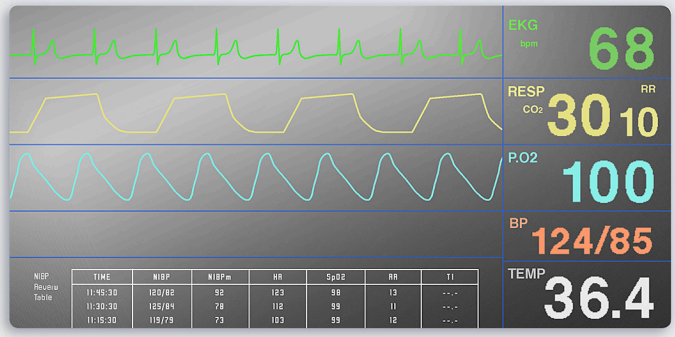
eISSN: 2589-9392
ISSN: 2589-9384

eISBN: 978-1-68108-721-4
ISBN: 978-1-68108-722-1

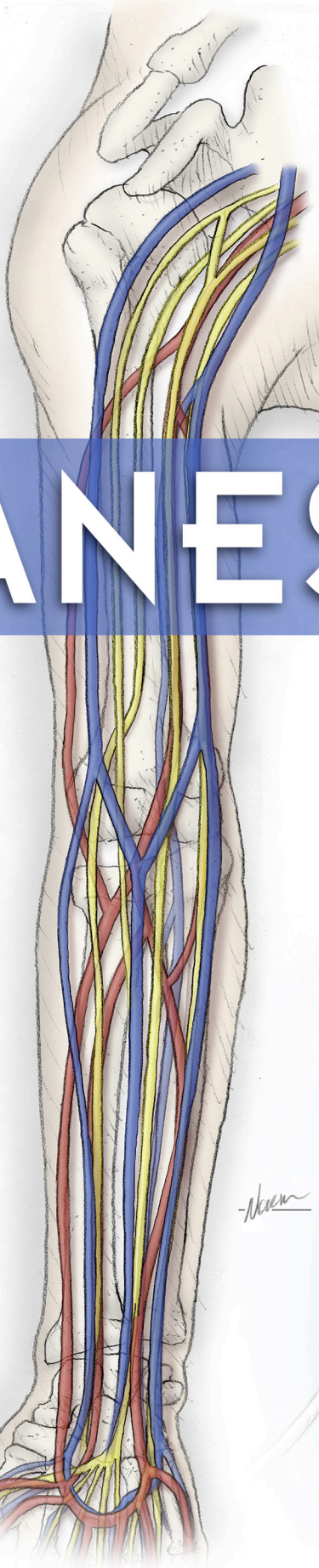
Recent Advances in Anesthesiology Volume 1

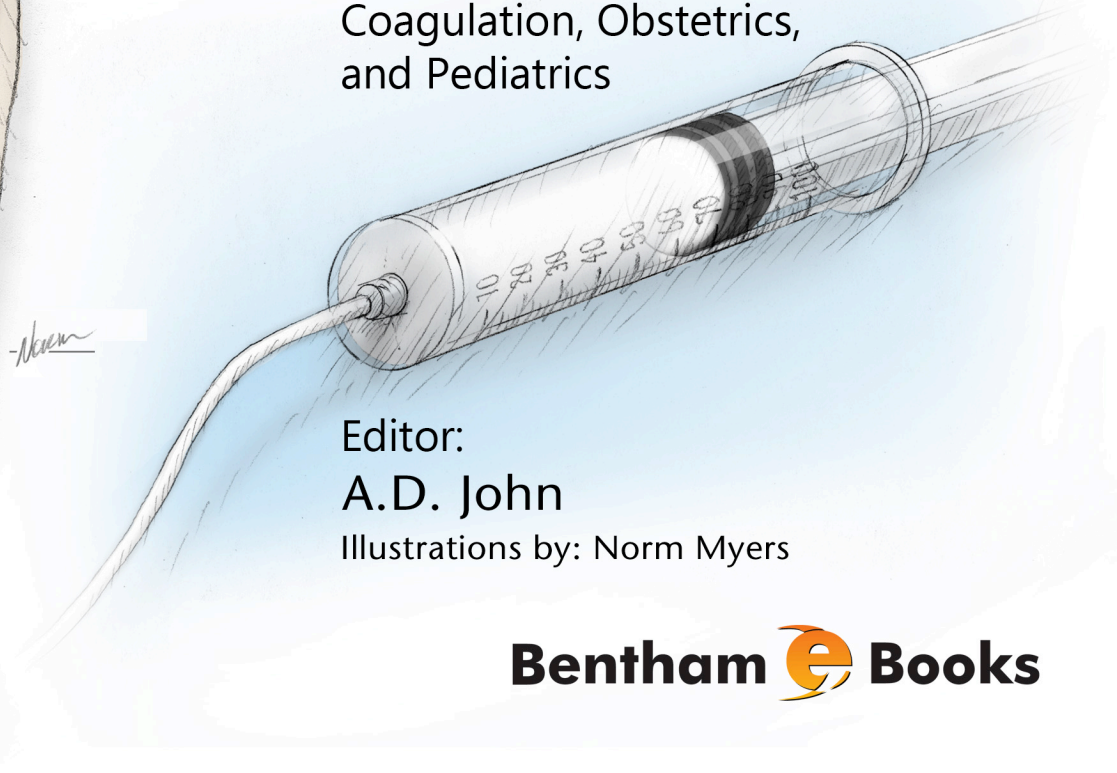


ANESTHESIA

Essential Clinical Updates for Practitioners

Regional, Ultrasound, Coagulation, Obstetrics, and Pediatrics





Editor:
A.D. John
Illustrations by: Norm Myers

Bentham Books

Recent Advances in Anesthesiology

(*Volume 1*)

Anesthesia: Essential Clinical Updates for Practitioners - Regional, Ultrasound, Coagulation, Obstetrics, and Pediatrics

Edited by

Amballur D. John
Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine Baltimore, MD, USA

Recent Advances in Anesthesiology

Volume # 1

Anesthesia: Essential Clinical Updates for Practitioners -
Regional, Ultrasound, Coagulation, Obstetrics, and Pediatrics

Editor: Amballur D. John

ISSN (Online): 2589-9392

ISSN (Print): 2589-9384

ISBN (Online): 978-1-68108-721-4

ISBN (Print): 978-1-68108-722-1

General:

1. Any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims) will be governed by and construed in accordance with the laws of the U.A.E. as applied in the Emirate of Dubai. Each party agrees that the courts of the Emirate of Dubai shall have exclusive jurisdiction to settle any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims).
2. Your rights under this License Agreement will automatically terminate without notice and without the need for a court order if at any point you breach any terms of this License Agreement. In no event will any delay or failure by Bentham Science Publishers in enforcing your compliance with this License Agreement constitute a waiver of any of its rights.
3. You acknowledge that you have read this License Agreement, and agree to be bound by its terms and conditions. To the extent that any other terms and conditions presented on any website of Bentham Science Publishers conflict with, or are inconsistent with, the terms and conditions set out in this License Agreement, you acknowledge that the terms and conditions set out in this License Agreement shall prevail.

Bentham Science Publishers Ltd.
Executive Suite Y - 2
PO Box 7917, Saif Zone
Sharjah, U.A.E.
Email: subscriptions@benthamscience.org

CONTENTS

PREFACE

The purpose of this work is to provide a quick update for practitioners on the major topics in Anesthesia. Medicine is a rapidly changing field. In this series:

VOLUME 1 deals with specific anesthetic issues such as regional anesthesia.

Recent Advances in Anesthesiology Vol 1: ***ANESTHESIA: Essential Clinical Updates for Practitioners – Regional, Ultrasound, Coagulation, Obstetrics, and Pediatrics***

VOLUME 2 deals with major systems.

Recent Advances in Anesthesiology Vol 2: ***ANESTHESIA: A Topical Update – Thoracic, Cardiac, Neuro, ICU and Interesting Cases***

Despite one's best effort and the efforts of various professional societies, it is often difficult to keep abreast in all aspects of anesthesia. Over time, every practitioner settles into a daily practice and keeps current in that area. However, the nature of modern anesthetic practice requires flexibility to fill various staffing needs. This often necessitates practitioners to do cases that they are not always facile with. There are a variety of resources available to acquire the requisite knowledge from detailed tomes to introductory manuals. The goal of this work is to provide practitioners with current updates on key aspects of anesthesia with a quick read of 15-20 minutes per topic so that a practitioner will be able to rapidly refresh their knowledge and skills. The chapters contained herein are written by outstanding specialist clinicians who are excellent teachers at the foremost anesthesia training programs. My deepest gratitude and sincere thanks to the authors who have taken the time and effort to do this onerous work, and apologizes for the inordinate delays incumbent in the publication process.

My sincere gratitude to the following individuals for their guidance and direction over the years. Dr. Eugenie Heitmiller: Genie is the epitome of excellence and positivity. As a young resident; I was fortunate to have had the opportunity and privilege of working with Genie. Dr. James Schauble who taught me to intubate and do anesthesia. Dr. William Merritt – who always took the time to teach and ensure that I was fed and watered no matter how horrid the day. Dr. Frederick Sieber: Fritz is my boss and friend. Special thanks to Warren Zapol M.D., Chairman Emeritus the Massachusetts General Hospital Harvard Medical School, and Edward Miller Jr. M.D., Emeritus Dean and CEO of Johns Hopkins Medicine, for their kindness and for hiring me.

ACKNOWLEDGEMENTS

My profound gratitude to the outstanding contributors who took time and effort to share their knowledge by writing the chapters on their areas of expertise, and to Fariya Zulfiqar and Shehzad Naqvi, project managers at Bentham. Thanks to Javita Jenkins and Audra Beard for their help with typing the manuscript. I am grateful to Jessica Terzigni who was able to work with all involved. The opportunity of working with Norm Myers – the illustrator, has been an enlightening educational experience.

A.D. John, M.D.
Department of Anesthesiology and Critical Care Medicine
Johns Hopkins University School of Medicine
Baltimore, MD, USA
E-mail: ajohn1@jhmi.edu

DEDICATION

This book is dedicated to my amazing and supportive parents, David and Lily John.

List of Contributors

Aaron S. Hess	Department of Anesthesiology, University of Wisconsin, Madison, WI, USA
Arun Kalava	Mayo Clinic, Jacksonville, Florida, USA
Blaine Easley	Baylor College of Medicine/Texas Children's Hospital, Houston, Texas, USA
De QH Tran	McGill University, Montreal, Canada
Dheeraj Goswami	Baylor College of Medicine/Texas Children's Hospital, Houston, Texas, USA
John R. Hess	Transfusion Medicine, Department of Laboratory Medicine, University of Washington, Seattle, WA, USA
Karen Lindeman	Johns Hopkins Medical Institution, Baltimore, MD, USA
Lawrence I. Schwartz	Colorado Children's Hospital, Aurora, CO, USA
Margaret K. Menzel Ellis	Oregon Health and Sciences University, Portland, Oregon, USA
Monica B. Pagano	Transfusion Medicine, Department of Laboratory Medicine, University of Washington, Seattle, WA, USA
Monica Hoagland	Colorado Children's Hospital, Aurora, CO, USA
Nathanial McQuay	University Hospital Cleveland, Cleveland, Ohio, USA
Neal S. Gerstein	Department of Anesthesiology and Critical Care Medicine, University of New Mexico, Albuquerque, New Mexico, USA
Peter M. Schulman	Oregon Health and Sciences University, Portland, Oregon, USA
Roy Greengrass	Mayo Clinic, Jacksonville, Florida, USA
Tessa Mandler	Colorado Children's Hospital, Aurora, CO, USA

CHAPTER 1

Trauma

Nathaniel McQuay, Jr.*

University Hospitals Cleveland, Cleveland, Ohio, USA

Abstract: Trauma is one of the primary causes of death for patients under the age of 44. Traumatic injuries are "time sensitive" where initial interventions are based on physiological derangements, and classical signs and symptoms which commonly occur based on the mechanism and pattern of injury. The primary survey focuses on maintaining life with the assessment of airway, breathing, circulation with hemorrhage control, and evaluation of neurological disability. Once exposure is obtained and the patient is stabilized, a detailed history is obtained and a complete physical examination must be done. This is the secondary survey. Thoracic injury, abdominal, pelvic and extremity injury are evaluated as well as the possibility of traumatic brain injury. The initial management of acute traumatic shock follows well established guidelines with the principle focus being damage control in order to optimize the patient's likelihood of a successful outcome.

Keywords: Abdominal compartment syndrome, Adult Trauma Life Support (ATLS), Airway, Damage control, Glascow Coma Scale (GCS), Hemorrhage control, Primary survey, Secondary survey, Shock, Trauma, Triad of hypothermia, coagulopathy and acidosis.

INTRODUCTION

In patients under the age of 44, trauma is the principle cause of death. This has been true since the seventeenth century B.C.E. as evidenced by the oldest surviving trauma text – the Edwin Smith papyrus [1, 2]. These "time sensitive" injuries require prompt evaluation, ongoing resuscitation and early identification of life and limb threatening injuries with timely definitive care implemented. The approach to the acutely injured/ill patient is in stark contrast to that of the traditional medical patient. Instead of emphasis on making the diagnosis prior to interventions, the approach to the trauma patient is exactly the opposite. Initial interventions are based on physiologic derangements, clinical signs and symptoms that commonly occur based on the pattern in injury.

* **Corresponding author Nathaniel McQuay, Jr.:** University Hospitals Cleveland, Cleveland, Ohio, USA; Tel: (216) 844-8088; E-mail: Nathaniel.McQuay@UHHospitals.org

Amballur D. John (Ed.)

Therefore, all injury associated information is vital to assist the provider in recognizing patterns of injury based on mechanism. It is this management approach that the following paragraphs will focus upon in reviewing the pre-arrival resource organization (Fig. **1**), phases of care (Fig. **2**) and injury specific management as it relates to the anesthesia provider.

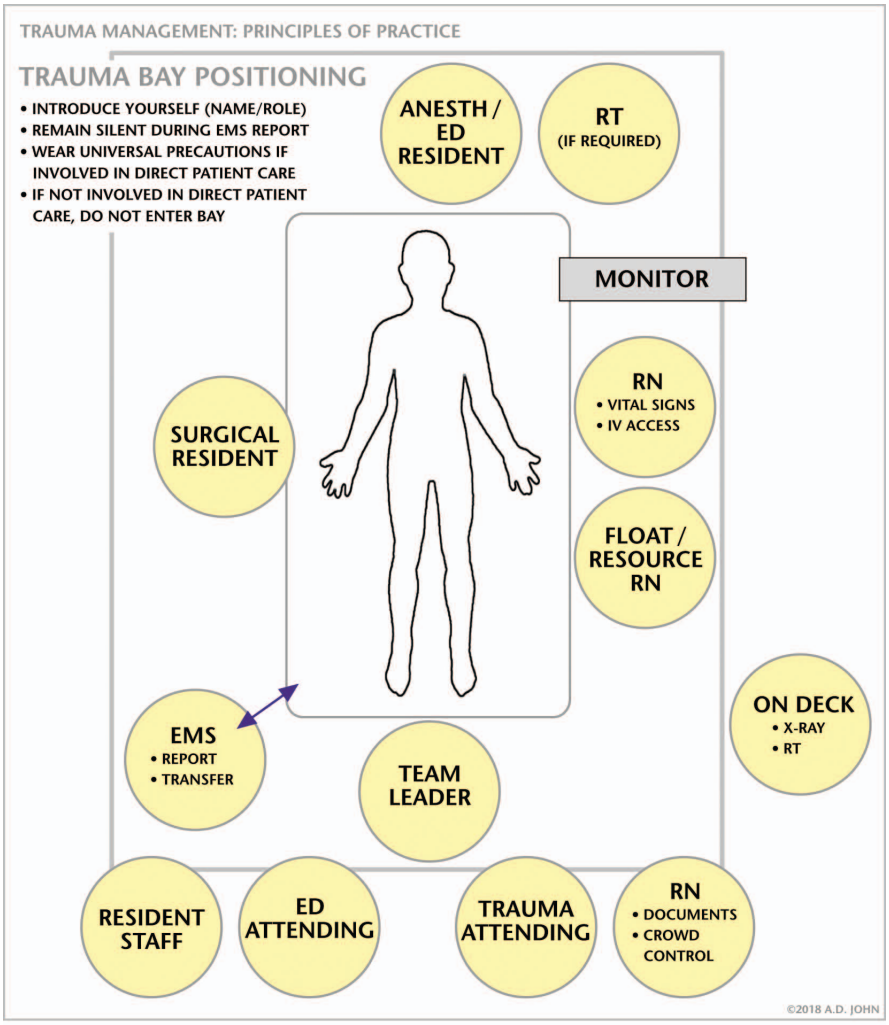


Fig. (1). Trauma resuscitation position diagram.

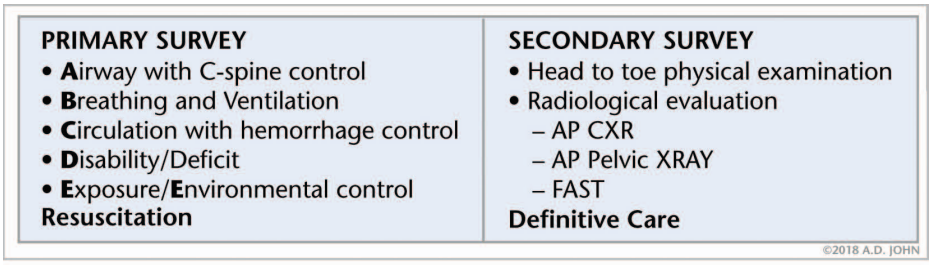


Fig. (2). Adult Trauma Life Support based phases of care for the acutely injured patient.

PRIMARY SURVEY

Airway Maintenance with Cervical Spine Protection

According to the Adult Trauma Life Support® (ATLS) [3] program, regardless of the injury, a standardized approach to the initial evaluation and management of the trauma patient must be undertaken in order to ensure an optimal successful outcome (Fig. **3**). Securing an airway, along with administration of supplemental oxygen and supporting ventilation, takes priority over all other conditions. The patient is first evaluated for patency of the airway by assessing his/her ability to speak. Clear uninterrupted speech is a good indication of airway patency. Caution must remain as the status of the airway may change and this requires frequent reassessment. In cases where airway patency is of question, the mouth and posterior pharynx should be suctioned and cleared of secretions and obstructions. Meanwhile, supplemental oxygen should be given. If necessary, a jaw thrust or insertion of an oral airway may be employed to open the posterior pharynx. In patients with facial fractures 1-5% may have concomitant cervical spine injury so cervical spine stabilization is done in order to avoid exacerbating a potential cervical spine injury [4 - 7]. Until the cervical spine has been examined both clinically and radiologically it is best to maintain cervical spine immobilization. The presence of airway problems requires definitive airway management – the placement of an endotracheal tube [2]. If a difficult airway is encountered a surgical airway must be obtained [3]. Facial trauma may present with violation of the cranial vault and so it is best to avoid the placement of nasal tubes whether nasogastric or nasotracheal.

Breathing and Ventilation

Breathing and ventilation in acutely injured patients especially those with severe facial and thoracic trauma may present challenges with both oxygenation and ventilation. In the patient requiring respiratory support, it is requisite to support both oxygenation and ventilation. Effective ventilation is often achieved by use of

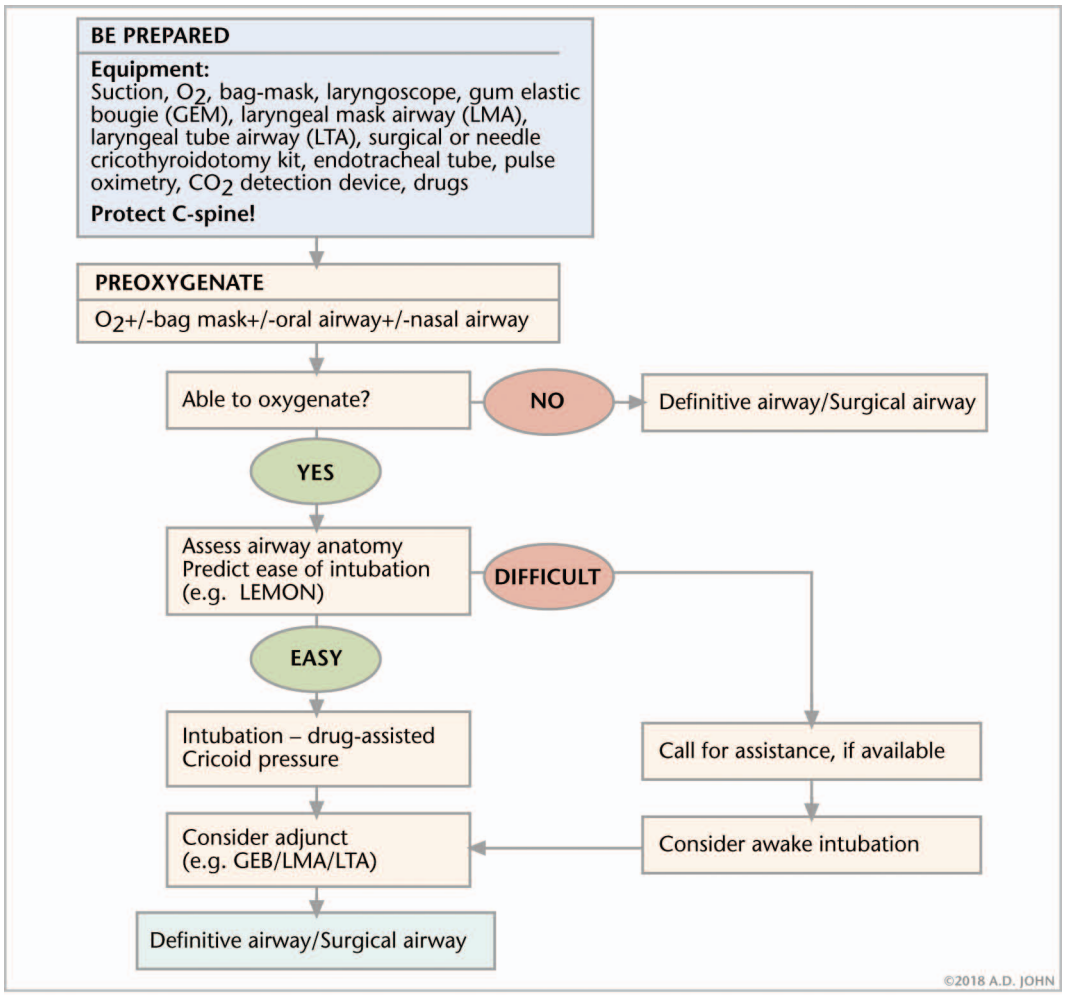


Fig. (3). Airway Decision Algorithm.

bag-valve mask techniques. One and two-person bag valve mask techniques are described, with the preference for two-person technique whenever feasible [8]. During bag valve mask ventilation, gastric distention may develop putting the patient at risk for emesis and aspiration. Excessive gastric distension can cause vagal induced hypotension and bradycardia. If intubation is required, an orogastric tube should be routinely placed to prevent such complications. In assessing the hypoxic patient an evaluation of the respiratory system with focus on a respiratory cause must be done even when airway compromise assumed. Penetrating injuries should be assessed for trajectory as missiles may arrest in the neck or thoracic cavity. Blunt injuries in the head, neck or chest may also affect respiratory efforts. The presence of subcutaneous emphysema should prompt

further investigation to rule out injury to the upper airway, aerodigestive tract, or tracheobronchial tree. A supine portable CXR serves as the initial adjunct study for further assessment of the hypoxic or tachypneic patient. Clinical findings consistent with a tension pneumothorax (absent breath sound, tracheal deviation, hypoxemia and hemodynamic lability) require immediate needle decompression with subsequent placement of thoracostomy tube. Hypoxemia in the stable patient with evidence of a pneumothorax or hemothorax is managed with placement of a thoracostomy tube.

Circulation with Hemorrhage Control

Acute hemorrhage continues to be the second most common cause of death in the trauma population [9]. Fatal traumatic hemorrhage accounts for a large portion of early deaths, with the majority of exsanguinations occurring within the first 48 hours [10, 11]. Following stabilization of the airway and breathing, circulation with hemorrhage control is the next priority in assessing acutely injured patients. **The best way to control hemorrhage in the acute setting is with well-placed direct pressure.** This concept is central in the management of the acutely injured patient with hemorrhage. Following placement of intravenous access, the potential sites of hemorrhage are assessed to determine the source of blood loss. **Common sites of major hemorrhage include chest, abdomen, pelvis, thighs and external wounds.** Each site is screened with adjunct diagnostic and imaging techniques for evidence of blood loss. The **chest** is evaluated with a supine CXR looking for evidence of major vascular injury or pneumo/hemothorax. Diagnostic peritoneal lavage historically has been used to evaluate the **abdomen**, but currently ultrasonography in the form of the FAST (Focused Abdominal Sonography for Trauma) is the standard screening modality. The presence of fluid in the dependent areas of the abdomen is assumed to be blood until proven otherwise. In addition to the abdominal windows, the FAST also includes a cardiac view to assess for the presence of pericardial fluid producing pericardial tamponade. The **pelvis** is assessed by a pelvic XRAY to identify acute fractures. The presence of certain fracture patterns is associated with potential retroperitoneal hemorrhage and therefore, the pelvic XRAY also indirectly assesses the retroperitoneum for potential hemorrhage source. **External sources** for hemorrhage are identified *via* the physical exam and include scalp lacerations and facial fractures in addition to open wounds. Scalp lacerations, due to the vast vasculature of the face, may serve as the sole source of hypotension and therefore must not be minimized as a potential cause of hypotension. Initial management includes application of direct pressure and suture control for arterial bleeders. Scalp laceration in patients on anticoagulants may require the administration of reversal agents to assist in hemorrhage control. Nasal fractures are often associated with bleeding. Direct pressure on the nares often controls epistaxis

from an anterior source. Significant bleeding from a posterior source may require nasal packing, balloon compression or both to obtain hemostasis. Patients with complex facial fractures due to either blunt or penetrating trauma have multiple sites of bleeding that may prove difficult to control. Encompassing the concept of direct pressure, facial packing and compressive dressing techniques have been described to achieve hemostasis [12]. Packing of the oropharynx following airway control is in essence similar to the four quadrant packing of the abdomen in an attempt to obtain hemorrhage control [13 - 16]. **When bleeding is refractory to compressive methods, angioembolization is employed for definitive control.**

Shock, defined as an abnormality of the circulatory system that results in inadequate organ perfusion and tissue oxygenation, is managed under the assumption that it is due to hypovolemia until proven otherwise. Although resuscitation is central in shock management, the provider's priority remains the identification of the source of hemorrhage to facilitate early control. Initial management consists of obtaining adequate intravenous access and the administration of liters of warmed crystalloids. Large caliber peripheral IV (14-16 gauge) should be placed preferably in the antecubital fossa bilaterally to facilitate rapid infusion of warmed fluid and blood products. When peripheral access is unable to be obtained, central venous access (Internal Jugular, Subclavian, Femoral) is obtained *via* the standard Seldinger technique. An alternative IV access is that of the intraosseous catheter. Historically shock classification was used to assess and guide management. **Assessment of the patient's response to therapy has now replaced the shock classification method and assists in the guidance of subsequent interventions** (Table **1**). Resuscitative strategies emphasizing large volumes of crystalloids have given way to more current strategies emphasizing early use of blood and blood products. This will be further discussed later in this chapter.

Disability

The initial neurological evaluation includes the assessment of the pupillary response and the computation of the Glascow Coma Score (GCS) [17]. This rapid evaluation assesses the patient's level of consciousness, presence of lateralizing signs and level of spinal cord injury. Unequal pupillary size, abnormal response and/or a low GCS score indicate the presence of a traumatic brain injury (TBI) requiring Computed Tomography (CT) scan of the brain for further assessment.

Table 1. Response to resuscitation in hemorrhagic shock.

	Rapid Response	Transient Response	Minimal or No Response
Vital Signs	Return to Normal	Transient improvement, Recurrence of decreased Blood pressure and increased heart rate	Remain abnormal
Estimate blood loss	Minimal (10-20%)	Moderate and ongoing (20-40%)	Severe (>40%)
Need for more crystalloid	Low	High	High
Need for blood	Low	Moderate to high	Immediate
Blood preparation	Type & Cross	Type specific	Emergency blood release
Need for operative intervention	Possibly	Likely	Highly likely
Early presence of surgeon	Yes	Yes	Yes

The provider must be vigilant of the possibility of a TBI by continually reassessing the patient for evidence of neurological deterioration as a lucid interval can occur in the setting of an epidural hematoma. Spinal cord injuries present with varying degrees of neurological deficits depending on the level involved. The patient is to remain immobilized during the assessment period. Computed Tomographic scan is the diagnostic imaging of choice to further evaluate the degree of cord injury. When either a TBI or spinal cord injury is diagnosed, prompt neurosurgical and/or spine surgery consults should ensue.

Exposure/Environmental Control

Exposure of the patient by removing all clothing allows for unobstructed evaluation for associated injuries. After completion of the examination, warmed blankets should be used to cover the patient. During the initial evaluation, a warmed environment should be provided. Although uncomfortable for the providers, patients exposed to cold environments are prone to the development of hypothermia. In trauma care the importance of preventing hypothermia cannot be overemphasized; since hypothermia may contribute to the development of coagulopathy, thus it is imperative to warm the room and use warmers to warm the fluids and the patient.

SECONDARY SURVEY

Upon stabilization of the patient after the primary survey, then and only then does one continue with the process and begin the Secondary Survey. During this stage

potential life threatening injuries elucidated and defined in order to be appropriately addressed. **A detailed history must be obtained and complete physical examination performed.** It is in the secondary survey that mechanum of injury and information obtained from prehospital personnel is compiled and analyzed to form the assessment that will guide appropriate interventions and care. The **AMPLE** (Allergies, Medications, Past illness/Pregnancy, Last meal, Events/Environment) is obtained to assist with establishing the patient's baseline physiological status. The importance of the information pertaining to the mechanism of injury (MOI) and details of the event provided by the pre-hospital personnel cannot be overstated. The provider should provide time for the pre-hospital report to be given as patterns of injury are associated with certain MOI. This relationship often can assist in the formulation of differential diagnosis as well as anticipate the needs of the patient. The physical examination must be organized and methodical to minimize missed injuries. Once the examination is completed, appropriate imaging studies, (CXR, Pelvic XRAY, FAST, CT scan) are performed.

Traumatic Brain Injury

The early management of TBI involves both prevention and empiric medical management. The primary focus during the initial management should be the prevention of hypotension and hypoxia as both have been documented to worsen neurologic outcomes [18]. The assessment of injury severity in patients with TBI is performed using the GCS. The injuries are then classified as minor (GCS13-15), moderate (GCS9-12) and severe (GCS<8). **Patients with GCS 8 or lower require intubation as a definitive airway.** This should be performed as soon as possible and by an experienced provider as poor outcomes have been documented following poorly performed intubations. Pre-hospital intubation has been associated with worse outcomes in TBI patients with multiple contributing factors postulated. Once intubated, pCO_2 levels should be maintained with targeted range of 30-40 mmHg as part of the empiric medical management [19]. Patients who present with clinical evidence of elevated intracranial pressure due to a space occupying lesion (Unequal pupils), should receive Mannitol.25-1g/kg, hyperventilation with target pCO_2 30-40 mmHg, Phenytoin 1 gm and an urgent head CT scan. Steroids use in the management of traumatic brain injury has been demonstrated to worsen outcomes [20] and are no longer recommended. Maintenance of blood pressure to ensure adequate brain perfusion as episodes of hypotension below 90mmHg have been associated with worse outcomes [21]. A systolic blood pressure of at least 90mmHg should be targeted with ongoing resuscitation. Next, the provider must determine the type of injury present (diffuse, focal) by obtaining a non-contrast CT when patient's condition safely allows.

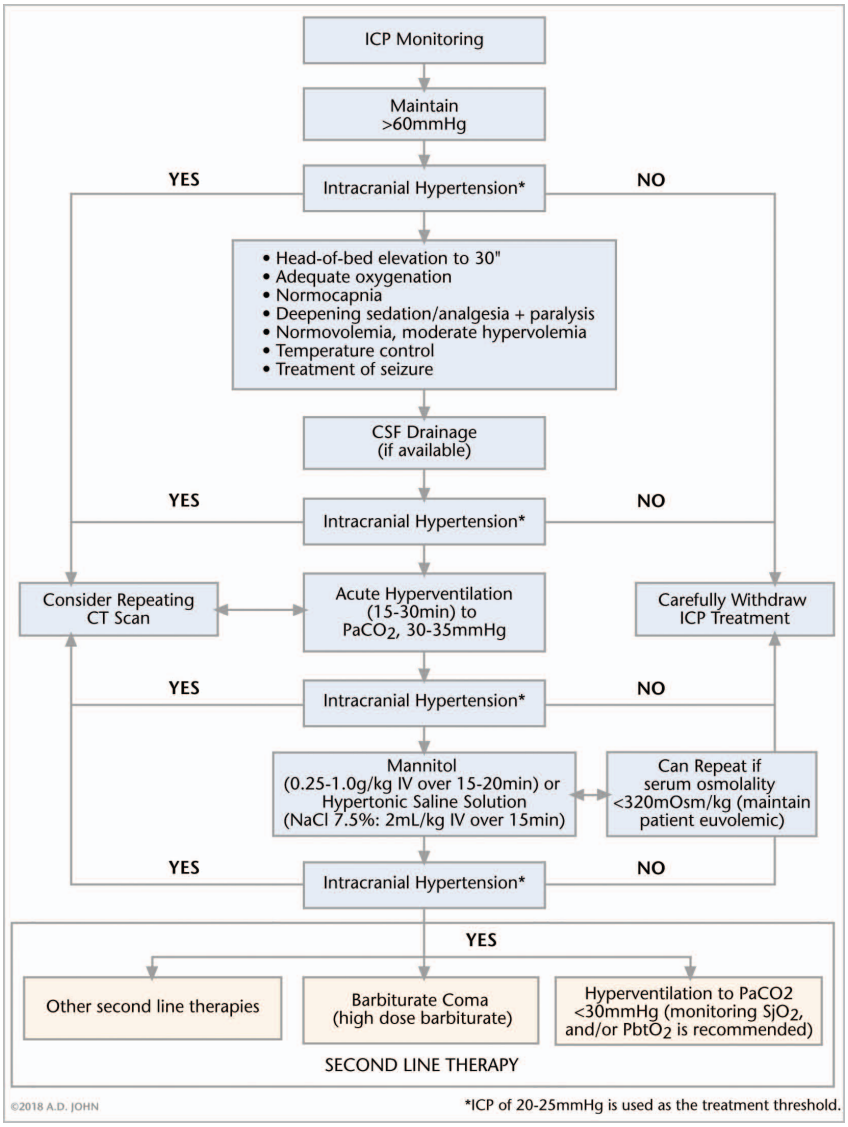


Fig. (4). Traumatic brain injury treatment algorithm.

Intensive care unit management of patients with traumatic head includes maintenance of ICP, cerebral perfusion pressure (CPP), seizure prophylaxis. Elevated ICP is managed with hyperosmolar therapy (Mannitol, Hypertonic Saline), Sedation, Analgesics, Cerebral spinal fluid drainage, and even paralysis in refractory and recalcitrant cases (Fig. **4**). Additional medical management issues include the assurance of euvolemia, adequate glycemic control, correction

of coagulopathy and appropriate prophylaxis for the prevention of thromboembolic events. Both mechanical and chemical prophylaxis offers the best prevention in this high risk population. Although concerns exist for potential bleeding associated with chemical prophylaxis, recent data reveal that this concern is minimized as the use of low molecular weight heparin has been proven effective as well as safe [22, 23]. Patients who remain refractory to medical therapies are often candidates for decompressive craniotomy [24].

Thoracic Injury

Traumatic thoracic injuries represent a significant cause of morbidity and mortality. Most injuries, blunt or penetrating, can be successfully managed without surgical intervention, but require an astute provider to recognize their presence and provide timely and appropriate management. The majority of moderate to serious injuries result in hypoxia, and therefore making the timely diagnosis and management imperative. The most common injury is that of rib fractures. Simple fractures usually require analgesics and pulmonary toilet. Adjuncts such as intercostal blocks and epidural catheters have been proven effective in attaining the goal of enabling adequate ventilation in blunt thoracic trauma patients [25]. Patients with multiple fractures who meet criteria for flail chest (two or more fractures in two or more places) may require more aggressive support measures as the underlying pulmonary contusion contributes to the hypoxia. This injury complex results in disruption of the integrity of the chest wall with paradoxical movement of the flail segment during the respiratory cycle. Initial management is similar to that for rib fractures. More severe cases require the patient to be placed on ventilator support to ensure both adequate ventilation and oxygenation.

Most injuries that are life threatening (Pnuemothorax, Hemothorax, Tension Pneumothorax) are managed with bedside thoracostomy tube placement. The provider should be careful as the hypoxia may be attributed to airway difficulty resulting in the conversion of a simple pneumothorax to a tension pneumothorax. If a tension pneumothorax is encountered, a large caliber needle decompression on the affected side is rapidly placed followed by thoracostomy tube placement. A hemothorax of <1500cc following thoracostomy tube placement serves as definitive management as bleeding is usually self-limited. Indications for operative intervention include >1500cc immediate output, 200cc/hr for 2-4hours or if blood transfusion is required.

Cardiac injuries may result from either blunt or **penetrating injuries**. But, blunt injuries are associated with poor outcomes. Penetrating injuries present in various ways from clinically occult to profound hemorrhagic shock resulting from either

tamponade physiology or free bleeding into the hemithorax *via* the associated laceration of the pericardial sac. Diagnosis of pericardial tamponade requires a high index of suspicion. Usually wound trajectory in proximity to the heart (below clavicles, medial to midclavicular lines and superior to costal margins) a cardiac injury should be excluded. The use of ultrasound has significantly improved the appropriately trained provider's ability to diagnose cardiac tamponade in a rapid fashion. FAST detects pericardial sac fluid with high sensitivity and specificity [26]. One should be cautious of a negative FAST in the setting of a hemothorax as the blood could be decompressing into the hemithorax giving a false negative study [27]. In settings where a qualified surgeon is available, operative intervention to definitively repair the injury is warranted. If a surgeon is not readily available, pericardiocentesis can be both diagnostic and therapeutic in the hands of a skilled provider. Subxyphoid placement of the needle/catheter complex allows for aspiration of blood contents which relieves the positive pressure within the pericardial sac facilitating cardiac filling. Placement of a flexible catheter that is connected to a three-way stopcock allows for intermittent drainage. All patients with a positive pericardiocentesis in the setting of cardiac tamponade require surgical exploration to evaluate the heart and repair the injury. These patients are then transferred to an appropriate facility for definitive care.

Patients with **blunt myocardial injury** may present as a spectrum of injury patterns from simple wall contusions to cardiac disruption (cardiorrhexis). Recently updated guideline recommended workup for cardiac contusions include a screening 12-lead ECG. Also, all patients are to have a Troponin I obtained. A normal test sufficiently excludes a cardiac injury and no further testing is warranted. An abnormal test should prompt admission for 24 hour observation with telemetry and Troponin I levels followed serially. The development of dysrhythmia or hemodynamic lability, a transthoracic or transesophageal echocardiography should be obtained [28].

Abdomen and Pelvic Trauma

Abdominal trauma continues to be a vexing problem to even the seasoned provider. The abdomen has often been referred to as the "black box" due to the difficulty in its assessment. Although this issue has been addressed with technological advancement, abdominal injuries continue to be a common cause of preventable death in the acutely injured patient. Factors such as intoxication, drugs, and associated neurological injury can affect the physical exam findings that may serve as a harbinger of an intra-abdominal injury. Historically diagnostic peritoneal lavage served as an adjunct to assist the provider is the assessment for possible intra-abdominal injury in the unevaluable patient. With advancement in technology, ultrasound (FAST) has supplanted DPL and is routinely used by

trained providers to identify the presence of fluid which is assumed to be blood. Advantages of FAST are its noninvasiveness, repeatability and allows for early diagnosis during either the primary or secondary survey in the trauma resuscitation area. A hemodynamically labile patient with a positive FAST exam warrants expeditious exploratory laparotomy as FAST in this scenario is greater than 95% sensitive. The FAST exam has less of a diagnostic role in penetrating abdominal trauma. Patients who are hemodynamically stable are safe for travel to the CT scan for further evaluation. Computed tomography allows for a more detailed evaluation of injuries resulting in a paradigm shift from operative to nonoperative management of most injuries [29].

Blunt abdominal trauma, MVC, MCC, Fall, Pedestrian struck, Crush, Assault, commonly result in injury to the solid organs of the abdomen. Liver, spleen, kidney and pancreatic injuries that were once managed operatively are now mostly managed nonoperatively based on established and validated CT criteria. Computed tomography provides organ specific injury type, extent and the presence/absence of free or intra-organ hemorrhage. Classification scales grade injuries from I to V/VI based on severity with high rates of success [30, 31]. Patients are followed clinically with serial abdominal exams and laboratory values. Development of derangement from baseline exam findings or lab values indicates failure of non-operative management and the patient is transferred to either the radiology suite for angiographic embolization or to the operating theatre for an exploratory laparotomy. Blunt hollow organ injures occur with less frequency but are more difficult to detect. Double (PO and IV) or triple (PO, IV and rectal) contrast enhanced abdominopelvic CT scan assists in making the early diagnosis of hollow viscus and retroperitoneal injuries that are often diagnosis in a delayed fashion with serial physical examinations.

Penetrating abdominal trauma, GSW, Stab, Impalement, tends to be relatively straightforward, however the determination of whether there has been peritoneal violation is sometimes difficult. Wound location is important as Intra-abdominal injuries can occur with lower chest (Thoracoabdominal) injuries. This is due to the fact that diaphragm elevation may occur up to the level of the nipple placing the upper abdominal organs at risk of injury. Recommended diagnostic modalities that assist in the evaluation of peritoneal violation include CT scan, Diagnostic Laparoscopy and Exploratory Laparotomy [32]. Computed tomography allows for determination of trajectory by following the injury tract. Peritoneal violation is an indication for operative exploration. Diagnostic laparoscopy represents a minimally invasive modality that not only allows for direct visualization of the peritoneum, as well as the diaphragm. The use of diagnostic laparoscopy has resulted in a decrease in the negative laparotomy. Abdominal vascular injuries mainly result from penetrating trauma and carry a high mortality.

Cardiopulmonary arrest or hemorrhagic shock is the usual state upon presentation to the trauma center. Aggressive resuscitative measures, including resuscitative thoracotomy, and rapid access to operative intervention is crucial to survival. The recent introduction of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) to the trauma arena has shown promising results in early studies [33, 34]. Most penetrating injuries are managed operatively, but non-operative management of certain injuries can be accomplished safely [35, 36].

Pelvic injuries are most commonly due to blunt mechanisms (MVC, MCC, Pedestrian struck). Pelvic ring disruption results from the application of a large amount of force. Types of severe pelvic fractures based on patterns of force include lateral compression, anterior-posterior compression and vertical shear. When encountered, pelvic fractures are often associated with injuries to intraperitoneal, retroperitoneal and extraperitoneal structures. Injuries to the bladder, urethra, rectosigmoid colon, uterus should be common and should be sought. Extra-peritoneal injuries include axial spine fractures, extremity fractures and aortic injuries. Patient with associated hypotension should be routinely assessed for common sources of life-threatening hemorrhage. The pelvis is palpated for tenderness and stability as these are indirect indicators for the presence of a severe fracture. An AP pelvic XRAY may be obtained if appropriate. If the patient's condition precludes XRAY evaluation, the pelvis is temporarily stabilized with a bedsheet or a commercial compression device (T-Pod® Pyng Medical Corp). The purpose is to decrease the volume within the pelvis that results from the fracture pattern in order to arrest posterior pelvic venous or internal iliac branch hemorrhage. Definitive management of pelvic bleeding is obtained in the angiography suite *via* angioembolization.

Abdominal compartment syndrome (ACS) is often encountered in the surgical intensive care units and warrants discussion. The World Society of Abdominal Compartment Syndrome defines ACS as a sustained intra-abdominal pressure >20mmHg (with or without abdominal perfusion pressure <60mmHg) that is associated with new organ dysfunction/failure. Abdominal compartment syndrome is classified as primary, secondary or recurrent based on etiology. Primary ACS is associated with pathology that originates from within the abdominal cavity (Hemoperitoneum, Ischemic bowel, Acute pancreatitis, ileus). Secondary ACS is associated with conditions that do not originate from within the abdomen (Massive crystalloid resuscitation). Recurrent ACS occurs following surgical decompression, prior to or after definitive closure. Organ failure develops as a result of the sustained elevation of intra-abdominal pressure >20mmHg causing decreased organ perfusion. The elevated pressure can affect any organ system but commonly involved systems include respiratory (Peak airway pressure >40mmHg), renal (Acute Kidney Injury), cardiovascular (decrease CO) and

gastrointestinal (Ileus, splanchnic hypoperfusion). Several intra-abdominal as well as extra-abdominal risk factors for ACS have been identified. (Table **2**) Diagnosis of ACS is made *via* the standard method of bladder pressure measurement utilizing an arterial line transducer [37 - 39]. Pressures in excess of 20-25mmhg in the appropriate clinical setting is suggestive of ACS [40]. Management options are broadly categorized as surgical or medical. Surgical options include percutaneous catheter drainage and decompressive laparotomy. Medical options include sedation, analgesia, paralysis, body positioning, intestinal decompression, restrictive fluid administration. Implementation of medical options in conjunction with serial bladder pressure measurements may prevent the progression of intra-abdominal hypertension. However, once end organ dysfunction occurs, surgical decompression is the treatment of choice. High index of suspicion along with preventive measures in high risk patients are key in improving survival.

Table 2. Clinical and objective risk factors for the development of Abdominal Compartment Syndrome.

Risk Factors for Abdominal Compartment Syndrome
1. Diminished abdominal wall compliance Acute respiratory failure Abdominal surgery with tight fascial closure Major Trauma, Major Burns High body index, central obesity
2. Increased Intra-fuminal contents Ileus (Gastroparesis)
3. Increased abdominal contents Ascites (Hemoperitoneum)
4. Early presence Hypotension Hypothermia (temp <33℃) Massive transfusion (>10units PRBC/24hrs) Coagulopathy (INR >1.5) Pancreatitis Sepsis Damage control laperotomy/Major Trauma Major Burn ©2018 A.D. JOHN

DAMAGE CONTROL

The initial approach in the acute management of traumatic shock follows well established guidelin.es [3, 41]. Damage control management of severe hemorrhage represents several phases of care for the patient approaching or in extremis (Hypothermic, Acidotic, Coagulopathic) [42, 43]. The phases of initial

resuscitation, operative, critical care and definitive care address both life threatening injuries and blood loss based on the physiological limitations of the patient. This physiological embarrassment results from both hemorrhage and tissue damage. The end result is a maldistribution of perfusion (Shock), anaerobic metabolism and the development of systemic inflammatory response (SIRS). Although the various phases occur in isolated environments (Trauma bay, OR, ICU, IR suite) the approach represents a continuum of care with the goal of addressing the reversal of the shock state and restoration of equilibrium (Fig. **5**).

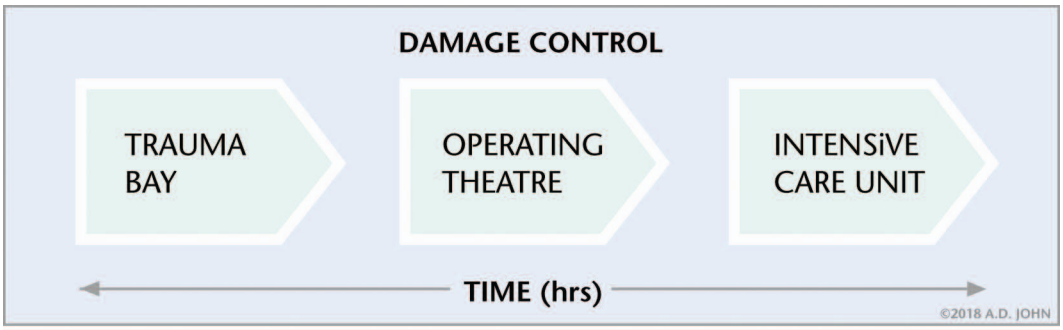


Fig. (5). Damage control management represents a continuum concept that begins shortly after injury and during all phases of care.

Early identification of the patient in extremis is key in the damage control approach. Pre-hospital evaluation of the acutely injured patient often provides information that may serve as early indicators for the presence of shock [44]. The presence of shock is assumed to be secondary to hemorrhage as this is the most common cause. **Traditional signs (BP, HR, UO) and symptoms have mostly been replaced with more objective indicators (Base deficit, Lactate) often referred to as endpoints.** These endpoints of resuscitation and more importantly the time to correction, have been associated with reduced mortality [45, 46]. Advancement in technology now allows for these endpoints to be obtained in the trauma bay *via* point of care devices. This information provides evidence of the depth of shock and assists the provider in recognizing the patient with physiological exhaustion, *i.e*. extremis. Aggressive fluid resuscitation is often employed when signs and symptoms of shock are present. However, this concept has been noted to contribute to several problems including increasing SIRS, ARDS, MOF and the promotion of hemorrhage by the dislodgement of formed clot and the production of a dilutional coagulopathy. These and other resuscitation induced comorbidities have resulted in several advances in the approach to resuscitation. **Damage control resuscitation strategy includes the combination of permissive hypotension and blood component transfusion.** The transfusion of thawed plasma in at least a 1:1 ratio with PRBCs, has been increasingly

employed in the resuscitation management of the patient in extremis due to exsanguination resulting in a significant survival benefit [47]. While the initial resuscitation is in progress, the operative phase of care commences with the primary goal of definitive hemorrhage control.

The trauma laparotomy encompasses two parts: Damage control and reconstruction. **Damage control surgery** includes control of hemorrhage, injury identification and the control of contamination designed to ensure immediate survival. Trauma deaths that occur in the operating room are mostly due to uncontrolled hemorrhage [48]. Stone *et al*. in 1983 observed the development of coagulopathy in these severely injured and exsanguinating patients during prolonged operative procedures [49]. The authors propose abbreviation of the procedure, reversal of the coagulopathy and return to the theatre at a later time for definitive repair. These damage control concepts were increasingly applied to the management of patients with penetrating abdominal injuries. Rotondo *et al*. in 1993 reported on their experience with the use of damage control management and improved survival [50]. **Reconstruction**, which usually occurs 24-48 hours after the initial procedure, involves the definitive repair of injuries following physiologic restoration as patients in extremis lack the reserve to tolerate both damage control and reconstruction during a single operation. Definitive procedures should not be attempted as this will only contribute further to the development of the "bloody vicious cycle" [51]. This concept as evolved from Halstead's original description of "intrahepatic packing" to the multidisciplinary approach that is currently used today. Indications for the use of damage control techniques are well documented [52].

During the trauma laparotomy, the anesthesiologist is responsible for the ongoing restoration of the patient's physiologic reserve. **The triad of hypothermia, coagulopathy and acidosis is often times not aggressively addressed.** Patients should receive warmed intravenous fluids, including blood products *via* a Level 1 rapid infuser (Level1Technologies, Marshfield, MA); room temperature should be approximately 80-85°F and placement of a conductive warming device (Bair Hugger, Augustine Medical Inc., Eden Prarie, Minn.) to prevent hypothermia. Serial assessment of endpoints should guide ongoing resuscitation. Acid-Base imbalances should be managed primarily with fluids and blood products. The degree of coagulopathy is assessed serially *via* point of care testing and managed with aggressive transfusion of FFP and PLTs. The attainment of these goals is facilitated by the utilization of massive transfusion protocols. This transfusion concept is initiated during the primary resuscitation by the trauma team leader. However, it is commonly not practiced during the damage control operative procedure. This critical and often overlooked portion of the damage control management is vital in optimizing survival. Recommendations for intra-operative

fluid resuscitation, ratio based blood component transfusion and acid-base management have been published [53] (Table **3**).

Table 3. Intraoperative goals of resuscitation during damage control surgery.

Resuscitation Goals During Damage Control Surgery*
Systolic blood pressure 90mmHg
Heart rate <120 beats per minute
Pulse oximeter functioning, SaO_2 >95%
$PaCO_2$ <50torr
Urine outpt ≥0.5ml/kg/hr
pH >7.25
Hematocrit >25%
Lactate stable or decreasing
Ionized calcium >1.0
International normalized ratio <1.6
Platelets >50,000 Normothermia
Deep anesthesia
*Low blood pressure may be tolerated as long as acidosis is not worsening ©2018 A.D. JOHN

The critical care phase follows completion of the damage control procedure. The goal during this phase of care is the continuation of resuscitation (Secondary resuscitation), optimization of oxygen delivery, and organ system support. The "bloody viscous cycle" is attenuated by correction of acidosis, reversal of coagulopathy and reversal of hypothermia [54]. Resuscitative gains are assessed serially and once the patient's is physiologically captured, the definitive phase can begin. Timing to planned reoperation is dependent not only upon physiological restoration, but is also determined by the nature of the injury. Correction of hypothermia, acidosis and coagulopathy signal the point at which the patient is safe for reoperation [55]. During the **definitive procedure** all previously placed packs are removed, re-exploration occurs to evaluate previous repairs and missed injuries. Definitive repairs are completed and the abdomen closed when possible. Unplanned reoperation may occur due to ongoing bleeding or the development of abdominal compartment syndrome [56].

The damage control management is a multi-staged approach to the patient in extremis representing a continuum of care. **Not only is the surgical procedure of importance, but ALL phases must be emphasized to optimize patient outcome.** If one critically evaluates all aspects of the damage control

management, many would agree it is often underutilized. Cold operating theaters, transfusion of cold blood products, lack of adequate resuscitation in the operating room are often not emphasized as the primary focus is on the damage control portion of the trauma laparotomy. The term damage control is added to all phases of care (Damage control surgery, Damage control resuscitation, Damage control transfusion, Damage control anesthesiology) to further emphasize the important contribution of each in the management of the exsanguinating patient.

CONCLUSION

Trauma is one of the primary causes of death for patients under the age of 44. Traumatic injuries are "time sensitive" where initial interventions are based on physiological derangements, and classical signs and symptoms which commonly occur based on the mechanism and pattern of injury. The primary survey focuses on maintaining life with assessment of airway, breathing, circulation with hemorrhage control, and evaluation of neurological disability. Once exposure is obtained and the patient is stabilized a detailed history is obtained and a complete physical examination must be done. This is the secondary survey. Thoracic injury, abdominal, pelvic, and extremity injury are evaluated as well as the possibility of traumatic brain injury. The initial management of acute traumatic shock follows well established guidelines with the principle focus being damage control in order to optimize the patient's likelihood of a successful outcome; where damage control is multifaceted concept and approach.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENT

Declared none.

REFERENCES

[1] Breasted JH. The Edwin Smith Surgical papyrus (facsimile and hieroglyphic transliteration with translation and commentary, in two volumes). Chicago: The University of Chicago Press 1930.

[2] WISQARS fatal injuries: mortality reports. http://webappa.cdc.gov.proxy.lib.mcw.edu/sasweb/ncipc/mortrate.html Accessed June1, 2015.

[3] American College of surgeons Committee on Trauma: Advanced Trauma Life Support. 9th ed., Chicago, IL: American College of Surgeons 2012.

[4] Gwyn PP, Carraway JH, Horton CE, Adamson JE, Mladick RA. Facial fractures--associated injuries

and complications. Plast Reconstr Surg 1971; 47(3): 225-30.
[http://dx.doi.org/10.1097/00006534-197103000-00004] [PMID: 5101680]

[5] Davidson JS, Birdsell DC. Cervical spine injury in patients with facial skeletal trauma. J Trauma 1989; 29(9): 1276-8.
[http://dx.doi.org/10.1097/00005373-198909000-00016] [PMID: 2769811]

[6] Hackl W, Fink C, Hausberger K, Ulmer H, Gassner R. The incidence of combined facial and cervical spine injuries. J Trauma 2001; 50(1): 41-5.
[http://dx.doi.org/10.1097/00005373-200101000-00007] [PMID: 11231667]

[7] Luce EA, Tubb TD, Moore AM. Review of 1,000 major facial fractures and associated injuries. Plast Reconstr Surg 1979; 63(1): 26-30.
[http://dx.doi.org/10.1097/00006534-197901000-00005] [PMID: 432322]

[8] Joffe AM, Hetzel S, Liew EC. A two-handed jaw-thrust technique is superior to the one-handed "EC-clamp" technique for mask ventilation in the apneic unconscious person. Anesthesiology 2010; 113(4): 873-9.
[http://dx.doi.org/10.1097/ALN.0b013e3181ec6414] [PMID: 20808210]

[9] Sauaia A, Moore FA, Moore EE, *et al.* Epidemiology of trauma deaths: a reassessment. J Trauma 1995; 38(2): 185-93.
[http://dx.doi.org/10.1097/00005373-199502000-00006] [PMID: 7869433]

[10] Acosta JA, Yang JC, Winchell RJ, *et al.* Lethal injuries and time to death in a level I trauma center. J Am Coll Surg 1998; 186(5): 528-33.
[http://dx.doi.org/10.1016/S1072-7515(98)00082-9] [PMID: 9583692]

[11] Hoyt DB, Bulger EM, Knudson MM, *et al.* Death in the operating room: an analysis of a multi-center experience. J Trauma 1994; 37(3): 426-32.
[http://dx.doi.org/10.1097/00005373-199409000-00016] [PMID: 8083904]

[12] Naimer SA, Nash M, Niv A, Lapid O. Control of massive bleeding from facial gunshot wound with a compact elastic adhesive compression dressing. Am J Emerg Med 2004; 22(7): 586-8.
[http://dx.doi.org/10.1016/j.ajem.2004.09.004] [PMID: 15666266]

[13] Calne RY, McMaster P, Pentlow BD. The treatment of major liver trauma by primary packing with transfer of the patient for definitive treatment. Br J Surg 1979; 66(5): 338-9.
[http://dx.doi.org/10.1002/bjs.1800660512] [PMID: 444853]

[14] Carmona RH, Peck DZ, Lim RC Jr. The role of packing and planned reoperation in severe hepatic trauma. J Trauma 1984; 24(9): 779-84.
[http://dx.doi.org/10.1097/00005373-198409000-00001] [PMID: 6481827]

[15] Feliciano DV, Mattox KL, Burch JM, Bitondo CG, Jordan GL Jr. Packing for control of hepatic hemorrhage. J Trauma 1986; 26(8): 738-43.
[http://dx.doi.org/10.1097/00005373-198608000-00010] [PMID: 3488413]

[16] Svoboda JA, Peter ET, Dang CV, Parks SN, Ellyson JH. Severe liver trauma in the face of coagulopathy. A case for temporary packing and early reexploration. Am J Surg 1982; 144(6): 717-21.
[http://dx.doi.org/10.1016/0002-9610(82)90557-8] [PMID: 6756183]

[17] Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2(7872): 81-4.
[http://dx.doi.org/10.1016/S0140-6736(74)91639-0] [PMID: 4136544]

[18] Chesnut RM, Marshall LF, Klauber MR, *et al.* The role of secondary brain injury in determining outcome from severe head injury. J Trauma 1993; 34(2): 216-22.
[http://dx.doi.org/10.1097/00005373-199302000-00006] [PMID: 8459458]

[19] Warner KJ, Cuschieri J, Copass MK, Jurkovich GJ, Bulger EM. Emergency department ventilation effects outcome in severe traumatic brain injury. J Trauma 2008; 64(2): 341-7.
[http://dx.doi.org/10.1097/TA.0b013e318160dfb3] [PMID: 18301196]

[20] Roberts I, Yates D, Sandercock P, *et al.* Effect of intravenous corticosteroids on death within 14 days in 10008 adults with clinically significant head injury (MRC CRASH trial): randomised placebo-controlled trial. Lancet 2004; 364(9442): 1321-8.
[http://dx.doi.org/10.1016/S0140-6736(04)17188-2] [PMID: 15474134]

[21] Chesnut RM, Marshall LF, Klauber MR, *et al.* The role of secondary brain injury in determining outcome from severe head injury. J Trauma 1993; 34(2): 216-22.
[http://dx.doi.org/10.1097/00005373-199302000-00006] [PMID: 8459458]

[22] Knudson MM, Morabito D, Paiement GD, Shackleford S. Use of low molecular weight heparin in preventing thromboembolism in trauma patients. J Trauma 1996; 41(3): 446-59.
[http://dx.doi.org/10.1097/00005373-199609000-00010] [PMID: 8810961]

[23] Dudley RR, Aziz 1, Bonnici A, *et al.* Early venous thromboembolic event prophylaxis in traumatic brain injury with low-molecular-weight heparin: risks and benefits. J Neurotrauma 2010; 27(12): 2165-72.
[http://dx.doi.org/10.1089/neu.2010.1366] [PMID: 20939698]

[24] Bullock MR, Chesnut R, Ghajar J, *et al.* Surgical management of traumatic parenchymal lesions. Neurosurgery 2006; 58(3) (Suppl.): S25-46.
[PMID: 16540746]

[25] Simon BJ, Cushman J, Barraco R, *et al.* Pain management guidelines for blunt thoracic trauma. J Trauma 2005; 59(5): 1256-67.
[http://dx.doi.org/10.1097/01.ta.0000178063.77946.f5] [PMID: 16385313]

[26] Rozycki GS, Feliciano DV, Ochsner MG, *et al.* The role of ultrasound in patients with possible penetrating cardiac wounds: a prospective multicenter study. J Trauma 1999; 46(4): 543-51.
[http://dx.doi.org/10.1097/00005373-199904000-00002] [PMID: 10217216]

[27] Ball CG, Williams BH, Wyrzykowski AD, Nicholas JM, Rozycki GS, Feliciano DV. A caveat to the performance of pericardial ultrasound in patients with penetrating cardiac wounds. J Trauma 2009; 67(5): 1123-4.
[http://dx.doi.org/10.1097/TA.0b013e3181b16f30] [PMID: 19901678]

[28] Clancy K, Velopulos C, Bilaniuk JW, *et al.* Blunt cardiac injury, Screening for. J Trauma 2012; 73: S301-6.
[http://dx.doi.org/10.1097/TA.0b013e318270193a] [PMID: 23114485]

[29] Peitzman AB, Richardson JD. Surgical treatment of injuries to the solid abdominal organs: a 50-year perspective from the Journal of Trauma. J Trauma 2010; 69(5): 1011-21.
[http://dx.doi.org/10.1097/TA.0b013e3181f9c216] [PMID: 21068605]

[30] Stassen NA, Bhullar I, Cheng JD, *et al.* Blunt hepatic injury, selective nonoperative management of. J Trauma 2012; 73: S288-93.
[http://dx.doi.org/10.1097/TA.0b013e318270160d]

[31] Stassen NA, Bhullar I, Cheng JD, *et al.* Blunt splenic injury, selective nonoperative management of. J Trauma 2012; 73: S294-300.
[http://dx.doi.org/10.1097/TA.0b013e3182702afc] [PMID: 23114484]

[32] Penetrating abdominal trauma, selective nonoperative management of. J Trauma 2010; 68: 721-33.
[http://dx.doi.org/10.1097/TA.0b013e3181cf7d07] [PMID: 20220426]

[33] Brenner ML, Moore LJ, DuBose JJ, *et al.* A clinical series of resuscitative endovascular balloon occlusion of the aorta for hemorrhage control and resuscitation. J Trauma Acute Care Surg 2013; 75(3): 506-11.
[http://dx.doi.org/10.1097/TA.0b013e31829e5416] [PMID: 24089121]

[34] Ogura T, Lefor AT, Nakano M, Izawa Y, Morita H. Nonoperative management of hemodynamically unstable abdominal trauma patients with angioembolization and resuscitative endovascular balloon occlusion of the aorta. J Trauma Acute Care Surg 2015; 78(1): 132-5.

[http://dx.doi.org/10.1097/TA.0000000000000473] [PMID: 25539214]

[35] Lamb CM, Garner JP. Selective non-operative management of civilian gunshot wounds to the abdomen: a systematic review of the evidence. Injury 2014; 45(4): 659-66.
[http://dx.doi.org/10.1016/j.injury.2013.07.008] [PMID: 23895795]

[36] Velmahos GC, Constantinou C, Tillou A, Brown CV, Salim A, Demetriades D. Abdominal computed tomographic scan for patients with gunshot wounds to the abdomen selected for nonoperative management. J Trauma 2005; 59(5): 1155-60.
[http://dx.doi.org/10.1097/01.ta.0000196435.18073.6d] [PMID: 16385294]

[37] World Society of the Abdominal Compartment Syndrome. Mission statement http://www.wsacs.org

[38] Malbrain ML, De laet IE. Intra-abdominal hypertension: evolving concepts. Clin Chest Med 2009; 30(1): 45-70, viii.
[http://dx.doi.org/10.1016/j.ccm.2008.09.003] [PMID: 19186280]

[39] Malbrain M, Jones F. Intra-abdominal pressure measurement techniques.Abdominal Compartment Syndrome. Georgetown, TX: Landis Bioscience 2006; pp. 19-68.

[40] Cheatham ML, Malbrain ML, Kirkpatrick A, *et al.* Results from the International Conference of experts on intra-abdominal hypertension and abdominal compartment syndrome, II. Recommendations. Intensive Care Med 2007; 33(6): 951-62.
[http://dx.doi.org/10.1007/s00134-007-0592-4] [PMID: 17377769]

[41] American College of Surgeons. Committee on Trauma PHTLS: Basic and Advanced Prehospital Life Support. 8th ed., Chicago: American College of Surgeons 2014.

[42] Kauvar OS, Wade CE. The epidemiology and modern management of traumatic hemorrhage: US and International perspectives. Critical Care 2005; 9 Supp;·5:S1-S9.

[43] Bowley DM, Barker P, Boffard KD. Damage control surgery--concepts and practice. J R Army Med Corps 2000; 146(3): 176-82.
[http://dx.doi.org/10.1136/jramc-146-03-05] [PMID: 11143684]

[44] Eastridge BJ, Malone D, Holcomb JB. Early preditors of transfusion and mortality after injury: a review of the data-based literature. J Trauma 2006; 60 (Suppl. 6): 720-4.

[45] Abramson D, Scalea TM, Hitchcock R, Trooskin SZ, Henry SM, Greenspan J. Lactate clearance and survival following injury. J Trauma 1993; 35(4): 584-8.
[http://dx.doi.org/10.1097/00005373-199310000-00014] [PMID: 8411283]

[46] Blow 0, Magliore L, Claridge JA, Butler K, Young JS. Detection and correction of occult hypoperfusion within 24 hours improves outcome from major trauma. J Trauma 1999; 47(5): 964-9.
[http://dx.doi.org/10.1097/00005373-199911000-00028] [PMID: 10568731]

[47] Malone DL, Hess JR, Fingerhut A. Massive transfusion practices around the globe and a suggestion for a common massive transfusion protocol. J Trauma 2006(Sup 6):S91-96.

[48] Hoyt DB, Bulger EM, Knudson MM, *et al.* Death in the operating room: an analysis of a multi-center experience. J Trauma 1994; 37(3): 426-32.
[http://dx.doi.org/10.1097/00005373-199409000-00016] [PMID: 8083904]

[49] Stone HH, Strom PR, Mullins RJ. Management of the major coagulopathy with onset during laparotomy. Ann Surg 1983; 197(5): 532-5.
[http://dx.doi.org/10.1097/00000658-198305000-00005] [PMID: 6847272]

[50] Rotondo MF, Schwab CW, McGonigal MD, *et al.* 'Damage control': an approach for improved survival in exsanguinating penetrating abdominal injury. J Trauma 1993; 35(3): 375-82.
[http://dx.doi.org/10.1097/00005373-199309000-00008] [PMID: 8371295]

[51] Kashuk JL, Moore EE, Millikan JS, Moore JB. Major abdominal vascular trauma--a unified approach. J Trauma 1982; 22(8): 672-9.
[http://dx.doi.org/10.1097/00005373-198208000-00004] [PMID: 6980992]

[52] Cushman JG, Feliciano DV, Renz BM, *et al.* Iliac vessel injury: operative physiology related to outcome. J Trauma 1997; 42(6): 1033-40.
[http://dx.doi.org/10.1097/00005373-199706000-00008] [PMID: 9210537]

[53] Dutton RP. Damage Control Anesthesia. International Trauma Care, Fall 2005.

[54] Sagraves SG, Toschlog EA, Rotondo MF. Damage control surgery--the intensivist's role. J Intensive Care Med 2006; 21(1): 5-16.
[http://dx.doi.org/10.1177/0885066605282790] [PMID: 16698739]

[55] Hirshberg A, Sterin M, Adar R. Re-operation, planned and unplanned in Damage Control Surgery. Surg Clin North Am 1997; 77(4): 897-907.
[http://dx.doi.org/10.1016/S0039-6109(05)70592-2] [PMID: 9291989]

[56] Richardson JD, Trinkle JK. Hemodynamic and respiratory alterations with increased intra-abdominal pressure. J Surg Res 1976; 20(5): 401-4.
[http://dx.doi.org/10.1016/0022-4804(76)90112-8] [PMID: 933497]

CHAPTER 2

Upper Extremity Blocks

De Q.H. Tran*

McGill University, Montreal, Canada

Abstract: Upper extremity blocks are becoming increasingly popular for Orthopedic and Ambulatory Anesthesia. Since pain originates from the periosteum, knowledge of osseous innervation is important for a successful block. Choosing the correct approach will allow one to successfully operate on the shoulder, clavicle and proximal humerus, or the distal humerus, forearm and hand. The risks associated with the blocks help determine the approach used. The interscalene and supraclavicular approaches have a high risk of diaphragmatic paralysis. The infraclavicular approach has a potential for vascular puncture and difficulty with external compression due to the depth of the vessel, and is usually contraindicated in patients with same side cardiac pacemakers. Axillary blocks should be avoided in patients who cannot abduct their arm.

Keywords: Axillary block, Brachial plexus, Interscalene block, Infraclavicular block, Neurostimulation, Radial nerve block, Supraclavicular block, Ulnar nerve block, Ultrasound guidance.

INTRODUCTION

This chapter represents an essential summary of the works [1] **by De Q. H. Tran, M.D., in order to present a concise, useful guide for practitioners in the areas of Dr. Tran's expertise – the Upper Extremity Block.**

By providing anesthesia and analgesia to the entire upper limb, brachial plexus blocks have contributed to advances in Orthopedic and Ambulatory Anesthesia. Furthermore, with the advent of ultrasonography, upper extremity blocks are becoming increasingly popular. Navigating the plethora of published studies can be a daunting task. This chapter aims to present a practical discussion of approaches and techniques for brachial plexus blockade.

The term "approach" will refer to the site where the brachial plexus is accessed (interscalene, supraclavicular, infraclavicular, axillary). In contrast, the term

* **Corresponding author De Q.H. Tran:** McGill University, Montreal, Canada; Tel: 514-934-1934; Fax: 514-93--8249; E-mail: de_tran@hotmail.com

Amballur D. John (Ed.)

"technique" will refer to the modality (neurostimulation, ultrasonography) or endpoints (single or multiple injections) employed for a given approach.

CLINICAL ANATOMY OF THE BRACHIAL PLEXUS

The anatomy of the brachial plexus is presented in (Fig. **1**). Although its complexity may appear overwhelming, one should focus on certain key facts:

While textbooks recommend selecting nerve blocks based on the skin innervation of the surgical site, knowledge of the osseous innervation (Fig. **2**) is far more important, as pain originates from periosteal and not cutaneous trauma.

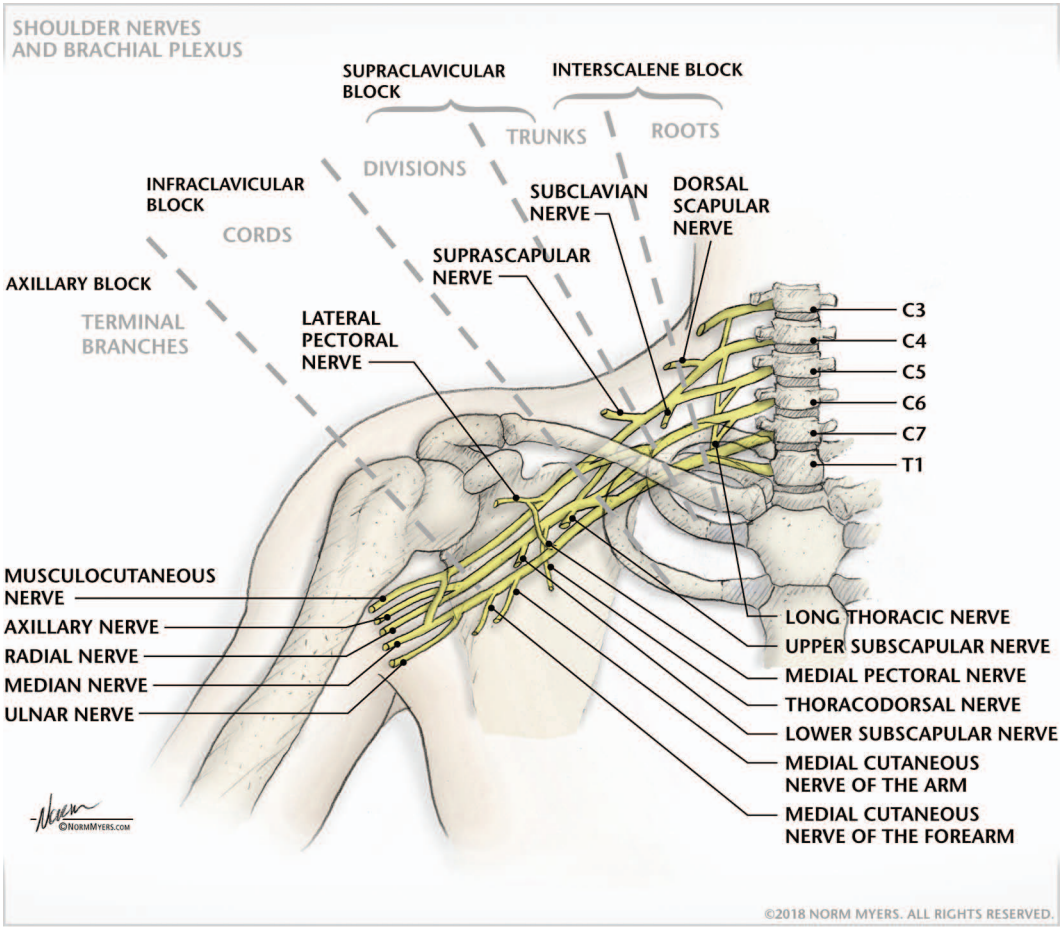


Fig. (1). Shoulder nerves and brachial plexus. Image provided by Norm Myers.

