like:
  - Somatization disorder
  - Conversion disorder
  - Hypochondriasis
  - Depression.
- Determines contribution of affective and behavioral factors to perception of pain.

Waddell's Nonorganic Signs

- Consists of a group of physical signs which may indicate nonorganic/psychological component of low backache
- These are:
  - Tenderness: Superficial sensitivity to light touch over lumbar spine/tenderness over large area
  - Simulation: Axial loading where light pressure is applied to skull in upright position, simulated rotation of lumbar spine with shoulders
  - Distraction: More than 40 difference in sitting vs supine straight leg raising test
  - Regional disturbances:
    - Motor: Generalized giving way
    - Sensory: Nondermatomal loss of sensation to pin prick in lower limbs.
- Overreaction: Disproportionate pain response to testing
- Any individual sign marks its category as positive
- When three or more categories are positive, the finding is considered clinically significant
- Detects nonorganic component to pain but does not exclude organic cause.

Minnesota Multiphasic Personality Inventory

- Consists of a 566 item true-false questionnaire
- Defines patient's personality on 10 clinical scales
- Three validity scales identify patients who are deliberately trying to hide traits or alter results
- Test is lengthy and some questions may be insulting
- Cannot reliably distinguish organic and functional pain but gives an idea about the role of psychological factors.

Beck's Depression Inventory

Used to identify patients with major depression.

Symptom Check List 90

- 90 items problems checklist
- Allows examinee to rate symptoms of physical and emotional distress on a 5 point scale.

Multidimensional Pain Inventory (MPI)
Medical Outcomes Survey 36 Item Short Form (SF 36)
Pain Disability Index (PDI)
Oswestry Disability Questionnaire (ODQ)

Evaluation of Outcome of Pain

- Success of treatment regime can be decided only if a positive response lasts for more than 3 weeks
- Evaluation graded in terms of quality of life too and not just with the pain score.

PAIN EVALUATION IN CHILDREN[1,2,3,15]

Introduction

- Evaluation of pain in children is tricky as:
  - Pediatric patient may not be able to express pain in suitable words
  - Children may not reveal pain for fear of injections.
- Physiological fetal pain perception systems develop at around 26 weeks of gestation
- Babies have a mature nervous system, able to feel pain and which is unfortunately coupled with an immature ability to produce neurochemicals which can inhibit pain.

Clinical Assessment

- Mostly indirect assessment in neonates by observing physiological changes or behavioral responses of neonate/infant to pain
- Physiological changes:
  - Tachycardia
  - Tachypnea
  - Hypertension
  - Palmar diaphoresis
  - Behavioral changes:
    - Changes in facial expressions:
      - Eyebrow bulge
      - Eye squeeze
      - Nasolabial furrow
      - Streeting of mouth
      - Pursing of lips
      - Taut tongue
      - Chin quivering.
    - Changes in body movement: Diffuse body movement to noxious stimuli
    - Changes in type of cry.

Pain Measurement in Preschool Children

Happy-Sad Face Scale

- Also useful in illiterate people
- Shows child's face in different moods
- Child asked to select facial expression which best reflects pain expression
- Assesses affective and fear component of pain.

Oucher Scale

- Shows photos of a Caucasian child face with increasing levels of discomfort
- Child selects facial expression which best reflects their experience of hurt
- These photos are used for children who cannot count
- On the left is a numerical scale for older children who can count till 100.

Nancy-Hester's Poker Chip Pain Rating Scale

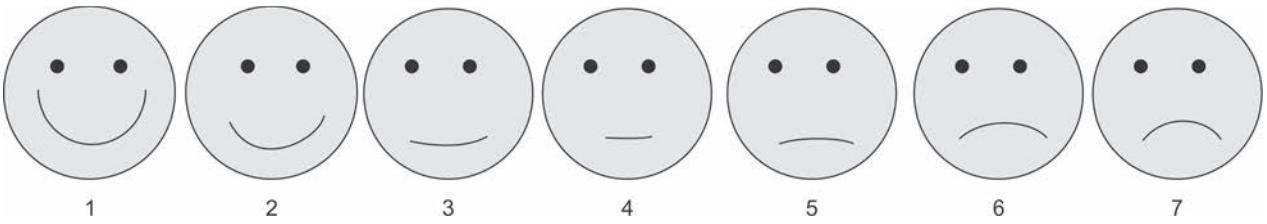
- Four red poker chips are aligned horizontally in front of child
- Child is told that the chips are pieces of hurt and that the 1st chip is just a little hurt, 2nd a little more hurt, and 4th is most hurt
- Ask the child how many pieces of hurt do you have and assess according to the response.

Color Scale

- Child asked to select a color using marker/crayons which is like their worst hurt, then a color like a little less hurt, even less hurt and finally no hurt
- A numerical value can be placed on each color
- Asking the child to select a color which is most like the pain they are currently experiencing can then assess pain intensity.

Wong-Baker's Faces Scale

Consists six faces ranging from very happy to tearful face.



Description[2,3,15]	Alert	No humor	Furrowed brow	Wrinkled nose	Slow blink	Eyes closed
	Smiling	Serious face	Pursed lips	Raised upper lip	Open mouth	Moaning
			Breath holding	Rapid breathing		Crying
Category	No pain	Pains little bit	Pains little more	Pains even more	Pains whole lot	Pains worst
Score	0	1	2	3	4	5
Alternate score	0	2	4	6	8	10



Activity Tolerance Scale

Pain[2,3,15]	Score
No pain	0
Can be ignored	2
Interferes with tasks	4
Interferes with concentration	6
Interferes with basic needs	8
Bedrest required	10

Comfort Scale

- Eight indicators used:
  a. Alertness
  b. Calmness/agitation
  c. Muscle tone
  d. Blood pressure
  e. Respiratory response
  f. Physical movement
  g. Facial tension
  h. Heart rate.
- Each indicator scored between 1–5 based on behavior exhibited
- Patient observed for 2 minutes and total score is calculated
- Ranges between 8–40
- Range between 17–26 indicates adequate sedation and pain control
- Useful in ICU environment.

FLACC Behavioral Pain Assessment Tool

- Uses Faces, Legs, Activity, Cry and Consolability (FLACC)
- Each of these is scored between 0–2 to provide a score ranging 0–10.

Cheops Scale
(Children Hospital of Eastern Ontario Pain Scale)

- *Gold standard* for comparative purposes
- Has 6 categories of behavior which are scored individually (0.2 or 1.3)
- These are then totalled for a score between 4–13
- Complicated and impractical to use.

Chipps Scale
(Children Infants Postoperative Pain Scale):

- Includes 5 behavioral items found to be consistently indicative of pain in children
- These items are:
  – Crying
  – Facial expression
  – Posture of trunk
  – Posture of legs
  – Motor restlessness.

Others

- Ladder scale
- Linear analogue scale
- Objective pain scale
- ***Abu-Saad*** pediatric pain assessment tool
- ***Varini-Thompson*** pediatric pain questionnaire
- Premature Infant Pain Profile (PIPP).

Pain Measurement in School Aged Children

- Able to read and write and comprehend what is explained to them
- Scales used are:
  – Six point (0–5) numerical verbal pain score: Used in children > 9 years to assess headache
  – 0–100 numerical scale
  – Visual analogue scale
  – Macgills pain questionnaire
  – Wong Bakers FACES pain rating scale
  – Comfort scale
  – Activity tolerance scale.

PHANTOM LIMB PAIN[1,2]

Introduction

- Phenomenon occurring in an amputated limb where sensation persists that the amputated limb is still there and moving like the other parts of body.
- In case of the limb, most of these sensations are painful and is made worse by stress, anxiety and weather changes.

- ***Phantosmia***: Perception of an odorant where none is there.
- ***Phantogeusia/dysgeusia***:
  - Distortion in the perception of a taste
  - Perception of a taste where there has been no tastant ingested.

Incidence

Occurs in up to 80% of amputations.

Location of Pain

- Peripheral limb following amputation
- Tooth pain following tooth extraction
- Breast pain following mastectomy
- Appendix following appendicectomy.

Pathogenesis

- Phantom limb pain occurs due to ***law of projection*** which states that no matter where a particular sensory pathway is stimulated along its course to the cortex, the conscious sensation produced is referred to the location of receptor
- The ends of the nerve cut at the time of amputation form nerve tangles called neuromas
- These may discharge spontaneously or when pressure is applied on them
- The impulses generated in them are in the nerve fibers which previously came from sense organs of the amputated limb
- Thus sensations are projected to where the receptors used to be.

Mechanism

Caused by central and peripheral mechanisms:

- Peripheral mechanisms:
  - Due to formation of neuromas
  - Increased C fiber activity in amputated limb
  - Increased Na^+ channel activation.
- Central mechanism: ***Reorganization of Somatosensory Cortex theory***:
  - Abnormal firing of internuncial neurons occurs, due to development of new synaptic connections in cerebral cortex
  - Area of somatosensory cortex representing the hand lies in close proximity to that representing the arm and face
  - Thus, when the hand is amputated, new synaptic connections are formed between the areas representing arm, hand and face
  - Thus, sensations from arm and face are transmitted to the amputated stump where the hand used to be.

Manifestations

- Pain may be immediate, occurring at the time of amputation
- Most commonly, pain occurs within first few days following amputation
- Pain is not felt all the time, only few days in a month
- Most sensations are of warmth, itching, squeezing, tingling
- Aggravated by stress, anxiety and weather changes
- 50% patients experience reduction in pain over time
- In remaining 50% patients, pain increases or remains unchanged.

Prophylaxis

- Preemptive analgesia is important as brain seems to implant sensation from preoperative state
- This can be done by:
  - Perioperative epidural infusion of opioids/local anesthetics/clonidine
  - Continuous brachial plexus block with memantine (an NMDA antagonist)
  - Opioids/neuroleptanalgesia.

Treatment

- Pharmacological methods:
  - Antidepressants
  - Neuroleptics
  - Sodium channel blockers
  - Opioids
  - Gabapentin (NMDA antagonist).
- Nonpharmacological methods:
  - Heat application
  - Relaxation techniques: Reduce stress
  - Massage of amputated area
  - Transcutaneous Electrical Nerve Stimulation (TENS)
  - Biofeedback
  - Spinal cord stimulation
    - Electrical stimulator is implanted under skin
    - Electrode is placed next to spinal cord
    - The nerve pathway in the spinal cord is stimulated
    - This interferes with pain impulses projected to the brain, which cause phantom limb pain.

POSTDURAL PUNCTURE HEADACHE[1,2,3]

Introduction

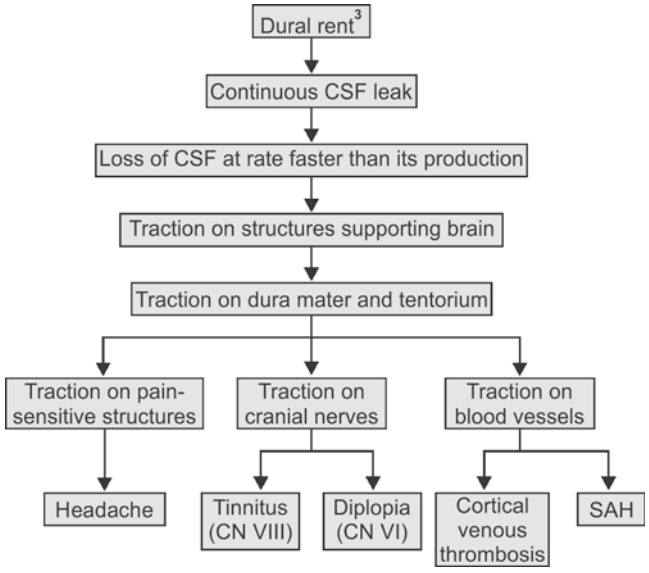
Headache resulting from any breach of the dura mater, occurring with an incidence as high as 25%.

Etiology

- Diagnostic lumbar tap
- Myelogram
- Spinal anesthesia
- Epidural wet tap.

Pathophysiology

- Dura is under longitudinal strain
- Thus, a slit which is oriented perpendicular to this longitudinal tension will be pulled open
- A slit oriented parallel to this tension will be pulled to close the slit.



Factors Increasing Incidence

- Age: More common in young patients
- Gender: Female more affected than males
- Pregnancy: More common in pregnant patients
- Needle size: More common with larger needles (27 or 25 G preferred)
- Needle bevel: Less when needle bevel is parallel to long axis of dura
- Needle type: More common with cutting tip than pencil tip (***Whitacres*** *needle preferred*)
- Dural punctures: More common with multiple punctures.

Clinical Features

- Headache:
  - Occurs 12–72 hrs following procedure
  - Usually occurs immediately after procedure
  - Bilateral, frontal/retro-orbital headache
  - May be occipital and extend into neck and shoulder
  - Associated with nausea and photophobia
  - *Hallmark* association with body position where headache increases with sitting/standing and reduced on lying down
  - Increased during coughing/staining.
- Associated features:
  - Tinnitus (CN VIII traction)
  - Diplopia (CN VI traction)
  - Cortical venous thrombosis
  - Subarachnoid hemorrhage rarely
  - Subdural hemorrhage rarely.

Management

- Conservative management:
  - Bed rest decreases the hydrostatic pressure which drives CSF leak
  - Adequate IV or oral fluid administration
  - Analgesics: NSAIDs, sumatriptan
  - Caffeine:
  - Stimulates CSF production and also causes vasoconstriction of intracranial vessels
  - 300–500 mg P.O/IV Q12H
  - Stool softeners and soft diet to minimize Valsalva straining.
- Invasive management:
  - Epidural blood patch:
    - Very effective in treating PDPH
    - 90% patients respond to single patch
    - 90% of initial nonresponders obtain relief from second patch
    - Done after giving a trial of conservative therapy for 12–24 hrs
    - Mechanism of action:
      - Forms a clot over the dural rent
      - This prevents further CSF leaks
    - Injected blood spreads over spinal segments more in the cranial direction
    - Technique requires two clinicians

- Epidural puncture is done at same space or one space lower
- Once in epidural space, 15–20 ml of blood is drawn from forearm under aseptic conditions
- Blood is slowly injected through the back until pain is felt in the back
- Patient placed supine for 1–2 hrs following procedure to reduce CSF leak from dural rent
- Prophylactic epidural patch not very effective in preventing PDPH
- Side effects of blood patch:
  - Backache
  - Radicular pain
  - Epidural hematoma
  - Bradycardia
  - Cranial nerve palsies.

– Epidurally administered fibrin glue is an effective alternative
– Epidural saline bolus/ACTH hormone requires further investigation
– Surgical closure of dural rent: Last resort.

PAIN THERAPY IN CANCER PATIENTS[1,2,3]

Introduction

Management of cancer pain is multifaceted and includes:

- Antineoplastic treatment
- Pharmacological management
- Interventional management
- Behavioral and psychological management
- Hospice care.

Mechanism of Cancer Pain

Somatic/Nociceptive Pain

- Originates from skin, muscle and bone
- Through A and C fibers
- For example, due to tumor infilteration of bone/joints.

Visceral Pain

- Originates from solid or hollow visceral organs
- Mediated by visceral sympathetic efferent fibers
- For example, due to obstruction of hollow viscus.

Sympathetic Pain

- Occurs after nerve or limb injury
- Associated with allodynia, hyperpathia, sudomotor dysfunction
- Poorly responsive to opioids
- For example, Radiation nerve injury.

Neuropathic Pain

- Sharp lancinating pain
- Poorly responsive to opioids
- For example, Vinca alkaloid induced neuropathy.

Causes

I. Cancer itself
II. Cancer therapy pain

- Chemotherapy:
  – Mucositis: Peripheral neuropathy
  – Constipation: Diarrhea
  – Abdominal cramps.
- Radiotherapy:
  – Mucositis
  – Peripheral neuropathy.
- Surgical treatment:
  – Postoperative pain: Phantom limb pain
  – Stump pain: Postmastectomy pain.

Assessment

- Simple Descriptive Pain Distress Scale
  – None
  – Annoying
  – Uncomfortable
  – Dreadful
  – Horrible
  – Agonizing.
- Numerical Pain Distress Scale
  – 0 – no pain
  – 5 – distressing pain
  – 10 – agonizing pain.
- Visual Analogue Scale
  – 0 – no pain
  – 10 – unbearable pain.

Modalities of Management

Pharmacological

- Analgesics:
  – NSAIDs
  – Opioids.
- Adjuvants:
  – Antidepressants

- Anticonvulsants
- Neuroleptics
- Corticosteroids
- Systemic local anesthetics
- α2 adrenergic agonists
- Botulinum toxin.

Nonpharmacological

- Injection techniques:
  - Somatic and sympatheic nerve blocks
  - Intrathecal and epidural neurolytics
  - Cryoanalgesia.
- Neuroablative techniques:
  - Radiofrequency denervation
  - Pituitary injection of alcohol.
- Neurostimulatory techniques:
  - Transcutaneous Electrical Nerve Stimulation: TENS
  - Spinal Cord Stimulation: SCS
  - Intracerebral Stimulation: ICS.
- Complementary/alternative approaches:
  - Massage
  - Hot/cold sponges
  - Paraffin baths
  - Fluidotherapy.
- Psychological interventions:
  - Lifestyle changes.
  - Yoga
  - Biofeedback relaxation.
- Palliative:
  - Deep X-rays
  - Tumor excision
  - Radiotherapy.
- Rehabilitation approaches.

Pharmacotherapy

PCT and NSAIDs

No	Drug	Dosage	Side Effects
1	Acetami-nophen	650 mg Q4H PO	
		10 – 15 mg/kg Q4H PO	
		15 – 20 mg/kg Q4H PR	
2	Ibuprofen	400 – 600 mg Q6H PO	Peptic ulceration
		10 mg/kg Q6H PO	Gastric erosions
			Nausea vomitting
3	Ketorolac	60 mg initially	Bleeding diathesis
		30 mg Q6H IM	Thrombocytopenia
		Not to exceed 5 days	Hepatorenal dysfunction

Opioids

No	Drug[2,3]	Oral	Parenteral	Side Effects
1	Morphine	30 mg Q3-4H	10 mg Q3-4H	Sedation
2	Morphine SR	90–120 mg Q12H	NA	Nausea constipation
3	Hydromorphone	6 mg Q3-4H	1.5 mg Q3-4H	Respiratory depression
4	Methadone	20 mg Q6-8H	10 mg Q6-8H	Myoclonus
5	Codeine	60 mg Q3-4H	60 mg Q2H IM or SC	Tolerance
6	Oxycodone	10 mg Q3-4H	NA	Physical dependance
7	Fentanyl	Trandermal 25/50/100 μ (lasts for 72 hrs)		GI toxicity

Adjuvant Analgesics

No	Drug[2,3]	Dose	Indications
1	Dexamethasone	High dose regimen–100 mg/day	Acute severe pain
		Low dose regimen: 10–20 mg/day PO/IV	Bone pain
			Raised ICT, visceral pain
2	Prednisone	40–100 mg PO	Bone pain
			Raised ICT, visceral pain
3	Carbamazepine	200–1600 mg PO	Trigeminal neuralgia
			Neuropathic pain
4	Phenytoin	300–500 mg PO	Neuropathic pain
5	Amitryptiline	25–150 mg PO	Neuropathic pain with depression

Contd…

Contd…

No	Drug[2,3]	Dose	Indications
6	Lidocaine	5 mg/kg IV/SC	
7	Mexiletene	450–600 mg PO	
8	Dextroamphetamine	5–10 mg PO	
9	Methylphenidase	10–15 mg PO	
10	Ketamine	0.15 mg/kg/hr IV	Refractory pain resistant to opioids
11	Gabapentin	100–300 mg/day upto 3600 mg/day	Trigeminal neuralgia
			Post herpetic neuralgia
			Diabetic peripheral neuropathy
12	Pregabalin	75–150 mg Q12H PO	Trigeminal neuralgia
			Post herpetic neuralgia
			Diabetic peripheral neuropathy

Nonpharmacological Approaches

- Physical Modalities:
  - Rehabilitation
  - Heat application
  - TENS
  - Therapeutic exercise and massage.
- Behavioural Interventions:
  - Meditation
  - Hypnosis
  - Music therapy
  - Systemic desensitization.
- Complementary Medicine:
  - Acupuncture.

Radiation and Chemotherapy

Palliative Surgeries

Special Procedures

Neurolytic Neural Blockade

No	Type of pain	Type of block
Peripheral Nerve Blocks		
1	Facial and neck pain	Trigeminal Nerve, Glossopharyngeal Nerve
2	Chest and abdominal wall	Intercostal/paravertebral nerve block
3	Intrathoracic malignancy	Intercostal Nerve block
4	Perineal	Sacral Nerve
Sympathetic Nerve Blocks		
1	Head, neck, arm pain	Stellate ganglion block
2	Pancreas, upper abdominal pain	Celiac plexus block
3	Pelvic pain	Hypogastric plexus block
4	Leg pain	Lumbar sympathetic block

Transcutaneous Electrical Nerve Stimulation

- Stimulates larger afferent fibers
- May provide pain relief in neuropathic cancer pain
- Electrodes are placed in the same dermatome as the pain
- Stimulated periodically by direct current from a generator.

Spinal Cord Stimulation

- Activates descending modulating systems
- Inhibits sympathetic outflow
- Most effective for neuropathic pain
- Electrodes placed in epidural space and connected to subcutaneous generator.

Intracerebral Stimulation

- Electrodes implanted into periacqueductal and periventricular grey matter
- May cause infections and hemorrhage.

Intrathecal Pumps

- Used in patients with unmanageable side effects of opioids
- Should have life expectancy > 3 mths
- 1/10 th IV dose required for epidural pumps
- 1/100 th IV dose required for intrathecal pumps
- Expensive procedure.

Radiofrequency Ablation

- Radiofrequency current into affected nerve destroys it
- Used for intercostal N, trigeminal N, paravertebral N.

PATIENT-CONTROLLED ANALGESIA[1,2,3]

Introduction

Technique of pain management which allows patient to administer their own analgesics on demand.

Types

- Patient Controlled Intravenous Analgesia (PCA)
- Patient Controlled Epidural Analgesia (PCEA)
- Patient Controlled Intranasal Analgesia (PCINA)
- Patient Controlled Transdermal Analgesia (PCTA)
- Patient Controlled Regional Analgesia (PCRA)
- Subcutaneous Patient Controlled Analgesia.

Variables

Bolus Dose/Demand Dose

- Dose which is delivered when patient activates PCA due to severe pain
- Optimal dose to be chosen
- Optimal dose causes good analgesia with minimal side effects
- High dose can cause respiratory depression.

Lockout Interval

- Time from end of delivery of first dose until machine responds to another demand
- Effectively, a safety feature of PCA pumps
- Ranges from 5–20 minutes
- Affects efficacy of PCA
- Too long lockout: Inadequate analgesia
- Too short lockout: Increased side effects.

Background Infusion

- Improves analgesia and prevents arousal with severe pain
- Usually reserved for opioid tolerant patient with chronic pain
- Also used in pediatric population
- Opioids will be delivered regardless of level of sedation.

Dose Limits

- Safety feature
- Limits maximum amount of drug that can be delivered over a certain period
- 1 hr and 4 hr limits present
- Commonly 10 mg in 1 hr and 30 mg in 4 hrs for morphine
- Prevents overdose of analgesics.

Loading Dose

- Total opioid dose initially required to provide analgesia
- Administered by presetting PCA pump.

Assessment During PCA

- Analgesia levels: VAS scores
- Sedation levels: ***Richmond Agitation Sedation Scale*** (RASS Score)
- Respiratory assessment
- Pulse oximetry: Especially for obesity, OSAS, old patient
- Capnography: For respiratory depression.

Indications

- Postoperative pain management
- Chronic pancreatitis
- Post trauma
- Burns
- Sickle cell crisis.

Contraindications

- Pulmonary disease
- Obstructive sleep apnea
- Renal/hepatic dysfunction
- Congestive cardiac failure
- Closed head injury
- Altered mental status
- Lactating mothers
- Very young children (< 5 yrs)
- If > 2 risk factors are present, PCA avoided in standard dosing regimens.

Advantages

- Superior pain relief with less medications
- Reduces delay between request for pain medication and administration
- Improves postoperative pulmonary function
- Reduces postoperative pulmonary complications
- Less potential for overdose when smaller doses are prescribed
- Lesser daytime sedation
- Higher patient acceptance and satisfaction
- Improved sleep pattern
- Earlier postoperative mobilization.

Disadvantages

- Narcotic dependance
- High cost: Requires special equipment
- Patient factors:

- Requires mental alertness
- Physical ability to press the button
- Ability to understand concept of PCA
- Caution required in patients with liver/renal/pulmonary disease.

Complications

- Nausea, vomiting
- Constipation
- Pruritis
- Excessive sedation
- Faulty equipment:
  - Failure of antireflux valve
  - Faulty program
  - Patient tampering
  - Use of pump close to MRI machine.

Drugs Used

- Most commonly morphine
- Hydromorphone
- Fentanyl
- Sufentanyl
- Tramadol.

Regimens

IV PCA

No	Opioid	Demand dose	Lockout	Basal infusion
1	Morphine	1–2 mg	6–10 min	0–2 mg/hr
2	Hydromorphone	0.2–0.4 mg	6–10 min	0–0.4 mg/hr
3	Fentanyl	20–50 µg	5–10 min	0–50 µg/hr
4	Sufentanyl	4–6 µg	5–10 min	0–8 µg/hr
5	Tramadol	10–20 mg	6–10 min	0–20 mg/hr

PCEA[1,3]

No	Drug	Continuous	Demand dose	Lockout interval
1	0.05% bupivacaine	4 ml/hr	2 ml/hr	10 min
	5 µg/ml fentanyl			
2	0.0625% bupivacaine	4–6 ml/hr	3–4 ml/hr	10–15 min
	5 µg/ml fentanyl			
3	0.1% bupivacaine	6 ml/hr	2 ml/hr	10–15 min
	5 µg/ml fentanyl			
4	0.2% ropivacaine	5 ml/hr	2 ml/hr	20 min
	5 µg/ml fentanyl			

Adjuvants to PCA

- Ketamine maybe added to reduce side effects and inprove analgesia
- Antiemetics like droperidol and cyclizine added to reduce nausea.

PREEMPTIVE ANALGESIA[1,2,3]

Introduction

Antinociceptive treatment that prevents establishment of altered central processing of afferent input from injuries.

Pathophysiology

- Tissue injury produces biphasic response
- ***Peripheral sensitization:***
  - Due to local release of neurotransmitters
  - Substance-P, prostaglandins, bradykinins, serotonin, histamine.
- ***Central sensitization:***
  - Continued barrage of afferent input from site of injury
  - Activation of NMDA receptors in spinal cord occurs
- Noxious stimuli sensitize nervous system to subsequent stimuli
- Normal pain response curve shifts to left
- Causes hyperalgesia and allodynia
- Preemptive analgesia aims to prevent sensitization
- Two essential requirements:
  - Establishment of effective level of analgesia
  - Inhibition of inflammatory mediators.

Preemptive Analgesia Strategies

- Infilteration with local anesthetics
- Nerve blocks
- Epidural block with catheter
- Subarachnoid block
- Drugs:
  - NSAIDs, COX-2 inhibitors: Paracetamol, ketorolac, etoricoxib
  - NMDA antagonists: Ketamine, magnesium
  - Alpha 2 agonists: Clonidine, dexmedetomidine
  - Glucocorticoids: Dexamethasone
  - Cholinergic drugs: Nicotine
  - Gabapentin, pregabalin.

Principles of Preemptive Analgesia

- Depth of analgesia must be adequate to block nociceptive input

- Technique of analgesia should be extensive enough to include entire surgical field
- Duration of analgesia should include both surgery and postsurgery.

Use

- Preemptive epidural analgesia effective in reducing analgesic consumption
- Preincision infilteration with local anesthetics beneficial
- Multimodal approach addressing multiple sites along pain pathway needed to prevent central sensitization.

No	Drug	Route	Initial dose	Continuous dose
	Epidural analgesia			
1	Morphine	Epidural	3 mg	1–2 mg/hr
2	Buprenorphine	Epidural	0.1 mg	0.02–0.03 mg/hr
	Supraspinal analgesia			
3	Ketamine	Intravenous	1 mg/kg	0.5 mg/kg/hr

Efficacy

- Controversy surrounding use in clinical setting despite being effective in animal models
- Not all clinical trials demonstrate efficacy
- May reduce risk of developing chronic postoperative pain
- Reduces incidence of phantom limb pain post limb amputation.

POSTOPERATIVE PAIN RELIEF[1,2,3]

Adverse Effects of Acute Pain

- Cardiovascular:
  - Tachycardia
  - Hypertension
  - Increased cardiac workload.
- Respiratory:
  - Respiratory muscle spasm
  - Atelectasis
  - Hypoxia
  - Increased risk of LRTI.
- Gastrointestinal: Increased postop ileus
- Renal:
  - Increased risk of oliguria
  - Urinary retention
- Coagulation: Increased risk of thromboemboli
- Immunological: Impaired immune function
- Muscular: Muscle weakness and fatigue
- Psychological: Anxiety, fear and frustration.

Clinical Assessment

- Categorical Rating Scale
- Visual Analogue Scale
- Verbal Numerical Rating Scale.

Management

- Preemptive analgesia: Started before onset of pain
- Balanced analgesia: by multimodal approach.

PHARMACOLOGICAL SYSTEMIC OPIOIDS

Codeine

- Weak opioid
- Combined with paracetamol.

Dextropropoxyphene

- Weak opioid
- Combined with paracetamol.

Methadone

- Used in maintenance therapy in opioid addicts
- Used for chronic pain
- Limited use in acute pain.

Fentanyl

- Strong opioid
- Fast onset
- No active metabolites
- 1–5 µg/kg IV bolus dose
- Infusion 0.5–2 µg/kg/hr.

Morphine

- Morphine 6 glucuronide stronger than morphine
- 0.1–0.2 mg/kg IV bolus dose
- 20–30 µg/kg/hr infusion.

Pethidine

- Accumulation of norpethidine occurs
- Nausea, vomiting common
- 0.1–1 mg/kg IV bolus dose
- 200–300 µg/kg/hr infusion.

Tramadol

- Atypical centrally acting analgesic
- Opioid agonist
- Nausea and vomiting common

- 0.5–1 mg/kg IV bolus
- 0.1–0.2 mg/kg/hr infusion.

Buprenorphine

Routes of Administration

- Intravenous
- Subcutaneous: Unpredictable blood levels in hypovolemia
- Intramuscular
- Transdermal: Fentanyl patch 25–100 µg/hr
- Patient Controlled Analgesia
- Intrathecal opioids:
  - Fentanyl 5–25 µg
  - Morphine 100–500 µg
  - Sufentanyl 2.5–10 µg
- Epidural opioids:
  - Morphine 1–6 mg bolus, 0.1–1 mg/hr infusion
  - Fentanyl 25–100 µg bolus, 25–100 µg/hr infusion.

NONOPIOID ANALGESICS

Local Anesthetics

- Local infilteration
- Peripheral N/plexus block
- Continuous neuraxial block
- Safe, effective and reduces side effects of opioids.

NSAIDs

- Paracetamol 10–15 mg/kg PO Q6H
- Paracetamol 15–20 mg/kg PR Q6H
- Ibuprofen 6–10 mg/kg PO Q6H
- Ketorolac 30 mg IM Q6H
- Diclofenac 12.5–100 mg IV
- Rofecoxib 20–50 mg PO
- Parecoxib 20–40 mg IM/IV.

Analgesic Adjuvants

- Ketamine: 0.5 mg/kg /hr
- $\alpha 2$ agonists:
  - Clonidine 1–2 µg/kg intrathecal
  - Clonidine 2–3 µg/kg epidural
  - Clonidine 0.5 µg/kg intravenous
  - Dexmedetomidine 1 µg/kg IV over 1 minute
- Neostigmine: 25–100 µg intrathecal
- Corticosteroids: Dexamethsone 2–4 mg IV
- Gabapentin 900 mg PO 1–2 hr prior to surgery.

NONPHARMACOLOGICAL

Cryoanalgesia

- Intense cooling of peripheral nerves to < –5 to –20 °C
- Causes disintegration of axon and myelin sheath
- Does not disrupt perineurium and epineurium
- Cause interruption of nerve conduction for several weeks
- Intercostal N frozen in thoracotomy
- Ilioinguinal N frozen in hernia repair.

Electroanalgesia

- Transcutaneous Electrical Nerve Stimulation
- Acupuncture Like TENS (ALTENS)
- Percutaneous Neuromodulation Therapy
- Transcutaneous Acupoint Electrical Stimulation.

Others

- Ultrasound therapy
- Hypnotherapy
- Lazer stimulation.

Latest Advances

Capsaicin

- Can be used as cream form or injectable
- Acts on C–fiber nerve endings
- Has opioid sparing effect
- Cautious use in those with liver disease and ACE inhibitors.

Tapentadol

- New receptor antagonist
- 18 times affinity of morphine
- Inhibits norepinephrine uptake
- Contraindicated in asthma and paralytic ileus.

Liposome Encapsulated Local Anesthetic

Extended Release Epidural Morphine

- Acts for up to 48 hrs.

PERIOPERATIVE PAIN MANAGEMENT IN OPIOID-DEPENDENT PATIENT[1,2,3]

Introduction

Physiological state of adaptation to opioids characterized by emergence of a withdrawal syndrome during abstinence which maybe relieved in total or part by readministration of the substance.

Problems

- Require higher doses of opioids perioperatively
- Experience higher incidence of sedation
- Tolerance to other side effects of opioids
- Higher incidence of intraoperative awareness
- Ketamine interaction with depth of anesthesia monitors
- Disruption of sleep/altered sleep cycle
- Require longer duration of postoperative analgesia.

Goals

- Promote adequate perioperative analgesia
- Prevent drug withdrawal syndromes
- Maintain collaborative multidisciplinary approach
- Assist with psychiatric and behavioral issues.

Principles of Management

Multimodal Analgesia

- Local anesthetics
- Anticonvulsants
- NSAIDs
- Acetaminophen
- Nitrates
- Opioids
- α_2 agonists
- Tricyclic antidepressants
- Selective serotonin reuptake inhibitors.

Preoperative Management

- Evaluation:
  - For early recognition and high index of suspicion
  - Evaluate what opioid and nonopioid analgesic is being used preoperatively
  - Assess patients chronic baseline requirement
  - Calculate total opioid requirement
  - Mode of administration.
- Fentanyl challenge test:
  - Fentanyl given to levels which cause respiratory depression
  - Pharmacokinetic modeling done
  - Uses:
    - To predict intraop and postop opioid requirements
    - Calculation of PCA bolus dose and infusion rate.
- Assess history of:
  - Previous surgery or trauma resulting in undermedication
  - Inadequate analgesia or relapsing episodes
  - Patients fears and expectations
  - Reassure patient regarding pain control and anxiety
  - Patient education about management plan.
- Management
  - Anxiolytics as indicated
  - Consultation with pain specialist
  - Patient instructed to take normal opioid dose
  - Maintain fentanyl patch already present only if:
    - No significant fluid shift
    - No hypovolemia/peripheral vasoconstriction
    - No sweating affecting adhesion of patch
    - No pyrexia
  - Consider non opioid analgesics preoperatively:
    - Acetaminophen 1 gm 1–2 hrs preop
    - Celecoxib 1–2 hrs preop
    - Gabapentin/pregabalin preop.

Intraoperative Management

- Monitor intraop vital signs
  - Heart rate
  - Blood pressure
  - ECG
  - Pupil size
  - Respiratory rate
  - BIS/entropy.
- Place warming devices away from transdermal patch to avoid excess absorption
- Opioid strategies:
  - Maintain baseline opioids
  - Increase intraop and postop opioid dose to compensate for tolerance
  - Opioid rotation: Dose of new opioid < 50% of calculated equianalgesic dose
  - Ensure adequate intraoperative loading with long acting opioid if remifentanyl infusion used intraoperatively
  - Titrate fentanyl and morphine to respiratory rate of 8–10 breaths/min
  - Titrate opioids to moderately miotic pupils.
- Peripheral neural or plexus blockade
- Neuraxial analgesia when clinically indicated
- Adjuvant medications:
  - Use nonopioids as analgesic adjuvants
  - Ketamine 0.5 mg/kg followed by 2 μg/kg/min infusion
  - Ketorolac 0.5 mg/kg IV if not given preoperatively

- Acetaminophen 1 gm per rectally if not given preoperatively.

Assessment of Pain

- Dynamic measures of pain to be considered-ability to deep breathe and cough
- ***Functional Activity Score*** useful:
  - A: No limitation of relevant activity due to pain
  - B: Mild limitation of physical activity
  - C: Severe limitation of physical activity.

Postoperative Management

- Plan preoperatively for postop analgesia
- Use multimodal analgesia techniques
- Regional analgesia:
  - Removes need for additional systemic analgesia
  - Consider continuous catheter techniques
  - Neuraxial opioids may not prevent opioid withdrawal
  - Difficult to estimate appropriate safe dose as requirements maybe higher
  - Increases risk of respiratory depression if used concurrently with systemic opioids.
- Opioid strategies:
  - Maintain baseline opioid level
  - Incremental dosing regimens
  - Transdermal buprenorphine: 480 µg/day for 20 µg/hour delivery system
  - PCA with basal infusion used as primary therapy
  - PCA can be used to supplement epidural analgesia techniques
  - Use synergistic opioid mixtures (morphine and oxycodone):
    - Better pain control
    - Reduced side effects
    - Reduces individual drug dosage.
  - Continue neuraxial opioids (intrathecal/epidural infusion)
  - Tramadol good choice due to lower abuse potential.
- Opioid rotation:
  - Switching from one opioid to another
  - Use of opioid different from preadmission opioid
  - Improves analgesia and reduces opioid related side effects
  - Mechanisms:
    - Incomplete opioid cross tolerance
    - Differing receptor activity
    - Presence of active metabolites.
  - Opioid doses converted with opioid conversion ratios
  - Drugs commenced with 30–50% calculated equianalgesic dose.
- Nonopioid coanalgesic for opioid sparing properties:
  - Low dose ketamine:
    - 0.25–0.5 mg/kg bolus
    - 2–4 µg/kg/min infusion.
  - Acetaminophen 1 gm every 6 hrs
  - NSAIDs or COX-2 inhibitors
  - Gabapentin/pregabalin
  - α_2 agonists-clonidine also prevents withdrawal symptoms.
- During transition phase:
  - Period of transition from regional/parenteral techniques to oral opioids/adjuvants
  - Allow on demand use of short acting opioids every 3 hrs
  - Taper opioid doses towards preoperative doses.
- Prevention of withdrawal syndrome:
  - Maintain usual opioid dose equivalent
  - Continue other CNS depressants/stimulants
  - High index of suspicion
  - Methadone Maintenance Therapy (MMT):
    - Given once a day
    - Suppresses withdrawal symptoms for 24 hrs
    - Can be given PO/IV/IM/subcutaneously.
- Buprenorphine Maintenance Therapy (BMT):
    - Usually given once a day
    - Given as transdermal patch
    - 2–24 mg per day generally required.

Discharge Criteria

Reverse Pain Ladder

Step I
- Paracetamol
- ± NSAIDs
- ± Tramadol
- ± Additional opioids

Step II
- Paracetamol
- ± NSAIDs
- ± Tramadol

Step III
- Paracetamol
- ± NSAIDs.

INTRAVENOUS REGIONAL ANESTHESIA (IVRA)[1,2,3]

Introduction

- It is a method of producing analgesia of part of a limb with an IV injection of local anesthetic while the circulation to the limb is occluded
- Also called ***Biers block***
- First used by ***August Bier*** in 1908.

Indications

- For short procedures lasting less than 90 minutes
- Surgeries of forearm and hand:
  - Closed reduction of fractures
  - Carpal tunnel syndrome.
- Surgeries of foot
- ***Rydings*** method of digital IVRA: For paronychia.

Contraindications

- Obese patients: As tourniquet would be ineffective
- Where prolonged tourniquet time is contraindicated:
  - Sickle cell disease
  - Cellulitis.
- Hypersensitivity of local anesthetics
- Untreated heart block:
  - Relative contraindication
  - Sudden release of LA may convert partial block to complete block/precipitate asystole.
- Patients with cardiac diseases like uncompensated CCF as lidocaine reduces contractility.

Mechanism of Action

- This method uses vascular bed to bring LA to the nerve endings as well as nerve trunk
- The vascular channels in the core of the nerve lie close to nerve fibrils
- These channels carry the drug to the nerve from which it diffuses to the periphery causing nerve blockade.

Technique

- Fasting as for general anesthesia:
  - 6 hours for solids
  - 4 hours for liquids
  - 2 hours for clear liquids.
- IV sedation:
  - Useful as:
    - Improves patient comfort
    - Increases threshold for toxic effects.
  - But prevents early identification of CNS toxic effects if patient is deeply sedated.
- Check BP on operative side: Enables cuff inflation to correct pressure after exsan guination
- Resuscitation equipment kept ready
- Cannulation of vein:
  - Cannula removed if duration of surgery less than 1 hour
  - Kept in-situ and flushed with heparinised saline if duration more than 1 hour
  - Veins on dorsum of hand preferred
  - Cannulation of more proximal veins results in patchy block
  - Inflate cuff to above diastolic BP to make veins prominent and cannulate vein
  - Cannulate vein in other hand too, to administer fluids and drugs in case of toxicity
  - Long IV cannula not used as cannula tip may lie beyond tourniquet cuff
  - This may cause direct LA injection into systemic circulation
  - Exsanguinate limb using ***Esmarch bandage***/ limb elevation for 3 minutes.
- Tie tourniquet:
  - Double tourniquet is usually used
  - Cuff is inflated to above *occlusion pressure*:
    - It is the pressure at which radial pulse disappears
    - Usually *150 mm Hg more than systolic BP.*
  - If double tourniquet used:
    - First inflate proximal tourniquet and wait for anesthetic effect to take place
    - Then inflate distal tourniquet so that the area of tourniquet inflation is anesthetized.
- Local anesthetic injection:
  - 25 ml of 0.5% lidocaine for forearm
  - 50 ml of 0.5% lidocaine for arm
  - 100 ml of 0.5% lidocaine for thigh
  - Other local anesthetics: Lidocaine 1.5–3 mg/kg with prilocaine 3–4 mg/kg
  - LA solution to be preservative free as it can cause thrombophlebitis
  - LA solution should be without adrenaline
  - More concentrated LA results in use of lower volume causing patchy block.
- Release of tourniquet:
  - Minimum duration:
    - Tourniquet kept inflated for minimum of 30 minutes

- Release of tourniquet before this would be akin to directly injecting LA into systemic circulation.

– If it was kept inflated for 30–40 minutes:
- Deflate the cuff and then immediately reinflate within 30 seconds
- This releases a test dose of LA slowly into circulation
- Tourniquet can then be completely deflated after 1 minute.

– If tourniquet was inflated for more than 40 minutes:
- Tourniquet released directly
- If tourniquet pain occurs, deflate proximal tourniquet while keeping distal tourniquet inflated.

- Monitor:
  – Blood pressure
  – ECG, pulse oximetry
  – CNS status.
- Prolonging IVRA effect:
  – Leave IV catheter *in situ*
  – Reinjection of local anesthetic:
    - After 1 hour, tourniquet deflated and bleeding vessels are cauterized
    - Tourniquet is then reinflated and LA solution reinjected into vein
    - Half the initial dose of LA is usually sufficient.
  – Other techniques:
    - Dilute solution of levo-bupivacaine (0.125%) can be used
    - Adjuvants like tramadol, ketorolac and clonidine used after cuff deflation.

Advantages

- High success rate (96% success rate)
- Ease of performance
- Quicker onset: Within 5 minutes
- Controllable duration (duration governed by time for which tourniquet remains inflated and not on duration of action of local anesthetic)
- Controllable extent with tourniquet
- Rapid recovery after cuff release: Ideal for day care anesthesia
- Minor risk only, of systemic toxicity, if safely performed.

Disadvantages

- Tourniquet related complications: Pain and neuropathy
- Exsanguination of limb required
- Inability to provide bloodless field due to gradual venous engorgement due to intraosseus blood flow
- Rapid recovery: No postoperative analgesia possible
- Toxic reaction: LA toxicity.

Complications

- LA toxicity: CNS and CNS toxicity, methemoglobinemia
- Peripheral nerve damage: Tourniquet palsy
- Compartment syndrome
- Thrombophlebitis with chlorprocaine
- Absence of postoperative analgesia.

Factors Influencing LA Toxicity

- Leakage of LA before tourniquet release:
  – Leakage through intraosseus veins
  – Leakage through ordinary veins when venous pressure exceeds cuff pressure (as can happen during rapid LA injection)
  – Malfunctioning tourniquet.
- Incomplete exsanguination results in release of reservoir of LA on cuff deflation
- Arm movements after tourniquet release discouraged
- Repeated deflation and inflation of cuff reduces toxicity.

IV Regional Sympathetic Block

- Described by ***Hannington-Kiff***
- Monitor BP, secure IV line
- Patient placed on table which can be tilted
- Guanethidine 20 mg in 25 ml normal saline with 0.5% prilocaine (to reduce pain on injection)
- Reserpine 1–1.5 mg or bretelium 5 mg/kg also used
- Postural hypotension possible for 48 hours after block
- Effect can last as long as 4–6 weeks
- Advantages:
  – Can be used after *postsympathectomy escape phenomenon*
  – Useful for patients on anticoagulants
  – Avoids complications of stellate ganglion block
  – Prevents adhesions due to phenol in lumbar plexus block.

STELLATE GANGLION BLOCK[1,2,3]

Introduction

- Stellate ganglion belongs to the orthosympathetic system and is formed by the fusion of *first thoracic and inferior cervical ganglion*
- Sympathetic block produced; covers thorax, axillary region and upper limb
- Also called ***cervicothoracic sympathetic block.***

Regional Anatomy

- Cervical sympathetic chain lies between:
  - Anteriorly: Carotid sheath
  - Posteriorly: Prevertebral muscles
- Stellate ganglion extends from:
  - Transverse process of C_7 (*Vertebra prominens*) to neck of first rib
  - Between longus colli posteriorly and carotid and vertebral artery anteriorly.
- Ganglion lies in close contact with:
  - Subclavian artery
  - Recurrent laryngeal nerve
  - Inferior thyroid artery
  - Right side apical pleura.
- Usually blocks upper thoracic and all cervical ganglia.

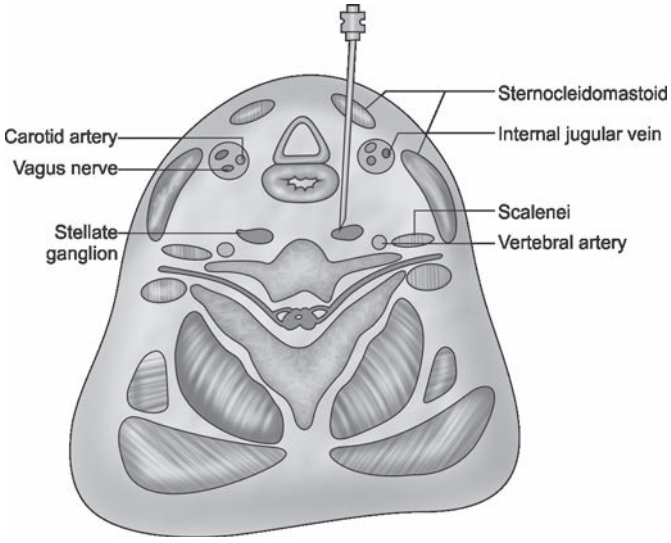


Fig. 9.1: Stellate ganglion[2]

Indications

- In children:
  - Severe circulatory disturbances of upper limb
  - Ventricular tachyarrhythmias due to familial prolonged QT interval syndromes.
- Treatment of pediatric herpes zoster ophthalmicus
- In adults:
  - Circulatory in sufficiency due to occlusive vascular diseases:
    - Chronic:
      - Raynauds disease
      - Scleroderma
      - Frostbite.
    - Acute:
      - Traumatic/embolic vascular occlusion
      - Accidental intra-arterial thiopentone injection.
  - Pain:
    - Post-traumatic syndrome *(causalgia)*
    - Causalgia following abdominal injury
    - Phantom limb***, Pagets disease***, neoplasms
    - Herpes zoster, trophic skin changes.
  - Others:
    - Hyperhydrosis, ***Sudecks dystrophy***
    - ***Shoulder–hand syndrome***
    - Stroke, ***Menieres disease***, amblyopia due to poisoning with quinidine.

Procedure

Paratracheal Approach

- Called ***anterior approach of Leriche***
- Patient should not talk during procedure
- Patient lies supine with head slightly lifted forward and tilted dorsally
- Done to stretch esophagus away from transverse cervical process on left side
- Palpate trachea and carotid pulse between sternocleidomastoid and trachea
- Palpate Chassaignac's tubercle at the level of cricoid cartilage
- Raise a skin wheal over this tubercle
- Two fingers now pressed down to the C_6 tubercle, pushing away carotid artery laterally and trachea towards midline
- 22 G, short bevelled, 4.5 cm long needle with 20 ml syringe attached is advanced till it hits the C_6 tubercle
- Hand holding needle is kept braced against the patient and needle is withdrawn 2 mm to clear from longus colli muscle
- Aspirate and check for CSF/blood

- Inject 2 ml of local anesthetic if no aspirate
- If high resistance occurs on injection: Prevertetral muscle present
- If radiating pain occurs on injection: Needle has penetrated nerve root
- 15–20 ml of bupivacaine/ropivacaine is injected
- Patient may feel lump in the throat and may be temporarily hoarse
- Food and fluids to be withheld till laryngeal reflexes become intact.

Continuous Technique

- Done with radio-opaque Teflon catheter
- This is introduced with X-ray control using paratracheal technique
- Stylet is withdrawn and catheter is fixed for continuous injection.

Chemical Stellate Ganglion Block

- 1–2 ml of 6% acqueous phenol/10% phenol in Conray dye used
- Complete cervicothoracic sympathetic blockade is not assured
- The arm might partially escape in which case injection at T_2-T_3 can be used as supplement
- This is rarely used owing to its close proximity to pleura
- Dural sheath may be entered and LA may migrate to medulla oblongata.

Signs of Successful Block

- Horners syndrome:
  - Ptosis
  - Miosis
  - Anhydrosis
  - Unilateral nasal stuffiness
  - Unilateral skin and conjunctival flushing.
- *Cobalt blue sweat test* also useful
- Increase in temperature of ipsilateral arm also suggests successful block.

Complications

- Nerve injuries:
  - Horners syndrome
  - Recurrent laryngeal nerve palsy
  - Neuralgia along chest wall and inner arm
  - Brachial plexus, phrenic nerve block.
- Inadvertent injection:
  - Intravascular injection: Vertebral artery, carotid artery, subclavian artery
  - Epidural, subarachnoid injection
  - Intradural injection: Slow onset of symptoms.
- Soft tissue:
  - Pneumothorax
  - Osteitis of transverse process
  - Mediastinitis due to esophageal puncture.

INTERSCALENE BLOCK[1,2,3]

Introduction

Developed as an alternative to supraclavicular approach to brachial sheath.

Advantages

- Can be used when proximal block is required: Shoulder surgeries
- Can be performed with arm in any position
- Pneumothorax risk is reduced
- Landmarks are usually clear, even in stout patients.

Disadvantages

- Essential to elicit paraesthesias
- Supplementary ulnar nerve block may be required
- Common but serious side effects
- Spares lowest branches of plexus (C_8 and T_1) which innervate ulnar forearm.

Indications

Shoulder, humerus and forearm surgeries.

Anatomy

- Cervical nerves of brachial plexus after leaving the respective intervertebral foramen pass laterally into a deep gutter/groove in superior surface of transverse process of cervical vertebrae
- This groove separates transverse process into anterior and posterior tubercles, which give rise to scalenus anterior and scalenus medius respectively
- After leaving transverse process, nerve roots of plexus pass into a plane between two scalenei called *paravertebral/interscalene groove or space* as trunks of brachial plexus
- This interscalene groove lies at level of cricoid cartilage
- The gutter on cervical transverse process is directed laterally downwards (45°) and forwards.

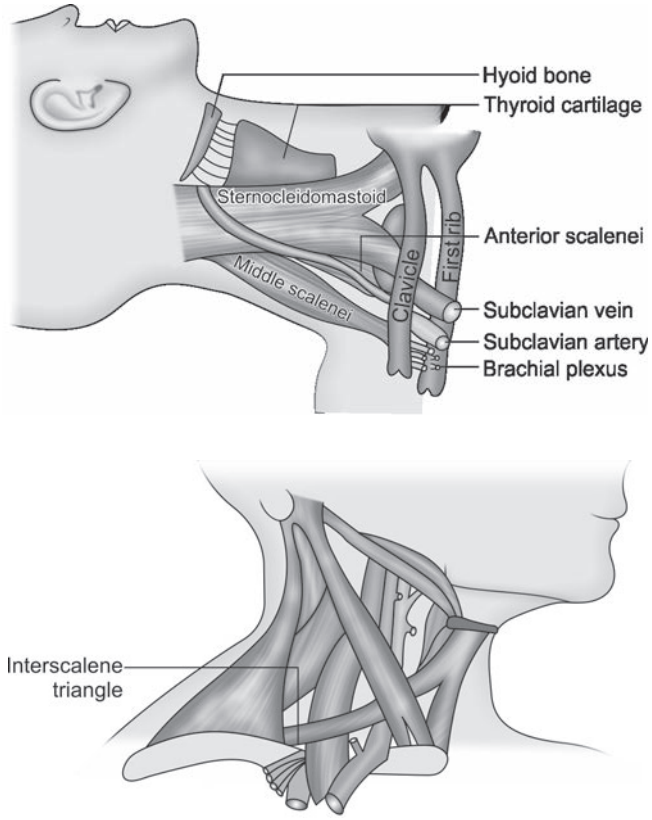


Fig. 9.2: Interscalene block[2]

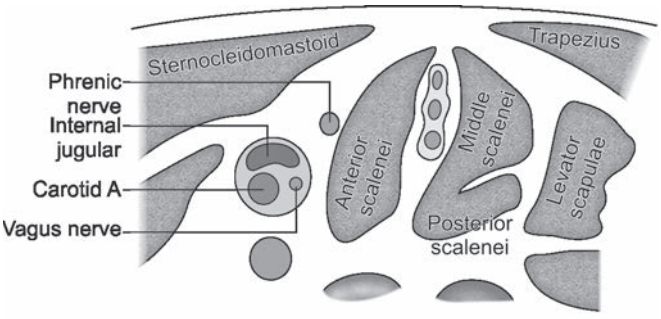


Fig. 9.3: Interscalene block cross-section[2]

Position

- Supine with neck straight, but head turned slightly to opposite side
- Arm is placed by the side with shoulder depressed as for supraclavicular nerve block.

Stimulation

- Deltoid: For shoulder surgery
- Elbow flexion: For humerus surgery.

Volume of Local Anesthetic

- 10–20 ml: For upper root analgesia
- 20–40 ml: For lower root analgesia
- 1% lidocaine or 1% prilocaine used
- 0.25–0.5% bupivacaine/levobupivacaine also can be used
- Use of long acting analgesics may provide analgesia for 12–14 hours.

Techniques

- ***Winnie's technique***:
  - Landmarks:
    - Cricoid cartilage
    - Posterior border of sternocleidomastoid
    - Interscalene groove.
  - Depth of insertion: 1–2 cm (very near surface)
  - Procedure:
    - Identify posterior border of sternocleidomastoid: Patient lifts head
    - Identify interscalene groove over belly of scalenus
    - Line drawn from cricoid cartilage to intersect interscalene groove
    - This is point of entry at the level of C_6 transverse process
    - External jugular vein might overlie this point
    - Digital pressure and massage might help in distant spread of LA.
  - Direction of needle:
    - Inward, 45° caudal and slightly backwards
    - Towards contralateral elbow/nipple.
- ***Mieirs approach***:
  - Indications:
    - Shoulder and humerus surgery
    - Difficult anatomy: Short neck resulting in poor identification of groove
    - Continuous catheter technique.
  - Depth of insertion: 3.5–5 cms
  - Landmarks:
    - Posterior border of sternocleidomastoid
    - Thyroid cartilage prominence (C_4)
    - Subclavian artery above clavicle.
  - Procedure:
    - Mark posterior border of sternocleidomastoid at level of thyroid prominence
    - Palpate subclavian artery over first rib behind clavicle
    - Line joining reduced these two marks approximate groove.

  - Direction of needle: Caudally, passing along long axis of interscalene groove towards subclavian artery
  - Advantages:
    - Reduced risk of epidural/intrathecal injection
    - Easier to place catheter due to angle of approach
    - Catheter placed using insulated Tuohy needle for shoulder arthroplasty.
- Posterior interscalene block: Pippas approach
  - Anatomical landmarks:
    - C_7 spinous process
    - C_6 spinous process
    - Cricoid cartilage
    - Sternocleidomastoid
  - Technique:
    - Seated position with cervical spine flexed backwards
    - Puncture site 3 cm away from midline between spinous processes of C_6 and C_7
    - Direction of needle 5–10° lateral and aimed at height of cricoid.
  - Puncture depth: 6–8 cms
- Ultrasound guided interscalene block.

Side Effects

- Nerve blocks:
  - Phrenic nerve block (100%)
  - Recurrent laryngeal nerve block (15%)
  - Stellate ganglion block (Horners syndrome).
- Epidural/spinal injection/spinal cord injury:
  - Easily detected if nerve stimulator is used
  - Avoid injecting when current responses are present at less than 0.4 mA
  - This suggests subarachnoid position of needle tip.
- Vertebral artery injection: Even 1–3 ml of LA solution can precipitate seizures as direct entry into brain occurs
- Intravenous injection: Slower onset LA toxicity
- Bilateral spread of interscalene block
- Pneumothorax due to advancing needle too far especially in a lateral direction
- C_6 neuropathy:
  - Occurs as needle may pin nerve root against tubercle
  - Suspect C_6 neuropathy if first injection of LA produces crampy pain sensation
  - This suggests intraneural position of needle tip
  - Withdrawal needle if so, as intraneural injection produces neuropathy.

Contraindications

- Not to be done in anesthetized patients
- Caution in patient with COPD or unilateral phrenic nerve palsy.

SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK[1,2,3]

Introduction

The brachial plexus is blocked at a point where it is most compactly arranged, at the level of the 3 trunks.

Advantages

- Brachial plexus blocked at a patient where it is most compactly arranged
- Whole brachial plexus is blocked: Excellent anesthesia of entire arm including hand
- Technique can be performed with arm in virtually any position
- Low volume of local anesthesia solution required.

Disadvantages

- Risk of pneumothorax
- Considerable experience required to master it.

Indications

Elbow, wrist, hand surgeries.

Contraindications

- Uncooperative patient
- Inexperienced practitioner
- Difficult stature patients in whom landmarks are not clear
- Respiratory cripples in whom pneumothorax or phrenic nerve palsy causes dyspnea
- Bilateral supraclavicular block not performed to avoid risk of bilateral phrenic nerve palsy.

Anatomy

- At the lateral border of anterior scalenii muscle, plexus passes between the first rib and clavicle to enter axilla
- Trunks are tightly oriented vertically on top of first rib, just posterior to subclavian artery
- Faster onset block due to perivascular sheath narrowing at this level
- Motor block faster than sensory as Mantle fibers are motor at this level
- Ulnar border of hand missed in 5% cases.

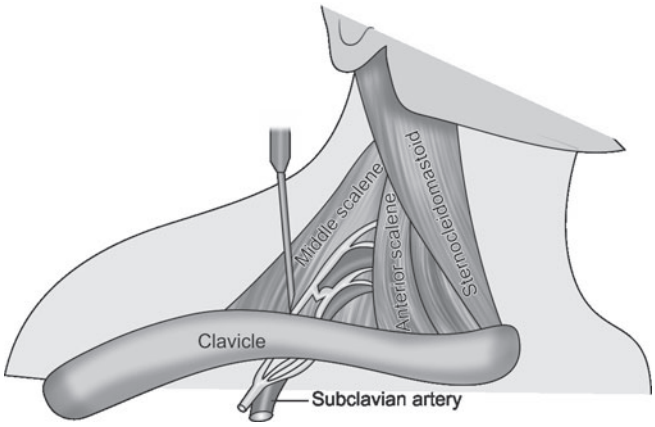


Fig. 9.4: Supraclavicular block[2]

Techniques

- Paresthesia technique
- Nerve stimulator technique
- USG guided block.

Position

- Patient is positioned supine without pillow
- Head is turned to 30° to contralateral side
- The ispilateral shoulder should be depressed downwards (caudal) and posteriorly by gentle pressure on the shoulder.

Approaches

- Classic approach:
  - Interscalene groove palpated at its most inferior point
  - This is just posterior to subclavian artery pulsation
  - The pulsation is felt in a plane just medial to midpoint of clavicle
  - Skin wheal raised with local anesthetic solution
  - 22G, 15 inch needle is directed caudally
  - Shaft of needle and syringe kept parallel to the plane of head and neck
  - Needle is directed, aiming at ipsilateral toe
  - Needle is advanced till paresthesia is felt or muscle contraction of forearm is seen
  - If muscle contraction still present with voltage of nerve stimulator decreased to 0.5 mA, 25–40 ml of LA is injected.
- Another technique:
  - Identify and measure width of clavicular head of sternocleidomastoid
  - Double the width and measure that distance from medial end of clavicle
  - The terminal part of interscalence groove should lie at this point, one finger breadth posterior to clavicle
  - Volume injected: 0.5 ml/kg upto 40 ml local anesthetic.
- ***Patrick technique***:
  - Used if no paresthesias are elicited, but the rib is contacted
  - LA solution is injected between skin and rib, behind the artery.
- If subclavian artery pulsation and landmarks are not felt:
  - The point where straight portion of EJV crosses the clavicle used to identify the midclavicular point
  - Asking patient to blow out his cheeks will make EJV prominent
  - Needle is inserted 1–2 cms behind midpoint of clavicle.

End Points

- Motor activity of forearm and hand: Inject LA solution
- Flexion and extension of wrist and fingers: Inject LA solution
- Blood in needle: Redirect needle more posteriorly and laterally
- Bone: Redirect needle and walk the needle more posteriorly and laterally
- No motor activity and depth of needle is equal to width of clavicle: Withdraw needle and reassess land marks
- Caution: Absolutely no medial angulation of needle.

Complications

- Pneumothorax/hemothorax:
  - Incidence 0.5–6%
  - Tall and thin patients with high apical pleura more at risk
  - Due to:
    - Needle puncturing pleura
    - More commonly needle pierces lung and lung surface gets torn by needle
    - Pneumothorax is then caused by air escaping from lung.
  - Suspect when cough/dypnea/pleuritic chest pain
  - Confirmed by chest X-ray

  - Majority take *up to 24 hrs to develop*
  - If extensive (≥ 50% involvement), continuous drainage occurs for 24–48 hrs
  - If lesser degree, air is removed, only if symptoms present with simple syringe aspiration
  - Takes weeks for complete absorption.
- Phrenic nerve palsy:
  - Occurs in 40–60% cases
  - If bilateral palsy in patients with underlying chest disease, signs of hypoxia may occur.
- ***Horners syndrome (Stellate ganglion block***):
  - Occurs in 70–90% cases when large volume of LA used (≥ 50 ml)
  - No treatment is necessary.
- Nerve damage/neuritis:
  - Uncommon complication
  - Occurs due to:
    - Faulty position of arm during surgery
    - Trauma by needle
    - Prolonged ischemia of nerve due to vasoconstrictor drug
    - Too concentrated LA solution.
- Local anesthetic toxicity:
  - Due to inadvertent intravascular injection/use of excessive LA
  - Prevented by repeated aspiration while injecting LA.

AXILLARY NERVE BLOCK[1,2,3]

Introduction

Provides excellent operative condition for surgeries of forearm and hand with reduced risk of major complications.

Indications

Surgeries of elbow, forearm, hand.

Limitations

- Arm must be abducted to perform the block
- Extent of anesthesia insufficient for shoulder/upper arm surgery without using large volume of solution
- Circumflex and musculocutaneous nerve are missed in single shot injection as they leave the axillary sheath proximal to the point of injection
- Radial nerve missed in 25% cases.

Anatomy

- Neurovascular bundle lies 1–2 cm below skin surface
- Subclavian artery becomes axillary artery just below clavicle where trunks of brachial plexus split into anterior and posterior divisions at lateral border of pectoralis minor
- In the axilla, musculocutaneous nerve has already left the sheath and lies within coracobrachialis muscle
- The fascial sheath in axilla might be multicompartmental with one compartment covering each nerve and the fascial septa may be responsible for patchy anesthesia
- Medial aspect of sheath (superficial): Subcutaneous tissue covering lies behind biceps/coracobrachialis and in front of triceps
- Relations in the sheath:
  - Median nerve: Lies anterior to axillary artery (above)
  - Ulnar nerve: Posterior to axillary artery (below)
  - Radial nerve: Posterior and lateral (below and laterally)
  - Musculocutaneous nerve: Anterior and lateral (within coracobrachialis)
  - Axillary vein: Medial to artery.

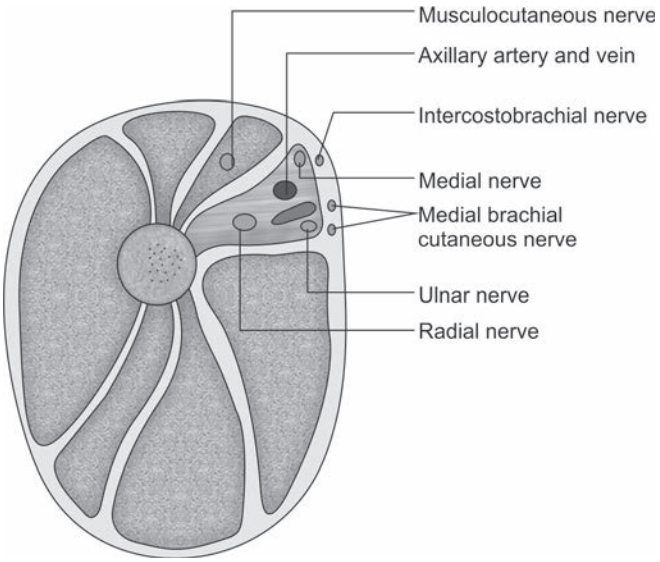


Fig. 9.5: Axillary block cross-section[2]

Landmark

- Axillary artery pulsations
- Pectoralis major insertion.

Depth of Insertion

10–15 mm.

Volume of Local Anesthetic

- 0.5 ml/kg upto 50 ml can be used
- 40 ml of LA solution reaches upto coracoid process thus blocking musculocutaneous nerve
- Increasing volume of solution above 40 ml does not improve spread to musculocutaneous nerve.

Techniques

- Perivascular technique:
  - Pulse of axillary artery identified as high in axilla as possible
  - Using immobile needle technique 22 G, 1.5 inch needle is directed parallel to neurovascular bundle, i.e. at apex of axilla
  - Oscillation of needle produced by arterial pulsations indicates that needle is atleast near the artery and thus probably within the sheath
  - Local anesthetic solution (15–20 ml) injected at this point
  - Same procedure applied for injection below pulsation.
- Transarterial technique:
  - Axillary artery pulsations identified
  - 22 G, 1.5 inch needle advanced till bright red blood aspirated
  - Needle advanced or withdrawn till aspiration ceases
  - LA injected (40 ml at once or 20 ml anterior and 20 ml posterior to artery).
- Paresthesia technique:
  - Useful if pulsations are not felt (fat patient)
  - Needle directed towards axillary artery to elicit single specific or multiple paresthesias
  - If concerned about septation, paraesthesias elicited in ulnar, median and radial nerve distribution and LA injected separately at these sites
  - Paresthesia only at surgical site also may be elicited
  - Regardless of whether single or multiple paresthesias are elicited, injected volume should be 40 ml.
- Nerve stimulator technique:
  - 2 inch and 22 G insulated simulating needle inserted proximal to hand palpating pulses, and appropriate muscle twitches are sought
  - Once identified and after reducing stimulation to less than 0.5 MA, witnessing fade of motor activity after 1 ml of LA is injection and negative aspiration of blood, local anesthetic is delivered
  - Nerve stimulation causes the following:
    - Median nerve: Flexion of index/middle finger
    - Ulnar nerve: Thumb adduction, little finger flexion
    - Radial nerve: Thumb extension
    - Musculocutaneous nerve: Elbow flexion
- Loss of resistance technique: Click/pop is felt on entering fascial sheath
- Continous axillary block:
  - 17/18 G needle, 20/22 G catheter used
  - Continuous infusion of 0.25% bupivacaine at 20–30 mg/hr is effective
  - First bolus dose given and then infusion started 1 hour after bolus
  - Not many toxic reactions
  - Used for long surgeries like reimplantation.
- Ultrasound guided axillary block: Using high frequency (10–15 MHZ) linear probe
- Tourniquet block:
  - Few ml of LA solution is deposited in subcutaneous tissues from biceps to triceps on medial surface of upper arm on withdrawal to block intercostobrachial nerve and its communication with medial cutaneous nerve of arm
  - This communication may cause tourniquet pain inspite of a successful axillary block.

Testing Block

- Pull-push-pin-pin test
- Pull (flexion of arm): Test musculocutaneous nerve
- Push arm against resistance: Tests radial nerve
- Pin: The thenar prominence: Tests median nerve
- Pin: Fifth digit: Tests ulnar nerve.

Promoting Proximal Flow within Sheath

- Important to increase chances of musculocutaneous nerve block
- Techniques of promoting proximal flow:
  - Digital pressure applied immediately distal to needle with index and middle fingers both during and immediately after injection
  - Tourniquet application
  - Adduct arm as soon as injection is completed: This removes effect of pressure of humeral head which may be limiting proximal spread.

Complications

Very low rate of complications:

- Intravascular injection
- Repeated elicitation of paresthesias cause neuropathy postoperatively: Ultrasound guidance and careful attention to injection pressures during block reduces incidence of neuropathy
- Hematoma if axillary artery is punctured (self-limiting)
- Infection.

PARAVERTEBRAL BLOCK[1,2,3]

Introduction

Potential space deep to endothoracic fascia that intercostal N traverses, on route to intercostal space.

Anatomy

- Wedge shaped space adjacent to vertebral body
- Spinal roots emerge and divide into dorsal and ventral rami
- Boundaries:
  - Anterolaterally: Pleura
  - Superiorly: Inferior aspect of upper rib
  - Inferiorly: Superior aspect of lower rib
  - Medially: Adjacent vertebra, intervertebral foramen
  - Posteriorly: Costotransverse ligament.

Indications

- Lower thoracic surgery
- Lumbar surgery
- Pelvic surgery
- Groin surgery (herniorraphy)
- Upper leg surgery
- Treatment of chronic pain syndromes:
  - Postthoracotomy
  - Postmastectomy
  - Nerve entrapment syndrome following herniorraphy.

Contraindications

- Local infections
- Mentally unstable patients
- LA sensitivity
- Surgery at site of block.

OT Preparation

- Emergency medications
- Airway equipment
- Antiseizure drugs
- Connect pulse oximeter, ECG, NIBP, Nerve stimulator if required.

Technique

Lumbar Paravertebral

- Prone position
- Aseptic precautions
- Palpate and mark each lumbar spinous process
- Draw horizontal line @ cephalad edge of each process
- Two vertical lines drawn parallel to and 3–5 cms from midline
- Raise skin wheal at points of intersection of the 2 lines
- 22 G, 8 cm needle perpendicular to skin until it touches transverse process @ depth of 3-5 cms
- Withdraw slightly and redirect to slide off caudal edge of transverse process
- Advance 1–2 cms deeper and inject 6–10 ml of local anesthetic.

Thoracic Paravertebral

- Prone position
- Aseptic precautions
- Palpate cephalad aspect of each spinous process
- 22 G 8 cms needle inserted perpendicular to skin and 2–3 cms lateral to spinous process
- Once transverse process is hit, withdraw needle little
- Advance it to pass cephalad to transverse until LOR is felt
- Inject 5 ml of LA per level.

Open Vision Technique

- Epidural catheter passed into open hemithorax via tuohy needle
- Small incision on parietal pleura and fascia covering paravertebral gutter
- Thread tip of catheter close to neurovascular bundle of cephalad intercostal space
- Suture to reduce spread of LA.

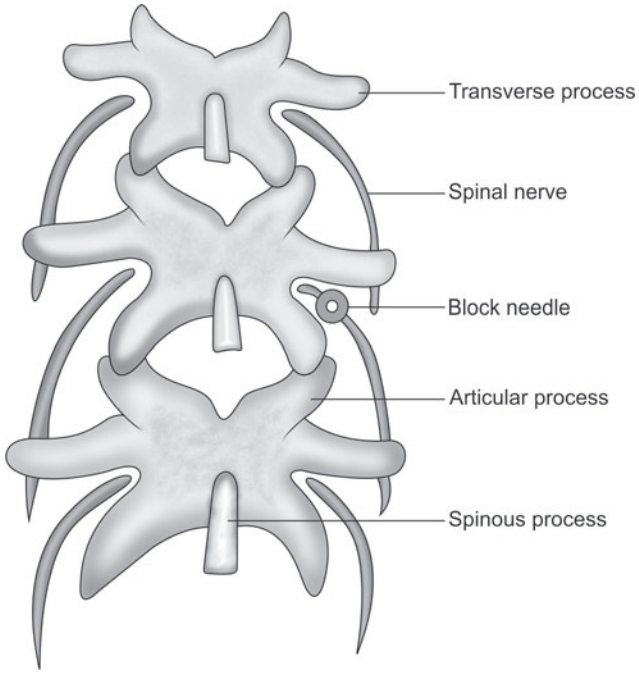


Fig. 9.6: Paravertebral block[2]

Continuous Paravertebral Block

- 0.1 ml/kg/hr of 0.5% bupivacaine
- 1 ml/10 kg/hr of 1% lidocaine (maximum 7 ml/hr)
- Can be combined with NSAIDs/opioids.

Complications

- LA toxicity
- Pneumothorax
- Subarachnoid/epidural space injection
- Intraperitoneal injection
- Puncture of retroperitoneal/intra-abdominal organs
- Infection/hematoma
- Paravertebral muscle pain/quadratus lumborum weakness
- Nerve injury.

Advantages Over Epidural

- Comparable analgesia
- Reduced neuraxial hematoma
- Reduced hypotension
- Fewer failed blocks
- Reduced nausea and urinary retention.

LUMBAR PLEXUS BLOCK[1,2,3]

Introduction

- Comprises of injection of local anesthetic into lumbar plexus in fascial plane within the posterior aspect of psoas major
- Also called *psoas compartment block.*

Anatomy

- Derived from ventral ramii of lumbar nerve roots L_1-L_4
- Contribution from T_{12} in 50% cases
- Made up of 7 nerves
  - Iliohypogastric T_{12}-L_1
  - Ilioinguinal L_1
  - Genitofemoral L_1-L_2
  - Lateral femoral cutaneous L_2-L_4
  - Obdurator L_2-L_4
  - Accessory obdurator L_3-L_4
  - Femoral L_2-L_4.
- After leaving intervertebral foramina courses via psoas compartment bounded:
  - Anteriorly: psoas muscle fascia
  - Posteriorly: quadratus lumborum fascia.
- Plexus blocked in psoas compartment.

Indications

- Analgesia:
  - Neuralgias of thigh
  - Fascia lata pain syndrome
  - Total knee replacement
  - Total hip replacement
  - Revision hip arthroplasty
  - Hemiarthroplasty
  - Surgeries on neck/shaft femur.
- Anesthesia:
  - Anterior cruciate ligament repair
  - Knee arthroscopy
  - Patellar tendon repair
  - Surgeries of thigh—skin graft/biopsy
  - Saphenous vein stripping.

Patient Preparation

- NPO status confirmed
- Consent taken
- Venous access secured
- IV midazolam 0.03–0.05 mg/kg can be administered
- Standard monitors applied – ECG, blood pressure, pulse oximetry.

OT Preparation

- Emergency drugs kept ready (thiopentone, adrenaline, atropine)

- Airway equipment (facemask, endotracheal tube, airways)
- Suction apparatus
- 1% lidocaine 0.5% bupivacaine in equal proportions
- Around 25–30 ml used
- 21 G 4 inch insulated stimulating needle
- 20 cc syringe.

Position

- Lateral decubitus (*Sims*) position
- Side to be blocked in non dependent position
- Hip on side to be blocked flexed to 30°
- Ipsilateral knee flexed to 90°.

Technique

- Line drawn connecting both iliac crests
- Posterior superior iliac spine identified
- Line drawn cephalad from PSIS parallel to vertebral column
- Intersection of both the lines represents most lateral position of lumbar plexus
- Insertion point 4 cm from midline
- Needle advanced perpendicularly at insertion point
- Loss of resistance felt on entry into psoas compartment
- When needle enters psoas compartment (70–90 mm) quadriceps twitch noted
- Reduce stimulation to < 0.5 mA while witnessing activity
- Witness fade of motor activity after injection of 1 ml of local anesthetic
- After negative aspiration of blood 25-40 ml local anesthetic injected.

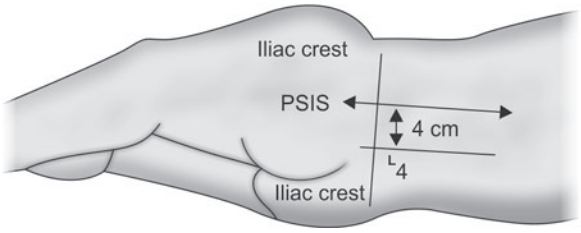


Fig. 9.7: Lumbar plexus block[2]

Advantages

- Lower pain scores
- Less morphine consumption
- Less hypotension/nausea/vomiting
- Reduces postoperative blood loss
- Greater patient satisfaction
- Earlier hospital discharge.

Disadvantages

- Deep anatomical location of plexus
- Needs large volumes of local anesthetic owing to size of plexus
- Serious complication rate
- Safer alternatives—femoral nerve block.

Complications

- Epidural/subdural injection
- Total spinal anesthesia
- Peripheral nerve damage
- Intravascular injection
- Puncture of renal pelvis
- Retroperitoneal hematoma
- Infection
- Neuropraxia/neurolysis
- Sympathetic block secondary to extravasation of local anesthetic.

THREE-IN-ONE BLOCK[1,2,3]

Introduction

Technique to block 3 of the 4 nerves of leg with single injection of local anesthetic:

- Femoral N
- Obdurator N
- Lateral cutaneous N

Also called *Inguinal Paravascular Technique* of lumbar plexus anesthesia.

Anatomy

- Nerves emerging from lumbar plexus lie between:
  - Anteriorly: Psoas major
  - Posteriorly: Quadratus lumborum
- Compartment formed extends beneath inguinal ligament
- Single femoral sheath forms closed space
- Sheath encloses all nerves involved in lumbar plexus
- Drugs injected into this sheath travel upwards
- Sufficient volume (> 25 ml) to be injected.

Supply

- Femoral Nerve:
  - Anterior and medial portion of thigh and knee
  - Cutaneous innervation of medial and lateral portion of thigh
  - Periosteum of femur.
- Lateral femoral cutaneous nerve
  - Sensory to lateral buttock
  - Sensory supply to lateral thigh and knee joint.

- Obdurator Nerve:
  - Medial thigh
  - Hip joint
  - Adductor muscles.

Indications

- Analgesia:
  - Post total knee arthroplasty
  - Post anterior cruciate ligament repair
  - Plaster applications femoral fractures
  - Fracture neck/shaft of femur
  - Above/below knee amputations.
- Anesthesia:
  - Skin graft/muscle biopsy anterior aspect of thigh
  - Knee surgery in combination with sciatic N block
  - Procedures on lower leg/foot in combination with lower leg.

Contraindications

- Burn/infection at injection site
- Local anesthetic allergy
- Coagulopathy
- Presence of prosthetic vascular graft of femoral artery
- Pre-existing neurological disease
- Patient refusal.

Complications

- Intravascular injection
- LA toxicity
- Femoral nerve trauma
- Prolonged motor blockade
- Hematoma formation
- Block failure.

Patient Preparation

- NPO status confirmed
- Consent taken
- Venous access secured
- IV midazolam 0.03–0.05 mg/kg can be administered
- Standard monitors applied – ECG, blood pressure, pulse oximetry.

OT Preparation

- Emergency drugs kept ready (thiopentone, adrenaline, atropine)
- Airway equipment (facemask, endotracheal tube, airways)
- Suction apparatus
- 1% lidocaine 0.5% bupivacaine in equal proportions
- Around 25–30 ml used
- 21–23 G 3–5 cm blunt needle
- 20 cc syringe.

Technique

- Supine position
- Stand opposite to side of block
- Aseptic precautions
- Site of insertion is 2 cms below line joining ASIS and pubic tubercle
- Needle inserted perpendicularly 2 cm lateral to femoral artery pulsations
- Needle advanced till 2 pops are felt (fascia lata and fascia iliaca)
- Paresthesias may be felt along femoral N innervation
- Quadriceps contractions identifies femoral N if nerve stimulator used
- Needle immobilized and pressure applied below needle
- 25–30 ml local anesthetic injected in graded aliquots after negative aspiration
- Distal pressure applied to ensure cephalad spread
- Needle removed and area massaged
- Lateral femoral cutaneous N often partially blocked with single injection
- Can be blocked simultaneously at anterior superior iliac spine.

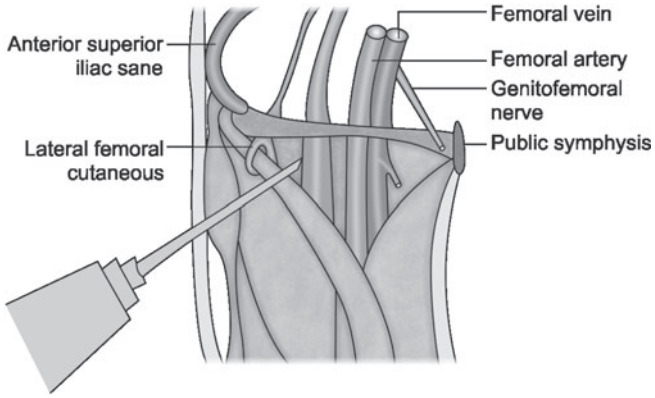


Fig. 9.8: Three-in-one block[2]

Advantages

- Single injection used
- Lesser local anesthetic needed
- High success rate

- Simple technique
- Can be used in geriatric population.

Disadvantages
- Lateral cutaneous femoral N sparing
- Obdurator N sparing
- Risk of permanent nerve injury.

FASCIA ILIACA BLOCK[1,2,3]

Introduction
Delivery of sufficient volume of local anesthetic behind fascia iliaca causes compartment block.

Anatomy
- Fascia Iliaca Compartment
- Potential space bounded by:
  - Anterior: Fascia Iliaca (overlaid by Fascia Lata)
  - Posterior: Iliopsoas muscle
  - Medial: Vertebral column
  - Craniolaterally: Inner lip of iliac crest
  - Craniomedially: Continuous with space between quadratus lumborum and its fascia
  - Contents:
    - Femoral N
    - Lateral femoral cutaneous N
    - Obdurator N
    - Genitofemoral N.

Supply
- Femoral Nerve:
  - Anterior and medial portion of thigh and knee
  - Cutaneous innervation of medial and lateral portion of thigh
  - Periosteum of femur.
- Lateral Femoral Cutaneous Nerve
  - Sensory to lateral buttock
  - Sensory supply to lateral thigh and knee joint.
- Obdurator Nerve:
  - Medial thigh
  - Hip joint
  - Adductor muscles.

Indications
- Perioperative analgesia or fracture neck or shaft of femur
- Adjuvant analgesia for hip surgeries
- Analgesia for total hip arthroplasties
- Analgesia for above knee amputation
- Analgesia for knee surgeries (in combiantion with sciatic N block)
- Analgesia for lower leg tourniquet pain.

Contraindications
- Previous femoral bypass surgery
- Patient refusal
- Anticoagulation
- Infection or inflammation over injection site
- Local anesthetic allergy.

Complications
- Block failure
- Intravascular injection
- LA toxicity
- Infection
- Perioperative injury secondary to numbness.

Patient Preparation
- NPO status confirmed
- Consent taken
- Venous access secured
- Standard monitors applied – ECG, blood pressure, pulse oximetry.

OT Preparation
- Emergency drugs kept ready (thiopentone, adrenaline, atropine)
- Airway equipment (facemask, endotracheal tube, airways)
- Suction apparatus
- 1% lidocaine 0.5% bupivacaine in equal proportions
- Around 25–30 ml used
- 3.5 inch 22 G Whitacre spinal needle
- 20 cc syringe.

Position
- Supine position
- Stand same side of block.

Technique
- Aseptic precautions
- Landmarks similar to femoral N block
- Line drawn from anterior superior iliac spine to pubic tubercle
- Junction of outer and middle thirds is identified
- 2 cms distal to junction is needle entry site
- Block does not require nerve stimulator
- Needle inserted perpendicular to skin till two 'pops' are felt
- First pop occurs as needle passes through fascia lata

- Second pop felt as needle passes through fascia iliaca
- Following negative aspiration 25–30 ml of local anesthetic injected
- Injection at 30° angle to skin in superior direction
- Pressure applied over injection site for 10 seconds following procedure.

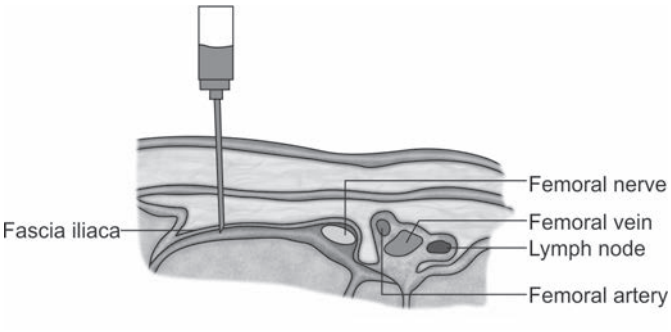


Fig. 9.9: Fascia iliaca block[2]

Advantages
- Does not require nerve stimulator
- Can be performed very quickly
- Not very painful
- Patients often do not require sedation
- Avoids injury to nerve and artery
- Catheter can be placed for continuous postoperative analgesia.

Disadvantages
- Inconsistent block success
- Femoral N blocked more consistently compared with lateral cutaneous femoral N and obdurator N.

LATERAL FEMORAL CUTANEOUS BLOCK[1,2,3]

Introduction
Superficial nerve block providing sensory anesthesia and analgesia to lateral thigh.

Anatomy
- Originates from lumbar plexus, dorsal divisions of L_2-L_3
- Traverses laterally from psoas muscle
- Courses anterolaterally along iliacus muscle
- Emerges inferior and medial to ASIS
- Passes between inguinal ligament and sartorius muscle
- Divides into anterior and posterior branches.

Supply
- Sensory to lateral buttock
- Sensory supply to lateral thigh and knee joint.

Indications
- Skin or muscle biopsy from lateral thigh
- Harvest site for skin graft
- In concurrence with femoral N block or fascia iliaca block
- Evaluation of lateral thigh pain
- Meralgia Parasthetica.

Contraindications
- Pre-existing peripheral neuropathy
- Previous femoral bypass surgery
- Patient refusal
- Anticoagulation
- Infection or inflammation over injection site
- Local anesthetic allergy.

Patient Preparation
- NPO status confirmed
- Consent taken
- Venous access secured
- IV midazolam 0.03–0.05 mg/kg can be administered
- Standard monitors applied – ECG, blood pressure, pulse oximetry.

OT Preparation
- Emergency drugs kept ready (thiopentone, adrenaline, atropine)
- Airway equipment (facemask, endotracheal tube, airways)
- Suction apparatus
- 1% lidocaine, 40 mg methylprednisolone if indicated
- Around 10–12 ml used
- 22 G 2 inch needle
- 10 cc syringe.

Position
- Supine or lateral
- Stand on same side of block.

Technique
- Strict asepsis
- As a field injection technique
- Point of injection 2 cm distal and 2 cm medial to ASIS
- Pop felt as needle passes through fascia lata
- Needle advanced slightly beyond resistance

- Needle repeatedly reinserted above and below fascia in lateral to medial direction
- Local anesthetic injected in fanwise technique as needle is reinserted
- Pressure applied over injection site for 10 seconds post injection to prevent ecchymosis.

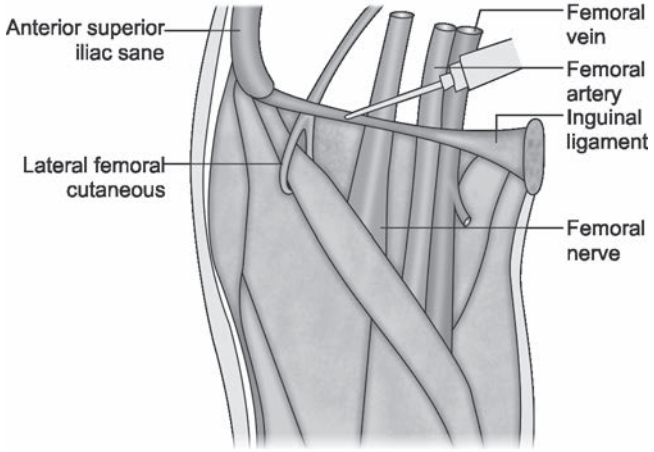


Fig. 9.10: Lateral femoral cutaneous nerve block[2]

Advantages

- Nerve stimulator not required
- Minimal complication rate
- Well tolerated
- Absence of motor block.

Disadvantages

- No continuous technique as catheter insertion not indicated.

Complications

- Low complication rate
- Postblock ecchymosis/hematoma
- Neuritis secondary to needle trauma or drug toxicity
- Inadvertant femoral N block
- Perforation of colon—intra-abdominal abscess.

OBDURATOR NERVE BLOCK[1,2,3]

Introduction

Provides anesthesia to medial thigh and relaxation to adductor muscles of hip.

Anatomy

- Mixed nerve derived from anterior primary rami of L_2, L_3 and L_4
- Runs within psoas major muscle during initial course
- Crosses close to bladder wall on its inferior/lateral portion
- Nerve exits pelvis and enters medial thigh through obdurator foramen
- Divides into anterior and posterior divisions to supply adductors of thigh.

Supply

- Sensory:
  - Medial thigh
  - Hip joint.
- Motor:
  - Adductor muscles of thigh
  - Articular branch to hip and knee.

Indications

- Adductor release procedure—adductor tenotomy
- Treatment of spasticity of thigh adductors due to hemiplegia/cerebral palsy
- To suppress '***Obdurator Reflex***' during TURBT
- As a supplement to femoral/sciatic N block
- Chronic pain secondary to knee arthrosis/pelvic tumors
- Diagnosis of hip pain.

Contraindications

- Burn/infection/inguinal lymphadenopathy at injection site
- Presence of prosthetic vascular graft of femoral artery
- Pre-existing obdurator neuropathy
- Paresis of adductor group of muscles
- Local anesthetic allergy
- Coagulopathy
- Patient refusal.

OT Preparation

- Emergency drugs kept ready (thiopentone, adrenaline, atropine)
- Airway equipment (facemask, endotracheal tube, airways)
- Suction apparatus
- 1% lidocaine or 0.5% bupivacaine
- Around 15–20 ml used
- 21 G 4 inch needle
- 10 cc syringe.

Patient Preparation
- NPO status confirmed
- Consent taken
- Venous access secured
- IV midazolam 0.03–0.05 mg/kg can be administered
- Standard monitors applied—ECG, blood pressure, pulse oximetry.

Position
- Supine position
- Thigh slightly abducted and externally rotated
- Stand on the side of block.

Technique
- ***LABATT's*** classical technique
- Aseptic precautions
- Needle inserted perpendicular to skin, 1.5 cm lateral and 1.5 cm inferior to pubic tubercle
- Needle advanced posterior direction towards superior pubic ramus
- Local anesthetic injected as needle is advanced
- On contacting bone needle redirected in lateral and caudal direction and advanced
- Needle enters obdurator foramen at 2–4 cms depth
- Adductor motor response of thigh elicited
- Reduce stimulation to < 0.5 mA
- Witness fade of motor activity after injection of 1 ml local anesthetic
- 15–20 ml local anesthetic injected in graded aliquots after negative aspiration of blood.

Advantages
Prevents bladder perforation during TURBT.

Disadvantages
- Technically difficult
- Lack of clear landmarks
- Block complexity
- Inconsistent results
- High complication rate.

Complications
- Adductor muscle spasm
- Hematoma
- Perforation of bladder/rectum/spermatic cord
- Peripheral nerve damage—obdurator neuropathy due to:
  - Needle trauma
  - Intraneural injection
  - Nerve ischemia
  - LA toxicity.
- Intravascular injection
- LA Systemic Toxicity—LAST
- Infection
- Neuropraxia/neurolysis.

SCIATIC NERVE BLOCK[1,2,3]

Introduction
Sciatic nerve, the terminal branch of sacral plexus is the largest nerve in the body.

Anatomy
- Originates from lumbosacral trunk
- Terminal branch of sacral plexus
- Formed by anterior primary rami of spinal roots L_{4-5} S_{1-3}
- Exits pelvis through greater sciatic notch
- Travels between gluteus maximus and piriformis muscle
- Continues towards posterior thigh between greater trochanter and ischial tuberosity
- Divides into 2 branches in superior aspect of popliteal fossa:
  - Tibial N
  - Common peroneal N.

Supply
- Sensory:
  - Posterior hip capsule
  - Knee joint
  - Lower extremity distal to knee except along anteromedial aspect.
- Motor:
  - Hamstring muscles
  - All lower extremity muscles distal to knee.

Indications
- Diagnosis and treatment of sciatic nerve entrapment
- Pyriformis syndrome
- In combination with femoral or lumbar plexus blocks
- Below knee amputations
- Foot and ankle surgeries.

Contraindications
- Burn/infection at injection site
- Local anesthetic allergy
- Coagulopathy
- Pre-existing neurological disease.

OT Preparation

- Emergency drugs kept ready (thiopentone, adrenaline, atropine)
- Airway equipment (facemask, endotracheal tube, airways)
- Suction apparatus
- 1% lidocaine 0.5% bupivacaine in equal proportions
- Around 15–25 ml used
- 21 G 4 inch insulated needle
- 10 cc syringe.

Patient Preparation

- NPO status confirmed
- Consent taken
- Venous access secured
- IV midazolam 0.03–0.05 mg/kg can be administered
- Standard monitors applied—ECG, blood pressure, pulse oximetry.

Technique

Classic Posterior Approach of Labatt

Position

- Lateral decubitus position (Sims position)
- Operative extremity nondependant.

Technique

- Strict asepsis
- Line drawn from greater trochanter to posterior superior iliac spine (GT-PSIS line)
- Second line drawn from greater trochanter to sacral hiatus (GT-SH line)
- Line drawn perpendicular to midpoint of GT-PSIS line in caudal direction
- Intersection of this perpendicular and GT-SH line is needle insertion point
- Needle advanced perpendicular to skin
- After eliciting gluteal stimulation, needle advanced further
- Motor response of distal ankle, foot or toes elicited
- Reduce stimulation to < 0.5 mA
- Witness fade of motor activity after injection of 1 ml local anesthetic
- 20–25 ml local anesthetic injected in graded aliquots after negative aspiration of blood
- Pressure applied for 10 seconds and patient made to lie supine immediately after injection.

Lithotomy Approach of Raj

Position

- Lithotomy position.

Technique

- Strict asepsis
- Midpoint between greater trochanter and ischial tuberosity identified
- Needle inserted at this point and advanced perpendicular to skin
- Motor response elicited in distal ankle, foot or toes
- Reduce stimulation to < 0.5 mA
- Witness fade of motor activity after injection of 1 ml local anesthetic
- 15–20 ml local anesthetic injected in graded aliquots after negative aspiration of blood.

Anterior Approach of Meier

Position

- Supine position
- Legs in slight internal rotation.

Technique

- Strict asepsis
- Line drawn between pubic tubercle and anterior superior iliac spine
- Second line drawn parallel to inguinal ligament starting from greater trochanter and going medially across anterior thigh
- First line is divided into 3 parts and perpendicular drawn from junction of middle and inner thirds
- Point of intersection of perpendicular and second line is point of insertion of needle
- Needle inserted perpendicular to skin
- Advanced till motor response of distal ankle or foot or toes noted
- Reduce stimulation to < 0.5 mA
- Witness fade of motor activity after injection of 1 ml local anesthetic
- 15–20 ml local anesthetic injected in graded aliquots after negative aspiration of blood.

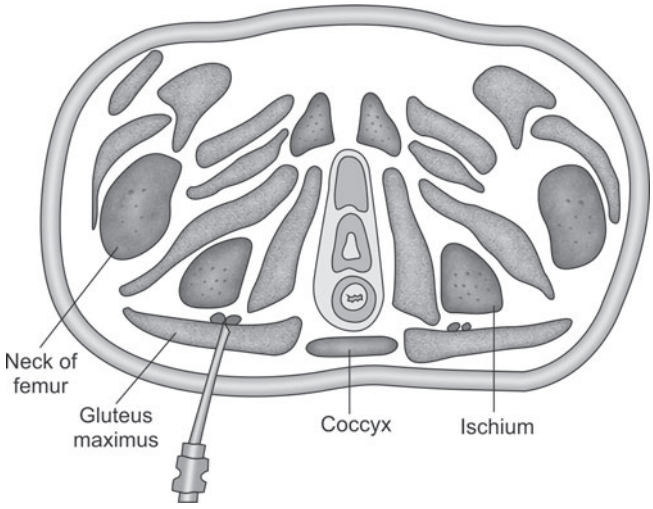


Fig. 9.11: Sciatic nerve block[2]

Advantages

- Multiple approaches.

Disadvantages

- Block takes long onset time as it is resistant to LA penetration
- Difficult positioning especially in lower limb fractures
- Block crosses multiple muscle planes—painful
- Risk of injury to major vessels
- Incomplete sensory block below knee—requires supplemental saphenous N block
- Almost always requires a supplemental block
- Anterior approach is very distal—sparing of posterior cutaneous nerve of thigh.

Complications

- Partial block—injection distal to branching of sciatic N
- Intraneural injection—neuropraxia/neurolysis
- Hematoma—damage to inferior gluteal vessels
- Intravascular injection
- LA Systemic Toxicity (LAST)
- Infection.

POPLITEAL BLOCK[1,2,3]

Introduction

Involves blocking sciatic nerve in the popliteal fossa.

Anatomy

Boundaries of popliteal fossa:

- Lateral: Biceps femoris tendon
- Medial:
  - Semimembranosus
  - Semitendinosus
- Contents:
  - Popliteal A (immediately lateral to semitendinosus)
  - Popliteal V (lateral to artery)
  - Tibial N
  - Common peroneal N (lateral to vein, medial to biceps femoris)
- Tibial N continues deep to gastrocnemius muscle
- Common peroneal N passes between head and neck of fibula to supply lower leg.

Indications

- Tourniquet analgesia for calf tourniquet
- Sural N biopsy
- Short saphenous nerve stripping
- Foot and ankle surgeries
- In conjunction with saphenous N block for complete anesthesia distal to knee.

Contraindications

- Burn/infection at injection site
- Local anesthetic allergy
- Coagulopathy
- Pre-existing neurological disease.

OT Preparation

- Emergency drugs kept ready (thiopentone, adrenaline, atropine)
- Airway equipment (facemask, endotracheal tube, airways)
- Suction apparatus
- 1% lidocaine 0.5% bupivacaine in equal proportions
- Around 25–30 ml used
- 22 G 2 inch insulated stimulating needle
- 20 cc syringe.

Patient Preparation

- NPO status confirmed
- Consent taken
- Venous access secured
- IV midazolam 0.03–0.05 mg/kg can be administered

- Standard monitors applied – ECG, blood pressure, pulse oximetry.

Technique

Posterior Approach

Position

Prone position.

Technique

- Strict asepsis
- Boundaries of popliteal fossa identified and popliteal crease drawn inferiorly
- 8–10 cm perpendicular line drawn cephalad from midpoint of popliteal crease
- Insertion point is 1 cm below apex of triangle and 1 cm lateral to perpendicular line
- Needle inserted perpendicular to skin and advanced
- Motor response sought in distal ankle, foot or toes
- Reduce stimulation to < 0.5 mA while witnessing activity
- Witness fade of motor activity after injection of 1 ml of local anesthetic
- After negative aspiration of blood 30–40 ml local anesthetic injected.

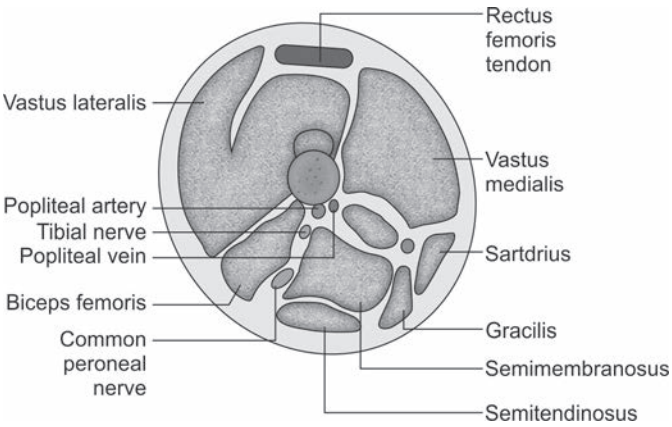


Fig. 9.12: Popliteal nerve block[2]

Lateral Approach

Position

Supine position.

Technique

- Palpate intertendinous groove between vastus lateralis and biceps femoris
- Groove present 10–12 cms proximal to superior notch of patella
- Needle advanced at 30° to skin, posteriorly angled
- Motor response elicited in distal ankle, toes or foot
- Reduce stimulation to < 0.5 mA while witnessing activity
- Witness fade of motor activity after injection of 1 ml of local anesthetic
- After negative aspiration of blood 25–40 ml local anesthetic injected.

Advantages

- Preserves hamstring function
- Allows early mobilization of postoperative patient
- Prolonged postoperative analgesia.

Disadvantages

- Variable success rate.

Complications

- Block failure
- Heel necrosis
- Intraneural injection
- Intravascular injections—LA Systemic Toxicity (LAST)
- Hematoma
- Infection.

SAPHENOUS NERVE BLOCK[1,2,3]

Introduction

Allows rapid anesthetization of anteromedial lower extremity, including medial malleolus.

Anatomy

- Largest terminal sensory branch of femoral N
- Derived from L_3L_4 nerve roots
- Travels through femoral triangle, lateral to vessels
- Beyond femoral triangle, it lies between sartorius and gracilis
- Distal to knee, it proceeds caudally along medial aspect of leg, with saphenous vein
- Provides sensory innervation to medial aspect of lower leg between knee and medial malleolus.

Indications

- Saphenous vein harvesting
- Knee arthroscopy
- Anterior cruciate ligament reconstruction
- Analgesia following medial meniscectomy
- Wound exploration/abscess drainage medial malleolus

- Usually in conjunction with popliteal block for medial foot/ankle surgery
- Usually not performed alone.

Contraindications
- Pre-existing peripheral neuropathy
- Patient refusal
- Anticoagulation
- Infection or inflammation over injection site
- Local anesthetic allergy.

OT Preparation
- Emergency drugs kept ready (thiopentone, adrenaline, atropine)
- Airway equipment (facemask, endotracheal tube, airways)
- Suction apparatus
- 1% lidocaine
- Around 10–12 ml used
- 22 G 10 cm needle
- 10 cc syringe.

Patient Preparation
- NPO status confirmed
- Consent taken
- Venous access secured
- IV midazolam 0.03–0.05 mg/kg can be administered
- Standard monitors applied – ECG, blood pressure, pulse oximetry.

Position
- Supine position
- Thigh abducted and externally rotated.

Technique

Below Knee Field Block Approach
- Strict aspsis
- Subcutaneous infilteration of local anesthetic (7–10 ml)
- Infilteration starts from tibial tuberosity, directed medially
- Infiltration completed near posterior aspect of leg.

Transsartorial Approach
- Strict asepsis
- Identify sartorius muscle on medial aspect of leg, just above knee
- Needle inserted 2 cms above patella, slightly posterior and caudal to coronal plane
- Needle advanced through body of satorius until it reaches subsartorial plane
- 7–10 ml local anesthetic injected.

Paravenous Approach
- Strict asepsis
- Tourniquet placed proximal to knee
- Leg placed over side of bed to make vein palpable
- Injection site along medial side of leg, just below patella
- 5 ml local anesthetic deposited on either side of vein in subcutaneous tissue.

Complications
- Block failure
- Postblock ecchymosis/hematoma
- Neuritis secondary to needle trauma or drug toxicity
- Intravascular injection—Local Anesthetic Systemic Toxicity (LAST)
- Infection.

ANKLE BLOCK[1,2,3]

Introduction
Ankle block accomplished by blocking 5 nerve trunks:
- Tibial N (L_{45}, S_{123})
- Sural N
- Deep peroneal N (L_{45}, S_{12})
- Superficial peroneal N (L_{45}, S_{12})
- Saphenous N (L_{234}).

Indications
- Heal spur excision
- Mortons neuroma excision
- Lacerations of foot
- Heal spur excision
- Diabetic foot
- Toe amputation.

Contraindications
- Localized infection of foot
- Young children
- Allergy to local anesthetics
- Patient noncompliance.

Advantages
- Ease of administration
- Safe technique
- Rapid onset of anesthesia
- Avoids neuraxial or general anesthetic complications.

Disadvantages
- Purely sensory
- Requires at least 3 separate injections
- Uncomfortable for patient.

Complications
- Infection
- Residual paresthesias
- Hematoma
- Vascular puncture
- Nerve injury
- Block failure.

Patient Preparation
- NPO status confirmed
- Consent taken
- Venous access secured
- IV midazolam 0.03–0.05 mg/kg can be administered
- Standard monitors applied—ECG, blood pressure, pulse oximetry.

OT Preparation
- Emergency drugs kept ready (thiopentone, adrenaline, atropine)
- Airway equipment (facemask, endotracheal tube, airways)
- Suction apparatus
- 1% lidocaine 0.5% bupivacaine in equal proportions
- Around 30 ml used
- 25 G 3–5 cm needle
- 10 cc syringe.

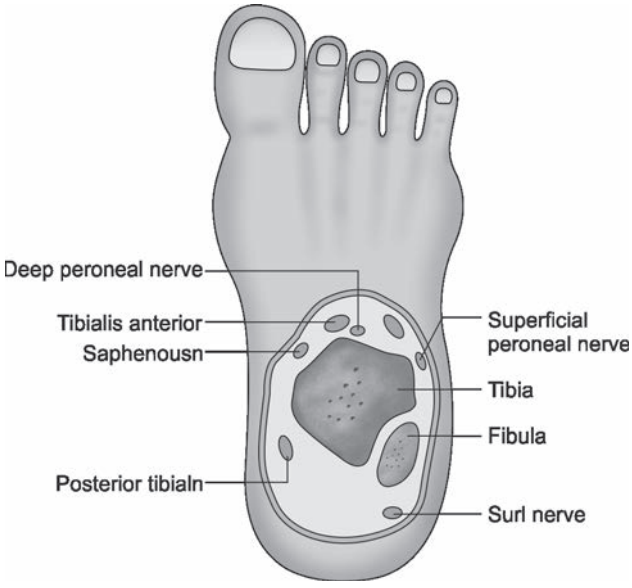


Fig. 9.13: Ankle block[2]

Position
- Supine
- Blanket/pillow under lower leg.

Technique
Tibial N

Anatomy
- Lies behind posterior tibial artery
- Anteromedial to achilles tendon
- Deep to flexor retinaculum.

Supply
- Sole and plantar portion of toes up to nails.

Technique
- 3–5 cms 25G needle
- Directed at right angle to tibia
- Medial to Achilles tendon at level of upper border of medial malleolus
- Advanced until paresthesia elicited or bone contacted
- 5–7 ml local anesthetic injected near posterior aspect of tibia
- Equal volume injected during withdrawal.

Sural N

Anatomy
- Located posterior to lateral malleolus
- Resides in superficial plane
- Accompanies short saphenous vein
- Extends to third digit.

Supply
- Cutaneous sensation of lower posterolateral ankle, lateral foot, fifth toe.

Technique
- Subcutaneous infilteration from lateral malleolus to Achilles tendon
- Given at upper border of lateral malleolus
- 5–10 ml of local anesthetic injected.

Deep Peroneal N

Anatomy
- Courses midway between malleoli
- Assumes position between anterior tibial and extensor hallucis longus tendons
- Present beneath extensor retinaculum at dorsum of foot
- Lies lateral to deep peroneal artery.

Supply
- Innervates short extensors of toe
- Skin sensations to interdigital cleft between great and second toes.

Technique
- Patient dorsiflexes foot
- Tendon of extensor hallucis longus identified
- 25G 3–5 cm needle used
- Needle inserted perpendicular to skin along line joining malleoli
- Point of insertion lateral to dorsalis pedis artery
- LOR felt during passage through extensor retinaculum
- Advanced until tibia is felt
- Paresthesia may be felt between great and second toe
- 3–5 ml local anesthetic injected.

Superficial Peroneal N

Anatomy
- Located on dorsal lateral aspect of foot
- Lie superficially above fascial plane.

Supply
- Cutaneous sensation to dorsum of foot and toes
- All areas supplied except between great and second toes.

Technique
- Inject local anesthetic subcutaneously
- Injected laterally from site of injection of deep peroneal N
- Directed towards superficial aspect of lateral malleolus
- 5–10 ml local anesthetic solution injected.

Saphenous N

Anatomy
- Runs anterior to medial malleolus near long saphenous N
- Lies deep and posterior to great saphenous vein.

Supply
- Cutaneous innervation to anteromedial side of lower leg
- Medial foot midway to toes.

Technique
- 3–5 ml local anesthetic injected subcutaneously
- Medially posterior to great saphenous vein
- Local anesthetic injected at anterior aspect of medial malleolus.

ASRA 2010 GUIDELINES[1,2,3]

Warfarin
- Stop 5 days before NAB with normalization of INR (< 1.5) before NAB
- Check inr before nab if patients recieve initial dose of warfarin before surgery.
- Monitor INR daily in patients recieving warfarin therapy during epidural anesthesia.
- Remove indwelling catheter when INR < 1.5 in patients recieving thromboprophylaxis with warfarin.
- Caution while removing catheter if INR between 1.5 to 3
- Assess CNS status before removal and continue till INR has stabilized.
- If INR > 3 hold warfarin dose or reduce dose if indwelling catheter present.
- Avoid concurrent drugs which alter hemostasis (NSAIDs, Ticlopidine)
- Monitor sensory and motor function, use low local anesthetic (LA) concentration to minimise degree of motor blockade.

Unfractionated Heparin

Twice Daily Dosing
- No contraindication for NAB if dose <10000 IU per day
- Provided PT, aPTT and platelet counts are normal.

Thrice Daily Dosing (> 10,000 IU/day)
- Increased risk of surgical bleeding
- Safety of NAB not established
- Unclear whether increased risk of spinal hematoma
- Assess risk benefit ratio on individual basis
- Apply techniques to detect neurodeficits:
  - Enhanced CNS monitoring
  - Minimal LA concentration.

Nab During Intraoperative Anticoagulation
- Avoid the technique if other coagulopathies
- Delay heparin for 1 hr after needle placement
- Remove catheter 2 hrs after last dose
- Restart heparin 1 hr after catheter removal
- Assess CNS status frequently postremoval
- Use low LA concentration
- Delay next UFH dose for 24 hrs if bloody tap.

Low Molecular Weight Heparin

Preoperative LMWH

- NAB after 12 hrs of last LMWH dose if prophylactic dosing regimen
- NAB after 24 hrs of last LMWH dose if therapeutic dosing regimen
- NAB contraindicated if LMWH given within 2 hrs preoperative.

Postoperative LMWH

Single daily regimens:

- First LMWH dose 8 hrs postcatheter placement
- Second LMWH dose > 24 hrs after 1st dose
- Catheter removed 12 hrs after last LMWH dose
- Subsequent LMWH > 2 hrs after catheter removal.

Twice daily regimens:

- Increased risk of spinal hematoma.
- 1st LMWH dose > 24 hrs post NAB placement.
- Avoid indwelling catheter.
- Remove indwelling catheter before initiating LMWH therapy.
- Initiate LMWH at least 2 hrs after catheter removal.
- LMWH therapy delayed > 24 hrs postop if bloody tap.
- Avoid drugs which affect hemostasis concomitantly.

NSAIDs

- No contraindication. Can be continued intraoperative.

Antiplatelet

- Discontinue ticlopidine for 14 days
- Discontinue clopidogrel for 7 days
- Can continue aspirin and dipyridamole intraoperatively.

Direct Thrombin Inhibitors: Thrombolytics

- NAB contraindicated with DTIs, streptokinase and alteplase.

Fondaparinux

- Actual risk of hematoma unknown.
- Atraumatic needle placement recommended.
- Single needle pass technique.
- Avoid indwelling catheter.

GP IIb-IIIa Antagonists

- Discontinue abxicimab for 48 hrs before NAB.
- Discontinue eptifibatide and tirofiban for 48 hrs before NAB.

Herbal Therapy

- No added risk of spinal hematoma by themselves.
- No evidence to recommend mandatory discontinuation.
- Consider drug interactions.

COMPLEX REGIONAL PAIN SYNDROME[1,2,3]

Introduction

CRPS formerly known as *reflex sympathetic dystrophy*, is a debilitating neuropathic pain disorder causing severe burning pain and vasomotor instability, due to autonomic nervous system dysfunction, usually in an extremity.

Types

CRPS Type I

- ***Reflex sympathetic dystrophy***
- Minor injuries/fractures of limb precede onset of symptoms.

CRPS Type II

- ***Causalgia***
- Develops after injury to major peripheral nerve.

Etiology

Highest incidence between 50–70 yrs age

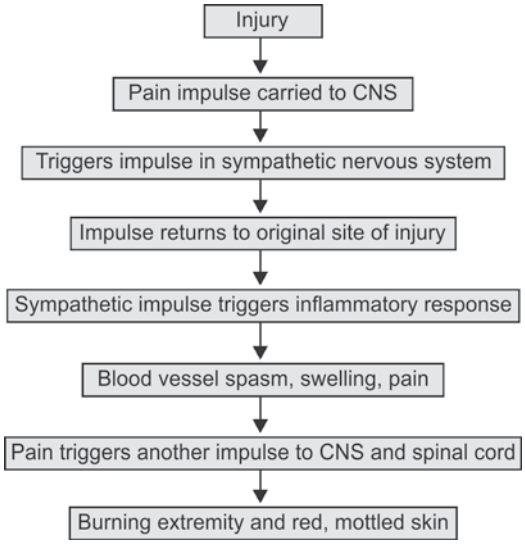
More frequently in women

- Trauma affecting distal part of extremity
- Postsurgical condition
- Contusions
- Strain/sprain
- CNS lesions:
  - Spinal cord injuries
  - CVA
  - Cardiac ischemia.

Pathophysiology

Various Theories

- Genetic predisposition
- Immobilization of limb
- Unregulated sympathetic nervous system
- Exaggerated neurogenic inflammation.



Clinical Features

Pain

- Poorly controlled
- Distal extremity
- Burning, spontaneous pain
- Disproportionate intensity to the inciting event
- Increases with limb in dependant position.

Autonomic Disturbances

- Swelling, sweating in the distal extremity
- Affected limb warmer than normal limb
- Hyper or hypohydrosis of affected limb.

Trophic Changes

- Abnormal nail growth
- Increased/decreased hair growth
- Thin, glossy skin
- Osteoporosis in chronic cases
- Restriction of passive limb movements
- Weakness of all muscles of extremity
- Movement disorders:
  - Loss of voluntary control
  - Bradykinesia
  - Dystonia
  - Myoclonus, tremors.

CRPS type II has all these features in addition to focal deficits due to lesions of peripheral nerve.

Stages

- *Warm stage*: With initial vasomotor symptoms
- *Intermediate stage*: With sudomotor symptoms
- *Cold stage*: With dystrophic and motor changes.

Diagnosis

Modified IASP Diagnostic Criteria (Budapest Criteria)

- Continuing pain disproportionate to inciting event
- At least one symptom in each category of:
  - Sensory:
    - Hyperesthesia
    - Allodynia.
  - Vasomotor:
    - Temperature asymmetry
    - Skin color changes
    - Skin color asymmetry in affected region.
  - Sudomotor/edema:
    - Edema
    - Sweating changes
    - Sweating asymmetry in affected region.
  - Motor/trophic:
    - Decreased range of motion
    - Motor dysfunction (weakness, tremor, dystonia)
    - Trophic changes (hair, nails, skin) in affected region.
- At least one sign in 2 or more categories:
  - Sensory: Evidence of:
    - Hyperalgesia to pin prick
    - Allodynia to light touch and/or deep somatic pressure and/or joint movement.
  - Vasomotor: Evidence of:
    - Temperature asymmetry
    - Skin color changes and/or asymmetry.
  - Sudomotor/edema: evidence of:
    - Edema
    - Sweating changes
    - Sweating asymmetry.
  - Motor/trophic: evidence of:
    - Decreased range of motion
    - Motor dysfunction (weakness, tremor, dystonia)
    - Trophic changes (hair, skin, nails).
- No other diagnosis better explains the signs and symptoms.

Treatment

Options

- Antinflammatory agents:
  - Naproxen
  - Ketorolac
  - Prednisone

  - Intravenous immunoglobulins
  - Anti-TNF monoclonal antibodies.
- Free radical scavengers:
  - Topical DMSO
  - Vitamin C.
- Inhibition of pain sensitization:
  - Intrathecal baclofen
  - Topical capsaicin
  - Carbamazepine oral
  - Gabapentin oral
  - Nifedipine oral
  - Ketamine oral
  - Intrathecal glycine
  - Intravenous lidocaine
  - Intrathecal morphine.
- Sympatholytic agents:
  - Topical clonidine
  - Intravenous lidocaine + guanethidine
  - Phenoxybenzamine
  - Reserpine.

Goals

- Relative pain reduction of at least 50%
- Reduction of VAS score by 30 mm on 100 mm scale.

Guidelines

- General:
  - Immobilize affected limb
  - Careful contralateral physiotherapy – ***acute treatment of choice***
  - Assume passive physical therapy of affected limb once resting pain subsides
  - Active isometric strengthening in combination with sensory desensitization programs till restoration of complete motor function.
- Analgesics:
  - NSAIDs: COX-2 inhibitors (etodolac, aceclofenac) ***first line analgesics***
  - Gabapentin, pregabalin: ***First line coanalgesics***
  - Opioids
  - Antidepressants
  - Calcium regulation agents: If refractory pain.
- Antiinflammatory:
  - Corticosteroids.
- Muscle relaxants:
  - Tizanidine
  - Baclofen
  - Clonazepam.
- Sympatholytic procedures:
  - Sympathetic ganglion blocks:
    - Stellate ganglion blocks
    - Lumbar sympathetic blocks.
  - Continuous intrathecal drug delivery systems:
    - ***Continuous Intrathecal Pump Implantation (CIPI)***
    - With intrathecal baclofen
    - Exorbitant cost.
  - ***Radiofrequency Neurolysis (RFN):***
    - Decreased incidence of neuritis
    - Avoids tinnitus
    - Avoids blindness
    - Avoids urethral stricture.
  - ***Spinal Cord Stimulation***
  - ***Endoscopic Thoracic Sympathectomy (ETS)***
  - ***Motor Cortex Stimulation.***
- Psychological support:
  - Cognitive behavioral therapy
  - Transcendental meditation.

CHAPTER

10

ICU and Mechanical Ventilation

HYPONATREMIA[1,2,3,10,12,18,19]

Introduction

Serum sodium levels < 135 mEq/L is called hyponatremia.

Etiology[2]

- Pseudohyponatremia: Hyponatremia with normal or increased plasma osmolality:
  - Hyponatremia with normal plasma osmolality:
    - Hyperlipidemia (chylomicronemia)
    - Hyperproteinemia: Glycine during TURP
  - Hyponatremia with increased plasma osmolality:
    - Hyperglycemia
    - Mannitol.
- True hyponatremia with low plasma osmolality:
  - With increased total body sodium:
    - CCF, nephrotic syndrome
    - Idiopathic edema
    - Cirrhosis, chronic renal failure
    - Hypoalbuminemia.
  - With low total body sodium:
    - Renal wasting:
      - Thiazide diuretics/mineralocorticoid deficiency
      - Renal tubular acidosis, cerebral salt wasting syndrome.
    - Extrarenal losses:
      - Vomiting, diarrhea
      - Integumentary loss, third spacing.
  - With normal total body sodium:
    - SIADH, primary polydipsia
    - Drug induced: Chlorpropamide, cyclophosphamide
    - Fluid overload due to CRF
    - Glucocorticoid deficiency
    - Hypothyroidism.
- True hyponatremia with normal plasma osmolality:
  - globulins
  - Lithium
  - THAM.
- Causes as related to volume status:
  - Hypovolemic hyponatremia:
    - Hemorrhage
    - Burn wound edema
    - Peritonitis
    - Cerebral salt wasting syndrome.
  - Hypervolemic hyponatremia:
    - CCF, nephrotic syndrome
    - Cirrhosis, TURP syndrome.
  - Euvolemic hyponatremia:
    - SIADH
    - Pseudohyponatremia
    - Iatrogenic administration of vasopressin
    - Increased AVP secretion from:
      - Small cell carcinoma of lung
      - Duodenal and pancreatic carcinoma.

Cerebral Salt Wasting Syndrome

- Severe salt wasting diathesis due to secretion of brain natriuretic peptide, in which ADH levels are normal unlike SIADH
- Predisposing factors:
  - Cerebral lesions due to trauma
  - Subarachnoid hemorrhage
  - Tumors, infections.
- Hydrocortisone 1200 mg/day prevents cerebral salt wasting syndrome.

Pathophysiology

- Acute hyponatremia:
  - Rapid reduction in plasma sodium occurs
  - Blood brain barrier is more permeable to water
  - Rapid reduction in plasma sodium increases both ECF and ICF brain water
  - Fall in plasma sodium levels causes hypoosmolality
  - Hypoosmolality rather than hyponatremia causes symptoms due to cerebral edema.
- Chronic hyponatremia:
  - Gradual compensatory lose of intracellular solutes occurs
  - Gradual rate of loss restores cell volume to normal
  - Thus, edema is absent even though hyponatremia occurs.

Pathogenesis

- Hyponatremia with low total body sodium:
  - Occurs due to loss of both sodium and water
  - But the loss of sodium is more than that of water
  - When intravascular deficient reaches 10% non-osmotic ADH secretion is activated
  - This occurs through:
    - Atrial stretch receptors
    - Carotid baroreceptors from preoptic muscles in hypothalamus.
  - This causes decreased renal free water elimination resulting in hyponatremia
  - In hyponatremia due to vomiting:
    - Chloride is lost from the gastrointestinal tract
    - Kidney starts bicarbonaturia as a compensatory mechanism
    - Thus sodium is also lost along with bicarbonate ions
    - Hence, urinary sodium is usually more than 20 mEq/L.
- Hyponatremia with increased total body sodium (TBN):
  - Aquaporin is upregulated in CCF, cirrhosis and CRF
  - Progressive impairment of renal free water excretion occurs due to:
  - Nonosmotic ADH release
  - Decreased delivery of fluid to distal diluting segment in nephrons.
- Hyponatremia with normal TBN:
  - Occurs in adrenal hypofunction
  - Occurs due to cosecretion of ADH along with corticotropin releasing factor
  - Common in AIDS due to CMV and mycobacterial infection of adrenal gland.

Clinical Features

- Primarily neurological manifestations
- Burning of hand and face is earliest symptom
- Severity depends on rate of development of extracellular hypoosmolality
- Mild to moderate hyponatremia are frequently asymptomatic
- Severe hyponatremia (< 120 mEq/L) causes symptoms of cerebral edema
- Acute hyponatremia:
  - Neurological manifestations:
    - Cerebral edema when serum Na^+ < 123 mEq/L
    - Apathy, lethargy
    - Agitation, altered consciousness
    - Headache, obtundation
    - Disordered reflexes and thermoregulation
    - Muscle twitching, seizures, coma.
  - Cardiovascular manifestations:

    Symptoms usually seen serum Na^+ < 100 mEq/L
    - Vasoconstriction and increased PVR causing HTN
    - Bradycardia
    - Increased blood flow to liver and kidneys
    - Decreased blood flow to skin and muscles.
  - Musculoskeletal:
    - Muscle cramps
    - Weakness during strenuous exercise.
  - Renal:
    - Dilute urine
    - Urine Na^+ < 10 mEq/L indicates extrarenal losses with intact renal sodium handling
    - Urine Na^+ > 20 mEq/L indicates intrinsic renal tubular damage.
  - Gastrointestinal:
    - Usually occurs early and first
    - Anorexia, nausea, vomiting.
- Chronic hyponatremia:
  - Focal weakness, hemiparesis
  - Weakness, ataxia
  - Positive Babinski sign.

Treatment[1,2,3]

- Treatment of cause:
  - Treat underlying disease

- Remove offending drugs
- Hyponatremia with normal or high serum osmolality: Remove nonsodium solute:
  - Glucose
  - Mannitol
  - Urea.
- Hyponatremia with low serum osmolality:
  - High total body sodium:
    - Restrict salt and water
    - Improve renal perfusion:
      - Increase cardiac output
      - Inotropes
      - Vasodilators.
    - Increase renal blood flow:
      - Dopamine
      - Diuresis
      - Dialysis.
  - Low total body sodium:
    - Restore blood volume: Saline
    - Eliminate sodium losses
    - Treat adrenal insufficiency
    - Cortisol.
  - Normal total body sodium:
    - Restrict water
    - Loop diuretic
    - Urinary sodium replacement with 0.9% or 3% saline
    - Lithium, demeclocycline
    - Thyroid replacement, hemodialysis
    - V_2 receptor antagonists:
      - Conivaptan
      - Tolvaptan.

- Replacement of sodium:[2]
  - Choice of fluid:
    - Hypertonic saline given if:
      - Seizures
      - Severely symptomatic
      - Serum $Na^+ < 110$ mEq/L
      - Rapid development of hyponatremia
      - More than 0.5 mEq/L/hr reduction in sodium levels.
    - Isotonic saline: Fluid of choice in mild-moderate cases
  - Rate of administration:
    - Not to exceed 0.6–1 mEq/L/hr
    - If Na^+ levels reach 125 mEq/L, water restriction alone is sufficient
    - Hypertonic saline at 1–2 ml/kg/hr to increase Na^+ by 1–2 mEq/L/hr
    - Rate can be reduced if symptoms improve.
  - Amount to be administered:
    - Na^+ deficit = TBW × [(desired Na^+) – (present Na^+)]
    - Free water excess = TBW × 125/(Measured plasma Na^+)
    - Urine volume for diuresis = FWE x [1–urine Na^+]/154
  - Duration of administration:
    - First half of deficit given over 8 hours
    - Next half—given over 1–3 days if symptoms persist.
  - Monitoring:
    - Serial serum Na^+ levels (every 2 hours)
    - Used to prevent correction at more than 1–2 mEq/L/hr or 8 mEq/L in 24 hours.
  - Recovery:
    - CNS signs and symptoms usually improve within 24 hours
    - It may require 4 days for complete recovery
- Newer modalities: Urea administration is under investigation
- Complications of therapy:
  - Delayed correction causes neurological injury
  - Cerebral hemorrhage/CCF if rapid rates of correction
  - Complications of using hypertonic saline:
    - Pulmonary edema
    - Hypokalemia
    - Hyperchloremic metabolic acidosis
    - Transient hypotension
    - Coagulation defects: Raised PT and aPTT
  - *Central pontine demyelination/osmotic demyelination:*
    - Lesion occurring due to correction of sodium levels at a rate faster than brain can adapt to higher osmolality
    - Pathophysiology:
      - Rapid correction causes abrupt brain dehydration
      - This causes neuronal crenation
      - This results in permanent neurological sequelae.
    - Risk factors: More likely if:
      - Hyponatremia has persisted for longer than 48 hours
      - Correction rates:
        - More than 20 mEq/L/day
        - More than 0.6 mEq/L/hr

- ° Associated alcoholism, poor nutritional status
- ° Liver disease, burns, hypokalemia.

- Clinical features:
  - ° Fluctuating levels of consciousness
  - ° Behavioral disturbances, dysarthria, dysphagia
  - ° Convulsions, pseudobulbar palsy, quadriplegia.
- Prognosis:
  - ° Improvement may occur after several weeks
  - ° Some patients may be permanently impaired.

Hyponatremia Severity

Serum Levels	ECG	CVS	CNS
120 mEq/L	Wide QRS complex	Hypotension	Restlessness
		Bradycardia	Confusion
115 mEq/L	Wide QRS complex	Cardiac depression	Nausea
	ST elevation		Somnolence
	Ectopics		
110 mEq/L	VT	CCF	Seizures
	VF		Coma

HYPERNATREMIA

Introduction

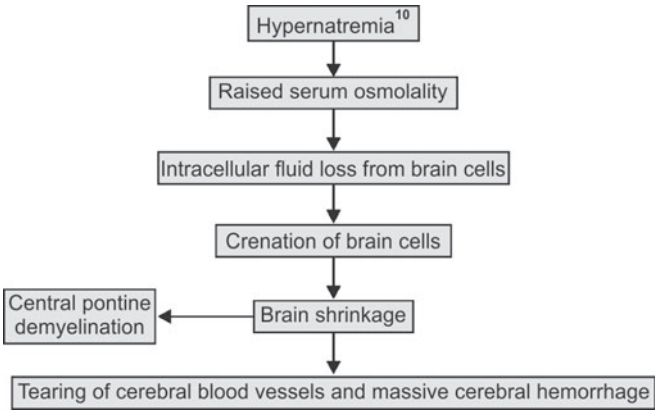
Refers to the condition where serum $Na^+ > 150$ mEq/L

Etiology

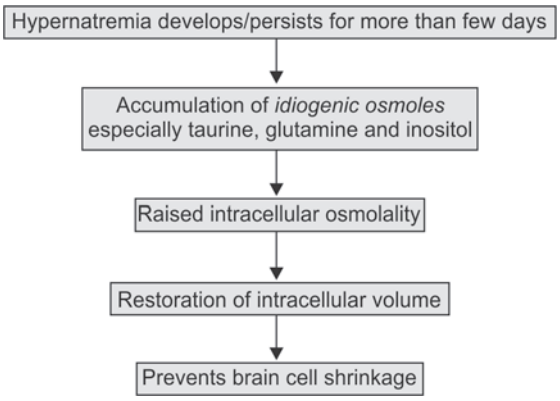
- Hypernatremia with low total body sodium: Hypotonic fluid loss:
  - – GI losses: Vomiting, diarrhea, intestinal fistula
  - – Skin loss: Burns, sweating
  - – Impaired renal concentrating ability:
    - Osmotic dieresis, hypercalcemia
    - Prolonged water intake, reduced protein intake
    - Sickle cell disease, multiple myeloma.
- Hypernatremia with normal total body sodium:
  - – Exercise, seizures, rhabdomyolysis
  - – Central and nephrogenic diabetes insipidus
  - – CNS disorders: Hypothalamic lesions.
- Hypernatremia with high total body sodium:
  - – Iatrogenic:
    - $NaHCO_3$ (contains 1000 mEq/L of sodium)
    - 3% hypertonic saline (contains 514 mEq/L of sodium).
  - – Deliberate/accidental ingestion:
    - Substitution of sugar with salt in infant feeds
    - Sea water ingestion/drowning.
  - – Mineralocorticoid/glucocorticoid excess:
    - Primary hyperaldosteronism
    - Cushings syndrome, ectopic ACTH production.
  - – Peritoneal dialysis.

Pathophysiology

Acute Hypernatremia



Chronic Hypernatremia



Clinical Features

- Common in:
  - – Debilitated patients who cannot drink
  - – Very old/young patients
  - – Patients with altered consciousness.

- Each liter of water deficit raises serum Na^+ by 3–5 mEq/L
- Acute symptoms occur once $Na^+ \geq 150$ mEq/L although rate for change of Na^+ is important
- Associated hypocalcemia may contribute to brain damage
- Fever can be a contributing cause/a result of hypernatremic dehydration
- Neurological symptoms predominant.

Osmolarity (Mosm/Kg)[1]	Manifestations
350–375 msom/kg	Restlessness, irritability
375–400 mosm/kg	Tremulousness, ataxia
400–430 mosm/kg	Hyper-reflexia, spasticity, twitching
≥ 430 mosm/kg (serum $Na^+ \geq$ 158 mEq/L)	Seizures, death

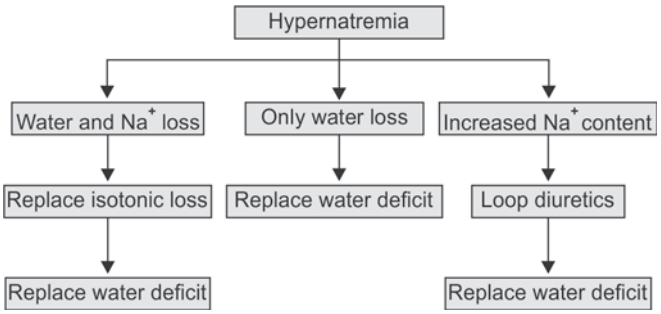
Complications

- Massive/multiple small parenchymal hemorrhagges
- Subdural/subarachnoid hemorrhage
- Cortical venous thrombosis
- Renal insufficiency and ARF
- Polyuria causing hydronephrosis and bladder distension.

Evaluation

- Hypovolemic hypernatremia:
  - Nonrenal losses:
    - U_{Na} less than 10–15 mEq/L
    - U_{OSM} more than 400 mosm/kg.
  - Renal water losses:
    - U_{Na} more than 20 mEq/L
    - U_{OSM} less than 300 mosm/kg.
- Euvolemic hypernatremia:
  - Nonrenal water losses:
    - U_{Na} variable
    - U_{OSM} more than 400 mosm/kg.
  - Renal water losses:
    - U_{Na} variable
    - U_{OSM} less than 290 mosm/kg.
- Hypervolemic hypernatremia:
  - Iatrogenic
  - Mineralocorticoid excess:
    - U_{Na} more than 20 mEq/L
    - U_{OSM} more than 300 mosm/kg.

Treatment



- Cornerstone of treatment is volume replacement and restoring plasma osmolality
- Calculation of free water deficit:

Free water deficit (L) = TBW × (Measured Na^+ – Normal Na^+)/Normal Na^+

- Rate of correction:
  - Not more than 1–2 mEq/L/hour
  - In chronic cases especially, correction of Na^+ deficit should be gradual
  - Rapid correction can cause brain cells to swell and cause edema
  - In acute cases, correction can be more rapid as no idiogenic osmoles will be present.
- Choice of fluids:
  - Hypernatremia with low total body sodium:
    - Isotonic saline/fluids initially, for correction of hypernatremia
    - Hypotonic solution given later, for correction of TBW deficit
  - Hypernatremia with high total body sodium: Treated with D_5W
  - Hypernatremia with normal total body sodium: Treated with D_5W.
- Role of normal saline: NS can be used even in hypernatremia as:
  - Na^+ in solution, will be less than patients serum Na^+
  - In most hypernatremia situations, there is total body sodium deficit
  - Use of NS allows more gradual reduction in serum Na^+ levels.
- Duration of therapy:
  - Serial sodium levels and osmolalities to be obtained
  - Plasma expanding fluids continued till tissue perfusion is restored
  - Urine output should be more than 0.5 ml/kg/hour
  - This is done with 0.45 NS or hypotonic solutions.

- Treat diabetes insipidus:
  - Nephrogenic DI:
    - Salt and water restriction
    - Thiazide diuretics.
  - Central DI:
    - DDAVP 1–4 µg S/C or 5–20 µg intranasally every 12–24 hours
    - Aqueous vasopressin can be used.
  - Partial central DI:
    - Chlorpropamide (potentiates vasopressin)
    - Carbamezepine (increases vasopressin secretion).

Anesthetic Implications

- Postpone elective surgery if serum sodium > 150 mEq/L until corrected
- Both water and isotonic fluid deficits have to be corrected completely prior to surgery
- Hypernatremia increases MAC value of volatile anesthetics
- Reduction in cardiac output and increased MAC values results in increased use of volatile agents
- Reduced V_d for IV anesthetics warrants a reduction in IV dose
- Hypernatremia associated hypovolemia and cardiac depression causes hypoperfusion of tissues and precipitous hypotension due to anesthetic induced vasodilatation.

Prognosis

When plasma osmolality exceeds 350 mosm/kg, mortality rate reaches 40–55%.

Example

70 kg man with serum sodium level of 160 mEq/L:

- Normal TBW × 140 = Present TBW × Present Na^+
- (70 × 0.6) × 140 = Present TBW × 160
- Thus, present TBW = 36.7 L
- Water deficit = Normal TBW – Present TBW = 42–36.7 = 5.3 L
- This volume has to be replaced over 48 hours
- Thus, 110 mL/hr of D_5W has to be given over 48 hours for correction of sodium levels.

HYPOKALEMIA[1,2,3,10,12,14,18,19]

Introduction

- Normal potassium levels are 3.5–5 mEq/L
- Hypokalemia defined as K^+ levels < 3.5 mEq/L.

Etiology[2,3]

There are two main causes of hypokalemia:

1. Transcellular shift: (ECF to ICF shift):
   - Administration of exogenous catecholamines:
     - Isoproterenol, ritodrine
     - Terbutaline, epinephrine
   - Alkalosis, increased plasma insulin
   - Hypothermia
   - Hypokalemic periodic paralysis.
2. Potassium depletion:
   - Insufficient intake:
     - Anorexia nervosa, geophagia
     - Starvation, primary aldosteronism
     - Alcoholism, secondary aldosteronism.
   - Increased losses:
     - GI losses:
       - Vomiting, malabsorption
       - Diarrhea (especially secretory)
       - Enteric fistulas.
     - Renal losses:
       - Barrters syndrome, hypomagnesemia
       - Diuretics, impermeant anion
       - Renal tubular acidosis.
     - Antibiotics: Carbenicillin, penicillin, ticarcillin
     - Sweat losses: Heat stroke, heavy exercise, fever
   - K^+ shifts from ECF to ICF:
     - Vitamin B_{12} therapy, lithium
     - Acute alkalosis, stress related catecholamine release
     - Insulin therapy, hypokalemic periodic paralysis.

Pathophysiology

- K^+ is the principle intracellular cation
- 98% of K^+ in body is intracellular
- Extracellular K^+ is found mainly in muscles
- Reduction in ECF K^+ leads to reduction in the resting membrane potential (RMP)
- This causes reduced responsiveness to sodium shifts into the cell
- Therefore, cellular excitability reduces
- Chronic K^+ loss causes ratio of ICF: ECF K^+ to remain stable
- Acute K^+ loss causes redistribution from ECF to ICF, causing changes in RMP
- This causes hyperpolarization of cardiac cell resulting in:

- Ventricular premature ectopics
- Reentrant phenomenon
- Ectopic tachycardias.

Clinical Features

- Cardiovascular system:
  - Autonomic neuropathy
  - Orthostatic hypotension
  - ECG changes:
    - U waves
    - T wave inversion
    - ST depression
    - QT shortening
  - Dysrhythmias: Ventricular ectopics and AF most commonly.
- Neuromuscular:
  - Malaise, fatigue, weakness, hyporeflexia
  - Cramps, paralysis
  - Paresthesias, rhabdomyolysis
- Gastrointestinal: Paralytic ileus
- Renal:
  - Metabolic alkalosis, parodoxical aciduria
  - Nephrogenic diabetes insipidus, increased ammonia production
  - Low GFR, chronic intestitial damage.
- Endocrine: Glucose intolerance.

ECG Changes

- Changes do not correlate with the severity of hypokalemia
- Narrow QRS complexes
- ST depression
- QT_c prolongation
- T wave inversion and flattening
- U waves
- Predisposed to torsades de-pointes, ventricular fibrillation.

Treatment[3,10,12]

- Treat any condition that promotes transcellular K^+ shifts:
  - Correct alkalosis
  - Stop β_2 agonist/insulin therapy
  - Warm the patient.
- Correcting potassium deficit: 1 mEq/L reduction in serum K^+ level represents 10% loss of total body K^+ stores (100–200 mEq of K^+)
  - Oral replacement:
    - In stable patients with mild-moderate hypokalemia
    - Should be able to tolerate oral intake
    - 20 mEq/L K^+ given every hour until optimum levels are achieved
    - Salt substitutes, K^+ supplements used.
  - Monitoring:
    - Blood pressure
    - Pulse oximetry
    - ECG
    - Bedside K^+ levels
  - Foods rich in K^+:
    - Oranges, tomatoes
    - Grapes, banana
    - Coconuts water, raisin
  - Intravenous replacements:
    - Solutions:
    - KCL:
      - 1 and 2 mEq/ml available
      - Packed as 10–40 mEq per ampoule.
    - K phosphate:
      - 4.5 mEq K^+ and 3 mMol phosphate per ml
      - Solutions should be diluted due to high osmolality
      - Especially used for DKA where phosphate levels are low.
  - Infusion rate and method:

$$\text{KCL required in mL} = \frac{(\text{Body weight}) \times (\text{Potassium deficit})}{2} \times \frac{1}{3}$$

    - Maximum rate is 0.5 mEq/kg/hr or 250 mEq/day
    - Add 20 mEq K^+ to 100 ml of NS and infuse over 1 hour
    - Maximum rate of infusion set at 10–20 mEq/hr
    - 40 mEq/hr K^+ may be used if serum level < 1.5 mEq/L
    - Continuous ECG monitoring required for infusion at 40 mEq/hr
    - Given via infusion pump.
  - Choice of vein:
    - Central vein usually preferred for infusion at 20 mEq/hr due to irritant nature of the hyperosmotic K^+
    - Infusion at 40 mEq/hr should be given through peripheral line as:
      - Risk of hyperkalemia is right heart chamber if central line is used
      - This can lead to cardiac arrest

    - So the K^+ dose is split and is infused via two peripheral veins
- Correct cause of K^+ depletion:
  - Treat fever, diarrhea and vomiting adequately
  - Stop use of diuretics
  - Consider change if antibiotics.
- Refractory hypokalemia:
  - Could be due to hypomagnesemia
  - Check serum magnesium levels and correct if low.

Anesthetic Implications

- Following factors considered before cancelling surgery
  - Urgency of surgery
  - Medications given
  - Acid-base balance
  - Suddenness of electrolyte imbalance.
- Postponement of surgery:
  - All patients undergoing elective surgery to have normal K^+ levels
  - Postponement of surgery not required if $K^+ > 2.8$ mEq/L
  - $K^+ < 3.5$ in cardiac surgery is associated with increased perioperative arrhythmias.
- Plasma K^+ concentration measured 1–3 days before surgery is 0.2–0.8 mEq/L higher than if measured immediately before surgery
- Beta blockers like propranolol can be used to prevent this effect
- Patients with ESRD should undergo dialysis except during emergency surgery
- Prevent hypokalemia from anxiety by premedication with clonidine
- No change in anesthetic requirements immediately perioperatively
- Avoid hyperventilation: Aggravates hypokalemia by causing respiratory alkalosis
- Prolonged NMB action expected post surgery: Delayed recovery.

HYPERKALEMIA[1,2,3,10,12,14,18,19]

Introduction

Serum potassium levels above 5 mEq/L is called hyperkalemia.

Etiology[1,3,10]

- Potassium overload:
  - Potassium supplements, potassium rich foods and IV potassium administration
  - Potassium containing drugs: Potassium penicillin
  - *In-vivo* hemolysis
  - Transfusion of old blood at ≥ 120 mL/min
  - Gastrointestinal bleeding
  - Cell death:
    - After chemotherapy
    - Rhabdomyolysis
    - Crush injuries
    - Extensive tissue necrosis, burns
  - Following cardiopulmonary bypass due to cardioplegia
  - Reperfusion injury.
- Altered internal potassium balance:
  - Acidosis, DKA, insulin deficiency
  - Hypoaldosteronism, hyporeninemic hypoaldosteronism
  - Malignant hyperthermia
  - Periodic paralysis
  - Drugs:
    - Succinylcholine
    - Non-selective β-blockers
    - Digitalis
  - Advanced age
  - Increased chloride reabsorption: *Gordons syndrome,* cyclosporine.
- Altered external potassium balance:
  - Reduced excretion in CRF patients
  - Reduced excretion of potassium
  - Type IV renal tubular acidosis, SLE
  - Sickle cell disease, renal transplant
  - Obstructive uropathy.
- Drugs:
  - Potassium sparing diuretics: Spironolactone, triamterene, amiloride
  - NSAIDs: Inhibit prostaglandin mediated renin release
  - ACE inhibitors and AT-II antagonists:
    - Interfere with AT-II mediated aldosterone release
    - Especially common in CCF patients
  - Trimethoprin, pentamidine
  - Heparin: Interferes with aldosterone secretion
  - Mannitol, cyclosporine.
- *Pseudohyperkalemia:*
  - Causes:
    - Sample lysis *in vitro*, tourniquet use
    - Technical problem, leucocytosis, thrombocytosis

  - Clotted blood K^+ is more than K^+ in heparinized sample by 0.4–0.5 mEq/L
  - This is because K^+ gets extruded from RBCs during clotting
  - Diagnosed by comparing serum and plasma K^+ levels from same sample
  - Stored blood ≥ 21 days contain K^+ upto 19–30 mEq/L.
- Effect of succinylcholine on potassium levels:
  - Succinylcholine in a normal patient raises serum K^+ by 0.5 mEq/L
  - This is because being a depolarizing agent, it causes Na^+ uptake into the cell
  - In exchange, K^+ is thrown out of the cell, causing hyperkalemia
  - Hyperkalemia with succinylcholine occurs in:
    - Metabolic acidosis and hypovolemia
    - Severe abdominal infections
    - Closed head injury
    - After massive trauma: Patients are susceptible for atleast 60 days
    - Conditions causing proliferation of extrajunctional ACH receptors:
      - Guillaine-Barré syndrome
      - Cerebrovascular accidents with hemiplegia
      - Muscular dystrophy.

Pathophysiology

- Hyperkalemia causes:
  - Reduction in RMP of cardiac cells
  - Reduction in duration of myocardial action potential
  - Reduction in upstroke velocity.
- *Sine wave pattern:*
  - Hyperkalemia reduces rate of ventricular depolarization
  - This coincides with beginning of repolarization in some areas of myocardium
  - Other areas of the myocardium are still undergoing depolarization
  - This causes a progressive widening of QRS complexes
  - These merge with T waves, to yield *sine wave pattern.*
- Hyperkalemic cardiotoxicity is enhanced by hyponatremia and hypocalcemia
- Skeletal muscle weakness occurs due to:
  - Sustained depolarization
  - Inactivation of Na^+ channels of muscle membrane.

Clinical Features

- Mainly skeletal muscle and cardiac manifestations
- Neuromuscular manifestations:
  - Neuromuscular dysfunctional weakness
  - Areflexia, ascending paralysis
  - Paresthesias, muscle weakness and flaccid paralysis
  - Inability to phonate and respiratory arrest in severe cases.
- Gastrointestinal: Nausea, vomiting and diarrhea
- Cardiovascular:
  - Cardiac effects are negligible when K^+ is less than 6 mEq/L
  - Death occurs due to diastolic arrest or ventricular fibrillation.

ECG Changes

- However, it is an insensitive and nonspecific method of detecting hyperkalemia
- ECG changes may be the first indicator of hyperkalemia
- Mild hyperkalemia: 5.5–6.5 mEq/L:
  - Increased PR interval
  - Tall, peaked T waves
- Moderate hyperkalemia: 6.5–8 mEq/L:
  - Loss of P wave
  - Prolonged QRS complex
  - ST-elevation
  - Ectopic beats
  - Escape rhythms
- Severe hyperkalemia: More than 8 mEq/L:
  - Progressive QRS widening
  - Sine wave ventricular flutter
  - Ventricular fibrillation
  - Asystole
  - Axis deviation
  - Bundle branch block
  - Fascicular blocks.

Treatment[1,3,10,12]

- General measures:
  - Confirm hyperkalemia by repeat blood sample, if no cardiac derangements
  - Monitor ECG and serum potassium levels
  - Stop further K^+ administration
- Treatment of causes:
  - Aldosterone agonists: 9-fludrocortisone 0.025–0.10 mg/day

- Digitalis intoxication:
  - Resistant to treatment
  - Attempts to shift K^+ into the cell are ineffective
  - Consider digoxin specific antibodies.
- Drugs contributing to hyperkalemia are stopped
- Physiological antagonism:
  - Calcium:
    - Mechanism of action:
      - Stabilizes myocardium
      - Reverses membrane excitability
    - Dosage:
      - 1 gm calcium chloride over 3–5 minutes
      - 1 gm calcium gluconate given over 10 minutes
      - 2–3 gms can be given over 5 minutes in emergencies.
    - Onset of action: 1–3 minutes
    - Duration of action: 30–50 minutes.
- Shift potassium back into the cell:
  - Insulin:
    - Mechanism of action:
      - Through Na^+-H^+ antiporter
      - When Na^+ enters the cell, H^+ is extruded from it
      - This is done to maintain electrical neutrality
      - K^+ must therefore enter the cell, for the same purpose
      - This reduces ECF potassium levels.
    - Dosage:
      - 5–10 IU regular insulin given IV
      - Given along with 25–50 gms dextrose
      - Alternatively, 2 ampoules of 50 ml 50% dextrose can be given
      - 0.15 IU/kg insulin with 1 ml/kg of 50% dextrose is alternative
    - Onset of action 10–20 minutes
    - Peak action takes upto 1 hour
    - Duration of action 4–6 hours.
  - Sodium bicarbonate:
    - Mechanism of action:
      - Increases extracellular fluid pH
      - This increases potassium influx into the cell
      - It is not useful when used alone however
    - Dosage:
      - 50–100 mEq given over 5–10 minutes
      - Alternatively, 1 mEq/kg IV
    - Onset of action 5–10 minutes
    - Duration of action 1–2 hours
  - β-agonists:
    - Mechanism of action:
      - Increase Na^+-K^+ ATPase activity
      - Bind to cell surface of receptors and upregulate cAMP
      - Increase potassium influx in skeletal muscle.
    - Dosage:
      - 10–20 mg salbutamol via nebulization
      - 0.18 mg salbutamol via MDI
      - 0.5–2 mg/min epinephrine
    - Onset of action within 30 minutes
    - Duration of action 2 hours.
  - Hyperventilation:
    - Mechanism of action:
      - Promotes respiratory alkalosis
      - Potassium is therefore shifted intracellularly, in exchange for H^+ ions
      - Each 0.1 change in pH changes K^+ by 0.4–1.5 mEq in opposite direction.
    - Dosage: Maintain $PaCO_2$ around 25–35 mm Hg
- Eliminate potassium from the body:
  - Sodium polysterone sulphonate:
    - Mechansim of action: Exchanges K^+ for Na^+ in GIT
    - Dosage:
      - 30 gms given orally
      - Alternatively, 50 gms in 200 ml 20% sorbitol given as enema
    - Onset of action 1–2 hours
    - Duration of action 4–6 hours
  - Diuretics:
    - Mechanism of action: Promotes kaliuresis
    - Dosage: 20–40 mg furosemide given IV
    - Onset of action variable
    - Duration of action variable
  - Dialysis:
    - Mechanism of action:
      - Exchange of K^+ with hypokalemic dialysate
      - This reduces extracellular K^+ levels
    - Effectiveness:
      - Hemodialysis is more effective than peritoneal dialysis
      - Hemodialysis removes 25–50 mEq/hr of potassium
      - Peritoneal dialysis removes 10–15 mEq/hr of potassium.

- Onset of action within minutes
- Duration of action variable.

Anesthetic Considerations[1,11]

- All patients undergoing elective surgery to have normal K^+ levels
- Delaying surgery not recommended if K^+ level is less than 5.9 mEq/L
- Stress during surgery itself causes serum K^+ to fall by 0.2–0.8 mEq/L
- Patients ESRD should undergo dialysis except in emergencies like imminent exsanguination
- Factors consider before cancelling surgery:
  - Urgency of surgery
  - Degree of hyperkalemia
  - Medications given
  - Acid-base balance
  - Suddenness of electrolyte imbalance.
- Careful ECG monitoring mandatory
- Neuromuscular function is monitored as hyperkalemia potentiates effects of NMBAs
- Succinylcholine is contraindicated
- K^+ containing solutions like RL contraindicated
- Avoid respiratory and metabolic acidosis
- Mild hyperventilation is desirable.

HYPOCALCEMIA[1,10,12]

Introduction

- Hypocalcemia is diagnosed on the basis of plasma ionized calcium concentration
- Plasma ionized Ca^+ less than 4 mg/dl or 1 mmol/L or 4.5 mEq/L is called hypocalcemia
- Hypocalcemia is called true hypocalcemia when free Ca^{2+} levels are low.

Incidence

- Hypocalcemia occurs in 88% of critically ill patients
- Occurs in 66% of less severely ill ICU patients
- Multiple trauma and post-CPB patients are at higher risk for hypocalcemia.

Causes[10]

- Low albumin level is most common cause
- Hypoparathyroidism:
  - Parathyroidectomy: Due to *hungry bones* post-surgery
  - Suppression of PTH by:
    - Severe hypo/hypermagnesemia
    - Burns, sepsis
    - Pancreatitis, I^{131} therapy
    - Hemosiderosis, hemochromatosis
    - Idiopathic causes
  - As a part of multiple endocrine defects (most commonly adrenal insufficiency).
- *Pseudohypoparathyroidism:*
  - Familial unresponsiveness of PTH
  - Vitamin D dependant rickets type II
  - Occurs due to abnormalities in G-protein function
  - Characterized by short stature, obesity, round face and short metacarpals.
- Vitamin D deficiency:
  - Nutritional, inadequate sunlight exposure
  - Malabsorption: Post-surgical (postgastrectomy), IBD
  - Altered Vitamin D metabolism:
    - Anti-convulsant therapy
    - Vitamin-D dependent rickets type I
- Hyperphosphatemia:
  - Overzealous phosphate therapy
  - Tumor lysis secondary to chemotherapy
  - Rhabdomyolysis, chronic renal failure
  - ***Osteitis fibrosa cystica*** following parathyroidectomy.
- Precipitation of calcium salts:
  - Pancreatitis:
    - Causes precipitation of calcium with fats (soaps)
    - This occurs following release of lipolytic enzymes and fat necrosis
  - Rhabdomyolysis, fat embolism
- Chelation of calcium:
  - Multiple transfusions $\geq$ 5 PRBCs or $\geq$ 1.5 ml/kg/min
  - Rapid infusion of large volumes of albumin and isotonic saline.
- Alkalosis:
  - Acute hyperventilation
  - Sodium bicarbonate therapy
  - Post-CPB patients
  - Nasogastric suctioning, diuresis
  - Occurs due to more calcium binding to albumin with rising pH.
- Miscellaneous and rare causes:
  - Calcitonin secreting medullary carcinoma of thyroid
  - Osteoblastic neoplastic disease (breast and prostate).

- Drugs:
  - Phosphates (enema, laxatives)
  - Phenytoin, phenobarbital
  - Gentamycin, tobramycin, actinomycin
  - Heparin, protamine
  - Theophylline, $MgSO_4$
  - Diuretics (loop), citrate
  - Glucagon, glucocorticoids
  - Sodium nitroprusside.

Clinical Features[1,3,10,12]

- General:
  - Weakness, fatigue are usually the first symptoms
  - Parasthesia also occurs commonly
  - Hypocalcemia becomes symptomatic when serum ionized calcium is below 0.7 mmol/L.
- Neurological:
  - Increased neuronal membrane irritability
  - Muscle spasm, circumoral and digital paresthesias
  - Tetany, Chvostek sign, Trosseaus sign
  - Seizures, abdominal cramps, biliary colic, urinary frequency
  - Papilledema
  - Seizures:
    - Maybe focal/jacksonian/petitmal/grand-mal/cerebral tetany
    - *Cerebral tetany:*
      - Generalized tetany followed by tonic spasms
      - Treatment with standard anti-convulsants is ineffective
  - Extrapyramidal disturbances, Parkinsonism
- Psychiatric:
  - Anxiety, depression
  - Dementia, hallucination, confusion, psychosis
- Cardiovascular system:
  - Dysrhythmias
  - Digitalis insensitivity, congestive cardiac failure
  - Hypotension
  - ECG:
    - Prolonged QTc
    - Long and flattened ST segment
    - Heart block
- Respiratory:
  - Laryngeal spasm
  - Bronchospasm
  - Apnea, respiratory arrest
- Skeletal:
  - Osteodystrophy
  - Rickets, osteomalacia
- Dermatological:
  - Dry scaly skin, brittle nails
  - Coarse hair, metastatic soft tissue calcification
- Miscellaneous:
  - Cataract, dental hypoplasia
  - Reduced insulin secretion
- Tests for latent hypocalemia:
  - ***Chvostek sign:***
    - Tapping on facial nerve at angle of mandible
    - This causes ipsilateral facial muscle spasm/masseteric spasm
    - Eyelid contraction during Chvostek sign is almost diagnostic of hypocalcemia.
  - ***Trosseaus sign:***
    - Sphygmomanometer cuff inflated for 3 minutes to 20 mm Hg above SBP
    - This produces characteristic carpopedal spasm
    - Occurs due to the increased muscle irritability caused by hypocalcemia
    - This is aggravated by ischemia of radial and ulnar nerves
    - Characteristics of carpopedal spasm:
      - Spastically extended at inter-phalangeal joints
      - Flexed at metacarpophalangeal joints
      - Flexed at wrist joint
      - Pronated forearm
      - Clinically, it is more reliable than Chvosteks sign.

Investigations

- ECG manifestations:
  - Severity of ECG manifestations do not correlate with degree of hypocalcemia
  - ECG changes usually occur at serum calcium less than 6 mg/dL
  - Heart block:
    - Hypocalcemia prolongs plateau phase of action potential
    - This causes a delay in ventricular repolarization
    - Thus, ventricles do to respond to next electrical impulse from SA node
    - This results in a 2:1 type of heart block.
  - Prolonged QT_C (more than 44 msec)
  - Long, flat ST segment, heart block

- X-ray features:
  - Metastatic soft tissue calcification occurs
  - Calcium deposits in and around blood vessels of basal ganglia
  - This may cause extrapyramidal effects.

Treatment[10,12,18]

- Treatment of cause:
  - Improve overall nutrition in critically ill patients with low albumin levels
  - Remove offending drugs
  - Repletion of magnesium if hypomagnesemia present
  - Removal of phosphate if hyperphosphatemia
  - Correct hyperkalemia:
    - Hyperkalemia potentiates hypocalcemia induced cardiac abnormalities
    - Thus, in a setting of hypocalcemia with hyperkalemia correct hypocalcemia first
    - Hypokalemia protects against hypocalcemic tetany
    - Thus, correction of hypokalemia first may provoke tetany
    - Thus, in a setting of hypocalcemia with hypokalemia also, correct hypocalcemia first.
- Replacement of calcium:
  - Administration of calcium: Rules of '10's
    - Intravenous regimen:
      - 10–20 ml of 10% calcium gluconate given over 10 minutes
      - Followed by elemental Ca^{2+} 0.3–2 mg/kg/hr infusion
      - 10 ml of 10% calcium chloride contains 272 mg elemental Ca^{2+} (1.36 mEq/mL).
      - 10 ml of 10% calcium gluconate contains 93 mg elemental Ca^{2+} (0.45 mEq/mL)
    - Oral regimen:
      - 500–1000 mg elemental calcium Q6H
      - Available as calcium lactate, glubionate, carbonate, ascorbate, gluconate
      - Once ionized Ca^{2+} is in range of 4–5 mg/dL, oral therapy can replace parenteral supplemetation.
  - Administration of Vitamin D:
    - Indications:
      - If calcium supplementation fails to maintain serum Ca^{2+} levels
      - If hypercalciuria develops
    - Preparations:
      - Ergocalciferol 1200 µg/day ($T_{1/2}$: 30 days)
      - Dihydrotachysterol 200–400 µg/day ($T_{1/2}$: 7 days)
      - 1,25 dihydrocholecalciferol 0.25–1 µg/day ($T_{1/2}$: 1 day)
- Monitors:
  - ECG: heart block, ventricular fibrillation
  - Serum calcium, potassium, magnesium, phosphate and creatinine levels
  - Urinary calcium: To prevent hypercalciuria (> 5 mg/kg/day).
- Mode of administration:
  - Choose larger peripheral vein to prevent irritation and thrombosis
  - Calcium to be diluted in 50–100 ml D_5W to reduce irritation and thrombosis
  - Extravated $CaCl_2$ causes severe tissue destruction
  - Thus, *calcium gluconate is considered safer*
  - Not to be mixed with phosphate or bicarbonate to prevent precipitation
  - Given with caution in digitalized patients as calcium increases digoxin toxicity
  - Dosage adjusted to keep serum calcium in low normal range.
- Adverse effects of therapy:
  - Hypercalcemia
  - Hypercalciuria
  - Renal stones.

Anesthetic Considerations[1,11]

- Hypocalcemia to be corrected preoperatively:
  - 10–20 ml calcium gluconate given at 5 mL/min
  - 10 mL/min 10% Ca gluconate in 500 ml D_5W over 6 hours
- Normalize serum magnesium and phosphate levels also
- Maintain serum ionized calcium in lower half of normal range in patients with chronic hypoparathyroidism
- Monitors:
  - Serial ionized calcium measurements done intraoperatively
  - Preoperative ECG useful to maintain QT_C levels
- Intraoperatively:
  - Hypocalcemia potentiates negative inotropic effects of barbiturates and volatile anesthetics
  - NMBA blockade requires close monitoring with nerve stimulator
  - Avoid hyperventilation and alkalosis
  - IV calcium to be given following rapid transfusion of blood/albumin.

HYPERCALCEMIA[1,2,3,10,11,12,14,18,19]

Introduction

Hypercalcemia refers to:

- Total serum calcium more than 10.5 mg/dL (standard definition)
- Ionized calcium levels above 1.5 mmol/L.

Etiology[1,3,10,12]

- Endocrinopathies
  - Hyperparathyroidism:
    - Primary hyperparathyroidism:
      - Parathyroid secretion increases independent of serum calcium levels
      - Occurs due to adenomas secreting PTH
    - Secondary hyperparathyroidism:
      - Parathyroid secretion increases due to chronic hypocalcemia
      - Occurs in chronic renal failure
    - Tertiary hyperparathyroidism:
      - Autonomous PTH secretion
      - Occurs following prolonged secondary hyperparathyroidism
    - MEN II syndrome
  - Hyperthyroidism, pheochromocytoma
  - Adrenal insufficiency, acromegaly
- Malignancy: *Humoral hypercalcemia of malignancy:*
  - Squamous cell carcinoma of lung
  - Breast carcinoma:
    - *Most common cause*
    - Causes 25–50% of malignancy associated hypercalcemia
  - Renal cell carcinoma, leukemias
  - Multiple myeloma: Hypercalcemia occurs due to:
    - Bone destruction
    - Derangement of RANK-L/osteoprogenerin system
    - Secretion of hormones:
      - PTH-like peptide
      - Prostaglandins, cytokines
      - $IL_{1\alpha}$ and $IL_{1\beta}$ and also TNF which stimulates osteoclast activity
- Drugs:
  - Hypervitaminosis D and A
  - Thiazide diuretics, lithium
  - Hormonal therapy for breast cancer
- Granulomatous diseases:
  - Sarcoidosis, histoplasmosis
  - Tuberculosis, coccidioidomycosis
  - Hypercalcemia occurs due to conversion of calcidiol to calcitriol by granulomatous tissue
- Miscellaneous:
  - Acidosis, post-renal transplantation
  - Immobilization and *Pagets disease of bone*
  - Recovery from acute renal failure, phosphate depletion syndrome
  - Hypocalciuric hypercalcemia, *milk alkali syndrome*
  - Hypoalbuminemia: Serum calcium levels reduce 0.8 mg/dL for every 1 g/dL drop in albumin levels
  - Idiopathic hypercalcemia of infancy, aluminium intoxication.

Severity

- Mild hypercalemia:
  - Serum levels 10.5–11.5 mg/dL
  - Usually asymptomatic
- Moderate hypercalcemia:
  - Serum levels 11.5–13 mg/dL
  - Lethargy, anorexia, nausea, polyuria
- Severe hypercalcemia:
  - Serum levels more than 13 mg/dL
  - Muscle weakness, depression
  - Impaired memory, emotional lability
  - Lethargy, stupor, coma
- Serum levels more than 20 mg/dL causes cardiac arrest.

Clinical Features

- General:
  - Malaise, polydypsia
  - Weakness, dehydration
- Central nervous system:
  - Confusion, proximal muscle weakness
  - Impaired memory, muscular dystrophy
  - Headache, irritability
  - Ataxia, hypotonia
  - Mental retardation in infants.
- Psychiatric:
  - Apathy, depression
  - Stupor, hallucinations
- Cardiovascular:
  - Hypertension, arrhythmias (heart block)
  - Vascular and myocardial calcification
  - Increased digitalis sensitivity
  - ECG changes:
    - QT_c shortening

- Coving of ST segment
- Normal or increased QRS duration
- Widening of T wave.

- Gastrointestinal:
  - Anorexia, weight loss
  - Nausea, vomiting
  - Constipation, abdominal pain
  - Peptic ulcer disease due to increased gastrin production
  - Pancreatitis
- Genitourinary:
  - Polyuria, nocturia
  - Renal insufficiency
  - Polydipsia, proximal (Type II) RTA
- Skeletal:
  - Pathological fractures, osteopenia, osteoporosis
  - Bony pain especially along anterior margin of tibia
  - Osteitis fibrosa cystica
- Metastatic calcification:
  - Band keratopathy, conjunctivitis, pruritus
  - Brain, kidney, blood vessels, myocardium.

Investigations

- Double antibody PTH assay:
  - Differentiates between malignancy/hyperparathyroidism induced hypercalcemia
  - Serum PTH levels are low in malignancy but high in hyperparathyroidism
- Radio immunoassay for PTH: Most useful confirmatory test of hyperparathyroidism.

Treatment[10,12]

- Supportive therapy:
  - Ensure adequate hydration
  - Correct associated abnormalities
  - Remove offending drugs
  - Dietary calcium restriction
  - Increase physical activity
  - Monitors:
    - ECG, cardiovascular status
    - Serum calcium, magnesium and potassium levels
    - Total serum calcium more than 14 mg/dL is treated as a medical emergency.
- Calciuresis:
  - Volume repletion:
    - Normal saline dilutes serum calcium and promotes calciuresis
    - Reduces serum calcium by 1.5–3 mg/dL
  - Diuretics:
    - Furosemide increases calcium excretion by increasing tubular sodium
    - Can achieve net calcium excretion rate of 2000–4000 mg/day
    - 40–100 mg frusemide given IV Q2-4H
    - Maintain urine output at 200–300 mL/hr
    - Diuretics, if given before volume replacement may aggravate hypercalcemia by causing additional volume depletion.
- Reduce calcium resorption:
  - Increased physical activity
  - Bisphosphates:
    - First line therapy for acute hypercalcemia
    - Inhibits osteoclast function and viability
    - Drugs used:
      - Pamidronate:
        - Most commonly used
        - 60–90 mg given IV
        - Is avoided if serum creatinine > 2.5 mg/dL
      - Alendronate: Gastrointestinal side effects present
      - Risedronate: Less gastrointestinal side effects
      - Zoledronate:
        - 4 mg given IV
        - Most rapid onset of action
        - Long acting drug which worsens ARF
  - *Salmon calcitonin:*
    - Second line therapy for acute hypercalcemia
    - Inhibits bone resorption directly
    - Acts within minutes of IV administration
    - It is more effective if combined with glucocorticoids
    - Reduces serum calcium by only 1–2 mg/dL
    - 25% patients may not respond to therapy
    - 2–8 IU/kg given subcutaneously
    - Alternatively, 100–400 U Q12H given subcutaneously
    - Acts in 24–48 hours if given subcutaneously.
  - Hydrocortisone:
    - Indications:
      - Lymphatic malignancy, hypervitaminosis
      - Sarcoidosis, breast cancer, myelomas
    - 3 mg/kg/day given IV in divided doses
  - Phosphates:
    - Reduce serum calcium by deposition of calcium in bone and soft tissue

- IV route not preferred due to risk of metastatic calcification in kidney and myocardium
- IV route only used if life threatening hypercalcemia
- Rarely used and given oral if used.

– Hemodialysis:
- Removes upto 6000 mg/day
- Used if concomitant CRF/CCF

– Mithramycin: 15–25 mg/kg given IV
– Gallium nitrate: Reduces solubility of base crystals, use avoided in renal failure

• Treatment of cause:
– Parathyroidectomy:
- Treatment of choice for primary hyperparathyroidism
- Indications:
  ° Age less than 50 years
  ° Serum calcium more than 11.5 mg/dL
  ° More than 30% reduction in GFR
  ° Severe bone demineralization.

– Calcimetics:
- Used for primary, secondary and tertiary hyperparathyroidism
- Also reduces inorganic phosphorus levels
- Indicated if patient refuses surgery or is medically unfit for surgery
- Sensitizes PTH calcium receptor to calcium
- Thus, it is also useful in tertiary hyperparathyroidism.

– Secondary hyperparathyroidism:
- Calcium supplementation
- Phosphate binders, Vitamin D analogues
- Calcimetics.

Anesthetic Considerations[11]

• Hypercalcemia is a medical emergency
• 200–400 ml/hr normal saline given preoperatively
• Careful monitoring to avoid fluid overload
• Correct hypercalcemia if possible before anesthetic administration
• Monitors:
– Ionized calcium, magnesium, potassium levels and ECG
– Neuromuscular function with nerve stimulator
– CVP and PA catheter advisable for patients with reduced cardiac reserve.
• Controlled ventilation to avoid:
– Acidosis: Worsens hypercalcemia
– Alkalosis:
- Reduces plasma K^+ levels
- This causes unopposed hypercalcemia resulting in tetany

• Avoid thiazides, maintain hydration and urine output with sodium containing fluids
• Reduce dose of NMBA in those with muscle weakness.

HYPOMAGNESEMIA[1,2,3,10,12,14,18,19]

Introduction

Hypomagnesemia is diagnosed when serum Mg^{2+} is less than 1.8 mEq/L.

Causes[10]

• Slight hypomagnesemia in:
– Athletes
– Hypermetabolic states (pregnancy)
– Cold weather
– Use of β-agonists
• Inadequate GI intake: Rare
– Alcoholics (30% are hypomagnesemic)
– Total parenteral nutrition
– Refeeding syndrome
• Inadequate GI absorption: Most common cause:
– Malabsorption syndrome
– Prolonged diarrhea
– Prolonged nasogastric suction
– Pancreatitis
• Increased losses:
– GI/biliary fistulas
– Intestinal drains
• Increased renal losses:
– Advanced renal disease, following renal transplant
– Polyuria due to volume expansion/diuretics, alcoholism
– Recovery phase of acute tubular necrosis
– Colony stimulating factor therapy
– Drugs:
- Aminoglycosides
- Amphotericin B
- Cisplatin, cardiac glycosides
- Diuretics, theophylline, pentamidine.

• Intracellular magnesium shifts:
– SIADH, hyper/hypo parathyroidism
– Hyngry bone syndrome following parathyroidectomy
– Thyroid hormone/insulin administration

- DKA, alcoholic ketoacidosis
- Primary hyperaldosteronism
- Barrters syndrome.

Pathophysiology

- Hypomagnesemia increases myocardial sensitivity to digitalis
- Hypomagnesemia may cause hypokalemia as Na^+-K^+ pump is magnesium dependant
- Hypokalemia correction may not occur without magnesium replacement
- Severe hypomagnesemia can reduce PTH secretion and cause hypocalcemia
- It also reduces end-organ response to parathyroid hormone.

Clinical Features

- Neurological:
  - Irritability, weakness, confusion
  - Fasciculations, tetany, seizures
  - Ataxia, nystagmus, vertigo, hyper-reflexia
  - Chvostek sign, Trosseaus sign
  - Obtundation, coma.
- Cardiovascular:
  - Electrical irritability
  - Atrial fibrillation, heart failure, hypotension
  - Potentiates digoxin toxicity
  - ECG changes:
    - Prolonged PR interval
    - Prolonged QT_C
    - Atrial fibrillation.
- Gastrointestinal: Anorexia, dysphagia, nausea, anemia
- Other electrolytes:
  - Hypocalcemia (due to reduced PTH secretion)
  - Hypokalemia (due to renal K^+ wasting)
  - Hyponatremia
  - Hypophosphatemia.

Severity[1,10]

Serum level	Clinical features
1.2–1.8 mg/dL	Neuromuscular irritability
	Hypocalcemia
	Hypokalemia
< 1.2 mg/dL	Tetany
	Arrhythmias
	Seizures

ECG Changes

- Low P-wave voltage
- Increased PR internal
- Wide QRS complexes
- Increased QT_c interval
- ST segment depression
- Flat/inverted T-waves especially in precordial leads
- Prominent U-waves
- Predisposed to AF, torsades de pointes, long QT Syndrome.

Investigations

- Peripheral lymphocyte magnesium concentration:
  - Correlates with skeletal and cardiac magnesium content
  - Serum magnesium may not reflect intracellular Mg^{2+} content
- 24-hour urinary magnesium excretion:
  - Hypomagnesemia with urinary magnesium > 3–4 mEq/day suggests renal etiology
  - Hypomagnesemia with urinary magnesium < 1–2 mEq/day suggests extrarenal etiology
- Magnesium loading test: Urinary Mg^{2+} measured for 24 hours after IV magnesium load.

Treatment

- Magnesium supplementation:
  - Severe deficiency (< 1 mg/dL) or symptomatic patients:
    - IV regimen:
      - 1–2 gms (8–16 mEq) of magnesium sulphate loading dose over 15 minutes
      - Followed by continuous infusion of 2–4 mEq/hr (250–500 mg/hr)
      - 1 gram $MgSO_4$ = 4 mmol = 8 mEq = 98 mg of elemental magnesium
      - Rate of infusion kept at less than 1 mEq/min
      - If acute arrhythmias are present, 1–2 gm is given over 5 minutes
      - Replacement is added to daily magnesium requirements of 0.3–0.4 mEq/kg/day.
    - IM regimen: 10 mEq Q4-6H
  - Mild deficiency:
    - Oral 60–90 mEq/day of MgO or $MgSO_4$ heptahydrate
    - Restoration of magnesium stores requires 5–7 days of therapy
    - After this, daily maintenance doses of magnesium should be provided

- Hypocalcemic and hypomagnesemic patients should receive magnesium as $MgCl_2$ as sulphate can chelate calcium and aggravate hypocalcemia.

- Monitors:
  - Serum Mg^{2+}, Ca^{2+}, K^+ levels
  - BP and cardiac output and ECG
  - Patellar reflexes: Withhold magnesium if decreased reflexes
  - Caution if renal failure present.
- Treat associated conditions: Isolated hypomagnesemia is rare:
  - Hypokalemia
  - Hypocalcemia
  - Hypophosphatemia.

Anesthetic Considerations[11]

- Increase risk of perioperative arrhythmias
- Hence hypomagnesemia is corrected before elective surgery
- Decreased muscle power intraoperatively: Elective postoperative ventilation preferred
- Prolonged action of neuromuscular blockers
- Increased respiratory depression with sedation
- Correct hypokalemia, hypocalcemia and hypophosphatemia prior to surgery.

HYPERMAGNESEMIA[1,2,3,10,11,12,14,18,19]

Introduction

- Hypermagnesemia is diagnosed when the serum magnesium levels are more than 2.5 mg/dL
- Therapeutic levels of serum magnesium is 4–6 mEq/L.

Etiology

- Iatrogenic:
  - During ecclampsia therapy
  - Magnesium containing antacids
  - Enemas
  - Parenteral nutrition especially in CRF patients
- Endocrine:
  - Hypothyroidism
  - Addisons disease
- Miscellaneous
  - Chronic renal failure
  - Lithium therapy
  - Familial hypocalciuric hypercalcemia
  - Rhabdomyolysis

Pathophysiology

- Antagonizes release and effect of ACH at neuromuscular junction
- Thus depressed skeletal muscle function results
- Potentiates neuromuscular blockade and reduces K^+ release in response to succinylcholine.

Clinical Features

Serum levels[1]	Clinical features
2.5–5 mg/dL	Decreased cardiac conduction, nausea
	Wide QRS complexes
	Increased PR interval
5–7 mg/dL	Sedation
	Hypoventilation
	Decreased deep tendon reflexes
	Muscle weakness
7–12 mg/dL	Hypotension
	Bradycardia
	Diffuse venous dilation
	Loss of deep tendon reflexes
More than 12 mg/dL	Areflexia
	Respiratory paralysis
	Coma
	Cardiac arrest, complete heart block

ECG Changes

- Prolonged PR internal
- Widening of QRS complexes
- Elevated T waves
- If severe hypermagnesemia, atrioventricular/intraventricular conduction disturbances occur
- Cardiac arrest occurs if serum levels exceed 15 mEq/L.

Treatment

- Stop all magnesium containing preparations (antacids)
- Antagonize effects of magnesium: IV calcium 5–10 mEq over 5 minutes
- Eliminate magnesium:
  - Expand extracellular volume with half normal saline with 5% dextrose
  - Induce diuresis with 40–80 mg furosemide IV
  - Hemodialysis done with low magnesium bath
  - Diuresis with normal saline is not recommended as:

- This reduces the likelihood of iatrogenic hypocalcemia
- Hypocalcemia potentiates effects of hypermagnesemia.

Anesthetic Considerations[11]

- Monitor ECG, BP and neuromuscular function, serial Ca^{2+} and Mg^{2+} levels
- Potentiates action of local anesthetics
- Potentiates NMBA by causing presynaptic neuromuscular blockade
- Reduce dose of NMBA used intra-operatively by 25–50%
- Can precipitate severe weakness in:
  - Patients with Eaton-Lambert syndrome
  - Myasthenic patients
  - Patients treated with small doses of defasciculating agonist.
- Prolongs action of depolarizing agents like succinylcholine
- Prevents succinylcholine provoked K^+ release
- Potentiates vasodilatation and negative inotropic action of anesthetics
- Urinary catheter to be used if diuretics are used
- Aminoglycoside antibiotics potentiate NMBAs and muscle weakness
- Avoid in PPH and pregnancy: Uterine atony and neonatal hypotonia
- Aggravates hypotension with spinal anesthesia.

HYPOPHOSPHATEMIA[1,10,11,12,14,18,19]

Introduction

Hypophosphatemia refers to inorganic phosphorus level less than 2.5 mg/dL.

Causes[1,10]

- Intracellular shift of phosphorous:
  - During treatment of DKA:
    - Occurs due to insulin induced cellular uptake of phosphorous
    - Occurs 12–24 hours after initial therapy
  - Hyperalimentation
  - *Nutritional recovery syndrome*
  - Carbohydrate induced hypophosphatemia: *Refeeding syndrome*
  - Change from catabolic state to anabolic state
  - Respiratory alkalosis:
    - Increases rate of glycolysis
    - This in turn increases intracellular consumption of phosphorous
    - Effects of hyperventilation progress even after cessation of hyperventilation.
  - Therapeutic hyperthermia
  - Acute correction of acidosis
  - Gram-negative sepsis and salicylate poisoning due to respiratory alkalosis
  - *Neuroleptic malignant syndrome.*
- Excessive renal losses:
  - Hyper-parathyroidism
  - Chronic alcoholics and alcohol withdrawal: Most common cause
  - Diuretic therapy
  - Renal tubular defects, acute renal failure, following renal transplantation
  - Severe hypomagnesemia.
- Excessive GI losses:
  - Phosphorus binding antacids
  - Malabsorption syndrome.

Pathophysiology

Hypophosphatemia results in:

- Low levels of ATP
- Low levels of 2,3-DPG
- Membrane phospholipid dysfunction: Results in:
  - Defective phagocytosis
  - Defective chemotaxis
  - Reduced bactericidal activity.

Clinical Features

- Severe life threatening organ dysfunction when serum P_i levels < 1 mg/dL
- Central nervous system:
  - Circumoral and finger tip paresthesias
  - Myopathy, reduced deep tendon reflexes, malaise
  - Encephalopathy, seizures, delirium, coma.
- Cardiovascular:
  - Impaired myocardial function
  - Low cardiac output, hypotension
- Hematological:
  - Dysfunction of WBC, RBC and platelets
  - Reduced chemotaxis, phagocytosis, bactericidal activity
  - Immune dysfunction
  - Reduced survival of WBC, RBC, platelets: Spherocytosis
  - Tissue hypoxia due to low 2,3-DPG levels
  - Metabolic acidosis.
- Miscellaneous:
  - Respiratory failure
  - Rhabdomyolysis if severe hypophosphatemia.

Investigations

Urinary phosphorus:

- If urinary P_i < 100 mg/day: Suggests extrarenal causes
- If urinary P_i > 100 mg/day: Implies renal loss of P_i.

Treatment[10,12]

- Calculation of P_i deficit:
  - P_i deficit = V_d {(desired P_i level) – (current P_i level)}
  - V_d = 400 ml/Kg
  - The calculated deficit to be given at not more than 0.25 mmol/kg over 4–6 hours.
- Phosphorous repletion:
  - Severe or symptomatic hypophosphatemia
    - 0.2–0.68 mmol/kg or 5–16 mg/kg elemental phosphorus
    - Rate of infusion ≤ 0.25 mmol/kg over 4–6 hours to avoid hypocalcemia
  - Moderate hypophosphatemia: 15 mmol boluses (465 mg) with 100 ml NS over 2 hours
  - Mild hypophosphatemia:
    - Oral phosphorus ≤ 30 mmol/day (1 g/day) as higher doses cause diarrhea
    - Available as sodium or potassium phosphate
    - Milk (contains 100 mg/dL or 33 mmol/L of phosphorus).
- Choice of fluid and duration of therapy:
  - Potassium phosphate: 93 mg/dL of phosphorus
  - Sodium phosphate: 93 mg/dL of phosphorus
  - Oral phosphorus started once serum P_i ≥ 2 mg/dL
  - P_i supplements continued for 5–10 days to replenish body stores.
- Monitors: Phosphorus and other electrolytes after 6 hours of initiating therapy
- Precautions:
  - Administer cautiously in hypocalcemic patients: Risk of precipitating severe hypocalcemia
  - If hypercalcemia present, P_i administration may cause metastatic calcification
  - Use with caution if renal failure present and avoid hyperphosphatemia.

Anesthetic Considerations[11]

- Hyperglycemia and respiratory alkalosis have to be avoided
- Avoid DNS and dextrose containing fluids
- Neuromuscular blockade monitoring
- Postoperative ventilation may be required if severe hypophosphatemia.

HYPERPHOSPHATEMIA[1,10,11,12,14,18,19]

Introduction

Hyper-phosphatemia refers to serum inorganic P_i levels more than 5 mg/dL.

Etiology[1,10]

- Increased intestinal absorption:
  - Phosphorus containing cathartics
  - Granulomatous diseases
  - Vitamin-D therapy
- Parenteral administration
  - IV phosphate salts
  - IV lipid infusions
- Internal redistribution:
  - Acute metabolic/respiratory acidosis
  - Reduced insulin levels
  - Clonidine administration
- Binding to serum proteins:
  - Plasma cell dyscrasias
  - Liver failure
- Cellular release:
  - Rhabdomyolysis
  - Tumor lysis as in:
    - *Burkitts lymphoma*
    - Lymphoblastic lymphomas
  - Sepsis
- Decreased renal excretion:
  - Renal insufficiency when GFR ≤ 25 mL/min
  - Hypoparathyroidism, pseudohypoparathyroidism
  - Tumoral calcinosis
  - Pseudoxanthoma elasticum
  - Infantile hypophosphatasia
  - Hypoparathyroidism, hyperthyroidism, adrenal insufficiency
  - Bisphosphonate therapy.

Clinical Features

Those of:

- Hypocalcemia
- Hypomagnesemia
- Renal failure
- Risk of metastatic calcification if: Calcium x phosphorus product ≥ 70 mg^2/dL^2.

Investigations

- Normal renal function with P_i excretion more than 1500 mg/day suggests excessive P_i supply
- Abnormal renal function with low GFR suggests reduced renal P_i excretion

- Normal function and P_i excretion less than 1500 mg/day suggests P_i reabsorption.

Treatment[10,12]

- Eliminate cause
- Correct hyperphosphatemia:
  - Restrict intake of calcium phosphate to less than 200 mg/day
  - Increase renal elimination:
    - 1–2 L of normal saline over 4–6 hours
    - Acetazolamide 500 mg QID
  - Increase GIT losses:
    - Enteric aluminium hydroxide 30–45 mg Q6H
    - Sucralfate, calcium citrate, calcium carbonate
  - Calcimetics: Useful in patients with renal failure
  - Phosphorus binders use with caution in patients with ARF:
    - *Sevelamer hydrochloride:* Binds bile acids
    - *Lanthanum carbonate*
  - Hemodialysis and peritoneal dialysis
- Correct hypocalcemia: Give calcium supplements only when serum $P_i < 2$ mmol/L or 6 mg/dL.

Anesthetic Considerations

- Monitor renal functions, serum P_i and Ca^{2+} levels
- Secondary hypocalcemia to be excluded
- Neuromuscular monitoring
- Avoid hypoventilation and acidosis.

PARACETAMOL/ACETAMINOPHEN POISONING[1,2,3,10,12,14,18,19]

Introduction

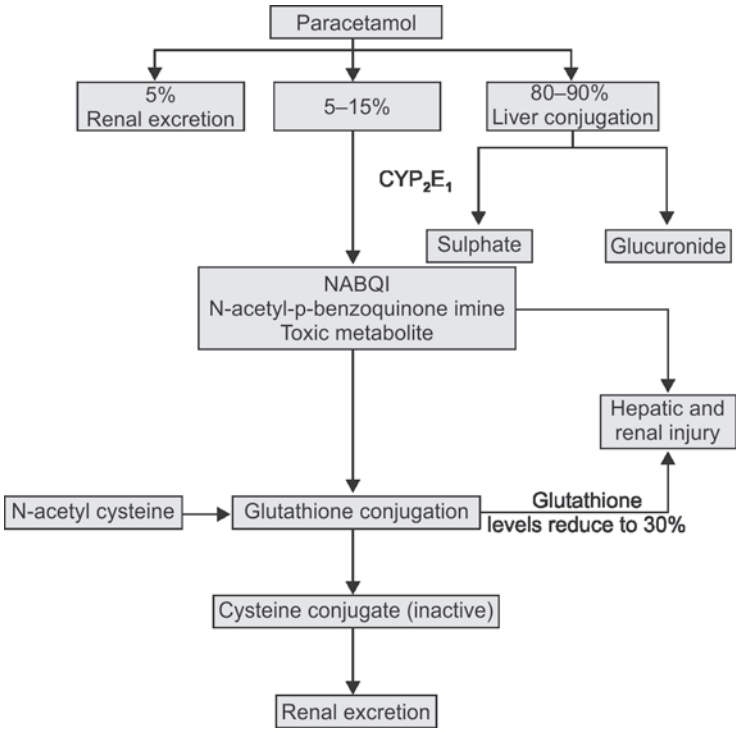
Analgesic-antipyretic which is used very commonly.

Mechanism of Toxicity

- Where there is ingestion of high levels of paracetamol, excessive amount of NABQI is formed
- This overwhelms the hepatic glutathione conjugation capacity
- When the glutathione stores are depleted to 30%, NABQI precipitates proteins in the liver and kidney by oxidant injury
- This causes liver failure, centrilobular hepatic necrosis and acuter tubular necrosis
- Centrilobular necrosis seen as CYP_2E_1, which produces NABQI is maximally concentrated around the central veins and minimally around the portal triad.

Fatal Dose

- 150 mg/kg or > 10 gms in adults
- More than 250 mg/kg is fatal



- 5–6 g/day for a few days in alcoholics (as alcohol induces CYP_2E_1)
- Fatal dose is lesser in children who have decreased glucuronide conjugating capacity
- Fatal dose is lesser in malnutrition and INH ingestion (lower glutathione stores)
- Lesser in those with induced cytochrome P_{450} activity:
  - Alcoholics
  - Concurrent anticonvulsant administration
  - Antitubercular drugs.

Fatal period: 3–5 days

Clinical presentation: Four stages of toxicity:[10]

Stage I:
- Between 0–24 hours
- Symptoms absent or nonspecific: Pallor, anorexia
- If present, nausea, vomiting, upper abdominal pain
- No clinical/laboratory evidence of hepatic injury.

Stage II:
- Between 24–72 hours
- Minimal/absent clinical manifestations: Right hypochondriac pain and tenderness
- No clinical evidence of hepatic injury
- Lab evidence of hepatic injury begins to appear
- Elevated levels of AST: Most sensitive
- Raised ALT, bilirubin.

Stage III:
- Between 72–96 hours
- Clinical evidence of hepatic and renal injury
- Jaundice, hypoglycemia, coagulopathy, encephalopathy, flapping tremors
- Peak levels of AST attained.

Stage IV:
- Presents beyond 96 hours
- Hemorrhagic pancreatitis, DIC, cardiac arrhythmias
- Confusion, coma
- Death within 3–5 days
- If patient survives hepatic failure, complete resolution with recovery occurs.

Circumstances of Poisoning

- Very rarely suicidal
- Most often due to accidental overdose
- Especially common in children due to inadequate glucuronide conjugating ability.

Diagnosis

- Routine blood investigations:
  - Complete blood count
  - ESR, hemoglobin
  - Bleeding time, clotting time: Coagulopathy common
- Liver function tests
- Renal function tests
- Plasma drug levels:
  - Plasma acetaminophen levels obtained between 4–24 hours
  - Useful to predict the risk of hepatotoxicity
  - Uses a *Rummack-Mathew* nomogram
  - If the plasma level falls in the high risk region:
    - Risk of hepatoxicity is 60%
    - This necessitates antidote therapy
  - If plasma levels are in the low risk region:
    - Risk of hepatotoxicity is only 1–3%
    - Antidote therapy is not required.

Treatment[10,12,14,18,19]

- Monitor:
  - BT, CT to check for coagulopathies
  - Prothrombin time helpful to predict course of liver disease
  - FDPs and D-dimer assay to diagnose DIC
  - Plasma levels of PCT
  - Serum amylase levels to detect pancreatitis
  - Fractional excretion of sodium, blood urea and creatinine to detect ATN
  - Strict intake output chart maintenance.
- Nonspecific measures:
  - Airway:
    - Check if airway is patent
    - Use head tilt, chin lift and jaw thrust maneauver
  - Breathing:
    - Check if spontaneously breathing
    - Mechanical ventilation may be required if efforts are inadequate
  - Circulation:
    - Check for pressure of carotid pulse
    - Secure IV lines and start IV fluids
    - Avoid IM injections to prevent hematomas due to coagulopathy
  - Gastric lavage:
    - Very effective within 2 hours

- Can be done upto 8 hours after ingestion as toxin is resecreted into stomach
- Induced vomiting: With Syp. Ipecac 3 ml in child, 5 ml in adults

– Activated charcoal:
- 1 g/kg recommended only in first 4 hours after overdose
- PCT is completely absorbed from GIT within first 4 hours.

• Specific:
– Goal of therapy is to replenish glutathione levels in liver
– N-acetyl cysteine (glutathione analogue) is given which replenishes the stores
– N-acetyl cysteine (NAC):
- In early PCT poisoning (≤ 8 hrs after ingestion):
° Prevents binding of NABQI to hepatic macromolecules
° This is done by:
* Acting as a glutathione precursor/substitute
* Acting as a sulphate precursor
* Directly reducing NABQI back to PCT.
- In established PCT toxicity (≥ 24 hrs after ingestion):
° NAC reduces hepatic necrosis by:
* Acting as an antioxidant
* Reducing neutrophil infiltration
* Increasing precirculatory blood flow
- IV regimen: 20% NAC (200 mg/ml) used:
° 150 mg/kg in 200 ml of 5% dextrose over 60 minutes
° 50 mg/kg in 500 ml of 5% dextrose over 4 hours
° 100 mg/kg in 1000 ml of 5% dextrose over 16 hours
- Oral regimen: 10% NAC (100 mg/ml) used:
° 140 mg/kg initial dose
° 70 mg/kg Q4H for 17 doses
– Methionine therapy:
- Less effective than NAC
- 2.5 mg orally Q4H upto a total of 10 grams

• Complication management:
– Protein restriction, lactulose and oral neomycin for hepatic encephalopathy
– FFP and heparin for DIC
– Antibiotic prophylaxis
– Liver transplant: Early transplant beneficial
– Fulminant hepatic failure:
- NAC therapy continued past standard regimen until:
° Patient recovers
° Receives transplant/dies
- Correct coagulopathy and acidosis
– Hemodialysis: May be required in severe cases with high plasma levels of PCT
– Monitor and aggressively treat cerebral edema.

Complications of Therapy

• Anaphylactic reactions with IV regimen
• Rotten egg taste with oral NAC regimen (due to –SH group)
• Nausea and vomiting with oral NAC regimens:
– Avoided by diluting the 10–20% NAC solutions to 5% using chilled beverages
– Odor can be minimized by using NG tube to administer the solution
– Persistent nausea and vomiting may require metoclopramide 0.1 mg/kg IV.
• NG tube administration of NAC may be required to prevent vomiting
• Dose dependent diarrhea with NAC oral regimens which resolves on continual therapy.

Poor Prognosticators

• Metabolic acidosis, pH < 7.3 despite fluid resuscitation
• Combination of coagulopathy (PT > 100)
• Renal insufficiency (creatinine > 3.3 mg/dL)
• Grade III/IV hepatic encephalopathy.

ORGANOPHOSPHORUS POISONING[1,2,10,12,14,18,19]

Introduction

• These compounds are derivates of phosphoric acid, used mainly as insecticides
• They have also been used as chemical warfare agents.

Classification

• Alkyl phosphates:
– HETP, OMPA
– TEPP, malathion
– Trichlorfon
• Aryl phosphates:
– Parathiol (follidol), chlorothion
– Paraoxon, diazion (TIK-20)
– Methylparathion.

Absorption
- GI tract, transconjunctival
- Transdermal, mucous membrane
- Inhalation.

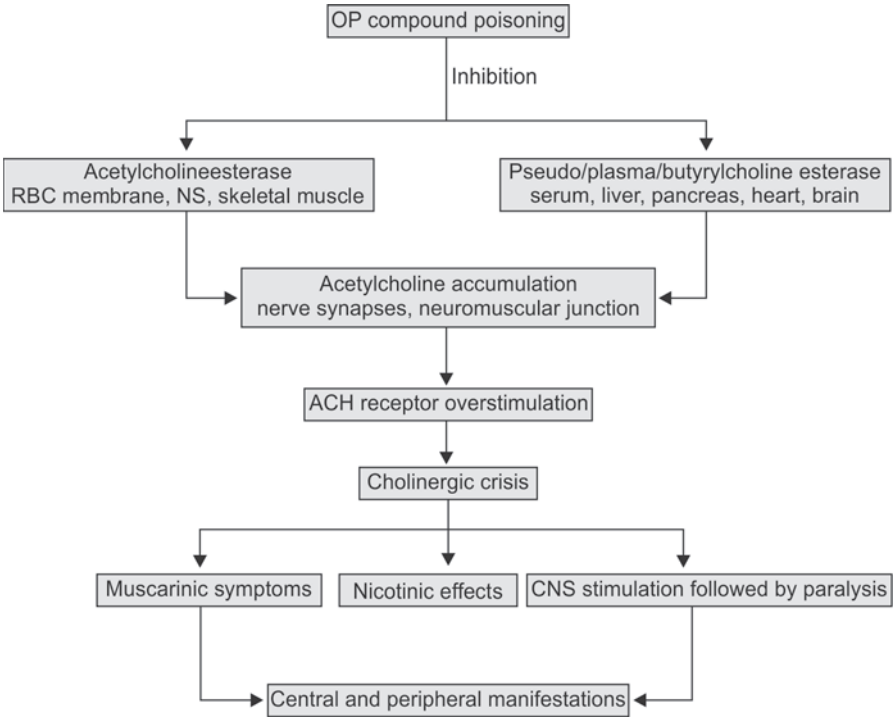
Fatal Dose
- Parathion: 80 mg IM/175 mg orally
- Malathion and diazinon: 1 gm orally

Fatal Period
- Less than 24 hours in untreated cases
- Complete recovery in 10 days if treated early.

Causes of Death
- Respiratory muscle paralysis
- Respiratory arrest due to failure of respiratory center
- Intense bronchoconstriction
- Late death (15 days after ingestion): VF/VT.

Pathophysiology
Refer flow chart.

Clinical Features[10,12,14]
- Immediate sequelae:
  - Onset is most rapid following inhalation and least following skin absorption
  - Begins within 5 minutes, usually in 8 hours
  - Manifests maximally in 24 hours
  - RS/GI symptoms are more marked depending on route of entry
  - Hydrocarbon/garlic like odor from patient
  - Muscarinic manifestations:
    - S: Salivation
    - L: Lacrimation
    - U: Urination
    - D: Defecation
    - G: GI pain/distress
    - E: Emesis
    - Respiratory:
      - Bronchoconstriction, dyspnea
      - Bronchorrhea, cyanosis
      - Persistent reactive airway disease rarely
    - Gastrointestinal:
      - Anorexia, cramps
      - Nausea, diarrhea
      - Vomiting, fecal incontinence
      - Tenesmus
    - Cardiovascular:
      - Bradycardia, hypotension
      - Pulmonary edema
    - Pupils:
      - Miosis occasionally unequal
      - Blurred vision



  - Nicotinic manifestations:
    - Striated muscle:
      - Fasciculations, cramps, areflexia, paralysis
      - Respiratory paralysis, acute respiratory failure and death
    - Sympathetic ganglia: Hypertension, tachycardia, pallor, mydriasis
    - Neurological:
      - Restlessness, drowsiness, emotional lability, slurred speech
      - Headache, ataxia, tremors, weakness
      - Confusion, coma, convulsions
    - *Chromolachryorrhea:*
      - Formation of red tears
      - Occurs due to porphyrin accumulation in lacrimal glands
- Delayed sequelae:
  - *Intermediate syndrome (IMS):*
    - Occurs 1–4 days after exposure
    - Symptoms usually resolve in 4–18 days
    - Paralysis of neck flexors and cranial nerves
    - Proximal limb and respiratory muscles also affected
    - Aggressive antidote therapy and respiratory support
  - *Organophosphate induced delayed neuropathy (OIDN):*
    - 1–3 weeks after exposure
    - Mixed sensorimotor syndrome
    - May resemble Guillaine-Barré syndrome
    - Antidotal therapy does not help
    - Occurs due to inhibition of neuropathy target esterase
    - Irreversible neuropsychiatric deficits may occur after OP poisoning
    - Persistent reactive airway disease occurs rarely.

Diagnosis

- Mainly clinical diagnosis
- Symptoms, signs and garlicky odour from patient
- Atropine test:
  - 2 mg atropine given IV/6 mg given IM
  - Normal persons will have marked atropinization
  - In OP poisoning, symptoms are relieved and secretions decrease.
- RBC and plasma cholinesterase levels:
  - Reduce to less than 50% of baseline values
  - RBC cholinesterase is a more accurate indicator of synaptic cholinesterase
  - Plasma cholinesterase levels, however are more readily available.
- Nonspecific indicators:
  - Leucocytosis
  - Hypo/hyperglycemia
  - Abnormal LFTs
  - Raised serum amylase: Pancreatitis like findings
  - Pulmonary edema on chest X-ray
  - ECG:
    - Heart block, prolonged QT_c
    - Idioventricular rhythm
    - VF/torsades-de-pointes.
- Electromyography:
  - Helps identify OP poisoning
  - Quantifies ACHE at the neuromuscular junction.

Treatment

- General measures:
  - Wear protective clothing
  - Neoprene/nitrile gloves used instead of latex for better protection
  - Remove the patient from the source of exposure
  - Remove all contaminated clothing
  - Wash exposed areas with soap, water and alkaline solution
  - A second wash with diluted ethanol may be done
  - Irrigate conjunctival recesses, skin and skin folds, fingernails, scalp and hair.
- Airway:
  - Keep airway patent: Head tilt, chin lift, jaw thrust
  - Gentle suctioning to remove secretions
  - Intubation/tracheostomy if:
    - Coma, bronchospasm
    - Respiratory failure, excess secretions, seizures
  - Succinylcholine may cause prolonged paralysis.
- Stomach wash:
  - If poison is ingested, stomach wash with 1:5000 $KMnO_4$
  - Activated charcoal 1 gm/kg to be used for stomach wash.
- Hypotension:
  - IV line taken and baseline blood sample taken for ACHE levels
  - Large fluid boluses of normal saline given
- Cardiac arrest: Resuscitate as per recent guidelines

- Atropine:
  - 2–4 mg IV given as test dose
  - If no effect, repeat every 5–10 mins until muscarinic symptoms relieved
  - IV infusion can be used to maintain full atropinization
  - Characteristics of full atropinization:
    - Dry skin
    - Tachycardia > 110 bpm
    - Hypertension
    - No secretions
    - Dilated pupils
  - Full atropinization has to be maintained for atleast 24 hours.
- Cholinesterase reactivators:
  - Agents used:
    - *Pralidoxime* (2-pyridine aldoxime methiodide)
    - *Diacetyl monoxime* (DAM)
    - *Obidoxime*
  - Rationale:
    - Restores ACHE activity by regenerating phosphorylated ACHE
    - Reactivators have to be started as early as possible
    - Given before aging of ACHE occurs (usually within 24 hours)
    - These are continued till the patient is clinically well
    - Reduce nicotinic, muscarinic and CNS symptoms.
  - Dosage:
    - 1–2 gm (20–40 mg/Kg) given IV as 5% solution over 5 mins
    - Can also be given in 150 ml of normal saline over half-hour
    - This can be repeated at 6–12 hour intervals for 24–48 hours
  - Continuous infusion:
    - Given at 500 mg/hr or 5–10 mg/kg/hr
    - Continuous infusion is preferable to repeated boluses
  - Maximum dose: Less than 12 gms in 24 hours
  - Not to be administered in:
    - Asymptomatic patients
    - Patients with carbamate poisoning and minimal symptoms
- Treatment of complications:
  - Convulsions:
    - Oxygenate, benzodiazepines and antidotal therapy
    - Anticonvulsants: Barbiturates/phenytoin
  - Pulmonary edema and bronchospasm: Oxygen, intubate, CPPV, atropine
  - Bradycardia: Usually secondary to bronchospasm: Atropine useful
- Avoid SCH, ester anesthetics and blockers as they may potentiate poisoning.

CARBON MONOXIDE POISONING[1,10,12,14,18,19]

Introduction

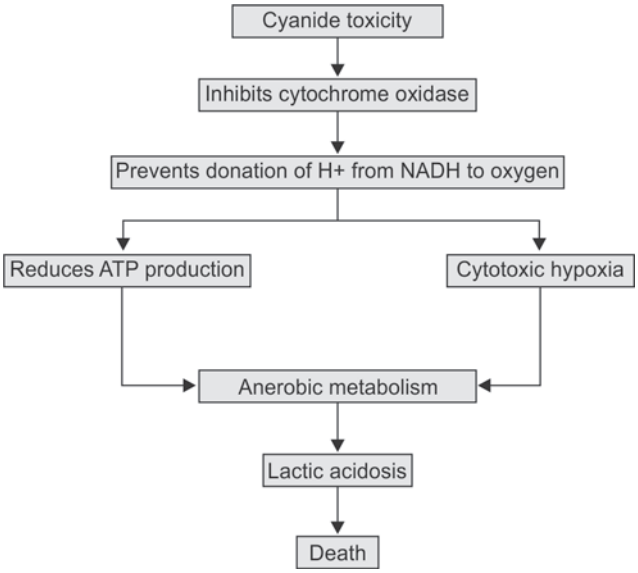
Occurs due to incomplete combustion of carbonaceous fuels.

Etiology

- Incomplete combustion of carbonaceous fuels
- Fires and natural disasters
- Automobile exhaust
- Closed space burns.

Pathophysiology

- Shifts oxyhemoglobin dissociation curve to the left: *Hemotoxic*
- Binds with myoglobin: *Cardiotoxic, Musculotoxic*
- Causes peroxidation of lipids and damage to the brain: *Neurotoxic.*



Clinical Features

Features of hypoxia with no cyanosis is *characteristic.*

Central Nervous System

- Headache
- Nausea

- Vomiting
- Dizziness
- Seizures
- Altered mental state
- Stupor
- Coma.

Cardiovascular System

- Hypotension
- Tachycardia
- Tachypnea
- Dyspnea
- Arrhythmias
- Myocardial infarction.

Delayed Neurological Sequelae

- Cognitive impairment
- Impaired memory
- Dementia
- Movement disorders.

Diagnosis

- Pulse oximetry: Normal as carboxyhemoglobin interpreted as hemoglobin
- Venous/arterial samples for carboxyhemoglobin levels:
  - > 5% in normal individuals
  - > 10% in smokers
- ECG: Features of ischemia
- Cardiac enzymes elevated
- CT scan
- ABG: Lactic acidosis.

Treatment

100% Oxygen

- Reduces half life of carboxyhemoglobin from 4–6 hrs to 1–2 hrs

Hyperbaric Oxygen Therapy

- Reduces half life of carboxyhemoglobin to 15–30 mins
- Reduces incidence of delayed neurological sequelae
- Use is controversial as most patients survive without hyperbaric therapy.

Airway Burns

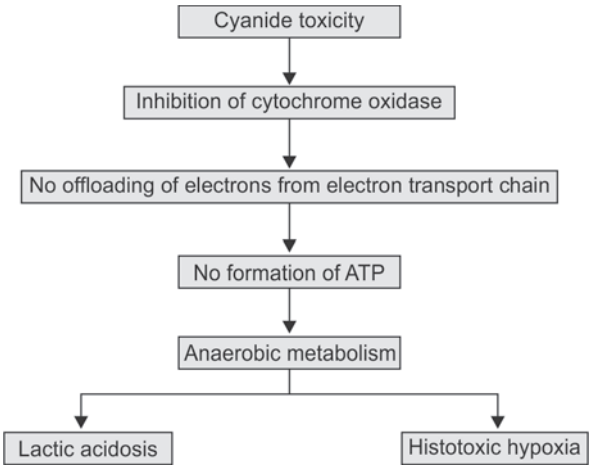
- Intubation
- Moist 100% oxygen
- Lavage
- Chest physiotherapy
- Bronchodilator therapy
- Heparin 10000 IU in 4 ml saline for nebulization
- N-acetyl cysteine nebulization.

CYANIDE POISONING[1,10,12,14,18,19]

Etiology

- Homicidal
- Suicidal
- Common in jewelers, industrial workers, lab workers
- Inhalation of hydrogen cyanide.

Pathophysiology



Clinical Features

Signs of hypoxia with no cyanosis *characteristic*.

Central Nervous System

- Headache
- Nausea
- Vomiting
- Dizziness
- Seizures
- Altered mental state
- Stupor
- Coma.

Cardiovascular System

- Hypotension
- Tachycardia
- Tachypnea
- Dyspnea
- Arrhythmias
- Myocardial infarction.

Diagnosis
- ABG: Profound lactic acidosis
- Normal pulse oximetry.

Treatment

Supportive
- Administer 100% oxygen
- IV cannulation
- Secure Airway Breathing.

Amyl Nitrite
- Available as volatile liquid in ampule
- Ampule broken and kept in front of victims mouth
- Done for 15 seconds followed by an interval of 15 seconds
- Acts by forming methemoglobin
- Cyanides bind more to methemoglobin than to cytochrome oxidase
- Thus it frees cytochrome oxidase enzyme.

Sodium Nitrite
- 10 ml IV or 0.2 ml/kg IV
- Followed after 2 hrs by 5 ml or 0.1 ml/kg IV
- Maintains methemoglobin concentration between 20–30%
- Same mechanism of action as amyl nitrite.

Sodium Thiosulfate
- 50 ml IV or 1.65 ml/kg IV
- Acts by hastening conversion of cyanide to thiocyanate by rhodanase.

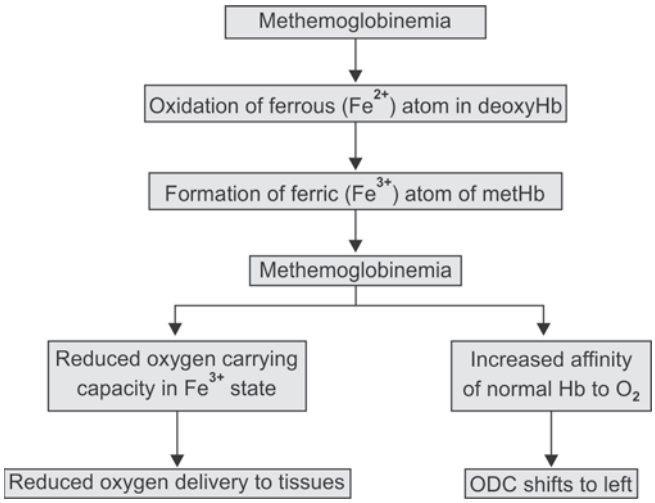
Hydroxocobalamine
- 70 mg/kg IV (maximum 5 gms)
- Converts cyanide to cyanocobalamine (vitamin B12).

METHEMOGLOBINEMIA[1,10,12,14,18,19]

Introduction
Due to formation of dyshemoglobin causing oxidation of ferrous atom in deoxyhemoglobin.

Etiology
- Congenital
- Acquired:
  - Lidocaine
  - Prilocaine
  - Benzocaine
  - Quinolines
  - Nitroglycerine
  - Sodium nitroprusside
  - Nitric oxide
  - Dapsone
  - Sulfonamides
  - Amyl nitrate
  - Closed space burns.

Pathophysiology[10,12]



Clinical Features
- Depends on methemoglobin levels
- Cyanosis occurs when methHb levels exceed 10% (1.5g/dL).

No[1,10]	Methemoglobin level	Features
1	0–15%	Asymptomatic
2	15–50%	Dyspnea on exertion
		Cyanosis
3	50–70%	Seizures
		Coma
		Cyanosis
		Profound acidosis
4	> 70%	Cardiac arrest
		Death

Investigations
- *Cooximetry* to detect methHb levels *diagnostic*
- Pulse oximetry characteristic in methHb:
  - SpO2 constant between 70–90%
  - Usually constant at 84%
  - Occurs as absorption at 660 nm and 940 nm is equal.

Treatment

Supportive Therapy

- 100% Oxygen
- Secure Airway, Breathing, Circulation.

Methylene Blue

- 1–2 mg/kg over 5 min
- Converted to leucomethylene blue by NADPH
- Leucomethylene blue reduces metHb to Hb
- Repeated every 60 mins as short acting
- Continued benzocaine absorption from adipose tissue may cause toxicity.

Blood Transfusion

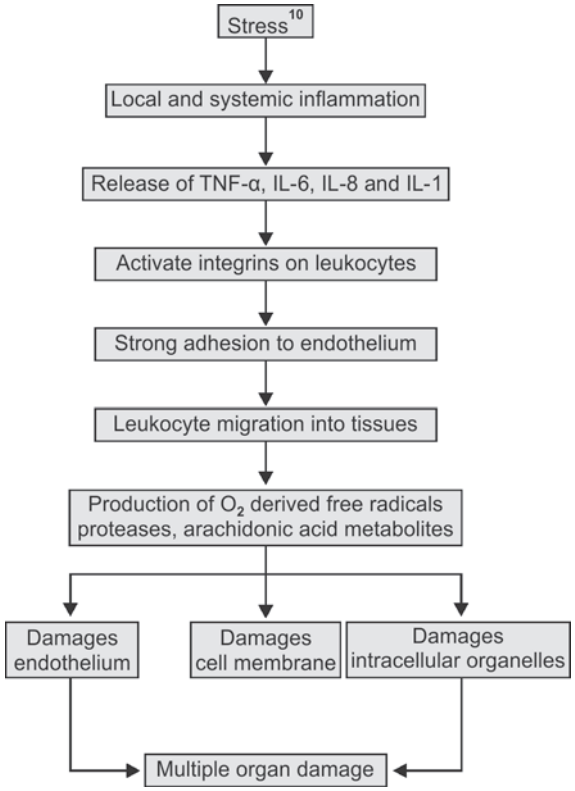
MULTIPLE ORGAN DYSFUNCTION SYNDROME[10,12,14,18,19]

Introduction

- Development of potentially reversible physiological derangement involving more than 2 organ systems, not involved in the disorder resulted in ICU admission is called multiple organ dysfunction syndrome.
- Multiple organ failure/multisystem organ failure (MSOF).

Pathogenesis[10]

- Gut hypothesis:
  - Due to splanchnic hypoperfusion and mucosal ischemia
  - Increased gut permeability and translocation of bacteria
  - Tissue injury due to immune response.
- Endotoxin macrophage hypothesis:
  - Gram-negative infections are common
  - Endotoxins are principal mediators
  - Pro-inflammatory mediators: TNF- α, IL-1, IL-6, TXA_2, PAF, NO
- Tissue hypoxia-microvascular hypothesis:
  - Due to macro and microvascular changes
  - Insufficient supply of oxygen occurs
- Integrated hypothesis: Combination of other 3 hypothesis
- Altered metabolism:
  - Extreme protein catabolism causes *auto-cannibalism*
  - Ketone body ratio (Aceto-acetate: β-hydroxy butyrate) less than 0.4 is *characteristic* of MODS.



Pathology[10]

- Cardiovascular:
  - Reduced peripheral vascular tone due to nitric oxide
  - Increased capillary permeability
  - Alteration in regional blood flow
  - Microvascular occlusion and stasis
  - Myocardial depression affecting right heart.
- Respiratory:
  - Failure of normal gas exchange and arterial hypoxemia
  - Atelectasis and ventilation-perfusion mismatch
  - Increased capillary permeability and alveolar flooding
  - Volutrauma and barotrauma aggravate lung injury.
- Gastrointestinal:
  - Reduced regional blood flow
  - Impaired motility and altered microbial flora
  - Hyperbilirubinemia and cholestasis.
- Genitourinary:
  - Reduced renal blood flow due to systemic hypotension
  - Altered regional perfusion

- Hematological:
  - Impaired delayed type hypersensitivity
  - Altered antibody production
  - Development of nosocomial infections.

Clinical Features[10,12,14]

- General:
  - Fever, tachycardia, tachypnea, leucocytosis
  - Rapid reduction in muscle mass, marked protein catabolism
- Neurological:
  - Encephalopathies, myopathy
  - Heterogenous neuropathies
  - Critical illness neuropathy
  - Coma
- Cardiovascular:
  - Hypotension, tachycardia
  - Reduced cardiac output and SVR
  - Diffuse capillary leak and anasarca
  - LV and RV dysfunction, low output failure
  - Supraventricular arrhythmias.
- Respiratory:
  - Hypoxemia and respiratory distress
  - Atelectasis, wasted ventilation, V/Q mismatch
  - ALI develops in 24–72 hours: Most common manifestation
  - Acute respiratory failure.
- Gastrointestinal:
  - Splanchmic ischemia
  - Upper GI bleeding and stress ulceration
  - Intolerance of enteral feeds: Ileus
  - Abdominal distension and diarrhea
  - Hyperbilirubinemia and cholestasis, liver failure
  - Pancreatitis, hepatitis.
- Genitourinary:
  - Prerenal/renal azotemia
  - Oliguric acute renal failure
  - Fluid and electrolyte derangement.
- Endocrine:
  - Hyperglycemia and insulin resistance
  - Side euthyroid syndrome
  - Relative adrenal insufficiency.
- Metabolic:
  - Hyperglymia due to increased gluconeogenesis and decreased glucose clearance
  - Lipolysis, hypertriglyceridemia
  - Low ketone levels
  - Increased oxygen consumption
  - Increased energy expenditure.
- Hematological:
  - Leukocytes, mild anemia due to bone marrow suppression
  - Thrombocytopenia and DIC
  - Nosocomial infections: Gram-negative infections are common.

Clinical Staging[10,12]

Stage I:
- Increased volume requirement
- Mild respiratory alkalosis
- Associated with oliguria, hyperglycemia, increased insulin requirement

Stage II:
- Tachypnea, hypocapnea, hypoxemia
- Moderate liver dysfunction
- Possible hematological abnormalities

Stage III:
- Shock with azotemia
- Acid-base disturbances
- Significant coagulation abnormalities

Stage IV:
- Patient is vasopressor dependant
- Oliguric/anuric
- Ischemic colitis/lactic acidosis.

Treatment[10,12,14,18,19]

- Resuscitation:
  - Aimed at maintaining gastric intramucosal pH above 7.35
  - Maintain hyperdynamic state to decrease oxygen debt/perfusion deficit
  - Volume loading more than 40 mL/kg in first hour in pediatric patients
  - Use colloids/crystalloids for volume expansion
  - Blood transfusion is not very beneficial
  - Effect of inotropes on splanchnic perfusion unpredictable.
- Control precipitating factors:
  - Appropriate antibiotics if infection
  - Control bleeding early if trauma is cause
  - Prompt surgery
  - Early fracture fixation
  - Early burn excision.
- Supportive therapy:
  - Cardiovascular:
    - Inotropes and vasopressors
    - Effect on splanchnic perfusion is unpredictable
    - Maintain adequate perfusion pressure and DO_2 to cells

  - Respiratory:
    - Endotracheal intubation and ventilation
    - Avoid high intrathoracic pressure
  - Renals:
    - Maintain renal perfusion with fluid therapy and inotropes
    - Renal dose dopamine may be detrimental
    - Start renal replacement therapy early.
  - Hematological support if DIC manifests
- Metabolic:
  - Goal is to obtain nitrogen equilibrium
  - Early enteral nutrition helps to stimulate blood flow to gut
  - Vitamin-E, zinc, omega-3 fatty acids, glutamine and arginine are under investigation
  - Growth hormone can improve nitrogen balance.
- Reduce stress response:
  - Sedation and analgesia
  - Prevent hypothermia
  - Remove residual foci of inflammation
  - Avoid secondary catheter-related sepsis.
- Experimental therapy:
  - Anti-inflammatory and anti-cytokine therapy
  - Monoclonal anti-TNF- therapy
  - Platelet activating factor and phospholipase A_2 antagonists
  - Antioxidants:
    - N-acetyl-cysteine
    - ATP-$MgCl_2$
    - Inhibitors of NO synthase.

Prevention

System[10]	Convincing evidence	Controversial
Cardiovascular	Restrict transfusion above Hb 7g%	Supranormal oxygen delivery
		Non-crystalloid fluids
		Swann-Ganz catheter
Respiratory	Pressure/volume limited ventilation	Liquid ventilation
		HFOV
Gastrointestinal	Stress ulcer prophylaxis with H_2 blockers	Gastric tonometry
	Enteral nutrition	
	Selective decontamination of digestive tract	
Renals	Avoid nephrotoxins	CVVHF
Endocrines		Corticoids in late sepsis
Hematology	DVT prophylaxis	Anticoagulant therapy
		Anticytokine therapy

Prognosis: *Mod Score:*[10]

Characteristic	Score				
	0	1	2	3	4
GCS score	15	13–14	10–12	7–9	< 6
R/P ratio	< 10	10.1–15	15.1–20	20.1–30	> 30
PaO_2/FiO_2	> 300	226–300	151–225	76–150	< 75
Serum bilirubin (μmol/L)	< 20	21–60	61–120	121–240	> 240
Serum creatinine (μmol/L)	< 100	101–200	201–350	351–500	> 500
Platelet count	> 120000	81000–120000	51000–80000	21000–50000	< 20000

Number of failing systems	Mortality
0	< 10 %
1	10–30 %
2	20–50 %
3	40–80 %
4	60–100 %
> 5	> 80%

NONINVASIVE VENTILATION[1,3,4]

Introduction

Technique of providing ventilation without the use of an artificial airway, using a mask or similar device.

Mechanism of Action

- Reduces inspiratory muscle work
- Reduces work of breathing
- Reduction in pressure-time product (PTP) of inspiratory muscles
- Also causes recruitment of alveoli
- Increases FRC
- Increases V/Q ratio.

Types of NIPPV

Type	Term	Description
NPPV	Noninvasive positive press vent	May be used as CPAP or BIPAP
CPAP	Continuous positive airway pressure	Positive pressure during spontaneous breathing
		No mechanical breaths given
		Active when IPAP = EPAP
PEEP	Positive end-expiratory pressure	Positive pressure applied at end-expiratory phase
		Applied during mechanical breaths
Bilevel PAP	Bilevel positive airway pressure	Provides IPAP & EPAP
		Also known as BIPAP
IPAP	Inspiratory PAP	Controls peak inspiratory pressure
EPAP	Expiratory PAP	Controls end expiratory pressure
		Used as PEEP when IPAP > EPAP
		Used as CPAP when IPAP = EPAP

Indications: *British Thoracic Society (BTS) 2002 guidelines:*

- Level I evidence: Using RCTs:
  - Acute hypercapneic respiratory failure due to COPD exacerbation
  - Facilitating weaning/extubation in patients with COPD
  - Cardiogenic pulmonary edema
  - Immunosuppressed patients with hypoxemic respiratory failure.
- Level II evidence: Individual cohort studies:
  - Do not intubate status
  - End stage patients as palliative measure
  - Extubation failure (COPD/CCF: As a preventive measure)
  - Community acquired pneumonia in COPD
  - Post-operative respiratory failure (prevention and therapy)
  - Prevention of acute respiratory failure in asthma.
- Level III evidence: Case control studies:
  - Neuromuscular diseases/kyphoscoliosis
  - Treatment of respiratory failure in asthma
  - Thoracic trauma
  - Partial upper airway obstruction
  - For ventilation in postoperative patients.
- Level IV evidence: Case series:
  - Very old age ≥ 75 yrs
  - Cystic fibrosis
  - *Obesity hypoventilation syndrome.*

Patient Selection Criteria

- Patient criteria:
  - COPD
  - Cardiogenic pulmonary edema
  - Decompensated OSAS
  - Chest wall deformity
  - Neuromuscular disorders.
- Clinical criteria:
  - Sick, but not moribund
  - Conscious and cooperate
  - Able to protect airway
  - No excessive respiratory secretions
  - Hemodynamically stable
  - Few comorbidities.
- Blood gas criteria:
  - Respiratory acidosis with:
    - $PaCO_2 > 45$ mm Hg
    - pH < 7.35
    - $H^+ > 45$ nmol/L
  - Low P (A-a) O_2 gradient.

Goals of NIPPV

- Short-term goals:
  - Relieve symptoms
  - Reduce work of breathing
  - Improve gas exchange
  - Optimize patient comfort
  - Good patient-ventilator asynchromy
  - Minimize risk
  - Avoid intubation.

- Long term goals:
  - Improve sleep duration and quality if OSAS
  - Maximize quality of life
  - Enhance functional status
  - Prolong survival.