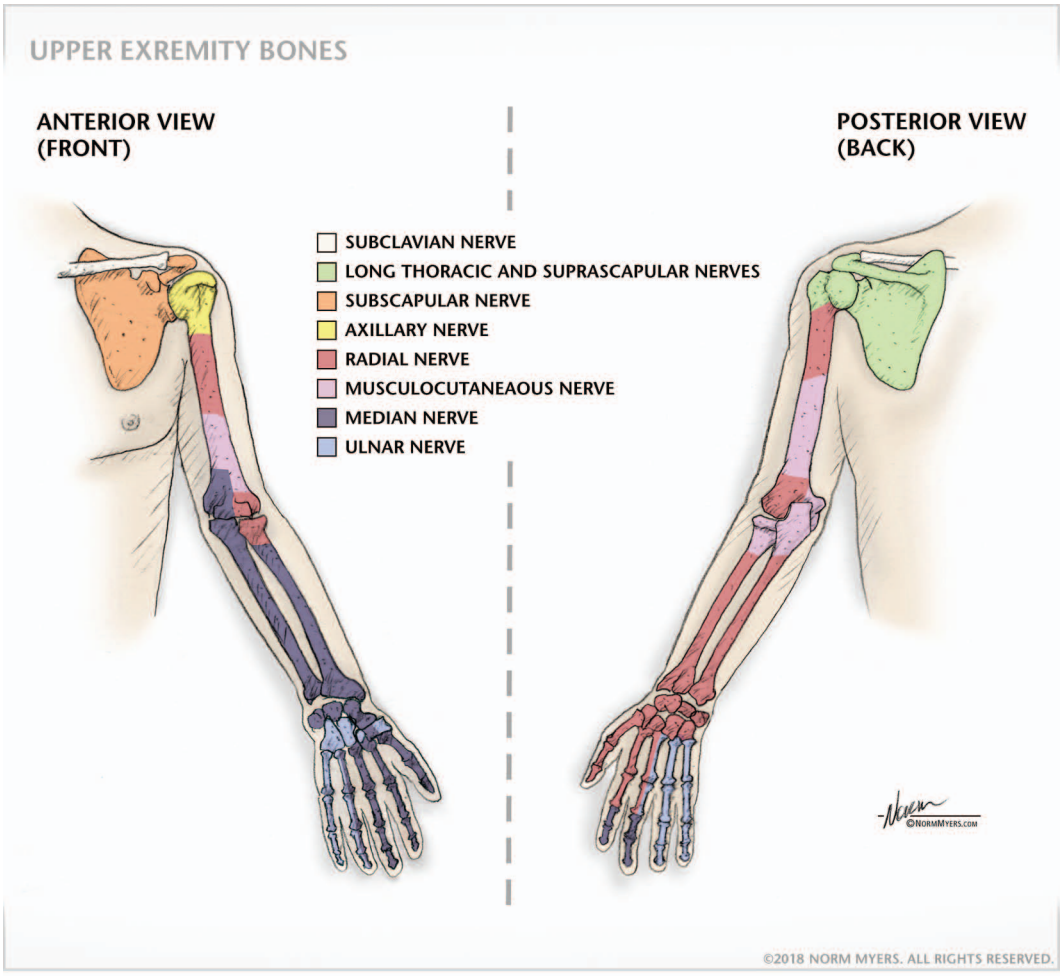


Fig. (2). Upper Extremity Bone Innervation. Image provided by Norm Myers. Reference Source: By permission - Upper Extremity Nerve Blocks, ©2012 Springer Science + Business Media, LLC.

The medial and lateral pectoral nerves originate from the medial and lateral cords, respectively. Thus pectoral contraction is an acceptable evoked motor response for neurostimulation-guided interscalene block. However pectoral contraction should not be accepted for neurostimulation-guided infraclavicular block since it could result from direct stimulation of the pectoral muscles.

The suprascapular nerve originates from the superior trunk and supplies the posterior aspect of the shoulder. For surgical procedures involving the shoulder joint, it is important to block this nerve prior to its take-off. This is best achieved with an interscalene or supraclavicular approach.

The subclavian nerve originates from the superior trunk and is responsible for the bony innervation of the clavicle. An interscalene or supraclavicular approach will anesthetize this nerve prior to its take-off.

SELECTING THE RIGHT APPROACH

In order to select the correct approach, one need only to know if surgery will take place in the area of the shoulder/clavicle/proximal humerus or in the region of the distal humerus/forearm/hand.

Surgery of the Shoulder, Clavicle and Proximal Humerus

The clavicle and posterior aspect of the shoulder joint/proximal humerus are innervated by the subclavian and suprascapular nerve, respectively (Fig. **2**). Because they target these nerves prior to their take-off from the superior trunk, the interscalene and supraclavicular approaches should be selected. Although subtle differences may exist between the interscalene and posterior cervical paravertebral approaches, from a practical standpoint, the latter should simply be conceptualized as a posterior approach to the interscalene block.

Surgery of the Distal Humerus, Forearm and Hand

The supraclavicular, infraclavicular and axillary approaches can be used for surgical procedures involving the distal humerus, forearm and hand. When optimal techniques are utilized for each approach, supraclavicular, infraclavicular and axillary blocks result in similar success rates [1]. In light of the comparable efficacy, the selection between the 3 approaches should be dictated by potential adverse events and patient characteristics. For instance, supraclavicular blocks, and their inherent risk of phrenic paralysis, should be avoided in patients with pulmonary compromise. Infraclavicular blocks may be contraindicated in subjects with cardiac pacemakers. Axillary blocks should be avoided in patients whose fracture precludes comfortable abduction of the upper limb.

INTERSCALENE APPROACH

The Theory

The interscalene approach anesthetizes the brachial plexus at the level of the roots and trunks. Identification of the plexus in the interscalene groove can be achieved with nerve stimulation or ultrasonography. Comparison of the 2 modalities has yielded contradictory results. In one study, ultrasound guidance improved the rate of surgical anesthesia as well as the onset and offset times [2]. In contrast, another trial observed no differences in performance time, surgical anesthesia and

postoperative neural deficits [3].

The Practice: Nerve Stimulation

The patient is supine with the head turned towards the contralateral side. At the level of the cricoid cartilage, posterior to the sternocleidomastoid muscle, the neck is palpated to identify the groove between the anterior and middle scalene muscles. To ensure that the correct groove has been identified, palpation of the latter above the clavicle should reveal an arterial pulsation (subclavian artery) (Fig. **3**).

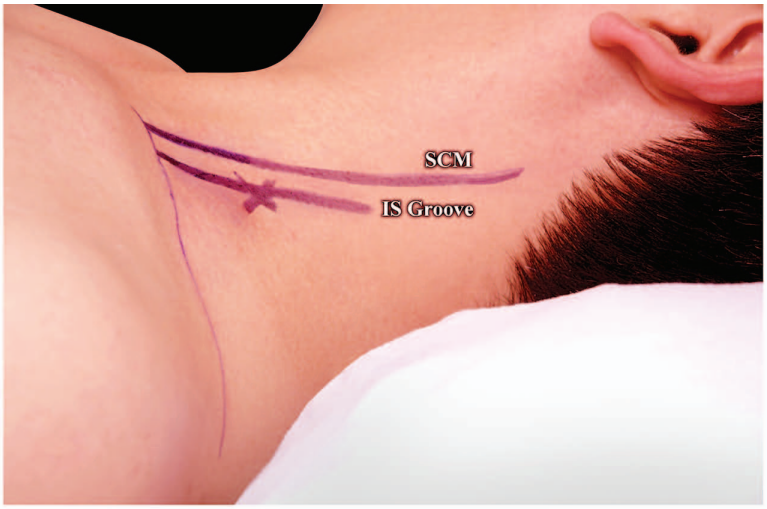


Fig. (3). To ensure that the correct groove has been identified, palpation of the latter above the clavicle should reveal an arterial pulsation (subclavian artery). Image provided by De Tran, M.D., McGill University.

The skin is infiltrated with local anesthesia (0.3 ml). A 5cm block needle, connected to a nerve stimulator set at a current of 1.5mA, a pulse width of 0.1ms and a frequency of 2Hz, is inserted in the interscalene groove. The needle is oriented in a slight caudad direction to avoid penetration of the intervertebral foramen. Typically, contraction of the deltoid, biceps, triceps or pectoral muscles is seen. All 4 constitute acceptable evoked motor responses. If diaphragmatic contraction (stimulation of the phrenic nerve) is encountered, the needle tip is too anterior thus should be redirected posteriorly. Conversely, if the needle is too posterior, stimulation of the dorsal scapular nerve and shoulder elevation (contraction of the rhomboid and levator scapulae muscles) will occur. After ensuring that the evoked motor response is still present at a current ≤0.8mA, 20ml of local anesthetic are injected. Although currents ≤0.5mA are commonly recommended to indicate proximity of the needle tip with the nerve, this threshold

originates (arbitrarily) from a 1969 case series pertaining to obturator nerve block [4]. The optimal stimulatory threshold warrants further investigation. In his practice, the author obtains high success rates with stimulating currents as high as 0.8mA.

Ultrasound Guidance

The patient is placed in a semi-sitting position with the head turned towards the contralateral side. The supraclavicular area is scanned to locate the subclavian artery. Typically, the brachial plexus (cluster of trunks and divisions) is situated superolateral to the latter. Next the plexus is slowly traced cephalad towards the cricoid cartilage until it becomes a column of hypoechoic nodules (roots/trunks) (Fig. **4A**, **4B**). Using an in-plane technique and a lateral to medial direction, the skin and subcutaneous tissues are infiltrated with local anesthesia. A 5cm block needle is then inserted. The target for this block is situated between the first and second nodules. A volume of 20ml of local anesthetic is commonly used.

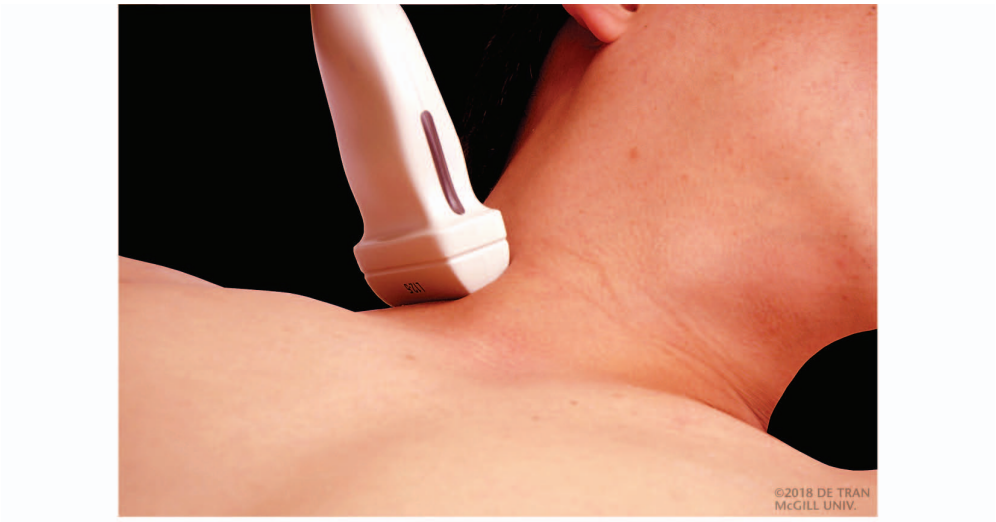


Fig. (4A). The patient is placed in a semi-sitting position with the head turned towards the contralateral side. The supraclavicular area is scanned to locate the subclavian artery. Typically, the brachial plexus (cluster of trunks and divisions) is situated superolateral to the latter. Next the plexus is slowly traced cephalad towards the cricoid cartilage until it becomes a column of hypoechoic nodules (roots/trunks) (Fig. **4A, 4B**). Image provided by De Tran, M.D., McGill University.

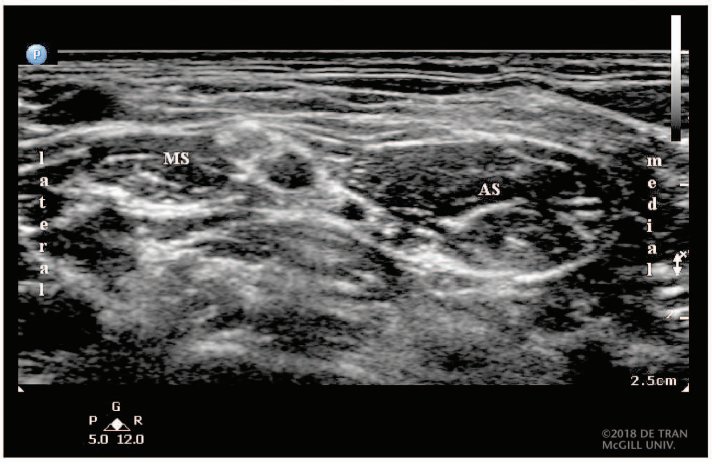


Fig. (4B). Ultrasound image of interscalene groove. Image provided by De Tran, M.D., McGill University. AS = anterior scalene muscle; MS = middle scalene muscle.

Complications

Due to the proximity of the cervical sympathetic chain and the recurrent laryngeal nerve, Horner syndrome and hoarseness can occur. These side effects are seldom problematic. With appropriate technique and equipment, some complications can be prevented: a slight caudad orientation of the needle will minimize the risk of dural cuff/vertebral artery/neuraxial puncture. The most vexing side effect remains the 100% incidence of ipsilateral hemidiaphragmatic paralysis (due to migration of local anesthetics to the C3-5 roots or the phrenic nerve) [5]. Usually well tolerated by healthy subjects, it becomes a prohibitive risk in patients with pulmonary compromise. To date, no preventive measure can reliably sidestep this adverse event. Even an injectate as small as 5ml can result in a 45% incidence of diaphragmatic paralysis [6]. There exist 2 clinical strategies to tackle pulmonary patients who require regional anesthesia for shoulder/proximal humerus surgery. Since the anterior and posterior shoulder joints are supplied by the axillary and suprascapular nerves, respectively, one can perform selective axillary and suprascapular nerve blocks [7]. However, the author does not favor this tactic because it provides no coverage for the posterior aspect of the upper humerus, which is also supplied by the radial nerve (Fig. **2**). A better strategy would be to combine selective suprascapular nerve block and infraclavicular brachial plexus block [8]. The latter would anesthetize both the axillary and the radial nerves.

SUPRACLAVICULAR APPROACH

The Theory

The supraclavicular approach anesthetizes the brachial plexus at the level of the

trunks and divisions. This block can be performed with neurostimulation or ultrasonography. Compared to neurostimulation, ultrasonography results in a similar success rate coupled with a lower incidence of phrenic nerve block [9].

The Practice: Nerve Stimulation

Because of the inherent risk of pneumothorax, the author strongly recommends that ultrasound guidance be employed for supraclavicular blocks.

Ultrasound Guidance

The classic technique remains the "Eight Ball, Corner Pocket" technique, whereby local anesthetic is injected at the intersection of the first rib and subclavian artery [10]. The patient is positioned semi-sitting with the head turned towards the contralateral side. Using a high frequency probe, the supraclavicular area is scanned to identify a short axis view of the subclavian artery (Fig. **5**). Superolateral to the latter, a collection of hypoechoic structures (trunks/divisions) can be seen. It is crucial to visualize the first rib underneath the subclavian artery: it serves as a backstop and prevents pleural breach.

The skin and subcutaneous tissues are infiltrated with local anesthesia (3ml). Using an in-plane technique and a lateral to medial direction, a 5cm block needle is directed towards the "corner pocket" *i.e.* the intersection between the subclavian artery and the first rib (Fig. **5**). A volume of 30-35ml of local anesthetic is commonly used.

Fig. (5A). The patient is positioned semi-sitting with the head turned towards the contralateral side. Using a high frequency probe, the supraclavicular area is scanned to identify a short axis view of the subclavian artery (Fig. **5A, 5B**). Image provided by De Tran, M.D., McGill University.

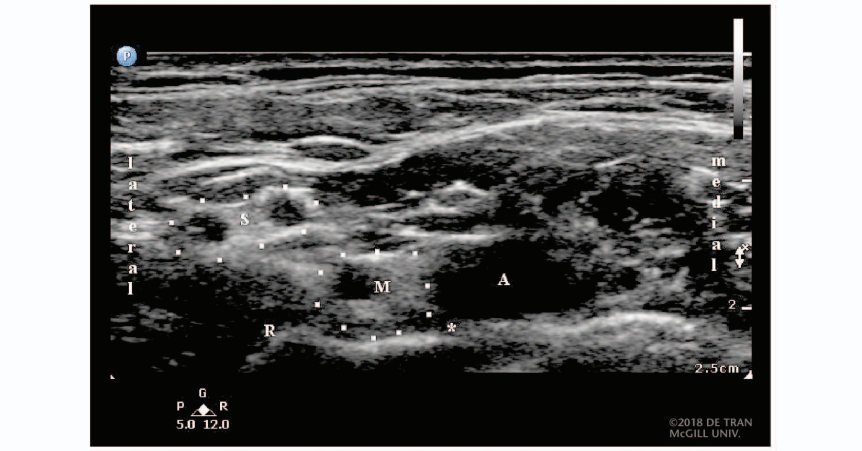


Fig. (5B). Supraclavicular ultrasound image. Image provided by De Tran, M.D., McGill University. A = subclavian artery; M = main neural cluster; S = satellite cluster.

Recently, the author has described a new method for ultrasound-guided supraclavicular block: the "targeted intracluster injection" (TII) technique [11]. The principle is simple. With the "corner pocket" technique, local anesthetic molecules, deposited at the intersection of the first rib and subclavian artery, are free to migrate and surround the neural clusters. In contrast, the TII technique aims to inject local anesthetic directly inside the main and satellite neural clusters (Fig. **5**). As a result, the onset time is significantly shorter.

Complications

Vascular puncture, recurrent laryngeal nerve paralysis and Horner syndrome can occur after supraclavicular blocks. The risk of pneumothorax can be as high as 6% with neurostimulation. Because phrenic nerve blockade can occur in 67% of cases, like its interscalene counterpart, the supraclavicular approach should be avoided in patients with pulmonary compromise [12].

INFRACLAVICULAR APPROACH

Theory

The infraclavicular approach anesthetizes the brachial plexus at the level of its cords (lateral, posterior and medial). It can be performed with neurostimulation or ultrasonography. Comparison of the 2 modalities has yielded mixed results. Two trials found similar rates of surgical anesthesia and onset times while another study reported a higher rate of surgical anesthesia and a shorter performance time with ultrasonography [13 - 15].

The Practice: Nerve Stimulation

The patient is in placed in the supine position. A point 2cm medial and 2cm caudad to the tip of the coracoid process is identified (Fig. **6**). The skin and subcutaneous tissue are infiltrated with local anesthesia (3ml). A 5-10cm block needle, connected to a nerve stimulator set at an initial current of 1.5mA, a pulse width of 0.1ms and a frequency of 2Hz, is inserted perpendicularly to the skin. Usually elbow flexion (lateral cord stimulation) is encountered first. Using a parasagittal plane, the needle tip is redirected in a caudad direction in search of flexion/extension of the wrist or fingers. In order to minimize the risk of pneumothorax, the needle should never be directed medially. After ensuring that the evoked motor response is still present at a current ≤0.8mA, 30-35ml of local anesthetic are injected.

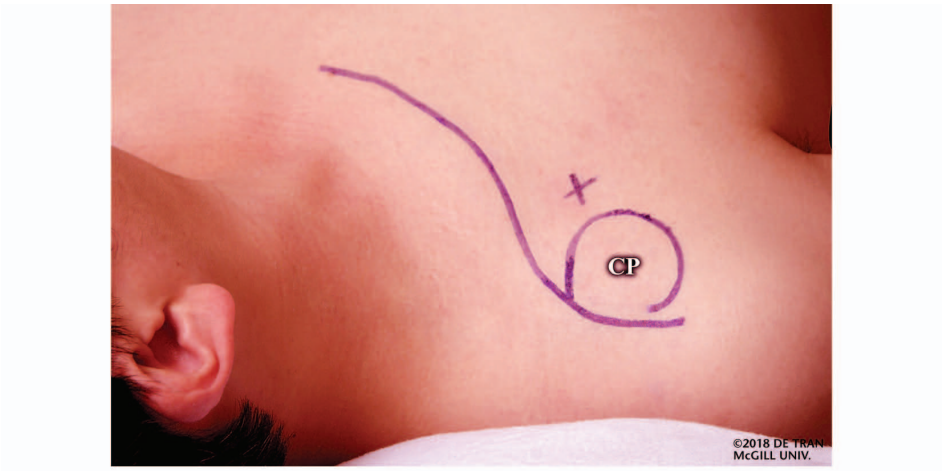


Fig. (6). The patient is in placed in the supine position. A point 2 cm medial and 2 cm caudad to the tip of the coracoid process (CP) is identified. Image provided by De Tran, M.D., McGill University.

Ultrasound Guidance

The patient is positioned supine. The arm is flexed so that the forearm and hand can rest comfortably on the torso. A high frequency ultrasound probe is placed in the infraclavicular fossa, medial to the coracoid process, to obtain a short-axis view of the axillary vessels (Fig. **7A**). The axillary artery and vein can be found under the pectoralis major and minor muscles. The pleura can sometimes be seen under the vessels (Fig. **7B**). Local anesthetic (3 ml) is used to infiltrate the skin, subcutaneous tissues and pectoralis muscles. Using an in-plane technique and a cephalad to caudad direction, a 10cm block needle is advanced until the tip lies just dorsal to the artery. Usually, a pop can be felt just before the needle assumes the correct position. Thirty to thirty-five (30-35) ml of local anesthetic agent are administered. Injection of the first few ml of local anesthetic will give rise to a

picture resembling a "double bubble" [16]. The superior bubble represents the axillary artery in a short axis and the "inferior bubble", the pool of local anesthetic. As more local anesthetic is deposited, the inferior bubble will turn into a U shape, wrapping itself around the artery and the latter will be gently pushed ventrally. If the artery fails to rise, the needle tip may be too dorsal in relation to the artery; thus it should be repositioned to lie immediately adjacent to the latter. Occasionally, 2 axillary veins (cephalad and caudad to the artery) or 2 arteries can be present. In such a situation, another approach should be selected to ensure singularity of the target and to avoid vascular puncture.

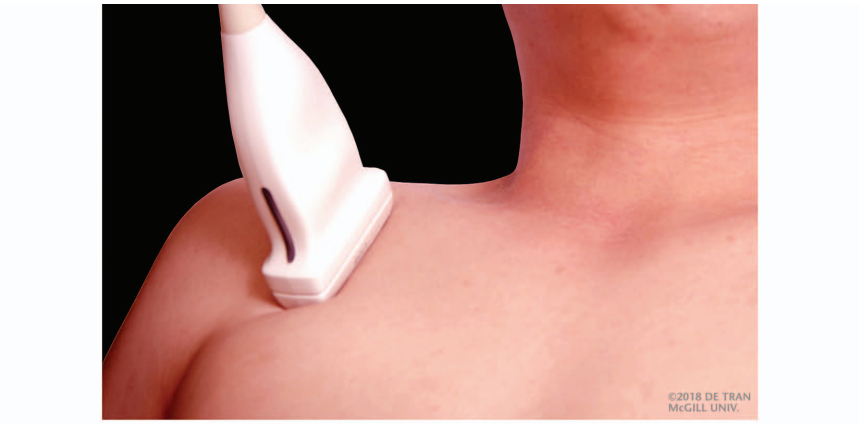


Fig. (7A). The patient is positioned supine. The arm is flexed so that the forearm and hand can rest comfortably on the torso. A high frequency ultrasound probe is placed in the infraclavicular fossa, medial to the coracoid process, to obtain a short-axis view of the axillary vessels. Image provided by De Tran, M.D., McGill University.

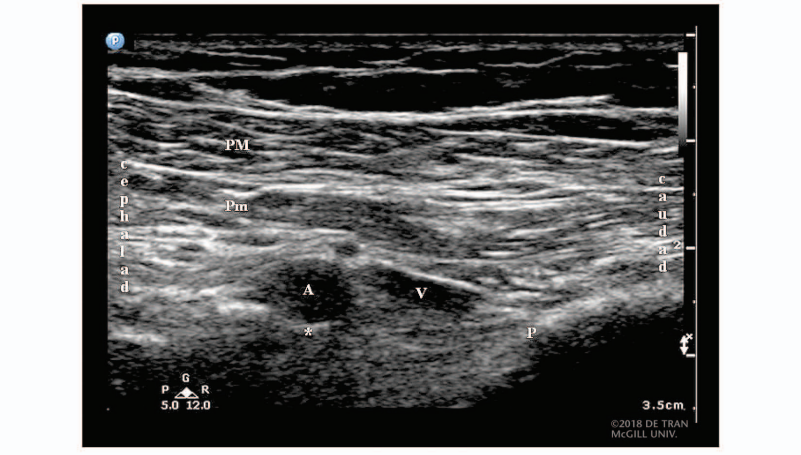


Fig. (7B). The axillary artery and vein can be found under the pectoralis major and minor muscles. The pleura can sometimes be seen under the vessels. Image provided by De Tran, M.D., McGill University. A = axillary artery; P = pleura; PM = pectoralis major muscle; Pm = pectoralis minor muscle; * = needle target.

Complications

Vascular puncture can occur. Because of the depth of the vessels, external compression can be tricky. Thus caution should be exercised in coagulopathic patients. Phrenic paralysis can occur in a minority of patients. There have been anecdotal reports of Horner syndrome and pneumothorax associated with infraclavicular blocks.

AXILLARY APPROACH

The Theory

The axillary approach anesthetizes the brachial plexus at the level of its 4 main terminal branches (musculocutaneous, median, radial and ulnar nerves). Performing this block with fascial clicks, elicitation of paresthesia, trans-arterial injection and single nerve stimulation yields only modest success rates (70-80%). Thus most practitioners prefer multiple-nerve stimulation and ultrasound guidance. Compared to a multiple-stimulation technique, a higher success rate and shorter onset time have been reported with ultrasonography [17]. However, another trial found no differences [18].

The Practice: Nerve Stimulation

The patient is positioned supine with the shoulder abducted and the elbow flexed. The axilla is palpated to identify the axillary artery. The musculocutaneous and median nerves are usually situated above the artery whereas the radial and ulnar nerves can be found below the latter. Two distinct puncture sites (above and below the artery) are required (Fig. **8**). The skin is infiltrated with local anesthesia (0.3ml per puncture site). A 5cm block needle, connected to a nerve stimulator set at an initial current of 1.5mA, a pulse width of 0.1ms and a frequency of 2Hz, is used. The block needle is first inserted above the artery to locate the musculocutaneous nerve (elbow flexion). After ensuring that the evoked motor response is still present at a current ≤0.8mA, 5-7ml of local anesthetic are deposited.

If elbow flexion cannot be obtained, the musculocutaneous nerve can be blocked by contacting the humerus and injecting local anesthetic as the needle is pulled back into the belly of the coracobrachialis muscle. Two or three passes (with different angulations) are required. Subsequently, the needle is repositioned to locate the median nerve (above the artery) and radial nerve (below the artery). Wrist/finger flexion is sought for the former whereas wrist/finger extension is sought for the latter. For each of these two nerves, a local anesthetic volume of 10-14ml is injected after ensuring that the evoked motor response is still present at

≤0.8mA. Electrolocation of the ulnar nerve is not required for successful neurostimulation-guided axillary block [19].

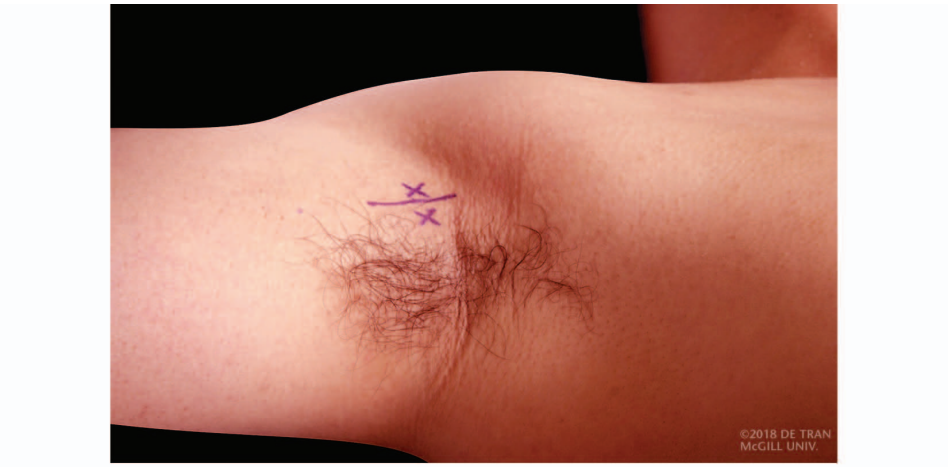


Fig. (8A). The patient is positioned supine with the shoulder abducted and the elbow flexed. The axilla is palpated to identify the axillary artery. The musculocutaneous and median nerves are usually situated above the artery whereas the radial and ulnar nerves can be found below the latter. Two distinct puncture sites (above and below the artery) are required. Image provided by De Tran, M.D., McGill University.

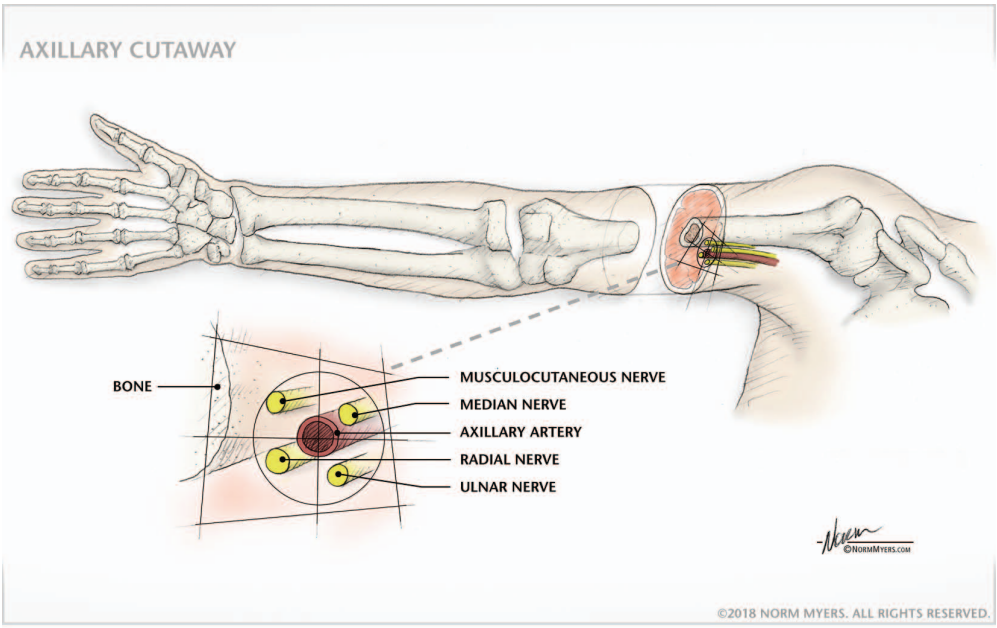


Fig. (8B). Axillary Cutaway. Image provided by Norm Myers.

Ultrasound Guidance

The patient is positioned with the shoulder abducted and the elbow flexed. The axilla is scanned with a high frequency, linear ultrasound probe to identify a short axis view of the axillary artery (Fig. **9A**). The musculocutaneous nerve, a hyperechoic structure can be found anterior and lateral to the artery, in a fascial plane between the coracobrachialis and biceps muscles (Fig. **9B**). Using an in-plane technique, the skin and subcutaneous tissues are infiltrated with local anesthesia (3ml). A 5cm block needle is then inserted. The needle is first directed towards the musculocutaneous nerve. Six ml of local anesthetic are deposited. Subsequently, the needle is redirected towards the six o'clock position of the axillary artery [20]. If the needle tip is correctly positioned inside the neurovascular sheath, injection of a few mL will result in a "silhouette sign" (blurring of the arterial wall due to the contiguity of anechoic blood and anechoic local anesthetic).

If a "silhouette sign" fails to form, the needle tip may be too dorsal in relation to the vessel; thus it should be repositioned to lie immediately adjacent to the latter. Twenty-five (25) ml of local anesthetic are then injected. This typically results in the axillary artery being surrounded by local anesthetic (donut sign). In some patients, the musculocutaneous nerve cannot be visualized between the biceps and coracobrachialis muscles, as it travels with its median/radial/ulnar counterparts inside the neurovascular bundle. In such cases, the entire volume of local anesthetic is injected at the 6o'clock position of the axillary artery after obtaining a "silhouette sign".

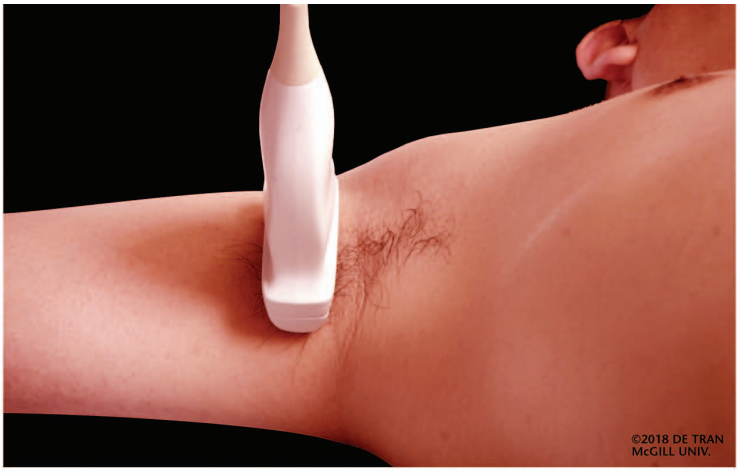


Fig. (9A). The patient is positioned with the shoulder abducted and the elbow flexed. The axilla is scanned with a high frequency, linear ultrasound probe to identify a short axis view of the axillary artery (Fig.**9A**). Image provided by De Tran, M.D., McGill University.

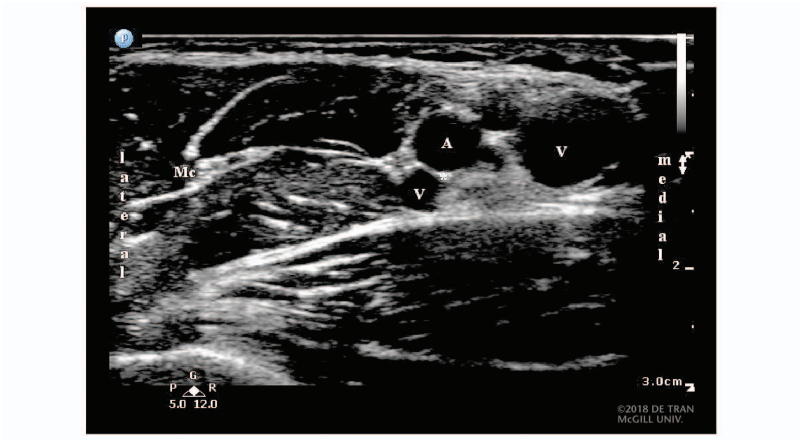


Fig. (9B). The musculocutaneous nerve, a hyperechoic structure can be found anterior and lateral to the artery, in a fascial plane between the coracobrachialis and biceps muscles. Image provided by De Tran, M.D., McGill University. A = axillary artery; Mc = musculocutaneous nerve; V = axillary vein.

Complications

Transient numbness, vascular puncture, intravascular injection, bruising and soreness at the injection site have been reported but the overall safety margin for the axillary approach is very high.

SUPPLEMENTAL BLOCKS

In the event of an incomplete brachial plexus block, missing nerves can be anesthetized at a more distal location.

Suprascapular Nerve Block

The Theory

In his practice, the author combines suprascapular nerve block with infraclavicular brachial plexus block to anesthetize the shoulder for patients who are unable to undergo interscalene/supraclavicular blocks due to pulmonary compromise. The suprascapular nerve can be blocked with neurostimulation or ultrasonography. To date, no study has compared these 2 modalities.

The Practice: Nerve Stimulation

Due to the elaborate landmarks required by the neurostimulation-guided technique, the author suggests using ultrasonography for suprascapular nerve block.

Ultrasound Guidance

The patient is positioned in the lateral decubitus position so that the side to be blocked is uppermost. Using a high frequency, linear ultrasound probe, the area cephalad to the scapular spine is scanned to identify the suprascapular fossa (Fig. **10A, 10B**). The skin and subcutaneous tissues are infiltrated with local anesthesia (3ml). Using an in-plane technique, a 10cm block needle is advanced towards the suprascapular fossa. After bony contact by the needle tip, a volume of 10ml of local anesthetics is deposited in the suprascapular fossa.

Fig. (10A). The patient is positioned in the lateral decubitus position so that the side to be blocked is uppermost. Image provided by De Tran, M.D., McGill University.

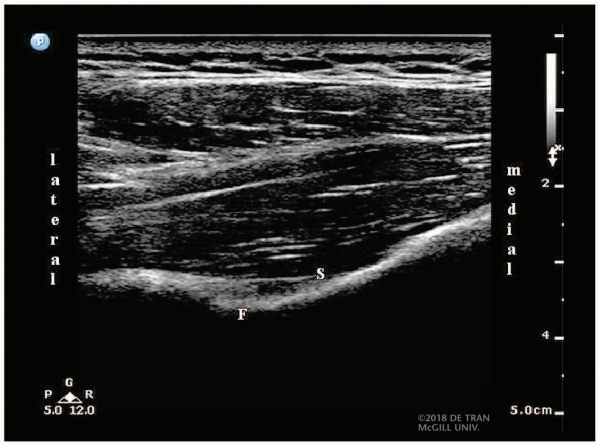


Fig. (10B). Using a high frequency, linear ultrasound probe, the area cephalad to the scapular spine is scanned to identify the suprascapular fossa. Image provided by De Tran, M.D., McGill University. F = suprascapular fossa; S = fascia of supraspinatus muscle.

Intercostobrachialis Nerve Block

Although many textbooks recommend supplementing brachial plexus blocks with an intercostobrachialis nerve block (subcutaneous infiltration of the medial arm with 5-7 ml of local anesthetic) for tourniquet tolerance, this step is not necessary. Tourniquet-related pain stems from muscular compression, which is covered by the brachial plexus block. In contrast, the intercostobrachialis nerve only provides sensory innervation to the skin.

DISTAL NERVE BLOCKS AT THE ELBOW

The Theory

The radial, median and ulnar nerves can be blocked at the elbow. To date, no study has compared neurostimulation and ultrasonography.

The Practice: Nerve Stimulation

Since the distal blocks at the elbow are usually performed to rescue a failing brachial plexus block, it is paramount that they succeed. With this mindset, the author suggests to use ultrasonography instead of neurostimulation: in addition to preventing vascular puncture, ultrasound guidance will ensure circumferential spread of local anesthetic around the target nerve.

Ultrasound Guidance

Radial and Median Nerve

The patient is positioned supine with the upper extremity abducted. At the level of the elbow crease, a high frequency, linear ultrasound probe is used. The radial nerve appears as a hyperechoic crescent (Fig. **11A, 11B**). The median nerve is located medial to the brachial artery (Fig. **12**). Using an in-plane technique, a 5cm block needle is advanced towards the 2 nerves. A volume of 5-7ml of local anesthetic is deposited around each nerve. If the median nerve cannot be visualized, a perivascular injection can be carried out medial to the brachial artery.

Ulnar Nerve

The patient is positioned supine. The elbow is flexed and the forearm internally rotated so that its radial aspect rests comfortably on the torso. A high frequency, linear ultrasound probe is used to scan the proximal forearm. The ulnar nerve appears as a hyperechoic structure (Fig. **13A, 13B**). Using an in-plane technique, a 5cm block needle is advanced towards the nerve. A volume of 5-7ml of local anesthetic is deposited around the nerve.

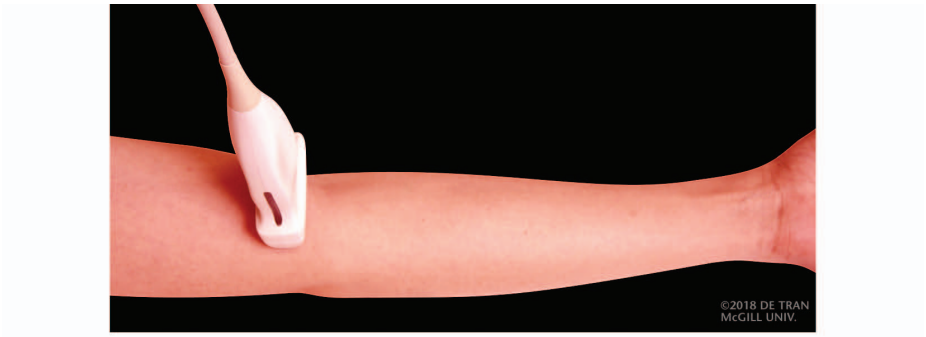


Fig. (11A). The patient is positioned supine with the upper extremity abducted. Image provided by De Tran, M.D., McGill University.

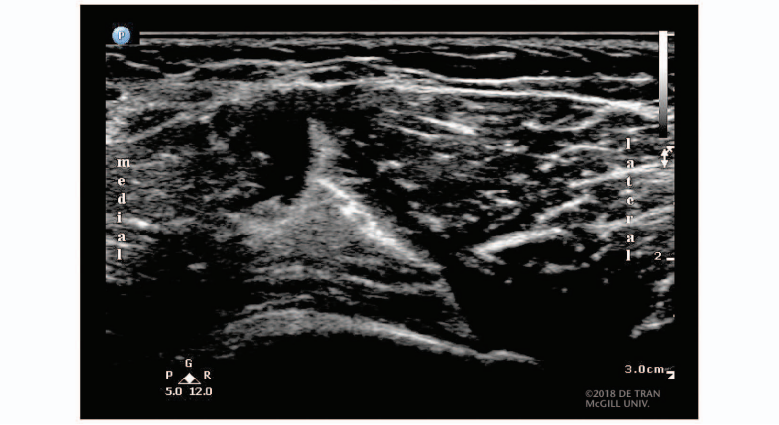


Fig. (11B). At the level of the elbow crease, a high frequency, linear ultrasound probe is used. The radial nerve appears as a hyperechoic crescent. Image provided by De Tran, M.D., McGill University.

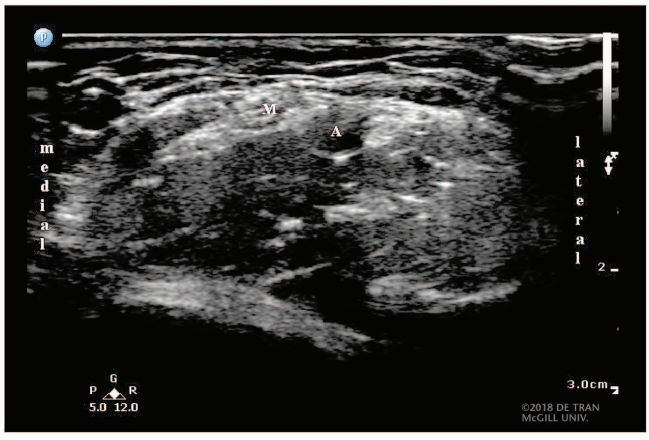


Fig. (12). The median nerve is located medial to the brachial artery. Image provided by De Tran, M.D., McGill University. A = brachial artery; M = median nerve.

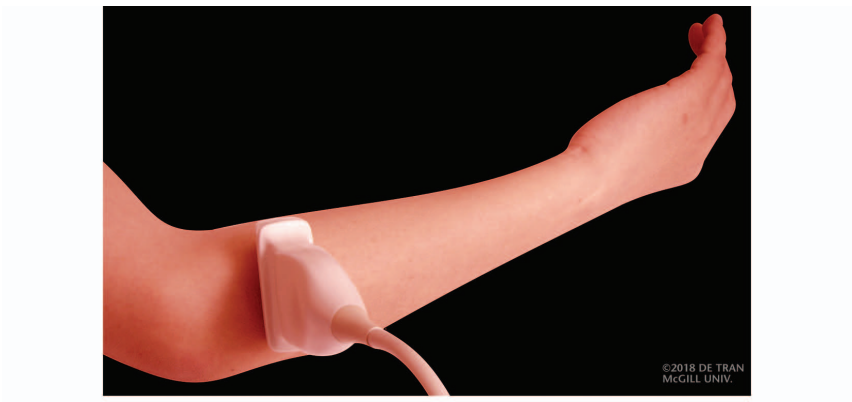


Fig. (13A). The patient is positioned supine. The elbow is flexed and the forearm internally rotated so that its radial aspect rests comfortably on the torso. Image provided by De Tran, M.D., McGill University.

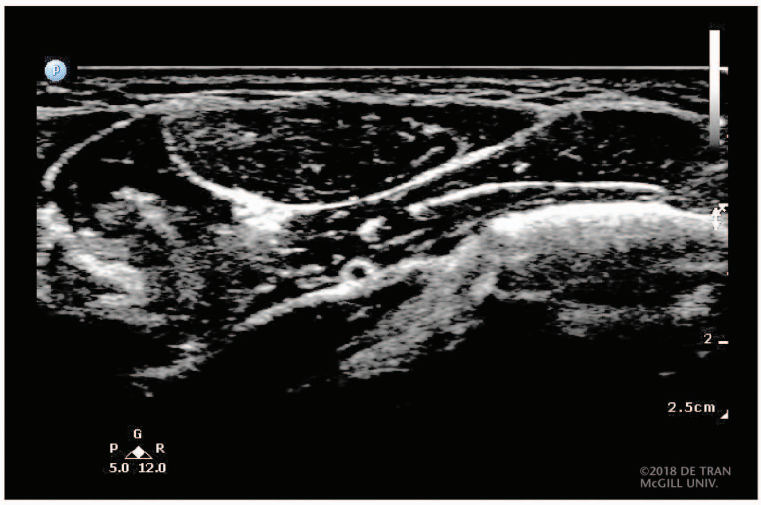


Fig. (13B). A high frequency, linear ultrasound probe is used to scan the proximal forearm. The ulnar nerve appears as a hyperechoic structure. Image provided by De Tran, M.D., McGill University.

Complications

Most supplemental blocks possess a high safety profile. Vascular puncture (brachial artery) can occasionally occur with median nerve blocks.

SELECTING THE LOCAL ANESTHETIC AGENT (TABLE 1)

In order to select the correct local anesthetic agent, the operator must decide whether the aim is postoperative analgesia, surgical anesthesia or both.

Table 1. Local anesthetic dose. Table provided by De Tran, M.D., McGill University.

Local Anesthetic	Toxic Dose (mg/kg)	Approximative Duration of Anesthesia (hours)*
Lidocaine	5	2-3
Lidocaine with epinephrine	7	3-6
Bupivacaine	2.5	6-8
Bupivacaine with epinephrine	3	8-10
Mepivacaine	6	2-3
Mepivacaine withepinephrine	7	3-4
Ropivacaine	3	6-8
*The duration of analgesia usually exceeds that of anesthesia. ©2018 A.D. JOHN		

If the brachial plexus block is performed to maximize postoperative analgesia, block duration should be the overriding concern. Thus long(est) acting agents (such as bupivacaine or ropivacaine) should be selected. In his practice, the author uses bupivacaine 0.25% with epinephrine 5µg/ml for the following reasons: **1)** bupivacaine lasts longer than ropivacaine. **2)** with technical proficiency and ultrasound guidance, intravascular injection can be avoided. Furthermore, incremental injection (with repeated negative aspiration) and the presence of epinephrine (which signals intravascular injection through tachycardia) impart additional layers of safety. Thus, though less cardiotoxic, ropivacaine provides minimal benefits for the author.

If the block is performed to ensure surgical anesthesia, onset time should be the main concern. Thus quickest(est) acting agents should be selected. In his practice, the author uses lidocaine 1.5% with epinephrine 5µg/ml. However, because of its short duration, lidocaine provides limited postoperative analgesia.

If the operator wishes to achieve both surgical anesthesia and postoperative analgesia, 3 options exist. Firstly, the brachial plexus block is performed with bupivacaine at least 45 minutes before surgery to provide enough soak time. This strategy requires an induction room as well as an assistant to monitor the patient while the anesthesiologist blocks the next one. Secondly, the brachial plexus block is performed with lidocaine (thus ensuring a swift onset) and a perineural catheter is inserted. Postoperatively, the latter is injected with bupivacaine to ensure long lasting analgesia. Albeit the most versatile, this strategy is most demanding in terms of technical skills, performance time and equipment costs. Finally, a mix of lidocaine 1%-bupivacaine 0.25% (obtained by combining equal parts of lidocaine 2% and bupivacaine 0.5%) with epinephrine 5µg/ml is

employed. While the mix does not have an onset time as swift as pure lidocaine or a duration as long as bupivacaine, it represents an attractive option because of its simplicity. In his practice, the author favors options 2 and 3.

PRECAUTIONARY MEASURES

Irrespective of the approach (interscalene/ supraclavicular/ infraclavicular/ axillary) and technique (neurostimulation/ ultrasonography) used for brachial plexus blockade, the author recommends implementation of the following precautionary measures: **1)** A peripheral nerve block is an invasive procedure that carries a risk of complications (nerve damage, local anesthetic toxicity). Thus adequate training (for the operator) and informed consent (from the patient) is paramount. **2)** While sedation can be provided for procedural discomfort, it should never obtund the patient's ability to report paresthesia or reflexic withdrawal to pain. **3)** Local anesthetic injection should always be carried out in a slow, deliberate manner with negative aspiration between every 5ml-increment. Furthermore, nerve blocks should always be performed in a monitored setting with ready access to resuscitative equipment and drugs (such as Intralipid). **4)** Toxic doses of local anesthetic agents should not be exceeded.

CONCLUSION

Brachial plexus blocks have contributed to advances in Orthopedic and Ambulatory Anesthesia. Ultrasonography has made upper extremity blocks more accessible and more popular Rather than focusing solely on dermatomal – skin innervation, knowledge of periosteal innervation is important for a successful block. Choosing the correct approach allows one to successfully operate on the shoulder, clavicle, proximal humerus, distal humerus, forearm, and hand. This chapter has aimed to present a practical discussion of approached and techniques for brachial plexus blockade. The risks associated with the blocks helps determine the approach used for each individual patient. The interscalene and supraclavicular approaches have a high risk of diaphragmatic paralysis, Horner's syndrome, and vascular absorption. The infraclavicular approach has a potential for vascular puncture and difficulty with external compression due to depth of the vessel, a potential for pneumothorax, and is usually contraindicated in patients who cannot abduct their arm. The duration of anesthesia provided is dependent on the medication chosen and whether an indwelling catheter is used.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

The author would like to thank Drs. Prangmalee Leurcharusmee, Vanlapa Arnuntasupakul and Daniel Chora De La Garza for their assistance with the figures.

REFERENCES

[1] **Dr. Tran's works used as a basis for this chapter include the following:** De Q. H. Tran. Upper Extremity Nerve Blocks, Essentials of Regional Anesthesia, 2012 Techasuk, Wallaya, Andrea P. González, Francisca Bernucci, Tracy Cupido, Roderick J. Finlayson, and De QH Tran. A Randomized Comparison Between Double-Injection and Targeted Intracluster-Injection Ultrasound-Guided Supraclavicular Brachial Plexus Block, Anesthesia & Analgesia, 2014. Yazer, Murray S., Roderick J. Finlayson, and De Q.H. Tran. A Randomized Comparison Between Infraclavicular Block and Targeted Intracluster Injection Supraclavicular Block, Regional Anesthesia and Pain Medicine, 2014. Tran, De Q.H., Kevin Pham, Shubada Dugani, and Roderick J. Finlayson. A Prospective, Randomized Comparison Between Double-, Triple-, and Quadruple-Injection Ultrasound-Guided Axillary Brachial Plexus Block, Regional Anesthesia and Pain Medicine, 2012. Tran, DQH, Russo GL, Munoz L, Zaouter C, Finlayson RJ. A Prospective, Randomized Comparison Between Ultrasound-Guided Supraclavicular, Infraclavicular and Axillary Brachial Plexus Blocks. Reg Anesth Pain Med. 2009; 34: 366-371. Tran DQH, Russo GL, Munoz L, Zaouter C, Finlayson RJ. A Prospective, Randomized Comparison Between Ultrasound-Guided Supraclavicular, Infraclavicular and Axillary Brachial Plexus Blocks. Reg Anesth Pain Med 2009; 34: 366-71.
[PMID: 19574871]

[2] Kapral S, Greher M, Huber G, *et al.* Ultrasonographic guidance improves the success rate of interscalene brachial plexus blockade. Reg Anesth Pain Med 2008; 33(3): 253-8.
[http://dx.doi.org/10.1097/00115550-200805000-00010] [PMID: 18433677]

[3] Liu SS, Zayas VM, Gordon MA, *et al.* A prospective, randomized, controlled trial comparing ultrasound *versus* nerve stimulator guidance for interscalene block for ambulatory shoulder surgery for postoperative neurological symptoms. Anesth Analg 2009; 109(1): 265-71.
[http://dx.doi.org/10.1213/ane.0b013e3181a3272c] [PMID: 19535720]

[4] Magora F, Rozin R, Ben-Menachem Y, Magora A. Obturator nerve block: an evaluation of technique. Br J Anaesth 1969; 41(8): 695-8.
[http://dx.doi.org/10.1093/bja/41.8.695] [PMID: 5810129]

[5] Urmey WF, Talts KH, Sharrock NE. One hundred percent incidence of hemidiaphragmatic paresis associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. Anesth Analg 1991; 72(4): 498-503.
[http://dx.doi.org/10.1213/00000539-199104000-00014] [PMID: 2006740]

[6] Riazi S, Carmichael N, Awad I, Holtby RM, McCartney CJL. Effect of local anaesthetic volume (20 *vs*. 5 ml) on the efficacy and respiratory consequences of ultrasound-guided interscalene brachial plexus block. Br J Anaesth 2008; 101(4): 549-56.
[http://dx.doi.org/10.1093/bja/aen229] [PMID: 18682410]

[7] Price DJ. Axillary (circumflex) nerve block used in association with suprascapular nerve block for the control of pain following total shoulder joint replacement. Reg Anesth Pain Med 2008; 33(3): 280-1.
[http://dx.doi.org/10.1097/00115550-200805000-00022] [PMID: 18433689]

[8] Martínez J, Sala-Blanch X, Ramos I, Gomar C. Combined infraclavicular plexus block with

suprascapular nerve block for humeral head surgery in a patient with respiratory failure: an alternative approach. Anesthesiology 2003; 98(3): 784-5.
[http://dx.doi.org/10.1097/00000542-200303000-00031] [PMID: 12606927]

[9] Renes SH, Spoormans HH, Gielen MJ, Rettig HC, van Geffen GJ. Hemidiaphragmatic paresis can be avoided in ultrasound-guided supraclavicular brachial plexus block. Reg Anesth Pain Med 2009; 34(6): 595-9.
[http://dx.doi.org/10.1097/AAP.0b013e3181bfbd83] [PMID: 19916254]

[10] Soares LG, Brull R, Lai J, Chan VW. Eight ball, corner pocket: the optimal needle position for ultrasound-guided supraclavicular block. Reg Anesth Pain Med 2007; 32(1): 94-5.
[PMID: 17196502]

[11] Techasuk W, González AP, Bernucci F, Cupido T, Finlayson RJ, Tran DQ. A randomized comparison between double-injection and targeted intracluster-injection ultrasound-guided supraclavicular brachial plexus block. Anesth Analg 2014; 118(6): 1363-9.
[http://dx.doi.org/10.1213/ANE.0000000000000224] [PMID: 24842181]

[12] Knoblanche GE. The incidence and aetiology of phrenic nerve blockade associated with supraclavicular brachial plexus block. Anaesth Intensive Care 1979; 7(4): 346-9.
[PMID: 525758]

[13] Sauter AR, Dodgson MS, Stubhaug A, Halstensen AM, Klaastad Ø. Electrical nerve stimulation or ultrasound guidance for lateral sagittal infraclavicular blocks: a randomized, controlled, observer-blinded, comparative study. Anesth Analg 2008; 106(6): 1910-5.
[http://dx.doi.org/10.1213/ane.0b013e318173280f] [PMID: 18499631]

[14] Taboada M, Rodríguez J, Amor M, *et al.* Is ultrasound guidance superior to conventional nerve stimulation for coracoid infraclavicular brachial plexus block? Reg Anesth Pain Med 2009; 34(4): 357-60.
[http://dx.doi.org/10.1097/AAP.0b013e3181ac7c19] [PMID: 19574869]

[15] Brull R, Lupu M, Perlas A, Chan VWS, McCartney CJL. Compared with dual nerve stimulation, ultrasound guidance shortens the time for infraclavicular block performance. Can J Anaesth 2009; 56(11): 812-8.
[http://dx.doi.org/10.1007/s12630-009-9170-2] [PMID: 19728002]

[16] Tran DQH, Charghi R, Finlayson RJ. The "double bubble" sign for successful infraclavicular brachial plexus blockade. Anesth Analg 2006; 103(4): 1048-9.
[http://dx.doi.org/10.1213/01.ane.0000239077.49794.a5] [PMID: 17000840]

[17] Chan VWS, Perlas A, McCartney CJL, Brull R, Xu D, Abbas S. Ultrasound guidance improves success rate of axillary brachial plexus block. Can J Anaesth 2007; 54(3): 176-82.
[http://dx.doi.org/10.1007/BF03022637] [PMID: 17331928]

[18] Casati A, Danelli G, Baciarello M, *et al.* A prospective, randomized comparison between ultrasound and nerve stimulation guidance for multiple injection axillary brachial plexus block. Anesthesiology 2007; 106(5): 992-6.
[http://dx.doi.org/10.1097/01.anes.0000265159.55179.e1] [PMID: 17457131]

[19] Sia S, Bartoli M. Selective ulnar nerve localization is not essential for axillary brachial plexus block using a multiple nerve stimulation technique. Reg Anesth Pain Med 2001; 26(1): 12-6.
[http://dx.doi.org/10.1097/00115550-200101000-00005] [PMID: 11172505]

[20] Bernucci F, Gonzalez AP, Finlayson RJ, Tran DQHA. A prospective, randomized comparison between perivascular and perineural ultrasound-guided axillary brachial plexus block. Reg Anesth Pain Med 2012; 37(5): 473-7.
[http://dx.doi.org/10.1097/AAP.0b013e3182576b6f] [PMID: 22660484]

ADDITIONAL EDUCATIONAL MATERIAL

Tran QH, Clemente A, Doan J, Finlayson RJ. Brachial plexus blocks: a review of approaches and techniques. Can J Anaesth 2007; 54(8): 662-74.
[http://dx.doi.org/10.1007/BF03022962] [PMID: 17666721]

Neal JM, Gerancher JC, Hebl JR, *et al.* Upper extremity regional anesthesia: essentials of our current understanding, 2008. Reg Anesth Pain Med 2009; 34(2): 134-70.
[http://dx.doi.org/10.1097/AAP.0b013e31819624eb] [PMID: 19282714]

Annual Meeting of the American Society of Regional Anesthesia (ASRA): https://www.asra.com/meetings

CHAPTER 3

Paravertebral Block

Roy Greengrass*

Mayo Clinic, Jacksonville, Florida, USA

Abstract: The paravertebral nerve block (PVB) allows the blockade of mixed nerve roots after they leave the intervertebral foramina. This provides anesthesia and analgesia for a variety of procedures and conditions including: breast surgery, thoracic surgery (thoracotomies, thoracoscopies, VATS), multiple rib fractures, herniorrhaphies, abdominal wall procedures; and to provide analgesia and anesthesia in the presence of severe scoliosis, kyphosis or Harrington rods; and also to treat chronic pain syndromes. The principal contraindications remaon infection, major coagulopathy, neuropathy of unknown origin and patient refusal. The use of catheters permits a longer duration of therapy. Complications include possible pneumothorax, intraneural injection, epidural spread and local anesthetic toxicity. This is a very useful technique to master.

Keywords: Breast surgery, Herniorrhaphies, Paravertebral catheter, Paravertebral nerve block (PVB), Rib fractures, Thoracoscopies, Thoracotomy, VATS.

INTRODUCTION

The paravertebral block (PVB) is a very useful block to master, because it allows one to provide regional anesthesia in situations where an epidural block may not be possible. The paravertebral block (PVB) blocks mixed nerve roots after they have exited the intervertebral foramina. Thus one can provide anesthesia and analgesia for a variety of procedures including: breast surgery (both cancer surgery – mastectomy and cosmetic – augmentation and mammoplasty), thoracic surgery (thoracotomies, thoracoscopies, and VATS), herniorrhaphies and abdominal wall surgeries. Post-surgical analgesia for thoracic procedures open cholecystectomy, open nephrectomy, appendectomies and rib fractures can be provided by paravertebral block, as well as analgesia for chronic mastectomy pain, post thoracotomy pain, post herpetic neuralgia, chronic cancer pain and refractory angina pectoris.

* **Corresponding author Roy Greengrass:** Mayo Clinic, Jacksonville, Florida, USA; Tel: 904-953-2000; E-mail: Greengrass.Roy@mayo.edu

Amballur D. John (Ed.)

ANATOMY

The paravertebral space is a well-defined wedge shaped [1, 2] anatomical compartment which is bounded antero-laterally by the parietal pleura, posteriorly by the superior costo-transverse ligament, medially by the vertebral bodies, intervertebral discs and intervertebral foramina, superiorly and inferiorly by the ribs (Fig. **1**). Within the space are the spinal roots dividing into ventral and dorsal rami, white and grey rami of the sympathetic chain, areolar tissue, fat and blood vessels. A local anesthetic infiltration thus provides unilateral sensory, motor and sympathetic blockade.

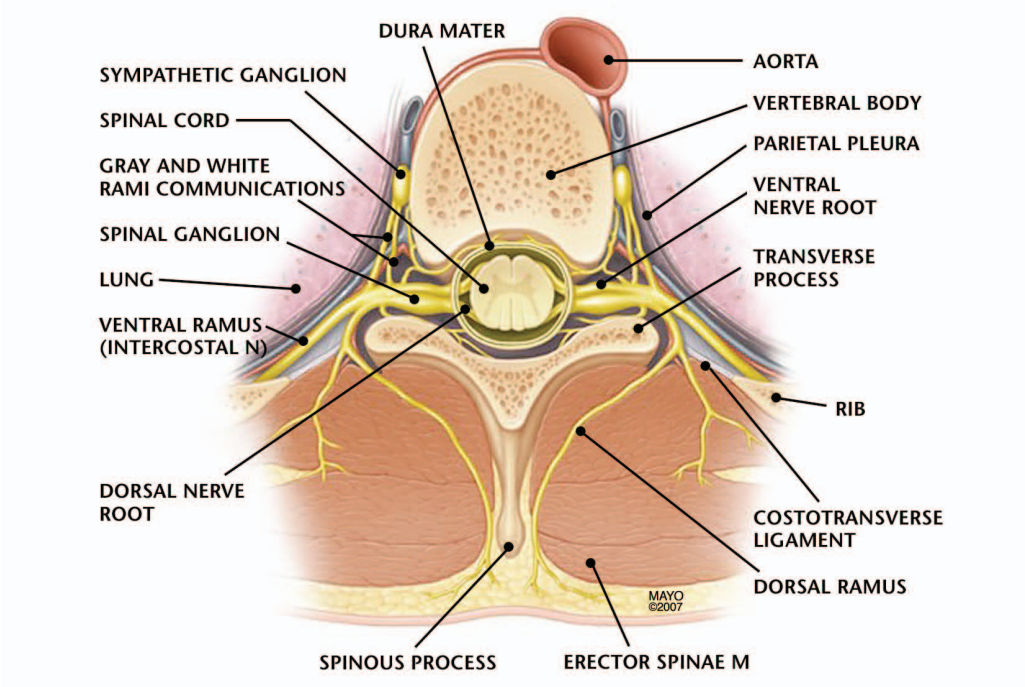


Fig. (1). Thoracic Paravertebral Space. Image provided by Roy Greengrass, M.D., Mayo Clinic.

INDICATIONS

PVB can be used both as the primary anesthetic and also to provide post-surgical analgesia.

PVB can be applied as primary anesthetic for most breast surgeries [3], rib resections, inguinal hernias [4], procedures in interventional radiology suites such as liver mass radiofrequency ablation [5], percutaneous transhepatic biliary drainage [6] and percutaneous nephrolithotomy [7] and gastrostomy tube placement.

Post-surgical analgesia can be effectively provided in patients having video assisted thoracoscopy [8], thoracotomy [9], minimally invasive mitral valve replacement [10], transapical transcatheter aortic valve replacement [11], open cholecystectomy [12], appendectomy [13], open nephrectomy [14], percutaneous nephrolithotomy [15] *etc*. and for providing analgesia in patients with rib fractures [16].

Chronic pain patients can benefit from PVB for chronic post mastectomy pain [17], post thoracotomy pain [17] and post herpetic neuralgia [18]. This can also be used in chronic regional pain syndrome, cancer pain [19] and refractory angina pectoris [20].

PVB catheters can be utilized to prolong the duration of analgesia [21].

TECHNIQUE

Equipment

22G Tuohy needle with graduated marking of 1cm (B. Braun Medical, Bethlehem, PA), clear extension tubing, skin marker, antiseptic solution, local anesthetic for skin wheal (2% lidocaine + 1:200,000 epinephrine), sterile gloves and gauze is used. For continuous catheters, an 18G or 17G Tuohy is used with an epidural catheter with a soft tip (Braun). Soft tip catheters stay in the paravertebral space more reliably.

Levels

Depending on the surgical procedure, the appropriate levels are chosen. For breast surgery involving the axilla, levels T1-T6 are blocked. For minimally invasive mitral valve repair, right T3-T7 are blocked. For inguinal herniorrhaphy levels T11-L1 are chosen.

Anatomical Landmarks (Fig. 2)

The landmarks are placed after positioning the patient in a sitting posture (preferred over lateral decubitus and prone position) with neck flexed, back arched out and shoulders relaxed.

The superior aspect of the spinous process is marked and from the middle of this mark the needle entry is marked 2.5cm lateral to each spinous process ipsilateral to the site of the surgery. These marks should overlie the transverse process (TP) of the vertebra immediately caudal to it.

A good guide for anatomical land marks are the C7 spinous process (most

prominent spinous process felt when the patient flexes the neck) which when marked, would correspond to the T1 spinal nerve root, the spine of the scapula corresponds to the T4 spinous process and the inferior tip of scapula corresponding to the T7 spinous process.

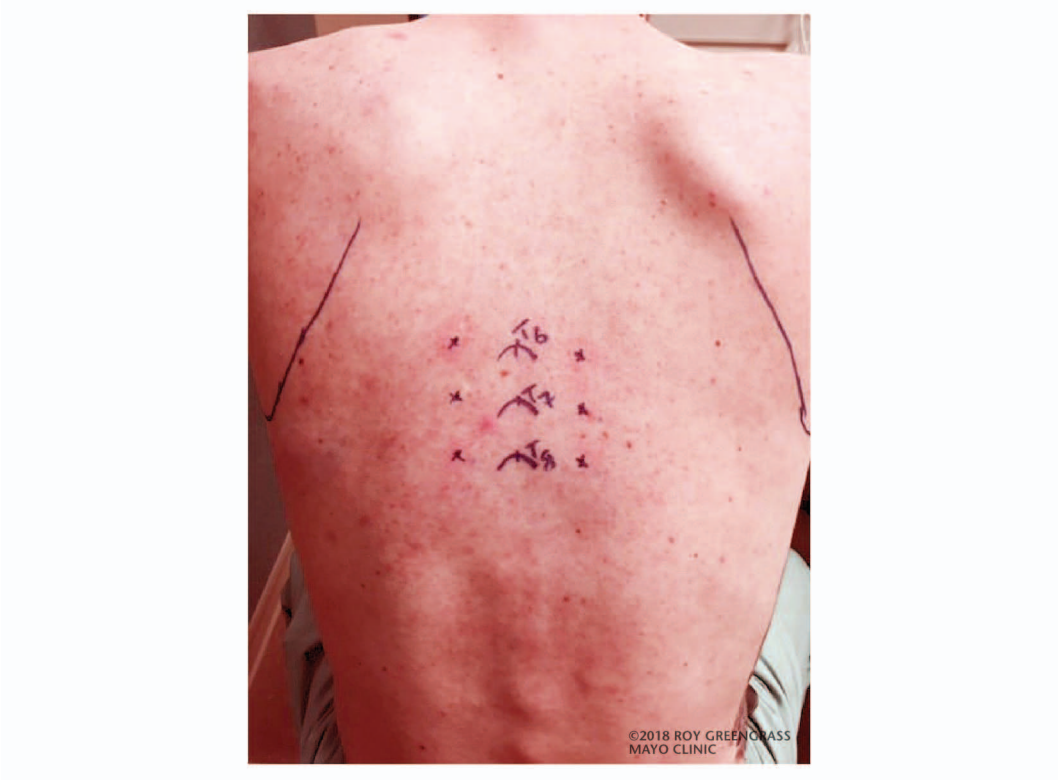


Fig. (2). Landmarks for Thoracic Paravertebral Block. Image provided by Roy Greengrass, M.D., Mayo Clinic.

Placement (Fig. 3)

Under aseptic precautions, a skin wheal is raised at the points of insertion that were marked. Using a graduated 22G, 3.5inch Tuohy needle (B. Braun) attached *via* clear extension tubing to a syringe, the shaft of the needle is grasped by the dominant hand of the operator. To estimate depth to the TP one can assume depth to the epidural space and subtract 1-2cm since the TP angles posteriorly (thus is more superficial). In an average adult the TP is usually contacted at a depth of 3-5cm. Alternatively the depth to the TP can be measured using ultrasound. (See US section) The needle is inserted through the skin wheal, perpendicular to the skin, until contact with the TP is made. If bone is not contacted with initial insertion, the needle is most likely between the transverse processes, and the needle is then

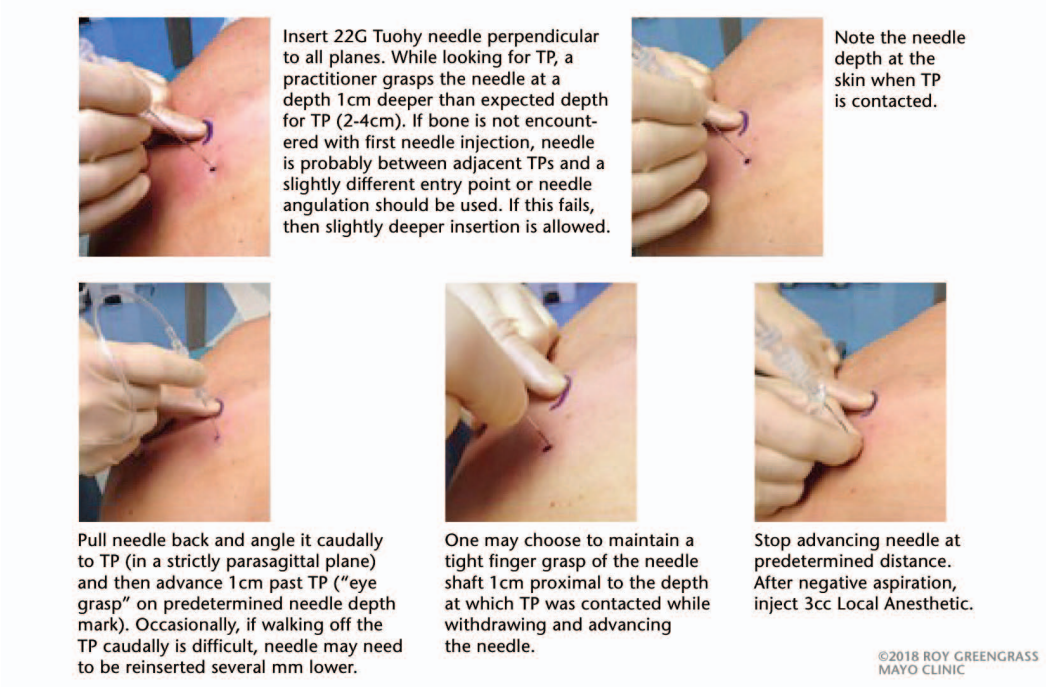


Fig. (3). Illustration of the classical landmark technique of performing a Thoracic Paravertebral Nerve Block. Images provided by Roy Greengrass, M.D., Mayo Clinic.

directed caudad then cephalad in an attempt to contact bone. If bone is still not contacted the needle is grasped 1cm deeper and the process repeated till the TP is successfully contacted. Once the TP is contacted, the depth is noted which will be a guide to the approximate depth to subsequent transverse processes. While on the TP the needle is grasped 1cm from the skin, then withdrawn and redirected caudally off the TP until the fingers contact skin (*i.e*. walking 1cm caudad off the TP). A loss of resistance ("pop") is appreciated as the needle passes through the superior costotransverse ligament. After aspiration, 1ml of local anesthetic is injected (to reduce the risk of intraneural injection of large volume of anesthetic) followed by another 2-4ml. It is recommended that while performing thoracic PVB, the provider should start at the lower most marked PVB first and proceed cephalad as the depth to the TP from the skin increases moving cephalad. It is important to experience a loss of resistance or subtle "pop" as the needle passes through the superior costotransverse process in the thoracic region. In the lumbar region, the transverse processes are very small compared to the ones in the thoracic area. area. The recommended depth of insertion off the TP in the lumbar area is 11/2-2cm as the lumber roots are deeper. There is no costotransverse ligament in this area. If a distinct "pop" is sensed here, then the needle has likely

punctured the psoas fascia and hence, should be withdrawn to a shallower depth. Injection for both thoracic and lumbar blocks should be easy and have little resistance.

Choice of Local Anesthetic

For surgical anesthesia, ropivacaine 0.5%-1% is used, which would also facilitate post procedural analgesia for 12-24hours. For continuous PVB, 0.2% or 0.3% ropivacaine at 6ml/hr with or without additional patient bolus of 6ml every hour is used.