Monitoring During NIPPV

- Subjective responses: Assessment of:
  - Patient comfort level and consciousness
  - Respiratory rate and heart rate
  - Chest wall motion
  - Accessory muscle recruitment
  - Coordination with ventilator.
- Physical responses:
  - Reduction in respiratory rate in first or second hour is most consistent sign
  - Reduced sternocleidamastoid activity
  - Abdominal paradox and heart rate reduces
  - Patient breathes in synchrony with ventilator.
- Gaseous exchange:
  - Pulse oximetry
  - E_TCO_2
  - ABG after 4–6 hrs of initiating therapy and Q1-2H thereafter
  - Spirometry before discharge.

Interfaces for NIPPV[4]

- Nasal mask:
  - Most *commonly* used interface:
  - Cannot be used in dyspneic patients as they are mouth breathers: Increases gas leak chances
  - Advantages:
    - Comfortable
    - Increased patient compliance
  - Disadvantages:
    - Gas leaks through mouth
    - Nasal dryness/drainage
    - Less effective at reducing $PaCO_2$
- Facial mask:
  - Advantages: Good seal possible
  - Disadvantages:
    - Claustrophobia
    - Non-compliance with therapy
    - Regurgitation and aspiration
    - Asphyxiation in cases of power/gas failure
    - Alarms and monitors may be necessary.
  - In acute setting, use facemask initially and change to nasal mask after 24 hrs as patient improves.
- Nasal pillows:
  - Resembles nasal mask but is smaller in size
  - Contains two cushions which fit under nose
  - Has pressure range of 3–20 cm H_2O
  - Used for CPAP
  - More comfortable, but gas leaks possible
- CPAP helmet.

Problems with Interfaces

- Gas leaks
- Pressure points sores/dry eyes
- Nasal congestion/discharge
- Nasal airway drying
- Skin breakdown/irritation
- Sensitive front teeth.

Initiating NIPPV

- Done in appropriate location and with appropriate monitors
- Patient in bed/chair, sitting at 30° angle
- Select and fit interface, select ventilator
- Apply headgear, avoid excessive strap tension: 1–2 fingers under strap
- Encourage patient to hold mask
- Connect interface to ventilator tubing and turn on ventilator
- Start with low pressure/volume in spontaneously triggered mode:
  - IPAP: 8–12 cm H_2O
  - EPAP: 3–5 cm H_2O
  - Tidal volume 10 ml/Kg
- Gradually change the settings:
  - Increase IPAP to 10–20 cm H_2O
  - Increase tidal volume to 10–15 ml/kg as tolerated, as indicated by:
    - Alleviation of dyspnea
    - Reduced respiratory rate
    - Increased tidal volume
    - Good patient-ventilator synchrony.
- Provide oxygen supplementation, keep $SpO_2 > 90\%$
- Check for air leaks, readjust straps
- Add humidifier as needed
- Consider mild sedation (IV lorazepam 0.5 mg) in agitated patients
- Encourage, reassure, frequently check and make adjustments
- Monitor ABGs every 1–2 hours.

Weaning from NIPPV: *BTS 2002 guidelines*:

- Criteria for weaning:
  - Respiratory rate < 24 breaths/min
  - SpO_2 > 90% on FiO_2 < 40%
  - Compensated pH > 7.35
  - Heart rate < 110 bpm
- Breaks can be made for drugs/meals, etc
- Ventilate as much as possible during first 24 hrs/until patient improves.

Contraindications to NIPPV

- Absolute contraindications:
  - Respiratory arrest
  - Cardiac arrest
  - Improperly fitting mask
- Relative contraindications:
  - General:
    - Agitated and uncooperative
    - Cannot protect airway
    - Clinically unstable patients
  - Local:
    - Facial trauma
    - Burns
    - Deformity
  - Upper airway:
    - Upper airway obstruction
    - Recent upper airway/GI/facial surgery
    - Increased secretions
    - Increased risk of aspiration/vomiting.
  - Systemic:
    - Severe comorbidity
    - Focal consolidation on chest X-ray
    - Undrained pneumothorax
    - Life threatening hypoxemia
    - Hemodynamic instability
    - Bowel obstruction
    - Nonrespiratory organ failure:
      - Encephalopathy
      - Severe upper GI bleed.

Advantages of NIPPV

- No neuromuscular paralysis
- Reduced work of breathing
- Reduced intubation complications: Injury to teeth, vocal cords and larynx
- Preserves airway defense mechanisms
- Allows patients to eat, drink and verbalize
- Reduces infectious complications: VAP, sinusitis
- Can be administered outside ICU settings
- Reduces hospital stay
- Reduces cost.

Complications

- Mask related:
  - Discomfort
  - Claustrophobia
  - Facial skin erythema
  - Nasal bridge ulceration
  - Acneform rashes
- Air pressure/flow related:
  - Nasal congestion
  - Eye irritation
  - Sinus/ear pain
  - Gastric insufflation
  - Nasal/oral dryness
  - Air leaks
- Major complications:
  - Aspiration pneumonia
  - Hypotension
  - Pneumothorax.

WEANING CRITERIA[1,10,12]

Criteria

Category	Examples	Values
Ventilatory criteria	Spontaneous breathing trial	Tolerates 30–120/min
	$PaCO_2$	< 50 mm Hg with normal pH
	pH	7.35–7.45
	Spontaneous tidal volume	5–8 ml/kg
	Spontaneous respiratory rate	< 30 breaths/min
	Minute volume	< 10 L/min
	Vital capacity	≥ 10–15 ml/kg

Contd...

Contd...

Category	Examples	Values
Oxygenation criteria	PaO_2 without PEEP	≥ 60 mm Hg at FiO_2 40%
	PaO_2 with PEEP	≥ 100 mm Hg at FiO_2 40%
	PaO_2/FiO_2	≥ 200 mm Hg
	SaO_2	≥ 90% at FiO_2 40%
	Intrapulmonary shunt (Qs/Qt)	≤ 20%
	$P(A\text{-}a)O_2$	< 350 mm Hg at FiO_2 100%
Pulmonary reserve	Maximum voluntary ventilation	Twice the minute volume at FiO_2 40%
	Maximum inspiratory pressure	> –20 to –30 cm H_2O in 20 seconds
Pulmonary measurements	Static compliance	> 30 ml/cm H_2O
	Airway resistance	Normally 0.6–2.4 cm H_2O/L/sec
	VD/VT	< 60%
Combined weaning indices	***RSBI***	< 100 breaths/min/L
	Simplified weaning index	< 9/min
	CROP index	≥ 13 mL/breath/min

Introduction

Process of abruptly or gradually withdrawing ventilatory support.

Prerequisites

- Patient to breath spontaneously for 3 minutes off ventilator prior to measuring:
  - Vital capacity
  - Tidal volume
  - Spontaneous respiratory rate
- In patients with anemia/dyshemoglobinemias, PaO_2 and SaO_2 do not reflect true oxygenation states.

Calculations

Maximum Inspiratory Pressure

- Also called negative inspiratory force
- Amount of negative pressure a patient can generate in 20 seconds when inspiring against an occluded measuring device.

Airway Resistance

- Airway resistance = $\frac{PIP–P_{plat}}{\text{Constant inspiratory flow rate}}$
- No critical weaning value has been established for airway resistance
- Higher airway resistance causes greater work of breathing.

Intrapulmonary Shunt Fraction

$$\frac{Q_S}{Q_T} = \frac{CcO_2–CaO_2}{CcO_2–CvO_2}$$

- Where:
  - Qs/QT = Shunt percent
  - CcO_2 = End capillary O_2 content in volume %
  - CaO_2 = Arterial O_2 content in volume %
  - CvO_2 = Mixed venous O_2 content in volume %.
- Interpretation:
  - 10–20% = Mild physiological shunt
  - 20–30% = Moderate physiological shunt
  - 30% = Severe physiological shunt.

Simplified Weaning Index

Simplified Weaning Index

$$= \frac{F_{mv}(PIP–PEEP)}{MIP} \times \frac{PaCO_{2mv}}{40}$$

Where,

- F_{mv} = Ventilator frequency
- PIP = Peak inspiratory pressure
- MIP= Maximal inspiratory pressure
- $PaCO_{2mv}$ = Arterial CO_2 tension while on ventilator.

- SWI evaluates patients ventilatory endurance and efficiency of gas exchange
- SWI < 9/min suggests 93% chances of weaning success
- SWI > 11/min suggests 95% chances of weaning failure.

Compliance Rate Oxygenation and Pressure Index

$$\text{CROP index} = \frac{C_{DYN} \times MIP \times PaO_2/P_AO_2}{f}$$

- Where:
  - C_{DYN} = Dynamic compliance
  - MIP= Maximum inspiratory pressure
  - PaO_2 = Arterial oxygen tension
  - P_AO_2 = Alveolar oxygen tension
  - f = Spontaneous respiratory rate per min.
- Evaluates patients gas exchange and balance between respiratory demand and respiratory neuromuscular reserve
- CROP index ≥ 13 ml/breath/min indicates increased likelihood of weaning success.

Rapid Shallow Breathing Index

Introduction

- Determines ratio of spontaneous respiratory rate to spontaneous tidal volume
- Also called *Tobin Index*.

Calculation

- $\text{RSBI} = \frac{\text{f (number of breaths/min)}}{\text{Tidal volume (in liters)}}$
- $\text{RSBI rate} = \frac{\text{RSBI}_2 - \text{RSBI}_1 \times 100}{\text{RSBI}_1}$

Significance

- RSBI > 100 suggests potential weaning failure and unsuccessful weaning trial
- RSBI 80–100 suggests weaning may or may not be successful
- RSBI < 80 implies weaning may be successful
- RSBI rate < 20% indicates chances of successful weaning trial.

Measurement

- Explain procedure to patient
- Ensure ventilator sensitivity is appropriately set
- Patient taken off ventilator and allowed to breath spontaneously for 3 minutes or until a stable breathing pattern has been established
- Alternately, RSBI measured on CPAP of 5 cm H_2O and pressure support 5 cm H_2O for 5 minutes
- Measure minute expired volume (V_E) and respiratory rate for 1 minute (f)
- V_T calculated by dividing V_E by f
- Divide f by V_T to obtain RSBI.

Basis

- Better compliance and greater inspiratory effort is associated with adequate gas exchange and lower respiratory rate
- Thus, greater is probability of sustaining spontaneous ventilation
- Hence weaning is more likely to be successful if respiratory rate is lower and tidal volume is higher.

Advantages

- Noninvasive measure
- Can be obtained at bedside with portable device (ventilator)
- Easily reproducible
- Can be performed in short period of time
- No need for laboratory data.

Current Status

- Not yet established routine as ventilatory pressure support still offers aid to inspiration
- However, it eliminates delay in extubation of patients
- Used to reduce failure of premature weaning.

SPONTANEOUS BREATHING TRIAL[9,10,12,14,18,19]

Introduction

- Spontaneous breathing trial is a trial of unassisted breathing during which patient is observed for signs of respiratory failure
- Usually done for period of 30 minutes: *Grade A, LOE I Critical Care 2000*
- Can be carried out for upto 2 hours.

Methods

- Using T piece
- Using pressure support and PEEP (minimal support with PS 5 cm H_2O and PEEP 5 cm H_2O)
- Using CPAP alone.

Criteria to Assess Readiness for SBT:

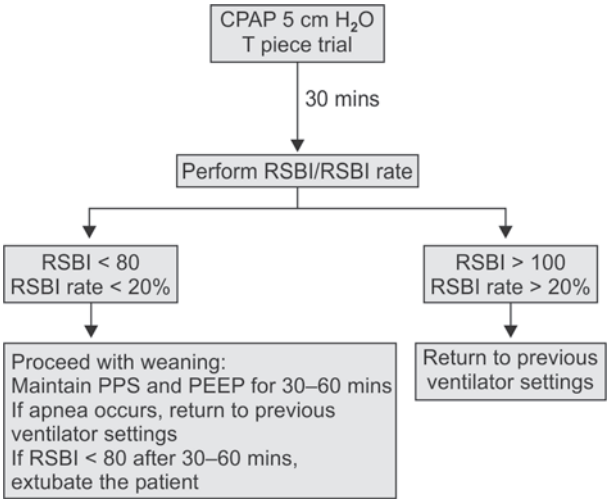
Wean Screen

Criteria	Value
Reversal of respiratory failure	Evidence of some reversal of underlying cause of respiratory failure
	$f/V_T < 105$
Adequate oxygenation	$PaO_2/FiO_2 \geq 150–200$
	PEEP ≤ 5–8 cm H_2O
	$FiO_2 \leq 40–50\%$
	pH ≥ 7.25
Hemodynamic stability	Absence of MI
	Absence of significant hypotension
	Minimal vasopressors
	Dopamine/dobutamine ≤ 5 µg/kg/min
Respiratory drive	Able to initiate inspiratory effort

Procedure[9,10]

Adjust ventilator settings:

PS 5 cm H_2O with PEEP 5 cm H_2O



T-Piece Trial

- May use new aerosol setup or existing ventilator circuit
- Let patient breathe spontaneously for up to 5 minutes every 30–180 minutes
- Return patient to mechanical ventilation after 5 minutes
- Increase duration of spontaneous breathing gradually for upto 2 hours at a time
- If patient tolerates trial with good ABG and stable vital sings, extubate the patient.

Termination Criteria[9,10,12]

- Change in mental status:
  - Coma
  - Agitation
  - Anxiety
  - Somnolence
- Signs of increased work of breathing:
  - Nasal flaring
  - Paradoxical breathing movement
  - Use of accessory respiratory muscles
  - Onset of worsening discomfort/diaphoresis
- Unstable ventilatory/respiratory pattern:
  - Respiratory rate ≥ 30 breaths/minute
  - Change in respiratory rate of ≥ 50%
- Inadequate gaseous exchange:
  - SpO_2 < 85–90%
  - PaO_2 < 60 mm Hg
  - pH < 7.32
  - Rise in $PaCO_2$ ≥ 10 mm Hg
- Hemodynamic instability:
  - Heart rate ≥ 140 bpm
  - Sustained change in heart rate ≥ 20%
  - SBP < 90 or > 180 mm Hg
  - Change in BP ≥ 20%
  - Requirement of vasopressorsl

Current Status

- Led to superior outcome and increased weaning and extubation success in several randomized controlled trials
- Tolerance of a 2 hour SBT suggests an 85% chance of successfully staying off the ventilator for more than 48 hours
- Currently, controversies exist regarding:
  - CPAP vs T-piece use for 1 hour
  - T-piece vs plain pressure support 7 cm H_2O for 1 hour
  - Duration of SBT 30 minutes vs 120 minutes.

PERCUTANEOUS TRACHEOSTOMY[1,3,6,9,10,12]

Introduction

PDT is a procedure in which placement of a tracheostomy tube is achieved after establishing a tracheal stoma through dilatation rather than surgical creation of a stoma.

Indications[1,10,12]

- Need for prolonged mechanical ventilation ≥ *7 days:*
  - Pneumonia refractory to treatement
  - Severe COPD
  - ARDS
  - MODS
  - Severe brain injury
- Airway protection against aspiration: Laryngeal incompetence due to:
  - Critical illness
  - Polyneuropathy
  - Bulbar palsy
- Upper airway obstruction:
  - Inflammatory diseases
  - Benign laryngeal pathology (web/cysts/papilla)
  - Malignant laryngeal tumors
  - Bilateral recurrent laryngeal nerve palsy
  - Laryngeal trauma/stenosis
  - Tracheal stenosis.
- Facilitation of pulmonary toilet
- Facilitation of weaning in patients with COPD
- Obstructive sleep apnea syndrome.

Timing

- *1989 Consensus Conference on Artificial Airways, ACCP guidelines*
- Tracheostomy indicated if artificial airway is anticipated for ≥ 7 days.

Contraindications[1,10]

- Age < 15 years
- Emergency airway access
- Known or suspected difficult intubation
- Local infection
- Unstable fractures of cervical spine
- Gross distortion of neck anatomy:
  - Hematoma/tumor
  - Thyromegaly
  - High innominate artery
  - Scars from previous surgery
  - Previous radiotherapy to neck.
- Bleeding diathesis:
  - PT/APTT > 1.5 times reference
  - Platelet count ≤ 50,000/µL
  - Bleeding time ≥ 10 minutes.
- Need for PEEP ≥ 15 cm H_2O.

Advantages of Translaryngeal Intubation

- Ease and rapidity of insertion
- Avoids acute surgical complications
- Lower cost
- Avoids late surgical complications (stenosis, infection, RLN palsy)
- Reduces risk of VAP.

Advantages of Tracheostomy

- Improved patient comfort
- Reduced need for sedation and analgesia
- Effective airway suctioning
- Reduced airway resistance
- Reduced work of breathing
- Reduced tube dead space
- Increased ease for speech
- Able to eat orally
- More secure airway: Reduced risk of extubation
- Easy tube reinsertion
- Improved oral, nasal, facial hygiene
- Facilitates oral communication and speech
- Improves patient appearance
- Improves patient mobility
- Facilitates nursing care of airway
- Facilitates more rapid weaning off ventilator.

Advantages of Percutaneous Tracheostomy

- Time required is shorter compared to surgical tracheostomy
- Avoids transport of critically ill patients to operation theater
- Less expensive.

Techniques

All have similar success rates:

- *Sheldons trocar*
- *Ciaglias percutaneous dilation tracheostomy* (PDT) 1985:
  - Needle guide wire airway access
  - Serial dilation with sequentially large dilators
- *Schachners Rapitrach technique* 1989:
  - Contains dilating forceps device with beveled metal cones
  - Advanced forcibly over a wire into airway
- *Griggs guidewire dilating forceps (GDWF) technique* 1990:
  - Similar to Rapitrach forceps
  - Forceps has no cutting edge on tip of instrument
- *Fantoni's translaryngeal technique:*
  - Initial puncture of the trachea is carried out with the needle directed cranially
  - Tracheal cannula inserted with a pull-through technique along the orotracheal route in a retrograde fashion
  - Cannula is then rotated downward using a plastic obturator
  - Advantages:
    - Minimal amount of skin incision required
    - Minimal bleeding observed
  - Disadvantages:
    - Procedure can only be carried out under endoscopic guidance
    - Rotating the tracheal cannula downward may pose a problem.

Equipment

- PDT kit:
  - # 22 needle, syringe
  - 11 F short punch dilator
  - Guide wire
  - 8 F guiding catheter
  - 18 F, 21 F, 24 F, 28 F, 36 F, 38 F dilators
  - ***Shiley 8*** size tracheostomy tube
  - Fibreoptic bronchoscope.

- Rapitrach kit:
  - # 12 needle and syringe
  - Guidewire, scalpel
  - Rapitrach PCT dilator
  - Standard portex # 8 tracheostomy tube with curved obturator
  - Fibreoptic bronchoscope.
- GWDF kit:
  - # 14 needles and syringe
  - Guide wire (J tipped Seldinger type)
  - Scalpel
  - *Howard Kelly forceps*
  - Shiley 8 # double cannula tracheostomy tube with curved obturator
  - Fibreoptic bronchoscope.

Types of Tracheostomy Tubes[6,9]

- Depending on cuff:
  - Cuffed tubes:
    - High volume low pressure cuffs preferred
    - Cuff pressure not to exceed 25 cm H_2O
    - Higher pressures can cause tracheal mucosal ischemia.
  - Uncuffed metallic tubes:
    - *Jacksons 3 cannula*
    - *Fullers tube*
- Depending on number of cannula:
  - Single cannula tube
  - Double cannula tube:
    - If cannula gets blocked, inner cannula is removed and cleaned everyday
    - Outer cannula is not removed on 1st 3 days to allow track formation
- Depending on fenestration:
  - Fenestrated tubes
  - Unfenestrated tubes:
    - Fenestrated has opening in posterior part of outer tube
    - If tube is cuffed, fenestration lies above cuff
    - Deflation of cuff allows air to pass through trachestomy lumen and fenestration
    - Maximal airflow then occurs through upper airways
    - This aids in speech.

Investigations

- Complete blood count: Platelets ≥ 50000/µL
- PT/APTT > 1.5 reference
- Bleeding time ≤ 10 minutes
- Blood urea nitrogen < 40 mg/dL, creatinine < 4 mg/dL
- Chest X-ray for tracheal air column (AP and lateral view).

Preparation for Tracheostomy

- NPO orders
- Induce with 50–100 µg fentanyl and 1–2 mg/kg ketamine IV
- 5 mg morphine, 10 mg atracurium IV
- Patient kept on FiO_2 1 from atleast 15 minutes before surgery
- Withdraw ETT under FOB vision to place cuff just under vocal cords
- Monitor ECG, NIBP, SpO_2, E_TCO_2.

Position

- Patient kept supine
- Sand bag under neck and shoulder to hyperextend neck
- Head placed in neutral position
- Surface marking done for thyroid, cricoid cartilage and suprasternal notch marked.

Technique: Griggs

- Intensivist stands at head end of patient
- ETT cuff deflated and tidal volume increased to twice desired volume with increase in peak inspiratory pressure limit
- Cleanse and drape neck below cricoid cartilage and upper chest
- Infiltrate skin and subcutaneous tissue with 2% xylocaine with 1:100000 adrenaline
- Identify puncture site by applying pressure between 2nd and 3rd tracheal rings
- ETT withdrawn from puncture site
- Pass FOB through ETT
- 1.5 to 2 cm midline transverse incision made between T_2 and T_3
- Pass needle (14# IV cannula with syringe attached) through tracheal wall and pass guidewire through it when air drawn into syringe
- Visualize entry of needle with FOB
- Remove needle as soon as air bubbles into syringe and advance sheath till it enters trachea
- Thread conical dilator to dilate soft tissue and enter trachea with continuous gentle pressure, verify with FOB
- Remove dilator, dilate trachea with both hands
- Suction out bleeding
- Thread TT over guide wire under FOB vision.

Ciaglia

- Uses rhinos for dilation
- Technique is similar to Griggs otherwise
- Rhinos become smooth when placed in water
- With rhinos, dilation of trachea is more controlled
- In Griggs, dilation is done with forceps and force to be applied to place tube has to be learnt by trial and error.

Postoperative Care[6,9,10]

- Airway entry checked by auscultation and respiratory plethysmography
- Chest X-ray taken to confirm position
- Provide humidified gases:
  - *Trach mask/mist collar*
  - Heat and moisture exchanger
  - Suction blood and secretions
- *Antiseptic wound and stoma care everyday*
- Monitor tube position to prevent dislodgement
- Suction tracheostomy tube when:
  - Audible rales or mucus rattling
  - Patient unable to generate effective cough
  - Visible secretions in airway
  - Increased respiratory rate or work of breathing
  - During cuff deflation
  - Before feeds.
- Avoid frequent suctions to prevent buildup of secretions
- Feeding with tracheostomy:
  - Suction tracheostomy tube before feeding
  - Encourage fluid intake which helps in loosening secretions
  - *Deflate cuff to enable swallowing*
  - *Use speaking valve, if present to make swallowing easier*
  - Monitor for vomiting and aspiration.
- *Deflate balloon for 15 mins every hour for 1st 24 hours and then leave balloon inflated*
- *Clean inner cannula once every 8 hours*
- Tracheostomy tube exchange
  - *Done every 2 weeks if single lumen TT*
  - *Done every month if double cannula TT*
- Tube exchange to prevent obstruction and also formation of granulation tissue around tube.

Decannulation

- The patient is decannulated when:
  - Able to obey commands in non-neurologically compromised patients
  - Cough reflex is sufficient
  - Suctioning is rarely needed
  - Mechanical ventilation has not been needed for more than 24 hours
  - FiO_2 is reasonably low
  - Airway is spontaneously patent
  - No new infilterates on chest X-ray
  - Tolerates cuff deflation for more than 24 hours
  - Tolerates speaking valve for more than 12 hours
  - Tolerates decannulation cap for upto 4 hours.
- At discharge from ICU to the ward with a tracheal cannula in place:
  - Tracheal cannula should be without cuff (to avoid risk of total airway occlusion)
  - An individual plan for decannulation should be presented.

Complications[6,9,10]

Perioperative Complications (< 24 hours postoperatively)

- Hemorrhage
- Hypoxia
- False passage:
  - Most common with short and thick neck
  - Paratracheal insertion
- Posterior tracheal wall peforation:
  - Due to guiding catheter/guidewire instability
  - Can cause pneumothorax/subcutaneous emphysema
- Subcutaneous emphysema:
  - False tracheostomy tube placement
  - Tracheal wall trauma
- Tension pneumothorax
- Accidental extubation
- Death.

Postoperative Complications (> 24 hours postoperatively)

- Hemorrhage: Common if:
  - Multisystem disease
  - Sepsis
  - Coagulopathies
  - Renal failure
  - Tracheoarterial fistula
  - Stomal granulation.
- Granulation tissue: Due to perichondritis of cricoid/tracheal cartilages
- Tracheoarterial fistula:
  - Tip of tube erodes into posterior branch of brachiocephalic artery

  - Risk is minimized if TT puncture is between 2–3 tracheal rings
- Stomal infections
- Tracheoesophageal fistula.

Late Complications (≥ 6 months postoperatively)

- Voice change
- Scar formation
- Tracheal stenosis:
  - Symptomatic if ≥ 75% lumen obstructed
  - Incidence reduced by using properly sized TT
  - High volume, low pressure cuff preferred
  - Flexible connecting tube between TT and ventilator reduces traction on TT and pressure on trachea
  - Place TT between T_2 and T_3 or T_1 and T_2 to reduce risk of cricoid cartilage injury
- Tracheocutaneous fistula:
  - Due to excessive granulation tissue and chronic infection of stoma
  - Usually stoma closes within 2–5 days of decannulation.

VENTILATION IN ARDS[1,10,12]

Definition

1994 American-European Consensus Conference (AECC) guidelines:

- Acute onset arterial hypoxemia
- PaO_2/FiO_2 < 200 mm Hg
- Bilateral infilterates on chest X-ray
- No evidence of left atrial HTN/CCF
- Pulmonary Capillary Wedge Pressure (PCWP) < 18 mm Hg.

ARDS Score[10]

No	Component	Value	Score
1	Chest X-Ray score:		
	No alveolar consolidation	–	0
	Consolidation confined to one compartment	–	1
	Consolidation confined to two quadrants	–	2
	Consolidation confined to three quadrants	–	3
	Consolidation in all four quadrants	–	4

Contd...

Contd...

No	Component	Value	Score
2	Hypoxemia score:		
	PaO_2/FiO_2	> 300	0
	PaO_2/FiO_2	225–299	1
	PaO_2/FiO_2	175–224	2
	PaO_2/FiO_2	100–174	3
	PaO_2/FiO_2	< 100	4
4	PEEP Score:		
	PEEP	< 5 cm H_2O	0
	PEEP	6–8 cm H_2O	1
	PEEP	9–11 cm H_2O	2
	PEEP	12–14 cm H_2O	3
	PEEP	> 15 cm H_2O	4

$$\text{Final Value} = \frac{\text{Aggregate sum}}{\text{Number of components used}}$$

Category	Score
No lung injury	0
Mild-moderate lung injury (ALI)	0.1 – 2.5
Severe lung injury (ARDS)	≥ 2.5

Risks of Ventilation in ARDS

- Ventilation may cause *Ventilator Induced Lung Injury (VILI)* by:
  - Atelectrauma
  - Barotrauma
  - Volutrauma
  - Biotrauma
- Oxygen toxicity if high FiO_2:
  - Retrolental fibroplasia
  - Reduced surfactant.

Goals of Ventilation

ARDS Network protocol

- Oxygenation:
  - PaO_2 55–80 mm Hg or SpO_2 88–94%
  - SpO_2 > 94% if concomitant pregnancy/stroke/intracranial HTN
- Tidal volume 4–6 ml/kg of Ideal Body Weight
- Plateau pressure ≤ 30 cm H_2O
- Respiratory rate ≤ 35 breaths/min
- pH between 7.30–7.45.

Ventilation Strategies[6,9,10]

Lung Protective Strategies

- Open collapsed lung units with recruitment maneuvres
- Keep recruited units open with appropriate PEEP

- Prevent alveolar over-distension:
  - Limit plateau pressure ≤ 30 cm H_2O
  - Limit tidal volume to 4–6 ml/kg of IBW
- Permissive hypercapnea.

Other Ventilatory Strategies

- *Prone ventilation*
- *Liquid ventilation*
- *Airway pressure release ventilation (APRV)*
- *Inverse ratio ventilation*
- Tracheal gas insufflation
- ECMO
- High frequency ventilation.

Newer Strategies

- Continuous Lateral Rotation Therapy
- *NAVA*
- *Upright ventilation*
- *Negative pressure ventilation.*

RECRUITMENT[1,10,12,14,18,19]

Introduction

Dynamic process of reopening collapsed alveoli through an intentional transient increase in transpulmonary pressure.

Mechanism

Three steps to open lung alveoli:

- Overcome critical opening pressure during inspiration
- Maintain opening pressure for sufficient time
- Use auto-PEEP/apply high PEEP at expiration to prevent collapse
- ***Hysteresis***: For a given inflation pressure, lung volume is larger during exhalation than inhalation.

Indications

- ARDS/ALI
- Atelectasis during general anesthesia
- After ETT suctioning.

Contraindications

- Raised ICP
- Hemodynamic instability
- Existing barotrauma
- Predisposition to barotrauma:
  - Apical bullous lung disease
  - Focal lung pathology (lobar pneumonias).

Factors Affecting Recruitment

- Type of lung injury, pulmonary or extra-pulmonary origin
- Differences in the severity of lung injury
- The transpulmonary pressures reached during recruitment maneuvers
- The type of recruitment maneuver applied
- The PEEP levels used to stabilize the lungs after the recruitment maneuver
- Differences in patient positioning (prone position more favorable)
- Use of different vasoactive drugs, which may affect distribution of pulmonary blood flow, thus modifying gas-exchange.

Consequences of Recruitment Maneuver

- Raised ICP
- Increased oxygenation
- *Stretch reflex* of alveoli stimulated: Increased surfactant secretion
- Increased intrapulmonary shunt
- Barotrauma
- Increased pulmonary arterial pressure
- Decreased cardiac output.

Types of Recruitment Maneuvers

- Sustained inflation maneuvers
- Pressure controlled ventilation applied with escalating PEEP and constant driving pressure
- Incremental PEEP limiting maximum inspiratory pressure
- Intermittent sighs to reach specific plateau pressure in VC or PC ventilation modes
- RAMP maneuver: Long slow increase in inspiratory pressure upto 40 cm H_2O.

Procedure

Sustained inflation maneuver

- FiO_2 increased to 1.0 for 5–10 minutes before recruitment maneuver (RM) is attempted
- Patient requires sedation to tolerate high airway pressures
- 30 cm H_2O PEEP is applied for 30–60 seconds during first recruitment maneuver
- Assess the results of first recruitment maneuver
- If inadequate response, but good patient tolerance, repeat maneuver in 15–20 minutes
- Second maneuver is done at higher PEEP (35–40 cm H_2O)
- If second RM is unsuccessful, use third RM at 40 cm H_2O

- If RM is successful, PaO_2/FiO_2 ratio becomes ≥ 300 mm Hg
- Maintain high PEEP values post RM to prevent *de-recruitment* of alveoli.

Monitoring During Recruitment Maneuver

Discontinue RM if:

- SaO_2 decreases by 5%
- Systolic BP falls by 30 mm Hg
- Heart rate decreases by 20 bpm
- Occurrence of arrhythmias.

Advantages

- Effective in reducing lung atelectasis
- Improves oxygenation and respiratory mechanics
- Prevents endotracheal suctioning-induced alveolar derecruitment.

Disadvantages

- Effects are short-lived
- Associated with circulatory impairment
- Increased risk of barotrauma/volutrauma
- Reduces net alveolar fluid clearance.

Validation

- *Alveoli Trial:* Trial concluded that:
  - Recruitment maneuvers demonstrate only modest effect on oxygenation
  - No difference in requirement for oxygenation support
- *Express and Lovs Trial:* Concluded that:
  - No mortality advantage with high PEEP compared with moderate PEEP levels
  - High PEEP is not recommended in ARDS patients
- *Cochrane review 2009:* Concluded that:
  - No significant difference in 28 day mortality
  - No statistical difference in risk of barotrauma
  - Causes increased oxygenation for brief periods which was not sustained.

POSITIVE END EXPIRATORY PRESSURE[1,6,9,10,12]

Introduction

Airway pressure strategy in ventilation which increases end-expiratory/baseline airway pressure to a value greater than atmospheric pressure.

Indications

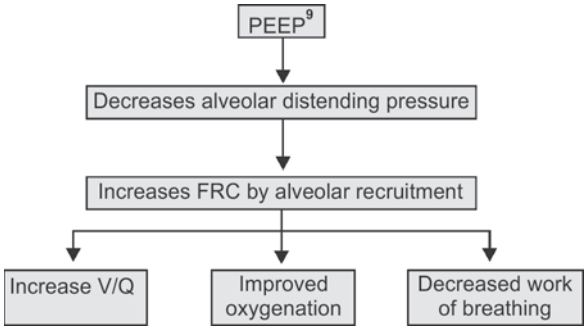
- Refractory hypoxemia, when patients PaO_2 is less than 60 mm Hg with FiO_2 of > 50%
- Intrapulmonary shunt due to:
  - Atelectasis
  - V/Q mismatch
- ARDS/ALI
- Cardiogenic pulmonary edema
- Diffuse pneumonia requiring mechanical ventilation.

Contraindications

- Raised ICP
- Pneumothorax in the absence of ICD
- Bronchopleural fistula
- Recent pulmonary resection surgery
- Hypovolemia
- Hemodynamic instability
- Right heart failure/pulmonary HTN
- Post cardiac surgeries like *Glenns/Fontans* shunt.

Physiology

- PEEP reinflates collapsed alveoli and maintains alveolar inflation during expiration
- Normally alveolar end expiratory pressure equals atmosphere pressure
- Average pleural pressure is around –5 cm H_2O
- Thus, alveolar distending pressure (i.e, alveolar – pleural pressure) is + 5 cm H_2O
- This alveolar distending pressure overcomes elastic recoil of alveolar wall
- Thus, PEEP of 5 cm H_2O is sufficient to maintain normal end expiratory alveolar volume.



Mechanisms of PEEP

Improves arterial oxygenation by:

- Redistributing lung water from alveoli to interstitial space
- Recruiting aletelectatic alveoli
- Improves V/Q mismatch
- Decreases intrapulmonary shunting
- Restores lung volumes.

Types of Positive End Expiratory Pressure

- PEEP:
  - Called PEEP when positive pressure is applied in assist or control modes of ventilation
  - Patient may increase respiratory rate in addition to present mechanical respiratory rate
- Continuous Positive Airway Pressure (CPAP):
  - Positive pressure continuously applied to spontaneously breathing patient is called CPAP
  - Used on patients who can breathe adequately
  - CPAP is a pressure applied by constant gas flow
- End-expiratory Positive Airway Pressure (EPAP): Positive pressure is applied at the end of expiratory phase alone.

Procedure

- Sedate or paralyze the patient
- Suction respiratory secretions
- Ensure tight ETT cuff seal
- Begin PEEP at 5 cm H_2O
- Increase or decrease PEEP in increments of 2 or 3 cm H_2O
- After each adjustment of PEEP, assess effects on:
  - Pulmonary function
  - Pressure-volume relationships
  - Oxygenation
  - Hemodynamics
- Goal of titration is to achieve optimal PEEP.

Optimal PEEP

Defined as level of PEEP that allows:

- The lowest FiO_2 or FiO_2 less than 50% if achievable
- While maintaining adequate oxygenation:
  - PaO_2 greater than 60 mm Hg
  - SaO_2 greater than 90%
- Achieving maximal static lung compliance
- Reducing intrapulmonary shunt fraction to less than 15%
- And avoiding adverse effects induced by PEEP.

Beneficial Effects of PEEP

- Improves oxygenation
- Recruits and stabilizes alveoli
- Improves lung compliance
- Improves FRC and prevents end expiratory collapse
- Minimizes potential for VILI.

Complications

- Decreased venous return:
  - Pleural pressure becomes more positive with application of PEEP (increases PIP and MAP)
  - This decreases pressure gradient between RA and central venous drainage
  - This decreases venous return
  - This causes decreased cardiac output and hypotension.
- Barotrauma:
  - Increased risk of barotrauma if:
    - PEEP > 10 cm H_2O
    - Mean Airway Pressure > 30 cm H_2O
    - Peak inspiratory pressure > 50 cm H_2O
  - Causes of barotrauma:
    - Pneumothorax
    - Tension pneumothorax
    - Pneumomediastinum
    - Pneumopericardium
    - Pneumoperitoneum
    - Subcutanous emphysema.
- Raised ICP:
  - More common in patients with normally compliant lungs
  - Raised intrathoracic pressure impedes venous return from superior vena cava
  - This causes venous congestion and retrograde increase in ICP
  - Rare in patients with ARDS/noncompliant lungs
  - Excessive pressure due to PEEP is not transmitted to superior vena cava in ARDS
  - Thus, there is no increase in ICP in ARDS patients.
- Renal function:
  - PEEP reduces perfusion to glomeruli
  - Glomerular filtration is less effective and reduced urine output results
- *Wasted ventilation:* Occurs as blood vessels around alveoli compressed by high alveolar pressure
- Others:
  - Decreased cardiac output.
  - Increased pulmonary vascular resistance; right ventricular failure
  - Decreased cerebral perfusion pressure
  - Septal shift to left.

Recommendations

ARDS Net protocol: Presently, there is no consensus on level of PEEP which is optimal in ARDS.

PERMISSIVE HYPERCAPNEA[9,10,12,14]

Introduction

- Intentional hypoventilation of patient by reducing tidal volume to 4–6 ml/kg, when arterial $PaCO_2$ is allowed to rise above the normal range and no attempts are made to compensate for the subsequent changes in blood pH
- This is a central component of protective lung ventilatory strategy.

Mechanism of Action

- Reduced tidal volume allowing permissive hypercapnea causes:
  - Reduced peak inspiratory pressures
  - Reduced mean airway pressure
  - Reduced likelihood of barotrauma.
- Attenuation of inflammatory response of ALI:
  - Interferes with the coordination of the immune response by reducing cytokine signalling
  - Inhibits the release of TNF-α and IL-1
  - Modulates neutrophil expression of selectins and intercellular adhesion molecules.
- Effects on free radical generation and activity:
  - Attenuates free radical production
  - Modulates free radical induced tissue damage
  - Production of superoxide by stimulated neutrophils is decreased at acidic pH
  - Reduces free radical tissue injury following pulmonary ischemia/reperfusion.

Effects of Hypercarbia

Central Nervous System

- For each 1 mm Hg increase in CO_2, CBF increases by 1.8 ml/100 g/min
- Increased CO_2 crosses BBB and causes:
  - Raised pH of CSF
  - Cerebral vasodilatation
  - This increases ICP
  - $PaCO_2$ > 90 mm Hg causes decreased seizure threshold.

Respiratory System

- Hypercarbia increases pulmonary vascular resistance
- Increases hypoxic pulmonary vasoconstriction
- Maximal stimulation of pulmonary vasculature occurs when $PaCO_2$ is around 100 mm Hg.

Cardiovascular

- Increased plasma epinephrine and norepinephrine
- Increases heart rate and BP
- Very high level cause hypotension and bradycardia.

GIT and Renals

- Increases hepatic and portal venous blood flow
- Retention of HCO_3^- in renal tubules
- Metabolic alkalosis (compensatory).

Metabolic: Potassium leakage from cells into plasma.

Indications

- Acute Respiratory Distress Syndrome (ARDS)
- Acute Lung Injury (ALI)
- Status asthmaticus
- COPD.

Contraindications

- Cerebral hemorrhage, raised ICP
- Known seizure disorder
- Hemodynamically unstable patients
- Hypovolemia
- Pulmonary HTN and right heart failure
- Arrhythmias
- Active coronary artery disease.

Advantages

- Reduced peak airway pressures
- Minimizes occurrence of VILI/VALI
- May exert direct protective effects in ALI states by attenuating inflammatory process
- Achieves faster weaning and improves survival rates

Lower PEEP/Higher FiO_2 Strategy[9]

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18–24

Higher PEEP/Lower FiO_2[9]

FiO_2	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5	0.5–0.8	0.8	0.9	1	1
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22	24

- Decreases incidence of chronic lung diseases
- Improved long term neurological outcome.

Disadvantages

- Potential for hypercarbia and carbon dioxide retention
- May cause hyperventilation
- Respiratory acidosis, CNS dysfunction
- Intracranial HTN, neuromuscular weakness
- Cardiovascular impairment and increased pulmonary vascular resistance.

Recommendations

- For $PaCO_2$ and pH:
  - Hypoxemia may occur concomittantly: Use higher FiO_2
  - Maintain pH between 7.15–7.20
  - Hypercarbia upto 60 mm Hg and pH upto 7.15 well tolerated if adequately sedated
  - Actual $PaCO_2$ is of less importance
  - In case of extreme respiratory acidosis:
    - Use buffering agents if:
      - pH < 7.15 in respiratory acidosis
      - pH < 7.28 if patient is at risk of simultaneous metabolic acidosis
    - Use sodium bicarbonate/0.3 M THAM
    - Dosage of THAM: Body weight (in kgs) × Base deficit (mEq/L)
    - In the absence of a correction of the primary problem, buffering a hypercapnic acidosis with bicarbonate is not likely to be of benefit
    - Limit carbon dioxide production:
      - Antipyretics
      - External cooling
- For airway pressure:
  - Tidal volume in a range of 4–6 ml/kg
  - Plateau airway pressure (PAP) more than 30 cm H_2O avoided
  - If PAP less than 30 cm H_2O inspite of tidal volume of 10–12 ml/kg, permissive hypercarbia not likely to be needed
  - Atelectasis: PEEP maybe used if airway pressure is acceptable
  - Higher PAP accepted if decreased chest wall compliance as in:
    - Tense ascites
    - Morbid obesity
    - Chest wall trauma.

Conclusion

- Adverse effects of alveolar over-distension and end expiratory collapse are more detrimental to patient outcome than adverse effects of intentional respiratory acidosis
- Currently hypercarbia cannot be a therapeutic target
- Efforts must be made to minimize hypercarbia with context of low V_T-P_{plat} ventilation
- The potential risks of hypercapnia must be weighed against the risks of ARDS, and therapy individualized.

LIQUID VENTILATION[1,3,6,9,10,12]

Introduction

Alternative mode of ventilation in ARDS.

Rationale for Use

- ARDS is associated with loss of surfactant
- This causes increased surface tension
- Increased surface tension leads to alveolar collapse
- Filling lung with liquid removes air-liquid interface
- This supports alveoli and decreases chances of collapse
- Thus liquid ventilation improves compliance of lungs.

Indications

- ARDS/ALI
- Experimental uses:
  - Meconium aspiration syndrome
  - Inhalation syndromes
  - Cystic fibrosis
  - Pulmonary alveolar proteinosis
  - To study topical administration of drugs like antibiotics.

Mechanism of Action

- Decreases surface tension
- Alveolar recruitment and selective distribution to dependant regions
- Increases surfactant synthesis and secretion
- Improves arterial oxygenation as liquid used has PFC
- Anti-inflammatory property:
  - Indirect: By mitigation of VILI
  - Direct: Decreases release of TNF-α , IL-1, IL-8
- Increases lung compliance.

Ideal Properties of Liquid

Liquid used should have:

- High solubility for oxygen and carbon dioxide to maintain gas exchange
- Greater density compared to body fluids so it can descend to dependant lung regions
- Low surface tension to improve lung compliance
- To be volatile to allow elimination in acceptable time.

Choice of Agent

- Perflubron/perfluorooctylbromide/*liquivent most commonly* used
- Perfluorocarbons used as they:
  - Eliminate air-liquid interface
  - Lower surface tension
  - Dissolve oxygen and carbondioxide
  - Fill collapsed alveoli to prevent closure
  - Accumulate in dependant areas of lung as it is heavier than water
  - Thus, action concentrated to lung regions at most risk for VILI
  - Non toxic and minimally absorbed
  - Easily eliminated by evaporation from lungs
  - Chemically inert.

Types of Liquid Ventilation

- Total liquid ventilation:
  - Entire lung filled with liquid
  - Uses PFCs instead of gas to obtain gas exchange
  - Uses special ventilator with pump, membrane oxygenator, etc to oxygenate the PFC
  - Usually applied after a short period of partial liquid ventilation
  - Difficult and expensive.
- Partial liquid ventilation:
  - Lung filled to FRC with liquid
  - Tidal volumes are delivered with a conventional volume regulated ventilator.

Character[1,10]	TLV	PLV
Ventilator	Liquid ventilator	Conventional ventilator
Tidal volume delivered	Oxygenated PFC	Gas
Lungs are filled	Completely by PFC	Filled till FRC by PFC
Feasibility	Experimental	Yes
Disadvantages	–	Loss gas by evaporated
		Costly

Procedure[1,10]

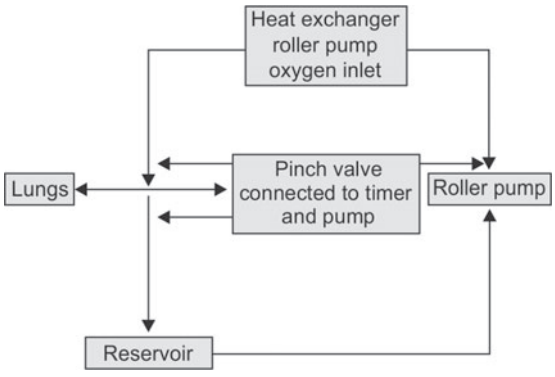
Total Liquid Ventilation

- Liquid ventilation is initiated after sedation and skeletal muscle paralysis
- Conventional mechanical ventilation is stopped
- The lungs are gradually filled with warmed oxygenated PFC
- A volume of 30 ml/kg of PFC is introduced initially
- Further quantities are administered until the lung has been completely filled
- As soon as the air has been completely expelled, the patient is connected to the special ventilator
- Tidal volume is subsequently set at 15–20 ml/kg of PFC
- Respiratory rate is regulated to 4–5 breaths per minute
- The maximum inspiratory pressure is 30 cm H_2O
- Pressure of between 15 and 20 cm H_2O is usually sufficient
- The negative pressure required during the expiratory phase ranges from –15 to –30 cm H_2O
- At the end of the treatment conventional artificial ventilation is started
- Ventilation can be continued until the PFC has evaporated from the lungs.

Partial Liquid Ventilation

- A volume of 10 ml/kg of PFC is introduced via ETT over 15 minutes
- This dose is repeated till:
  - A sustained meniscus is seen in the ETT at the sternal level
  - Or till the infused volume reaches 30 ml/kg
- This replaces the functional residual capacity
- A further 10 ml/kg of PFC is added every hour to replace redistribution or evaporative losses
- The PFC is redosed daily for 5–7 days
- Conventional ventilation with standard setting was continued throughout.

Liquid Ventilator



Adjuncts to Liquid Ventilation

Additive effect of PLV occurs in combination with:
- Nitric oxide
- Exogenous surfactant
- Conventional PEEP
- High Frequency Oscillatory Ventilation (HFOV)
- Prone ventilation.

Advantages of Liquid Ventilation

- As PFCs are heavier than body fluids, PLV mobilizes purulent secretions from lungs
- Improves pulmonary hygiene as PFCs allow gas exchange
- Allow oxygenation during therapeutic lavage
- Useful in diseases with secretions
- Improves lung compliance
- Reduces intrapulmonary right-left shunt
- Accumulates in dependent areas, where ARDS is more severe.

Disadvantages

- Can causes mucus plugging of airway and ETT
- Increased chances of pneumothorax
- Hypoxia and hypotension
- Lactic acidosis
- Hypercarbia due to high viscosity of PFCs
- Interference with radiography due to radio-opaque nature of some PFCs.

Current Status

- Conventional ventilation showed decreased 28 days mortaility and more ventilator free days when compared with PLV/TLV
- Two published trials have confirmed safety but not efficacy
- Several problems remain to be solved:
  - Safety of liquid ventilation over prolonged periods of time
  - Return to conventional gas ventilation from liquid ventilation
  - Hemodynamic effects in the presence of pulmonary hypertension
  - Significant degree of lactic acidosis and the increase in hypoxemia in inhomogeneous lung pathology
  - The metabolism of PFC with regard to damage from long term persistence.
- Thus, PLV is not routinely recommended in ARDS patients.

INVERSE RATIO VENTILATION[1,9,10]

Introduction

IRV is a mechanical ventilation with inspiratory-expiratory time ratio more than 1 (I:E = 2:1 or 4:1).

Mechanism of Action

Improves oxygenation by:
- Decreasing intrapulmonary shunt
- Improvement of V/Q matching
- Decreasing dead space ventilation
- Increasing mean airway pressure
- Presence of auto PEEP.

Physiological Changes

Increased	Decreased	No Change
Mean airway pressure	PEEP requirement	FiO_2
Central venous pressure	Peak airway pressure	Intrinsic PEEP
Pulmonary arterial pressure	Cardiac output	Blood pressure
PaO_2		$PaCO_2$

Physiological Basis

- Mean airway pressure:
  - Requires lower peak airway pressure and PEEP but higher mean airway pressure
  - Higher MAP recruits alveoli without generating high PAP
  - This reduces shunting and improves oxygenation.
- Auto-PEEP:
  - Breath stacking occurs due to longer I time and shorter E time
  - Increased end expiratory pressure occurs as time is not enough for complete expiration
  - Presence of auto-PEEP reduces shunting and improves oxygenation.

Types

Can be applied to volume controlled/pressure controlled ventilation:
- Volume controlled-IRV:
  - Inspiratory time extended with slow inspiratory flow
  - End expiratory pause/decelerating inspiratory flow also other features
  - Any ventilator can be adjusted to deliver VC-IRV

  - Allows control of minute volume and inspiratory flow
  - Requires careful monitoring of airway and alveolar pressure.
- Pressure controlled-IRV:
  - More commonly used
  - Constant pressure applied for duration of inspiration
  - Causes decelerating gas flow into lungs
  - Permits exact adjustment of airway pressure
  - May cause variation in tidal and minute volume
  - Requires special ventilators.

Adverse Effects

- Increased of chances of barotrauma due to:
  - Increased mean airway pressure
  - Presence of auto-PEEP
  - Increased mean alveolar pressure and volume
- Increased rate of transvascular fluid flow/flooding due to increased alveolar pressure
- May worsen preexisting pulmonary disease
- Requires sedation and NMBA as patients are often agitated.

PRONE VENTILATION[1,9,10,12]

Introduction

Mechanism of Action

- Causes alveolar recruitment
- Redistribution of ventilation occurs towards dorsal areas, which remain well perfused
- Homogenization of tidal volume distribution occurs due to better fitting of lungs with chest wall
- Gradient of transpulmonary and pleural pressure are reduced
- Dorsal chest wall becomes more compliant
- Causes position dependent alteration is pulmonary ventilation
- Position dependent alteration in pulmonary perfusion due to which blood flow distributes preferentially to dorsal lung independent of position
- Reversal of dependent collapse.

Other Effects

- Increases FRC
- Improved ventilation of previously dependent regions due to:
  - Difference in diaphragmatic movement
  - Decreased chest wall compliance in prone position
  - Redistribution of tidal volume and atelectatic dorsal region
  - Weight of heart may affect ventilation.
- Improved cardiac output
- Better drainage of secretions
- Improved lymphatic drainage.

Patient Selection Criteria

Most severely ill patients with:

- $PaO_2/FiO_2 < 88$
- SAPS II score > 49
- High tidal volume > 12 ml/kg.

Timing

- In patients with ARDS lasting > 24 hrs or on second day
- Frequency of once a day
- Duration of 2–20 hrs/day.

Positioning Aids

- Circular electric bed
- Manual two step, light weight, portable support frame
- Vollmans prone positioner.

Contraindications

- Refractory raised ICP
- Unstable bony fractures, pelvic fractures, unstable spine
- Left ventricular failure
- Hemodynamic instability
- Active intra-abdominal pathology.

Complications

- Accidental extubation
- Removal of invasive catheters
- Facial injury
- Retinal ischemia
- Myositis ossificans of shoulder
- Peripheral nerve injury
- Nipple ischemia.

Current Status

- No randomized controlled trials to study benefits of proning
- Proning is safe feasible and dramatically relives hypoxia
- No impact on mortality.

TRACHEAL GAS INSUFFLATION[10,12,18,19]

Introduction

TGI is an adjunct to mechanical ventilation where trachea is filled with a stream of fresh gas at the end of exhalation.

Rationale

- Without TGI, trachea is filled with alveolar gas at end of exhalation
- This CO_2 rich air is forced back into alveoli at next inspiration
- With TGI a stream of fresh gas at 4–8 L/min is insufflated through a small catheter or channel into walls of ETT in lower trachea
- This flushes carbon dioxide from upper airways, prior to next inspiration
- Provides gas flow near carina thus washing carbon dioxide out of large airways.

Mechanism of Action

- Reduces dead space
- Useful to decrease carbon dioxide and acidosis due to small tidal volume ventilation
- Enhanced gas mixing distal to TGI catheter tip due to turbulence at high gas flows through TGI catheter.

Procedure

- TGI catheter passed to position through the ETT lumen using sidearm adaptor
- Fresh gas flow 4–8 L/minute used
- TGI may be selectively timed during expiration: Also called Expiratory Wash Out or EWO
- EWO can be used to offset increases in Tv and airway pressure, seen with continuous TGI.

Side Effects

- Dessication of secretions
- Airway mucosal injury
- TGI catheter may be nidus for accumulation of secretions
- May causes auto-PEEP and increase airway pressure from expiratory flow
- May cause increased tidal volume delivery.

Current Status

Ravenscraft found $PaCO_2$ decreased from 53 to 45 mm Hg when catheter was at 1 cm from carina and FGF at 6 L/min.

AIRWAY PRESSURE RELEASE VENTILATION[9,10,12,14,18,19]

Introduction

Bilevel form of ventilation with sudden and short releases in pressure to rapidly reduce FRC and permit ventilation.

Indications

- ALI/ARDS
- Refractory hypoxemia
- Massive atelectasis.

Components

- Contains CPAP circuit
- Release valve is expiratory limb of CPAP circuit to accomplish rapid release of CPAP.

Principle

- A ventilatory mode which sets a level of CPAP which intermittently time cycles to a lower airway pressure to maintain alveolar recruitment throughout respiratory cycle
- Provides two levels of CPAP
- Allows spontaneous breathing at both levels when spontaneous effort is present
- Can work in apneic/spontaneously breathing patients
- Contains CPAP circuit which maintains baseline airway pressure above ambient
- Augmentation of alveolar ventilation determined by APRV rate and tidal volume
- If APRV release frequency and tidal volume are sufficient to reduce $PaCO_2$ below apneic threshold, controlled ventilation results
- Weaning from APRV done by lowering release frequency until patient is breathing with CPAP without any APRV.

Mechanism

- Provides two levels of airway pressure P_{high} and P_{low}, during two set time periods T_{high} and T_{low}
- APRV strategy is for long T_{high} and short T_{low}
- Accomplished by setting P_{high} well above closing pressure of recruitable alveoli
- The set T_{high} generally maintains this pressure and alveolar recruitment for several seconds
- Set T_{low} is of duration adequate to assist in carbon dioxide removal.

Advantages

- Augmented alveolar ventilation with low peak airway pressure
- Prevents over-distension of lung parenchyma
- Improves patient ventilator synchrony
- Improves mean airway pressure
- Reduces physiological dead space
- May be used with mask in patients already receiving NI-CPAP

- Reduces peak airway pressure, mean airway pressure and mean intrathoracic pressure
- Decreases incidence of VILI
- Allows IRV with or without spontaneous breathing.

Disadvantages

- Variable tidal volume delivered
- Could be harmful in COPD/asthma patients
- Auto-PEEP usually present
- Asynchrony if spontaneous breaths are out of sync with release time
- Requires presence of active exhalation valve
- Caution in hemodynamically unstable patients.

HIGH FREQUENCY VENTILATION[1,9,10,12,14,18,19]

Introduction

Ventilation with supra-physiological respiratory rates and tidal volumes equal to or less than dead space (usually 60–3000 breaths/minute).

Methods

- Small tidal volume, rapid respiratory rate with conventional mechanical ventilator
- High frequency percussive ventilation
- Various forms of external chest oscillation
- High frequency positive pressure ventilation (HFPPV)
- High frequency jet ventilation (HFJV)
- High frequency oscillatory ventilation (HFOV).

Mode[10]	Rate	Tidal volume	Exhalation	Gas
HFPPV	60–100 cycles/min	3–5 ml/kg	Passive	None
HFJV	100–150 cycles/min	2–5 ml/kg	Passive	Yes
HFOV	Upto 2400 cycles/min	< 3 ml/kg	Active	Yes

Advantages

- Reduced peak airway pressure: Decreases barotrauma
- Reduced tidal volume: Less volutrauma
- Alveolar recruitment maintained:
  - Increases oxygenation
  - Decreases oxygen toxicity
- More efficient carbon dioxide removal
- Avoids cyclical expansion and collapse of alveoli: Decreases lung damage
- Decreased need for surfactant therapy
- Prevents bronchopulmonary dysplasias
- Decreased need for ECMO.

Theories of Gas Transport in HFOV[10]

Direct Alveolar Ventilation Theory

Some proximal alveoli receive bulk gas flow.

Interregional Gas Mixing Theory

- Called Pendelluft
- Alveoli with short time constants fill early in inspiration
- These may empty into alveoli with longer time constants which are still filling.

Corrective Streaming Theory

- Air in the center of airway moves faster than air in contact with airway walls during inspiration
- In expiration all gases move slowly
- Thus gas flows rapidly into central alveoli while it flows away from alveoli, along the walls.

Augmented Dispersion Theory: Taylor

- Gas flowing through has a parabolic front
- This increases dispersion of gas across the front of moving column (Axial diffusion)
- This also causes molecular dispersion of gas along concentration gradients occurring laterally (Radial diffusion).

Cardiogenic Mixing Theory

Due to heartbeat induced oscillations in airway.

Molecular Diffusion Theory

Due to simple diffusion across alveolar capillary membrane along a concentration gradient.

Indications[9,10]

- Pulmonary:
  - Neonatal RDS/Hyaline membrane disease
  - Adult respiratory distress syndrome (ARDS)
  - Air-leak syndromes:
    - Pneumothorax
    - Bronchopleural fistula
  - *Oxygenation index* more than 13.
- Persistant pulmonary HTN:
  - Meconium aspiration
  - Neonatal asphyxia
  - Congenital diaphragmatic hernia
  - Congenital heart defects with pulmonary HTN.
- Ventilation during procedures: HFJV and HFPPV:
  - Direct laryngoscopy, bronchoscopy
  - Endoscopic laser surgery

  - Upper airway and tracheal surgeries
  - One lung ventilation.
- Difficult airway algorithm: Percutaneous tracheal HFJV
- Others:
  - Ventilation in hemodynamically unstable patients
  - During weaning.

Determinants of Gas Exchange

- FiO_2
- Mean airway pressure (P_{aw}):
  - Increased P_{aw} will improve oxygenation
  - P_{aw} used in HFOV is higher than that used in conventional ventilation
  - P_{aw} upto 35–40 cm H_2O is used in HFOV.
- Amplitude (Power/ΔP):
  - Determines displacement of piston
  - Increasing amplitude/power of pressure wave increases tidal volume
  - This causes increased CO_2 elimination
  - Power adjusted till chest movement is optimal *(Chest wiggle).*
- Rate/frequency:
  - Increasing frequency shortens inspiratory and expiratory times
  - Thus, tidal volume decreases
  - Thus, in HFOV, increasing frequency reduces MV and increases carbon dioxide levels
  - Frequency adjusted between 3–15 Hz (180–900 breaths/min)
  - Also increased frequency increases barotrauma.
- Bias flow:
  - Maintains P_{aw} and washes carbon dioxide out
  - Bias flow can be increased to 40–60 L/min
- I and E TIME: Inspiratory time usually fixed at 33%.

Complications

- Cardiovascular depression
- Decreased venous return and cardiac output in initial stages
- Barotrauma and air-leak syndromes due to dynamic hyperinflation
- Necrotizing tracheobronchitis
- Inspissated airway secretions
- Slow movement of airway columns: May take upto 45 minutes for ABG changes to occur.

Contraindications

- No absolute contraindications
- Obstructive airway disease:
  - As HFV devices have very short expiratory time
  - Asthma and bronchiolitis
  - Combination of active recruitment, high pressure and short expiratory time can cause barotrauma
- Hemodynamically unstable patients
- Severe acidosis
- Pregnancy.

HIGH FREQUENCY POSITIVE PRESSURE VENTILATION[10,12,14]

Introduction

- Use of conventional ventilator to deliver tidal volumes of 3–4 ml/kg at frequency of 1–2 Hz through a flow interrupter.
- Also called ***High Frequency Flow Interrupter***

Example: *Infrasonics Infant Star Ventilator.*

Working Principle

- Essentially IPPV with increased respiratory rate and reduced tidal volume
- Breaths may be PC/VC with gas flow directed through insufflation catheter placed in airway or through side arm of pneumatic valve attached to an ETT or bronchoscope
- Requires ventilator with:
  - Low internal and circuit compliance
  - Negligible compressible volume
- Tidal volume 3–4 ml/kg
- Respiratory rate 60–100 breaths/min
- Inspiration: Expiration < 0.3
- Frequency of 1–2 Hz.

Current Status

- Not gained widespread use
- Studies showed no difference in mortality.

HIGH FREQUENCY JET VENTILATION[10,12]

Introduction

Intermittent high pressure jet of gas delivered at high frequency (100–200 Hz) through small bore cannula built along sides of modified ETT.

Example: *Bunnel Life Pulse Jet Ventilator.*

Working Principle

- Frequency of 4–11 Hz
- Total volume 3–4.5 ml/kg

- Respiratory rate 100–150 breaths/min
- 1:E= 0.1 to 0.5
- Expiration is passive
- Driving pressure = 10–40 PSI.

Mechanism

- High pressure jet entrains stream from conventional ventilator
- Thus, due to Venturi effect, actual tidal volume delivered is higher than volume of gas delivered from jet catheter, as entrainment of additional ambient gas occurs
- Has synergistic effect when used with recruitment maneuvers.

Procedure

- Small 14–16 G cannula placed within specially designed ETT
- Less commonly, catheter is placed directly into trachea
- Ancillary circuit providing continuous humified gas flow is directed via side port into ETT
- Humidification by coaxial flow of saline in front of jet cannula
- Saline is nebulized by jet flow and humidifies air
- Tidal volume is adjusted by altering inspiratory time/driving pressure.

High Frequency Flow Interruption

- Variation of HFJV
- High pressure source of gas is interrupted by valve
- Pulsatile flow is delivered to patients airway
- Emerson rotating ball used to interrupt flow.

Current Status

- Safe, but not superior to CMV in neonatal RDS
- Requires reintubation with special ETT in unstable patients
- Role is yet to be defined and thus, it has not found widespread use.

HIGH FREQUENCY OSCILLATORY VENTILATION[10,12]

Introduction

Uses continuous flow of gas and piston/loud speaker diaphragm to generate high frequency sinusoidal waves in this column of gas.

Example

- *Sensormedics 3100 A* (for patients weighing less than 45 kgs)
- *Sensormedics 3100 B* (for patients weighing more than 90 kgs).

Working Principle

- Tidal volume 1–3 ml/kg
- Frequency between 3–15 Hz
- Respiratory rate up to 2400 breaths/min
- Expiration is *active*.

Physics

- Back and forth motion of piston creates active expiratory phase which is unique to HFOV
- Mean airway pressure is constant
- Peak pressure gradually falls from proximal to distal airway
- Small tidal volume provides for relatively higher mean airway pressure
- This higher MAP may recruit lung more effectively than PEEP.

Mechanism

- A bias flow of fresh, heated, humidified gas is provided at proximal ETT
- Bias flow is typically 20-40 L/min
- P_{aw} at proximal ETT is set at high level (25–35 cm H_2O)
- Oscillating piston vibrates the flowing gas
- P_{aw} modified by adjusting bias flow rate/back pressure.

Inspiration

- Is an *active* process
- HFOV device placed in line with ETT
- Gas source placed perpendicular to ETT
- Fresh Gas Flow (FGF) is driven into ETT by waves from oscillator.

Expiration

- Is also an *active* process
- Expiratory limb placed perpendicular to ETT but opposite to FGF
- Expiratory limb has high impendence to oscillations but low impendence to steady gas flow
- Rigid interconnecting tubes used to ensure proper transmission of oscillatory waves.

Care of Patient

- Change in posture Q6H
- Encourage oral feeds

- DVT prophylaxis
- Consider weaning to conventional ventilation within 24 hrs.

Weaning Criteria

- Mean airway pressure < 25 cm H_2O in adults
- Mean airway pressure < 20 cm H_2O in children
- Frequency < 5 Hz.

Current Status

- Proven by randomized controlled trial to be safe and effective in children with severe lung disease
- Not yet shown to improve outcome.

VENTILATOR INDUCED LUNG INJURY[6,9,10,12]

Introduction

- Acute Lung injury produced by positive pressure mechanical ventilation
- Also called *Ventilator Associated Lung Injury/VALI.*

Incidence

- More in earlier days with conventional tidal volumes of 12–15 ml/kg
- Presently lesser incidence
- Mortality rate of 31–40%.

Mechanisms

Overdistention

- Small area of normal aeration receives bulk of volume
- Varies in different regions of lung
- This causes volutrauma.

Shear Injury

- Shearing forces develop in alveoli adjacent to collapsed areas
- Occurs as collapsed alveoli do not move during mechanical ventilation
- Transpulmonary pressure at junction of atelectatic and normal alveoli is higher than overall transpulmonary pressure
- This causes *barotrauma*.

Cyclical Collapse

- *Repeated Airwary Collapse and Expansion: RACE*
- Alveoli in dorsal dependent portion of lungs collapse and expand with every respiratory cycle in ARDS
- In diseased lung, alveoli collapse at the end of inspiration due to deactivation of surfactant
- These alveoli can be stabilized with PEEP
- This causes *atelectrauma.*

Systemic Inflammation

- Systemic effects occurring due to release of inflammatory mediators
- Cytokine response produced due to over distention of lungs
- Increased IL-1, IL-6, IL-8 and TNF-α levels in bronchoalveolar lavage fluid
- Thus causes *biotrauma.*

Pathophysiology

- Altered gene expression and cellular metabolism
- Upregulated inflammatory response
- Translocation of bacteria from lungs to systemic circulation
- *Mechanotransduction:* Transduction of mechanical stimuli (like cell deformation) into biochemical alteration
- Alterations in surfactant.

Types of Vili

Barotrauma

- Occurs due to high airway pressure
- May present as:
  - Pneumothorax
  - Pneumoperitoneum
  - Pneumomediastinum
  - Air embolism
  - Intestitial emphysema.

Volutrauma: Due to overdistention

Atelectrauma: Due to shear forces and RACE

Biotrauma: Due to systemic cytokine response

Strategies to Prevent Vili

Lung Protective Strategies

ARDS Net trial:

- Tidal volume 4–6 ml/kg IBW
- Plateau pressure ≤ 30 cm H_2O
- Mean airway pressure ≤ 50 cm H_2O
- Goal of oxygenation 88–92%
- Permissive hypercapnea with pH ≥ 7.2.

PEEP: No consensus on adequate PEEP level

Lower PEEP/Higher FiO_2 Strategy

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1
PEEP	5	5	8	8	10	10	10	10	12	14	14	16	18	18–24

Higher PEEP/Higher FiO_2 Strategy

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5–0.8	0.8	0.9	1	1
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22	24

Use of Pulmonary Mechanics

- Use tidal volume such that pressure does not exceed upper limit
- Over distention identified as breaking on pulmonary P-V loop
- Stress index used to identify tidal hyperinflation
- With stress index 1 and no hyperinflation, line is straight
- Upward concavity suggests hyperinflation

Prone Ventilation

- Causes recruitment and redistribution of ventilation
- Done early in course of ARDS
- Done for 2–20 hrs/day.

Continuous Lateral Rotation Therapy (CLRT)

- Causes redistribution of weight of edematous lung
- Also helps to remove secretions and permits recruitment
- Used when proning is unsafe.

Upright Mechanical Ventilation

- Decreases intrapulmonary shunting
- Permits better alveolar recruitment
- Increases FRC
- Improves gastric emptying
- Causes faster recovery of diaphragmatic function
- Effects not proven in any trials.

Negative Pressure Ventilation

- Reduces pulmonary dead space
- Better V/Q matching.

Airway Pressure Release Ventilation (APRV)

- Best if spontaneous ventilation is present
- Better recruitment of alveoli.

High Frequency Oscillation

- Low tidal volume: 1–2 ml/kg
- Frequency of 2400 breaths/min.

Neutrally Adjusted Ventilatory Assist (NAVA)

- Uses diaphragmatic electric activity to trigger inspiration
- Less trigger delay and better patient-ventilator synchrony
- Reduced work of breathing
- Ventilatory assistance increases with diaphragmatic contraction.

VENTILATOR ASSOCIATED PNEUMONIA[9,10,12]

Introduction

Pneumonia arising more than 48 hours after endotracheal intubation with no clinical evidence suggesting presence of pneumonia at the time of initial intubation.

Types

- Early onset VAP: Pneumonia occurring within 4 days of intubation
- Late onset VAP: Pneumonia occurring after 5 days of intubation.

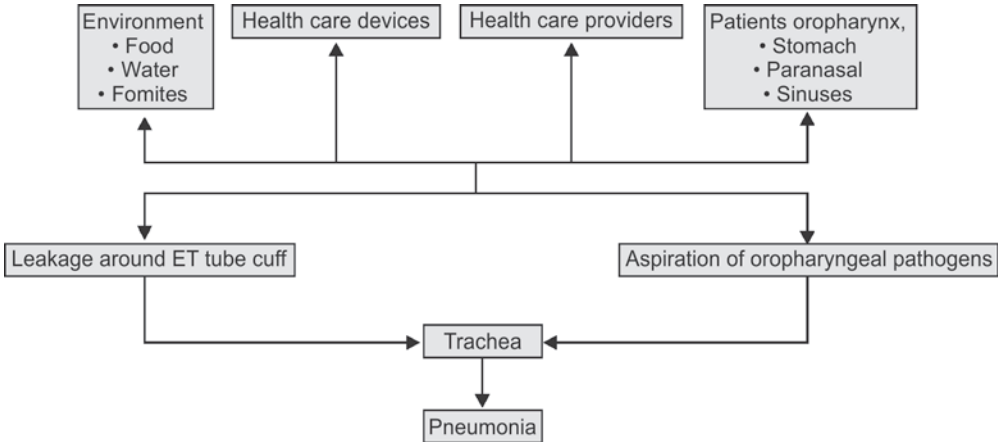
Incidence

- Likelihood of developing VAP increases with the duration of mechanical ventilation
- Incidence of > 15% at 1 week of ICU stay and > 20% at 2 weeks.

Etiology

- Gram-negative bacteria:
  - Klebsiella, E.coli
  - Pseudomonas, acinetobacter
- Gram-positive bacteria:
  - Staphylococcus aureus
  - Hemophilus influenza
  - Pneumococcus
- Anerobic: Rare, usually occurs following aspiration in nonintubated patients
- Fungal:
  - Candida
  - Aspergillus fumigates
- Viral: Influenza A
- Usually, early onset VAP is caused by:
  - Hemophilus influenza
  - Staphylococcus aureus
  - Pneumococcus
- Late onset pneumonia caused by:
  - Methicillin resistant staphylococcus aureus
  - Pseudomonas
  - Acinetobacter.

Pathogenesis[12]



Risk Factors

- Nonmodifiable risk factors:
  - Advanced age
  - Male sex
- Modifiable risk factors:
  - Burns, trauma
  - Coma, COPD
  - Thoracic or abdominal surgery
  - Longer duration of surgery
  - Immunosupression.

Prevention[10,12,14]

- Mechanical ventilation:
  - Risk of VAP increases 6–21 fold when ventilated for more than 3 days
  - Care of endotracheal tube:
    - Use cuffed endotracheal tube
    - Use of oropharyngeal ETT and orogastric tube reduces incidence
    - Use of nasopharyngeal and nasogastric tubes increases incidence
    - Incidence reduced by maintaining cuff pressure above 20 cm H_2O.
  - *Continuous subglottic suction:*
    - Also called CASS: Continuous aspiration of subglottic secretions
    - This reduces incidence of VAP
  - Factors which do not influence incidence of VAP:
    - Frequent change in ventilator circuit
    - Use of passive humidifiers
    - Use of heat and moisture exchangers.
- Drugs:
  - Sedatives and paralytic agents: Incidence of VAP decreased by limiting their use
  - *Selective decontamination of digestive track (SDD):*
    - Involves application of a poorly absorbable mixture of:
      - Polymyxin
      - Amphotericin B
      - Aminoglycoside
    - Avoid use of systematic antibiotics for SDD
  - *Selective decontamination of oral cavity (SDO):*
    - Chlorhexidine mouth wash used to decontaminate oral cavity
    - Advantages: Prevents antibiotic resistance
  - Alternatives: Use mixture of:
    - 2% gentamicin
    - 2% colistin
    - 2% vancomycin
    - Applied as paste Q6H to oral cavity.
  - Antacids:
    - Avoid using PPI and H_2 blockers
    - Reducing gastric acidity enhances colonization of stomach
    - When required, sucralfate is a better option.
- Blood products:
  - Avoid unnecessary use of blood
  - Transfusion trigger of 7 g% rather than 9 g% reduces risk of VAP
- Others:
  - Position head of bed 30° above horizontal
  - Oscillating beds reduce risk of VAP
  - Staff education
  - Strict adherence to alcohol based disinfection techniques
  - Feeding:
    - Late administration of enteral foods (beyond 5 days of intubation)
    - Practice post-pyloric feeding

- Immunonutrition (parenteral/enteral): Comprises of:
  - Selenium
  - Vitamin C, Vitamin E
  - Arginine, glutamine
  - Omega-3 fatty acids

– Prophylactic immunization in patients with neutropenia for:
  - Influenza
  - Pneumococcus

– *FAST-HUG approach:*
  - F- Feeding
  - A-Analgesia
  - S-Sedation
  - T-Thrombopropylaxis
  - H-Head end elevation 30–40°
  - U-Ulcer prophylaxis
  - G-Glycemic control.

Diagnosis

- Suspected if patient has X-ray infilterates (new/progressive) with fever, purulent sputum, leucocytosis or reduction in systemic oxygenation
- Invasive strategies:
  – Include collecting of bronchial specimens and quantifying the bacterial load
  – Examples:
    - Endotracheal aspirate: Threshold of > 10^6 CFU/mL
    - BAL sample ≥ 10^4 CFU/mL (CFU: Colony forming unit)
    - Protected specimen brush (PSB) ≥ 10^3 CFU/ml
- Levels of soluble triggering receptor (STREM-I):
  – Expressed on myeloid cells
  – It is strongest predictor of pneumonia.

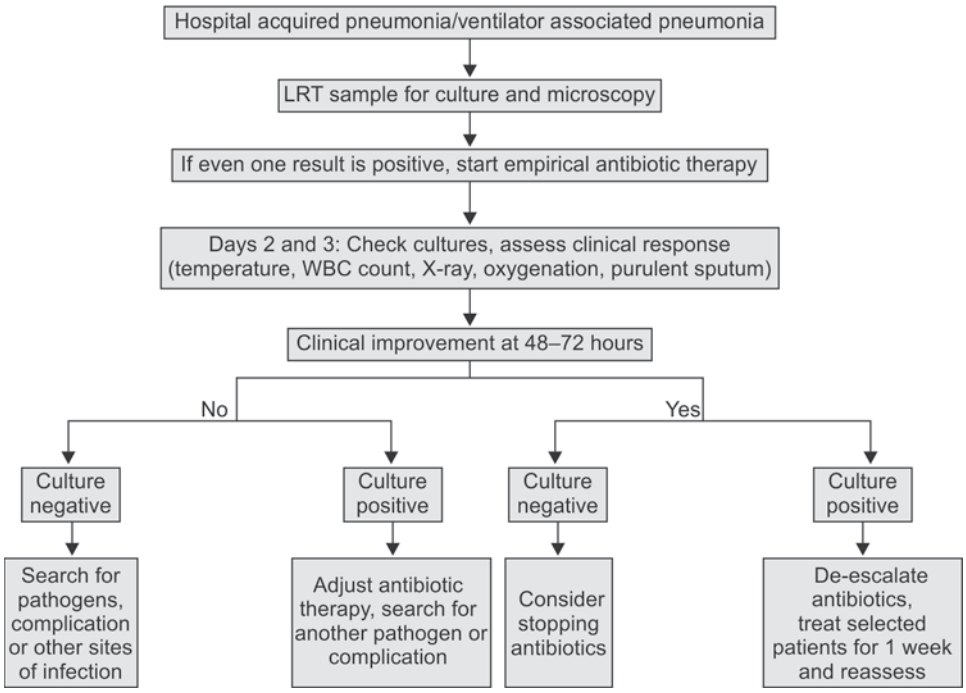
Clinical Pulmonary Infection Score (CPIS)

	0	1	2
Fever[10,12]	> 36.5, < 38.4	38.4 – 38.9	> 38.9
Tracheal secretion	Rare	Abundant	Purulent
Leucocytosis	4000 –11000	< 4000 or > 11000	< 4000
			> 11000 with > 500 band forms
PaO_2/FiO_2	> 240, ARDS	< 240, no ARDS	
X-ray infilterates	Absent	Patchy/diffuse	Localized
Microbiology	Negative		Positive
CPIS Score more than 6 diagnostic of Ventilator Associated Pneumonia			

Management[9,10,12]

- Criteria for admission to ICU: 1 major OR 3 minor criteria required of:
  – Minor criteria:
    - Respiratory rate more than 30 cycles/min
    - Leucopenia (total count less than 4000 cells/mm^3)
    - Thrombocytopenia (less than 100000 cells/dL)
    - Confusion/disorientation
    - Hypotension requiring rapid fluid administration
    - Uremia (BUN > 20 mg/dL)
    - X-ray infilterates
    - Hypothermia (< 36 °C)
    - $PaO_2/FiO_2 < 250$.
  – Minor criteria:
    - Invasive mechanical ventilation
    - Septic shock with need for vasopressors.
- Antibiotic therapy:
  – Empirical therapy:
    - β-lactam with either azithromycin or respiratory fluoroquinolone
    - If pseudomonas, antipseudomonal β-lactam + azithromycin + aminoglycoside
    - If MRSA, add vancomycin/linezolid
  – Monotherapy vs combination therapy:
    - Higher rates of therapy failure and nephrotoxicity with combination therapy
    - It also fails to prevent resistance
    - Combination therapy used only if MDR or pseudomonas is suspected.
  – Continuous vs intermittent infusion: Continuous infusion maintains drug concentration above the MIC for longer duration
  – Aerosolized antibiotics:
    - Polymyxin or aminoglycosides for MDR gram-negative bacteria
    - Especially useful in patients not improving with systemic therapy
  – *Antibiotic rotation/holiday:* May reduce incidence of resistance
  – Duration of therapy:
    - Shorten duration from 14–21 to 8 days, provided organism is not pseudomonas
    - If low suspicion of VAP (CPIS of ≤ 6), stop after 3 days
- Supportive therapy:
  – Chest physiotherapy
  – Postural drainage
  – Humidification, aerosolization with bronchodilators.

De-escalating Therapy (ATS 2005 Guidelines)



Prognosis

- 30–70% mortality in late onset VAP/HAP
- In general, these patients have longer duration of hospital stay and mechanical ventilation.

EXTRACORPOREAL MEMBRANE OXYGENATION[9,10,12]

Introduction

Oxygenation of blood outside the body using a membrane oxygenator.

Indications

- Primary pulmonary HTN of newborn (PPHN):
  - Idiopathic PPHN
  - Meconium aspiration syndrome
  - Respiratory distress syndrome
  - Asphyxia
  - Group-B streptococcal sepsis.
- Pulmonary vaso-reactive crisis following repair of congenital heart defect
- Congenital Diaphragmatic Hernia
- *Low Cardiac Output Syndrome* due to:
  - Right/Left/biventricular failure
  - Following repair of congenital heart defect
- As a bridge to cardiac surgery in patients with severe end organ damage
- As a bridge to cardiac transplant.

Patient Selection Criteria[9]

- General criteria:
  - Gestational age ≥ 34 weeks
  - Birth weight ≥ 2000 grams
  - Failure of maximal medical therapy
  - When more than 80% risk of mortality exists, if conventional methods are used.
- Ventilation criteria:
  - Reversible lung injury
  - On mechanical ventilation for less than 14 days
- Systemic criteria:
  - No intracranial hemorrhage
  - No significant coagulopathy/uncontrolled bleeding
  - No lethal malformation.

ECMO Criteria[9]

These are qualifying criteria which apply only when infant has reached maximum ventilatory support of 100% FiO_2 with peak inspiratory pressure ≥ 35 cm H_2O.

- *Alveolar–Arterial oxygen pressure gradient {P(A-a)O2}:*
  - Calculated with patient on 100% O_2
  - P(A-a) O_2 = Barometric pressure – 47 – $PaCO_2$ – PaO_2
  - P(A-a) O_2 of 605–620 mm Hg at 100% FiO_2 for 4–12 hours indicates need for ECMO therapy.

- ***Oxygen Index:***
  - Oxygen index = $\frac{mP_{aw} \times FiO_2}{PaO_2}$
  - Index of 0.35–0.6 for 0.5–6 hours with $mP_{aw} \geq 20$ cm H_2O is indication for ECMO
- Acute deterioration: Taken as:
  - $PaO_2 \leq 30$–40 mm Hg for 2 hours
  - pH ≤ 7.25 for ≥ 2 hours
  - Intractable hypotension.

ECMO Circuit

- Uses modified heart-lung bypass machine
- Consists of:
  - Roller pump with raceway tubing
  - Venous reservoir
  - Membrane oxygenator
  - Countercurrent heat exchanger.
- Blood pump can be either:
  - Single roller pump
  - Vortex centrifugal pump
- Oxygenators can be either:
  - Bubble oxygenator
  - Membrane oxygenator
  - Hollow fiber oxygenator.

Safety Devices and Monitors

- Air bubble detectors
- Arterial line filters between heat exchanger and arterial cannula to trap air, thrombi and other emboli
- Pressure monitors
- Continuous venous O_2 saturation monitor
- Temperature monitors.

Types

- Venoarterial (VA) ECMO:
  - Blood drawn from RA via IJV
  - Oxygenated blood back into aortic arch via right common carotid artery
  - Oxygenates blood and support cardiac function as blood flow to aorta is supported by ECMO
  - Most common route for ECMO.
- Venovenous (VV) ECMO:
  - Blood drawn from RA via right IJV
  - Oxygenated blood back to RA via femoral vein
  - Only oxygenates blood, does not support cardiac output
  - Blood flow from right heart to left heart remain sole function of the heart.

Venoarterial ECMO[9,10]	Venovenous ECMO
Requires arterial cannula	Requires only venous cannula
Provides cardiac support to assist systemic circulation	Does not provide cardiac support
Bypasses pulmonary circulation	Maintains pulmonary blood flow
Reduces pulmonary arterial pressure	Elevates mixed venous PO_2
Lower perfusion rates needed	Higher perfusion rates needed
Higher PaO_2 achieved	Lower PaO_2 achieved

Technique

- Prime circuit with the freshest available blood
- Venoarterial/Venovenous bypass established
- General care:
  - Obtain cultures from circuit atleast once a week
  - Strict aseptic precautions
  - Minimum sedation with fentanyl/morphine/midazolam after stabilization
  - Doses of other inotropes maybe reduced once patient is on ECMO
  - Antacids and H_2 blockers.
- Central nervous system:
  - Avoid paralytic agents
  - Frequent CNS assessment
  - Phenobarbital for seizures
- Respiratory management:
  - Ventilator settings:
    - FiO_2 21–30%
    - PIP 15–25 cm H_2O
    - Rate 10–20 breaths/min
    - PEEP 3–5 cm H_2O
  - ETT suction done regularly
  - Daily chest X-ray
- Cardiovascular management:
  - Maintain systemic perfusion and intravascular volume
  - Inotropes to increase cardiac output
  - Echo to exclude congenital defects.
- Renals:
  - Oliguria and ATN common in first 24–48 hours
  - Diuretic phase, beginning within 48 hours is one of earliest signs of recovery
  - If oliguria ≥ 48–72 hrs, use diuretics
  - Hemofiltration/hemodialysis filters added to circuit if ARF does not improve.
- Blood:
  - Epsilon aminocaproic acid maybe required to reduce bleeding during procedure
  - Maintain hemoglobin between 12–15 gm%

  - Maintain platelet count > 1,00,000/μL
  - Maintain ACT between 180–240 sec
- Fluid balance:
  - Hyperalimentation for catabolic states
  - Fluid retention occurs in first 1–3 days.

Contraindications

- Gestational age ≤ 34 weeks
- Weight ≤ 2000 gms
- Patient with preexisting intracranial hemorrhage as heparin is given during ECMO
- Coagulopathies
- If mechanically ventilated for ≥ 2 wks before initiation of ECMO due to increased chances of chronic lung disease which ECMO cannot reverse.

Weaning Criteria

- Patient demonstrates adequate gas exchange with reasonable ventilator settings
- Patient tolerates pump flow of 10–20 ml/kg/min with minimum of 200 ml/min.

Complications[9,10]

- Mechanical complications:
  - Failure of pump
  - Airlock due to air in circuit
  - Rupture of tubing
  - Oxygenator failure
  - Hypothermia due to heat exchanger malfunction
  - Clots in ECMO circuit
  - Damage to IJV with mediastinal bleeding during cannulation.
- Physiological complications:
  - Bleeding due to increased heparin
  - Intracranial hemorrhage or infarcts due to:
    - Carotid artery ligation
    - Systemic heparinization
    - Thrombocytopenia
    - Coagulopathies
  - Seizures
  - Pulmonary hemorrhage
  - Cardiovascular complications:
    - Hypovolemia/hypervolemia
    - Hypo/hypertension
    - Arrhythmias
    - Pericardial tamponade
    - Symptomatic PDA
    - Altered renin-angiotensin-aldosterone cycle due to non-pulsatile perfusion.
  - Blood:
    - Anemia
    - Thrombocytopenia
    - Leukopenia
    - Increased chances of infection.
  - GIT complications:
    - Gut hemorrhage
    - Biliary calculi
    - Direct hyperbilirubinemia.
- Metabolic complications:
  - Acidosis/alkalosis
  - Hyper/hyponatremia
  - Hypo/hyperkalemia
  - Hyper/hypocalcemia
  - Hypo/hyperglycemia.

Current Status

- ECMO use as safe means to ventilate neonates has not been realized
- Carotid artery which is used to cannulate patient is permanently ligated: Effects of single carotid artery as patients gets older is to be determined.
- Expensive and requires round the clock monitoring.

Prognosis

- High rate of complication
- Feeding difficulty occurs after ECMO decannulation
- Epilepsy occurs in 2% patients
- Increased rate of rehospitilization for pulmonary complications within 6 months after ECMO
- 6% chances of sensory-neural disabilities
- Psychosocial morbidity: Increased incidence of ADHD and academic difficulties
- Neuromotor deficits ranging from mild hypotonia to gross motor delay and spastic quadriparesis.

APACHE SCORE II

Introduction

- The Acute *Physiological Assessment and Chronic Health Evaluation (APACHE)* score is a widely used method for assessing severity of illness in acutely ill patients in ICUs, taking into account a variety of routine physiological parameters
- Outlined by ***Knauss*** in 1985
- Scores ranged from 0.71 with higher scores indicating greater severity of illness and increased risk of death.

Applications

- Lower age for application is not specified but a good limit is to use the score only for patients above 15 years of age
- Some procedures and medicines are only given to patients with a certain Apache II score
- Apache II score can be used to describe mortality of a patient when comparing the outcome with other patients
- Predicted mortalities are averaged for groups of patients in order to specify the groups mortality.

Calculation

- A point score is calculated from 12 routine physiological measurements during first 24 hours after admission
- Information about previous health status also is obtained at admission
- The resulting score is interpreted in relation to the illness of the patient
- After initial score has been determined within 24 hours of admission, no new score can be calculated during the hospital stay
- If a patient is discharged from ICU and readmitted, a new score can be calculated
- Using the patients Apache score and principle diagnosis at admission the predicted mortality can be calculated.

Parameter	Range	Score
Age in years	Less than 44 years	0
	45–54 years	2
	55–64 years	3
	65–74 years	5
	More than 75 years	6
Severe organ insufficiency	Yes, non-operative/ emergency postop patient	5
Immunocompromized status	Yes, elective postop patient	2
	No	0
Rectal temperature	More than 40.9 °C	4
	39–40.9 °C	3
	38.5–38.9 °C	1
	36–38.4 °C	0
	34–35.9 °C	1
	32–33.9 °C	2
	30–31.9 °C	3
	Less than 30 °C	4

Contd...

Contd...

Parameter	Range	Score
Heart rate	More than 179 bpm	4
	140–179 bpm	3
	110–139 bpm	2
	70–109 bpm	0
	55–69 bpm	2
	40–54 bpm	3
	Less than 40 bpm	4
Respiratory rate	More than 49/min	4
Non–ventilated or ventilated	35–49/min	3
	25–34/min	1
	12–24/min	0
	10–11/min	1
	6–9/min	2
	Less than 6/min	4
Mean arterial pressure	More than 159 mm Hg	4
	130–159 mm Hg	3
	110–129 bpm	2
	70–109 bpm	0
	50–69 bpm	2
	Less than 50 bpm	4
Oxygenation	A–a gradient > 499	4
Use PaO2 if FiO2 < 50%	A–a gradient 350–499	3
Else, use alveolar-arterial gradient	A-a gradient 200–349	2
	A-a gradient < 200 if FiO_2 > 49 or PaO_2 >70	0
	If FiO_2 less than 50%	
	PaO_2 61–70	1
	PaO_2 55–60	3
	PaO_2 less than 55	4
Arterial pH	More than 7.69	4
	7.6–7.69	3
	7.5–7.59	1
	7.33–7.49	0
	7.25–7.32	2
	7.15–7.24	3
	Less than 7.15	4
Serum sodium levels	More than 179 mmol/L	4
	160–179 mmol/L	3

Contd...

Contd...

Parameter	Range	Score
	155–159 mmol/L	2
	150–154 mmol/L	1
	130–149 mmol/L	0
	120–129 mmol/L	2
	111–119 mmol/L	3
	Less than 111 mmol/L	4
Serum potassium levels	More than 6.9 mmol/L	4
	6–6.9 mmol/L	3
	5.5–5.9 mmol/L	1
	3.5–5.4 mmol/L	0
	3–3.4 mmol/L	1
	2.5–2.9 mmol/L	2
	Less than 2.5 mmol/L	4
Serum creatinine	More than 3.4 mg/dL and ARF	8
	2–3.4 mg/dL and ARF	6
	1.5–1.9 mg/dL and ARF	4
	More than 3.4 mg/dL and CRF	4
	2–3.4 mg/dL and CRF	3
	1.5–1.9 mg/dL and CRF	2
	0.6–1.4 mg/dL	0
	Less than 0.6 mg/dL	2

Contd...

Contd...

Parameter	Range	Score
Hematocrit	More than 59.9%	4
	50–59.9%	2
	46–49.9%	1
	30–45.9%	0
	20–29.9%	2
	Less than 20%	4
WBC count	More than 39000/mm^3	4
	20000–38900/mm^3	2
	15000–19900/mm^3	1
	3000–14900/mm^3	0
	1000–2900/mm^3	2
	Less than 1000/mm^3	4

Mortality Prediction

Total of all points Apache score is then calculated:

Apache score	Mortality Rate
0–4	4%
5–9	8%
10–14	15%
15–19	25%
20–24	40%
25–29	55%
30–34	75%
More than 35	85%

CHAPTER

11

Anesthetic Pharmacology

DRUG INTERACTIONS[1, 2, 3, 7, 20]

Classification

- Pharmaceutical interactions
- Pharmacokinetic interactions:
  - Absorption
  - Distribution
  - Cardiac output alterations
  - Ion trapping
  - Protein binding
  - Metabolism
  - Hepatic biotransformation
  - Elimination.
- Pharmacodynamic interactions:
  - Affecting hemodynamics
  - Affecting analgesia/hypnosis.

Problems Due to Drug Interactions

- One drug may antagonize action of other
- Toxicity due to drug interaction
- Reduced therapeutic window of warfarin/digoxin/theophykine
- Unable to identify the drug producing clinical effect
- Increased idiosyncratic reactions: MAO inhibitors with meperidine.

Pharmaceutical Interaction

Introduction

Chemical/physical interaction which occurs before a drug is administered/absorbed systemically.

Types

- Incompatibility between two drugs in solution:
  - Thiopentone precipitates when given with succinylcholine
  - Soda bicarb reduces solubility of bupivacaine and precipitates it
  - Soda bicarb inactivates catecholamines.
- Drugs forming toxic compounds:
  - Halogenated agents + Baralyme $\rightarrow$ CO + heat
  - Sevoflurane + Baralyme $\rightarrow$ Sevo-olefin
  - $NO + O_2 \rightarrow NO_2$ (toxic at > 10 ppm concentration).

Pharmacokinetic Interactions

Absorption

- Altered mechanism of absorption:
  - Oral tetracycline inactivated with $Mg^{2+}/Ca^{2+}/Al^{3+}$ antacids
  - Oral antidiarrheals (kaolin/pectin) absorb digoxin
  - Bile acid binding residue cholestyramine binds to warfarin and reduces absorption.
- Reduced regional perfusion:
  - Reduced local anestheic absorption when adrenaline added.

Distribution

- Cardiac output altering distribution:
  - Thiopentone/propofol/remifentanyl causes reduced cardiac output
  - Volatile anesthetics reduce cardiac output and have increased CNS effect.

- Ion trapping:
  - Drug induced changes in pH causing altered distribution
  - Antacids/H_2 blockers/proton pump inhibitors reduce absorption of acidic drugs
  - Altered urinary pH affects renal clearance of drugs.
- Plasma protein binding:
  - Displacement of bilirubin by sulfonamides causing *kernicterus*
  - Displacement of warfarin by phenylbutazone/phenytoin.

Metabolism

- Acetylcholine esterases/nonspecific esterases:
  - Neostigmine/pyridostigmine increases succinylcholine effects
  - Neostigmine increases action of ester local anesthetics:
    - Procaine
    - Cocaine
    - Tetracaine.
- MAO inhibitors interaction:
  - They increase action of indirect acting sympathomimetics:
    - Ephedrine
    - Amphetamine.
  - They may cause hypertensive crises due to tyramine present in aged cottage cheese: ***Wine and cheese reaction***
  - They increase action of direct acting sympathomimetics to a lesser extent:
    - Epinephrine
    - Norepinephrine.
  - When given with meperidine it causes ***serotonin syndrome***:
    - Excitation and hyperpyrexia
    - HTN, diaphoresis, rigidity
    - Seizures, coma and death.

Hepatic Biotransformation

- Drugs with high extraction ratio (ER > 0.7):
  - Examples of drugs with high ER:
    - Lidocaine
    - Propranolol.
  - Blood flow to liver is rate limiting as metabolism is at maximum
  - Lidocaine concentration increases due to:
    - Reduced hepatic blood flow due to reduced cardiac output
    - Vasopressors: Isoproterenol and noradrenaline.
- Drugs with low extraction ratio (ER < 0.3):
  - Examples of drugs with low ER:
    - Diazepam
    - Mepivacaine
    - Alfentanyl.
  - Activity of hepatic enzymes is rate limiting as enzyme induction can increase metabolism
  - Midazolam and fentanyl are competitive inhibitors of CYP3A4
  - Propofol inhibits CYP3A4 and reduces clearance of midazolam by 37%
  - Erythromycin increases effect of alfentanyl
  - Cimetidine inhibits metabolism of warfarin, diazepam, phenytoin and morphine
  - Ketoconazole inhibits clearance of midazolam, theophylline, warfarin and digoxin
  - Etomidate inhibits cytochrome P450 dependent 17 hydroxylase and 11 hydroxylase
  - This causes reduced synthesis of cortisol and aldosterone.
- Enzyme inducers:
  - Phenobarbitone
  - Phenytoin
  - Rifampicin
  - Carbamezipine
  - Ethanol.
- Enzyme inhibitors:
  - Cimetidine
  - Ketoconazole
  - Erythromycin
  - Disulfiram
  - Ritonavir.

Elimination

- Ion trapping: Phenobarbital (weak acid) excretion is increased in acidic urine
- Ion secretion:
  - Probenecid inhibits secretion of penicillin
  - Quinidine reduces Vd and clearance of digoxin.

Pharmacodynamic Interactions

Additive Interactions

- Occurs when drugs with similar mechanism of action are combined
- Rocuronium + vecuronium: Additive effect
- 2 volatile anesthetics or N_2O + VA: Additive efffect.

Antagonistic Interaction

- SCH + NDMR
- Neostigmine + NDMR
- Flumazenil + Benzodiazepines
- Naloxone + opioid
- Butorphanol + midazolam: Increased sedation but less anterograde amnesia than midazolam alone.

Synergistic Interaction

- Small doses of 2 drugs producing larger effects
- Opioids potentiation by NSAIDS
- NDMR potentiation by volatile anesthetics
- Aminosteriod + benzylisoquinoline NDMR.

Pharmacodynamic Interactions Affecting Hemodynamics

- Tricyclic antidepressants can increase effects of direct/indirect acting agonists
- β2 agonists may cause tachycardia and ectopic rhythms.

Interactions Affecting Analgesia/Hypnosis

- Opioid – hypnotic:
  - Fentanyl reduces barbiturate need
  - Opioids potentiate propofol
- Opioid – Benzodiazepine:
  - Fentanyl potentiates midazolam
- Opioid – volatile anesthetic:
  - Fentanyl at 1.67 ng/ml blood concentration reduces isoflurane MAC by 50%
  - Butorphanol and nalbuphine also reduces MAC
- Benzodiazepine – hypnotic
  - Thiopentone potentiates midazolam
  - Propofol hypnosis increased with midazolam
- 2 agonist interaction:
  - Dexmedetomidine potentiates opioids and benzodiazepines (BZDs)
  - Dexmedetomidine reduces halothane MAC by almost 100%
- Three way interactions:
  - Propofol dose reduces by 86% in combination with midazolam and alfentanyl
  - Enflurane MAC reduces with dexmedetomidine and fentanyl.

THIOPENTONE[1,2,3,7,20]

Introduction

This is a thio-barbiturate which is commonly used as a hypnotic inducing agent and anticonvulsant.

Chemistry

- Derivative of barbituric acid formed by condensation of urea and malonic acid
- Oxygen replaced by:
  - Sulfur at urea derived carbon position 2
  - Branched chain group at carbon position 5.
- This gives the drug short duration of action
- S(–) isomers of thiopental are more potent than R(+) isomers
- Commercial preparations are racemic mixtures.

Presentation

- Hygroscopic yellow powder
- Clinically used as 2.5% solution
- Contains thiopentone with 6% Na_2CO_3 stored under atmosphere of nitrogen
- Nitrogen prevents precipitation of insoluble acid formed by atmospheric carbon dioxide
- Solution has highly alkaline bacteriostatic properties with pH of 10.8 and pKa of 7.6.

Mechanism of Action

- At GABAA receptors:
  - Causes positive allosteric modulation: Increases channel opening time of Cl^- channels
  - Reduces dissociation of GABA from receptors: Causes sustained inhibition of RAS
  - Mimics GABA action by directly stimulating GABAA receptors.
- Stimulates glutamate receptors
- Stimulates adenosine receptors
- Stimulates neuronal nicotinic ACH receptors (n-ACHRs)
- Reduces transmission in sympathetic ganglia causing hypotension
- At high concentration it depresses enzymes for glucose oxidation, inhibits ATP formation and Ca^{2+} dependent action potentials.

Pharmacodynamics

- Central nervous system: Cerebroprotective effect:
  - Sedation
  - Rapid induction of anesthesia
  - *Antalgesic in lower doses:* Reduces pain threshold
  - Anticonvulsant
  - Depresses respiratory center
  - Depresses vasomotor center
  - *Retrograde amnesia: Midazolam causes anterograde amnesia*

  - Reduced cerebral blood flow, cerebral vasoconstriction
  - Reduces ICP, depresses cerebral metabolism
  - Reduces intraocular pressure.
- Respiratory system:
  - Depresses respiratory center:
    - Causes transient apnea
    - This is followed by a more prolonged period of respiratory depression
  - Preserves laryngeal reflexes
  - Coughing, laryngeal spasm, bronchoconstriction especially in asthmatics
  - Reduces ventilatory response to hypercarbia.
- Cardiovascular system:
  - Hypotension and tachycardia
  - Negative inotropism
  - Reduces cardiac output by about 20%
  - Reduces peripheral vascular resistance.
- Genitourinary system:
  - Reduces renal plasma flow
  - Increases ADH secretion
  - Reduces urine output
  - Uterine tone is unaffected
  - Crosses blood-placental barrier
  - Fetal plasma concentration is lower and more delayed.
- Autonomic nervous system:
  - Reduces intestinal activity
  - Constriction of splanchnic vasculature
  - Inhibits vasomotor center
  - Constriction of pupil followed by dilatation
  - Loss of pupillary and eyelash reflexes
- Metabolic: Transient reduction in K^+ levels.

Dosage

- Intravenous: Given as 2.5% solution (25 mg/ml) in a dose of 3–5 mg/kg
- Can be given rectally as 5–10 % solution in a dose of 50 mg/kg body weight.

Pharmacokinetics

- Absorption: Absorbed when given orally/rectally.
- Distribution:
  - 72–86% protein bound, mostly to albumin
  - Volume of distribution 2.5 L/kg
  - Lipid soluble unionized form of the drug crosses BBB
  - Rapid onset of action as:
    - High blood flow to brain
    - Lipophilicity of drug
    - Low degree of ionization
  - Action of drug seen within one brain arm circulation time (30 seconds).
- Redistribution:
  - Initial high uptake of drug by the brain causes plasma concentration to decrease
  - This results in reversal of the concentration gradient
  - This causes movement of the drug back into blood subsequently
  - Accounts for the brief duration of anesthesia following bolus dose of thiopentone.
- Metabolism:
  - Hepatic metabolism with extraction ratio of 0.15 (low)
  - Oxidation, formation of active metabolite pentobarbital
  - Initially after bolus dose decay follows first order kinetics
  - With longer infusions and higher doses hepatic metabolic capacity is exceeded causing zero order kinetics.
- Excretion:
  - Predominantly in urine
  - Excreted as inactive metabolic
  - Less than 1% is directly eliminated unchanged in urine.

Implications of Pharmacokinetics

- Dose should be reduced in CRF and liver failure patients as serum albumin will be low: More amount of free drug in circulation.
- Concurrent administration of warfarin and aspirin may displace thiopentone from proteins resulting in toxicity.
- Dose should be reduced in hypovolemia as blood flow to skeletal muscle is reduced while brain and heart perfusion is maintained.

Clinical Uses

- Induction of anesthesia:
  - 3–5 mg/kg IV is induction dose
  - Loss of consciousness (LOC) occurs in one brain-arm circulation time (30 seconds)
  - LOC lasts for around 5–15 minutes.
- Treatment of raised ICT:
  - Produces cerebral vasoconstriction and reduces cerebral blood flow

  - 37.5 mg/kg thiopentone required to produce isoelectric EEG
  - Hemodynamic instability may complicate high dose thiopentone
  - Thiopentone is preferred to isoflurane for raised ICT
  - Isoflurane requires 2 MAC to produce equivalent EEG suppression.
- Cerebral protection:
  - Useful in focal ischemia, but not global cerebral ischemia like in cardiac arrest
  - Reduces incidence of neuropsychiatric complications following cardiopulmonary bypass
  - Cerebral protection occurs due to:
    - Reduction in $CMRO_2$
    - Reverse steal phenomenon ***(Robin Hood effect)*** on CBF
    - Free radical scavenging
    - Stabilization of lysosomal membranes
    - Excitatory amino acid receptor blockade.
- To verify wet epidural tap:
  - Used to verify if the fluid coming out of the epidural catheter is CSF or LA
  - Local anesthetic (LA) solutions are highly acidic preparations
  - If fluid coming out of catheter is LA solution, thiopentone being highly alkaline will precipitate on being added.

Side Effects

- Cardiovascular:
  - Myocardial depression especially when given in high doses
  - Hypotension due to peripheral venodilatation
  - Histamine release: Hypotension
  - Heat loss and hypothermia due to vasodilation.
- Respiratory:
  - Transient apnea
  - Bronchospasm/laryngospasm during intubation if inadequate depression of laryngeal reflexes by barbiturates.
- Liver: Modest reduction in hepatic blood flow
- Kidney: Modest reduction in renal blood flow and GFR
- Tolerance
- Venous thrombosis:
  - Due to deposition of barbiturate crystals in the vein
  - Occurs frequently when vecuronium is given after thiopentone injection
  - Diluting thiopentone injection to 2.5% reduces this incidence.
- Intra-arterial injection:
  - Clinical features:
    - Immediate intense pain
    - Vasoconstriction with blanching of extremity
    - This can result in cyanosis and gangrene.
  - Mechanism of action:
    - Endothelial damage causes inflammatory response
    - This leads to arteritis and microembolization causing occlusion of artery.
  - Treatment and prevention:
    - Use only 2.5% solution thiopentone
    - Let angiocatheter remain in place
    - If angiocatheter has been removed:
      - Inject vasodilator into more proximal location in artery
      - Injected more proximally because affected artery will be in spasm.
    - Inject saline into angiocatheter to dilute the drug
    - Lidocaine, papaverine and phenoxybenzamine used to produce vasodilation
    - Heparin/urokinase is considered if thrombosis occurs
    - Sympathetic blockade: Stellate ganglion/brachial plexus block may be used.
- Allergic reaction:
  - May occur even without prior exposure to thiopentone
  - Aggressive and early therapy with epinephrine, fluids and steroids
  - Unusually high mortality rate.
- Immunosuppression:
  - Bone marrow suppression and leucopenia occurs
  - Also inhibits neutrophil function
  - Occurs with long term and high dose administration
  - Results in increased incidence of nosocomial infections.

Contraindications

- Porphyria
- Status asthmaticus
- Shock, pericardial tamponade
- Uncompensated myocardial disease.

PROPOFOL[1,2,3,7,20]

Introduction

Propofol is a substituted isopropylphenol which is commonly used as an induction agent in anesthesia.

Chemistry

- Chemically 2–6 disopropylphenol
- Propofol unlike ketamine and thiopentone is a non-chiral compound.

Presentation

- Propofol is an oily compound which is insoluble in water
- Therefore, it requires a lipid vehicle for emulsification
- Commercial preparations contain propofol molecule, a carrier and preservative compound
- Preservatives are used because the lipid carrier acts as a potent medium for bacterial growth.

Preparations

- There are various preparations for propofol depending on:
  - Carrier molecule
  - Propofol concentration
  - Preservative compound.
- The various preparations are:
  - Generic propofol:
    - Contents:
      - 1% propofol
      - 2.25% glycerol
      - 10% soybean oil
      - 1.2% egg phosphatide
    - Preservative used: Sodium metabisulfite
    - pH: 4.5–6.5.
  - Cremaphor EL:
    - Earlier used as the carrier
    - Withdrawn due to anaphylaxis.
  - Diprivan:
    - Contents:
      - 1% propofol
      - 2.25% glycerol
      - 10% soybean oil
      - 1.2% egg phosfatide.
    - Preservatives: NaOH, disodium edetate (EDTA)
    - pH: 7–8.5.
  - Ampofol (low lipid emulsion):
    - Contents:
      - 1% propofol
      - 0.6% egg lecithin
      - 0.5% soybean oil.
    - Preservatives: None because of low lipids
    - Equipotent to diprivan but causes more pain or injection
    - Less bacterial growth.
  - Aquavan:
    - Alternative to lipid emulsion formulations
    - It is water soluble
    - Contains pro-drug *fospropofol* (phosphorylated pro-drug)
    - Propofol is liberated after hydrolysis by alkaline phosphatases
    - Prevents lipid associated side effects like:
      - Pain, hypertriglyceridemia
      - Pulmonary embolism.
    - Properties:
      - Larger V_d
      - Higher potency
      - Longer time to peak effect
      - Prolonged pharmacological action.
  - Nonlipid formulations with cyclodextrin carrier:
    - Structurally sugar molecules
    - Forms guest-host complexes which migrate between hydrophilic center of the cyclodextrin molecular and the water soluble phase
    - After injection, propofol migrates out of the cydodextrin into blood.
  - 2% formulations:
    - Contains 2% propofol and medium to long chain fatty acids
    - Decreased incidence of pain on injection due to long chain and medium chains
    - Mixing of propofol with any drug is not recommended
    - May be mixed with lignocaine to reduce pain on injection
    - This may result in coalescence of oil droplets causing pulmonary embolism.

Mechanism of Action

- $GABA_A$ receptor:
  - Propofol binds to β subunit of $GABA_A$ receptor and γ2 subunits also contribute to modulatory effects of propofol on $GABA_A$
  - Prevents dissociation of GABA from the receptor
  - This causes prolonged activation of the receptor
  - Chloride influx occurs as a result causing hyperpolarization and inhibition of post-synaptic neurons.

- Inhibits ACH release in hippocampus through $GABA_A$ action
- Inhibits NMDA receptor.

Pharmacodynamics

- Central nervous system:
  - Rapid smooth induction
  - Rapid and clear headed recovery
  - Cerebroprotective:
    - Antioxidant properties
    - Reduces intracranial pressure, $CMRO_2$ and cerebral perfusion pressure.
  - Cerebrovascular autoregulation and reaction to changes in $PaCO_2$ not affected
  - Produces burst suppression on EEG: Anticonvulsant
  - Produces same degree of memory impairment as midazolam
  - Seizures and abnormal motor activity may sometimes occur
  - Tolerance occurs to repeated dosing
  - Increases dopamine in *nucleus accumbens*: results in drug abuse.
- Cardiovascular system:
  - Decrease in:
    - Arterial blood pressure:
      - Reduction in systolic, diastolic and mean pressures
      - Effects exaggerated in old patients, hypovolemia and LV dysfunction due to CAD
      - Inhibits baroreceptor reflex to hypotension.
    - PVR: Due to more impotent inhibition of sympathetic nervous tone
    - Cardiac output, stroke volume index and cardiac index:
      - Occurs due to reduced intracellular Ca^{2+} availability
      - This is secondary to inhibition of transsarcolemmal Ca^{2+} influx.
  - Heart rate:
    - May increase, decrease or remain unchanged
    - Response depends on hypotension and baroreceptor suppression
    - Causes bradycardia and asystole sometimes
    - Heart rate response to atropine is attenuated
    - Bradycardia is reversed by isoprenaline.
  - Does not alter SA node or AV node function: Safe in WPW syndrome and ablative procedures
  - Suppresses supraventricular tachycardia
  - Potentiates oculocardiac reflex.
- Respiratory system:
  - Produces short duration apnea (30–60 sec) after induction in 25–30% patients
  - Decreases tidal volume and frequency of breathing
  - Response to CO_2 and hypoxemia is reduced by direct action on carotid body receptors
  - Produces bronchodilation and reduces intraoperative wheezing
  - Hypoxic pulmonary vasoconstriction is intact but attenuated
  - *Laryngeal reflexes are lost.*
- Hepatic and renal functions:
  - Prolonged infusion:
    - Causes hepatocellular injury resulting in acidosis
    - Increases phenols in urine:
      - This causes phenoluria resulting in green color urine
      - However, it does not alter renal function.
  - Urinary uric acid excretion increases resulting in turbid urine
  - Decreases hepatic blood flow.
- Intraocular pressure:
  - Decreases intraocular pressure following intubation
  - Potentiates oculocardiac reflex.
- Coagulation: Does not alter coagulation profile.

Pharmacokinetics

- Distribution:
  - Volume of distribution 3.5–4.5 L/kg
  - 97 % is plasma protein bound
  - Onset of action: 30–45 seconds (one brain-arm circulation time)
  - Duration of unconsciousness produced is around 10 minutes
- Metabolism: Undergoes hepatic and extrahepatic metabolism:
  - Hepatic metabolism:
    - Rapid metabolism
    - Conjugation to soluble, inactive compounds with glucuronide and sulfate
    - Cytochrome P450 actions:
      - Ring hydroxylation occurs forming 4-hydroxypropofol
      - This has one-third the hypnotic activity of propofol.

- *Extrahepatic metabolism:*
  - Lungs:
    - Are responsible for 30% uptake and first pass elimination after bolus dose
    - Propofol is metabolized to 2-disopropyl-quinol.
  - Kidney and brain: Contains UDP-glucuronyl transferase.

- Excretion:
  - Less than 0.3% excreted unchanged in kidneys
  - Metabolites are also excreted in kidney
  - 2% is eliminated in feces
  - No influence of renal dysfunction on renal clearance
  - Hepatic dysfunction also does not affect elimination.
- Fospropolol:
  - Endothelial cell alkaline phosphatase hydrolyses it to release propofol
  - Each mg of fospropofol liberates 0.54 mg of propofol.

Clinical Uses

- Induction of anesthesia:
  - Results in rapid induction with rapid and smooth recovery
  - Induction dose: 1.5–2.5 mg/kg IV in adults
  - Higher doses in children due to higher central compartment volume and clearance rate
  - Complete awakening results without residual CNS effects.
- Intravenous sedation:
  - 25–100 µg/kg/min IV infusion
  - Prompt recovery occurs following stoppage of infusion
  - Low incidence of postoperative nausea and vomiting.
- Maintenance of anesthesia:
  - 100–300 µg/kg/min IV infusion
  - Used only for short procedures
  - Longer procedures (72 hours): Propofol not preferred due to higher cost.
- Nonhypnotic therapeutic applications:
  - Antiemetic effects:
    - Due to:
      - Reduced release of glutamate and aspartate in olfactory cortex
      - Inhibits CTZ and vagal nuclei
      - Has antidopaminergic properties
      - Also reduces serotonin levels in *area postrema.*
    - 10–15 mg given IV (subhypnotic doses)
  - Effective for PONV especially if nonvagal in nature and chemotherapy induced vomiting.
- Antipruritc actions:
  - 10 mg propofol given IV
  - Due to ability to depress spinal cord activity
  - Used for:
    - Pruritis due to intrathecal opioids
    - Cholestatic jaundice associated pruritis.
- Anticonvulsant: 1 mg/kg IV reduces seizure duration in patients undergoing ECT
- Chronic intractable headache: 20–30 mg IV given every 3–4 minutes (maximum 400 mg)
- Also used for laryngospasm and for cerebroprotection.

Immediate Side Effects

- Hypotension and bradycardia: Augmented by concomitant opioids
- Pain on injection:
  - Most common side effect
  - Occurs especially on injection into smaller veins
  - Preventive measures:
    - Inject into larger veins
    - Avoid veins on dorsum of hand
    - Pretreatment with opioids/NSAIDs
    - Prior administration of 1% lidocaine
    - Change carrier composition to long and medium chain fatty acids.
- Allergic reactions:
  - Was more with cremaphor-EL which was withdrawn from production
  - Occurs due to isopropyl side chain and phenol nucleus.
- Proconvulsant action:
  - Spontaneous excitatory activity due to increased subcortical activity
  - Caution in administration of propofol with poorly controlled epileptic patients
  - Myoclonus associated with meningismus occurs in some cases.

Side Effects on Prolonged Administration

- Bacterial growth:
  - Lipid carrier is a potent culture medium
  - Supports the growth of E. coli and pseudomonas

  - Preventive measures:
    - Aseptic technique: Disinfect neck of ampule with 70% isopropyl alcohol
    - Withdraw drug with sterile syringe
    - Discard unused contests within 6 hours
    - Flush IV cannula after administration of drug.
- Abuse potential:
  - Due to dopamine accumulation in nucleus accumbens
  - Causes intense dreaming, amorous behavior and sexual fantasies
  - Hallucinations occur on recovery from effects of propofol.
- Propofol infusion syndrome
- Pancreatitis: Due to prolonged administration of preparations with lipid carriers
- Thrombophlebitis in rare cases
- Hypertriglyceridemia
- Immunosuppression:
  - Inhibits phagocytosis and killing of bacteria
  - Reduces proliferative lymphocyte activity.

PROPOFOL INFUSION SYNDROME[1,2,3,7,20]

Introduction

- Features which occurs in patients receiving propofol infusions for long duration (> 48 hrs).

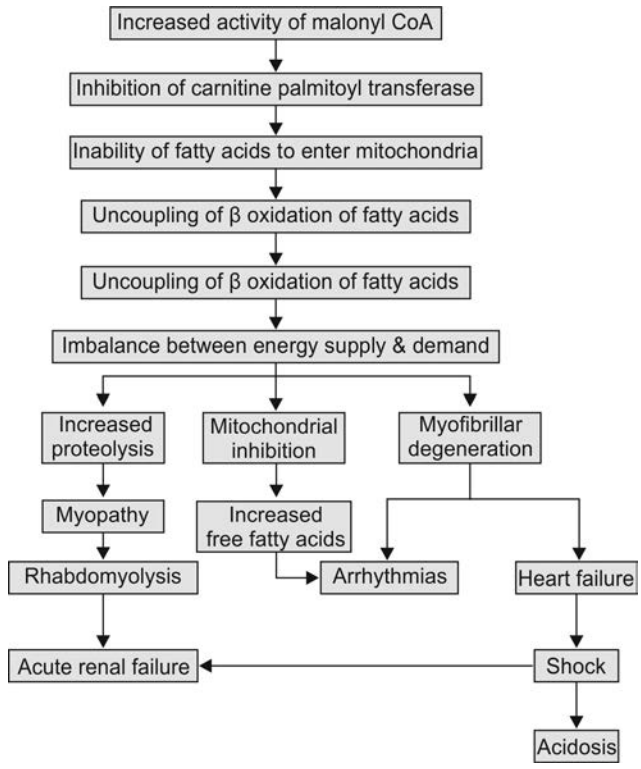
Incidence

- More commonm in children
- More common if used for sedation in TBI
- Can occur with prolonged infusion (> 48 hrs).

Risk Factors

- Pediatric age group
- Cumulative dose:
  - > 75 µg/kg/min
  - > 4 mg/kg/hr
- Duration of infusion > 48 hrs
- Severe inciting illness
  - CNS origin (TBI)
  - Sepsis
  - Respiratory origin
  - Pancreatitis
- Catecholamines/corticosteroid supplementation
- Inadequate delivery of carbohydrates
- Subclinical mitochondrial disease.

Pathophysiology[1,3]



Clinical Features

- Profound metabolic acidosis (base deficit > 10 mmol/l)
- Lactic acidosis
- Hyperkalemia
- Hyperlipidemia hypertriglyceridemia
- Acute refractory bradycardia, sinus arrest, asystole
- Cardiomyopathy, cardiac failure, hypotension
- Fatty liver, hepatomegaly
- Skeletal myopathy, rhabdomyolysis
- Acute renal failure.

Early Markers

- Unexplained metabolic acidosis
- Elevated serum lactate
- Elevated creatinine kinase
- Elevated myoglobin levels
- Hyperlipidemia
- ECG changes (ST segment elevation in V1 to V3).

Investigations

- ABG for metabolic acidosis
- Triglycerides
- Lactate

- Creatinine kinase
- Myoglobin.

Prevention

- Avoid high dose propofol
- Minimize duration of infusion
- Avoid infusion in:
  - Children
  - Mitochondrial disease
- Early and adequate carbohydrate intake
- Avoid lipid overload
- High index of suspicion: Serum triglycerides after 2 days of continuous infusion.

Treatment

- Mainly supportive
- Stop propofol infusion
- Start alternative sedation
- Hemodynamic maintenance:
  - IV crystalloids/colloids
  - Vasopressors/inotropes
  - Transvenous pacing.
- Nutritional support:
  - Avoid additional lipids
  - Add dextrose to IV fluids (4–8 mg/kg/hr glucose).
- Renal support:
  - Dialysis
  - Continuous renal replacement therapy.
- Maintain oxygenation
- ECMO has been tried.

KETAMINE[1,2,3,7,20]

Introduction

This is a phencyclidine derivative widely used for induction of anesthesia.

Chemistry

- Phencyclidine derivative
- Two optical isomers:
  - S(+) and R(–) ketamine
  - Racemic mixture of the two is usually used commercially
  - Isomers are pharmacodynamically and pharmacokinetically different

No	Property	S(+) isomer	R(–) isomer
1	Action[7]	More intense	Less intense
2	Potency	Analgesia is four time more potent	Less potent
3	Metabolism	Rapid hepatic biotransformation	Slower bio-transformation
4	Recovery	More rapid	Slower
5	Emergence reaction	Lower incidence	Higher incidence
6	Salivation	Less	More
7	EEG suppression	More potent	Less potent
8	Apoptosis	More antiapoptotic	Less
9	Therapeutic index	More	Less
10	Affinity	More receptor affinity	Less

Preparation

- Available in 1%, 5% and 10% concentrations
- It is partially water soluble, 5 to 19 times as lipid soluble as thiopentone
- Preparation has a pKa of 7.5
- Preservative:
  - Benzethonium chloride used as preservative which is neurotoxic
  - S(+) isomer preparations do not have preservative (less neurotoxic)
  - Only these preservative free preparations are used for intrathecal administration.

Mechanism of Action

- NMDA receptor:
  - Causes noncompetitive inhibition of NMDA receptor
  - Decreases presynaptic glutamate release
  - Potentiates GABA effect.
- Opioid receptors: Interacts with μ, κ and δ receptors
- Monoaminergic receptor: Interacts and thus interferes with pain pathway
- Muscarinic receptors:
  - Acts as an antagonist at muscarinic receptors
  - This causes the bronchodilator and delirious effects of ketamine.
- Sodium channels: Attributes mild local anesthetic like properties
- Cytokines:
  - Suppresses neutrophil production of cytokines
  - Also, directly inhibits cytokines in circulation causing analgesic properties.

Pharmacokinetics

- Distribution:
  - Less plasma protein bound
  - Large volume of distribution (V_d = 3 L/kg)
  - Rapid onset of action as:
    - Highly lipid soluble (5–10 times that of thiopentone)
    - Ketamine induced vasodilatation:
      - Causes increased cerebral blood flow
      - This causes increased drug delivery.
  - Onset of action 30–60 seconds.
- Redistribution:
  - Following initial rapid distribution to CNS, the plasma concentration falls
  - The drug then re-enters plasma from the central compartment and gets redistributed to the less perfused areas.
- Metabolism:
  - Occurs through cytochrome P450 enzyme
  - Demethylated to form norketamine
  - Norketamine has one-third to one-fifth the activity of ketamine
  - Norketamine is hydroxylated and conjugated with glucuronide
  - Ketamine can also induce cytochrome P450 enzyme
  - This causes tolerance and drug dependence
  - High hepatic clearance rate (more than 1 L/min)
  - Reduction in hepatic blood flow reduces metabolism.
- Excretion:
  - Less than 4% is excreted unchanged in urine
  - Less than 5% is excreted in feces
  - Remaining conjugated metabolites excreted via urine.

Pharmacodynamics

- Central nervous system:
  - Analgesia:
    - Greater for somatic nonvisceral pain
    - Reduces spinal cord sensitization by blocking NMDA receptors in dorsal horn
    - Also reduces transmission of impulses in medullary RAS: Important for affective component of pain.
  - Anesthesia: Called *Dissociative Anesthesia*:
    - Definition: Cataleptic state where profound analgesia and amnesia occurs even though patient appears conscious and maintains protective reflexes.
    - Mechanism:
      - Causes dissociation between thalamocortical tract and limbic system
      - Inhibition of thalamocortical tract occurs with stimulation of limbic system
      - This causes functional disorganization of nonspecific pathways in midbrain and thalamus.
    - Characteristics:
      - It is a *cataleptic state*
      - Open eyes with slow and nystagmic gaze
      - Appears awake but noncommunicative
      - Various degrees of hypertonus and purposeless skeletal muscle movements
      - Amnesia: No recall of surgery/anesthesia
      - Cough, swallowing and corneal reflexes are present
      - Reflexes should not be assumed to be protective
      - Profound analgesia present.
  - Intracranial pressure:
    - Potent vasodilator
    - Increases cerebral blood flow by 60%
    - Increases ICP in normocapneic patients
    - May cause reduction in ICP in ventilated patients
    - Cerebrovascular response to CO_2 is preserved.
  - Neuroprotection:
    - Antagonist of NMDA receptors
    - This causes neuroprotection in cerebral ischemic states
  - EEG:
    - Abolishes α-rhythm
    - β-rhythm slowly progresses to δ-rhythm, which coincides with loss of consciousness
    - High doses cause burst suppression pattern
    - Has anticonvulsant activity though myoclonus may present occasionally.
- Autonomic nervous system:
  - Pupillary dilation, nystagmus
  - Increased salivation and lacrimation.
- Cardiovascular system:
  - Blood pressure:
    - Increases blood pressure
    - SBP increases by 20–40 mm Hg, DBP by smaller amount
    - Rise in BP occurs progressively during first 3–5 minutes

- This is followed by a fall over next 20–30 minutes.

– Critically ill patients:
  - In these patients catecholamine stores are exhausted
  - Direct negative inotropic effect of ketamine may manifest in critically ill patients
  - Administration on ketamine may therefore cause cardiovascular collapse.
– Also increases heart rate, cardiac output, cardiac work, myocardial oxygen demand
– Enhances arrhythmogenecity of adrenaline
– Mechanisms of cardiovascular effect:
  - Direct stimulation of CNS resulting in increased central sympathetic flow
  - Inhibition of baroreceptor reflex through NMDA receptors in nucleus tractus solitarius
  - Inhibition of norepinephrine reuptake in postganglionic sympathetic nervous system: Results in increased plasma catecholamine concentration.

- Respiratory system:
  – Ventilation:
    - No significant depression of ventilation occurs
    - Has no effect on central respiratory drive
    - Ventilatory response to CO_2 is preserved
    - Breathing frequency reduced for 2–3 minutes after administration
    - Apnea can occur with large dose/with concomitant benzodiazepines.
  – Upper airway reflexes:
    - Airway reflexes are preserved
    - However airway is not completely protected as silent aspiration may occur.
  – Salivary and tracheobronchial secretions:
    - Ketamine increases tracheobronchial and salivary secretion
    - Secretions are especially problematic in children as it causes laryngospasm
    - Pretreatment with anti-sialogogues mandatory.
  – Bronchodilation:
    - Maybe useful in asthmatics
    - Bronchodilation occurs due to:
      ° Reduced uptake of catecholamines
      ° Increased levels of circulating catecholamines
      ° Muscarinic antagonism
      ° Inhibition of Ca^{2+} channel.
- Coagulation: Inhibits platelet aggregation by reducing formation of inositol 1, 4, 5 – triphosphate
- Hepatic and renal function: Not significantly altered.

Clinical Uses

- Analgesia:
  – 0.2–5 mg/kg IV analgesic dose of ketamine
  – Indications:
    - Cancer pain
    - Chronic central and peripheral neuropathic pain
    - Fibromyalgia, migraine
    - Phantom limb and ischemic limb pain
    - Complex regional pain syndrome.
- Neuraxial analgesia:
  – 0.5–1 mg/kg neuraxial dose of ketamine
  – Mechanism of action:
    - Due to systemic and spinal effects
    - Spinal effects:
      ° Action on spinal opioid receptors
      ° LA action through sodium channels.
  – Affinity of ketamine is 10,000 times weaker than morphine
  – S(+) isomer preparations with no preservative is used
  – Preservative in the racemic mixture formulation is neurotoxic.
- Induction of anesthesia:
  – Induction doses:
    - 1–2 mg/kg IV dose
    - 4–8 mg/kg IM dose
  – Consciousness is lost in 30–60 seconds after IV administration
  – Loss of consciousness occurs 2–4 minutes after IM administration
  – Return of consciousness occurs after 10–20 minutes
  – Full orientation attained 60–90 minutes after last dose
  – No retrograde amnesia present
  – Preferred agent in:
    - Children
    - Skin grafting/debridement/burn dressing
    - Hypovolemic shock
    - Known asthmatics/bronchospasm
    - Congenital heart disease especially with right to left shunts
    - Septic shock, provided catecholamine stores are intact.

- Sedation:
  - 2 mg/kg/hr IV infusion used for postoperative sedation
  - Especially useful in pediatric patients for:
    - Cardiac catheterization
    - Radiotherapy/radiological studies
    - Dressing change
    - Dental work.
- Adjunct to regional anesthesia:
  - 0.5 mg/kg IV given along with 0.03 mg/kg midazolam
  - Used during application of painful blocks.
- Reversal of opioid tolerance:
  - Useful in reversing opioid tolerance
  - Acts through interactions between NMDA, nitric oxide pathway, and μ-opioid receptors.
- Improvement of mental depression:
  - Postoperative depression unproved in patients with mental depression
  - Improves depression apart from providing analgesia in chronic pain syndrome.
- ***Restless legs syndrome***: Inhibits neuroinflammation in spinal cord.

Contraindications

- Raised ICP, head trauma
- Open ocular injury: As ketamine increases IOP
- Ocular examination/operations: As ketamine causes nystagmus
- Schizophrenia, delirium tremens
- Coronary artery disease
- Pulmonary hypertension, right heart failure
- Systemic hypertension
- Vascular aneurysmal surgery.

Side Effects

- Central nervous system:
  - Raised intracranial pressure, myoclonus
  - Nystagmus, raised intraocular pressure
- Central nervous system: Raised systemic BP, tachycardia
- Respiratory:
  - Transient apnea in rare cases
  - Sialorrhea and laryngospasm especially in children.
- Allergic reactions: Very rare
- Tolerance and drug abuse
- Increased bleeding tendency
- Emergence reaction:
  - Description: Emergence from ketamine anesthesia is associated with visual, auditory and proprioceptive illusions which may progress to delirium.
  - Clinical features:
    - Transient cortical blindness, altered short term memory
    - Vivid and brightly colored dreams with morbid content and nightmares
    - Hallucinations:
      - May occur up to 24 hours after administration of ketamine
      - Usually disappear within a few hours
    - Extracorporeal experiences:
      - Patient feels a sensation of floating out of body
      - This is due to lack of appreciation of gravity
      - Occurs due to reduced somatic and proprioceptive sensation.
  - Incidence: Increased incidence in:
    - Females
    - Age more than 15 years: As children are unable to communicate the dreams occurance
    - Doseage more than 2 mg/kg IV
    - History of personality problems/frequent dreaming.
  - Mechanisms:
    - Due to depression of inferior colliculus and medical geniculate body
    - This causes mis-interpretation of auditory and visual stimuli resulting in illusions
    - Extracorporeal experiences due to κ-receptor stimulation.
  - Prevention:
    - Pretreatment with benzodiazepines: Midazolam best
    - Coadministration of thiopental, inhaled anesthetics or propofol
    - Benzodiazepines given 5 minutes IV before ketamine usage
    - Prospective discussion with patients about side effects.

Drug Interactions

- Hemodynamic depression rather than stimulation when used with:
  - Inhaled agents
  - Diazepam/midazolam
  - Verapamil

- Enhances neuromuscular blocking actions of non-depolarizing drugs
- Pancuronium enhances cardiac stimulating properties
- Succinylcholine apnea may be prolonged
- Seizures when aminophylline is given along with ketamine
- When used with tricyclic antidepressants (TCAs):
  - TCAs and ketamine prevent norepinephrine reuptake
  - This results in severe hypotension, cardiac failure and myocardial ischemia.

MIDAZOLAM[1,2,3,7,20]

Introduction

This is a commonly used short acting benzodiazepine.

Chemistry

- Water soluble compound
- Imidazole ring present which accounts for:
  - Water solubility
  - Short duration of action
  - Rapid metabolism
- Nonchiral in nature: No isomers.

Preparation

- Clear, colorless solution
- 1/2/5 mg/ml of solution for IV injection
- Midazolam syrup preparation has 2 mg/ml
- Acidic pH of 3.5
- Compatible with lactated Ringers solution
- Characterized by pH dependent ring opening phenomenon:
  - At pH less than 4, ring remains open and thus it is water soluble
  - At pH more than 4 (physiological pH), ring closes and it becomes a highly lipid soluble drug.

Mechanism of Action

- Acts mainly through BZD receptors:
  - Found at synapses concentrated in cortex and midbrain
  - These are closely related to $GABA_A$ receptors
  - BZD receptors facilitate $GABA_A$ receptor opening
  - *This opens up chloride channels:* Causes hyperpolarization of the synaptic membrane.
- Kappa opioid agonist activity which explains spinal analgesia.

Routes of Administration

- Oral administration: 0.25 mg/kg given as 2 mg/ml syrup
- Intramuscular administration: 0.07–0.08 mg/kg
- Intravenous administration: 0.02–0.03 mg/kg
- Intrathecal administration: 0.3–2 mg given usually
- Epidural administration: 0.03–0.05 mg/kg.

Pharmacodynamics

- Central nervous system:
  - Hypnosis, sedation, anxiolysis
  - *Anterograde amnesia* which is more potent and longer lasting than sedative effect
  - Reduces cerebral metabolic oxygen requirements which has a ceiling effect
  - Reduces cerebral blood flow, especially in regions associated with arousal, attention and memory
  - Little or no change in intracranial pressure
  - Potent anticonvulsant, no cerebroprotective effects
  - When administered intrathecally or epidurally, it has antinociceptive effect
  - Muscle relaxant through actions on spinal internuncial gamma neurons.
- Cardiovascular system:
  - Reduces systolic BP by 5% and diastolic BP by 10%
  - *No effect on cardiac output*: Most useful in congestive cardiac failure
  - Reduces peripheral vascular resistance
  - Increases heart rate.
- Respiratory system:
  - Reduction in tidal volume but increase in respiratory rate
  - Dose dependant reduction in ventilation with 0.15 mg/kg IV
  - Transient apnea with doses more than 0.15 mg/kg
  - Impaired ventilatory response to hypercapnea
  - Better avoided in COPD patients
  - Ventilatory depression more when 0.05 mg/kg IV used for induction.
- Others:
  - Reduces hepatic and renal blood flow
  - Reduces adrenergic but not cortisol response to stress

- Inhibits phagocytosis and leucocyte bactericidal activity.

Pharmacokinetics

- Absorption:
  - Absorbed well and very quickly when given orally
  - Oral bioavailability 50%
  - IM bioavailability 80–100%
- Distribution:
  - V_d of 1–1.5 L/kg may increase to 3 L/kg in critically ill patients
  - 96% plasma protein bound
  - Short duration of action due to:
    - High lipid solubility
    - Rapid redistribution
    - Short context sensitive half time: Can be used for continuous infusion.
- Metabolism:
  - By hepatic and small intestinal by cytochrome P450
  - Converted to 1 and 4 hydroxy-midazolam
  - 1-hydroxy-midazolam has half the activity of midazolam
  - This may be responsible for prolonged sedation in renal insufficiency
  - Metabolism is slowed in the presence of cytochrome P450 inhibitors:
    - Cimetidine, erythromycin
    - Calcium channel blockers, antifungal drugs
  - Hepatic clearance is also reduced by concomitant fentanyl administration
  - Finally 1 and 4 OH-midazolam are conjugated with glucuronide.
- Excretion:
  - In urine as glucuronide conjugates
  - Renal impairment has little effect
  - Elimination half life of 1.5–3.5 hours
- Onset of action within 30–60 seconds
- Peak effect within 3–5 minutes
- Duration of action 15–80 minutes.

Uses

- Preoperative medication:
  - Most commonly used premedication in children for conscious sedation
  - Oral midazolam syrup 2 mg/ml in dose of 0.25 mg/kg
  - Administered at least 20 minutes prior to surgery.
- Intravenous sedation:
  - 0.03–0.05 mg/kg given IV
  - Continuous IV infusion can be used at 4 µg/kg/min
  - Useful for:
    - Endoscopy and procedures performed under local anesthesia
    - Monitored anesthesia care
  - Used with caution in patients with COPD and old age.
- Induction of anesthesia:
  - 0.1–0.2 mg/kg IV
  - Causes slower onset of unconsciousness compared with thiopental
  - Onset can be quickened by prior administration of opioids
  - Fentanyl 50 or 100 µg IV can be given preceding midazolam by 1–3 minutes.
- Maintenance of anesthesia:
  - 0.25 to 1 mg/kg/hour
  - Used as supplement to opioids and propofol
  - Reduces MAC of volatile agents by around 15%
  - Produces gradual awakening which is rarely associated with nausea or emergence reactions.
- Postoperative sedation: 1–7 mg/hr IV in intubated patients
- *Paradoxical vocal cord motion:*
  - Causes nonorganic upper airway obstruction and stridor
  - Midazolam 0.5–1 mg IV can be used effectively
- Chronic pain including deafferentiation syndrome.

Side Effects

- Occasional discomfort at site of injection
- Ventilatory depression and apnea especially with doses > 0.15 mg/kg
- Withdrawal phenomenon like irritation and insomnia in prolonged infusions
- Transient apnea in geriatric patients and those with COPD
- May accelerate cognitive decline in elderly patients with long-term use
- May inhibit platelet aggregation by causing conformational change in platelet membranes.

Drug Interactions

- Antacids and food reduce absorption from GIT
- Cimetidine, erythromycin, calcium channel blockers inhibit metabolism of midazolam

- Metabolism of midazolam is also inhibited by fentanyl
- Alcohol, inhaled anesthetics, opioids and α_2 agonist exert synergistic sedative effects
- Analgesic actions of opioids are reduced by BZDs
- Depressant actions of opioids are potentiated by BZDs
- Flumazenil:
  - It is specific antagonist at BZD receptor
  - Reverses all effects except respiratory depression.

DIAZEPAM[1,2,3,7,20]

Chemistry

- Lipid soluble benzodiazepine.
- Nonchiral compound with no isomers.

Presentation

- Available as tablets containing 2/5/10 mg
- Syrup contains 0.4 mg/1 mg/ml
- 10 mg suppository or 2/4 mg/ml solution available for rectal administration
- Clear yellow solution with 5 mg/ml for IM/IV injection
- Insoluble in water and thus dissolved in organic solvent like propylene glycol
- Slightly acidic with pH of 6.6–6.9
- Also available as soybean formulation for IV injection.

Mechanism of Action

- Acts mainly through BZD receptors:
  - Found at synapses concentrated in cortex and midbrain
  - These are closely related to $GABA_A$ receptors
  - BZD receptors facilitate $GABA_A$ receptor opening
  - This opens up chloride channels: Causes hyperpolarization of the synaptic membrane.
- Kappa opioid agonist activity which explains spinal analgesia.

Routes of Administration

- Oral dose of up to 60 mg/day in divided doses in adults
- Intravenous dose: 5–20 mg, increasing according to clinical effect
- Rectally used in children with febrile seizures.

Pharmacodynamics

- Central nervous system:
  - Anxiolytic and decreases aggression
  - Paradoxical excitement may occur
  - Sedation, hypnosis, a*nterograde amnesia*
  - Anticonvulsant activity:
    - Act by selectively inhibiting limbic system especially hippocampus
    - This is different from bartiturates
    - Barbiturates inhibit seizures by nonselective CNS depression.
  - Analgesic: Especially with spinal analgesia
  - Muscular relaxation through actions on spinal gamma internuncial neurons.
- Cardiovascular system:
  - Transient reduction in BP and systemic vascular resistance
  - Reduction in cardiac output
  - Reduction in myocardial oxygen consumption
  - Coronary blood flow increases secondary to coronary vasodilation.
- Respiratory system:
  - Ventilatory depression causing reduced tidal volume
  - Large doses may produce apnea
  - Ventilatory depression reversed by surgical stimulation but not by naloxone
  - Depressant action exaggerated in:
    - Patients with COPD
    - Concomitant administration of other CNS depressants (alcohol, opioids).

Pharmacokinetics

- Absorption:
  - Rapidly absorbed after oral and rectal administration
  - Bioavailabitity of 86–100%
  - Absorption after intramuscular administration is slow and erratic.
- Distribution:
  - Volume of distribution:
    - V_d of 1–1.5 L/kg
    - Increase in fat content of body, as with old age and female gender, increases the V_d
  - Plasma protein binding:
    - 96–98% plasma protein bound, mainly to albumin

- Reduced levels of plasma proteins:
  - Occurs in cirrhosis and CRF
  - Reduction in plasma levels of albumin occurs
  - This causes a reduction in plasma protein binding
  - Increased propensity of side effects of diazepam occurs.

– Diazepam rapidly crosses placenta.

- Metabolism:
  – Metabolized by hepatic microsomal enzymes by N-demethylation (oxidation)
  – Desmethyl-diazepam, oxazepam and temazepam are the active metabolites formed
  – Contribute to return of drowsiness which occurs 6–8 hours after administration of diazepam
  – Metabolites are then conjugated with glucuronide
  – Metabolism is inhibited by cytochrome P450 enzyme inhibitors
  – Enterohepatic circulation present.
- Elimination:
  – Excreted in urine as glucuronide derivative
  – Less than 1% is excreted unchanged
  – Elimination half-life of 20–40 hours
  – This is prolonged in cirrhosis due to reduced protein binding of drugs
  – Elimination half life also prolonged in elderly due to fat content causing increased Vd
  – Context sensitive half time longer than midazolam.

Uses

- Short-term treatment of anxiety
- Premedication in adults
- Status epilepticus, febrile seizures in children
- Delirium tremens and alcohol withdrawal (second drug of choice to chlordiazepoxide)
- Treatment of local anesthetic induced seizures 0.1 mg/kg IV
- Tetanus, lumbar disk prolapse and other spastic conditions for muscle relaxation.

Side Effects

- Drowsiness, ataxia, headache
- Tolerance, dependence
- Withdrawal symptoms: Insomnia, anxiety, confusion, psychosis, perceptual disturbances
- Gastrointestinal: Nausea, vomiting, abdominal pain
- Allergic reactions and rashes
- Thrombophlebitis:
  – Highly irritant to veins
  – Soybean oil preparation is less irritant and may be preferred
- CNS intoxication when plasma concentration is 1000 ng/ml
- Ventilatory depression especially in COPD and old patients.

Drug Interactions

- Reduces MAC value of inhaled anesthetic
- Diazepam potentiates nondepolarizing muscle relaxants
- Cimetidine reduces clearance of diazepam by inhibiting cytochrome P450
- Drug cannot be removed by hemodialysis due to the high protein binding
- Synergistic CNS depression on administration with opioids and alcohol.

REMIFENTANYL[1,2,3,7,20]

Introduction

Ultra short-acting synthetic opioid with ester side chain, susceptible to metabolism by blood and tissue esterases.

Mechanism of Action

- 4-anilido-piperidine compound
- Pure μ-receptor agonist
- μ-receptor stimulation causes intracellular calcium accumulation
- This increases K^+ conductance causing hyperpolarization of excitable cell membranes
- This reduces membrane excitability causing pre- and post-synaptic effects.

Pharmacodynamics

- Central nervous system:
  – Minimal sedative/hypnotic activity
  – Dose dependant analgesic effects
  – Peak effect occurs between 1–3 minutes
  – Concentration dependant slowing of EEG
  – Muscle rigidity with bolus doses
  – Drug is injected over 60 seconds to avoid muscle rigidity
  – Lesser suppression of motor evoked potentials (compared with other opioids)
  – Preserves cerebral autoregulation (if < 0.5 μg/kg/min)
  – Miosis from stimulation of Edinger-Westphal nucleus
  – MEAC = 0.75 ng/ml.

- Respiratory system:
  - Dose dependent ventilatory depression (maximum with 2 µg/kg IV)
  - Reduces tidal volume and respiratory rate
  - Reduces ventilatory response to hypoxia and hypercarbia
  - No bronchospasm as it does not cause histamine release
  - Respiratory parameters recover more rapidly than other opioids.
- Cardiovascular system:
  - Brief increase in systolic BP and heart rate if bolus dose > 1 µg/kg is given
  - Dose dependent reduction in SBP and heart rate otherwise (causes 20% reduction in MAP)
  - Greater hemodynamic changes in CAD patients
  - May also reduce contractility and cardiac output.
- Gastrointestinal:
  - Dose dependant nausea and vomiting
  - Delays gastric emptying and biliary drainage
  - Effects resolve more quickly.

Pharmacokinetics

- Ultra short acting opioid
- Termination of action by:
  - Redistribution of drug from effect site
  - Hydrolysis by blood and tissue nonspecific esterases.
- Absorption:
  - Not effective orally
  - Volume of distribution: 0.3–0.5 L/kg
  - 70% plasma protein bound.
- Metabolism: By blood and tissue nonspecific esterases
- Excretion:
  - Clearance = 3–5 L/min
  - Elimination half-life = 10 minutes
  - Context sensitive half-life = 4 minutes after 4 hour infusion.

Uses in Anesthesia

- Induction and maintenance of anesthesia
- Conscious sedation in ESWL and colonoscopy
- Component of TIVA
- Fast-track cardiac anesthesia
- Postoperative analgesia
- Reduces MAC of isoflurane by 65%
- Reduces MAC-BAR by 60%
- Obstetric analgesia.

Dosage and Administration

- Induction of general anesthesia:
  - Opioid induction: 2–5 µg/kg bolus
  - Balanced anesthesia: 1 µg/kg over 60 seconds followed by 0.25–0.5 µg/kg/min.
- Maintenance of anesthesia:
  - Balanced anesthesia: 0.2–0.25 µg/kg/min
  - High dose opioid maintenance: 1–3 µg/kg/min
  - Nitrous-narcotic technique: 0.6 µg/kg/min
  - Cardiac surgery: 1–3 µg/kg/min and reduced during hypothermia.
- TIVA: 0.25–0.5 µg/kg/min
- Conscious sedation:
  - 12.5–25 µg boluses intermittently
  - 0.01–0.2 µg/kg/min infusion
  - 0.2–0.25 µg/kg/min for colonoscopy/ESWL
  - 0.05–0.1 µg/kg/min as an adjunct to LA or RA.
- Postoperative pain: 0.05–0.15 µg/kg/min
- Monitored anesthesia care:
  - 0.1 µg/kg/min given 5 minutes prior to stimulus
  - Wean to 0.05 µg/kg/min as tolerated
  - Adjust, increase/decrease in increments of 0.025 µg/kg/min
  - Reduce dose accordingly at the time of administration of midazolam/propofol
  - Avoid administration of bolus doses.
- Labor analgesia:
  - May have maternal, fetal and neonatal side effects
  - 0.2–1 µg/kg boluses with lock out intervals of 1–5 minutes
  - 0.1 µg/kg/min infusion may be used.

Dose Adjustments

- Pediatric patients may require twice as much remifentanyl (0.15 µg/kg/min)
- 50% reduction in dose required in old age
- No dosage adjustments required in CRF.

Side Effects

- Respiratory depression
- Muscle rigidity
- Transient hypertension and tachycardia, bradycardia
- Postoperative shivering and pruritus
- *Subjective side effects*: Dry mouth, itching, flushing, sweating
- Impaired performance of psychomotor tests.

Disadvantages

- Rapid loss of analgesia with development of opioid induced hyperalgesia postoperatively

- Opioid tolerance
- Intraoperative awareness as it has minimal hypnotic properties.

Contraindications

Not used in spinal/epidural as additive as the preparation has glycine.

CLONIDINE[1,2,3,7,20]

Introduction

Selective partial α_2 agonist which is an aniline derivative .

Mechanism of Action

Primarily sympatholytic action:

Acute Use

- Direct action:
  - Direct sympatholytic action on spinal preganglionic sympathetic neurons
  - This reduces sympathetic tone and increases vagal tone.
- Indirect action:
  - Stimulates prejunctional α_2 receptors as it is structurally similar to norepinephrine
  - This opens up K^+ channels and presynaptic Ca^{2+} channels
  - This causes inhibition of adenylyl cyclase resulting in reduced neurotransmitter release
  - Therefore, postsynaptic transmission reduces from pontine locus ceruleus
  - This results in sedation and analgesia
  - Also, reduced postsynaptic transmission causes reduced central sympathetic outflow
  - This results in hypotension and bradycardia.

Chronic Use

Acts by reducing responsiveness of blood vessels to vasoactive substances and sympathetic stimulation.

Pharmacokinetics

- Absoption:
  - Rapidly absorbed orally
  - Oral bioavailability around 70–90%.
- Distribution:
  - 20–40% plasma protein bound
  - Volume of distribution 2 L/kg
  - Peak plasma levels in 60–90 minutes.
- Metabolism and excretion:
  - Half life = 12–24 hours
  - 50% metabolized in liver to glucoromide conjugates
  - 50% excreted unchanged in urine
  - Elimination half-life = 9–12 hours.
- Duration of action:
  - Hypotension after single dose for 8 hours
  - Transdermal administration requires around 48 hours to achieve therapeutic levels.

Pharmacodynamics

- Receptor-wise action:
  - α_{2a}: Sedation, analgesia, anxiolysis
  - α_{2b}: Reduces shivering and vasoconstriction
  - α_{2c}: Startle response
  - α_2: α_1 = 220:1 for clonidine.
- Central nervous system:
  - Supraspinal (*locus ceruleus*), spinal (*substantia gelatinosa*) and peripheral analgesia
  - Sedative and anxiolytic
  - Reduces shivering and cerebral blood flow
  - Reduces IOP.
- Cardiovascular:
  - Cardioprotective properties
  - Hypotension (due to reduces central and peripheral sympathetic outflow)
  - Reduction in SBP more than reduction in DBP
  - Transient HTN may occur immediately after injection due to α_1 action
  - No effect on baroreceptor reflexes
  - Bradycardia, well maintained cardiac output.
- Respiratory:
  - Does not induce profound respiratory depression
  - Mildly potentiates opioid induced respiratory depression.
- Gastrointestinal: Reduces gastric motility, antisialogogue
- Genitourinary: Maintains GFR and renal blood flow
- Endocrines: Reduces catecholamine, renin levels and insulin secretion.

Indications

- Anesthetic indications:
  - Premedication:
    - Oral 2.5–4.5 µg/kg preoperatively reduces anxiety
    - Transdermal patch:
      - 0.2 µg/day patch is applied on the night before surgery
      - This is continued for 72 hours postoperatively.

  - Protection against perioperative MI:
    - 300 µg clonidine P.O 90 minutes before surgery
    - This is continued for 72 hours at 200 µg/day .
  - Induced hypotension
  - Reduce intubation response
  - Analgesia:
    - Epidural clonidine for reflex sympathetic dystrophy, intraop and postop pain
    - 1–1.5 µg/kg IV bolus (up to 2 µg/kg)
    - 1–2 µg/kg/hour IV infusion.
  - As an additive to prolong neuraxial blockade
  - Postoperative shivering:
    - 75 µg bolus can be given IV
    - 1 µg/kg as it reduces vasoconstriction.
  - Postoperative nausea and vomiting
  - PICU sedation: 1 µg/kg/hour with midazolam 350 µg/kg/hour
  - Clonidine can be used with lidocaine for IVRA.
- Nonanesthetic uses:
  - Severe hypertension, rennin dependant HTN: 0.2–0.3 mg/day
  - Pheochromocytoma:
    - Aids in diagnosis of pheochromocytoma
    - 300 µg clonidine is administered orally
    - This reduces catecholamine concentration in normal patients
    - Catecholamines remain raised in the presence of pheochromocytoma
  - Treatment of opioid withdrawal, panic disorder
  - Treatment of cancer chemotherapy associated emesis and diabetic diarrhea
  - Treatment of spasticity, attention deficit hyperkinetic disorder, schizophrenia.

Dose

- 1–2 µg/kg: IV, IM, caudal, spinal and epidural routes
- 2–4 µg/kg: Rectal and nasal routes
- 4–5 µg/kg: Oral dose
- 0.2 mg/day via transdermal route.

Anesthetic Advantages

- General anesthesia:
  - Reduced anesthetic requirements:
    - Volatile anesthetics:
      - Reduced by 40–60% if acute clonidine use
      - Reduced by 10–20% if on chronic clonidine therapy
    - Also has opioid sparing and MAC sparing properties.
  - Hemodynamics:
    - More stable cardiovascular course
    - Reduced stress response
    - Reduces laryngoscopic and intubation response
    - Obtunds tourniquet induced hypertension.
  - Postoperative:
    - Better pain relief especially postoperatively
    - Reduces postoperative agitation in children
    - Reduces postoperative shivering, nausea and vomiting
    - Reduces postoperative oxygen consumption.
  - Others:
    - Reduced dose of cardioactive anesthetics
    - Blocks narcotic induced muscle rigidity
    - Reduces propofol requirement for LMA insertion.
- Regional anesthesia:
  - Prolongs duration of analgesia (50% prolongation of bupivacaine)
  - Reduces peak plasma concentration of local anesthetics
  - Slight sedation provided for 1 to 3 hours postoperatively
  - Does not cause urinary retention after neuraxial block
  - Reduces duration of motor block.

Side Effects

- Drowsiness, dry mouth, constipation, impotence
- Bradycardia and hypotension (especially if intrathecal dose ≥ 150 µg)
- Orthostatic hypotension (rare)
- Rashes (rare) and fluid retention
- Glucose intolerance
- Rebound hypertension:
  - Occurs in patients taking more than 1.2 mg/day
  - Occurs 18 hours after sudden discontinuation of clonidine
  - Lasts for around 72 hours
  - Characterized by:
    - Hypertension and tachycardia
    - Insomnia, flushing, headache, apprehension, and sweating.
  - Treatment:
    - Hydralazine, SNP
    - Restart clonidine (transdermally if patient has vomiting).

Drug Interactions
- Coadministration of TCAs, phenothiazines and butyrophenones can precipitate hypertensive crisis
- Reduces anesthetic requirements.

Contraindications
- Avoid in first 6 months of life as respiratory depression can occur due to reduced clearance in neonates
- Reduce dose if GFR is less than 10 ml/min and in liver disease.

DEXMEDETOMIDINE[1,2,3,7,20]

Introduction
Selective and complete α-agonist introduced in 1999 which is more selective for α_2 receptors than clonidine.

Chemistry
- D-enantiomer of medetomidine
- High ratio of specificity for α_2 receptors ($\alpha_1 : \alpha_2 = 1600:1$)
- Belongs to imidazole subclass of α_2 agonists
- Freely soluble in water.

Pharmacokinetics
- Distribution:
  - 94% plasma protein bound
  - Volume of distribution 2–3 L/kg
  - Rapid onset of action within 5 minutes
  - Peak effect within 15 minutes
  - Context sensitive half-life:
    - 4 minutes after 10 minute infusion
    - 250 minutes after 18 hours infusion.
- Metabolism: Metabolized in liver:
  - N-methylation and hydroxylation reactions
  - This is followed by conjugation with glucuronide.
- Elimination:
  - Via kidney and feces
  - Elimination half-life 2–3 hours
  - Clearance of 10–30 ml/kg/min.

Mechanism of Action
- Dexmedetomidine selectively activates α_2 receptors (G-protein coupled receptors)
- 3 types of α_2 receptors exist:
  - α_{2a} receptors:
    - Present in peripheral tissues
    - *Postsynaptic* α_{2a} stimulation causes vasoconstriction
    - *Presynaptic* α_{2a} stimulation inhibits norepinephrine release
    - This inhibits vasoconstriction.
  - α_{2b} and α_{2c} receptors:
    - Present in brain and spinal cord
    - α_{2b} and α_{2c} stimulation causes sympatholysis, sedation and analgesia.
- α_2 activation by dexmedetomidine causes the following changes:
  - Reduction in activity of adenylyl cyclase
  - Increase in K^+ channel activity
  - Inhibition of opening of voltage gated Ca^{2+} channels.

Pharmacodynamics
- Central nervous system:
  - Causes arousable sedation
  - Sedation: hypnosis (α_2 stimulation in locus ceruleus)
  - Analgesia:
    - Supraspinal analgesia: Locus ceruleus
    - Spinal analgesia: Substantia gelatinosa.
  - Anxiolysis, dose dependant amnesia
  - Preserves cerebral oxygen supply-demand ratio
  - Reduces cerebral blood flow by α_2 mediated vasoconstriction
  - Reduces cerebral metabolic rate.
- Respiratory system:
  - Reduces minute volume
  - Maintains ventilatory response to carbon dioxide
  - Demonstrates hypercarbic arousal phenomenon like natural sleep.
- Cardiovascular system:
  - Reduces heart rate, SVR, myocardial contractility and cardiac output
  - Hypotension and bradycardia for 5 minutes after loading dose
  - Limiting bolus dose to 0.4 µg/kg reduces incidence of hypotension
  - Reduces incidence of perioperative MI
  - Increases sweating threshold, reduces vasoconstriction and shivering threshold.

Side Effects
- Systemic hypotension with rapid IV boluses (give less than 0.4 µg/kg over 20 minutes)
- Bradycardia, AV dissociation, sinus arrest/cardiac arrest
- Dryness of mouth, transient hypertension.

Uses

- ICU sedation:
  - FDA approved for sedation less than 24 hours duration in adults
  - Loading dose of 0.5–1 µg/kg followed by 0.1–1 µg/kg/hr infusion
  - Has opioid sparing properties with more stable hemodynamics
  - Useful for conducting daily wake-up tests in mechanically ventilated patients
  - Reduced incidence of delirium and coma.
- Off-label indications:
  - Premedication:
    - 0.33–0.66 µg/kg IV given 15 minutes before surgery
    - 1 µg/kg given transmucosal
    - 3–4 µg/kg given orally
    - 2.5 µg/kg IM given 45–90 minutes before surgery
    - Advantages of dexmedetomidine premedication:
      - Reduces thiopentone requirement by 30%
      - Reduces volatile anesthetic requirement by 25%.
  - Maintenance of anesthesia:
    - 0.5–0.8 µg/kg IV bolus
    - Followed by 0.4 µg/kg/hr infusion
    - Advantages:
      - Opioid sparing properties
      - Reduces narcotic requirement in OSAS patients
      - Low postoperative pain scores.
  - TIVA: Useful when:
    - Spontaneous ventilation has to be maintained
    - Access to airway difficult
    - Rapid awakening is required.
  - Monitored anesthesia care:
    - Dose: 0.7 µg/kg/min IV infusion
    - Indications:
      - Patients receiving LA/RA
      - Pediatric patients undergoing MRI
      - Awakes craniotomies requiring patient cooperation
      - Awake carotid end-arterectomy
      - Cardiac catheterization studies in children
      - Awake fiberoptic intubation:
        * 1 µg/kg loading dose IV over 10 minutes
        * 0.2–0.7 µg/kg/hr maintenance dose.
  - IVRA: 0.5 µg/kg added to lidocaine improves quality of anesthesia and postoperative analgesia
  - Treatment of narcotic, benzodiazepine, alcohol and recreational drugs withdrawal.

Advantages

- Excellent sedation
- Potentiates benzodiazepine induced hypnosis and opioid induced analgesia
- Potent MAC sparing and opioid sparing properties
- Reduces BP, heart rate and plasma catecholamine levels
- Little respiratory depression while weaning off mechanical ventilation
- Improved cardiac outcome in noncardiac patients
- Reduces emergence delirium associated with ketamine.

Drug Interactions

- Sedation antagonized with ***atipamezole*** 50 µg/kg (α_2 antagonist)
- Reduces volatile anesthetic requirements (by 25%)
- Reduces opioid requirements
- Potentiates benzodiazepine mediated hypnosis and opioid analgesia
- INH and other cytochrome inhibitors may increase dexmedetomidine levels.

MAGNESIUM SULFATE[1,2,3,7,20]

Introduction

- Mg^{2+} is the second most prevalent intracellular cation after K^+
- Therapeutic range = 4–6 mEq/L.

Presentation

- Clear, colorless solution
- Contains 2.03 mmol/L of ionic Mg^{2+}.

Physiology

- It is a natural physiological antagonist of calcium
- Up to one half of total body magnesium is present in bones (50%)
- 20% is present in skeletal muscle
- 1% is present in ECF, 30% is plasma protein bound
- Activates up to 300 enzyme systems
- ATP becomes fully functional only after chelation to magnesium

- Regulates calcium access into cells and action of calcium within cells
- Presynaptic release of ACH depends on action of magnesium.

Mechanism of Action

- Anticonvulsant action:
  - Mechanism is unclear
  - CNS depressant action
  - Reduces CNS irritability
  - Secondary action through cerebral vasodilation which reverses cerebral vasospasm.
- Muscle relaxation:
  - Reduces NMJ irritability
  - Reduces presynaptic release of ACH
  - Reduces sensitivity to ACH
  - Reduces uptake and binding of intra cellular Ca^{2+}
- Antihypertensive actions:
  - Vasodilatation by direct action on blood vessels
  - Reduces sympathetic tone by sympathetic blockade
  - Reduces catecholamine release.

Pharmacodynamics

- Central nervous system:
  - CNS depressant, reduces CNS irritability
  - Anticonvulsant
  - Possible analgesic effect by antagonism at NMDA receptors.
- Cardiovascular system:
  - Cardioprotective action
  - Vasodilation, reduces SVR, hypotension
  - Slows SAN impulse formation and prolongs SA conduction time
  - Prolongs PR interval and AV nodal effective refractory period: Bradycardia
  - Attenuates arrhythmogenic and vasoconstrictive action by adrenaline
  - Reduces reperfusion injury with minimal myocardial depression.
- Respiratory system:
  - Effective bronchodilator due to smooth muscle relaxation
  - Attenuates hypoxic pulmonary vasoconstriction
  - Maintains intact respiratory drive.
- Gastrointestinal:
  - Osmotic laxative if given orally
  - Antacid properties.
- Genitourinary:
  - Renal vasodilatation, diuresis
  - Uterine tocolytic, increased placental perfusion.
- Others:
  - Inhibits platelet function
  - Prolongs clotting time
  - Reduces thromboxane A_2 synthesis
  - Inhibits thrombin induced platelet aggregation.

Pharmacokinetics

- Absorption: 25–65% of ingested magnesium is absorbed
- Distribution: 30% plasma protein bound
- Excretion: More than 50% of magnesium dose is excreted in kidney.

Clinical Uses

- Central nervous system:
  - Subarachnoid hemorrhage:
    - Reduces new ischemic deficits and improves outcome
    - To be started within 4 days of subarachnoid hemorrhage.
  - Postoperative shivering: 30 mg/kg IV
  - Cerebral edema.
- Cardiovascular system:
  - Antiarrhythmic:
    - 1–2 gm IV over 5–10 minutes
    - Followed by 1–2 gm/hour IV
    - Alternatively, 25–50 mg/kg IV over 10–20 minutes.
  - For treatment of:
    - Torsades-de-pointes, QTc prolongation
    - Intractable VT, VF, multifocal atrial tachycardia
    - Dysrhythmias associated with:
      - Alcoholism
      - Hypokalemia
      - Digitalis toxicity
      - MI, catecholamine release
      - Postcardiac surgery.
  - In supraventricular tachycardias:
    - 2–2.5 gm IV bolus followed by 1.75 gm/hr infusion
    - Rarely used now: Only used for rate control in SVT.
  - As a component of cardioplegia: To reduce effects of calcium

  - To treat autonomic hyper-reflexia secondary to spinal cord injury.
- Respiratory system:
  - Suppression of intubation response
  - To reduce fasciculation after succinylcholine administration
  - Management of intractable bronchospasm
  - Spasms occurring with tetanus
- Gastrointestinal system:
  - As a component of total parental nutrition
  - Antiaspiration prophylaxis: Antacid properties of MgO useful.
- Genitourinary:
  - Severe PIH:
  - *Drug of choice* for seizure control and prevention
  - IV regimen:
    - 4 gms in 20% solution IV given over 10 minutes
    - This is followed by 1 gm/hour infusion
    - Alternatively, 40–60 mg/kg IV bolus followed by 15–30 mg/kg/hr.
  - IM regimen:
    - 5 gms (10 ml of 50% solution) IM in both buttocks
    - This is followed by 5 gms Q4H in alternate buttocks
    - Continued till 24 hours postpartum.
  - Preterm labor:
    - 4 gms IV over 15 minutes loading dose
    - This is followed by 1–4 gm/hr infusion.
  - Antepartum hemmorrhage.
- Dyselectrolytemias:
  - Hypomagnesemia
  - Refractory hypokalemia
  - Refractory hypocalcemia.
- Others:
  - Thrombophlebitis
  - Malignant hyperthermia therapy
  - Patients undergoing pheochromocytoma resection
  - Patients undergoing surgeries involving aortic cross-clamping
  - Barium poisoning.

Interactions

- Neuromuscular blocking agents:
  - Prolongs action of NMBAs (by reducing ACH release and sensitivity to ACH)
  - 30–50% of normal dose of NMBAs used in the presence of $MgSO_4$
  - More interaction seen with vecuromium.
- Succinylcholine:
  - Prevents K^+ release and reduces fasciculations
  - Reduces incidence and severity of muscle pain
  - May prolong phase-II block.
- Opioids: Enhances sedative action of opioids.

Side Effects

- Minor side effects: Warmth, flushing, nausea, headache, dizziness
- May cause fetal and neonatal hypermagnesemia when used in PIH
- Pain on IM injection of $MgSO_4$
- Reduced DTR is useful sign to predict magnesium toxicity.

Serum level[1]	Clinical features
2.5–5 mg/dl	Reduced cardiac conduction, nausea
	Wide QRS
	Increased PR interval
5–7 mg/dl	Sedation and hypoventilation
	Reduced deep tendon reflexes
	Muscle weakness
7–12 mg/dl	Hypotension
	Bradycardia
	Diffuse venous dilation
	Loss of DTR
More than 12 mg/dl	Areflexia
	Respiratory paralysis
	Coma
	Cardiac arrest, complete heart block

SUGAMMADEX[1,2,3,7,20]

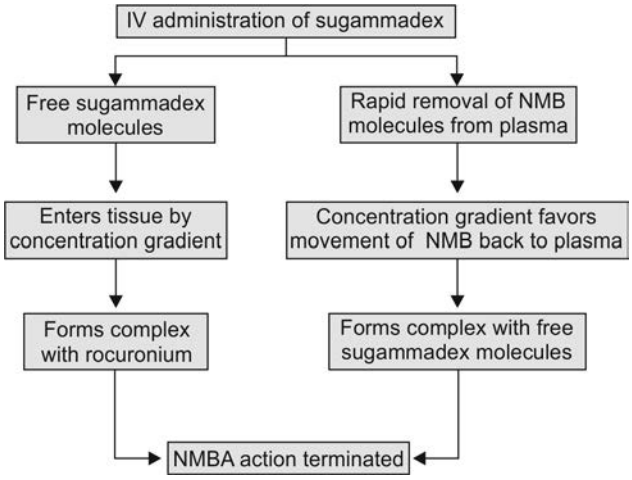
Introduction

- Novel selective reversal binding agent
- Also called ORG 25969.

Structure

- Modified γ-cyclodextrin
- Lipophilic core and hydrophilic periphery
- Modification of the γ-cyclodextrin extended the cavity size
- This allowed greater encapsulation of rocuronium molecule.

Mechanism of Action



Pharmacokinetics

- Volume of distribution = 12–15 L
- Plasma half-life = 2.2 hours
- No metabolism occurs
- Clearance = 90 mL/min.

Key Features

- Unique mode of action
- Rapid reversal from any depth of NM blockade
- Faster speed of reversal than neostigmine
- Usually well tolerated
- Low risk of residual blockade
- Dosing for multiple situations: Immediate, moderate and deep block reversal.

Advantages

- Useful in conditions where succinylcholine is contraindicated:
  - Ocular surgeries
  - Hyperkalemia
  - Burns
- Avoids side effects of SCH
- Useful for RSI with rocuronium
- Avoids need and side effects of cholinesterase inhibitors
- 9–12 times faster than neostigmine
- Immediate reversal of NMBA (3 minutes after rocuronium dose)
- Recurarization is rare and occurs only insufficient sugammadex doses
- Same efficacy for vecuronium and rocuronium but as vecuronium is 7 times more potent, blockade is less.

Dosage

- Routine reversal:
  - 2 mg/kg given IV
  - Used if some amount of spontaneous recovery has occurred
  - Up to occurence of T2 following NMB.
- Profound blockade:
  - 4 mg/kg given IV
  - Used if 1–2 post-tetanic convulsions have occurred
- Immediate reversal:
  - 16 mg/kg given IV
  - Used within 3 minutes after rocuronium administration.

Side Effects

- Interacts with remifentanyl
- Anaphylaxes
- Caution in patients with renal dysfunction
- Impairment of taste (bitter metallic taste).

Present Status

- Still undergoing trials
- Has no effect on succinylcholine/mivacurium/atracurium
- Not used regularly due to concern over rare allergic reactions.

EPHEDRINE[1,2,3,7,20]

Introduction

Sympathomimetic amine used as a stimulant, appetite suppressant, concentration aid, decongestant and to treat hypotension associated with anesthesia.

Chemistry

- Alkaloid derived from ephedra vulgaris
- Four stereoisomers are present: D(+) ephedrine and L(–) ephedrine
- It is a substituted amphetamine and structural methamphetamine analoge
- Enantiomers with opposite stereochemistry around chiral center is called ephedrine while those with same stereochemistry is called pseudoephedrine.

Mechanism of Action

- Sympathomimetic amine
- Indirect stimulation of adrenergic receptors by increasing the activity of norepinephrine on post-synaptic α_1, α_2 and β_1 receptors

- Direct α receptor activation: Controversial
- Also crosses blood brain barrier: Weak CNS activation.

Pharmacokinetics

- T½ of 3–6 hours
- Onset of action 5 minutes
- Duration of action 1 hour
- Biotransformation in liver
- Excreted mostly unchanged in urine.

Indications

- Treatment of anesthesia induced hypotension:
  - Especially following spinal anesthesia
  - 750 µg/kg IV in titrated doses.
- Treatment of bronchitis:
  - Due to bronchodilator action
  - Pseudoephedrine has less bronchodilator action.
- ECA stack:
  - Component of thermogenic weight loss pills
  - Contains ephedrine, caffeine and aspirin
  - Speeds up metabolism and causes faster burning of food
  - Taken by body builders before work-outs to increase concentration, alertness and energy levels.
- ***Coast guard cocktail***:
  - Along with promethazine (25 mg), ephedrine 25 mg forms part of coastguard cocktail
  - Used to combat sea sickness
  - Promethazine prevents vomiting
  - Ephedrine fights drowsiness due to promethazine.

Adverse Reactions

- Neurological:
  - Restlessness, insomnia
  - Hallucination (rare), hostility
  - Confusion, mania, delusion, paranoia
- Cardiovascular:
  - Tachycardia, arrhythmias
  - Angina, hypertension
- Respiratory: Dyspnea, pulmonary edema
- Gastrointestinal: Anorexia, nausea
- Genitourinary:
  - Diuresis due to increased renal blood flow
  - Difficult micturition due to internal urethral sphincter constriction (rare).
- Dermatological: Flushing, diaphoresis, acne vulgaris
- Miscellaneous:
  - Dizziness, headache
  - Tremors, hyperglycemia.

Dosage

- Intramuscular/subcutaneous: 25–50 mg repeated as per BP response
- Intravenous: 750 µg/kg or 25 mg/cm^2 of body surface area.

Contraindications

- Absolute contraindications:
  - Asymmetrical septal hypertrophy: Obstruction increases due to increased contractility
  - Pheochromocytoma
  - Tachyarrhythmias: Ventricular tachyarrhythmias
  - Hypersensitivity.
- Relative contraindications:
  - Hypoxia, hypercarbia, acidosis
  - Closed angle glaucoma
  - Hyperthyroidism, hypertension, hypovolemia
  - Diabetes insipidus, impaired adrenal function
  - Prostatic hypertrophy, pregnancy (category C drug).
- Abuse potential:
  - Ephedrine increases concentration more than caffeine: Used by students and athletes
  - Used to synthesize methamphetamine by Birch reduction (using ammonia and Li^{2+}).

Drug Interactions

- Not to be used with SSRIs (Serotonin and Norepinephrine Reuptake Inhibitors)
- Not to be used with bupropion: Increases norepinephrine levels
- Not to be used with MAO inhibitors
- Caution with concomitant use of halothane: sensitizes to arrhythmias.

PHENYLEPHRINE[1,2,3,7,20]

Introduction

Synthetic sympathomimetic agent which acts as a vasoconstrictor.

Chemistry

- Chemically m-hydroxy α [(methyl-amino) methyl] benzyl alcohol hydrochloride
- Molecular formula: $C_9H_{13}NO_2$.

Clinical Pharmacology
- Predominantly α_1 adrenergic agonist
- No direct stimulating effects on CNS
- Peripheral vasoconstrictor and causes reflex bradycardia
- Onset of action:
  - 10–15 minutes following IM/subcutaneous
  - Onset is immediate following IV administration.
- Duration of action:
  - 1–2 hours for IM/subcutaneous administration
  - 20 minutes for IV administration.

Pharmacokinetics
- Metabolized in liver by MAO enzyme
- Route of elimination of metabolites not identified.

Indications
Hypotensive states:
- Circulatory failure
- Central neuraxial block
- Following labor analgesia (preferred to ephedrine)
- Drug induced hypotension.

Dosage
- In adults:
  - IM or subcutaneous administration: 2–5 mg with further 1–10 mg supplements
  - Intravenous administration:
    - 100–500 µg at rate of 180 µg/min
    - Taper to 30–60 µg/min according to response.
- In children: 100 mg/kg IM or subcutaneous.

Contraindications
- Patients on MAO inhibitors or within 14 days of ceasing such therapy
- Severe hypertension, hyperthyroidism
- Ischemic heart disease
- Occlusive vascular disease: Atherosclerosis, hypertension, aneurysm
- Arrhythmias, diabetes mellitus, closed angle glaucoma.

Adverse Effects
- Extravasation may cause tissue necrosis
- Hypertension: Headache, vomiting, cerebral hemorrhage, pulmonary edema
- Reflex bradycardia, arrhythmias, angina, palpitation, cardiac arrest, dizziness, flushing
- Urinary retention, difficulty in micturition
- Altered glucose metabolism
- Transient tingling sensation, cooling of skin.

Drug Interactions
- May cause VF if used with halothane/cyclopropane
- May increase risk of arrhythmias if given along with cardiac glycosides, quinidine/TCA
- Reverses action of antihypertensives.

Overdose
- Headache, vomiting, hypertension, reflex bradycardia, cardiac arrhythmias, acidosis
- Treat symptomatically with supportive measures
- Counter hypertension with α-blocker like phentolamine 5–60 mg IV over 10–30 minutes and repeat as necessary.

DOPAMINE[1,2,3,5,7,20]

Introduction
Endogenous catecholamine which is immediate precursor to norepinephrine.

Chemistry and Presentation
- Naturally occurring catecholamine
- It is a nonchiral compound
- Presented as a clear, colorless solution
- Contains 40/160 mg per ml of dopamine hydrochloride
- 200 mg of dopamine present per ampoule.

Mechanism of Action
- Direct action is by action on receptor
- Indirect action occurs by releasing norepinephrine
- 25% of IV dose is converted to norepinephrine
- Dose wise difference in the site of action
- Site of action:
  - At dose of 0.5 µg/kg/min: On D_1 and D_2 receptors
  - At dose of 5–10 µg/kg/min: On β_1 and β_2 receptors
  - At dose of more than 10 µg/kg/min: α_1 action predominates.

Dosage
- Given only as continuous infusion as it is rapidly metabolized
- Diluted in D5/normal saline as alkaline solutions inactivate dopamine

- Central vein is preferred for infusion
- Lowest dose should be used to maintain the desired BP
- Usually used in doses of 5–15 µg/kg/min.

Pharmacodynamics

- Central nervous system:
  - Nausea and vomiting by stimulation of CTZ
  - Raised intraocular pressure.
- Autonomic nervous system:
  - Vasodilatation of splanchnic circulation
  - Reduces gastrointestinal motility.
- Cardiovascular system: Dose dependent action:
  - At dose of 0.5 µg/kg/min:
    - Causes vasodilatation
    - Decreases diastolic BP.
  - At dose of 5–10 µg/kg/min:
    - Positive inotropic effect
    - Increased chronotropism
    - Venoconstriction: Causes reduction in preload
    - Systemic vasodilatation: Causes reduction in afterload
    - Modest increase in systemic BP
    - Predisposes to arrhythmias due to norepinephrine release.
  - At dose of more than 10 µg/kg/min:
    - Raised systolic BP but no increase in cardiac output
    - Causes nonepinephrine release
    - Coronary vasoconstriction.
- Respiratory system:
  - Reduces ventilatory response to hypoxia
  - Increases intrapulmonary shunting.
- Genitourinary:
  - Reduces renal vascular resistance
  - Increases renal blood flow and causes diuresis
  - Creatinine clearance is unaltered.
- Endocrine:
  - Aggravates partial hypopituitarism
  - Reduces growth hormone secretion in critically ill patients
  - Aggravates sick euthyroid syndrome
  - Inhibits insulin secretion: Hyperglycemia
  - Inhibits aldosterone secretion causing diuresis.

Pharmacokinetics

- Absorption:
  - Not effective orally
  - Volume of distribution 1.8–2.5 L/kg.
- Metabolism:
  - 75% of administered dose:
    - Rapidly metabolized in plasma, liver and kidneys
    - Metabolized by MAO and COMT
    - Metabolized to homovanillic acid and 3, 4 dihydroxyphenyl acetic acid.
  - 25% of administered dose: Converted to norepinephrine in adrenergic nerve terminals
- Excretion:
  - Excreted in urine as homovanillic acid
  - Small fraction is excreted unchanged
  - Elimination half life of 2 minutes.
- Onset of action within 5 minutes
- Duration of action 10 minutes.

Side Effects

- Pain on extravasation:
  - Most common due to intense vasoconstriction
  - Treated by local infilteration of phentolamine
- Cardiovascular:
  - Tachycardia, arrhythmias
  - Angina and hypertension
  - Palpitation
- Others:
  - Mesenteric ischemia
  - Hyperglycemia
  - Potentiates development of MODS
  - Raised intraocular pressure
  - Nausea and vomiting due to stimulation of CTZ
  - Gangrene of extremities when used in occlusive vascular diseases and DM.

Uses

- Low cardiac output states
- Septic shock
- Following cardiopulmonary bypass
- To maintain blood pressure in postsurgery patients.

Contraindications

- Right heart failure
- Pulmonary hypertension
- Pheochromocytoma
- Tachyarrhythimias.

Drug Interactions

- Concurrent use of volatile anesthetics predisposes to arrhythmias

- Inactivated by alkaline solutions like $NaHCO_3$
- Dopamine action is blocked by phenothiazines (metoclopramide and droperidol)
- Phosphodiesterase inhibitors may accentuate action of dopamine.

Renal Dose Dopamine

- Refers to continuous small dose infusion (0.5 µg/kg/min)
- Causes improvement in urine output when used in low doses
- This is thought to be due:
  - An overall improvement in cardiac output with dopamine
  - This causes an increased renal blood flow and inhibits aldosterone secretion
  - This results in improved urine output.
- Diuresis is not due to any specific action of dopamine
- No studies to prove reduction in incidence of ARF when dopamine is administered to patients at risk for developing ARF
- No evidence of improved creatinine clearance or reduced need for dialysis with dopamine administration
- May increase risk for MODS by causing GI mucosal ischemia and translocation of bacterial toxins.

DOBUTAMINE[1,2,3,5,7,20]

Chemistry

- It is a synthetic isoprenaline derivative
- It has two isomers, levo (L–) and dextro R(+).

Presentation

- 12.5/50 mg/ml of dobutamine hydrochloride
- Presented as a clear colorless solution
- 250 mg of dobutamine per ampoule

Mechanism of Action

- Mainly β_1 agonist:
  - Stimulates adenalyl cyclase
  - This causes an increase in c-AMP levels
  - This increases cell membrane permeability to calcium.
- Also acts as a weak β_2 agonist
- At doses above 5 µg/kg/min levo-dobutamine also exerts weak α_1 action.

Route of Administration

- Ineffective when administered orally
- Used with 5% dextrose/normal saline to avoid inactivation by alkaline solution
- Usually in doses of 5–15 µg/kg/min (> 20 µg/kg/min causes tachyarrhythmias).

Pharmacodynamics

- Central nervous system: Stimulation at highest doses
- Cardiovascular system:
  - Positive inotropic effect
  - Increases SA node automaticity: Tachycardia
  - Increases AV nodal conduction velocity
  - Increases myocardial perfusion
  - Causes coronary vasodilation
  - Improves cardiac index
  - Reduces left ventricular end diastolic pressure
  - Reduces systemic vascular resistance
  - Reduces pulmonary arterial occlusion pressure
- Genitourinary:
  - Increased urine output due to increase in cardiac output
  - It has no renal vasodilator effect.
- Others:
  - Reduces blood glucose
  - Increases natural-killer cell activity
  - Increases cutaneous heat loss due to cutaneous vasodilatation.

Pharmacokinetics

- Absorption: Not effective orally
- Distribution: Volume of distribution = 0.2 L/kg
- Metabolism:
  - Mainly by COMT methylation
  - Converted to 3-O-methyl-dobutamine and conjugated with glucuronide.
- Excretion:
  - In urine as conjugated products
  - 20% excreted in feces
  - Elimination half life of 2 minutes.
- Onset of action within 1–2 minutes
- Duration of action 10 minutes.

Uses

For inotropic support in:

- Myocardial infarction
- Cardiomyopathy

- Low output cardiac failure
- Cardiogenic shock
- Septic shock
- Postcardiac surgery
- For cardiac stress testing in those in whom exercise testing cannot be done.

Side Effects

- Arrhythmias, tachycardia, hypertension, angina
- Fatigue, nervousness, headache, paresthesias, tremors
- Allergy, tachyphylaxis
- Increased heat loss
- Dyspnea, nausea.

Contraindications

- Cardiac tamponade
- *Aortic stenosis*
- Mitral stenosis
- Allergy.

VASOPRESSIN[1,2,3,5,7,20]

Introduction

Hormone secreted by posterior pituitary gland.

Chemistry and Preparation

- Nanopeptide, containing 8-L-arginine vasopressin
- Molecular formula $C_{46}H_{65}N_{15}O_{12}S_2$
- 1 ml ampoules with 40/20 IU of vasopressin
- Molecular weight 1084.23.

Physiology

- Synthesized as prohormone in *magnocellular neuron cell bodies* of *supraoptic and paraventricular nuclei* of posterior hypothalamus
- Bound to a neurohypophysin and transported to axonal terminals
- Synthesis transport and storage takes 1–2 hours.

Stimuli for Release of Vasopressin

- Increased plasma osmolarity
- Hypercapnea
- Pain
- Nausea
- Severe hypovolemia
- Hypoxia
- Hypoxia
- Stress
- Pharyngeal stimuli

Chemical mediators

- ACH
- Histamine
- Angiotensin
- Dopamine
- Prostaglandins
- Catecholamine

Mechanism of Action

No	Receptor	Location	Mode of action	Actions
1	V1	Renal coronary	G protein receptors	Direct vasoconstrictor
		Systemic circulatn	Activate phospholipase C	Pulmonary vasodilator(NO)
		Myometrium		
		Platelets		
2	V2	Distal tubule	G protein receptors	Antidiuretic action
		Collecting ducts	Activate adenalyl cyclase	Induces factor VIII release
			Increase cAMP	Induces vWF release
			Mobilize aquaporin channel	
			Aquaporin channels inserted	
			into apical membrane of	
			renal collecting duct cells	
3	V3	Pituitary gland	G protein receptor	Neurotransmitter in memory
			Increases intracellular Ca^{2+}	consolidation
			Mediated by NO	Regulates body temperature
				Stimulates ACTH release

Pharmacodynamics

Cardiovascular

- Potent splanchnic portal cerebral pulmonary coronary vasoconstrictor
- Contracts especially capillaries small arterioles and venules
- Platelet aggregation and thrombus formation through endothelial vWF.

Central Nervous System

- Stimulates ACTH release from anterior pituitary
- Neurotransmitter for memory, body temperature and BP.

Renals

- Antidiuresis by increasing water resorption by renal tubules
- Contraction of bladder uterus GIT.

Pharmacokinetics

- Administered IV/IM/SC
- Duration of action 2–8 hrs
- Not protein bound
- Vd = 140 ml/kg
- Plasma T1/2 = 10 – 35 mins
- Normal plasma concentration < 4 pg/ml
- Metabolized in liver
- Excreted by kidneys (65%) and metabolism by vasopressinase (35%).

Indications

Cardiopulmonary Resuscitation

- VF/PEA/Asystole
- As alternative to epinephrine
- Causes sustained increase in MAP as opposed to epinephrine
- 40 mg IV repeated every 3–5 mins regardless of initial rhythm
- Pediatric CPR: Dilute 1 IU/kg in 50 ml NS and infuse @ 1 ml/hr (0.33 IU/kg/min).

Shock

- Septic: 0.01–0.04 IU/min
- Anaphylactic: 2–10 IU bolus followed by 2–6 IU/hr
- Hemographic: 2–10 IU bolus followed by 0.8 IU/kg/min titrated to BP
- Vasodilatory: 2–6 IU/hr in postcardiotomy patients

Abdomen

- Abdominal Distention:
  - 5 IU IM increased to 10 IU IM and repeated at 3–4 hr intervals.
- Variceal Bleed:
  - 20 IU in 100 ml 5% D over 15 mins bolus
  - Given IV or rarely intra-arterial infusion
  - Reduces portal blood flow and variceal pressure.

Central Diabetes Insipidus

- Given IV/intranasally on cotton pledgets/sprays
- 5–10 IU IM or SC TID/BD
- 2.5–10 IU IM/SC TID or QID for children.

Bleeding Anomalies

- In von Willibrands disease and mild hemophilia
- Impaired platelet function due to NSAIDs/renal failure.

Other Vasodilatory States

- Hypotension with SAB/epidural
- Triple H therapy with phenylephrine
- Hormone replacement in brain death
- Preoperative refractory hypotension in patients on ACE inhibitors
- Shock after pheochromocytoma excision resistant to catecholamines
- Carcinoid crisis as sympathomimetics are contraindicated.

Side Effects

- Local/systemic allergic reactions
- Abdominal cramps
- Nausea vomiting flatus
- GIT ischmia
- Tremors, vertigo, severe headache
- Bronchospasm, sweating, urticaria
- Cutaneous gangrene on extravasation
- Thrombophlebitis
- Water intoxication: Hyponatremia drowsiness headache coma.

Contraindications

- Anaphylaxis
- Hyperbilirubinemia
- Chronic renal failure
- Peripheral vascular disease
- A/c bowel ischemia/MI

- Caution in:
  - Migraine
  - Asthma
  - Epilepsy
  - Heart failure.

Pregnancy: Category C

Drug Interactions

Potentiation of ADH Action By

- Carbamazepine
- Clofibrate
- Fludrocortisone
- Chlorpropamide
- Tricyclic antidepressants.

Potentiation of Pressor Action By

- Ganglion blocking agents

Negate ADH Action

- Demeclocycline
- Lithium
- Alcohol
- Heparin
- Norepinephrine.

MECHANISM OF ACTION OF LOCAL ANESTHETICS[1,2,3,5,7,20]

Pharmacokinetics

- Only 1–2% of local anesthetic volume injected eventually reaches the nerve fiber
- The action is exerted on the nerve fiber in three phases:
  - Delivery phase:
    - Drug diffuses through many layers before it reaches the axons
    - Two main types of movement of drugs occurs:
      - Mass movement (due to injection)
      - Diffusion along concentration gradient
    - Factors affecting drug delivery:
      - Amount of fat and fibrous tissue surrounding the nerve
      - Absorption into vascular and lymphatic channels.
    - Example:
      - More amount of fat and fibrous tissue is present in sciatic nerve
      - Spinal nerve roots on the other hand, are almost naked in CSF
      - LA gets absorbed into blood vessels around peripheral nerves
      - Thus, lesser amount of local anesthetic is available for delivery to the sciatic nerve
      - Addition of vasoconstrictor thereby increases drug delivery
      - Drugs like bupivacaine are extensively bound to plasma proteins
      - Thus, less amounts of free drug is available for vascular absorption
      - Therefore, adding epinephrine to bupivacaine does not increase its duration of action.
  - Induction phase:
    - Refers to diffusion of local anesthetic from nerves outer surface towards center
    - Thus, axons at the outer layer of nerve (mantle fibers) supplying proximal part of limb are blocked earlier than those in the inner layer (core fibers), supplying distal part of limb.
    - Implications:
      - In IVRA, local anesthetics are present in veins of axon
      - These are more densely packed in core region
      - Local anesthetic molecules diffuse from core to mantle
      - Hence, the block progresses from distal to proximal
      - In supraclavicular blocks, paresis precedes analgesia
      - This is because motor fibers of shoulder girdle area are present in mantle position of nerve fibers.
  - Recovery phase:
    - During recovery phase, the diffusion gradient is reversed
    - Nerve core contains higher concentration of LA
    - Therefore, it loses drug for more time (as more drug has to diffuse out)
    - Thus, proximal limb area recovers faster than distal areas.

Molecular Basis of Action

- Locus of action:
  - Voltage gated sodium channels:
    - LA acts on inactivated and activated channels more than resting state channels
    - This is according to *Modulated receptor hypothesis*

- Thus binding of LA stabilizes the channels in a nonconducting state.
  - Voltage gated K^+ channels
  - L-type Ca^{2+} channels
  - NMDA receptors
  - Nicotinic ACHR.
- Active species:
  - Local anesthetics have a pKa of 7.5–9.5
  - Thus they are more often electrically charged molecules
  - The neutral form of LA is necessary to pass through axonal membrane
  - But, protonated form is necessary to block Na^+ channels.
- Types of blockade:
  - Phasic blockade/use dependent blockade:
    - Refers to potentiation of anesthetic block by repetitive depolarization
    - Greater number of Na^+ channels are blocked at same drug concentration by repetitive stimulation
    - This is because more channels are in open state
    - This results in potentiation by repetitive depolarization.
  - Tonic blockade:
    - Refers to degree of inhibition of single impulses measured without preceding stimulus
    - Indicates reduction in number of Na^+ channels in open state for a given drug concentration
    - Use dependant blockade is explained by modulated receptor hypothesis.
  - Other drugs with local anesthetic action:
    - Ketamine, inhaled anesthetics
    - Pethidine, tricyclic antidepressants.

Neurophysiological Implications

- Myelination of nerve fibers:
  - LA have to diffuse through lesser tissue to reach axons in small diameter fibers
  - Thus, smaller diameter fibers are more sensitive to LA action
  - Also, myelin stores LA at induction but draws them away from axon during drug diffusion
  - Thus myelinated fibers are blocked by LA slowly
  - Type B autonomic preganglionic and type C fibers are therefore more sensitive.
- Minimum blocking concentration(C_m):
  - Lowest concentration of LA *in vitro* which will block given nerve within reasonable time (usually 10 minutes) is called C_m
  - This is similar to MAC value of inhaled anesthetics
  - Factors affecting C_m:
    - Dilution by tissue fluid
    - Fibrous tissue barriers
    - Drug absorption and metabolism
    - Elimination and distribution of LA.
- Differential nerve blockade:
  - Refers to complete blockade of 1 nerve modality (sympathetic) with partial blockade of other modalities (sensory and motor)
  - Occurs due to 3 reasons:
    1. Impulse in smaller fibers (B and C) blocked before larger fibers (Aδ and Aγ)
    2. Some fibers are more susceptible due to lack of myelin (C fibers)
    3. Axons per se may be differentially sensitive to block as some may have K^+ channels while some do not.
  - Increasing concentration of LA ensures C_m of larger fibers is attained
  - This negates differential blockade occurring commonly
  - Orderly progression of block from first to last:
    - Temperature
    - Proprioception
    - Motor
    - Sharp pain
    - Light touch
- Threshold block phenomenon/Wedensky block
  - Phenomenon where, when C_m of a nerve fiber has been reached, it no longer conducts a single impulse but allows 2nd/3rd member of a train of impulses to breach the block
  - Occurs as the conducted impulse briefly lowers the firing threshold of the nerve
  - Another nerve impulse arriving during this phase will induce just enough depolarization to trigger an action potential
  - This phenomenon is more pronounced in thinner axons
  - Noxious stimuli trigger impulses in high frequency barrages through thin axons
  - Thus, patient may not feel pain to a pin prick but may react to a high intensity stimulus like a surgical incision

  - As anesthetic concentration progressively rises above the C_m, fewer impulses in a train are conducted as blockade becomes more profound.
- Decremental conduction:
  - Sufficient volume of LA is required to suppress conduction across a critical length of nerve fiber
  - As membrane depolarization from an action potential spreads passively across a nerve fiber a critical length of fiber should be blocked to prevent passive firing of AP from adjacent membrane/Nodes of Ranvier
  - Too short an exposure length allows impulse to skip over membranes and bigger APs
  - Concentration of LA, which blocks 84% of sodium channel conductance at 3 successive Nodes of Ranvier, prevents any impulse propogation.

Cardiac Action of Local Anesthetics

- Local anesthetics can be both proarrhythrogenic and is also used to Rx arrhythemias.
- Use of lidocaine in arrhythmias:
  - Mainly used in ventricular tachyarrhythmias
  - Lidocaine targets open cardiac Na^+ channels
  - It limits the rate of firing in ventricular tissue by increasing AP threshold in a phasic manner
  - Thus, due to faster firing rates in VT, more number of Na^+ channels are open and also remain open for longer times
  - Thus, use dependant blockade helps to reduce rate of ectopic ventricular firing while not affecting normal impulses
  - This occurs due to two main differences between heart and peripheral nerves:
    - At RMP, few channels are in open state while in peripheral nerve, 30% may be in active state
    - Cardiac action potential produces depolarization which lasts several 100 milliseconds while neuronal impulse is only 1 msec.
  - Lidocaine thereby acts by delaying rate of spontaneous phase 4 depolarization by preventing or diminishing the gradual decrease in K^+ permeability that occurs
  - In higher doses, lidocaine reduces conduction in AV node and Purkinje fibers.
- Bupivacaine toxicity:
  - Bupivacaine differs from lidocaine (mainly bradycardiogenic) in being arrhythmogenic
  - It effects the storage and release of cytoplasmic Ca^{2+} thus affecting membrane excitability.

LOCAL ANESTHETIC TOXICITY[1,2,3,5,7,20]

Introduction

Adverse reactions with local anesthetics include systemic toxicity, localized neural and skeletal muscle toxicity and drug specific side effects.

Mechanism of LA Toxicity

- Local anesthetics inhibit carnitine acyl carnitine translocase
- This prevents transfer of acyl COA across mitochondrial membrane
- This reduces fatty acid metabolism and reduces available energy at the cellular level
- This results in cardiac arrest.

Systemic Toxicity

- Most toxic reactions involve CNS
- CVS depression is rare but is more serious and difficult to manage
- Neurotoxicity:
  - Factors affecting CNS toxicity:
    - Rate of drug injection also influences toxicity
    - Anesthetic potency:
      - Convulsions occur at:
        - Dose of 5 mg/kg of bupivacaine
        - Dose of 20 mg/kg of lidocaine.
      - Thus, CNS toxicity relationship of lidocaine: Kupivacaine is 4:1.
  - Phases of toxicity:
    - Initial phase of excitation: Due to selective blockade of inhibitory pathways
    - Later, CNS depression due to inhibition of both inhibitory and facilitatory pathways.
  - Respiratory acidosis, hypercarbia and acidosis decrease toxic threshold as:
    - Hypercarbia increases cerebral blood flow: More LA delivery to brain
    - Acidosis reduces plasma protein binding: Decreased V_d and more free drug for diffusion
    - Decreased intracellular pH causes:
      - Increased conversion to cationic form which is responsible for LA action
      - Conversion to poorly diffusible cationic form: Increases intracellular LA concentration.
  - Cauda equina syndrome:
    - 5% lidocaine and 0.5% tetracaine on repeated doses pool around cauda equina

- Neurotoxic potential: From most toxic to least toxic:
  - Lidocaine = tetracaine
  - Bupivacaine
  - Ropivacaine.
- Sodium metabisulfate and low pH propentiate development of cauda equina.

– *Transient neurological symptoms*:
- 5% lidocaine, lithotomy position, obesity and outpatient status are risk factors for TNS
- Occurs due to:
  - Local nerve root irritation in lithotomy position
  - More common with continuous injection of lidocaine via intrathecal catheters
  - This causes chromatolysis and vacuolysis of spinal neurons in ***Obersteiner-Redlich*** zone.

- Cardiovascular toxicity:
  – Local anesthetics cause increased conduction time and myocardial depression
  – This results in:
    - Prolonged PR interval, QRS duration
    - SA node depression, sinus bradycardia and sinus arrest
    - AV nodal dissociation and idioventricular rhythm.
  – Dose dependent negative inotropism: More intense with more potent LA
  – CC/CNS ratio:
    - Refers to ratio of dose required for causing cardiac to that required for neurotoxicity
    - CC/CNS ratio is 7 for lidocaine
    - This means 7 times as much lidocaine is required for cardiovascular collapse as for convulsions
    - CC/CNS ratio is 3.5 for bupivacaine.
  – Cocaine causes HTN and VPCs which are treated with CCBs and adrenergics
  – Bupivacaine more cardiotoxic due to:
    - Molecular structure per se
    - Also due to higher lipid solubility and protein binding.
- Peripheral vascular toxicity:
  – It has biphasic action on smooth muscles of blood vessels
  – Vasoconstriction occurs, followed by vasodilatation
  – Cocaine is an exception which produces only vasoconstriction by inhibiting norepinephrine uptake
  – Increased heart rate, BP and cardiac output
  – This is followed by profound cardiovascular depression and circulatory collapse.
- Other system toxicity:
  – Membrane stabilizing property results in:
    - Neuromuscular blockade
    - Ganglion blockade
    - Anticholinergic activity.
  – Hematological: Lidocaine inhibits coagulation by:
    - Inhibiting thrombosis
    - Inhibiting platelet aggregation
    - Enhanced fibrinolysis.

Local Tissue Toxicity

- Localized skeletal muscle damage:
  – Mostly commonly by bupivacaine and etidocaine
  – Muscle damage is reversible
  – Occurs due to hypercontraction which causes lytic degeneration and necrosis
  – Rapidly reversed within 3-4 weeks of injection.
- Local ischemia or neurotoxicity may occur.

Drug Specific Toxicity

- Methemoglobinemia:
  – Following large doses (> 600 mg) of prilocaine
  – Due to formation of O-toluidene in liver which:
  – Oxidizes hemoglobin to methemoglobin
  – Spontaneously reversible
  – Treated with IV methylene blue.
- Drug allergy:
  – More to amino esters like procaine
  – Rare with amino-amides
  – Due to drugs being derivatives of PABA
  – Allergy also to preservatives sodium metabisulfite/methyl paraben.

Treatment

- Stop local anesthetic injection
- Instruct patient to hyperventilate if conscious
- Minor reactions may be allowed to resolve spontaneously
- Protect airway: Intubate if necessary
- Provide supplemental oxygen if seizures present
- Anticonvulsants:
  – Thiopentone 50–75 mg or diazepam 2.5–10 mg IV

  - Midazolam 2 mg, propofol 1 mg/kg IV.
- Cardiac arrest:
  - Transvenous/transarterial pacing
  - ACLS protocol based resuscitation
  - Use amiodarone/bretylium instead of lidocaine for ventricular arrhythmias
  - Vasopressors like epinephrine, vasopressin and norepinephrine
  - Massive doses of atropine/adrenaline required for bupivacaine cardiotoxicity
  - *IV lipid emulsion (Intralipid)* in refractory cases
  - Cardiopulmonary bypass.
- Local ischemic or neurotoxicity due to vascular compromise:
  - Warm compresses
  - IV phentolamine
  - Nitroglycerine cream.
- Treat methemoglobinemia
  - If methemoglobin > 30% methylene blue IV at 1–2 mg/kg
  - Up to 50 mg/kg can be given in adults
  - Given as 1% solution in 5 minutes and repeated in 1 hour
  - Ascorbic acid 200–500 mg orally
  - N-acetylcysteine can also be used
  - Exchange transfusion recommended in severe cases.
- Drug scavenging nano particles:
  - Structure:
    - Contain yellow oil hydrophobic core with soluble hydrophilic cover
    - Also contains a nonionic polymer made of ethylene oxide and polypropylene oxide.
  - Mechanism of action:
    - Nanoparticles have large surface area to volume ratios
    - This aids in the treatment of LA toxicity
    - Nanoparticles are made of polyacrylic acid spheres
    - These can soak up drug molecules in the body like a sponge
    - Thus, they sequester bupivacaine from the acqueous phase of human blood.
  - Advantages:
    - Can penetrate deep into tissues through fine capillaries due to small size
    - Enter cells to evade detection by RES.

PREVENTION OF LAST[1,2,3,5,7,20]

Procedural

- Use ultrasound guided nerve blocks
- Avoidance of multiple simultaneous nerve blocks
- Use low dose while giving blocks with high LA absorption
- (Intercostal > epidural > brachial)
- Use of adrenaline as marker for intravenous injection
- Aspiration before injection of LA
- Injection in graded aliquots
- Use of continuous catheter techniques as:
  - Allows use of less toxic drugs (lidocaine rather than bupivacaine)
  - Avoids rapid injection of high doses
  - Allows sufficient time interval between doses.

Drugs

- Use of less toxic drugs (lidocaine, prilocaine > ropivacaine, levobupivacaine > bupivacaine)
- Restrict total anesthetic dosage to lowest effective dose
- When large doses are required fractionate doses
- Allow sufficient time interval before subsequent drug dosages
- Avoid rapid epidural injections
- Avoid combination of LA as toxic doses of combinations not known
- Use adjuvants to reduce dosage of LA
- Avoid excessive sedation to allow early LAST detection.

Patient Factors

- Reduced LA dose in those with:
  - Obesity
  - Pregnancy
  - Old age
  - Cardiac failure
  - Liver failure
  - Renal failure.

LIPID EMULSION THERAPY FOR LA TOXICITY[1,2,3,7,20]

Introduction

- First clinical application by *Rosenblatt and Litz*
- It is used only when more conventional methods of treatment have failed.

Pharmacological Basis

- Lipid emulsion on administration creates a lipid bank

- Wayward local anesthetic molecules are deposited into this bank
- Thus, concentration of LA molecules into this bank prevents progression of toxicity
- This prevents progression of CNS to CVS toxicity
- This is advantageous as there are a number of options to revert CNS toxicity, but CVS toxicity is refractory to most resuscitative techniques.

Mechanism of Action of Lipid Emulsions

- Prevents LA induced inhibition of carnitine acyl carnitine translocase
- Lipid droplets also segregate the unbound bupivacaine
- Provides instant energy source as it contains fat molecules
- Acts on nitric oxide pathway and reverses inhibitory effects of bupivacaine.

Indications

- Toxicity of any lipid soluble drug:
  - Sertraline, quetiapine, bupropion
  - Lamotrigine, clomipramine
  - Verapamil, bupivacaine, ropivacaine.
- Intralipid forms a component of parenteral nutrition formulations
- Some propofol and etomidate preparations use propofol as carrier.

Composition of Intralipid

- Available in 10, 20 and 30% concentrations
- Contains emulsion of soybean, egg phospholipids and glycerine (Lytic cocktail)
- Provides omega 6 essential fatty acids, linoleic acid and linolenic acid.

Dosage

Weinberg regimen:

- Intralipid used as 20% solution, 1 ml/kg given over 1 minute
- Dose can be repeated every 3–5 minutes up to a dose of 3 ml/kg
- This is followed by an infusion of 0.25 mL/kg/min which is continued till hemodynamic stability is achieved
- Rate is increased to 0.5 ml/kg/min if hypotension occurs
- A total maximum dose of 8 ml/kg is recommended.

Side Effects

- Altered reticuloendothelial system function and inflammatory responses
- Increased risk of infections and thrombophlebitis
- Allergy and anaphylaxis, especially if soybean is present
- Pulmonary, splenic and cerebral fat emboli
- Pulmonary hypertension
- May cause raised ICP after traumatic brain injury
- May induce weakness and seizures in children.

Drug Interactions

- Causes warfarin resistance by facilitating its binding to albumin
- May interfere with ECMO circuit.

HEPARIN[1,2,3,5,7,20]

Introduction

- Discovered in 1916
- One of the strongest acids found in nature (negatively charged anion)
- Anticoagulant which delays clotting by direct and indirect actions on coagulation system.

Chemistry

- It is negatively charged anion
- Extracted from bovine lung/porcine intestinal mucosa
- Also present in basophils, mast cells, liver, lymph nodes and thymus
- It is a glycosaminoglycan formed by altering residues of D-glucosamine and L-iduronic acid
- Mixture of highly sulfated glycosaminoglycans which are acid mucopolysaccharides
- Molecular weight of 3000–60000 Da (with mean of 15,000 Da: UFH).

Presentation

- Packed in two formulations:
  - Heparin sodium containing 1000/5000/25000 IU/ml
  - Heparin calcium containing 25000 IU/ml.
- 1 IU of heparin is defined as that volume of heparin containing solution which will prevent 1 ml of citrated sheep blood from clotting for 1 hour after addition of 0.2 ml of 1:100 calcium chloride
- Heparin must contain atleast 120 USP (United States Pharmacopeia) units per ml
- 1 mg of heparin = 100 IU.

Mechanism of Action

- Anticoagulant action:
  - Indirect action:
    - Pentasaccharide sequence of heparin binds to scaffolding present on antithrombin
    - This increases antithrombotic activity of AT by 1000 times
    - AT then inactivates factors V, VII, IX, X, XI and XII
    - Arginine center of AT binds to these serine proteases and inhibits them
    - Factor IIa is 10 times more sensitive than Xa to inhibition by UFH
    - Principal action is inhibition of thrombin induced activation of factors V and VII
    - Anti-thrombin is therefore also called *Heparin cofactor*
  - Direct action:
    - Also directly binds to several serine proteins (IX, X, XI, XII)
    - This facilitates their action on AT.
- Antithrombotic action: Inhibits platelet function by:
  - Inhibiting platelet aggregation
  - Inhibiting vWF and collagen cross linking.

Routes of Administration

- Poorly absorbed from GIT as it is less lipid soluble: oral dose is ineffective
- Subcutaneous and intravenous administration preferred
- IM dose avoided as increases risk of hematoma formation.

Pharmacokinetics

- Absorption:
  - Poorly absorbed orally
  - Bioavailability is the same (40%) for IV/subcutaneous administration
  - Onset of action:
    - IV administration is immediate
    - S/C administration is delayed by 1–2 hours.
- Distribution:
  - One-third of dose binds to antithrombin III
  - Remaining two-third of dose binds to:
    - Albumin, fibrinogen
    - Proteases, platelet factor 4
    - Histidine rich glycoprotein, fibronectin, vitronectin and vWF.
  - Volume of distribution 40–100 ml/kg
  - Highly plasma protein bound.
- Metabolism: Desulfated and depolymerized in liver, kidney and RES by heparinases
- Excretion:
  - Mainly by depolymerization in endothelium and macrophages (JPME)
  - Small amounts excreted unchanged in kidney
  - Clearance: 0.5–2 ml/kg/min
  - Elimination half-life: 2.5 hours
  - Elimination and thus duration of action is prolonged in:
    - High dose (thus, dose response curves are not linear)
    - Hepatic and renal dysfunction
    - Hypothermia < 37 °C (as during CPB).
  - Does not cross placenta unlike warfarin: Not teratogenic.

Pharmacodynamics

- Anticoagulant: Inhibits factors V, VII, IX, X, XI, XII, XIII
- Anti-thrombotic: Inhibits platelet aggregation
- Lipolysis:
  - It is precursor of lipoprotein lipase
  - Also increases other lipase activity in plasma
  - This reduces plasma free fatty acid concentration.
- Anti-inflammatory action: Through mast cells
- Angiogenesis: Inhibits vascular smooth muscle proliferation
- Osteolytic:
  - Suppresses osteoblast formation
  - Stimulates osteoclasts and causes bone loss.
- Increases blood vessel permeability.

Lab Evaluation

- Lee-Whites whole blood clotting time
- aPTT: Kept at 1.5–2.5 times the normal value (30–35 seconds)
- ACT:
  - Kept at more than 480 seconds for CPB
  - 180–480 seconds: Questionable anticoagulant effect
  - If less than 180 seconds: Inadequate anticoagulant effect.
- Thrombin time: More than 16 seconds preferred (normal is 14–16 seconds)
- BART (Blood activated recalcification time): Normal 65–125 seconds
- No need of monitoring for LMWH due to its higher bioavailablity and half life.

Clinical Uses

- Venous thromboembolism prophylaxis: 3500 IU S/C Q8H, started 2 hours before surgery
- Fat embolism: Increased lipase action and clears FFA from blood
- Treatment of pulmonary embolism
- Disseminated intravascular coagulation: 50–100 IU/kg bolus followed by 10–15 IU/kg/hr
- Priming of cardiopulmonary bypass and hemodialysis circuits: 300–500 IU/kg
- Maintaining patency of indwelling catheters (IBP, CVP): 3–4 IU half hourly
- Coronary Artery disease:
  - Unstable angina, Non-Q-wave STEMI
  - 5000 IU IV followed by 32000 IU/24 hour infusion.
- Atrial fibrillation with embolic complication while on standard dose warfarin and in pregnant patients with prosthetic valves: long-term heparin therapy.

Contraindications

- Absolute contraindications:
  - Bleeding diathesis, thrombocytopenia
  - Intraocular surgeries
  - Intracranial surgeries
  - History of allergy to heparin
  - Threatened abortion.
- Relative contraindications:
  - Patients undergoing neuraxial blockade
  - For tests which involve complement and Ig osmotic fragility
  - Severe hypertension, endocarditis
  - Hemorrhoids, GIT ulcers, large malignancies, tuberculosis
  - Chronic alcoholics, hepatic and renal dysfunction.

Side Effects

- Hemorrhage:
  - *Most common* side effect
  - Risk increases with:
    - Pre-existing coagulation defects
    - Concurrent use of other drugs which inhibit coagulation
    - Chronic alcoholism
    - Other serious concurrent illness.
- Allergy: As heparin is derived from animal tissues
- Cardiovascular changes:
  - Reduces MAP, pulmonary arterial pressure and SVR on rapid infusion
  - This is due to direct relaxant effect on vascular smooth muscle.
- Osteoporosis:
  - Occurs if high dose heparin given for more than 5 months
  - This is because heparin inhibits osteoblasts and stimulates osteoclasts.
- Aldosterone suppression
- Altered cellular morphology:
  - Heparin alters cellular morphology of stored blood
  - Heparinized blood is hence not used for tests which involve osmotic fragility.
- Increased thrombotic tendency:
  - Heparin may reduce antithrombin activity to one-third of normal
  - It may therefore paradoxically increase thrombotic tendency.
- Heparin resistance:
  - Occurs due to antithrombin deficiency
  - This may necessitate high doses of heparin together
  - Administration of FFP may restore AT III levels to normal
  - This is seen in inflammatory disorders due to raised plasma protein concentration
  - This reduces the amount of free drug available for action.
- Heparin induced thrombocytopenia.

Drug Interactions

- Nitroglycerine increases heparin requirement
- Increased concentration of free propranolol and diazepam when administered with heparin as heparin displaces these drugs from protein binding sites
- OCPs (estrogen containing): Reduce levels of AT and thus may cause heparin resistance
- Increased bleeding tendencies when used with aspirin and clopidogrel
- Alcohol increases risk of heparin induced bleeding.

Heparin Reversal

- Protamine
- Platelet factor 4:
  - Heparin binding protein which is present in α-granules of platelets
  - It is released during platelet aggregation and reverses heparin anticoagulation
  - Recombinant PF4 can be used in protamine allergy.

- Heparinase I: Heparin degrading enzyme which lyses heparin at its α-glycoside linkages
- Histidine rich glycoprotein, vitronectin: Physiologically present.

HEPARIN INDUCED THROMBOCYTOPENIA[1,2,3,5,7,20]

Introduction

Life threatening prothrombotic complication of heparin administration.

Incidence

- 2.6% incidence with UFH, 0.2% incidence with LMWH
- 8% patients have antibodies to heparin
- 3% of these patients develop thrombocytopenia
- Only 1% patients undergo thrombotic complications.

Mechanism

- Mechanism of HIT I:
  - Nonimmune mediated mechanism
  - Occurs due to drug binding to platelets
  - This inhibits platelet aggregation.
- Mechanism of HIT II:
  - Immune mediated mechanism
  - Heparin complexes with PF4 and forms the antigen
  - IgG antibodies develop against this antigen and bind to heparin-PF4 complexes
  - This causes endothelial injury, complement activation and heparin neutralization
  - This results in platelet aggregation and platelet (white) clots.

Risk Factors

- Can occur with any dose of heparin, any route of administration
- Highest incidence with full dose UFH
- Bovine UFH > porcine UFH > LMWH > danaparoid
- Surgical patients > medical patients.

Clinical Features

- Onset on day 5–10 after heparin exposure
- Triad of signs in heparin induced thrombocytopenia:
  - Thrombocytopenia
  - Tachyphylaxis to heparin and heparin resistance
  - Thrombotic complication.
- Thrombocytopenia:
  - It may begin within hours in patients previously exposed
  - It can even occur with catheter flush doses
- Tachyphylaxis: Antibodies disappear within 3 months of discontinuation
- Thrombotic complications:
  - It can cause venous/arterial thrombii in iliac arteries and aorta
  - Manifestations:
    - DVT, pulmonary embolism
    - DIC, stroke, MI, splanchnic ischemia
    - Gangrene of legs and arms.
  - Risk of thrombosis persists up to 30 days after cessation of heparin
  - Highest risk within first 10 days of diagnosis.

Types

Feature	HIT I[3]	HIT II
synonym	Heparin associated thrombocytopenia	Heparin induced platelet activation
Incidence	More common	Less common
Severity	Mild	Severe, life threatening
Incidence	30–40% of heparinized patients	0.5–6% patients
Type	Nonimmunological	Immunological
Mechanism	Drug induced platelet aggregation	Due to heparin interaction with PF4
Antiplatelet antibodies	Absent	Present
Platelet count	Less than 1,00,000 / mm^3	Less than 50,000 / mm^3
Onset	Less than 3 days of therapy	6–10 days of heparin therapy
Resolution	Spontaneous	Not spontaneous
Complications	Benign	Severe with end organ damage
Thrombosis	Not seen	Causes stroke and amputation
Diagnosis	Solely clinical	Enzyme assays
Therapy	No specific therapy	Specific therapy indicated

Determination of Risk

- *Warkentins criteria*
- To determine probability of heparin induced thrombocytopenia:

Criteria	2 Points	1 Point	0 point
Thrombocytopenia	> 50% fall	30–50% fall	< 30% fall
Onset	Onset on day 5–10	Onset after day 10	Platelet count fall too early
	< 1 day if heparin in past 3 months		No recent heparin exposure
Sequelae	New thrombosis	Progressive thrombosis	None
	Skin necrosis	Erythematous skin lesion	
	Post-heparin acute reaction		
Other causes	No other cause	Other cause possible	Definite other cause
Pretest probability score			
6–8	High probability		
4–5	Intermediate probability		
0–3	Low probability		

DIAGNOSIS

- Platelet aggregation studies: Simple and cost effective
- Antibody assays:
  - Functional assays:
    - PF4-Ig assay
    - Serotonin release assay: Gold standard.
  - ELIZA: Easy and rapid.
- Mainly clinical diagnosis: Suspect HIT if:
  - Declining platelet count to less than 50% of baseline value
  - Occurs within 5–10 days of heparin therapy
  - Other causes of thrombocytopenia have been excluded
  - Condition resolves after cessation of therapy.

Prevention of HIT

- Immediate evaluation if heparin resistance/tachyphylaxis
- Minimize dose and duration of heparin
- Use LMWH/porcine heparin
- No heparin bonded vascular catheters
- Heparinless catheter flush solution
- Avoid platelet transfusion: Helps in formation and extension of thrombus
- Add heparin to list of drug allergies in patients medical chart.

Treatment

- HIT I requires no specific treatment
- HIT II:
  - Discontinue heparin immediately
  - Anticoagulation for CPB with HIT:
    - Give antithrombotic drugs which do not produce immune mediated thrombocytopenia Alternatives:
      - Warfarin, aneroid
      - Orgaran, danaparoid.
  - Platelet transfusion if platelet count is low
  - LMWH have a high incidence of cross reaction with heparin dependant antibodies and is not useful.

Anticoagulation in HIT

Anticoagulation in Active HIT

Avoid heparin in any route:

Procedure	Agent	Dose	Monitor
CPB	Lepirudin	0.25 mg/kg bolus	ECT
		0.5 mg/kg infusion	
	Argatroban	0.1 mg/kg bolus	ACT
		5–10 µg/kg/min infusion	
PCI	Argatroban	350 µg/kg bolus	ACT
		25 µg/kg/min infusion	
	Danaparoid	2250 IU bolus	
		200 IU/hr infusion	

Anticoagulation in Subacute HIT

Avoid heparin in any route:

Drug	Dose	Monitor
Lepirudin IV	0.4 mg/kg	aPTT
	0.15 mg/kg/hr	
Argatroban IV	2 µg/kg/hr	aPTT
Danaparoid S/C	1500–2250 IU Q12H	Anti-Xa levels

Anticoagulation in Patients with History of HIT:

- Heparin re-exposure considered for short-term anticoagulation (CPB)
- Alternative anticoagulants to be used for long-term indication.

Anticoagulation in Pregnancy with History of HIT

- No heparin use in active/subacute HIT
- Danaparoid can be used
- Not known if fondaparunix/DTI crosses placenta.

Differential Diagnosis

- Aplastic anemia, septicemia
- Leukemia, DIC
- Alcoholism
- Drugs: drug induced thrombocytopenia:
  - Quinidine, cytotoxic drugs
  - Gold, rifampicin
  - Sulfa drugs, valproate.

Feature	HIT	DIT
Platelet count	50,000 /mm^3	Less than 10000/mm^3
Mechanism	F_{cr} activation	F_{ab} mediated
Thrombosis	Yes	No
Bleeding	Rarely	Yes

LOW MOLECULAR WEIGHT HEPARIN[1,2,3,5,7,20]

Introduction

They are produced from unfractionated heparin by chemical and enzymatic depolymerization.

Chemistry

- Mean molecular weight 4000–6500 Da
- Ranges from 2000–10,000 Da
- Fragments are one-third the size of heparin
- Chain length of 13–22 sugars.

Types

- Nadroparin: By N_2O depolymerization
- Enoxaparin: Benzylation followed by alkaline depolymerization
- Dalteparin: N_2O depolymerization
- Ardeparin: Peroxidative depolymerization
- Tinzaparin: Enzymatic depolymerization with heparinase
- Reviparin: N_2O depolymerization
- Danaparoid: Prepared from animal gut mucosa.

Mechanism of Action

- Smaller size molecule and thus retains full anti-Xa activity with less anti-IIa activity
- Anti Xa: Anti IIa = 4:1
- Also binds directly to factor VII and reduces production of prothrombinase.

Pharmacokinetics

- Route of administration: Subcutaneous
- Absorption: Absorbed completely, 90% bioavailability
- Distribution:
  - Less protein bound (only 10%)
  - Half-life is 2–4 times longer than UFH.
- Metabolism: Partially by desulfonation and depolymerization
- Excretion:
  - Not depolymerized by endothelial cells which occurs rapidly
  - Excreted only through renal route
  - Thus the duration of action is prolonged.

Monitoring

- Monitoring is generally not required as anticoagulant effect is predictable
- LMWH also reduces risk of bleeding
- aPTT is a relatively insensitive indicator
- Anti-Xa levels are measured to monitor LMWH (should be kept at 0.5–0.8 IU/ml)
- PT and INR also used.

Uses

- Prevention of VTE:
  - Enoxaparin 20–40 mg S/C given 6 hours preoperatively
  - LMWH continued once daily thereafter.
- Treatment of VTE
- Treatment of unstable angina and NQWMI: 1 mg/kg enoxaparin Q12H.

Reversal

Reversal of low molecular weight heparin:

- 1 mg protamine given for every 100 anti-Xa units (for enoxaparin)
- Protamine is given within first 8 hours of administering LMWH
- If bleeding continues, 0.5 mg protamine/100 anti-Xa units can be administered

- Smaller doses needed beyond 8 hours after LMWH administration
- Protamine neutralizes 65% of anti-Xa activity and 90% of anti-IIa activity.

Advantages Over UFH

- Protects against VTE better
- Greater efficacy: Safety ratio
- Once daily dose possible due to long DOA
- No monitoring required
- Less hemorrhage, osteoporosis, HIT.

Classification of Anticoagulants

- Used *invitro:*
  - Heparin
  - Sodium citrate: 1.65 gm/350 ml of blood
  - Sodium oxalate
  - Sodium edetate.
- Used *invivo:*
  - Parenteral agents:
    - Heparin (UFH, LMWN)
    - Heparinoids:
    - Heparan sulfate
    - Ancrod
    - Dextran sulfate.
  - Oral anticoagulants:
    - Coumarin derivatives:
      - Warfarin, acenocoumarin
      - Dicoumarol, ethyl bicoumacetate.
    - Inandione: Phenindione.

HEPARIN ALTERNATIVES[1,2,3,5,7,20]

Classification

- Direct thrombin inhibitors:
  - Lepirudin, bivalirudin
  - Debigatran etixilate
  - Argatroban, ximelagatran.
- Anti-Xa agents:
  - Danaparoid, rivaroxaban
  - Fondaparinux.
- Warfarin
- Defibrinogenating agents: Ancrod.

Direct Thrombin Inhibitors

Introduction

In contrast to the indirect inhibition of thrombin caused by heparin, DTIs require no preceding interaction prior to their effect on thrombosis (factor IIa).

Properties

- More specific
- Do not cross-react with HIT antibodies
- Acts on both soluble and thrombus bound thrombin
- Anti-inflammatory property
- Suppresses platelet function
- Used to treat arterial/venous thrombotic disorders.

Lepirudin/Desirudin

- Chemistry:
  - Recombinant hirudin derivative
  - Is present in saliva of *hirudo medicinalis*
  - Derived from yeast cells.
- Kinetics:
  - Half-life of 1.3 hours with peak effect in about 4 hours
  - Eliminated through renal clearance and effect is therefore prolonged in renal failure.
- Indications:
  - Anticoagulation with renal replacement therapy
  - CPB in heparin induced thrombocytopenia.
- Dose:
  - 0.4 mg/kg bolus followed by 0.15 mg/kg/hr infusion
  - When INR reaches 2, reduce lepirudin rate by 50%
  - Stop infusion when INR reaches 2.5
  - aPTT titrated to 1.5–2.5 times baseline.
- Monitoring:
  - ECT (Ecarin clotting time)
  - aPTT, ACT
  - PT, INR, TEG.
- Contraindications:
  - Patients with recent biopsy
  - Stroke, major surgery
  - Major bleeding, uncontrolled hypertension.
- Benefits:
  - Rapid onset of action
  - Short half-life
  - Does not cross react with HIT antibodies
  - Risk of bleeding is not increased.
- Reversal:
  - No antidote, factor VIIa may be tried for reversal
  - Emergency reversal can be done with plasmapheresis, hemofilteration and peritoneal dialysis.