Ultrasound (US) Technique

US can be utilized to complement an anatomic technique by determining the distance to the TP and directing the needle onto the TP prior to walking off the TP. US can also be utilized for the entire procedure [22, 23]. A linear or curvilinear probe may be used, curvilinear preferentially used in obese patients. The probe is placed transversely on the back and the spines identified and marked (if not visible). Skin marks are made 2.5cm lateral to the spines. The probe is then placed parasagitally 2.5cm from the midline to image the lateral aspect of the TP and the TP rib junction (Fig. **4**). The TP is imaged just above the midpoint of the probe. The block needle is then inserted at the midpoint of the probe paramedially and directed to contact the TP (Fig. **5**). After contacting the TP an anatomic technique can be used where the needle is walked caudally off the TP to traverse the SCTL. The needle can also be directed caudally off the TP under US guidance to traverse the SCTL after which injected local anesthetic may result in visible anterior displacement of the pleura. The needle may also be imaged and inserted to pierce the SCTL without contacting the TP. It is recommended the needle always be directed caudad with all approaches particularly an exclusive US guided approach, to avoid vessels and nerves which are located in the cephalad part of the PV space. As with other blocks, hydrodissection can greatly assist US needle guidance, particularly in patients with difficult anatomy

Nerve Stimulator Technique

A nerve stimulator can be used as an adjunct to the anatomical approach to locate the nerve root that one plans on blocking however, as mentioned, directing the needle cephalad to locate the nerve may result in injury to nerve or vessels.

Complications

Pleural puncture, pneumothorax, epidural/spinal spread, extrapleural hematoma, hypotension, local anesthetic toxicity are the potential complications of PVB.

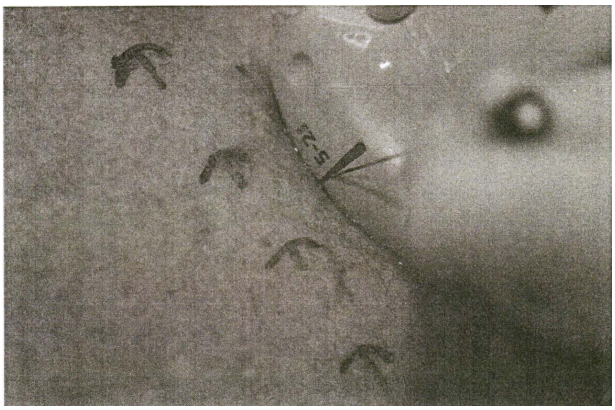


Fig. (4). US probe placed 2.5cm lateral to midline. Needle will be directed to contact caudal part of TP then redirected caudally off the TP.

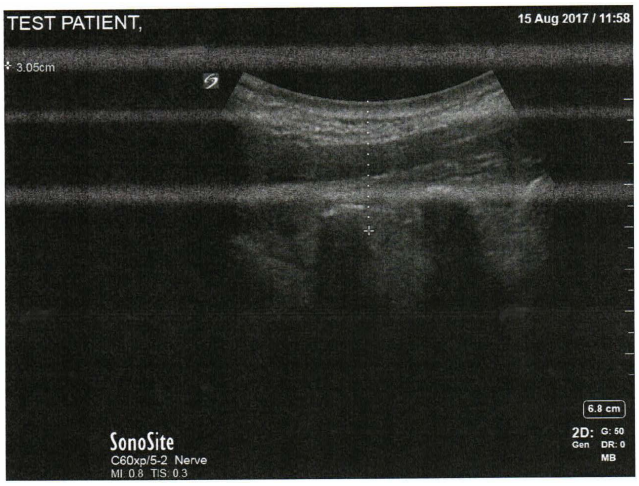


Fig. (5). Measured depth to caudal part of the TP simulating path of needle.

Contraindications to PVB

As with any regional anesthetic, PVBs are contraindicated in patients with local infection (infected skin, empyema *etc.*,) coagulopathy, indeterminate neuropathy and patient refusal.

CONCLUSION

Thus, the paravertebral block is a useful block to have in one's armamemtorium. It allows one to provide regional anesthesia in situations not amenable to an epidural because the paravertebral block (PVB) blocks mixed nerve roots after they have exited the intervertebral foramina. So, in the presence of severe scoliosis, hyphosis, or instrumentation such as Harrington rods it is possible to

provide regional anesthesia and analgesia. In addition, a variety of procedures including: breast surgery (both cancer surgery – mastectomy and cosmetic – augmentation and mammoplasty), thoracic surgery (thoracotomies, thoracoscopies, and VATS), herniorrhaphies, and abdominal wall surgeries can be covered by paravertebral blocks. PVB's can provide post-surgical analgesia for thoracic procedures, open cholecystectomy, open nephrectomy, appendectomies and rib fractures. The paravertebral block is a useful tool providing analgesia for chronic mastectomy pain, post thoracotomy pain, post herpetic neuralgia, chronic cancer pain, and refractory angina pectoris. The principle contraindications are infection, coagulotherapy, neuropathy of unknown origin and patient refusal. Although possible pneumothorax, intraneural injection, epidural spread, and local anesthetic toxicity, the paravertebral block is a very useful technique.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Greengrass RA, Duclas R Jr. Paravertebral blocks. Int Anesthesiol Clin 2012; 50(1): 56-73. [http://dx.doi.org/10.1097/AIA.0b013e318216c03e] [PMID: 22227423]

[2] Greengrass R, Buckenmaier CC III. Paravertebral anaesthesia/analgesia for ambulatory surgery. Best Pract Res Clin Anaesthesiol 2002; 16(2): 271-83. [http://dx.doi.org/10.1053/bean.2002.0238] [PMID: 12491557]

[3] Coveney E, Weltz CR, Greengrass R, *et al.* Use of paravertebral block anesthesia in the surgical management of breast cancer: experience in 156 cases. Ann Surg 1998; 227(4): 496-501. [http://dx.doi.org/10.1097/00000658-199804000-00008] [PMID: 9563536]

[4] Weltz CR, Klein SM, Arbo JE, Greengrass RA. Paravertebral block anesthesia for inguinal hernia repair. World J Surg 2003; 27(4): 425-9. [http://dx.doi.org/10.1007/s00268-002-6661-5] [PMID: 12658486]

[5] Piccioni F, Fumagalli L, Garbagnati F, Di Tolla G, Mazzaferro V, Langer M. Thoracic paravertebral anesthesia for percutaneous radiofrequency ablation of hepatic tumors. J Clin Anesth 2014; 26(4): 271-5. [http://dx.doi.org/10.1016/j.jclinane.2013.11.019] [PMID: 24856797]

[6] Culp WC Jr, Culp WC. Thoracic paravertebral block for percutaneous transhepatic biliary drainage. J Vasc Interv Radiol 2005; 16(10): 1397-400. [http://dx.doi.org/10.1097/01.RVI.0000174285.84995.7F] [PMID: 16221913]

[7] Borle AP, Chhabra A, Subramaniam R, *et al.* Analgesic efficacy of paravertebral bupivacaine during percutaneous nephrolithotomy: an observer blinded, randomized controlled trial. J Endourol 2014;

28(9): 1085-90.
[http://dx.doi.org/10.1089/end.2014.0179] [PMID: 24828850]

[8] Vogt A, Stieger DS, Theurillat C, Curatolo M. Single-injection thoracic paravertebral block for postoperative pain treatment after thoracoscopic surgery. Br J Anaesth 2005; 95(6): 816-21.
[http://dx.doi.org/10.1093/bja/aei250] [PMID: 16199417]

[9] Fibla JJ, Molins L, Mier JM, Hernandez J, Sierra A. A randomized prospective study of analgesic quality after thoracotomy: paravertebral block with bolus *versus* continuous infusion with an elastomeric pump. Eur J Cardiothorac Surg 2015; 47(4): 631-5.
[http://dx.doi.org/10.1093/ejcts/ezu246] [PMID: 24966147]

[10] Neuburger PJ, Ngai JY, Chacon MM, *et al.* A Prospective Randomized Study of Paravertebral Blockade in Patients Undergoing Robotic Mitral Valve Repair. J Cardiothorac Vasc Anesth 2015 Jan 22. pii: S1053-0770(14)00477-7.

[11] Poltak JM, Cobey FC, Augoustides JG, Connors CW. Paravertebral analgesia in transapical transcatheter aortic valve replacement. Heart Lung Vessel 2015; 7(1): 91.
[PMID: 25861599]

[12] Paleczny J, Zipser P, Pysz M. [Paravertebral block for open cholecystectomy]. Anestezjol Intens Ter 2009; 41(2): 89-93. [Paravertebral block for open cholecystectomy].
[PMID: 19697826]

[13] Splinter WM, Thomson ME. Somatic paravertebral block decreases opioid requirements in children undergoing appendectomy. Can J Anaesth 2010; 57(3): 206-10.
[http://dx.doi.org/10.1007/s12630-009-9239-y] [PMID: 20063137]

[14] Baik JS, Oh AY, Cho CW, Shin HJ, Han SH, Ryu JH. Thoracic paravertebral block for nephrectomy: a randomized, controlled, observer-blinded study. Pain Med 2014; 15(5): 850-6.
[http://dx.doi.org/10.1111/pme.12320] [PMID: 24341324]

[15] Ak K, Gursoy S, Duger C, *et al.* Thoracic paravertebral block for postoperative pain management in percutaneous nephrolithotomy patients: a randomized controlled clinical trial. Med Princ Pract 2013; 22(3): 229-33.
[http://dx.doi.org/10.1159/000345381] [PMID: 23257888]

[16] Karmakar MK, Critchley LA, Ho AM, Gin T, Lee TW, Yim AP. Continuous thoracic paravertebral infusion of bupivacaine for pain management in patients with multiple fractured ribs. Chest 2003; 123(2): 424-31.
[http://dx.doi.org/10.1378/chest.123.2.424] [PMID: 12576361]

[17] Kirvelä O, Antila H. Thoracic paravertebral block in chronic postoperative pain. Reg Anesth 1992; 17(6): 348-50.
[PMID: 1286056]

[18] Naja ZM, Maaliki H, Al-Tannir MA, El-Rajab M, Ziade F, Zeidan A. Repetitive paravertebral nerve block using a catheter technique for pain relief in post-herpetic neuralgia. Br J Anaesth 2006; 96(3): 381-3.
[http://dx.doi.org/10.1093/bja/ael007] [PMID: 16431881]

[19] Antila H, Kirvelä O. Neurolytic thoracic paravertebral block in cancer pain. A clinical report. Acta Anaesthesiol Scand 1998; 42(5): 581-5.
[http://dx.doi.org/10.1111/j.1399-6576.1998.tb05170.x] [PMID: 9605376]

[20] Moore R, Groves D, Hammond C, Leach A, Chester MR. Temporary sympathectomy in the treatment of chronic refractory angina. J Pain Symptom Manage 2005; 30(2): 183-91.
[http://dx.doi.org/10.1016/j.jpainsymman.2005.02.016] [PMID: 16125034]

[21] Luyet C, Siegenthaler A, Szucs-Farkas Z, Hummel G, Eichenberger U, Vogt A. The location of paravertebral catheters placed using the landmark technique. Anaesthesia 2012; 67(12): 1321-6.
[http://dx.doi.org/10.1111/j.1365-2044.2012.07234.x] [PMID: 23130724]

[22] Hara K, Sakura S, Nomura T, Saito Y. Ultrasound guided thoracic paravertebral block in breast surgery. Anaesthesia 2009; 64(2): 223-5.
[http://dx.doi.org/10.1111/j.1365-2044.2008.05843.x] [PMID: 19143711]

[23] O Riain SC, Donnell BO, Cuffe T, Harmon DC, Fraher JP, Shorten G. Thoracic paravertebral block using real-time ultrasound guidance. Anesth Analg 2010; 110(1): 248-51.
[http://dx.doi.org/10.1213/ANE.0b013e3181c35906] [PMID: 19933536]

CHAPTER 4

Lower Extremity Blocks

Roy Greengrass* and **Arun Kalava**

Mayo Clinic, Jacksonville, Florida, USA

Abstract: Lower extremity blocks provide anesthesia and analgesia for a variety of orthopedic, vascular and cosmetic procedures involving the hip, the thigh, the knee, the leg, the ankle and the foot. Lower extremity blocks include the femoral nerve block, (FNB), the sciatic nerve block, the popliteal sciatic nerve block, the saphenous nerve block, the posterior lumbar plexus block and the ankle block. A combination of lumbar plexus and sciatic block provides complete anesthesia of the lower extremity. The femoral nerve block is among the easiest, safest, and the most successful blocks to master. This block can provide analgesia for a fractured hip, a femoral fracture, knee arthroplasty and the harvesting of skin from the thigh. The popliteal block when combined with the saphenous block provides complete anesthesia below the knee. When the ankle block is performed above the malleoli, complete anesthesia of the foot can be achieved. The use of regional-lower extremity blocks helps to avoid the risks of general or neuroaxial anesthesia especially for those who are frail, debilitated, with multiple co-morbidities and cardiovascular risk factors. In addition, lower extremities blocks can provide significant post-operative analgesia. The blocks maybe performed with the use of the ultrasound or with peripheral nerve stimulation.

Keywords: Adductor canal block, Ankle block, Femoral nerve blocks, Lower extremity blocks, Lumbar plexus block, Popliteal block, Saphenous nerve block, Sciatic nerve block.

INTRODUCTION

Lower extremity blocks provide anesthesia and analgesia for a variety of orthopedic, vascular and cosmetic procedures involving the hip, the thigh, the knee, the leg, the ankle and the foot. Lower extremity blocks include the femoral nerve block (FNB), the sciatic nerve block, the popliteal sciatic nerve block, the saphenous nerve block, the posterior lumbar plexus block and the ankle block. A combination of the lumbar plexus and the sciatic nerve the sciatic block provides far complete anesthesia of the lower extremity. The femoral nerve block is among the easiest, safest and the most successful blocks to master.

* **Corresponding author Roy Greengrass:** Mayo Clinic, Jacksonville, Florida, USA; Tel: 904-953-2000; E-mail: Greengrass.Roy@mayo.edu

Amballur D. John (Ed.)

This block can provide analgesia for a fractured hip, a femoral shaft fracture, knee arthroplasty, and the harvesting of skin from the thigh. The popliteal block when combined with the saphenous block provides far complete anesthesia below the knee. When the ankle block is performed above the malleoli, the complete anesthesia of the foot can be achieved. The use of regional- lower extremity blocks helps avoid the risks of general or neuroaxial anesthesia especially for those who are frail, debilitated, with multiple co-morbidities and cardiovascular risk factors. In addition, lower extremity blocks can provide significant postoperative analgesia. These blocks may be performed with the aid of ultrasound or with peripheral nerve stimulation.

ANKLE BLOCK

Anatomy

The foot is innervated by the saphenous, posterior tibial, superficial peroneal, deep peroneal and the sural nerve. For a successful ankle block, all five nerves at the ankle have to be anesthetized. A simple and easy way of providing anesthesia and postoperative analgesia [1] to the foot is by performing an ankle block above the malleoli (supra-malleolar) [2].

Method

Ankle block is performed using an ultrasound [3, 4] **and/or infiltration technique**. The posterior tibial nerve can also be stimulated [5]. After appropriate sedation, the foot to be anesthetized is elevated using a stack of sheets, (Fig. **1**) the malleolar and supra-malleolar area is prepped with chlorhexidine and a high frequency linear probe is used to scan and identify individual nerves. Posterior tibial, deep peroneal and sural nerves are consistently visualized (Fig. **2**). The posterior tibial nerve is visualized in the vicinity of the posterior tibial artery, posterior to the medial malleolus (Fig. **3**). The deep peroneal nerve is visualized lateral to the anterior tibial artery between the malleoli (Fig. **4**). The sural nerve can be visualized in the vicinity of the small saphenous vein posterior to the lateral malleolus (Fig. **5**). The superficial peroneal and saphenous nerves are difficult to visualize using an ultrasound and hence, are blocked using the infiltration technique. The deep peroneal nerve can also be anesthetized anatomically at the superior malleolar level between the tendons of the extensor hallucis longus and tibialis anterior. The needle is inserted perpendicular to the skin to touch bone after which it is withdrawn a millimeter prior to injection. The needle is then fanned medially and laterally from the initial insertion site. A 25-gauge hypodermic needle attached *via* clear extension tubing to a syringe containing local anesthetic is used to perform the block. Care should be taken to minimize the number of needle punctures made during the block. The authors

suggest using the same puncture site and directing the needle medially and laterally to inject the local anesthetic. 20ml of local anesthetic (usually 0.5-1% ropivacaine) is usually sufficient to perform an ankle block.

Complications

As with any regional anesthetic technique, infection, bleeding, nerve injury, local anesthetic toxicity and compartment syndrome [6] are possible, but rare.

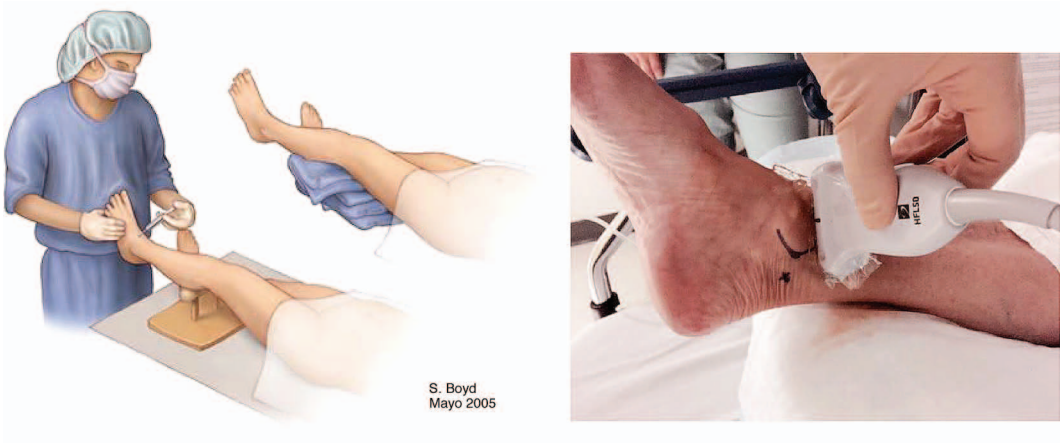


Fig. (1). Positioning for of the leg for an ankle block Supramalleolar placement of the ultrasound probe. Images provided by Mayo Clinic.

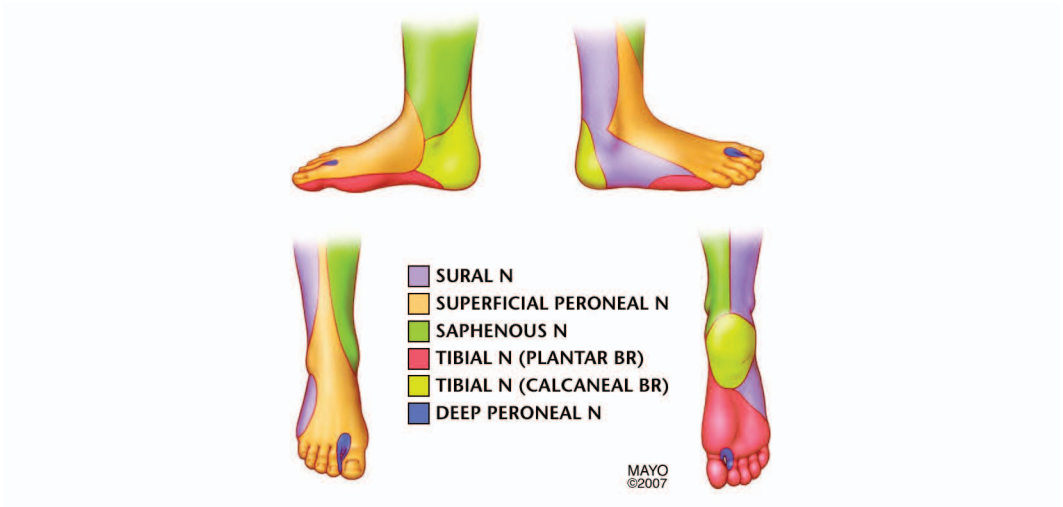


Fig. (2). Innervation of the Foot and Ankle. Images provided by Mayo Clinic.

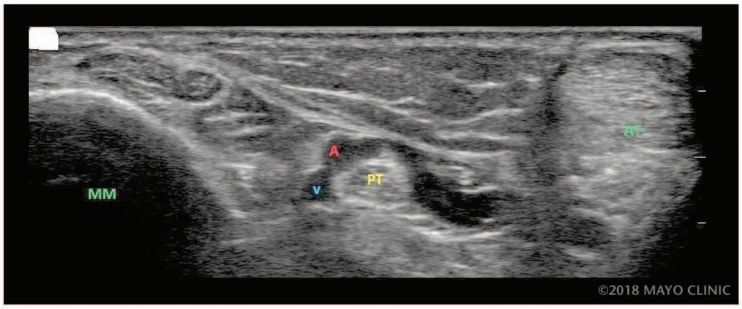


Fig. (3). Ultrasound image of the PT: Posterior Tibial Nerve, A: Posterior Tibial Artery, V: Posterior Tibial Vein, AT: Achille's Tendon and MM: Medial Malleolus. Images provided by Mayo Clinic.

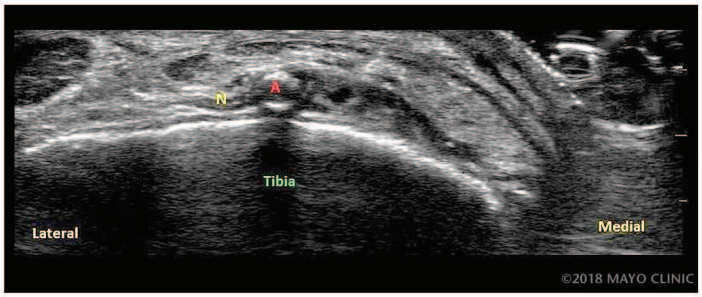


Fig. (4). Ultrasound image of the N: Deep Peroneal Nerve and A: Anterior Tibial Artery. Image provided by Mayo Clinic.

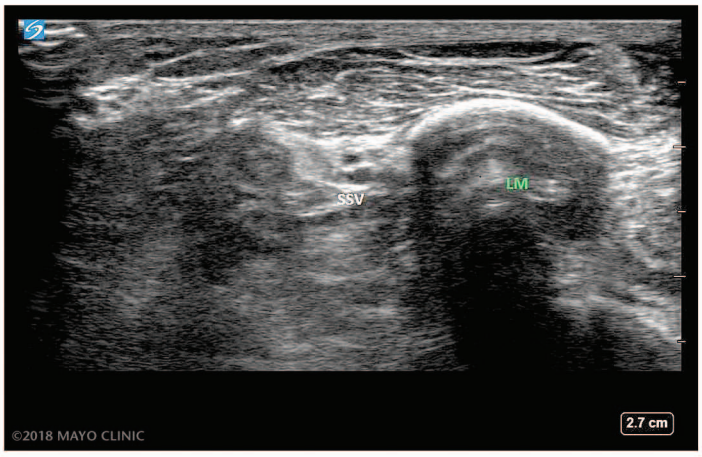


Fig. (5). Ultrasound image with LM: Lateral Malleolus and SSV: Short Saphenous Vein. Injection of LA should be done in the proximity of the SSV for a reliable sural nerve block. Image provided by Mayo Clinic.

SAPHENOUS NERVE (ADDUCTOR CANAL) BLOCK

The adductor canal block is becoming a more en vogue technique to provide analgesia of the lower extremity in the saphenous nerve distribution while theoretically sparing blockage of the motor branches of the femoral nerve; however, this is debatable [7]. The indications [8] for adductor canal block include TKA, and to complement sciatic block for procedures below the knee.

Anatomy

The adductor canal or Hunter's canal is a potential space in the middle compartment of the thigh that extends from the inguinal ligament to the adductor hiatus. The canal is bordered by the sartorius muscle anteromedially, the adductor longus and magnus muscles posteromedially and the vastus medialis muscle laterally. In addition to the saphenous nerve, the nerve to the vastus medialis and branches of the obturator nerve are also contained within the canal (Fig. **6**).

Ultrasound Technique

Without ultrasound guidance the canal can be reliably accessed with a blind anatomy technique by identifying the mid-point between the anterior superior iliac spine and the genu of the knee and the midpoint of the thigh from anterior to posterior. Where these lines intersect will be the insertion point of the needle. After aseptic preparation, a short bevel needle is then advanced perpendicular to all planes encountering two successive "pops" before entering the canal.

These changes in resistance are the facia of the Sartorious muscle. The capacitance of the canal is quite small, less than 15ml local anesthetic will be sufficient to fill the space [9].

An ultrasound guided block [10] is also very easily done. Most techniques to perform adductor canal block identify the sartorius muscle. A linear array probe is positioned in a transverse plane to the mid-thigh. The sartorius muscle appears as an oval shape beneath the subcutaneous layer of adipose tissue (Fig. **7**). The femoral artery beneath the muscle is identified. The saphenous nerve is infrequently seen on the ultrasound image; however, sometimes it is visualized as a small round hyperechoic structure medial to the artery. A femoral vein accompanies the artery and saphenous nerve, which are all usually seen at 2-3cm of depth. A short bevel needle can then be advanced in or out of the plane to below the sartorius muscle and medial or lateral to the artery before depositing 10-15ml of local anesthetic. A continuous catheter is usually placed to prolong analgesia.

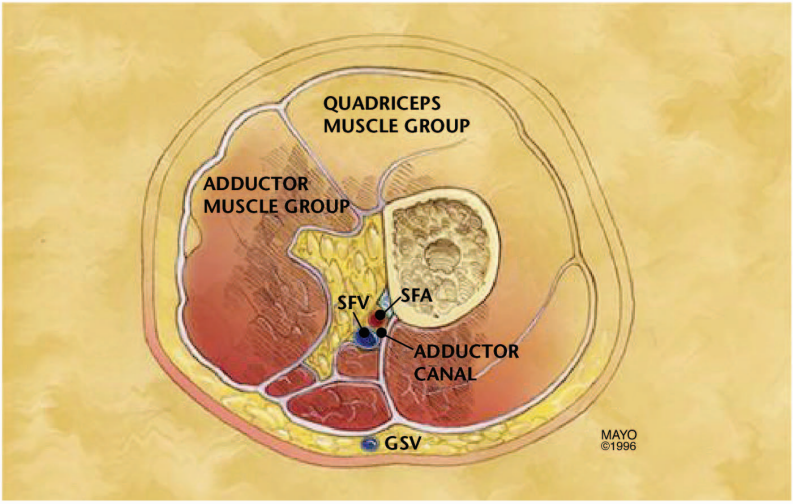


Fig. (6). Cross-sectional image of the adductor canal SFA = Superficial Femoral Artery, SFV=Superficial Femoral Vein, GSV = Great Saphenous Vein. Images provided by Mayo Clinic.

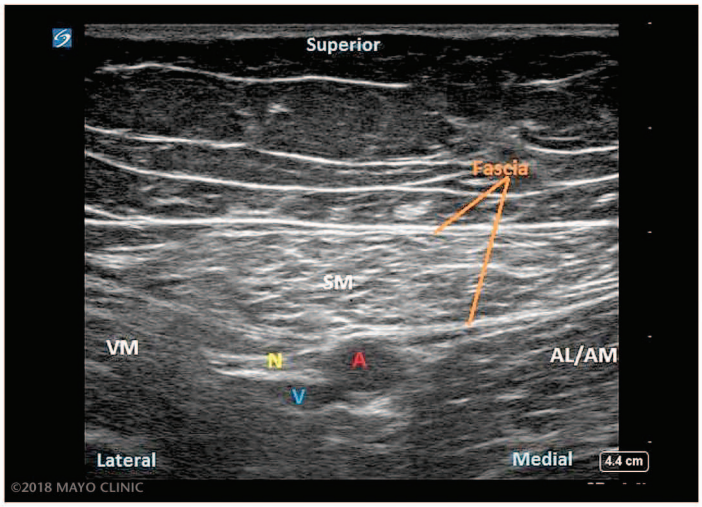


Fig. (7). Ultrasound image of the Adductor Canal with N=Saphenous Nerve, A = Superficial Femoral Artery, V = Superficial Femoral Vein, SM = Sartorius Muscle, VM = Vastus Medialis and AL/AM = Adductor Longus and Adductor Magnus. Image provided by Mayo Clinic.

POPLITEAL SCIATIC NERVE BLOCK

Blockade of the sciatic nerve in the popliteal fossa is utilized for surgery below the knee. When combined with a saphenous block complete anesthesia below the knee can be achieved.

Anatomy

The Sciatic nerve descends in the posterior thigh medial to the biceps femoris muscle and lateral to the semitendinosus before dividing into its separate components the common tibial (medial) and common peroneal (lateral) nerves, usually 5-7cm proximal to the popliteal crease [11]. It is here that the popliteal block is performed (Fig. **8**).

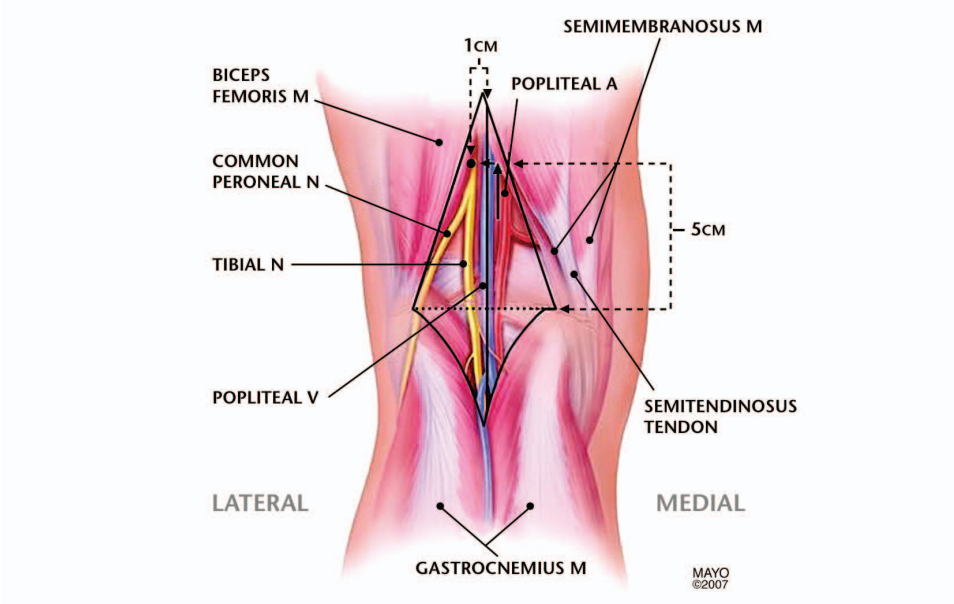


Fig. (8). Popliteal fossa and the approximate needle insertion point at the bifurcation of the sciatic nerve into Common peroneal and Tibial Components. Image provided by Mayo Clinic.

Technique

Although this block can be performed with NS guidance in a lateral or prone approach, **we usually utilize an ultrasound guided approach at our institution**. The technique described here will be that of Ultrasound guidance.

Positioning can be performed in several ways to optimize visualization of the tibial and peroneal nerves under Ultrasound. Because of patient body habitus and risk of possible airway issues, risk with sedation if the patient is positioned prone, we prefer the patient to be positioned semi lateral with the side to be blocked uppermost. The non-dependent leg is partially flexed to aid in patient comfort while the block is performed (Fig. **9**).

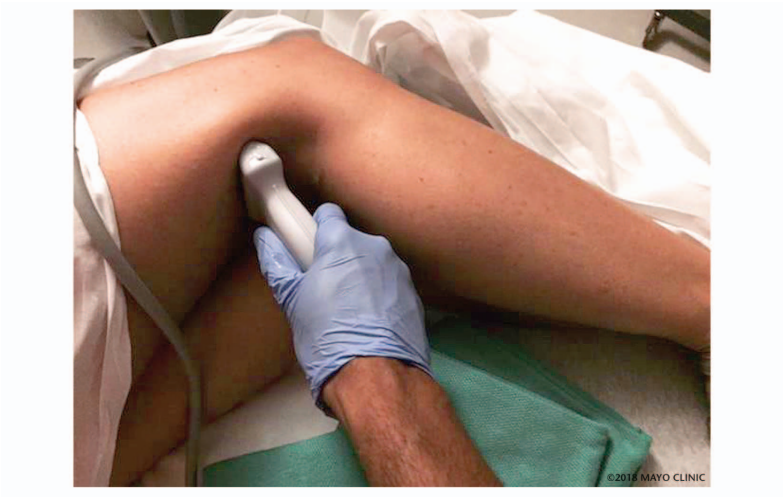


Fig. (9). Positioning of the leg and ultrasound probe to perform a popliteal sciatic nerve block in the lateral decubitus position. Image provided by Mayo Clinic.

A high frequency linear array probe is used for this block although occasionally, a low frequency probe may be needed because of patient habitus. The probe is positioned transversely to the path of the nerve about 5-7cm from the popliteal crease and scanned until the two components of the sciatic nerve at their division in short axis are seen laterally and more superficial to the popliteal artery (Fig. **3**). This is sometimes referred to as bow-tie sign. If difficulty in visualizing the structures is encountered, dorsiflexion and plantar flexion of the foot will cause the sciatic nerve to rock back and forth in a see-saw or teeter-totter pattern unlike any other structure in the field of view. Alternatively, the tibial nerve can easily be visualized above the popliteal artery at the popliteal crease and traced proximally to the point where it joins the peroneal nerve.

Once the ideal image is obtained, (Fig. **10**) a 9cm 22 gauge Tuohy needle is utilized for the block. Alternatively, a 9 cm insulated short bevel needle can be used particularly if nerve stimulation is necessary for nerve confirmation. The needle is advanced in plane from lateral to medial position until the nerve is encountered after which, 20-30ml of local anesthetic can be deposited in a slow controlled manner with frequent aspirations, inside the common sheath, rather than outside for quicker onset and better quality of block [12]. Perineural catheters can be placed easily and the correct positioning of the tip [13] of the catheter inside the common sheath should be confirmed.

As with all other nerve blocks there is risk of infection, hematoma and potential nerve injury and rarely pressure ulcers due to insensate extremity [14] or fracture

from stumbling [15] when performing this block and care must be taken to minimize these risks.

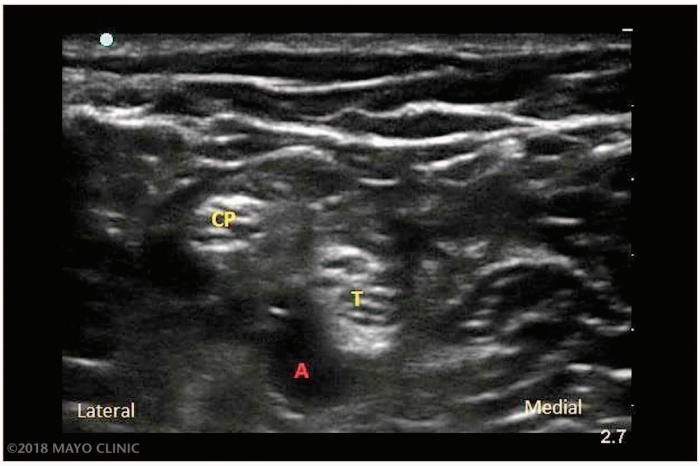


Fig. (10). Ultrasound image of the Sciatic Nerve in the popliteal fossa as it bifurcates into CP=Common Peroneal and T=Tibial components. Also seen is the A=Popliteal Artery. Image provided by Mayo Clinic.

FEMORAL NERVE BLOCK

The **femoral nerve block (FNB)** is one of the easiest blocks to master and has a wide range of clinical applications for lower extremity surgery [16]. Aside from being a relatively simple block it also carries a low risk of complication and very high success rate [17]. FNB can be utilized for a number of procedures including femoral shaft fractures, total knee arthroplasty, harvesting of skin grafts, analgesia for fractured hip [18] *etc*., For both peripheral nerve stimulator and ultrasound FNB, **identification of the inguinal crease is essential** as the femoral nerve arborizes just below the inguinal crease and a catheter placed below this may not be functional.

Anatomy

The femoral nerve is the largest branch of the lumbar plexus, arising from the dorsal divisions of the ventral rami (posterior rami) of nerve roots L2, L3 and L4. The nerve descends within the iliopsoas muscle before assuming a more superficial path below the inguinal ligament at which it is lateral to the femoral artery and beneath the facia iliaca but above the iliacus muscle (Fig. **11**). There is no vested fascial compartment to surround the femoral nerve at this level unlike that of the femoral artery and vein situated medially. This helps explain why placing the needle within the vascular fascia will result in a failed block because the fascia iliaca separates the femoral artery from the nerve (Fig. **12**).

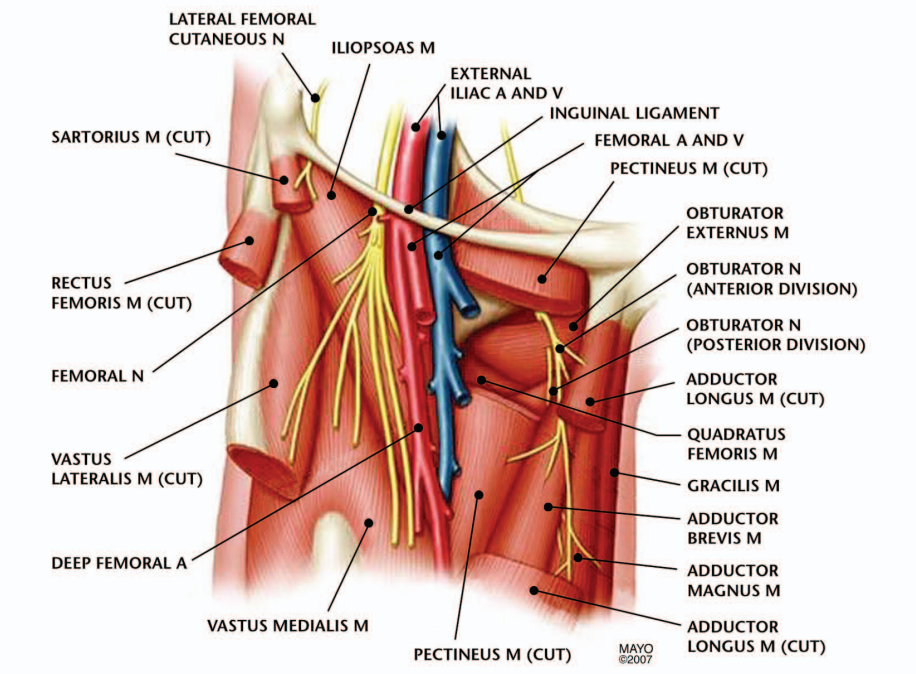


Fig. (11). Anatomical relationships of the femoral nerve at the groin. Image provided by Mayo Clinic.

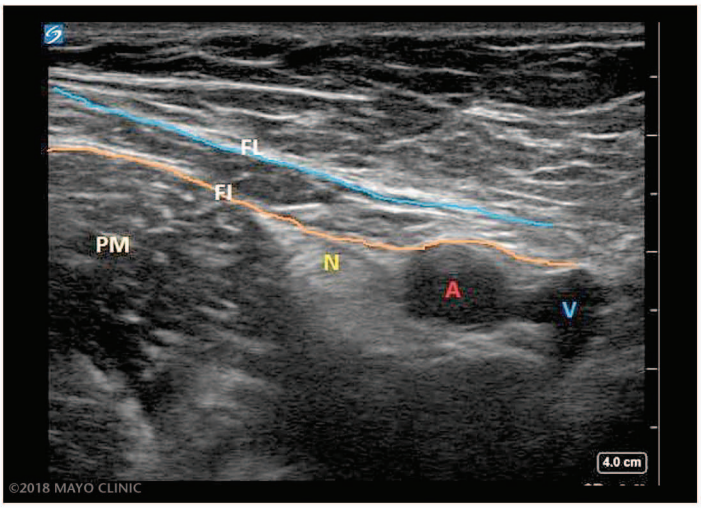


Fig. (12). Ultrasound image of the N=Femoral Nerve at the inguinal crease. FL = Facial Lata, FI = Fascia Iliaca, A = Femoral Artery, V = Femoral Vein and PM = Psoas Muscle. Images provided by Mayo Clinic.

The femoral nerve supplies muscular innervation for the anterior thigh including the iliacus and pectineus muscle except for the tensor facia lata which is innervated by the superior gluteal nerve. The femoral nerve also gives cutaneous innervation to the anterior and medial thigh and anterior knee.

After innervating the muscles and skin of the anterior thigh the anterior branch of the **femoral nerve continues as the saphenous nerve within the adductor canal (see adductor canal block)** and the medial cural cutaneous nerves that supply the patella and skin of the medial leg.

Peripheral Nerve Stimulator (PNS) Technique

Draw a line above the inguinal crease from the anterior superior iliac spine to the pubic ramus. At the midpoint of this line the femoral pulse is always palpable. With the finger of the non- dominant hand on the femoral pulse a needle is placed just lateral to the pulse directed slightly cranially. After traversing the fascia lata and iliaca, contraction of the quadriceps is elicited. If a twitch is not elicited the needle is inserted initially laterally then slightly medially until a twitch is observed after which incremental injection of up to 20ml of local anesthetic is injected. If a medial twitch (sartorius) is elicited the needle is moved deeper and more lateral to elicit a twitch of the quadriceps.

Ultrasound Guided FNB

The Ultrasound transducer is placed parallel to the inguinal crease and moved laterally and medially till the femoral vessels are appreciated. The nerve or branches of it may also be appreciated. The probe is positioned so that the artery is just medial to the midpoint of the probe. A needle is then inserted out of plane (or in-plane: Fig. **13**) lateral to the artery to pass through the facia lata and iliaca. 1ml of local anaesthetic is injected to assure the needle is through the facia iliaca but not directly into the psoas muscle. Injection 20ml of local anesthetic is then made incrementally. The nerve will often be more observable after injection of local as a hyperechoic flat structure. Continuous perineural catheters can be routinely placed to prolong analgesia.

SCIATIC NERVE BLOCK

The sciatic nerve is the largest nerve in the body and there have been several methods described on how to best anesthetize it, including Labat [19] in 1922, Pitkin [20] in 1953, Winnie [21] in 1974 and others. The sciatic nerve block when combined with a posterior lumbar plexus block can anesthetize the whole lower extremity.

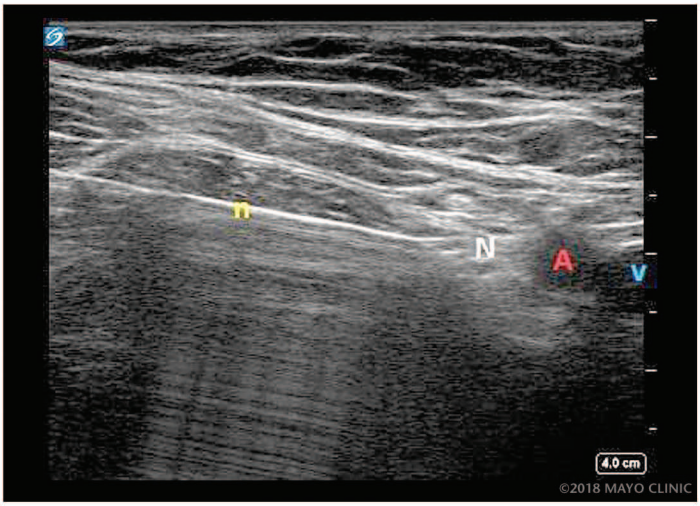


Fig. (13). Ultrasound guided in-plane approach to femoral nerve block, n = Needle, N = Femoral Nerve, A = Femoral Artery, V = Femoral Nerve. Image provided by Mayo Clinic.

Anatomy

The sciatic nerve originates from the ventral rami of L4, 5, S1, 2, 3-S3 and has two components, the tibial nerve medially and the common peroneal (fibular) nerve laterally. The nerve exits the pelvis *via* the greater sciatic foramen and passes deep to the piriformis muscle before assuming a more vertical and midline route between the greater trochanter and ischial tuberosity, deep to the gluteus maximus. Proximal to the popliteal fossa the tibial and peroneal components of the sciatic nerve separate to form two distinct nerves.

The sciatic nerve innervates all the muscles of the leg and the muscles of the posterior compartment of the thigh. Cutaneous coverage of the sciatic includes the posterior thigh and the entire leg except the medial aspect which is innervated by the saphenous nerve.

Technique

Nerve Stimulator Guidance

The most common method performed to block the sciatic nerve proximally is the trans-gluteal approach described by Labat and modified by Winnie (Fig. **14a**). Other approaches described are parasacral [22] (Fig. **15**), gluteal [23], sub-gluteal [24], Raj's approach where the sciatic nerve is blocked at the level of the ischial tuberosity with the patient in lithotomy [25] and the anterior approach described by Beck [26].

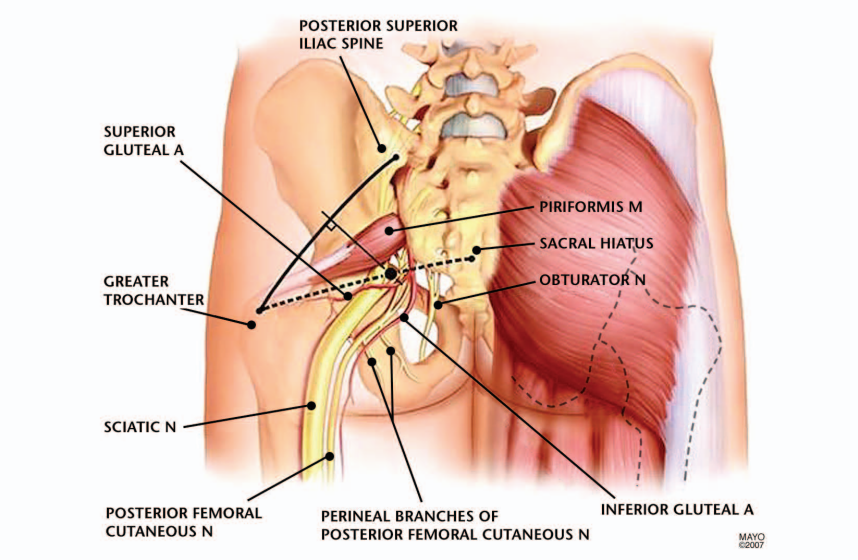


Fig. (14a). Posterior Classic Labat approach with corresponding landmarks-Greater Trochanter, Sacral Hiatus and Posterior Superior Iliac Spine. Image provided by Mayo Clinic.

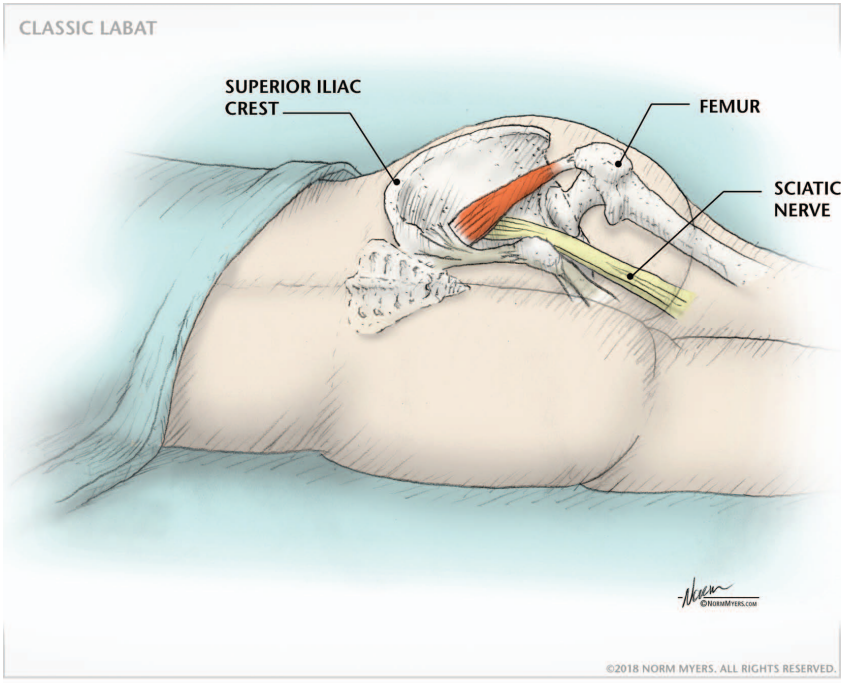


Fig. (14b). Sciatic – Classic Labat. Image provided by Norm Myers.

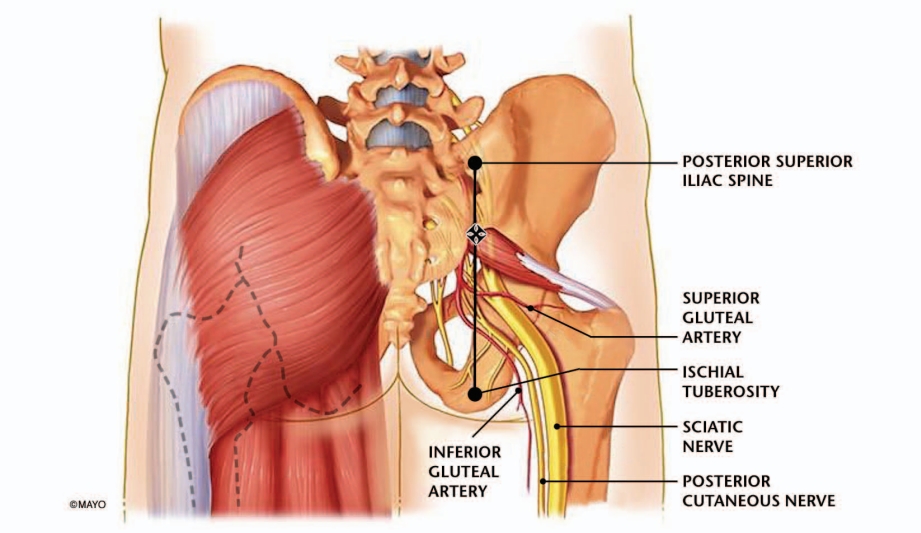


Fig. (15). Parasacral approach to sciatic nerve block (Mansour): Posterior Superior Iliac Spine and Ischial Tuberosity. Image provided by Mayo Clinic.

We describe the **transgluteal approach** described by Labat as is the most common approach we reliably use to block the sciatic nerve. To perform this block one must identify the surface anatomic landmarks of the greater trochanter of the femur and the posterior superior iliac spine (PSIS). The patient is positioned in the Sims position in lateral decubitus, with the side to block up.

The dependent leg is extended and the non-dependent leg is flexed at the hip and at the knee, while the buttock is rotated anteriorly. A line is drawn to connect the PSIS and greater trochanter. From the midpoint of this line a perpendicular line is drawn caudally. Another line is point of needle insertion. This point should correspond to an intersecting transverse line drawn from the sacral hiatus to the greater trochanter. Where the line drawn from the midpoint of the PSIS/trochanter line intersects the latter line is the point of insertion (Fig. **14a and 14b**).

Using a 9 cm short bevel insulated needle, the needle is advanced perpendicular to all planes until the sciatic nerve is stimulated. The needle is adjusted until a twitch at 0.5mA is elicited following which approximately 15-20ml of local anesthetic is deposited in small incremental doses.

Complications from this block are rare but can include infection, nerve injury, hematoma and accidental intravascular injection. It must be noted that the inferior gluteal vessels are large and multiple in this area and can increase the potential for complication.

Ultrasound Guidance

Transgluteal Approach [27]

Owing to the depth of the sciatic nerve a low frequency**curvilinear probe** is usually needed to visualize the nerve and at times is difficult to visualize and the authors suggest that one should combine use of nerve stimulation while using ultrasound guidance.

With the patient positioned in the same fashion as for a nerve stimulation guided sciatic block the Ultrasound probe is positioned mid gluteal. The sciatic nerve is seen as a flattened hyper echoic structure between the lesser trochanter and ischial tuberosity (Fig. **16**). A 9cm insulated needle can then be passed out of plane to contact the nerve (and verify *via* stimulation if desired) and after negative aspiration 15-20ml of local anesthetic is deposited incrementally with frequent aspiration.

Infra-Gluteal Approach

A high or low frequency probe is used depending on the body habitus to scan under the gluteal fold, where sciatic nerve can be seen as a hypo or hypoechoic structure under the hamstrings (Fig. **17**).

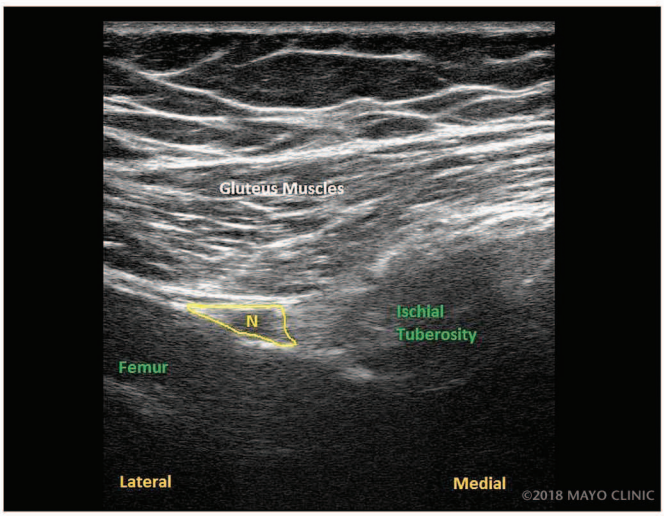


Fig. (16). Ultrasound image of transgluteal approach to N=sciatic nerve blockade. Image provided by Mayo Clinic.

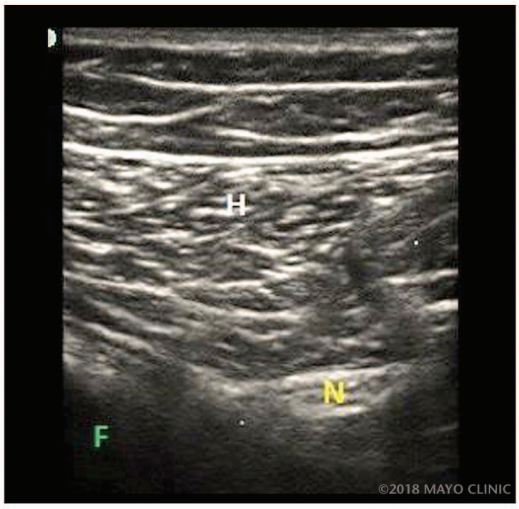


Fig. (17). Ultrasound image of Infragluteal approach to blockade of N=Sciatic nerve; H=Hamstrings and F=Femur. Image provided by Mayo Clinic.

Anterior Approach [28]

With patient supine, a curvilinear probe is placed about 8cm below the mid inguinal point [29] and the nerve is identified medially and posterior to the lesser trochanter of the femur (Fig. **18**). Nerve stimulator guidance usually increases efficacy. Readers should be aware that the anterior approach (both anatomical or ultrasound) does not anesthetize the posterior cutaneous nerve of the thigh.

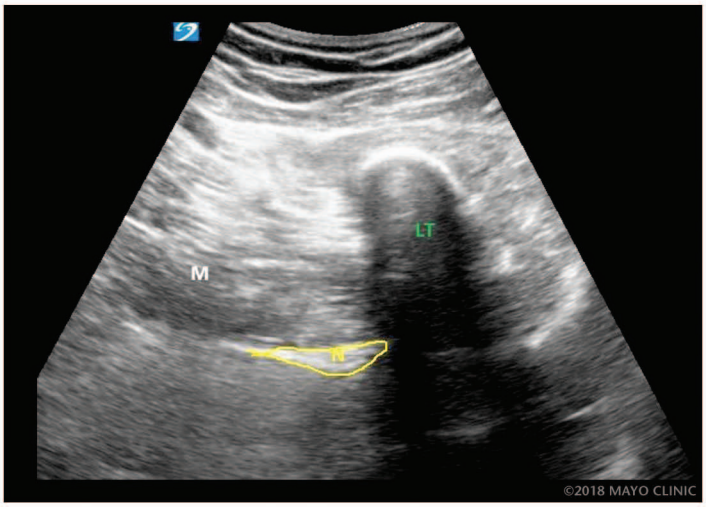


Fig. (18). Ultrasound image of the N=Sciatic nerve, lying below the M=Muscles of the anterior thigh, postero-medial to the LT=Lesser trochanter of the femur. Image provided by Mayo Clinic.

Our preferred method of needle insertion for ultrasound guided sciatic nerve blocks has been an out of plane approach as the needle localization is relatively difficult when using the in-plane approach.

POSTERIOR LUMBAR PLEXUS BLOCK

Anatomy

The lumbar plexus emanates from the first to the fifth lumbar roots (Fig. **19**). The sacral plexus emanates from the first to the fifth sacral roots. Unlike upper extremity blocks where a single injection can provide anesthesia and analgesia for surgery, lower extremity blocks often require a block of both the lumbar and sacral plexus. Lower extremity blocks can be performed using nerve stimulation, ultrasound, or a combination of both.

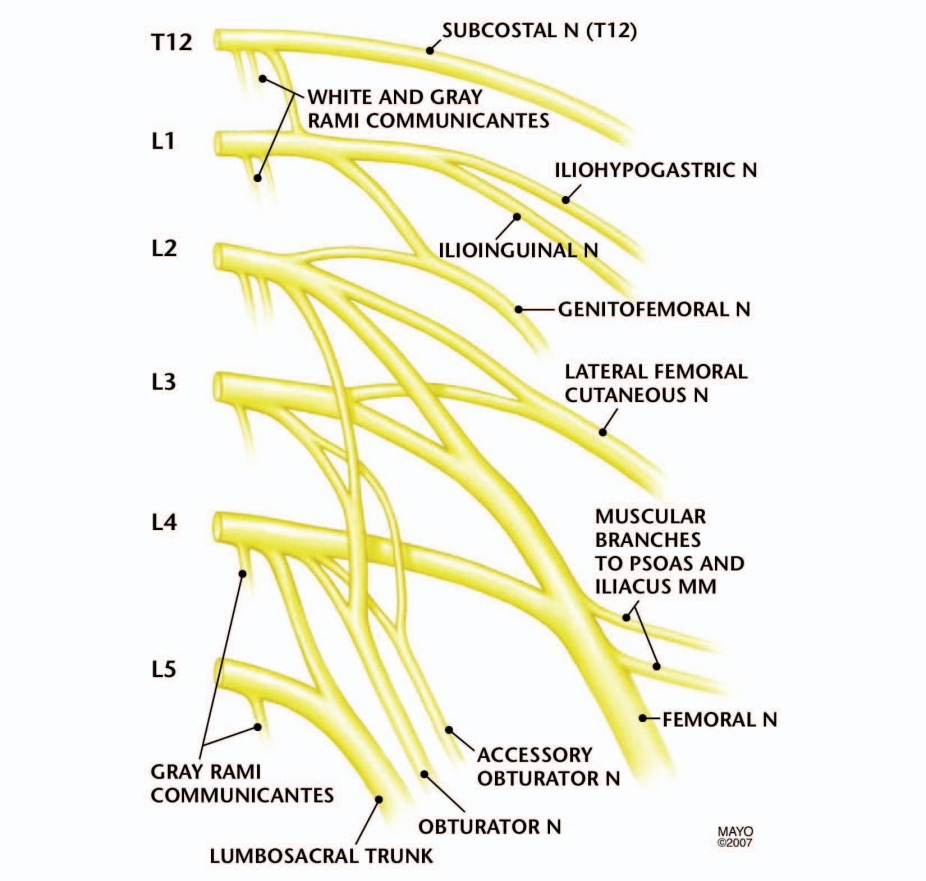


Fig. (19). Lumbar Plexus. Image provided by Mayo Clinic.

Posterior Lumbar Plexus Block (PLPB)

PLPB are performed at the level of the roots of the lumbar plexus. Thus single injection PLPB will successfully anesthetize all nerves of the lumbar plexus relevant to a lower extremity block. *e.g*. Musculocutaneus (L2-3), femoral (L2-4 posterior rami) and obturator (L2-4 anterior rami).

PLPB Nerve Stimulation Technique

The PLPB method described by Winnie [30, 31] **is the safest and most logical method to block the lumbar plexus** as it provides an anatomical landmark, the posterior superior iliac spine (PSIS) which compensates for the patients age, size and gender.

A line is drawn through the most cephalad part of the iliac crests (the intercristal line) (Fig. **20**). This line generally runs through the L3-L4 interspace or the L4 spinous process. A line connecting the lumbar spines is then made. The PSIS is palpated and a line from the PSIS parallel to the spines is made. Where this line intersects the intercristal line is the point of needle insertion.

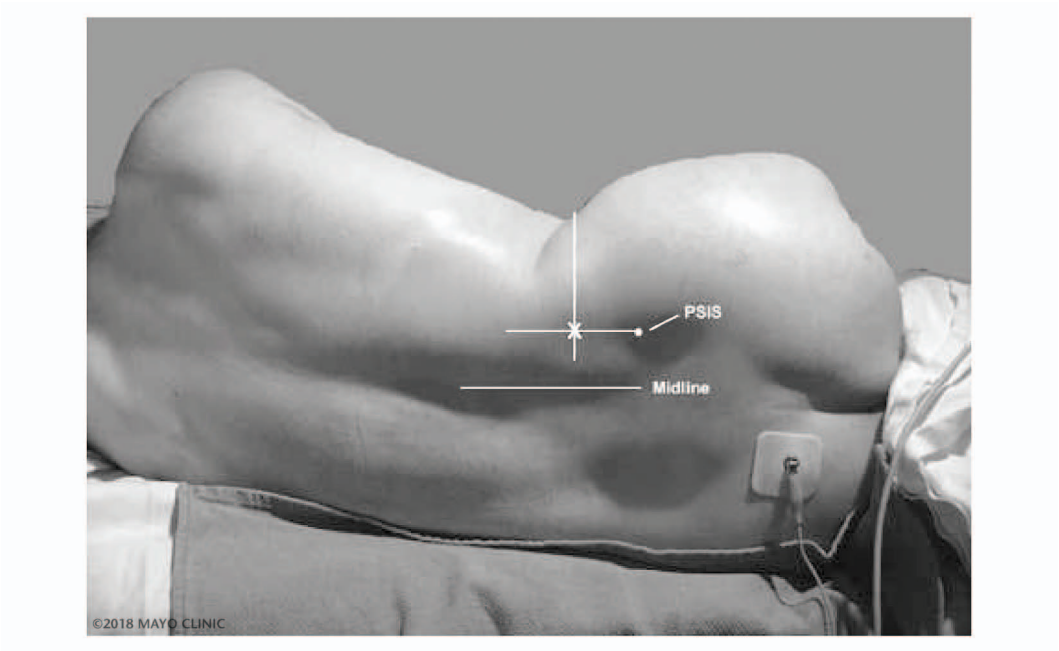


Fig. (20). Positioning for a Posterior Lumbar Plexus Block. Image provided by Mayo Clinic.

The needle is inserted perpendicularly through the skin point and inserted 5-9cm in adults (depending on the body habitus of the patient) until a contraction of the

quadriceps is elicited (nerve stimulator set at 1.5mA and turned down to 0.5-.07mA with an appreciable twitch). The needle is then fixed and 20-30ml of local anesthetic is incrementally injected. If the lumbar plexus is not stimulated on initial insertion of the needle the needle is withdrawn to skin and redirected slightly medial to be at depth approximately 1cm closer to midline. This is repeated if necessary. If the lateral aspect of the transvers process is contacted the needle is stabilized grasped 2cm from the skin and walked caudally off the transvers process up to 2cm till a twitch is appreciated.

Note: If a sacral stimulation (*e.g.* Hamstrings) is elicited the needle has been inserted too far medially and the chance of significant epidural spread is 30%.

Ultrasound Guided Block

Using a curvilinear probe, a parasacral scan [32 - 34] is performed to define the sacrum and move cranially to define the forth transverse process which is marked at the middle of the probe (Fig. **21**). The depth to the transvers process can be measured and the needle can then be inserted out of plane to contact the transverse process. The needle is then walked caudally off the transverse process a further 2cm (as with nerve stimulation technique) after which local anesthetic is incrementally injected. Alternatively, the needle can be directed in plane from cephalad to caudad to contact the transverse process then walked off as before.

Another technique [35] would be by locating the lumbosacral junction (L5-S1 gap) on a paramedian sagittal scan and then counting cranially to locate the lamina and transverse processes of the L3, L4, and L5 vertebrae. The modified paramedian transverse scan through the lumbar intertransverse space is then performed with the transducer positioned 4cm lateral to the midline in the transverse orientation at the L3-L4 intervertebral level. The needle is then advanced into the posterior aspect of the psoas muscle until either needle-lumbar plexus contact is visualized or there is a quadriceps twitch elicited.

It is important to realize that ultrasound techniques which guide the needle onto the transverse process may direct the needle too medially along the process then (as with sacral stimulation techniques) the chance of a significant epidural or intrathecal injection is possible.

Complications

In addition to infection, local anesthetic toxicity and nerve injury [36], PLPB can result in spinal [37] and or epidural spread [38], transient lumbar plexopathy secondary to psoas hematoma [39] and renal hematoma [40].

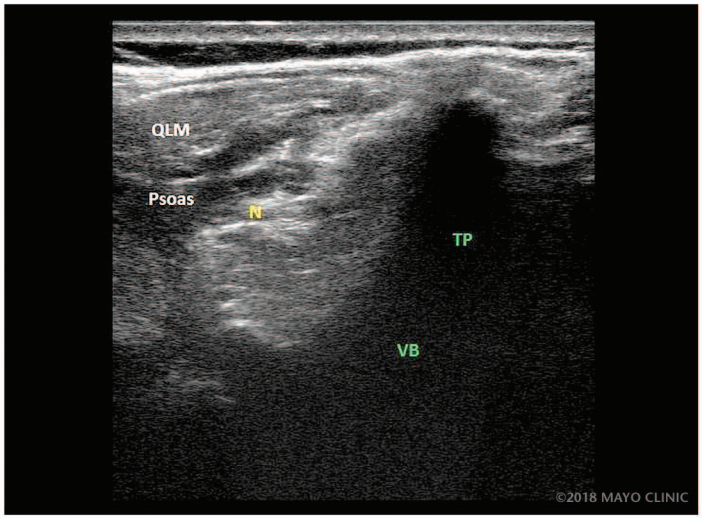


Fig. (21). Ultrasound image of the lumbar plexus with the probe lateral to the midline, in a transverse position at the level of lumbar vertebra 4. N = lumbar plexus, QLM = Quadratus lumborum muscle, TP = Transverse process of L4 and VB = Vertebral body of L4. Image provided by Mayo Clinic.

CONCLUSION

Thus, lower extremity blocks-femoral nerve block, sciatic nerve block, popliteal block, lumbar plexus block and ankle block, maybe done with the aid of the ultrasound or peripheral nerve stimulator. The combination of lumbar plexus and sciatic nerve block provides for complete anesthesia of the lower extremity. The femoral nerve block which is among the easiest, safest, and successful blocks provides for analgesia for a hip fracture, a femoral shaft fracture, knee arthroplasty, and skin harvesting from the thigh. The popliteal block when combined with saphenous nerve blocks provide for complete anesthesia below the knee. When the ankle block is performed above the malleoli complete anesthesia of the foot can be achieved; but, bear in mind tourniquet pain is not covered. In patients who are frail, debilitated who have multiple comorbidities and cardiovascular risk factors, regional anesthesia with lower extremity blocks may help to avoid the risk of subjecting the patient to a general or neuraxial anesthetic.

Contraindications to lower extremity blocks include infection, major coagulopathy, unknown neuropathy, and patient refusal. Complications include hematoma formation, introneural injection, intravascular absorption, and local anesthetic absorption. When performing regional anesthesia one should be familiar with the anatomy, equipment, anesthetic toxicity, and always use standard ASA/monitors and have all resuscitative equipment immediately available, along with enough adequately trained personal.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Needoff M, Radford P, Costigan P. Local anesthesia for postoperative pain relief after foot surgery: a prospective clinical trial. Foot Ankle Int 1995; 16(1): 11-3.
[http://dx.doi.org/10.1177/107110079501600103] [PMID: 7697147]

[2] Delgado-Martinez AD, Marchal-Escalona JM. Supramalleolar ankle block anesthesia and ankle tourniquet for foot surgery. Foot Ankle Int 2001; 22(10): 836-8.
[http://dx.doi.org/10.1177/107110070102201011] [PMID: 11642537]

[3] Doty R Jr, Sukhani R, Kendall MC, *et al.* Evaluation of a proximal block site and the use of nerve-stimulator-guided needle placement for posterior tibial nerve block. Anesth Analg 2006; 103(5): 1300-5.
[http://dx.doi.org/10.1213/01.ane.0000244323.30306.59] [PMID: 17056973]

[4] Redborg KE, Sites BD, Chinn CD, *et al.* Ultrasound improves the success rate of a sural nerve block at the ankle. Reg Anesth Pain Med 2009; 34(1): 24-8.
[http://dx.doi.org/10.1097/AAP.0b013e3181933f09] [PMID: 19258984]

[5] Redborg KE, Antonakakis JG, Beach ML, Chinn CD, Sites BD. Ultrasound improves the success rate of a tibial nerve block at the ankle. Reg Anesth Pain Med 2009; 34(3): 256-60.
[http://dx.doi.org/10.1097/AAP.0b013e3181a343a2] [PMID: 19587626]

[6] Noorpuri BS, Shahane SA, Getty CJ. Acute compartment syndrome following revisional arthroplasty of the forefoot: the dangers of ankle-block. Foot Ankle Int 2000; 21(8): 680-2. [SAPHENOUS NERVE]. [ADDUCTOR CANAL]. [BLOCK].
[http://dx.doi.org/10.1177/107110070002100809] [PMID: 10966367]

[7] Barton J, Wilson SH. Adductor canal block: a great block, but not a panacea. Reg Anesth Pain Med 2015; 40(3): 292-3.
[http://dx.doi.org/10.1097/AAP.0000000000000230] [PMID: 25899964]

[8] Jaeger P, Grevstad U, Henningsen MH, Gottschau B, Mathiesen O, Dahl JB. Effect of adductor-cana--blockade on established, severe post-operative pain after total knee arthroplasty: a randomised study. Acta Anaesthesiol Scand 2012; 56(8): 1013-9.
[http://dx.doi.org/10.1111/j.1399-6576.2012.02737.x] [PMID: 22834681]

[9] Andersen HL, Andersen SL, Tranum-Jensen J. The spread of injectate during saphenous nerve block at the adductor canal: a cadaver study. Acta Anaesthesiol Scand 2015; 59(2): 238-45.
[http://dx.doi.org/10.1111/aas.12451] [PMID: 25496028]

[10] Mariano ER, Kim TE, Wagner MJ, *et al.* A randomized comparison of proximal and distal ultrasound-guided adductor canal catheter insertion sites for knee arthroplasty. J Ultrasound Med 2014; 33(9): 1653-62. [POPLITEAL SCIATIC NERVE BLOCK].
[http://dx.doi.org/10.7863/ultra.33.9.1653] [PMID: 25154949]

[11] Barbosa FT, Barbosa TR, da Cunha RM, Rodrigues AK, Ramos FW, de Sousa-Rodrigues CF. Anatomical basis for sciatic nerve block at the knee level. Braz J Anesthesiol 2015; 65(3): 177-9. [http://dx.doi.org/10.1016/j.bjane.2014.03.010] [PMID: 25925028]

[12] Lopez AM, Sala-Blanch X, Castillo R, Hadzic A. Ultrasound guided injection inside the common sheath of the sciatic nerve at division level has a higher success rate than an injection outside the sheath. Rev Esp Anestesiol Reanim 2014; 61(6): 304-10. [http://dx.doi.org/10.1016/j.redar.2013.11.018] [PMID: 24556512]

[13] Elsharkawy H, Salmasi V, Abd-Elsayed A, Turan A. Identification of location of nerve catheters using pumping maneuver and M-Mode-a novel technique. J Clin Anesth 2015; 27(4): 325-30. [http://dx.doi.org/10.1016/j.jclinane.2015.03.003] [PMID: 25837495]

[14] Ilfeld BM. Continuous peripheral nerve blocks: a review of the published evidence. Anesth Analg 2011; 113(4): 904-25. [http://dx.doi.org/10.1213/ANE.0b013e3182285e01] [PMID: 21821511]

[15] Saporito A, Sturini E, Petri J, Borgeat A, Aguirre JA. Case report: unusual complication during outpatient continuous regional popliteal analgesia. Can J Anaesth 2012; 59(10): 958-62. [FEMORAL NERVE BLOCK]. [http://dx.doi.org/10.1007/s12630-012-9758-9] [PMID: 22829027]

[16] Vloka JD, Hadzić A, Drobnik L, Ernest A, Reiss W, Thys DM. Anatomical landmarks for femoral nerve block: a comparison of four needle insertion sites. Anesth Analg 1999; 89(6): 1467-70. [http://dx.doi.org/10.1213/00000539-199912000-00028] [PMID: 10589630]

[17] Szucs S, Morau D, Iohom G. Femoral nerve blockade. Med Ultrason 2010; 12(2): 139-44. [PMID: 21173942]

[18] Watson MJ, Walker E, Rowell S, *et al.* Femoral nerve block for pain relief in hip fracture: a dose finding study. Anaesthesia 2014; 69(7): 683-6. [SCIATIC NERVE BLOCK]. [http://dx.doi.org/10.1111/anae.12683] [PMID: 24862655]

[19] Labat G, Mayo WJ. Regional anesthesia: its technique and clinical application. Philadelphia, London: W. B. Saunders company 1922; pp. 289-91.

[20] Pitkin GP, Southworth JL, Hingson RA. Conduction Anesthesia: Clinical Studies of George P Pitkin. Philadelphia: Lippincott 1953.

[21] Winnie AP, Ramamurthy S, Durrani Z, Radonjic R. Plexus blocks for lower extremity surgery. Anesthesiol Rev 1974; 1: 11-6.