Argatroban

- Small (molecular weight of 500 Da) arginine derivative
- Promotes nitric oxide release
- Half-life of 40–50 minutes
- Undergoes hepatic metabolism and excretion and is therefore useful in CRF
- FDA approved for use in PCI
- Dose: 2 µg/kg/min infusion
- Monitor ACT and aPTT
- Maintain aPTT at 1.5–3 times baseline
- Contraindicated when there is active bleeding.

Bivalirudin

- Direct thrombin inhibitor
- Dose: 0.75 mg/kg followed by 1.75 mg/kg/hr infusion.

Ximelagatran

- Oral prodrug of DTI melagatran
- Converts to melagatran which binds to clot bound and free thrombin
- Elimination half-life of 3 hours, cleared by kidneys
- Monitoring of coagulation is not necessary during therapy
- Does not increase incidence of bleeding
- Withdrawn from market due to hepatotoxicity: transiently increases transaminase levels.

Dabigatran Etexilate

- New oral prodrug of DTI dabigatran used for DVT prophylaxis
- Has low molecular weight
- Dosage: 200 mg OD 1–4 hours after surgery
- Epidural avoided for 36 hours after a dose and 12 hours before next dose.

ANTI-Xa Agents

Danaparoid

- Derived from porcine intestinal mucosa
- Composed of heparin, dermatan and chondroitin sulfate
- It is a univalent DTI and anti-Xa agent
- Anti-Xa: Antithrombin activity = 28:1
- Molecular weight of 527 Da
- Half-life of 40–50 minutes with elimination by renal clearance
- In heparin induced thrombocytopenia, 25 µg/kg/min to 350 µg/kg
- Monitoring:
  - ACT maintained at 250–300 seconds
  - Anti-Xa assay (0.5–0.8 U/ml is normal)
- It has low-risk of bleeding
- Emergency clearance can be done by plasmapheresis.

Fondaparinux

- Synthetic anticoagulant
- Contains 5 saccharide units
- These bind to antithrombin and inhibit factor Xa directly and indirectly
- 100% oral bioavailability
- Rapid onset of action (25 minutes after subcutaneous injection)
- Peak action 1–2 hours
- Elimination half-life 15 hours
- Elimination unchanged by kidneys and is therefore prolonged in CRF
- Useful to prevent DVT and pulmonary embolism
- Given 2.5 mg subcutaneously once daily.

Rivaroxaban

- Potent, selective *oral* Xa inhibitor
- 10 mg Q6–8H after surgery
- Remove epidural at least 20 hours after initial dose
- Next dose of epidural is delayed 4 hours after catheter removal.

Defibrinogenating Agents

Ancrod

- Defibrinogenating agent
- It is derived from Malayan pit viper venom
- Multiple mechanisms of action:
  - Cleaves fibrinogen to prevent clot formation
  - Reduces blood viscosity causing improved blood flow: Reperfusing agent
  - Thrombus modification
  - Altered hemostasis.
- It also limits brain damage in stroke
- Half-life of 3–5 hours, mainly eliminated via renal clearance
- Given subcutaneously or via IV infusion
- Contraindications:
  - Bleeding disorders, platelet counts < 1,00,000 / mm^3 (except HIT)
  - Planned surgery
  - Active GIT ulcers, renal stones
  - Uncontrolled hypertension.

EPSILON AMINO CAPROIC ACID[1,2,3,5,7,20]

Introduction

6-amino-hexanoic acid which acts as an inhibitor of fibrinolysis.

Chemistry

- Chemically, it is 6-amino-hexanoic acid
- Molecular formula: $C_6H_3NO_2$
- Packed as 250 mg/ml of EACA with 0.9% benzyl alcohol as preservative.

Pharmacokinetics

- Volume of distribution: 30 ± 8 liters
- Distributes throughout extravascular and intravascular compartments
- Penetrates RBCs and other tissue cells
- Eliminated renally with clearance = 116 ml/min
- Elimination half-life of approximately 2 hours.

Indications

Excessive bleeding due to:

- Systemic fibrinolysis: Pathological condition associated with:
  - Cardiac surgery, portocaval shunt
  - Hematological disorders like aplastic anemia
  - Abruptio, liver cirrhosis
  - Carcinoma of prostrate, lung, stomach.
- Urinary fibrinolysis: Normal physiological phenomenon associated with:
  - Complications following severe trauma
  - Following anoxia and shock.

Dosage

- Priming dose of 5 gms oral/IV (through slow infusion)
- Followed by 1–1.25 g doses at hourly intervals
- This is continued for 8 hours or until bleeding stops
- Dose more than 30 grams in 24 hour period is not recommended.

Contraindications

- When there is evidence of active intravascular clotting process
- In presence of DIC without using concomitant heparin
- Hematuria of upper urinary tract origin:
  - EACA can cause intrarenal obstruction
  - Form clots in renal pelvis and ureters causing obstruction
- Early pregnancy unless benefits out-weighs the risks as teratogenicity not established
- Not recommended in children and neonates:
  - Preservative benzyl alcohol can cause *Gasping syndrome*
  - Syndrome consists of:
    - Gasping respiration
    - Hypotension, bradycardia
    - Cardiovascular collapse.

Adverse Effects

- General:
  - Edema, headache, malaise
  - Hypersensitivity, anaphylaxis.
- Local: Injection site reaction, pain, necrosis
- Neurological:
  - Confusion, dizziness
  - Convulsion, hallucinations
  - Delirium, intracranial hypertension
  - Stroke, syncope.
- Cardiovascular:
  - Bradycardia
  - Hypotension (especially if rapid IV boluses)
  - Peripheral ischemia
  - Thrombosis.
- Respiratory:
  - Dyspnea
  - Nasal congestion
  - Pulmonary embolism.
- Genitourinary: Raised blood urea nitrogen, renal failure
- Dermatological: Pruritis, rashes
- Musculoskeletal:
  - Raised CPK levels, myalgia
  - Muscle weakness, myopathy
  - Myositis, rhabdomyolysis.
- Hematological:
  - Agranulocytosis
  - Leukopenia
  - Coagulation disorders, thrombocytopenia.

Overdose

Causes transient hypotension, ARF and death.

NITROUS OXIDE[1,2,3,5,7,20]

Introduction

Prepared by *Joseph Priestly* in 1776

Properties

- Colorless, odorless, inorganic gas
- Nonexplosive and noninflammable but supports combustion
- Gas at room temperature, becomes liquid under pressure
- Manufactured by heating ammonium nitrate in a controlled process
- Low blood gas partition coefficient (BGPC 0.47%)
- High MAC value (105%)
- Poor solubility but more soluble than oxygen
- More soluble than nitrogen (35 times)
- 1.5 times heavier than air.

Pharmacodynamics

Central Nervous System

- Weak anesthetic
- Powerful analgesic
- Mild evaluation of ICP as it increases CBF and CBV
- Increases cerebral O_2 consumption
- Maximum analgesic effect at 35% concentration.

Neuromuscular

- No muscle relaxation
- Skeletal muscle rigidity at high concentration.

Respiratory System

- Increased respiratory rate, reduces tidal volume
- Reduces ventilatory response to hypoxia and hypercarbia
- *Diffusion hypoxia* on emergence.

Cardiovascular System

- Slight direct myocardial depression
- Offset by sympathetic stimulation
- Opioids can block sympathomimetic effects
- Increases pulmonary vascular resistance.

Hepatic and GIT

- Reduces hepatic blood flow
- May cause PONV by stimulating CTZ and vomiting center in medulla

Renals

- Increases renal vascular resistance
- Reduces renal blood flow: Reduced GFR and urine output.

Pharmacokinetics

- Mainly eliminated unchanged through lungs
- <0.01% undergoes reductive metabolism by anerobic bacteria in GIT
- Small amounts diffuse through skin.

Mechanisms of Action

- Analgesic action through stimulation of opioid receptors
- Anxiolytic action through stimulation of GABA receptors.

Anesthetic Uses

- As a supplement to anesthesia
- As carrier gas for inhalational agents
- As analgesic agent in: *As entonox*
  - Obstetrics for labor analgesia
  - Burn dressing
  - Dental pain
  - Acute trauma and fracture reduction.

Contraindications

Absolute

- Neurosurgery
- Middle ear surgeries
- Congenital heart diseases with pulmonary HTN
- Significant respiratory compromise
- Laparoscopic surgeries
- Pneumothorax/air embolism/bowel obstruction.

Relative

- History of stroke/hypotension
- Vitamin B_{12}/folate deficiency
- Pregnancy.

Effects on Closed Gas Spaces

Highly Compliant Spaces

- Spaces normally contain nitrogen which:
  - Has low solubility
  - BGPC of nitrogen is 0.015
  - BGPC of N_2O is 0.47
- Therefore, entrance of N_2O into the space is not countered by an equal loss of N_2
- This increases the volume of the space
- Expansion occurs in cases of:
  - Pneumothorax, pneumoperitoneum
  - Air embolus
  - ETT cuff and cuff of inflatable balloons (Swann Ganz catheter).

- 75% N_2O in pneumothorax doubles the volume in 10 min and triples it by 30 mins
- 4 hrs of N_2O at 100% increases ETT cuff volume by 300–350%.

Poorly Complaint Spaces

- Increased IOP after intravitreal SF_6 for retinal detachment surgery
- Middle ear pressure: tympanic membrane rupture and displacement of TM graft during tympanoplasty
- Increased ICP during neurosurgery.

TOXICITY

Bone Marrow Toxicity

- It can cause bone marrow depression: Megaloblastic anemia and pernicious anemia
- Irreversibly oxidizes cobalt atom in vitamin B_{12}
- This inhibits vitamin B_{12} dependent enzymes
  - Methionine synthetase: Myelin formation
  - Thymidylate synthetase: DNA synthesis.
- Complete bone marrow failure after several days of exposure
- More than 12 hrs exposure causes mild and > 24 hrs causes marked changes.

Neurotoxicity

- Neurodeficits on prolonged exposure:
  - Peripheral neuropathy
  - Subacute degeneration of cord after several months.
- Prevented by pretreating patients with large doses of folinic acid
- This gets converted to 5, 10 methylene THF and causes thymidine synthesis.

Reproductive Toxicity

- No significant effect on sperms
- Reduced fertility and increased spontaneous abortion rates on chronic exposure
- Teratogenic effects.

Immunological Toxicity

- Alters chemotaxis
- Alters neutrophil mobility.

Environmental Toxicity

NIOSH recommendation

Theatre pollution: Recommended maximum level of N_2O < 25 ppm parts of air.

Desirable Properties

- Inexpensive
- Poor solubility: Ensures quick induction and recovery
- ***Second gas effect:*** Accelerates anesthetic effect
- Lessens respiratory irritation produced by isoflurane/sevoflurane
- Weak anesthetic but powerful analgesic
- It has little effect on respiration
- It has little effect on BP and heart rate.

Undesirable Properties

- Limited potency, MAC of 105
- It cannot produce anesthesia alone
- MAC awake for N_2O suppresses awareness but not recall
- Reduces delivered O_2 concentration and thus increases risk of hypoxia
- Diffusion hypoxia at emergence
- Impaired pulmonary function: Increased risk of hypoxia
- It can expand bowel gas, pneumothorax, air embolism, ETT cuff volume
- It can increase ICP, IOP and middle ear pressure
- Increases $CMRO_2$, CBF, ICP
- Increases pulmonary vascular resistance
- It does not provide ischemic preconditioning like volatile anesthetics
- Increases muscle tone and rigidity when used alone
- It can cause bone marrow depression and neurotoxicity
- Supports combustion.

Current Status

Due to increased number of undesirable properties, it is proposed that eliminating N_2O use leads to safer anesthetic delivery devices.

NITRIC OXIDE[1,2,3,5,7,20]

Introduction

- Vasoactive gas naturally produced from L-arginine, primarily in endothelial cells which is an important messenger molecule
- Formerly called endothelium derived relaxation factor (EDRF).

Chemistry

- Colorless, odorless, corrosive
- Only slightly soluble in water

- Unstable in air, undergoes spontaneous oxidation and forms NO_2.

Presentation

- Stored in aluminium or stainless steel cylinders
- Typically have 40 L capacity at high pressures (2000 PSIG)
- Stored as 100/1000/2000 ppm of NO in nitrogen.

Sites at Which Nitric Oxide is Biological Mediator

- Vascular endothelium
- Platelets
- Marcrophages
- Brain tissue.

Diseases Associated with Abnormal Nitric Oxide Production

- Ageing, smoking
- HTN, obesity, Type I and II DM, atherosclerosis
- Dyslipidemias:
  - Hypercholesterolemia
  - Hypertriglyceridemia.
- Heart failure
- Multiple sclerosis
- Ulcerative colitis
- Arthritis.

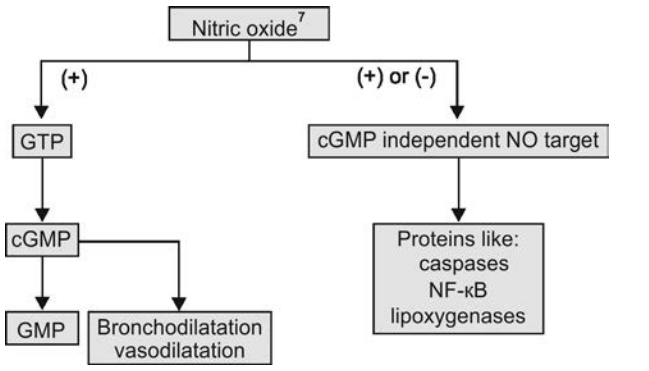
Administration

- Injected into patient limb of inspiratory circuit of ventilator
- To be stored prediluted in nitrogen
- Not injected between patient and ventilator to avoid over-dosage
- Not allowed to contact air/oxygen until it is used (to prevent NO_2 formation)
- Use of sodalime in inspiratory limb to absorb the formed NO_2 is advocated
- Delivered safely via face mask/nasal cannula/ET tube.

Mechanism of Action

- Nitric oxide diffuses out from endothelial cells and enters vascular smooth muscle
- It then stimulates guanylate cyclase and increases c-GMP levels causing vasodilation
- NO also causes vasodilation by reducing cytosolic calcium.

No Signalling Pathway



Pharmacokinetics

- Absorption:
  - Highly lipid soluble
  - Freely diffuses across cell membranes.
- Metabolism:
  - Rapidly converted to nitrates and nitrites in presence of oxygen
  - Reacts with oxidized hemoglobin to form methemoglobin
  - Half-life less than 5 seconds.

Pharmacodynamics

- Central nervous system:
  - Acts as neurotransmitter in CNS
  - Important role in modulation of:
    - State of arousal
    - Pain perception
    - Apoptosis
    - Long-term neuronal depression and excitation.
  - Peripheral neurons with NO control regional blood flow in corpus cavernosum.
- Cardiovascular:
  - Direct vasodilatation
  - Indirect vasodilatation by inhibiting AT-II medicated vasoconstriction
  - Antithrombotic effect by inhibiting platelet aggregation
  - Antiproliferative action by inhibiting smooth muscle hyperplasia
  - Anti-inflammatory by inhibiting leukocyte adhesion to vascular endothelium
  - Anti-apoptotic.
- Respiratory:
  - Selective pulmonary vasodilator when inhaled
  - Preferentially increases blood flow to well ventilated areas

  - Selective to pulmonary blood vessels as it rapidly binds to hemoglobin with high affinity and gets inactivated before reaching systemic circulation
  - Improves ventilation-perfusion relationship
  - Bronchodilatation
  - Anti-inflammatory.
- Gastrointestinal:
  - Determinant of GI motility
  - Modulates morphine induced constipation.
- Genitourinary:
  - Role in regulation of renin production
  - Role in Na^+ homeostasis in kidney
  - Physiological mediator of penile erection.
- Immunological:
  - Toxic to pathogens, important in host-defense mechanisms
  - Inhibits leucocyte adhesion to vascular endothelium
  - Scavenges superoxide anion.
- Hematological:
  - Reduces platelet aggregation
  - Prolongs bleeding time by inhibiting platelet function.

Advantages

- Selective pulmonary vasodilator
- Devoid of systemic action
- Dilates blood vessels in those lung regions which are well ventilated
- Favorably affects ventilation-perfusion relationship
- Low toxicity if safety precautions followed.

Disadvantages

- Stringent safety precautions required
- NO_2 induced pulmonary edema
- Methemoglobinemia
- Ciliary depletion in terminal bronchioles on chronic use
- Corrosive to metal
- Requires monitoring.

Uses

- Pulmonary hypertension:
  - For persistent pulmonary HTN secondary to:
    - Meconium aspiration
    - Pneumonia, sepsis
    - Hyaline membrane disease
    - Congenital diaphragmatic hernia
    - Pulmonary hypoplasia
  - Inhalational NO called INO_{max}
  - Recommended dose: 0.5–20 ppm (up to 80 ppm)
  - Lowest effective dose to be used
  - Onset time for reducing PVR and RV-SWI: 1–2 minutes
  - Should be maintained up to 14 days or until underlying oxygen desaturation has resolved.
- ARDS:
  - Effect on outcome not demonstrated conclusively
  - Mechanism of action in ARDS:
    - Selective pulmonary vasodilatation
    - Reduces pulmonary capillary pressure
    - Reduces pulmonary transvascular albumin flux
    - Improves oxygenation.
- Intraoperative:
  - Used for lung and cardiac transplants
  - Reduces the incidence of fatal pulmonary HTN post-transplant
  - Pulmonary vasoreactivity testing in catheterization laboratory
  - To treat pulmonary HTN following CABG: 20–40 ppm
  - Pulmonary hypertensive crises following congenital heart disease repair: 10 ppm
  - Insertion of LVAD: To reduce PVR after LVAD insertion.
- Pulmonary diseases:
  - Reduces rate of bronchopulmonary dysplasia but additional studies needed
  - COPD patients and bronchospasm:
  - Improves oxygenation when used with 1 L/min O_2 via facemask
  - If used alone, it may reduce oxygenation.
- Indirect effects:
  - Drugs like NTG (releasing NO) for angina
  - Drugs altering NO activity protects brain in stroke, Alzheimer and Parkinsons.

Monitoring NO Levels

- Chemiluminescent reaction:
  - $NO + O_3 \rightarrow NO_2 + O_2 + light$
  - Light is detected by photodetector
- Electrochemical analysis.

Toxic Effects

- Methemoglobinemia:
  - Neonates at greater risk as they have reduced levels of methemoglobin reductase

  - If inhaled concentration around 500–2000 ppm
  - Occurs 8 hours after inhalation.
- Pulmonary edema if NO_2 levels more than 10 ppm
- Acute lung injury and pneumonitis:
  - Due to elevated NO_2 levels which gets converted to HNO_3 in presence of water
  - This results in the formation of ***Acid Rain***
  - Occurs if environmental levels 25 ppm for more than 8 hours.
- Chronic use/sustained elevation:
  - Direct tissue toxicity
  - Results in ciliary depletion and epithelial hyperplasia of terminal bronchioles
  - Cardiovascular collapse associated with septic shock.
- Abrupt discontinuation:
  - Worsens PaO_2 and oxygenation
  - Increase in pulmonary artery pressures.
- Headache in hospital staff
- Others:
  - Alveolar hemorrhage, sepsis
  - Atelectasis, hyperglycemia
  - Stridor, cellulitis
  - Hematuria.
- Raised LV filling pressure due to direct negative inotropic actions
- Caution in patients with severe LV dysfunction.

Contraindications

In neonates dependant on right-left shunt.

XENON[1,2,3,5,7,20]

Properties

- Colorless, odorless, nonexplosive
- Density is 3.2 times that of air
- Viscosity is 1.7 times that of air
- BGPC = 0.15, MAC value = 63%
- Boiling point = 108.1 ºC
- Molecular weight = 54 kDa.

Ideal Anesthetic Agent

- Smooth induction, rapid emergence
- Environmentally safe, no occupational hazards
- Nontoxic, nonallergic
- No carcinogenic potential
- No fetoxicity
- Very low chances of diffusion hypoxia
- Produces anesthesia, analgesia and some degree of muscle relaxation
- It does not cause respiratory depression to the point of apnea
- Cardiac stable, not metabolized in body and eliminated completely by lungs.

Mechanism of Action

- Inhibits NMDA receptors: Anesthetic and analgesic actions
- Serotonin inhibitor: Used in management of PONV
- Central and peripheral nociception.

Stages of Xenon Anesthesia

Four stages of anesthesia with 70% xenon and 30% oxygen

- *Stage 1:* Whole body paresthesia and hypoalgesia
- *Stage 2:* Euphoria, increased psychomotor activity
- *Stage 3:* Analgesia, partial amnesia (after 3–4 minutes)
- *Stage 4:* Surgical anesthesia with degree of muscle relaxation.

Pharmacodynamics

- Central nervous system:
  - Neuroprotective as:
    - NMDA antagonist
    - Antiapoptotic effects
    - Activation of K^+ channels.
  - Some degree of muscle relaxation
  - Increases ICP and CBF in traumatic brain injury patients
  - Produces anesthesia and amnesia.
- Cardiovascular:
  - Mild sympatholytic effect
  - Negative inotropic effects
  - Ischemic preconditioning: Protects from brief periods of ischemia
  - No significant change in blood pressure.
- Respiratory:
  - Increases airway resistance
  - Increases turbulence and work of breathing due to increase in density and viscosity
  - Very low BGPC (0.115): Low chances of diffusion hypoxia.

Use in Anesthesia

- Xe^{133} isotope is most commonly used
- MAC value of 63%
- MAC_{awake} of 33%
- 50% xenon causes increase in pain threshold and reduces consciousness

- 80% xenon produces profound analgesia
- Delivered via ***Physioflex*** machine with rotating meters to measure gas flow.

Other Uses

- Induction agent
- Nuclear medicine to diagnose ventilation-perfusion mismatch
- To find out functional capacity of lung parenchyma
- CT scans of brain and lungs to:
  - Diagnose early infarct and vasospasm
  - Evaluation of head trauma
  - Confirmation of brain death
  - Locate seizure foci.

Disadvantages

High cost and low availability.

HALOTHANE HEPATITIS[1,2,3,7,20]

Definition

Jaundice occurring in a patient who is previously exposed to halothane within 3 weeks with fever, rashes and lab evidence of raised liver enzymes like SGOT, SGPT and antibodies.

Incidence

- Male : Female : 1 : 2
- Type I halothane hepatitis: 25–30%
- Type II halothane hepatitis: 1: 6000–35000
- In children: 1: 1,00,000–2,00,000 (rare).

Classification

- Type I halothane hepatitis:
  - Mild form
  - Benign features
  - Self-limiting disease
  - Mild rise in serum transaminase and glutathione-S-transferase
- Type II halothane hepatitis:
  - Severe form
  - Causes massive centrilobular necrosis
  - Results in fulminant liver failure.

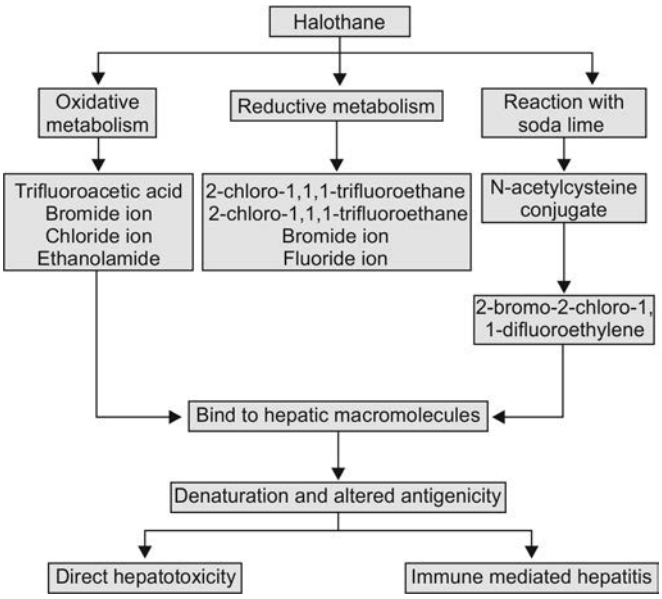
Clinical Features

- High grade fever lasting for 3–14 days
- Jaundice: Onset within 1–2 days after fever
- Nausea, vomiting anorexia
- Chills, myalgia, rash
- Moderate liver enlargement with tenderness.

Lab Findings

- Raised serum bilirubin
- Raised serum ALT, AST and alkaline phosphatase
- Increased prothrombin time
- Increased GST > 2 is specific index.

Metabolism and Mechanism



Risk Factors

- Multiple exposures at intervals < 6 weeks
- Prior history of postanesthetic fever/jaundice
- Duration: Prolonged exposure, major surgeries
- Obesity, middle age, pregnancy
- Male : Female ratio: 1 : 2
- Enzyme induction (alcohol/barbiturates)
- Drug allergy, recent viral hepatitis.

Predisposing Factors

- Pregnancy
- Viral hepatitis
- Burns
- Hypoxia, hypercarbia.

Guidelines for Safe Use

Avoid halothane if:

- Age more than 70 years
- Obese females
- Pre-existing liver disease/biliary surgery
- If family history of unexplained jaundice after halothane
- Recent halothane exposure within six weeks.

Prognosis

- If fulminant liver failure occurs, 50% deaths
- Hepatic encephalopathy also results in 50% deaths.

NEPHROTOXICITY OF FLUORINATED AGENTS[1,2,3,7,20]

Mechanisms of Nephrotoxicity

- Reduced renal blood flow
- Inorganic fluoride production is directly nephrotoxic
- Vinyl halide production
- BCDFE induced nephrotoxicity.

FLUORIDE INDUCED NEPHROTOXICITY

Mechanism

- Fluoride inhibition of adenylate cyclase:
  - Prevents normal action of ADH on DCT
  - Therefore unable to concentrate urine.
- Fluoride induced intrarenal vasodilation:
  - Shunting of blood from cortex to medullary area
  - This interferes with counter current multiplier mechanisms.

Toxic Levels

Sl No	Fluoride levels	Manifestations
1	< 50 µmol/l	No evidence of toxicity
2	50–80 µmol/l	Moderate injury
3	80–120 µmol/l	Severe injury
4	> 120 µmol/l	Most often fatal

Clinical Features

- Polyuria (inability to concentrate urine)
- Hyperosmolarity
- Hypernatremia
- Increased plasma creatinine.

Factors Affecting Toxicity

Individual Agents

- Methoxyflurane *most nephrotoxic* and causes high output renal failure
- Enflurane: Only transient reduction in renal concentrating ability
- Isoflurane:
  - Resistant to defluorination
  - No significant increased in fluoride concentration on prolonged administration.
- Sevoflurane:
  - Due to low blood solubility, even though fluoride concentration increases, it falls very rapidly after surgery and toxicity is very rare
  - Not nephrotoxic.
- Desflurane:
  - No evidence of nephrotoxicity
  - No biotransformation
- Halothane: Not nephrotoxic.

Metabolism

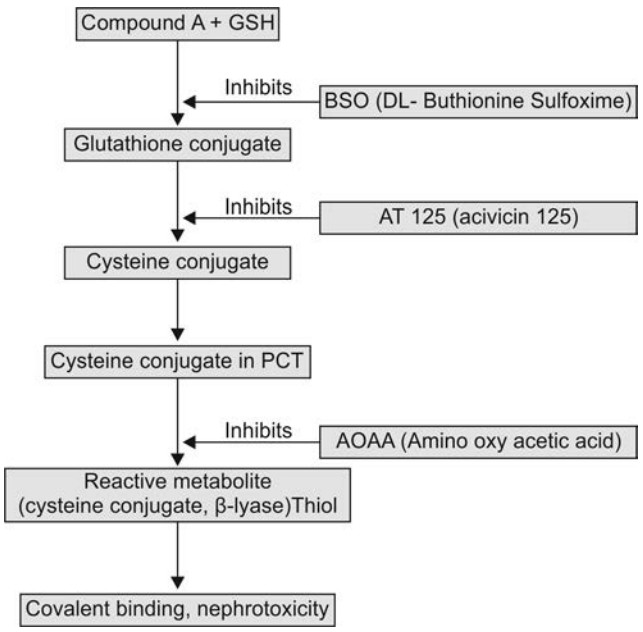
- Intrarenal metabolism causes more nephrotoxicity than metabolism in liver
- Methoxyflurane and enflurane undergo more intrarenal metabolism to fluoride
- Therefore they are more nephrotoxic
- Sevoflurane undergoes more hepatic metabolism
- Thus sevoflurane is less nephrotoxic even though fluoride concentration is more.

VINYL HALIDE NEPHROTOXICITY

Mechanism

Reaction of fluorinated volatile anesthetic agents with CO_2 absorbent produces trifluromethylvinyl ether *(Sevoolefin/compound A)*.

β-LYASE PATHWAY



Factors Affecting Toxic Levels

- Total exposure rather than absolute concentration is more important determinant of toxicity
- 150–300 ppm-hours of compound A exposure (i.e. 50 ppm for 3 hrs)
- Compound A production more with baralyme than sodalime
- More production occurs with increased temperature of absorbent
- Hyperventilation causes increased temperature increasing compound A levels.

Recommendations to Reduce Nephrotoxicity

- Use fresh gas flow of at least 2 L/min while using sevoflurane to prevent accumulation of metabolites in breathing circuit
- Most important factor determining blood levels is inspired FGF rate
- Renal changes with prolonged sevoflurane exposure is usually transient
- Patients with pre-existing renal disease not to be exposed to sevoflurane
- Lower threshold for renal toxicity is 150 ppm — hrs of compound A.

BCDFE Induced Nephrotoxicity

- Produced due to reaction of halothane with CO_2 absorbent
- 75% less nephrotoxic than compound A
- BCDFE is *bromochlorodifluoro ethane*
- Chance of BCDFE causing nephrotoxicity when halothane is used as sole anesthetic is negligible.

Methods of Studying Nephrotoxicity

- Creatinine clearance
- Maximal urinary osmolality
- Urinary N-acetyl β-macroglobulin
- Urinary excretion of alanine aminopeptidase.

HERBAL TOXICITY

Sl No	Drug	Common use	Toxicity
1.	Ephedra	Weight loss Antitussive Bacteriostatic	Halothane arrhythmias MAO-I: Increased sympathetic effect Oxytocin: HTN Stroke, HTN, cardiac arrest
2.	Garlic	Lipid lowering Antiplatelet Antihypertensive Antioxidant	Potentiates warfarin Reduces platelet aggregation
3.	Echinacea	Common cold prevention	Hepatotoxic Inhibits CYP1A2 Induces CYP 3A
4.	Ginger	Nausea Antispasmodic	Inhibits thromboxane A2 synthetase
5.	Gingko	Circulatory stimulant	Inhibits platelet activating factor Increases bleeding
6.	Kava	Anxiolytic	Hepatotoxic Potentiates BZDs Potentiates barbiturates
7.	Licorice	Gastric ulcer Gastritis Cough, bronchitis	Hypokalemia Hypertension Edema
8.	Vitamin E	Antiageing Reduce stroke Reduce atherosclerosis Improve wound healing	Increased bleeding Hypertension Reduces platelet aggregation
9.	St. Johns wort	Depression	Reduces digoxin efficacy Reduces warfarin efficacy Reduces anticonvulsant efficacy Prolongs emergence Cardiovascular toxicity CYP3A induction
10.	Valerian	Sedative Anxiolytic	Potentiates barbiturates

INTRATHECAL/EPIDURAL OPIOIDS[1,2,3,7,20]

Introduction

Analgesia provided by intrathecal administration of opioids is not associated with sympathetic denervation, skeletal muscle weakness or loss of proprioception.

Mechanism of Action

- Analgesia following epidural placement of opioids is by diffusion across dura mater
- They act on the μ receptors present in substantia gelatinosa of the spinal cord
- Lipophilic opioids rely mainly on systemic absorption from epidural space to act on systemic opioid receptors
- Epidural administration of these drugs (fentanyl/sufentanyl) may therefore offer no clinical advantages over IV administration
- Analgesia is specific for visceral rather than somatic pain.

Pharmacokinetics

- Epidural opioids:
  - Movement of opioids from epidural space depends on their lipid solubility
  - Lipid soluble opioids:
    - Have a quick onset and short duration of action
    - Opioids can get absorbed into epidural fat and CSF
    - They also get absorbed into systemic circulation via *Batsons plexus*
    - Time for peak CSF concentration after epidural administration:
      - Fentanyl: 20 minutes
      - Sufentanyl: 6 minutes
      - Morphine: 1–4 hours.
    - Time for peak blood concentration after epidural administration:
      - Fentanyl: 5–10 minutes
      - Morphine: 10–15 minutes.
    - Only 3% of epidural morphine reaches CSF
    - Addition of epinephrine to epidural opioids reduces systemic absorption
    - Lipophilic drugs get absorbed more into systemic circulation than CSF
    - They also depend more on systemic opioid receptors on epidural administration.
  - Water soluble opioids:
    - Water soluble opioids get absorbed more into CSF
    - Absorption into CSF however is slower
    - Therefore, they have slower onset but longer duration of action
    - They depend less on systemic receptors for their action.
- Intrathecal opioids:
  - Cephalad movement of opioids in CSF is dependent on their lipid solubility
  - Lipid soluble opioids are limited in cephalad migration by uptake into spinal cord
  - Less lipid soluble opioids remain in CSF for transfer to more cephalad location
  - The cause of ascent is bulk flow of CSF
  - This can be increased by coughing/straining (but not position of patient)
  - They can reach up to cisterna magna, 3rd, 4th and lateral ventricles (within 3–6 hours) through bulk flow.

Dosages

(epidural close = 5–10 times SA dose)

- Fentanyl:
  - Intrathecal: 5–25 μg
  - Epidural: 50–100 μg
  - Onset of action: 5–10 minutes (faster)
  - Duration of action: 2–4 hours (shorter).
- Morphine:
  - Intrathecal: 0.1–0.3 mg
  - Epidural: 1–5 mg
  - Onset of action: 30–60 minutes (delayed)
  - Duration of action: 6–24 hours (longer).
- Alfentanyl: Epidural: 0.5–1 mg
- Sufentanyl:
  - Intrathecal: 2–10 μg
  - Epidural: 10–50 μg.
- Hydromorphone: Epidural: 0.5–1 mg
- Diamorphone:
  - Intrathecal: 1–2 mg
  - Epidural: 4–6 mg.
- Meperidine/Pethidine:
  - Intrathecal: 10–30 mg
  - Epidural: 20–60 mg.
- Methodone: Epidural: 4–8 mg
- Butorphanol:
  - Intrathecal: 5–25 μg/kg
  - Epidural: 1–4 mg.

Advantages of Neuraxial Opioids

- Longer duration of analgesia: Better postoperative pain control
- No associated sympathetic denervation
- No associated muscle weakness
- No loss of proprioception.

Side Effects of Neuraxial Opioids

- Side effects are less common in those chronically exposed to opioids
- Pruritis:
  - *Most common* side effect of neuraxial opioids: 1% incidence
  - More common in obstetric patients due to interaction with estrogen receptors
  - It may be localized to face, neck, thorax or generalized
  - Due to cephalad migration and interaction with μ receptors in trigeminal nucleus
  - Treatment:
    - Antihistaminics and naloxone
    - Naltrexone and nalbuphine also can be used.
- Urinary retention:
  - More common in young males
  - Occurs due to interaction with μ receptors in sacral spinal cord
  - This causes inhibition of sacral parasympathetic outflow: Increased bladder capacity
  - Epidural morphine also causes detrusor relaxation within 15 mins, lasting up to 16 hrs
  - Treatment: Low dose naloxone (0.5–1 μg/kg).
- Ventilatory depression:
  - It may be early or late ventilatory depression
  - Incidence of 1% and is equal to incidence following IV administration of opioids
  - Early depression: Within 2 hours of injection:
    - More with lipophilic opioids, unlikely with morphine
    - Occurs due to systemic absorption of LA
    - Cephalad migration of opioids in CSF might also be responsible.
  - Delayed depression: After 72 hours of injection:
    - More common with hydrophilic opioids
    - Occurs due to cephalad migration of LA
    - LA subsequently interact with opioid receptors in ventral medulla
    - Characteristically occurs 6–12 hours after epidural or intrathecal morphine
    - Usually does not occur after 24 hours of administration.
  - Factors increasing risk:
    - Concomitant IV sedative administration
    - Coughing, straining
    - Advanced age, raised intrathoracic pressure.
  - Obstetric patients are at low risk due to ventilatory stimulation by progesterone
  - Treatment:
    - Naloxone 0.5–1 μg/kg up to 1–2 μg/kg
    - Infusion: 0.5–5 μg/kg/hr.
- Nausea and vomiting:
  - Due to spread to area postrema in medulla oblongata
  - More common with hydrophilic opioids
  - Treatment:
    - Metaclopramide (0.2 mg/kg), ondansetron 4 mg IV
    - Droperidol 25–50 μg/kg, transdermal scopolamine patch (1.25 mg)
    - Naloxone 0.5–1 μg/kg.
- Sedation:
  - More often with sufentanil
  - May be due to depression of ventilation causing carbon dioxide narcosis
  - Paranoid psychosis, catatonia, hallucinations which are naloxone reversible also occur.
- CNS excitation:
  - Tonic rigidity similar to seizures occurs rare
  - Myoclonus progressing to grand mal seizures
  - It may be due to cephalad migration and interaction with nonopioid receptors in brainstem and basal ganglion
  - This causes blockade of glycine/GABA mediated inhibition.
- Viral reactivation:
  - Reactivation of herpes simplex virus
  - Occurs commonly 2–5 days after epidural morphine in obstetric patients
  - Occurs due to cephalad migration and interaction with trigeminal nucleus.
- Neonatal morbidity:
  - It may cause increased blood levels in neonates: respiratory depression
  - Negligible concentration in breast milk (fenta/sufenta).
- Miscellaneous:
  - Sexual dysfunction: Sustained erection, inability to ejaculate
  - Ocular: Miosis, nystagmus, Vertigo (naloxone reversible)
  - Delayed gastric emptying

- Peripheral edema due to:
  - Oliguria
  - Water retention due to release of vasopressin (from cephalad migration).
- Spinal cord damage due to preservatives: Spasms, paresis, paralysis.

STEROID THERAPY IN PERIOPERATIVE PERIOD[1,2,3,7,20]

Introduction

Increasingly used in perioperative period.

Indications

- Perioperative steroid replacement therapy
- Postoperative nausea and vomiting (PONV)
- Daycare surgery
- Anaphylaxis
- Septic shock
- Anti-inflammatory uses
- Hyper-reactive airway
- Analgesic adjunct
- Cerebral edema
- Spinal cord injuries
- Specific surgeries.

Comparison of Steroids

Compound[7]	Anti-inflammatory potency	Na retention potency	DOA	Equivalent dose
Cortisol	1	1	8–12 h	20
Cortisone	0.8	0.8	8–12 h	25
Dexamethasone	25	0	36–72 h	0.75
Prednisone	4	0.8	12–36 h	5
Prednisolone	4	0.8	12–36 h	5
Triamcinolone	5	0	12–36 h	4
Betamethasone	25	0	36–72 h	0.75

Steroid Replacement Therapy

Indications

- Adrenal suppression
- Axis separation due to steroid intake — > 5 mg prednisone for at least one month in past six months
  - Rhematoid arthritis
  - Ulcerative colitis
  - Bronchial asthma.

Dosage

Kehlet and Salem et al:

For patient currently on steroids:

< 10 mg/day prednisolone	Assume normal HPA axis	Additional cover not required
> 10 mg/day prednisolone	Minor surgery	25 mg hydrocortisone @ induction
	Moderate surgery	• Usual preoperative steroid • 25 mg hydrocortisone at induction • 100 mg/day for 24 hrs
	Major surgery	• Usual preoperative steroid • 25 mg hydrocortisone at induction • 100 mg/day for 48–72 hrs
High dose immunosuppression		Usual immunosuppressive dose at induction

For patients stopped taking steroids:

< 3 months	Treat as if on steroids
> 3 months	No perioperative steroids necessary

Advantages

- Prevents stress induced hypotension and shock
- Prevents secondary adrenal insufficiency
- Prevents hypothalmo pituitary axis suppression.

Disadvantages

- Catabolic effects
- Affects wound healing
- Impairs glucose metabolism.

Anti-inflammatory Uses

Indications

- Anaphylactic reactions:
  - Blood transfusions
  - Drug allergies.
- Solid organ transplant
- Spinal cord injuries (within 8 hrs of injury)
- Autoimmune disorders.

Mechanism of Action

- Inhibit production of interleukins, cytokines, chemotactic agents
- Reduced secretion of proteolytic enzymes
- Decreased leucocyte margination
- Diminished inflammatory response.

Hyper-reactive Airways

Indications
- History of asthma
- Recent upper respiratory tract infection
- Difficult airway
- Multiple intubation attempts
- Aspiration
- Airway surgeries
- COPD
- Foreign body bronchus.

Mechanism of action
- Anti-inflammatory
  - Decreased mucosal edema
  - Prevents bronchoconstictor release.
- Enhance efficacy of bronchodilators.

Postoperative Nausea and Vomiting

Optimal dose 10 mg IV
Most effective if given before induction

Mechanism of action:
- Decreased production of inflammatory mediators
- Improves blood brain barrier function
- Synergistic effect with 5-HT3 antagonists.

Day Care Surgery

12 mg betamethasone IM 30 minutes prior to surgery

Mechanism of action:
- Decreased incidence of PONV
- Decreased postoperative pain
- Establishes early oral intake
- Elevates level of endorphins.

Anaphylaxis

100 mg hydrocortisone IV after initial therapy with epinephrine 0.5 ml of 1:1000 IM or SC
IV methylprednisolone 125 mg Q6H in very severe cases.

Cerebral Edema

Loading dose dexamethasone 8–32 mg IV.

Mechanism of action:
- Reduces vasogenic edema
- Stabilizes cerebral endothelium
- Increases cerebral glucose utilization
- Electrolyte shifts favoring trancapillary efflux of fluid
- Inhibits release of free radicals
- Increased lysosomal activity of cerebral capillaries.

Spinal Cord Injury

Methylprednisolone 30 mg/kg IV loading dose
5.4 mg/kg/hr infusion for 23 hrs
To be used within 8 hrs of cord injury.

Specific Surgeries

250 mg methylprednisolone prior to and for 2 days post esophageal resection.

ICU SEDATION[1,2,3,7,10,20]

Aims
- Improve patient comfort
- Analgesia
- Reduce incidence of ICU delirium
- Facilitate mechanical ventilation
- Facilitate therapeutic interventions.

Drugs Used

Induction Agents
- Propofol: < 75 µg/kg/min for < 48 hrs to avoid PRIS (FDA recommendation)
- Thiopentone: To treat refractory raised ICP (BTF 2007)
- Ketamine.

Benzodiazepines
- Midazolam: Accumulation of metabolites (hydroxy-midazolam) in ARF
- Lorazepam: Causes increased incidence of ICU delirium.

Opioids
- Morphine: Accumulates on prolonged usage
- Fentanyl, alfentanil, sufentanil: Long context sensitive T1/2
- Remifentanil: Useful adjunct, 0.1–0.15 µg/kg/min.

Inhalational

AnaConDa for isoflurane use.

α_2 Agonist
- Dexmedetomidine 0.1–1 µg/kg/hr infusion for duration < 24 hrs (FDA recommendation)
- Clonidine 4 µg/kg/hr in NICU sedation protocols.

Antipsychotics
- Olanzapine
- Quetiapine
- Haloperidol.

Types
- Hypnotic based sedation
- Analgosedation with remifentanil.

Recommendations
- Ideally should be protocol based sedation
- Titrated to sedation scores
- Should resemble normal sleep wake cycle
- Avoid over/under sedation
- Avoid neuromuscular blocking agents
- Sedation holiday.

ICU Sedation Protocols

Patient Targeted Sedation Protocols
- Once in 4 hrs assessment of pain and distress
- Bolus doses given by nurse
- Continuous infusion started if increased frequency of boluses.

Daily Interruption of Continuous Sedation
- Continuous infusion
- Interrupted daily
- Assess distress and pain
- Restart at half the previous dose if increased distress.

Sedation Assessment
Ramsays sedation scale:

Score	Description
1	Confused, irritable
2	Comfortable, oriented
3	Responds to vocal commands
4	Brisk response to auditory stimulus/glabellar tap
5	Sluggish response to auditory stimulus/glabellar tap
6	No response

Advantages
- Better patient comfort
- Pain free
- Reduced anxiety and ICU delirium
- Reduced post-traumatic stress syndrome
- Facilitates mechanical ventilation and therapeutic interventions.

Disadvantages
Oversedation
- ICU sedation itself is risk factor for delirium
- Respiratory depression
- Hypoxia, hypercarbia in extubated patients
- Hemodynamic instability
- Delayed weaning
- Long ICU stay, long hospital stay.

Undersedation
- Pain, delirium, anxiety
- Self-extubation
- Ventilator asynchrony
- Raised airway pressure
- HTN, arrhythmias, MI.

ROLE OF NEUROMUSCULAR BLOCKERS IN ICU[1,2,3,7,10,20]

Indications for NMB in ICU
- To facilitate mechanical ventilation:
  - To facilitate endotracheal intubation
  - Enable patients to tolerate ventilation
  - High pulmonary inflation pressure: ARDS
  - Prone ventilation.
- Facilitate permissive hypercapnea
- Hyperventilation for raised ICP
- Facilitate therapeutic/diagnostic procedures
- To reduce oxygen consumption:
  - Abolish shivering
  - Reduce work of breathing.
- Treatment of tetanus and status epilepticus.

Complications of Muscle Paralysis in ICU
- Short-term use:
  - Specific drug side effects
  - Inadequate ventilation if ventilator failure/disconnection
  - ICU awareness: Inadequate sedation/analgesia.
- Long-term use:
  - Complications of immobility:
    - DVT, pulmonary embolism
    - Peripheral nerve injuries
    - Decubitus ulcers
  - Inability to cough: Retention of secretions, pneumonia
- Dysregulation of nACH receptors
- Residual paralysis:
  - Persistent neuromuscular blockade
  - *Critical illness myopathy*
  - *Critical illness neuropathy*
  - Use of vecuronium in renal failure patients
  - High dose steroids in asthmatics.

- Unrecognized effects of drugs/metabolites:
  - Succinylcholine, 3-desacetylvecuronium, laudanosine
  - Metabolic acidosis
  - Hypovolemia
  - Cerebral excitation.

Risk Factors for Development of Neuromuscular Dysfunction

- Female sex, steroid administration
- Hypercapnea, increased duration of mechanical ventilation
- Sepsis
- Dysfunction of more than two organ systems.

Recommendations for Neuromuscular Blockade in ICU[1,3]

- Avoid use of neuromuscular blockers:
  - Maximize use of analgesics and sedatives
  - Manipulate ventilator modes and parameters.
- Minimize use of succinylcholine as:
  - Upregulation of AChRs occurs due to immobilization
  - This causes high incidence of cardiac arrest due to hyperkalemia
  - Contraindicated in patients with total body immobilization for more than 24 hours.
- Minimize dosage of neuromuscular blocking agents:
  - Use only in patients who cannot be managed otherwise
  - Administer only when required and to achieve a well defined goal
  - Administer as bolus doses rather than continuous infusions
  - Use peripheral nerve stimulator with TOF monitoring
  - Continuously allow recovery from paralysis
  - Do not administer NMBAs for more than 2 days continuously
  - Drug requirement increases with time due to receptor upregulation
  - Avoid combining nondepolarizing agents with steroids.
- Choice of nondepolarizing muscle relaxants:
  - Steroid based relaxants like vecuronium/pancuronium have prolonged action
  - These drugs may cause residual palsy
  - Atracurium causes residual palsy in 70% cases if NM blockade exceeds 2 days
  - Cisatracurium is better as lesser chances of residual palsy
  - Laudanosine accumulation is less with cisatracurium compared with atracurium.
- Consider alternative therapy:
  - Avoid vecuronium in females with renal failure
  - Use isoflurane in place of muscle relaxants for treatment of status asthmaticus
  - Reduce dose of steroids in asthma patients.

THIOPENTONE VS PROPOFOL

Property	Thiopentone	Propofol
Chemistry	Thiobarbituric acid	2,6-di-isopropyl phenol
	S(+) and R(-) isomers present	Nonchiral compound: No isomers
Presentation	Hygroscopic yellow powder	Oily emulsion
	Water soluble	Fat soluble
	6% Na_2CO_3 preservative	Sodium metabisulphite preservative
	Used as 2.5% solution	Used as 1% solution
	Alkaline pH 10.8	Acidic pH 4.5–6.5
	Bacteriostatic due to alkalinity	Promotes bacterial growth due to lipid carrier
Mechanism of action	Direct and indirect action on $GABA_A$	No direct $GABA_A$ action
	Also on n-AChR and glutamate receptors	Acts on NMDA receptors

Contd...

Contd...

Property	Thiopentone	Propofol
Pharmacodynamics		
Central nervous system	Residual effects: hangover	Clear headed recovery
	Anticonvulsant	Causes myoclonus
	Antalgesic	Analgesic
Cardiovascular	Tachycardia	Rarely bradycardia and asystole
Respiratory	Bronchospasm, laryngospasm	Bronchodilatation
	Preserved laryngeal reflexes	Laryngeal reflexes are blunted
Hepatic	Reduces hepatic blood flow	Hepatocellular injury on long-term infusions
Renal	Reduces urine output	Phenoluria: Green color urine
Pharmacokinetics	Absorbed rectally	Not absorbed
	V_d 2.5 L/kg	V_d 3.5–4.5 L/kg
	72–86% plasma protein bound	97% plasma protein bound
	Hepatic oxidative metabolism	Hepatic metabolism by hydroxylation
	No extrahepatic metabolism	Extrahepatic metabolism in lungs and kidney
	Excreted in urine	Excreted in urine and feces
	Enzyme inducer	No enzyme induction
Uses	Induction agent 3–5 mg/kg	Induction agent 1.5–2 mg/kg
	Raised ICP	Anticonvulsant
	Cerebroprotection	Antiemetic 10–15 mg IV
	Checking wet epidural tap	Antipruritic 10 mg IV
Side effects	Hypotension, tachycardia	Asystole, bradycardia
	Allergy due to histamine release	Allergy due to cremaphor-EL
	Arterial thrombi	Not common
	No increased risk	Increased risk of pancreatitis
	Rare	Pain on injection common
	Not common	Liver damage on prolonged infusion (PRIS)
Contraindications	Porphyria	Drug allergy
	Status asthmaticus	
	Cardiac tamponade, shock	

DOPAMINE VS DOBUTAMINE

Property	Dopamine	Dobutamine
chemistry	Natural endogenous catecholamine	Synthetic derivative
	Nonchiral compound	Two isomers present: L(–) and R(+)

Contd...

Contd...

Property	Dopamine	Dobutamine
Presentation	40 mg/mL of dopamine	50 mg/mL of dobutamine
	200 mg/ampoule of dopamine	250 mg/ampoule of dobutamine
Mechanism of action	α_1, β_1, β_2, D_1, D_2 receptors	β_1, weak β_2 and α_1 actions
	Dosewise variation in action:	Less than 5 µg/kg/min: β_1 action
	0–5 µg/kg/min: D_1 and D_2 action	More than 5 µg/kg/min: α_1 action
	5–10 µg/kg/min: β_1 and β_2 action	No indirect action
	More than 10 µg/kg/min: α_1 action	
Pharmacodynamics		
Cardiovascular		
Cardiac output	Increased	Increased
Heart rate	Increased	Increased (less likely)
Arrhythmias	Stimulates	Stimulates
Coronary vasculature	Vasoconstriction	Vasodilatation
Myocardial O_2 demand	Increased	Not increased
Systemic vascular resistance	Increased	Decreased
	Vasodilatation in brain and kidney	Vasodilatation in skin and skeletal muscle
	Increases pulmonary artery pressure	Decreases pulmonary artery pressure
Renal blood flow	Increased	Increased (less prominent effect)
Pharmacokinetics	V_d = 1.8–2.5 l/kg	V_d = 0.2 l/kg
	Onset of action within 5 minutes	Onset of action within 1–2 minutes
	Eliminated in urine	In urine and feces
Uses	Postsurgery cases	Low cardiac output states
	Not used commonly	Stress testing
	Septic shock	Not used commonly
	Not used	Corpulmonale, right heart failure
	Mainly in cardiac surgical ICU	Mainly in cardiac CCU
Side effects	Nausea and vomiting prominent	Rare
	Rare	Allergy present
	Raised IOP	No increase in IOP
	Hyperglycemia	Reduces blood glucose
	Potentiates development of MODS	Does not potentiate
Contraindications	Pulmonary HTN, cor pulmonale	Used in these patients
	Used in these patients	Aortic stenosis, mitral stenosis
	Allergies are rare	Allergies

MIDAZOLAM VS PROPOFOL

Property	Midazolam	Propofol
chemistry	Benzodiazepine, imidazole ring	2,6-diisopropyl phenol
	Water soluble	Lipid soluble
Presentation	Syrup with 2 mg/mL	No oral preparation
	IV preparation with 1/2/5 mg/ml	1% solution
	pH of 3.5	pH of 4.5–6.5
	pH dependant ring opening phenomenon	Not present
	No preservative	EDTA or sodium metabisulfite
	Mixed with lactated ringers	Not recommended
Mechanism of action	Agonist at BZD receptor	$GABA_A$ stimulant
	κ-opioid agonist	Inhibits ACH release from hippocampus
	No action on NMDA receptor	NMDA inhibition
Routes of administration	Oral, IV, IM, epidural, intrathecal	Only IV administration
Dose	1.5–2 IV	1.5–2 mg/kg IV
Pharmacodynamics		
Central nervous system	Anterograde amnesia	Absent
	Muscle relaxant	No muscle relaxation
	Not cerebroprotective properties	Cerebroprotective
	Not present	Myoclonus, abnormal motor activity
	Cannot produce isoelectric EEG	Can produce isoelectric EEG
Cardiovascular system	No reduction in cardiac output	Reduced cardiac output
	Not present	Bradycardia and asystole
Respiratory system	Intact laryngeal reflexes	Laryngeal reflexes lost
Others	Absent	Phenoluria possible
	No hepatocellular injury	Hepatocellular injury on long infusion
Pharmacokinetics	V_d of 1–1.5 L/kg	V_d of 3.5–4.5 L/kg
	96–98% plasma protein bound	97% plasma protein bound
	Onset of action 30–60 seconds	Onset of action 30–45 seconds
	Duration of action 15–80 minutes	Duration of action 10 minutes
	Only hepatic metabolism	Extrahepatic metabolism present
	Excreted in urine	Excreted in urine and feces
	Elimination $T_{1/2}$ 1.5–3 hours	Elimination $T_{1/2}$ 10–70 minutes
Uses	Mainly as premedication	Mainly as induction agent
	Also useful as anticonvulsant	Also used for cerebroprotection
	Used in paradoxical vocal cord motion	Used as antiemetic and antipruritic
Side effects	Rare	Pain on injection
	Ventilatory depression	Transient apnea
	Withdrawal phenomenon on long-term use	Dependence and abuse potential common

MIDAZOLAM VS DIAZEPAM

Property	Midazolam	Diazepam
Chemistry	Water soluble BZD	Lipid soluble BZD
Preservative	Syrup: 2 mg/mL	Syrup: 0.4 mg/mL
	IV presentation: 1/2/5 mg/mL	5 mg/mL solution
	Not available	Available as rectal suppository
	No solvent required	Propylene glycol as solvent
	Water soluble	Fat soluble
	pH 3.5	pH 6.6–6.9
	pH dependent ring opening phenomenon	No such phenomenon
	Not available	Soybean formulation to reduce pain
Route of administration	Oral/IV/IM/epidural/spinal	Oral/IV/IM/rectal
Pharmacokinetics	50% oral bioavailability	86–100 % oral bioavailability
	80–100% IM bioavailability	IM absorption slow and erratic
	V_d 1–1.5 l/kg	V_d 1–1.5 l/kg
	96–98% plasma protein bound	96–98% plasma protein bound
	Duration of action 15–80 minutes	Longer duration of action
	Onset of action 30–60 seconds	Onset of action late
	Short context sensitive half-life	Very long context sensitive half-life
	Metabolized by hepatic hydroxylation	
	1 hydroxy-midazolam active metabolite	Desmethyl-diazepam active metabolite
	Hepatic clearance 10 times faster	Hepatic clearance slow
	Renal elimination	Renal elimination
	Elimination $T_{1/2}$ 1.5–3 hours	Elimination $T_{1/2}$ 20–40 hours
	Absent	Enterohepatic circulation present
	No effect	Produces coronary vasodilatation
Uses	Mainly premedication in children	Rarely used in children
	Used for IV sedation and induction	Used in alcohol withdrawal, delirium
	Can be used as infusion for ICU sedation	Not used as infusion
Side effects	Inhibits platelet aggregation	Does not inhibit aggregation
	No pain	Pain on injection common
	Less common	Allergic reactions
	Less common	Nausea and vomiting

UFH VS LMWH

Property	UFH	LMWH
mean molecular weight	15,000 Da	4000 Da
Anti-Xa: IIa activity	1:1	4:1
Inhibition of platelets	Yes	No
Bioavailability	40%	90%
Protein binding	More	Less (10%)
Excretion and metabolism	Endothelial cells and kidney	Only kidney
Elimination $T_{½}$:	Shorter	Longer
$T_{1/2}$ IV administration	1 hour	2 hours
$T_{1/2}$ S/C administration	2 hours	4 hours
Monitoring	Required	Not essential
VTE prevention	Lesser	Better
Thrombocytopenia	High (2–6%)	Low (0.2%)
Hemorrhage	High	Low
Osteoporosis	High	Low
Protamine neutralization	Full	Anti-Xa 65%, anti-IIa 90% reversed
Anticoagulant effect	Inconsistent	Consistent

CLONIDINE VS DEXMEDETOMIDINE

Clonidine	Dexmedetomidine
$\alpha_2 : \alpha_1 = 220 : 1$	$\alpha_2 : \alpha_1 = 1600 : 1$
Aniline derivative	Imidazole derivative
Primarily analgesic adjuvant	Primary sedative
Antihypertensive	Analgesic
Vd = 2 l/kg	V_d = 2–3 l/kg
T ½ = 12–24 hours	T ½ = 2 hours
20–40% protein bound	94% protein bound
Elimination T ½ = 9–12 hours	Elimination T ½ = 2–3 hours
PO, IV, transdermal, epidural routes of administration	IV, IM, PO, transmucosal
Doses: 4–5 µg/kg oral, 1–2 µg/kg IV	0.5–1 µg/kg IV, 2–4 µg/kg PO, 1–2 µg/kg nasal
Uses: Antihypertensive, PMI prophylaxis	Mainly ICU sedation and MAC

CHAPTER

12

Miscellaneous Topics

ASA FUNCTIONAL STATUS CLASSIFICATION[1,2,3]

Introduction

- ASA classification is a system designed for assessing fitness of patients before surgery
- Originally consisted of 6 categories which described the physical status of the patient
- This was revised in 1961 ***by Dripps*** to 5 classes.

Classification

Category I

- Healthy patient
- No comorbidities
- Mortality 0.05%.

Category II

- Mild systemic disease with no functional limitation
- *Examples:* Bronchial asthma or well controlled hypertension
- Mortality 0.4%.

Category III

- Severe systemic disease with functional limitation
- *Examples:* Chronic renal failure on dialysis, class II CCF
- Mortality 4.5%.

Category IV

- Severe systemic disease which constantly threatens survival
- *Examples:* Acute MI, respiratory failure requiring mechanical ventilation
- Mortality 25%.

Category V

- Moribund disease
- Not expected to survive more than 24 hours with or without surgery
- Mortality 50%.

Category VI

- Currently it has been removed
- Declared brain dead patient whose organs are being removed for donor purposes.

Category VII

- Additional code for emergency surgery
- Called emergency if delay in treatment would significantly increase threat to patients life or body part.

Uses

- Used to indicate patient's overall physical health/sickness preoperatively
- Regarded by lawyers and hospitals as a scale to predict risk and decide if a patient should have had an operation
- Used to predict operative risk, planning anesthetic management and monitoring technique
- As the ASA grade increases, mortality risk also rises.

Trial of Ratings Modification

Class Ia: Normal healthy individual.

Class Ib:

- Mild systemic disease
- Healthy individual with operative or anesthetic risk.

Class IIa
- Moderate systemic disease
- Mild systemic disease with anesthetic/operative risk.

Class IIb
- Moderate-severe systemic disease with no functional impairment
- Moderate systemic disease with operative/anesthetic risk.

Class III: Severe systemic disease with functional limitation.

Class IV: Severe systemic disease which constantly threatens survival.

Class V: Moribund disease, not expected to survive more than 24 hours with or without surgery.

Limitations
- Subjective score:
  - Physical status classification is a rating conferred by the practitioner.
  - So individual variation existed, i.e. it was subjective score rather than objective.
- There exists no class for diseases which are moderate (only mild and severe are mentioned).
- Class of a patient suffering simultaneously from more than two diseases is not clear.
- The word systemic creates a lot of confusion as:
  - MI, although grave, is a local disease with poor post surgery survival rates.
  - However it does not fit in any category of ASA classification, being a local disease.
- The classification assumes that age has no relation to physical fitness which is not true as neonates and elderly even in the absence of any systemic disease tolerate similar anesthetics poorly compared to young adults.
- Classification ignores malignancy entirely.
- Does not consider age, sex, pregnancy status, operative/difficult airway risk.

Other Health Grading Systems
- ***APACHE II score, Goldman index***
- ***APGAR score, Malinas score***
- ***Barnes akathisia score***
- ***Blaktyre coma scale***
- ***Glasgow coma scale.***

DRUG ERRORS IN ANESTHESIA[1,2,3,7]

Introduction
Leading cause of morbidity and mortality in hospitalized patients.

Types
- *Omission:* Drug not given
- *Repetition:* Extra dose
- *Substitution:* Incorrect drug/drug swap
- *Insertion:* Unintended drug use
- *Incorrect dose:* Wrong dose
- *Incorrect route:* Wrong route of administration.

Risk Factors
- Inadequate experience
- Inadequate familiarity with equipment
- Carelessness, haste
- Lack of staff
- Odd working hours
- Fatigue
- Poor communication
- Failure to perform routine check
- Inadequate familiarity with surgery
- Teaching activity underway.

Mechanisms
- *Slips:* Due to attention failures
- *Lapses:* Due to memory failure
- *Rule based errors:* Lack of expertise
- *Fixation errors:* Misapplication of knowledge due to fixed ideas
- *Violation:* Deliberate deviation from standard instructions.

Drugs Involved
- Induction agents:
  - Ketamine
  - Thiopentone
- Muscle relaxants
- Narcotics
- Anticholinergics
- Local anesthetics.

Error Reduction in OT
APSF recommendation:
- Color coding
- Drug labels
- Checking labels with second observer
- Double checking before labeling syringe and before administration of drug
- Pre filled syringes
- Bar codes with audible readers on syringes
- Smart pumps
- Preparation of IV medication in pharmacy rather than at point of care

- Standardization of preparation procedures
- Standardization of preparation syringes
- Standardization of infusion concentrations and units
- Standardization of drug workspace layout
- Radiofrequency identification (RFID)
- Computerized order entry (CPOE)
- Avoid storing hazardous concentrated solutions like KCL in syringes.

Error Reduction in ICU

- Reduce physician work hours
- Computerized devices
- Computerized physician order entry.

ASTM Label Standards

1	Induction agents	Yellow
2	Tranquilizers	Orange
3	Relaxants	Fluorescent red
4	Narcotics	Blue
5	Relaxant antagonists	Fluorescent red/white stripes
6	Narcotic antagonists	Blue/white stripes
7	Anticholinergics	Green
8	Local anesthetics	Grey
9	Hypotensive agents	Violet/white stripes
10	Vasopressors	Violet
11	Narcotic/tranquilizer combination	Blue/salmon
12	Major tranquilizers	Salmon

EVIDENCE-BASED MEDICINE[1,2,3]

Introduction

Optimal integration of the best research evidence with clinical expertise and patient preferences to aid in clinical decision-making.

Advantages

- Minimizes errors in patient care
- Reduces cost of treatment
- Optimizes quality of patient care
- Clinicians updated on latest developments.

Disadvantages

- RCTS do not guarantee absence of publication bias-more likelihood of positive trials being published than negative trials
- Difficult to practice clinically
- Suppresses clinical freedom
- Not useful in many clinical situations.

Grading Systems

- Hierarchy of Study Types
- SIGN methodology
- GRADE methodology.

Hierarchy of Study Types

- Systematic reviews and meta analyses of RCTS
- Randomized controlled trials
- Nonrandomized intervention studies–case control studies
- Observational studies–case series/reports
- Nonexperimental studies
- Expert opinion, pathophysiological inference.

Grade Methodology

- *Quality of evidence:* Extent to which one can be confident that an estimate of effect is correct
- *Strength of recommendation:* Extent to which one can be confident that adherence to the recommendation will do more good than harm.

STRENGTH OF RECOMMENDATIONS

Factors Affecting Strength of Recommendations

- Quality of evidence
- *Specificity:* Should be specific to patient groups
- *Trade offs:* Involves compromises between benefits and risks.

No	Class	Benefit[21]	Recommendation
1	I	Benefit >>> Risk	General consensus-treatment is useful
			Procedure should be performed
2	IIa	Benefit >> Risk	Weight of evidence favoring usefulness
			Additional studies with focussed objectives needed
			Reasonable to administer treatment
3	IIb	Benefit ≥ Risk	Usefulness less well established by evidence
			Additional studies with broad objective required
			Treatment may be considered
4	III	Risk ≥ Benefit	Evidence exists that treatment not useful/may be harmful
			No additional studies required
			Procedure/Treatment should not be performed

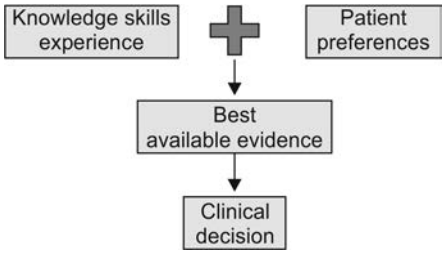
LEVELS OF EVIDENCE

Factors Affecting Levels of Evidence

- *Study design:* Should minimize bias
- *Study quality:* Should use appropriate randomization blinding methods
- *Consistency:* Indicates similarity of effect in different studies
- *Directness:* Extent to which patients and interventions are similar to those of population of interest.

LOE[21]	Description
A (HIGH)	Multiple (3–5) population risk strata evaluated
	Sufficient evidence from multiple RCTS/meta analyses
	General consistency of direction and magnitude of effect
B (LOW)	Limited (2–3) population risk strata evaluated
	Limited evidence from single RCT/nonrandomized studies
C (V LOW)	Very limited population risk strata evaluated
	Only expert opinion/case studies

Clinical Use[21]



HYPERBARIC OXYGEN THERAPY[1,2,3,5,10,21]

Introduction

- Refers to administration of oxygen at higher than atmospheric pressure.

Indications

Undersea and Hyperbaric Medical Society guidelines:

- Global hypoxia:
  - Carbon monoxide poisoning
  - Cyanide poisoning
  - Severe anemia
  - During therapeutic lung lavage.
- Regional hypoxia:
  - Crush/thermal injuries
  - Nonhealing wounds/ulcers
  - Meleneys ulcer
  - Acute peripheral vascular insufficiency
  - Compromised surgical graft
  - Flap osteonecrosis
  - Osteoradionecrosis
  - Radiation cystitis.
- Infections:
  - Gas gangrene/clostridial myonecrosis
  - Necrotising fascitits
  - Fourniers gangrene
  - Refractory osteomyelitis
  - Mucormycosis.
- Gas lesions:
  - Gas embolism
  - Decompression sickness/Caissons disease.
- Others:
  - Septic shock
  - ARDS
  - Plastic surgery
  - Cancer therapy
  - Congenital cardiac anomalies
  - Disseminated sclerosis
  - Acute cerebral edema.

Physiological Effects of Hyperbarism

- Trapped Air Pockets:
  - Contract on compression and expand on decompression
  - Middle ear, paranasal sinuses, intestinal gas, pneumothorax have air pockets.
- Altered Temperature:
  - Increased heat production and increased chamber temperature during compression
  - Cooling and reduced chamber temperature during decompression.
- Elevation of Absolute Pressure:
  - Causes High Pressure Nervous Syndrome
- Elevated Partial Pressure of Oxygen:
  - Raised PaO_2
  - Raised blood oxygen content
  - Vasoconstriction
  - Antibacterial action especially against anaerobes.
- Elevated Inert Gas Pressure:
  - Elevated nitrogen pressure
  - Associated with narcosis – Nitrogen narcosis
  - Causes euphoria, memory loss, unconsciousness.
- Reversal of Anesthesia:
  - Both intravenous and inhalational anesthetics reversed
  - Insignificant at clinically used pressures.

Mechanism of Action

- In global hypoxia:
  - Competes with CO molecules for Hb and eliminates CO
  - Increases dissolved oxygen in plasma
  - Shifts oxygen dissociation curve to right.
- In regional hypoxia:
  - Increases oxygen gradient at tissue level by increasing PaO_2
  - Increases oxygen delivery to tissues
  - Stimulates angiogenesis due to improved fibroblast function.
- Infections:
  - Inhibits clostridial alpha toxins
  - Improves osteoclast function
  - Leucocyte oxidative killing when O_2 tension > 130 mm Hg
  - Inhibits growth of microorganism:
    - Clostridium welchii
    - Clostridium tetanii
    - Staphylococcus aureus
    - Pseudomonas pyocyanea.
- Gas lesions:
  - Reduces volume of embolus
  - Increases arterial hydrostatic pressure
  - Improves oxygen delivery to tissues downstream of emboli
  - Maximizes gradient for removal of gas from emboli.
- Others:
  - Increases sensitivity of cells to radiotherapy
  - Improves collateral flow in grafts – reduces area of ischemia.

Rationale

- Increases PIO_2 and thus improves PAO_2
- Increases oxygen carried in plasma
- O_2 dissolved in plasma at 3 atm pressure is 6 ml/100 ml blood (0.3 ml/100 ml blood at 1 atm pressure)
- Tissues oxygenated even if blood flow reduced by half
- DO_2 can be increased without using O_2 bound to Hb
- Tissues can survive anoxia for longer time.

Methods of Administration

- Single Person Chamber:
  - Made of transparent acrylic
  - Only patient is subject to compression
  - Staff remains outside.
- Multiperson Chamber:
  - Made of steel/aluminium
  - Can be used for surgery
  - Staff breathes compressed air
  - Patient breathes 100% O_2 at pressure from mask/ETT
  - Used for critically ill patients.

Technique

- For decompression sickness:
  - 2.8 atm followed by slow decompression to 1.9 atm
  - Periods of oxygen breathing interspersed with 5–15 min periods of breathing room air
  - Technique reduces oxygen toxicity.

Limitations

- Contraindicated if pulmonary blebs/bullae
- Factors limiting dose and duration of therapy:
  - Oxygen toxicity
  - Decompression sickness of accompanying staff
  - Difficulty with monitoring
  - Patient discomfort.

Side Effects

- Decompression Sickness:
  - Gaseous emboli
  - Rupture of tympanic membrane
  - Can be reduced by reducing decompression rate
  - Reduced by O_2 inhalation before decompression.
- Oxygen Toxicity:
  - CNS reduced cerebral blood flow, convulsions
  - RS pulmonary edema, CO_2 narcosis, absorption atelectasis
  - Retrolental fibroplasia
  - Testicular damage.
- Barotrauma:
  - Pneumothorax
  - Pneumomediastinum
  - Gas embolism.
- Visual Disturbances:
  - *High pressure myopia:* Effect of high pressure on lens shape/refractory index
  - Retrolental fibroplasia
  - Cataract.
- High Pressure Nervous Syndrome:
  - Nausea, vomitting, vertigo, tinnitus, parasthesia, anxiety
  - Involuntary muscle movement
  - Occurs at > 15–20 atm pressure.

ANESTHESIA UNDER HYPERBARIC OXYGEN THERAPY[1,2,3,21]

Indications

- Carotid endarterectomy
- Therapeutic broncheoalveolar lavage
- Emergency surgery in a saturation dive
- Injured divers
- Open heart surgery
- Radiation therapy for cancer.

Evaluation

- Ability to vent middle ear – eustachian tube patency on Valsalva maneuver
- Chest X-ray for blebs/bullae
- Visual acuity checks for hyperbaric myopia
- Anxiolytic therapy initiated if claustrophobic.

Machines

- Standard machines used in chamber
- Cylinders and reducing valves function normally
- Gases piped from outside should be at higher pressure (> 60 PSIG)
- Flowmeters show high value due to increased gas density
- Flowmeters calibrated to higher pressure levels
- Expiredgases absorbed and vented outside.

Monitors

- Most instruments left outside chamber
- View oscillometric measurements through glass port in chamber
  - Blood Pressure:
    - Ordinary/fluid filled BP cuffs
    - Finger plethysmography/intra-arterial catheter
    - Aneroid manometer preferred to mercury manometer
  - ECG and EEG:
    - Standard equipment
    - Recording apparatus placed outside
  - Blood Gas:
    - Machine placed in adjacent lab
    - Polarographic microelectrodes recommended
  - Respiratory Function: With normal instruments.

Technique of Anesthesia

- Regional Anesthesia:
  - Safe and effective
  - Avoids need for mechanical ventilation
  - Extreme aseptic precautions as increased bacterial growth in warm and humid chamber
- *General anesthesia:* Less preferred.

Inhaled Anesthetics

- Can pollute chamber
- Effect of volatile agents proportional to partial pressure of anesthetic and not alveolar concentration
- Effect of 1% halothane at 1 atm equivalent to 0.5% at 2 atm
- Prefer nonexplosive agents
- Standardized vaporizers used
- Recalibrate vaporizers within chamber.

Nitrous Oxide

- Maybe used as sole anesthetic
- Induction rapid (< 60 sec)
- Increased ATM pressure allows MAC to be exceeded
- Induction with nitrous oxide associated with HTN, tachycardia, tachypnea
- Rapid emergence but severe PONV
- May cause embolism during decompression
- Dilutional hypoxia possible.

Intravenous Anesthetics

- Behavior unaffected by pressure
- No pharmacokinetic alteration up to 6 ATM pressure.

Intravenous Fluids

- Air volume in drip chamber shrinks during compression and expands during decompression
- Exclude glass bottles to avoid risk of explosion during decompression
- Use plastic infusion bottles
- Infusion pumps to be capable of handling pressure differential.

Tubes

- ETT cuff inflated with water to avoid volume changes during compression/decompression
- Intragastric tube left open
- Bladder catheters filled with saline
- Repressure pressure bags during compression and vent out during decompression
- PA balloon ports left open to chamber during compression and decompression.

Ventilation

- Pressure controlled/volume controlled used

- Pressure controlled ventilation needs frequent adjustment of PC level
- Risk of fire hazard due to O_2 build-up in ventilator case
- ETT cuff inflated in chamber and released before decompression.

HIGH ALTITUDE[1,2,3,21]

Introduction

No.	Level	Height
1	Baseline	3000 mts above sea level
2	Mild high altitude	3000—3600 mts
3	Moderate high altitude	4200—4800 mts
4	Extreme high altitude	> 4800 mts

Pathophysiological Changes

Central Nervous System

- Vasodilatation causing:
  - Raised ICP
  - Increased cerebral blood flow
  - Altered behavior
  - Drowsiness, incoordination
  - Lack of judgment
  - Sleep–speech disturbances
  - Unconsciousness, seizures.

Cardiovascular

- Tachycardia
- Hypertension
- Increased blood volume by 30%
- Increased erythropoeisis
- Hematocrit increases from 40 to 65 %
- Local vasodilation due to tissue hypoxia
- Pulmonary HTN due to hypoxic pulmonary vasoconstriction.

Hypothermia

Causes:

- Arrhythmias
- AV block
- Hypotension
- Negative inotropism.

Respiratory System

- Reduced PIO_2
- Reduced ambient pressure
- Reduced gas density
- Increased diffusion capacity (normal 2.1 ml/mm Hg /min)
- Reduced oxygen gradient leading to ventilation perfusion mismatch
- Hypoxia induced hyperapnea: leftward shift of ODC
- Pulmonary edema due to:
  - Increased hydrostatic pressure
  - Increased pulmonary vascular permeability
  - Coagulation defect
  - Increased oxygen free radicals
  - Increased autonomic activity causing neurogenic pulmonary edema.

Anesthetic Considerations

- Remote site:
  - Suboptimal equipment
  - Increased risk of infection and pollution–lack of properly built OT
  - Risk of fire hazard and explosion.
- Risk of perioperative hypoxia–supplemental oxygen therapy very important
- Hypothermia common–maintain OT temperature between 21 and 24 °C
- Warm intravenous fluids essential
- Judicious fluid doses to avoid pulmonary edema
- Increased bleeding tendency due to:
  - Raised venous pressure
  - Increased capillary density
  - Venodilation
  - Raised blood volunme
  - Coagulopathies
  - Increased risk of aspiration.

Preoperative Preparation

- NPO 6 hours
- Informed consent
- Opioid/benzodiazepine premedication
- Antisialogogues–glycopyrrolate/atropine
- Antibiotic prophylaxis
- Antiaspiration prophylaxis
- DVT prophylaxis.

Machine

- Boyles type F with Goldman vaporizer for halothane
- Spirometers used to calibrate flowmeters
- Flowmeters show low reading at high flows due to low gas density
- Hazardous if low flow anesthesia used with high nitrous oxide concentration

- Oxygen analyzers show false low reading unless calibrated
- Oxygen analyzer essential if low flow used
- Venturi devices deliver higher O_2 than at sea level
- Venturi mask delivering 35% at sea level delivers 41% at 10000 feet
- Reduce fire hazard by:
  - Avoiding ether
  - Use battery operated lights in OT
  - Reduced overall fire risk as PIO_2 is low.

Regional Anesthesia

- Increased incidence of bowel and bladder distension after SAB
- Increased incidence of postdural puncture headache due to:
  - Chronically increased CSF pressure
  - Dehydration
- Duration of action of local anesthetics shortened
- Prevent Phrenic N palsy during:
  - Interscalene block
  - Supraclavicular block
  - Stellate ganglion block.

Induction

- All patients at risk of aspiration due to delayed gastric emptying
- Rapid sequence induction preferred
- Thiopentone has slower onset due to prolonged brain arm circulation time at high altitude
- Propofol, etomidate, benzodiazepines safe
- Larger amounts of propofol required
- Ether induction slow and requires high concentration
- Gas volume in ETT cuff and PAC balloon expands
- Periodic checking of blood glucose levels as high altitude increases glucose consumption.

Inhalational Agents

- Potency proportional to partial pressure and not percentage in mixture of O_2
- Nitrous oxide potency reduced as barometric pressure reduces
- Nitrous oxide to be given at 50% to be effective
- Fixed concentration of volatile anesthetics have reduced potency
- Halothane can be used:
  - Ideal for rapid induction and recovery
  - High potency
  - Noninflammable
  - Reduced incidence of laryngospasm.
- Delivery of halothane increased at high altitude though partial pressure remains constant
- Isoflurane also suitable.

Neuromuscular Blockade

- Succinylcholine safe for short duration surgery
- NDMR action prolonged in hypothermic patients
- Continue assisted ventilation till patient regains complete consciousness
- Complete reversal mandatory as patients are dependant on hyperventilation for oxygenation
- Maintain PaO_2 and $PaCO_2$ at baseline levels rather than normal values.

Ventilation

- High oxygen concentration to be given due to:
  - Anesthetic deprived compensatory mechanisms
  - Reduced PIO_2 and PAO_2 at high altitude
  - Hypoxic brain damage at lower PaO_2
  - Reduced compensation for acidosis at high altitude
- Ventilation at high altitude dependant on hypoxic drive
- Administration of narcotics blunts hypoxic drive and precipitates hypoxia.

Temperature

- Warm OT and warm IV fluids mandatory
- Warming blankets
- Humidified inspired gases
- Heated peritoneal/bladder/colonic lavage.

Fluid Balance

- Challenging due to preexisting hypovolemia and hypoosmolarity
- Fluid bolus prior to induction in hypovolemic patients
- Avoid aggressive fluid challenges in patients at high- risk for High Altitude Pulmonary Edema
- Titrate to maintain renal perfusion
- Clear IV lines of air bubbles as development of R to L shunts through ***Patent Foramen Ovale*** common in high altitude.

Deep Vein Thrombosis

- Common due to:
  - Hypercoagulability
  - Polycythemia
- Increased risk of postoperative stroke/TIA/DVT.

Dissociative Anesthesia

- Advantageous as:
  - Minimally suppresses ventilation
  - Reduces dose of opioids.
- Ketamine 1–6 mg/kg total dose + atropine 20 µ/kg + midazolam 0.05 mg/kg for TIVA useful
- Useful if supplemental O_2 not available for use.

ANESTHESIA IN SPACE[1,2,3,21]

Physiological Changes in Space

- Cardiovascular changes:
  - Increase in LV end diastolic volume
  - Paradoxical reduction in CVP due to microgravity
  - Reduced LV mass due to cardiac atrophy/injury
  - Central redistribution of blood
  - Facial edema
  - Diuresis with plasma volume depletion (≥ 20%).
- Autonomic dysfunction:
  - Especially on return to earth
  - Occurs due to:
    - Cardiovascular deconditioning
    - Reduced intravascular volume
    - Increased NO expression
    - Downregulation of α-adrenergic receptors
    - Ventricular atrophy
    - Changes in arterial stiffness.
- G forces:
  - Increase in gravitational forces during launch as space craft accelerates to orbital speed
  - Absence of gravitational stress (microgravity) during the period in space.
- *Neuromuscular changes:* Skeletal muscle atrophy even after short missions.

Technical Challenges

Airway

- Difficult intubation due to facial edema
- Both intubator and patient to be secured
- Intubator to stabilize head of patient by holding it between knees
- Use smaller size ETT if vocal cord edema is present
- LMA, intubating LMA, cuffed oropharyngeal airway used alternatively.

Fluid Therapy

- Hypovolemia may not be adequately treatable due to reduced quantity of supplies
- Air fluid interface in IV fluids generate bubbles as fluids and gases do not separate on basis of differing densities due to lack of gravity
- Air bubbles do not rise up but remain mixed in solution
- IV bag to be degassed before flight/removed by inline filtration as IV fluid bags contain fluids akin to foam.

Neuromuscular Blockade

- Succinylcholine to be avoided as it may cause cardiovascular collapse.
- Disuse and skeletal muscle atrophy due to immobilization causes proliferation of extrajunctional receptors causing hyperstimulation and cardiac arrest on SCH use.
- Resistance to NDMR may occur
  - *Subarachnoid Block:* Increased risk of cardiovascular collapse due to autonomic dysfunction.

Vaporizers

- Devices which depend on gravity induced separation of fluids and gases malfunction
- This is because vaporizers require gravity to confine liquids to bottom of reservoir.

Closed Environment

- Safe use of anesthetic gases difficult in space craft
- Drugs used in flight should not be capable of reaching crew through the closed cabinet atmosphere
- Dumping of exhaust O_2 into cabin atmosphere avoided to prevent fire hazard
- Minimum flow system for xenon may be useful.

Complications

Nephrolithiasis and Osteoporosis:

- Due to gravitational unloading
- This causes loss of calcium from bones along with hypercalciuria.

Space Motion Sickness

- GERD may occur during flight and after landing
- Dizziness, drowsiness, nausea and vomiting
- Increased risk of aspiration.

Hemorrhage and Hypovolemia

- Reduced chances of bleeding
- This is because due to high surface tension of blood, it will remain on surface of wound

- Chances of arterial bleeds spilling out still remains
- Hypotension may be increased by preexisting volume loss and increased G forces during re-entry.

Ebullism

- Cabin pressure in space craft is 760 mm Hg
- That of extra-vehicular activity (EVA) space suits is 222 mm Hg
- This reduced pressure in EVA suit increases risk of decompression sickness
- If the suit is disrupted during EVA, astronauts ambient pressure quickly drops to zero
- This causes generalized bubble formation called ebullism
- Body fluid boils due to ambient pressure being lower than saturated water vapor pressure.

Hypoxia

- Astronauts breathe 100% oxygen in EVA suits
- Disruption of the suit causes hypoxia.

Electrolyte Disturbances

Hypokalemia and hypomagnesemia common due to reduced dietary intake.

Other Advantages

- On board diagnostic tools like remotely guided USG examination
- Remote robotic surgery substituted for onboard surgeon.

INTRAOPERATIVE ANAPHYLAXIS[1,2,3]

Introduction

Rapid systemic reaction, with potentially life-threatening consequences, to a substance to which the individual is already sensitized.

Types

- Allergic anaphylaxis:
  - Type I IgE mediated release of inflammatory mediators
  - Involves mast cells and basophils.
- Anaphylactoid reaction:
  - Direct nonimmune mediated release of inflammatory mediators
  - Direct complement activation contributory.

Risk Factors

- Female gender
- Old age
- History of pulmonary/cardiovascular disease
- History of atopy
- Food allergy
- Latex allergy
- Intravenous drug administration.

Etiology

- Muscle relaxants: Most common: Succinylcholine, Rocuronium, Atracurium.
- Natural rubber: Latex gloves, Tourniquets, Foleys catheter.
- Antibiotics: Penicillins, Betalactams, Bacitracin, Vancomycin, Polymyxins, Amphotericin.
- Hypnotics: Thiopentone, Propofol.
- Opioids: Morphine, Meperidine.
- Colloids: Dextran, Gelatin, Mannitol.
- Drugs affecting coagulation: Aprotinin, Heparin, Protamine.
- Others: Bupivacaine, Ester local anesthetics, β-blockers, Radiocontrast allergy, Povidone iodine.

Mechanism

- Initial exposure to antigens causes IgE release
- IgE binds to mast cells and basophils
- Reexposure to multimeric antigen causes cross linking of IgE receptors
- Degranulation of mast cells and basophils
- Release of inflammatory mediators: Histamine Tryptase, Prostaglandins, Kinins, Serotonin, Leukotrienes.

Symptoms

- Flushing, Generalized rashes, Urticaria, Localized edema, Dyspnea, Periorbital/perioral edema, Wheezing.

Signs

- Hypotension, Tachycardia, Bronchospam, Angioedema, Cardiovascular collapse, Pulmonary HTN, Arrhythmias Acute tubular necrosis, Laryngeal edema Pulmonary edema.

Signs Under Anesthesia

- Increased peak inspiratory pressure
- Increased end tidal carbon dioxide
- Decreased oxygen saturation
- Decreased urine output
- Disseminated Intravascular Coagulation.

Severity

Ring and Meissner scale:

Severity	Description
Grade I	Erythema, pruritis
	Angioedema, urticaria
Grade II	Urticaria, erythema
	Hypotension, tachycardia, presyncope
	Dyspnea,wheezing, bronchospasm
	Nausea, vomiting, diarrhea
Grade III	Profound hypotension, arrhythmias
	Bradycardia, cardiovascular collapse
	Laryngeal edema, bronchospasm, hypoxia
	Confusion, unconsciousness
Grade IV	Pulseless electrical activity
	Cardiac arrest

Investigations

General

- Carboxypeptidase levels
- Complement C3 and C4 levels elevated at 30 mins, 1 and 4 hours postepisode
- Tryptase Estimation:
  - Blood sample taken 30 minutes after onset of reaction
  - Values > 20 ng/ml suggestive of anaphylaxis
  - Half-life of tryptase 2 hours
  - Serum levels decrease over time
  - Repeat sample at 6 and 24 hours after reaction for tryptase levels
  - Does not differentiate anaphylaxis and anaphylactoid reaction
  - Maybe absent in the presence of anaphylaxis.

In Vivo Tests

- Skin Prick Testing:
  - Done 4–6 weeks after anaphylactic episode due to mast cell depletion
  - Test with suspected agents and positive and negative controls
  - Freshly prepared diluted drugs used
  - Skin pricked with needle containing small quantity of allergen
  - On front of forearm/back of trunk.
- Intradermal Skin Testing:
  - Done 4–6 weeks after anaphylactic episode due to mast cell depletion
  - Done only if skin prick test is negative
  - Drug concentration of prick test diluted by 1:10
  - 0.2–0.3 ml introduced intradermally with hypodermic needle
  - Slightly greater risk of systemic reaction.
- Scratch test: Deep dermal scratch done with blunt bottom of lancet
- Patch test: Patch containing allergen applied to skin
- Bronchial Challenge Test:
  - In cases of strong suspicion
  - Patient inhales nebulized histamine or methacholine
  - Degree of airway obstruction measured with spirometry
  - Patients with airway hyperreactivity respond to lower dose of drug
  - Postbronchodilator maybe used to differentiate asthma from COPD
  - Done only with availability of full resuscitation facilities.

In Vitro Tests

- Radioallergosorbent test (***RAST***):
  - Measures presence of specific IgE antibodies in serum
  - Insoluble disk coupled with specific drug added to patients serum
  - Radiolabelled antihuman antibody added to mixture
  - Radiolabelled antihuman antibody binds to IgE antibodies already bound to antigen
  - Unbound IgE antibodies washed away
  - Amount of radioactivity proportional to serum IgE for allergen.

Management

General

- Stop administration of offending drug
- Terminate or rapidly complete surgery
- IV fluids:
  - Loss of 40–50% IV volume
  - Rapid administration to compensate for peripheral vasodilatation
  - 1–2 liter boluses of balanced salt solution
  - Titrate to maintain SBP > 90 mm Hg.

Airway

- Administer 100% oxygen
- Endotracheal intubation:
  - Secure airway early
  - Those with apnea, coma, increasing hypercapnea, exhaustion

- Rapid sequence intubation
- Largest sized ETT used if no airway edema to minimize resisitance
- Ventilatory strategy:
  - Small tidal volume (6–8 ml/kg)
  - Slower respiratory rate
  - Shorter inspiratory time
  - Longer expiratory time (I:E = 1:4 or 1:5)
  - Permissive hypercapnea
- Delay extubation as airway edema may continue for 24 hours.

Bronchodilators

- Ipratropium bromide 0.03%–500 µg in 2.5 ml NS nebulization
- Albuterol 0.3% 2.5–5 mg in 3 ml NS nebulization
- Albuterol 100–200 µg IV bolus
- Terbutaline 250–500 µg subcutaneously repeated every 20 min for 3 doses
- Aminophylline 5 mg/kg IV over 20–30 minutes.

Epinephrine

- *Drug of choice* as α 1 supports blood pressure while β2 supports bronchodilation
- Highest peak blood levels with intramuscular administration in anterolateral thigh
- Subcutaneous injection provides uncertain and delayed absorption
- 0.2–0.5 mg IM (1 : 1000), repeat every 5–15 minutes if no improvement (*Class I, LOE C*)
- 50–100 µg IV boluses if anaphylactic shock (*Class I, LOE B*)
- 5–15 µg/min infusion to maintain blood pressure in shock (*Class IIa, LOE C*)
- 2–2.5 mg in 10 ml instilled endotracheally.

Antihistaminics

- Diphenhydramine (H1 blocker) – 0.5–1 mg/kg IV
- Ranitidine (H_2 blocker) – 1 mg/kg IV.

Corticosteroids

- Methylprednisolone 0.5–1 mg/kg bolus followed by 0.8 mg/kg Q4–6H
- Hydrocortisone 1–5 mg/kg IV bolus followed by 2.5 mg/kg Q4–6H
- Decrease airway edema and reduce recurrence
- Hydrocortisone preferred due to fast onset.

Vasopressors

- Other vasopressors useful in those cases unresponsive to epinephrine (*Class IIb, LOE C*)
- Dopamine 2–20 µg/kg/min infusion
- Norepinephrine 0.05 µg/kg/min infusion
- Vasopressin:
  - 1–2 IU IV for hypotension
  - 40 IU IV for cardiac arrest
- Methoxamine and metaraminol other alternatives.

Others

- Ketamine: May be useful if intubation planned.
- Heliox:
  - Mixture of 70% helium and 30% oxygen
  - Reduces turbulence in airflow
  - Not useful if > 30% oxygen required.
- Volatile anesthetics:
  - Isoflurane/sevoflurane in refractory bronchospasm
  - Increases ease of mechanical ventilation.
- Glucagon:
  - 20–30 µg/kg or 1–5 mg bolus followed by 5–15 µg/min infusion.
- Magnesium sulfate:
  - 40–60 mg/kg or 2 gms IV bolus
  - Used for refractory bronchospasm.

Extracorporeal Life Support

- Cardiopulmonary bypass for anaphylaxis followed by cardiac arrest (*Class IIb, LOE C*)
- Requires equipment and expertise.

Differential Diagnosis

- Pulmonary embolism
- Acute myocardial infarction
- Aspiration
- Vasovagal reaction.

ELECTRICAL SAFETY IN OPERATING ROOM[1,2,3,4]

Introduction

- Operating theater is at a high-risk for fire hazards as:
  - Variety of electrical equipment are close to each other
  - Unconscious patient who cannot protect himself.

Predisposing Factors

- Confined space
- Electrical items
- Electrically sensitive persons:
  - Patient with breaks in skin—abrasions
  - Wet dressings

  - Implanted pacemakers
  - Monitoring lines connected to transducer
- Inflammable materials:
  - Oxygen
  - Ether
  - Bowel gas.

Risk Factors

Circumstantial

- Nonuniformity of electrical fixtures
- Poorly designed electrical distribution system
- Poor maintenance.

Human

- Unskilled electrician
- Nonadherence to regulations
- Overloaded cables
- Excessive fuse sizes
- Inadequate earthing.

Environmental

- Heat
- Humidity
- Animals: Rats and rodents.

Types of Electrical Hazard

- *Shock:* When person becomes final component that closes electrical circuit
- *Electrocution:* When amount or path of flow of current through person becomes lethal
- Burns
- Fires
- Explosions
- Failure of equipment.

Classes of Electrical Equipment

Describes method of electrical protection.

Class I

- Any conducting part of equipment is earthed
- Fuses present at wall socket, live and neutral sides of equipment
- Any electrical leakage channeled to earth and breaks circuit.

Class II

- Accessible conducting parts have doubly reinforced insulation
- This prevents possibility of accessible part becoming live
- Earthing wire not required.

Class III

- Uses voltages not higher than Safety Extra Low Voltage (SELV)
- Usually less than 25 V for AC and 60 V for DC
- Unlikely for electrocution at such low voltages
- Equipment which uses either batteries or SELV transformers
- Can cause microshock
- Does not meet current standards as limitation of voltage alone not sufficient to ensure patient safety.

ELECTROCUTION[1,2,3,4,21]

Mechanisms

Resistive Coupling

- Person touches faulty wire or equipment while in contact with earth
- Body becomes part of an electrical circuit
- Leakage current passes through the body to the earth.

Capacitative Coupling

- Occurs in presence of high frequency current
- Equipment attached behaves like one of the plates of the capacitor
- Body becomes part of an electrical circuit
- Current passes through the body.

Factors Affecting Severity

- *Type of current:* AC current more dangerous
- *Size of current:* 50–60 Hz frequency most dangerous
- Electrical path (especially current density through the heart)
- Duration of current flow
- Timing in relation to ECG.

No	Strength of current	Injury
1	< 1 mA	Nil
2	1 mA	Tingling
3	5 mA	Pain
4	15 mA	Muscular tetany, pain, asphyxia
5	50 mA	Expiratory respiratory arrest
6	75 mA	Arrhythmias
7	100 mA	Ventricular fibrillation
		Cardiac arrest
8	> 5 Amp	Sustained asystole
		Contact burns

Injuries Caused

- Functional disruption of tissues
- Burns
- Respiratory failure
- Ventricular fibrillation
- Blunt trauma.

Types of Shocks

Macroshock

- *Most common*
- 100–300 mA current, as low as 50 mA
- Electrical charge occurs through intact skin
- Travels to heart and out again
- Current distributed somewhat evenly through body parts
- Examples:
  - Contact with faulty class I equipment
  - Defibrillator use.

Microshock

- Very low level shocks which go undetected
- Usually < 1 mA current
- Charge directly delivered to heart muscle
- *Examples:*
  - Shock delivered via central line/pacemaker wire.

Precautions

Technical Measures

- Polarities to be correctly identified
- Prevent interruption of neutral conductor
- Earth connections on all socket outlets in an area to be interconnected by a low resistance conductor
- Exposed metal objects to be interconnected to a good earth
- Earth leakage trip device
- Regular testing and maintenance
- International standard theater electrical equipment
- Do not block access to electrical panels with carts/equipment.

Cautery Measures

- Keep cautery forceps in protective quiver
- Use of buzzer which is activated on depression of foot switch
- Proper plugging in of cautery plate
- Use of bipolar cautery in the presence of pacemakers.

Utilization Measures

- Plug equipment into wall receptacles with power switches in off position
- Do not unplug equipment by grasping cord
- Check for frayed or exposed wiring on equipment cords
- Do not drape cord over hot/sharp objects
- Do not plug in equipment with wet hands
- Do not plug in equipment when cord is wet
- Ensure patient is not in contact with earthed objects
- Wear antistatic shoes.

Appropriate Selection of Equipment

Types of electrical equipment: Describes degree of protection of medical equipment:

Type B

- Equipment maybe class I, II or III
- Maximum leakage current not to exceed 100 µA
- Not suitable for direct connection to heart.

Type BF

- Equipment maybe class I, II or III
- Maximum leakage current not to exceed 100 µA
- Uses *floating/isolated circuit.*

Type CF

- Provides highest degree of protection
- Have maximum leakage current < 10 µA
- Suitable for direct cardiac connection
- Examples:
  - ECG leads
  - Pressure transducers.

TOTAL INTRAVENOUS ANESTHESIA[1,2,3,7,21]

Introduction

Method of inducing and maintaining general anesthesia by drugs administered exclusively by intravenous route in the absence of all inhalational agents including nitrous oxide.

Ideal Intravenous Anesthetic

- Rapid onset of action
- Rapid offset of action
- Noncumulative
- Nonactive metabolites
- Nontoxic metabolite.

Aims

- Achieve smooth general anesthesia:
  - Smooth induction
  - Reliable and titratable maintenance of anesthesia
  - Rapid emergence on termination of infusion.
- Avoid undesirable clinical effects
- Avoid under or overdosing
- Allow rapid and smooth emergence.

Indications

- Previous history of PONV
- *High-risk of PONV:* Orchidopexy, strabismus
- *Scoliosis surgery:* Intraoperative Wake-up test
- History of malignant hyperthermia/malignant hyperthermia susceptible
- Airway procedures
- *Neurosurgery:* Endoscopic neurosurgeries for hypotensive anesthesia
- Thyroid surgeries for recurrent laryngeal nerve monitoring.

Advantages

- Avoids the peaks and troughs of repeated bolus dosing
- Better hemodynamic control–controlled hypotension
- Reduced stress response
- Reduced bleeding
- Reduced intraocular pressure
- Improved V/Q matching
- Increases maximum attainable FiO_2
- Reduces OT pollution
- Smooth emergence
- Lesser hangover
- Reduced bowel distention
- Reduced PONV.

Disadvantages

- Delay to peak effect (equivalent of four to five drug elimination $T_{1/2}$)
- Decrease in plasma concentration at transition from loading dose to maintenance dose
- No single intravenous anesthetic provides all components of anesthesia
- Combination of drugs necessary
- Early or late respiratory depression
- Opioid side effects–muscle rigidity, gastroparesis, pruritis
- Adverse effects if IV line disrupted
- Risk of awareness.

Modes of Delivery

- Simple intravenous boluses
- Variable rate continuous infusion.

Instruments Used

- Controllers
  - Drops (Exadrop)
  - Volumetric (Dosifix)
- Pumps
  - Syringes (Intrafusor)
  - Volumetric (Infusomat)
  - Peristaltic drops (Digifusa).

TIVA Alarms

- Occlusion
- Empty syringe
- Absent syringe
- Wrong syringe position
- Low battery
- Bolus delivery
- Setting changes.

Monitoring During TIVA

- ASA minimum monitoring standards:
  - Pulse oximetry
  - Electrocardiogram
  - NIBP
  - Capnography.
- Depth of anesthesia:
  - BIS
  - Auditory Evoked Potential
  - Entropy.

Drugs Used

- *Hypnotic agents:* Propofol, benzodiazepines, ketamine, barbiturates
- *Analgesic agents:* Remifentanyl, alfentanil, fentanyl, morphine
- *Muscle relaxants:* Vecuronium, atracurium, rocuronium.

Drug Dosages

Opioids

- Fentanyl 2µg/kg bolus followed by 0.2 µg/kg/min infusion
- Alfentanil 20 µg/kg bolus followed by 0.25 µg/kg/min infusion
- Sufentanil 0.15 µg/kg bolus followed by 0.003 µg/kg/min infusion
- Remifentanil 1µg/kg bolus followed by 0.02 µg/kg/min.

Hypnotics

Propofol 1.5–2 mg/kg induction followed by:
- 100–150 µg/kg/min first 10 mins
- 90–140 µg/kg/min from 10 mins to 2 hours
- 75–125 µg/kg/min beyond 2 hours
- Turn off propofol 5–10 mins prior to desired time of emergence.

Ketamine
- No initial bolus
- Infusion started at 1 mg/min, maintained up to 1 hour
- 1–4 hrs: 0.6 mg/min
- > 4 hrs: 0.4 mg/min
- Turned off 15–30 mins prior to end of surgery.

Infusion Schemes

- BET infusion scheme:
  - B = Loading dose
  - E = Terminal elimination
  - T = Transfer to peripheral compartment.
- Open Loop System:
  - Blood or brain drug concentration chosen
  - Microprocessor of pump adjusts rate of infusion
  - Microprocessor maintains effect site drug concentration
  - No feedback signal of output.
- Closed loop system:
  - Future technology
  - Feedback signal of effect site concentration built into delivery system.

TIVA Models

- *Roberts* manual infusion regimen
- *Marsh'* weight based regimen
- *Schnider* model
- *Kateria, Pedifuser* pediatric models.

Recent Advances

- Newer hypnotics:
  - Remimazolam
    - Sedation with 6 mg initial loading dose
    - Followed by 3 mg doses at > 2 min intervals
    - Recovery within 16 minutes for 90% patients
  - Dexmedetomidine
  - S+ketamine enantiomer
  - Propofol prodrug
- Closed loop anesthesia
- Target Controlled Infusion
- Noninvasive monitoring of propofol concentration.

TARGET-CONTROLLED INFUSIONS (TCI)[1,2,3,7,21]

Introduction

TCI is an infusion controlled in such a manner as to attempt to achieve a user defined drug concentration at the effect site.

Goals

- Avoid overdosage
- Ensure constant concentration
- Allow accurate titration
- Account for patient covariates.

Advantages

- Improves stability and titration
- Minimal workload—convenient to use
- Displays calculated blood concentration
- Good control of depth of anesthesia
- Optimizes drug properties
- Cardiovascular stability—lower heart rate, less stress hormones
- Improved ciliary function postoperatively
- Reduced intracranial pressures
- Quickens recovery
- Helps anticipating recovery—predicts patient waking time
- Avoids OT pollution
- Less incidence of PONV.

Disadvantages

- Concentration calculation errors
- Possibility of awareness when used with muscle relaxants
- Requires dedicated IV cannula for administration
- IV access needs constant check for occlusion.

Components

- User interface for patient details
- Software with pharmacokinetic model validated for specific drug
- Infusion device—capable of infusion rates up to 1200 ml/hr with precision of 0.1 ml/hr
- Communication between control unit and pump hardware.

Functions of TCI Pump

- *Bolus:* Ability to rapidly increase plasma concentration
- *Flow rate*: Accurate function at low flow rates
- *ALARMS:* Facilitates identification of improper positioning of syringe in pump

- *Tight syringe fitting:* Prevents syringe from moving when pump is in action
- *Battery indicator.*

TCI Pharmacokinetic Model

- ***Marsh*** model used by Diprifusor for propofol
  - Assumes that central compartment volume proportional to weight alone
  - Age is entered but not used in calculations.
- Schuttler and White-Kenny models for propofol
- Schneider model for propofol
  - Incorporated in newer generation TCI pumps
  - Follows a three compartment model
  - Age, height, weight are entered into the system
  - Calculated lean body mass used to calculate infusion rates.
- ***Kataria*** model for children
  - Minimum age of 3 years and body weight 15 kg
- ***Paedfusor*** model for children
  - Minimum age limit is 1 year and lowest body weight permissible is 5 kg
- ***Minto*** model for remifentanil
  - Uses three compartment model
  - Covariates age, weight, height and gender considered for calculation of dose
  - Questionable efficacy owing to fixed context sensitive half life of remifentanil
  - May producer higher concentrations in elderly or sick patients.

Rationale

- End result always a variation of Bolus, Elimination and Transfer scheme
- Pharmacokinetic model used in reverse
- Desired effect site concentration chosen
- Computer calculates rate of administration using pharmacokinetic model
- Calculations done to keep desired concentration in target compartment constant every 10 seconds
- Infusion pump changes infusion rate depending upon target concentration.

Usage

- Initial programming of pump based on patients age, height, weight and sex
- Initial induction blood propofol levels of 6–8 μg/ml
- Caution in elderly and those with cardiovascular disease
- Reassessment of dosage during airway manipulation
- Target concentration adjusted subsequently based on response to surgical stimulus
- Coadministration of benzodiazepines and opioids necessitate dose adjustments
- Target concentration reduced towards end of case to promote rapid recovery
- Infusion stopped once final sutures applied
- Time to awakening displayed by machine, usually at propofol concentration of 1 μg/ml.

Precautions

- High concentration of drugs that run at slow speeds avoided
- Syringe pump connected closer to patient
- Vasoactive drugs should not be combined with primary drug
- Pump should not be placed above level of patient
- Use separate IV access for TCI infusion.

Validation

- *Median Prediction Error* (MDPE): Median of procentual difference, positive or negative
- *Median Absolute Prediction Error* (MDAPE): Median of procentual difference between measured and predicted concentration in absolute value
- *Divergence:* Slope of linear regression analysis of evolution in time of MDAPE
- *Wobble:* Median of variability in individual patients.

MONITORED ANESTHESIA CARE[1,2,3,5,7,21]

Introduction

Refers to instances in which an anesthesiologist has been called upon to provide specific anesthesia services to a patient undergoing a planned procedure and is in control of the patients nonsurgical or nonobstetrical medical care (including monitoring patients vital signs, and is available to administer anesthetics or provide medical care as appropriate).

Requirements

- Performance of preanesthetic examination and evaluation
- Prescription of anesthetic care
- Personal participation in, or medical direction of entire plan of care
- Continuous physical presence of anesthesiologist
- Proximate presence of anesthesiologist for diagnosis and management of emergencies.

Goals

- To maintain patient safety and sense of well-being
- To alleviate pain and minimize discomfort

- Administration of sedatives, hypnotics, anesthetic agents and other medications
- To minimize psychological response: Anxiolysis, analgesia and amnesia
- To control behavior
- Support of vital functions
- Diagnosis and treatment of clinical problems which occur during the procedure
- Provision of other medical services as needed to complete the procedure safely
- To return patient to preprocedural state.

End Points

- Providing patient comfort
- Maintaining cardiorespiratory stability
- Improving operative conditions
- Prevent recall of unpleasant perioperative events.

Contraindications

- Severe comorbidity (ASA III, IV)
- Morbid obesity
- Documented history of sleep apnea
- Increased risk of airway obstruction:
  - Sleep apnea/stridor
  - Dysmorphic facies
  - Oral abnormalities: Macroglossia
  - Neck abnormalities: Neck mass
  - Jaw abnormalities: Micrognathia.
- Inability to follow simple commands:
  - Cognitive dysfunction
  - Intoxication
  - Psychological problems
  - Acutely agitated
  - Uncooperative patients.
- Medical problems associated with alcohol/drug abuse
- Patients of extreme age: Younger than 18 years, older than 70 years
- History of intolerance to standard sedatives:
  - Chronic opioid use
  - Chronic benzodiazepine use.
- Spasticity or movement disorders
- Pregnancy
- Prolonged procedures requiring deep sedation.

Preoperative Assessment

- Similar to preanesthetic evaluation of other patients
- Patient's ability to lie motionless and actively cooperate is assessed
- Ability to verbally communicate with the patient assessed as it:
  - Is a means of reassuring the patient
  - Allows requests for active participation by the patient
  - Assists in monitoring level of sedation and cardiorespiratory function.

Monitoring

- Visual, tactile and auditory assessment:
  - Response to verbal stimulation evaluated for effective titration of sedation
  - Rate, depth and pattern of breathing
  - Peripheral perfusion and capillary refill
  - Diaphoresis, shivering, cyanosis and changes in neurological status.
- *Auscultation*: Precordial stethoscope
- Pulse oximetry
- Capnography
- ECG
- BP recorded at least every 5 minutes
- Temperature for prolonged procedures.

Drugs Used

- *Benzodiazepines:* Midazolam 1–2 mg IV before propofol/remifentanil infusion
- Diazepam 2.5–5 mg IV.

Opioids

- Alfentanyl 5–20 µg/kg IV bolus 2 minutes before stimulus
- Fentanyl 0.5–2 µg/kg IV bolus 2 minutes before stimulus
- Remifentanyl 0.1 µg/kg/min infusion 5 mins before stimulus, 0.05 µg/kg IV maintenance as tolerated.

Others

- Propofol 250–500 µg/kg bolus, 25–75 µg/kg/min infusion
- Ketamine 0.25–1 mg/kg IV bolus
- Dexmedetomidine 0.5–1 µg/kg loading dose over 10 minutes, 0.2–0.7 µg/kg/hr infusion.

ANESTHESIA FOR DAYCARE SURGERY[1,2,3,21]

Introduction

An operation or procedure, an office or outpatient operation/procedure, where the patient is discharged on the same working day—International Association of Ambulatory Surgery (IAAS).

Advantages

- Reduced dependence on availability of hospital beds
- Greater flexibility in scheduling surgeries
- Shorter surgical waiting lists
- Lower overall procedural costs
- Lower requirements of nursing and medical supervision
- Greater turnover of patients
- Minimal psychological disturbances, especially children
- Less incidence of hospital acquired infections
- Lesser incidence of respiratory complications
- Reduced incidence of venous thromboembolism.

Procedure Requirements

- Minimal risk of postoperative hemorrhage
- Minimal risk of postoperative airway compromise
- Rapid return to normal fluid and food intake
- Postoperative pain controllable by outpatient management techniques
- Postoperative care managed by patient/responsible adult.

Patient Requirements

- ASA I and ASA II patients
- ASA III patients whose disease is well controlled preoperatively
- Should have understanding of the process and be able to follow discharge instructions
- Patients place of residence to be within easy access to surgical facilities
- Normal term infants of over 6 weeks age
- Expremature infants more than 52 weeks postconceptual age.

Common Day Care Surgeries

General Surgery

- Herniorraphy
- Hemorrhoidectomy
- Herniotomy
- Upper and lower gastrointestinal tract endoscopy/biopsy
- Lymph node excision biopsy
- Laparoscopic procedures.

Plastic Surgery

- Otoplasty
- Excision skin lesions
- Scar revision.

Gynecology

- D & C
- Hysteroscopy
- Vaginal hysterectomy
- Tubal ligation.

Orthopedics

- Implant removal
- Arthroscopy
- Closed reduction procedures.

Urology

- Circumcision
- Cystoscopy
- Lithotripsy
- Prostate surgery
- Orchidectomy/orchidopexy.

Otolaryngology

- Myringotomy
- Mastoidectomy
- Tympanoplasty
- Adenoidectomy
- Tonsillectomy
- Polypectomy.