[22] Souron V, Eyrolle L, Rosencher N. The Mansour's sacral plexus block: an effective technique for continuous block. Reg Anesth Pain Med 2000; 25(2): 208-9. [PMID: 10746538]

[23] Sutherland ID. Continuous sciatic nerve infusion: expanded case report describing a new approach. Reg Anesth Pain Med 1998; 23(5): 496-501. [PMID: 9773704]

[24] Di Benedetto P, Casati A, Bertini L, Fanelli G. Posterior subgluteal approach to block the sciatic nerve: description of the technique and initial clinical experiences. Eur J Anaesthesiol 2002; 19(9): 682-6. [http://dx.doi.org/10.1097/00003643-200209000-00011] [PMID: 12243293]

[25] Raj PP, Parks RI, Watson TD, Jenkins MT. A new single-position supine approach to sciatic-femoral nerve block. Anesth Analg 1975; 54(4): 489-93. [http://dx.doi.org/10.1213/00000539-197507000-00020] [PMID: 1170786]

[26] Beck GP. Anterior approach to sciatic nerve block. Anesthesiology 1963; 24: 222-4. [http://dx.doi.org/10.1097/00000542-196303000-00011] [PMID: 13970060]

[27] Alsatli RA. Comparison of ultrasound-guided anterior *versus* transgluteal sciatic nerve blockade for

knee surgery. Anesth Essays Res 2012; 6(1): 29-33.
[http://dx.doi.org/10.4103/0259-1162.103368] [PMID: 25885498]

[28] Tsui BC, Ozelsel TJ. Ultrasound-guided anterior sciatic nerve block using a longitudinal approach: "expanding the view". Reg Anesth Pain Med 2008; 33(3): 275-6.
[PMID: 18433684]

[29] Chelly JE. Sciatic nerve block. Tech Reg Anesth Pain Manage 7(1): 18-25. [POSTERIOR LUMBAR PLEXUS BLOCK].
[http://dx.doi.org/10.1053/trap.2003.123521]

[30] Awad IT, Duggan EM. Posterior lumbar plexus block: anatomy, approaches, and techniques. Reg Anesth Pain Med 2005; 30(2): 143-9.
[PMID: 15765457]

[31] Greengrass RA. Posterior lumbar plexus block. Tech Reg Anesth Pain Manage 2003; 7: 3-7.
[http://dx.doi.org/10.1053/trap.2003.123517]

[32] Karmakar MK, Ho AM, Li X, Kwok WH, Tsang K, Ngan Kee WD. Ultrasound-guided lumbar plexus block through the acoustic window of the lumbar ultrasound trident. Br J Anaesth 2008; 100(4): 533-7.
[http://dx.doi.org/10.1093/bja/aen026] [PMID: 18344573]

[33] Kirchmair L, Entner T, Kapral S, Mitterschiffthaler G. Ultrasound guidance for the psoas compartment block: an imaging study. Anesth Analg 2002; 94(3): 706-10.
[http://dx.doi.org/10.1097/00000539-200203000-00042] [PMID: 11867402]

[34] Kirchmair L, Entner T, Wissel J, Moriggl B, Kapral S, Mitterschiffthaler G. A study of the paravertebral anatomy for ultrasound-guided posterior lumbar plexus block. Anesth Analg 2001; 93(2): 477-81.
[PMID: 11473883]

[35] Karmakar MK, Li JW, Kwok WH, Hadzic A. Ultrasound-guided lumbar plexus block using a transverse scan through the lumbar intertransverse space: a prospective case series. Reg Anesth Pain Med 2015; 40(1): 75-81.
[http://dx.doi.org/10.1097/AAP.0000000000000168] [PMID: 25469756]

[36] Güngör I, Zinnuroğlu M, Taş A, Tezer T, Beyazova M. Femoral nerve injury following a lumbar plexus blockade. Balkan Med J 2014; 31(2): 184-6.
[http://dx.doi.org/10.5152/balkanmedj.2014.13179] [PMID: 25207194]

[37] Dogan Z, Bakan M, Idin K, Esen A, Uslu FB, Ozturk E. Total spinal block after lumbar plexus block: a case report. Braz J Anesthesiol 2014; 64(2): 121-3.
[http://dx.doi.org/10.1016/j.bjane.2013.03.002] [PMID: 24794455]

[38] Muravchick S, Owens WD. An unusual complication of lumbosacral plexus block: a case report. Anesth Analg 1976; 55(3): 350-2.
[http://dx.doi.org/10.1213/00000539-197605000-00014] [PMID: 945016]

[39] Klein SM, D'Ercole F, Greengrass RA, Warner DS. Enoxaparin associated with psoas hematoma and lumbar plexopathy after lumbar plexus block. Anesthesiology 1997; 87(6): 1576-9.
[http://dx.doi.org/10.1097/00000542-199712000-00040] [PMID: 9416746]

[40] Aida S, Takahashi H, Shimoji K. Renal subcapsular hematoma after lumbar plexus block. Anesthesiology 1996; 84(2): 452-5.
[http://dx.doi.org/10.1097/00000542-199602000-00027] [PMID: 8602680]

CHAPTER 5

Vascular Access

Margaret K. Menzel Ellis[1], Neal S. Gerstein[2,*] and **Peter M. Schulman[1]**

[1] *Oregon Health and Science University, Portland, OR, USA*

[2] *Department of Anesthesiology and Critical Care Medicine, University of New Mexico, Albuquerque, New Mexico, USA*

Abstract: Vascular access is critical in managing the perioperative patient. In critical situations, establishing adequate vascular access is often difficult, invasive, and carries significant risks. Ultrasound is an invaluable tool in facilitating efficient and safe vascular access. Ultrasound helps to verify the presence, position and potency of the target vessel prior to the needle puncture and provides real time imaging of the needle throughout the vasculature (puncture process. The following chapter reviews the basics of ultrasound physics and machine knobology for optimizing image acquisition. The specifications of establishing central access – internal jugular vein, subclavian vein, axillary vein, and femoral vein; as well as obtaining arterial access are discussed in detail. Sources that are useful to continue one's education are also included.

Keywords: Acoustic impedence, Arterial access, Axillary vein, Doppler effect, Femoral vein, Refraction, Scattering, Spatial resolution, Subclavian vein, Ultrasound, Ultrasound for difficult intravenous access, Ultrasound for internal jugular vein.

INTRODUCTION

Establishing adequate vascular access is crucial to the management of the perioperative patient. However, vascular access procedures are invasive, carry serious risks, and are sometimes difficult to perform [1]. Ultrasound technology has emerged as an invaluable tool for increasing the efficacy and safety of vascular access procedures [2 - 4]. Ultrasound is used to facilitate vascular cannulation by **1)** "pre-scanning" to verify the presence, position, and patency of a suitable target vessel before needle puncture, and/or **2)** imaging the trajectory of the needle in real-time throughout the vessel puncture process [2].

This chapter reviews the basics of ultrasound physics and knobology for optimizing image acquisition, summarizes the literature supporting ultrasound

[*] **Corresponding author Neal S. Gerstein:** Department of Anesthesiology and Critical Care Medicine, University of New Mexico, Albuquerque, New Mexico, USA; Tel: (503) 706-5516; E-mail: ngerstein@gmail.com

Amballur D. John (Ed.)

use, provides a practical overview of specific ultrasound guided vascular access procedures, and offers tips for obtaining vascular access in challenging situations.

BASICS OF ULTRASOUND PHYSICS AND KNOBOLGY

Basic Principles of Ultrasound Physics

Ultrasound refers to sound waves with a frequency greater than the human ear can sense; typically, frequencies greater than 20,000 Hertz (Hz). Diagnostic ultrasound technology transmits high-frequency (1-12megahertz (MHz)) sound waves within tissue media of various densities to compose an image. The ultrasound machine produces electrical signals from an alternating current that generates vibrations within a set of piezoelectric crystals contained within the ultrasound transducer. During an ultrasound examination, the transducer acts as both a transmitter and receiver. When transmitting, an electric potential is applied to the piezoelectric crystals causing the crystals to mechanically deform. This deformation engenders the formation of acoustic waves in a process known as the **piezoelectric effect**. When the sound waves encounter a boundary between tissues or structures of varying density, some waves are reflected and travel back toward the transducer while other waves continue more deeply to other boundaries before ultimately being reflected. The amplitude of the returning sound waves (which are proportional to the signal strength) is sensed by the piezoelectric crystals and reconverted into an electrical signal. The ultrasound machine's computer processor analyzes and compiles these electrical signals into a real-time image based upon the time it takes for the various sound waves to return to the transducer as well as the strength and direction of the returning waves. Since the velocity of sound waves in soft tissue is relatively constant, the time from the emission of an ultrasound pulse and the reception of a reflected signal is dependent on the distance traveled (the depth of the reflecting structure).

Two-dimensional ultrasound produces a gray-scale image, the appearance of which is determined by the interaction of the ultrasound waves with the structures they encounter. Ultrasound waves interact with tissues in multiple ways. **This interaction is described as ultrasound wave attenuation, reflection, refraction, or scattering.** When ultrasound waves pass through a uniform medium, the path is a straight line and a uniform image is displayed. When the medium is heterogeneous and composed of multiple interfaces, the ultrasound wave path is altered due to one or more of the four possible interactions. Tissue interfaces that include air and bone are strong reflectors due to minimal transmission of the ultrasound waves. Strong reflectors appear bright with ultrasound imaging and are referred to as **"echodense", "hyperechoic",** or

"echogenic." In tissues such as water, blood, and fat, ultrasound waves are transmitted with minimal loss of energy or attenuation; hence, they appear dark and are described as **"echolucent"** or **"hypoechoic."** Structures that allow complete passage of ultrasound waves appear black on the ultrasound image, and are described as **"anechogenic."**

Acoustic impedance is the resistance of a given tissue to the passage of ultrasound waves. The mismatch between the acoustic impedance of two tissues at their interface determines the reflection of sound waves from that interface, which allows discrimination between different tissue structures. **Refraction** is a type of deflection of the ultrasound waves as they pass through structures with different acoustic impedance and can lead to an image display in a location that differs from the actual structure location. **Scattering** occurs when ultrasound waves encounter structures that are less than one wavelength in their lateral dimension causing the ultrasound beam to be radiated in multiple directions.

Spatial resolution is the ability to distinguish one object from another and is categorized as **axial** (objects aligned parallel to the ultrasound beam) or **lateral** (objects aligned perpendicular to the ultrasound beam). **Axial resolution** is determined by the frequency of the ultrasound beam when encountering an object. Higher frequency waves provide better axial resolution. **Lateral resolution** is determined by the width of the ultrasound beam when encountering objects; the ultrasound waves that comprise a narrower beam are closer together, providing more discrimination and better lateral resolution [5].

Knobology, Image Optimization, And Transducer Selection

Each ultrasound machine has a proprietary configuration of knobs and buttons on the ultrasound control panel. Here, the control panel of a SonoSite© ultrasound machine is depicted. The depth control is outlined in yellow. The gain controls, including the near and far field gain adjustment buttons, are outlined in pink. The color Doppler controls are outlined in green, and the auto-optimization button is outlined in blue. The controls for focus, frequency, and several other ultrasound functions are contained within the upper portion of the image, outlined in white. These buttons correspond to menu options that are displayed on the ultrasound screen, allowing the user to toggle through various options for each setting. The "2D" button, located in the right lower corner of the panel just below the Doppler controls, can be used to immediately return the ultrasound to default settings.

The ultrasound probe can be moved or repositioned in four distinct ways. To **align** the probe, slide or translate it in any direction. To **rotate** the probe, twist it around its vertical axis. To **tilt** the probe, move it along its horizontal axis to change the angle between the probe and the patient. Finally, sometimes applying

or releasing downward **pressure** is useful to optimize the image or to help identify structures.

When using ultrasound for vascular access procedures it is important to optimize the image. **A major component of image optimization involves correct transducer selection and use of the correct machine settings.** Optimal image generation is partly accomplished by understanding the impact of acoustic speed, wavelength, frequency and their relationship to image resolution. Resolution is the ability to discern the differences between structures of interest and it is directly related to frequency and inversely related to wavelength. Of these variables, frequency is the one that is can be modified by transducer selection and machine settings. Resolution is typically described as axial or lateral, both of which are constituents of the overall spatial resolution. Axial resolution relates to the ability to distinguish between structures in the same plane as the ultrasound wave. Lateral resolution refers to the ability to distinguish between adjacent structures perpendicular to the ultrasound wave. Typically, **there are five variables that can be adjusted to optimize a given image: frequency, depth, gain, focus, and Doppler modes** (Fig. **1**).

Fig. (1). Ultrasound controls. Images provided by Margaret K. Menzel Ellis, M.D., Oregon Health Sciences University and Neal S. Gerstein, M.D., FASE, University of New Mexico Department of Anesthesiology and Critical Care Medicine, Albuquerque, New Mexico, USA.

Frequency

The frequency of the ultrasound wave determines the degree of spatial resolution and is determined by transducer as well as machine settings. **Typical linear transducers used for vascular access have a frequency range of 6-13MHz.** At a higher frequency, more frequent oscillations of the sound wave are produced resulting in a greater interaction with tissue interfaces at shallower depths. Hence, imaging with a higher frequency results in higher resolution images at the expense of imaging depth, since the frequent oscillations also result in more rapid loss of energy of the ultrasound waves. The converse principle exists for lower frequency imaging; lower frequency imaging enables imaging at deeper depths due to less attenuation but at the expense of lower resolution. In order to achieve the most optimal image, one should choose a transducer that corresponds to the desired frequency. **High-frequency transducers often have a linear array surface and are ideal for imaging shallow structures, while low-frequency transducers often have a curvilinear array surface and provide better imaging of deeper structures** [6]. Variable-frequency transducers allow for adjustment of the frequency within a narrow high- or low-frequency range to further optimize the quality of the image [7]. Several different transducers are shown in (Fig. **2**).

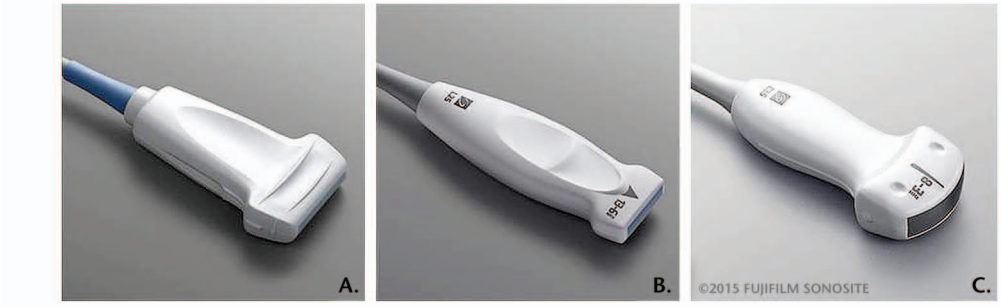


Fig. (2). Ultrasound probes. Large (a) and small (b) 13-6 MHz linear array ultrasound transducers are pictured here, as well as an 8-13 MHz curvilinear (c) transducer. Images ©2015 FUJIFILM SonoSite, Inc. All Rights Reserved, used with permission.

Depth

The depth of the vessel of interest should be one of the principle considerations when choosing a given ultrasound transducer and adjusting the settings. The depth of the field should be adjusted so that the region of interest and other relevant structures are visualized in the middle of the ultrasound display. For most bedside ultrasound systems, centering the structure of interest allows optimal image focus and resolution of the given structure and other relevant adjacent structures.

Gain

Increasing or decreasing the gain affects the brightness of the displayed screen image. Gain is described as a post-processing function, meaning that changes in gain only affect the image display after the returning ultrasound signals have been received. In other words, increasing the gain increases the energy of the returning ultrasound waves ("signal") after the piezoelectric crystal have received them. Increasing gain results in an increase in the energy of all returning waves, thus increasing the brightness of all of the imaged structures and increasing the ratio of signal to "noise" (background artifact). Decreasing the gain darkens the entire field and decreases the ratio of signal to noise [5]. In addition to adjusting an image's total gain, the gain setting can also be adjusted to diminish or increase the returning ultrasound signals from varying tissue depths. This function is called **time-gain compensation** and allows one to adjust the bright and dark areas of the field to best provide a clear image of the structures of interest. A gain setting that permits adequate contrast between the vascular structure of interest and adjacent structures, without excess brightness or dimness, is typically optimal for visualizing vascular structures.

Focus

The focal zone is the narrowest portion of the ultrasound beam as it passes through tissue. Imaging in the focal zone provides the best lateral resolution because the individual ultrasound waves are closest together in this portion of the beam. The focal zone is adjusted based on the depth of the structures of interest within the ultrasound field in order to concentrate the ultrasound beam at the most appropriate depth. Certain ultrasound machines allow for the focal zone to be manually adjusted, while other systems automatically adjust the focal zone based on imaging depth.

Color Doppler

Typically, veins are in close proximity to arteries, hence it is sometimes challenging to identify the vessel of interest. Color Doppler can be useful in these situations. Color Doppler mode utilizes the Doppler effect. **Doppler effect** theory describes that the frequency of sound waves reflected from a moving object will change depending on the velocity and direction of the moving object relative to the observer. For example, a person sitting at a train station hears the approaching train's whistle. The whistle produces sound waves at a single frequency. However, the pitch of the whistle perceived by the sitting person changes based on whether the train is moving quickly or slowly as well as towards or away from the person. The change in perceived frequency by the sitting person as compared to the true whistle pitch is due to the Doppler effect. Analogously, ultrasound

waves reflected from a moving object exhibit slight differences in the time required for the wave to be returned to the receiver. These differences can be measured as time differences or as a phase shift from which the Doppler frequency is calculated.

In medical ultrasound, the receiver/observer is the ultrasound probe and the moving object is typically red blood cells. The velocity and direction of blood travel relative to the transducer generates a Doppler signal which the ultrasound machine then assigns a color based upon red blood cell velocity and direction. The color Doppler mode interprets these alterations and typically displays shades **of red (higher frequency, red blood cells moving toward the transducer)** and **blue (lower frequency, red blood cells moving away from the transducer)**. However, because the color scale can be manipulated, it is important to verify the direction of flow relative to the color scale being utilized. The pulsatility of flow can also be assessed with color Doppler, since red blood cells within a pulsatile blood vessel move at varying velocities depending on the cardiac cycle. During systole velocity increases, and flow is typically antegrade, while during diastole flow velocity decreases, and flow may either cease or flow retrograde. Hence, the color Doppler image of a vessel with arterial flow will have varying color and velocity during systole and diastole, while venous flow on color Doppler will likely display a low velocity pattern.

Auto-Optimization

Many ultrasound machines have an auto-optimization option, in which pushing a single button (such as iSCAN [Philips] and TEQ [Siemens]) results in a balanced image based upon the computer's interpretation of the incoming signals. While this feature does not always provide an ideal image, it often provides a useful starting point from which further fine-tuning can be done if necessary.

Transducer Orientation

Ultrasound machines have an orientation marker on one side of the transducer that corresponds to an indicator displayed on one side of the ultrasound screen. When performing ultrasound-guided procedures, align the transducer marker with the screen indicator so that the right and left side of the transducer corresponds to the right and left side of the screen respectively. Once the transducer is oriented correctly relative to the screen, its position can be adjusted in several ways to optimize the image (Fig. **3**).

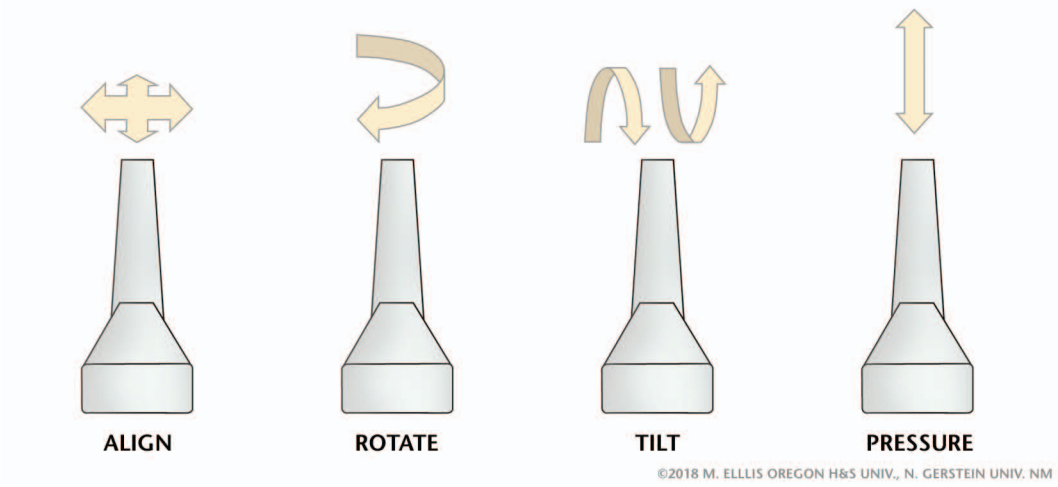


Fig. (3). Standard probe movements. Images provided by Margaret K. Menzel Ellis, M.D., Oregon Health Sciences University and Neal S. Gerstein, M.D., FASE, University of New Mexico Department of Anesthesiology and Critical Care Medicine, Albuquerque, New Mexico, USA.

Ultrasound for Central Venous Cannulation

Indications for central venous cannulation during the perioperative period include administration of vasoactive medications, monitoring of hemodynamic indices (*i.e.* central venous pressure), insertion of pulmonary artery catheters or cardiac pacing leads, performance of temporary hemodialysis, or any other situation requiring direct access to the central circulation [8]. As compared to the landmark technique, ultrasound-guided central line placement is associated with a higher first attempt and overall success rates of cannulation [9 - 12]. Furthermore, the use of ultrasound guidance rather than landmark-based techniques is advocated by multiple specialty societies and national organizations [13 - 15].

The utility of ultrasound for obtaining central venous access was first described in 1984, when a technique involving Doppler ultrasound to locate the internal jugular vein (IJV) was found to be more successful than a landmark-based technique [16]. Several small studies subsequently compared various ultrasound-guided techniques to landmark-based techniques, all of which consistently demonstrated greater success and fewer complications with ultrasound-guided placement. An early study involving more than 1000 patients, prospectively compared real-time ultrasound-guided cannulation of the IJV with a landmark technique and found higher success rates, faster time to cannulation, and fewer complications with the use of ultrasound [17].

More recently, numerous additional studies have demonstrated improved safety and efficacy when real-time ultrasound guidance was used to facilitate cannulation of the subclavian (SCV) or femoral (FV) veins [3, 9, 18 - 20]. As medical trainees become more accustomed to and reliant upon ultrasound guided techniques and as ultrasound technology becomes increasingly accessible and affordable, **ultrasound is rapidly becoming the standard of care for central venous cannulation** [3, 4].

PRINCIPLES OF ULTRASOUND-GUIDED CENTRAL LINE PLACEMENT

Preparing for the Procedure

Site Selection

The **three common anatomic sites** for central line placement are the **IJV, SCV**, and **FV**. Anatomic site selection should be based on the clinical situation, relative risks and benefits of using one site instead of another, and skill and experience of the operator [21].

Historically, the SCV was associated with the least risk of infection when compared to the IJV or FV [22, 23]. Femoral venous lines were associated with the most frequent infectious complications, however the modern day central line bundle and fastidious line stewardship protocols have improved the safety of this approach [24 - 26]. Evidence suggests that fewer occurrences of catheter colonization are associated with SCV lines when compared to femoral lines, but rates of catheter-related sepsis are equivocal [22, 27]. Recent studies also demonstrate no difference catheter-related sepsis or catheter-related bloodstream infection between the SCV site and IJV site [22, 28].

The risk of mechanical complications (pneumothorax, hemothorax, catheter tip malposition) and guidewire issues (including kinking, entrapment, knotting, fracturing, and embolization) was historically considered to be higher with SCV access as compared to the IJV or FV sites [29]. However, more recent data suggests that the SCV site is associated with fewer mechanical complications as compared to the IJ site and fewer thrombotic complications as compared to the femoral site [22, 30, 31]. Nevertheless, given the **multiple case reports describing aortic injury, hemothorax, and tamponade with IJV and SCV central venous cannulation**, the anesthesiologist should remain vigilant for these complications following supradiaphragmatic central venous cannulation [21]. Non-infectious complications of femoral lines are uncommon but include arterial puncture, bleeding, and damage to surrounding structures.

Safety

Barring an emergency, **informed written consent must be obtained** before performing any medical procedure. For central venous cannulation, complications such as infection, bleeding, and damage to surrounding structures (notably hemothorax and pneumothorax for SCV and IJV lines) should be discussed. **A procedural 'time-out' and appropriate procedural checklists should be completed and verified prior to commencing with central line placement** [32]. Continuous electrocardiography and pulse oximetry monitoring, as well as any other monitoring appropriate for the patient's condition, should be used throughout the procedure.

Following the completion of the procedure, all sharps should be properly disposed in approved sharps containers. Scalpels should be retracted into their protective sleeves. Lastly, if more than one central line kit was opened for any reason, ensure that all guidewires are accounted for. There are case reports involving an unrecognized guidewire embolus associated with the use of multiple kits [33].

Sterile Precautions

Since performing a central venous access procedure carries the risk of serious infection, the importance of using universal sterile precautions is paramount. These precautions include hand washing, wearing a sterile gown and gloves, surgical cap, mask, and eye protection. Once the patient is positioned, prepare the skin using an appropriate antiseptic and cover the area with a sterile full body fenestrated drape. Be sure to include all landmarks within the sterile field. At the end of the procedure, apply a sterile dressing before removing the drape.

Equipment

Most necessary equipment is found in commercially prepared kits and includes: skin preparation solution, sterile towels or drapes sufficient to cover the entire body, 1-2% lidocaine, sterile 4x4 gauze, non-luer lock ("slip-tip") syringes that are easy to remove from the needle, #11-blade scalpel, sterile saline or heparinized flushing solution, catheter with the appropriate length and number of lumens, compatible skin dilator (usually one French larger than the catheter), appropriate size needle, guidewire of compatible size which will pass through the catheter and needle, suture, and needle driver for curved needles. Sterile transduction gel, an acoustically transparent sterile transducer sheath, and sterile rubber bands or clips to secure the sheath around the transducer are also required and are often packaged together.

Since there are a wide variety of central venous catheters available, selection should be based on the indication for and site of line placement. In adults, 7-8 French double or triple lumen catheters of either 15 or 20cm length are most commonly used. For resuscitation, short, large-bore, single-lumen catheters are superior because fluid flow is proportional to catheter diameter. Patients who need central venous access for hemodialysis or plasmapheresis require catheters designed specifically for these purposes. **For children and small adults, 4 and 5 French catheters are available.**

When choosing the appropriate ultrasound transducer to use for central line placement, consider the relative benefits and drawbacks of different transducers. While linear-array high-resolution vascular transducers are preferred for central line placement due to their superior resolution for imaging relatively shallow central veins, low-frequency lower-resolution curvilinear transducers may be beneficial in patients with large body habitus or with excessive soft tissue at the procedure site.

The Ultrasound-Guided Seldinger Technique

The basic steps of the Seldinger technique are illustrated here: **1)** puncture the skin and advance the needle into the target blood vessel **2)** thread a guidewire through the needle and into the blood vessel, and remove the needle **3)** use a scalpel to make a small skin incision at the skin entry site of the guidewire **4)** thread a rigid dilator over the wire and through the soft tissue underlying the skin entry site **5)** thread the catheter over the guidewire and into the target vessel, maintaining control of the external end of the wire at all times, and **6)** advance the catheter over the wire and into the blood vessel, then remove the guidewire and secure the catheter in place.

Once the target vessel has been located on ultrasound, its depth can be measured. The skin entry point should be chosen based on the planned angle of approach and the depth of the target vessel. This figure illustrates the ultrasound probe, with its plane penetrating the skin and the blood vessel below. By measuring the distance (**a**) between the skin and the vessel on the ultrasound screen, and then estimating the angle between the needle and the skin (**x**), the length of the hypotenuse of the resulting triangle (**c**) and the appropriate distance between the needle the probe (**b**) can be estimated.

In 1953, the Swedish radiologist Sven-Ivan Seldinger pioneered the technique that bears his name for percutaneous catheter placement. Prior to this time interventional vascular access procedures either required a surgical cut-down or were accomplished with large vascular access trocars which had a high rate of associated complications [34]. The **Seldinger technique** has since become a

foundational technique for vascular access procedures; the incorporation of ultrasound into these procedures has given rise to a modified version of the Seldinger technique. The vast majority of modern percutaneous medical procedures, including all of those described herein, are performed using the Seldinger or modified Seldinger technique, the basic steps of which are illustrated in (Fig. **4**).

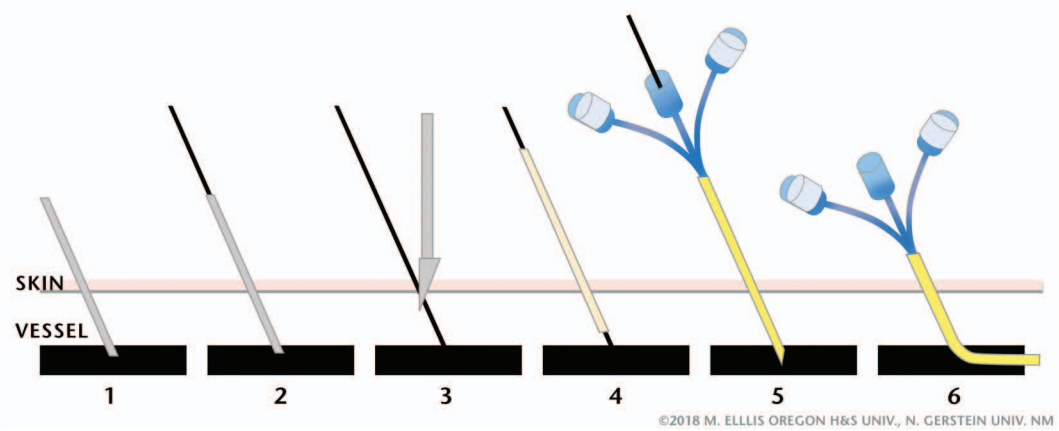


Fig. (4). Basic Seldinger technique. Images provided by Margaret K. Menzel Ellis, M.D., Oregon Health Sciences University and Neal S. Gerstein, M.D., FASE, University of New Mexico Department of Anesthesiology and Critical Care Medicine, Albuquerque, New Mexico, USA.

Preparation

First, establish a sterile field using universal sterile precautions. Next, prepare the ultrasound transducer. To prepare the transducer, place enough sterile acoustic gel to cover the transducer surface into a sterile transducer sheath. Next, have an assistant carefully insert the transducer into the sheath and through the gel. Slide the end of the sheath toward the assistant, being careful not to break sterility by touching the assistant's glove or any portion of the ultrasound transducer. Hold the sterile sheath containing the ultrasound transducer head as the operator pulls and lengthens the sheath away from the operator over the transducer wire. The interface between the end of the sheath and the imaging surface of the ultrasound transducer should be free of wrinkles and air bubbles to ensure optimal acoustic coupling. Secure the sheath around the transducer using sterile rubber bands or plastic clips. To complete acoustic coupling, apply a small amount of sterile ultrasound gel to the covered ultrasound transducer or to the patient's skin. Because the sterilely covered ultrasound transducer is used intermittently throughout the procedure, it is necessary to identify a convenient sterile area on which the transducer can be placed when it is not in use. This step should precede local anesthetic infiltration, because the exact location of infiltration may change slightly once the target vessel is imaged with the sterile-covered transducer.

Use ultrasound to visualize the target vein; the details of obtaining an optimal view of the target vein are specific to the site of the line placement and are described in detail in subsequent sections of this chapter. Based on the estimated depth of the most superficial aspect of the vein determined by the ultrasound image, choose a skin entry point such that the needle tip will reach the target vein just as it passes through the ultrasound beam (Fig. **5**). This ensures that the needle tip can be visualized as it enters the vein. In a patient who is awake or sedated, use a small needle to infiltrate the skin overlying the planned insertion site with a local anesthetic (*i.e.* 1-2% lidocaine) to help minimize discomfort during insertion. Flush all lumens of the catheter with saline or heparinized saline, and then remove the cap from the port through which the guide wire will be threaded. This is commonly the longest lumen and is frequently designated by a brown-colored port.

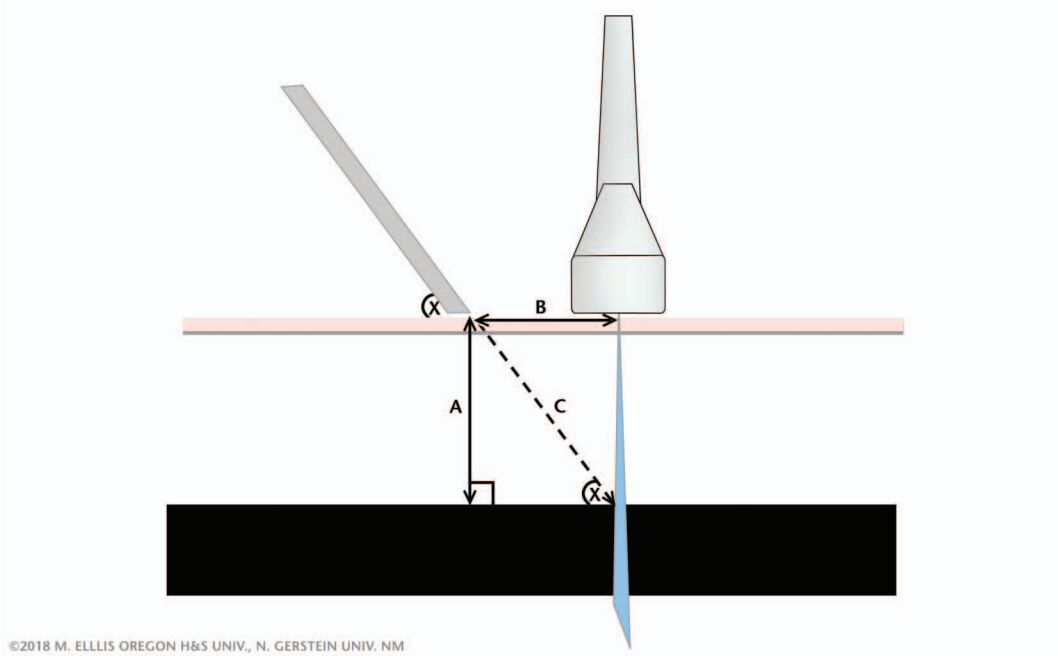


Fig. (5). Skin entry point and ultrasound beam. Images provided by Margaret K. Menzel Ellis, M.D., Oregon Health Sciences University and Neal S. Gerstein, M.D., FASE, University of New Mexico Department of Anesthesiology and Critical Care Medicine, Albuquerque, New Mexico, USA.

Cannulation

Advance a thin-walled 18-gague needle with an attached slip-tip syringe through the skin, maintaining negative pressure on the syringe at all times. During this portion of the procedure, watch the ultrasound screen while also frequently

checking for a return of blood in the syringe, signifying needle entry into a vessel. Once the tip of the needle lies completely within the lumen of the target vein, blood should be continuously aspirated into the syringe without any resistance. Once appropriate blood flow is confirmed, carefully place the ultrasound transducer in a sterile location and disconnect the syringe while stabilizing the needle. The ultrasound transducer should remain sterile and available throughout the remainder of the procedure, as it can be useful for troubleshooting technical issues, including confirming guidewire location within the vessel, assessing for the presence of a hematoma, and ruling out iatrogenic pneumothorax [35, 36].

Confirming Intravenous Access and Passing the Wire

Confirm that the blood flow is non-pulsatile; bright red pulsatile blood is suggestive of arterial puncture. However, dark or non-pulsatile blood does not exclude the possibility of arterial puncture, particularly in patients with hypoxemia or low cardiac output. Once the vessel is accessed, pass the J-tip of a flexible guidewire through the needle into the vessel's lumen. During this and all subsequent steps, it is imperative to maintain complete control of the external portion of the wire, as it can be inadvertently lost within the patient if inserted fully. When passing the wire through the SCV or IJV, it is also important to watch for arrhythmias or ectopy on telemetry monitoring, as the wire can pass into the right heart and cause myocardial irritation and possible hemodynamic instability. If an arrhythmia does occur, withdraw the wire until it stops.

At this point, **ultrasonography should be utilized to confirm intravenous wire placement; the guidewire within the lumen of the vein should be clearly apparent on the screen in both cross-sectional and longitudinal views.**

If the location or path of the wire is unclear, fluid column manometry or pressure transduction can be utilized for confirmation. First, advance a small catheter or angiocatheter (typically 20Ga. x 1-3/4inches (4.45cm)) over the guidewire and remove the wire. To perform fluid column manometry, attach a short length of IV tubing to the angiocatheter, and hold the distal end below the level of the patient's heart to allow the tubing to fill with blood. Next, elevate the end of the tubing above the level of the patient's heart. Free blood flow from the tubing back to the patient confirms a low intravascular pressure suggesting venous placement; however, if the blood in the IV tubing is pulsatile or rises continuously through the IV tubing, arterial placement is more likely. Alternatively, the blood pressure within the accessed vessel can be measured directly by connecting the angiocatheter to a sterile pressure transducer. Once the possibility of arterial placement is excluded, reinsert the guidewire through the catheter and then remove the catheter while leaving the guidewire in place.

Some central line kits include an angiocatheter pre-loaded onto the venous access needle; if this kit is used, advance the angiocatheter over the access needle into the vein once free blood flow is established, and remove the needle. Perform fluid manometry or pressure transduction to confirm a low intravascular pressure as described above, then advance the wire through the angiocatheter and confirm its intravenous placement using ultrasound visualization.

Dilation and Catheter Placement

Next, withdraw the needle or angiocatheter and leave the wire in place. Using a scalpel, make a small superficial incision at the wire entry point, taking care not to cut the guidewire. There should be no skin "bridge" between the wire entry site and the skin incision. Thread a dilator over the guidewire, being certain to maintain control of the guidewire at all times, and advance the dilator 1-2cm by holding it close to the tip and rotating it. It should be noted that the dilator is used to dilate the soft tissue rather than to specifically dilate the vein itself. Be careful not to introduce a bend or kink in the guidewire. Remove the dilator (increased bleeding at the site of puncture is expected) while continuing to maintain control of the guidewire. A gauze pad can be applied to the insertion site to minimize blood loss.

Once the dilator is removed, feed the catheter over the guidewire while maintaining control of the external end of the wire. This typically requires pulling the guidewire out of the patient until the external end of the guidewire passes through the length of the catheter, extends out of the catheter hub, and can be grasped. While grasping the external end of the wire, advance the catheter over the wire and through the skin using a rotating motion. If resistance is met, the tract may not have been adequately dilated. In this case, remove the catheter and repeat the dilation portion of the procedure. Once the catheter passes smoothly over the wire, insert the catheter to a depth that places the tip at the junction of the superior vena cava and the right atrium.

Final Steps

Remove the guidewire and check for blood return in all ports. Aspirate all the air from each catheter lumen, and then flush each lumen with sterile saline. Place caps on the hubs and suture the line in place, using at least two anchor points to ensure the line does not become displaced with patient movement. Finally, cover the insertion site with sterile gauze or a sterile dressing prior to removing the drapes or breaking the sterile field in any way.

CHALLENGES IN ULTRASOUND-GUIDED CENTRAL LINE PLACEMENT

Visualizing the Needle

While visualizing the needle tip on the screen is ideal, it is not always possible. When a cross-sectional technique is used (target vessels are imaged in cross-section and appear as circular structures on ultrasound) the needle is also imaged in cross section and will appear as a small, bright dot on the screen. This makes the determination of the exact location of the needle tip more difficult, since only a single cross section of the needle shaft can be seen. However, all attempts should be made to keep the tip of the needle under direct ultrasound visualization once it appears as a dot on the ultrasound image.

The use of short in and out or tapping movements may facilitate visualizing the trajectory of the needle. In addition, the location of the needle tip may be visualized by tilting the transducer back and forth or by withdrawing of the needle and realigning it. When the needle passes underneath the transducer, the resulting soft tissue tenting will also appear on the ultrasound screen; it is most important to watch the wall of the target vessel invaginate as it is pierced by the needle.

In the **cross-sectional** (also referred to as "**short axis**" or "**out-of-plane**") technique, the vessels appear circular on the ultrasound image, and the needle appears as a small, bright dot in cross-section. Conversely, a **longitudinal** (also referred to as "**long-axis**" or "**in-plane**") view of the vein is also possible. In the longitudinal technique, the vessel appears as an echolucent stripe, with the anterior wall of the vessel located closest to the transducer. This view can be achieved by rotating the ultrasound transducer 90degrees after achieving an optimal longitudinal view of the target vein. While the cross-sectional technique is often preferred because it allows the vein, artery, and other adjacent structures of interest to be imaged simultaneously in a single view, a longitudinal technique may be used to visualize the entire length of the needle as it advances towards and penetrates the vein. However, the entire length of the needle must lie exactly within the plane of the ultrasound beam; otherwise, the view of the needle will be foreshortened, and the tip will still not be visualized.

Regardless, ultrasonography does not necessarily confirm the location of the tip. A "flash" of blood followed by free, continuous aspiration of blood into the syringe is the best marker of intravenous needle tip positioning. Challenging venous access requiring multiple attempts should lead to increased suspicion of arterial puncture, and should prompt careful confirmation as described above.

Troubleshooting

Pre-scanning the anticipated site of central line insertion prior to preparation of the sterile field may identify anatomical issues that could complicate placement. Pre-scanning may be especially useful in complex patients with concurrent indwelling central venous hardware, previous central lines, prior chest trauma, surgery, radiation, or a recent or current upper extremity venous thrombosis [21]. If concerns about the safety or feasibility of line placement emerge after pre-scanning, consider evaluating a different site.

During the initial venous access portion of the procedure, the tip of the needle may only compress the wall of the target vessel, rather than puncture it. The vessel wall may invaginate on ultrasound, but no blood will be aspirated into the syringe. This is more likely to occur when larger gauge needles are used. In this situation, a short quick thrust of no more than a few millimeters may be sufficient for the needle to "pop" through the vessel wall and into the lumen. If the needle has been advanced to the anticipated depth of the target vessel, but no "flash" has been seen or blood cannot be freely aspirated, slowly withdraw the needle while maintaining gentle negative pressure on the attached syringe. In an easily collapsible vein, entry may only become evident as the needle is withdrawn and pressure on the vein is relieved. Occasionally, pressure from the ultrasound transducer may also compress the vein; hence, only the minimal pressure required for adequate acoustic coupling of the transducer should be applied.

If the guidewire will not thread through the needle, it may be necessary to adjust the placement of the needle since it may have inadvertently been advanced or withdrawn during manipulation. If so, adjust the needle and re-aspirate to be sure that the needle tip is still located within the vessel lumen. If blood flow cannot be re-established, remove the needle and start over. Finally, presence of a blood clot in the needle will further complicate assessment of whether the vein has been successfully entered. If blood has previously been aspirated into the needle, remove it and flush it thoroughly with saline to clear any obstructing clot before reattempting placement of the line.

Complications

Central venous cannulation is an invasive procedure that can result in serious or even life threatening complications, including arterial puncture, vascular injury, bleeding, hemothorax, pneumothorax, thoracic duct injury (with left SCV attempts), myocardial injury, arrhythmia, nerve damage, and catheter malposition.

If arrhythmias occur following SCV or IJ catheter placement and guidewire removal, the catheter might be in the right atrium or ventricle. Always confirm the

catheter's position with a post procedure chest radiograph and if necessary pull it back so that it is ideally positioned in the cavo-atrial junction.

During insertion, it is critical to prevent air entrainment through a needle or catheter open to atmospheric pressure, as this can precipitate a venous air embolism (VAE), especially if the heart is lower than the accessed vessel. Hypovolemia, tachycardia, upright position, spontaneous ventilation, and open catheter ports are all risk factors for VAE during central line placement [37] If VAE is suspected, the patient should be administered 100% oxygen and placed in the left-lateral decubitus and head down position to facilitate right ventricle apex air trapping and to speed air reabsorption.

Arterial injury is an emergency. Unintended placement of a large bore catheter into a central artery will be evident by bright red pulsatile blood return from the catheter. However, in patients with low cardiac output, hypoxemia, and/or continuous flow ventricular assist devices, it may be difficult to differentiate venous from arterial blood based on color or pulsatility. Ideally, possibility of this complication should be recognized early on in the procedure. If arterial placement is suspected based on ultrasonography, fluid column manometry, or pressure transduction, do not dilate the vessel or place the catheter. **Immediately abort the procedure, hold firm manual pressure over the insertion site, and only reattempt line placement once hemostasis is achieved.** If the dilator or catheter is suspected of already being intraarterial, it should be left in-situ, and the need for surgical arterial repair should be immediately assessed by an appropriate surgeon.

In the case of persistent bleeding at the catheterization site at the end of the procedure, apply direct pressure, considering evaluating coagulation studies, and replace blood products as necessary. Persistent bleeding may be another sign of an arterial injury or an indicator of a venous injury, and a vascular surgeon should be consulted if the bleeding cannot be controlled with direct pressure and correction of coagulopathy.

Occasionally, air may be aspirated into the syringe. If this occurs, check the syringe to be sure that the needle or catheter and syringe are firmly attached. If air continues to be aspirated during IJV or SCV line placement despite firm connections, or if the patient develops respiratory distress, immediately remove the needle or catheter as a pneumothorax may have occurred. In mechanically ventilated patients, lung injury can rapidly result into tension pneumothorax. Immediately obtain a chest radiograph and insert a chest tube if necessary. Do not attempt to place the central line in a supradiaphragmatic location on the contralateral side because of the risk of contralateral pneumothorax and further respiratory compromise.

SITE-SPECIFIC CONSIDERATIONS

Cannulation of The Internal Jugular Vein

Indications and Contraindications

In 1966, a landmark-based technique for locating and cannulating the IJV was described [38], and it remains a frequent first choice site for central venous access due to its accessible location and easily identifiable anatomy. In the operating room, an IJV line is often ideal, since it may be the only site accessible to the anesthesiologist throughout many surgical procedures. The relatively straight path from the right IJV to the superior vena cava makes it an ideal site for placement of large, stiff lines such as hemodialysis catheters. Furthermore, if central access is needed for pulmonary artery catheter placement, the right IJV site offers the shortest and most straightforward path to the pulmonary circulation.

Do not place a central line in the IJV if there has been recent surgery, burn, or infection of the skin overlying the vein, or if surgery is planned that would involve the IJV site. The ability of the patient to tolerate a pneumothorax on the side of line placement should be considered; if pneumothorax would be catastrophic, avoid IJV line placement. Finally, if manipulation of the neck is contraindicated, such as in patients with cervical spine instability, proper positioning for IJV central line placement will not be possible.

Ultrasound Visualization of the Neck Vessels

The large vessels of the right neck are seen here in cross-section. The internal jugular vein (**IJV**) appears as a large, hypoechoic, ovoid structure, which is compressible with application of downward ultrasound probe pressure. The carotid artery (**CA**) lies just medial and deep to the IJV. It should appear pulsatile, and should not be compressible with the ultrasound probe. The sternocleidomastoid (**SCM**) muscle can be seen superficial to the vessels in this view.

Unless clinically contraindicated, position the patient supine, in slight Trendelenburg position, to increase venous engorgement and minimize the risk of venous air embolus. Stand at the patient's head. Next, turn the patient's head slightly toward the contralateral side. Avoid turning the head too far as excessive head rotation can bring the IJV directly in front of the carotid artery [39, 40].

The IJV lies just lateral to the common carotid artery and is commonly cannulated within the anatomical triangle bordered inferiorly by the clavicle, and medially and laterally by the anterior (sternal) and posterior (clavicular) heads of the

sternocleidomastoid muscle respectively. Once the sterile field, ultrasound, and equipment are ready, place the ultrasound transducer within the superior aspect of the triangle, parallel to the clavicle. Ensure proper transducer is alignment; the left and right sides of the transducer should correlate with left and right on the ultrasound screen. The IJV should be readily visible in cross section as a large, black, oval shaped structure, which can be compressed by applying pressure to the skin with the ultrasound transducer. The carotid artery is visualized just medial and deep to the vein and is identified by its muscular vessel wall, pulsatility and lack of compressibility [41] (Fig. **6**). If the transducer is translated closer to the clavicle, the apex of the lung may be seen as bright, sliding pleura just deep to the dark shadow cast by the first rib. In order to minimize the risk of iatrogenic pneumothorax, translate the transducer cephalad to access the vein as superiorly along its trajectory as possible. Adjust the position of the transducer as needed so that the IJV is in the center of the monitor screen.

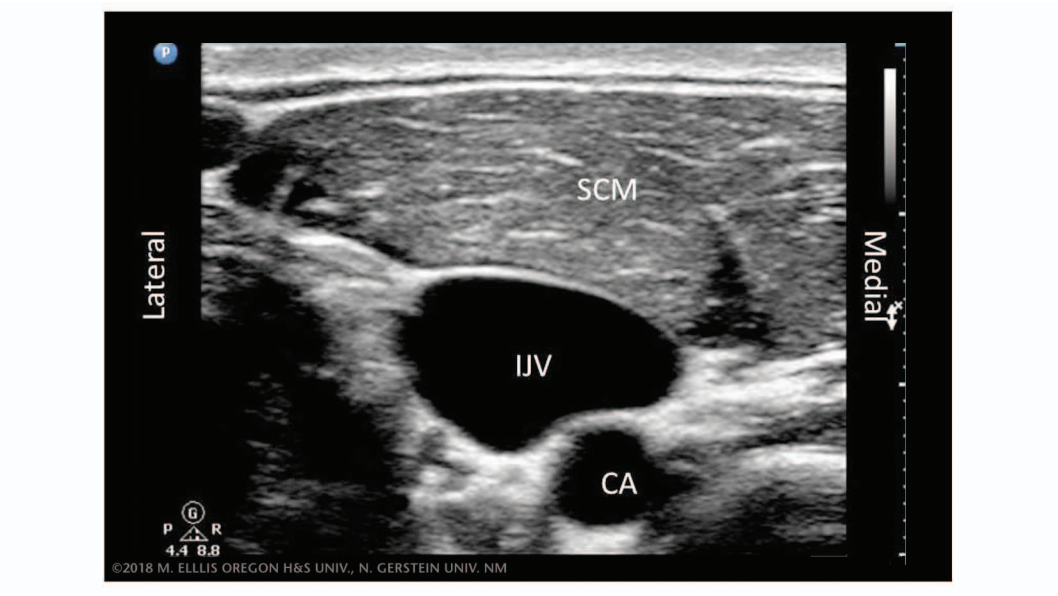


Fig. (6). Ultrasound view of the neck vessels. Images provided by Margaret K. Menzel Ellis, M.D., Oregon Health Sciences University and Neal S. Gerstein, M.D., FASE, University of New Mexico Department of Anesthesiology and Critical Care Medicine, Albuquerque, New Mexico, USA.

Internal Jugular Vein Cannulation

Once the ideal view is obtained and local anesthesia has been administered (if indicated), puncture the skin with the access needle superior to the ultrasound transducer, with an entry point perpendicular to the mid-point of the ultrasound

transducer. Advance the needle, aiming slightly laterally toward the center of the vein to avoid inadvertent carotid artery puncture. Once the vessel is accessed with the needle and blood flow is established, the remainder of the procedure is performed using the Seldinger technique.

Cannulation of The Subclavian Vein, Indications and Contraindications

SCV cannulation may be indicated when conditions that affect the IJ or FVs, such as occlusion due to thrombosis or scarring, or when the IJ landmarks have been obscured or distorted by trauma, recent or planned surgery, or other anatomic anomalies such as goiter or morbid obesity [42]. In patients with significant cervical spine trauma or instability, accessing the IJ or moving the head and neck may not be possible, making SCV cannulation the best option. Additionally, in cardiac transplant it may prudent to choose the SCV to minimize potential scarring of the IJ, thereby facilitating future cardiac biopsy surveillance.

Specific contraindications for placing a central venous line in the SCV include infection or significant burns in the area overlying the insertion site, fracture or trauma to the clavicle or proximal ribs, or occlusion or thrombosis of the target vein. Coagulopathy, while not an absolute contraindication, should be of somewhat greater concern when considering the SCV approach as the position of the clavicle can prevent effective application of pressure to the subclavian vessels if needed to prevent hematoma formation. The inability to tolerate a pneumothorax is also a relative contraindication to SCV cannulation, although the use of ultrasound decreases this risk when compared to a landmark-guided approach [43].

Based upon current literature, real-time ultrasound-guided SCV cannulation is likely superior to the use of a landmark-based technique [44]. SCV central line placement using ultrasound guidance is associated with fewer procedural complications including a reduction in average access time, fewer placement attempts, and lower risk of arterial puncture, hematoma, hemothorax, pneumothorax, brachial plexus injury, phrenic nerve injury, and cardiac tamponade [9, 11, 14].

Ultrasound Visualization of the Subclavian Vessels

Unless contraindicated, position the patient in a small amount (15-20degrees) of Trendelenburg position to decrease the risk of air embolism and engorge the SCV. Placing a small roll under the midline of the patient's upper back often optimizes positioning. If possible the patient's ipsilateral arm should be fully adducted.

Identify the clavicle (Fig. **7**). The SCV most closely approximates the clavicle just under the middle third of the clavicle, and the artery runs posterior and superior to the vein. The middle third of the clavicle begins at the point where the clavicle angles posteriorly and is joined by the costoclavicular ligament.

Probe placement for subclavian central line placement.

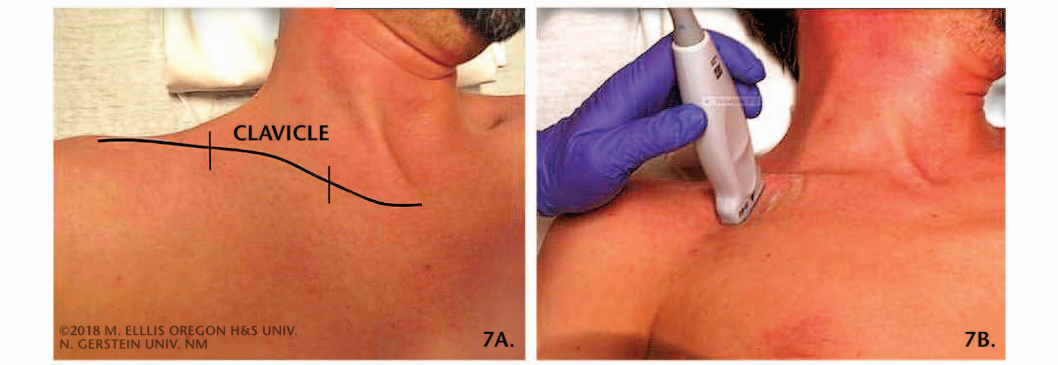


Fig. (7). A: Surface anatomy of the clavicle; the * indicates the junction of the lateral and medial thirds of the clavicle. **B**: The appropriate starting position of a linear ultrasound probe placed perpendicular to the junction of the lateral and medial thirds of the clavicle. Figs. (**7A and 7B**) provided by Margaret K. Menzel Ellis, M.D., Oregon Health Sciences University and Neal S. Gerstein, M.D., FASE, University of New Mexico Department of Anesthesiology and Critical Care Medicine, Albuquerque, New Mexico, USA.

Once the sterile field, ultrasound, and equipment have been prepared, place the ultrasound transducer inferior and perpendicular to the middle third of the clavicle, and direct the transducer marker cephalad (Fig. **7**). A cross-sectional image of the SCV and SCA should be readily identifiable; however, it may be necessary to translate the transducer slightly cephalad to achieve this view. In that case, a portion of the ultrasound transducer may overly the clavicle. The clavicle is identified as a bright echogenic line at the left of the screen; however, the acoustic shadow cast by the clavicle is frequently seen rather than the clavicle itself. This shadow will appear as a dark area lateral (on the left side of screen) and adjacent to the SCA. If the surface of the transducer footprint is completely inferior to the clavicle, only the SCV, SCA, and pleura will be visualized on the ultrasound screen (Fig. **8**). Tilting the transducer medially and laterally may further optimize the view.

The SCV will be located towards the right of the screen and deep to the clavicle. The SCA is typically between the clavicle (or its shadow) and the SCV. The pleura appears as a thin, echogenic, linear structure below and to the right of the SCV and SCA (Fig. **8**). When distinguishing between the artery and vein, it is useful to note that the SCV is typically larger, more compressible, and non-

pulsating, while the SCA should be smaller, pulsatile, and more difficult to compress. To ensure the patency of the vein, gently compress the vein with the transducer; minimal pressure should be sufficient to collapse the lumen. In a situation in which the identity of the artery and vein is unclear, location and patency can be further assessed with color flow Doppler ultrasound; venous biphasic flow will be seen in the SCV, while the SCA will have pulsatile systolic flow. At this stage, it also helpful to use the depth marker located at the side of the ultrasound imaging screen to determine the approximate depth of the SCV and pleura location. Finally, if the patient is awake, a Valsalva maneuver can be useful to increase intrathoracic pressure, dilate the SCV, and confirm its identity (unless contraindicated).

Ultrasound view of the subclavian vessels during central line placement

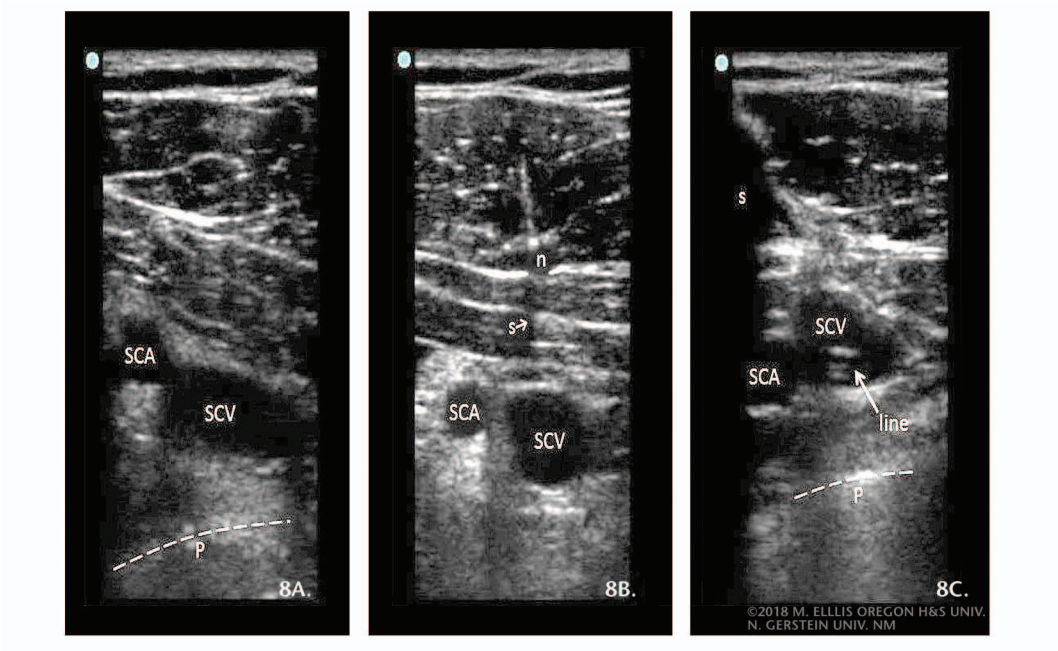


Fig. (8). A: Cross-sectional image of subclavian artery (SCA), subclavian vein (SCV), and pleura (P). **B**: Image of needle (n) and needle trajectory towards SVC, acoustic shadow from needle (s, indicated by arrow), SCA. **C**: Cross-sectional image post-cannulation; acoustic shadowing from clavicle (s), SCA; SCV with echogenic catheter noted in lumen (indicated by arrow). Fig. (**8A-8C**) provided by Margaret K. Menzel Ellis, M.D., Oregon Health Sciences University and Neal S. Gerstein, M.D., FASE, University of New Mexico Department of Anesthesiology and Critical Care Medicine, Albuquerque, New Mexico, USA.

Subclavian Vein Cannulation

Once you have prepared the insertion site and equipment using the sterile technique described above, establish local anesthesia by infiltration at the insertion site if appropriate. With a thin-walled, hollow needle, puncture the skin just distal to the transducer, and advance the needle at a 30degree angle to the skin, aiming toward the sternal notch, maintaining gentle negative pressure in the attached syringe per the Seldinger technique. Although the SCV is typically accessed immediately beneath the clavicle, the needle may not encounter the vein for several centimeters after skin entry depending on patient anatomy and body habitus. Continuous assessment of the depth of needle insertion relative to the previously measured depth of the target vein may decrease the risk of inadvertent pleural puncture and subsequent pneumothorax. Proceed with the remainder of the central line placement procedure using the Seldinger technique described above.

After the procedure is completed and the line is covered with a sterile dressing, an ultrasound scan of the bilateral IJ veins and contralateral and SCV can quickly assess for catheter malposition. On confirmatory, post-procedural chest radiography, the tip of catheter should be less than 2.9 cm distal to the tracheobronchial tree to ensure the catheter is not entering the right atrium [45].

The Axillary Vein

The **axillary vein** can also be cannulated in a very similar procedure to SCV cannulation. The axillary vein begins at the lower margin of the teres major muscle as a continuation of the brachial vein, and becomes the SCV once it crosses the lateral border of the first rib. Depending on whether the first rib or pleura can be visualized during the ultrasound scanning and the degree of medial *versus* lateral placement of the ultrasound transducer, the axillary vein may be the actual target cannulated.

There may be a number of advantages to **axillary vein** as compared to SCV cannulation. As compared to accessing the SCV, axillary vein cannulation may have less of an acute entry angle and trajectory comparatively. Hence, axillary vein cannulation may be associated with less mechanical stress on central line catheters or implanted cardiac device leads leading to less catheter obstruction or lead failures, respectively [46]. Furthermore, the axillary vein's course is outside the boundaries of the thoracic cage and may be associated with a lower risk of hemothorax or pneumothorax [47, 48]. If an arterial injury does occur during attempts to access the axillary vein, the axillary artery is more easily manually compressed and surgery access is more straightforward as compared to the SCA [49].

CANNULATION OF THE FEMORAL VEIN

Indications and Contraindications

Cannulation of the FV may be indicated whenever central venous access is needed and the IJV or SCV sites are not available due to trauma, recent surgery, or other conditions that affect the neck or chest. Cannulation of the FV is particularly useful in emergency situations when other procedures (cardiopulmonary resuscitation, endotracheal intubation, chest tube placement) are concurrently being performed and limit access to the patient's neck and upper chest. The FV is also a useful site for emergency hemodialysis or plasmapheresis access given its relatively straight trajectory. IJV or SCV access should arguably be avoided and might be difficult whenever the Trendelenburg position is contraindicated, for instance in the setting of elevated intracranial pressure or in patients at high risk for aspiration. In these situations, the FV may also be the best approach.

The FV should not be cannulated if recent trauma, surgery, or infection obscures the skin overlying the vein or distorts the surrounding anatomy. Furthermore, if the patient has a known proximal deep venous thrombosis or an injury to the ipsilateral iliac vein or the inferior vena cava, the connection between the FV and the heart may be interrupted and a femoral line should not be placed. The FV is not an ideal site for placement in an ambulatory patient or a patient who frequently flexes his or her hips, as repeated movement may lead to dislodgement or fracture of the catheter.

Ultrasound Visualization of the Femoral Vessels

Ultrasound View of the Femoral Vessels

The FV is located just medial to the femoral artery within the femoral triangle. This anatomical region is bordered superiorly by the inguinal ligament, medially by the adductor longus muscle, and laterally by the sartorius muscle. Position the patient supine and in slight reverse Trendelenburg to promote femoral venous engorgement. Stand at the patient's side, facing the patient's head. Once the sterile field, ultrasound, and equipment have been prepared, place the ultrasound transducer parallel and just distal to the inguinal ligament, within the femoral triangle. Ensure that the left and right sides of the ultrasound transducer correlate with left and right on the monitor, and translate the transducer medially and laterally until the femoral artery and vein are visualized in the center of the ultrasound screen. The vein may be less distinctly seen due to its depth, however color Doppler can be used to distinguish and confirm the location of the both vessels (Fig. **9**).

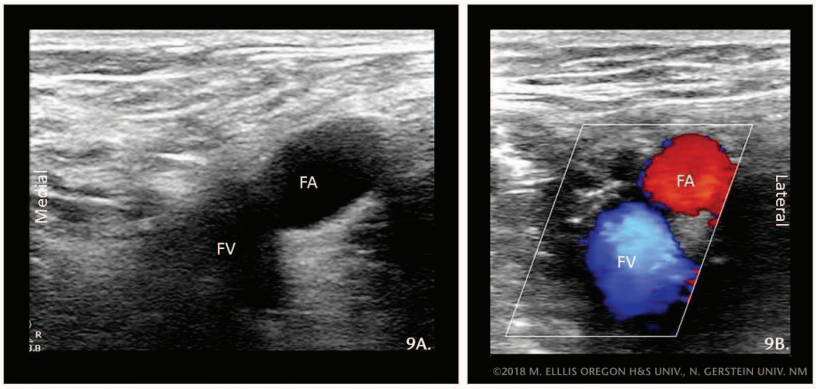


Fig. (9). A: A cross-sectional view of the left femoral artery (FA) and femoral vein (FV) is shown in this image. The artery lies just superficial and lateral to the vein. Not the indistinctness of the margin of the vein and between the two vessels. **B**: Color Doppler is used to distinguish arterial and venous blood flow Figs. (**9A and 9B**) provided by Margaret K. Menzel Ellis, M.D., Oregon Health Sciences University and Neal S. Gerstein, M.D., FASE, University of New Mexico Department of Anesthesiology and Critical Care Medicine, Albuquerque, New Mexico, USA.

Femoral Vein Cannulation

Insert the needle at a 45-degree perpendicular to the mid-point of the ultrasound transducer. Aim the needle cephalad and medial to avoid femoral artery puncture and advance, maintaining gentle negative pressure on the attached syringe. Once the needle enters the vein and free blood return has been established, complete the remainder of the procedure per the ultrasound-guided Seldinger technique described above. Of note, a longer catheter (20cm) is often preferable for FV central line placement given the greater distance between the entry site and the heart. A confirmatory radiograph is not necessary following FV central line placement, as there is no risk of pneumothorax with this procedure.

Ultrasound for Arterial Access

Arterial line placement for continuous blood pressure measurement and arterial blood gas sampling is frequently required in patients who are undergoing surgery or are critically ill. **There are many possible sites for placing an arterial line including the radial, ulnar, axillary, brachial, femoral, and dorsalis pedis arteries.**

Placing an arterial line first involves cannulating the artery, which is typically accomplished by identifying anatomical landmarks and palpating the pulse. Although this approach is often straightforward, it sometimes requires multiple attempts and is associated with relatively high failure rates. Numerous conditions such as anatomical variability, obesity, peripheral edema, and peripheral arterial

disease can further complicate placement. Arterial cannulation in patients with a weak or completely non-palpable pulse is especially challenging. **Non-pulsatile blood flow in the setting of a ventricular assist device or extracorporeal membrane oxygenation makes arterial cannulation *via* the traditional landmark and palpation method nearly impossible.** Moreover, every failed attempt at arterial line placement makes subsequent attempts significantly more challenging, as hematoma formation, vasospasm, and arterial dissection can obscure landmarks, making a previously bounding pulse difficult to palpate.

Ultrasound guided arterial line placement has emerged as an alternative to using landmarks and palpation, and the efficacy and superiority of ultrasound for this purpose is now fairly well established. In fact, prospective studies demonstrate that ultrasound-guided arterial line placement, as compared with traditional methods, results in higher success rates and shorter procedure times [50]. In one meta-analysis, ultrasound-guided arterial line placements were accomplished more frequently on the first attempt, with fewer attempts overall and a reduced incidence of hematoma formation [51].

As with central venous line placement, arterial line placement should be considered a sterile procedure, and sterile precautions should be taken. While uncommon, arterial catheter-related bloodstream infections (CRBSI) have been reported in several studies, and a large meta-analysis found that the rate of arterial line-related blood stream infection may even approach the rate of CRBSI seen with short-term central venous line [52].

Ultrasound Guided Radial Arterial Line Placement

The most frequent site for arterial line placement is the **radial artery**. It is an easily accessible peripheral location, and having a catheter in the radial artery is associated with a low incidence of complications, is generally well tolerated, and does not restrict patient movement to the same degree as a catheter that is placed in other sites such as the femoral artery or foot. Regardless of whether ultrasound or a more traditional method is used to locate the artery, arterial cannulation is almost always accomplished *via* the Seldinger or modified Seldinger technique as described above [53].

Ultrasound Visualization of the Radial Artery

The radial artery (RA, indicated by arrow) is a small, round, pulsatile structure when imaged in cross-section. It is often found at a very shallow distance; this image has a depth of field of 1cm, so the radial artery is approximately 0.3cm deep to the skin.

During ultrasound guided radial arterial line placement, supinate the patient's arm, extend the hand slightly, and secure the hand and arm (frequently on a foam or plastic arm board) to prevent movement. Stand or sit adjacent to the patient so that the angiocatheter or needle can be directed toward the patient's proximal arm. Prepare and drape the site and ultrasound transducer in the usual sterile fashion. Hold the ultrasound transducer with your non-dominant hand and position it 2-3 fingerbreadths proximal to the prominent joint of the scaphoid bone and distal radius in the patient's wrist [54]. Align the ultrasound transducer so its left and right sides correlate with left and right on the monitor. The radial artery appears as a small, round, black, pulsatile structure (Fig. **10**), and is difficult or impossible to compress with the ultrasound transducer. Color Doppler can be used to confirm blood flow within the artery. Once the artery is located, optimize the ultrasound image by increasing or decreasing the depth of field and translating the transducer medially or laterally so that the artery is in the center of the ultrasound screen.

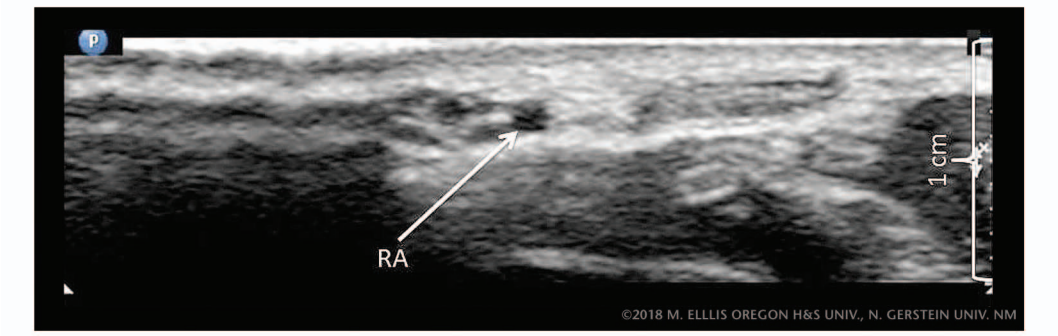


Fig. (10). Ultrasound view of the radial artery. Images provided by Margaret K. Menzel Ellis, M.D., Oregon Health Sciences University and Neal S. Gerstein, M.D., FASE, University of New Mexico Department of Anesthesiology and Critical Care Medicine, Albuquerque, New Mexico, USA.

Ultrasound Artery Cannulation

Insert and advance the angiocatheter (or needle) at about a 45degree angle to the skin, while continuously watching the ultrasound screen and frequently checking for a "flash" of blood in the angiocatheter. Given the small size of the artery, only very slight adjustments in the catheter's position are generally required to maintain or alter the desired trajectory. Once the artery is entered and pulsatile blood flow is seen, flatten the catheter's angle, verify that pulsatile flow is still present, then insert a guide wire and complete the procedure by advancing the catheter into the lumen of the artery over the guide wire.

Not infrequently, a small "flash" of blood is briefly seen in the chamber of the angiocatheter, but brisk, continuous arterial blood flow is not obtained. When this

situation occurs, utilizing the "through and through" technique can be helpful. When performing this technique, first purposefully advance the angiocatheter through the back wall of the artery without altering its trajectory. Next, remove the needle, and then slowly withdraw the angiocatheter until its tip is within the lumen of the artery, at which time brisk, pulsatile arterial blood flow will be obtained. At this point, pass a guidewire through the angiocatheter, then advance the catheter over the guidewire and into the artery. Finally, remove the guidewire and then secure the catheter in place. This technique has been shown to be faster and more reliable than the modified Seldinger technique in at least one randomized study [53].

When radial arterial line placement is especially difficult, a longitudinal view can be used to advance the guidewire and confirm its location within the lumen of the artery. Obtain a longitudinal view by rotating the ultrasound transducer orthogonal to (90degrees from) the cross-sectional view, such that the transducer is oriented parallel to the artery. Use the longitudinal view to confirm the position of the guidewire position prior to advancing the catheter.

As mentioned above, numerous other sites can be used for arterial line placement. **Ultrasound guidance is especially useful for accessing deeper arteries (*i.e.* brachial or axillary)**, but can be successfully employed for any of these procedures.

Ultrasound for Difficult Peripheral Intravenous Access

Numerous conditions complicate peripheral intravenous (IV) catheter placement. Obesity hinders placement of peripheral intravenous catheters [55, 56] because in these patient's peripheral veins can be deep, and thus difficult or impossible to palpate or visualize. Patients with chronic kidney disease are prone to develop vascular scarring from repeated vascular access procedures, making peripheral intravenous catheter placement difficult. Furthermore, the presence of an arteriovenous fistula generally precludes tourniquet placement and peripheral intravenous catheter placement on the extremity in which the fistula is located [57]. Chemotherapy patients often have veins that are sclerotic or scarred, as chemotherapeutic agents can cause local vascular damage or systemic tissue changes. Similar changes can be seen following radiation therapy [58]. Patients who have undergone mastectomy with axillary lymph node dissection, or other cancer surgeries that disrupt the lymphatic system, are at risk for lymphedema that may be exacerbated by intravenous infusion and can also complicate peripheral intravenous line placement. Establishing vascular access in intravenous drug users tends to be difficult [59 - 61]. Illicit drugs can damage veins because they are often prepared with caustic ingredients, are generally not sterile, and are

sometimes injected using a heated solution. Since illicit drugs tend to have a short duration of peak effect, users often inject themselves multiple times per day. Veins in this patient population may be sclerotic, thrombosed, or infected. Moreover, venous insufficiency in these patients leads to venous stasis and edema in the affected limbs [62].

In the patient with known or suspected difficult IV access, ultrasound-guided peripheral intravenous line placement offers a number of benefits over a traditional approach, including a reduction in the number of attempts needed, reduced total procedure time, and improved patient satisfaction [63]. Furthermore, in emergency department patients with difficult peripheral IV access, the use of ultrasound-guidance carries a higher success rate than external jugular vein cannulation [60]. Ultrasound allows deep veins such as the basilic and cephalic veins of the upper arm, which are rarely visible or palpable on physical examination, to be accessed [64, 65]. In patients with challenging peripheral intravenous access, the increased success rate with ultrasound guidance can sometimes prevent the unnecessary insertion of central venous lines [66].

Technique for Ultrasound Guided Peripheral Intravenous Line Placement

Ultrasound guidance should be considered after two failed attempts at standard IV catheter placement, or if the patient **endorses a history of difficult intravenous placement** [67]. As with any invasive procedure, universal precautions and hand washing are mandatory for this procedure, although sterile gloves are not needed.

Ultrasound Visualization of a Target Peripheral Vein

A linear array probe is used to locate and cannulate a peripheral vein in the forearm. The vein (**v**) can be clearly seen (**a**) as a round structure in this cross-sectional view, which easily compresses with downward pressure (**b**) from the approaching needle (**n**, indicated by arrow). The tip of the needle is seen penetrating the superficial wall of the vein (**c**). Finally, the angiocathteter (circled) can be seen as a hyperechoic structure outlined) within the vein (**d**).

Apply a tourniquet and then use a cross-sectional view to evaluate the sonoanatomy and identify a suitable target vein. **A linear array transducer with a frequency of 5-13megahertz is recommended for this procedure** [67]. Veins are thin walled and are easily compressible (Fig. **11**), while arteries are thicker walled, are not easily compressible and are visibly pulsatile [67]. Adjust the depth and gain, and translate the transducer side-to-side to optimize the view of the target vein. **Color Doppler** can be used to help distinguish a deep vein from an artery; an artery will have pulsatile flow while a vein will be pulseless. Note that

larger diameter veins with a depth less than 1.6cm are easier to cannulate [68]. For deeper veins, the use of a longer-length catheter may be necessary [67, 69].

Once a suitable target vein is identified, clean the skin with an antiseptic swab, and clean the ultrasound transducer with an appropriate cleaning solution or apply a sterile ultrasound sleeve. Apply ultrasound gel or lubricant to the target area. Select an angiocatheter of appropriate gauge and length based on the size and depth of the target vein. Either a longitudinal or cross-sectional technique can be used for ultrasound-guided peripheral intravenous line placement [70]. To find the longitudinal view, first locate the vein in cross-sectional and then rotate the ultrasound transducer 90° to visualize the vein longitudinally. **Ensure the ultrasound transducer is aligned so its left and right sides correlate with left and right on the monitor; the target vessel should be in the center of the screen.**

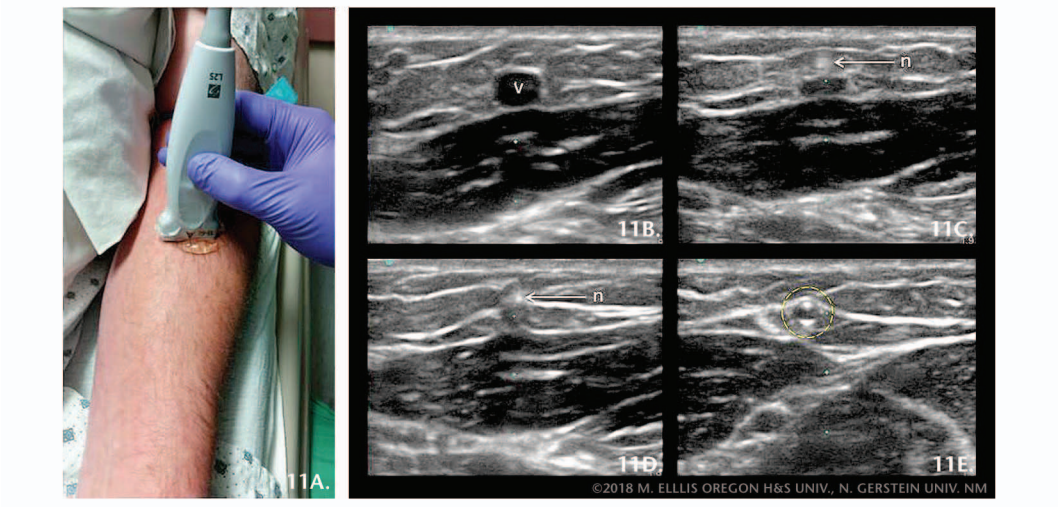


Fig. (11). Peripheral venous line placement with ultrasound. Images provided by Margaret K. Menzel Ellis, M.D., Oregon Health Sciences University and Neal S. Gerstein, M.D., FASE, University of New Mexico Department of Anesthesiology and Critical Care Medicine, Albuquerque, New Mexico, USA.

Cannulation of The Peripheral Vein

Insert and advance the needle through the skin distal to the ultrasound transducer at an angle of approximately 45degrees, while observing the trajectory of the needle on the ultrasound screen. In a cross-sectional technique, the needle will appear as a bright dot as it passes beneath the ultrasound transducer (Fig. **11**). If using a longitudinal technique, as long as the needle is perfectly aligned with the ultrasound plane, the entire length of the needle including its tip will be visible throughout the procedure. When the tip of the needle enters the lumen of the vein,

a "flash" of blood is seen in the chamber of the angiocatheter. At this point, flatten the angle of the angiocatheter, advance the angiocatheter over the needle and into the vein, and release the tourniquet. Confirm proper placement by drawing back on the angiocatheter and injecting saline. Blood should draw back freely, and there should be no resistance or evidence of extravasation when saline is injected. In addition, the ultrasound can be used to locate the angiocatheter in the lumen of the vein, in either the cross-sectional (Fig. **11**) or longitudinal view.

Occasionally, blood flow is achieved even though the angiocatheter cannot be advanced completely into the vein without meeting resistance; often this situation occurs because of an intravenous valve. In this situation, use the modified Seldinger technique to insert a guidewire through the angiocatheter and open the valve, then advance the angiocatheter over the guidewire into the lumen of the vessel [65]. The location of the guidewire can also be confirmed with ultrasound.

CONCLUSION

The use of ultrasound for central, peripheral, and arterial vascular access procedures has significantly improved the safety, efficacy, and range of possibilities when performing these procedures. Becoming familiar with practical use of ultrasound technology, including its various applications for vascular access (Figs. **12 - 14**), strengthens the anesthesiologist's role as a perioperative and hospital-wide consultant.

RESOURCES FOR PROVIDERS

Several excellent resources are available for continued ultrasound-guided vascular access education, including:

New England Journal of Medicine videos: These free, online videos published by the New England Journal of Medicine provide concise, clearly illustrated instruction for a wide variety of medical procedures, including ultrasound- guided central line, arterial line, and peripheral line placement. They can be accessed through the New England Journal of Medicine website (http://www.nejm.org/multimedia/medical-videos).

Medscape: Medscape offers free, concise online descriptions of several ultrasound-guided vascular access procedures, which can be accessed through searching their website. Registration is required. (http://reference.medscape.com)

LearnICU: This resource from the Society of Critical Care Medicine offers educational materials for a variety of critical care procedures and can be accessed after free registration online. (https://www.learnicu.org)

Product specific education: Many ultrasound machine manufacturers offer on-site training and additional resources for customers or prospective customers. Information about these resources can often be found under the "education" section of the manufacturer's website.

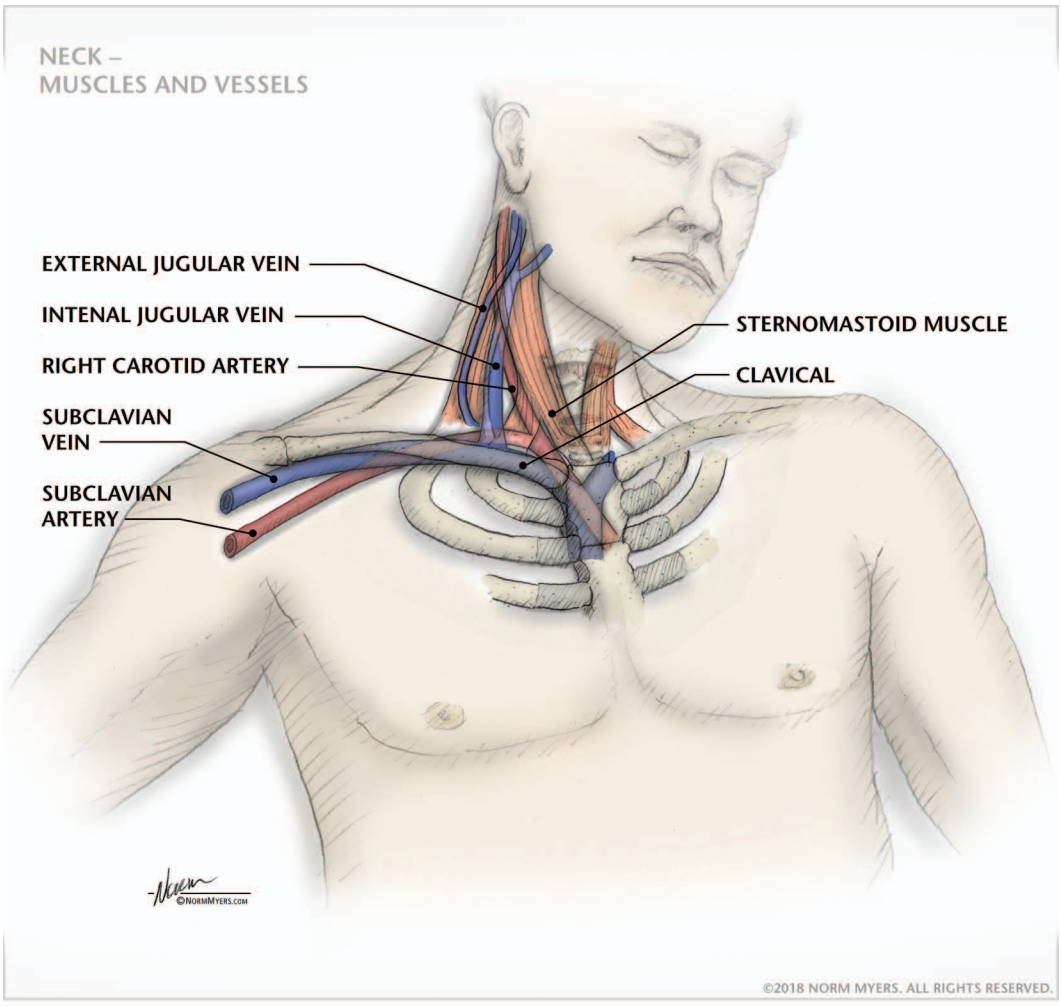


Fig. (12). Neck (Muscles and Vessels). Image provided by Norm Myers.

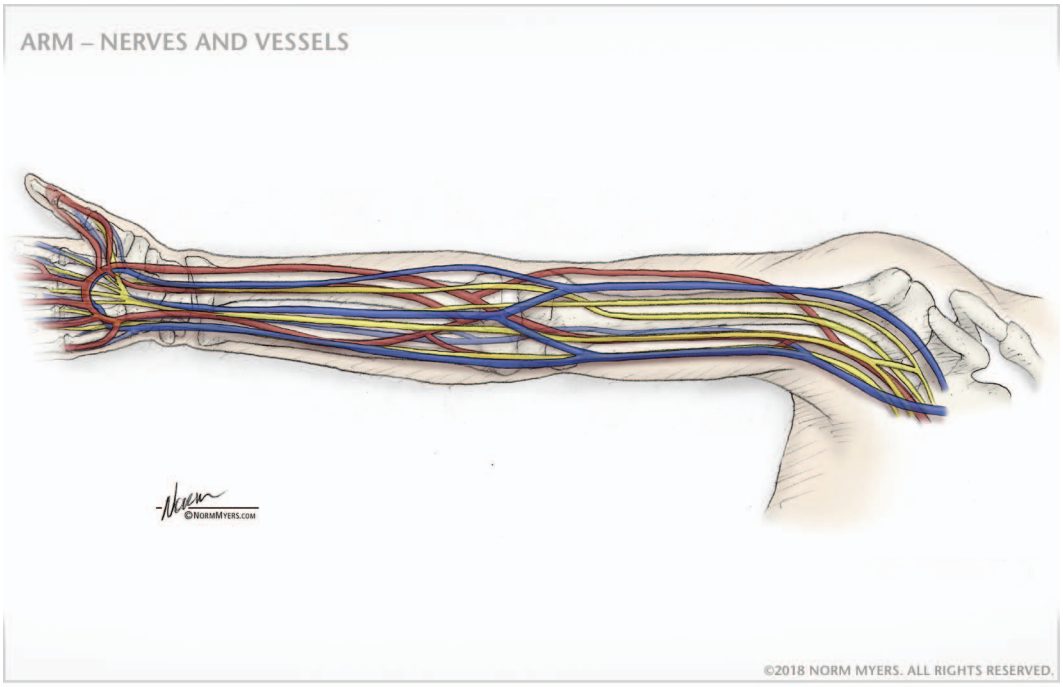


Fig. (13). Arm (Nerves and Vessels). Image provided by Norm Myers.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

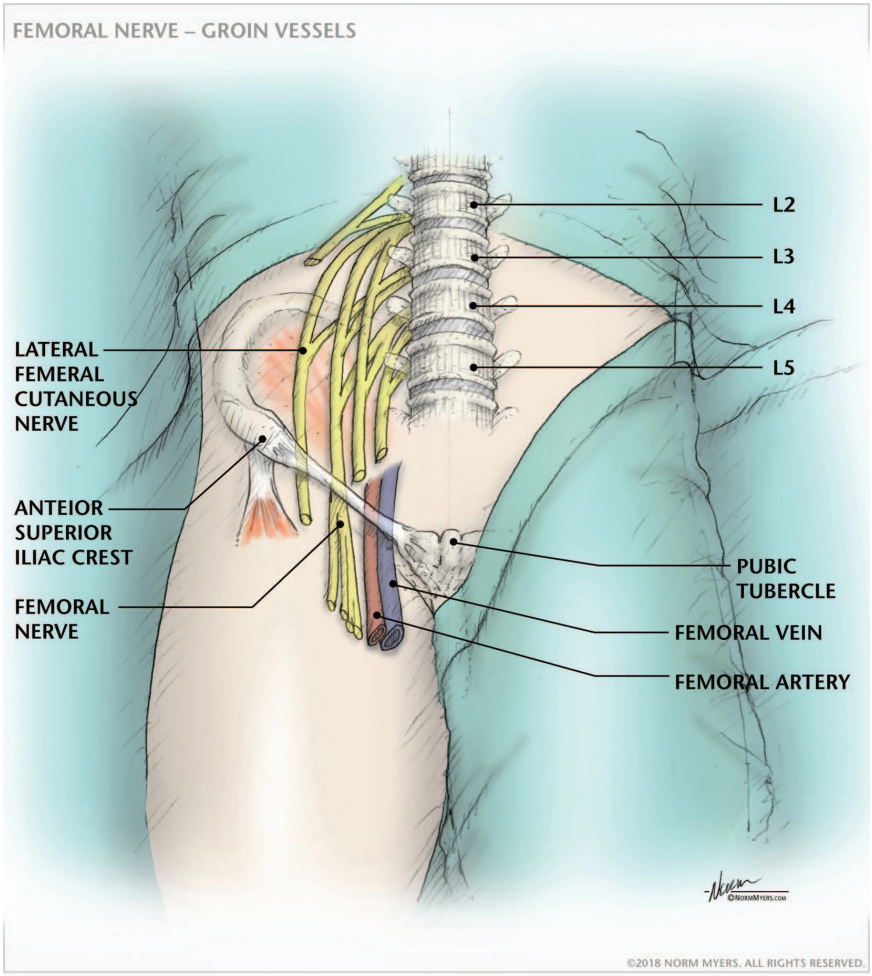


Fig. (14). Femoral Nerve (Groin Vessels). Image provided by Norm Myers.

REFERENCES

[1] Vezzani A, Manca T, Vercelli A, Braghieri A, Magnacavallo A. Ultrasonography as a guide during vascular access procedures and in the diagnosis of complications. J Ultrasound 2013; 16(4): 161-70. [http://dx.doi.org/10.1007/s40477-013-0046-5] [PMID: 24432170]

[2] Lamperti M, Bodenham AR, Pittiruti M, *et al.* International evidence-based recommendations on ultrasound-guided vascular access. Intensive Care Med 2012; 38(7): 1105-17. [http://dx.doi.org/10.1007/s00134-012-2597-x] [PMID: 22614241]

[3] Brass P, Hellmich M, Kolodziej L, Schick G, Smith AF. Ultrasound guidance *versus* anatomical landmarks for subclavian or femoral vein catheterization. Cochrane Database Syst Rev 2015; 1: CD011447. [Review]. [PMID: 25575245]

[4] Shekelle PG, Wachter RM, Pronovost PJ, *et al.* Making health care safer II: an updated critical analysis of the evidence for patient safety practices. Evid Rep Technol Assess (Full Rep) 2013; (211): 1-945.
[PMID: 24423049]

[5] Arbona FL, Khabiri B, Norton JA. Ultrasound basics for the busy novice practitioner. Int Anesthesiol Clin 2011; 49(4): 34-51.
[http://dx.doi.org/10.1097/AIA.0b013e318219b6b4] [PMID: 21956076]

[6] Enriquez JL, Wu TS. An introduction to ultrasound equipment and knobology. Crit Care Clin 2014; 30(1): 25-45, v. [v.].
[http://dx.doi.org/10.1016/j.ccc.2013.08.006] [PMID: 24295840]

[7] Shanthanna H. Review of essential understanding of ultrasound physics and equipment operation. World Journal of Anesthesiology 2014; 3(1): 12.
[http://dx.doi.org/10.5313/wja.v3.i1.12]

[8] Ortega R, Song M, Hansen CJ, Barash P. Videos in clinical medicine. Ultrasound-guided internal jugular vein cannulation. N Engl J Med 2010; 362(16): e57.
[http://dx.doi.org/10.1056/NEJMvcm0810156] [PMID: 20410510]

[9] Fragou M, Gravvanis A, Dimitriou V, *et al.* Real-time ultrasound-guided subclavian vein cannulation *versus* the landmark method in critical care patients: a prospective randomized study. Crit Care Med 2011; 39(7): 1607-12.
[http://dx.doi.org/10.1097/CCM.0b013e318218a1ae] [PMID: 21494105]

[10] Hind D, Calvert N, McWilliams R, *et al.* Ultrasonic locating devices for central venous cannulation: meta-analysis. BMJ 2003; 327(7411): 361.
[http://dx.doi.org/10.1136/bmj.327.7411.361] [PMID: 12919984]

[11] Brooks AJ, Alfredson M, Pettigrew B, Morris DL. Ultrasound-guided insertion of subclavian venous access ports. Ann R Coll Surg Engl 2005; 87(1): 25-7.
[http://dx.doi.org/10.1308/1478708051441] [PMID: 15720903]

[12] Gualtieri E, Deppe SA, Sipperly ME, Thompson DR. Subclavian venous catheterization: greater success rate for less experienced operators using ultrasound guidance. Crit Care Med 1995; 23(4): 692-7.
[http://dx.doi.org/10.1097/00003246-199504000-00018] [PMID: 7661944]

[13] Troianos CA, Hartman GS, Glas KE, *et al.* Guidelines for performing ultrasound guided vascular cannulation: recommendations of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. J Am Soc Echocardiogr 2011; 24(12): 1291-318.
[http://dx.doi.org/10.1016/j.echo.2011.09.021] [PMID: 22115322]

[14] Troianos CA, Hartman GS, Glas KE, *et al.* Special articles: guidelines for performing ultrasound guided vascular cannulation: recommendations of the American Society of Echocardiography and the Society Of Cardiovascular Anesthesiologists. Anesth Analg 2012; 114(1): 46-72.
[http://dx.doi.org/10.1213/ANE.0b013e3182407cd8] [PMID: 22127816]

[15] O'Grady NP, Alexander M, Burns LA, *et al.* Guidelines for the prevention of intravascular catheter-related infections. Am J Infect Control 2011; 39(4) (Suppl. 1): S1-S34.
[http://dx.doi.org/10.1016/j.ajic.2011.01.003] [PMID: 21511081]

[16] Legler D, Nugent M. Doppler localization of the internal jugular vein facilitates central venous cannulation. Anesthesiology 1984; 60(5): 481-2.
[http://dx.doi.org/10.1097/00000542-198405000-00016] [PMID: 6711857]

[17] Denys BG, Uretsky BF, Reddy PS. Ultrasound-assisted cannulation of the internal jugular vein. A prospective comparison to the external landmark-guided technique. Circulation 1993; 87(5): 1557-62.
[http://dx.doi.org/10.1161/01.CIR.87.5.1557] [PMID: 8491011]

[18] Karakitsos D, Labropoulos N, De Groot E, *et al.* Real-time ultrasound-guided catheterisation of the

internal jugular vein: a prospective comparison with the landmark technique in critical care patients. Crit Care 2006; 10(6): R162.
[http://dx.doi.org/10.1186/cc5101] [PMID: 17112371]

[19] Leung J, Duffy M, Finckh A. Real-time ultrasonographically-guided internal jugular vein catheterization in the emergency department increases success rates and reduces complications: a randomized, prospective study. Ann Emerg Med 2006; 48(5): 540-7.
[http://dx.doi.org/10.1016/j.annemergmed.2006.01.011] [PMID: 17052555]

[20] Weiner MM, Geldard P, Mittnacht AJ. Ultrasound-guided vascular access: a comprehensive review. J Cardiothorac Vasc Anesth 2013; 27(2): 345-60.
[http://dx.doi.org/10.1053/j.jvca.2012.07.007] [PMID: 22995457]

[21] Rupp SM, Apfelbaum JL, Blitt C, *et al.* Practice guidelines for central venous access: a report by the American Society of Anesthesiologists Task Force on Central Venous Access. Anesthesiology 2012; 116(3): 539-73.
[http://dx.doi.org/10.1097/ALN.0b013e31823c9569] [PMID: 22307320]

[22] Ge X, Cavallazzi R, Li C, Pan SM, Wang YW, Wang FL. Central venous access sites for the prevention of venous thrombosis, stenosis and infection. Cochrane Database Syst Rev 2012; (3): CD004084. [Review].
[PMID: 22419292]

[23] Parienti JJ, du Cheyron D, Timsit JF, *et al.* Meta-analysis of subclavian insertion and nontunneled central venous catheter-associated infection risk reduction in critically ill adults. Crit Care Med 2012; 40(5): 1627-34.
[http://dx.doi.org/10.1097/CCM.0b013e31823e99cb] [PMID: 22511140]

[24] Deshpande KS, Hatem C, Ulrich HL, *et al.* The incidence of infectious complications of central venous catheters at the subclavian, internal jugular, and femoral sites in an intensive care unit population. Crit Care Med 2005; 33(1): 13-20.
[http://dx.doi.org/10.1097/01.CCM.0000149838.47048.60] [PMID: 15644643]

[25] Marik PE, Flemmer M, Harrison W. The risk of catheter-related bloodstream infection with femoral venous catheters as compared to subclavian and internal jugular venous catheters: a systematic review of the literature and meta-analysis. Crit Care Med 2012; 40(8): 2479-85.
[http://dx.doi.org/10.1097/CCM.0b013e318255d9bc] [PMID: 22809915]

[26] Timsit JF, Bouadma L, Mimoz O, *et al.* Jugular *versus* femoral short-term catheterization and risk of infection in intensive care unit patients. Causal analysis of two randomized trials. Am J Respir Crit Care Med 2013; 188(10): 1232-9.
[http://dx.doi.org/10.1164/rccm.201303-0460OC] [PMID: 24127770]

[27] Mermel LA, McCormick RD, Springman SR, Maki DG. The pathogenesis and epidemiology of catheter-related infection with pulmonary artery Swan-Ganz catheters: a prospective study utilizing molecular subtyping. Am J Med 1991; 91(3B): 197S-205S.
[http://dx.doi.org/10.1016/0002-9343(91)90369-9] [PMID: 1928165]

[28] Marik PEFM, Flemmer M, Harrison W. The risk of catheter-related bloodstream infection with femoral venous catheters as compared to subclavian and internal jugular venous catheters: a systematic review of the literature and meta-analysis. Crit Care Med 2012; 40(8): 2479-85.
[http://dx.doi.org/10.1097/CCM.0b013e318255d9bc] [PMID: 22809915]

[29] Eisen LA, Narasimhan M, Berger JS, Mayo PH, Rosen MJ, Schneider RF. Mechanical complications of central venous catheters. J Intensive Care Med 2006; 21(1): 40-6.
[http://dx.doi.org/10.1177/0885066605280884] [PMID: 16698743]

[30] Malinoski D, Ewing T, Bhakta A, *et al.* Which central venous catheters have the highest rate of catheter-associated deep venous thrombosis: a prospective analysis of 2,128 catheter days in the surgical intensive care unit. J Trauma Acute Care Surg 2013; 74(2): 454-60.
[http://dx.doi.org/10.1097/TA.0b013e31827a0b2f] [PMID: 23354238]

[31] McGee DC, Gould MK. Preventing complications of central venous catheterization. N Engl J Med 2003; 348(12): 1123-33.
[http://dx.doi.org/10.1056/NEJMra011883] [PMID: 12646670]

[32] Goeschel CA, Holzmueller CG, Cosgrove SE, Ristaino P, Pronovost PJ. Infection preventionist checklist to improve culture and reduce central line-associated bloodstream infections. Joint Commission journal on quality and patient safety / Joint Commission Resources 2010; 36(12): 571-5.
[http://dx.doi.org/10.1016/S1553-7250(10)36085-5]

[33] Song Y, Messerlian AK, Matevosian R. A potentially hazardous complication during central venous catheterization: lost guidewire retained in the patient. J Clin Anesth 2012; 24(3): 221-6.
[http://dx.doi.org/10.1016/j.jclinane.2011.07.003] [PMID: 22495087]

[34] Higgs ZCJ, Macafee DAL, Braithwaite BD, Maxwell-Armstrong CA. The Seldinger technique: 50 years on. Lancet 2005; 366(9494): 1407-9.
[http://dx.doi.org/10.1016/S0140-6736(05)66878-X] [PMID: 16226619]

[35] Lichtenstein DA, Mezière G, Lascols N, *et al.* Ultrasound diagnosis of occult pneumothorax. Crit Care Med 2005; 33(6): 1231-8.
[http://dx.doi.org/10.1097/01.CCM.0000164542.86954.B4] [PMID: 15942336]

[36] Vezzani A, Brusasco C, Palermo S, Launo C, Mergoni M, Corradi F. Ultrasound localization of central vein catheter and detection of postprocedural pneumothorax: an alternative to chest radiography. Crit Care Med 2010; 38(2): 533-8.
[http://dx.doi.org/10.1097/CCM.0b013e3181c0328f] [PMID: 19829102]

[37] Flanagan JP, Gradisar IA, Gross RJ, Kelly TR. Air embolus--a lethal complication of subclavian venipuncture. N Engl J Med 1969; 281(9): 488-9.
[http://dx.doi.org/10.1056/NEJM196908282810907] [PMID: 5796967]

[38] English ICWFR, Frew RM, Pigott JF, Zaki M. Percutaneous cannulation of the internal jugular vein. Thorax 1969; 24(4): 496-7.
[http://dx.doi.org/10.1136/thx.24.4.496] [PMID: 5795652]

[39] DeAngelis V, Denny J, Chyu D, *et al.* The Optimal Angle of Head Rotation for Internal Jugular Cannulation as Determined by Ultrasound Evaluation. J Cardiothorac Vasc Anesth 2015; 29(5): 1257-60.
[http://dx.doi.org/10.1053/j.jvca.2015.02.007] [PMID: 25998069]

[40] Wang R, Snoey ER, Clements RC, Hern HG, Price D. Effect of head rotation on vascular anatomy of the neck: an ultrasound study. J Emerg Med 2006; 31(3): 283-6.
[http://dx.doi.org/10.1016/j.jemermed.2005.12.026] [PMID: 16982362]

[41] Maecken T, Marcon C, Bomas S, Zenz M, Grau T. Relationship of the internal jugular vein to the common carotid artery: implications for ultrasound-guided vascular access. Eur J Anaesthesiol 2011; 28(5): 351-5.
[http://dx.doi.org/10.1097/EJA.0b013e328341a492] [PMID: 21150630]

[42] Braner DA, Lai S, Eman S, Tegtmeyer K. Videos in clinical medicine. Central venous catheterization--subclavian vein. N Engl J Med 2007; 357(24): e26.
[http://dx.doi.org/10.1056/NEJMvcm074357] [PMID: 18077803]

[43] Lalu MM, Fayad A, Ahmed O, *et al.* Ultrasound-Guided Subclavian Vein Catheterization: A Systematic Review and Meta-Analysis. Crit Care Med 2015; 43(7): 1498-507.
[http://dx.doi.org/10.1097/CCM.0000000000000973] [PMID: 25803646]

[44] Fragou M, Gravvanis A, Dimitriou V, *et al.* Real-time ultrasound-guided subclavian vein cannulation *versus* the landmark method in critical care patients: a prospective randomized study. Crit Care Med 2011; 39(7): 1607-12.
[http://dx.doi.org/10.1097/CCM.0b013e318218a1ae] [PMID: 21494105]

[45] Aslamy Z, Dewald CL, Heffner JE. MRI of central venous anatomy: implications for central venous

catheter insertion. Chest 1998; 114(3): 820-6.
[http://dx.doi.org/10.1378/chest.114.3.820] [PMID: 9743173]

[46] Mirza B, Vanek VW, Kupensky DT. Pinch-off syndrome: case report and collective review of the literature. Am Surg 2004; 70(7): 635-44.
[PMID: 15279190]

[47] Lin CP, Wang YC, Lin FS, Huang CH, Sun WZ. Ultrasound-assisted percutaneous catheterization of the axillary vein for totally implantable venous access device. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 2011; 37(5): 448-51.
[http://dx.doi.org/10.1016/j.ejso.2011.01.026]

[48] Uhlenkott MC, Sathishkumar S, Murray WB, McQuillan PM, Das Adhikary S. Real-time multimodal axillary vein imaging enhances the safety and efficacy of axillary vein catheterization in neurosurgical intensive care patients. J Neurosurg Anesthesiol 2013; 25(1): 62-5.
[http://dx.doi.org/10.1097/ANA.0b013e318264542e] [PMID: 22871952]

[49] Sharma A, Bodenham AR, Mallick A. Ultrasound-guided infraclavicular axillary vein cannulation for central venous access. Br J Anaesth 2004; 93(2): 188-92.
[http://dx.doi.org/10.1093/bja/aeh187] [PMID: 15220180]

[50] Shiver S, Blaivas M, Lyon M. A prospective comparison of ultrasound-guided and blindly placed radial arterial catheters. Acad Emerg Med 2006; 13(12): 1275-9.
[http://dx.doi.org/10.1197/j.aem.2006.07.015] [PMID: 17079789]

[51] Gu WJ, Tie HT, Liu JC, Zeng XT. Efficacy of ultrasound-guided radial artery catheterization: a systematic review and meta-analysis of randomized controlled trials. Crit Care 2014; 18(3): R93.
[http://dx.doi.org/10.1186/cc13862] [PMID: 24887241]

[52] O'Horo JC, Maki DG, Krupp AE, Safdar N. Arterial catheters as a source of bloodstream infection: a systematic review and meta-analysis. Crit Care Med 2014; 42(6): 1334-9.
[http://dx.doi.org/10.1097/CCM.0000000000000166] [PMID: 24413576]

[53] Pancholy SB, Sanghvi KA, Patel TM. Radial artery access technique evaluation trial: randomized comparison of Seldinger *versus* modified Seldinger technique for arterial access for transradial catheterization. Catheter Cardiovasc Interv 2012; 80(2): 288-91.
[http://dx.doi.org/10.1002/ccd.23445] [PMID: 22419562]

[54] Brzezinski M, Luisetti T, London MJ. Radial artery cannulation: a comprehensive review of recent anatomic and physiologic investigations. Anesth Analg 2009; 109(6): 1763-81.
[http://dx.doi.org/10.1213/ANE.0b013e3181bbd416] [PMID: 19923502]

[55] Gregg SC, Murthi SB, Sisley AC, Stein DM, Scalea TM. Ultrasound-guided peripheral intravenous access in the intensive care unit. J Crit Care 2010; 25(3): 514-9.
[http://dx.doi.org/10.1016/j.jcrc.2009.09.003] [PMID: 19836193]

[56] Juvin P, Blarel A, Bruno F, Desmonts J-M. Is peripheral line placement more difficult in obese than in lean patients? Anesth Analg 2003; 96(4): 1218.
[http://dx.doi.org/10.1213/01.ANE.0000050570.85195.29] [PMID: 12651688]

[57] Scheer B, Perel A, Pfeiffer UJ. Clinical review: complications and risk factors of peripheral arterial catheters used for haemodynamic monitoring in anaesthesia and intensive care medicine. Crit Care 2002; 6(3): 199-204.
[http://dx.doi.org/10.1186/cc1489] [PMID: 12133178]

[58] S Wells. Venous access in oncology and haematology patients: part one. Nurs Stand 2007; 22(52): 39-46.
[PMID: 18494446]

[59] Brannam L, Blaivas M, Lyon M, Flake M. Emergency nurses' utilization of ultrasound guidance for placement of peripheral intravenous lines in difficult-access patients. Acad Emerg Med 2004; 11(12):

1361-3.
[http://dx.doi.org/10.1197/j.aem.2004.08.027] [PMID: 15576530]

[60] Costantino TG, Kirtz JF, Satz WA. Ultrasound-guided peripheral venous access *vs*. the external jugular vein as the initial approach to the patient with difficult vascular access. J Emerg Med 2010; 39(4): 462-7.
[http://dx.doi.org/10.1016/j.jemermed.2009.02.004] [PMID: 19303238]

[61] Egan G, Healy D, O'Neill H, Clarke-Moloney M, Grace PA, Walsh SR. Ultrasound guidance for difficult peripheral venous access: systematic review and meta-analysis. Emerg Med J 2013; 30(7): 521-6.
[http://dx.doi.org/10.1136/emermed-2012-201652] [PMID: 22886890]

[62] MD Stein. Medical Complications of Intravenous Drug Use. J Gen Intern Med 1990; 5: 249-58.
[http://dx.doi.org/10.1007/BF02600544] [PMID: 2187962]

[63] Costantino TG, Parikh AK, Satz WA, Fojtik JP. Ultrasonography-guided peripheral intravenous access *versus* traditional approaches in patients with difficult intravenous access. Ann Emerg Med 2005; 46(5): 456-61.
[http://dx.doi.org/10.1016/j.annemergmed.2004.12.026] [PMID: 16271677]

[64] Keyes LEFB, Frazee BW, Snoey ER, Simon BC, Christy D. Ultrasound-guided brachial and basilic vein cannulation in emergency department patients with difficult intravenous access. Ann Emerg Med 1999; 34(6): 711-4.
[http://dx.doi.org/10.1016/S0196-0644(99)70095-8] [PMID: 10577399]

[65] Mahler SA, Wang H, Lester C, Conrad SA. Ultrasound-guided peripheral intravenous access in the emergency department using a modified Seldinger technique. J Emerg Med 2010; 39(3): 325-9.
[http://dx.doi.org/10.1016/j.jemermed.2009.02.013] [PMID: 19303241]

[66] Au AK, Rotte MJ, Grzybowski RJ, Ku BS, Fields JM. Decrease in central venous catheter placement due to use of ultrasound guidance for peripheral intravenous catheters. Am J Emerg Med 2012; 30(9): 1950-4.
[http://dx.doi.org/10.1016/j.ajem.2012.04.016] [PMID: 22795988]

[67] Joing S, Strote S, Caroon L, *et al.* Ultrasound-Guided Peripheral IV Placement. N Engl J Med 2012; 366(25): e38-40.
[http://dx.doi.org/10.1056/NEJMvcm1005951] [PMID: 22716992]

[68] Panebianco NL, Fredette JM, Szyld D, Sagalyn EB, Pines JM, Dean AJ. What you see (sonographically) is what you get: vein and patient characteristics associated with successful ultrasound-guided peripheral intravenous placement in patients with difficult access. Acad Emerg Med 2009; 16(12): 1298-303.
[http://dx.doi.org/10.1111/j.1553-2712.2009.00520.x] [PMID: 19912132]

[69] Elia F, Ferrari G, Molino P, *et al.* Standard-length catheters *vs*. long catheters in ultrasound-guided peripheral vein cannulation. Am J Emerg Med 2012; 30(5): 712-6.
[http://dx.doi.org/10.1016/j.ajem.2011.04.019] [PMID: 21703801]

[70] Mahler SA, Wang H, Lester C, Skinner J, Arnold TC, Conrad SA. Short- *vs*. long-axis approach to ultrasound-guided peripheral intravenous access: a prospective randomized study. Am J Emerg Med 2011; 29(9): 1194-7.
[http://dx.doi.org/10.1016/j.ajem.2010.07.015] [PMID: 20951527]

CHAPTER 6

Bleeding and Clotting: Blood and Drugs

Monica B. Pagano[1,*], **Aaron S. Hess**[2] and **John R. Hess**[1]

[1] *Transfusion Medicine, Department of Laboratory Medicine, University of Washington, Seattle, WA, USA*

[2] *Department of Anesthesiology, University of Wisconsin, Madison, WI, USA*

Abstract: Uncontrolled hemorrhage from trauma, surgery, or post-partum is a major cause of death, but more people die from clotting, as heart attacks, strokes, or thromboembolism. The coagulation system underlies this complex interaction between bleeding and clotting. There are numerous blood components, biologicals, and drugs that affect bleeding and clotting; a basic understanding is requisite for successful perioperative care. This chapter provides an essential review of primary and secondary hemostasis and fibrinolysis, conventionally available tests of coagulation, common causes of hemorrhage, and commonly used anticoagulant drugs and platelet inhibitors. Finally, it discusses current concepts of the use of blood components to reverse coagulopathy and the transfusion reactions that can complicate blood therapy.

Keywords: Anticoagulants, Antiplatelet agents, ACT, Clotting, Coagulation testing, Congenital clotting disorders, Fibrinolysis, Hemorrhage, Primary hemostasis, Secondary hemostasis, Thrombosis, Von Willibrands Disease.

INTRODUCTION

- **Uncontrolled bleeding is a major cause of death**. Each year, approximately 15,000 trauma patients die in U.S. hospitals of uncontrolled hemorrhage. Mortality in cardiac surgery and transplant surgery are strongly correlated with total blood use. Post-partum hemorrhage is the most common cause of maternal death [1].
- **At least ten times more patients die each year of clotting**. Heart attacks, ischemic strokes, and thromboembolic disease account for more than 65% of all U.S. mortality [2]. The benefits of primary prevention of cardiovascular disease through smoking cessation and treatment of hypertension, diabetes, and hyperlipidemia are blunted by epidemic obesity and greater lifespan with their accompanying vascular complications. Many chronically ill and elderly individuals take anticoagulants.

[*] **Corresponding author Monica B. Pagano:** Department of Laboratory Medicine, University of Washington, Seattle, WA, USA; Tel: 206-543-2100; E-mail: monibea@uw.edu

Amballur D. John (Ed.)

- At the intersection of bleeding and clotting, patients taking anticoagulants present with intracranial bleeds and need hemorrhage control without worsening the thrombotic complications of the underlying reason they were placed on anticoagulants in the first place [3]. Patients with complex thromboses such as mesenteric artery or portal vein clots need effective anticoagulation that will not lead to bleeding. Patients with stented coronary and carotid arteries frequently are treated with multiple drugs and present with emergent complications.
- Care of such patients caught at the interface of bleeding and clotting is complicated by the large number of blood components, biologicals, and drugs available and by the relatively small number of readily available and useful laboratory tests to help manage these situations. This chapter will review physiologic hemostasis, laboratory tests to assess hemostasis, bleeding and thrombosis, and the clinical rational for the use and the complications of available procoagulant and anticoagulant therapies.

BLOOD COAGULATION AND FIBRINOLYSIS

Remember
• ***Primary Hemostasis*** is the formation of a **platelet plug** at a site of endothelial disruption that provides a platform for coagulation.
• ***Secondary Hemostasis*** is the formation of a **fibrin clot** through activation and amplification of the clotting cascade at the platelet plug (Fig. **1**).
• Normal coagulation is a local process, contained by antithrombotic factors including antithrombin, Protein C, and Tissue Factor Pathway Inhibitor.
• In contrast to the classical two-pathway teaching, most physiological clotting occurs through the extrinsic pathway, amplified by the intrinsic pathway factors.
• Plasma-based clot breakdown is mediated by plasmin, and plasminogen activator inhibitor inactivation by activated Protein C in the setting of trauma can lead to massive fibrinolysis.

- **A blood clot is made of platelets and fibrin [4]. Blood coagulation starts with platelets and the formation of a primary platelet plug, so called *primary hemostasis*.** When endothelial integrity is breached, type III collagen in the subendothelial matrix is exposed. Platelets localize at such sites of endothelial disruption because von Willebrand factor (vWF) binds with one end to the exposed type III collagen and with the other end to platelet glycoprotein 1b. This vWF binding tethers platelets to the site of injury and blood flow-related shear stress on the tethered 1b receptor leads to platelet activation. Activated platelets racemize phospholipids in their membranes, shed vesicles, secrete the contents of their granules, and open their integrin receptors to support aggregation. Racemization of phospholipids places negatively charged

phosphotidyl serine and phosphotidyl ethanolamine on the outer surface where they condense to form negatively charged phospholipid rafts that bind calcium and the vitamin K dependent coagulation factors (FII, FVII, FIX, FX). Shed vesicles increase this reactive surface area and the dispersion of this activity. Secreted alpha-granules release proteins such as vWF, FV, and fibrinogen and dense granules release salts such as calcium, serotonin, ADP, and mid-length polyphosphates for the activation of more platelets and coagulation factors and the induction of local vasoconstriction. Activated integrins open to become strong receptors, 1a2a for collagen and 2b3a for fibrinogen. As 2b3a receptors on different platelets adhere to the opposite ends of a single fibrinogen molecule, the platelets aggregate. Platelet aggregates physically limit blood loss and provide an environment ideal for plasma coagulation.

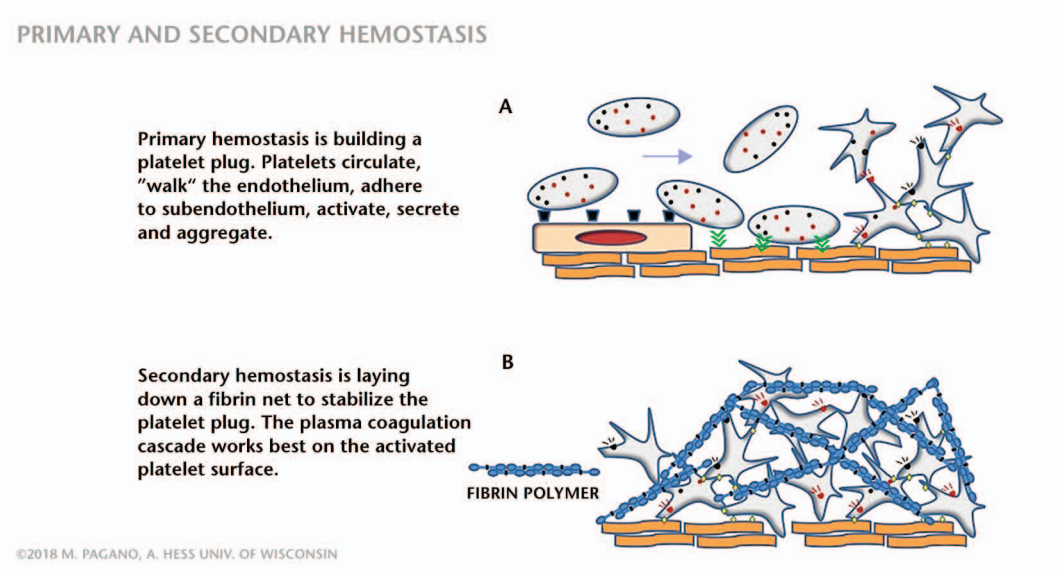


Fig. (1). Primary and Secondary Hemostasis. Provided by John R. Hess, MD, University of Washington.

- ***Secondary hemostasis*** **is the formation of the fibrin clot through the coagulation factor cascade**. During the initiation phase plasma coagulation initiates at breaks in endothelial integrity where subendothelial tissue factor-bearing cells are exposed. Factor VII (FVII) from the circulation binds to the exposed tissue factor (TF) and self-activates (TF-FVIIa complex) and activates factors IX and X. FXa activates FII (prothrombin) to IIa (thrombin) which in turn activates small amounts of factors V, VIII, XI, and XIII, but then is inactivated by anti-thrombin. During the amplification phase, FIXa, less susceptible to inactivation by anti-thrombin, migrates to an adjacent activated

platelet surface where it binds its cofactor VIIIa and produces larger amounts of FXa. FXa in turn binds its cofactor Va, either on the platelet or the activated endothelial cell edge, and in the propagation phase produces large amounts of thrombin. This burst of thrombin generation cleaves fibrinogen to make fibrin monomers, and more factor Va, VIIIa, XIa, and XIIIa. Fibrin monomers nucleate to form gel chains which are then cross-linked by FXIIIa to make fibrin polymer (Ref Hoffman 2003).

- **Clotting is highly localized** by the requirement for tissue factor initiation at the site of the endothelial break and for collocation with activated platelets for the FIX-driven amplification phase. **Amplification** comes from the marked increase in enzyme activity associated with the assembly of complexes of activated enzymes and cofactors on the negatively charged phospholipid rafts on the outer membranes of the supporting cells and platelets. This amplification can be 10,000- to a million-fold at each successive stage from the TF-VIIa complex initiation phase, to the platelet bound factors IXa and VIIIa amplification phase, to the prothrombinase complex of Xa and Va propagation phase. The speed and intensity of this propagation phase determine the rate of fibrinogen activation to fibrin monomer formation, which in turn determines the rates and ratios of fibrin polymer nucleation and chain extension that determine the ultimate structure of the fibrin clot. This structure is further stabilized by FXIII cross-linking and thrombin-activated fibrinolysis inhibitor (TAFI) that removes the lysine binding sites for plasmin (see below) from fibrin polymer to slow its breakdown.
- **Plasma coagulation is also highly localized by plasma anticoagulant activity present in the form of anti-thrombin, tissue factor pathway inhibitor (TFPI), and proteins C and S**. Anti-thrombin circulates free in plasma and stoichiometrically binds the activated coagulation enzyme factors thrombin, FXa, and FXIa to abolish their activity. Tissue factor pathway inhibitor binds the TF-FVIIa complex to turn off the initiation phase of coagulation. Activated protein C with its cofactor activated protein S inactivate factors VIIIa and Va to shut down the amplification and propagation phases of thrombin generation and clot formation. Because protein C and S are activated by thrombin bound to thrombomodulin on the surface of healthy endothelial cells away from the edges of wounds, it serves to prevent clot from spreading beyond the sites of coagulation-activating injury.
- Most of us were taught that there are intrinsic and extrinsic coagulation factor cascades [5]. The above description represents the modern view that most clotting follows the extrinsic pathway from factor VIIa to Xa to IIa, and that the intrinsic pathway factors function most commonly as participants in shorter feedback loops that reinforce and amplify the extrinsic pathway [6]. The intrinsic pathway probably does function physiologically when FXII is activated on extra cellular DNA nets and the subsequent plasma coagulation helps to

immobilize pathologic organisms. It probably functions pathologically when high energy injury results in cell ruptures with widespread activation of FXII on extra cellular DNA leading to disseminated intravascular coagulation (DIC) with factor consumption and the severe form of the acute coagulopathy of trauma. Normally, FXII deficiency is not a bleeding disease.

- **Once formed, blood clots are broken down either by a plasma process called fibrinolysis or by a cellular process mediated by neutrophil elastase** [7]. The plasma process is based on the enzyme plasmin which digests polymeric fibrin to yield D-dimers and other fibrin degradation products. Plasmin is an enzyme activated by limited proteolysis from a plasma precursor, plasminogen. This activation is mediated by tissue plasminogen activator which is secreted by endothelial cells in response to low blood pressure or flow. This system is inhibited by anti-plasmin and plasminogen activator inhibitor. Inactivation of plasminogen activator inhibitor by activated protein C following high energy injury can lead to massive fibrinolysis.

COAGULATION TESTING

Readily and rapidly available tests of blood coagulation are limited [8, 9]. At the bedside, the activated clotting time **(ACT)** is the simplest and most widely available test. Many institutions can only perform basic coagulation testing, including platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen concentration, and D dimer or fibrin split products. Various platelet functional measures and assays of coagulation proteins are available but typically only in reference laboratories and with considerable delay. There are also viscoelastic measures of whole blood coagulation and fibrinolysis.

Remember
• **Activated Clotting Time (ACT)** measures whole-blood clotting time and is useful in tracking intra-operative heparinization; it is widely variable from patient to patient • **Prothrombin Time (PT)/International Normalization Ratio (INR)** measures extrinsic pathway function and can be used to regulate warfarin anticoagulation or to detect the acute coagulopathy of trauma • **Partial Thrombin Time (PTT)** measures intrinsic pathway function and can be used to regulate heparin anticoagulation or to detect multi-factor deficiencies • **Fibrinogen** assays can be used to direct fibrinogen therapy • **D-dimer** measures fibrin breakdown and can be used to detect DIC or clot breakdown • **Thromboelastogram (TEG)** measures whole-blood cloth strength over time and can be used to direct blood component resuscitation; it does not provide specific information about the mechanisms of coagulopathy except for fibrinolysis

The **ACT** is a whole blood clotting time. Whole blood is placed in a standard tube, coagulation is activated by mixing with an anionic surface like the clay kaolin, and the tube tilted every 30 seconds until the blood stops flowing. Time

from mixing to clot is typically about 3 minutes. The test is sensitive to the actions of heparin, making it possible to follow anticoagulation in heparinized cardio-pulmonary bypass circuits.

The **platelet count** as part of the complete blood count is very accurate over the whole clinical range. Most platelets in circulation can be expected to function adequately, except in patients with congenital platelet functional disorders, patients on anti-platelet drugs, patients with uremia, and patients whose platelets are injured by partial activation by cardiopulmonary bypass circuits or high-energy traumatic injury. Platelet dysfunction can be confirmed with tests of platelet secretion and aggregation, tests of aperture closure time such as the PFA100, and viscoelastic tests of plasma or whole blood maximum clot strength. Tests of whole blood platelet aggregation to screen for or dose adjust antiplatelet drugs are labor intensive and not very accurate.

The **PT** and **aPTT** are rapid tests of the integrity of the extrinsic and intrinsic coagulation pathways that measure the speed of clotting of recalcified citrated plasma under different initiator conditions. They are widely available, accurate, and useful in specific contexts. The PT is specifically sensitive to **FVII concentration**, which makes it useful to regulate warfarin anticoagulation and to detect the acute coagulopathy of trauma. The **aPTT** is sensitive to multifactor deficiency but frequently confounded by lupus anticoagulants. Neither test is a useful screen for low concentrations of fibrinogen. Neither is a useful screening test for mild coagulation dysfunction in general surgical patients.

The **Claus fibrinogen assay** is widely available and accurate but takes 30 minutes as typically implemented. It can be read sooner but only in a high complexity lab set up and approved to do so. Its accuracy is important as a guide to therapy with fibrinogen concentrates or cryoprecipitate.

The **D-dimer assay** is a semi-quantitative assay for a specific breakdown product of cross-linked fibrin polymer. The D-E-D structure of normal fibrinogen or fibrin monomer means that D-D only occurs when fibrin has been polymerized and secondarily broken down by plasmin or neutrophil elastase. The assay is useful for the detection of DIC and the breakdown of clots. It is not useful after surgery, when clots are expected, but can be used to determine if clot breakdown has stopped after therapy for thrombosis.

Alternative tests of coagulation such as **thromboelastography (TEG)** are available but are limited by poor reproducibility, lack of automation, and cost [10]. TEG can provide rapid estimates of global coagulation function and fibrinolysis which have been shown to reduce total blood use but mostly by driving the early use of plasma or platelets and tranexamic acid, now standard

ways of resuscitating massively bleeding patients. The tests provide little information about specific mechanisms of coagulation disorders.

HEMORRHAGE

Remember
• In cases of **uncontrolled hemorrhage**, blood component resuscitation is best achieved with 1:1:1 transfusion of RBCs, platelets, and plasma under the guidance of an institutional massive transfusion protocol • Bleeding patients with **congenital clotting disorders** should be treated in a targeted manner, *e.g.,* fVIII for Hemophilia A, rfXIIIα for fXIII deficiency, DDAVP for Type 1 vWD, *etc*. • Bleeding patients with **acquired clotting disorders** such as liver or marrow failure are difficult to resuscitate and may require expert consultation

Uncontrolled hemorrhage is rapidly fatal and a surgical emergency. Rapid control of vascular sources of bleeding is generally effective, and the need to replace acute blood losses should be weighed against the acute and chronic risks of transfusion (See Table **1** – Acute transfusion reactions). For situations of sustained uncontrolled hemorrhage, ongoing support of intravascular volume, oxygen delivery (by means of red blood cells (RBC) transfusions), and hemostasis (by means of plasma and platelet transfusions) can be lifesaving. This is best accomplished by administering a 1:1:1 ratio of units of plasma, platelets and RBC according to a massive transfusion protocol that has been developed and its activation tested under the auspices of the institutional transfusion committee [11]. Because 85-90% of the platelets administered in the U.S. are collected by **apheresis** (single donor platelet units) and a unit of apheresis platelets is equivalent to about 6 units of the old whole blood derived platelets (whole blood platelet units), the actual ratio of bags of products given is most often 6 units of plasma to one unit of apheresis platelets to 6 units of RBCs (See Fig. **2** – Effect of Ratios of Standard Blood Components). Significant deviations from this ratio are associated with excess mortality.

Table 1. Acute Transfusion Reactions. Provided by Monica B. Pagano, M.D., University of Washington.

Reaction Type	Typical Cause	Presentation	Management	Comments
Acute Hemolytic	- ABO incompatible RBC transfusion, recipient anti-A/anti-B causing intravascular hemolysis.	- Can include fever, flank/lumbar pain, pain at infusion site, rigors, felling of "impending doom," hematuria, DIC (increased bleeding)	- If immediate transfusion required, switch to Group O RBC, AB plasma/FFP - Maintain U/O ≥ 100ml/hr. - Analgesics	- May present with minimal/no symptoms - Hemolysis can vary from minimal to catastrophic

(Table 1) cont.....

Reaction Type	Typical Cause	Presentation	Management	Comments
Febrile Non-Hemolytic	- Cytokine release from WBC and platelets	- Fever *(typically < 1.5C)*, chills, occasional nausea, vomiting, headache	- Acetaminophen: 650 mg (adult dose)	- Diagnosis of exclusion - Can occur with leuko reduced products (still contain some WBC)
Allergic	- Preformed IgE against proteins in donor plasma, histamine release from mast cells	- Mild: pruritus, red urticarial rash – mild reaction - Moderate: Respiratory symptoms (wheeze, stridor, hypoxia), or angioedema - Severe: Anaphylaxis near start of transfusion	- Mild: diphenhydramine 25-100mg IV - Moderate: consider additional anti-histamine, *e.g.* ranitidine 50-100mg IV Severe: Epinephrine 0.2-0.5ml of 1:000 S/C, IM or IV	Severe Reactions/Anaphylaxis: - Rarely caused by recipient anti-IgE towards IgA in IgA deficient patient. - Consult transfusion medicine for additional workup/ management recommendations for this.
Transfusion Associated Circulatory Overload (TACO)	- Patient CVS unable to accommodate sudden rise in intravascular volume - acute pulmonary edema	- Dyspnea, hypertension, tachypnea, desaturation, wheeze, may require intubation, *increased* CVP	- IV diuretics *e.g.* furosemide 10-20mg IV: caution in patients with renal failure	- Extremes of age more at risk - Can occur in ANY patient who is rapidly transfused - CXR: indistinguishable from TRALI
Transfusion Related Acute Lung Injury (TRALI)	- Donor anti-HLA, anti-neutrophil antibodies against corresponding recipient antigen - Bioactive lipids present in product as result of storage	- Fever, hypertension (may see hypotension), dyspnea, tachypnea, desaturation, wheeze, may require intubation, *decreased* CVP	- No response to diuretics (helps distinguish this from TACO) - Care is supportive - Resolves after 24-72 hs - ≤ 10-20% mortality	- Occurs within 6 hrs. of transfusion, but typically occurs within 2 hs. - If suspicion, consult transfusion medicine for input - All plasma containing blood products implicated
Bacterial Contamination	- Introduction of bacteria into product bag, typically at time of collection	- Presentation dependent on bacteria species and count. - Fever (often > 1.5C), chills, rigors, profound hypotension (if large amount gram negative endotoxin)	- Patient blood cultures - Empiric antibiotic therapy until culture results available	- Important to notify transfusion medicine ASAP, because other products from same blood donation will need to be quarantined

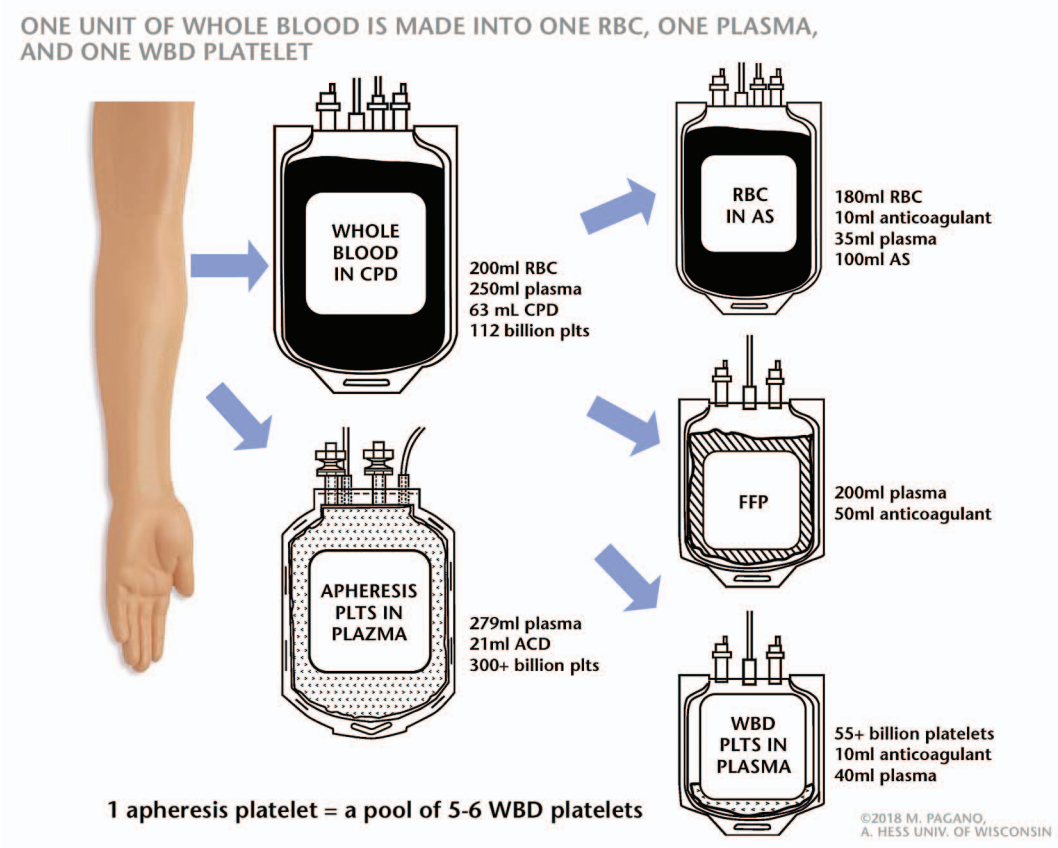


Fig. (2). Manufacture and Contents of Standard Blood Components. Provided by John R. Hess, MD, University of Washington.

Congenital causes of uncontrolled bleeding include von Willebrand disease (vWD), deficiencies of coagulation factors called hemophilias, syndromes of platelet dysfunction such as Glanzmann's thrombesthenia, and disorders that threaten vascular integrity such as arteriovenous malformations or hereditary hemorrhagic telangiectasia. For the most common hemophilias, **hemophilia A (FVIII deficiency)** and **B (FIX deficiency**), recombinant coagulation factors exist and are available from regional hemophilia centers along with expertise in their use and testing to support their management. **Trauma centers** often keep a single emergency dose of factors VIII and IX available, along with four-factor **prothrombin complex concentrates (PCC)** (containing factors II, VII, IX, and X) and a FVIII:von Willebrand factor mix. Deficiencies of factors I (fibrinogen) and XIII are treated with **cryoprecipitate**, and the remaining factors V and XI with plasma. Patients with congenital platelet disorders are also generally managed by hematologists associated with regional hemophilia centers or

children's hospitals. Their expertise is critical to balance the benefits of platelet transfusion against the risks of alloimmunization and refractoriness to future platelet transfusions. Patients with large vessel vascular abnormalities such as arteriovenous malformations and Ehlers-Danlos syndrome benefit from specialized vascular surgical care.

vWD is the most common bleeding defect occurring in at least one out of every 100 people [12]. A problem with the circulating vWD protein behaves as a platelet function defect with mucocutaneous bleeding. Common forms include **vWD Type 1**, which is a quantitative defect with low plasma concentrations of the normal multimers caused by a defect in endothelial secretion, and less often, a shorter half-life. **vWD type 2**, is a qualitative defect with normal or low multimers of abnormal function. There are **four different subclassifications** based on altered function, including **Type 2A** (increased proteolysis by ADAMTS13), **Type 2B** (increased affinity to platelet receptor GP 1b), **Type 2M** (decrease affinity to platelet receptor GP 1b) and **Type 2N** (decrease affinity to factor VIII). Type 1 vWD can often be treated with DDAVP, and type 2 with replacement of Factor VIII:vWF complex using specific concentrates. A **rare Type 3 vWD** is characterized by the complete absence of vWF, with no multimers present and no activity.

Acquired causes of bleeding disorders in adults are typically associated with liver disease, disorders of platelet number and function, and drugs [13]. Drugs will be discussed in more detail below. The question of whether the abnormal coagulation tests associated with liver disease represent coagulation abnormalities is best determined by assessing the cirrhotic patient for evidence of non-variceal bleeding [14]. Acquired low platelet counts from immune thrombocytopenia purpura (ITP), splenic disease, or marrow failure are frequently complicated by platelet transfusion refractoriness requiring expert consultation, treatment with immune modulators, or transfusion with multiple units of platelets.

THROMBOSIS

Remember
• **Arterial thromboembolii** are typically platelet-rich and best inhibited with antiplatelet agents • **Venous thromboembolii** are typically factor-rich and best inhibited with anticoagulants

Arterial thrombosis is the most common cause of heart attacks and strokes. It typically affects medium-sized arteries. Arterial thromboembolism is less common and typically comes from clots on artificial heart valves and aortic plaques or areas with stasis such as the left atrium in patients with atrial fibrillation. Microscopic thrombi occur in DIC and other thrombotic microangiopathies. Arterial thrombi are typically **"white"**, composed of platelets

and fibrin without a substantial RBC component, **they are best inhibited with antiplatelet agents** as reflected in the general recommendation that almost everyone over 60 or 70 years of age should take low-dose **aspirin**. More severe arterial disease or the presence of foreign bodies such as stents may require "dual anti-platelet" therapy. Exceptions to this rule are that cardiac valves and atrial fibrillation, associated with stasis, do better with plasma anticoagulants.

Venous thrombosis is very common **affecting 8%** of the population between the ages of **20 and 60years, 900,000 incident cases/yr** [15]. Venous thromboembolism is responsible for at least 100,000 deaths per year. Venous clots form in association with injury, stasis, and hypercoagulable states**(Virchow's triad)**. In the capacitance vessels of the calf, thigh, and pelvis venous thrombi can grow to very large size and use RBC trapped in a fibrin matrix to form large **"red clots"**. The red cell bulk is necessary as the total volume of platelets in a normal person is only 10ml. As a result of their fibrin-rich nature, these clots are best **treated with plasma anticoagulants**.

There is a strong association of unprovoked venous thrombosis in individuals less than 40years old with **hypercoagulable states** [16]. Congenitally acquired states include antithrombin, protein C, and protein S deficiencies, activated protein C resistance (Factor V Leiden, especially in those of European descent), increased concentrations of clotting factors (I, II, VIII, especially in those of African descent, IX, and XI), and increased concentrations of plasminogen activator inhibitor or histidine rich glycoprotein. Acquired hypercoagulable states occur with smoking, the use of oral contraceptives, and pregnancy. **Vascular injuries** classically associated with an increased risk of thrombosis include ankle, tibial, and femoral fractures with immobilization of a leg in a cast, hip and knee replacement, pelvic injuries, and intravascular catheter placement. All of these situations are potential indications for prophylactic anticoagulation. In these provoked situations of venous thrombosis, searching for a congenital hypercoagulable state is not useful, as it does not change treatment for the patient and is rarely helpful for family members.

ANTICOAGULANT DRUGS

The exact choice of drugs to prevent or treat thrombosis has become complex as licensed drugs have increased in number, trials of their use in clinical situations have increased, and patterns of complications have become apparent [17]. In the individual patient, safety, effectiveness, ease of use, and cost determine choice of drug and dose. Commonly used anticoagulant and antiplatelet drugs are listed in (Table **2**).

Remember
• Anticoagulants increase the risk of bleeding • **Heparin** is an antithrombin III activator, used for a wide variety of anticoagulant applications, monitored by aPTT or Xa activity, reversible by protamine, and associated with the complication of heparin-induced thrombocytopenia (HIT) • **Low-molecular weight heparins** such as enoxaparin have less frequent dosing than heparin, a lower incidence of HIT, and are at least partially reversible with protamine • **Fondaparinux** is a synthetic heparinoid with an 18-hour half-life and no reversal agent • **Warfarin** is a vitamin K antagonist affecting factors II, VII, IX and X, used for venous thromboembolism prophylaxis and in patients with prosthetic cardiac valves, monitored by INR, reversible by vitamin K or clotting factor replacement, and complicated by warfarin skin necrosis • **Argatroban** and **bivalirudin** are **direct thrombin inhibitors**, used to treat HIT, monitored by aPTT or ACT, and require continuous infusion owing to rapid hepatic and renal clearance, respectively • **Dabigatran** is an oral direct thrombin inhibitor, safer than warfarin and can be reversed with idrucizumab. It has a 12-hour half-life and renal excretion • **Rivaroxaban**, **apixaban**, and **endoxaban** are oral direct **Xa inhibitors**, used for long-term venous thromboembolism prophylaxis, not routinely monitored, and can be reversed with andexinet alpha.

Table 2. Emergency/Urgent Reversal.

Agent	Mechanism Action	Urgent/Emergency Reversal	Laboratory Test	Comments
Warfarin	Inhibits synthesis vitamin K dependent coagulation factors (II, VII, IX, X) and protein S & C	- Vitamin K 5-10mg slow IV infusion - 4-factor PCC 20-50 IU/kg - Monitor response to therapy	PT/INR	- If 4 factor PCC not available give 3-factor PCC 25-50 IU/kg AND 2-4U FFP/Plasma - Monitor response to therapy
Heparin - Unfractionated	Binds AT, and inhibits "Xa and IIa"	- Stop infusion - Protamine sulfate: 1mg for each 100U of active heparin	aPTT Anti-Xa activity	- FFP contraindicated (provides additional AT which may potentiate anticoagulation) - Infuse slowly (*i.e.* < 5mg/minute) to avoid protamine induced hypotension or bronchospasm
LMWH - Enoxaparin - Daltaparin	Binds AT and the complex inactivates Xa	- Protamine sulfate, 1mg for each 1mg LMWH	Anti-Xa activity (APTT – ref. range varies between hospitals)	- Protamine only offers partial reversal

(Table 2) cont.....

Agent	Mechanism Action	Urgent/Emergency Reversal	Laboratory Test	Comments
Direct Thrombin Inhibitors (DTIs) - Dabigatran - Bivalirudin	Direct IIa inhibitors - Dabigatran inhibits both free and clot based Thrombin	- No specific antidotes* Life threatening bleeding - 4-factor PCC (20-50IU/kg), if not available: 3-factor PCC with FFP/Plasma, adjunctive Rx: DDAVP (0.3 µg/kg), TXAω, EACA? Dabigatran - Activated charcoal if last dose < 2-3 hrs. - - Consider dialysis if drug level supratherapeutic as last resort	aPTT Plasma diluted TT Dabigatran drug levels	- Normal APTT indicates no dabigatran effect - Reversal with PCC does not fully correct coagulation testing results
Selective Xa Inhibitors - Argatroban - Rivaroxaban - Apixaban	Inhibit Xa	- No specific antidotes* - For all, consider FFP/plasma & cryoprecipitate Life threatening bleeding - 4-factor PCC (20-50IU/kg) OR 3-factor PCC with FFP/Plasma, OR consider rVIIa (10-90 µg/kg) & FFP/Plasma if no PCC available, aPCC (FEIBA) Rivaroxaban - Consider activated charcoal if last dose < 2-3 hours - - Consider plasma exchange if drug level supratherapeutic as last resort	aPTT - Argatroban Anti-Xa Activity - Rivaroxaban - Apixaban PT - Rivaroxaban - Apixaban	- Normal laboratory results indicate no anticoagulant effect
Pentasaccharides - Fondaparinux	Inhibit Xa through AT	- No specific antidote	Anti-Xa activity	- Protamine has no effect - Hemodialysis reduces drug ≈ 30%
Cox Inhibitors - Aspirin	Inhibit COX Aspirin – irreversible NSAIDS - reversible	- Transfuse 1U apheresis platelets or 4-6U pooled WBDP** - - Consider DDAVP 0.3 µg/kg (Caution ICH)	Platelet function assay - PFA-100 - - TEG / platelet mapping	- Reversal in 15-30 minutes

(Table 2) cont.....

Agent	Mechanism Action	Urgent/Emergency Reversal	Laboratory Test	Comments
Thienopyridines - Clopidogrel - Ticlopidine	Inhibit platelet $P2Y_{12}$ ADP receptor	- Transfuse 1U apheresis platelets or 4-6U pooled WBDP** - - Consider DDAVP 0.3 µg/kg (Caution ICH)	Platelet function assay - PFA-100 - - TEG / platelet mapping	- Reversal in 15-30 minutes
Warfarin	Inhibits synthesis vitamin K dependent coagulation factors (II, VII, IX, X) and protein S & C	- Vitamin K 5-10mg slow IV infusion - 4-factor PCC 20-50 IU/kg - Monitor response to therapy	PT/INR	- If 4 factor PCC not available give 3-factor PCC 25-50 IU/kg AND 2-4U FFP/Plasma - Monitor response to therapy
Heparin - Unfractionated	Inhibits AT, Xa and IIa	- Stop infusion - Protamine sulfate: 1mg for each 100U of active heparin	aPTT Anti-Xa activity	- FFP contraindicated (provides additional AT which may potentiate anticoagulation) - Infuse slowly (*i.e.* < 5mg/minute) to avoid protamine induced hypotension or bronchospasm
LMWH - Enoxaparin - Daltaparin	Binds AT and the complex inactivates Xa	- Protamine sulfate, 1mg for each 1mg LMWH - Consider activated PCC (FEIBA)	Anti-Xa activity (APTT – ref. range varies between hospitals)	- Protamine only offers partial reversal
Direct Thrombin Inhibitors (DTIs) - Dabigatran - Bivalirudin	Direct IIa inhibitors - Dabigatran inhibits both free & clot based IIa	- No specific antidotes* <u>Life threatening bleeding</u> - 4-factor PCC (20-50IU/kg), if not available: 3-factor PCC with FFP/Plasma, adjunctive Rx: DDAVP (0.3 µg/kg), TXAω, EACA? <u>Dabigatran</u> - Activated charcoal if last dose < 2-3 hrs. - Consider dialysis if drug level supratherapeutic as last resort	aPTT Plasma diluted TT Dabigatran drug levels	- Normal APTT indicates no dabigatran effect - Reversal with PCC does not fully correct coagulation testing results

(Table 2) cont.....

Agent	Mechanism Action	Urgent/Emergency Reversal	Laboratory Test	Comments
Selective Xa Inhibitors - Argatroban - Rivaroxaban - Apixaban	Inhibit Xa	- No specific antidotes* - For all, consider FFP/plasma & cryoprecipitate Life threatening bleeding - 4-factor PCC (20-50IU/kg) OR 3-factor PCC with FFP/Plasma, OR consider rVIIa (10-90 µg/kg) & FFP/Plasma if no PCC available, aPCC (FEIBA) Rivaroxaban - Consider activated charcoal if last dose < 2-3 hours - Consider plasma exchange if drug level supratherapeutic as last resort	aPTT - Argatroban Anti-Xa Activity - Rivaroxaban - Apixaban PT - Rivaroxaban - Apixaban	- Normal laboratory results indicate no anticoagulant effect
Pentasaccharides - Fondaparinux	Inhibits Xa through AT	- No specific antidote	Anti-Xa activity	- Protamine has no effect - Hemodialysis reduces drug ≈ 30%
Cox Inhibitors - Aspirin	Inhibit COX Aspirin – irreversible NSAIDS - reversible	- Transfuse 1U apheresis platelets or 4-6U pooled WBDP** - Consider DDAVP 0.3 µg/kg (Caution ICH)	Platelet function assay - PFA-100 - TEG / platelet mapping	- Reversal in 15-30 minutes
Thienopyridines - Clopidogrel - Ticlopidine	Inhibit platelet $P2Y_{12}$ ADP receptor	- Transfuse 1U apheresis platelets or 4-6U pooled WBDP** - Consider DDAVP 0.3 µg/kg (Caution ICH)	Platelet function assay - PFA-100 - TEG / platelet mapping	- Reversal in 15-30 minutes

* At time of writing no specific antidotes are licensed for direct thrombin inhibitors or selective Xa inhibitors; however several agents are currently in phase III clinical trials. ωTXA – tranexamic acid. ? EACA – epsilon amino-caproic acid.** WBDP – whole blood derived platelets.

Unfractionated Heparin (UFH) is the oldest available anticoagulant drug, functioning as an anti-thrombin enhancing agent to bind factors IIa and Xa. A unit of heparin activity is the amount that prevents the clotting of 1ml of whole blood for 24 hours *in vitro*. *In vivo*, the dose remains the same, 5000 units for a normal sized adult with a 5000 ml blood volume, but the *in vivo* half-life of UFH is only

1hour, so dosing is typically repeated every 4 hours or the drug is given in a continuous infusion to maintain a constant plasma concentration. Problems with UFH include the requirement for parenteral administration, marked individuality in dose and metabolism, difficulty with monitoring the clinical effect with either the PTT or the heparin anti-Xa activity, and the not rare complications of **heparin-induced thrombocytopenia (HIT) with thrombosis (HITT)**. Wide usage of heparin in deep venous thrombosis (DVT) prophylaxis, catheter maintenance, dialysis, and cardiopulmonary bypass means that constant vigilance is required to know if sick hospital patients are receiving the drug and blood specimens are contaminated with it. The presence of heparin is suggested by a prolonged **thrombin time (TT)** and can be confirmed by repeating the test after heparinase or protamine sulfate treatment. UFH activity can be reversed with protamine sulfate, with **1-1.5mg of protamine binding 100U of heparin**. Protamine can cause allergic, anaphylactic, and anaphylactoid reactions so it is customary to give a 5mg dose and observe the effect before giving the full dose.

Low molecular weight heparins, dalteparin, enoxaparin, or tinzaparin, function as **indirect Xa inhibitors** through the enhanced activity of antithrombin. They have the advantages of once or twice daily subcutaneous dosing and less frequent HIT. Their activity is at least partially reversible by protamine sulfate. The drugs are all eliminated through the kidney, and they require reduced dosing in renal failure. Low molecular weight heparins have been associated with a **risk of spinal epidural hematomas** when given in association with spinal, epidural anesthesia or lumbar puncture.