Ophthalmology

- Examination under anesthesia
- Lacrimal duct probing
- Strabismus correction

Contraindications

- Serious life-threatening diseases
- Morbid obesity complicated by CVS and RS symptoms
- Chronic use of centrally acting drugs
- Extremely premature infants (< 60 weeks postconceptional age)
- Lack of responsible adult at home to take care of patient postdischarge
- Surgical procedures involving:
  - Major fluid shifts
  - Significant blood loss
  - Significant postoperative pain
  - Significant PONV.

Preoperative Evaluation

- Detailed history with specific focus on comorbidities
- Identify difficult airway
- Recording of vital signs

- Preoperative counseling to allay fear and anxiety
- Written and verbal communication regarding arrival time and fasting guidelines
- Need for a responsible adult to accompany patient specified
- Investigations:

Age	Male	Female
< 40 yrs	Nil	Hematocrit
		Pregnancy test
40–49 yrs	ECG	Hematocrit
		Pregnancy test
50–64 yrs	ECG	Hematocrit
		ECG
65–74 yrs	Hematocrit	Hematocrit
	ECG	ECG
	BUN	BUN
	Glucose	Glucose
> 75 yrs	Hematocrit	Hematocrit
	ECG	ECG
	BUN	BUN
	Glucose	Glucose
	Chest X-ray	Chest X-ray

Anesthetic Goals

- Smooth onset of action
- Adequate intraoperative analgesia and amnesia
- Good surgical conditions
- Rapid recovery
- Minimal adverse effects.

Choice of Anesthetic Technique

- General anesthesia most commonly preferred
- Central neuraxial blockade not encouraged as persistant motor block delays discharge
- Local nerve and plexus blocks are good options for peripheral surgeries.

Choice of Drugs

Induction agents: Propofol, ketamine.

Analgesics: Fentanyl, alfentanil, sufentanil, remifentanil.

Maintenance: Nitrous oxide along with sevoflurane, desflurane or propofol.

Muscle relaxants: Succinyl choline, atracurium, cisatracurium, mivacurium.

Regional Anesthesia

- Short acting drugs like lignocaine and procaine desirable for central NAB
- Bupivacaine used if anticipated duration of surgery > 2 hours
- Intrathecal fentanyl and sufentanil prolong sensory blockade without affecting motor block
- Low spinal is recommended.

CRITERIA FOR DISCHARGE FROM PACU[1,3]

Introduction

Minimum mandatory stay in PACU is not required and patients must be observed until:

- They are no longer at risk for ventilatory depression
- Their mental status is clear/has returned to baseline
- They are hemodynamically stable.

Recommendations for Discharge

- Minimum mandatory stay not required
- Vital signs stable and within acceptable limits
- Patient should be alert, oriented/mental status returned to baseline
- Discharge after patient meets certain criteria
- Scoring system used to document fitness for discharge
- Requirements to urinate and retain clear fluids are not part of routine criteria
- Outpatients discharged with responsible adults who will accompany their home
- Written instructions regarding postprocedure diet, medications and emergency phone number provided.

Scoring Systems Modified Aldrete Scoring System

Respiration	
Able to take deep breath and cough	2
Dyspnea/shallow breathing	1
Apnea	0
Oxygen Saturation	
Maintains SpO_2 > 92 on room air	2
Needs oxygen to maintain SpO_2 > 90%	1
SpO_2 < 90% even with supplemental oxygen	0
Consciousness	
Fully awake	2
Arousable on calling	1
Not responding	0
Circulation	
BP + 20 mm Hg preoperatively	2
BP + 20–50 mm Hg preoperatively	1
BP + 50 mm Hg preoperatively	0

Contd…

Contd…

Respiration	
Activity	
Able to move four extremities voluntary/on command	2
Able to move two extremities	1
Unable to move extremities	0
Score more than 9 required for discharge	

Postanesthesia Discharge Scoring System

Vital Signs	
BP and pulse within 20% preoperative level	2
BP and pulse within 20–40% preoperative level	1
BP and pulse more than 40% preoperative level	0
Activity	
Steady gait, no dizziness, meets preoperative level	2
Requires assistance	1
Unable to ambulate	0
Nausea and Vomiting	
Minimal/treated with oral medications	2
Moderate/treated with parenteral medications	1
Severe/continues despite therapy	0
Pain	
Controlled with oral analgesics and acceptable to patient:	
Yes	2
No	1
Surgical Bleeding	
Minimal—no dressing changes	2
Moderate—up to two dressing changes required	1
Severe—more than three dressing changes required	0
Score more than 9 required for discharge	

Discharge after Regional Anesthesia

- Must meet same criteria as patients recovering from general anesthesia
- Additional criteria present, to ensure safe ambulation if neuraxial block or major lower limb nerve block has been administered
- Before ambulation, patients with neuraxial must have:
  - Return of normal sensation, muscle strength, proprioception and sympathetic function
  - Normal perianal sensation (S_4 and S_5)
  - Ability to plantar flex toes
  - Proprioception of big toe
  - Advisable to void before discharge.

CLINICAL TESTS FOR CORRECT PLACEMENT OF ET TUBE

Introduction

Detection of esophageal intubation is significant as it contributes to 15% of major anesthetic catastrophies.

Clinical Tests

- Direct visualization of tube passing through larynx
- Observation of chest movement
- Observation of abdominal movements
- Observation of moisture condensation in ETT: tracheal mist
- Auscultation of breath sounds
- Auscultation of epigastrium
- Movement of reservoir bag in unparalyzed patients.

Diagnostic Aids

- Exhaled carbon dioxide:
  - Exhaled CO_2 waveform observed for a minimum of 3 cycles
  - False positives occur when:
    - Alveolar gas forced into stomach during mash ventilation
    - Ingestion of carbonated soft drinks preoperatively.
- Esophageal detector device (EDD):
  - It is a 60 ml catheter tip syringe fitted with one end of 15 mm tracheal tube.
  - Works on principle that esophagus is a fibromuscular tube with no intrinsic structure to maintain patency.
  - Trachea is kept patent by C-shaped cartilaginous rings.
  - Withdrawal of plunger of EDD will aspirate gases from lung if ETT is in trachea with minimal resistance.
  - However, if ETT is in esophagus, withdrawal of plunger will cause opposition of esophageal walls around syringe.
  - This occludes lumen causing increased resistance when plunger is pulled back.
  - Inflated stomach may give false positive result: EDD to be applied before starting ventilation through the tube.
- ***Ellicks evacuator bulb***: Modification of EDD
- Transtracheal illumination:
  - Lighted stylet placed inside ETT jurst proximal to the cuff, with cricoid pressure and overhead light dimmed.

  - When stylet was introduced into esophagus, no transesophageal illumination can be demonstrated.
  - Disadvantages: Cannot be used in midline neck masses and red rubber ETT.
- Fiberoptic scope:
  - *Best method* of confirming tracheal intubation
  - Visualization of carina and tracheal rings
  - Impractical for routine use but mandatory for doubtful cases and difficult intubation.

VICARIOUS LIABILITY[1,21]

Introduction

An employer is responsible not only for his own negligence but also for the negligence of his employees, if such acts occur in the course of employment and within its scope, by the principle of respondent superior (let the master answer).

Explanation

Employees are liable under the law principle '*qui facit per alium facit per se*', i.e. one who acts through another, acts in his or her own interests.

Prerequisites

Three conditions must be satisfied to prove vicarious liability:

- There must be an employer-employee relationship
- The employees conduct must occur within the scope of his employment
- While on the job.

Determination of Negligence

Fourfold test to determine negligence:

- It must be established that there is a duty of care (between a doctor and patient, this can be taken for granted).
- It must be shown that duty of care has been breached, using ***Bolam*** test, as falling below the standard of a responsible body of medical men means the doctor may be considered negligent.
- Should be shown that there was a *causal link* between the breach of duty and harm.
- It must be shown that the harm was not too remote.

Implications in Medicine

- The principal doctor becomes responsible for any negligence of the assistant. Both may be used by the patient even though the principal has not been professionally concerned. The same applies where the principal employs nonmedical servants.
- When two doctors practice as partners, each is liable for the negligence of the other, even though one may have no part in the negligent act.
- When two or more independent doctors are attending to a patient, each may be held liable for the negligence of others that he observes, or in the ordinary course should have observed and allows it to continue without objection.

PREOPERATIVE EVALUATION CLINIC[1,2,3,21]

Introduction

The preoperative evaluation clinic was developed with the goal of focusing all preoperative clinical services into hospital location to establish a center of visibility competitiveness and efficiency.

Operative Goals

- Provide a centralized site for preoperative evaluation
- Avoid logistic shuffling of patients to multiple hospital sites
- Provide anesthesia consultation for evaluation of medically complex patients
- Establish rapport with patients and reduce anxiety
- Improve patient care by provide personalized care, comfort and convenience
- Improved education of patients and families about their surgical procedure and proposed anesthesia care, including postoperative pain control options
- Educate patients about what to expect regarding postoperative feeding and discharge needs
- Ensure cost effective ordering of preoperative laboratory and diagnostic studies
- Reduce number of cancellation and delays in operative procedures on the day of surgery
- Ensure availability of medical records at the time of preoperative evaluation
- Ensure patients and surgeon satisfaction.

Components

Preoperative evaluation clinic is a visible collaboration between departments of surgery, anesthesia, nursing and hospital administration.

Requisite Facilities

- Registration and reception area
- Adequate number of examination rooms
- Patient and family education room
- Phlebotomy and ECG room
- Area for admitting, financial and insurance services
- Computer support room and rest rooms.

Importance

- PAE clinic aims at evaluating patient for potential risks during surgery and postoperative period
- Patients should be screened and triaged to determine patients current health status
- Standardization of preoperative process done in PAC. This is useful as:
  - Allows for development and implementation of clinical algorithms to optimize preoperative medical management and reduce complications
  - This can reduce cost of admission and length of stay
  - Allows more accurate data collection
  - Minimize complications caused by communication errors.

PAE Clinic Activities

- Surgeon office schedules PAC appointment. Flexibility in scheduling appointment is required to accommodate patients with urgent surgical requirements
- Anesthetist interviews and examines patient, obtains relevant medical information and determines appropriate diagnostic, laboratory, ECG and other evaluation requirements
- Phlebotomy/ECG and hospital admitting and insurance registration are available at the clinic
- Patients ECG is assessed during the visit and lab results evaluated at the end of each clinic day. Thus, significant abnormalities can be addressed immediately and cases cancelled the day before surgery
- A nurse educator trained in perioperative teaching discusses the surgery and hospital process with each patient and family member to increase patient awareness and comfort, thus reducing fear and anxiety.

Role of Anesthetist

- The anesthetist is the only specialist who can decide on whether the patient is appropriate for anesthesia and stable to proceed
- The anesthetist should develop leadership and management position in the preanesthetic evaluation program.

THIRD SPACE LOSS[1,2,3]

Introduction

Third space loss refers to the sequestration of fluid in the third space, which is not usually perfused with fluids, i.e. the space other than the intestitial and intravascular compartment which normally make up the ECF.

Sites of Third Spacing

- *Brain:* Due to cardiac arrest causing cerebral edema
- *Lungs:* Cardiogenic/noncardiogenic pulmonary edema
- *Bowel:* Intra-abdominal hypertension (IAP more than 12 mm Hg)
- *Extremites:* Peripheral edema.

Etiology

- Medical conditions:
  - Acute gastric dilatation
  - Acute peritonitis
  - Acute intestinal obstruction
  - Acute pancreatitis.
- Mechanical injuries:
  - Burns
  - Acute spreading cellulitis
  - Crush injuries.
- Surgical insult:
  - Following abdominal and pelvic surgeries: Accumulation in peritoneum, bowel wall, etc.
  - Following abdominal aortic aneurysmal surgery after clamp is released:
    - Declamping phenomenon
    - Fluid accumulates in ischemic area of lower limbs.

Composition

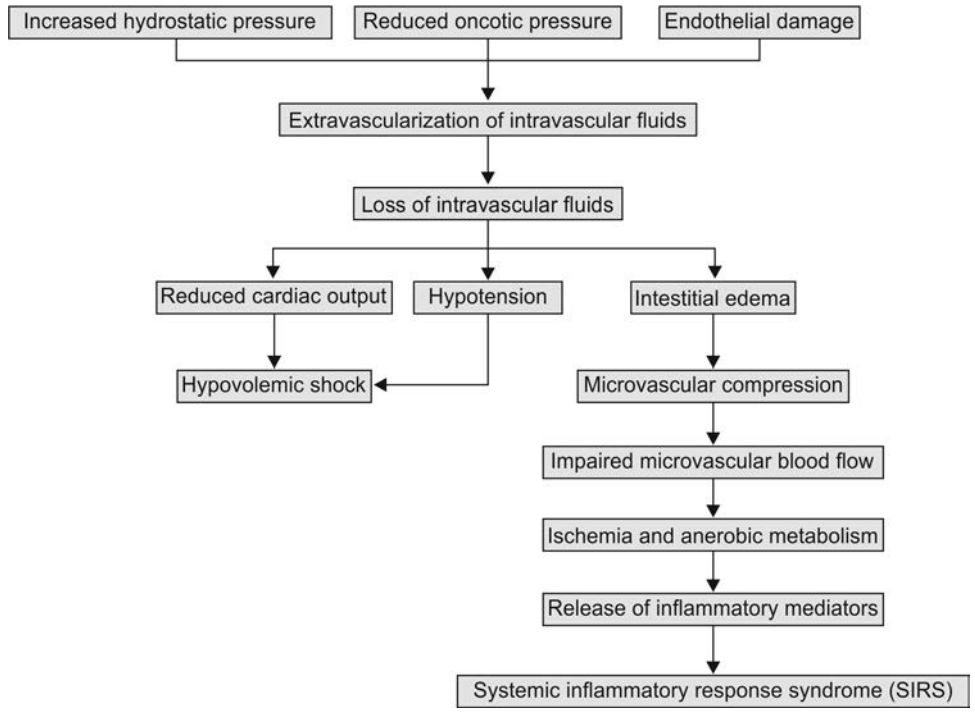
- Contains extracellular fluid
- Electrolytes
- Small amounts of proteins.

Pathogenesis

Mechanisms of fluid accumulation:

- Physiological type I fluid shift:
  - Fluid is protein free
  - Shift is due to alterations in *Frank-Starling forces*.
- Pathological type II fluid shift:
  - Fluid has proteins
  - Shift is due to disruption of *double barrier* formed by endothelial cell line and glycocalyx
  - Causes are:
    - Increased capillary permeability by surgical manipulation
    - Increased capillary permeability by inflammatory mediators
    - Increased capillary permeability by reperfusion injury
    - Iatrogenic fluid overload causing glycocalyx degradation.

Pathophysiology



Calculation of third Space Loss

- When plasma exudes out of blood stream, RBCs are now suspended into smaller volume of plasma
- Thus hematocrit increases
- This increase in hematocrit can be used to calculate plasma loss

  Plasma deficit = [normal blood volume]
  – [(normal blood volume)
  × (measured initial HCT)]
- Intra-abdominal procedures with small incisions like hysterectomies may require 2 ml/kg/hr to replace third space loss
- Major bowel resections have third space losses of around 4–6 ml/kg/hr.

Complications

- Hypovolemic shock, MI, CCF, pulmonary edema
- SIRS, anastomotic leak, paralytic ileus
- Cerebral edema
- Anasarca: Compartment syndrome
- Pulmonary Edema, reduced FRC, hypoxia, pneumonia, respiratory failure
- Intraabdominal hypertension/abdominal compartment syndrome:
  - Called IAH if sustained/repeated increase of IAP more than 12 mm Hg
  - Normal intra-abdominal pressure (IAP) = 5–7 mm Hg
  - Grading of intra-abdominal HTN:
    - Grade I intra-abdominal HTN: IAP 12–15 mm Hg
    - Grade II intra-abdominal HTN: IAP 16–20 mm Hg
    - Grade III intra-abdominal HTN: IAP 21–25 mm Hg
    - Grade IV intra-abdominal HTN: IAP more than 26 mm Hg.

Management

- *Goal directed therapy* with:
  - Central venous pressure
  - Mean arterial pressure
  - Serum lactate
  - Mixed venous oxygen saturation (MVO_2)
  - Cardiac output monitoring.
- Closely monitor:
  - Vital signs
  - Urine output (maintain more than 0.5 ml/kg/hr)
  - Peripheral perfusion
  - Mental status (for raised ICP)

  - Investigations:
    - Hematocrit, hemoglobin, serum electrolytes
    - Blood urea nitrogen, serum creatinine, serum lactate
- Intra-abdominal pressure: Measured using:
  - Serial abdominal girth measurements
  - Bladder pressure measurement with Foleys catheter Q4H when urine output is less
- Fluid resuscitation:
  - Isotonic saline/lactated Ringers preferred for dehydration
  - Boluses of colloid to increase oncotic pressure for acute hypovolemia
  - Small doses of furosemide to prevent ARF and increase renal output
  - Infuse PRBCs or whole blood:
    - Increase oxygen carrying capacity of blood
    - Also increases intravascular oncotic pressure.
- Guidelines for fluid replacement:
  - ***Parklands formula*** for burns:
    - 4 ml RL/kg/% TBSA burned
    - Gives minimum amount of fluid to be given over 24 hrs
    - Half the value obtained, is given over first 8 hrs post burns
    - Remaining half is given over next 16 hrs
  - ***Thompsons guidelines*** for postoperative fluid management.

ANESTHETIC CONSIDERATIONS OF PRONE POSITION[1,2,3,21]

Introduction

- In the classic prone position, the face, chest, abdomen, front of thighs, knees, toes and some surface of hands and arms all touch the supporting surface
- Also called *concorde position or face down position.*

Modifications

- *Jack-knife position*:
  - Used for anorectal surgeries
  - Patient lies flexed on table with pelvis at flexion point
- *Knee-chest position:*
  - Exaggeration of jack knife position
  - Knee and chest are supported
- ***Buie position***:
  - For proctological work
  - Patient kneels on a padded shelf, places chest on table proper
  - Table is tilted to head down position
- ***Georgia position***: For perineal and rectal work
- ***Overholt position***:
  - Used for thoracic problems
  - To prevent drainage of infected material and blood from the involved lung into the other lung
- ***Sellor-Brown position***:
  - Lower part of body in one plane
  - Chest neck and head are on a lower plane
  - Used to drain blood and infected material from the uninvolved lung
- Crouching or Carpenters rule position:
  - Knees and hips are flexed maximally
  - Patients weight rests on back of legs
  - Abdomen rests on front of thigh
  - Associated with:
    - Knee injury
    - Femoral venous obstruction
    - Abdominal wall restriction.

Indications

- Posterior cervical and occipital surgeries
- *Spine surgeries:* Laminectomy, spinal fusion, scoliosis
- Thoracotomy by posterior approach
- Adrenal exploration, renal biopsies, percutaneous nephro-lithototripsy, PCN
- Surgeries on back of leg, e.g. varicose vein stripping, tendon repair
- Prone ventilation for ARDS
- Ano-rectal surgery in jack-knife position.

Contraindications

- Crush injury to chest, flail chest
- Contusion of heart
- Severe *pectus excavatum.*

Problems

- Care must be taken in keeping head safe in relation to rest of body
- Body weight against abdominal wall leads to:
  - Reduced diaphragmatic movement: Reduced FRC
  - Reduced tidal volume
- Increased intra-abdominal pressure causes reduced venous return
- Pressure on body prominences and toes: Pressure injuries.

Physiological Effects

- Cardiovascular system:
  - Blood supply to brain must be protected:
    - Avoid severe twisting or neck extension
    - This may impede flow through vertebral artery
  - Venous return from head may get occluded:
    - Eyelid edema, swollen and engorged eye vessels
    - Headache, subglottic edema can occur macroglossia
  - Pressure on carotid sinus may cause severe arrhythmias
  - Pressure on inferior vena cava and femoral vein:
    - Causes reduced venous return
    - This leads to hypotension
    - This is compounded by sympathetic block associated with SAB/GA
  - Venous air embolism
  - Increased bleeding from abdominal pressure due to epidural venous engorgement.
- Respiratory system:
  - Less airway pressure is required to ventilate patient in prone position
  - This is because weight of chest and abdominal wall does not have to be lifted
  - Patients thorax and pelvis should be raised by support
  - A hand should be able to pass between abdomen and bed
  - Body weight against abdominal wall leads to reduced diaphragmatic movement and tidal volume.

Complications

Neurological Complications:

- Ophthalmological:
  - Corneal abrasions: Eyes may be injured during:
    - Turning patient
    - Protracted pressure in prone position during long duration surgeries
  - *Anterior Ischemic Optic Neuropathy (AION)*
  - *Posterior Ischemic Optic Neuropathy (PION)*
  - *Central Retinal Artery Occlusion (CRAO*)
  - Cortical blindness.
- Facial nerve injury in infraparotid region
- Brachial plexus injuries due to:
  - *Neck rotation:* Stretching of nerve roots
  - Compression of plexus between ribs and clavicle
  - Injury to neurovascular bundle from head of humerus
  - Compression of ulnar nerve before, within or after the cubital tunnel
  - Lateral compression of radial nerve proximal to elbow.
- *Ulnar nerve:* At risk against sharp edges of supporting devices when arms are positioned above the head
- Spine injury if hips and shoulder not in same plane always
- Jack-knife position:
  - Can injure femoral nerve
  - Lateral cutaneous nerve of thigh injury causing meralgia paraesthetica.
- Injury to nerves and tendons of dorsum of foot.

Other Injuries

- Orbital compression can cause retinal ischemia and blindness
- Nasotracheal tubes:
  - To be positioned carefully
  - Avoid pressure on nasal cartilage in anterior margin
- Pressure necrosis of maxilla and forehead in prolonged procedures
- In cervical and posterior fossa procedures:
  - Flexion of neck causes reduced anteroposterior diameter of hypopharynx
  - This leads to compression ischemia of base of tongue and macroglossia
  - This causes unexpected postextubation airway obstruction.
- Ear cartilage damage if folded over
- Turning an extended neck causes:
  - Neck muscle spasm and headache postoperatively
  - This is due to pressure on C_2 between atlas and axis vertebrae
- Chest support devices may block venous return from neck
- In females:
  - Breasts may get injured along sternal border
  - Common if breast prosthesis is present
  - Thus, medial and cephalad displacement of breast should be done
- *Male genitals:* Electrocautery grounding plate should not touch them
- Skin overlying iliac crest should be protected
- Compartment syndrome in prolonged kneeling position

- Toes should be protected using pillows under ankles
- Air embolism is a risk when operating field is higher than the heart.

Accidental Extubation

In prone position there is:
- Poor access to airway
- Traction from head movements and circuit
- Loosening of adhesive tapes due to sweating/saliva.

ANESTHETIC CONSIDERATIONS OF LITHOTOMY POSITION[1,2,3,21]

Introduction

It is the position in which the patient is on his back with the legs and thighs flexed to right angles.

Modification

- For combined vaginal-abdominal approach to pelvic viscera:
  - Leg elevation is less
  - Flexion of thigh to abduction is less than 90°
- ***Walcher position*** for obstetrics: Thighs pressed firmly onto trunk and legs left dangling
- ***Blandys position*** for TURP where legs are supported in such a way that thighs create an obtuse rather than acute angle with the body.

Types of Lithotomy Position

- Low lithotomy position:
  - Used for most urological procedures
  - Degree of thigh elevation is only 35–40°.
  - Reduces perfusion gradients and improves perineal access
- High lithotomy position:
  - Thigh flexed to 90° or more on trunk
  - Legs are almost fully extended on thighs by suspending patients feet from high poles
  - Significant uphill perfusion gradient exists
  - Poorly tolerated in less mobile patients
  - Complications:
    - Sciatic nerve stretching
    - Compression of contents of femoral canal.
- Exaggerated lithotomy position:
  - For transperineal approach to retropubic area
  - Patient's pelvis is flexed ventrally on the spine
  - Thighs are flexed on trunk with lower legs aimed skywards
  - Significant uphill perfusion gradient exists for feet perfusion
  - Restricted ventilation: Controlled ventilation necessary
  - Avoided in preexisting lumbar spine diseases
  - High frequency of compartment syndrome of lower limbs.
- Tilted lithotomy position:
  - Lithotomy position with head down tilt
  - Patient may slide cephalad and have head injuries
  - Cranial vascular compression and raised ICP
  - Use of shoulder brace to prevent cephalad displacement:
    - This may compress neurovascular bundle in neck
    - May also compress subclavian neurovascular bundle between clavicle and first rib
  - Weight of abdominal viscera on the diaphragm limits ventilation
  - It also causes gravitational accumulation of blood in the poorly ventilated lung apices
  - During controlled ventilation higher airway pressures are required to expand the lung.

Indications

- Perineal and rectal surgeries
- Vaginal surgery
- Urological operations: TURP, cystoscopy, retrograde pyelography, etc.

Contraindications

- Painful lumbar spine diseases
- Obese patients: Relative contraindication
- Decompensated CCF
- Raised ICP: Tilted lithotomy position contraindicated.

Physiological Changes

- Respiratory system:
  - Vital capacity reduces by 18%
  - Thus is due to:
    - Restriction of diaphragmatic movement
    - Reduced volumetric expansion of lung due to pulmonary vascular congestion
  - Tidal volume reduces by 3%
  - FEV1 increases by 9% due to:
    - Weight of abdominal viscera acts as a belt
    - This improves resting position of diaphragm
    - This increases inspiratory reserve
    - This adds force to maximum expiratory effort.

  - Increase in postoperative respiratory complications due to paralysis of abdominal muscles with resultant inability to cough following SAB/epidural anesthesia.
- Cardiovascular system:
  - Sudden elevation of lower limb causes increased venous return to right heart and precipitates CCF
  - Sudden lowering of lower limb may cause significant hypotension.

Complications

- Venous stasis: Any patient placed in lithotomy position for more than 15 mins should have legs protected by elastic stockings
- Damage to hip and knee especially of elderly women
- Injury to hand and fingers when caudal portion of table is lowered
- Sudden hypotension, congestive cardiac failure
- Compartment syndrome in high and exaggerated lithotomy position
- Peripheral nerve injuries:
  - Obdurator nerve ($L_{2,3,4}$):
    - Due to acute flexion of thigh on groin
    - Causes paralysis of thigh adductors.
  - Femoral nerve:
    - Due to acute thigh flexion with angulation against underlying surface of pubic ramus
    - Causes abnormal gait and numbness.
  - Saphenous nerve:
    - Compression of leg to knee brace medially
    - Causes loss of sensation on medial aspect of leg.
  - Common paroneal nerve (L_4-S_2):
    - Due to pressure on head of fibula
    - Causes foot drop due to tibialis anterior palsy.
  - Stretching of sciatic nerve: Foot drop
  - Compression of popliteal neurovascular bundle by edges of holder
  - Improper technique of lowering legs may cause torion stress on lumbar spine
  - ***Transient Neurological Symptoms (TNS):***
    - Especially common with 5% lidocaine and 1% tetracaine
    - Neuronal damage due to:
      - Increased release of glutamate causing increased intracellular calcium levels
      - This causes vacuolation and central chromatolysis of neurons in *Obersteiner-Redleich zone.*
    - More common when:
      - 5% lidocaine used for spinal anesthesia
      - In lithotomy position due to stretching of nerve fibers.

NEURONAL TRANSMISSION[1,2,3,21]

Definitions

- *Action potential:* Brief localized spikes of positive charge/depolarization on the cell membrane caused by rapid influx of Na^+ ions down its electrochemical gradient
- *Threshold potential:* The point at which the rate of depolarization abruptly increases.

Types of Impulses

- Local, nonpropagated disturbances in potential: *Synaptic potential*
- Propagated disturbances in potential: *Action potential*
- Measurement of electrical events in living tissue is done with *cathode ray oscilloscope.*

All or None Law

- Whether or not an impulse is conducted across the nerve fiber is determined by all or none law
- Once the threshold intensity is reached, a full fledged action potential is fired
- Further increase in intensity of stimulus produce no increment or change in action potential
- If the stimulus is subthreshold in magnitude, action potential fails to occur
- Thus, action potential is ***all or none*** in character.

Electrogenesis of Action Potential

- Two factors contribute to electrical potential in cells:
  - Concentration gradient of ions across membrane
  - Selective permeation of ions through membrane
- Electrogenic Na^+ K^+ ATPase complex:
  - Transports 3 Na^+ ions out of the cell, for every 2 K^+ ions it moves into the cell
  - This creates a concentration gradient which favors movement of extracellular Na^+ into the cell and intracellular K^+ out of the cell
  - This gradient thus produces forces which tend to move the ions
- At rest:
  - The membrane is more permeable to K^+ than Na^+
  - Thus, a relative excess of negatively charged ions (anions) accumulates intracellularly

  - This accounts for the resting membrane potential (RMP) (-70 mv)
  - This RMP is close to the MP of K^+ (-80 mv).
- On application of a mechanical/chemical/electrical stimulus:
  - Depolarization occurs which fires an action potential when it exceeds the threshold potential (-55 mv)
  - This occurs as depolarization causes opening of VGSC (*voltage gated sodium channels)*
  - This causes influx of Na^+ ions and thus, a progressive reduction of negative polarity.
- When the membrane potential reaches + 35 mv:
  - A sudden inactivation of Na^+ channels causes a drop in Na^+ permeability
  - This occurs along with an increased conductance of K^+ out of the cell
  - This returns the membrane to its resting potential
  - After reaching baseline, persistent K^+ efflux causes *after-hyperpolarization.*
- After hyperpolarization:
  - Minor changes in the Na^+ and K^+ concentrations occur during this process
  - Baseline concentrations are then established using Na^+K^+ ATPase.

Impulse Conduction

- Inward current entering the axon during depolarization flows within axoplasm and spreads to adjacent inactive regions
- These regions are rapidly depolarized by this local circuit current to levels far in excess of threshold potential, thus generating its own inward current
- Depending on presence of myelin, three types of conduction occur:
  - *Saltatory conduction:*
    - Occurs in myelinated axons where depolarization jumps from one ***node of Ranvier*** to the next
    - Thus, myelinated axons conduct upto 50 times faster than unmyelinated fibers
  - *Orthodromic conduction:* Conduction of impulses in one direction from synaptic junction along axons to their termination
  - *Antidromic conduction:* Conduction in opposite direction.

Factors Affecting Neuronal Responsiveness

- *pH:* Alkalosis increases excitability (seizures common in hyperventilated patients)
- *Hypoxia:* Total inexcitability of neurons within 3–5 seconds
- Inhaled anesthetics increase threshold for excitation and thus, reduce activity.

Synaptic Fatigue

Refers to a reduction in number of discharges by post-synaptic membrane, when synapses are repetitively and rapidly stimulated.

Post Tetanic Facilitation

- Increased responsiveness of post-synaptic neuron to stimulation after a rest period which was preceded by repetitive stimulation of an excitatory synapse
- This occurs due to increased release of neurotransmitters due to increased permeability to Ca^{2+}
- This may be responsible for mechanism ***of short term memory.***

CONCENTRATION EFFECT[1,21]

Definition

- Increasing inspired concentration of an anesthetic agent not only increases alveolar concentration but also the rate of rise of alveolar concentration (i.e. FA/FI ratio)
- Predominantly seen for N_2O as it has low blood gas partition coefficient (0.47).

Factors Causing Concentration Effect

- *Concentrating effect:*
  - When a certain amount of gas is taken up by the blood (i.e. uptake), the alveolar size reduces
  - This reduction in alveolar size concentrates the gas remaining in the lung
  - The magnitude of this effect is influenced by concentration of gas within the lung
  - For example:
    - When the lung is filled with 1 part N_2O and 99 parts of O_2:
      - If one half of N_2O is taken, 0.5 parts N_2O and 99 parts of O_2 remains
      - Thus N_2O concentration is 0.5% (0.5/99.5)
    - If the same lung is filled with 80 parts of N_2O and 20 parts of O_2:
      - If one half of N_2O is taken, 40 parts of N_2O and 20 parts O_2 remain
      - Thus, concentration of N_2O remaining is 67% (40/60)

- When inspired gas contains 100% of N_2O:
  - If 50% of N_2O is taken up, 50 parts of N_2O is present in 50 parts of alveolar gas
  - Thus, concentration remains 100%.

- *Augmented inflow effect:*
  - When N_2O is taken up by blood, the alveolar volume reduces
  - To prevent alveolar collapse, additional inflow of gas occurs due to negative pressure and gas is drawn from trachea
  - This fresh inflow of gas replaces the volume of N_2O lost by uptake in blood
  - Thus, increased alveolar ventilation makes alveolar gas more like inspired gas
  - This reduces FI/FA concentration difference
  - For example:
    - If one half of N_2O is taken from an 80 parts N_2O and 20 parts O_2 mixture:
    - 40 parts of N_2O and 20 parts of O_2 remain
    - N_2O concentration will be 67%
    - The remaining 40 parts of gas is again filled by an 80% N_2O and 20% O_2 mixture, i.e. by 32 parts of N_2O (80% of 40 parts) and 8 parts of O_2 (20% of 40 parts)
    - Thus, total volume is now made by 72 parts of N_2O (40 + 32) and 28 (20 + 8) parts of O_2
    - Thus, N_2O concentration becomes 72%.

SECOND GAS EFFECT[1,21]

Definition

Uptake of a large volume of first or primary gas (usually N_2O) from alveoli, increases rate of rise in alveolar concentration of a second gas given concomitantly.

Factors Causing Second Gas Effect

- *Concentrating effect:*
  - Uptake of large volume of N_2O causes a reduction in alveolar volume
  - Thus, concentration of all remnant gases in alveolus increases, including that of inhaled anesthetics
  - This is especially important for less soluble agents as their uptake into blood is less.
- *Augmented inflow effect:*
  - The loss of volume of alveoli when large volume of N_2O is taken up by blood is replaced by fresh gas inflow with more inhaled anesthetic
  - This also increases alveolar concentration of inhaled anesthetic
  - This is especially important for more soluble agents as their uptake into blood is larger.

Clinical Importance

Since uptake of large volume of N_2O is limited to first 5–10 minutes of induction, these effects are important only during this period.

Controversy

Sun-X 1999 anesthesia analogue demonstrated that N_2O did not effect alveolar/blood concentration of enflurane under controlled ventilation.

DIFFUSION HYPOXIA/FINK EFFECT[1,21]

Definition

Desaturation of a patient on termination of anesthetic which includes nitrous oxide within 5–10 minutes.

Etiology

- As N_2O has low BGPC (0.47), large volume of N_2O diffuses from blood into alveoli upon termination of N_2O administration
- This occurs within 5–10 minutes of termination
- This has a two-fold effect to cause hypoxia:
  - Displacement of alveolar oxygen:
    - N_2O diffusing into alveolus displaces alveolar O_2
    - If only room air is being administered during this time, fraction of alveolar O_2 can fall below 0.21 and cause hypoxia.
  - Displacement of alveolar carbon dioxide:
    - N_2O also displaces CO_2
    - If this causes the fraction of alveolar CO_2 to fall below the level needed to maintain $PaCO_2$ sufficient to drive ventilation, hypoventilation results
    - This causes further hypoxia
    - This is more important when residual narcotics are present or in patients with COPD
    - Diffusion hypoxia is prevented by administration of 100% O_2 for 5–10 minutes on termination of N_2O.

PRINCIPLES AND USE OF ULTRASOUND IN ANESTHESIA[1,2,3,4]

Introduction

- Ultrasound is a form of mechanical sound energy which travels through a conducting medium (e.g. body tissue) as a longitudinal wave producing

compressions (high pressure) and rarefactions (low pressure)
- Human hearing range is 20–20,000 Hz
- Frequency of ultrasound wave is 20,000 Hz
- Medical ultrasound commonly is 2.5–15 mHz range.

Generation of Ultrasound Wave

- An ultrasound wave is generated when a strong electrical field is applied to an array of piezoelectric crystals located on the transducer surface
- Electrical stimulation causes distortion of these crystals which then start vibrating
- This results in production of sound waves and is called *converse piezoelectric effect*
- Each crystal generates an ultrasound wave
- The summation of all these waves produces an ultrasound beam
- The waves are generated in intermittent trains called pulses
- *Pulse length* is the distance travelled by one pulse
- *Pulse repetition frequency (RPF):*
  - Refers to the rate at which pulses are generated by the transducer (number of pulses per unit time)
  - This is important as ultrasound pulses must be spaced with enough time between pulses to permit the waves to reach the target, and return to the transducer before the next pulse is generated.

Attenuation

- As the ultrasound beam travels through tissue layers, the amplitude of the original signal reduces and depth of penetration increases.
- This is due to:
  - Absorption (conversion of acoustic energy to heat)
  - Reflection
  - Scattering at interfaces.
- The attenuation caused by each tissue is represented by its *attenuation coefficient*
- Thus tissues like bone have a high attenuation coefficient and severely limits beam transmission
- Attenuation also varies with frequency of the ultrasound wave
- High frequency waves are more attenuated and thus have lesser tissue penetration and vice versa.

Generation of Image

- The transducer waits to receive the returning wave (echo) after each pulsed wave
- The transducer then converts the echo (mechanical energy) into an electrical signal which is displayed on screen
- This is called *piezoelectric effect*.

Components of Ultrasound Scanner

- *Pulser:* Applies high amplitude voltage to energize crystals
- *Transducer:* Converts mechanical to electrical energy and vice versa
- *Receiver:* Receives and amplifies weak signals
- *Memory:* Stores video display
- *Display:* Displays ultrasound signals in a variety of modes.

Modes of Display

- Amplitude (A) mode
- Brightness (B) mode
- Motion (M) mode
- B-modes is most often used for regional blocks.

Echogenecity

- When an echo returns to the transducer, its amplitude is represented by the degree of brightness of a dot on display (*echogenicity*)
- Strong specular reflection produce bright dots (*hyperechoic shadows*):
  - Diaphragm
  - Pericardium
  - Bone
  - Gall and bladder stones.
- Weaker diffuse reflections produce grey dots (*hypoechoic shadows*), e.g. solid organs
- No reflection produces dark dots (*anechoic shadows*), e.g. blood and fluid filled structure as the beam passes through without any reflection
- Nerves exhibit the phenomenon of ***anisotrophy***:
  - Phenomenon where the echogenecity of the nerve varies with angle of insonation
  - Thus at 90°, reflection from the scanned nerve is maximal and image is best.

Resolution

- Spatial resolution determines the degree of image clarity
- Resolution refers to the ability of ultrasound machine to distinguish two structures that are close together as separate
- Spatial resolution is influenced by axial and lateral resolution

- Axial resolution refers to the ability of to distinguish two structures which lie along the axis of ultrasound beam as separate and distinct
- Lateral resolution refers to resolution of objects lying side by side, i.e. perpendicular to beam axis.

Imaging Plane and Approaches

- Nerves can be imaged in either short (transverse) axis or long (longitudinal) axis
- Blocks are usually performed in short axis (SAX) view
- With this view, identification of nerve fibers as modular structures is easy with good resolution
- Circumferential spread of LA on injection is also viewable.

Color Doppler

- Instrument used to characterize blood flow and useful in identifying blood vessels in close proximity to nerves.
- Doppler effect:
  - Occurs when there is a moving source (RBCs) and a stationary listener (USG transducer)
  - There is an apparent change in frequency of returning echoes due to relative motion between sound source and receiver
  - RBCs moving towards transducer are perceived as higher frequency (red)
  - RBCs moving away from transducer are perceived as lower frequency (blue).

Uses of Ultrasound in Anesthesia

- First used by ***La Grange*** in 1978 for supraclavicular block
- In 1994 detailed paper on the same published by *Stephen Kapral*
- Ultrasound guided nerve blocks:
  - Regional anesthesia
  - Chronic pain.
- Ultrasound guidance for vascular access
- Diagnostic modality:
  - Pleural/pericardial effusion
  - Intra-abdominal hemorrhage
  - Perforated hollow viscus
  - Trauma patients.
- Monitoring:
  - Transesophageal echocardiography
  - Cardiac output monitoring
  - Transthoracic echocardiography.

Advantages of Ultrasound Guided Nerve Blocks

- Higher rate of success with failure rate 20% with paresthesia technique
- Reveals nerve localization and surrounding vascular structures
- Real time imaging guidance during needle advancement
- Images local anesthetic spread pattern during injection (***Doughnut sign***)
- Improves quality of sensory block, onset time and success rate compared to nerve stimulator technique
- Reduces number of needle attempts and the risk of nerve injury
- Prevents intravascular and intraneural injection.

Ultrasound Guided Vascular Access

- Advantages:
  - High success rate
  - Less number of punctures: Reduces skin transfer of pathogens
  - Reduced incidence of complications
- Limitations:
  - *Impractical:* USG probes/sterile scanner manipulation
  - Unavailability of equipment
  - Lack of trained personnel.

OCULOCARDIAC REFLEX[1,2,3,7,21]

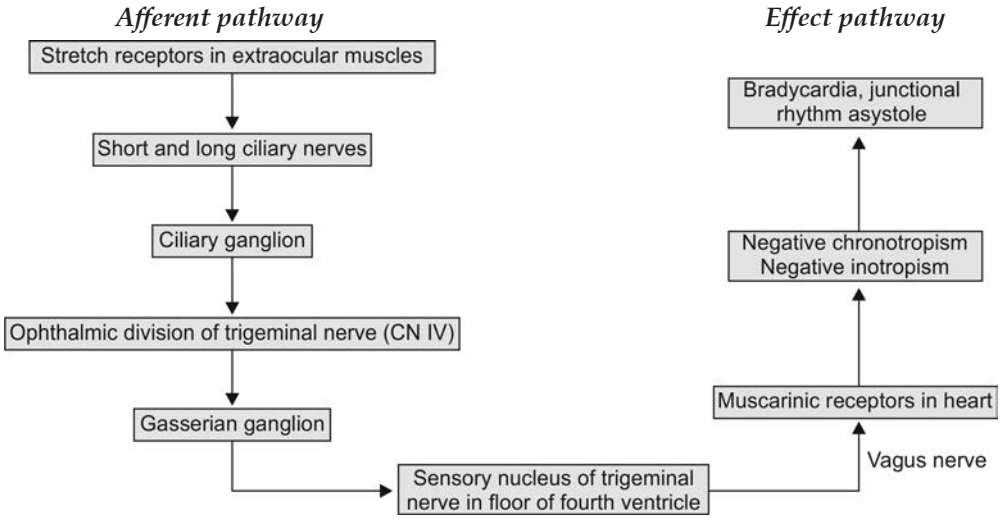
Introduction

- Oculocardiac reflex is a trigeminovagal reflex response which results in bradycardia, junctional rhythm or asystole, secondary to traction on eye/extraocular muscle
- First described by ***Aschner and Dagmini*** in 1908.

Prevalence

- 30–90% prevalence in ocular surgery
- More common in children and young adults undergoing strabismus surgery.

Pathway[21]



Triggers

- Pressure on eyeball
- Traction on extraocular muscles/conjunctiva/periosteum/any orbital structure
- Orbital trauma
- Orbital hematoma
- Manipulation of globe
- ***Forced duction test***
- Raised intraocular pressure
- During retrobulbar block.

Occurrence

Common during:

- Retrobulbar block:
  - Occurs due to retrobulbar hemorrhage
  - May occur upto 1.5 hours after surgery, as additional blood extravasates out.
- Strabismus surgery (medical rectus is most sensitive to manipulation)
- Enucleation, cataract surgery
- Retinal detachment surgery (during giving retrobulbar block)
- Non-ocular surgery if pressure applied on eyeball
- Ocular trauma and pain
- Ocular manipulation.

Aggravating Factors

- Can occur in an empty orbit from extraocular muscle stimulation or traction on orbital remnants following enucleation
- Hypoventilation, hypercarbia and acidosis augments the risk
- Light planes of anesthesia
- Anesthesia technique which includes fentanyl, remifentanyl and sufentanyl increases risk
- Reduced incidence of OCR with:
  - Sevoflurane, as compared with halothane
  - Pancuronium, as compared with other NDMR.

Manifestations

- *Most common in pediatric patients undergoing strabismus surgery*
- Triad of bradycardia, nausea and syncope
- Somnolence and nausea in awake patients
- *Sinus bradycardia most common manifestation*
- Nodal/junctional rhythm may manifest
- AV block, wandering pacemaker, asystole
- Ventricular trigeminy, multifocal VPCs, VT, VF.

Prevention

- Retrobulbar block as it inhibits afferent links of reflex arc.
- Gentle manipulation of ocular muscle
- Avoid hypoventilation and hypercarbia
- Communication between anesthetist and surgeon
- Deep planes of anesthesia
- Avoid fentanyl/remifentanyl/sufentanyl
- IV premedication:
  - Done with IV atropine/glycopyrrolate
  - Given within 30 minutes prior to surgery

- IM premedication is ineffective
- Especially useful in those patients with:
  - History of conduction block
  - Vasovagal response
  - Currently on-blocker therapy.

Management

- Ask the surgeon to stop manipulation of muscle
- Ensure adequate oxygenation, ventilation and adequate depth of anesthesia
- Most often, heart rate and rhythm return to baseline within 20 seconds if these 2 steps are done
- Deepen anesthetic plane and maintain normocarbia
- IV Atropine:
  - 7 µg/kg increments is used
  - Given if conduction disturbance persists
  - To be given only once surgeon stops manipulation of EOM
  - If it is given when OCR is still active, more dangerous arrhythmias may occur.
- IV Glycopyrrolate:
  - 10 µg/kg increments can also be used
  - It causes less tachycardia
  - Takes 3–4 minutes to act
- In recalcitrant episodes, infilterate rectus muscle with local anesthetics
- Repeated stimulation of EOM causes fatigue of the reflex arc at level of cardio-inhibitory center
- Cardiopulmonary resuscitation, if asystole, as it helps to circulate atropine.

Postoperative Management

- Reflex may occur up to 1½ hours after uncomplicated retrobulbar block
- It may occur late due to:
  - Expanding retrobulbar hemorrhage
  - Persistent bleeding causing raised IOP
- Careful monitoring is therefore warranted
- Maintain adequate oxygenation and ventilation.

Controversy

- Atropine may be hazardous as:
  - Elderly patients with CAD will not tolerate tachycardia
  - It may cause VPCs, LBBB, VT and VF if halothane is used concurrently.

RAPID SEQUENCE INDUCTION[1,2,3,6,21]

Introduction

- Rapid intravenous induction and muscle relaxation to aid endotracheal intubation, combined with cricoid pressure to reduce risk of pulmonary aspiration
- Virtually simultaneous administration of sedative hypnotic and neuromuscular blocking agent to render a patient rapidly unconscious in order to facilitate emergency tracheal intubation (*within 60–90 seconds*) and to minimize risk of aspiration by applying *Sellicks maneuver.*

Indications

Full stomach patients:

- Pregnancy
- Intestinal obstruction
- Preoperative gastro-esophageal reflux, esophageal dilatation
- Hiatus hernia, strangulated hernia
- Inadequate NPO status:
  - Less than 6 hours for solids
  - Less than 4 hours for breast milk
  - Less than 2 hours for clear fluids.
- Trauma, head injury, burns
- Maxillofacial trauma
- Autonomic neuropathy, associated with delayed gastric emptying.

Principles for Rapid Sequence Induction

- Adequate preoxygenation must be performed (3–5 minutes)
- Sufficient dose of IV drugs to be given to ensure patient is adequately anesthetized
- Intubation within 60–90 seconds is considered acceptable
- Cricoid pressure:
  - Applied subsequent to injection of induction agent
  - Removed after checking position of ETT and inflating cuff.

Preparation for Rapid Sequence Induction (RSI)

- Trained assistant
- Working suction
- Tilting trolley

- Tested cuffed endotracheal tube
- Two functioning laryngoscopes, gum elastic bougie
- Routine monitoring, IV cannula
- Drawn up predefined dose of induction agent and succinylcholine
- Emergency drugs
- Plan for failed RSI.

Conduct of RSI

- Check equipment
- Take baseline BP, heart rate, SPO_2 on room air
- Switch on suction and place within easy reach
- Preoxygenate with atleast tidal volume breathing with tight fitting face mask for:
  - Atleast 3 minutes
  - Or, until ETO_2 reaches 90%
- Thiopentone 3–5 mg/kg administered IV
- Cricoid pressure at 30 N/3 kg force (9.8 N = 1 kg)
- Succinylcholine 1.5 mg/kg
- Intubate, inflate cuff, check position of ETT in sniffing position
- Remove cricoid pressure and continue anesthesia
- Nasogastric tube inserted to deflate stomach
- Awake extubation in lateral position.

Other Methods of Rapid Muscle Relaxation

- *Priming technique*:
  - 10% of intubating dose of NMBA, administered 2–4 minutes before intubation dose
  - This accelerates onset of action of NMBA by 30–60 seconds
  - But, intubating condition not very good
  - Also, associated with aspiration and difficulty in swallowing.
- *High dose neuromuscular blocking agents:*
  - Useful with rocuronium
  - Increasing dose of rocuronium from 0.6 mg/kg IV to 1.2 mg/kg IV reduces onset of action from 90 seconds to 60 seconds.
- *Combination of NMBAs:*
  - Mivacurium and rocuronium used in combination often
  - Does not have consistent effect.

Adverse Effects of RSI

- Hemodynamic instability:
  - Due to excessive dose of induction agent
  - Hypertension, tachycardia and awareness if inadequate anesthesia
- Problems with cricoid pressure:
  - BURP (backwards, upwards, rightwards pressure) improves view but increases chances of airway obstruction
  - Impedes laryngoscopy and distorts view
  - May cause esophageal rupture
  - Cricoid cartilage fracture, especially if patient is on steroids.

Failed RSI Regimen after Succinylcholine

- Announce failed intubation and call for help
- Maintain cricoid pressure
- Insert oral airway
- Ventilate with face mask and 100% oxygen
- Try four handed bag and mask ventilation with extra person
- *Insert LMA:* Release cricoid force temporarily as LMA is swept into place
- Reapply cricoid force and attempt ventilation
- Release cricoid force and attempt ventilation
- If ventilation not possible, emergency cricothyrotomy if patient is not waking up or spontaneously breathing.

Other Techniques to Prevent Aspiration

- *Newcastle technique:*
  - Based on assumption that patient cannot hyperventilate and vomit simultaneously
  - Uses hyperventilation with N_2O, O_2 and ether
- 20° head down tilt in lateral position
- 40° head up tilt:
  - Maneuver raises larynx by 19 cms above lower esophageal sphincter
  - It prevents passive reflux, but increases likelihood of aspiration if vomiting occurs.

Special Situations

- Myasthenia gravis:
  - May be resistant to succinylcholine
  - Use 1.5 mg/kg succinylcholine with vecuronium 0.01 mg/kg IV.
- Pediatric patients:
  - May not cooperate for preoxygenation
  - Desaturation occurs faster
  - Force for cricoid pressure not yet established
  - Gentle face mask ventilation after induction
  - If uncuffed tube used, put throat pack to prevent intraoperative aspiration
  - Succinylcholine is preceded by atropine to prevent bradycardia
  - Nasogastric tube inserted after intubation.

CRICOID PRESSURE[1,2,3,6]

Introduction

- Temporary occlusion of upper end of esophagus by backward pressure on cricoid cartilage against body of C5/C6 vertebra
- Also called *Sellicks maneuvre*.

Indications

- Pregnancy
- Intestinal obstruction
- Preoperative gastroesophageal reflux, esophageal dilatation
- Hiatus hernia, strangulated hernia
- Inadequate NPO status:
  - Less than 6 hours for solids
  - Less than 4 hours for breast milk
  - Less than 2 hours for clear fluids.
- Trauma, head injury, burns
- Maxillofacial trauma
- Autonomic neuropathy, associated with delayed gastric emptying.

Contraindications

- Suspected cricotracheal injury
- Active vomiting
- Unstable cervical spine injury
- May be difficult in patients with history difficult intubation.

Mode of Application

- Position:
  - Tonsillectomy position/sniffing position
  - Extension on neck, cervical spine flexed on thorax.
- Timing:
  - Upon initiation of induction
  - Incremental forces:
    - 20 N while patient is conscious
    - 30 N upon loss of consciousness.
- Methods of application:
  - Single handed cricoid pressure:
    - Thumb and middle finger placed on cricoid cartilage
    - Index finger placed above, to prevent lateral movement of cricoid cartilage.
  - Double handed cricoid pressure:
    - Counter pressure with hand placed beneath cervical vertebrae to support neck
    - One hand placed under hyperextended neck
    - Other hand applies cricoid pressure
    - Better in cervical spine pathology.
- Cricoid yoke:
  - Hand held device with foam contact cushion molded to fit over cricoid cartilage
  - Applies pressure set at predetermined values.
- Nasogastric tube:
  - NGT must be left open to atmosphere to vent air/liquid
  - This limits rise in intragastric pressure during induction
  - Presence of NGT may reduce incidence of aspiration
  - Chances of passive regurgitation maybe higher
  - If NGT already present, empty stomach before induction.

Withdrawal of Cricoid Pressure

After tube position is checked and ETT cuff is inflated.

Complications of Cricoid Pressure

- Insufficient pressure may allow aspiration
- Excessive pressure (more than 40 N):
  - Completely occludes laryngeal lumen, especially in young females
  - Difficulty in laryngoscopy and intubation
  - Difficulty with fall mask ventilation
  - Difficulty with LMA insertion
  - Esophageal rupture
  - Cricoid cartilage fracture, especially if patient is on long term steroids (asthmatics).

VENTURI PRINCIPLE[1,2,3,21]

Introduction

- It is a reduction in fluid pressure which results when a fluid flows through a constricted section of pipe
- ***Coanda effect***: If such a constriction occurs at a bifurcation, due to increase in velocity and decrease in pressure, fluid (air, blood) tends to stick to one side of the branch causing maldistribution.

Explanation

- Any apparatus containing a tube with a constriction and an opening at the constriction will suck in air/fluid due to low pressure at that site (*Bernoullis principle*). Such an apparatus is called Venturi apparatus

- When a gas passes through a tube with a narrowed diameter, its pressure is reduced
- So as to keep the energy constant, velocity of the gas increases.

Applications

Clinical Signs

- *Obstructive sleep apnea syndrome:* Collapse of airway occurs due to turbulent flow through obstructed airways
- Mucus plug present at branching of tracheobronchial tree may cause maldistribution of gases
- *Pulsus bisferiens* in aortic regurgitation
- Unequal flow may occur due to plaques in vascular tree (*coronary steal* due to Coanda effect).

Venturi Devices

- Venturi mask:
  - Color coding:
    - Color of the mask's aperture determines the FiO_2
    - FiO_2 delivered by blue mask 24%
    - FiO_2 delivered by white mask is 28%
    - FiO_2 delivered by yellow mask is 35%
    - FiO_2 delivered by red mask is 40%
    - FiO_2 delivered by green mask is 60%.
  - Working principle:
    - Oxygen mask having different diameter ports at the distal end
    - It thus entrains air into oxygen flow
    - At point A, 100% oxygen flows into wider point B via narrow orifice
    - Due to narrowing, oxygen speeds up and pressure drops at that point is below atmospheric pressure
    - Thus, room air is drawn to this point, diluting the 100% oxygen to a calibrated value set by the colored nozzle
    - The nozzle has a varying aperture open to room air, which sets the entrapment ratio and thus the FiO_2 given to the patient.
- Oxygen tents
- *Pethick's test* for checking Bains circuit
- Nebulizer:
  - Oxygen passes through the liquid present in reservoir containing medication
  - Water droplets containing medication is generated which is inhaled.
- Vaporizers, humidifier
- Jet ventilation:
  - HFJV through a small catheter in trachea
  - Oxygen flow through catheter entrains air
- *Saunders injector* in Venturi ventilation for bronchography:
  - Two 16 gauge cannulae are attached to proximal end of bronchoscope
  - A jet of oxygen blows through the cannula
  - This will generate sufficient force to draw in room air and deliver air at substantial positive pressure.
- PEEP valve
- For driving gases in a ventilator
- Suction apparatus
- Use of helium for treating laryngospasm:
  - Helium is a gas of low density and hence reduces turbulent flow
  - This reduces velocity of gas flow through the narrow laryngeal orifice
  - Therefore, laryngeal obstruction is relieved.

INFORMED CONSENT[1,2,3,21]

Introduction

Legal and moral imperitives for informed consent are based on ethical principle of respect for patient autonomy, i.e. ability to choose without controlling interference by others and without personal limitations which prevent meaningful choices.

Components

- Name and purpose of diagnostic test or procedure
- Most significant risks of test/procedure
- Benefits of intervention, including chances of success if pertinent
- Probable outcome of intervention/refusal of proposed plan
- Possible alternatives and procedure
- Patient must be free from concerns.

Definition

- Consent requires an active communication between doctor and patient wherein the physician educates the patient explaining the nature and purpose of the proposed procedure or therapy, along with the attendant risks and benefits
- In the Indian context, informed consent was nonexistent till Consumer Protection Act was made applicable to medical profession.

Documentation of Consent

- Hand written note:
  - Is the best evidence of discussion and consent
  - Time consumed in the process however, is unacceptable.
- Separate anesthesia consent form required, with common risks detailed in separate form
- Reliance on surgical consent is not very reliable.

Ethical Aspects of Consent

- Ethical obligation to respect patients autonomy
- Obligation to respect patients right to be involved in decisions which affect them
- Patient must be supplied adequate information to make a balanced decision free from coercion
- Need to respect autonomy may conflict with other obligations like *principles of beneficience (doing good)*
- For example, patient may decline life saving therapy and this may have to be respected.

Legal Aspects of Consent

- Touching a patient without consent may lead to chain of battery or assault
- Treating doctor is responsible for ensuring that patient has consent for treatment
- Consent is valid if given voluntarily by appropriately informed patient who has capacity to exercise a choice
- Patient without capacity to consent, may be treated without consent, if it is in their best interest/consent is taken from guardian
- Pain, illness, premedication does not necessarily render a patient incompetent to consent.

Informed Refusal

- Informed consent is meaningless if patient cannot also refuse medical treatment
- For example:
  - Request to withdraw life support and care in ICU
  - Do not resuscitate (DNR) orders in operation theater
  - Jehovahs witness patients who refuse blood transfusion
  - Patient refusing preoperative testing like HIV and pregnancy test.

Disclosure

- Informed consent requires honest disclosure of medical information to patient
- Therapeutic privilege cited if stress of discussing risk can harm patient psychologically/physically
- Physician must discuss therapy, its alternatives and no therapy
- He should also disclose the common and serious risks
- Two standards of disclosure:
  - *Reasonable person standard*: Physician must disclose any information which a reasonable person would want to know
  - *Subject to standard*:
    - Some patient may have special need to special information
    - When the need is obvious, information must be disclosed.
    - For example, violinist has specific need to know about nerve damage from axillary nerve block.

Outcome

- Patient will have sufficient knowledge to make an educated decision whether or not to undergo the proposed therapeutic intervention
- Physicians have ethical obligation to avoid exploiting their influence on patients and to coerce or manipulate than into decision by threats/misinterpreting information.

COMPUTERS IN ANESTHESIA

Introduction

Various applications of computers in anesthesia are:

- Hospital information systems
- Electronic health record
- Computerized order entry
- Decision support system/artificial intelligence
- Telemedicine
- Computer integrated PCA devices
- Target control infusion.

Hospital Information System

- Network of interfaced subsystems, both hardware and software, which coexist to serve the multiple computing requirements of a hospital including:
  - Admission and discharge
  - Transfer
  - Billing
  - Laboratory, radiology.
- Component elements:
  - Administrators

- Clinical documentation
- Billing systems
- Business systems.

Electronic Health Record

- It is a computerized record of patient care
- It includes:
  - ICU record
  - Out patient record
  - Emergency department record
  - Nursing home electronic record
  - Dialysis electronic record.
- Core function (benefits) includes:
  - Management of patients health information and data
  - Presentation of results acquired from patients testing
  - Computerized order entry
  - *Decision support:* Autogenerated reminder to inform the behavior of clinician.
- Patient support tools like discharge directions generated automatic billing management, insurance validation
- Internal and external reporting requirements simplified.

Computerized Ordered Entry

- It is a computer based ordering system, designed to automate the ordering process
- Example, for drugs, pathology/radiology tests
- Benefits of computerized order entry:
  - Identification of prescribers
  - Standardized legible orders
  - Link to adverse drug reporting system
  - Cost management
  - Reduce confusion of drug name
  - Improved order turn around.

Decision Support System/Artificial Intelligence

- Provides immediate access to current medical knowledge, institutional best practices, billing compliance information, administrative function and facilitates cost control
- Acts in three ways:
  - *Passive system:* Responds when information is asked
  - *Semiactive system:* Provides alarms only when certain condition are met
  - *Active/autonomous system:* Generates order and manages medical process automatically
- *For example:* Automated weaning of mechanical ventilator.

Telemedicine

- Application of health care server across space, time, social and cultural barriers
- Useful in underserved areas and providing access to specialist in remote areas
- Allowing patients to receive medical attention at home when physical contact is not a critical element
- New technologies like teleimmersion, telepresence, telesurgery are coming up.

ANESTHESIA FOR SCOLIOSIS CORRECTION[1,2,3,6,11,21]

Introduction

Deformity characterized by coronal, sagittal and horizontal plane deviation of spine associated with rotation of vertebrae.

Classification

Nonstructural/Mobile Scoliosis

- Sciatica
- Leg length discrepancy
- Hip contracture causing pelvic tilt.

Structural Scoliosis

- Idiopathic:
  - Infantile < 3 yrs
  - Juvenile 3–10 yrs
  - Adolescent >10 yrs.
- Congenital:
  - Hemivertebrae
  - Spinal dysmorphism
  - Fused ribs.
- Syndromes:
  - *VATER anomaly*
  - *Von – Recklinghausens*/neurofibromatosis
  - *Marfans syndrome*
  - Rheumatoid arthritis
  - *Ehler Danlos syndrome.*
- Post Trauma:
  - Vertebral fracture
  - Postsurgery
  - Post-thoracoplasty
  - Postradiation
  - Postburns contracture.

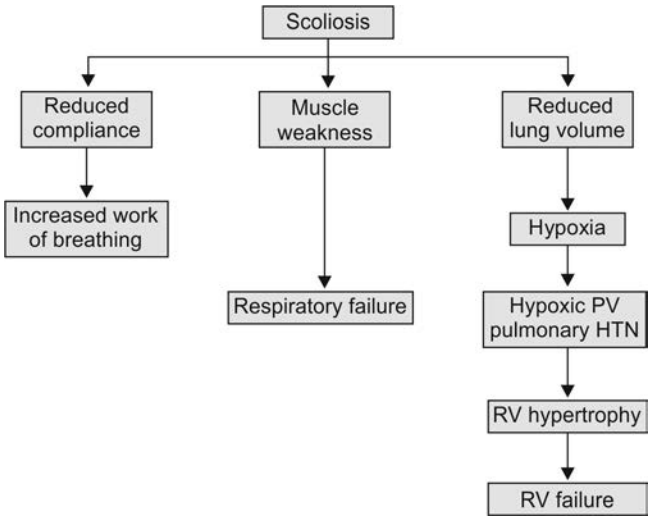
- Neuromuscular:
  Neuropathic:
  - Cerebral palsy
  - Polio myelitis
  - Spinal cord injury
  - *Freidrichs ataxia*
  - Meningomyelocele.

  Myopathic:
  - *Duchennes muscular dystrophy*
  - Myotonic dystrophy.

Pathophysiology

- Pulmonary:
  - Reduced vital capacity
  - Reduced total lung volume
  - Reduced functional residual capacity
  - Ventilation perfusion mismatch
  - Hypoxia, hypercarbia
  - Respiratory failure.
- Cardiovascular:
  - Pulmonary HTN
  - RV hypertrophy and failure
  - Associated defects:
    - Mitral valve prolapse
    - Coarctation of Aorta
    - Mitral regurgitation
    - Cyanotic heart disease
    - Aortic regurgitation

Scoliosis



Assessment of Severity

Severity increases with:

- Greater number of vertebrae involved
- More cephalad location of curve
- Loss of normal thoracic kyphosis
- Increased COBBS angle.

Cobbs Angle Measurement

- Perpendicular drawn from bottom of lowest vertebrae whose bottom tilts towards concavity of curve
- Perpendicular from top of highest vertebra whose top tilts towards concavity
- Angle at which perpediculars intersect is Cobbs angle.

No	Angle	Implication
1	< 20°	Benign
		Monitored every 4 months by X-ray
		No surgery required
2	> 40°	Cardiorespiratory impairment present
		Restrictive lung disease
3	> 100°	Severe cardiorespiratory involvement
		Severe impairment of gaseous exchange

Indications for Surgery

- Cobbs angle > 50º
- Neurological involvement
- Pain
- Cosmetic purposes.

Surgical Technique

- Posterior spinal fusion with:
  - *Herrington rod*
  - *Cotrel Dubousset instrumentation*
- Anterior approach
  - Thoracotomy
  - Transdiaphragmatic
  - Transabdominal.
- Combined posteroanterior approach.

Preoperative Evaluation

- Cardiovascular, respiratory and neuromuscular status
- Cobbs angle
- Associated congenital anomalies
- Neurological deficits especially on neck rotation.

Investigations

- Complete blood count: Increased HCT due to chronic hypoxia
- *Coagulation profile:* PT and INR on day of surgery
- ECG for cor pulmonale

- Pulmonary function tests:
  - Reduced vital capacity, TLC, FRC, IC, ERV
  - Normal FEV1/FVC.
- PEFR as bedside test to assess severity
- 2D ECHO as mitral valvce prolapse MR, AR and cardiomyopathy possible
- *ABG–baseline values noted:* Reduced PaO_2 with normal $PaCO_2$ and pH
- X-ray spine, CT thorax, preoperative myelogram/MRI for cysts/lipomas/teratomas.

Preoperative Preparation

- Preoperative teaching of incentive spirometry and coughing
- Aggressive pulmonary toilet
- Bronchodilator therapy if COPD
- If intraop wakeup test planned:
  - Rehearse the test
  - Reassure patient about lack of pain
- Discuss with the patient:
  - Autologous transfusion
  - Awake intubation/tracheostomy
  - Postop ventilation
  - Postop pain management
  - Sleep apnea syndrome
  - Prone position and inability to lie flat.

Premedication

- Sedatives avoided if neuromuscular disease/pulmonary HTN
- Antisialogogues: Glycopyrrolate
- Antibiotics before catheterization/laryngoscopy
- Steroids if any neurodeficits
- DVT prophylaxis.

Monitors

- *General:*
  - Pulse oximeter
  - IBP for hypotensive anesthesia
  - End tidal CO_2
  - CVP/PA catheter for pulmonary HTN
  - ECG
  - Urine output
  - Temperature
  - Esophageal stethoscope
  - Thromboelastography
  - Neuromuscular monitoring.
- *Spinal cord monitoring:*
  - Intraop wake up test
  - Somatosensory evoked potentials (SSEPS-posterior column)
  - Motor evoked potentials (MEPS-anterolateral tracts).

Anesthetic Considerations

- Long duration surgery
- Blood loss:
  - Blood conservation strategies
  - Hypotensive anesthesia.
- Hypothermia due to large surgical field exposure
- *Difficult airway*
- *Remote airway*
- Difficult regional anesthesia technique
- One lung ventilation if anterior approach
- Restrictive lung defect:
  - Increased risk of postop respiratory insufficiency
  - Retention of secretions
  - Postop respitatory failure
  - Right ventricular failure and pulmonary HTN postoperative.
- Increased risk of *Malignant hyperthermia*.

Induction

- On trolley with all monitors
- Thiopentone/etomidate/propofol as induction agents
- Fentanyl and nondepolarizing neuromuscular blocking agents
- Succinylcholine avoided in muscular dystrophy
- Intubate with fibreoptic bronchoscopy
- Sometimes tracheostomy done
- Fix tube properly as remote airway
- Armoured tube to avoid kinking
- DLT/bronchial blocker with one lung ventilation if anterior approach
- Nasogastric tube as *postop ileus* common.

Maintenance

O_2 + N_2O + volatile agents + fentanyl + vecuronium

Or

TIVA with propofol and remifentanyl infusion.

Position

- Prone position:
  - If posterior approach
  - Prevent neck extension to minimize venous pressure and blood loss
  - Abdomen should be free to avoid IVC compression

  - Protect pressure points
  - Eye protection
  - *Wilson frame/Jackson table* to free chest and abdomen.
- Lateral position:
  - If anterior approach
  - Pad pressure points adequately.

Ventilation

- Avoid hypoxia hypercarbia and acidosis.

Hemodynamics

- Deliberate hypotension:
  - MAP between 60–70 mm Hg to maintain spinal cord perfusion
  - NTG/SNP/esmolol/propranolol used.
- Maintain normothermia/normocarbia
- Warming devices for patients and fluids
- Moderate third space losses: Replace with BSS at 5–7 ml/kg/hr.

Blood Conservation

- Preop optimization of Hb
- Modest hypotension
- Coagulation control
- *Cell salvage*
- Antifibrinolytic agents
- Autologous blood transfusion
- *Isovolemic hemodilution*
- Reduce intrabdominal pressure:
  - NMBAs to avoid increased abdominal wall tension
  - Careful positioning
  - Deep plane of anesthesia.

Extubation

- Most need elective postop ventilation
- Extubate patients with mild–moderate PFT abnormalities
- Extubation parameters:
  - Vital capacity > 10 ml/kg
  - Tidal volume > 5 ml/kg
  - Spontaneous respiratory rate < 30/min
  - Negative inspiratory force > 30 cm H_2O.
- Postop ventilation if:
  - Severe restrictive lung defects
  - Vital capacity < 30% predicted
  - CO_2 retention
  - *Duchennes muscular dystrophy*
  - Cerebral palsy.

Postoperative

Complications

- Pneumothorax, hemothorax/pleural effusion
- Atelectasis, hypoxia
- Ventilation perfusion mismatch
- Disseminated intravascular coagulation
- SIADH
- Infections
- Paralytic ileus
- Spinal cord injury
- Thoracic duct injury: *Chylothorax*
- Thromboembolism.

Monitoring

- Pulse oximetry blood pressure
- ABG X-ray
- Blood urea nitrogen serum creatinine
- PT INR Urine output
- Platelet count Serum electrolytes Q12H for 24 hrs.

Pain

- Epidural analgesia
- Patient controlled analgesia
- Intravenous opioids
- Intrathecal opioids
- Paravertebral blocks
- Extrapleural catheters
- Multimodal analgesia.

Management

- Aggressive chest physiotherapy:
- Incentive spirometry
  - Deep breathing
  - Coughing
  - Bronchodilator therapy
- Maintain urine output > 0.5 ml/kg/hr
- Avoid hypotonic fluids for 1st 24–36 hrs postop
- Compression stockings/pneumatic leg pumps for DVT prophylaxis.

WAKE UP TEST[1,2,3,6]

Introduction

- Intraop awakening of patient after completion of spinal instrumentation to assess integrity of spinal motor pathways
- Described first time by *Vauzelle*.

Preparation

- One to two assistants to be available in the event of excessive movement
- Discontinue propofol and muscle relaxants 30–45 minutes before test
- Discontinue volatile agents 20 minutes before test
- Continue opioid infusion to allow patient to tolerate pain
- Patients usually respond within 5 minutes
- Avoid naloxone as it causes pain and patient may become agitated
- If necessary naloxone 0.3–0.5 μg/kg boluses every 2–3 mins
- Reversal of NM blockade unnecessary if 3 twitches are present on TOF
- Excessive movement rare if nitrous-narcotic-relaxant technique used.

Procedure

- Patient instructed to squeeze anesthetists hand: Confirms responsiveness
- Then asked to move feet and toes
- If patient moves hands but unable to move feet reduce amount of distraction and repeat test
- Once patient moves feet deepen plane of anesthesia with benzodiazepines, thiopentone and muscle relaxant.

Interpretation

- Patient moves hands and feet: Correct screw placement
- Patient moves hands but not feet: Screws need realignment
- Patient does not move hands/feet: Patient not awake.

Disadvantages

- Only one time indicator
- Cannot be done in children/mentally retarded
- Rarely maybe false negative: Patient can have neurodeficit at the end of surgery
- Replaced largely by SSEP/MEP.

Complications

- Prone position extubation
- Intraoperative awareness
- Self injury
- Dislodgement of instruments
- Air embolus from open venous sinus if patient inhales vigorously
- Myocardial infarction.

ANESTHESIA FOR ESOPHAGECTOMY[1,2,3,11]

Approaches

No[1]	Approach	Lesion	Incision
1	***Ivor-Lewis***		2 Incisions:
	Laparotomy and right thoracotomy		Upper abdominal midline
			Rt 5th and 6th ICS thoracotomy
2	Left thoracoabdominal	Lower esophagus	Rt lateral thoracotomy
			Extended to left upper lateral abdomen
			One incision
3	***Orringer***	Lower esophagus	2 Incisions:
	Transhiatal	Mid esophagus	Upper abdomen midline
			Left neck
4	***McKewan 3 stage***	Upper esophagus	3 Incisions:
	Combined chest neck and abdomen	Mid esophagus	Right thoracotomy
			Laparotomy
			Left cervical anastomoses
5	Minimally invasive thoracoscopy and laparoscopy		1 or 2 incisions Avoids blunt dissection in chest Neck incision in end

Anesthetic Considerations

For All Patients

- Remote airway
- Distant airway
- Poor preop nutritional status
- Increased risk of aspiration
- Hypothermia due to extensive resection
- Large fluid shifts
- Preoperative chemotherapy which reduces immunity
- Postoperative TPN.

Transthoracic Approach

- One lung ventilation
- Intraoperative position change from supine/prone to right/left lateral.

Transhiatal Approach

- Double lung ventilation
- Cardiac compression during dissection.

Minimally Invasive Approach

- One lung ventilation desirable
- Pneumoperitoneum causing:
  - Hypercarbia
  - Hemodynamic changes.

Premedication

- NPO 6–8 hrs
- Informed consent
- IV midazolam 0.03–0.05 mg/kg for anxiolysis
- IV glycopyrrolate 0.01 mg/kg
- *Antiaspiration prophylaxis*
  - IV ranitidine 1 mg/kg
  - IV metaclopramide 0.15 mg/kg
  - 30 ml of 0.3 M sodium citrate.

OT Preparation

- Suction
- *Oxygen source:* Pipeline and cylinder
- *Airway:* Facemasks, airways, endotracheal/double lumen tube
- *Pharmacy:* Opioids, induction agents and muscle relaxants
- *Monitors:* Arterial line, central line
- *Emergency drugs:* Atropine, adrenaline, phenylephrine, ephedrine.

Monitors

- Pulse oximetry
- ECG
- $EtCO_2$
- Core temperature
- NIBP
- Urine output
- IBP and CVP
- Blood glucose
- Entropy
- Neuromuscular monitoring
- Left IJV avoided as esophageal anastomoses in left neck
- ABG with hematocrit intraoperatively.

Induction

- *Rapid sequence induction* with cricoid pressure
- Thiopentone + succinylcholine + fentanyl for induction
- Nasogastric tube inserted which is removed during resection
- Nasogastric tube reinserted with surgical guidance following anastomoses.

Ventilation

- One lung ventilation during thoracotomy
- Left sided DLT for lung collapse
- Ventilate dependent lung with:
  - 5 ml/kg tidal volume
  - 5 cm H_2O PEEP.
- Change DLT to SLT to improve surgical access prior to cervical anastomoses.

Hemodynamics

- Cardiac compression during intrathoracic mobilization
- Crystalloids @ 10 ml/kg/hr
- Colloids and PRBCS for blood loss
- Torrential hemorrhage possible–blood should be ready
- Require large third space fluid administration and inotropes
- Watch for metabolic acidosis secondary to reduced tissue perfusion
- Keep patient warm: Fluid warmer, forced air blankets.

Extubation

- Early extubation preferred
- If not possible replace DLT with SLT and ventilate postop
- Postoperative ventilation if cold or hemodynamically unstable.

Postoperative Management

- Early enteral feeding with jejunostomy/nasoduodenal tube
- Maintain minimal urine output 1 ml/kg/hr
- Total parenteral nutrition.

Analgesia

- Multimodal
- Thoracic epidural:
  - 3 ml of 0.25% bupivacaine boluses
  - 5 mg diamorphine in 50 ml 0.167 % bupivacaine @ 2–8 ml/hr
- Paravertebral LA injection
- *Patient Controlled Analgesia* with morphine
- NSAIDs.

Complications

- Highest morbidity and mortality in thoracic surgeries

- Intrathoracic anastomotic leakage
- Sepsis
- Gastric necrosis
- Respiratory complications:
  - ARDS
  - ALI.
- Anastomotic stenosis.

TRANSPLANT PATIENT FOR NON-TRANSPLANT SURGERY[1,2,3,11]

Pathophysiology

Cardiovascular Disease

- Hypertension:
  - Native kidney disease
  - Allograft dysfunction
  - Steroid therapy
  - Weight gain
  - Transplant renal artery stenosis.
- Coronary artery disease
- Congestive cardiac failure: Fluid overload
- Ventricular hypertrophy
- Cerebrovascular disease
- Peripheral vascular disease.

Bone Disorders

- Persistent hyperparathyroidism:
  - Poor allograft function
  - Vitamin D deficiency.
- Gout:
  - Cyclosporine
  - Impaired renal uric acid clearance.
- Osteonecrosis: High dose steroids
- Osteoporosis:
  - Steroid therapy
  - Hyperparathyroidism
  - Vitamin D deficiency/resistance
  - Phosphate depletion.

Electrolyte and Acid Base Imbalance

- Hyperkalemia:
  - Cyclosporine induced impairment of tubular potassium secretion
  - Poor graft function
  - Excessive intake
  - ACE inhibitors.
- Hypophosphatemia:
  - Residual hyperparathyroidism
  - Glucocorticoids
  - Low Vitamin D state.
- Hypercalcemia:
  - Persistent hyperparathyroidism
  - Coadministration of Vitamin D and calcium.
- *Hypomagnesemia:* Cyclosporine
- *Metabolic acidosis:* Distal Tubular Acidosis:
  - Cyclosporine
  - Graft rejection
  - Residual hyperparathyroidism.

Anesthetic Considerations

- Potential for infectious complications: Wound infections, UTI, pneumomia
- Potential for malignancies: Lymphoproliferative malignancies
- Difficult airway if lymphoproliferative disease due to tonsillar obstruction
- Drug interactions:
  - Calcium channel blockers promote cyclosporine and prednisolone toxicity
  - Cyclosporine potentiates NMBAS.
- Adverse effects of immunosuppressants:
  - *Cyclosporine:* Nephrotoxic, hepatotoxic, neurotoxic, hyperkalemia, HTN
  - *Tacrolimus:* Hypertrophic Obstructive Cardiomyopathy, diabetes
  - *Azathioprine:* Bone marrow depression, hepatotoxicity, pancreatitis
  - *Mycophenolate:* Nephrotoxic, hepatotoxic, bone marrow depression, GI bleeds
  - *Sirolimus:* Bone marrow depression, buccal ulcers, diarrhea.
- Transfusion of only CMV- negative blood products
- Difficult perioperative glucose control due to steroid therapy.

Preoperative Evaluation

Clinical Evaluation

- Evaluate complications of immune suppression:
  - *CNS:* Lowered seizure threshold
  - *CVS:* HTN,
    - Hyperlipidemia
    - Atherosclerosis.
  - *Renals:* Redued GFR
    - Hyperkalemia
    - Hypomagnesemia.
  - *Hematology:* Increased risk of infection
    - Increased risk of malignancy
    - Pancytopenia.

  - *Others:* DM
    - Osteoporosis
    - Poor wound healing.
- Evaluate signs of acute graft rejection or infection: Postpone surgery and optimize status
- Level of renal dysfunction to decide drugs and dose modification
- Airway evaluation especially if lymphoproliferative malignancies.

Investigations

- Complete blood counts: Anemia, leucopenia, thrombocytopenia
- Serum electrolytes: Hyperkalemia, hypophosphatemia, hypomagnesemia
- ECG: Hyperkalemia, hypercalcemia
- ECHO
- Liver function tests
- Coagulation studies: Hypercoagulability with cyclosporine
- Renal function tests: For graft rejection
- Pulmonary function tests
- ABG: Metabolic acidosis common
- *Chest Xray:* Rule out infection
- *Urinanalysis:* Graft function and infection.

Preoperative Optimization

- Minimal disruption of antibiotics, antivirals, antifungals and immune suppression agents
- Maintain therapeutic blood levels of immunosuppressants: Tacrolimus or cyclosporine 4–7 hrs before surgery
- DVT prophylaxis
- Avoid drugs causing renal dysfunction:
  - Cyclosporin, tacrolimus
  - Amphoterecin
  - Ranitidine/cimetidine
  - Vancomycin/gentamicin/tobramycin
  - NSAIDs
  - Cotrimoxazole
- Antiaspiration prophylaxis: Avoid metaclopramide
- *Antisialogogues:* Glycopyrrolate has prolonged duration of action.

Intraoperative Considerations

Monitors

- Routine:
  - ECG
  - NIBP
  - Pulse oximetry
  - Capnography
  - ABG and blood sugar monitoring
  - Neuromuscular monitoring important as:
    - Prolonged NMBA action due to cyclosporine
    - Muscle weakness due to dyselectrolytemias.
- Invasive monitors:
  - Limited to minimum
  - Used only when necessary
  - Strict aseptic precautions.

Induction

- *Rapid sequence induction* preferred: Propofol/thiopentone with reduced doses
- Ketamine best avoided
- Etomidate preferred if hemodynamic compromise
- Preoxygenation important as anemia and increased risk of CVA
- LMA and mask best avoided
- Nasal intubation avoided to reduce risk of infection
- Difficult intubation if diabetic/lymphoproliferative malignancy.

Maintenance

- Isoflurane/desflurane preferred
- Halothane not recommended for repeat use
- Enflurane and sevoflurane avoided as nephrotoxic
- Succinylcholine avoided if hyperkalemia
- Rocuronium maybe used for RSI
- Atracurium/cisatracurium *drug of choice*
- Vecuronium may cause renal vasoconstriction and prolonged action in acidosis.

Hemodynamics

- Maintain euvolemic status at all times to prevent graft dysfunction
- Use potassium free fluids if hyperkalemia
- Osmotic diuretics preferred over tubular diuretics.

Infection

- Strict aseptic technique: Gowns, gloves, handwashing
- Routine perioperative antibiotic prophylaxis: 30 minutes before skin incision
- Intravenous lines and invasive monitors only if specifically indicated, removed as soon as no longer necessary for patient care
- Use antiseptic impregnated catheters.

Immunosuppression

- Maintain intraoperative immunosuppressant levels

- Preop administration of immunosuppressants
- Postpone elective surgery if WBC count < 2000/cc[3]
- Intraoperative monitoring of blood levels as hemodilution and bleeding during surgery can decrease blood levels.

Transfusion

- Adequate blood arranged in advance
- Cross matching might be delayed
- Transfusion reactions and transmission of infection possible
- Refractoriness to platelet transfusion common
- Leucocyte poor/irradiated blood products preferred.

Renal Transplant Patients

- Maintain renal perfusion
- Adequate CVP/TEE guided volume replacement
- Avoid nephrotoxic agents.

Lung Transplant Patients

- Increased risk of pneumonia as cough reflex maybe reduced
- Compare preop CXR PFT and ABG with prior studies
- Increased risk of bronchospasm as increased airway reactivity
- Regional anesthesia techniques advantageous
- Avoid depression of intercostal muscle function
- Invasive monitors for intraoperative fluid status
- CVP inserted on side of native lung
- Tracheal cuff positioned just beyond vocal cords to avoid site of anastomoses
- Early extubation is preferred.

Heart Transplant Patients

- Transplanted hearts usually denervated
- Do not respond to indirectly acting agents like dopamine, ephedrine and atropine
- Norepinephrine and epinephrine used for refractory cardiogenic shock
- Beta effects of epinephrine/norepinephrine exaggerated
- Isoprenaline is mainstay of chronotropic therapy
- GA preferred as denervated heart does not reflexly compensate for hemodynamic changes
- Preoperative ECG, ECHO, stress testing and myocardial biopsy as required
- ECG shows 2 P waves:
  - Native atrium not conducted
  - Implanted atriums waves.

Others

- Use minimally invasive techniques both for surgery and anesthesia
- Careful positioning to avoid pathological fractures
- Frequent blood gas determination for acidosis and dyselectrolytemia
- Increased risk of perioperative arrhythmias
- Impaired respiratory muscle power: Hyperkalemia, hypophosphatemia, hypomagnesemia
- Early extubation preferred.

Postoperative Care

Analgesia

- NSAIDs avoided due to risk of nephrotoxicity
- Opioids may cause increased PONV due to synergism with chemotherapeutic agents
- Morphine and pethidine avoided if renal function deranged
- Epidural, regional blocks and topical infilterations useful
- Multimodal analgesia useful.

Maintenance

- Maintain hematocrit > 30% and normothermia
- Intensive physiotherapy
- Early mobilization
- Early removal of catheters and drains
- Continuation of immunosuppressive therapy.
- DVT prophylaxis.

Complications

- CMV sepsis
- Infection
- Graft rejection
- B-cell lymphomas
- Visceral perforation.

ANESTHETIC MANAGEMENT OF PATIENT WITH LIVER DISEASE[1,2,3,6,11]

Preoperative Evaluation and Preparation

Preoperative Evaluation

History Taking

- History of platypnea (dyspnea in upright position)
- Risk factors:
  - Blood transfusion
  - Alcohol abuse
  - Illicit drug use
  - Tattoos
  - Personal/family history of jaundice.

Physical Examination

- Encephalopathy
- Altered sleep wake cycles
- Jaundice
- Scleral icterus
- Halitosis
- Parotid enlargement
- Gynecomastia
- Spider angioma
- Clubbing
- Leuconychia
- Palmar erythema
- Asterixis
- Hepatosplenomegaly.

Investigations

- Complete blood count: Anemia
- *Blood urea nitrogen, serum creatinine:* Prerenal azotemia or hepatorenal syndrome
- Blood sugar levels
- Liver function tests
- Serum albumin, globulin, albumin: Globulin ratio
- *Serum electrolytes:* Hypokalemia due to diuretic use
- Coagulation profile: Altered PT INR very sensitive indicator
- *ECG:* Dyselectrolytemias
- *Chest X-ray:* Pleural effusion more commonly on right side
- Echocardiography.

Classification Systems

Child Pugh classification of severity of liver disease:

No	Parameter	1 point	2 points	3 points
1	Bilirubin (mg/dl)	< 2	2–3	> 3
2	Albumin (gm/dl)	> 3.5	2.8–3.5	< 2.8
3	Increase in prothrombin time (s)	1–3	4–6	> 6
4	Ascites	None	Slight	Moderate
5	Encephalopathy	None	1–2	3–4

Child Pugh grades:
5–6 points: Grade A
7–9 points: Grade B
10–15 points: Grade C

Preoperative Preparation

Goals

- Optimize nutritional status
- Optimize cardiopulmonary function
- Medical control of ascites
- Correct dyselectrolytemias.

Preparation

- Fluid restriction
- Diuretics
- Paracentesis for large volume ascites
- Preoperative antibiotics to reduce infection
- Prophylactic H_2 blocker for 4–6 wks
- Fresh frozen plasma and Vitamin K to correct coagulopathy
- Cryoprecipitate and DDAVP if bleeding time prolonged
- Lactulose and Neomycin if encephalopathy
- Antiaspiration prophylaxis:
  - Ranitidine 1 mg/kg IV
  - Metaclopramide 10 mg IV.

INTRAOPERATIVE MANAGEMENT

Anesthetic Considerations

Preoperative Considerations

- Antiaspiration prophylaxis
- Increased chances of infection: Antibiotic coverage
- Poor preoperative nutritional status
- Electrolyte imbalances
- Avoid preoperative sedation
- Coagulopathy:
  - Avoid regional anesthesia
  - Avoid intramuscular injections
  - Adequate blood ready
  - Blood conservation strategies.

Intraoperative Considerations

- Universal precautions if indicated
- *Increased risk of aspiration:* Rapid sequence induction
- Avoid traumatic intubation
- Careful nasogastric tube placement as esophageal varices possible
- Altered drug metabolism:
  - Increased volume of distribution
  - Reduced plasma protein levels
  - Reduced drug metabolism
  - Reduced excretion
  - Increased duration of action of succinylcholine, cisatracurium *relaxant of choice*.
- Titrated dose NMBAS and sedatives
- Avoid halothane, nitrous oxide

- Drug interactions:
  - Neomycin increases duration of neuromuscular blockade
  - Cimetidine potentiates relaxant drug action
- Massive intraoperative fluid shifts: Invasive BP monitor mandatory
- Profound hypotension on induction: Graded doses of induction agents
- *Increased third spacing:* Hypotension on draining ascitic fluid
- Careful to avoid fluid overload
- Titrate fluids to maintain urine output > 0.5 ml/kg/hr and CVP between 2–5 mm Hg
- Use sodium free fluids: Albumin is fluid of choice
- Increased blood loss due to coagulopathy
- Careful blood transfusion to avoid encephalopathy
- Citrate toxicity possible due to reduced liver function
- *Large operative field exposure:* Hypothermia common.

Postoperative

- Expect delayed recovery
- Avoid NSAIDs for pain
- Increased chances of complications:
  - Hepatic encephalopathy
  - Hepatorenal syndrome
  - Hepatopulmonary syndrome.

Monitors

- Pulse oximetry
- NIBP
- ECG
- Capnography
- Temperature probe
- Neuromuscular monitoring
- *Arterial line:* For invasive BP/repeated blood sampling
- Central venous access: For prolonged procedures with potential for blood loss
- Pulmonary artery catheterization for:
  - Anticipated prolonged vascular exclusion
  - Preoperative sepsis.
- Periodic arterial blood gas analysis
- Periodic blood sugar as prone for hypoglycemia
- Point of care testing:
  - Blood chemistry for anemia
  - Coagulation analysis.

Induction

- *Rapid sequence induction* as high-risk for aspiration
- Reduced induction dosage of thiopentone
- Propofol maybe preferred as it avoids phase II metabolism
- Two large bore intravenous cannulas to be available
- Restrict fluid administration during induction of anesthesia.

Maintenance

- O_2 + air + isoflurane/sevoflurane/desflurane
- Avoid halothane
- Supplemental narcotic agent: Fentanyl is *opioid of choice*
- Atracurium *muscle relaxant of choice*
- Pass anesthetic gases through large capacity heat moisture exchanger
- Fluids passed through warmer
- Forced warm air devices on upper and lower parts of body.

Hemodynamics

Goals

- Avoid undesired hypovolemia
- Avoid vasodilation to prevent low peripheral perfusion pressures
- Autologous blood donation and intraoperative blood recovery systems where necessary
- Judicious use of norepinephrine or vasopressin to restore perfusion pressures
- Maintain CVP around 2–5 mm Hg
- Maintain urine output > 0.5 ml/kg/hour.

Colloids

- Reduces extravascular translocation of fluids
- Improves mesenteric perfusion
- Rapid restoration of postoperative gut function
- Preferred fluids:
  - 5% albumin
  - 20 % albumin
  - Hetastarch in a balanced salt solution.

Crystalloids

- Intraoperative use restricted to minimum
- Causes fluid extravasation.

Blood Products

- Fresh frozen plasma: Used as maintenance fluid in coagulopathy
- Packed red cells: *Transfusion trigger* 25%.

Extubation

- Fully awake and warm with stable vital signs
- Fully reversed and extubated.

HEPATORENAL SYNDROME[1,2,3,10]

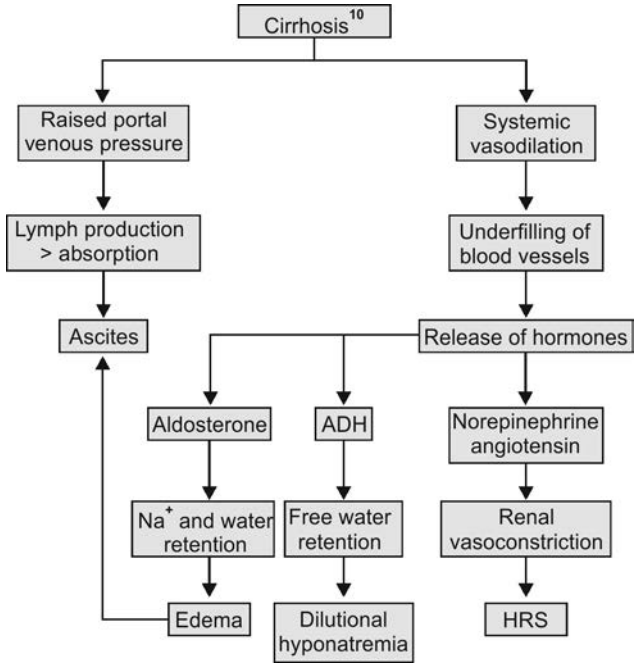
Introduction

Complication of cirrhosis which is almost always irreversible.

Precipitating Factors

- Progression of cirrhosis
- Rapid correction of ascites
- Large volume paracentesis
- Diuretic therapy
- Diarrhea
- Sepsis
- Major surgery
- Major bleeding
- GI bleeding.

Pathogenesis



Types

	Type I hrs	Type II hrs
1	Progressive oliguria	Insiduous symptoms
2	Rapid rise in serum creatinine	Moderate renal function impairment
3	Commonly precipitated by Spontaneous bacterial peritonitis	Seen in refractory ascites
4	Poor prognosis	Better prognosis

Diagnostic Criteria

International Ascites Club criteria:

Major Criteria

- Absence of response to 1.5 L fluid load
- Low GFR
  - Creatinine clearance < 20 ml/min
  - Serum creatinine > 2.5 mg/dl
  - Proteinuria < 500 mg/day.
- Normal renal ultrasound
- Absence of intrinsic renal disease
- Absence of infections, nephrotoxins and shock.

Minor Criteria

- Oliguria < 500 ml/day
- Urinary Na^+ < 10 m Eq/L
- Serum Na^+ < 130 m Eq/L.

Treatment

Supportive Therapy

- Support Airway Breathing
- Maintain renal perfusion:
  - Colloids to maintain perfusion (albumin preferred)
  - Vasopressors
  - Inotropes.
- *Avoid nephrotoxins:* NSAIDS
- Protein restriction.

Vasopressors

- Help by increasing systemic vasoconstriction
- Reduce renal vasoconstriction
  - Midodrine (α_2 agonist) 5–10 mg TID per orally
  - Octreotide 100 µg subcutaneously BD
  - Terlipressin.

Others

- TIPSS considered if vasopressor therapy fails
- Dialysis for renal support.

Orthoptic Liver Transplant

- Only definitive therapy
- Reverses HRS if performed early.

Treat Complications

- Hyponatremia
- Hyperkalemia
- Hypokalemia.

Prevention

- Avoid high dose diuretics
- Slow treatment of ascites
- Early management of infections, hemorrhage and dyselectrolytemia.

Differential Diagnosis

No	Investigation	Prerenal Arf	Hrs	Arf
1	Urine sodium	< 10 mEq/L	< 10 mEq/L	> 30 mEq/L
2	Urine: Plasma creatinine	> 30:1	> 30:1	< 20:1
3	Urine: Plasma osmolarity	100 m Osm	100 m Osm	0 m Osm
4	Urinary sediment	Normal	Unremarkable	Casts, debris

OBESITY[1,2,3,11,21]

Introduction

Disease characterized by abnormally high percentage of body weight as fat.

Pathological Changes

- Respiratory System:
  - Pulmonary function tests:
    - Reduced FRC, VC, TLC, ERV
    - Normal FEV1, FVC.
  - Obstructive sleep apnea
  - Obesity hypoventilation syndrome: ***Pickwickian syndrome***:
    - Obesity (BMI > 30 kg/m^2)
    - Awake arterial hypercapnea ($PaCO_2$ > 45 mm Hg).
  - Small airway obstruction, asthma
  - Pulmonary HTN, corpulmonale.
- Cardiovascular System:
  - Increased total blood volume
  - Increased cardiac output: Up to 20–30 ml per kg of excess fat
  - Left ventricular hypertrophy, reduced ventricular compliance
  - Increased left ventricular filling pressures, diastolic dysfunction
  - Pulmonary edema, biventricular failure
  - Dormant CAD
  - Cardiac arrhythmias due to:
    - Fatty infilteration of conduction system
    - CAD, myocardial hypertrophy
    - Hypoxia and hypercapnea, OSAS
    - Electrolyte imbalance
    - Increased circulating catecholamines.
  - ECG changes:
    - Low voltage QRS complexes
    - LVH, left atrial enlargement, left axis deviation
    - T-wave inversion in inferior and lateral leads.
  - Hypertension:
    - SBP increases by 3–4 mm Hg with every 10 kg weight gained
    - DBP increases by 2 mm Hg with every 10 kg weight gained
    - Occurs due to RAS stimulation causing sodium retention and HTN.
- Gastrointestinal tract:
  - Predisposed to aspiration:
    - Gastric volumes > 25 ml
    - Gastric pH > 2.5 causes increased pneumonitis if aspiration occurs
    - Delayed gastric emptying
    - GERD, acid peptic disease, hiatus hernia.
  - Colonic carcinoma, cholelithiasis
  - Non Alcoholic Fatty Liver Disease (NAFLD)
  - Non Alcoholic Steato-Hepatitis (NASH).
- Genitourinary system:
  - ESRD
  - Macrosomia
  - Prostatic carcinoma
  - Urinary incontinence
  - Menorrhagia, ecclampsia, preeclampsia.
- Endocrine system:
  - Type II diabetes mellitus
  - Dyslipidemia
  - Hypothyroidism
  - *Insulin resistance, metabolic syndrome.*
- Central nervous system:
  - Carpal tunnel syndrome
  - *Pseudotumor cerebri*
  - Stroke
  - Endogenous depression.
- Blood:
  - Hypercoagulability: Increased factor VII, vWF, PAI-I
  - Relative polycythemia.
- Musculoskeletal system:
  - ***Acanthosis nigricans***
  - Gout
  - Osteoarthritis
  - Rheumatoid arthritis.

Anesthetic Considerations

- Difficult intubation
- Difficult IV access
- Difficult monitoring
- Difficult positioning
- Increased dosage of anesthetic agents
- Judicious fluid administration as CCF may be precipitated
- Increased chances of nerve injuries
- Difficult regional anesthetic technique.

Regional Anesthesia

- Useful alternative to GA
- Technically difficult as:
  - Difficult to identify bony landmarks
  - Higher regional block failure rates
  - Easier in lumbar region as less fat in this area
- Longer needles, sitting position, USG and fluoroscopy used to make procedure easier
- Dose requirement for epidural analgesia may be reduced due to:
  - Vascular engorgement
  - Fatty infilteration which reduces volume of the space.
- Subarachnoid block:
  - Not as difficult as epidural
  - Height of block is difficult to control causing fast upward spread of the LA
  - Continuous catheter SAB is better
- Combination of epidural and GA:
  - Allows use of larger oxygen concentration
  - Provides optimal muscle relaxation
  - Provides option for postoperative analgesia.

Ambulatory Anesthesia

- Done in obese individuals with stable concomitant diseases
- Morbidly obese patient with unstable comorbidities and no patient escort are unsuitable
- Individual evaluation and proper selection is important
- Use of regional blocks where feasible, rapidly dissipating anesthetic agents and appropriate sized equipment should be combined
- Technically challenging as dose titration is required.

Preoperative Evaluation

- Respiratory system:
  - Pulmonary function tests: Reduced ERV is the *most sensitive* indicator for pulmonary impairment
  - Sleep study: May be necessary in patients with OSA/OHS.
- Cardiovascular system:
  - *ECG:* RVH, RAD, RV strain: pulmonary HTN
  - *ECHO:* Tricuspid regurgitation is confirmatory for pulmonary HTN
  - Stress test:
    - Patients lead a sedentary lifestyle
    - These patients may have a dormant CAD without symptoms
    - Thus, stress test maybe necessary.
- Blood tests:
  - Serum glucose and thyroid hormone status
  - Serum electrolytes especially important in a setting of chronic hypercapnea
  - Serum creatinine
  - Serum vitamin B_{12}, folate, iron and calcium levels: *Acute postgastric reduction surgery polyneuropathy*
  - Arterial blood gas
  - Liver function tests:
    - Raised alanine aminotransferase *most commonly* seen
    - Clearance is usually preserved even in the presence of abnormal LFTs.
- Airway: Difficult airway due to:
  - Short, thick neck
  - Excessive tissue folds in the mouth and pharynx
  - Thick suprasternal, presternal, submental fat pads
  - Limited movement of atlanto-occipital joints by low cervical fat pads: Causes reduced thyromental distance.
- Neck circumference:
  - *Neck circumference > 40 cms* indicates increased incidence of OSA
  - This is *single biggest predictor* of difficult intubation in these patients
- Difficult venous access: CVP may be necessary for venous access.

Preoperative Medications

- All medications to be continued on morning of surgery except insulin and OHAs
- Anxiolysis with benzodiazepines
- Antiaspiration prophylaxis:
  - 30 ml of nonparticulate sodium citrate
  - 50 mg ranitidine IV
  - 10 mg metoclopramide or 8 mg ondansetron IV.

- DVT prophylaxis:
  - S/C heparin 5000 IU before surgery and every 12 hours after surgery till fully mobile
  - S/C enoxaparin 40 mg Q12H.

Intraoperative Care

Position

- Specially designed *Hercules table* available
- Particular care of pressure points as increased chances of:
  - Nerve injuries
  - Rhabdomyolysis
  - Pressure sores.
- *Walters Henderson maneuver* for shifting patient on and off table
- Supine position:
  - IVC and aortic compression
  - Reduced FRC and oxygenation
  - Worsened in head down position.
- Prone position: Reduced lung compliance and ventilation
- Lateral decubitus position: *Best preferred* as better diaphragmatic movement
- Position at intubation:
  - Stacking with towels or pillows to bring chin above the level of chest
  - *Head ELevated Laryngoscopy Position (HELLP):*
    - Done with *troop elevation pillows*
    - Brings external auditory meatus in line with sternal angle.

Monitors

- Pulse oximetry
- $ETCO_2$
- ECG
- Precordial stethoscope
- NIBP cuff size may be small for arm circumference
- Invasive arterial BP monitoring required as spuriously high BP values may result from small cuffs
- PA catheter inserted if pulmonary hypertension present
- Temperature, neuromuscular monitoring, urine output.

Pharmacological Considerations

- Increased blood volume in obese patients reduces the plasma concentration of drugs injected
- Fat has low blood flow and thus, calculating the dose based on TBW may cause excess plasma concentration
- Calculating initial dose based on LBW with subsequent doses based on pharmacological response is best approach
- LBW in obese persons calculated by adding 20–30% to the ideal body weight (IBW)
- IBW = $22 \times \text{height}^2$
- IBW = height (cm) – x, where:
  x = 100 in males
  x = 105 in females
- Repeated injection accumulates in fat and causes prolonged response.

Induction

- Difficult mask ventilation: Gather fat pads in cheek around the mask for better fit
- Preoxygenation:
  - Preoxygenate adequately as rapid desaturation occurs due to reduced FRC
  - Four vital capacity breaths with 100% oxygen within 30 seconds *recommended*.
- Induction agents:
  - Larger doses are required
  - Dose of all agents except succinylcholine is calculated according to LBW
  - Dosage of succinylcholine is according to TBW as the pseudocholinesterase increases proportionately to TBW.
- Intubation:
  - Difficult intubation anticipated
  - LMA, gum elastic bougie kept ready
  - Use *polio blade with short handle*
  - Awake fibreoptic intubation preferred
  - Sedation with dexmedetomidine useful
  - Head ELevated Laryngoscopy Position (HELLP)
  - Xylocard 1.5 mg/kg IV given prior to intubation if hypertensive
  - Intubation attempted when expired oxygen ≥ 90%.

Maintenance

- TIVA or balanced anesthesia with inhalation agents can be used
- Nitrous oxide:
  - May be a good choice
  - Avoid if pulmonary HTN present
  - High oxygen demand limits its use
  - Also causes abdominal distention reducing FRC further.
- Desflurance may be preferred due to better hemodynamic stability
- Halothane avoided as:
  - Increased sensitization to catecholamines
  - Increased chances of halothane hepatitis.

- Short acting opioids facilitate rapid and smooth emergence
- Cisatracurium, vecuronium and rocuronium useful
- Dexmedetomidine may be a useful sedative and analgesic.

Ventilation

- Pressure control mode very useful
- Tidal volumes > 10 ml/kg offer no added advantages
- Maintain minute volume of around 5 liters
- PEEP:
  - Improves lung compliance and oxygenation
  - Prevents V-Q mismatch
  - Detrimental if pulmonary HTN present.

Hemodynamics

- Judicious fluid administration as CCF maybe precipitated
- Adipose tissue masks tissue perfusion: Fluid balance may be difficult to assess
- Blood loss is greater due to more extensive dissection to reach the surgical site
- Early colloid and blood product infusion required as these patients are less able to compensate for blood loss.

Postoperative Care

Extubation

- Prompt extubation necessitated as patient may become ventilator dependent
- Extubated in semi-recumbent position as this has lesser adverse effect on respiration
- Reversal:
  - Prompt and early reversal but slow full recovery seen with neostigmine induced reversal of vecuronium
  - Neostigmine dosed according to TBW.
- Sugammadex:
  - Modified cyclodextrin derivative
  - Encapsulates rocuronium
  - Causes rapid and complete reversal of rocuronium induced neuromuscular blockade.

Management

- Walter Henderson maneuver with patient transfer device to safely transfer patient
- Nursed in semi-recumbent position
- Respiratory care:
  - Adequate analgesia
  - Use of elastic binder
  - Early ambulation
  - Deep breathing exercises
  - Incentive spirometry
  - CPAP or bilevel positive airway pressure initiated for those with OSAS.

Monitors

- Pulse oximetry
- IBP, ECG, temperature
- Blood sugar, arterial blood gas monitoring.

Postoperative Analgesia

- Epidural analgesia:
  - Useful analgesia with opioids and local anesthetics
  - Allows early ambulation and prevents DVT
- Patient controlled analgesia:
  - Done with morphine-PCA
  - Nausea and pruritis is also reduced
- Local infilteration of wound with bupivacaine
- Multimodal analgesia:
  - Combines PCA and local infiltration
  - Better analgesia than either techniques done alone.

OBSTRUCTIVE SLEEP APNEA[1,2,3,6,11,21]

Definition

- Obstructive sleep apnea:
  - Complete cessation of airflow
  - Lasting 10 seconds or longer
  - Despite maintaining ventilatory effort
  - Occurring ≥ 5 times per hour of sleep
  - Reduction of at least 4% in SaO_2.
- Obstructive sleep hypopnea:
  - Partial cessation of airflow (≥ 50%)
  - Lasting ≥ 10 seconds
  - Despite maintaining ventilatory efforts
  - Occurring ≥ 15 times per hour of sleep
  - Reduction of at least 4% in SaO_2.
- Obesity hypoventilation (Pickwickian) syndrome:
  - Obesity (BMI > 30 kg/m^2)
  - Awake arterial hypercapnea ($PaCO_2$ > 45 mm Hg)
  - Absence of other causes of hypoventilation.

Grading

- Done using the *apnea hypopnea index (AHI)* which is derived from polysomnography
- $$AHI = \frac{\text{Number of episodes of apnea/hypopnea}}{\text{Total sleep time in hours}}$$

- Normal limit of AHI = 5–10 events per hour
- Grading of OSAS:
  - Mild disease = 5–5 events/hr
  - Moderate disease = 16–30 events/hr
  - Severe disease = 30 events/hr.
- *Total arousal index (TAI)* = Total no of arousals/hr
- *Respiratory disturbance index* = AHI + TAI.

Pathophxsiology

Sleep apnea causes hypoxia and hypercapnea which results in:

- Systemic HTN due to systemic vasoconstriction
- Acute carbon dioxide retention due to chronic hypoventilation
- Polycythemia due to increased levels of TNF-α , IL1, ICAM, VCAM
- Excessive daytime somnolence and intellectual deterioration due to:
  - Cerebral dysfunction
  - Sleep fragmentation
  - Loss of deep sleep
  - Excessive motor activity.
- Left heart failure due to:
  - Reduced pleural pressure
  - Reduced intrathoracic pressure
  - Increased cardiac afterload.
- Sudden cardiac death due to:
  - Vagal bradycardia
  - Ventricular arrhythmias.
- Pulmonary HTN and corpulmonale due to hypoxic pulmonary vasoconstriction.

Preoperative Screening

- History of:
  - Heavy snoring with sudden awakening with choking
  - Daytime somnolence, headaches.
- On examination:
  - Nasal obstruction, tonsillar hypertrophy
  - Retrognathia, crowding of pharynx, macroglossia
  - Obesity, GERD
  - Pulmonary HTN, systemic HTN, intracranial HTN
  - IHD, right and left heart failure, arrhythmias.
- Investigations:
  - Blood urea and serum creatinine
  - Blood glucose and thyroid function tests
  - Serum electrolytes and ABG especially for chronic hypercapnea
  - *Raised LFTS:* Especially alanine aminotransferase
  - Cardiovascular:
    - Echocardiogram and ECG
    - *Stress tests:* As these patients may have dormant CAD due to sedentary life style.
  - Respiratory:
    - Sleep study or polysomnography
    - *Gold standard* for diagnosis
    - Monitors:
      - Electroencephalography
      - Electrocardiography
      - Electrooculography
      - Electromyography
      - Nasal/oral airflow, pulse oximetry, capnography
      - BP and esophageal pressure for GERD
      - Room noise.
    - Results expressed as AHI
    - Costly test.
  - Nasopharyngoscopy for assessing surgical benefits like uvulopharyngoplasty for obstruction
  - Overnight recording of SaO_2 by pulse oximetry can be used for diagnosis.

Choice of Anesthesia

- Regional anesthesia preferred as respiratory drive is not affected
- Difficult to establish land marks
- Should be ready for airway management if inadvertent respiratory paralysis
- If GA, intubation with controlled ventilation preferred.

Preoperative Preparation

- NPO orders
- Informed consent
- Preoperative sedation:
  - Usually with benzodiazepines
  - Sedation may increase airway obstruction
  - If sedation is given, SpO_2 should be monitored or patient should be placed on CPAP.
- Antiaspiration prophylaxis
- DVT prophylaxis
- Continue all preoperative medications except OHAs and insulin
- *Difficult venous access if patient is obese:* Central line maybe only venous access
- Facilitate ventilation:
  - CPAP is required in moderate to severe OSAS
  - If refractory to CPAP, noninvasive positive pressure ventilation is given (NIPPV).

Monitors

- Pulse oximetry, capnography, ECG
- Temperature, urine output
- Precordial stethoscope, neuromuscular monitoring
- Invasive arterial BP measurement preferred over NIBP as NIBP becomes unreliable due to cuff size
- PA catheter inserted and monitored if pulmonary HTN present.

Induction

- Preoxygenate with FiO_2 of 100% with APL value set to deliver 5–15 cm H_2O of CPAP for 3 minutes
- *Difficult mask ventilation:* Gather fat pads in cheek around mask for better seal
- Avoid large doses of drugs and longer acting drugs
- All drugs given according to lean body weight except for succinylcholine and neostigmine (according to TBW)
- *Rapid sequence induction* for emergencies with cricoid pressure and succinylcholine
- Difficult airway equipment and gum elastic bougie kept ready
- *McCoys laryngoscope, LMA* kept standby
- Awake intubation and extubation preferred in difficult airway
- *Awake fiberoptic intubation* preferred for elective cases
- Oxygen insufflation with nasopharyngeal catheter during intubation delays desaturation
- Cricothyrotomy set and ENT surgeon standby for Cant Ventilate Cant Intubate situation.