Fondaparinux is a synthetic version of the active 5-sugar site of heparin. It works through the **activation of antithrombin** to give high specificity to anti-Xa activity but is too small to have significant anti-IIa activity. In healthy individuals it has an 18hour half-life and very stable pharmacokinetics. It is renally excreted and contraindicated in patients with a creatinine clearance of less than 30ml/min. The long half-life and lack of a reversal agent are problems if hemorrhage occurs subsequently hemorrhage.

Warfarin, a vitamin K antagonist, and its congeners have been available for more than 50 years. **Vitamin K** is a cofactor in the post-translational processing of factors II, VII, IX, and X as well proteins C and S. As the historic oral anticoagulant, it is widely used in venous thromboembolism prophylaxis and treatment and for anticoagulating prosthetic cardiac valves. Its use is complicated by its competition with dietary vitamin K, by genetically determined differences in metabolism, and the need to start the drug slowly to avoid warfarin skin necrosis. As a result of the differences in drug metabolism between patients, dose is titrated against the PT/INR. Prophylaxis and treatment of DVT and venous

thromboembolism (VTE) uses INR values between 2 and 3 as the therapeutic target and prevention of thrombosis on artificial heart valves and vascular stents uses higher target ranges. **Reversal** of the drug effect can be accomplished by holding subsequent doses or giving oral or IV vitamin K. For patients with life threatening bleeding, rapid reversal of anticoagulation to control the bleeding can be achieved by replacement of the vitamin K coagulation factors II, VII, IX, and X as well proteins C and S using plasma, or preferably 4-factor prothrombin complex concentrates.

Intravenous direct thrombin inhibitors are a class of drugs used to treat HIT and include argatroban and bivalrudin. Both are small molecule blockers of the thrombin active site, and bivalirudin has a second blocking structure of the fibrin binding site attached by a short glycine chain. Because of their non-covalent binding and small size, they function as reversible inhibitors with short half-lives and so are given by continuous infusion with aPPT or activated clotting time monitoring. **Argatroban** is cleared in the liver in bile, and **bivalirudin** by the kidney, and consideration of limitations of the excretory path are a major reason for choosing one over the other.

Finally, a relatively new set of novel oral anticoagulant drugs (NOACs) including, the oral direct thrombin inhibitor dabigatran, and the oral FXa inhibitors rivaroxaban, apixaban and endoxaban [18]. These drugs are variably approved for a variety of indications including stroke prophylaxis in atrial fibrillation, thromboembolism prophylaxis in knee and hip replacement, and treatment of DVT and venous thromboembolic disease. The convenience of once or twice a day oral dosing, stable pharmacokinetics, and reproducible efficacy, eliminating the need for frequent blood tests, and better safety makes them attractive alternatives to warfarin.

Aspirin is a widely available over the counter drug used in low dose to prevent heart attacks and strokes and in high dose to treat pain and inflammation [19]. As an antiplatelet drug, it functions by irreversibly inactivating cyclooxygenase, breaking the linkage between platelet adhesion and activation. With low-dose aspirin therapy (81 mg once a day), all platelets in the body are affected. Activity returns slowly as new platelets replace the old ones at 10% a day over the normal 10day platelet lifespan. The aspirin itself has a short half-life and is largely gone in 4hours. Thus, a patient with a normal platelet count of 250K/μL who took their last aspirin 4days ago is expected to have a 100K/μL of functional platelets circulating and should be fine even for neurologic or ocular surgery.

ANTIPLATELET DRUGS

Also, most patients taking aspirin do not bleed because platelets can be activated

by strong activators like thrombin that bypass the adhesion-activation linkage. In the body, thrombin is normally made by the coagulation cascade on the surface of activated platelets. A few normal platelets will support the development of thrombin which will activate the larger number of locally adherent aspirin-poisoned platelets to produce clot. Exact platelet concentrations at which this occurs are variable but typically are around the 30K/μL range. As a result, a patient who has been off of aspirin for 30 hours or who has received one adult dose of platelets giving about 30K/μL of normal platelets will generally do well in general surgery along anatomic planes if allowance is made for the slightly higher threshold for clotting initiation.

Remember
• Antiplatelet agents increase the risk of bleeding • **Recovery** from anti-platelet agents depends on **1)** the half-life of the drug and **2)** the rate of platelet replacement, which is usually about 10% per day • If the patient's anti-platelet medication is cleared and they have a normal platelet count, approximately 30K/μL of normal platelets, *i.e.*, one unit of random-donor platelets, is usually sufficient to support the activity of the remaining circulating platelets • **Aspirin** prevents platelet aggregation by cyclooxygenase inhibition • **Abciximab, eptifibatide,** and **tirofiban** prevent platelet aggregation by inhibiting GP2b3a • **Clopidogrel** and **ticlodipine** prevent platelet activation by $P2Y_{12}$ADP inhibition • **Dipiridamole** and **cilostazol** prevent platelet activation by phosphodiesterase inhibition preventing the action of ADP, and are similar to clopidogrel and ticlodipine but with longer half-lives

Abciximab, eptifibatide, a**nd tirofiban** are all **inhibitors of platelet GP2b3a**, the integrin that serves as a fibrinogen and fibrin receptor. Inhibition of fibrinogen binding prevents platelet-to-platelet aggregation, and inhibition of fibrin binding prevents platelets from pulling the fibrin web tight in the process of clot retraction. **Abciximab** is a monoclonal antibody fragment that binds to the platelet and serves as an inhibitor for 12-48 hours. Its effect can be partially offset by giving more platelets, the drug may also affect transfused platelet function. **Eptifibatide** is an artificial cyclic polypeptide akin to a rattlesnake venom. The drug is administered IV, and rapidly but reversibly binds the GP2b3a integrin. It is excreted in urine and can accumulate in patients with renal failure. Monitoring during therapy is advised, but requires a test of platelet function such as the clotting time, aperture closure time, or thromboelastogram maximum amplitude. **Tirofiban** is a non-peptide viper venom analog that also functions as a reversible binder of the GP2b3a integrin. It must be given IV, has a short half-life, and renal excretion. Monitoring with the aPTT is suggested, but following the platelet count is also important because allergic reactions with thrombocytopenia occur.

Clopidogrel and **ticlopidine** are the two most commonly used non-aspirin platelet inhibitors. **Clopidogrel** is used because of its oral dosing, its "aspirin-like" irreversible inhibition of the $P2Y_{12}$ ADP receptor limiting platelet to platelet activation, and small molecule short half-life as an alternative or supplement to aspirin in the prevention of coronary, cerebrovascular, and stent thrombosis. Because the molecule, a prodrug, and its physiologically active metabolite are rapidly cleared, treatment of bleeding associated with its use is like that following aspirin. **Ticlopidine** has a similar activity but a longer half-life because of high protein binding.

Dipiridamole and **cilostazol** are blockers of phosphodiesterase which blocks the breakdown of cyclic-adenosine monophosphate (cAMP) normally induced by ADP, so they behave much like clopidogrel. The drugs have much longer half-lives because of protein binding and similar problems with stopping bleeding if it starts. They also cause vasodilation.

LOCAL PROCOAGULANTS

Remember
• A number of local procoagulant technologies exist to assist in control of hemorrhage

A variety of materials can be sprinkled, or sprayed, or pressed onto wounds to slow bleeding. They range from simple astringents like cotton and cornstarch, to fibrous materials which can contribute to clot activation and structure such as cellulose and collagen, to vasoactive materials such epinephrine, to biologic clot components such as bovine thrombin or fibrin glues made from human plasma, and finally structured materials such as dry fibrin sealant bandages or patches of hydrophobically modified chitosan. All of these materials have some efficacy and a place in the surgical armamentarium.

Burn surgeons used to cut deep with dermatomes to establish free bleeding as a sign that all injured tissue had been removed, but this led to massive blood loss. The current practice of shallow excision and the use of epinephrine-soaked gauze, pressure, and fibrin glue has reduced blood loss and cut red cell transfusion 81% in the care of patients with 50% whole body burns.

Whole blood is separated into components by centrifugation, first a "soft" spin to bring down the red cells allowing the platelet rich plasma to be removed and then a "hard" spin to bring down the platelets allows platelet concentrate to be separated from the platelet poor plasma. It is also possible to collect **RBCs**, platelets, and plasma separately by apheresis. Separation is important because RBCs store best in liquid suspension at 1-6°C (as cold as they can be without

freezing), **plasma** is best stored frozen (to limit protein degradation), and **platelets** store best at 20-24°C (as cold as possible above the 18°C lipid phase transition that leads to receptor aggregation).

BLOOD COMPONENTS

Remember
• Separation of whole blood into components is necessary because red blood cells (RBCs), platelets, and plasma have different optimum storage conditions • All blood products are labeled with their **ABO and Rh type** • All blood products are tested for a limited number of infectious diseases • **Packed RBCs** (PRBCs) have a hematocrit of approximately 55%, and will raise hemoglobin by approximately 1 g/dL • **Fresh-frozen plasma (FFP)** has an INR of approximately 1.1, and 10-20 ml/kg (4-8units) are required to have a clinically meaningful effect on INR • **Whole blood-derived platelets** have at least 55 x 10^9 platelets in 50ml, **apheresis platelets** have at least 300 x 10^9 in 300ml, and a dose of 6 whole blood-derived units (or one apheresis unit) will raise the platelet count by approximately 30k/μL • **Cryoprecipitate** is used to replete fibrinogen and factor XIII, and is usually issued in 5unit pools (one unit is the cryoprecipitate from one unit of plasma) • Current evidence supports using a hemoglobin of 7g/dL as a RBC transfusion trigger in most patients, 8g/dL for patients with active cardiac disease

Whole blood is typically collected in 450ml (pint) or 500ml (half-liter) quantities with the larger amount used to offset the losses associated with leukoreduction (see Fig. **1**). Anticoagulant, now almost always citrate, phosphate, and dextrose (CPD or CP2D), is present in the primary collection bag in a 1:7 volume ratio for the planned collection. Since the hematocrit (Hct) of eligible blood donors is typically about 42%, 3/7ths of the total volume, the remaining plasma is 4/7ths and mixed with the 1/7th anticoagulant means that all plasma in blood components starts as 80% plasma and is only diluted further by additive solutions. Almost all RBC units contain about 100ml of saline-based additive solution (AS), so their final composition is about 180ml of RBCs, 100ml of AS, 36ml of plasma, and 9ml of anticoagulant. See Table **3** for the **composition of all of the commonly available blood components**. A unit of plasma is typically 250ml of an 80% mixture of plasma and anticoagulant. Platelets are 50ml for whole blood-derived (WBD) and 300ml for apheresis-derived units of plasma with 55+ or 300+ billion platelets respectively. The approximate equivalence of **6 U of WBD** to **1 apheresis**-derived unit as one adult dose is important in calculating platelet support.

Table 3. Blood products. Provided by Monica B. Pagano, M.D., University of Washington, and Aaron Hess, M.D., PhD., University of Wisconsin.

Blood Product & Contents	Indications	Dosage & Anticipated Effect	Comments
Packed Red Blood Cells VOLUME ≈ 300ml CONTENTS: - 180-250ml RBC ≈50ml plasma	- No good guidelines in surgical patients, patients with ongoing hemorrhage, hemolysis or traumatic brain injury - Acute need for increased O2 carrying capacity - compensatory mechanisms insufficient (based in pulse, BP, T, SaO2, *etc*.) Massive transfusion: (*as part of a balanced transfusion protocol)* Symptomatic Anemia: - Stable hospitalized patient: Hb < 7.0g/dL - Stable patients with pre-existing cardiac disease & symptoms, or Hb < 7.0g/dL - Hb < 6.0 g/dL almost always requires transfusion - Hb ≥ 10g/dL. virtually never requires transfusion	DOSE : Adults: - 1U packed RBC Pediatrics : - 10 ml/kg EFFECT : - Increases Hb 1.0 g/dL & Hct 3% in non-bleeding non hemolyzing patient	- Transfusion based on Hb/Hct triggers alone sub-optimal. - Need to take into consideration if patient tolerating degree of anemia. *(This will be based on rapidity of anemia, degree of blood loss with hemorrhage e.g.* > 30% blood volume - and other co-existing medical conditions).
Platelets VOLUME: ≤ 300ml CONTENTS: ≥ 3 x 10^{11} platelets per - 1U apheresis platelets *OR* - 4-6U pool whole blood derived platelets ≈ 300ml plasma *OR* additive solution	Thrombocytopenia: < 10 x 10^9/L in stable, non-bleeding patient *(prophylactic transfusion)* < 100 x 10^9/L if intracranial hemorrhage or surgery < 50x 10^9/L lumbar puncture in uncomplicated, stable patient *(no good data, technique rather than count better predictor of bleeding)* < 50 x 10^9/L with hemorrhage or other major surgery Massive transfusion*(as part of a balanced transfusion protocol)* Abnormal Platelet Function: *(Transfusion decisions not based on absolute platelet count)* - Patient undergoing surgical procedure - Intracerebral hemorrhage - Antiplatelet medications - Congenital platelet function abnormality	DOSE Adults: - 1U apheresis platelets *OR* pool of 4-6U whole blood derived platelets Pediatrics: - 10-15ml/kg EFFECT: - Raises platelet count 20-50 x 10^9/L in non-bleeding, non-refractory patient without splenomegaly - 1-2 doses should provide sufficient hemostatic function in patients taking antiplatelet medication	- Often difficult to obtain platelet count ≥ 100 x 10^9/L severely thrombocytopenic patient refractory to platelet transfusion or with massive splenomegaly - Although platelets often transfused to patients with uremia, these are third line therapy behind DDAVP, dialysis, and conjugated estrogens

(Table 3) cont.....

Blood Product & Contents	Indications	Dosage & Anticipated Effect	Comments
FFP/Plasma VOLUME: - 250-300ml CONTENTS: - 1 IU/ coagulation factors per ml - 400mg fibrinogen	AABB 2010 Recommendations: include - Massive transfusion *(as part of a balanced transfusion protocol)* - Insufficient data to recommend for or against use in trauma or surgical patients *without* massive transfusion Other Indications: - Dilution Coagulopathy (*i.e. from high volume IV crystalloid fluids)* - Global factor deficiencies – with hemorrhage or undergoing surgery - Congenital factor deficiency where no factor concentrate is available (V, X, XI in USA) with hemorrhage or undergoing surgery -Urgent warfarin reversal where no 4 factor PCC available: 3 factor PCC *(lacks VII)* – give with 4U plasma and check response.	DOSE: - Based on desired % coagulation factor levels *versus* current levels Adults: - 10 mL/Kg (typically 4U) Pediatrics: - 10-20 ml/kg EFFECT: - Increases factor levels by 20-30% in non-bleeding patient - At lower PT/INR less response seen	- Usually only need 20-40% normal factor levels for adequate hemostatic function, but ≠ normal PT/INR (reflects mostly VII activity) - Plasma types include FFP, FP24 (frozen within 24 hrs. collection), 5 day thawed plasma, liquid plasma (never frozen). Are all essentially equivalent
Cryoprecipitate VOLUME: - 1U = 10-15ml - 5U pool = 50-75ml CONTENTS: 1U ≥150mg fibrinogen ≥80 IU VIII - 80-120 IU vWF - 40-60 IU XIII	- No good evidence based guidelines For Hypofibrinogenemia: - Acquired or congenital with hemorrhage, or for surgical prophylaxis Treat for fibrinogen concentration: < 100 mg/dL in patient undergoing surgery < 150-200 mg/dL trauma, massive transfusion < 200-400 mg/dL post-partum hemorrhage, surgery at end of pregnancy	DOSE: Adults: Fibrinogen < 100mg/dL - 5-10U Fibrinogen < 70mg/dL - 10-15U Pediatrics: 1U / 10kg EFFECT: - Should increase fibrinogen by 50-100mg/dL if no ongoing bleeding or fibrinolysis	- Some hospitals only provide 5U pools *(check with hospital transfusion service lab)* - Optimal target fibrinogen > 175-200mg/dL, *(recommendations are evolving)*

Cryoprecipitate is made from plasma, collecting the protein slush from the bottom when a unit of fresh frozen plasma is thawed in a refrigerator at 4°C. It is frequently pooled into 5U pools and serves as a source of fibrinogen and factor XIII. Plasma left over from making cryoprecipitate, "plasma cryoprecipitate reduced" can be used to treat TTP, but because of the low fibrinogen, should not be used as a source of fibrinogen.

A unit of RBCs typically raises the hematocrit of a 70kg patient by 3% or the hemoglobin (Hb) by 1g/dL. A dose of platelets typically raises the platelet count

by 30K/μL but with wide variability. A unit of plasma typically has little effect on plasma coagulation or the PT/INR, and a typical adult dose of 10-20ml/Kg of body weight (4-8 units of plasma) is necessary to provide approximately 30% of coagulation factor hemostatic activity.

All blood products are tested and labeled with their ABO and RhD type. **ABO** mismatch is the most important cause of acute hemolytic reactions. Errors in sample identification from patients and getting the correct units to the right patients remain common causes. **All blood is tested for** HIV 1 & 2, HTLV 1 & 2, Hepatitis B, Hepatitis C, and Syphilis. West Nile Virus, Chagas's disease, and now Babesiosis are tested for in certain areas of the country or times of the year. Testing is not done for a number of transfusion-transmitted diseases such as malaria and Rocky Mountain Spotted Fever. We trust to their rarity in the donor population, honest answers to pre-donation questions, and epidemiologic surveillance to protect the population. Apheresis platelets are cultured for bacteria 24 hours after collection and 12 hours before release. Still, the safest transfusion is the one not given.

Indications for transfusion are becoming more restrictive. We now transfuse most patients only when their hemoglobin falls below 7g/dL [20, 21]. Higher thresholds such as 8g/dL for patients with active cardiac disease or pregnant women with sickle cell disease are exceptions [22]. Most hospitalized cancer patients tolerate platelet counts of 10K/μL [23]. Mild and moderate prolongations of plasma coagulation times are well tolerated with some bruising [24]. Serious complications, such as brain bleeds are uncommon except following trauma.

PLASMA PRODUCTS

Remember
• A wide variety of plasma-derived or recombinant coagulation factors are available • **Prothrombin Complex Concentrates (PCCs)** are concentrates of factors II, VII, IX, X and Protein C and Protein S, and are indicated for emergent correction of warfarin anticoagulation in the setting of intracranial bleeding or uncontrolled hemorrhage

Some of the plasma collected with routine blood donation and more collected in plasma collection centers are manufactured into human plasma products. The first of these products were albumin and anti-hemophilia factors, but they now include IVIgG and a number of specialized coagulation products. Such products made from pooled plasma were historically associated with massive transmission of hepatitis and HIV, but plasma collections are now routinely tested before manufacture and the products subjected to pathogen reduction by nanofiltration, solvent-detergent treatment, and where possible, heat inactivation. Most anti-hemophilia factors are now made using recombinant protein expression in cell

culture or transgenetically in mammalian milk. Table **4** is a list of the human coagulation factors and best sources for them.

Table 4. Coagulation factors. Provided by John R. Hess, MD, University of Washington.

Coagulation Factors and How to Find Them
1. **Fribrinogen deficiency**: cryoprecipitate from the blood bank is the best source. Give one or two 5-unit pools initially. On a gram basis, 1.5 grams of fibrinogen in a 5 unit pool of cryoprecipitate replaces about 1/6 of normal 10 grams whole body blood. Increase the dose for peripartum bleeding.
2. Factor II (prothrombin) deficiency: 4 Factor Prothrombin Complex Concentrate (PCC) such as Kcentra™, can be obtained from the pharmacy. It is given on a unit bases at 25 – 50 U/Kg based on INR for critical bleeding in patients receiving warfarin. Also given with vitamin k 1-10 mg.
3. Factors III, IV and VI,no longer used.
4. Factor V Deficiency: platelets from the blood bank or plasma depending on circumstances. Give one platelet unit and and get Hematology or Transfusion Medicine consultation.
5. Factor VII deficiency: Recombinant factor VIIa, such as NovoSeven™ can be obtained from the pharmacy. Initial dose 1 mg IV.
6. Factor VIII deficiency: Recombinant factor VIII. Give 5000U adult dose and consult hemophilia center (Hematology, Transfusion Medicine)
7. Factor XI deficiency: Recombinant factor IX, give 8000U adult dose and consult hemophilia center (Hematology, Transfusion Medicine)
8. Factor X: It is present in prothrombin complex concentrate (Kcentra™), which can be obtained from the pharmacy. The promary indication is to reverse warfarin anticoagulation and its dose calculation is based on INR. It is given in combination with vitamin K (1-10 mg).
9. Factor XI deficiency: thawed plasma from the blood bank is the best resource. Adult dose: 15-20 ml/Kg
10. Factor XIII deficiency: cryoprecipitate from the blood bank is the best resource. Give one or two 5-unit pools initially.
11. Von Willebrand factor deficiency: Common type I with reduced secretion should be treated with desmopressin (DDAVP) to increase secretion. It can be obtained from the pharmacy, Other types of Von Willebrand disease with low or abnormal factor need factor replacement with factor VIII and von Willebrand factor complex, such as HumateP™ and others.

Use of anti-hemophilia factors is highly specialized and other than emergency use should be coordinated with a hemophilia center to optimize care and minimize wastage. The normal concentration of human coagulation factors is 1U/ml and the normal blood content is 3000U of any factor in the 3L of plasma. For factor VIII deficiency (hemophilia A), only 60% of the replacement dose remains intravascular, so one needs to give more, 5000U total to achieve full correction. Factor VIII comes in vials of 2500U to facilitate dosing to achieve 50% and 100% correction of normal sized individuals.

Coagulation Factors and How to Find Them

Since donor plasma contains all factors in near normal amounts, it is the appropriate initial replacement for patients with massive uncontrolled hemorrhage who have or are at risk for coagulopathy. However, get laboratory early and often to guide resuscitation and direct diagnostic and therapeutic thinking.

Prothrombin complex concentrates (PCCs) are concentrates of the vitamin K dependent factors II, VII, IX, and X and the anti-coagulant factors protein S and C. They are collected and concentrated on calcium columns. They provide rapid correction of warfarin effect and are useful when intracranial or other critical bleeding requires rapid correction of warfarin anticoagulation. For the typical elderly patient with atrial fibrillation who develops an intracranial bleed, PCCs can correct the coagulation defect quickly.

ANTI-FIBRINOLYTICS

Remember
• Tranexamic acid and ε-aminocaproic prevent fibrinolysis and are indicated for limiting blood loss in some elective surgeries with high anticipated blood loss • Tranexamic acid **given in the first three hours** after traumatic injury is associated with lower mortality

Tranexamic acid and **ε-aminocaproic acid** are small molecule analogues of lysine that block the binding of plasmin to fibrin. In this manner they block fibrinolysis. They appear to be highly effective for reducing blood loss in a variety of circumstances. Randomized trials in craniosynostosis surgery in infants, hip and knee replacement, and spinal surgery all show about 50% reductions in blood loss and use.

Fibrinolysis complicates severe trauma when activation of protein C inactivates plasminogen activator inhibitor allowing plasmin to be continuously activated and clot to be continuously broken down. In the large CRASH-2 trial, giving tranexamic acid to all injured patients within 3hours of injury resulted in a significant net savings of life [25, 26].

GETTING HELP

The management of bleeding and clotting comprises an array of complex situations. Expertise in all aspects is uncommon. Seeking help from acute care and vascular surgeons, critical care, and hematologic physicians, and transfusion medicine or laboratorians may each be appropriate in different situations (Tables **5 and 6**).

Talking to The Blood Bank

Table 5. Talking to the Blood Bank. Provided by Monica B. Pagano, M.D., University of Washington, and Aaron Hess, M.D., PhD., University of Wisconsin.

ABO - ABO is the major human blood antigen group. A and B are sugars, O is German "Ohne" (without). Group "O" red cells lack A and B antigens and can serve as universal donor red cells. Humans share these antigens with bacteria in their gut, so they make antibodies against the antigens they do not have on their red cells (reciprocal antibodies). These antibodies are generally IgM, can fix complement, and cause acute intravascular hemolytic transfusion reactions. Incompatible RBCs can lead to death so we have rules and procedures to prevent incompatible transfusions. Because these antibodies can sometimes be strong, we use group AB plasma (without antibodies) as universal donor plasma but can use A low-titer-B plasma as well.
Rh - Refers to both the major non-ABO RBC antigen, RhD, and to the whole family of 50+ Rh antigens found on the 2 Rh proteins. Antibodies to these antigens can cause delayed hemolytic transfusion reactions and hemolytic disease of the fetus and newborn. The "D" antigen is so common, present in 85% of people, and reactive, immunizing approximately 50% of negative individuals, that its presence is labeled on every unit as "Positive" or "Negative". The Rh antigens are relatively few in number on RBCs and the antibodies generally IgG so they rarely fix complement and hemolysis occurs by antibody mediated phagocytosis and lysosomal breakdown inside macrophages. This is extravascular hemolysis without free hemoglobin, complement anaphylotoxins, or changes in haptoglobin. Such reactions can be detected by falling hematocrit and increases in direct bilirubin and LDH.
Alloantibodies - Can arise after exposure to non-self-alleles of RBC proteins and sugars and, like Rh antibodies, cause delayed hemolytic transfusion reactions and hemolytic disease of the fetus and newborn. Kell, Duffy, Kidd, and MNS are the most common proteins and Lewis and P the most important sugars. All RBCs and patient sera are tested with an antibody screen to look for these common alloantibodies, and such testing may identify other antibodies that are less common or important. Finding RBCs for patients who have one or several alloantibodies can take time and may require reference laboratories or going to the National Rare Donor Registry.
Autoantibodies - Are pathologic antibodies against RBCs or other blood components that can arise with viral infections, B-cell malignancies, and other uncommon causes. Mycoplasma-related cold aggulutinins or B-cell related warm RBC autoantibodies are common examples of this wider group of problems. Testing for antibody on RBCs, a direct antiglobulin (Coombs') test, is the typical starting place to evaluate for such problems.

Table 6. Common causes of bleeding in surgical patients. Provided by Monica B. Pagano, M.D., University of Washington, and Aaron Hess, M.D., PhD., University of Wisconsin.

Anemia
Thrombocytopenia
Platelet function disorders
Coagulation factors deficiency
Disseminated Intravascular Coagulation (DIC)
Excess fibrinolysis

CONCLUSION

This chapter outlines a structural framework for those providing operative and

perioperative care to understand the basics bleeding and coagulation. There are now numerous drugs, biologicals, and blood components that affect coagulation, and grasping the basics of coagulation is essential for safe and successful patient care. Bearing in mind that one of the major causes of death is uncontrolled hemorrhage whether from trauma, surgery, or postpartum, the reality remains that ten times more people die from heart attacks, stroked and thromboembolic disease – that is clotting – than they do from hemorrhage. An understanding of hemostasis, blood components, and their interactions with medications helps to understand the issues involved on patients who have bleeding or clotting disorders. Laboratory testing alone will not reflect what is happening acutely; in acute and rapidly evolving clinical situations, measured use of all available resources and expert consultation is imperative.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The author (editor) declares no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Hess JR. Massive Hemorrhage. In: Murphy MF, Roberts DJ, Yazer MH, Eds. Practical Transfusion Medicine. 5th ed., Wiley 2015.

[2] Francis CW. Clinical practice. Prophylaxis for thromboembolism in hospitalized medical patients. N Engl J Med 2007; 356(14): 1438-44.
[http://dx.doi.org/10.1056/NEJMcp067264] [PMID: 17409325]

[3] Baron TH, Kamath PS, McBane RD. Management of antithrombotic therapy in patients undergoing invasive procedures. N Engl J Med 2013; 368(22): 2113-24.
[http://dx.doi.org/10.1056/NEJMra1206531] [PMID: 23718166]

[4] Furie B, Furie BC. Thrombus formation *in vivo*. J Clin Invest 2005; 115(12): 3355-62.
[http://dx.doi.org/10.1172/JCI26987] [PMID: 16322780]

[5] Furie B, Furie BC. Mechanisms of thrombus formation. N Engl J Med 2008; 359(9): 938-49.
[http://dx.doi.org/10.1056/NEJMra0801082] [PMID: 18753650]

[6] Hoffman M. A cell-based model of coagulation and the role of factor VIIa. Blood Rev 2003; 17 (Suppl. 1): S1-5.
[http://dx.doi.org/10.1016/S0268-960X(03)90000-2] [PMID: 14697207]

[7] Longstaff C, Kolev K. Basic mechanisms and regulation of fibrinolysis. J Thromb Haemost 2015; 13 (Suppl. 1): S98-S105.
[http://dx.doi.org/10.1111/jth.12935] [PMID: 26149056]

[8] Segal JB, Dzik WH. Paucity of studies to support that abnormal coagulation test results predict

bleeding in the setting of invasive procedures: an evidence-based review. Transfusion 2005; 45(9): 1413-25.
[http://dx.doi.org/10.1111/j.1537-2995.2005.00546.x] [PMID: 16131373]

[9] Fowler A, Perry DJ. Laboratory monitoring of haemostasis. Anaesthesia 2015;70 Suppl 1:68-72, e24.
[http://dx.doi.org/10.1111/anae.12919]

[10] Goodman MD, Makley AT, Hanseman DJ, Pritts TA, Robinson BR. All the bang without the bucks: Defining essential point-of-care testing for traumatic coagulopathy. J Trauma Acute Care Surg 2015; 79(1): 117-24.
[http://dx.doi.org/10.1097/TA.0000000000000691] [PMID: 26091324]

[11] Holcomb JB, Tilley BC, Baraniuk S, *et al.* PROPPR Study Group. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 *vs*. a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. JAMA 2015; 313(5): 471-82.
[http://dx.doi.org/10.1001/jama.2015.12] [PMID: 25647203]

[12] Ng C, Motto DG, Di Paola J. Diagnostic approach to von Willebrand disease. Blood 2015; 125(13): 2029-37.
[http://dx.doi.org/10.1182/blood-2014-08-528398] [PMID: 25712990]

[13] Tripodi A, Anstee QM, Sogaard KK, Primignani M, Valla DC. Hypercoagulability in cirrhosis: causes and consequences. J Thromb Haemost 2011; 9(9): 1713-23.
[http://dx.doi.org/10.1111/j.1538-7836.2011.04429.x] [PMID: 21729237]

[14] Roberts LN, Bernal W. Management of bleeding and thrombosis in critically Ill patients with liver disease. Semin Thromb Hemost 2015; 41(5): 520-6.
[http://dx.doi.org/10.1055/s-0035-1550431] [PMID: 26080305]

[15] Riva N, Donadini MP, Ageno W. Epidemiology and pathophysiology of venous thromboembolism: similarities with atherothrombosis and the role of inflammation. Thromb Haemost 2015; 113(6): 1176-83.
[http://dx.doi.org/10.1160/TH14-06-0563] [PMID: 25472800]

[16] Nakashima MO, Rogers HJ. Hypercoagulable states: an algorithmic approach to laboratory testing and update on monitoring of direct oral anticoagulants. Blood Res 2014; 49(2): 85-94.
[http://dx.doi.org/10.5045/br.2014.49.2.85] [PMID: 25025009]

[17] Baron TH, Kamath PS, McBane RD. Management of antithrombotic therapy in patients undergoing invasive procedures. N Engl J Med 2013; 368(22): 2113-24.
[http://dx.doi.org/10.1056/NEJMra1206531] [PMID: 23718166]

[18] Gehrie E, Tormey C. Novel oral anticoagulants: efficacy, laboratory measurement, and approaches to emergent reversal. Arch Pathol Lab Med 2015; 139(5): 687-92.
[http://dx.doi.org/10.5858/arpa.2013-0677-RS] [PMID: 25927153]

[19] Scharf RE. Drugs that affect platelet function. Semin Thromb Hemost 2012; 38(8): 865-83.
[http://dx.doi.org/10.1055/s-0032-1328881] [PMID: 23111864]

[20] Carson JL, Grossman BJ, Kleinman S, *et al.* Red blood cell transfusion: a clinical practice guideline from the AABB*. Ann Intern Med 2012; 157(1): 49-58.
[http://dx.doi.org/10.7326/0003-4819-157-1-201206190-00429] [PMID: 22751760]

[21] Carson JL, Terrin ML, Noveck H, *et al.* Liberal or restrictive transfusion in high-risk patients after hip surgery. N Engl J Med 2011; 365(26): 2453-62.
[http://dx.doi.org/10.1056/NEJMoa1012452] [PMID: 22168590]

[22] Reeves BC, Rogers CA, Murphy GJ. Liberal or restrictive transfusion after cardiac surgery. N Engl J Med 2015; 373(2): 193.
[PMID: 26154794]

[23] Kaufman RM, Djulbegovic B, Gernsheimer T, *et al.* Platelet transfusion: a clinical practice guideline from the AABB. Ann Intern Med 2015; 162(3): 205-13.

[http://dx.doi.org/10.7326/M14-1589] [PMID: 25383671]

[24] Tinmouth A. Evidence for a rationale use of frozen plasma for the treatment and prevention of bleeding. Transfus Apheresis Sci 2012; 46(3): 293-8.
[http://dx.doi.org/10.1016/j.transci.2012.03.019] [PMID: 22521566]

[25] Tinmouth A. Evidence for a rationale use of frozen plasma for the treatment and prevention of bleeding. Transfus Apheresis Sci 2012; 46(3): 293-8.
[http://dx.doi.org/10.1016/j.transci.2012.03.019] [PMID: 22521566]

[26] Shakur H, Roberts I, Bautista R, *et al.* Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet 2010; 376(9734): 23-32.
[http://dx.doi.org/10.1016/S0140-6736(10)60835-5] [PMID: 20554319]

CHAPTER 7

Anesthesia for Obstetrical Emergencies

Karen Lindeman*

Johns Hopkins Medical Institution, Baltimore, MD, USA

Abstract: Anesthesia for obstetrical emergencies presents some of the most difficult decision making quandaries in anesthesiology due to the double considerations of both mother and fetus. Concerns for the mother often compete with concerns for the fetus. In the following chapter, several topics will be discussed including emergency cesarean section in patients with comorbidities such as asthma, morbid obesity and eclampsia. A cesarean section may have to be done without a spinal, epidural, or general anesthetic; that is a cesarean section done using only local anesthesia. Non-hemorrhagic emergencies during labor such as umbilical cord prolapse, breach presentation and shoulder dystocia are elaborated. Recommendations for hemorrhage- antepartum due to placenta previa, placental abruption, trial of labor after cesarean section, and uterine rupture; as well as those for postpartum- hemorrhage due to placenta accreta, increta, percreta, as well as uterine atony and uterine inversion are discussed. The pregnant patient undergoing nonobstetrical surgery presents with other challenges that are also addressed in the chapter.

Keywords: Asthma, Breach presentation, Eclampsia, Emergency cesarean section, Morbid obesity, Obstetrical emergencies, Placenta abruption, Placenta accreta, Placenta increta, Placenta percreta, Placenta previa, Shoulder dystocia, TOLAC (trial after trial of labor after cesarean section), Umbilical cord prolapse, Uterine atony, Uterine rupture.

INTRODUCTION

Anesthesia for obstetrical emergencies presents some of the most difficult decision-making quandaries in anesthesiology due to double considerations of both the mother and fetus. In many situations, concerns for the mother (Fig. **1**) compete with considerations for the fetus.

In general, categories of obstetrical emergencies that require anesthetic intervention include emergency cesarean delivery in patients with comorbidities,

* **Corresponding author Karen Lindeman:** Johns Hopkins Medical Institution, Baltimore, MD, USA; Tel: 410-95--5608; E-mail: klindema@jhmi.edu

Amballur D. John (Ed.)

non-hemorrhagic emergencies that arise before or during labor, and hemorrhagic emergencies.

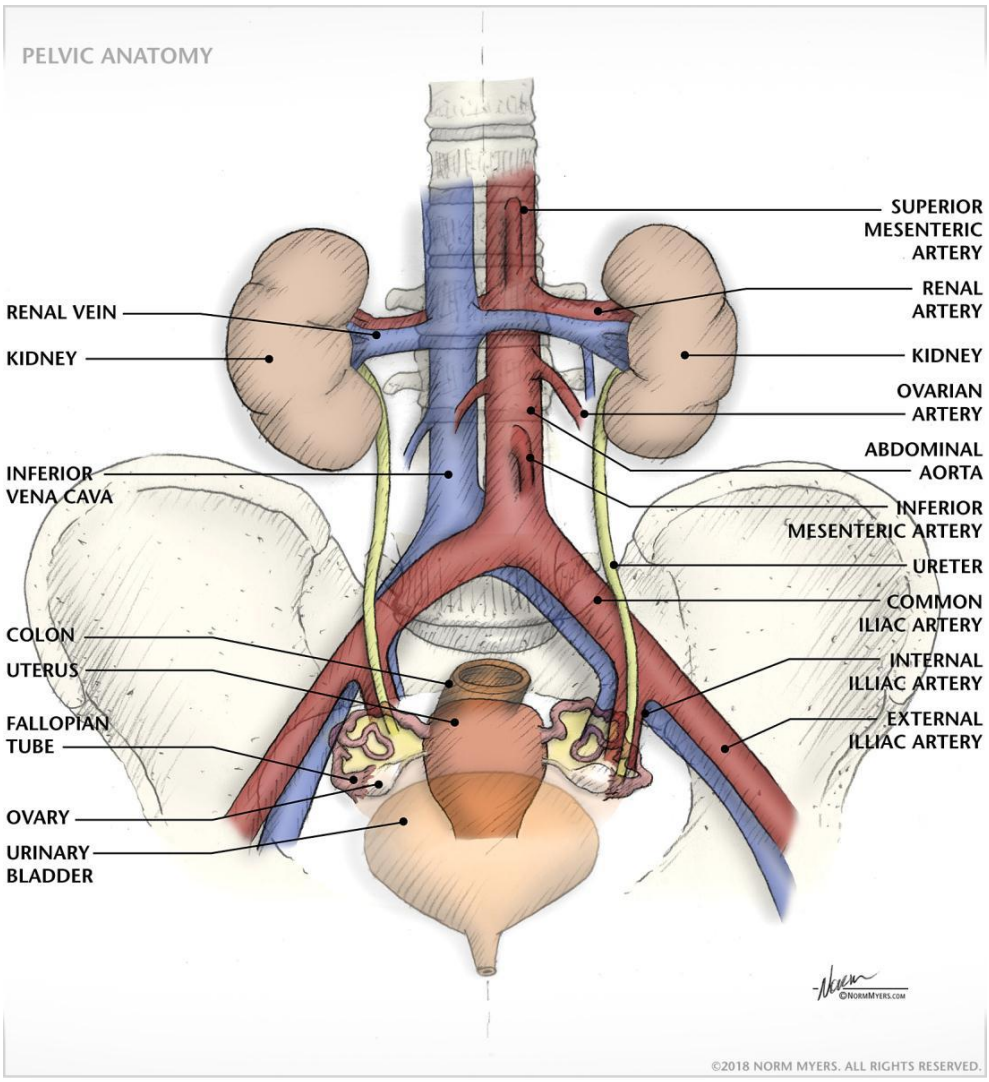


Fig. (1). Pelvic Anatomy. Image provided by Norm Myers.

EMERGENCY CESAREAN SECTION IN PATIENTS WITH COMORBIDITY

Emergency cesarean section in healthy patient incurs significant risk, but this risk can be multiplied many fold in patients with concomitant diseases.

Asthma

For emergency cesarean section, patients with asthma are at increased risk of exacerbation due to reflex-induced bronchospasm during laryngoscopy and intubation of the trachea. Regional anesthesia, which obviates the necessity of airway manipulation, minimizes this risk. Although practitioners should strongly consider the use of neuraxial anesthesia in cases of active asthma, the decision to use regional or general anesthesia depends on the urgency of the situation and nature of the emergency. Since in emergency situations, regional anesthesia may not be possible in a timely fashion, general anesthesia with endotracheal intubation may be required. **Methods to attenuate reflex-induced bronchospasm** include pretreatment with a α-adrenergic agonist [1], administration of intravenous lidocaine [2], and induction of anesthesia with either propofol or ketamine.

For maintenance anesthesia in asthmatic subjects, high concentrations of inhaled anesthetics provide protection against intraoperative bronchospasm. Because these agents also cause dose-dependent relaxation of uterine muscle, the risk of postpartum hemorrhage is concomitantly increased. If uterine atony does occur, treatment with **oxytocin and methylergonovine maleate** is preferable to **15-methyl prostaglandin** $F_2\alpha$, since the latter is more likely to stimulate bronchoconstriction in asthmatic subjects. Thus, maintenance general anesthesia in asthmatic subjects requires repeated assessments of airway and uterine conditions to determine optimal management.

Morbid Obesity

Morbid obesity, generally defined as body mass index greater than **30kg/m^2**, increases the risk of maternal morbidity and mortality. In an obstetrical emergency, these patients often present technical difficulties with blood pressure measurement, intravenous placement, neuraxial anesthesia, and general anesthesia. In addition, pulmonary changes exaggerate already reduced functional residual capacity and increased oxygen consumption, so that these women more rapidly develop hypoxemia during periods of apnea [3].

Choices for blood pressure measurement include a proper size blood pressure cuff placed on the upper arm, a regular size blood pressure cuff on the forearm, or an intra-arterial catheter if necessary. Successful intravenous catheter placement may be accomplished *via* peripheral approaches, sometimes aided by ultrasound visualization, or *via* a central approach.

Neuraxial anesthesia is more difficult to accomplish in morbidly obese patients. To find the midline, some practitioners locate the spinous processes with a long

needle [4] or use ultrasound guidance [5] when palpation is impossible. Since these procedures require additional time that might not be available, general anesthesia is often required in an emergency.

Emergency general anesthesia in a morbidly obese patient incurs increased risks of rapid oxygen desaturation, aspiration of gastric contents, and difficult mask ventilation and endotracheal intubation. As for the patient with normal body mass index, administration of a nonparticulate oral antacid shortly before the induction of anesthesia increases intragastric pH to mitigate the effects of potential aspiration. Many practitioners situate morbidly obese patients in a "ramped" position, by placing folded blankets beneath the chest and head until the external auditory meatus aligns horizontally with the sternal notch, to facilitate mask ventilation (if needed) and endotracheal intubation [6]. Videolaryngoscopy has been advocated, but no randomized trials have demonstrated its superiority over conventional direct laryngoscopy in morbidly obese pregnant subjects.

Eclampsia

Eclampsia, defined as otherwise unexplained seizures or coma in the setting of preeclampsia, constitutes a medical emergency. Thus, the immediate goal is to terminate the seizures. Secondary objectives include minimizing complications, especially inadequate ventilation, aspiration, cardiac dysrhythmias, and severe hypertension. At the onset of a seizure, monitoring airway patency, oxygen saturation, blood pressure, and electrocardiogram will assist in the detection of potential problems. Once the patient is medically stable, anesthetic plans for either vaginal delivery or cesarean section will depend on patient condition.

Eclamptic seizures can be isolated or recurrent. In either situation, **$MgSO_4$** is the agent of choice to prevent further seizures [7]. An initial loading dose of 4-6g over 20minutes, followed by a continuous infusion of 1-2g/h, usually yields therapeutic serum concentrations of 5-9mg/dL. An additional bolus of 2g may be required for repeated seizures. Concomitant administration of small doses of a benzodiazepine, such as midazolam 1-2mg, affords additional anticonvulsant effects in the acute setting, but incurs the risk of prolonged sedation. Propofol, with its anticonvulsant properties, might also provide benefit in small doses, but no studies have documented whether subanesthetic doses enhance the effects of $MgSO_4$ in preventing recurrence of seizures.

During an eclamptic seizure, proper airway management promotes ventilation and therefore helps to mitigate the risk of hypoxemia. Although in a spontaneously breathing patient supplemental oxygen *via* face mask, left sided tilt, and conservative measures to maintain an open airway may be sufficient, repeated seizures may necessitate endotracheal intubation to limit the risk of aspiration.

Guidelines for pharmacologic treatment of acute hypertension associated in the setting of eclampsia have not been clearly defined. Citing an association between acute systolic hypertension and intracranial hemorrhage in preeclampsia, the American College of Obstetrics and Gynecology (ACOG) recommends treatment to lower systolic blood pressures to 160mm Hg in preeclampsia or eclampsia [8]. However, no randomized trials have demonstrated reduced morbidity/mortality in eclamptic subjects when following this guideline. Nevertheless, most practitioners agree upon the treatment of acute hypertension at some level to prevent intracranial hemorrhage. **Pharmacological methods** to treat acute hypertension include intravenous labetalol, hydralazine, nitroprusside, and nicardipine, or, if the patient is sufficiently alert, oral nifedipine. Because sudden, acute drops in blood pressure can decrease uterine blood flow, the target decrease in blood pressure is usually limited to 20% of baseline in the first 30minutes. After termination of the seizures, a neurological examination can provide clues to the presence of intracranial pathology, such as an intracranial hemorrhage, which can be diagnosed *via* CT scan or MRI.

During or shortly after an eclamptic seizure, emergency cesarean delivery requires weighing the risks against the benefits. Transient fetal bradycardia often accompanies eclampsia [9], but emergency cesarean delivery for fetal concerns is generally limited to cases in which fetal bradycardia does not resolve.

For emergency cesarean section in an eclamptic patient, general anesthesia presents numerous potential hazards. As in a preeclamptic patient, airway edema can obscure visualization of the trachea during direct laryngoscopy, and sudden, severe hypertension during laryngoscopy can promote intracranial hemorrhage. Specifically, for the eclamptic patient, hypoxemia would likely occur more rapidly if the patient had aspirated during a seizure. In addition, acute increases in intracranial pressure during laryngoscopy could compromise neurologic function if intracranial pressure were already elevated from a recent seizure. If emergency general anesthesia is unavoidable, blood pressure monitoring with an arterial catheter would facilitate recognition and treatment of acute hypertension. A variety of difficult airway adjuvants and endotracheal tube sizes should be available. Useful measures to prevent acute hypertension include **pretreatment** with a short-acting antihypertensive agent, such as sodium nitroprusside (25-50 mcg), and/or using a generous dose of an induction agent, such as propofol (2-mg/kg) during rapid sequence induction. Awake fiberoptic tracheal intubation is a consideration in patients with significant facial edema, but this may be difficult to accomplish quickly in an emergency.

CESAREAN SECTION WITH ONLY LOCAL ANESTHESIA

In some cases, the situation mandates rapid delivery of the fetus in a patient who is not sufficiently prepared to undergo either major regional or general anesthesia. Under these circumstances, the obstetrician can utilize local anesthesia to deliver the fetus while preserving the mother's life.

Because large volumes of local anesthetics are required when performing cesarean section, amide local anesthetics can cause neuro- or cardiac toxicity in this situation. **Chloroprocaine (1.0-1.5%)**provides rapid anesthesia with limited toxicity due to its metabolism by nonspecific plasma esterases. The obstetrician initially infiltrates intracutaneously with 10-20ml chloroprocaine. Following incision, the obstetrician injects approximately 20ml of the local anesthetic deeper into the rectus fascia and incises the fascia. To anesthetize the peritoneum as well as the retroperitoneal uterine surface, the obstetrician then pours a large volume (60-100ml) of the local anesthetic into the abdomen. He/she can then incise the uterus and deliver the infant. **Supplemental sedation with ketamine (10mg bolus, up to 1mg/kg) provides analgesia and amnesia with limited respiratory effects on the neonate.** After delivery of the infant, additional chloroprocaine can be used to complete the operation if risks of induction of general anesthesia remain too high.

The **disadvantages** to this local anesthesia for cesarean section include incomplete anesthesia and the ensuing difficulties of managing an uncomfortable patient, unsatisfactory anesthesia if more extensive surgery is required, and unfamiliarity of the obstetrician with the technique. However, in extreme circumstances, this technique can help preserve the life of both the mother and the fetus.

NON-HEMORRHAGIC EMERGENCIES DURING LABOR

Umbilical Cord Prolapse

In some circumstances the umbilical cord prolapses through the cervix, either in the presence or absence of labor. When this occurs, compression of the cord between the fetal head and the cervix could reduce uterine blood flow and cause fetal bradycardia. Obstetricians therefore respond to this condition by manually elevating the fetal head *via* the vagina, until the infant can be delivered by cesarean section. **In the absence of fetal bradycardia**, neuraxial anesthesia, particularly spinal anesthesia with its rapid onset, is a reasonable choice for urgent cesarean section. **In cases of prolonged fetal bradycardia**, general anesthesia would be the technique of choice.

Breech Presentation

In breech presentation (Fig. **2**), the fetal buttocks and/or lower extremities are closest to the cervix. The three types of breech presentation include **frank breech**, in which the hips are flexed and the knees extended, **complete breech**, in which the hips and knees are flexed, and **incomplete breech**, in which one or both lower extremities is/are extended. Potential fetal complications that necessitate emergency intervention include umbilical cord prolapse, umbilical cord compression with or without prolapse, and entrapment of the head due to insufficient cervical dilation. These scenarios more likely arise with incomplete breech, due to the limited cervical dilation from the fetus's lower extremities.

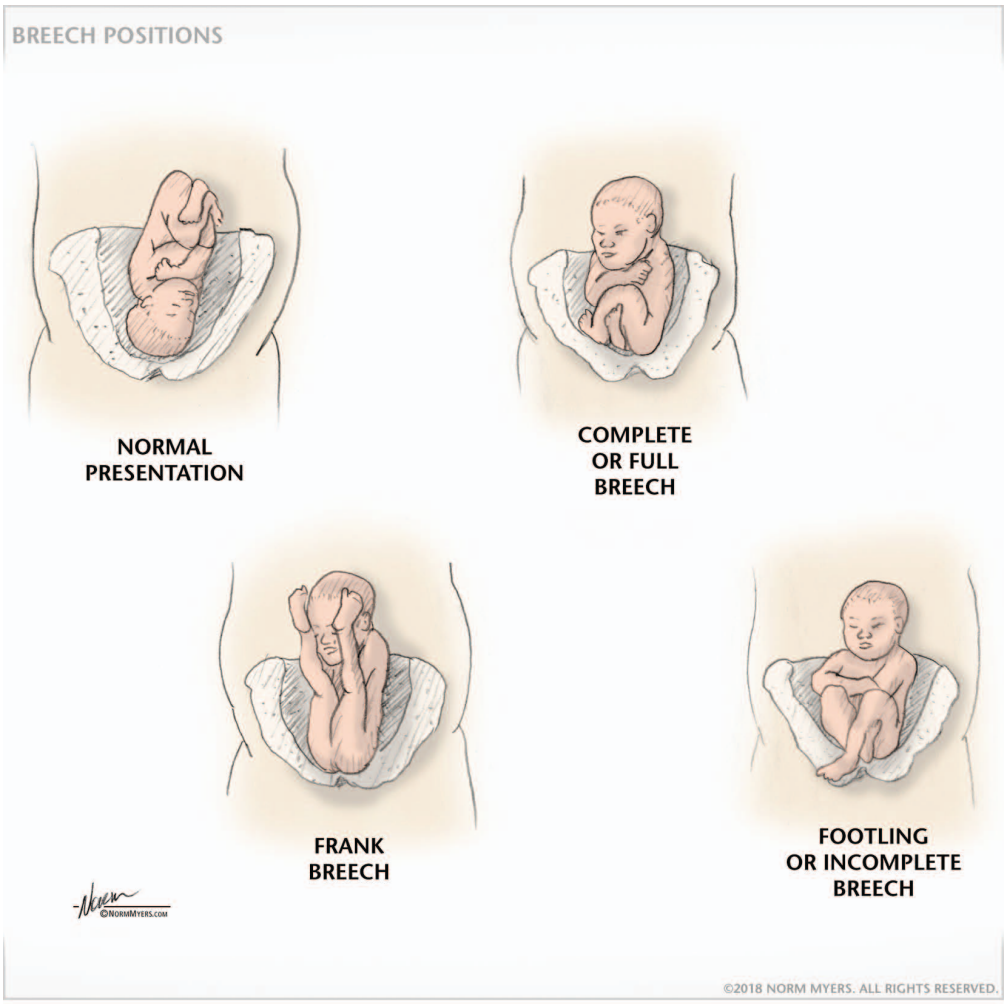


Fig. (2). Breech Positions. Image provided by Norm Myers.

For planned vaginal delivery, **epidural analgesia** for labor provides pain relief for the first stage of labor. In the second stage, epidural analgesia not only provides analgesia for obstetrical maneuvers, but also provides perineal relaxation to assist with instrumental vaginal deliveries, including forceps, which are commonly required to deliver the breech infant. If the head becomes entrapped, **intravenous nitroglycerin (50-250 mcg)** relaxes the uterus when excessive uterine contraction is contributing to head entrapment. More commonly, the cervix is not sufficiently dilated. Occasionally, the obstetrician may be able to deliver the entrapped head by incising the uterus, but at the risk of significant maternal hemorrhage. A labor epidural catheter can also be used to provide anesthesia for emergency cesarean section if cord prolapse, cord compression with fetal bradycardia, or entrapment of the fetal head occurs.

Shoulder Dystocia

During the majority of vertex vaginal deliveries, delivery of the fetal head provides the greatest obstacle to complete delivery of the infant. In a small percentage of cases, the anterior shoulder of the fetus has difficulty passing below the pubic symphysis after delivery of the fetal head. **Shoulder dystocia** becomes an emergency if umbilical cord compression causes fetal asphyxiation and ensuing bradycardia. To release the fetus' shoulder, the obstetrician will need to perform additional maneuvers, such as suprapubic pressure with traction on the fetal head and hyperflexion of the maternal thighs. Labor epidural analgesia would provide maternal pain relief and perineal relaxation to assist these maneuvers. If no epidural catheter was present for the first stage of labor, the use of spinal anesthesia would depend on time constraints. **Intravenous nitroglycerin (50-250mcg)** to relax the uterus may assist with the obstetrician's maneuvers. If these maneuvers fail to release the anterior shoulder, the obstetrician might need to reposition the fetal head back into the vagina and deliver the infant *via* emergency cesarean section. In the absence of a labor epidural catheter, general anesthesia would be needed.

ANTEPARTUM HEMORRHAGIC EMERGENCIES

Abnormal Placental Implantation

Placenta previa (Fig. **3**) occurs when the placenta implants ahead of the fetal presenting part. Three varieties of placenta previa include **total**, **partial**, and **marginal placenta previa**, meaning that the placenta completely covers the cervical os, partially covers the cervical os, or lies adjacent to the cervical os, respectively.

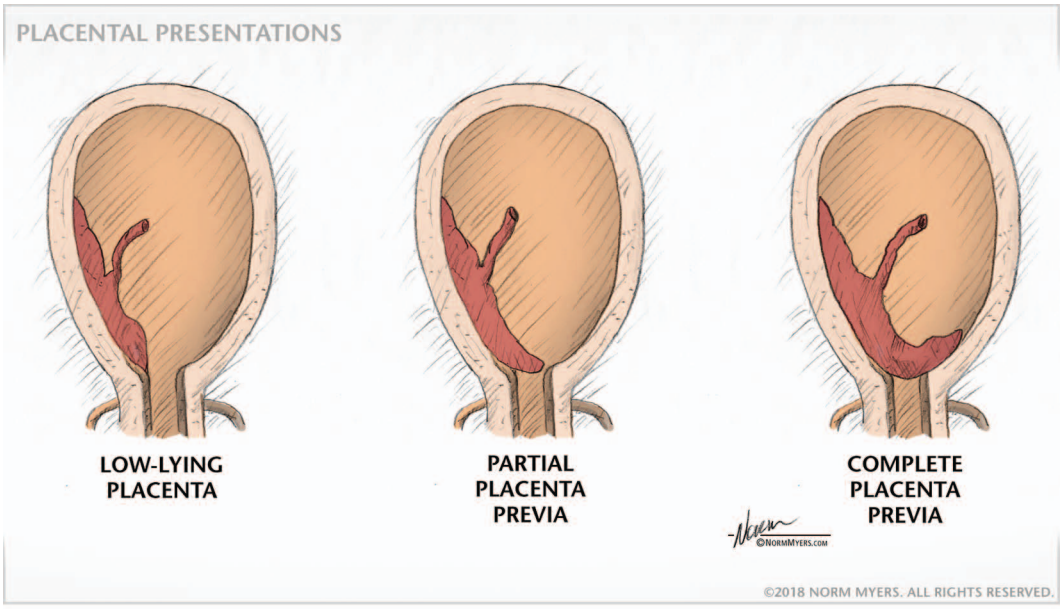


Fig. (3). Placental Presentations. Image provided by Norm Myers.

Placenta previa classically presents as painless vaginal bleeding. Transvaginal ultrasonography provides the most accurate diagnosis of placenta previa [10] and has made the "double set-up" essentially obsolete. Women with placenta previa usually require cesarean section, unless a marginal previa lies sufficiently distant from the cervical os. Patients with placenta previa are at increased risk of also having abnormal placental implantation, described below.

Placenta previa becomes an emergency when it results in either significant maternal hemorrhage or fetal distress, either of which might result from sudden placental separation. Although many practitioners select neuraxial anesthesia for patients with stable placenta previa, general anesthesia allows more rapid initiation of surgery while avoiding severe hypotension in the presence of fetal distress and/or significant maternal hemorrhage.

Placental Abruption

Placental abruption occurs when a normally implanted placenta separates before delivery of the fetus. The magnitude of the separation usually determines its clinical consequences. Large abruptions can result in fetal compromise, massive hemorrhage, and coagulopathy, presumably due to release of thromboplastic substances into maternal circulation and ensuing disseminated intravascular coagulation [11].

In contrast to placenta previa, **placental abruption typically causes painful vaginal bleeding**. Characteristically, the pain is constant rather than limited to contractions. Depending on the magnitude of the abruption, hemodynamic instability might accompany vaginal bleeding. In other cases, however, hemorrhage that remains intrauterine behind the placenta may be difficult to detect. Other symptoms and signs of placental abruption include constant uterine pain, uterine tenderness, and increased uterine tone. Changes in fetal heart rate patterns show variable or late decelerations with or without reduced short-term variability, or fetal bradycardia [12]. Ultrasonography may or may not help determine the diagnosis, since this technique is not very sensitive, especially in cases of concealed hemorrhage [13].

During labor, placental abruption can become an **emergency** and necessitate cesarean section for either fetal considerations or for hemorrhage. In either case, practitioners should prepare for significant hemorrhage by obtaining large bore intravenous access, assuring blood availability, and checking coagulation parameters to evaluate for disseminated intravascular coagulation. In a patient with labor epidural analgesia, extension of the labor block for cesarean section can provide rapid anesthesia in the case of fetal compromise, as long as the patient does not suffer from severe intravascular volume depletion. Alternatively, a hemodynamically stable patient might also be a candidate for spinal anesthesia, if a normal coagulation status can be confirmed. In cases of coagulopathy, severe volume depletion, or in the absence of labor epidural anesthesia, general anesthesia would be the technique of choice.

Trial of Labor After Cesarean Section

The choice of whether to undergo trial of **labor after cesarean section (TOLAC)** involves many complex considerations. One of the most important considerations is the likelihood of uterine rupture that most likely would occur at the site of the previous uterine scar [14]. The previous uterine incision most amenable to a subsequent TOLAC is a lower segment transverse incision. The lower uterine segment contains a lower density of uterine smooth muscle and is therefore less likely to result in scar dehiscence during the forceful myometrial contractions that constitute labor. With a classical cesarean section, the uterine incision is oriented vertically within the uterine corpus, which contains a higher density of smooth muscle. Both the vertical orientation of the scar and the location in the density of smooth muscle contribute to the increased probability of uterine rupture during labor.

Another factor that might increase the probability of uterine rupture is the use of oxytocin to stimulate uterine contractions. Stronger, oxytocin-induced uterine

contractions might cause uterine rupture more readily than contractions in the absence of oxytocin. In the absence of data from randomized trials, observational studies showed mixed results regarding effects of oxytocin in increasing the probability of uterine rupture during TOLAC.

Methods suggested to detect uterine rupture include changes in fetal heart rate pattern, loss of pressure with an intrauterine pressure catheter, or a sudden increase in pain during labor. Continuous fetal heart rate monitoring remains the most sensitive indicator of uterine rupture during labor. The other potential methods are neither sensitive nor specific indicators.

Anesthetic Considerations

In a woman approved to undergo TOLAC, intravenous access is essential to provide fluids in case of uterine rupture, as is access to blood and blood products. Although in the past some obstetricians argued against labor epidural analgesia based on the concern of masking signs and symptoms of uterine rupture, most obstetricians now agree that other indicators, as described above, would provide sufficient warning if this did occur. In TOLAC patients, labor epidural analgesia not only provides excellent analgesia for the first stage of labor, but also provides anesthesia for cesarean section if TOLAC does not succeed. There are no randomized trials comparing labor epidural analgesia to controls with respect to probability or detection of uterine rupture.

Uterine Rupture

Uterine rupture, which involves a full-thickness disruption of the uterine wall, occurs more frequently in women with previous uterine surgery, such as cesarean section. Although uterine rupture can occur in the absence of labor, factors that increase the strength of uterine contractions, such as induction of labor and/or use of oxytocin and prostaglandins, increase the probability of uterine rupture.

Diagnosis of uterine rupture can be challenging. In TOLAC patients, uterine scar dehiscence, in which only the pre-existing scar separates, can be asymptomatic and only detected if repeat cesarean section is needed. Signs of full thickness uterine rupture include abnormal fetal heart rate patterns, constant or more severe abdominal pain, hemodynamic changes, bleeding, and cessation of uterine contraction.

Anesthetic management depends on the nature of the emergency. In stable labor patients with labor epidural analgesia, surgical anesthesia *via* the epidural catheter is appropriate. Women who exhibit hemodynamic instability or apparent massive hemorrhage should undergo general anesthesia.

POSTPARTUM HEMORRHAGE

Placenta Accreta, Increta, and Percreta

Placenta accreta (Fig. **4**) occurs when the placenta implants abnormally into the uterine myometrium. In the most frequent amongst the three varieties, the placenta implants on the surface of the myometrium, while in **placenta increta** the placenta invades into the myometrium [15]. In **placenta percreta**, the least common, the placenta invades through the entire wall of the uterus to implant in the uterine serosa or outside the uterus. The placenta adheres abnormally to the uterus and may be impossible to separate from the uterine wall. These conditions are life-threatening due to massive blood loss, especially for placenta increta and placenta percreta, followed at times by coagulopathy, renal dysfunction, and acute respiratory distress syndrome.

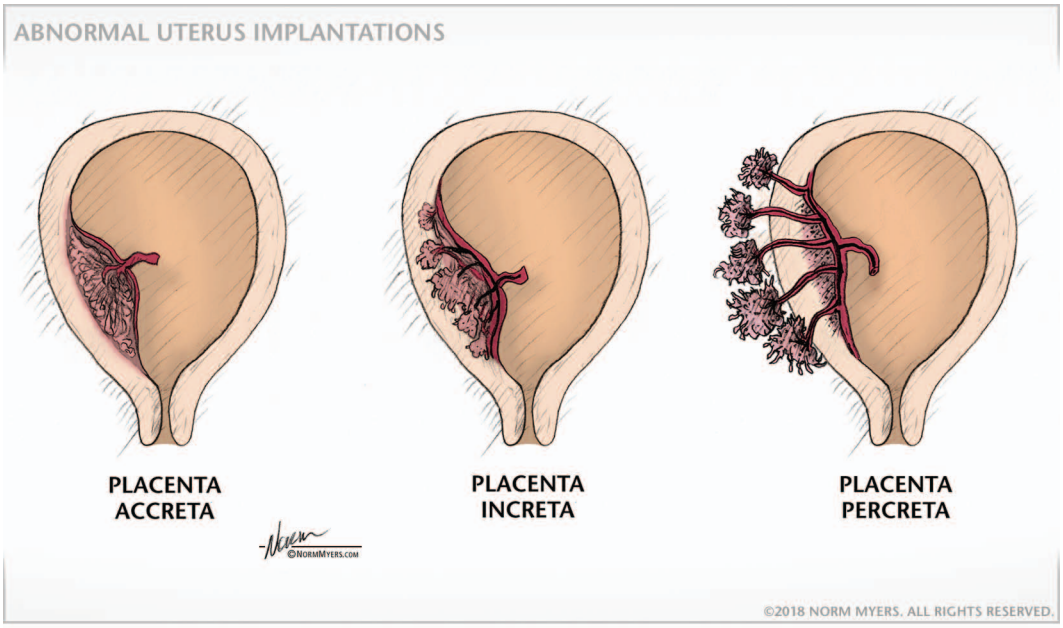


Fig. (4). Abnormal Implantations into Uterus. Image provided by Norm Myers.

Repeated cesarean delivery dramatically increases the probability of subsequent placenta accreta, increta, and percreta [16]. Although obstetricians often make the diagnosis of placenta accreta when the placenta fails to separate normally following delivery, antenatal ultrasonography or MRI may detect these conditions before delivery. Practitioners should be suspicious about the presence of placenta accrete in cases when the placenta overlies a previous uterine scar.

Anesthetic management entails preparation for massive hemorrhage during cesarean section and/or hysterectomy. Supportive management for additional complications, as outlined above, is also necessary. Especially with placenta percreta, a variety of surgical specialties may become involved to complete the surgery.

Uterine Atony

The mechanisms underlying the transformation of the uterine state of quiescence during pregnancy to rhythmic contractions during labor to sustained, forceful contraction in the postpartum period are not well understood. Failure to maintain this sustained contraction in the postpartum period inevitably leads to hemorrhage from bridging arteries across the myometrium remaining open. **Conditions** that cause overdistention of the uterus, such as macrosomia, multiple gestation, or polyhydramnios, increase the likelihood of uterine atony. Prolonged intrapartum exposure of the uterus to oxytocin can downregulate oxytocin receptors and therefore predispose to postpartum uterine atony. Intrapartum use of tocolytic agents, such as $MgSO_4$ for preeclampsia or α-adrenergic agonists for asthma or in utero fetal resuscitation, also increase the probability of uterine atony in the postpartum period.

Prophylactic therapy against uterine atony usually includes an intravenous infusion of oxytocin, since rapid bolus administration of a bolus dose oxytocin, which cases vasodilation, results in hypotension. Although neither minimum nor maximum doses of oxytocin have been firmly established, the doses generally range from 10-60units over one hour. **Other ecbolic agents**, drugs that contract the uterus, include ergot alkaloids, such as methylergonovine maleate, and prostaglandins, especially 15-methyl prostaglandin $F_2\alpha$ At least part of the mechanism of action of ergot alkaloids includes activation of α-adrenergic receptors on the surface of myometrial cells [17]. Thus, side effects from α-adrenergic receptor activation on vascular or airway smooth muscle cells include hypertension and, in susceptible individuals such as asthmatic subjects, bronchospasm. 15-methyl prostaglandin $F_2\alpha$ activates contractile prostaglandin receptors on airway and myometrial cells to stimulate contraction. Because airways of asthmatic subjects are often exquisitely sensitive to prostaglandin stimulation, but less so α-adrenergic stimulation, methylergonovine maleate would be a better choice in these subjects.

Uterine Inversion

Post-partum **acute uterine inversion**, when the uterus turns inside-out, requires emergency intervention due to the potential for severe hemorrhage with orwithout maternal bradycardia. Inversion may be obvious from visual inspection or hidden,

sometimes visualized on ultrasonography.

Obstetrical management centers on situating the uterus in its proper location, and therefore uterine relaxation may facilitate the required maneuvers. Intravenous nitroglycerin (50-250mcg) relaxes the uterus.

If the patient underwent labor epidural analgesia, the epidural catheter can be used to provide anesthesia. Alternatively, general anesthesia with high concentrations of a potent inhalational anesthetic can provide both uterine relaxation and anesthesia for obstetrical maneuvers.

Anesthetic Considerations for Obstetrical Hemorrhage

Anesthetic management for obstetrical hemorrhage centers on volume resuscitation to maintain euvolemia. This usually entails placement of multiple large bore peripheral and/or central venous catheters to administer crystalloid and colloid solutions (5% albumin), as well as blood products. A rapid infusion device can replace lost fluids quickly. Placement of an intra-arterial catheter allows continuous blood pressure monitoring and frequent blood sampling to assess adequacy of resuscitation and presence of complications, including coagulopathy, hypothermia, hypocalcemia, and acidosis.

Blood transfusion can include whole blood and/or blood components. Although whole blood provides the ideal replacement for significant hemorrhage, its limited availability often necessitates the utilization of blood component therapy. Packed red blood cells (PRBC), fresh frozen plasma (FFP), cryoprecipitate, and platelets can be transfused separately depending on the patient's needs. If cross-matched blood is not available, then administration of type-specific or O-negative blood would be second choices.

No clinical trials have determined the optimum ratio of PRBC to other blood components in massive transfusion for obstetrical hemorrhage. The potential risk of ongoing coagulopathy by transfusing relatively higher ratios of PRBC's should be weighed against known risks of complications associated with plasma and platelet transfusion with lower ratios. In trauma [18], a multi-center randomized trial, comparing ratios of 1:1:1 with 1:1:2 for transfusions of platelets, FFP, and PRBC's, failed to demonstrate differences in 30day mortality but did show lower mortality due to exsanguination in the 1:1:1 group. Whether these results can be extrapolated to obstetrical patients remains uncertain. In fact, studies showing accelerated consumption of coagulation factors in obstetrical hemorrhage [19] suggest that the pathophysiology of obstetrical hemorrhage differs from that of trauma and that therefore such extrapolations may not be tenable.

Hemostatic monitoring, such as thromboelastography, can be useful to direct therapy for transfusion-associated coagulopathy. In thromboelastography, abnormalities of the first phase of the readout suggest deficits at the beginning of clot formation that may be amenable to treatment with FFP. Abnormalities of the second phase, which involves further generation of the clot, may result from reduced fibrinogen and platelet quantity and/or quality. Administration of platelets and cryoprecipitate may be indicated. In the third phase, which reflects clot stability, abnormalities suggest hyperfibrinolysis that can be treated with an antifibrinolytic agent such as tranxemic acid. Normal ranges of thromboelastography differ during pregnancy and reflect the baseline hypercoagulable state [20].

Cell salvage was once thought to be contraindicated in obstetrics due to the possibility of administering amniotic fluid contamination and its potential for a syndrome similar to amniotic fluid embolism. However, modern cell salvage techniques have proven to be safe and effective in massive obstetrical hemorrhage [21].

For severe hemodynamic instability due to obstetrical hemorrhage, cross clamping the aorta provides a useful adjuvant to other resuscitation measures [22]. The aorta can be cross clamped below the level of the kidneys to minimize organ damage.

Although the choice of general anesthesia or regional anesthesia depends on volume status of patient and presence or absence of epidural catheter for labor, in most cases of severe hemorrhage practitioners use general anesthesia to minimize hemodynamic changes. Because of its sympathomimetic properties, rapid sequence induction with ketamine, rather than propofol, provides greater hemodynamic support during hemorrhage, except in cases of catecholamine depletion [23]. Lacking sufficient intravascular volume to maintain blood pressure during moderate depths of anesthesia, these patients may require intravenous adjuvants, such as benzodiazepines or scopolamine, to ensure amnesia. Following massive transfusion, extubation of the trachea may not be possible, mandating postoperative care in an intensive care unit.

ANESTHESIA FOR EMERGENCY NON-OBSTETRICAL SURGERY IN THE OBSTETRICAL PATIENT

When compared to emergency surgery in patients who are not pregnant, emergency surgery during pregnancy incurs additional risks to the mother and to the fetus. For the mother, physiologic changes of pregnancy increase anesthetic risk, while for the fetus, the primary risk is from preterm labor. Additional considerations for the fetus include changes in uterine blood flow and direct

effects of pharmacologic agents administered to the mother.

Many physiologic changes of pregnancy, including cardiovascular and pulmonary changes, begin in the first trimester and accelerate through the second trimester. Increased blood volume, primarily from increased plasma volume, reaches a peak at the end of the second trimester and results in an overall decrease in hematocrit. The enlarged uterus begins to produce significant vena caval obstruction at approximately the midpoint of gestation. In the respiratory system, increased oxygen consumption with concomitant reduced functional residual capacity leads to rapid maternal hypoxemia during periods of apnea as might occur with induction of general anesthesia. Changes in anatomy of the upper airway have been debated for decades. Although the question of whether visualization of the airway during **direct laryngoscopy in pregnant women is more difficult** has not been fully answered, physicians should prepare for this possibility. Physiologic changes to the gastrointestinal system increase the risk of aspiration of gastric contents in pregnant women who undergo surgery. Hormonally-mediated changes, including relaxation of the physiologic lower esophageal sphincter, begin early in the pregnancy, while changes resulting from the enlarged uterus, such as elevated intragastric pressure and alteration of the angle of the stomach with respect to the esophagus, become important when the uterus enlarges at the end of the second trimester.

Pregnant women who undergo emergency non-obstetrical surgery should have an obstetrical consultation before surgery, if time permits. Assuming that fetal monitoring is available at a particular institution, the obstetrical team may or may not recommend intraoperative fetal monitoring, depending on type of surgery and gestational age of the fetus. No randomized trials provide clinical outcome data with or without fetal monitoring, but the American College of Obstetricians and Gynecologists (ACOG) has released general guidelines in this regard. ACOG recommends that “if the fetus is considered previable, it is generally sufficient to ascertain the fetal heart rate by Doppler before and after the procedure” [24]. For a viable fetus, ACOG recommends a minimum of fetal heart rate and contraction monitoring before and after surgery, with intraoperative monitoring when additional conditions, including the physical ability to monitor the fetus and the possibility of performing emergency cesarean section, are met.

Preterm labor/fetal loss remains the major risk to the fetus in non-obstetric surgery during pregnancy. The mechanism for this observation is unknown, but surgery involving or closer to the uterus seems to incur greater risk. Although some practitioners have advocated prophylactic tocolysis to prevent preterm labor in nonobstetrical surgery, evidence for this is limited. Teratogenicity from anesthetics has been difficult to study due to the lack of randomized trials in

human subjects. Animal studies suggest that physiologic alterations, such as hypoxia, hypercarbia, and hypotension, expose potential teratogenic effects. Many of the studies implicating specific agents in humans, such as diazepam, require chronic administration throughout the pregnancy, including the first trimester, and are observational studies only.

Anesthetic technique of choice depends on the nature of the surgery and condition of the patient. In general, regional anesthesia mitigates risk of aspiration and, depending on the surgical location and the type of regional anesthesia, might provide the most stable hemodynamic profile. No controlled studies have demonstrated a difference in risk of preterm delivery with either regional or general anesthesia.