Maintenance

- TIVA or balanced anesthesia with inhalation agents can be used
- Nitrous oxide:
  - May be a good choice
  - Avoid if pulmonary HTN present
  - High oxygen demand limits its use
  - Also causes abdominal distention reducing FRC further.
- Desflurance may be preferred due to better hemodynamic stability
- Halothane avoided as:
  - Increased sensitization to catecholamines
  - Increased chances of halothane hepatitis
- Short acting opioids facilitate rapid and smooth emergence
- Cisatracurium, vecuronium and rocuronium useful
- Dexmedetomidine may be a useful sedative and analgesic.

Ventilation

- Tidal volumes > 10 ml/kg offer no added advantages
- Maintain minute volume of around 5 liters
- PEEP:
  - Improves lung compliance and oxygenation
  - Prevents V-Q mismatch
  - Detrimental if pulmonary HTN present.

Hemodynamics

- Judicious fluid administration as CCF maybe precipitated
- Early colloid and blood product infusion required as these patients are less able to compensate for blood loss.

Extubation

- Consider short period of postoperative mechanical ventilation if:
  - Duration of surgery is longer
  - Upper airway surgeries where serious compromise of upper airway is expected
- Fully awake extubation with patient is sitting or reverse Trendelenburg position
- Adequate suctioning and cricoid pressure during extubation may prevent aspiration.

Postoperative Care

Position

- Head elevated to 30° to increase upper airway stability
- Lateral posture relieves upper airway obstruction.

Complications

- *Respiratory:* Hypercapnea, desaturation (episodic)
- *Cardiovascular:* HTN, MI, arrhythmias.

Management

- Nursed in high dependency unit for few days if:
  - Severe BMI/OSAS
  - Severe cardiovascular disease
  - Severe intraoperative complication
  - High postoperative opioid requirement.
- Maintenance of CPAP:
  - Insert NG tube before initiation of therapy to prevent distension of stomach
  - Even if NG tube is present, CPAP can be used but leakage may be present
  - 2–4 L/min of oxygen via side port on CPAP mask achieves adequate FiO_2.

- Advantages of CPAP:
  - CPAP reduces risk of complication
  - Sedative analgesic drugs can be used safely
  - After nasal surgery, surgeon may use naso-pharyngeal airway with packing around it
  - CPAP is very useful in this scenario to prevent dangerous desaturation.

Postoperative Analgesia

- Multimodal analgesia is best
- Opioids:
  - Patient controlled analgesia useful
  - Basal rate set at zero and dosing is restricted
  - Morphine is preferred opioid.
- Local infiltration of incision site
- Epidural analgesia:
  - Allows early ambulation
  - Reduces risk of DVT
  - NSAIDs can be used.

POLYSOMNOGRAPHY

Introduction

- Comprehensive recording of the biophysical changes which occur during of sleep
- Usually done at night except for patients with Circadian rhythm sleep disorders.

Indications

- Narcolepsy, parasomnias
- Restless leg syndrome
- REM behavioral disorder
- Obstuctive sleep apnea syndrome
- Circadian rhythm sleep disorder
- Congenital central hypoventilation syndrome *(Ondines curse).*

Monitors

- Electroencephalography
- Electrooculography
- Electromyography
- Electrocardiography
- Nasal and oral airflow
- Jaw and chin movements
- Abdominal and chest wall movements
- Pulse-oximetry.

Interpretation

- *Sleep latency*: Time taken to fall asleep from the time lights were switched off (normally < 20 min)
- *Sleep efficiency*:
  - Calculated as:
    - Number of minutes of sleep
    - Number of minutes in bed.
  - Normally > 85–90%.
- Sleep stages:
  - REM sleep and NREM sleep (stages I–IV)
  - 20–25% of sleep is REM sleep
  - Majority of sleep is stage II sleep.
- Breathing irregularities:
  - Obstructive sleep apnea:
    - Complete cessation of air flow
    - Lasting more than 10 seconds
    - Despite maintaining ventilatory effort
    - Occurs more than 5 times per hour of sleep
    - Reduction of at least 4% in SaO_2.
  - Obstructive sleep hypopnea:
    - Partial cessation of airflow
    - Lasting more than 10 seconds
    - Despite maintaining ventilatory efforts
    - Occurs more than 15 times per hour of sleep
    - Reduction of at least 4% in SaO_2.
- *Arousals:* Sudden shifts in brain wave activity due to leg movements, environmental noise, etc.
- Cardiac rhythm abnormalities
- Leg movements
- Body position during sleep
- Oxygen saturation during sleep.

CPAP Titration Study

- Polysomnography done for an OSAS patient after CPAP mask is applied
- This is done to determine:
  - Correct CPAP mask size
  - Correct amount of pressure
  - Tolerance to treatment.
- When CPAP titration and diagnostic polysomnography are done on the same night the study is called *split night study.*
- Minimum of 2 hours of polysomnography required to diagnose OSAS before a CPAP mask is applied in a *split night study.*

Alternatives

- Nowadays polysomnography is replaced by *actigraphy* which is used to measure gross motor activity
- Usually measured by an actigraph unit at the wrist.

TURP SYNDROME[1,2,3,10,21]

Introduction

Term used to describe the signs and symptoms which occur with excessive absorption of irrigating solution during TURP, primarily due to circulatory overload, water intoxication and occasionally toxicity from the irrigating fluid.

Etiopathogenesis

- Resection of the gland opens up the prostatic venous sinuses
- This causes absorption of fluids across the venous sinuses
- This causes:
  - Fluid overload resulting in:
    - Hypertension, bradycardia
    - Pulmonary edema, CCF, MI
    - Hypoosmolality and hyponatremia.
  - Hypoosmolality resulting in:
    - Cerebral edema, Cushings reflex
    - Hypertension, bradycardia.
  - Dilutional hyponatremia resulting in:
    - Confusion, restlessness
    - Seizures, coma.
- Syndrome occurs due to absorption of large amounts of hypotonic fluids
- About 20 ml/min of fluids is absorbed
- This can go up to 200 ml/min
- When ≥ 2 liters of fluid is absorbed, TURP syndrome results
- $\text{Volume absorbed} = \frac{\text{Preoperative } Na^+}{\text{Postoperative } Na^+} \times \text{ECF} - \text{ECF}.$

PREDISPOSING FACTORS

- Hydrostatic pressure of irrigating fluid (> 60 cm H_2O)
- Duration of surgery ≥ 60 minutes
- Size of gland ≥ 45g
- *Hemorrhage:* Causes opening of sinuses
- *Irrigation fluid:* Distilled water increases risk
- Poorly controlled preoperative CCF.

Clinical Features

CNS and ₹	CNS	Metabolic	Others
Hypertension (SBP and DBP) Brady/ tachyarrythmias CCF Pulmonary edema MI Shock	Agitation Confusion Restlessness Seizures Coma Transient visual disturbances	Hyponatremia Hyperglycine-mia Hyperglycemia Hyperammone-mia Hypoosmolarity	Hemolysis ARF

Sodium level	CNS disturbance	ECG findings
120 mEq/L	Confusion Restlessness	Occasionally QRS widening
115 mEq/L	Somnolence Nausea	Widening of QRS complexes ST segment elevation
110 mEq/L	Seizures Coma	Ventricular tachycardia Ventricular fibrillation

Prevention

- Optimize preoperative Na^+ levels ≥ 130 mEq/L
- Treat CCF preoperatively adequately
- Conservative treatment of BPH in critically ill (medical therapy/balloon dilatation)
- Avoiding distilled water for irrigation
- Limit hydrostatic pressure by reducing height of pole to:
  - 60 cm during initial half of surgery
  - 30 cm in the last part of surgery
- Avoid overdistension of bladder
- Restrict duration of surgery to ≤ 1 hour
- Microdrip set for IV fluids in cardiac/renal patients
- Use of vasopressors to control regional anesthesia induced hypotension instead of fluids.

Management

- Ensure adequate oxygenation with face mask or nasal cannula
- Terminate surgery as soon as possible
- Consider insertion of invasive monitor if cardiovascular instability present
- Attach 12 lead ECG
- Collect blood for estimation of:
  - Creatinine, glucose
  - Serum electrolytes, ABG
- Correction of hyponatremia:
  - If asymptomatic, (Na^+ > 120 mEq/L): Fluid restriction with diuretics
  - If symptomatic hyponatremia:
    - Amount of Na^+ required = TBW (desired Na^+ – present Na^+)
    - Correction rates:
      - Mild symptoms: 0.5 mEq/L/hr
      - Moderate symptoms: 1 mEq/L/hr
      - Severe symptoms: 1.5 mEq/L/hr
      - Avoid rapid correction to prevent *central pontine demyelination*
    - Choice of fluids:
      - Isotonic saline for mild-moderate symptoms
      - 3% saline (or 5%) if severe symptoms or serum Na^+ < 110 mEq/L

- ° Stop hypertonic saline when symptoms cease or $Na^+ > 120$ mEq/L
- ° Rate of 3% NaCL should be < 100 ml/hr.

- Treatment of complications:
  - ° Seizures:
    - * Midazolam 2–4 mg IV
    - * Diazepam: 3–5 mg IV
    - * Thiopentone: 50–100 mg IV
    - * Phenytoin: 15–20 mg/kg at ≤ 50 mg/min.
  - ° Pulmonary edema:
    - * Diuretics
    - * CPAP ventilation
    - * Intubation and positive pressure ventilation.

CHRONIC RENAL FAILURE[1,2,3,6,11,21]

Introduction

- Chronic renal failure is a clinical syndrome characterized by progressive and irreversible decline in renal function over the course of 3–6 months causing GFR to reduce below *25 ml/min.*
- ESRD is renal dysfunction which would be fatal without renal replacement therapy and occurs when GFR reduces to *10 ml/min.*

Etiology

- Diabetes mellitus (45%)
- Glomerulonephritis
- Pyelonephritis
- Polycystic kidney disease
- Hypertension
- Systemic lupus erythematosus.

Calculation of GFR

Cockroft-Gault formula:

$$\text{GFR/creatinine clearance (ml/min)} = \frac{(140 - \text{age}) \times (\text{weight in kgs})}{72 \times (\text{serum creatinine})} \quad \text{in males}$$

Classification

KDOQI staging system

GFR range (ml/min/1.73 m²)	Diagnosis
100–120	Normal
60–100	Reduced renal reverse
40–60	Mild renal impairment
25–40	Moderate renal impairment
≤ 25	Chronic renal failure
≤ 10	ESRD

Clinical Features

- Central nervous system:
  - – Peripheral neuropathy, uremic encephalopathy
  - – Autonomic neuropathy, asterixis, myoclonus
  - – Muscle twitching, confusion, seizures, coma.
- Cardiovascular system:
  - – Hypertension, arrhythmias
  - – Fluid overload, CCF, conduction block
  - – Uremic pericarditis, accelerated atherosclerosis.
- Respiratory system:
  - – Interstitial/alveolar edema
  - – Pleural effusion.
- Gastrointestinal system:
  - – Anorexia, nausea, vomiting
  - – Mucosal ulcerations, acid peptic disease
  - – GI hemorrhage
  - – Delayed gastric emptying, adynamic ileus
  - – Hiccoughs.
- Endocrine system:
  - – Glucose intolerance
  - – Secondary hyperparathyroidism
  - – Hypertriglyceridemia.
- Metabolic:
  - – Hyponatremia (hypernatremia rare)
  - – Hyperkalemia (hypokalemia rare)
  - – Hypocalcemia, hypoalbuminemia
  - – Hypermagnesemia, hyperphosphatemia, hyperuricemia
  - – High anion gap metabolic acidosis/hyperchloremic normal anion gap metabolic acidosis.
- Hematological:
  - – Anemia, platelet dysfunction
  - – Leukocyte dysfunction.
- Musculoskeletal system:
  - – Renal osteodystrophy
  - – Periarticular calcification.
- Skin: Hyperpigmentation, pruritus, ecchymosis.

Pharmacological Considerations

- Effects of CRF on drug disposition:
  - – Dose adjustment usually required if GFR < 50 ml/min
  - – *Absorption of drugs:* Delayed due to delayed gastric emptying
  - – *Distribution:* V_d increased or decreased depending on TBW
  - – *Protein binding:*
    - Reduced for acidic drugs due to hypoalbuminemia: Increased free drug levels
    - Increased for basic drugs due to increase in α1-glycoprotein: Reduced free drug levels

  - Elimination: Increased T½ for drugs eliminated by kidney.
- Volatile anesthetics:
  - Sevoflurane releases *compound A (sevo-olefin)* which is nephrotoxic
  - It also increases fluoride levels
  - Isoflurane and desflurane are safe.
- Neuromuscular blockers:
  - Avoid succinylcholine if serum $K^+ > 5.5$ mEq/L
  - Atracurium and cisatracurium are better choices
  - Cisatracurium is *drug of choice* due to:
    - Reduced incidence of histamine release
    - Drug is more potent
    - Less production of laudanosine
    - Has shorter duration of action.
  - Vecuronium and rocuronium have long duration of action.
- Induction agents:
  - Thiopentone requires lesser dose and lower rate of administration as:
    - Volume of distribution is increased
    - Reduced plasma protein binding.
  - *Propofol:* Dose is unchanged but causes profound hypotension.
- Anticholinesterases:
  - *Neostigmine clearance reduced:* Causes prolonged parasympathetic activity
  - Use glycopyrollate instead of atropine.
- Nonopioid analgesics:
  - *Contraindicated* including COX 2 inhibitors
  - Paracetamol is safe.
- Opioids analgesics:
  - Morphine:
    - Metabolized to:
      - Morphine-3-glucuronide which reduces seizure threshold
      - Morphine-6-glucuronide which causes delayed onset of sedation and respiratory depression.
    - Reduce dose and frequency of morphine.
  - Fentanyl: Reduced clearance
  - Tramadol:
    - Forms O-demethyl tramadol which is excreted by kidneys
    - This may be epileptogenic: Reduce dose and increase dosing interval.
  - Pethidine: Forms normeperidine which causes seizures, altered mentation
  - Alfentanil and remifentanyl are safe.
- Local anesthetics:
  - Shorter duration of action due to altered protein binding
  - Reduce dose by 25% as altered protein binding reduces seizure threshold.

Regional Anesthesia Considerations

- Reasons to avoid neuraxial blockade in CRF:
  - Uremic encephalopathy:
    - Raised ICT
    - Uncooperative patient.
  - Hemodynamically unstable
  - *Platelet dysfunction common:* Possibility of hematoma
  - *Heparin administered during hemodialysis:* Possibility of hematoma.

Anesthetic Management

Preoperative Evaluation

- History:
  - Establish cause of CRF
  - Duration of therapy
  - Evaluate and explain possible need for dialysis postoperatively
  - *History of comorbidities:* HTN, DM, IHD, SLE and details of therapy.
- Examination:
  - *Blood pressure:* Standing and sitting position
  - Flow murmur due to anemia
  - Pericardial rub.
- Ankle edema due to CCF/hypoproteinemia
- *Investigations:*
  - Complete blood count: Anemia, thrombocytopenia
  - Serum electrolytes for hyperkalemia/hyponatremia/hypocalcemia
  - BUN and serum creatinine for assessing severity
  - Blood glucose for glucose intolerance
  - BT and CT especially if regional anesthesia considered
  - ABG for acid base status and hypoxemia
  - *ECG:* For hyperkalemia *(sigma waves)* and hypocalcemia (prolonged QT_c)
  - *ECHO:* For cardiac function and pericardial effusion
  - *Chest X-ray:* For signs of fluid overload, pleural effusion, cardiomegaly
  - *Arteriogram/renal Doppler:* If renal artery stenosis is suspected.

Preoperative Optimization

- NPO orders
- Informed consent
- Preoperative sedation:
  - Given only if patient is stable
  - Avoid sedation if unstable hemodynamics
  - Reduced dose of benzodiazepines used for sedation
  - Midazolam is relatively safe.
- Promethazine 2.5–25 mg IM used for sedation and antiemesis
- Antiaspiration prophylaxis:
  - 30 ml of non-particulate sodium citrate
  - 50 mg ranitidine IV
  - 10 mg metoclopramide or 8 mg ondansetron IV.
- Continue all drugs on the day of surgery, especially antihypertensives
- Stop morning dose of oral hypoglycemics and insulin on day of surgery
- Preoperative blood transfusion:
  - Avoid unnecessary blood transfusions
  - Transfuse if Hb < 6–7 g/dL
  - Target Hb > 10 g/dL
  - But difficult to maintain Hb levels above 10 g/dL.
- Preoperative dialysis:
  - Done to optimize electrolyte status
  - Hemodialysis is more effective than peritoneal dialysis
  - Hypovolemia is common post-dialysis
  - Optimize BP and serum potassium levels post-dialysis
  - Optimize ACT as heparin is used during dialysis.

Care of Arteriovenous Fistula

- Made between:
  - Radial artery and cephalic vein
  - Brachial artery and basilic vein
  - Usually made on nondominant hand.
- Purpose is to improve venous access for subsequent dialysis
- Complications of AV fistula:
  - Infection
  - Stenosis
  - Thrombosis
  - Aneurysm
  - Limb ischemia.
- Done under GA/local infilteration/brachial plexus block
- If patient is dialysis dependent:
  - Dialysis to finish 4–6 hrs preoperatively to allow fluid shift
  - Heparin to be eliminated
  - Full blood count, BU, SC, BT and CT should be measured postdialysis
  - Protect limb with fistula carefully
  - BP cuff and IV line to be on other hand/leg
  - Avoid application of pressure on the fistula
  - Pad the fistula adequately at the time of positioning to avoid pressure
  - Give slow and titrated doses of induction agents.

Monitoring

- Pulse oximetry and capnography
- ECG for hyperkalemia/hypocalcemia
- *Blood pressure:* NIBP cuff not to be tied in arm with AV fistula as occlusion may occur
- Neuromuscular monitoring, precordial stethoscope
- *Urine output:* Maintain > 0.5 ml/kg/hr
- IBP if major fluid shifts expected
- CVP, PA monitoring for fluid optimization in unstable patients
- Regular ABGs for acid base status.

Induction

- Preoxygenate for 5–6 minutes as anemia with increased cardiac output increases oxygen demand
- Opioids:
  - Avoid morphine as high levels of M-6-G may cause respiratory depression
  - Fentanyl is relatively safe.
- Induction agents:
  - Reduced dose of thiopentone (2–3 mg/kg) and etomidate (0.2–0.4 mg/kg)
  - Induction agents given slowly to avoid hypotension
  - Ketamine and propofol (1–2 mg/kg) relatively safe
  - Induction with inhalational agents is safe as reversal is easy.
- Muscle relaxants:
  - Succinylcholine safe if serum K^+ levels is normal
  - Atracurium, cisatracurium and mivacurium safe
  - Vecuronium and rocuronium duration of action prolonged 1½ times
  - *Atracurium/cisatracurium preferred*: Cistracurium is better.
- *Rapid sequence induction* with cricoid pressure if history of nausea, vomiting/GI bleed

- Beta blocker (esmolol, propranolol) or lidocaine used to blunt intubation response
- Use of LMA is safe and advantages as:
  - It avoids intubation response
  - Avoids need for paralysis.

Maintenance

- Avoid:
  - Morphine and alfentanyl as action is prolonged
  - Meperidine as it causes prolonged CNS excitation.
- Fentanyl and remifentanyl:
  - Pharmacokinetics is unaffected
  - Can be used safely.
- Volatile anesthetics:
  - Avoid sevoflurane and enflurane
  - Isoflurane, desflurane best preferred as least effect on renal blood flow and CO.
- Nitrous oxide:
  - Used with caution in:
    - Patients with ventricular dysfunction
    - Severe anemia with Hb < 7 g/dL.
  - Otherwise can be used safely.
- Controlled ventilation preferred as inadequate spontaneous ventilation with progressive hypercarbia can cause respiratory acidosis circulatory depression and hyperkalemia
- Reversal of neuromuscular blockade requires no change in dose.

Hemodynamics

- Maintenance of cardiac output essential as in the presence of anemia, reduction of cardiac output may be deleterious
- Superficial operation requires only correction of insensible fluid loses with 5% dextrose
- Choice of fluids:
  - Ringer lactate avoided as it contains:
    - 5 mEq/L of potassium
    - 29 mmol/L of lactate.
  - Normal saline is the *best maintenance fluid*
  - Glucose free solutions to be used as glucose intolerance might be worsened
  - Avoid starches as it can accumulate and worsen CRF
  - Gelatin containing fluids are safe
  - Replacement of blood loss with packed cells is best.
- Management of hypotension:
  - Judicious fluid therapy to treat hypotension
  - Avoid precipitating fluid overload and CCF
  - If inadequate response with fluid therapy:
    - β-receptor agonists or dopamine used
    - Phenylephrine useful as vasopressor.
- Antihypertensives:
  - Furosemide and thiazide action is prolonged
  - Propranolol, esmolol and labetolol: No change
  - Nifedipine, diltiazem and verapamil: No change
  - Nitroglycerine is safe
  - Sodium nitropusside less desirable as cyanide toxicity occurs on prolonged use
  - Hydralazine:
    - Duration of action is prolonged
    - Cautious use advised.

Postoperative Care

Complications

- *Bleeding and infections more common:* Due to lymphocyte and platelet dysfunction
- Worsening renal function
- Worsening acidosis
- Electrolyte imbalance/anemia
- Recurarization.

Monitors

- SpO_2
- ECG
- BP
- Frequent ABGs
- Check BUN
- Creatinine
- Hb
- Urine output.

Analgesia

- Avoid NSAIDs, morphine, pethidine
- Fentanyl, remifentanyl effective
- Epidural analgesia if normal coagulation profile
- Early mobilization.

RENAL REPLACEMENT THERAPY[1,2,3,10]

Introduction

RRT used to describe all available approaches to mechanical artificial support of nonendocrine kidney functions.

Indications[1]

- Clinical signs of uremic toxicity
- Anuria: Oliguria (diuresis < 200 ml in 12 hrs)

- Anasarca/severe fluid overload
- Multiple organ failure with renal dysfunction and SIRS or sepsis
- Severe metabolic acidosis (pH < 7.10)
- Hyperkalemia (K^+ > 6.5 mEq/L)
- Severe dysnatremia (Na^+ <115 or > 160 mEq/L)
- Hyperazotemia (BUN > 80 mg/dL or creatinine > 4 mg/dL)
- Hyperthermia (> 40 °C without response to medical therapy).

Principles[1]

- Blood flows through semipermeable membrane
- Exchange of substances occurs through:

  Diffusion:
  - Movement of small molecular weight solutes across membrane
  - Movement occurs from high concentration to low concentration compartment
  - Ineffective for larger molecular weight substances (> 5000 Da).

  Convection:
  - Movement of water by mass transport across pressure gradient
  - Removes both small and larger molecular weight substances
  - *Ultrafilteration* causes movement of water across the membrane.

Techniques[1]

Intermittent Techniques

- Intermittent hemodialysis
- Hemodiafilteration
- Isolated ultrafilteration.

Continuous Techniques

- Peritoneal dialysis
- Slow continuous ultrafilteration
- *Hemofilteration:* CAVH, CVVH
- *Hemodialysis:* CAVHD, CVVHD
- *Hemodiafilteration:* CAVHDF, CVVHDF
- Extended daily dialysis.

Hybrid Techniques

- Slow low efficiency daily dialysis (SLEDD)
- Sustained low efficiency daily dialysis with filteration (SLEDD-F).

Intermittent Hemodialysis

- Most common technique for chronic renal failure
- Blood and dialysate circulated in countercurrent manner without contact
- Ultrafilteration rate = Scheduled weight loss
- Typically performed 4 hrs thrice weekly or daily.

Peritoneal Dialysis

- Blood circulating along capillaries of peritoneal membrane exposed to dialysate
- Access by insertion of peritoneal dialysis catheter
- Abdominal instillation of dialysate
- Can be continuous or intermittent.

Slow Continuous Ultrafilteration (SCUF)

- Blood driven through a highly permeable filter
- Uses extracorporeal circuit in venovenous mode
- Ultrafilterate produced = Weight loss
- Used only for fluid control in overloaded patients.

Continuous Venovenous Hemofilteration (CVVH)

- Blood driven through highly permeable filter
- Uses extracorporeal circuit in venoneous mode
- Ultrafilterate replaced to achieve blood purification and volume control
- *Predilution hemofilteration:* Replacement fluid delivered before filter
- *Postdilution hemofilteration:* Replacement fluid delivered after filter.

Continuos Venovenous Hemodialysis (CVVHD)

- Blood driven through low permeability dialyzer
- Uses extracorporeal circuit in venovenous mode
- Countercurrent flow of dialysate in dialysate compartment
- Ultrafilterate produced = Weight loss.

Hemoperfusion (HP)

- Patients blood circulated on bed of coated charcoal powder
- Removes solutes by adsorption
- Indicated in cases of poisoning and intoxication with agents removed by charcoal
- Causes platelet and protein depletion.

Plasmapheresis (PP)

- Uses specific plasma filters to filter plasma as a whole
- Blood reconstituted by infusion of plasma products like albumin/frozen plasma
- Used to remove proteins and protein bound solutes.

High Flux Dialysis (HFD)

- Uses highly permeable membrane
- Ultrafilteration control system incorporated
- Ultrafilteration occurs in proximal part of filter
- Counterbalanced by positive pressure applied on dialysate compartment
- Backfilteration occurs in distal part of filter
- Convective passage of dialysate occurs into blood.

High Volume Hemofilteration

- Hemofilteration with a high volume setting > 45 ml/kg/hr
- Uses highly permeable membrane.

High Permeability Hemofilteration

- Uses high cutoff permeable membranes.

Conduct of RRT

No[1]	Clinical variable	Operational variable	Setting
1	Fluid balance	Net ultrafilteration	Continuous negative balance
			100–300 ml/hr in unstable pts
			Monitor CVP IBP ECG SpO_2
2	Dosage	Clearance/modality	2000–3000 ml/hr
			35 ml/kg/hr for CRRT
3	Acid base balance	Solution buffer	Bicarb buffered solution preferred in lactic acidosis/hepatic failure
4	Electrolytes	Replacement	Solution without K^+ in hyperK$^+$
			Manage accurately with $MgPO_4$
5	Goal		Urea clearance > 2 L/hr
6	Timing	Schedule	Early and intense RRT
7	Protocol	Staff/Machine	Well trained staff

Anticoagulation During RRT

- Contact occurs between blood and tubing of circuit
- Activation of coagulation cascade occurs
- Techniques used:

  Mechanical:
  - Adequate sized vascular access
  - Avoid kinking of circuit tubing
  - Blood flow rate > 100 ml/min
  - Continuous monitoring of venous bubble trap
  - Keep plasma filteration fraction < 20%.

  Pharmacological:
  - *Unfractionated heparin:* 5–10 IU/kg/hr
  - LMWH
  - Prostacyclines
  - Citrate
  - Danaparoid/argatroban/irudine.

CONTINUOUS RENAL REPLACEMENT THERAPY[1,2,3,10]

Introduction

Replaces renal function by gradual and continuous removal of surplus fluid retained in the body.

Indications

Renal Causes

- Marked azotemia with fluid overload
- Maintaining electrolyte and acid base balance
- Persistent oliguria, hyperkalemia
- Pericarditis/refractory pulmonary edema
- Hypothermia/hyperthermia
- Poisoning with dialyzable poison
- Serial rise in blood urea/creatinine
- ARF with cardiovascular instability.

Nonrenal Causes

- SIRS
- Crush syndrome
- Lactic acidosis
- Congestive heart failure.

Types

- Hemodialysis
- Hemofilteration
- Hemodiafilteration
- High flux dialysis.

Access

Arteriovenous Access

- Femoral artery and vein access
- *Advantages:* No pump required
- Disadvantages:
  - ischemia of limb
  - atheroembolism
  - hematoma formation
  - arterial wall injury
  - arterial apasm
  - hemorrhage.

Venovenous Access

- Double lumen cannula inserted into femoral or internal jugular vein
- 12–14 Fr catheters used
- Advantages:
  - Rapid and consistent blood flow rates: Up to 300 ml/min
  - Reduced clotting chances
  - Improved dialysis performance
  - Ease of cannulation.
- Disadvantages:
  - Air embolism
  - Hemorrhage
  - Central vein thrombosis.

Dialysate Characteristics

- *Dialysate A:* 4.5 L electrolyte solution with Ca Mg lactic acid
- *Dialysate B:* 8.4 % bicarbonate
- *Replacement Fluids:*
  - Normal saline with calcium chloride
  - Normal saline with magnesium sulfate
  - Half normal saline
  - Half normal saline with sodium bicarbonate.

Anticoagulation

- Need for continuous anticoagulation
- If platelet count < 50000/mm^3, no need of anticoagulation
- Continuous anticoagulation causes increased risk of bleeding and thrombocytopenia.

Advantages

- Useful in hemodynamically unstable patients as lower rates of fluid removal
- Excellent control of azotemia, electrolyte and acid base balance
- Efficient removal of fluid in special circumstances like ARDS and pulmonary edema
- Helps in administration of parenteral nutritiion, IV medication and inotropes
- Hemofilteration reduces intracranial tension
- *Removes proinflammatory mediators:* IL-1, IL-6, IL-8, TNF.

Disadvantages

- Requires regular monitoring of hemodynamic status
- Requires regular infusion of dialysate
- Requires continuous anticoagulation
- Expensive.

Complications

Technical

- Vascular access site malformation
- Air embolism
- Circuit blood clotting
- Fluid and electrolyte imbalance.

Clinical

- Bleeding
- Thrombosis
- Infection/sepsis
- Membrane bioincompatibility
- Hypothermia
- Nutrient losses.

RRT IN SEPSIS[1,3,10]

Introduction

RRT frequently used adjuvant therapy in sepsis.

Indications

- Acute renal failure of sepsis
- Severe vasopressor dependent septic shock
- Inability to maintain adequate ECF volume using diuretics
- Elevated lactate levels (> 4 mmol/L) which persists following initial resuscitation.

Principles

Peak Concentration Hypothesis

- Removes cytokines from blood compartment during proinflammatory phase of sepsis
- Assumes reduced blood cytokine levels decreases tissue effects and organ failure.

Threshold Immunomodulation Hypothesis

- Assumes proinflammatory process halted when blood cytokine levels fall to threshold level
- Threshold level unclear.

Mediator Delivery Hypothesis

- HVHF increases lymph flow 20–40 times
- Mediators and cytokines 'dragged' with lymph
- Pulls cytokines from tissues to blood from where it is removed
- Tissue levels of inflammatory mediators fall.

Vascular Access

(KDIGO recommendations)

- Site of vascular access in order of preference:
  - Right internal jugular vein
  - Femoral vein
  - Left internal jugular vein
  - Right subclavian vein.
- Ultrasound guided placement of catheters
- Chest X-ray confirmation of placement
- Avoid topical antibiotics over skin insertion site.

Intermittent Techniques

Advantages

- Relatively inexpensive
- Rapid correction of fluid overload
- Rapid removal of dialyzable drugs
- Rapid correction of electrolyte balance
- Minimizes anticoagulant exposure.

Disadvantages

- Hypotension common
- Cerebral edema
- Can cause renal ischemia
- Limited duration of therapy.

Continuous Techniques

Advantages

- Better hemodynamic stability
- Better volume control
- Stable intracranial pressure
- Disease modification by cytokine removal.

Disadvantages

- Anticoagulant requirement
- Higher potential for filter clotting
- Expensive.

Techniques

- CRRT equivalent to IHD for AKI according to *Surviving Sepsis guidelines*
- HVHF shown to have beneficial effects on hemodynamics
- 4.5–10 L/hr (atleast 35–40 ml/kg/hr) for ultrafiltration sessions lasting 4–8 hrs
- Using bicarbonate based solutions in which K^+ and Ca^{2+} are added
- This is followed by traditional CVVH.

Advantages

- Removes inflammatory mediators: Endothelin I,endogenous cannabinoids,myodepressants
- Improved macrophage function
- Improved hemodynamics:
  - Improved cardiac index, blood pressure and stroke volume
  - Reduced inotropic requirement.

Recent Advances

- Coupled Plasma Filteration Adsorption (CPFA)
- Slow Low Efficiency Extended Daily Dialysis (SLEDD)
- Prolonged Daily Intermittent RRT (PDIRRT)
- Extended Daily Dialysis (EDD)
- Extended Dialysis (ED).

Coupled Plasma Filteration Adsorption (CPFA)

- Separates blood from plasma using plasma filter
- Plasma is passed through synthetic resin cartridge and returned to blood
- Second blood filter used to remove excess fluid and small molecular weight toxins
- Removes almost 100% concentrations of TNF α and Ilβ
- Allows significant reduction of vasopressor dose-ages.

Extended Daily Dialysis (EDD)

- Dialysis performed with standard dialysis equipment
- Performed daily over extended treatment time
- Uses low dialysate and blood flow rates.

Slow Low Efficiency Extended Daily Dialysis (SLEDD)

- Conventional dialysis equipment
- Online dialysis fluid preparation
- Cardiovascular stability
- Reduced anticoagulation requirement
- Decreased costs compared to CRRT
- Phosphate supplementation required.

PHYSIOLOGICAL CHANGES DURING LAPAROSCOPY[1,2,3,6]

Introduction

Three major forces alter the patients physiology during laparoscopic surgery:

- Increase in intraabdominal pressure and volume, which are transmitted to the thorax

- Patient position
- Carbondioxide insufflation.

Effects of Carbon Dioxide Insufflation

- Procedure:
  - Gas is insufflated via a midline percutaneous puncture
  - Rate of insufflation 2–3 L/min
  - Insufflation occurs through a Verres needle
  - Laparoscope is passed into the expanded peritoneal cavity through a subumbilical incision
  - Once pneumoperitoneum is established gas flow is reduced to 200–300 ml/min
  - IAP is maintained at 14–20 mm Hg.
- Effects of carbondioxide pneumoperitoneum:
  - Effects on respiratory system:
    - $PaCO_2$ rises during first 15–30 mins of insufflation to reach a plateau
    - In an apneic patient $PaCO_2$ rises at the rate of 3–6 mm Hg/min
    - Rise in $PaCO_2$ during pneumoperitoneum occurs due to:
      - Absorption of CO_2 from peritoneal cavity due to raised IAP
      - Impairment of pulmonary ventilation
      - Due to patient position.
    - Hypercarbia and acidosis stimulate respiratory center
    - As a compensatory mechanism, minute volume increases
    - Each mm Hg rise in $PaCO_2$ increases ventilation by 2–3 L/min
    - Increase in respiratory rate is higher than increase in tidal volume
    - $PaCO_2$–E_TCO_2 gradient does not change significantly in normal patients
    - In ASA II and III patients $PaCO_2$ increases more than E_TCO_2
    - $PaCO_2$ between 35–45 mm Hg desirable.
  - Effects on cardiovascular system:
    - Direct effects of carbondioxide:
      - Direct myocardial depression causing:
        - Negative chronotropism
        - Increased bathmotropism
        - Stimulates myocardial irritability and arrhythmias
        - Mainly occurs due to acidosis.
      - Vasodilatation:
        - Hypercarbia directly causes vasodilation of all blood vessels, except pulmonary blood vessels
        - Hypercarbia also reduces responsiveness to catecholamines
        - In pulmonary blood vessels hypercarbia causes vasoconstriction.
    - Indirect effects of hypercarbia:
      - Occurs secondary to CNS and sympathoadrenal stimulation
      - Results in:
        - Increased cardiac output and heart rate
        - Increased force of contraction, BP and CVP
        - Reduced peripheral vascular resistance.
  - Effects on central nervous system:
    - CO_2 first used as an anesthetic by Hickman in 1824
    - CO_2 causes nitrous oxide like narcosis at 90–120 mm Hg
    - Slight elevation of $PaCO_2$ causes:
      - Direct cortical depression
      - Increased seizure threshold
    - Further elevation causes cortical and subcortical depression
    - Carbondioxide is the most important factor in regulating of cerebral blood flow:
      - Hypercarbia increases CBF and ICP
      - Each 1 mm Hg rise in $PaCO_2$ increases cerebral blood flow (CBF) by 1.8 ml/100gm/min
  - Effects on regional hemodynamics:
    - Urine output, renal plasma flow and GFR reduce to less than 50% of baseline values
    - Causes bicarbonate retention and compensatory metabolic alkalosis
    - *Reduces splanchnic and hepatic blood flow:* Reduces drug metabolism
    - Increases cerebral blood flow velocity
  - *Neuroendocrine effects:* Increases levels of:
    - Epinephrine, norepinephrine
    - Renin, cortisol
    - Antidiuretic hormone, atrial natriuretic peptide.

Effects of Raised Intra-abdominal Pressure

- Effects on respiratory system:
  - Reduces thoracopulmonary compliance by 30–50%
  - Reduces FRC and aids development of atelectasis due to diaphragmatic displacement

- Increases airway pressures and causes VQ mismatch
- Increases risk of aspiration by reducing esophageal sphincter tone
- Can cause various complications:
  - Subcutaneous emphysema
  - Pneumothorax
  - Capnothorax
  - Carbondioxide air embolism
  - Endobronchial intubation.

- Effects on cardiovascular system:
  - Causes reduced cardiac output due to:
    - Reduction in venous return occurring due to:
      - Pooling of blood in lower limbs
      - Inferior vena caval compression
      - Increased venous resistance.
    - Direct negative inotropism
    - Increase in systemic vascular resistance occurring due to:
      - Raised intrathoracic pressure
      - Stimulation of peritoneal stretch receptors
      - Increased vascular resistance of intraabdominal organs.
  - Increases propensity for arrhythmias:
    - Occurs due to sudden stretching of peritoneum during insufflations
    - This causes increased vagal tone
    - This may result in sinus bradycardia and even asystole.
- Effects on central nervous system:
  - Raised IAP reduces venous return from the upper body
  - This causing venous engorgement
  - This may result in raised ICP and IOP.

Effects of Patient Position

- Usually Trendelenburg position with head down tilt preferred
- Effects on respiratory system:
  - Reduction in FRC, TLV, pulmonary compliance
  - Favors development of atelectasis.
- Effects on cardiovascular system:
  - I*ncrease in CVP, cardiac output and BP:* May precipitate CCF
  - Sudden hypotension on lowering limbs.
- Effects on central nervous system:
  - Causes raised ICP, CBF and IOP
  - Increased incidence of nerve injuries:
    - Brachial plexus
    - Obdurator nerve
    - Femoral nerve
    - Common peroneal nerve.

LAPAROSCOPIC SURGERY[1,2,3,6]

Introduction

Laparoscopy (or peritoneoscopy) is a minimally invasive procedure allowing endoscopic access to the peritoneal cavity after insufflation of a gas (CO_2) to create a space between anterior abdominal wall and viscera.

Advantages

- *Better cosmesis:* Smaller non-muscle splitting incision
- Reduced blood loss intraoperatively
- Lesser incidence of postoperative complications:
  - Pain, respiratory muscle dysfunction
  - Ileus, infection
  - Dehiscence of wound.
- Shorter hospitalization and convalescence
- Lower cost
- Lesser incidence of incisional hernia
- Reduced levels of C-reactive protein and IL_6
- Lesser incidence of hyperglycemia and leucocytosis postoperatively.

Disadvantages

- Narrowed two dimensional visual field
- Need for longer duration of general anesthesia
- Longer learning curve for surgeons
- Increased incidence of PONV:
  - Occurs in 40–75% patients
  - PONV can be reduced with:
    - Propofol based anesthesia
    - *Intraoperative gastric emptying:* Nasogastric tube
    - IV fluid administration perioperatively
    - Droperidol, ondansetron, palanosetron administration intraoperatively.
- Postoperative pain:
  - More of visceral pain:
    - Biliary colic
    - Pelvic spasm
  - *Referred shoulder tip pain common:* Occurs due to intrapleural carbonic acid formation
  - Reduced with preoperative administration of NSAIDs and COX II inhibitors
  - Dexamethasone is effective.

Choice of Gas for Pneumoperitoneum

- Carbon dioxide:
  - Insufflating agent of choice
  - Advantages:
    - Odourless, nontoxic, noncombustible
    - Readily available
    - 20 times more soluble in blood than air
    - *Blood Gas Partition Coefficient (BGPC)* of 0.8
  - Disadvantages:
    - Causes hypercapnea
    - *Gas embolism possible:* Least risk amongst other gases
    - Shoulder pain due to formation of carbonic acid intrapleurally.
- Nitrous oxide:
  - Advantages:
    - Less irritating to peritoneum
    - Lower potential for embolism compared to air/oxygen
    - Reduced risk of arrhythmias and shoulder pain.
  - *Disadvantages:* Supports combustion.
- Oxygen:
  - Causes explosion while using cautery
  - Possibility of gas embolism
  - It was used in 1993.
- Air:
  - Originally used to produce pneumovulgaris
  - High risk of causing air embolism
  - Delayed absorption causes shoulder pain.
- Inert gases:
  - Helium, argon and xenon used
  - Nonflammable but high risk of embolism
  - Avoids hyperoxia and hyperventilation
  - Not safe if gas embolism occurs as less soluble.

Gasless Laparoscopy

- Peritoneal cavity expanded using abdominal wall lift using a fan retractor
- Advantages:
  - Avoids hemodynamic and respiratory consequences of raised IAP and hypercarbia
  - Renal and splanchnic perfusion not altered
  - Incidence of port site metastasis after laparoscopic surgery is reduced
  - Good for patients with severe cardiopulmonary disease.
- Disadvantages:
  - Compromises surgical exposure
  - Increases technical difficulty
  - Combining gasless laparoscopy with low pressure CO_2 pneumothorax (< 5 mm Hg) may improve surgical condition.

Indications

- Urological:
  - Uncomplicated adrenelectomy
  - Nephrectomy.
- General surgery:
  - Cholecystectomy
  - Hernia repair, antireflux surgery
  - Splenectomy, appendicectomy
  - Bowel surgery.
- Gynecological:
  - Tubal surgeries, cystectomy
  - Hysterectomy, endometrial ablation.
- Thoracoscopic and neurosurgery without gas insufflations: Recent advances
- Lumbar discectomies and spine surgeries using anterior approach.

Contraindications

- Raised ICT, intracranial space occupying lesions (ICSOL)
- Ventriculoperitoneal shunt:
  - Continuous ICP monitoring and ventricular drainage may be required
  - Patients are at increased risk of:
    - Gas emboli
    - Shunt obstruction
    - Raised ICT.
- Severe cardiopulmonary disease (including bullae)
- Gastrointestinal disorders:
  - History of previously extensive surgery with adhesions
  - Large intrabdominal/abdominal wall tumor
  - Obesity, peritonitis
  - Diaphragmatic hernia.
- *Coagulopathy, sickle cell disease:* As acidosis precipitates crisis
- Hypovolemia, patient on β blockers
- Patient refusal, inexperienced surgeon
- *Pregnancy:* Was considered contraindication as:
  - Increased risk of damaging gravid uterus
  - Carbondioxide pneumoperitoneum may cause fetal acidosis
  - May cause miscarriage/premature labor.

Laparoscopy in Pregnancy

- Should be done during second trimester
- Ideally done at *less than 23 weeks* to:
  - Minimize risk of preterm labor
  - Maintain adequate surgical field.
- Tocolytics used intraoperatively, to arrest preterm labor
- Avoid blind/closed technique using *Veress needle*
- Use open laparoscopy for abdominal access using *Hasson cannula* to avoid damaging uterus
- Continuous fetal monitoring using transvaginal USG
- Mechanical ventilation adjusted to maintain material physiological alkalosis.

Choice of Anesthetia

- *General anesthesia with ETT and CMV:* Best as:
  - Duration of surgery may be long
  - Patient may be anxious
  - Dyspnea common in awake patient in Trendelenburg position
  - NGT/OGT may be uncomfortable in awake patient
  - Most importantly muscle paralysis essential as:
    - Raised IAP makes spontaneous breathing difficult
    - Provides quieter surgical field and better exposure
    - Bucking causes increased risk of pneumothorax and gas dissection
    - *Coughing increases IAP:* Hollow viscus perforation
    - Necessary to control ventilation to adjust for hypercarbia and acidosis.
- Role of GA with LMA:
  - Advantages:
    - Fewer cases of sore throat
    - Useful for short cases.
  - Disadvantages:
    - Does not protect airway against aspiration
    - Limits ability to apply positive pressure
    - Interferes with use of OGT.
- Role of local anesthesia:
  - Advantages:
    - Quicker recovery
    - Fewer cardiovascular changes
    - Reduced incidence of PONV
    - Allows early diagnosis of complications in awake patient.
  - Disadvantages:
    - Carbon dioxide may irritate peritoneum
    - OGT in awake patient is uncomfortable
    - Disadvantageous if conversion to open laparotomy.
- Regional anesthesia:
  - *May require high level sensory block (T4):* Results in dyspnea
  - OGT not tolerated
  - Hyperventilation causes excessive movement in surgical field
  - Sympathetic denervation results in hypotension and reduced cardiac output
  - *Shoulder tip pain:* Alleviated with opioids/clonidine.

Anesthetic Management

Preoperative Evaluation

- Examination:
  - Look for dyspnea, kyphoscoliosis, body weight distribution, URTI
  - Cardiac function evaluated in patients with heart disease
  - Patients with severe valvular disease and CCF are more prone for cardiac complications than patients with IHD
  - Patients with renal failure:
    - Optimize hemodynamics
    - Avoid nephrotoxic agents.
  - In patients with respiratory diseases, laparoscopy preferable.
- Investigations:
  - CBC, urinalysis, CT, BT, ECG, blood grouping and typing
  - Baseline electrolytes, ABGs, pulse oximetry and pulmonary function tests
  - *BUN and SC:* As possibility of oliguria during long surgery
  - Baseline CXR:
    - *To rule out active disease:* Bulla on X-ray contraindicates laparoscopy
    - Postoperative comparison of acute changes such as:
      - Emphysema
      - Pneumothorax
      - Pulmonary edema.

Preoperative Preparation

- Informed consent:
  - Inform about general complications of surgery

  - Explain about:
    - Specific complications of laparoscopic surgery
    - Postoperative referred pain.
  - Inform and obtain consent for possible laparotomy
- NPO orders:
  - 6 hrs solids
  - 2 hrs clear fluids.
- Premedication:
  - Preoperative sedation with midazolam/morphine
  - *Preoperative NSAIDs:* Reduce postoperative pain and opioid requirements
  - Clonidine and dexmedetomidine:
    - Reduce intraoperative stress response
    - Improves hemodynamic stability.
- Preoperative antibiotic prophylaxis as per hospital protocol
- DVT prophylaxis if long duration surgery
- Antiaspiration prophylaxis if delayed gastric emptying
- Complete bowel preparation preoperatively.

Monitors

- Mechanical monitors:
  - BP measurement
  - ECG with ST segment trending
  - *Pulse oximetry:* Watch for sudden bradycardia and SAN arrest during insufflation
  - Capnography mandatory:
    - E_TCO_2 stabilizes after 15–30 minutes of insufflation
    - If E_TCO_2 increases after 30 mins suspect:
      - Subcutaneous emphysema
      - Pneumothorax.
  - Nerve stimulator, indicators of FiO_2
  - Monitor minute volume and peak airway pressure
  - Temperature monitoring with esophageal probe
  - Arterial line for long surgeries/ASA III patients
  - TEE/Doppler/CVP for hemodynamically unstable patients
  - Serial ABGs to monitor $PaCO_2$–E_TCO_2 difference.
- Clinical monitors:
  - Skin:
    - Monitor color turgor and capillary refill
    - Head, neck and upper chest may become purplish in dependent position
    - Suggestive of hypercarbia.
  - Cornea and conjunctiva:
    - Monitor for edema
    - Important in:
      - Trendelenburg position
      - When oliguria occurs as it may indicate fluid overload.
  - *Upper chest wall:* Monitor for subcutaneous emphysema
  - *Pulse:* For volume and rhythm
  - Urine output:
    - Oliguria may occur despite adequate hydration
    - Common when IAP > 15 mm Hg
    - Also monitor color and concentration of urine.

Position

- Trendelenburg position used for urology
- Dorsolithotomy position used for gynecology
- Head-up position used for upper GI and biliary tract surgeries
- Lateral decubitus used for thoracoscopy, nephrectomy and adrenelectomy
- Precautions:
  - Adequate padding to protect from nerve compression
  - Shoulder braces used in Trendelenburg position
  - Patient tilt limited to 15–20
  - Tilting to be slow and progressive to avoid sudden cardiovascular changes
  - Position of ETT to be checked after any change in position
  - Endobronchial intubation possible in obese patient with Trendelenburg position.

Induction

- Adequate preoxygentaion
- Induction with thiopentone + fentanyl + muscle relaxant like vecuronium
- Rapid sequence induction if delayed gastric emptying present
- Lidocaine 1.5 mg/kg IV 90 seconds before intubation to prevent intubation response
- Insert orogastric/NG tube for:
  - Deflating stomach of air entry during mask ventilation
  - Prevention of regurgitation
  - During pneumoperitoneum, CO_2 continuously inflates stomach.
- Foleys catheter inserted to empty urinary bladder.

Maintenance

- Mixture of oxygen + air + isoflurane used
- Use of air + O_2 + inhalation agent mandates use of higher MAC of inhalation anesthetic
- Intermittent fentanyl and vecuronium boluses may be used to maintain balanced anesthesia
- Careful dosing as closure of laparoscopy procedure may be abrupt
- Avoid halothane as it can cause arrhythmias in the presence of hypercarbia
- TIVA:
  - Propofol maintenance results in fewer postoperative side effects
  - Propofol avoided in fertility procedures as it causes lower pregnancy rates
- Nitrous oxide:
  - Avoided as:
    - It distends bowel and disrupts surgical field
    - May cause increased incidence of PONV.
  - If used, N_2O limited to 50% of inspired mixture.
- *Maintain deep planes:* Bucking causes hollow viscus/blood vessel perforation by trocar
- Intermittent suctioning of OGT as CO_2 continues to diffuse into stomach and distend it
- Intermittent sequential compression stocking to be applied if long surgery
- Maintain intra-abdominal pressure < 15 mm Hg
- Adjuvants:
  - Vagolytic drugs:
    - To be available as bradycardia and sinoatrial arrest possible
    - Usually occurs during sudden peritoneal distension by gas.
- Vasodilating drugs:
  - Nicardipine, 2 blockers, remifentanyl useful
  - Improve hemodynamic stability
- Antiemetics:
  - *Droperidol:* Sedative, long acting and α-inhibitory action
  - *5 HT_3 blockers:* Ondansetron and palanosetron.

Ventilation

- Positive pressure ventilation preferred
- Maintain $ETCO_2$ between 35–40 mm Hg
- This requires a 15–25% increase in minute volume
- Increase in respiratory rate rather than tidal volume preferable in patients with COPD/spontaneous pneumothorax.

Hemodynamics

- Large bore angiocatheter placed due to possibility of major hemorrhage
- Minimal third space loss, blood loss and insensible water loss
- Maintenance fluids:
  - 2.5–4 ml/kg/hour of lactated Ringers ideal
  - Despite adequate hydration oliguria common
  - Volume of fluids infused may be mistakenly increased
  - This may lead to postoperative pulmonary edema
  - Thus restrict fluids to 2.5–4 ml/kg/hr as after deflating abdomen diuresis occurs.
- *Retained intraperitoneal saline*:
  - Volume of retained intraperitoneal saline should be added to maintenance fluids
  - Calculated as (Volume of fluids for irrigation–volume of fluid in suction containers).
- Vasodilators:
  - Nicardipine, 2 blockers, remifentanil useful
  - These reduce cardiovascular changes of pneumoperitoneum.
- Bradycardia common at the time of peritoneal distension.

Extubation

- Extubation might be delayed as high concentration of inhalation agents must be used
- Delayed extubation if patient has:
  - Edema
  - Venous congestion
  - Duskiness of head and neck
  - *Tongue, conjunctival and lid edema:* Keep head end up till edema subsides
  - *Oliguria:* Wait till diuresis has begun.

Postoperative Care

Monitors

- *Monitor SpO_2:* Supplemental oxygen mandatory even in healthy patients as O_2 demand increases after laparoscopy
- Monitor BP as hemodynamic changes induced by pneumoperitoneum outlast duration of pneumoperitoneum
- Temperature, urine output, ABG monitoring.

Management

- PONV:
  - 40–75% incidence

  - Treated with 5 HT_3 inhibitors, scopolamine and droperidol.
- *Chest X-ray:* Immediate chest X-ray taken if:
  - Respiratory distress
  - Subcutaneous emphysema
  - Suspected pneumothorax
  - Pulmonary edema
  - History of cardiac disease.
- Remove Foleys catheters and OGT if patient fully awake, stable and voiding adequately.

Analgesia

- Multimodal analgesia with opioids and NSAIDs
- Intraoperative peritoneal LA admininistration useful
- Wound site infilteration reduces incisional pain
- *Shoulder pain:* Opioids, clonidine.

Complications

- Post Operative Nausea and Vomiting (PONV)
- Shoulder tip pain
- Injuries from instruments:
  - Abdominal wall bleeding
  - Blood vessel/hollow viscus perforation, peritonitis
  - Subcutaneous emphysema, wound infection, hernia at trocar site
  - Hemorrhage
  - Staples and clips can causes nerve entrapment
  - Thermal injury from cautery/lazer.
- Complications of pneumoperitoneum:
  - Raised IAP:
    - Bowel ischemia
    - Omental/bowel herniation
    - Gastric regurgitation
    - IVC compression.
  - Reduced venous return:
    - Hypotension
    - Raised intrathoracic pressure.
  - Airleak syndromes:
    - Mediastinal emphysema
    - Subcutaneous emphysema
    - Capnothorax
    - Pneumothorax.
  - Air embolism
  - Postoperative nausea and vomiting (PONV)
  - Bradycardia, shoulder tip pain
  - Endobronchial intubation.
- Complications of hypercarbia:
  - Acidosis
  - HTN, tachycardia
  - Arrhythmias
  - Precipitation of sickle cell crisis
  - Raised ICT.
- Complications of Trendelenburg position:
  - Raised ICP, IOP, glaucoma
  - Corneal and conjunctival edema
  - Retinal hemorrhagge, retinal detachment
  - Upper airway edema
  - Hypoxemia, ventilation perfusion mismatch
  - Brachial plexus injury
  - Endobronchial intubation
  - Femoral and obdurator N injuries.
- Late complications:
  - Bowel obstruction due to injury, cautery, burns
  - Incisional hernia
  - Adhesions, DVT
  - Nerve injuries
  - Bowel necrosis
  - Cutaneous metastasis at port site.

PHEOCHROMOCYTOMA[1,2,3,6,11,21]

Introduction

- These are functional catecholamine secreting tumors of chromaffin tissue derived from neural crest
- Tumors are called *pheochromocytoma* when they are present in adrenal medulla
- When tumors are located extra-adrenally, they are called *paraganglionomas.*

Incidence

- Account for 0.1–1% of all cases of hypertension
- In adults 55–60% occur in females
- In children 70% occur in boys.

Syndromic Association

Can occur as part of:

- *MEN 2A syndrome (Sipples syndrome):*
  - Parathyroid adenomas
  - Medullary carcinoma of thyroid
  - Pheochromocytoma
- *MEN 2B syndrome (Gordins syndrome):*
  - Medullary carcinoma of thyroid
  - Pheochromocytoma
  - Marfanoid habitus, mucosal neuroma
  - *Von-Hippel-Lindau syndrome*
  - Hemangioblastoma of retina, cerebellum
  - Pheochromocytoma

- *Neurofibromatosis type I (Von-Recklinghausens disease):*
  - Neurofibromatosis
  - Pheochromocytoma
- *Familial paraganglionoma syndrome*
- Nonsyndromic familial pheochromocytoma.

Location

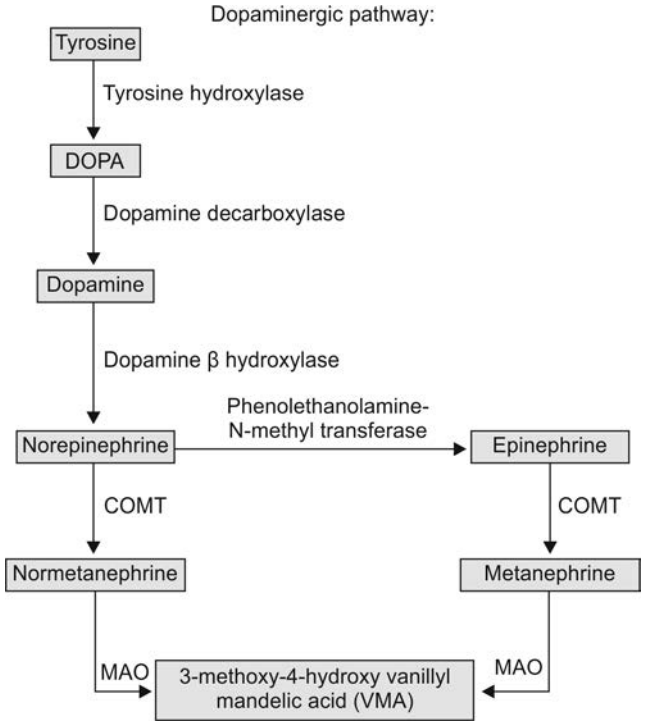
- Pheochromocytomas:
  - Adrenal medulla
  - Sympathetic ganglia.
- Paraganglionomas:
  - Thorax, right atrium
  - Urinary bladder, spleen, broad ligament of ovary
  - *Organs of Zuckerkandl* at aortic bifurcation.

Rule of Ten

- 10% of tumors occur in children
- 10% familial
- 10% malignant
- 10% extradrenal
- 10% bilateral.

Pathophysiology

- Pheochromocytomas predominantly secrete epinephrine and norepinephrine
- Malignant pheochromocytomas may secrete dopamine also.



Clinical Features

- Most commonly occur in young to mid-adult life
- In adults it is more common in females
- Considered greatest mimic due to varied clinical presentation
- Hypertension:
  - 5–15% cases are normotensive
  - Seen in 90% cases, intermittent or continuous
  - HTN with narrow pulse pressure and reflex bradycardia if norepinephrine secreting tumor
  - HTn with raised SBP, low DBP and tachycardia if epinephrine secreting tumor
- *Paroxysms/pheochromocytoma crisis:*
  - Presents with classical triad of headache, palpitation and sweating
  - Symptoms:
    - Fever due to raised BMR
    - HTN or orthostatic hypotension
    - Hyperglycemia, polyuria, polydipsia
    - Headache, palpitation, dyspnea, weakness
    - Panic attacks, blurred vision, weight loss
    - Atypical manifestations like:
      - Acute abdomen secondary to hemorrhagic rupture
      - *Catecholamine cardiomyopathy:*
        - Congestive cardiac failure, LVF
        - Myocardial infarction, acute pulmonary edema, arrythmias.
- Symptoms precipitated by:
  - Palpation of abdomen
  - Uterine contraction during labor
  - Defecation, changes in posture
  - Micturition (if tumor present in bladder)
  - Drugs:
    - Tricyclic antidepressants
    - MAO inhibitors
    - Phenothiazines, droperidol
    - *Metaclopramide*, naloxone
- Complications:
  - Patients are at high risk for cerebrovascular accidents
  - Rhabdomyolysis due to muscle ischemia from vasoconstricted state.

Indicators of Suspicion

- Family history of MEN/pheochromocytoma
- Paroxysmal headache/sweating and palpitation
- HTN at an early age (< 20 yr) or if resistant to therapy
- Unexplained grade III/IV retinopathy

- Orthostatic hypotension in patients who are not on antihypertensive therapy
- Incidentaloma in adrenal gland
- *Carneys triad:* Coexistence of three types of neoplasms in young women:
  - Gastric stromal tumor
  - Pulmonary chondromas
  - Extra-adrenal paraganglionomas.

Differential Diagnosis

- Thyrotoxic crisis
- Malignant hyperthermia
- Acute anxiety neurosis
- Toxemia of pregnancy.

Diagnosis

- Nonspecific investigations:
  - Raised hematocrit due to reduced intravascular volume and hemoconcentration
  - Hypercalcemia due to ectopic parathyroid related protein
  - Uncontrolled hyperglycemia
  - Raised BUN and serum creatinine due to myoglobinuric renal failure
  - ECG:
    - LVH, LBBB/RBBB
    - T wave changes, MI
    - Tachyarrythmias.
  - *Chest X-ray:* Cardiomegaly
  - *Echocardiography:* LVH, catecholamine cardiomyopathy.
- Specific investigations:
  - Urine 24 hour assay of adrenal hormones:
    - Considered as better screening test
    - Stat samples may have normal values as catecholamine secretion is paroxysmal
    - Urinary metanephrine is *most specific*
    - Normal values:
      - *Catecholamines:* Less than 100–150 µg/day
      - *Metanephrine:* Less than 1.3 mg/day
      - Vanillyl mandelic acid less than 7 mg/day.
    - In pheochromocytoma:
      - *Catecholamines:* More than 250 µg/day
      - *Metanephrine:* More than 1.3 mg/day
      - *Vanillylmandelic acid:* More than 14 mg/day.
  - Plasma catecholamines: Stat sample:
    - *Normal value:* Less than 1 µg/ml
    - *Pheochromocytoma:* More than 1 µg/ml.
  - Pharmacological tests:
    - Provocative test:
      - No longer used
      - Glucagon, histamine, tyramine.
    - Suppression test:
      - With clonidine and pentolinium
      - Used when other tests are negative but very strong clinical suspicion exists.
    - Tumor localization:
      - *CT scan:* Identities 90% tumors > 1 cm diameter
      - *MRI:* Useful in pregnancy as less radiation
      - Selective venous catheterization:
        - Useful in locating multiple extraadrenal tumors
        - Blood samples taken from vein draining tumor
        - Catecholamine levels are measured in these samples.
      - *Arteriography:* Rarely used as contrast releases catecholamines
      - MIBG scintigraphy:
        - With metaiodo-benzyl-guanethidine
        - To diagnose ectopic and multiple tumors
        - Guanethidine taken up by chromaffin granules
        - Tumor is then visualized with gamma camera.
      - *PET scan:* For extraadrenal tumors
      - *Ultrasonography and IV pyelography:* Insensitive.

Preoperative Preparation

- Have to be adequately prepared before surgery to resolve volume contracted state
- α-blockade should always precede β blockage to avoid unopposed vasoconstriction
- α-adrenergic blockage:
  - *Aim:* To restore blood volume status by reversing vasoconstriction
  - Duration:
    - At least 2 weeks before surgery for complete restoration of blood volume

- If ST-T wave changes are present:
  - Long term α-blockade (1–6 months) recommended
  - This produces clinical and ECG resolution of catecholamine cardiomyopathy.

– Drugs used:
- Phenoxybenzamine:
  - Provides nonselective noncompetitive irreversible α-blockade
  - Start with 10 mg bid/tid
  - Increase 10–20 mg every 3 days until maximum of 80–250 mg/day
  - Longer duration of action:
    * Facilities BID dosing
    * α-blockade may persist in postoperative period causing hypotension
  - Somnolence, headache, stuffy nose are side effects.
- Prazosin:
  - Started at 1 mg Q8H
  - Gradually increases dose till maximum of 8–12 mg/day
  - *First dose phenomenon*, so given at bed time.
- Doxazosin, terazosin
- Doxazosin allows once daily dosing
- $MgSO_4$, dexmedetomidine, calcium channel blockers, clonidine also used.

- β adrenergic blockade:
  – Commenced only after α-blockade has started
  – Only used if persistent tachycardia (> 100 bpm) or arrhythmias
  – β blockade may precipitate CCF in catecholamine cardiomyopathy
- Rapid IV α-blockade:
  – Done over atleast 3 days
  – Day 1:
    - Phenoxybenzamine 1 mg/kg in 500 ml 5% dextrose
    - Given over 2 hrs
    - Oral propranolol given if heart rate increases beyond 120 bpm.
  – Day 2:
    - Phenoxybenzamine 1–1.5 mg/kg in 500 ml of 5% dextrose
    - Given over 2 hours
    - Oral propranolol given if heart rate increases beyond 100 bpm.
  – Day 3:
    - Phenoxybenzamine 1.5–2 mg/kg in 500 ml 5% dextrose
    - Given over 2 hours
    - Oral propranolol given if heart rate increases beyond 100 bpm.
- α-methyl tyrosine:
  – Inhibits tyrosine hydroxylase which is rate limiting step in catecholamine biosynthesis
  – Reduces catecholamine production and secretion
  – Reserved for patients with metastatic disease or in whom surgery is contraindicated
  – Dose: 0.5–4 gms/day.

Roizens Criteria

Used for assessment of adequacy of preparation:
- No inhospital BP reading more than 160/90 mm Hg for 24 hrs prior to surgery
- Orthostatic hypotension with standing BP > 80/45 mm Hg
- ECG free of ST-T changes for 1 week prior to surgery
- No more than 1 ectopic beat every 5 mins
- *Other indicators:* Serial hematocrit, RBS control, improved psychological status.

Premedication

- NPO orders
- Informed consent
- *Sedatives/anxiolytics:* Useful as they prevent catecholamine release
- *Avoid use of:*
  – Morphine and pethidine as they cause histamine release
  – Metoclopramide and droperidol as they cause catecholamine release
  – Atropine as parasympathetic block causes unimposed sympathetic NS activity.
- Steroid supplementation if bilateral adrenelectomy planned
- *Adequate volume expansion:* Careful in patients with cardiomyopathy
- Drug to be avoided:
  – *Morphine, pethidine, curare, atracurium:* Histamine releasers
  – *Succinylcholine:* Catecholamine release
  – *Pancuronium:* Sympathomimetic effect
  – *Droperidol, metaclopramide:* Inhibits catecholamine reuptake and potentiates their action
  – *Halothane:* Sensitizes myocardium to catecholamines.

Induction

- Adequate preoxygenation
- Induction with etomidate/benzodiazepine/thiopentone/propofol
- Fentanyl as opioid and vecuronium as muscle relaxant
- Adequate depth of anesthesia before intubation is very important
- Intubation response:
  - IV lidocaine 1–1.5 mg/kg IV
  - Nitroglycerine infusion as alternative
  - Might be more severe as more catecholamine stores present in N terminals due to reuptake of already increased catecholamines
- Avoid use of:
  - *Morphine pethidine, atracurium:* Histamine release
  - *Pancuronium:* Sympathomimetic effect
  - Succinylcholine:
    - Releases catecholamines by increasing intra-abdominal pressure
    - Also has direct effect on sympathetic ganglia.

Maintenance

- Maintenance with O_2 with N_2O and isoflurane for balanced anesthesia
- Opioids (fentanyl/alfentanyl) with vecuronium as intermittent boluses
- Inhalational agents:
  - Isoflurane/sevoflurane preferred
  - Desflurane use is controversial
  - Avoid halothane as it sensitizes myocardium to catecholamines.
- Avoid use of:
  - Pancuronium, metoclopramide, droperidol
  - Ketamine, ephedrine
- Avoid hypoventilation as it causes sympathetic nervous system stimulation
- Handling of tumor may cause life threatening hypertensive crisis
- Hypotension may occur following ligation of venous supply to tumor.

Monitoring

- E_TCO_2, pulse oximetry, ECG monitoring
- IBP monitoring is *mandatory*
- Urinary catheter, temperature probe may be used
- Urinary output measurement hourly (≥ 0.5 ml/kg/hr)
- CVP and pulmonary wedge pressure in patients with cardiomyopathy
- Echocardiography may be done
- *Arterial blood gases, blood sugar:* Done second hourly.

Hemodynamics

- Hypertensive crisis:
  - Occurs during:
    - Intubation
    - Tumor manipulation for tumor removal
    - Also due to hypocalcemia, hypercarbia
    - If SBP ≥ 200 mm Hg for more than 1minute, treat HTN.
  - Drugs used:
    - *SNP:* 0.5–10 µg/kg/min as infusion
    - *NTG:* 0.5–10 µg/kg/min as infusion
    - Phentolamine 2–5 mg IV bolus or as infusion.
- Control of hypotension:
  - Occurs following ligation of venous drainage of tumor
  - Prevented by preoperative preparation
  - Treated by volume expansion and vasopressors like dopamine and phenylephrine.
- Laparoscopic surgery increases IAP and hypercarbia which cause catecholamine release
- Control of tachyarrhythmias:
  - β blockers:
    - Propranolol 1 mg increments
    - Atenolol, labetolol
    - *Esmolol:* Preferred as half life of 9 minutes.
  - *Amiodarone:* Supraventricular arrhythmias especially with CCF
  - *Lidocaine:* For ventricular arrhythmias.

Postoperative Care

Monitor

- Pulse oximetry
- *BP for hypotension/hypertension:* HTN more common
- Blood sugar levels
- Urinary output, ABG.

Analgesia

- Multimodal approach safest
- Epidural analgesia useful
- NSAIDs can be used as adjuvants
- *Opioids:* Lower doses preferred as patients will be somnolent.

Complications

- Hypertension:
  - Common usually upto 3 days postoperatively

  - If it persists more than 2 wks postoperatively, measure urinary plasma catecholamine levels
  - Done to rule out residual disease
  - Usually, catecholamine levels reduce to normal within 72 hrs
  - Other causes of HTN:
    - Pain, urinary retention
    - Hypoxia, hypercarbia.
- *Hypotension:* Occurs due to:
  - Sudden catecholamine withdrawal post surgery
  - Persistent α-blockade
  - If acute, it may indicate intra-abdominal hemorrhage
- Hypoglycemia:
  - Occurs due to disappearance of inhibition of β-cell function by catecholamines
  - This causes increased insulin secretion.
- Somnolence:
  - Commonly occurs for upto 48 hrs postoperatively
  - Occurs due to catecholamine withdrawal post surgery
  - Normal opioid doses may cause respiratory depression.

Role of Regional Anesthesia

- Epidural preferred over spinal anesthesia as:
  - Sudden drop in SVR with hypotension avoided
  - Level of block can be extended
  - Duration can be prolonged
  - Epidural anesthesia reduces catecholamine release.
- Epidural preferred over GA for hemodynamic benefits as:
  - Deep GA must be given to prevent tachycardia and HTN
  - This can cause myocardial depression
  - Vasopressors more effective during epidural rather than GA.

Pheochromocytoma in Pregnancy

- Investigations:
  - Difficult to localize the tumor with radiological studies due to risk of fetal radiation exposure
  - MRI is safest modality.
- Supine hypotension syndrome:
  - Aortocaval compression effects may be aggravated by volume constricted state
  - Also, left lateral tilt might stimulate catecholamine release by uterine compression of the tumor.
- Preoperative preparation:
  - α-blockers considered safe
  - α-blockade commenced before β-blocker therapy
  - β-blockers might cross placenta and cause fetal bradycardia and hypotension.
- Cesarean section:
  - *Vaginal delivery absolutely contraindicated*
  - Surgery for pheochromocytoma done during 1st trimester/3rd trimester at the time of caesarean section
  - Epidural anesthesia preferred over GA/SAB.
- Uterotonics:
  - Following delivery syntocinon given safely
  - Ergonovin/prostaglandin avoided as may precipitate hypertensive crisis.
- Magnesium sulfate:
  - Can be used to maintain cardiovascular stability
  - Hypomagnesemia occurs during pregnancy as increased utilization of magnesium occurs
  - Treated with 40–60 mg/kg IV bolus followed by 2 g/hr IV infusion
  - Magnesium not deleterious to fetus.

CLEFT LIP AND PALATE[1,2,3,6,11,21]

Introduction

Commonly occurring anomaly due to defective embryological development of the lip and palate.

Incidence

- *Occurs in 1:* 300–600 live births
- *Isolated cleft palate:* 1:2000 live births
- Cleft present in both lip and palate in 50% cases
- *Cleft lip with or without palate:* 1:1000 births (more common in boys)
- Isolated cleft palate more common in Asian girls.

Development

- Congenital clefts of upper lip occur due to failure of fusion of maxillary with medial and lateral nasal processes
- Face develops between 4–7 weeks of fetal life
- Palate development completed at 12 weeks
- Anatomy:
  - Cleft palate is divided into prepalatal and postpalatal clefts
  - The incisive foramen marks the boundary between the two
  - Prepalatal cleft involves anterior palate, alveolus, lip, nostril floor and ala nasi

  - Postpalatal cleft may extend from soft and hard palate to incisive foramen
- *Most common* cleft of palate is left complete cleft of pre and palatal structures
- Second most common is midline cleft of all soft palate and part of hard palate without a cleft is prepalatal area.

Pathophysiology

- Pharynx communicates more extensively with nasal fossae and oral cavity
- Thus, complex mechanisms of swallowing, breathing, hearing and speech are impaired
- Difficulty in feeding:
  - Presence of cleft lip and palate in neonates causes feeding difficulty
  - Presence of cleft makes creation of negative pressure difficult
  - Thus, baby cannot suck
  - Breast feeding is improbable and bottle feeding difficult.
- Chronic middle ear effusion/infection:
  - Abnormal anatomy of nasopharynx effects Eustachian tube function
  - Palatopharyngeus muscle function is impaired owing to the cleft palate
  - ASOM, SOM occur commonly
  - These cause conductive hearing loss.
- Abnormal speech:
  - Nasal septation between food and air is absent
  - Secondary defects in growth of ala nasi and velopharyngeal function can occur
  - This causes rhinolalea aperta
  - Speech of these children is typically nasal
  - Usually unable to pronounce *plosives (p, k, d, t) and fricatives (s, f).*

Conditions Associated with Cleft Lip and Palate

- Limb and ear deformities
- Club foot
- *Pierre-Robins syndrome:* Micrognathia, cleft palate, respiratory and digestive disorders
- *Downs syndrome*
- *Velocardiofacial syndrome*
- *Goldenhaar syndrome (facioauriculovertebral syndrome)*
- *Treacher-Collins syndrome:*
  - Antimongoloid slant of eyes
  - Eyelid colobomas (outer part of lower lid)
  - Pointed nasal prominence
  - Small oral cavity with normal sized tongue
  - Dental malocclusion
  - High arched palate/cleft palate
  - Increased anterior facial height
  - Hypoplastic cheeks, zygomatic arch, mandible
  - Microtia with possible hearing loss.

Indication and Timing of Closure

- Cleft lip:
  - Usually done at 3 months
  - Repaired early to improve scar and assist maternal bonding.
- Cleft palate:
  - Closure of soft palate at 6–9 months
  - Secondary closure of residual hard palate at 15–18 months of age.
- This repair provides total palatal closure before speech evolves
- If soft palate is repaired at the time of lip repair, additional anesthetic avoided.

Rule of Ten

Operate child when:
- Age less than 10 weeks
- Weight approximately 10 pounds
- Hemoglobin: 10 gm/dl or more
- WBC count ≤ 10,000/µl.

Preoperative Evaluation

- History of:
  - Repeated droplet infection:
    - Respiratory, ear, gastrointestinal infections
    - Treat with antibiotics
  - *Feeding problems:* Low body weight, anemia
  - Previous surgery or anesthetic exposure
  - Previous history of aspiration
  - Immunization and development milestones
- Investigations:
  - Complete blood count, blood grouping and cross matching
  - Bleeding time, clotting time
  - X-ray mandible, X-ray chest
  - Echocardiography if congenital heart disease suspected.

Preoperative Preparation

- NPO orders:
  - Clear fluids 2 hrs
  - Breast milk 4 hrs
  - Cows milk and solids 6 hrs.

- Informed consent
- Specific consent to be taken for suppository use
- 10% glucose solution started to avoid hypoglycemia at 4 ml/kg/hr
- Premedication:
  - Syrup phenergan 0.3 ml/kg 90 minutes prior to surgery
  - Syrup diazepam 0.2 mg/kg 1 hour prior to surgery
  - Oral midazolam 0.25–0.5 mg/kg 30 minutes prior to surgery as alternative
  - Atropine 20 µg/kg IM 30 minutes before surgery.

Induction

- *Two techniques of induction:* Inhalational induction or IV induction
- Inhalation induction:
  - Used when difficult airway suspected or when IV access is absent
  - Preoxygenate for 3–5 mins
  - $O_2 + N_2O$ + halothane/sevoflurane used
  - Concentration is slowly increased
  - Once limb is relaxed, IV line taken with 22 G cannula.
- Intravenous induction:
  - Used when IV access is available
  - Preoxygenate for 3–5 minutes
  - IV ketamine 1–2 mg/kg
  - IV thiopentone 4–5 mg/kg double diluted given slow intravenously
  - Succinylcholine 1–1.5 mg/kg or vecuronium 0.1 mg/kg IV as muscle relaxants.

Intubation

- Timing of intubation:
  - Deep intubation with child breathing spontaneously or,
  - Intubation following muscle relaxation.
- Laryngoscopy:
  - Straight forward in patients with cleft lip
  - In patients with cleft palate, insert gauze pack in cleft before laryngoscopy
  - Intubation done with a small, Millers laryngoscope
  - *Retromolar intubation:*
    - Done if left sided cleft palate or bilateral cleft with protruding premaxilla
    - In such cases slant laryngoscope from incisor, support on left molar
    - ET tube inserted through right cleft (retromolar intubation).
- Endotracheal tube:
  - RAE tube *(Ring-Adeyer-Ellwyn tube)*
  - Reinforced tube used, which resists compression
  - ET tube secured in midline after confirming air entry to avoid distortion and maintain symmetry.
- Throat is packed and eyes are protected
- NG tube inserted after intubation to empty stomach of gas and secretions which are removed before preparation of surgical field.

Position

- *Slight head up:* Reduces risk of aspiration
- *Neck extended:* Reduces bleeding
- *Shoulder support:* For better exposure.

Monitoring

- Heart rate, pulse oximetry, E_TCO_2
- Precordial stethoscope
- ECG, temperature, urine output
- *Blood loss:* Lesser compared with other surgeries.

Maintenance

- O_2 + N_2O + sevoflurane/isoflurane + fentanyl (1 µg/kg) + NDMR
- Clonidine and ketamine can be used as opioid sparing techniques
- Adrenaline infilteration of 1: 2,00,000 used to control bleeding
- Thus, halothane use is not advised as it sensitizes heart to arrhythmias
- *Dingmans gag* used by surgeon causes tongue swelling postoperatively
- Dexamethasone 0.1 mg/kg given to avoid postoperative tongue swelling
- IV fluid management using 4:2:1 rate *(Halliday formula).*

Extubation

- Reversal of NDMR with 0.02 mg/kg atropine and 0.06 mg/kg neostigmine IV
- Extubation after early/deep and proper suctioning (done gently)
- Fully awake extubation in head down and lateral decubitus position
- Nasal stents to maintain airway patency.

Postoperative Care

Monitoring

- Pulse oximetry and apnea alarm
- Blood pressure

- Urine output
- ABG with blood sugar levels.

Postoperative Management

- Elbow restraints for some days to prevent child from taking his hands to operation site
- Feeding started as soon as child is fully awake with clear water and half diluted milk.
- *Logans bow:*
  - Traction suture placed through tongue and tied loosely
  - Traction on the suture stimulates respiration
  - Done to prevent child from going into deep sleep and apnea
  - The suture is removed when child leaves PACU.

Analgesia

- LA infilteration by surgeon
- Regional blocks:
  - Infraorbital/palatine/nasopalatine block
  - Consider infraortbital nerve block for cleft lip repair
  - Nasopalatine with palatine block done for palatal surgery.
- *NSAIDs:* Paracetamol suppository/ketorolac (0.5 mg/kg IV up to maximum 30 mg)
- Opioid analgesics fentanyl (1 µg/kg IV) or morphine (0.1 mg/kg IV).

Complications

- Laryngeal edema/spasm (1 mm laryngeal edema causes 60% narrowing)
- Delayed recovery
- Respiratory depression
- Airway obstruction due to:
  - Closed palate
  - Small mandible pushing tongue into pharynx
  - Edema
  - Blood and residual anesthesia.
- Bleeding
- Hypothermia
- *Abbe-Estlander flap:*
  - Taken from lower lip to upper lip
  - Done to make up for tissue loss in bilateral cleft lip
  - Thus, problems of closed mouth is common like vomiting and aspiration.

ANESTHESIA FOR TONSILLECTOMY[1,2,3,21]

Introduction

Tonsillitis is infection of tonsil which are aggregates of lymphoid tissue, present on both sides of throat.

Anatomy

Waldeyers ring is formed by:

- Tubal tonsils
- Palatine tonsils
- Lingual tonsils
- Adenoid.

Indications

- Infections:
  - Chronic tonsillitis
  - Recurrent acute tonsillitis (more than 3 episodes of tonsils/adenoids per year)
  - Peritonsillar abscess unresponsive to medical therapy
  - Recurrent chronic otitis media/SOM
  - Chronic tonsillitis with streptococcal carrier state unresponsive to antibiotics with valvular heart disease.
- Obstruction:
  - OSAS, severe dysphagia
  - Sleep disorder
  - Cardiopulmonary complications due to hypertrophy
  - Dental malocclusion/affecting facial growth.
- Others:
  - Malignancy of tonsils for biopsy/resection
  - Persistent halitosis unresponsive to therapy due to chronic tonsillitis
  - Chronic nasal obstruction with rhinorrhea and obligate mouth breathing.

Contraindications

- Acute tonsillitis, abnormal coagulation people
- Uncorrected partial/complete cleft palate as adenoids help fill retropharyngeal gap and facilitate speech.

Methods for Tonsillectomy

- Conventional *cold steel* tonsillectomy:
  - Tonsillar snare used as dissector
  - More intraoperative bleeding
  - Less postoperative pain and post-tonsillectomy bleeding.

- Hot surgical techniques:
  - Bipolar radio frequency
  - Electrocautery, ultrasonic dissection
  - Laser powered microdebrider:
    - Less intraoperative bleeding
    - Increased postoperative pain and bleeding.

Clinical Features

- Pain in throat, fever, tachycardia
- Dysphagia/odynophagia, failure to thrive
- Mouth breathing, inflamed tonsil with discharge
- Cervical lymphadenopathy
- Corpulmonale:
  - If long standing hypoxia and hypercapnea due to airway resistance
  - Cardiac enlargement is reversible with digitalis and tonsillectomy.
- Two most common levels of obstruction during sleep are at soft palate and base of tongue
- Long standing hypoxia and hypercapnea:
  - This leads to increased airway resistance
  - This causes pulmonary artery constriction and pulmonary HTN
  - Ultimately right heart failure and cor-pulmonale results.

Anesthetic Considerations

- Shared airway
- Difficult airway if enlarged lymphoid tissue
- Obstruction of ETT/LMA by *Boyle-Davies* gag used by surgeons
- Maintain deep planes of anesthesia with rapid recovery of consciousness and reflexes.

Preoperative Assessment

- History:
  - *History of fever, pain, dysphagia:* Defer surgery
  - *Bleeding disorders:* Easy bruising/bleeding gums/epistaxis
  - Family history of bleeding disorders/intake of aspirin/NSAIDs
  - History of allergy/GERD sinusitis
  - History of rhinorrhea/post-nasal drip
  - History of anemia/sickle cell disease
  - History of antibiotics/antihistaminics/NSAIDs /previous surgeries.
- Examination:
  - Wheezing/rales for LRTI
  - *Inspiratory stridor/prolonged expiration:* Partial airway occlusion
  - *Loose/missing teeth:* Care during mouth gag application
  - Enlarged and tender lymph nodes (≥ 2 cms)
  - Tonsillar/pharyngeal exudate
  - Thorough airway assessment
  - *Adenoid facies:*
    - Long face, flat mid-face, open mouth
    - Retrognathia, high arched palate, hyponasal speech.

Investigations

- Complete blood count, blood grouping and typing
- Clotting profile, chest X-ray
- ECG if recent URTI/pneumonia/bronchitis/cor-pulmonale.

Premedication

- Avoid sedation if history of OSAS/airway obstruction
- In older children/adults, 0.05 mg/kg midazolam PO if age ≥ 2 years
- IV access taken after EMLA cream application
- 0.02 mg/kg glycopyrollate given IV
- IV fluids if dehydrated due to odynophagia
- Antibiotics before surgery if acute tonsillitis present
- Consent for rectal analgesia.

Technique of Anesthesia

- Local anesthesia:
  - Rarely done under local anesthesia
  - Used with GA for postoperative analgesia and bleeding
  - No single nerve block is adequate as multiple areas of nerve supply to tonsils
  - Following topical anesthesia of mucus membrane, three LA injections into:
    - Region of upper pole
    - In anterior pillar
    - In lower pole (between capsule and pharyngeal wall).
  - Care to prevent injection into blood vessel as it is a very vascular area
  - If local anesthetic spreads to glossopharyngeal nerve, airway reflexes may lost.
- *GA with ETT:* Most commonly used
- *GA with LMA:* Flexible LMA can be used
  - Advantages:
    - Avoids muscle relaxants
    - Reduces aspirations of blood

  - Reduces laryngospasm/bronchospasm/desaturation
  - *Requires light plane of anesthesia:* Faster recovery.
- Disadvantages:
  - Difficult to control situation if airway is lost during surgery
  - May get compressed on opening mouth gag
  - Access to inferior pole is difficult
  - Maneuvers to aid insertion:
    - Head extension
    - Lateral insertion of LMA
    - Pressure on tip of LMA with index finger
    - Anterior displacement of tongue
    - Use of laryngoscope.

Monitors

- Pulse oximetry
- $ETCO_2$
- NIBP
- ECG
- Precordial stethoscope
- Urine output
- Temperature.

Induction

- *Intravenous:* Propofol + fentanyl with or without short acting NDMR
- Inhalational:
  - In uncooperative children with poor venous access
  - *Difficult/slow in significant OSAS:* Also may cause hypoxia
- Intubation:
  - South facing ETT (nasal ETT used in some adults)
  - Intubate under deep inhalation/after administering muscle relaxants
  - Nasotracheal intubation may be used in adults as adenoids is absent
  - Secure ETT in midline and ensure that it lies correctly in Boyle Davies gag
  - Pack throat with petroleum gauze to prevent aspiration
  - Limit cuff pressure to avoid postextubation croup.

Position

- Eyes protected especially if gag is used
- Head extended and held by a sand bag/bolster kept under shoulder
- Mouth kept open by Boyle-Davies gag
- Advantages:
  - Direct view of tonsils
  - Posterior pharynx forms sump into which blood drains.

Maintenance

- Oxygen + N_2O + isoflurane 1 MAC
- Fentanyl is given in intermittent boluses
- Maintain adequate depth to prevent reflex induced HTN, tachycardia and bucking/straining during surgery
- Intraoperative dexamethasone 0.15 mg/kg IV to reduce edema
- Spontaneous ventilation/CMV with muscle relaxants can be used
- Care to prevent accidental extubation/aspiration of blood and secretions if throat pack displaced
- LA + adrenaline injected in tonsillar fossa:
  - Gives bloodless field
  - But, increases postoperative pain
  - If large volume is used, respiratory obstruction/aspiration can occur due to bilateral glossopharyngeal nerve block.

Hemodynamics

- Instrumentation of postnasal space may cause bradycardia
- Blood loss difficult to assess
- IV fluids like RL/DNS to maintain volume status
- Blood transfusion may be required in some cases.

Extubation

- No difference in rate of complications between extubating in deep/awake planes
- Fully awake plane with complete return of reflexes preferred
- Head down tilt with lateral position
- Avoid blind suctioning of pharynx to avoid trauma
- Suction done under vision after removal of throat pack: *Coroners clot* may result otherwise
- Antiemetic like ondansetron 0.15 mg/kg IV
- Neostigmine 0.05 mg/kg + atropine 0.01 mg/kg IV
- Remove LMA when patient opens eyes to command
- Transfer to recovery room in tonsillar position with oxygen inhalation.

Postoperative Care

Pain

- Moderate to severe pain present after tonsillectomy

- Oral syrup/rectal paracetamol and NSAIDs (do not increase bleeding)
- LA infilteration into tonsillar bed
- Opioids
- Avoid aspirin to prevent risk of bleeding
- Increased pain if laser or electrocautery used
- Pain is less in those who have had sharp surgical dissection and ligation of blood vessels.

Management

- IV fluid administration as swallowing maybe reduced due to pain
- IV cannula kept *in situ* in case of postoperative bleeding
- Dexamethasone 0.05–0.15 mg/kg to reduce PONV, pain and increase oral feed tolerance
- Continue antibiotics
- Metoclopramide 0.15 mg/kg IV to reduce PONV.

Complications

- Post-tonsillectomy bleeding: *Most common*
- Airway obstruction:
  - Due to upper airway edema, blood, secretions and laryngospasm
  - Greater incidence following ETT than LMA use
  - Avoided by giving topical anesthesia to upper airway.
- PONV:
  - During first 24 hours, incidence 30–65%
  - Due to pharyngeal irritation from surgery and swallowed blood
  - Decompress stomach with OGT
  - Ondansetron 0.1 mg/kg given IV
  - *May cause dehydration:* Start IV fluids.
- Pain and sore throat may last for 3-4 days
- *Creutzfeldt-Jacob disease:*
  - Transmission due to contamination of instruments with lymphoid tissue
  - Use disposable surgical and anesthesia equipment between December and January to reduce transmission
  - Single use ETT, laryngoscope blades, tongues and LMAs preferred.
- Pulmonary edema:
  - Due to increased pulmonary hydrostatic pressure from rapid relief of airway obstruction
  - Most cases resolve within 24 hours
  - Treat with ETT, PPV and PEEP application, diuretic therapy.

POST-TONSILLECTOMY BLEEDING

Introduction

- Most common complication following tonsillectomy
- It is an emergency procedure involving a hypovolemic, tachycardic child on full stomach
- Usually bleeding is venous in origin.

Incidence

- 0.1–8.1% incidence
- More common in older children (above 11 years age at 69% incidence)
- More common in chronic tonsillitis
- Most common in first 6–8 hours postoperatively and may occur till sixth day
- 67% of bleeds originate from tonsillar fossa
- 26% originate in nasopharynx and 7% from both tonsillar fossa and nasopharynx.

Types

- *Primary hemorrhage:* Occurs during surgery
- Reactionary hemorrhage:
  - Approximately 75% occurs in first 6 hours postsurgery
  - Remaining 25% occurs within 24 hours
  - Occurs due to:
    - Slippage of ligature from bleeding vessels
    - Dislodgement of clots due to retching/vomiting
    - Bleeding from adenoid bed common in first 4 hours.
- Secondary hemorrhage:
  - From 24 hours to 5–10 days post-surgery
  - Due to secondary infection with sloughing of tissues.

Blood Supply to Tonsil

- Superior pole of tonsil:
  - Ascending pharyngeal artery
  - Lesser palatine artery.
- Inferior pole:
  - Facial artery branches
  - Dorsal lingual artery
  - Ascending palatine artery.

Venous Return

- Plexus around tonsillar capsule
- Lingual vein
- Pharyngeal plexus.

Anesthetic Considerations

- *Hypovolemia:* Needs urgent fluid resuscitation
- *Full stomach:* Due to ingested food and swallowed blood
- Difficult intubation:
  - Active bleeding in airway
  - Formed clots obstructing airway access
  - Edema from previous instrumentation and surgery.
- *Residual narcotic effects:* Due to previous anesthesia
- Shared airway.

Preoperative Evaluation

- History:
  - Elicited from the mother
  - History of frequent swallowing
  - Vomiting with coffee brown vomitus.
- Previous anesthesia record:
  - Difficult intubation
  - Anesthetic agents used.
- Examination:
  - General:
    - Assess level of consciousness and look for signs of restlessness
    - Pallor and dehydration
    - *Stridor and intercostal retractions:* Suggests difficult intubation
    - Blood loss is difficult to assess as most of blood is swallowed.
  - Cardiovascular:
    - Hypotension (occurs late), tachycardia
    - Capillary refill time more than 2 seconds
    - Bradycardia in late stages.
  - *Respiratory:* Tachypnea, stridor, accessory muscle use
  - *Others:* Oliguria, cold extremities, metabolic acidosis.

Treatment

- If history of intermittent bleeding with no active bleed:
  - Observe
  - IV fluids
  - Coagulation parameters
  - If coagulation study abnormal, hematology consult
  - Complete blood count and hematocrit as baseline.
- If active minor bleeding:
  - IV fluid resuscitation
  - Ice water gargling and packing
  - If persistent and patient is uncooperative, reexploration is done.

Preoperative Preparation and Resuscitation

- Secure large bore IV access
- Resuscitation with crystalloids/blood/plasma:
  - 20 mL/kg repeated depending on clinical signs
  - Upto 40–60 mL/kg may be required
  - *Avoid hypotonic fluids:* 5% dextrose, 0.45% saline, 2.5% dextrose.
- Send blood for hematocrit, cross-matching and coagulation profile
- Avoid preoperative sedation
- *Antisialogogues:* Glycopyrollate 0.02 mg/kg IV
- Anti-aspiration prophylaxis:
  - IV metoclopramide 0.15 mg/kg
  - IV ranitidine 1 mg/kg
- Check blood pressure in erect and supine position for orthostatic changes.

OT Preparation

- Machine check, AMBU bag, masks
- Variety of ETT and laryngoscope blades
- Variety of large bore suction catheters as blood in airway may plug the catheter/ETT
- Tilting table
- *Emergency drugs:* Atropine, adrenaline
- Anesthetic agents.

Monitors

- Pulse oximetry
- $ETCO_2$
- NIBP
- Urine output
- ECG
- Precordial stethoscope
- Temperature.

Induction

Two techniques can be used:

- Inhalational induction with sevoflurane/halothane:
  - *Disadvantages:*
    - Challenging as position of patient is lateral to avoid aspiration
    - Can be slow
    - Blood may be inhaled and precipitate laryngospasm

- Tracheal intubation in lateral position is difficult
- Halothane may cause cardiac arrest.

– *Advantages:*
- Oxygenation is well maintained in spontaneous ventilation
- Lateral position helps in draining blood
- Clots can be easily suctioned.

- Rapid sequence IV induction with cricoid pressure:
  – *Preferred method*
  – Ketamine 2 mg/kg + succinylcholine 1 mg/kg + fentanyl 1 µg/kg used
  – Etomidate 0.2–0.4 mg/kg IV used as alternative
  – Avoid thiopentone and propofol due to risk of precipitous hypotension
  – Advantages:
    - Supine position with cricoid pressure reduces risk of aspiration
    - Less stressful to child.
  – Disadvantages:
    - Preoxygenating a bleeding child may be difficult
    - Face mask ventilation following succinylcholine may inflate stomach
    - Risk of hypoxia if difficult intubation with paralyed patient.
- Technique:
  – Adequate preoxygenation with 100% oxygen for 3–5 minutes
  – Rapid sequence induction with cricoid pressure
  – Head down tilt to keep blood away from larynx
  – 0.5-1 mm smaller than appropriate sized ETT as airway edema will be present
  – Decompress stomach with Ryles tube after intubation
  – Dexamethasone 0.1 mg/kg IV to reduce airway edema
  – Ondansetron 0.1 mg/kg IV to prevent vomiting
  – Suction to be readily available.

Maintenance

- O_2 + N_2O + isoflurane 1 MAC used for maintaining balanced anesthesia
- Fentanyl and vecuronium given in intermittent boluses
- Intermittent positive pressure ventilation.

Hemodynamics

- Continue volume resuscitation throughout surgery
- IV fluids and blood as per clinical signs and hematocrit
- Maintain temperature.

Extubation

- Head down lateral position
- Extubate when fully awake with normal cough and gag reflex, and stable hemodynamics
- Neostigmine 0.05 mg/kg + glycopyrollate 0.02 mg/kg IV for reversal of NM blockade
- Avoid coughing during extubation to prevent reactionary hemorrhage due to slippage of ligature.

Postoperative Care

Management

- Nurse in tonsil position/*Fowlers position*
- *Tonsil position:* Pillow under chest so that head falls below chest level and fluids drain from mouth
- May require midazolam/opioids to tolerate post nasal packs
- Oxygen administration till fully awake
- Maintain normal temperature
- Continue IV fluids and blood as per hematocrit.

Analgesia

- Adequate analgesia to prevent restlessness
- Opioids/NSAIDs used in combination.

Monitors

- Pulse oximetry
- ECG
- NIBP
- Temperature
- Urine output
- Serial hematocrit
- Monitor for further bleeding.

PHYSIOLOGICAL CHANGES WITH AGING[1,2,3,7]

Introduction

- Progressive, universally prevalent physiological process producing measurable changes in the structure and decrementals alteration in function of tissues and organs
- Generally, patients more than 65 years are called geriatric
- *65–74 years:* Elderly
- *75–84 years:* Aged
- *More than 85 years:* Very old.

Central Nervous System Changes

- Reduction in brain mass, starts at 50 years
- 10% reduction in brain weight occurs at 80 years
- Atherosclerosis of cerebral blood vessels
- Reduced cerebral blood flow
- *Reduced neurotransmitters:* Dopamine, serotonin, GABA, acetylcholine
- Increased incidence of postoperative delirium and cognitive decline.

Cardiovascular System Changes

- Cardiac output:
  - Cardiac output is stroke volume dependent as heart rate is low
  - Reduced maximal cardiac output
  - Output is volume dependent but volume intolerance.
- Structural changes:
  - Stiffening of myocardium, arteries and veins causing:
    - Slow diastolic filling
    - Postural hypotension with mild hypovolemia.
  - *Increased capillary permeability:* Increased chances of pulmonary edema.
- Conduction system:
  - Fibrosis of conduction system
  - Loss of sinoatrial node cells
  - Atrial fibrillation common, sick sinus syndrome, complete heart block.
- Blood pressure:
  - Old age represents a volume contracted state
  - Increased sympathetic nervous system activity and reduced parasympathetic activity
  - Labile blood pressure during anesthesia
  - Reduced PNS activity may limit increase in heart rate in response to administration of atropine
  - *Reduced arterial compliance:* Systolic HTN and widened pulse pressure.
- Defective ischemic preconditioning as protective effect of angina is absent.

Respiratory System Changes

- Structure:
  - More upper airway obstruction
  - Stiffening of chest wall, barrel shaped chest
  - Increased elasticity of lung parenchyma
  - *Reduced alveolar surface area:* Reduced resting PaO_2
  - *Less effective cough:* Increased chances of aspiration
  - *Flattened diaphragm and loss of muscle mass:* Increased dyspnea.
- Physiology:
  - Increased anatomical and physiological dead space
  - Ventilation-perfusion mismatch
  - Increased closing capacity
  - Closing capacity exceeds FRC in mid 60s
  - *50% reduction in ventilatory response to hypoxia and hypercarbia:* Increased risk of postoperative apnea
  - PaO_2 falls steadily $\left\{PaO_2 = \frac{(100 - age)}{4}\right\}$
  - Reduced minute volume requirements as O_2 consumption and CO_2 production reduces
  - Patients tolerate longer periods of apnea
  - *Edentulous patient:* Maintenance of patent airway and face mask seal difficult.

Endocrine System Changes

- Insulin resistance
- Insulin secretion reduces in response to glucose load
- Reduced estrogen, testosterone and GH production
- Subclinical hypothyroidism in females.

Hepatocellular Changes

- Reduced liver mass, 20–40% reduction in liver blood flow
- Size of liver reduces to 40% by 80 years
- Reduced hepatic function
- Reduced phase I metabolism and bile secretion with age
- Reduced plasma cholinesterase in men.

Renal Changes

- Reduced renal cortical mass by 20–25%
- Loss of upto half the glomeruli by 80 years
- Reduction in GFR by 1 ml/min/year after 40 years age
- Increased risk of acute renal failure perioperatively.

Body Composition and Fluid Homeostasis

- Gradual loss of skeletal muscle and body fat
- Reduced total body water and plasma albumin
- Low responsiveness to ADH
- *Reduced aldosterone secretion:* Altered Na^+ homeostasis
- Reduced ability to conserve Na^+ and concentrate urine
- Reduced basal metabolism.

Thermoregulation

- Prone to hypothermia as:
  - Reduced subcutaneous fat insulation
  - *Reduced BMR:* Reduced heat production.
- Ineffective shivering and vasoconstriction
- Vasoconstriction not activated till temperature falls by more than 4 °C.

Hematology

- Hypercoagulability and DVT
- Anemia more common
- *Reduced immune response:* Increased infection.

Musculoskeletal

- Reduced muscle mass fragile skin
- *Osteoporosis:* Positional fractures and dislocations
- *Osteoarthritis/rheumatoid arthritis deformities:* Difficult IV line
- *Increased chances of nerve injuries:* Pad pressure points
- Osteoporosis, ligament laxity and calcification causes difficult spinal.

Drug Pharmacology

- Reduced body mass
- Reduced total body water
- Relative reduction in fat
- Reduced albumin
- Increased acid glycoprotein
- Reduced cardiac output
- Mildly contracted blood volume
- Reduction in hepatic and renal clearance
- Also altered drug responses as in:
  - Drugs have more pronounced effect
  - Bolus doses take longer time to act
  - Increased drug interactions
  - Target organs more sensitive to drug level
  - Increased context sensitive half life.
- Examples:
  - Use meperidine only for shivering
  - *Fentanyl, sufentanyl, remifentanyl, alfentanyl and morphine:* 50% reduction in dosage
  - Thiopentone and propofol warrant 20% reduction in dose
  - Midazolam requires modest reduction in dose at 60 years and 75% reduction in dose at 90 years
  - Vecuronium, rocuronium, cisatracurium and succinylcholine:
    - Have slower onset of action
    - Increased incidence of residual paralysis especially if multiple doses used.
  - Residual paralysis occurs due to drug accumulation
  - Neostigmine dose increases with age in some studies
  - Decrease in MAC value of volatile anesthetics with age
  - Reduced sensitivity to β agonists, antagonists and digoxin with age
  - Increased chances of renal failure and GI bleed with NSAIDs
  - Increased hypotension with CCBs, nitrates and diuretics due to volume contracted state.

ANESTHETIC MANAGEMENT OF GERIATRIC PATIENT[1,2,3,21]

Introduction

With geriatric population on the rise, anesthetist is bound to encounter more number of elder patients in the near future.

Preoperative Evaluation

- Preoperative risk factors:
  - Emergency surgery
  - ASA class ≥ 3
  - Low functional status
  - Clinical evidence of CCF.
- Coexisting diseases:
  - History of cardiac (MI/CCF), respiratory (COPD), renal/hepatic diseases
  - History of RA/OA deformities:
    - Difficult IV access
    - Cervical instability.
  - Polypharmacy and drug interactions are common
  - Dehydration, malnutrition are very common: *Anorexia of ageing*.
- History and evaluation:
  - History of previous illness, medication history
  - Current functional status of all organ systems
  - Assessment of level of physical activity for CVS and RS status is limited due to bone and joint disease
  - Mental status examination important
  - Low albumin levels associated with increased morbidity and mortality.
- Preoperative management:
  - Continue all medication except OHAs
  - Avoid sedatives, especially benzodiazepines and pethidine

  - Perioperative β-blockade considered
  - Care towards *Do Not Resuscitate orders*
  - Optimize preoperative medical status
  - Postpone elective surgery until concurrent illnesses are optimized.

Regional Anesthesia

- Use wherever possible
- Commonly used for TURP, herniorrhaphy, gynecological surgeries, hip fractures
- Requires alert and cooperative patient
- Advantages:
  - Reduced chances of DVT, early mobilization
  - Low incidence of postoperative cognitive decline
  - Rapid recognition of CNS changes and onset of angina pectoris
- Spinal anesthesia:
  - Difficult spinal due to ligament calcification and laxity
  - Prolonged duration of action due to reduced vascular absorption of LA due to atherosclerosis
  - Profound hypotension on induction due to volume contracted state
  - T_8–T_{10} level acceptable for most cases.
- Epidural anesthesia:
  - More gradual onset of hypotension than spinal anesthesia
  - Dose required to produce sensory block lesser as progressive occlusion of intervertebral foramina with connective tissue occurs.

Conduct of General Anesthesia

Monitoring

- Pulse oximetry
- Capnography
- NIBP
- ECG
- Temperature
- Urine output
- BP/CVP considered in cardiac patients
- Neuromuscular monitoring (residual palsy).

Positioning

- Osteoporosis increases chances of positional injuries
- Intermittently relieve pressure points in long duration surgeries
- Positional changes should be gradual as defectives baroreceptor function.

Induction

- Smaller induction doses used
- Difficult IV access due to thin veins and bony deformities
- Onset of IV induction delayed due to longer brain-arm circulation time
- Significant hypotension with induction
- Difficult mask ventilation in edentulous patients
- Precautions to prevent aspiration as:
  - Blunted airway reflexes
  - Increased incidence of hiatus hernias in elderly
- ET tube to be used where possible.

Maintenance

- Reduced MAC value of volatile anesthetics
- Reduced doses of intravenous drugs
- Reduced fentanyl, sufentanyl, alfentanyl, remifentanyl and morphine requirements by 50%
- Reduce doses of muscle relaxants as high incidence of residual muscular paralysis
- Forced air warmers to prevent hypothermia.

Ventilation

- Mechanical ventilation with supplemental oxygen preferred to spontaneous ventilation
- High tidal volume with PEEP used to prevent atelectasis
- Avoid hyperventilation if patient receiving digoxin to prevent hypokalemia.

Postoperative Care

Monitors

- Pulse oximetry
- NIBP
- ECG
- Urine output
- Temperature
- Neuromuscular monitoring
- ABG
- Fluid balance.

Management

- Early establishment of nasogastric tube feeding
- Early mobilization, physiotherapy and thromboprophylaxis, elastic support stockings
- Maintain hemoglobin level at 9–10 g% if cardiac disease present
- Continue oxygen for 24 hours except in minor surgeries
- Monitor fluid balance and fluid overload.

Postoperative Analgesia

- May be more tolerant of acute pain
- Delirium and cognitive decline hinder pain reporting by patient
- More difficulty with visual analogue scale rather than verbal/numerical scales
- Epidural analgesia superior, it also reduces opioid requirements
- NSAIDs used with caution and reduces opioid requirement.

Complications

- Pain causing:
  - Sleep deprivation
  - Gastric ileus
  - Suboptimal mobilization
  - Insulin resistance
  - Tachycardia, perioperative MI.
- Cardiovascular system:
  - Myocardial infarction, cardiac arrest
  - Arrhythmias.
- Respiratory system:
  - *Pneumonia:* If more than 48 hours on ventilator
  - Reintubation
  - Atelectasis.
- Central nervous system:
  - *Stroke:* Usually occurs more than 7 days postoperatively
  - Delirium, cognitive decline.

ANESTHESIA FOR TOTAL HIP REPLACEMENT[1,2,3,21]

Introduction

Performed commonly in geriatric patients who usually have associated comorbidities.

Preoperative Evaluation

History

- Underlying medical illness and review of organ systems
- *Drug history:* For *polypharmacy*
- Surgical history and anesthetic history.

Examination

- Deafness, dementia and cognitive dysfunction common
- *Vital parameters:* BP, heart rate, rhythm, respiratory rate
- CVS, RS, CNS, abdominal examination
- Difficult IV access in rheumatoid arthritis if small joints of wrist and foot are involved
- Check if patient can tolerate lying flat after spinal (orthopnea may limit lying flat).

Investigations

- Routine blood, urea, creatinine, clotting profile
- *Chest X-ray:* Pleural effusion, interstitial fibrosis
- Echocardiography for LV function, RWMA, valve abnormality
- Dobutamine stress test:
  - Exercise tolerance is limited by hip disease
  - Hence, cardiovascular reserve may be difficult to assess
- Lung function tests, ABG and SpO_2 on room air
- Renal function tests may be impaired due to chronic NSAIDs use.

Airway Assessment

- In rheumatoid arthritis, cervical spine and TMJ may be involved
- Atlantoaxial subluxation occurs in 25% patients with severe rheumatoid arthritis
- *Treat as unstable spine:* Use Manual in-line Stabilization maneuver
- TMJ involvement may cause restricted mouth opening.

Preoperative Preparation

- NPO orders
- Informed consent
- Optimize comorbidities
- Two units of cross matched blood to be available
- Antibiotic prophylaxis
- 16–18 G large bore IV cannula in nondependent arm for laterally positioned patients
- Time DVT prophylaxis as per ASRA guidelines for regional anesthetic techniques
- Invasive monitors if severe disease/large blood loss is anticipated
- ACE inhibitors stopped to avoid sudden hypotension
- Continue other antihypertensives
- Stop morning dose of hypoglycemic agents
- Avoid NSAIDs, especially if neuraxial block planned.

Anesthetic Considerations

- Anesthetic consideration of lateral position
- Hypotensive anesthetic technique may be preferred

- *Keep patient warm:* OT may be set at 18–20 °C
- OT temperature usually set at 18–20 °C to prevent premature cement setting
- Ensure adequate volume filling prior to cementing
- Watch for *bone cement implantation syndrome*
- Patient warming device and warm fluids should be used where possible
- Blood loss may be around 300–500 ml
- Strategies to avoid blood transfusion:
  - Avoid HTN and tachycardia
  - Regional anesthesia technique
  - Hypotensive anesthesia
  - Acute normovolemic hemodilution
  - Intraoperative and postoperative blood salvage.
- Anterior restraints used in lateral position may prevent chest expansion.

Choice of Anesthetic Technique

- Regional anesthesia:
  - *Advantages:*
    - Reduces blood loss intraoperatively
    - Reduced need for blood transfusion
    - Improved cement bonding due reduced bleeding
    - Reduced incidence of DVT and PE
    - Avoids effects of GA on pulmonary function
    - Good postoperative analgesia
    - Low cost.
  - Conduct of anesthesia:
    - *Monitors:* NIBP, SpO_2, ECG, urine output
    - Preload with IV fluid 10 ml/kg
    - Subarachnoid block with 0.5 % heavy bupivacaine
    - Phenylephrine better for treating hypotension
    - Protect pressure points with gel pads, cotton pads and gamgee rolls
    - Patient warming devices connected
    - Tranexemic acid 500 mg in NS given over 30 minutes pre-incision and postoperatively
    - Sedate with midazolam and fentanyl combination
    - Oxygen by face mask at 4–6 L/min
    - 10° head down tilt with normal to slight hypervolemia when hypotensive anesthesia planned
    - Basal BP restored after cementing is complete.
- Epidural anesthesia:
  - For longer and more complex surgery
  - Also for postoperative analgesia
  - Insert urinary catheter if epidural anesthesia given
  - Time removal of catheter with DVT prophylaxis.
- Peripheral nerve blocks for THR:
  - No single peripheral nerve block is sufficient for THR
  - Lumbar plexus block gives effective analgesia
  - Three in one femoral block is easier to perform but less effective.
- General anesthesia:
  - *Advantages:*
    - Better in patients unable to the flat
    - Safer in patients with fixed cardiac output states like aortic stenosis
    - Patients comfortable
    - Less likely to require urinary catheterization.
  - Expect:
    - Late recovery from GA
    - Reduced MAC values
    - Increased benzodiazepine requirements
    - Increased LA concentration as albumin levels are lower in blood.

Anesthetic Problems

Preoperative Problems

- *Deafness, dementia and cognitive impairment:* Difficult to communicate
- *Difficult to assess cardiac status:* Stress dobutamine test
- *Volume contracted state if hypertensive:* Judicious preloading
- *Associated comorbities:* DM, HTN, polypharmacy, ARF, NSAID nephropathy
- *May have reduced FRC and V-Q ratio:* Pulmonary function test done
- Anemia of chronic disease
- Antiaspiration prophylaxis as reduced LES tone and airway reflexes
- DVT prophylaxis as prolonged immobilization.

Intraoperative Problems

- Lateral position:
  - Might decrease FRC more
  - May be dangerous in patients prone for pathological fractures
  - Padding to prevent brachial plexus injuries
- Blood loss of around 500 ml: Use blood conservation strategies

- Bone cement implantation syndrome
- Fat embolism syndrome from femur reaming
- Judicious fluid management to prevent fluid overload
- Prone for hypothermia as thermoregulatory center impaired
- Profound fall in BP after SAB if isolated systolic HTN exists preoperatively
- If general anesthesia chosen:
  - Prolonged and late recovery as although weight is less, fat proportion is increased
  - *Difficulty airway:* Atlantoaxial joint and TMJ involvement
  - *Unstable cervical spine:* Use MILS maneuver.

Postoperative Care

Position: Supine with legs abducted using pillow.

Ventilation

- Oxygen therapy for 24 hrs postoperatively
- Given for 72 hrs postoperatively in those at high risk for M1.

Monitors

- NIBP
- SpO_2
- ECG
- Urine output
- Drains
- Hemoglobin 24 hrs postoperatively.

Postoperative Analgesia

- Less severe compared with TKR
- Multimodal analgesia preferred
- Patient controlled analgesia may be used
- Use NSAIDS with caution as renal impairment may occur in elderly
- Epidural analgesia very useful
- Time the removal of catheter with DVT prophylaxis regimen
- Epidural infusion of 0.125% bupivacaine and fentanyl 2–4 µg/ml for 48 hrs at 6–10 ml/hr started around 2 hrs after SAB.

ARTERIAL TOURNIQUET[1,2,3,21]

Introduction

Use of arterial tourniquet greatly facilitates bloodless field during upper and lower limb orthopedic surgeries.

Indications

- For intravenous regional anesthesia or Biers block
- To provide bloodless field for surgery:
  - For better identification of structures
  - Reduced operative time
  - Reduced surgical complications
  - Reduced need for blood transfusion.

Guidelines for Use

- *Position:* Point of overlap of tourniquet to be placed 180° from neurovascular bundle as there is some area of reduced compression at overlap point
- Cuff width:
  - Width of inflated cuff to be more than half the limb diameter
  - To be more than 7 cms, especially for leg, to minimize drainage to skin.
- Tourniquet time:
  - Minimum time for IVRA is 30 minutes
  - Maximum duration of inflation:
    - 2 hours as increased risk of rhabdomyolysis and nerve palsy if longer duration
    - 5 minutes of intermittent perfusion allowed beyond 2 hour inflation
    - This is followed by repeat exsanguination through elevation and compression of limb
    - This may allow prolonged use of tourniquet.
- Tourniquet pressure:
  - Systolic BP + 150 mm Hg for IVRA
  - Systolic BP + 100 mm Hg for lower limb surgeries
  - Systolic BP + 50 mm Hg for upper limb surgeries.

Changes on Cuff Deflation

- Mild systemic metabolic acidosis (preinflation pH of 7.4 reduces to 6.9, two hours after deflation)
- Increased $PaCO_2$ (1–8 mm Hg)
- Raised lactate levels
- Increased K^+ levels (5–10 % increase)
- Transient rise in $ETCO_2$ levels
- Transient fall in systolic BP: 14–19 mm Hg
- Transient fall in heart rate: 6–12 bpm
- Transient fall in temperature by 0.7 °C
- All these changes are due to release of toxic metabolites from the occluded limb, like carbon dioxide, lactic acid and potassium.

Contraindications

- Peripheral vascular disease *(Raynauds disease)*
- Deep vein thrombosis
- AV fistula/arterial calcific disease

- Peripheral neuropathy/CNS disorder
- Severely injured/traumatized limb
- Severe infection in limb
- Bone abscess
- *Sickle cell disease*: Use is controversial as sickling is promoted by hypoxia/acidosis.

Complications

Tourniquet Pain

- Occurs in 66% cases 30–60 minutes after giving RA
- Due to faster recovery of unmyelinated C fibers from SAB as the block wanes, as compared to A fibers
- Bupivacaine is associated with reduced tourniquet pain as it blocks C unmyelinated fibers in a better way
- Likelihood of pain varies with anesthetic technique:
  - IVRA > epidural > SAB > GA
  - Hyperbaric tetracaine > isobaric bupivacaine.
- Clinical features:
  - Dull, deep, burning and poorly localized pain
  - Hypertension, tachycardia, diaphoresis.
- Treatment:
  - Definitive treatment is cuff deflation
  - Sedatives, IV opioids
  - Double cuff application
  - EMLA cream application under cuff
  - TENS/vibratory massages: Not useful.

Hemodynamic Changes

- Exsanguination:
  - Results in movement of blood from peripheral to central circulation
  - Causes increased SVR and preload to heart.
- 10–15% increase in heart rate and HTN on cuff inflation
- Cardiac arrest, LV failure
- Deflation of cuff:
  - Causes reduced SVR
  - This causes acute blood loss which may continue for 24 hours
  - Also causes release of metabolites: May require cardiac support with inotropes.

Touniquet Hypertension

- Occurs due to tourniquet pain
- Begins three-fourths to one hour after cuff inflation.

Pulmonary Embolism

- Pulmonary embolism possible following exsanguinations/cuff deflation in TKR
- Silent DVT may be the cause and high index of suspicion is required.

Metabolic Changes

- Increased $PaCO_2$ (1–8 mm Hg), reduced pH, increased lactate and K^+ levels
- Only increase in $PaCO_2$, in head injury patients may cause increased CBF and raised ICP
- Body temperature increases in pediatric patients during tourniquet inflation.

Postoperative EDEMA

- Due to return of exsanguinated blood and post-ischemic reactive hyperemia
- Can be due to arterial flow with no venous return during cuff inflation
- *Post tourniquet syndrome:* Pale and swollen limb for 1–6 weeks postoperatively
- Cold compression of limb is useful.

Bleeding

- Bleeding during tourniquet inflation:
  - More commonly due to intramedullary blood flow in long bones
  - Particularly common in skeletally immature patients
  - Also due to small arteries between two long bones in distal limb.
- Post-tourniquet release, bleeding may continue for 24 hours.

Tourniquet Failure

Occurs due to:

- Inadequate pressure and exsanguination
- Calcified arteries.

Delayed Return of Blood Flow after Tourniquet Release

Causes are:

- Arterial injury
- Compartment syndrome
- Reperfusion injury due to formation of lipid peroxides which is reduced by propofol (which inhibits superoxide formation).

Trauma

- Skin trauma:
  - Due to improper placement of padding under cuff
  - Causes bruising, abrasions and blistering.

- *Arterial trauma:* Causes arterial spasm, arterial thrombus
- *Venous trauma:* Venous thrombus due to stagnant blood
- *Muscle rhabdomyolysis:* If inflation time more than 2 hours
- Nerve injury:
  - Called *tourniquet palsy*
  - Paroneal and tibial nerve palsy common following TKA with tourniquet inflation ≥ 2 hours.

BONE CEMENT

Introduction

Bone cement consists of polymethyl-methacrylate which interdigitates with intestices of cancellous bone and strongly binds prosthetic device to patients bone during TKR/THR.

Components

- Components of ampoule:
  - Methylmethacrylate monomer
  - N, N-dimethyl paratoluidene
  - Hydroquinone.
- Components of powder:
  - Methylmethacrylate styrene copolymer
  - $BaSO_4$.
- Hydroquinone prevents premature polymerization which occurs due to exposure to light or elevated temperatures
- N, N-dimethylparatoluidene promotes cold curing of finished therapeutic compound
- $BaSO_4$ for contrast for X-ray examination.

Indications

- Fixation of prosthesis to living bone:
  - Osteoarthritis
  - Rheumatoid arthritis
  - Traumatic arthritis
  - Avascular necrosis
  - Sickle cell anemia
  - Collagen vascular diseases.
- Fixation of pathological fractures where loss of bone substance/recalcitrance of fracture renders conventional measures ineffective.

Contraindications

- Allergy to any of the components
- Infective arthritis/active joint infection/history of such injection
- Where loss of musculature/neuromuscular compromise in affected limb would render procedure unjustifiable.

Pathophysiological Changes

- Polymerization of methylmethacrylate:
  - It is an exothermic reaction
  - Temperatures can reach up to 110 ºC
  - This can cause RBC and bone marrow lysis.
- Methacrylic acid:
  - Residual methylmethacrylate monomers gets hydrolyzed to methacrylic acid
  - Significant fraction of circulating methacrylate is in the form of free acid and rather than methylester
  - This can cause vasodilation and reduced systemic vascular resistance.
- Femoral reaming and prosthetic implantation can cause embolization of fat, bone marrow and air into femoral venous channels due to intramedullary hypertension (≥ 500 mm Hg)
- Release of tissue thromboplastin may trigger platelet aggregation and microthrombus formation in lungs.

Complications

- Most frequent complications:
  - *Exothermic reaction:* Red cell and bone marrow lysis
  - Transient hypotension:
    - Occurs primarily in:
      - Patients with increased or high normal BP
      - Patients with hypovolemia
      - Those with preexisting cardiovascular abnormalities.
    - Onset of hypotension is within 10–165 seconds
    - Hypotension lasts for 30 seconds to 5–6 minutes.
  - Thrombophlebitis
  - Surgical wound infection, deep wound infection
  - Trochanteric bursitis, trochanteric separation
  - Hemorrhage and hematoma
  - Loosening and displacement of prosthesis.
- Most serious complications:
  - Cardiac arrest due to:
    - Direct embolization
    - Secondary to hypoxia due to pulmonary embolism
    - Myocardial infarction.
  - Cerebrovascular accidents

- Other complications:
  - Heterotopic bone formation
  - Short term cardiac conduction abnormalities.

Bone Cement Implantation Syndrome

Components

- Hypoxia (Increased pulmonary shunting)
- Hypotension
- Dysrhythmias including heart block and sinus arrest
- Pulmonary hypertension (increased pulmonary vascular resistance)
- Reduced cardiac output
- Fat embolization syndrome (FES)
- Cardiac arrest.

Risk Factors for Syndrome

- Revision surgery
- Long stem femoral prosthesis
- THA/TKA for pathological fractures
- Quantity of cement used.

Strategies Tominimize Embolization

- Increase FiO_2 prior to cementing: Prevents hypoxia
- Maintain euvolemia by monitoring CVP: Prevents hypotension
- Create vent hole in distal femur to relieve intramedullary pressure
- Perform high pressure lavage of femoral shaft to remove debris: Potential microemboli
- Use cementless prosthesis
- Discontinue N_2O several minutes prior to bone cement application.

FAT EMBOLISM[1,2,3,10,21]

Introduction

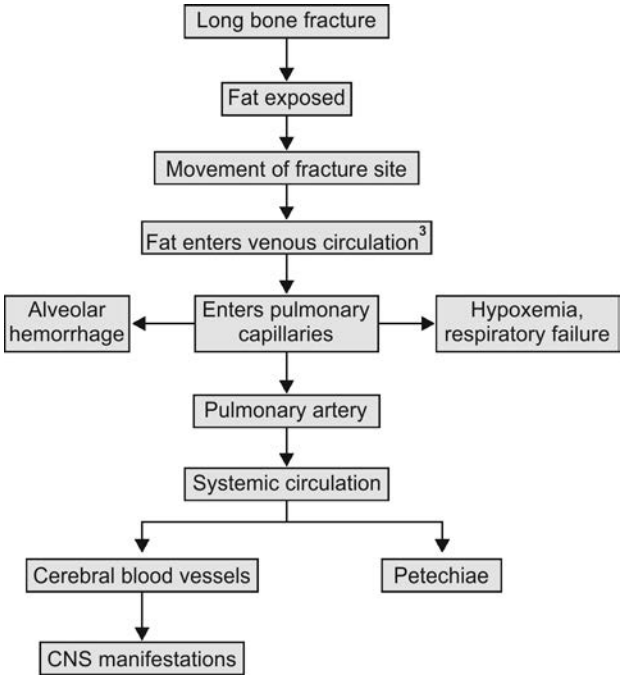
- Fat embolism can be defined as the presence of fat in peripheral circulation
- Fat embolism syndrome (FES) can be defined as the physiological response to fat within systemic circulation
- Seen in almost all patients who sustain a pelvic/femur fractures, but incidence of FES is < 1%.

Etiology

- Long bone/pelvic fractures
- Hip/knee replacement (during implantation of femoral prosthesis/during reaming)
- Following CPR, bone marrow transplant
- Lipid emulsion therapy or lipid infusion in parental feeding
- Liposuction
- Acute pancreatitis, acute fatty liver
- Acute sickle cell crisis: Bone marrow crisis.

Pathogenesis

- Two theories to explain FES: Mechanical theory and biochemical theory
- Mechanical theory:
  - Fat globules are released by disruption of fat cells in the fractured bone
  - These enter circulation through tears in medullary blood vessels.
- Biochemical theory: 2 mechanisms:
  - Toxic mechanism:
    - Free fatty acids released due to trauma
    - These directly affect pneumocytes in lung and cause ARDS
    - This is increased by trauma mediated release of catecholamines
    - Catecholamines increase mobilization of free fatty acids.
  - Obstructive mechanism:
    - Unspecified chemical event occurs at site of fracture
    - This causes release of mediators
    - These mediators affect lipid solubility, resulting in coalescence of lipids
    - Consequently, fat embolization occurs.
- Other predisposing factors like shock, hypovolemia, sepsis or DIC may be required to convert fat emboli to FES
- ARDS:
  - Increased fatty acid levels can have a toxic effect on capillary alveolar membrane
  - This leads to the release of vasoactive amines and prostaglandins
  - This causes development of SIRS/ARDS due to damage to pulmonary endothelium.
- Neurological manifestations are due to capillary damage to cerebral circulation and cerebral edema.



Risk Factors for Fat Embolism Syndrome (FES)[3]

- Male gender
- Age 20–30 yrs
- Hypovolemic shock
- Intramedullary instrumentation
- Total hip arthroplasty using cementing femoral stems
- Bilateral total knee arthroplasty.

Incidence

- Incidence of FES in isolated long bone fractures is 3–4%
- Mortatility rate associated with FES is 10–20%
- Self-limiting condition with adequate supportive therapy.

Types[3,10]

Subclinical FES

- Occurs in 50% patients with long bone fractures
- Can occur up to 3 days after injury
- Associated with mild hypoxemia and hematological abnormalities

Non Fulminant FES

- Occurs in 1–5 % cases of major trauma
- Develops within 12–72 hours gradually
- Severe hypoxia, respiratory depression, rashes fever, tachycardia, CNS symptoms.

Fulminant FES

- Rapid onset occurring within few hours
- Severe form associated with RVF, cardiac arrest, fat particles in systemic circulation, DIC
- It can occur during surgery causing fatal outcome.

Clinical Features

- Classically presents within 72 hrs following long bone fractures
- Males 20–30 yrs of age affected more often
- Dermatological manifestations:
  - Petechiae over axilla, neck, conjunctiva face *pathognomonic*
  - Occurs due to rupture of small blood vessels by fat globules.
- Respiratory manifestations:
  - Hypoxemia, tachypnea, dyspnea
  - Initial chest X-ray is normal, 10% have fluffy appearance
  - Less than 10% cases progress to frank ARDS
  - Inspiratory crackles due to RV failure.
- Central nervous system:
  - Drowsiness, confusion, coma, seizures
  - It can occur in the absence of respiratory complications
  - This may be due to passage of fat across ASD/other AV shunts.
- Others:
  - Pyrexia, tachycardia
  - *ECG:* RV strain pattern.
- Renals: Oliguria, lipiduria, hematuria, proteinuria.

Signs During General Anesthesia

- Hypotension, tachycardia, rashes
- Reduction in $ETCO_2$ and SpO_2 with increase in $ETCO_2$-$PaCO_2$ gradient
- Reduced alveolar-arterial gradient
- Raised pulmonary arterial pressure, reduced cardiac index
- *ECG:* ST elevation, right ventricular strain pattern
- Transesophageal echocardiography
- Delayed awakening following GA.

Investigations

- *Blood:* Thrombocytopenia (< 1.5 lakh/mm^3), anemia (unexplained cause)
- Fat globules in blood/urine/retina (*cotton wall spots*)
- Increased clotting time, hypocalcemia due to affinity of calcium to FFA
- Increased serum lipase may be present

- Increased levels of free fatty acids and triglycerides in blood
- ECG: RV strain pattern, ST elevation
- Transesophageal echocardiography, pulmonary artery catheter: For pulmonary HTN.
- MRI/CT scan
- *Bronchoalveolar lavage:* Macrophages with fat.

Gurds

Diagnostic Criteria for Fat Embolism Syndrome[3]

- Major features:
  - Respiratory insufficiency, tachypnea > 30 cycles/minute
  - Cerebral involvement
  - Petechial rashes.
- Minor features:
  - Pyrexia > 38 °C
  - Tachycardia
  - Jaundice
  - *Retinal changes:* Retinal fat globules
  - *Renal changes:* Urinary fat globules.
- Lab findings:
  - *Fat microglobulinemia:* Essential
  - Anemia, thrombocytopenia, raised ESR.
- *One major and four minor criteria with evidence of fat microglobulinemia required.*

Schonfield

Fat Embolism Syndrome Index[3]

Sign	Score
Petechial rash	5
Diffuse alveolar infilterates	4
Hypoxemia, PaO_2 < 70, FiO_2 100%	3
Confusion	1
Fever > 38 °C (> 100.4 °F)	1
Heart rate > 120 bpm	1
Respiratory rate > 30/min	1

- Ranks/score given according to incidence of presentation
- Score > 5 required for diagnosis of FES.

Management

Prophylactic

- Early stabilization of fracture
- Reduce intramedullary instrumentation and manipulation
- Use of cemented prosthesis
- Change in surgery such as converting IM nailing to external fixator application
- Reversal of possible risk factors such as hypovolemia.

Supportive

- *Monitor:* Pulse oximetry
- ECG
- Capnography
- Oxygen therapy:
  - Continuous positive pressure ventilation may be required
  - If SpO_2 < 90% tracheal intubation and mechanical ventilation
  - Ventilation with FiO_2 100% and respiratory rate > 35 breaths/min
  - Ventilation to be instituted before onset of respiratory failure
  - Only 10% cases require mechanical ventilation as symptoms resolve within 3–7 days.
- Correct hypovolemia, cardiac support with inotropes
- *Heparin:* Useful as it increases lipase action and clears FFAs from blood
- *Alcohol and dextran bind FFA:* Unproven role, results may be disappointing
- *Corticosteroids:* Beneficial especially if cerebral edema present
- Aspirin as prophylactic agent as it inhibits TXA_2 production.

AIRTRAQ

- *Single use:* No cross contamination
- Simple to use
- *Built in antifog system:* Offers good view
- Increased battery life
- *Optical wireless monitor and camera:* Good for training due to portability
- Integrated lens and light source
- Increases intubation success rate
- Anatomically shaped
- *Guiding channel:* Leads ETT through vocal cords
- Range of sizes:
  - *Small:* Fits 6–7.5 size ETT
  - *Regular:* Fits 7–8.5 size ETT
  - *Pediatric:* Fits 3.5–5.5 size ETT.

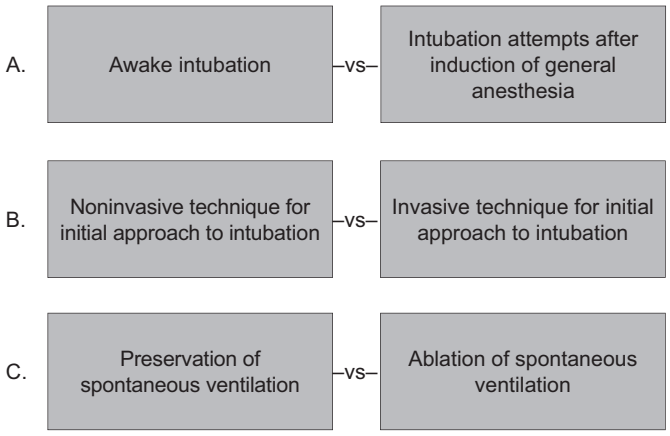
CHAPTER

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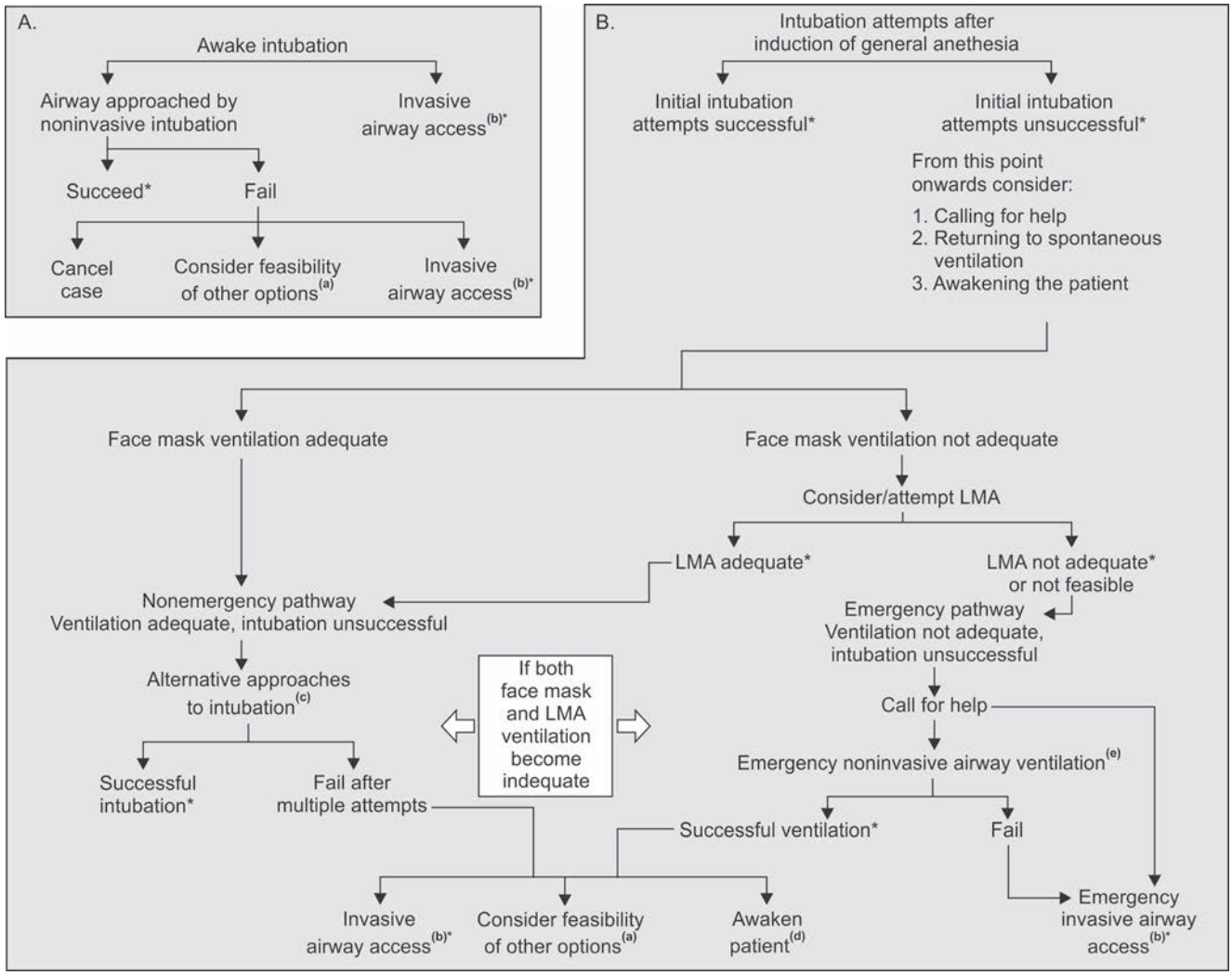
Algorithms

DIFFICULT AIRWAY ALGORITHM

1. Assess the likelihood and clinical impact of basic management problems:
   - Difficult ventilation
   - Difficult intubation
   - Difficulty with patient's cooperation or consent
   - Difficult tracheostomy
2. Actively pursue opportunities to deliver supplemental oxygen throughout the process of difficult airway management
3. Consider the relative merits and feasibility of basic management choices:



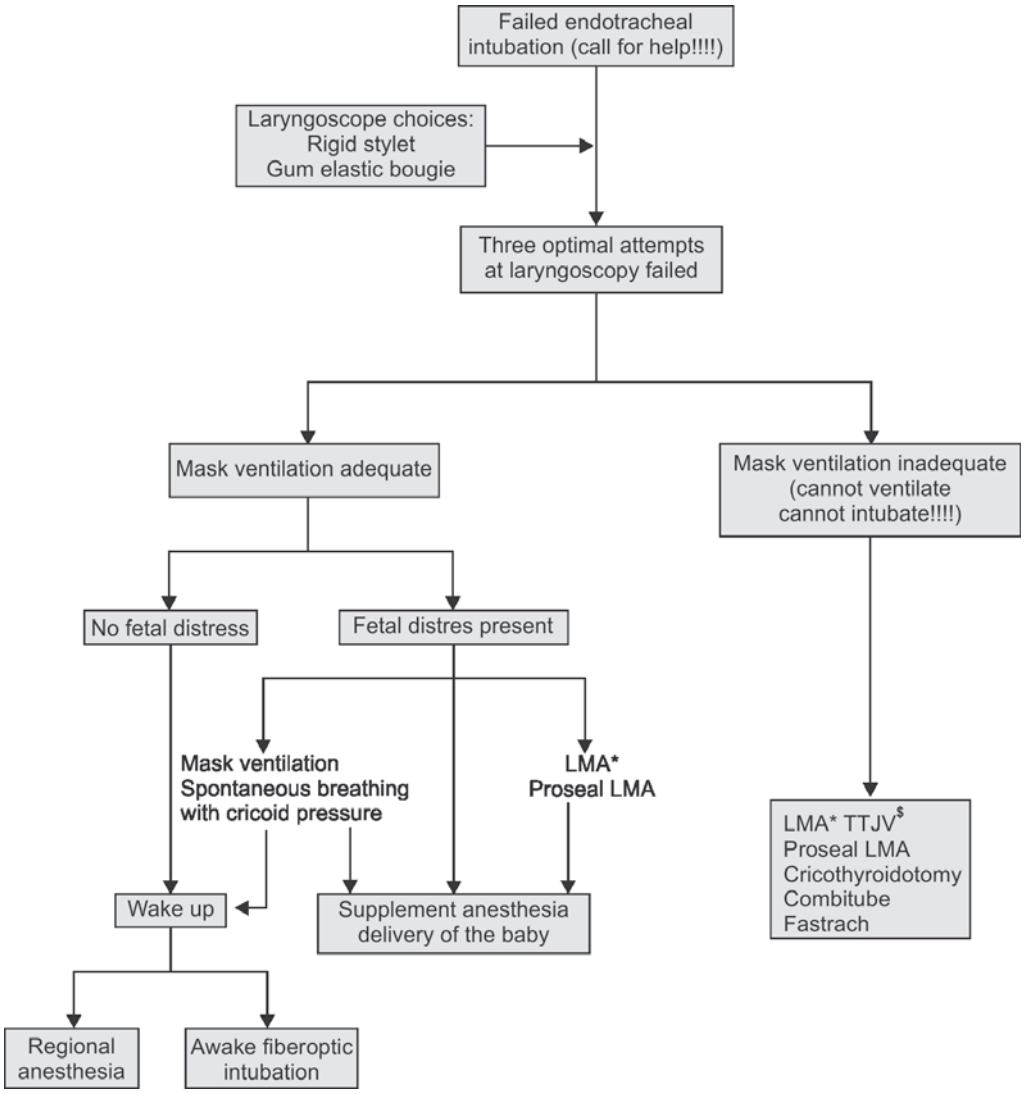
4. Develop primary and alternative strategies:



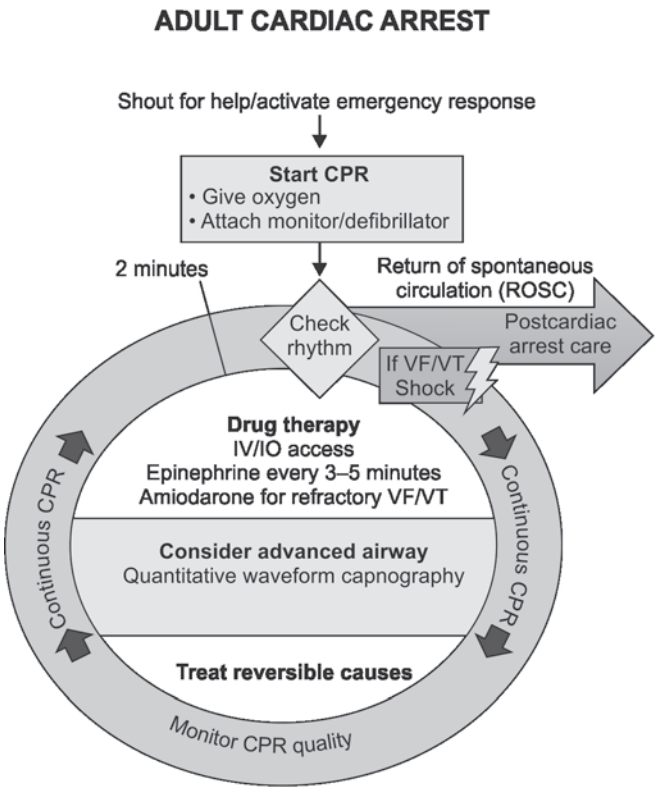
*** Confirm ventilation, tracheal intubation, or LMA placement with exhaled CO_2**

a. Other options include (but are not limited to) surgery utilizing face mask or LMA anesthesia, local anesthesia infiltration or regional nerve blockade. Pursuit of these options usually implies that mask ventilation will not be problematic. Therefore, these options may be of limited value if this step in the algorithm has been reached via the emergency pathway.
b. Invasive airway access includes surgical or percutaneous tracheostomy or cricothyrotomy
c. Alternative noninvasive approaches to difficult intubation include (but are not limited to) use of different laryngoscope blades, LMA as an intubation conduit (with or without fiberoptic guidance), fiberoptic intubation, intubating stylet or tube changer, light wand, retrograde intubation, and blind oral or nasal intubation.
d. Consider repreparation of the patient for awake intubation or canceling surgery.
e. Options for emergency noninvasive airway ventilation include (but are not limited to) rigid bronchoscope, esophageal-tracheal combitube ventilation or transtracheal jet ventilation.

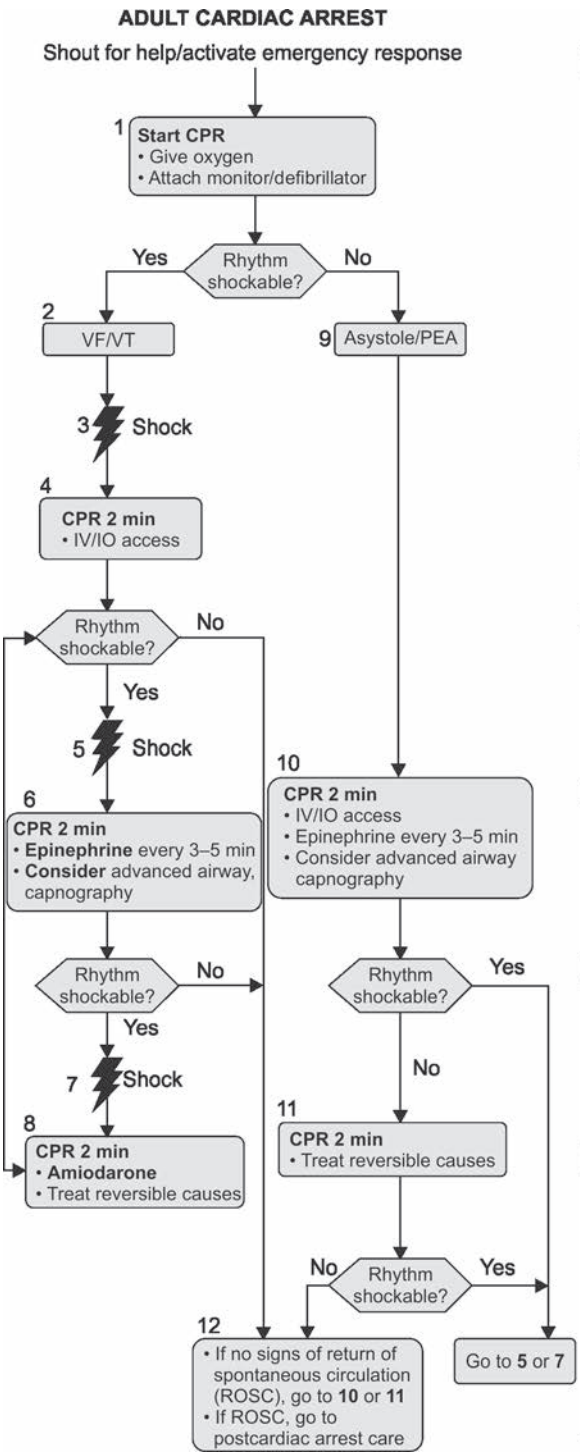
DIFFICULT AIRWAY ALGORITHM IN OBSTETRICS



Steps after trial of failed intubation during general anesthesia in an obstetric patient.
*Laryngeal mask airway.
$Transtracheal jet ventilation.



CPR quality
• Push hard (≥ 2 inches (5 cm) and fast (≥ 100/min) and allow complete chest recoil • Minimize interrruptions in compressions • Avoid excessive ventilation • Rotate compressor every 2 minutes • If no advanced airway, 30 : 2 compression-ventilation ratio • Quantitative waveform capnography – If $PETCO_2 \leq 10$ mm Hg, attempt to improve CPR quality • Intra-arterial pressure – If relaxation phase (diastolic) pressure ≤ 20 mm Hg, attempt to improve CPR quality.
Return of spontaneous circulation (ROSC)
• Pulse and blood pressure • Abrupt sustained increase in $PETCO_2$ (typically ≥ 40 mm Hg) • Spontaneous arterial pressure waves with intra-arterial monitoring.
Shock energy
• **Biphasic:** Manufacturer recommendation (e.g. initial dose of 120–200 J); if unknown, use maximum available. Second and subsequent doses should be equivalent and higher doses may be considered. • **Monophasic:** 360 J.
Drug therapy
• **Epinephrine IV/IO dose:** 1 mg every 3–5 minutes • **Vasopressin IV/IO dose:** 40 units can replace first or second dose of epinephrine. • **Amiodarone IV/IO dose:** First dose: 300 mg bolus. Second dose: 150 mg.
Advanced airway
• Supraglottic advaced airway or endotracheal intubation • Waveform capnography to confirm and monitor ET tube placement • 8–10 breaths per minute with continuous chest compressions.
Reversible causes
• **H**ypovolemia • **H**ypoxia • **H**ydrogen ion (acidosis) • **H**ypro-/hyperkalemia • **H**ypothermia • **T**ension pneumothorax • **T**amponade, cardiac • **T**oxins • **T**hrombosis, pulmonary • **T**hrombosis, coronary



CPR quality

- Push hard (≥ 2 inches [5 cm]) and fast (≥ 100/min) and allow complete chest recoil
- Minimize interruptions in compressions
- Avoid excessive ventilation
- Rotate compressor every 2 minutes
- If no advanced airway, 30 : 2 compression-ventilation ratio
- Quantitative waveform capnograhy:
  If $PETCO_2$ < 10 mm Hg, attempt to improve CPR quality
- Intra-arterial pressure:
  If relaxation phase (diastolic) pressure < 20 mm Hg, attempt to improve CPR quality.

Return of spontaneous circulation (ROSC)

- Pulse and blood pressure
- Abrupt sustained increase in $PETCO_2$ (typically ≥ 40 mm Hg)
- Spontaneous arterial pressure waves with intra-arterial monitoring.

Shock energy

- **Biphasic:** Manufacturer recommendation (e.g. initial dose of 120–200 J); if unknown, use maximum available. Second and subsequent doses should be equivalent, and higher doses may be considered
- **Monophasic:** 360 J.

Drug therapy

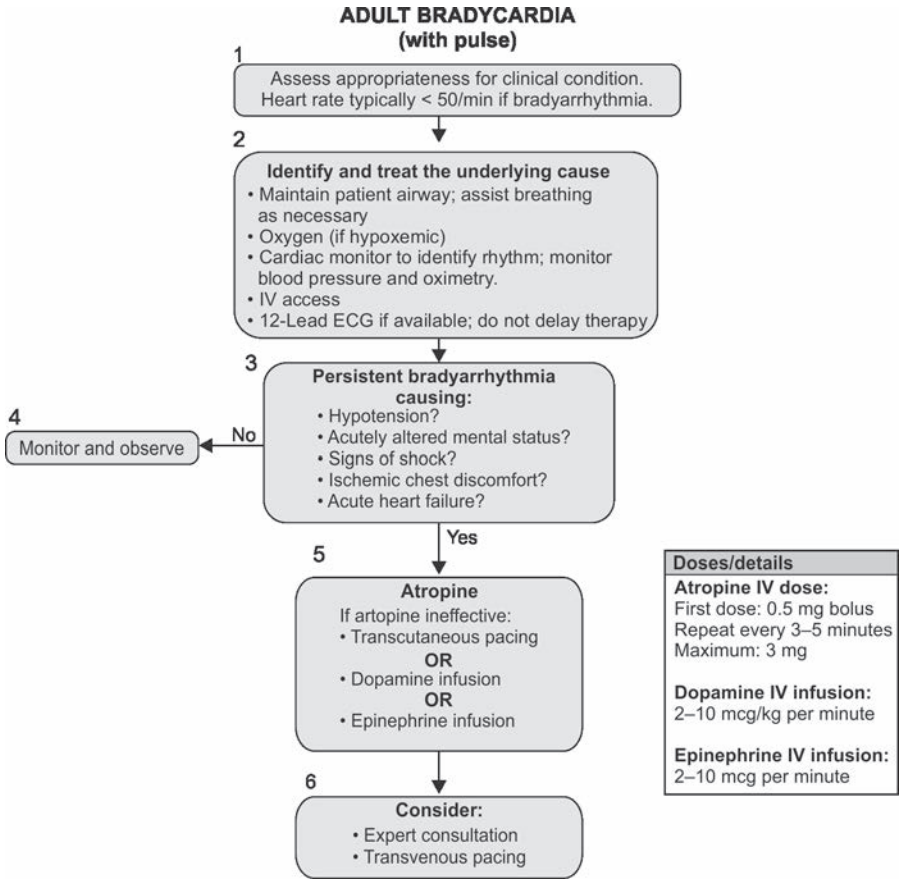
- **Epinephrine IV/IO dose:** 1 mg every 3–5 minutes
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- **Amiodarone IV/IO dose:** First dose: 300 mg bolus. Second dose: 150 mg.

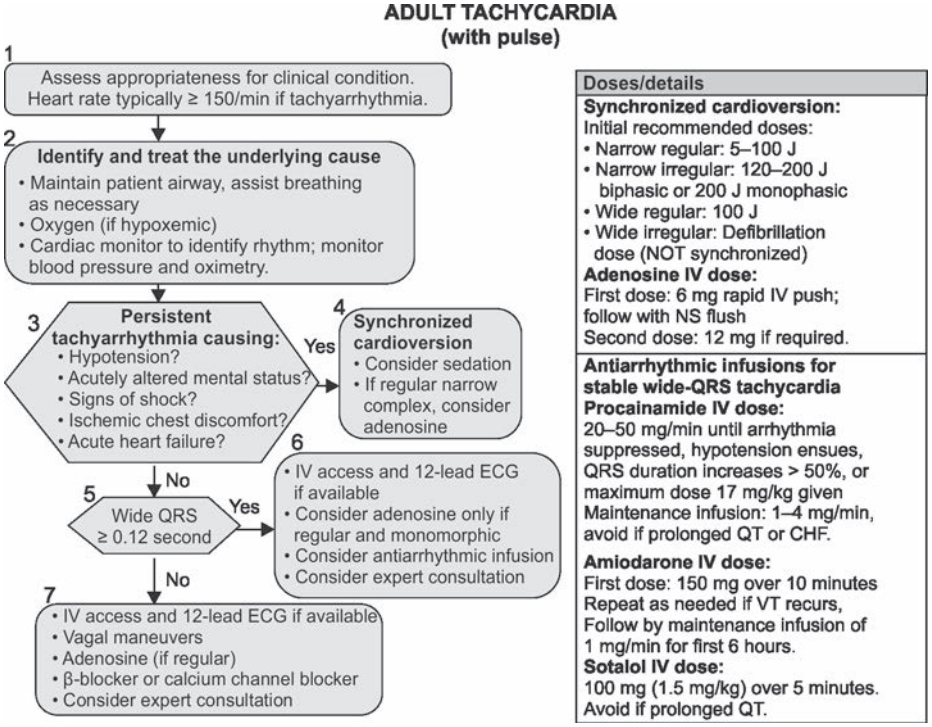
Advanced airway

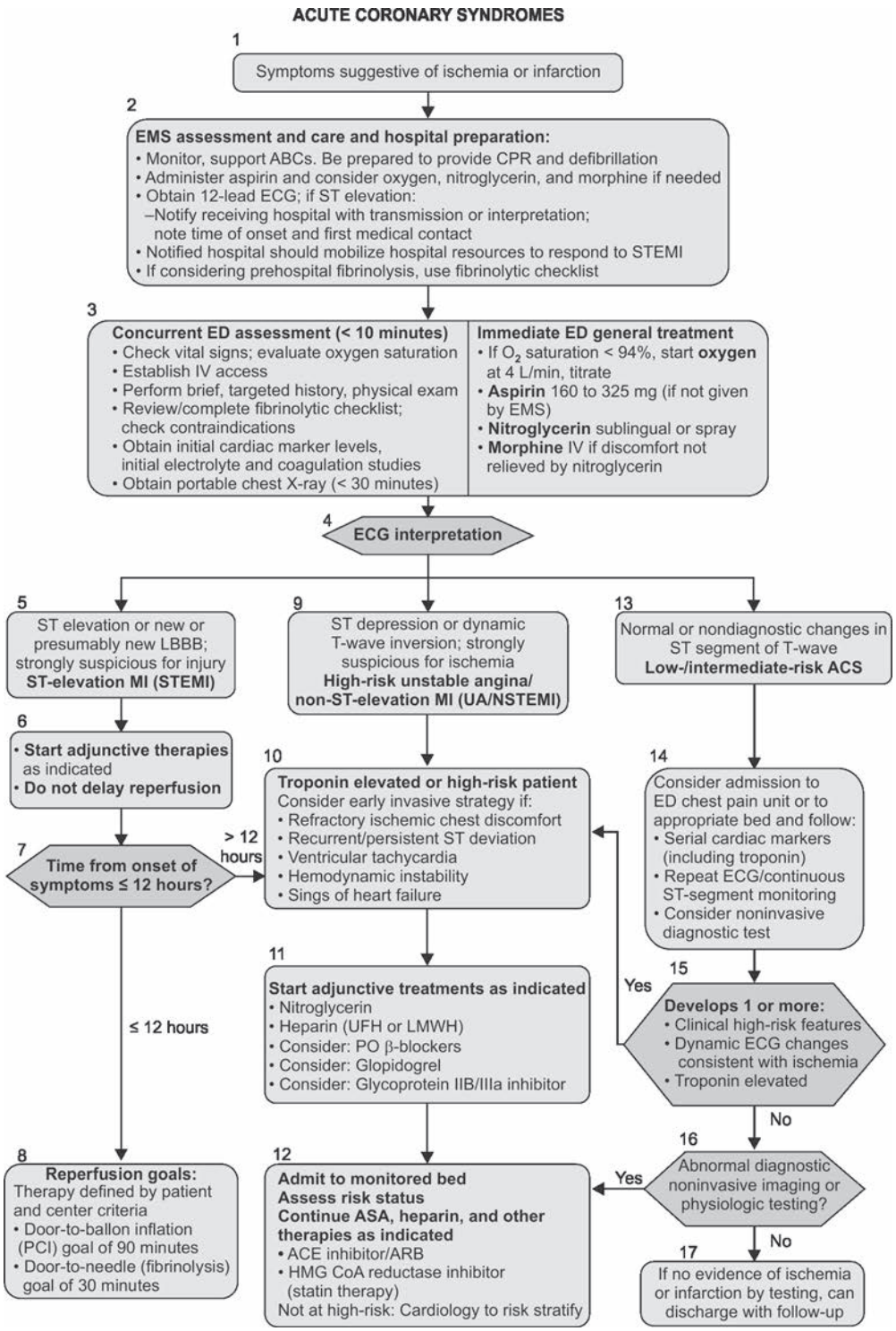
- Supraglottic advanced airway or endotracheal intubation
- Waveform capnography to confirm and monitor ET tube placement
- 8–10 breaths per minute with continuous chest compressions.

Reversible causes

- Hypovolemia
- Hypoxia
- Hydrogen ion (acidosis)
- Hypo-/hyperkalemia
- Hypothermia
- Tension pneumothorax
- Tamponade, cardiac
- Toxins
- Thrombosis, pulmonary
- Thrombosis, coronary


ADULT BRADYCARDIA
(with pulse)
1
Assess appropriateness for clinical condition.
Heart rate typically < 50/min if bradyarrhythmia.
2
Identify and treat the underlying cause
• Maintain patient airway; assist breathing as necessary
• Oxygen (if hypoxemic)
• Cardiac monitor to identify rhythm; monitor blood pressure and oximetry.
• IV access
• 12-Lead ECG if available; do not delay therapy
3
Persistent bradyarrhythmia causing:
• Hypotension?
• Acutely altered mental status?
• Signs of shock?
• Ischemic chest discomfort?
• Acute heart failure?
No
4
Monitor and observe
Yes
5
Atropine
If artopine ineffective:
• Transcutaneous pacing
OR
• Dopamine infusion
OR
• Epinephrine infusion
6
Consider:
• Expert consultation
• Transvenous pacing
Doses/details
Atropine IV dose:
First dose: 0.5 mg bolus
Repeat every 3–5 minutes
Maximum: 3 mg
Dopamine IV infusion:
2–10 mcg/kg per minute
Epinephrine IV infusion:
2–10 mcg per minute


ADULT TACHYCARDIA
(with pulse)
1
Assess appropriateness for clinical condition.
Heart rate typically ≥ 150/min if tachyarrhythmia.
2
Identify and treat the underlying cause
• Maintain patient airway, assist breathing as necessary
• Oxygen (if hypoxemic)
• Cardiac monitor to identify rhythm; monitor blood pressure and oximetry.
3
Persistent tachyarrhythmia causing:
• Hypotension?
• Acutely altered mental status?
• Signs of shock?
• Ischemic chest discomfort?
• Acute heart failure?
Yes
4
Synchronized cardioversion
• Consider sedation
• If regular narrow complex, consider adenosine
No
5
Wide QRS ≥ 0.12 second
Yes
6
• IV access and 12-lead ECG if available
• Consider adenosine only if regular and monomorphic
• Consider antiarrhythmic infusion
• Consider expert consultation
No
7
• IV access and 12-lead ECG if available
• Vagal maneuvers
• Adenosine (if regular)
• β-blocker or calcium channel blocker
• Consider expert consultation
Doses/details
Synchronized cardioversion:
Initial recommended doses:
• Narrow regular: 5–100 J
• Narrow irregular: 120–200 J biphasic or 200 J monophasic
• Wide regular: 100 J
• Wide irregular: Defibrillation dose (NOT synchronized)
Adenosine IV dose:
First dose: 6 mg rapid IV push; follow with NS flush
Second dose: 12 mg if required.
Antiarrhythmic infusions for stable wide-QRS tachycardia
Procainamide IV dose:
20–50 mg/min until arrhythmia suppressed, hypotension ensues, QRS duration increases > 50%, or maximum dose 17 mg/kg given
Maintenance infusion: 1–4 mg/min, avoid if prolonged QT or CHF.
Amiodarone IV dose:
First dose: 150 mg over 10 minutes
Repeat as needed if VT recurs,
Follow by maintenance infusion of 1 mg/min for first 6 hours.
Sotalol IV dose:
100 mg (1.5 mg/kg) over 5 minutes.
Avoid if prolonged QT.


ACUTE CORONARY SYNDROMES
1
Symptoms suggestive of ischemia or infarction
2
EMS assessment and care and hospital preparation:
• Monitor, support ABCs. Be prepared to provide CPR and defibrillation
• Administer aspirin and consider oxygen, nitroglycerin, and morphine if needed
• Obtain 12-lead ECG; if ST elevation:
–Notify receiving hospital with transmission or interpretation; note time of onset and first medical contact
• Notified hospital should mobilize hospital resources to respond to STEMI
• If considering prehospital fibrinolysis, use fibrinolytic checklist
3
Concurrent ED assessment (< 10 minutes)
• Check vital signs; evaluate oxygen saturation
• Establish IV access
• Perform brief, targeted history, physical exam
• Review/complete fibrinolytic checklist; check contraindications
• Obtain initial cardiac marker levels, initial electrolyte and coagulation studies
• Obtain portable chest X-ray (< 30 minutes)
Immediate ED general treatment
• If O_2 saturation < 94%, start oxygen at 4 L/min, titrate
• Aspirin 160 to 325 mg (if not given by EMS)
• Nitroglycerin sublingual or spray
• Morphine IV if discomfort not relieved by nitroglycerin
4
ECG interpretation
5
ST elevation or new or presumably new LBBB; strongly suspicious for injury
ST-elevation MI (STEMI)
9
ST depression or dynamic T-wave inversion; strongly suspicious for ischemia
High-risk unstable angina/ non-ST-elevation MI (UA/NSTEMI)
13
Normal or nondiagnostic changes in ST segment of T-wave
Low-/intermediate-risk ACS
6
• Start adjunctive therapies as indicated
• Do not delay reperfusion
7
Time from onset of symptoms ≤ 12 hours?
> 12 hours
≤ 12 hours
10
Troponin elevated or high-risk patient
Consider early invasive strategy if:
• Refractory ischemic chest discomfort
• Recurrent/persistent ST deviation
• Ventricular tachycardia
• Hemodynamic instability
• Sings of heart failure
11
Start adjunctive treatments as indicated
• Nitroglycerin
• Heparin (UFH or LMWH)
• Consider: PO β-blockers
• Consider: Glopidogrel
• Consider: Glycoprotein IIB/IIIa inhibitor
14
Consider admission to ED chest pain unit or to appropriate bed and follow:
• Serial cardiac markers (including troponin)
• Repeat ECG/continuous ST-segment monitoring
• Consider noninvasive diagnostic test
15
Develops 1 or more:
• Clinical high-risk features
• Dynamic ECG changes consistent with ischemia
• Troponin elevated
Yes
No
16
Abnormal diagnostic noninvasive imaging or physiologic testing?
Yes
No
17
If no evidence of ischemia or infarction by testing, can discharge with follow-up
8
Reperfusion goals:
Therapy defined by patient and center criteria
• Door-to-ballon inflation (PCI) goal of 90 minutes
• Door-to-needle (fibrinolysis) goal of 30 minutes
12
Admit to monitored bed
Assess risk status
Continue ASA, heparin, and other therapies as indicated
• ACE inhibitor/ARB
• HMG CoA reductase inhibitor (statin therapy)
Not at high-risk: Cardiology to risk stratify

MATERNAL CARDIAC ARREST

First Responder

- Activate maternal cardiac arrest team
- Document time of onset of maternal cardiac arrest
- Place the patient supine
- Start chest compressions as per BLS algorithm; place hands slightly higher on sternum than usual

Subsequent Responders

Maternal Interventions
Treat as per BLS and ACLS algorithms

- Do not delay defibrillation
- Give typical ACLS drugs and doses
- Ventilate with 100% oxygen
- Monitor waveform capnography and CPR quality
- Provide postcardiac arrest care as appropriate.

Maternal Modifications

- Start IV above the diaphragm
- Assess for hypovolemia and give fluid bolus when required
- Anticipate difficult airway; experienced provider preferred for advanced airway placement
- If patient receiving IV/IO magnesium prearrest, stop magnesium and give IV/IO calcium chloride 10 mL in 10% solution, or calcium gluconate 30 mL in 10% solution
- Continue all material resuscitative interventions (CPR, positioning, defibrillation, drugs, and fluids) during and after cesarean section.

Obstetric Interventions for Patient with an Obviously Gravid Uterus*

- Perform manual left uterine displacement (LUD)—displace uterus to the patient's left to relieve aortocaval compression
- Remove both internal and external fetal monitors if present

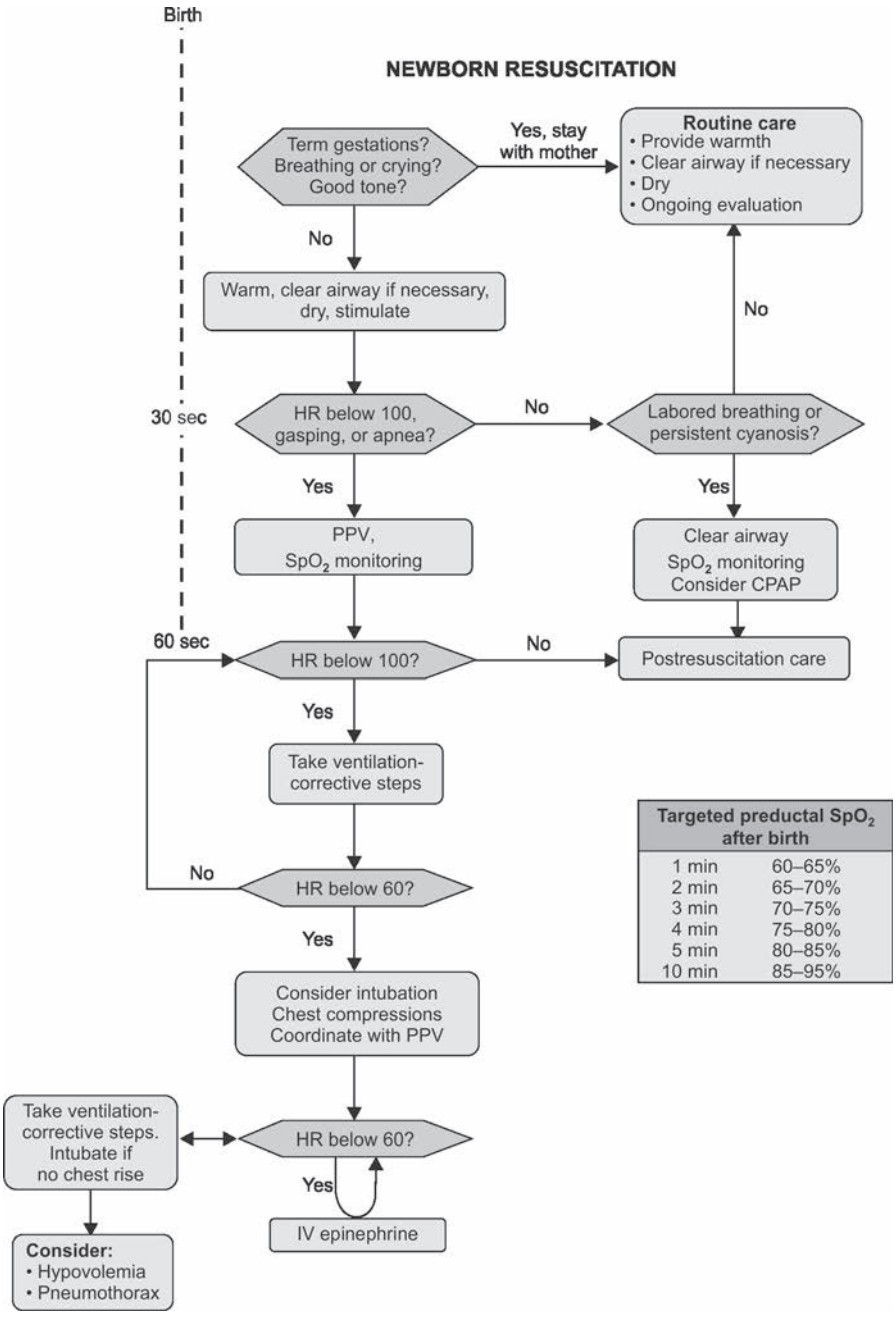
Obstetric and neonatal teams should immediately prepare for possible emergency cesarean section

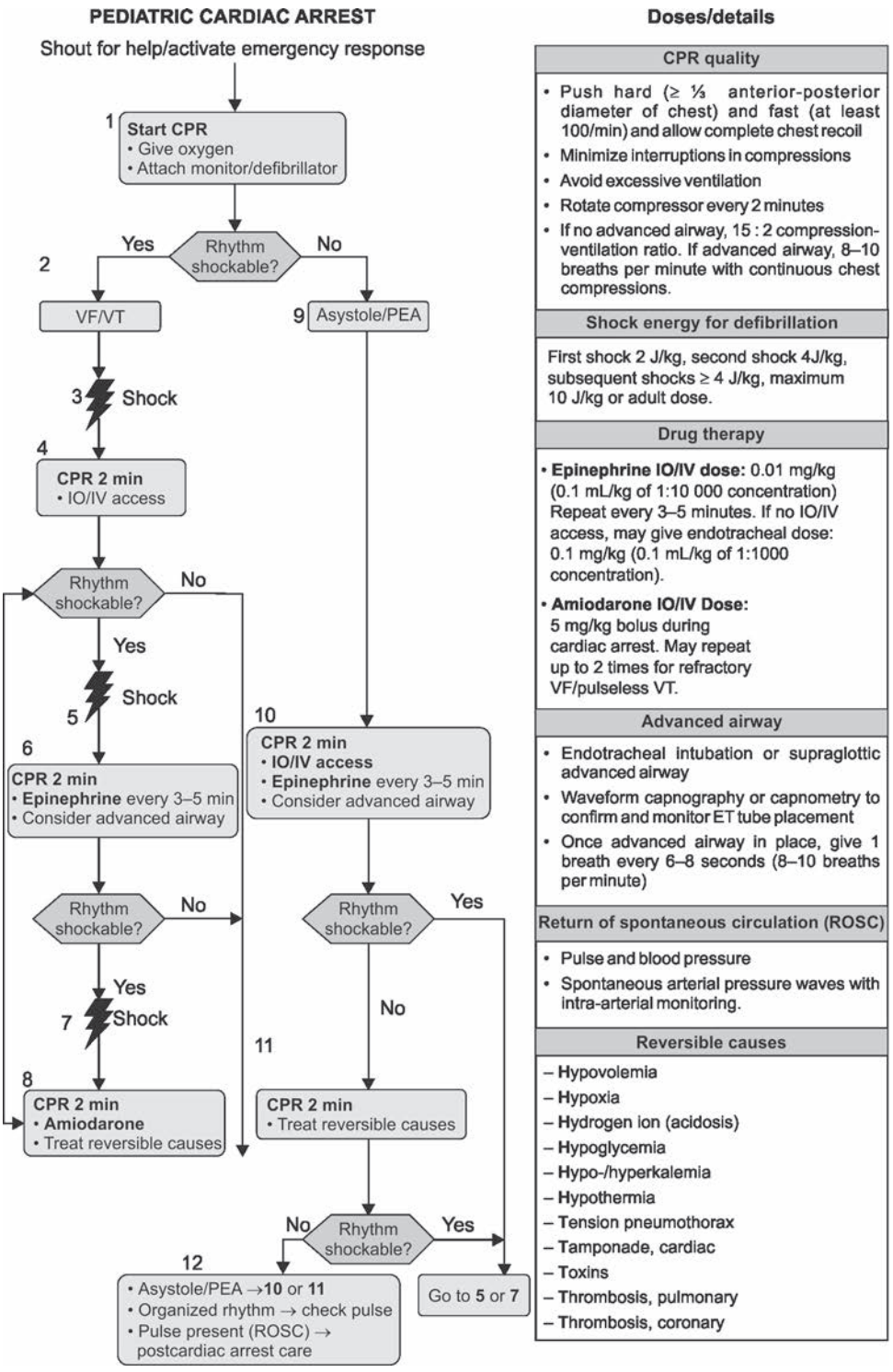
- If no ROSC by 4 minutes of resuscitative efforts, consider performing immediate emergency cesarean section
- If no ROSC by 4 minutes of resuscitative efforts, consider performing immediate emergency cesarean section
- Aim for delivery within 5 minutes of onset of resuscitative efforts

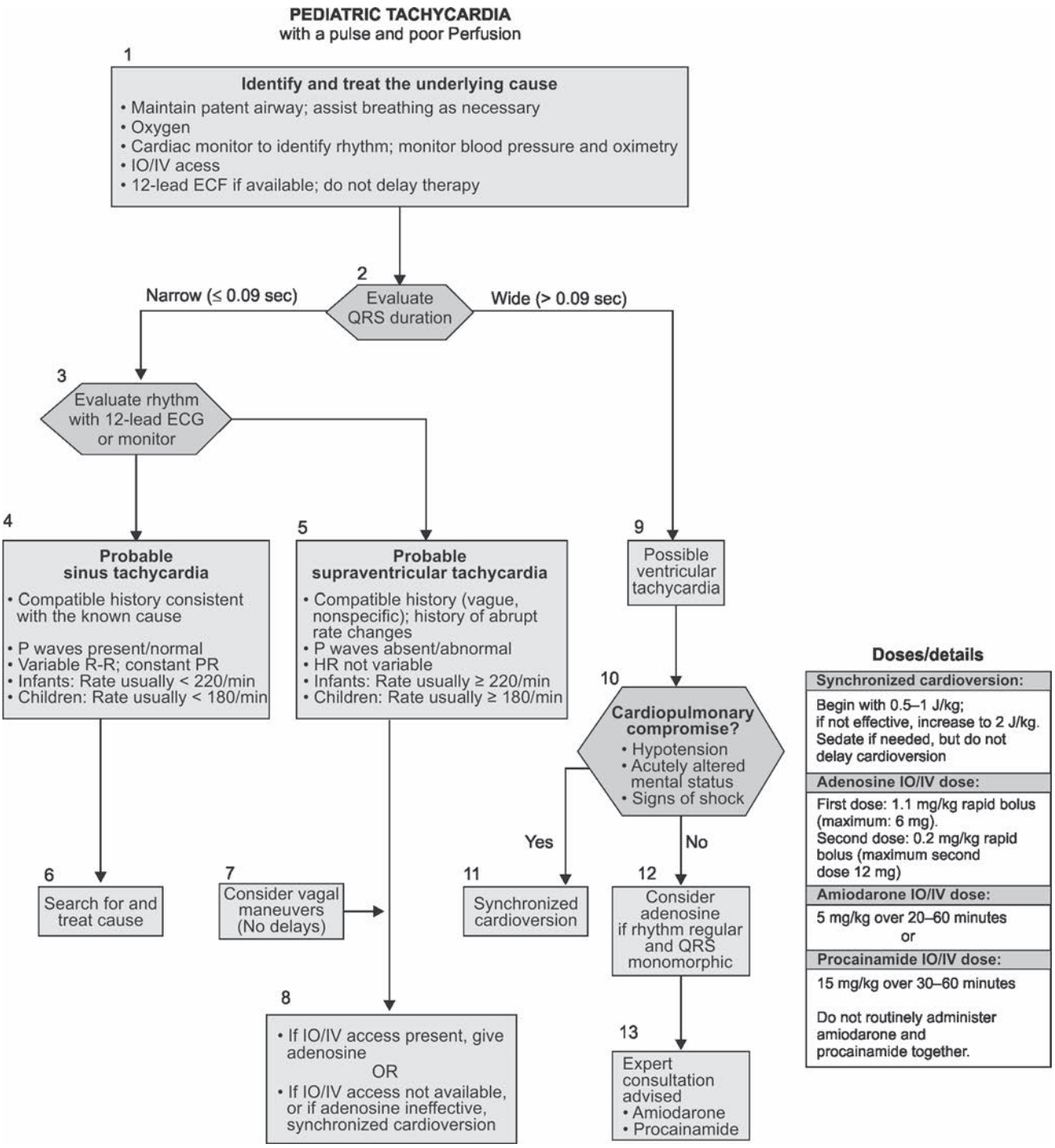
*An obviously gravid uterus is a uterus that is deemed clinically to be sufficiently large to cause aortocaval compression.

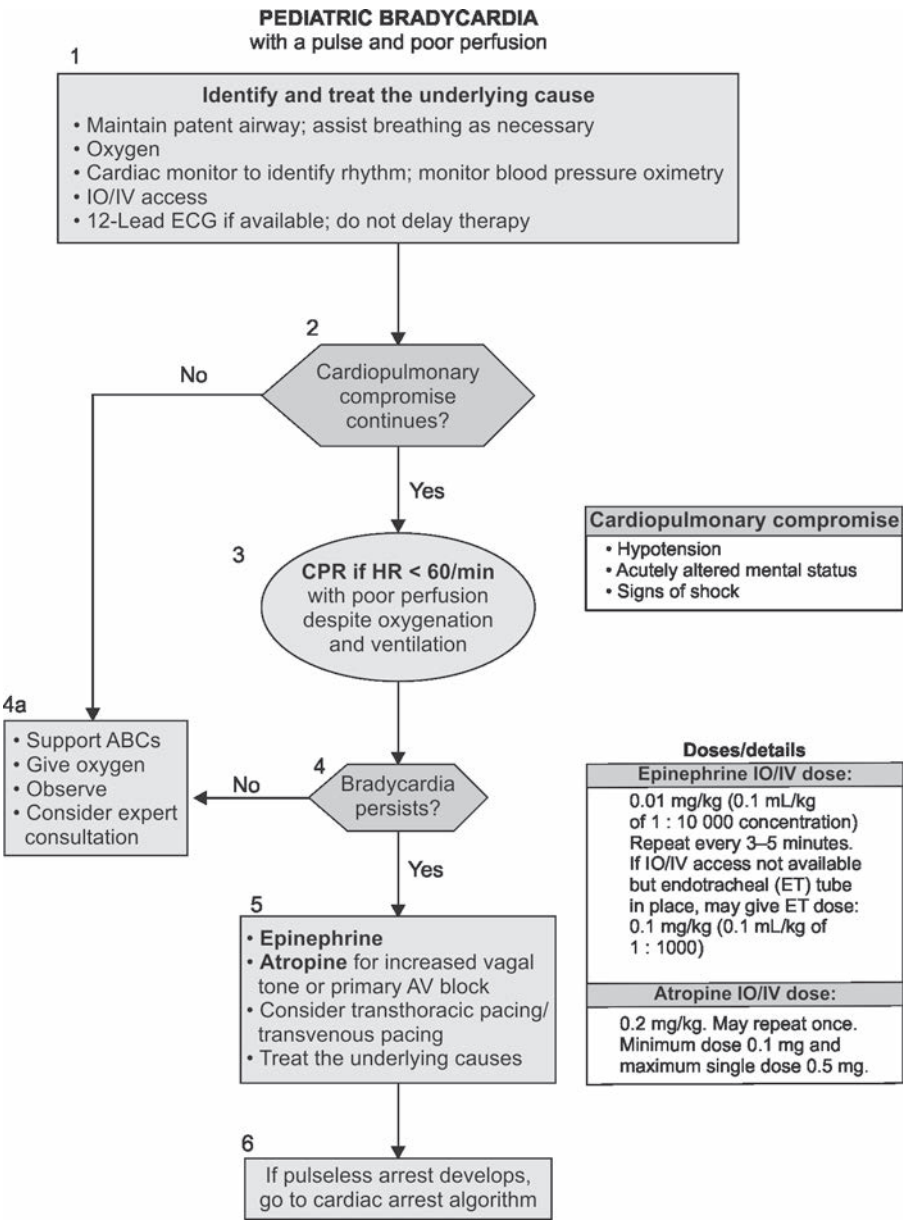
Search for and Treat Possible Contributing Factors (BEAU-CHOPS)

Bleeding/DIC
Embolism: Coronary/pulmonary/amniotic fluid embolism
Anesthetic complications
Uterine atony
Cardiac disease (MI/ischemia/aortic dissection/cardiomyopathy)
Hypertension/preeclampsia/eclampsia
Other: Differential diagnosis of standard ACLS guidelines
Placenta abruptio/previa
Sepsis

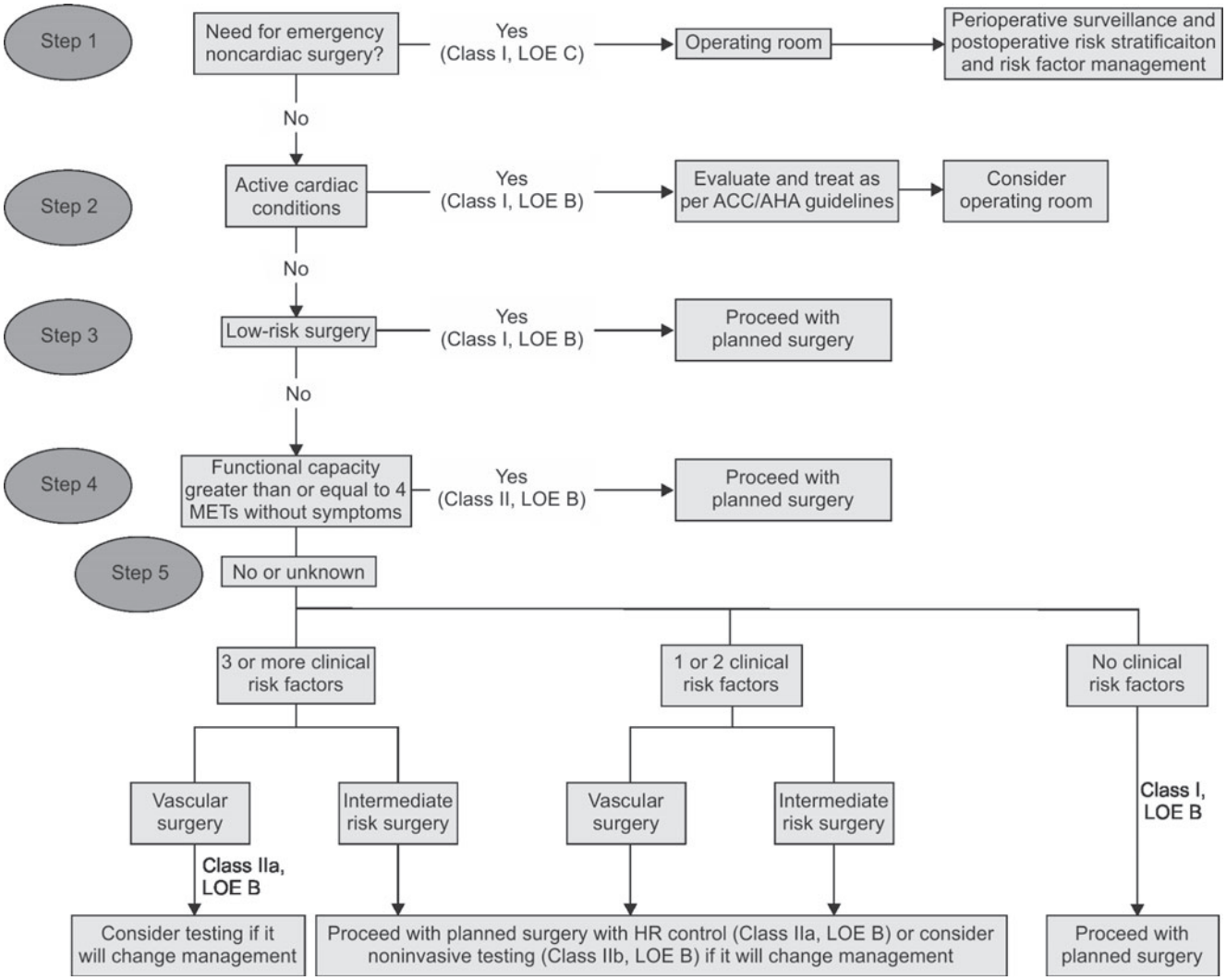

Birth
NEWBORN RESUSCITATION
Term gestations?
Breathing or crying?
Good tone?
Yes, stay with mother
Routine care
• Provide warmth
• Clear airway if necessary
• Dry
• Ongoing evaluation
No
Warm, clear airway if necessary, dry, stimulate
No
30 sec
HR below 100, gasping, or apnea?
No
Labored breathing or persistent cyanosis?
Yes
Yes
PPV, SpO2 monitoring
Clear airway
SpO2 monitoring
Consider CPAP
60 sec
HR below 100?
No
Postresuscitation care
Yes
Take ventilation-corrective steps
Targeted preductal SpO2 after birth
1 min 60–65%
2 min 65–70%
3 min 70–75%
4 min 75–80%
5 min 80–85%
10 min 85–95%
No
HR below 60?
Yes
Consider intubation
Chest compressions
Coordinate with PPV
Take ventilation-corrective steps. Intubate if no chest rise
HR below 60?
Yes
IV epinephrine
Consider:
• Hypovolemia
• Pneumothorax


PEDIATRIC CARDIAC ARREST
Shout for help/activate emergency response
1
Start CPR
• Give oxygen
• Attach monitor/defibrillator
Rhythm shockable?
Yes
No
2
VF/VT
9
Asystole/PEA
3
Shock
4
CPR 2 min
• IO/IV access
Rhythm shockable?
No
Yes
5
Shock
6
CPR 2 min
• Epinephrine every 3–5 min
• Consider advanced airway
Rhythm shockable?
No
Yes
7
Shock
8
CPR 2 min
• Amiodarone
• Treat reversible causes
10
CPR 2 min
• IO/IV access
• Epinephrine every 3–5 min
• Consider advanced airway
Rhythm shockable?
Yes
No
11
CPR 2 min
• Treat reversible causes
Rhythm shockable?
No
Yes
12
• Asystole/PEA →10 or 11
• Organized rhythm → check pulse
• Pulse present (ROSC) → postcardiac arrest care
Go to 5 or 7
Doses/details
CPR quality
• Push hard (≥ ⅓ anterior-posterior diameter of chest) and fast (at least 100/min) and allow complete chest recoil
• Minimize interruptions in compressions
• Avoid excessive ventilation
• Rotate compressor every 2 minutes
• If no advanced airway, 15 : 2 compression-ventilation ratio. If advanced airway, 8–10 breaths per minute with continuous chest compressions.
Shock energy for defibrillation
First shock 2 J/kg, second shock 4J/kg, subsequent shocks ≥ 4 J/kg, maximum 10 J/kg or adult dose.
Drug therapy
• Epinephrine IO/IV dose: 0.01 mg/kg (0.1 mL/kg of 1:10 000 concentration) Repeat every 3–5 minutes. If no IO/IV access, may give endotracheal dose: 0.1 mg/kg (0.1 mL/kg of 1:1000 concentration).
• Amiodarone IO/IV Dose: 5 mg/kg bolus during cardiac arrest. May repeat up to 2 times for refractory VF/pulseless VT.
Advanced airway
• Endotracheal intubation or supraglottic advanced airway
• Waveform capnography or capnometry to confirm and monitor ET tube placement
• Once advanced airway in place, give 1 breath every 6–8 seconds (8–10 breaths per minute)
Return of spontaneous circulation (ROSC)
• Pulse and blood pressure
• Spontaneous arterial pressure waves with intra-arterial monitoring.
Reversible causes
– Hypovolemia
– Hypoxia
– Hydrogen ion (acidosis)
– Hypoglycemia
– Hypo-/hyperkalemia
– Hypothermia
– Tension pneumothorax
– Tamponade, cardiac
– Toxins
– Thrombosis, pulmonary
– Thrombosis, coronary


PEDIATRIC TACHYCARDIA
with a pulse and poor Perfusion
1
Identify and treat the underlying cause
• Maintain patent airway; assist breathing as necessary
• Oxygen
• Cardiac monitor to identify rhythm; monitor blood pressure and oximetry
• IO/IV acess
• 12-lead ECF if available; do not delay therapy
2
Evaluate QRS duration
Narrow (≤ 0.09 sec)
Wide (> 0.09 sec)
3
Evaluate rhythm with 12-lead ECG or monitor
4
Probable sinus tachycardia
• Compatible history consistent with the known cause
• P waves present/normal
• Variable R-R; constant PR
• Infants: Rate usually < 220/min
• Children: Rate usually < 180/min
5
Probable supraventricular tachycardia
• Compatible history (vague, nonspecific); history of abrupt rate changes
• P waves absent/abnormal
• HR not variable
• Infants: Rate usually ≥ 220/min
• Children: Rate usually ≥ 180/min
9
Possible ventricular tachycardia
10
Cardiopulmonary compromise?
• Hypotension
• Acutely altered mental status
• Signs of shock
Yes
No
6
Search for and treat cause
7
Consider vagal maneuvers (No delays)
8
• If IO/IV access present, give adenosine
OR
• If IO/IV access not available, or if adenosine ineffective, synchronized cardioversion
11
Synchronized cardioversion
12
Consider adenosine if rhythm regular and QRS monomorphic
13
Expert consultation advised
• Amiodarone
• Procainamide
Doses/details
Synchronized cardioversion:
Begin with 0.5–1 J/kg;
if not effective, increase to 2 J/kg.
Sedate if needed, but do not delay cardioversion
Adenosine IO/IV dose:
First dose: 1.1 mg/kg rapid bolus (maximum: 6 mg).
Second dose: 0.2 mg/kg rapid bolus (maximum second dose 12 mg)
Amiodarone IO/IV dose:
5 mg/kg over 20–60 minutes
or
Procainamide IO/IV dose:
15 mg/kg over 30–60 minutes
Do not routinely administer amiodarone and procainamide together.


PEDIATRIC BRADYCARDIA
with a pulse and poor perfusion
1
Identify and treat the underlying cause
• Maintain patent airway; assist breathing as necessary
• Oxygen
• Cardiac monitor to identify rhythm; monitor blood pressure oximetry
• IO/IV access
• 12-Lead ECG if available; do not delay therapy
2
Cardiopulmonary compromise continues?
No
Yes
Cardiopulmonary compromise
• Hypotension
• Acutely altered mental status
• Signs of shock
3
CPR if HR < 60/min with poor perfusion despite oxygenation and ventilation
4a
• Support ABCs
• Give oxygen
• Observe
• Consider expert consultation
4
Bradycardia persists?
No
Yes
Doses/details
Epinephrine IO/IV dose:
0.01 mg/kg (0.1 mL/kg of 1 : 10 000 concentration) Repeat every 3–5 minutes. If IO/IV access not available but endotracheal (ET) tube in place, may give ET dose: 0.1 mg/kg (0.1 mL/kg of 1 : 1000)
Atropine IO/IV dose:
0.2 mg/kg. May repeat once. Minimum dose 0.1 mg and maximum single dose 0.5 mg.
5
• Epinephrine
• Atropine for increased vagal tone or primary AV block
• Consider transthoracic pacing/ transvenous pacing
• Treat the underlying causes
6
If pulseless arrest develops, go to cardiac arrest algorithm

NONCARDIAC SURGERY IN CARDIAC PATIENTS



DNB Question Paper

CARDIOVASCULAR SYSTEM

1. Air embolism during anesthesia
2. Methods, uses and complications of cannulation of internal jugular vein
3. Central venous pressure monitoring and uses
4. Cardiac arrhythmias during anesthesia
5. Discuss the etiology and management of supraventricular arrhythmias during surgical procedures.
6. Pulmonary artery catheter
7. Prevention and treatment of intraoperative myocardial infarction
8. Preoperative preparation and evaluation of a patient with history of exertional angina for surgery under general anesthesia
9. Management of multi focal ventricular ectopics during anesthesia
10. Monitored anesthesia care in a 75 years old man with *ischemic heart disease* for cataract surgery.
11. Define hypertension. How will you evaluate and prepare preoperatively a 40-year-old female patient scheduled for abdominal hysterectomy. Discuss the anesthetic and postoperative management of such a case.
12. Coronary circulation, *Goldmans* risk index
13. Describe the basic life support (BLS) measures in an adult, who has been brought into the emergency room of the hospital in a state of cardiac arrest.
14. *Myocardial protection* during cardiopulmonary bypass
15. Anesthesia in a patient with *artificial pacemaker*
16. Transesophageal echocardiography
17. Child with *tetralogy of Fallot* is posted for corrective surgery. Discuss the preoperative evaluation and anesthetic management of this case
18. Role of anesthetist in the management of a case with *thromboangitis obliterans*.
19. Factors affecting coronary circulation
20. Defibrillation
21. Cardioversion
22. Myocardial preservation
23. Pathophysiology of CAD. Discuss anesthetic management of a patient with angina.
24. Cardiac evaluation for noncardiac surgery
25. Classify congenital heart diseases. Explain with diagrams the blood flow before and after delivery in *patent ductus arteriosus.*
26. Clinical features of *infective endocarditis*, principle guidelines to use antibiotics as prophylaxis against, during surgery
27. Preoperative evaluation of a patient with *valvular heart disease*
28. A patient who has undergone *heart transplant* requires noncardiac surgery. What precautions must be undertaken by an anesthesiologist for this surgery?
29. Define *perioperative hypertension*. Describe the causes and management.
30. Discuss the anesthetic management in a patient of *myasthenia gravis* scheduled for thymectomy.
31. Advantages and disadvantages of off-pump coronary artery bypass graft surgery (OPCAB)
32. Determinants of cardiac output and noninvasive methods of measurement of CO
33. Anesthetic management of *mitral stenosis and atrial fibrillation* for balloon valvotomy
34. A hypertensive man with CAD for TURP: Discuss the anesthetic management
35. Anticoagulation and cardiopulmonary bypass
36. Cardioplegia
37. Anesthetic management of mitral stenosis for closed mitral valvotomy
38. Anesthesia in a patient with *coronary stent*
39. Perioperative problems and anesthetic management of mitral stenosis for elective LSCS

40. Anesthetic management of 3-year-old child scheduled for PDA ligation
41. Indication of mediastinoscopy, anesthetic implication
42. DVT-diagnosis, prophylaxis and management
43. Preoperative evaluation and anesthetic management of a patient with mediastinal tumor for thoracotomy
44. PCWP vs CVP
45. Anesthetic management in a patient with *abdominal aortic dissection* scheduled for aortic bypass graft
46. Describe the cardiac conduction system. How do you manage a patient with *paroxysmal supraventricular tachycardia*?

ENDOCRINE SYSTEM

1. *Pheochromocytoma*—preoperative preparation, anesthetic management and complications during removal of the tumor
2. Discuss the preoperative investigations, preparation and anesthetic management of *diabetic* patient presenting for an exploratory laparotomy.
3. Preoperative evaluation and preparation of a patient of *thyrotoxicosis.* Describe anesthetic and postoperative management of such a case.
4. *Myasthenia gravis*—clinical features, preoperative investigations, preparation, anesthetic management and complications for an interval appendicectomy
5. Management of *diabetic ketoacidosis*
6. Role of corticosteroids in the practice of anesthesiology
7. *Thyroid crisis*
8. *Malignant hyperthermia*—clinical features, laboratory finding and anesthetic importance
9. *Myxoedematous coma,* causes of airway obstruction following thyroid surgery and its management
10. *Carcinoid tumor* for removal: anesthetic management
11. Anesthetic management of a case of diabetes scheduled for open cholecystectomy
12. Diabetic patient with *autonomic neuropathy* for abdominal hysterectomy
13. Anesthetic management of a case of pituitary adenoma who is planned for transsphenoidal hypophysectomy
14. A 25-year-old man presents with marked features of acromegaly and is posted for transsphenoidal hypophysectomy. Discuss the anesthetic management.
15. A 60-year-old man presents for elective *parathyroidectomy.* Discuss the anesthetic management.
16. Discuss anesthetic management of 25-year-old female with *Cushing syndrome* for bilateral adrenalectomy.
17. Discuss anesthetic management of an inadequately managed diabetes mellitus patient with ketoacidosis posted for below knee amputation.
18. 50-year-old woman with *hypothyroidism* is scheduled for abdominal hysterectomy. Discuss the anesthetic management.
19. Evaluation of autonomic nervous system in diabetic autonomic neuropathy
20. Different methods used for *perioperative control of blood sugar* in diabetes with their advantages and disadvantages
21. Describe the manifestations and management of thyroid storm intraoperatively.

OPHTHALMOLOGY AND ENT

1. Problems during anesthesia for *laser surgery*
2. Anesthesia for *squint surgery.*
3. Anesthesia for *perforating injury* of the eye in a 3-year-old child
4. Anesthesia for *total laryngectomy*
5. *Oculocardiac reflex*
6. Anesthesia for *intraocular surgery*
7. *Post tonsillectomy bleeding*
8. Merits and demerits of *Retrobulbar vs Peribulbar block*
9. Anesthesia techniques practiced for cataract surgery and their complications
10. A 2-year-old child weighing 10 kg is scheduled for removal of organic foreign body in right bronchus. Discuss the anesthetic management.
11. Causes of hypertension in 20 years old female patient posted for *angiofibroma* of nose
12. Anesthetic management of a child with retropharyngeal abscess presenting for surgical drainage
13. A 22-year-old male patient with multiple papilloma of larynx is scheduled for laser excision. Describe the anesthetic management.
14. What is *monitored anesthesia care*? Describe the technique in an 80-year-old patient with ischemic heart disease scheduled for cataract surgery.

GIT, LIVER AND URO

1. Anesthetic management and postoperative care in a patient with uncontrolled hypertension (BP 180/120 mm Hg) for emergency laparotomy for *perforated duodenal ulcer*
2. *Hepatorenal syndrome*—etiology, pathophysiology prevention and management
3. Preoperative evaluation and anesthetic management of an emergency abdominal operation in a 60-year-old man who had myocardial infarction six weeks back
4. Problems of *laparoscopic surgery* and monitoring techniques used during the procedure
5. Upper intestinal obstruction for emergency laparotomy. Discuss the preoperative evaluation, preparation and anesthetic management of the case.
6. Anesthetic management of strangulated inguinal hernia in a patient with a recent myocardial infarction
7. *TURP Syndrome*
8. Assessment, preparation and problems of anesthesia in a chronic smoker for cholecystectomy
9. Preoperative preparation and risk assessment in a patient with *cirrhosis of liver*
10. *Hepatitis B* and the anesthesiologist
11. Electrolyte disturbances and preanesthestic correction in small gut obstruction
12. Assessment of risk factor for patient with moderate to severe liver disease
13. *Postoperative jaundice*
14. Preoperative evaluation of a case with *chronic renal failure* posted for renal transplant
15. Describe the *countercurrent mechanism* in the kidney. Discuss the renal protection strategies during preoperative period.
16. Role of kidney in acid base balance
17. Patient with permanent pacemaker posted for TURP
18. Discuss the anesthetic problems in a patient undergoing lienorenal shunt.
19. Anesthetic problems of *liver transplantation surgery*
20. Preoperative assessment and preparation for *thoraco-abdominal esophagectomy*. Describe your anesthetic problem during operation.
21. Preoperative preparation of diabetic patient with bleeding varices for lienorenal shunt operation
22. Anesthetic considerations in chronic liver failure
23. What are the problems associated with anesthesia for an elective surgery in patient of chronic renal failure?
24. A patient with *obstructive jaundice* is posted for Whipple's procedure. Discuss preoperative evaluation and anesthetic management of this case.
25. Discuss anesthetic management of a 20-year-old male with achalasia cardia and bronchial asthma for laparoscopic cardiomyotomy.
26. What are the problems related to *chronic hemodialysis*?
27. What are the anesthetic implications in a patient with transplanted kidney posted for incidental elective surgery?
28. Physiological changes associated with pneumoperitonium for laparoscopic cholecystectomy
29. Anesthetic management of a severely jaundiced patient
30. Describe the assessment and management of a 70-year-old patient posted for transurethral resection of prostate. What are the possible complications and how will you treat them?

INSTRUMENTS

1. Double lumen endotracheal tubes
2. Volutrauma
3. Application of venturi principle in anesthetic practice
4. Role of capnography during anesthesia
5. Sterilization of anesthesia equipments
6. Coaxial circuits
7. Pediatric circuit
8. Merits and demerits of laryngeal mask
9. Evolution of rotameter
10. PEEP and its application in modern ventilators
11. Check out procedure to be followed routinely before using an anesthesia machine and other monitoring equipment.
12. Pulse oximetry
13. Jugular venous oximetry
14. Characteristics of ideal vaporizer
15. Newer modes of ventilation
16. Physical principles of pulse oximetry
17. Operation theater safety

18. What is minimum monitoring standard? Describe the objectives and methods.
19. What is low flow anesthesia? Discuss its advantages and disadvantages.
20. Discuss different methods of humidification.
21. Draw a labeled diagram of a flexible fibreoptic bronchoscope and describe methods for its sterilization or high level disinfection.
22. Supraglottic airway devices
23. Link 25 proportioning system in anesthesia machine
24. Laryngeal mask airway—various modifications
25. Functional analysis of pressure reducing valve
26. Discuss principles of monitoring E_TCO_2
27. Classify vaporizers. Briefly mention the effects of altered barometric pressure on the performance of vaporizer.
28. Compare and contrast TOF and double burst
29. Discuss in brief the sites and devices for temperature monitoring.
30. Safety features in a modern day anesthesia machine
31. I Gel airway
32. LMA
33. Evolution of Boyles anesthesia machine
34. Sterilization of ventilators

NEUROANESTHESIA

1. Somatosensory evoked potential
2. Glasgow coma scale
3. Describe anesthetic and postoperative management of a patient undergoing intracranial aneurysm surgery.
4. Awareness during anesthesia
5. Monitoring and control of raised intracranial pressure in head injury
6. Preoperative management of a neonate for meningomyelocele surgery
7. Methods of decreasing increased intracranial pressure
8. Management of a 4 years old child scheduled for computerized tomographic scanning a brain using an iodine containing solution
9. Trigeminal neuralgia, clinical features and management
10. Regulation of cerebral blood flow
11. Regulation of intracranial tension
12. Hydrocephalus and its various methods of management
13. Preoperative evaluation of autonomic function
14. Horner's syndrome
15. Minimum monitoring for postspinal fusion in scoliosis
16. Anesthetic management of a patient with suspected posterior fossa tumor
17. Methods of monitoring of neuromuscular transmission during anesthesia
18. Methods of intracranial pressure (ICP) monitoring, uses and complication of ICP monitoring
19. Medical management of head injured patient
20. Describe the criteria and neurological test for brainstem death and preparing the patient for organ donation.
21. What is cerebral protection? Explain the methods adopted in clinical practice for cerebral protection.
22. Discuss the perioperative management of cerebral AVM (arteriovenous malformation).
23. Anesthesia for electroconvulsive therapy
24. Discuss the causes of delayed recovery from anesthesia and the management.
25. Guillain-Barre Syndrome: Discuss briefly etiology, pathogenesis, symptomatology and management including anesthetic management.
26. Intraoperative problems of neurosurgical procedure under anesthesia in sitting position
27. Preoperative evaluation and anesthetic considerations of a patient with Parkinson's disease
28. Compare and contrast TOF and double burst
29. What is bispectral index monitoring? What are its clinical applications in anesthesia practice?
30. How is cerebral blood flow regulated? What is the affect of various anesthetic drugs in cerebral blood flow?
31. Discuss the management of intracranial hypertension.
32. Hypotensive anesthesia in neurosurgery
33. What are the anesthetic problems of craniofacial surgery? Describe an appropriate anesthetic technique.
34. Central anticholinergic syndrome
35. Myasthenia gravis vs myasthenic syndrome
36. Causes of perioperative seizures

OBSTETRIC ANESTHESIA

1. HELLP syndrome
2. Discuss the pathophysiological changes in pre-eclampsia and eclampsia. Discuss your choice of anesthetic technique for such a patient for emergency cesarean section.
   a. A patient of coarctation of aorta is scheduled for cesarean section. Discuss the preoperative preparation, anesthetic management and post-operative care of the patient.
3. Draw a neat labeled diagram of fetal circulation and delineate the differences from adult.
4. Aspiration prophylaxis in obstetrics
5. Supine hypotension syndrome
6. Describe physiologic changes occurring during pregnancy and clinical implications to the anesthesiologist.
7. Modern trends in obstetrical analgesia
8. Cardiopulmonary resuscitation in pregnant women
9. Anesthetic management of emergency appendicectomy in a 16 weeks pregnant patient
10. Problems and management of pregnant patient with dilated cardiomyopathy on treatment for emergency LSCS
11. Preanesthetic evaluation of a patient of mitral stenosis for medical termination of pregnancy (MTP) and sterilization
12. Role of anesthesiologist in an obstetric unit
13. Regional versus GA in obstetric surgery
14. Anesthesia for a pregnant woman for non-obstetric surgery
15. Laparoscopy surgery in a pregnant patient
16. Describe innervation of female genital tract with a diagram and discuss methods of producing painless labor.
17. Discuss the preoperative evaluation and anesthetic management of a 30-year-old female patient who underwent mitral valve replacement 6 months ago and is now scheduled for medical termination of pregnancy (MTP) with laparoscopic sterilization.
18. Anesthetic implications of fetal surgery
19. Techniques to prevent hypotension after spinal anesthesia in cesarean section
20. Draw a labeled diagram of fetal circulation. What are the circulatory changes that occur at birth?
21. Amniotic fluid embolism
22. Neonatal resuscitation in labor room

ORTHO

1. Mechanism of reflex sympathetic dystrophy
2. Management of spinal injury
3. Post-traumatic fat embolism
4. The Golden Hour
5. An 80 Years old male is posted for total hip replacement. Discuss the preoperative evaluation, preparation and anesthetic management of this case
6. Discuss the preoperative assessment and the method of anesthesia in patient with TM ankylosis for the release of ankylosis.
7. Minimum monitoring for postspinal fusion in scoliosis
8. Assessment of an adult who sustained multiple trauma of few hours duration
9. Indication and contraindication for use of arterial tourniquet. What complication may arise from the use of such tourniquet?
10. Problems encountered by anesthetists during the orthopedic operative procedures
11. Anesthetic problems of total hip replacement in elderly patients
12. Anesthetic problems in scoliosis surgery
13. An 86-year-old patient is scheduled for open reduction and internal fixation of subtrochanteric fracture of femur. Discuss the preoperative evaluation and anesthetic management of patient
14. What is triage? What are the triage criteria in relation to trauma?
15. Discuss the anesthetic problems, preoperative preparation and anesthetic management of a case posted for correction of kyphoscoliosis.

OTHERS

1. Discuss the anesthetic techniques and postoperative problems in an obese patient for large hernia of interior abdominal wall.
2. Total intravenous anesthesia
3. Peripheral nerve injury under anesthesia
4. Describe airway management of a patient of ankylosing spondylitis with severe restriction of neck movement posted for total hip replacement.
5. Obesity: Anesthetic problems
6. Iatrogenic complications in anesthesia
7. Anesthesia for radiotherapy

8. Attenuation of laryngoscopic reaction to intubation
9. Etiology and management of hypotension during anesthesia
10. Enumerate various positions in relation to anesthesia and discuss in detail the problems associated with them.
11. Monitored anesthesia care
12. Simulator in anesthesia education
13. Computer-based patient record for anesthesia
14. APACHE score (acute physiology and chronic health evaluation)
15. Discharge criteria in outpatient anesthesia (day-stay surgery)
16. Minimum patient monitoring during anesthesia
17. Operating room pollution
18. Problems and role of anesthetists in a dental anesthesia
19. Oxygen therapy
20. Write down the physiology of sleep. How does it differ from anesthesia? What phases occur in various stages of anesthesia?
21. Informed consent
22. Infections related to anesthetic practice
23. Role of anesthetist in multiple trauma
24. MRI and anesthesia
25. Prevention of fire and explosion hazards in operation theaters
26. Jugular venous oximetry
27. Discuss the regulation of body temperature. How will you prevent hypothermia in a neonate posted for major abdominal surgery.
28. Recognition and management of anaphylaxis during general anesthesia
29. Methods of monitoring of neuromuscular transmission during anesthesia
30. Possible causes of delayed recovery from general anesthesia
31. Discuss in brief the problems of adult patient with Downs syndrome for multiple teeth extraction.
32. Third space loss—its importance to anesthesiologist
33. Anaphylactic reaction on the operation table
34. Preemptive analgesia
35. Anesthetists role in pain and palliative care
36. Acute pain management service
37. Anesthetic consideration for magnetic resonance imaging (MRI)
38. Myasthenic Syndrome
39. Causes and management of post anesthesia shivering
40. Enumerate risk factors for postoperative nausea and vomiting (PONV) and discuss its management.
41. A 40-year-old man weighing 140 kg has diabetes and hypertension and is scheduled for gastric banding. Discuss the anesthetic management
42. American Society of Anesthesiologists (ASA) physical status classification
43. Anesthetic management for radiodiagnostic procedures
44. Evidence-based medical education
45. Principle of ultrasonography. How is ultrasound useful in anesthesia?
46. Indication of mediastinoscopy, anesthetic implication
47. HIV disinfection in operating room working
48. Computers in anesthesia
49. Operating room pollution
50. Impact of cancer therapy on anesthetic management
51. Preanesthetic assessment clinic
52. Vicarious liability for negligence
53. Preoperative evaluation, preparation and anesthetic management of a known case of bronchial asthma posted for radical mastectomy
54. Postoperative hypoxemia—its causes, prophylaxis and management

PAIN

1. Patient controlled analgesia
2. Discuss the various methods of postoperative pain relief in pediatric surgery
3. World Health Organization regimen of chronic pain management
4. Postoperative analgesia in an infant for circumcision
5. The World Health Organization—three-step ladder pattern for pain relief in advanced cancer
6. Postoperative analgesia in children for inguinal hernia
7. What are the various routes of administration of opioids? Discuss the merits and demerits of each
8. Assessment of pain in children
9. Preemptive analgesia
10. Discuss the principles, assessment and methods of analgesia for pain relief in burns.

11. Acute pain relief in opioid dependent pain
12. Caudal epidural analgesia in anesthetic practice
13. Phantom limb pain
14. Pain management options in a patient with intractable pain due to carcinoma head of pancreas
15. Patient controlled analgesia (PCA) in anesthetic practice
16. Recent views of preemptive analgesia
17. Assessment of pain
18. Commonly used techniques and drugs for post operative pain relief
19. Pain relief in fracture ribs
20. Define and classify chronic pain. Describe the methods of treatment of complex regional pain syndrome in left upper limb in a 20-year-old male patient.

PEDIATRIC ANESTHESIA

1. Anesthetic management of a 2 days neonate for primary repair of tracheoesophageal fistula
2. Postoperative analgesia in pediatric patients
3. Heat loss during abdominal surgery in a newborn child
4. Postoperative analgesia in an infant for circumcision
5. Postoperative analgesia in children for inguinal hernia
6. Discuss the problems, preoperative preparation and anesthetic management of a neonate posted for repair of gastroschisis.
7. Recent advances in intraoperative pediatric fluid management
8. Neonatal resuscitation
9. Role of regional analgesia in pediatric surgery
10. Describe the anatomy and physiology of various types of tracheoesophageal fistula. Discuss the anesthetic management.
11. Anesthetic management of a 4-year-old with foreign body in right main bronchus. Discuss the problems.
12. Temperature regulation in neonate and prevention of hypothermia in neonate during perioperative period
13. Anesthetic problems of repair of congenital diaphragmatic hernia in a neonate.
14. Preoperative considerations in pediatric patients
15. A 10-months-old baby for hernia repair. Discuss anesthetic and postoperative pain management.
16. Anesthetic implications in neonatal anesthesia
17. Discuss the anesthetic considerations in a neonate for repair of cervical meningomyelocele.
18. Perioperative fluid requirement in small pediatric patients
19. Indications, technique and complications of spinal anesthesia in pediatric patient undergoing surgery
20. Fasting guidelines for children. How does premedication in adults differ from that in children?
21. New guidelines for neonatal resuscitation.
22. Preoperative assessment and anesthetic management of a 2-year-old child of hydrocephalous posted for shunt procedure
23. Preanesthetic assessment and preparation of 1 day old neonate for tracheaoesophageal fistula repair
24. Anesthetic management of congenital diaphragmatic hernia
25. Indication of caudal epidural in a pediatric patient, describe its technique and complications.
26. Anesthesia for bronchoscopy in children
27. Regional analgesia in children
28. How does the pediatric airway differ from that of an adult? What are the implications for an anesthesiologist?
29. Describe anesthetic management of a 6-month-old child with hydrocephalus scheduled for MRI.

PHARMACOLOGY

1. Hoffman degradation
2. Midazolam
3. Remifentanil
4. Rocuronium
5. Role of Nitric Oxide in ICU
6. Role of magnesium in anesthesia practice
7. Narcotic antagonists
8. Beta receptor blockade its relationship in anesthesia
9. What are the various routes of administration of morphine? Discuss the pharmacokinetics and pharmacokinetics of epidural morphine.
10. Nephrotoxicity of halogenated anesthetics
11. Propofol
12. Enzyme induction: Describe the mechanism with routine anesthesia examples
13. Mechanism of action of local anesthetic agents

14. Manifestations and treatment of beta adrenergic agonist toxicity
15. Sevoflurane
16. Untoward effects of intravenous sodium bicarbonate
17. Hepatotoxicity of halothane
18. Compare propofol with midazolam
19. Neuromuscular transmission
20. Propofol as compared to thiopentone
21. Elimination of atracurium from the body
22. Sevoflurane vs Desflurane
23. Rocuronium
24. Adenosine and its clinical uses
25. Ropivacaine
26. Isoflurane vs Sevoflurane
27. Human albumin
28. Transdermal opioids
29. Effect of esmolol pretreatment on cardiovascular system, neuromuscular junction and intraocular pressure
30. Mannitol in surgery
31. Pharmacokinetics of intravenous thiopentone
32. Clinical use of alpha 2 agonists in anesthesia
33. Enumerate the problems with the muscle relaxants.
34. Adrenergic agonists
35. Drug interactions
36. Compare and contrast dopamine and dobutamine as an inotropic agents.
37. What are the manifestations of hyponatremia and how will you treat it?
38. Perioperative blocker therapy
39. Concentration effect and second gas effect produced during uptake of inhalation agent
40. Mention the commonly used immunosuppressive drugs and their interaction with anesthetic drugs.
41. Clonidine in anesthesia practice
42. Lipid emulsion for the treatment of local anesthetic toxicity mechanism and dosage.
43. Nitrous oxide—current status
44. Adverse effects of neuromuscular blocking agents
45. Compare and contrast starch and gelatin as IV fluids.
46. Discuss the ECG abnormalities due to various electrolyte abnormalities.
47. What are the factors affecting neuromuscular blockage? Discuss various methods to monitor neuromuscular blockage.
48. Transdermal administration of drugs.
49. Dexmeditomidine, clinical application and complications
50. Rationale of premedication
51. Methods of prolonging effect of local anesthetics
52. Cardiovascular effects of newer anesthetic ethers
53. Adrenergic receptor antagonists and their uses
54. Classify antihypertensive drugs. Describe the management of hypertensive emergency.

POSTOPERATIVE ICU, CCU AND BLOOD

1. Complications and sequel of blood transfusion
2. Weaning modes of ventilation
3. Disseminated intravascular coagulation
4. Pressure controlled ventilation
5. Use of muscle relaxants in intensive care unit
6. Postoperative analgesia in pediatric patients
7. Present trend of blood component therapy
8. Newer modes of ventilation
9. Autologous blood transfusion
10. Hypokalemia
11. Crystalloid and colloid
12. Anesthesia for drainage of empyema thoracis
13. Total parenteral nutrition
14. Postanesthetic vomiting
15. Long-term ventilation and its complications
16. Care of organophosphorous poisoning in intensive care unit
17. Perioperative blood conservation
18. Discuss the pathophysiology, preventive and corrective measures of irreversible shock.
19. Airway management in an unconscious patient
20. Oxygen therapy in postoperative period
21. Uses, advantages and disadvantages of plasma expanders
22. Define multiple organ dysfunction syndrome. How do you plan to manage such a case.
23. Control of nosocomial infections in postoperative and intensive care unit
24. How is the diagnosis of dilutional hyponatremia made? What is its significance in anesthesia?
25. Disinfection

26. Principles of management of diabetic ketoacidosis
27. Management of mismatched blood transfusion
28. Septic shock
29. Autologous blood transfusion
30. Plasma volume expanders
31. Causes, diagnosis and treatment of hypo- and hyperkalemia
32. Describe PEEP (Positive End Expiratory Pressure) its mechanism of action, uses and complications.
33. The role of sedation in intensive care unit patients
34. Recent advances in cardiopulmonary resuscitation
35. Artificial blood (synthetic oxygen carrying substances)
36. Discuss the management of an unconscious young patient with history of drowning.
37. Discuss the management of a patient with snake bite.
38. What are the criteria for the diagnosis of SIRS? Discuss the principles of management in a patient of septic shock admitted in ICU.
39. What is autologous blood transfusion? Describe various techniques of autologous blood transfusion.
40. Anion gap
41. Recombinant Factor VII
42. Discuss the management of massive blood loss.
43. What is thromboelastography? Draw a labeled diagram to show a normal tracing. What are its implications?
44. Enteral feeding in critically ill patients
45. Enumerate five Hs and five Ts as possible causes of cardiac arrest. What is the management of pulseless electrical activity in an unconscious patient?
46. What is Triage? What are the triage criteria in relation to trauma?
47. What are the common nosocomial infections in ICU? Discuss the measures for prevention of ventilatory associated pneumonias.
48. Clinical features, diagnosis and management of paracetamol poisoning
49. Anemia and anesthesia
50. Coagulation of blood and management of hemophiliac patients
51. Physiological and biochemical changes of acute blood loss
52. How would you investigate the causes of increase bleeding during surgery? Give a brief account of various techniques employed to reduce bleeding.
53. Blood substitutes
54. Postoperative hypoxemia: Its causes, prophylaxis and management
55. Blood transfusion related disease transmission
56. How will you diagnose mismatched blood transfusion intraoperatively? Describe its management.
57. Enumerate the indications, contraindications and complications of invasive arterial blood pressure monitoring. Describe the technique.
58. What are the major buffer systems in the body? Enumerate the causes, effects and management of metabolic acidosis.

REGIONAL ANESTHESIA

1. Describe the nerve innervation of the foot with diagram and discuss the local anesthetic block at the ankle for the amputation of gangrenous toes in a patient.
2. Pulmonary function changes following central neuraxial blockade
3. Continuous subarachnoid block
4. Intravenous regional anesthesia
5. Postdural puncture headache
6. Management of local anesthetic toxicity
7. Regional analgesia in children
8. Epidural analgesia for postoperative pain relief
9. Peribulbar block
10. Epidural pressure and the various factors affecting the same
11. Complications of local anesthetics
12. Three in one block
13. Pulmonary edema in intraoperative and immediate postoperative period
14. Effect of intrathecal neostigmine on spinal anesthesia
15. Indications and methods of stellate ganglion block
16. Combined spinal epidural block
17. Caudal block
18. Modified combined spinal and epidural analgesia
19. Spinal anesthesia in children
20. Regional anesthesia in day care surgery
21. Describe the intrathecal and epidural opioids in clinical practice and their complications.
22. Describe the nerve supply of foot and the technique of ankle block for amputation of great toe.

23. Various epidural narcotics for management of postoperative pain
24. Indications, technique and complications of spinal anesthesia in pediatric patient undergoing surgery
25. Anatomy of epidural space and the methods of identification
26. Discuss one method brachial plexus block through supraclavicular approach and enumerate the complications associated with it.
27. Describe anatomy of paravertebral space and describe one method of establishing paravertebral block.
28. Describe with the help of labeled diagram the anatomy of lumbar plexus and describe the technique of lumbar plexus block.
29. Enumerate the guidelines for regional anesthesia in a patient on anticoagulant/antiplatelet therapy
30. Describe the anatomy of celiac plexus. Describe indications and measures to block celiac plexus.
31. Regional analgesia in children
32. IVRA technique and mode of action
33. Regional anesthesia techniques for upper extremity surgery.
34. Role of anesthesiologist in managing reflex sympathetic dystrophy
35. Complications of epidural anesthesia
36. Pain relief in fracture ribs
37. Innervation of foot and technique of performing ankle block
38. What is postdural puncture headache ? What are the factors affecting it? Describe the management of such a case.

RESPIRATORY

1. Minimum alveolar concentration (MAC)
2. Pressure controlled ventilation
3. Functional residual capacity
4. The factors influencing tissue oxygenation
5. Risk and management of pulmonary aspiration
6. Describe airway management of a patient of ankylosing spondylitis with severe restriction of neck movement posted for total hip replacement.
7. Problems and management in one lung anesthesia
8. Management of intraoperative bronchospasm
9. Oxygen therapy
10. Relevance of pulmonary function tests
11. Inverse ratio ventilation
12. Describe the pathogenesis and management of adult respiratory distress syndrome (ARDS).
13. Discuss the current concepts in the management of a case of chronic obstructive airway disease in respiratory failure.
14. Closing volume of the lungs and its measurement.
15. Discuss the pathophysiology and management of inhalational injury.
16. Tracheobronchial tree with diagram
17. Discuss anatomy of the diaphragm with a diagram. How does it behave under different stages of anesthesia?
18. Physiological changes associated with IPPV
19. Vocal cord palsies with the aid of diagrams of direct laryngoscopic view
20. Acute lung injury
21. Describe the anatomy of larynx with difference in adult and children. What is importance of recurrent laryngeal nerve in anesthesia practice?
22. Pulmonary edema in intraoperative and immediate postoperative period
23. Bronchopleural fistula
24. Evaluation of difficult airway
25. Respiratory monitoring in anesthesia
26. Difficult intubation
27. Tracheostomy techniques and complications
28. High frequency ventilation
29. Discuss the preoperative assessment and the method of anesthesia in patient with TM ankylosis for the release of ankylosis.
30. Hydropneumothorax
31. Predictive factors and intubation difficulty
32. Discuss the anesthetic management of a patient posted for pneumonectomy for carcinoma of right bronchus.
33. Oxygen toxicity
34. Pressure support ventilation
35. Management of an adult with smoke inhalational injury
36. Oxygen cascade, oxygen transport and oxygen dissociation curve
37. List the bed side tests available to predict the difficult intubation. Comment on their use.
38. Discuss the ventilatory management of ARDS (Adult Respiratory Distress Syndrome).
39. Anesthetic management of two years old child who is scheduled for therapeutic bronchoscopy

following inhalation of foreign body 2 days ago. Child could not exhibit any sign of airway obstruction

40. Postoperative pulmonary complications

41. What are the causes of hypercarbia during the intraoperative period? Discuss the effects and management.

42. Lung compliance

43. How will you anesthetize airway of a 40-year-old man for awake intubation?

44. Discuss the management of cannot intubate and cannot ventilate situation in the operation theater.

45. What is low flow anesthesia? Discuss its advantages and disadvantages.

46. Oxygen dissociation curve

47. Laryngospasm during anesthesia

48. Noninvasive ventilation: advantages, disadvantages and methods of administration

49. Discuss briefly different modes used for neonatal ventilation.

50. Criteria for weaning from prolonged ventilation

51. Percutaneous dilatational tracheostomy

52. Discuss the pathophysiology and management of a case of carbon monoxide poisoning.

53. Discuss the distribution of ventilation and perfusion in a normal lung with the help of labeled diagram. What are the factors affecting ventilation perfusion ratio?

54. Enumerate predictors of weaning from mechanical ventilation.

55. Hypoxic pulmonary vasoconstriction

56. Describe the techniques of chest physiotherapy. What is its role in postsurgical period?

57. Describe with diagram the flow volume loops.

58. Permissive hypercapnia

59. Methemoglobinemia and anesthesiologist

60. Pressure support ventilation

61. Prolonged use of ventilators

62. High frequency jet ventilation

63. Pulse oximetry in anesthetic practice

64. Oxygen cascade and oxygen flux

65. Modes of ventilation during bronchoscopy

66. Treatment of acute pulmonary edema

67. One lung anesthesia

68. CO_2 carriage in blood and effects of hypercapnia

69. A 40-year-old male with emphysematous bulla in right lung is scheduled for video-assisted thoracoscopic surgery (VATS) excision of bulla. Describe the anesthetic management.

70. Describe the metabolic functions of lung.

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