For many types of emergency surgery, regional anesthesia is not feasible and therefore general anesthesia will be the technique of choice. Because of vena caval compression, the uterus should be displaced to the left in pregnant subjects by 20 weeks' gestation. As for cesarean section, the potential benefits of administration of a nonparticulate oral antacid in reducing the risk of acid aspiration usually outweigh risks. Rapid sequence induction or awake intubation also limits the risk of aspiration. No credible evidence implicates any of the common induction agents in teratogenesis when used acutely for anesthesia. For maintenance anesthesia, other commonly used anesthetics, such as local anesthetics, opioids, muscle relaxants, and potent inhalational anesthetics, also appear to be safe with respect to potential teratogenesis. Normal oxygenation and blood pressure are important to maintain oxygen delivery to the fetus. In most cases, extubation of the trachea with the patient wide awake protects against aspiration at the end of the case.

CONCLUSION

Anesthesia for obstetrical emergencies often requires a plan of action before the emergency occurs. Improved care has come with coordination amongst anesthesiologists, obstetricians, neonatologists, radiologists, general surgeons, and intensive care specialists. As complicated situations occur with increasing frequency, the anesthesiologist will need to be prepared to take on a multitude of roles in perpipartum care to improve patient outcome.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Groeben H, Schlicht M, Stieglitz S, Pavlakovic G, Peters J. Both local anesthetics and salbutamol pretreatment affect reflex bronchoconstriction in volunteers with asthma undergoing awake fiberoptic intubation. Anesthesiology 2002; 97(6): 1445-50.
[http://dx.doi.org/10.1097/00000542-200212000-00016] [PMID: 12459670]

[2] Groeben H, Silvanus MT, Beste M, Peters J. Combined intravenous lidocaine and inhaled salbutamol protect against bronchial hyperreactivity more effectively than lidocaine or salbutamol alone. Anesthesiology 1998; 89(4): 862-8.
[http://dx.doi.org/10.1097/00000542-199810000-00010] [PMID: 9778003]

[3] Tanoubi I, Drolet P, Donati F. Optimizing preoxygenation in adults. Can J Anaesth 2009; 56(6): 449-66.
[http://dx.doi.org/10.1007/s12630-009-9084-z] [PMID: 19399574]

[4] Maitra AM, Palmer SK, Bachhuber SR, Abram SE. Continuous epidural analgesia for cesarean section in a patient with morbid obesity. Anesth Analg 1979; 58(4): 348-9.
[http://dx.doi.org/10.1213/00000539-197907000-00024] [PMID: 572187]

[5] Whitty RJ, Maxwell CV, Carvalho JC. Complications of neuraxial anesthesia in an extreme morbidly obese patient for Cesarean section. Int J Obstet Anesth 2007; 16(2): 139-44.
[http://dx.doi.org/10.1016/j.ijoa.2006.08.011] [PMID: 17270422]

[6] Collins JS, Lemmens HJM, Brodsky JB, Brock-Utne JG, Levitan RM. Laryngoscopy and morbid obesity: a comparison of the "sniff" and "ramped" positions. Obes Surg 2004; 14(9): 1171-5.
[http://dx.doi.org/10.1381/0960892042386869] [PMID: 15527629]

[7] Lucas MJ, Leveno KJ, Cunningham FG. A comparison of magnesium sulfate with phenytoin for the prevention of eclampsia. N Engl J Med 1995; 333(4): 201-5.
[http://dx.doi.org/10.1056/NEJM199507273330401] [PMID: 7791836]

[8] ACOG. Committee Opinion 623, February 2015.

[9] Paul RH, Koh KS, Bernstein SG. Changes in fetal heart rate-uterine contraction patterns associated with eclampsia. Am J Obstet Gynecol 1978; 130(2): 165-9.
[http://dx.doi.org/10.1016/0002-9378(78)90361-7] [PMID: 619657]

[10] Leerentveld RA, Gilberts EC, Arnold MJ, Wladimiroff JW. Accuracy and safety of transvaginal sonographic placental localization. Obstet Gynecol 1990; 76(5 Pt 1): 759-62.
[http://dx.doi.org/10.1097/00006250-199011000-00006] [PMID: 2216220]

[11] Hall DR. Abruptio placentae and disseminated intravascular coagulopathy. Semin Perinatol 2009; 33(3): 189-95.
[http://dx.doi.org/10.1053/j.semperi.2009.02.005] [PMID: 19464510]

[12] Oyelese Y, Ananth CV. Placental abruption. Obstet Gynecol 2006; 108(4): 1005-16.
[http://dx.doi.org/10.1097/01.AOG.0000239439.04364.9a] [PMID: 17012465]

[13] Glantz C, Purnell L. Clinical utility of sonography in the diagnosis and treatment of placental abruption. J Ultrasound Med 2002; 21(8): 837-40.
[http://dx.doi.org/10.7863/jum.2002.21.8.837] [PMID: 12164566]

[14] Rosen MG, Dickinson JC, Westhoff CL. Vaginal birth after cesarean: a meta-analysis of morbidity and mortality. Obstet Gynecol 1991; 77(3): 465-70.
[PMID: 1825136]

[15] Placenta Accreta. ACOG Committee Opinion No. 529. July, 2012.

[16] Getahun D, Oyelese Y, Salihu HM, Ananth CV. Previous cesarean delivery and risks of placenta previa and placental abruption. Obstet Gynecol 2006; 107(4): 771-8.
[http://dx.doi.org/10.1097/01.AOG.0000206182.63788.80] [PMID: 16582111]

[17] de Groot AN, van Dongen PW, Vree TB, Hekster YA, van Roosmalen J. Ergot alkaloids. Current status and review of clinical pharmacology and therapeutic use compared with other oxytocics in obstetrics and gynaecology. Drugs 1998; 56(4): 523-35.
[PMID: 9806101]

[18] Holcomb JB, Tilley BC, Baraniuk S, *et al.* Transfusion of plasma, platelets, and red blood cells in a 1:1:1 *vs*. a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. JAMA 2015; 313(5): 471-82.
[http://dx.doi.org/10.1001/jama.2015.12] [PMID: 25647203]

[19] Butwick AJ. Postpartum hemorrhage and low fibrinogen levels: the past, present and future. Int J Obstet Anesth 2013; 22(2): 87-91.
[http://dx.doi.org/10.1016/j.ijoa.2013.01.002] [PMID: 23473552]

[20] Polak F, Kolnikova I, Lips M, Parizek A, Blaha J, Stritesky M. New recommendations for thromboelastography reference ranges for pregnant women. Thromb Res 2011; 128(4): e14-7.
[http://dx.doi.org/10.1016/j.thromres.2011.04.007] [PMID: 21543108]

[21] Postpartum hemorrhage. ACOG Practice Bulletin No. 76. American College of Obstetricians and Gynecologists. Obstet Gynecol 2006; 108: 1039-47.
[http://dx.doi.org/10.1097/00006250-200610000-00046] [PMID: 17012482]

[22] Belfort MA, Zimmerman J, Schemmer G, Oldroyd R, Smilanich R, Pearce M. Aortic compression and cross clamping in a case of placenta percreta and amniotic fluid embolism: a case report. AJP Rep 2011; 1(1): 33-6.
[http://dx.doi.org/10.1055/s-0031-1274513] [PMID: 23705082]

[23] Gustafsson U, Sjöberg F, Lewis DH, Thorborg P. Influence of pentobarbital, propofol and ketamine on skeletal muscle capillary perfusion during hemorrhage: a comparative study in the rabbit. Int J Microcirc Clin Exp 1995; 15(4): 163-9.
[http://dx.doi.org/10.1159/000178971] [PMID: 8847176]

[24] Nonobstetric surgery during pregnancy. Committee Opinion number 474. ACOG. Obstet Gynecol 2011; 117: 420-1.
[http://dx.doi.org/10.1097/AOG.0b013e31820eede9] [PMID: 21252774]

CHAPTER 8

Pediatric Anesthesia

Monica Hoagland, Tessa Mandler and **Lawrence I. Schwartz***

Colorado Children's Hospital, Aurora, CO, USA

Abstract: CHILDREN ARE NOT SMALL ADULTS. In this chapter, we will discuss the resources and standards that must be in place, in order for community-based programs to be in a position to deliver quality anesthetic care to children. Patient and procedural selection policies, appropriate equipment, dedicated physical space, and knowledgeable and experienced providers are just some of what is required. Caring for children in a large children's hospital, where the entire system is geared toward pediatrics, can test the most experienced pediatric anesthesiologist. Children have unique physiologic, pharmacologic, pathophysiology, and behavioral characteristics which change and develop throughout their lives. We will examine the pre-operative, intra-operative, and post-operative aspects that make pediatric anesthesia different from the perioperative care of adults. Additionally, we will provide an overview of the anesthetic management of some of the more common ambulatory pediatric procedures which may be encountered in the community-based practice such as; myringotomy and tympanostomy tube insertion; tonsillectomy and adenoidectomy; genitourinary procedures – circumcision, hypospadias repair, inguinal hernia repair, and orchiopexy; and foreign body removal.

Keywords: Adenoidectomy, Bronchospasm, Children, Circumcision, Difficult pediatric airway, Foreign body removal, Hypospadial repair, Infants, Inguinal hernia, Laryngospasm, Myringotomy, Neonates, Orchiopexy, Pediatric anesthesia, Pediatric intraoperative fluid management, Pediatric surgery, Pediatric pain medication, Pediatric postoperative nausea and vomiting, PRAE (perioperative respiratory delirium), Postoperative pediatric pain control, Tonsillectomy, Tympanostomy.

INTRODUCTION

Children are not small adults. Pediatric patients greatly vary from 1000 gram premature infants to the morbidly obese adolescents, and each one presents a special set of challenges to the anesthesiologists who care for them.

* **Corresponding author Lawrence I. Schwartz:** Colorado Children's Hospital, Aurora, CO, USA; Tel: 720-77--4999; Fax: 720-777-7266; E-mail: Lawrence.Schwart2@childrenscolorado.org

Amballur D. John (Ed.)

These patients have unique physiologic, pharmacologic, pathophysiology, and behavioral characteristics which change and develop throughout their lives. Caring for children in a large children's hospital, where the entire system is geared toward pediatrics, can test the most experienced pediatric anesthesiologist. When these patients present to community based centers, with fewer resources and personnel focused on children, these challenges can be overwhelming and possibly compromise safe, quality pediatric anesthesia.

In this chapter, we will discuss the resources and standards that must be in place, in order for community-based programs to be in a position to deliver quality anesthetic care to children. Patient and procedural selection policies, appropriate equipment, dedicated physical space, and knowledgeable and experienced providers, are just some of what is required of institutions which desire to care for pediatric anesthesia patients. We will examine the pre-operative, intra-operative, and post-operative aspects that make pediatric anesthesia different from the perioperative care of adults. Additionally, we will provide an overview of the anesthetic management of some of the more common ambulatory pediatric procedures which may be encountered in the community based practice.

PATIENT AND PROCEDURE SELECTION

Current evidence has established that some children have a higher risk of perioperative morbidity and mortality. **Specifically, neonates, critically ill children, and children with complex comorbidities may benefit from care delivered in specialized hospitals.** However, historically, American Society of Anesthesiologists (ASA) classification 1 and 2 children have been safely cared for in community based hospitals and surgical centers. Community-based centers caring for children must develop, administer, and maintain a system that allows for the "correct" pediatric patients to be anesthetized by a dedicated group of anesthesia and surgical providers focused on providing safe and effective care for pediatric patients.

Routine pediatric surgeries are performed in several types of institutions (*i.e.* children's hospitals, adult hospitals, ambulatory surgery centers, *etc.*). The vast majority of pediatric surgical procedures are completed in an outpatient setting with an increasing number occurring in freestanding locations [1, 2]. Table **1** lists the most common Ambulatory procedures on patients younger than 15 years of age.

Table 1. Most common inpatient pediatric surgery procedures on pstients <15 years of age. Adapted from Centers for Disease Control and Prevention. National Survey of Ambulatory Surgery [3]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Most Common Ambulatory Surgery Procedures on Patients <15 Years of Age	
Total ambulatory procedures	**3,266,000**
Myringotomy and tubes	667,000
Tonsillectomy with or without adenoidectomy	530,000
Nose, mouth and pharynx excluding tonsillectomy with or without adenoidectomy and adenoidectomy	388,000
Orthopedic procedures	295,000
Miscellaneous diagnostic and therapeutic procedures	22,000
Ear excluding myringotomy and tubes	191,000
Operations on the male genital organs	166,000
Operations on the integumentary system (i.e. skin, subcutaneous tissue, breast)	166,000
Adenoidectomy	132,000
Eye surgeries	103,000
Hernia repair ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.	73,000

Despite the establishment and maturation of pediatric surgery as a subspecialty, approximately 40% of the most common pediatric inpatient surgical procedures are performed in non-pediatric hospitals [4]. However, complex pediatric surgeries are 6-16 times more common in a pediatric hospital than any other institution [5]. Table **2** lists the most common inpatient pediatric surgery procedures.

In 2014, a Task Force for Children's Surgical Care established guidelines for providing a "surgical and anesthetizing" level of care to pediatric patients undergoing surgical procedures. The purpose of center classification was to assure optimal resources to care for infants and children undergoing surgical intervention and to define the procedures and patients that are within the typical scope of practice of each level [6]. A summary of the Children's Surgical Center Standard and Scope of Practice are reviewed in Table **3**.

These recommendations have been endorsed by the board of the Society for Pediatric Anesthesia (SPA) and the American College of Surgeons (ACS). How these standards will impact pediatric care remains to be seen. Suffice it to say, that the needs to anesthetize children in community-based settings is only increasing and will require greater cooperative planning to facilitate safe and effective regional care.

Table 2. Most Common Inpatient Pediatric Surgery Procedures (Modified from Somme [5]). Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Most Common Inpatient Pediatric Surgery Procedures	
Type of Surgery	**Weighted Frequency**
Appendectomy	81,848
Central venous access	33,474
Pyloromyotomy	11,326
Burn debridement or grafting	10,844
Cholecystectomy	7,679
PDA ligation	5,653
Bladder/ureteral reconstruction	5,543
Antireflux procedure	5,355
Pediatric inguinal hernia repair	4,507
Gastrostomy/jejunostomy ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.	4,407

Table 3. A summary of the children's surgical center standard and scope of practice.

Level	**I – Comprehensive**	**II – Advanced**	**III – Basic**
Age	Any	Any	>6 months
ASA	1-5	1-3	1-2
Multidisciplinary management of comorbidities	Multiple medical and surgical specialties; pediatric anesthesiology	Typically single surgical specialties; neonatology; pediatric anesthesiology	None
Operations	Major congenital anomalies, complex diseases. Require significant multi-disciplinary coordination	Common anomalies and diseases typically treated by most pediatric surgical specialists. Do not require significant multidisciplinary coordination	Common, low-risk procedures typically performed by a single specialty.
Ambulatory ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.	ASA 1-3*	ASA 1-3*	ASA 1-2 Age older than 1 year

*Full term and preterm infants can be cared for as ambulatory patients based on written guidelines established by the pediatric anesthesiologist in charge of perioperative care. Institutional guidelines generally require full-term infants younger than weeks or preterm infants younger than 50 post-conceptual weeks to be monitored for at least 12 hours. Adapted from Task Force for Children's Surgical Care [6]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Resources Necessary for the Perioperative Care of Children

Table 4. Equipment Specific for Infant & Pediatric Patients [7 - 13]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Equipment Specific for Infant & Pediatric Patients [7, 8-13]	
Machine	Infant/pediatric appropriate that supports spontaneous and positive-pressure ventilation
Airway Devices	Appropriately sized airway equipment includes: face masks, oral airways, nasal airways, laryngeal mask airways (LMAís), cuffed and uncuffed straight, oral-rae, nasal-rae endotracheal tubes, straight and curved laryngoscope blades with laryngoscope handle, special airway devices for difficult airway (i.e. fiber optic scope, video laryngoscope, cricothyrotomy tray), self-inflating bag, working suction
Intravenous Equipment	Intravenous catheters +/- central venous catheters; intraosseous equipment; micro-drip infusion sets; vascular access technology (i.e. ultrasound, near-infrared devices such as transilluminator)
Warming Devices	Warming lamps, heat and moisture exchangers (HMEís), fluid warmers, heating mattress pad, and circulating warm-air devices
Monitors	Non-invasive blood pressure cuffs, pulse oximeters, temperature probes or thermometers, electrocardiography, capnography, anesthetic gas concentrations and inhaled oxygen concentration, +/- invasive arterial pressure measurement
Drugs	Induction, maintenance, emergence, emergency (i.e. atropine and succinylcholine for laryngospasm) ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.

Equipment

Prior to anesthetizing an infant or child, a comprehensive selection of pediatric equipment that is regularly stocked and maintained must be readily available to the anesthesiology care team (Table **4**). Airway equipment and intravenous catheters are manufactured in various sizes to meet the needs of children of all ages. In addition, emergency drugs and equipment including, a code cart with pediatric defibrillator pads and medications for resuscitation and malignant hyperthermia, and a difficult airway cart all need to be immediately accessible [7, 8]. Resuscitation drugs should be stocked in appropriate infant/pediatric concentrations. **Furthermore, even if the entire perioperative staff is well educated on pediatric emergency drug dosing and administration, it is prudent to have a clearly written pediatric dose schedule for these drugs easily accessible** [8, 9].

Monitors

Vigilant monitoring of patients under anesthesia significantly improves

perioperative morbidity and mortality. While properly trained, experienced anesthesiologists and their anesthetists are the foundation of patient safety during an anesthetic, monitors have augmented the practice of anesthesia in that they provide real-time, objective data, trends and/or warnings that may indicate a change in a patient's well-being or anesthetic equipment function. The American Society of Anesthesiologists' Committee on Standards and Practice Parameters has outlined standards for basic anesthetic monitoring for any patient undergoing monitored anesthetic care, regional anesthesia or general anesthesia [14]. Table **5** lists these standards and describes how information pertinent to each physiologic parameter can be obtained during an anesthetic.

Table 5. Basic Anesthetic Monitoring of Pediatric Patients [7, 12 - 15]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Basic Anesthetic Monitoring of Pediatric Patients [7, 12-15]	
Physiologic Parameter	Monitoring Method
Oxygenation	Physical Exam: color assessment Pulse Oximetry: blood oxygen saturation Mass spectroscopy, Oxygen Analyzer with Low Oxygen Concentration Limit Alarm, inspired and expired concentration of gases
Ventilation	Physical Exam: chest excursion, auscultation of breath sounds Capnography, Mass Spectroscopy: qualitative and quantitative measure of end-tidal carbon dioxide
Circulation	Physical Exam: pulse assessment Electrocardiogram: cardiac rhythm, rate, & ischemia detection Non-invasive arterial blood pressure: circulatory function
Temperature	Physical Exam: warmth assessment Temperature probe or thermometer: assess appropriate body temperature especially if change is suspected, intended or anticipated ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.

Well maintained and properly functioning anesthesia equipment is equally important to patient monitors. Improperly functioning equipment and/or broken equipment is associated with an increased risk of perioperative morbidity and mortality [16, 17]. Therefore, The American Society of Anesthesiology's Committee on Equipment and Facilities developed recommendations for the pre-anesthesia checkout. While the pre-anesthesia checkout can be completed by a qualified anesthesia and/or biomedical technician, **the anesthesia provider is ultimately responsible for the proper function of all equipment used to provide anesthesia care** [15, 18]. **These standards apply to the care of children in any anesthetizing location. Again, having appropriately sized monitoring equipment is essential**. Blood pressure cuffs must be correctly sized

for the patient. Cuffs which are too large may underestimate the actual blood pressure, while cuffs that are too small may overestimate the pressure and result in the provider possessing a false sense of security of hemodynamic stability. In children, the American Heart Association recommends that the cuff bladder width should be at least 40 percent of the arm circumference halfway between the olecranon and acromion; the cuff should then cover 80 percent or more of the arm circumference [19].

Admitting *vs*. Transfers

In order to provide the safest care possible to pediatric patients, clear guidelines need to be established and observed regarding their perioperative care. Institutions should practice within their respective surgical center level standards unless providing emergency services [8]. If the institution cannot provide comprehensive perioperative care for the patient, it must establish relationships and transfer agreements with a specialized pediatric institution. These contracted providers should collaborate to help further define these standards and scope of practice. **Fundamental to these guidelines are the indications for the transfer of infants and children with surgical needs to Level I or Level II Centers, which include patients characterized by the following: less than 60 weeks postmenstrual age, younger than 6 months of age, and need for intensive care unit** [8, 20].

Patients less than 60 weeks post-conceptual age (PCA) are at risk for post anesthetic apnea [1, 20, 21]. Prematurity, a history of apnea, anemia, and coexisting disease are all risk factors for postoperative apnea. Based on current literature, a widely accepted guideline is to monitor all infants less than 50 weeks post-conceptual age for at least 12 hours post-anesthesia; if the infant has a desaturation episode during this monitoring period, it is recommended to monitor for an additional 12 hours from the apnea episode [1, 22 - 24]. At our institution, **we observe the following guidelines:**

"Former premature infants born prior to 37 weeks gestational age who are less than 56 weeks PCA at the time of surgery are admitted overnight for cardiorespiratory monitoring or receive prolonged observation in the PACU prior to discharge.

Full term infants require overnight admission or extended PACU observation if they are less than 44 weeks PCA at the time of surgery" [25].

Another pediatric population that warrants strong consideration for post-operative admission are children with sleep disordered breathing who present for tonsillectomy and adenoidectomy. The American Academy of

Otolaryngology – Head and Neck Surgery recommends overnight admission for children less than 3 years of age with obstructive sleep apnea (OSA) or patients with severe OSA (*i.e.* apnea-hypopnea index of ≥10 events/hour or oxygen saturation ≤80%) due to the high incidence of perioperative respiratory complications after tonsillectomy [1, 26 - 28].

Personnel

Safe perioperative care of a neonate, infant, child or teenager requires a team of qualified, experienced, pediatric trained medical personnel, which includes anesthesiologists, surgeons, pediatricians and, nurses [7, 8]. Moreover, in order to provide optimal perioperative care, it is helpful for other health care team members and services that have roles in caring for surgical patients to have pediatric knowledge and experience. These other health care team members and services may include but are not limited to: radiologists, pathologists, pharmacists, respiratory therapists, phlebotomists, and child life specialists [7, 8, 20]. In essence, the institutional resources and personnel should be able to provide comprehensive perioperative care for pediatric patients [29]. If a facility is unable to meet these requirements, a clearly outlined transfer agreement and plan should be in place with a specialized pediatric center that can assume the perioperative care responsibility of a pediatric patient [8, 20, 30].

Institutions that routinely care for pediatric patients should have a written policy defining its scope of practice for their perioperative care. This policy should delineate which types of pediatric operative, diagnostic and therapeutic procedures requiring anesthesia are permitted on an elective or emergent basis. **Institution policy should also define how many times each procedure should be performed in order to maintain competency** [7, 20, 29]. In a similar vein, institutions should also define the requirements, minimal case number and types of pediatric cases each anesthesiology provider should perform in order to obtain and maintain institution credentials and practicing privileges [7, 8, 29].

The American Society of Anesthesiologist's Statement on Practice Recommendations for Pediatric Anesthesia designates privileges as "Regular Clinical Privileges" and "Special Clinical Privileges" [8]. According to this statement, an anesthesiologist who meets training and certification recommendations may provide and/or directly and immediately supervise anesthetics for pediatric patients. It is suggested that anesthesiologists providing and/or directly supervising the anesthetic care of pediatric patients in the categories designated by the facility's department of anesthesiology as being at increased risk for anesthetic complications (thus requiring special clinical privileges) should be graduates of pediatric anesthesiology fellowship training

programs accredited by ACGME or should be fully credentialed members of the department of anesthesiology who have demonstrated continuous competence in the care of such patients as determined by the department [8, 15].

Credentialing

The Society of Pediatric Anesthesia was founded in 1987 with the mission to "continually advance the safety and quality of anesthetic care, perioperative management, and alleviation of pain in children" [30]. Ten years later, The Accreditation Council for Graduate Medical Education (ACGME) first recognized pediatric anesthesiology as a subspecialty in anesthesiology, and the Anesthesiology Residency Review Committee developed standardized program requirements for the 1-year fellowship program [31, 32]. Then, in 2013, The American Board of Anesthesiology allowed diplomates who had successfully completed pediatric anesthesiology fellowship and non-pediatric anesthesiology fellowship trained anesthesiologists who met certain qualifications to take the first pediatric anesthesiology subspecialty examination (Table **6**) [33]. Most recently, in 2014, the Second Year Advanced Pediatric Anesthesiology Fellowship Network was created to promote additional pediatric anesthesiology education and training in the following areas: pediatric cardiac anesthesiology, pediatric anesthesiology education, pediatric anesthesiology pain medicine, pediatric anesthesiology quality and safety, and pediatric anesthesiology research [34, 35]. The ongoing evolution of the field of pediatric anesthesiology strive to continually improve the perioperative care to pediatric patients. It is the duty of anesthesiology practitioners to be knowledgeable on current trends and help define future standards.

Table 6. Pediatric anesthesiology certification requirements. Adapted from ASA statement on practice recommendations for pediatric anesthesia [8]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Pediatric Anesthesiology Certification Requirements
• American Board of Anesthesiology (ABA) Diplomate
• Maintain licensure requirements: permanent, unconditional, unrestricted, unexpired license to practice medicine or osteopathy in the United States or province of Canada
• Fulfillment of ABA defined subspecialty training
• Fulfillment of ABA defined subspecialty examination requirement
• In good professional standing, according to the ABA
• Capable of independently performing the entire scope of subspecialty practice without accommodation or with reasonable accommodation ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.

Establishing Pediatric Specific Guidelines

Nil Per Os

The American Society of Anesthesiologists developed recommendations for the minimum fasting period prior to elective procedures in order to allow for adequate post-prandial gastric emptying thereby reducing the incidence and severity of pulmonary aspiration, which occurs in approximately 0.02-0.04% of pediatric patients [36 - 38]. Children may be at risk for aspiration of gastric contents due to excessive aerophagia during crying, strenuous diaphragmatic activity during obstruction, and a shorter esophagus with decreased hydrostatic pressure gradient between the stomach and the larynx. The intent of the ASA NPO recommendations is to provide guidelines for healthy pediatric patients undergoing elective scheduled procedures (see Table **7**). Despite adherence to the fasting recommendations, gastric emptying may be incomplete and clinical judgment is of utmost importance in determining appropriate NPO time under circumstances such as, opioid treatment, altered mental status, neuromuscular diseases, trauma, systemic infection, gastric hypomotility, and impaired esophageal sphincter control [36, 38, 39]. It is also not uncommon for children to find food unbeknownst to their parents.

Table 7. Summary of fasting recommendations. *Adapted from the American Society of Anesthesiologists [36]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Summary of Fasting Recommendations	
Your child may enjoy the following prior to his/her procedure:	**Hours prior to scheduled surgery**
Clear liquids	2
Breast Milk	4
Infant formula	6
Light meal (i.e. food with low fat content: plain toast, fruit, vegetables, crackers, etc.) *Fried or fatty foods may prolong gastric emptying time requiring longer fasting time	6
©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.	

Prolonged fasting in young children is associated with perioperative patient discomfort, hypoglycemia, and dehydration with associated hypotension and/or difficult intravenous access. Allowing pediatric patients to enjoy clear liquids until 2 hours preoperatively, especially those that contain carbohydrates, prior to their NPO cutoff time, may ameliorate the adverse effects of prolonged fast, and produce a happier, more compliant patient and family [40 - 43]. In an effort to

decrease operating room downtime from a procedure delay or cancelation due to non-compliance with the fasting recommendations, several pediatric institutions have adopted fasting cutoffs based on facility arrival time for outpatients rather than scheduled procedure time [44, 45]. **Most important is to present a clear, easy to understand, consistent policy to patients, parents, and staff.**

PREOPERATIVE CARE

Developmental Pediatrics/Child Life Issues

A child's perception and comprehension of the world, and their place in it, varies vastly depending on his/her chronological and developmental ages. As a consequence, children of varied ages may have very different experiences during their hospital stay [46, 47]. Anesthesiologists caring for children must possess an understanding of child development in order to effectively develop rapport and trust with pediatric patients and their families and alleviate both patient and parental anxiety. Table **8** briefly outlines normal childhood development stages, and offers behavioral strategies which can be employed to create a more comfortable and less stressful experience for pediatric patients who require surgery and anesthesia.

Pre-Op Sedation/Parental Presence

The incidence of significant anxiety during the perioperative period occurs in up to 60% of children [55, 56]. Proper management of perioperative anxiety is important in order to avoid adverse outcomes such as uncooperative behavior during induction of anesthesia, increased postoperative pain, increased likelihood of emergence agitation, and negative postoperative behavioral changes [46, 57, 58]. The two most common practices to manage perioperative anxiety are pre-anesthesia sedation and parental presence at induction [55]; the debate has been longstanding regarding which is the best method. Although each practice possesses its own merits, there currently does not seem to be a failsafe practice applicable to every child (see Table **9**).

While objective data is essential to a pre-anesthesia interview, a subjective assessment is also important. Through observation and interaction, the child (*i.e.* crying, uncooperative child who is unwilling to socially engage with health care professionals), the anesthesiologist should be able to determine the need for special pre-operative interventions such as pre-operative sedation or parental presence [59]. Furthermore, the objective and subjective information obtained during the anesthesia pre-operative evaluation will enhance the anesthesiologist's overall assessment of the pediatric patient and his/her family [46]. This personalized knowledge facilitates the creation of a thoughtful and appropriate

perioperative care plan (and back-up plan) that will best align with the needs of the child and his/her family.

Table 8. Childhood Developmental Stages [46, 48 - 54]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Childhood Developmental Stages [46,48-54]		
Age	**Developmental Characteristics**	**Keys to Interaction**
Infants (<1year)	- Motivations based on basic human needs: food, shelter, etc. - Separation anxiety (~8-10 months) - Learn about surroundings by social referencing (referring to reactions/ emotions of caregiver)	- Minimize NPO time to decrease fussiness due to hunger - Active parental participation during hospitalization to emphasize sense of security - Allow comfort items (i.e. favorite toy or blanket)
Toddlers (1-3years)	- Well bonded to parents; difficulty separating from them during stress - Receptive > expressive language skills - Explorers - Fear pain and injury	- Allow comfort items (i.e. favorite toy, blanket, object) - Distraction techniques (i.e. stories, songs) - Use short, easy to understand terms - Engage in magical thinking (i.e. special sleeping medicine)
Preschoolers (3-5years)	- Egocentric view of the world - Fear pain and injury - Literal, concrete thinking	- Allow child to participate in care (i.e. help pick a mask flavor, hold the mask) - Honest, simple communication; encourage child to talk - Reassure child he/she will not be alone - Use play to show what will happen (i.e. stuffed animal patient)
School age children (6-12years)	- Transition from egocentric to sociocentric perspective; concerned about other people - Developing logical thought processes and problem solving ability - Goal-oriented activities	- Describing patient hospital experience in a non-threatening environment - Encourage patients to actively participate in their care (i.e. answer simple pre-operative questions regarding health history) - Rely on parent support and begin to seek peer support
Teenagers (13-18years)	- Develop skills of logical thought, deductive reasoning and systematic planning - Need for privacy and independence - Concerns about pain, losing control, waking up during surgery, not waking up and dying	- Include patients in discussions and decisions regarding care to provide a sense of control and independence - Reassurance that privacy will be respected - Provide clear explanations and assurances regarding perioperative fears - Increased teenager cooperation when physician perceived to be attentive and nonjudgmental
©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.		

Table 9. Comparison of pre-operative sedation and presence to reduce patient peri-operative anxiety. Adapted from Kain [55]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Comparison of Pre-Operative Sedation and Parental Presence to Reduce Patient Peri-Operative Anxiety		
Method	**Pro**	**Con**
Pre-Operative Sedation with benzodiazepine, alpha-2-agonist, or opioid	- Improved compliance during induction - Decreased parental anxiety especially in anxious parents - Decreased negative postoperative behavioral responses - Improved postoperative psychologic and pain recovery (in adults)	- Prolonged discharge times - Increased cost - Potential disruption to operating room flow - Adverse reactions to medications
Parental Presence during Induction of Anesthesia ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.	- Decreased need for pharmacologic anxiolysis - Decreased fear and anxiety of parent-child separation - Decreased parental anxiety - Increased parental satisfaction with separation process and perioperative care via "Family Centered Care"	- Crowded operating room - Parentsí possible adverse reactions (i.e. vasovagal episode, increased parental anxiety) - Prolonged anesthetic induction - Increased anesthesiologist stress especially if a complication arises

If parental presence during the induction to anesthesia is part of the anesthetic plan, it is helpful for family members to be familiar with expectations and responsibilities [60]. Preparation may begin during a pre-surgical tour either in person or video or through educational handouts on what to expect the day of surgery [47, 61]. Prior to induction of anesthesia, parents should be briefed on the potential changes their child may experience during anesthesia induction with reassurance that the changes are common and normal: nystagmus, disconjugate gaze, increased respiratory rate, signs of upper airway obstruction, rapid loss of consciousness, and/or uncoordinated movements. Lastly, to facilitate smooth separation from their child and allow the operating room team to focus on the patient, it is helpful to clearly state that family members will be escorted from the operating room as soon as their child is asleep or in the event of an emergency [57].

There are many advantages to the administration of pre-operative sedatives for anxious children of all ages who are facing surgery. These medications can alleviate fear and anxiety and help provide for a smooth, stress-free induction in a compliant, relaxed patient. They may also provide some amnesia regarding the arrival to the operating room and induction. The choice of which sedative to use varies widely depending on factors such as provider, facility, patient tolerance and procedure. Midazolam is the most commonly use pre-operative sedative, although

dexmedetomidine and ketamine are finding an increased utility among many pediatric anesthesiologists. The detailed pharmacology of these drugs are well published in multiple sources and will not be discussed here. The most common sedatives and dose schedules are listed for quick review in Table **10**:

Table 10. Pre-operative sedation option [62 - 71]. IM, intramuscular; IV, intravenous. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Pre-Operative Sedation Options [62-71]		
Medication	**Recommend Dose**	**Comments**
Midazolam	Oral: 0.2-0.5mg/kg/dose (maximum 20mg; approved for ≥6months of age) IM/IV: 0.05-0.1mg/kg/dose (maximum 10mg) Intranasal: 0.1-0.3mg/kg/dose (maximum 10mg; use 5mg/ml concentration)	- Water-soluble, fruit flavored oral formulation with bitter aftertaste - Clinical effect dose dependent: usual onset 10-15minutes post-oral administration, 5-10minutes post intranasal administration, <3-5 minutes IM/IV administration - IM administration can last up to 4-6hours - Paradoxical reactions (1-3%) may occur especially with higher doses - Burning sensation with intranasal administration
Dexmedetomidine	Oral: 2.5-4 mcg/kg Intranasal: 1-2 mcg/kg Generally given as a pre-medication to children >1year of age	- Usual onset 30-45minutes post intranasal administration, 45-60 minutes post oral administration - Prolonged postoperative sedation - "Arousable" and "Cooperative" sedation effects - Analgesic effects and decreased perioperative opioid administration - Costly compared to other sedatives
Ketamine	Oral: 4-10mg/kg/dose IM: 2-5mg/kg/dose IV: 0.5-2mg/kg/dose Intranasal (>1year of age): 5mg/kg/dose	- Adverse effects: increased secretions, nausea, vomiting, psychological disturbances (noted with IM/IV administration), prolonged recovery - IM administration useful in uncooperative patients who will not tolerate mask induction or IV placement - Onset: intranasal 5-10minutes; oral 10-15minutes; IM 3-5minutes; IV within 30seconds
Opioids ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.	Varies per drug	- Reserve for patients experiencing pain due to risk of adverse effects (i.e. respiratory depression, pruritus, nausea and vomiting)

EMERGENCY PLANNING

As discussed above, community based centers providing pediatric anesthesia services must be prepared to deal with children who present with emergent situations such as difficult airway, massive hemorrhage, malignant hyperthermia,

and cardiopulmonary collapse. This requires the resources, personnel, and knowledge to perform a resuscitation of a pediatric patient. The resuscitation of the pediatric patient goes beyond the scope of this chapter. However, it is imperative that all centers caring for children have algorithms and policies in place for dealing with these emergencies. At minimum, all providers must be trained and competent in Pediatric Basic Life Support, and Pediatric Advanced Life Support guidelines. A pediatric "code cart" containing resuscitative drugs in appropriate concentrations and doses, vascular access equipment including intraosseous needles, airway equipment, and dantrolene should be regularly stocked and maintained. It would be prudent policy to ensure providers remain up to date with the latest updates to practice guidelines, and keep up knowledge and skill through various educational activities includes practice drills and simulation.

INTRAOPERATIVE CARE

The intraoperative anesthetic management of pediatric patients differs from that of adult patients for a number of reasons including differences in pharmacology, physiology and the ability of pediatric patients to cooperate with medical procedures. Pharmacokinetic differences are most pronounced in neonates and infants with older children being more similar to adults. Neonates, infants and young children have decreased protein binding, an increased proportion of total body water, decreased fat and muscle stores and immature renal and hepatic function compared to adults [72]. These changes have a profound effect on pediatric dosing requirements. For instance, water-soluble drugs will require a higher bolus dose and either decreased maintenance dose or longer dosing interval to compensate for the changes in volume of distribution and renal clearance [73]. In addition, cardiac output, regional blood flow and receptor expression varies by age and further impacts the appropriate dosing of drugs. Unfortunately, up to 80% of drugs used in pediatrics have not been studied in children and dosing recommendations are usually based on adult dosing scaled to weight, which may not accurately predict appropriate dosing [72]. To complicate matters further, there is concern that some anesthetics, particularly agents targeting GABA and NMDA receptors, can have neurotoxic effects after exposure in neonates and infants [74]. However, two recent studies have shown that single early exposures to general anesthesia do not adversely affect neurodevelopmental outcomes after no anesthesia or regional anesthesia [75, 76]. Young children also have markedly different physiology compared to older children and adults. Cardiovascular and respiratory physiologic differences are of particular importance in pediatric anesthesia and will be discussed throughout the following sections.

Finally, pediatric patients often have limited ability to cooperate with medical procedures, and anesthetic techniques may be modified to accommodate these

limitations. Mask induction and deep extubation are more often performed in pediatric patients than adults. Regional anesthetics are rarely performed in the absence of general anesthesia. Non-invasive procedures, such as imaging studies, which would not require sedation in an adult often require general anesthesia in children. This section will address intraoperative anesthetic issues as they pertain to pediatric patients as well as review anesthetic considerations for common pediatric procedures.

Induction of Anesthesia

Anesthesia in children can be induced by either inhalation or intravenous routes, with most children preferring a mask induction followed by intravenous line placement after loss of consciousness. **Mask inductions are contraindicated for patients who are at risk for** aspiration and those who have medical conditions, such as malignant hyperthermia and muscular dystrophy, which preclude the use of inhalational anesthetics [77]. Benefits of mask inductions include patient satisfaction, the ability to maximize success for intravenous line placement, and the ability to titrate the anesthetic while maintaining spontaneous ventilation [78]. However, if the child has a respiratory emergency or becomes hemodynamically unstable during induction, the anesthesiologist will be unable to administer rescue medications or fluids until an intravenous line is obtained.

Inhalation induction is most often performed with a combination of nitrous oxide (N_2O) and sevoflurane. In a cooperative child, induction is started with 70% N_2O in oxygen for approximately one minute until the child begins to feel the effects of N_2O. At that point, sevoflurane is added to the circuit [78]. Sevoflurane can be added gradually in small increments or increased immediately to 8%. Rapidly increasing to a high concentration decreases the length induction and may increase the rate of apnea, but does not increase any other respiratory or cardiovascular complication [79]. An exception to this is children with Down syndrome who can have significant bradycardia with high inspired sevoflurane concentrations [80].

As the induction proceeds, airway muscle tone decreases and the child may begin to have obstructed breathing. Basic maneuvers, such as adjusting head position, opening the mouth and doing a chin lift or jaw thrust, should be performed. If obstruction continues, applying CPAP with 10-15 cm H_2O is the next step. Oral and nasal airways can be used to relieve obstruction, but if the patient is still in a light plane of anesthesia these may trigger laryngospasm [81]. While the intravenous line is being placed, the child should be maintained with spontaneous or assisted ventilation on the highest level of sevoflurane and nitrous oxide that he

will tolerate. If the child becomes apneic, the level of sevoflurane should be decreased and ventilation controlled until spontaneous ventilation resumes. If prolonged controlled ventilation is necessary, the anesthetic level must be decreased to avoid giving an accidental sevoflurane overdose. Once the intravenous line is obtained, N_2O is discontinued and additional drugs, such as propofol, fentanyl, or neuromuscular blocking agents can be given as needed in preparation for intubation. If the induction is prolonged or mask ventilation is difficult, gastric insufflation is likely. This can be especially problematic in infants and small children in whom gastric distention may significantly interfere with effective ventilation. Air should be evacuated from the stomach prior to or after intubation to improve ventilation [81].

Intravenous inductions should be performed whenever there is an intravenous line in place, when children are at risk for aspiration or when mask inductions are anticipated to be difficult due to patient's body habitus or potential for upper airway obstruction. This method of induction is preferred for adolescent patients who can cooperate with preoperative intravenous line placement. The drugs available for intravenous induction include propofol, ketamine, etomidate, fentanyl and midazolam. Indications and contraindications of these drugs are the same as for adults and will not be reviewed here. However, special consideration should be given to rapid sequence induction (RSI) in pediatric patients, especially young children. The classic RSI technique includes pre-oxygenation, cricoid pressure, muscle relaxation with succinylcholine and no positive pressure ventilation prior to intubation. This technique is associated with hypoxemia, bradycardia, hypotension and airway trauma in infants and young children due to rapid desaturation without ventilation, rushed attempts at intubation and distorted airway anatomy and decreased lower esophageal sphincter tone due to cricoid pressure [82, 83]. An alternative modified RSI for childhood consists of pre-oxygenation, no cricoid pressure, use of non-depolarizing muscle relaxants and gentle ventilation prior to intubation. This technique is associated with fewer desaturations and hemodynamic instability without any incidence of aspiration [84]. The use of succinylcholine in this situation is also controversial. Succinylcholine is contraindicated for use in routine airway management in children and adolescent patients. Although patients at risk for aspiration are not considered routine patients, some argue that with the availability of sugammadex, rocuronium should be used in place of succinylcholine for RSI in pediatric patients to provide rapid intubating conditions while minimizing the risks associated with succinylcholine. However, succinylcholine still provides more rapid intubating conditions than rocuronium and is also essential in the management of other airway emergencies. The decision of appropriate induction technique in this situation is left to the discretion of the anesthesiologist [85].

Airway Management

The pediatric respiratory system has significant anatomic and physiologic differences from adult patients that affect intraoperative airway management, many of which resolve by late childhood. **The pediatric airway is prone to obstruction at multiple points, which can make mask ventilation difficult.** The occiput is relatively large and places the neck in flexion while lying supine. The nasal passages and oropharyngeal space are relatively small and the tongue is large. Adenotonsillar hypertrophy can cause progressive obstruction starting in early childhood. The larynx in neonates is located at C2 and moves progressively down to its normal location near C5 in childhood. The combination of a high larynx and short jaw makes the airway appear more anterior during laryngoscopy. However, the airway is more easily manipulated by external pressure than in adults. The epiglottis is long, narrow and omega-shaped which can limit visualization of the vocal cords. In addition, **the vocal cords are angled anteriorly** and may make passage of an endotracheal tube difficult. If the endotracheal tube is caught at the anterior commissure, slight rotation may allow it to pass into the trachea [81, 83].

The **respiratory system is immature at birth and matures over months to years**. The breathing pattern in infants is irregular and periodic due to immature respiratory control, which improves over weeks to months. This can lead to severe apneas and is also associated with abnormal responses to hypercapnia and hypoxia. **Preterm infants** have an initial increase in ventilation in response to hypoxia for approximately one minute, followed by decreased ventilation and possibly apnea. Anesthetic drugs further impair respiratory responses. Oxygen consumption is higher in infants than adults, which requires an increased minute ventilation. Due to incomplete ossification of the thorax, chest wall compliance is increased, which limits the amount of negative intrapleural pressure that can be generated and makes infants prone to retractions and paradoxical chest wall motion during times of distress. In addition, infant airways are highly compliant and prone to collapse at extremes of pressure. The combination of these factors leads to a decreased functional residual capacity (FRC). The combination of increased alveolar ventilation and decreased FRC predisposes infants to rapid desaturation and hypoxemia [86]. Airway resistance is increased small children due to the small diameter of their airways, as expressed in Poiseuille's equation.

Techniques for endotracheal intubation and placement of laryngeal mask airways are similar to adults and will not be discussed in depth. Infants and young children often require a shoulder roll rather than a blanket under their heads to achieve optimal sniffing position for intubation due to their large occiputs. Appropriate sizing of airway equipment is essential for pediatric airway management. The

endotracheal tube size is approximated by the formula "age/4 + 4" for uncuffed tubes for children over 2 years old. A half to one full size smaller tube should be used for cuffed tubes. For younger children, approximate **appropriate sizes of cuffed tubes** are 3.0 for newborns, 3.5 starting at 4 months old and 4.0 starting at 12 months. Previous recommendations were that uncuffed endotracheal tubes should be used in patients under 8 years old. However, newer information shows that cuffed endotracheal tubes are associated with fewer intubation attempts and a better seal, resulting in better ventilation and oxygenation with a more reliable end-tidal carbon dioxide tracing. This is particularly important in cases when positive pressure ventilation is required and peak pressures may be elevated, such as during thoracic or abdominal procedures. Importantly, there is no increase in the rate of stridor as long as cuff pressures are monitored and kept below 20 cm H_2O [87]. Due to the short trachea length in infants, care must be taken when securing the endotracheal tube to ensure proper endotracheal tube positioning, particularly in cases where the patient or head may be moved intraoperatively [13]. Appropriate weight-based sizing for laryngeal mask airways is listed in Table **11**.

Table 11. Guide for Placement of LMA and Fiberoptic Intubation [89] *The pilot balloon on cuffed tubes will not pass through LMAs smaller than size 3. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Guide for Placement of LMA And Fiberoptic Intubation			
Body Weight (kg)	**LMA**	**ETT size ID (mm)***	**Fiberoptic Scope OD (mm)**
<5	1	3.0 uncuffed	2.5
5-10	1.5	3.5 uncuffed	2.8
10-20	2	4.0-4.5 uncuffed	3.5
15-30	2.5	5.0 uncuffed	4.1
30-50	3	5.5-6.0 cuffed	5.0
50-70	4	7.0 cuffed	– –
>70	5	7.5 cuffed	– – ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.

Intraoperative Airway Emergencies

The majority (53%) of intraoperative anesthesia-related adverse events in pediatric patients are due to airway complications. Adverse events are more likely to occur in infants, patients undergoing in ENT surgery, children requiring intubation and ASA class 3-5 patients. Hypoxemia, bronchospasm and laryngospasm are the most common adverse events [88]. Pediatric patients are far more likely to have difficulty with oxygenation and ventilation than to be difficult

to intubate. This is primarily due to an increase in functional airway obstruction, such as laryngospasm and bronchospasm, which are not covered in adult difficult airway algorithms [89].

Difficult Pediatric Airway

The incidence of difficult intubation in children ranges from 0.2-0.5%, although 80% of these were anticipated [90]. **Predictors of difficult intubation**in children include mandibular hypoplasia, limited mouth opening, facial asymmetry (including ear abnormalities), **stridor and obstructive sleep apnea** [89]. The incidence of unanticipated difficult intubation is 0.095% in children under 16 years old, but increases to 0.24% in infants [88]. Twenty percent of pediatric patients who are difficult to intubate have a complication related to intubation. Transient hypoxemia is the most common complication, but cardiac arrest due to hypoxemia occurs in 1.5% of patients. Complications are more common in patients with an unanticipated difficult intubation [90], likely due to a lack of personnel or alternative airway equipment to help manage the airway. **Due to the potential for significant morbidity related to pediatric airway management, all patients with a documented or anticipated difficult airway should be managed at a pediatric hospital with appropriate resources** [89]. If a child with a known difficult airway must be anesthetized outside of a pediatric hospital, consideration should be given to maintaining spontaneous ventilation with a supraglottic airway device if possible [83]. Although unanticipated difficult airways are rare, these patients are likely to be encountered at a community hospital and also have potential for significant complications.

Pediatric airway management can be divided into **1)** effective oxygenation and ventilation, **2)** intubation and **3)** airway rescue techniques (cannot ventilate, cannot intubate scenarios). The Difficult Airway Society (DAS) has published guidelines to address these scenarios in children (Figs. **1A - C**) [91].

Unexpected difficulty with facemask ventilation in pediatric patients ranges from 2.8-6.6% [82]. As previously discussed, unanticipated difficult intubation children carry a 20% risk of complications ranging from transient hypoxemia to cardiac arrest. The risk factors for complications include greater than two intubation attempts, persistent attempts at direct laryngoscopy (greater than three), patient weight less than 10 kg and micrognathia or other abnormal findings on the airway physical exam [90]. If initial laryngoscopy fails, intubating conditions, including patient position, depth of anesthesia and neuromuscular blockade, should be optimized prior to the second attempt [89]. Subsequent attempts should include a change in intubating technique (video laryngoscopy, fiberoptic intubation or

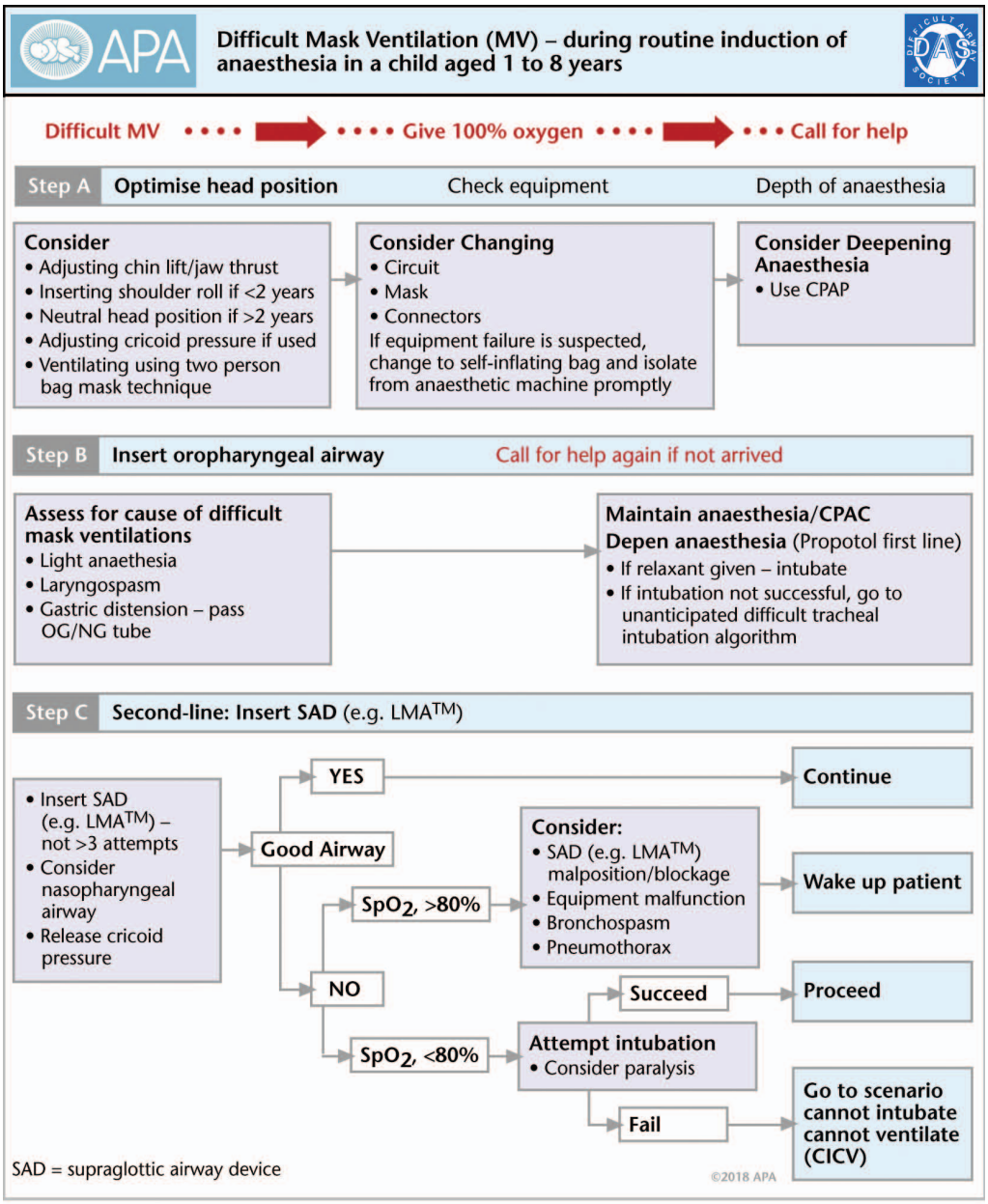


Fig. (1A). Difficult mask ventilation. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

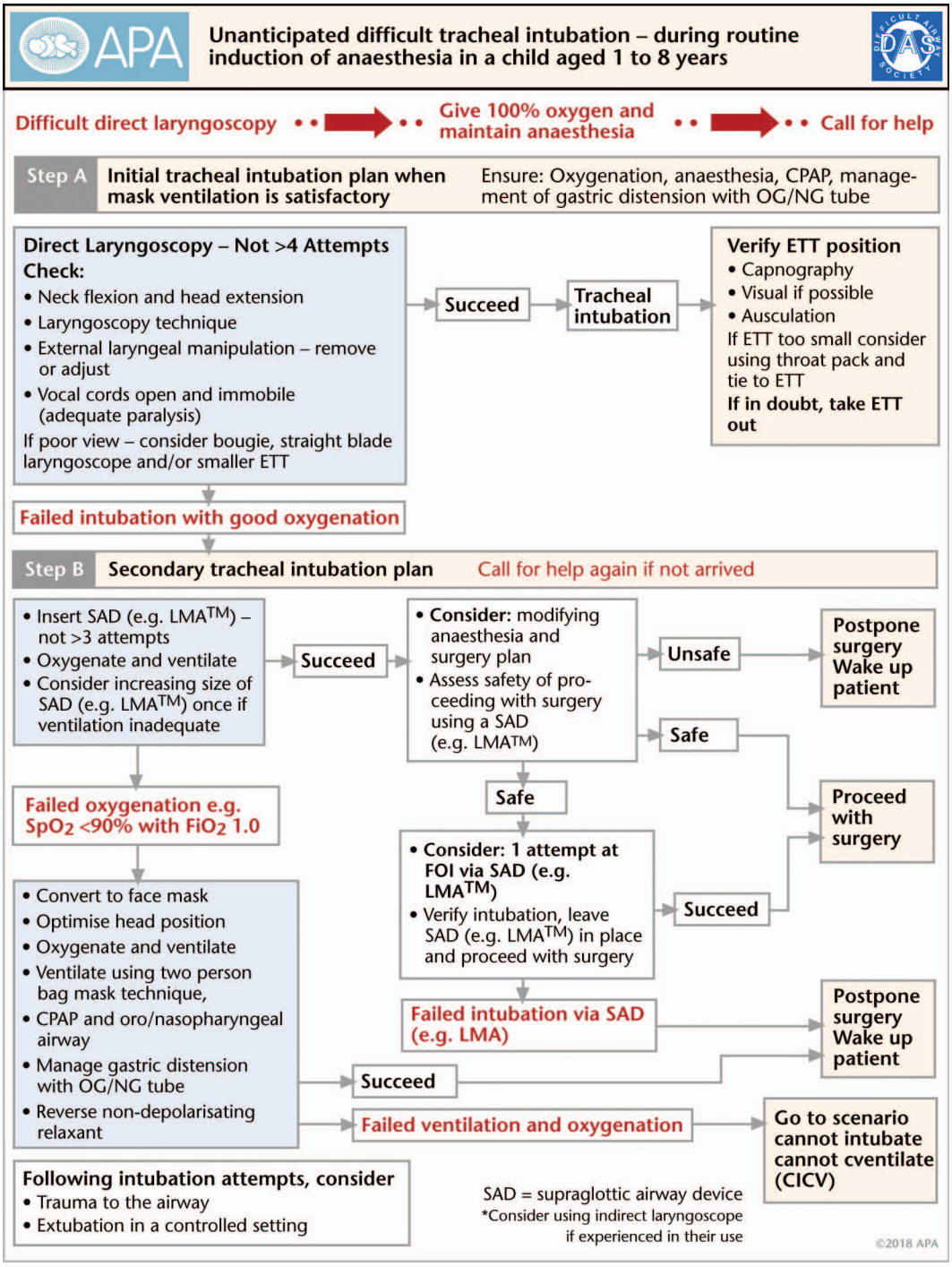


Fig. (1B). Unanticipated difficult tracheal intubation.

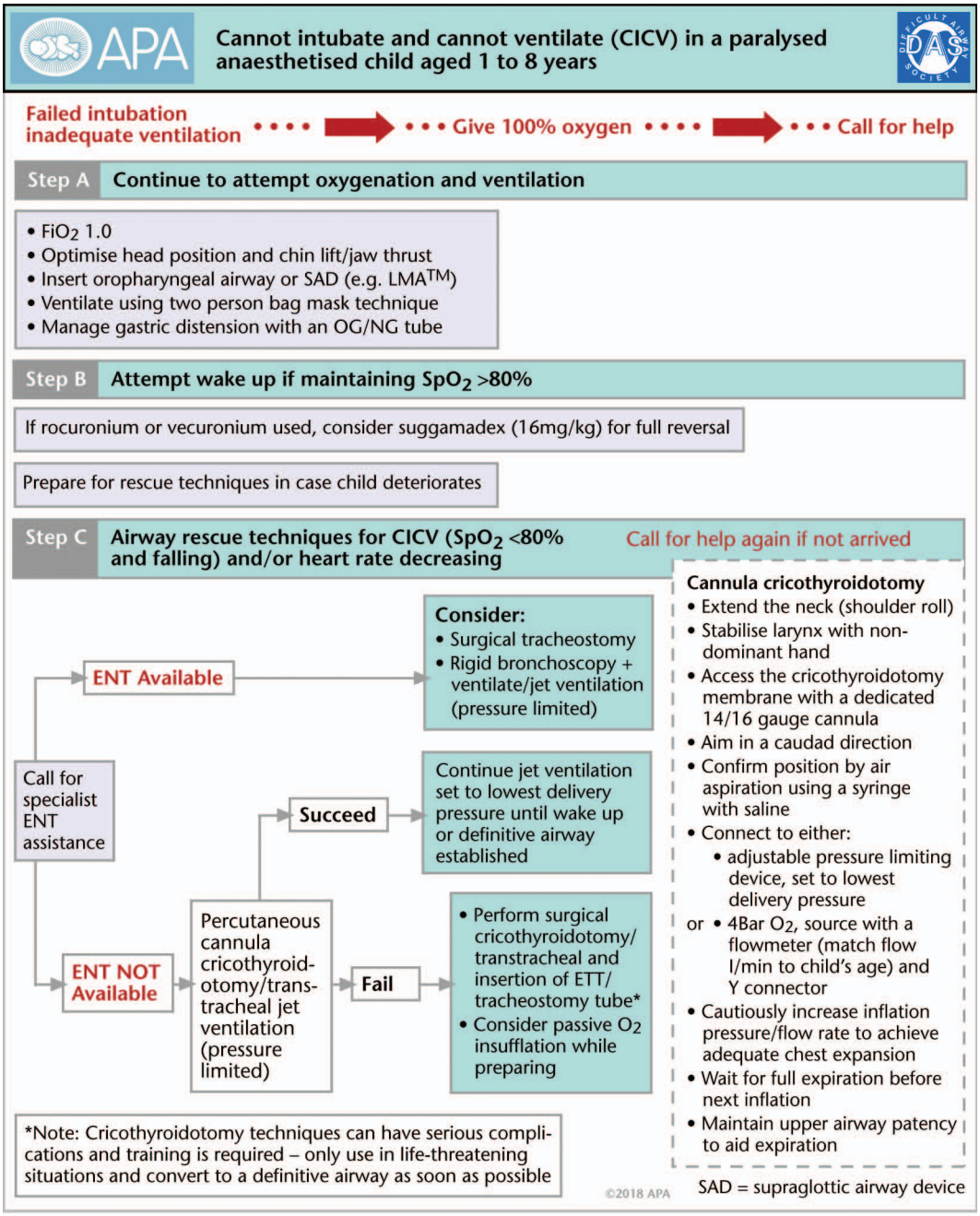


Fig. (1C). Cannot intubate and cannot ventilate (CICV).

intubation through a supraglottic airway) and/or change in operator to someone more experienced in pediatric airway management.

Guide for Placement of LMA and Fiberoptic Intubation

Different Airway Algorithms for Pediatrics

Figs. (1A - C): Guidelines for airway management in children age 1-8 published by the DAS (difficult airway society) at http://das.uk.com/guidelines/paediatric-difficult-airway-guidelines. Fig. **A**: Difficult mask ventilation. Fig. **B**: Unanticipated difficult tracheal intubation. Fig. **C**: Cannot intubate and cannot ventilate (CICV) [91].

Laryngospasm

Laryngospasm occurs more commonly in pediatric patients than in adults and is the most common respiratory cause of pediatric perioperative cardiac arrest [92]. The incidence of laryngospasm has been reported as 0.87% in the general population, increasing to 1.74% in children under 9 years old and 2.82% in infants under 3 months of age [93]. However, more recent studies have reported a lower incidence, possibly due to changes in anesthetic technique [88, 94]. Approximately half of laryngospasm occurs during emergence with the remainder divided between induction and maintenance. The time of highest risk is likely determined by the anesthetic technique and type of airway management. Patients with an endotracheal tube are most likely to have spasm during emergence, while those with an LMA or face mask anesthetic are more likely to have intraoperative spasm [94]. Patient risk factors for laryngospasm include young age, upper airway inflammation, asthma and tobacco exposure in the home. The risk is also increased with surgical procedures that involve the airway. Anesthetic risk factors include the use of sevoflurane for induction, intubation without the use of muscle relaxants and the use of invasive airways (endotracheal tubes) compared to supraglottic airway management (LMA and face mask) [81]. Signs of laryngospasm include respiratory effort with inspiratory stridor or absence of air movement, inability to give positive pressure ventilation and paradoxical chest and abdomen movement. It should be differentiated from other causes of airway obstruction, such as bronchospasm and supraglottic obstruction, and from breath holding. Prolonged laryngospasm can result in hypoxemia, bradycardia and cardiac arrest during the event or post-obstructive pulmonary edema and aspiration after resolution of laryngospasm [93].

The **treatment of laryngospasm** depends on the degree of airway obstruction and hypoxemia. The first-line treatment is removal of the offending stimulus, airway repositioning with jaw thrust and continuous positive pressure. However, if

complete laryngospasm is present, continuous pressure may increase gastric distention, placing the patient at risk for aspiration after resolution of laryngospasm. Due to the potential for rapid desaturation, especially in very young patients, pharmacologic therapy should not be delayed. Propofol at doses of 0.25-0.8 mg/kg will successfully resolve laryngospasm in up to 80% of cases. However, succinylcholine 0.1-3 mg/kg may be required and should be given immediately if propofol is not successful. Succinylcholine may cause bradycardia and is more likely to do so if the patient is already hypoxic. Atropine 0.02 mg/kg should be given if there are concerns for bradycardia. In the absence of intravenous access, succinylcholine 4 mg/kg can be given intramuscularly. Intubating conditions will be obtained in 3-4 minutes, but the relief of laryngeal spasm occurs much faster [25]. Rocuronium can be used if succinylcholine is contraindicated, though the onset will be delayed.

Maintenance of Anesthesia

Anesthesia can be maintained with inhalational or intravenous medications. Compared to inhalational anesthetics, maintenance with propofol may reduce the risk of PONV and postoperative behavioral problems in children. However, there is no difference in postoperative respiratory or cardiovascular complications or time to discharge [95]. For most patients, either technique can be used safely, but pharmacokinetic and pharmacodynamic differences in neonates and infants compared to adults must be taken into account when selecting appropriate drugs and dosing.

The induction and emergence characteristics and MAC values of volatile agents are different in neonates and infants compared to adults. The wash-in of inhalational agents is increased in neonates and infants due to an increased ratio of alveolar ventilation-to-functional residual capacity, a greater fraction of cardiac output being delivered to the vessel-rich tissue group and reduced blood and tissue solubility of volatile agents [96]. The net effect of these changes is to speed the induction and emergence from volatile anesthesia in infants compared to adults. MAC values vary significantly with age. For isoflurane and desflurane, MAC values are highest in infants and are decreased in neonates [97, 98]. For sevoflurane, values for neonates and infants are roughly equivalent [99]. MAC values for premature neonates have only been established for isoflurane [100]. For all volatile agents, the MAC values stabilize in childhood before eventually declining to adult levels. MAC values by age are listed in Table **12**.

Minimum Alveolar Concentration (MAC) Values by Age

Propofol is the most commonly used drug for intravenous maintenance in pediatric anesthesia. After intravenous administration, propofol distributes rapidly

to vessel-rich organs, accounting for its rapid onset. The effect of a single bolus is rapidly terminated by redistribution into the blood compartment, but the effects of repeated boluses or continuous infusions are terminated by hepatic clearance [101]. Neonates and infants have an increased volume of distribution and decreased hepatic function compared to adults, which affects dosing requirements [72]. The bolus dose (2.5-4 mg/kg) and initial infusion rates (250 mcg/kg/min) are increased in children compared to adults. Infusion rates in infants are likely even higher due to their increased volume of distribution. However, these increased infusion rates prolong the context-sensitive half-time of propofol after long infusions, which must be considered for emergence [102]. The duration of action of even a single dose of propofol can be prolonged in neonates, so caution should be exercised with drug re-dosing in this age group [101]. Similar pharmacologic considerations apply to initial and repeated dosing of all intravenous agents given to neonates and infants.

Table 12. Minimum Alveolar Concentration (MAC) Values by Age [97 - 100]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Minimum Alveolar Concentration (MAC) Values by Age			
Age	**Sevoflurane**	**Isoflurane**	**Desflurane**
Premature neonate	– –	1.3-1.4%	– –
Full-term neonate	3.3%	1.6%	9.2%
Infant	3.2%	1.8-1.9%	9.4-9.9%
Child	2.5%	1.6%	8.0-8.7%
Adult	1.7-2.1%	1.1-1.3%	6.0-7.3% ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.

Neuromuscular Blockade

Neuromuscular blockade in children is affected by a number of factors including immaturity of the neuromuscular junction, pharmacologic differences compared to adults, and restrictions on the use of succinylcholine. The neuromuscular junction in neonates and young infants is morphologically different from adults due to the presence of the fetal isoform of nicotinic receptors and extra-junctional receptors. In addition, decreased amounts of acetylcholine are released during neuromuscular transmission. These changes make the nicotinic receptors sensitive to non-depolarizing blockade and resistant to depolarizing blockade. The increased cardiac output in infants increases the speed of onset of blockade, while the increased volume of extracellular fluid contributes to the resolution of single doses of blockade. With repeated dosing, drug metabolism becomes a more important determinant of drug duration of action [103].

Succinylcholine doses are increased in neonates and infants due to the resistance of the immature neuromuscular junction to depolarizing blockade as well as the increased volume of drug distribution. The intravenous dose required for intubating conditions is 2 mg/kg in children and up to 3 mg/kg in infants. In the absence of intravenous access, 4-5 mg/kg can be given intramuscularly to obtain adequate intubating conditions in 3-4 minutes with an expected duration of 15-20 minutes. The use of succinylcholine in children is restricted to emergency airway management due to concerns for life-threatening hyperkalemia in young patients with undiagnosed muscular dystrophy. Additionally, succinylcholine carries a risk for bradycardia, particularly after administration of a second dose. Administration of atropine 20 mcg/kg IV should be considered in neonates receiving any succinylcholine or in older patients prior to receiving a second dose of succinylcholine [103]. Bradycardia after intramuscular administration is uncommon.

Neonates and infants require smaller doses of non-depolarizing blockade despite the increased volume of drug distribution because of increased sensitivity of the neuromuscular junction to non-depolarizing blockade. The recommended doses for non-depolarizing drugs in children are rocuronium 0.6 mg/kg, vecuronium 0.1 mg/kg and cisatracurium 0.15 mg/kg. Rocuronium 1.2 mg/kg is an alternative to succinylcholine for rapid sequence induction. These doses should be reduced for neonates and infants due to the increased sensitivity of the neuromuscular junction to blockade. The duration of action of rocuronium and vecuronium can be significantly prolonged in neonates and infants, especially after repeated dosing, due to immature hepatic metabolism in those patients. Cisatracurium may be a better choice for neuromuscular blockade in neonates as it undergoes spontaneous degradation [103].

Residual postoperative neuromuscular blockade is a common problem after pediatric anesthesia due to slow and variable spontaneous resolution of blockade. Potential complications of residual blockade include respiratory insufficiency, upper airway obstruction and aspiration. A peripheral nerve stimulator should be used to assess depth of neuromuscular blockade due to poor reliability of clinical findings [104]. For neonates and infants in whom twitch assessment is sometimes difficult, sustained leg lift can be used as a marker of adequate neuromuscular function [105]. The baseline activity level for infants should be noted preoperatively and used as a benchmark for return of appropriate muscle function postoperatively. The dose of neostigmine required to reverse a low degree of neuromuscular blockade in children is decreased compared to adults [104] Neostigmine 35mcg/kg and glycopyrrolate 10 mcg/kg should be given for reversal of blockade [103]. Sugammadex is currently available for the reversal of moderate neuromuscular blockade after rocuronium in pediatric patients with a

dose of 2 mg/kg. Higher doses of 16 mg/kg have been used to reverse profound block in adults, but are not currently approved for pediatric patients [104].

Analgesia

Pain in pediatric patients has historically been undertreated [106, 107]. An audit of children's hospitals in the United States found a 44% prevalence of moderate-to-severe pain among patients on surgical services [108]. The consequences of inadequate pain control are well-studied and include deleterious neuroendocrine stress responses, disrupted eating and sleep cycles and increased pain responses to subsequent painful procedures. There are multiple barriers to adequate pain treatment in children. Pain assessment can be difficult, particularly among preverbal or developmentally delayed children. Lack of provider familiarity with weight-based dosing and pediatric pharmacokinetics as well as limitations in pediatric research further contribute to insufficient pain control and place children at risk for medication-related adverse effects [109]. Finally, healthcare provider and parental fears of adverse medication effects, such as respiratory depression and addiction, may preclude their appropriate use in pediatric patients [106, 109]. A plan for perioperative pain management should be created preoperatively jointly between the anesthesia and surgical teams in consultation with the patient and/or family members to adequately address these issues. As in adults, multimodal pain therapy, which may include non-opioid analgesics, opioid medications and regional anesthetic techniques, provides optimal perioperative pain control [106, 107].

Pain Medications

Non-opioid analgesics, most commonly acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs), provide dose-dependent analgesia and decrease opioid requirements [108, 109]. However, they also have a ceiling effect which limits their effectiveness in treating severe pain. As such, they can be used as the sole treatment for mild postoperative pain and should be used as scheduled adjuncts for the treatment of moderate-to-severe pain unless contraindicated by the patient's age or medical comorbidities [109, 110]. When used for moderate-t--severe pain, around-the-clock dosing at fixed intervals is recommended [106].

Acetaminophen can be given intraoperatively by intravenous or rectal routes. The rectal absorption of acetaminophen is slow and variable and suppositories vary in composition and bioavailability, making dosing unpredictable [109, 111]. This route has fallen out of favor as intravenous acetaminophen has become more readily available. Intravenous administration results in higher serum concentrations, which may increase analgesic potency, compared to oral administration. The onset of analgesia begins within 15 minutes, though the time

to peak analgesia may still be 1-2 hours after administration [109, 111]. When administering acetaminophen to children by any route, caution must be taken not to exceed maximum daily dose recommendations, which would place children at risk for hepatotoxicity. This is especially important in the postoperative period when patients may be prescribed oral opioid-acetaminophen combination pills, and should be stressed to parents prior to discharge [109]. Due to pharmacokinetic differences, neonates and small infants have a lower allowable daily dose of acetaminophen compared to older children and may require smaller doses and/or increased dosing intervals to maintain therapeutic drug levels (Table **13**) [109, 112].

Dose Recommendations for Acetaminophen by Age

Table 13. Dose Recommendations for Acetaminophen by Age. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Dose Recommendations for Acetaminophen by Age				
	Maximum Daily Dose	**Oral**	**Rectal**	**Intravenous**
Neonate 28-32 weeks PCA	40mg/kg	10-15mg/kg every 12hours	15mg/kg every 12hours	7.5-10mg/kg every 6-8hours
Neonate 32-36 weeks PCA	60mg/kg	10-15mg/kg every 8hours	20mg/kg every 12hours	7.5-10mg/kg every 6hours
Full term neonate – 3months	60mg/kg	10-15mg/kg every 6-8hours	20mg/kg every 12hours	15mg/kg every 6hours
>3months	75mg/kg	10-15mg/kg every 4-6hours	20mg/kg every 6ours	15mg/kg every 6hours
Maximum Dose	4000mg	650-1000mg every 4-6hours	– –	1000mg every 6hours

PCA = postconceptual age.

The manufacturer guidelines for intravenous acetaminophen suggest a dose of 7.5 mg/kg every 6 hours in infants weighing <10 kg. However, pharmacokinetic studies indicate than 10 mg/kg is a more appropriate dose. Caution should be used when administering intravenous acetaminophen, which is supplied as 10 mg/ml, as 10-fold dosing errors have been reported in pediatric literature. Some dosing guidelines also recommend a loading dose of 20 mg/kg PO or 20-30 mg/kg PR prior to maintenance dosing [108 - 112].

Due to an increased risk of bleeding events, ketorolac should not be used in patients undergoing tonsillectomy [109]. Less commonly, NSAIDs may cause bronchospasm in children with asthma or other atopic symptoms and impair bone

healing [109, 111]. NSAIDs are generally not recommended for infants less than 6 months old, though some data do support the safe administration of ketorolac for young infants. However, neonates have decreased clearance of ketorolac with increased risk of bleeding events and should not routinely receive NSAIDs [110, 112]. Common perioperative NSAID doses are intravenous ketorolac 0.5 mg/kg (maximum 30 mg) every 6 hours and oral ibuprofen 6-10 mg/kg (maximum 600 mg) every 6 hours [109].

Other non-opioid analgesics used in pediatric pain management include benzodiazepines, ketamine and dexmedetomidine. Benzodiazepines, especially diazepam, can be helpful for treating muscle spasm, especially after orthopedic procedures or in cognitively impaired children who may have spasm or clonus at baseline [109]. In addition, the sedative effect of benzodiazepines may be helpful in treating the behavioral or emotional issues that often play a large role in pediatric pain [107, 110]. Intraoperative ketamine administration is associated with decreased pain scores and non-opioid analgesic use in the PACU. However, these benefits do not persist in the early postoperative period (6-24 hours) and an opioid-sparing effect has not been shown in children [113]. Caution should be exercised when using ketamine in neonates due to potential for neurotoxicity [108]. Studies of intraoperative dexmedetomidine use have shown decreased postoperative pain and rates of opioid use, but no reduction in total opioid consumption. Further studies regarding safety and hemodynamic side effects may be required [114].

Opioid analgesics are the mainstay of treatment for moderate-to-severe postoperative pain and have been well-studied for systemic and neuraxial administration in all age groups. Morphine is the most commonly used intravenous opioid with the greatest experience in children. Despite its excellent track record, morphine may not be well tolerated in children with hemodynamic instability, due to histamine-induced vasodilation, and should not be used in children with renal failure, due to the potential for accumulation of toxic metabolites. Fentanyl is also well-studied in the pediatric population and has the benefit of hemodynamic stability and shorter duration of action. Hydromorphone is less well studied in the pediatric population, but is still often used perioperatively. Although codeine has been commonly used for pediatric patients, it is no longer recommended for routine use due to safety and efficacy concerns [115]. Codeine is a prodrug that must be converted to its active metabolite, morphine, by the cytochrome P450 system. Unfortunately, significant variation in the activity of this enzyme exists between patients. Up to 30% of patients do not receive any analgesic effect from codeine. More importantly, a small number are at risk for overdose due to increased drug metabolism [109, 115].

Opioid dosing recommendations for oral and intravenous routes are presented in Table **14**. The clearance of morphine and fentanyl is significantly reduced in the neonatal period, resulting in a prolonged half-life for these drugs. Drug clearance increases with gestational age, reaching adult levels by approximately one month in full-term infants [111, 112]. In addition, neonates and infants less than six months of age are at increased risk for opioid-induced respiratory depression due to immature respiratory responses to airway obstruction, hypoxia and hypercapnia [109]. Due to these concerns, opioid doses should be reduced for neonates and infants less than six months of age. Young infants receiving opioids should be carefully monitored for respiratory depression and should be cared for in a setting where rapid airway intervention is possible [109, 112].

Table 14. Systemic Opioid Dosing Guidelines. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Systemic Opioid Dosing Guidelines			
	Potency Relative to Morphine	**Oral Dose**	**Intravenous Dose**
Morphine	1	0.3mg/kg every 3-4hours	Bolus: 0.1mg/kg every 2-4hours Infusion: 10-40mcg/kg/hr
Hydromorphone	5-7	40-80mcg/kg every 3-4hours	Bolus: 20mcg/kg every 2-4hours Infusion: 2-8mcg/kg/hr
Fentanyl	50-100	N/A	Bolus: 0.5-1mcg/kg every 1-2hours Infusion: 0.5-2mcg/kg/hr
Remifentanil	50-100	N/A	Bolus: 0.1-1mcg/kg Infusion: 0.05-4mcg/kg/min
Oxycodone	1-1.5	0.1-0.2mg/kg every 4-6hours	N/A
Hydrocodone	1-1.5	0.1-0.2mg/kg every 4-6hours	N/A ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.

Suggested doses should be reduced by 25% for infants under 6 months of age. Opioids may be administered by continuous infusion intra- or post-operatively. Continuous infusion may be used postoperatively as an alternative to PCA dosing in patients who are unable to use PCA. Potential exists for significant drug accumulation, sedation and respiratory depression. Patients receiving continuous opioids must be adequately monitored, likely requiring ICU-level care [108, 109, 111].

Regional Analgesia

Regional analgesia can play a critical role in pain management by reducing the need for systemic analgesic medications and attenuating the intraoperative stress response. This is particularly helpful in children at risk for respiratory depression, including neonates and small infants and patients with airway abnormalities, chronic lung disease or abnormal central respiratory control. There are, however, significant differences from adult regional anesthesia which must be addressed. These include differences in local anesthetic metabolism, the performance of nerve blocks while under general anesthesia and different approaches to neuraxial anesthesia.

The potential for local anesthetic toxicity is increased in small infants and neonates due to their low body weight and pharmacokinetic differences compared to adults. Neonates have immature cytochrome P450 systems, which are necessary for metabolism of amide local anesthetics. In addition, they have decreased plasma proteins compared to adults, which increases the free fraction of amide local anesthetics in circulation. Although single doses of amide anesthetics can be used safely, the potential exists for significant drug accumulation with repeated doses or continuous infusions, with subsequent development of toxicity. It is recommended that the bolus and infusion doses of amide anesthetics be reduced by 30% for infants less than 6 months of age to decrease the risk for toxicity.

Local anesthetic systemic toxicity **(LAST)** is a significant concern in small children, as it can occur after administration of small volumes of local anesthetics. In addition, prodromal symptoms, such as circumoral paresthesia, dizziness, and visual and auditory disturbances may not be apparent in children who are too young to report such symptoms or who are anesthetized. Objective signs, such as CNS excitation or depression, seizures, respiratory depression or arrest and cardiovascular findings (hypotension, bradycardia, dysrhythmias, ischemia and arrest), may be the first signs of LAST in anesthetized children [116]. A test dose of local anesthetic containing epinephrine 5 mcg/ml has been advocated for use as an indicator of intravascular local anesthetic injection. An epinephrine dose of 0.5 mcg/kg (maximum 15 mcg) should produce EKG changes (peaked T waves and ST elevation), an increase in heart rate by 10% and a transient increase in systolic blood pressure when given intravascularly. However, these findings are not always reliable in anesthetized children and false negative results can occur [116, 117]. A test dose of local anesthetic is not required, but should be given at the discretion of the anesthesiologist. Any modification of T waves or heart rate within 30-90 seconds should be considered a sign of accidental intravascular injection until proven otherwise. However, given the high rate of false negative

test doses, all subsequent local anesthetic injections should be preceded by catheter aspiration and given slowly in doses of 0.1-0.2 ml/kg with observation for signs of intravascular injection [117].

Approximately 95% of regional anesthetic blocks in children are performed under general anesthesia due to lack of patient cooperation in awake or mildly sedated children. The rates of regional blockade under general anesthesia are slightly lower in neonates, who have the highest rates of awake blocks (spinal anesthesia), and children over 10 years old who have the highest rates of blocks performed under sedation [118]. The most recent guidelines released by the American and European Societies for Regional Anesthesia state that the performance of pediatric regional anesthesia under general anesthesia or deep sedation is associated with acceptable safety and should be viewed as the standard of care. Although the overall complication rate is very low and no cases of paralysis have been reported, in the event of an unexpected outcome such as prolonged motor blockade, a high index of suspicion for neurological injury is warranted and appropriate diagnostic and therapeutic measures should be immediately performed [117].

Neuraxial techniques have historically been used more commonly than peripheral nerve blockade in children. However, there has recently been a trend towards increasing use of peripheral nerve blockade in pediatrics, likely due to the common use of ultrasound-guided techniques [119]. The techniques used and indications for peripheral nerve blockade in children are similar to adults and will not be reviewed in this chapter.

Neuraxial analgesia in neonates and infants differs from older children and adults for a number of reasons. The conus medullaris ends at L3 in neonates and ascends to the adult position of L1 by one year of age. Lumbar puncture should therefore only be attempted at the L4-5 or L5-S1 interspace. Infants and young children have a greater volume of cerebrospinal fluid per kilogram body weight with a higher rate of turnover compared to older children and adults. Intrathecal analgesia will therefore require higher doses of local anesthetic and have a shorter duration of action than in adults. Neuraxial anesthesia in infants and small children is associated with a greater degree of hemodynamic stability than in older children and adults. This is due to multiple factors including a preserved heart rate, lack of resting sympathetic peripheral vascular tone and a small venous capacitance in the lower extremities, all of which minimize the hypotension associated with sympathectomy and peripheral vasodilation. An extreme example of this is total spinal anesthesia in a neonate, which is characterized by apnea without a change in blood pressure [116].

The most common regional block in pediatric patients is a single-injection caudal block, accounting for 40% of regional anesthetics in pediatric patients. The overwhelming majority of these blocks are performed in children under three years old [120]. A single dose of 1 ml/kg of local anesthetic can produce a T4-6 sensory level and will reliably provide analgesia for infra-umbilical procedures, such as inguinal hernia repair, orchiopexy and extensive penile procedures, and for lower extremity procedures, such as clubfoot repair.

Common neuraxial medications include local anesthetics and adjuvants (opioids and clonidine) that may be added to enhance blockade. Recommended doses of these drugs are listed in Table **15**. Bupivacaine and ropivacaine are the most commonly used medications for neuraxial blockade, although chloroprocaine is the anesthetic of choice for neonates receiving continuous epidural analgesia. Bupivacaine 0.125-0.175% and ropivacaine 0.1-0.2% are commonly used for bolus dosing, but bupivacaine 0.25% can also be used if motor block is not a concern [109]. The local anesthetic concentrations and dose ranges for epidural infusion are listed in Table **15**.

Epidural Dosing Guidelines

Table 15. Epidural Dosing Guidelines. *The dose of bupivacaine should be decreased by 30% for infants less than 6 months of age. The rate of chloroprocaine infusion should be adjusted to deliver a volume of 0.2-0.8 ml/kg/hr [109, 116]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Epidural Dosing Guidelines ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP				
	Bolus Concentration	**Maximum Dose**	**Infusion Concentration**	**Dose Range**
Bupivacaine	0.125-0.25%	2.5mg/kg*	0.1%	0.2-0.4mg/kg/hr
Ropivacaine	0.1-0.2%	2.5mg/kg	0.1-0.2%	0.2-0.5mg/kg/hr
Chloroprocaine	– –	– –	1-1.5%	2-10mg/kg/hr
Fentanyl	– –	– –	2-3mcg/ml	0.3-1mcg/kg/hr
Hydromorphone	– –	– –	3-7mcg/ml	1-2.5mcg/kg/hr
Morphine	– –	– –	5-10mcg/ml	1-5mcg/kg/hr
Clonidine	– –	0.5-1mcg/kg	0.5-1mcg/ml	0.1-0.5mcg/kg/hr

Fluid Management

The goal for intraoperative fluid management is to maintain adequate circulating volume with normal hematocrit, glucose and electrolyte levels. Pediatric fluid management, particularly in neonates and small infants, is affected by differences in circulating blood volume, hematocrit and glucose requirements compared to

adults [121]. The circulating blood volume per kilogram of body weight is highest in premature neonates and declines with age. The blood volume is approximately 100 ml/kg for premature neonates, 90 ml/kg for full-term neonates, 80 ml/kg for infants, 75 ml/kg for children and 70 ml/kg for adults [53]. Neonates have an elevated hemoglobin of 17 g/dL, composed mostly of hemoglobin F, to compensate for low intrauterine oxygen tension. After the neonatal period, infants experience a physiologic anemia as hemoglobin F concentrations decline and hemoglobin A concentrations increase. Full-term infants reach a nadir of 9-11 g/dL at 8-12 weeks of age, while premature infants have a nadir of 7-9 g/dL at 3-6 weeks. Hemoglobin values reach approximately adult levels by one year of age [54].

Fasting, surgical stress and anesthesia have significant effects on glucose homeostasis in the perioperative period. Neonates and small infants have a higher metabolic rate and glucose consumption compared to adults, but also have limited energy reserves, making them prone to hypoglycemia with prolonged fasting [122]. Glucose levels tend to rise intraoperatively due to the hormonal stress response combined with decreased energy requirements under anesthesia [123, 124]. Neuraxial analgesia significantly decreases the hormonal stress response and may blunt the expected rise in glucose concentrations [125]. Hypoglycemia in healthy, fasting children presenting for surgery is rare and the incidence has decreased with the use of more liberal fasting guidelines [126, 127]. However, neonates and small infants require intraoperative glucose administration. Particularly high-risk patients are those who are premature or small-fo--gestational age, less than 48 hours old, undergoing long procedures, receiving glucose-containing solutions preoperatively or who have a neuraxial block [125, 128].

The **maintenance fluid requirement** in pediatric patients is estimated by the "4-2-1" rule. Patients should receive 4 ml/kg/hour for the first 10 kg, 2 ml/kg/hour for every kilogram from 10-20 kg and 1 ml/kg/hour for every kilogram above 20 kg [129]. Although it is common for pediatric patients to be given hypotonic fluids, this carries an unnecessary risk for iatrogenic hyponatremia and should be avoided [127]. Maintenance fluids should be isotonic with dextrose if required due to the patient's age or metabolic concerns. Administration of 5% dextrose infusions at maintenance rates to infants and young children causes perioperative hyperglycemia. To maintain euglycemia, the dextrose concentration can be decreased to 1-2.5% or 5% dextrose can be administered at half the maintenance rate [126, 130]. 10% dextrose infusions are commonly used preoperatively for neonatal patients due to their increased metabolic requirements. These infusions can be continued intraoperatively at a lower rate (1-3 ml/kg/hour) to maintain euglycemia. Separate non-glucose containing fluids should be used to replace the

fasting deficit and intraoperative losses. The decision to transfuse blood products is based on the patient's estimated blood loss, circulating blood volume and age-based target hemoglobin levels.

Emergence

At the conclusion of surgery, airway devices may be removed while patients are still deeply anesthetized or after emergence from anesthesia. Criteria for awake extubation are the same as in adults. Patients must have adequate ventilation and oxygenation as well as return of laryngeal reflexes and return to baseline consciousness, which may include eye opening, facial grimacing and purposeful movements. If a deep extubation is performed, the airway device is removed while the patient is breathing spontaneously, but still in a surgical plane of anesthesia with depressed airway reflexes [131, 132]. Patients who are at risk for aspiration and central respiratory depression and those with known or suspected difficult airways are not candidates for deep extubation. However, deep extubation may be beneficial for patients with upper airway irritation due to poorly controlled asthma or upper respiratory infection [131]. In addition, prevention of coughing during extubation is beneficial for surgical hemostasis in some cases. Patients who are extubated while anesthetized must be closely monitored, either by an anesthesiologist or dedicated PACU staff trained in basic pediatric airway management skills, until they have regained consciousness and control of airway reflexes [131]. This may require additional operating room time after extubation or an adjustment of PACU staffing assignments to accommodate safe patient recovery. These needs should be considered when deciding the appropriate time for extubation. Patients who are extubated while deeply anesthetized may have increased rates of airway obstruction relieved with airway maneuvers, while those extubated awake have increased coughing or hoarse voice [132]. However, in appropriately managed pediatric patients, the rates of major respiratory adverse events, including desaturation with oxygen requirement, laryngospasm and invasive airway management, are not different between the two groups [131 - 133]. During transport and on arrival to the PACU, care should be taken to minimize movement and stimulation of the patient until emergence is complete.

The timing of LMA removal remains controversial, with different studies showing mixed results. A meta-analysis for anesthetized *versus* awake LMA removal showed that coughing is more common when the LMA is removed awake, while airway obstruction is more common when the LMA is removed while the patient is still anesthetized. However, more serious complications, such as laryngospasm or desaturation are not different between the two groups [134] Therefore, timing of LMA removal should be at the discretion of the anesthesiologist.

COMMON PEDIATRIC SURGERIES MYRINGOTOMY AND TYMPANOSTOMY TUBE INSERTION

Otitis media with effusion is a common childhood condition. Up to 90% of children will have at least one episode of otitis media by 10 years old and up to 30-40% will have recurrent episodes, which can impact hearing and speech. Surgical treatment of otitis media decreases time with effusion and improves hearing in the short term compared to watchful waiting [135]. Myringotomy with or without insertion of tympanostomy tubes is one of the most commonly performed pediatric surgical procedures.

Myringotomy with tube insertion is a short procedure, usually lasting 10-15 minutes. Because of this, the procedure is usually performed with anesthesia by facemask alone with no invasive airway or intravenous access obtained, unless indicated by the child's other medical conditions. Chronic otitis media is often associated with rhinorrhea and recurrent upper respiratory infections. These conditions improve after surgical treatment for otitis. Surgery should therefore not be cancelled for these symptoms unless they are severe or worsened from the patient's baseline. Care should be taken to provide an adequate depth of anesthesia during surgical stimulation to avoid laryngospasm and bronchospasm. Anesthesia is maintained with sevoflurane with or without nitrous oxide and the patient is either breathing spontaneously or with assisted ventilation by bag mask. Care should be taken to keep the patient's head complete immobile during facemask ventilation, especially while the surgeon has sharp implements in the patient's ear. Despite the short duration of the procedure, the rates of postoperative pain and emergence agitation can be quite high when the anesthetic is sevoflurane alone [136]. Intranasal fentanyl 1-2 mcg/kg is the most commonly used analgesic regimen, though adding intramuscular ketorolac 0.5 mg/kg may give additional benefit to fentanyl alone [136, 137]. Intranasal dexmedetomidine does not provide any clinical benefit over fentanyl and is associated with increased PACU stays [138, 139]. Preoperative midazolam is associated with worse PACU outcomes, likely due to the long duration of drug effect relative to the short procedure duration [138]. Intravenous and intramuscular morphine 0.1 mg/kg have comparable outcomes to intranasal fentanyl [140]. When administering intranasal drugs, care should be taken to minimize the total volume and administer the drug slowly to prevent large volumes of fluid from passing through the nasopharynx and onto the vocal cords where they can cause irritation, laryngospasm and desaturation [140]. Pain control in the PACU usually consists of oral acetaminophen only.

Tonsillectomy and Adenoidectomy

Tonsillectomy and adenoidectomy are among the most commonly performed pediatric surgical procedures. The majority of surgeries are performed in the outpatient setting with a bimodal age distribution in early childhood (5-8 years old) and early adulthood (17-21 years old). The most common indications are sleep disordered breathing (SDB) and recurrent tonsillitis [141]. SDB encompasses a spectrum of breathing disorders ranging from primary snoring to obstructive sleep apnea (OSA). The prevalence of OSA in children is 1-3% in all age groups, with a peak prevalence at 3-6 years of age [142]. However, most children are not screened with a sleep study due to the cost, time and limited availability of this test. Therefore, clinical criteria, such as the **STBUR** (Snoring, Trouble Breathing, Unrefreshed) questionnaire (Table **16**), are often used to preoperatively identify children at risk for breathing disorders. Children with SDB, defined as a STBUR score >3, are at increased risk for perioperative respiratory adverse events (PRAE) and opioid-related adverse events (ORAE) [143].

The STBUR Questionnaire

Table 16. The STBUR Questionnaire [143]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

The STBUR Questionnaire
• While sleeping, does your child snore more than half the time?
• While sleeping, does your child snore loudly?
• While sleeping, does your child have trouble breathing or struggle to breathe?
• Have you ever seen your child stop breathing during the night?
• Does your child wake up feeling unrefreshed (not well rested) in the morning? ©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.

Respiratory complications are common after tonsillectomy and adenoidectomy. Minor complications, such as hypoxemia and persistent oxygen requirement, occur in 10-30% of patients. Major complications, including airway obstruction requiring reinstrumentation, positive pressure ventilation and pharmacologic intervention, occur in 5-20% of patients [133]. Respiratory complications occur more often in children with OSA, those younger than 2 years old and those with medical comorbidities. If a sleep study is done, an AHI >5 events per hour and nocturnal desaturations ≤80% are associated with an increased risk [142]. Specifically, children with OSA undergoing adenotonsillectomy are more likely to have supraglottic obstruction, breath holding and desaturation on induction and emergence and are more likely to require medical intervention for airway obstruction in the PACU than those without OSA [144]. Despite tonsil removal,

children remain at risk for airway obstruction for months after surgery and those with severe OSA can have numerous episodes of airway obstruction and desaturations on the first night after surgery [142]. These risks should be considered when selecting appropriate patients for ambulatory surgery. Although protocols differ by institution, children under 2-3 years old and those with significant OSA or medical comorbidities are not generally offered outpatient surgery for adenotonsillectomy.

The majority of patients undergoing tonsillectomy are managed with an endotracheal tube, although there is some evidence for the safe management of patients with a laryngeal mask airway. The endotracheal tube can be removed while the patient is deeply anesthetized or after return of airway reflexes. Either option can be used safely in children undergoing tonsillectomy, though consideration should be given to the patient's degree of OSA, ease of mask ventilation and intubation, other medical comorbidities and the ability to monitor for and manage airway complications in the PACU [132, 133]. The risk for laryngospasm after extubation can be decreased by administering topical lidocaine to the vocal cords during intubation or giving intravenous lidocaine or propofol prior to extubation [145, 146]. The flexible reinforced LMA has been increasingly used for tonsillectomy procedures, especially in Europe. Use of an LMA is associated with decreased airway irritation, especially in patients with URIs, and decreased hemodynamic disturbance on induction, with adequate airway protection from the blood and secretions associated with this procedure [147]. Concerns regarding adequate surgical access, kinking or displacement of LMA leading to difficult ventilation and oxygenation, and intraoperative laryngospasm are persistent, but some studies have shown the outcomes between endotracheal tubes and LMAs to be comparable [148]. The success of this technique is highly dependent on anesthesiologist and surgeon comfort and endotracheal intubation is still the most common means of airway management.

Patients recovering from tonsillectomy can have significant pain, including surgical site pain, dysphagia, referred otalgia and neck pain for 1-2 weeks postoperatively [149]. There is mixed data regarding the effect of surgical resection technique on postoperative pain and there is no evidence that administering local anesthetic at the surgical site improves postoperative pain [149, 150]. Acetaminophen is the mainstay of analgesia after tonsillectomy and should be used routinely [149]. NSAIDs are equianalgesic to opioids and are associated with decreased emesis after tonsillectomy [151, 152]. However, NSAIDs are typically avoided in the immediate perioperative period due to concerns for an increased risk of bleeding from platelet dysfunction.

Opioid medications are often required for postoperative analgesia, but should be

used cautiously given the high incidence of SDB in this patient population. Children with severe OSA are at increased risk for opioid-related adverse events (ORAE), including oxygen desaturation, over-sedation, use of supplemental oxygen and naloxone, and escalation of care [143]. This is due to a combination of diminished responsiveness to hypercarbia, which impairs their ability to arouse from over-sedation, as well as increased sensitivity to the analgesic effect of opioids [143, 153]. Children with OSA and chronic recurrent hypoxemia require half the total morphine dose to obtain the same degree of postoperative analgesia after adenotonsillectomy compared to children with OSA who do not have hypoxemia [153]. Therefore, children with OSA, and specifically those with nocturnal hypoxia, should receive a decreased opioid dose compared to those without OSA. One method is to give intraoperative opioids in small incremental doses up to a standard morphine dose of 0.05-0.1 mg/kg, titrated to the patient's respiratory pattern [142]. Children under 4-5 years old are usually not prescribed opioids after hospital discharge.

Postoperative vomiting (POV) can occur in more than 70% of children underdoing tonsillectomy without antiemetic prophylaxis and is the most common cause of delayed discharge or unscheduled overnight admission after tonsillectomy. Therefore, antiemetic prophylaxis should be routinely administered to these patients. Dual therapy with dexamethasone and a 5-HT_3 antagonist is the most effective prophylaxis for POV after tonsillectomy [154]. In addition to its antiemetic effect, dexamethasone reduces pain scores and improves the quality of oral intake for the first 24 hours after tonsillectomy and is associated with a delayed time to first analgesic requirement postoperatively [155].

Postoperative hemorrhage is the most common severe complication after tonsillectomy, occurring in 0.3-1% of patients. Primary hemorrhage occurs within the first 24 hours and is likely related to surgical technique. Secondary hemorrhage is due to disruption of the eschar, most commonly occurring on postoperative day 6-7 [149]. It is impossible to quantify the amount of preoperative blood loss from post-tonsillectomy hemorrhage due to the large amount of blood that is swallowed. As such, patients may be profoundly hypovolemic or anemic on presentation with an increased risk for aspiration [156]. Patients are most commonly managed with rapid sequence induction. Care should be taken not to dislodge any clot that is present during intubation and an extra suction set-up should be available in case of significant bleeding. Gastric contents should be aspirated after induction and the patient should be extubated awake to further decrease aspiration risk [157]. The most common adverse events are hypoxemia, bradycardia and hypotension. In a review, 2.7% of patients were difficult to intubate due to airway conditions, although none of these patients had difficult airways for their initial tonsillectomy [156].

Foreign Body Ingestion and Aspiration

Foreign body ingestion and aspiration are common events among children. Up to 75% of foreign body ingestions occur in children under 5 years old and the peak age group for foreign body aspiration is 1-2 years old [158, 159]. Ninety-eight percent of accidental ingestions of objects commonly found in the home [158]. Younger children are more likely to aspirate food products, while older children aspirate non-organic products. Aspiration events carry a high rate of morbidity and mortality, especially in children under 3 years old [159]. Many ingestions are not witnessed and children may not present with a clear history of choking or gagging. Presenting symptoms after ingestion include chest or abdominal pain, drooling, fussiness, fever, feeding refusal, stridor, wheezing, recurrent pneumonia and respiratory distress, or children may be asymptomatic [158, 159]. In the event of an unwitnessed ingestion, the diagnosis may be delayed for weeks due to the non-specific nature of symptoms [159]. Children with a suspected foreign body ingestion will have radiographs performed as part of their evaluation. Radio-opaque objects can be visualized and, possibly, identified. Button batteries can be differentiated from coins based on "double halo" and "step-off" signs, although these findings are not always reliable [158]. This differentiation has important implications for the urgency of intervention, but if there is any doubt, the object should be assumed to be a button battery and treated as such. Radiolucent objects will not be visualized, but signs of air trapping and atelectasis can indicate the presence of an airway foreign body [159].

The acute management of aspirated foreign bodies begins with appropriate pediatric basic life support. Children who are able to cough and make sounds should be allowed to clear the object on their own, while those with severe airwayobstruction should receive subdiaphragmatic abdominal thrusts or back blows and chest thrusts depending on age. Rigid bronchoscopy is the gold standard for diagnosis and treatment and should be performed as soon as the diagnosis of an airway foreign body is considered. Constant communication between the anesthesia and surgical teams is essential as the patient will have an unprotected airway shared between the two teams for the duration of the procedure [159]. Anesthesia can be induced by the inhalational or intravenous route. Patients are unlikely to be appropriately fasted for their procedure, raising concerns for intraoperative aspiration of gastric contents. For clinically stable patients with a foreign body in the distal airways, it may be appropriate to wait until the child is appropriately NPO prior to proceeding. However, patients with proximal airway obstruction or suspected aspiration of foreign bodies that are likely to cause significant airway inflammation (for instance, peanuts) require emergent treatment. The anesthesiologist may choose to perform a rapid sequence induction with intubation and gastric suctioning to decrease aspiration risk [159].

However, this may not be possible depending on the position of the foreign body and the endotracheal tube will have to be removed for the procedure, so this is not commonly done. Both spontaneous and controlled ventilation with a muscle relaxant can be used during this procedure. Spontaneous ventilation allows continuous ventilation during all stages of the procedure, but it can be difficult to maintain adequate depth of anesthesia to prevent laryngospasm and patient motion while also maintaining adequate respiratory drive. Controlled ventilation with muscle relaxants requires ventilation through the side-port of the bronchoscope. This is only possible while the bronchoscope is in the airway, so there may be prolonged periods of apnea during the case. In addition, positive pressure ventilation may push the foreign body more distally in the airway or increase the risk of ball-valve hyperinflation distal to the foreign body. Benefits of controlled ventilation include facilitation of foreign body removal in an immobilized airway and ease of maintaining an appropriate anesthetic level. Controlled ventilation decreases the rate of laryngospasm and patient movement and slightly decreases operative time, but there are no differences in the incidence of desaturation, laryngeal edema or anesthesia recovery time [160]. A variety of maintenance regimens including TIVA, sevoflurane or a combination of the two can be used. Maintenance with a volatile agent will result in operating room contamination and surgeon exposure to anesthetic agents. A combination of propofol and sevoflurane was found to have a lower incidence of adverse events (cough, breath holding, desaturation, broncho- or laryngospasm) compared to propofol and remifentanil, but outcomes such as duration of procedure, ventilation and success of foreign body removal were not different between the two groups [161]. Opioid administration is helpful to blunt the response to surgical stimulation of the airway, but care must be taken not to induce apnea in patients being managed with spontaneous ventilation. The choice for spontaneous *versus* controlled ventilation and intravenous *versus* inhalational maintenance ultimately depends on anesthesiologist and surgeon preference as well as institutional protocol.

The supraglottic and glottic structures should be anesthetized with topical lidocaine prior to beginning instrumentation of the airway. This will provide anesthesia during the procedure and will also allow an assessment of the depth of systemic anesthesia prior to surgical instrumentation. End-tidal carbon dioxide will not be reliably detected due to the lack of a controlled airway. Ventilation should be continuously monitored by chest rise, auscultation of breath sounds with a precordial stethoscope, visualization of vocal cord motion during bronchoscopy and oxygen saturation. Emergency drugs, including succinylcholine, atropine and albuterol, as well as airway equipment must be available for the treatment of desaturations, laryngospasm and bronchospasm. If the foreign body is lost during retrieval and obstructs the subglottis or trachea, it

should be pushed distally into a mainstem bronchus to allow ventilation of the contralateral lung before the next attempt at removal. Patients with a delayed diagnosis of airway foreign body may have significant airway inflammation or pneumonia at the time of removal and may require close postoperative monitoring for pulmonary compromise. Dexamethasone may be administered perioperatively at the request of the surgeon to decrease airway inflammation [159].

The management of foreign body ingestions depends on the type of object ingested, location within the gastrointestinal tract, presenting symptoms and size of the child. The majority of ingested foreign bodies are removed urgently (within 24-hour of presentation). Emergent removal (less than 2 hours) is indicated for patients with symptomatic foreign bodies, including inability to manage oral secretions, respiratory distress or signs of perforation. Emergent removal is also indicated for all esophageal and most gastric button batteries due to their high morbidity and mortality. The external electrolytic current created by the battery creates a caustic alkaline environment that causes tissue injury beginning within 15 minutes of exposure. These ingestions can be associated with esophageal perforation or stricture, tracheoesophageal fistula, mediastinitis, pneumothorax and aortoesophageal fistula with the potential for catastrophic GI bleeding. Magnet ingestion must also be treated emergently when multiple magnets are ingested, as these can create entero-enteric fistulae or bowel perforations when magnets in adjacent loops of small bowel are attracted to each other. Gastric coins and asymptomatic gastric button batteries in children over 5-years old can be allowed to pass on their own. If the foreign body is not moving on serial imaging, elective removal is indicated [158]. Esophageal and gastrointestinal foreign bodies are often removed endoscopically by gastroenterologists. However, if endoscopic removal is unsuccessful or there are concerns for other injuries such as bowel perforation or esophageal erosion with damage to surrounding structures, pediatric surgeons are likely to be required.

Patients with esophageal or gastric foreign bodies who require endoscopic removal usually require rapid sequence induction with placement of an endotracheal tube. This is especially important for patients who are unable to manage their oral secretions or patients who failed an oral challenge prior to presenting for foreign body removal. For uncomplicated extractions, postoperative pain is minimal, generally requiring only fentanyl, acetaminophen and/or ketorolac for analgesia. Patients with a button battery ingestion will need hospitalization with repeated evaluations to monitor for progression of tissue damage [158]. As these patients may need emergent surgical interventions, transfer of care to a tertiary children's hospital after initial stabilization may be required.

Genitourinary Procedures

Genitourinary procedures are commonly performed as ambulatory procedures in pediatric patients. These include penile surgeries, such as circumcision and hypospadias repair, and scrotal and inguinal procedures, such as inguinal hernia repair and orchidopexy. Many of these procedures occur electively in infancy, however, repair of incarcerated inguinal hernias and testicular torsion are performed emergently due to the risk of ischemic bowel or testicular injury [162]. Circumcision and hypospadias repairs are limited to the penile shaft [163]. Inguinal hernia repairs are performed through an inguinal incision and diagnostic laparoscopy may be performed to evaluate the contralateral side [162]. Orchidopexy may be performed through a scrotal, inguinal or abdominal incision depending on the location of the testis and may require laparoscopy [164]. Orchidopexy also requires traction on the spermatic cord, which is quite stimulating and can trigger laryngospasm in an inappropriately anesthetized patient [165]. The majority of genitourinary procedures are performed with general anesthesia and either caudal block or peripheral nerve blocks (dorsal penile nerve block or ilioinguinal nerve block). The choice for airway management depends on the duration of procedure, the anticipated degree of surgical stimulation and the fasting status of the patient.

Caudal anesthesia and peripheral nerve blocks provide better analgesia for outpatient pediatric urologic surgery than general anesthesia alone [166]. For distal penile surgery, such as circumcision and distal hypospadias repair, there is very limited evidence for improved analgesia with caudal block compared to penile block [167]. Given the risk for postoperative motor block, which can be bothersome to ambulatory children and may delay discharge, penile block is often preferred for these procedures. More extensive genitourinary surgery and bilateral procedures are often managed with a caudal block. A T4 level is required intraoperatively to block stimulation associated with traction on the spermatic cord, but a T10 level will provide adequate postoperative analgesia [165]. The volume of local anesthetic required to achieve adequate spread from the caudal space is estimated at 0.05 ml/kg/level, or approximately 0.5 ml/kg for lumbar levels, 1 ml/kg for lower thoracic levels and 1.25 ml/kg for mid-thoracic levels. High-volume blocks with dilute local anesthetic solutions are required to achieve adequate intraoperative spread for spermatic cord traction [165]. In addition, high volume/low concentration blocks provide prolonged postoperative analgesia with decreased motor block after hypospadias repair and orchidopexy compared to low-volume blocks using more concentrated solutions [165, 168]. The optimal concentrations for caudal local anesthetics appear to be bupivacaine 0.125-0.175% and ropivacaine 0.1-0.2% with volume calculated to stay below 2.5 mg/kg of local anesthetic in a single bolus [169]. The duration of analgesia is

limited to 4-8 hours, even with long-acting drugs such as bupivacaine. Adjuncts, such as morphine and clonidine, can prolong the duration of analgesia, but at the expense of delayed respiratory depression and sedation [169]. These medications are generally not used for children undergoing outpatient surgery due to unjustified safety risks and potential for delayed PACU discharge.

POSTOPERATIVE CARE

Routine Postoperative Care

The postoperative care of pediatric patients may occur in the postanesthesia care unit (PACU) or an age-appropriate intensive care unit (NICU or PICU) depending on the acuity of the patient and available hospital resources. The American Society of Anesthesiologists (ASA) has published guidelines for the postanesthetic care of patients. As in adult patients, children must have their vital signs routinely monitored and be assessed for return to baseline mental status and neuromuscular function. Patients must have a stable cardiorespiratory status and adequate control of pain and nausea prior to discharge. Appropriate nursing and physician staff, airway and resuscitation equipment and emergency drugs must be immediately available [170]. Particular concerns related to pediatric patients are outlined by the American Academy of Pediatrics (AAP). A full range of age- and size-appropriate medical equipment, including monitoring, airway, intravascular and resuscitation devices, must be readily available. In addition, resuscitation drugs must be available in appropriate pediatric concentrations. All staff caring for pediatric patients must have the ability to recognize a child in distress and provide immediate assistance with basic pediatric airway management and resuscitation techniques [171]. Importantly, these recommendations should be extended to all areas of the hospital where pediatric patients may be cared for perioperatively, including the inpatient ward, emergency department and radiology suites.

Children are generally admitted to a "first-stage" recovery unit until they have a stable airway and vital signs without respiratory or hemodynamic support, have return of baseline consciousness and motor function and pain and nausea are well-controlled. At that point, they are transitioned to a "second-stage" recovery unit with decreased nursing supervision until they reach discharge criteria [172]. The most commonly used discharge criterion is the modified Aldrete score. This score evaluates five components of patient recovery, including motor activity, respiration, blood pressure, consciousness and oxygen saturation. Each component is given a score of 0-2 with a maximum score of 10 points [173, 174]. Other discharge criteria specific for ambulatory surgery incorporate additional assessments of pain control, nausea and vomiting and surgical bleeding [175,

176]. Patients are no longer required to drink fluids or urinate prior to discharge, as this has been found to prolong PACU stay without patient benefit. In addition, there is no minimum duration of observation required prior to PACU discharge [170]. Regardless of which discharge criteria is used, a physician anesthesiologist must be responsible for each PACU patient to determine when discharge to home or the inpatient unit is appropriate.

Common Postoperative Problems

The rate of unplanned hospital admission after pediatric ambulatory surgery ranges from 1.8-3.7% in retrospective reviews. **Anesthesia-related reasons**, including postoperative nausea and vomiting (PONV), airway complications, poorly controlled pain and prolonged sedation, accounted for 35-40% of admissions [177, 178]. The rate of unplanned postoperative ICU admission after pediatric surgery is 0.6% [179, 180]. The rate of unplanned ICU admission due to anesthesia causes is 0.14-0.5% [179, 181]. Although the need for ICU admission is usually recognized intraoperatively or in the PACU, 20% of ICU admissions came from the inpatient floor after patients had been discharged from the PACU [181]. One study found a 0.3% incidence of rapid response team activation for emergent evaluation of inpatients recovering from anesthesia. Of these, 50% required transfer to an ICU [182]. The majority (56-73%) of anesthesia-related ICU admissions or emergent evaluations in children are due to airway or respiratory complications, which differs from adults who are more commonly admitted for cardiovascular problems [180 - 182]. Unplanned pediatric ICU admissions are often associated with underlying airway abnormalities and/or intraoperative hypoxia, especially in patients undergoing head and neck procedures and occur more often in children under 5 years of age [179 - 181]. These studies highlight the need for ongoing vigilance and staff training in pediatric care at all points during a child's postoperative recovery, not just while the child is in the perioperative environment. The prevention and management of problems that commonly affect children postoperatively are discussed below.

Respiratory Problems

Perioperative respiratory adverse events (PRAE) are a major cause of morbidity and mortality after pediatric surgery. Fifteen percent of children will have a respiratory event during the perioperative period, and 4% of children will have a respiratory event specifically in the postoperative period. The most common PRAE is oxygen desaturation, followed by persistent coughing, airway obstruction, laryngospasm, bronchospasm and stridor [183]. Most events are easily managed with no long-term sequelae, however, complications can include prolonged oxygen requirements, need for non-invasive ventilation or intubation,

need for unplanned hospital or ICU admission, negative pressure pulmonary edema and, in severe cases, cardiac arrest with neurologic sequelae or death [184]. Approximately half of pediatric perioperative cardiac arrests are related to anesthesia and, of those, one-quarter are due to respiratory events. Half of the anesthesia-related cardiac arrests that occur in the postoperative period are due to respiratory events [92].

The risk for PRAE is affected by patient, surgical and anesthetic factors. Patient factors associated with PRAE are young age, a history of wheezing or nocturnal dry cough, recent upper respiratory infection (URI), eczema, exposure to tobacco smoke and family history of atopy [183]. The risk for PRAE is highest in young children. The risk of any respiratory event decreases by 8% per year of age and the risk of laryngospasm decreases by 11% per year of age [183, 185]. URIs increase the risk for PRAE if patients have symptoms within two weeks of surgery. URI symptoms greater than two weeks prior to surgery are not associated with increased PRAE [183]. Eczema is used as an early marker for children who will eventually develop asthma or recurrent wheeze later in life [184]. Surgical procedures involving the airway, sudden surgical stimulation and emergency surgical procedures are associated with PRAE [183, 184]. Anesthetic factors that increase risk are premedication with midazolam, induction or maintenance with volatile agents as compared to propofol (desflurane is higher risk than sevoflurane) and spraying the vocal cords with lidocaine. Non-invasive airway management with face mask or laryngeal mask airway (LMA) is associated with decreased risk of PRAE compared to use of endotracheal tubes (ETT). Multiple attempts to secure the airway and the use of uncuffed ETTs also increase the risk of laryngospasm, while the use of muscle relaxants to facilitate intubation decreases this risk. The risk for PRAE is increased when LMAs are removed awake, when ETTs are removed under deep anesthesia and when non-pediatric trained anesthesiologists are managing the airway [183].

Respiratory events may present as obvious respiratory distress, but can also have more subtle features including anxiety or altered mental status, tachy- or bradycardia, hypertension and seizures. It is therefore important that all perioperative staff be trained to recognize the signs of pediatric respiratory distress and be able to begin initial treatment while awaiting specialist help. Initial maneuvers should include administering supplemental oxygen, repositioning the airway to relieve obstruction, suctioning the airway if secretions or blood are present and starting bag-mask ventilation if needed. The management of airway obstruction and laryngospasm has been discussed previously in this chapter. Negative pressure pulmonary edema can occur after the generation of strong inspiratory efforts against a closed glottis and may be seen after relief of laryngospasm or other upper airway obstruction. Patients may have significant

hypoxia, persistent tachypnea or tachycardia and pink frothy secretions. Symptoms usually resolve quickly, but patients may require supplementary oxygen, CPAP or ICU admission until resolution of symptoms [183].

Post-intubation croup manifests as stridor, hypoxemia and respiratory distress in the postoperative period, most often occurring in children 1-4 years old and less of often with increasing age. Symptoms typically begin within 1-4 hours postoperatively and resolve by 24 hours. Risk factors include traumatic intubation, tight-fitting ETT (leak greater than 20-25 cm H_2O), coughing with the ETT in place, changing the patient's position while intubated, intubation lasting more than one hour and surgery on the head and neck [186]. The incidence was previously found to be 1% among intubated children, but has decreased with the use of cuffed ETTs which are associated with lower rates of stridor. The treatment of stridor is nebulized racemic epinephrine (0.5 ml of 2% epinephrine in 3 ml sterile water). Children must be observed for 4 hours after the administration of racemic epinephrine for signs of rebound edema, which may necessitate and unplanned hospital admission. Dexamethasone is useful for croup after long-term ventilation. Although its benefit after intubations of shorter duration is unclear, it is still often used for postoperative post-intubation croup [184].

Emergence Delirium

Emergence delirium (ED) is a postoperative disturbance of cognition characterized by agitation, inconsolability, hallucinations or delusions, hypersensitivity to stimuli, lack of awareness of the surrounding environment and absence of eye contact with caregivers. In addition, patients have involuntary physical activity ranging from restlessness to combativeness [187 - 190]. The reported incidence is highly variable depending on the definition used and population studied. Rates of 12-18% have been reported in the pediatric literature [187]. The exact etiology of ED is unknown. It is more likely to occur in preschool-aged children (2-5 years old), patients with preoperative anxiety and poor adaptability and those undergoing ENT and ophthalmology procedures [187, 191]. Anesthetic risk factors include the use of inhalational anesthetics and rapid awakening, though there is no association with duration of anesthesia [187]. Inadequately controlled pain may contribute to ED, but it can also occur after anesthetics for non-painful procedures, such as radiology studies [188]. Children who develop ED are at increased risk for postoperative maladaptive behaviors, including anxiety, sleep disturbances, enuresis, temper tantrums and attention seeking behavior [190, 191].

Emergence delirium occurs in the early postoperative period, usually within the first 30 minutes of surgery. It is generally self-limited, lasting less than 15

minutes, and resolves without treatment, but may last as long as 45 minutes or require intervention [187 - 189]. It may be difficult to distinguish from other causes of agitation, such as pain, respiratory failure and hemodynamic instability [190]. Multiple assessment scales have been created, most of which assess emotional distress, agitation and lack of cooperation. These criteria overlap with those assessed in some pain scales [188]. The Pediatric Anesthesia Emergence Delirium (PAED) scale (Table **17**) assesses eye contact, purposeful movement, awareness of surroundings, restlessness and consolability. A score of 10 or more indicates the likely presence of emergence delirium [189].

Pediatric Anesthesia Emergence Delirium (PAED) Scale

Table 17. Pediatric Anesthesia Emergence Delirium (PAED) scale [127]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Pediatric Anesthesia Emergence Delirium (PAED) Scale e					©2018 L. SCHWARTZ, CO CHILDREN'S HOSP.
	Not at all	**Just a little**	**Quite a bit**	**Very much**	**Extremely**
The child makes eye contact with the caregiver.	4	3	2	1	0
The childís actions are purposeful.	4	3	2	1	0
The child is aware of his/her surroundings.	4	3	2	1	0
The child is restless.	0	1	2	3	4
The child is consolable.	0	1	2	3	4

The prevention of ED includes treatment of preoperative anxiety, anesthetic modification to minimize exposure to volatile agents and the use of analgesic and sedative medications to decrease the chance for development of ED. A recent meta-analysis of pharmacologic treatments found that midazolam premedication is not effective at preventing ED. Propofol given as a continuous infusion intraoperatively or as bolus prior to emergence prevents ED, but a propofol bolus on induction does not. Ketamine, clonidine, dexmedetomidine and fentanyl were all shown to decrease the incidence of ED [192]. Intraoperative dexmedetomidine is superior to propofol administration, but may increase the duration of PACU stay [190].

Although ED is generally self-limited, it should be treated when it is prolonged or potentially dangerous. Possible adverse events include disruption of the surgical site, accidental removal of intravenous catheters and drains, patient or caregiver injury and parental distress [187 - 189, 192]. In addition, prolonged ED requires extra nursing care, putting a strain on PACU resources [188, 189]. In one study,

60% of children with ED required physical restraint to prevent self-harm and 52% were treated with an opioid or benzodiazepine [187]. Pharmacologic treatments include midazolam 0.1 mg/kg, propofol 0.5-1 mg/kg, fentanyl 1-2.5 mcg/kg and dexmedetomidine 0.3-0.5 mcg/kg, all of which prolong the PACU stay [188, 190].

Postoperative Nausea and Vomiting

The incidence of postoperative nausea and vomiting (PONV) is increased in children compared to adults, with some studies showing a two-fold increase in PONV among pediatric patients [193, 194]. PONV can be associated with prolonged PACU stays or unplanned admissions, patient and family dissatisfaction and, rarely, medical complications, such as aspiration, volume depletion, electrolyte imbalance and wound disruption [172, 194]. Unlike adults, children often present with vomiting rather than nausea, as they are often unable to describe the sensation of nausea. For this reason, many pediatric studies focus on postoperative vomiting (POV), rather than PONV [195, 196]. There are four independent factors which increase the risk of PONV; duration of surgery >30 minutes, age >3 years, strabismus surgery, and a personal or family history of PONV. The incidence of POV ranged from 9% in patients with zero risk factors to 70% in patients with four risk factors [195].

The ASA has released Consensus Guidelines regarding the prevention and treatment of PONV, including recommendations for pediatric patients. Recommendations include reducing baseline risk factors for PONV, administering antiemetic prophylaxis to children at moderate-to-high risk of POV and treating POV with drugs of a different class than those that were used for prophylaxis. Strategies to reduce baseline risk include avoidance of general anesthesia by the use of regional anesthesia, avoidance of volatile agents and nitrous oxide, preferential use of propofol for induction and maintenance of anesthesia, minimizing perioperative opioid administration and providing adequate intravenous hydration. In the pediatric population, it is often not possible to avoid general anesthesia due to lack of patient cooperation with regional-only techniques. However, a combination of general and regional technique should be used when possible to provide adequate postoperative pain control with decreased opioid requirements. The common use of mask inductions makes complete avoidance of volatile agents and nitrous oxide impossible. However, in pediatric populations, subhyptonic doses of propofol (1 mg/kg bolus followed by a 20 mcg/kg/min infusion) have been shown to decrease POV in patients receiving volatile agents. Although the use of nitrous oxide does increase PONV in patients at risk, it has little impact when the risk of PONV is low. Routine gastric decompression and limiting oral intake postoperatively have not been shown to

decrease PONV [194].

Antiemetic prophylaxis should be administered to children at risk for POV, with those at moderate-to-high risk receiving combination therapy with at least two agents. The first line agents for pediatric POV are 5-HT_3 antagonists and steroids, each of which provides a 50-60% relative risk reduction in pediatric POV when used alone and an 80% relative risk reduction when used in combination. The recommended doses are ondansetron 50-100 mcg/kg (up to 4 mg) and dexamethasone 150 mcg/kg (up to 5 mg). Pediatric doses for other antiemetic agents can be found in the ASA Consensus Guidelines. As in adults, the main side effects from ondansetron are related to QT prolongation. The clearance of ondansetron is decreased in infants less than 6 months of age due to immaturity of the cytochrome P450 system. It is recommended that children younger than 4 months should be closely monitored after receiving ondansetron; however, this age group often does not receive antiemetic prophylaxis due to the lower incidence of POV. Dexamethasone should be avoided in children at risk for tumor lysis syndrome. Concerns for steroid effects on blood glucose and wound healing are similar to what is seen in adults [194]. Transdermal scopolamine is an effective antiemetic in adults; however, it **IS NOT** approved in children younger than 12 years old. The patch should not be cut or altered in any way, as this will have unpredictable effects on drug administration.

Rescue treatment with antiemetic drugs should be given to children who develop POV. If prophylaxis was given within the previous 6 hours, it is recommended that drugs of a different class be used for treatment as repeating administration of previously used agents does not improve outcomes. Any drug aside from dexamethasone, transdermal scopolamine, and longer-acting drugs such as aprepitant and palonosetron, can be repeated after 6 hours. In adults, 5-HT_3 antagonists, dexamethasone, droperidol, promethazine and small doses of propofol have been used as rescue therapy for PONV [194]. Unfortunately, there are no large-scale studies of rescue antiemetic therapy in children on which to base recommendations. However, smaller studies have shown effectiveness of antihistamines (dimenhydrinate) and dopamine antagonists (droperidol and metoclopramide) in pediatric patients. Side effects such as sedation and extrapyramidal effects must be considered prior to administering these medications [193].

Postoperative Pain

Poorly controlled pain can be a cause of prolonged PACU stay or unanticipated hospital admission and a source of patient and family dissatisfaction. As previously discussed, a plan for perioperative pain management should be created

and instituted prior to arrival in PACU. Children often have an exaggerated emotional and behavioral component to their pain due to increased anxiety and poor coping mechanisms. In addition, parental behavior plays and important role in pediatric pain. It is important to establish goals for postoperative analgesia prior to surgery [110]. Once in PACU, patients should be routinely assessed with developmentally appropriate pain scales and treated according to standardized protocols. There should be an anesthesiologist responsible for perioperative pain management available for consultation at all times. In addition, all perioperative staff should have ongoing education and training to ensure the ability to recognize and treat adverse effects due to analgesic therapies. In addition to analgesics, behavioral techniques and anxiolytics may play and important role in perioperative analgesia [107].

A number of scales have been created to evaluate pain among pediatric patients. As in adults, self-report scales are the preferred method of pain assessment. However, young children lack the cognitive skills to use a numerical scale, such as the visual analog scale (VAS) used for adults. Alternative scales, such as the Wong Baker Faces Pain Scale (Fig. **2**), rely on facial expressions rather than numerical values for self-report and have been validated in children as young as 3 years old. In many cases, it is still necessary to use behavioral observations to complement self-reported scores, particularly in preschool-aged children [109]. For children who are unable to or unwilling to rate their pain, observational scales can be used in place of self-report. Two commonly used scales are the FLACC and NIPS scales (Tables **18** and **19**), outlined below, though many observational pediatric scales exist [109, 112].

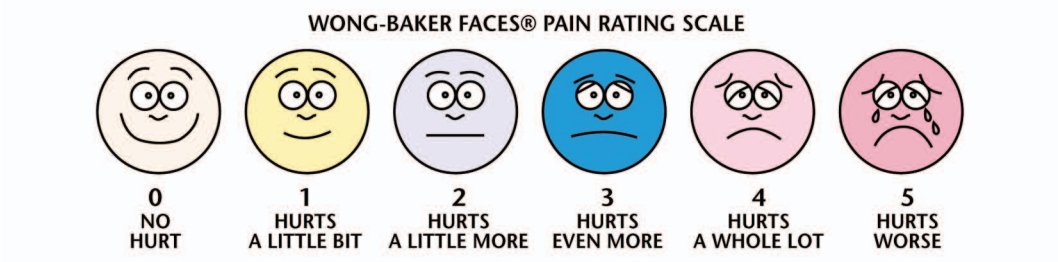


Fig. (2). Wong Baker Faces Pain Scale [109]. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital. ©1983 Wong-Baker FACES Foundation, www.WongBakerFACES.org. Used with permission. Originally published in Whaley & Wong's Nursing Care of Infants and Children. ©Elsevier Inc.

FLACC Behavioral Pain Scale Total Score Ranges from 0-10 Points

Table 18. FLACC Behavioral Pain Scale Total score ranges from 0-10 points. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

FLACC Behavioral Pain Scale Total Score Ranges From 0-10 Points.			
Scoring:	**0**	**1**	**2**
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Neonatal Infant Pain Scale Total Score Ranges From 0-7 Points. ≥4 Point Is Considered Pain

Table 19. Neonatal Infant Pain Scale. Total score ranges from 0-7 points. ≥4 point is considered pain. Provided by Drs. Monica Hoagland, M.D., Tessa Mandler, M.D., Lawrence I. Schwartz, M.D., Colorado Children's Hospital.

Neonatal Infant Pain Scale Total Score Ranges From 0-7 Points. >4 Point Is Considered Pain.			
Scoring:	**0**	**1**	**2**
Facial expression	Relaxed	Contracted	– –
Cry	Absent	Mumbling	Vigorous
Breathing	Relaxed	Different than baseline	– –
Arms	Relaxed	Flexed/stretched	– –
Legs	Relaxed	Flexed/stretched	– –
Alertness	Sleeping/calm	Uncomfortable	– –

Common pediatric oral and intravenous dosing requirements for acetaminophen and NSAIDs are discussed previously. Scheduled acetaminophen and NSAID administration should be continued in the postoperative period unless

contraindicated by the patient's medical comorbidities or surgical procedure. Given the multiple over-the-counter and prescription analgesics that contain acetaminophen and the multiple concentrations of ibuprofen available, there is a high potential for overdose of these medications among pediatric patients. For patients being discharged home from the PACU, it is extremely important to counsel parents regarding appropriate administration of these analgesics [109]. At some institutions, surgeons are also encouraged to prescribe stand-alone opioids (*i.e,* oxycodone instead of percocet) to eliminate the risk of accidental acetaminophen overdose in children.

Postoperative opioid administration is indicated for procedures with anticipated moderate-to-severe pain. Oral medications, such as oxycodone and hydrocodone should be used when possible. As previously discussed, codeine should not be used for pediatric patients. When intravenous opioid administration is indicated, medications are most commonly given on an as needed (PRN) schedule. However, this dosing regimen does not achieve stable blood levels and predisposes to periods of excessive sedation alternating with inadequate analgesia [109]. The preferred method for opioid administration is by patient controlled analgesia (PCA). Children over 7 years old are generally able to understand and self-administer PCA. Parents must be instructed not to administer opioids on behalf of their child, as this increases the risk of opioid overdose, sedation and respiratory depression [109]. For younger or developmentally delayed children, nurse- or caregiver-controlled analgesia (NCA/CCA) may be an option. In this scenario, a nurse or family member is authorized to administer opioids on behalf of the child. This technique requires significant education of family members regarding pain assessment, recognition of opioid side effects and scenarios in which the CCA should not be used. In addition, strict nursing protocols must be in place to appropriately monitor the patient's pain control, level of sedation and respiratory status [109, 110]. Due to the level of family education and monitoring required for NCA/CCA, this dosing regimen may not be appropriate for hospitals that do not routinely care for pediatric patients or patients may require admission to the intensive care unit for appropriate monitoring.

Opioids administered by any route carry a risk for respiratory depression, nausea, pruritis and urinary retention. The Anesthesia Patient Safety Foundation recommends respiratory monitoring, consisting of at least continuous pulse oximetry and respiratory rate (capnography), for children receiving PCA, serial parenteral or neuraxial opioids. However, adherence to these guidelines may be difficult in pediatric patients due to lack of cooperation. Patients at increased risk for opioid-induced respiratory depression, such as infants or patients with abnormal airway anatomy or respiratory control may require more frequent monitoring or ICU admission while receiving opioids. The level of sedation

should also be routinely monitored. Resuscitation and airway equipment in appropriate pediatric sizes must always be immediately available for any patient receiving opioids. Opioid side effects can be treated with intravenous naloxone 0.5-1 mcg/kg or 0.25 mcg/kg/hr. Nalbuphine 25-50 mcg/kg can be given intravenously every 6 hours to treat pruritis. When treating nausea, caution should be used with antiemetics that also cause sedation, as these can potentiate opioid-induced sedation and respiratory depression [109].

Patients with regional blockade require additional monitoring for appropriate block function and side effects. Patients receiving continuous regional analgesia must be evaluated at least daily by an anesthesiologist to assess block efficacy, manage medication administration and monitor for complications such as local anesthetic toxicity, nerve injury and infection.

CONCLUSION

Surgery is a time of anxiety, fear, and pain for children. The ability to alleviate their anxiety, quell their fear, and prevent and treat their pain is what makes pediatric anesthesia a greatly rewarding field for the anesthesia provider. The opportunity to care for this special patient population is a privilege which comes with great responsibility. Community based pediatric anesthesia programs have a responsibility to ensure that their institution is equipped to safely manage the children who will present to them for their anesthetic care. They must ensure that policies and resources specific to the pediatric patient are in place, and make certain that all personnel maintain the knowledge and skills necessary for this task. In doing so, the millions of children who present to community based centers for surgery each year will have access to the high quality of anesthesia care they deserve.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] August DA, Everett LL. Pediatric ambulatory anesthesia. Anesthesiol Clin 2014; 32(2): 411-29. [http://dx.doi.org/10.1016/j.anclin.2014.02.002] [PMID: 24882128]

[2] Rabbitts JA, Groenewald CB, Moriarty JP, Flick R. Epidemiology of ambulatory anesthesia for children in the United States: 2006 and 1996. Anesth Analg 2010; 111(4): 1011-5.
[PMID: 20802051]

[3] Centers for disease control and prevention. National Survey of Ambulatory Surgery 2006. http://www.cdc.gov/nchs/nsas.htm

[4] Cullen KA, Hall MJ, Golosinskiy A. Ambulatory surgery in the United States, 2006. Natl Health Stat Rep 2009; 28(11): 1-25.
[PMID: 19294964]

[5] Sømme S, Bronsert M, Morrato E, Ziegler M. Frequency and variety of inpatient pediatric surgical procedures in the United States. Pediatrics 2013; 132(6): e1466-72.
[http://dx.doi.org/10.1542/peds.2013-1243] [PMID: 24276846]

[6] Optimal resources for children's surgical care in the United States. J Am Coll Surg 2014; 218(3): 479-487, 487.e1-487.e4.
[http://dx.doi.org/10.1016/j.jamcollsurg.2013.10.028] [PMID: 24468231]

[7] Campbell S, Wilson G, Engelhardt T. Equipment and monitoring--what is in the future to improve safety? Paediatr Anaesth 2011; 21(7): 815-24.
[http://dx.doi.org/10.1111/j.1460-9592.2011.03553.x] [PMID: 21435095]

[8] American Society of Anesthesiology Pediatric Anesthesia Committee. ASA Statement on practice recommendations for pediatric anesthesia 2011 .http://www.asahq.org/quality-and-practice-management/standards-and-guidelines

[9] Feldman JM. Optimal ventilation of the anesthetized pediatric patient. Anesth Analg 2015; 120(1): 165-75.
[http://dx.doi.org/10.1213/ANE.0000000000000472] [PMID: 25625261]

[10] Jöhr M, Berger TM. Venous access in children: state of the art. Curr Opin Anaesthesiol 2015; 28(3): 314-20.
[http://dx.doi.org/10.1097/ACO.0000000000000181] [PMID: 25827277]

[11] Bouaziz H, Zetlaoui PJ, Pierre S, *et al.* Guidelines on the use of ultrasound guidance for vascular access. Anaesth Crit Care Pain Med 2015; 34(1): 65-9.
[http://dx.doi.org/10.1016/j.accpm.2015.01.004] [PMID: 25829319]

[12] Eichhorn JH, Cooper JB, Cullen DJ, Maier WR, Philip JH, Seeman RG. Standards for patient monitoring during anesthesia at Harvard Medical School. JAMA 1986; 256(8): 1017-20.
[http://dx.doi.org/10.1001/jama.1986.03380080063029] [PMID: 3735628]

[13] Eichhorn JH, Cooper JB, Cullen DJ, *et al.* Anesthesia practice standards at Harvard: a review. J Clin Anesth 1988; 1(1): 55-65.
[http://dx.doi.org/10.1016/0952-8180(88)90013-X] [PMID: 3078525]

[14] American Society of Anesthesiology, Committee on Standards and Practice Parameters. Standards for basic anesthetic monitoring 2015. http://www.asahq.org/~/media/Sites/ASAHQ/Files/Public/Resources/standards-guidelines/standards-for-basic-anesthetic-monitoring.pdf

[15] Merry AF, Cooper JB, Soyannwo O, Wilson IH, Eichhorn JH. International standards for a safe practice of anesthesia 2010. Can J Anaesth 2010; 57(11): 1027-34.
[http://dx.doi.org/10.1007/s12630-010-9381-6] [PMID: 20857254]

[16] Mehta SP, Eisenkraft JB, Posner KL, *et al.* Patient injury from gas delivery equipment: a closed claims update. Anesthesiology 2013; 119: 778-95.
[http://dx.doi.org/10.1097/ALN.0b013e3182a10b5e]

[17] Mehta SP, Posner KL, Domino KB. Burns from warming devices and heated materials: a closed claims update. Anesthesiology 2012; A1079.

[18] American Society of Anesthesiology, Committee on Equipment and Facilities. Recommendations for

Pre-Anesthesia Checkout Procedures 2008. https://www.asahq.org/resources/clinical-information/2008-asa-recommendations-for-pre-anesthesia-checkout

[19] Pickering TG, Hall JE, Appel LJ, *et al.* Recommendations for blood pressure measurement in humans and experimental animals: Part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Hypertension 2005; 45(1): 142-61. [http://dx.doi.org/10.1161/01.HYP.0000150859.47929.8e] [PMID: 15611362]

[20] American College of Surgeons. Optimal resources for children's surgical care in the United States 2015.https://www.facs.org/~/media/files/quality%20programs/acs%20csv_standardsmanual.ashx

[21] Laituri CA, Garey CL, Pieters BJ, Mestad P, Weissend EE, St Peter SD. Overnight observation in former premature infants undergoing inguinal hernia repair. J Pediatr Surg 2012; 47(1): 217-20. [http://dx.doi.org/10.1016/j.jpedsurg.2011.10.045] [PMID: 22244421]

[22] Optimal resources for children's surgical care in the United States. J Am Coll Surg 2014; 218(3): 479-487, 487.e1-487.e4. [http://dx.doi.org/10.1016/j.jamcollsurg.2013.10.028] [PMID: 24468231]

[23] Coté CJ, Zaslavsky A, Downes JJ, *et al.* Postoperative apnea in former preterm infants after inguinal herniorrhaphy. A combined analysis. Anesthesiology 1995; 82(4): 809-22. [http://dx.doi.org/10.1097/00000542-199504000-00002] [PMID: 7717551]

[24] Kurth CD, Coté CJ. Postoperative apnea in former preterm infants: general anesthesia or spinal anesthesia – do we have an answer? Anesthesiology 2015; 123(1): 15-7. [http://dx.doi.org/10.1097/ALN.0000000000000710] [PMID: 26001034]

[25] https://policyportal.childrenscolorado.org/policy/Documents/Perioperative_Admission%20for%20Former%20Premature%20Infants_Post%20Anesthetic%20and%20Post%20Sedation.pdf#search=anesthesia

[26] Bhattacharyya N. Ambulatory pediatric otolaryngologic procedures in the United States: characteristics and perioperative safety. Laryngoscope 2010; 120(4): 821-5. [http://dx.doi.org/10.1002/lary.20852] [PMID: 20213790]

[27] Goldman JL, Baugh RF, Davies L, *et al.* Mortality and major morbidity after tonsillectomy: etiologic factors and strategies for prevention. Laryngoscope 2013; 123(10): 2544-53. [PMID: 23595509]

[28] Statham MM, Elluru RG, Buncher R, Kalra M. Adenotonsillectomy for obstructive sleep apnea syndrome in young children: prevalence of pulmonary complications. Arch Otolaryngol Head Neck Surg 2006; 132(5): 476-80. [http://dx.doi.org/10.1001/archotol.132.5.476] [PMID: 16702561]

[29] Collins CE, Everett LL. Challenges in pediatric ambulatory anesthesia: kids are different. Anesthesiol Clin 2010; 28(2): 315-28. [http://dx.doi.org/10.1016/j.anclin.2010.02.005] [PMID: 20488397]

[30] Society for Pediatric Anesthesia Web Site. http://www.pedsanesthesia.org/about/mission-statement/

[31] The Accreditation Council for Graduate Medical Education Web Site. http://www.acgme.org/Specialties/Overview/pfcatid/6/Anesthesiology

[32] Benzon HA, De Oliveira GS Jr, Jagannathan N, Suresh S. Selection of subspecialty fellows in anesthesia for pediatric anesthesia: a national survey of program directors in the United States. Paediatr Anaesth 2015; 25(5): 487-91. [http://dx.doi.org/10.1111/pan.12608] [PMID: 25581298]

[33] The American Board of Anesthesiology Web Site. http://www.theaba.org/ Exams/Pediatric-Anesthesiology/Pediatric-Anesthesiology

[34] Andropoulos DB, Walker SG, Kurth CD, Clark RM, Henry DB. Advanced second year fellowship

training in pediatric anesthesiology in the United States. Anesth Analg 2014; 118(4): 800-8. [http://dx.doi.org/10.1213/ANE.0000000000000089] [PMID: 24651235]

[35] McGowan FX Jr, Davis PJ. The advanced pediatric anesthesiology fellowship: moving beyond a clinical apprenticeship. Anesth Analg 2014; 118(4): 701-3. [http://dx.doi.org/10.1213/ANE.0000000000000167] [PMID: 24651221]

[36] Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. Anesthesiology 2011; 114(3): 495-511. [http://dx.doi.org/10.1097/ALN.0b013e3181fcbfd9] [PMID: 21307770]

[37] Warner MA, Warner ME, Warner DO, Warner LO, Warner EJ. Perioperative pulmonary aspiration in infants and children. Anesthesiology 1999; 90(1): 66-71. [http://dx.doi.org/10.1097/00000542-199901000-00011] [PMID: 9915314]

[38] Tan Z, Lee SY. Pulmonary aspiration under GA: a 13-year audit in a tertiary pediatric unit. Paediatr Anaesth 2016; 26(5): 547-52. [http://dx.doi.org/10.1111/pan.12877] [PMID: 26990683]

[39] Neelakanta G, Chikyarappa A. A review of patients with pulmonary aspiration of gastric contents during anesthesia reported to the Departmental Quality Assurance Committee. J Clin Anesth 2006; 18(2): 102-7. [http://dx.doi.org/10.1016/j.jclinane.2005.07.002] [PMID: 16563326]

[40] Andersson H, Zarén B, Frykholm P. Low incidence of pulmonary aspiration in children allowed intake of clear fluids until called to the operating suite. Paediatr Anaesth 2015; 25(8): 770-7. [http://dx.doi.org/10.1111/pan.12667] [PMID: 25940831]

[41] Schreiner MS, Triebwasser A, Keon TP. Ingestion of liquids compared with preoperative fasting in pediatric outpatients. Anesthesiology 1990; 72(4): 593-7. [http://dx.doi.org/10.1097/00000542-199004000-00002] [PMID: 2321772]

[42] Friesen RH, Wurl JL, Friesen RM. Duration of preoperative fast correlates with arterial blood pressure response to halothane in infants. Anesth Analg 2002; 95(6): 1572-6. [http://dx.doi.org/10.1097/00000539-200212000-00018] [PMID: 12456418]

[43] Castillo-Zamora C, Castillo-Peralta LA, Nava-Ocampo AA. Randomized trial comparing overnight preoperative fasting period *vs*. oral administration of apple juice at 06:00-06:30 am in pediatric orthopedic surgical patients. Paediatr Anaesth 2005; 15(8): 638-42. [http://dx.doi.org/10.1111/j.1460-9592.2005.01517.x] [PMID: 16033337]

[44] https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0ahUKEwiSpJKMmbPNAhVozoMKHQdeAccQFgghMAA&url=http%3A%2F%2Fwww.cincinnatichildrens.org%2FWorkArea%2FDownloadAsset.aspx%3Fid%3D101370&usg=AFQjCNHlVMu794CSUODFdRHvSqJo8c34_Q

[45] https://www.texaschildrens.org/departments/surgery/preparing-surgery

[46] Capurso M, Ragni B. Psycho-educational preparation of children for anaesthesia: A review of intervention methods. Patient Educ Couns 2016; 99(2): 173-85. [http://dx.doi.org/10.1016/j.pec.2015.09.004] [PMID: 26603504]

[47] Hallowell LM, Stewart SE, de Amorim E Silva CT, Ditchfield MR. Reviewing the process of preparing children for MRI. Pediatr Radiol 2008; 38(3): 271-9. [http://dx.doi.org/10.1007/s00247-007-0704-x] [PMID: 18084752]

[48] Johnson CP, Blasco PA. Infant growth and development. Pediatr Rev 1997; 18(7): 224-42. [http://dx.doi.org/10.1542/pir.18-7-224] [PMID: 9203831]

[49] McCann ME, Kain ZN. The management of preoperative anxiety in children: an update. Anesth Analg 2001; 93(1): 98-105.

[http://dx.doi.org/10.1097/00000539-200107000-00022] [PMID: 11429348]

[50] de Rosnay M, Cooper PJ, Tsigaras N, Murray L. Transmission of social anxiety from mother to infant: an experimental study using a social referencing paradigm. Behav Res Ther 2006; 44(8): 1165-75. [http://dx.doi.org/10.1016/j.brat.2005.09.003] [PMID: 16288978]

[51] Lerwick JL. Psychosocial implications of pediatric surgical hospitalization. Semin Pediatr Surg 2013; 22(3): 129-33. [http://dx.doi.org/10.1053/j.sempedsurg.2013.04.003] [PMID: 23870205]

[52] Hearst D. The Runaway Child: managing anticipatory fear, resistance and distress in children undergoing surgery. Paediatr Anaesth 2009; 19(10): 1014-6. [http://dx.doi.org/10.1111/j.1460-9592.2009.03146.x] [PMID: 19754489]

[53] Skinner EA, Zimmer-Gembeck MJ. The development of coping. Annu Rev Psychol 2007; 58: 119-44. [http://dx.doi.org/10.1146/annurev.psych.58.110405.085705] [PMID: 16903804]

[54] Wright KD, Stewart SH, Finley GA. When are parents helpful? A randomized clinical trial of the efficacy of parental presence for pediatric anesthesia. Can J Anaesth 2010; 57(8): 751-8. [http://dx.doi.org/10.1007/s12630-010-9333-1] [PMID: 20499223]

[55] Kain ZN. Premedication and parental presence revisited. Curr Opin Anaesthesiol 2001; 14(3): 331-7. [http://dx.doi.org/10.1097/00001503-200106000-00009] [PMID: 17019112]

[56] Wollin SR, Plummer JL, Owen H, Hawkins RM, Materazzo F. Predictors of preoperative anxiety in children. Anaesth Intensive Care 2003; 31(1): 69-74. [PMID: 12635399]

[57] Bailey KM, Bird SJ, McGrath PJ, Chorney JE. Preparing parents to be present for their child's anesthesia induction: a randomized controlled trial. Anesth Analg 2015; 121(4): 1001-10. [http://dx.doi.org/10.1213/ANE.0000000000000900] [PMID: 26237623]

[58] Stargatt R, Davidson AJ, Huang GH, *et al.* A cohort study of the incidence and risk factors for negative behavior changes in children after general anesthesia. Paediatr Anaesth 2006; 16(8): 846-59. [PMID: 16884468]

[59] Kain ZN, Caldwell-Andrews AA, Maranets I, Nelson W, Mayes LC. Predicting which child-parent pair will benefit from parental presence during induction of anesthesia: a decision-making approach. Anesth Analg 2006; 102(1): 81-4. [http://dx.doi.org/10.1213/01.ANE.0000181100.27931.A1] [PMID: 16368808]

[60] Kain ZN, Maclaren J, Weinberg M, Huszti H, Anderson C, Mayes L. How many parents should we let into the operating room? Paediatr Anaesth 2009; 19(3): 244-9. [http://dx.doi.org/10.1111/j.1460-9592.2008.02889.x] [PMID: 19143951]

[61] Berghmans J, Weber F, van Akoleyen C, *et al.* Audiovisual aid viewing immediately before pediatric induction moderates the accompanying parents' anxiety. Paediatr Anaesth 2012; 22(4): 386-92. [http://dx.doi.org/10.1111/j.1460-9592.2011.03767.x] [PMID: 22176212]

[62] http://www.micromedexsolutions.com/micromedex2/librarian/CS/8F441E/ND_PR/evidencexpert/ND_P/evidencexpert/DUPLICATIONSHIELDSYNC/1B5DCC/ND_PG/evidencexpert/ND_B/evidencexpert/ND_AppProduct/evidencexpert/ND_T/evidencexpert/PFActionId/evidencexpert.DoIntegratedSearch?SearchTerm=midazolam&UserSearchTerm=midazolam&SearchFilter=filterNone&navitem=searchALL#

[63] Golparvar M, Saghaei M, Sajedi P, Razavi SS. Paradoxical reaction following intravenous midazolam premedication in pediatric patients - a randomized placebo controlled trial of ketamine for rapid tranquilization. Paediatr Anaesth 2004; 14(11): 924-30. [http://dx.doi.org/10.1111/j.1460-9592.2004.01349.x] [PMID: 15500492]

[64] Sajedi P, Habibi B. Comparison of the effects of intravenous premedication: Midazolam, Ketamine, and combination of both on reducing anxiety in pediatric patients before general anesthesia. J Res Pharm Pract 2015; 4(4): 187-92.

[http://dx.doi.org/10.4103/2279-042X.167050] [PMID: 26645024]

[65] Pasin L, Febres D, Testa V, *et al.* Dexmedetomidine *vs*. midazolam as preanesthetic medication in children: a meta-analysis of randomized controlled trials. Paediatr Anaesth 2015; 25(5): 468-76.
[http://dx.doi.org/10.1111/pan.12587] [PMID: 25559766]

[66] Funk W, Jakob W, Riedl T, Taeger K. Oral preanaesthetic medication for children: double-blind randomized study of a combination of midazolam and ketamine *vs*. midazolam or ketamine alone. Br J Anaesth 2000; 84(3): 335-40.
[http://dx.doi.org/10.1093/oxfordjournals.bja.a013435] [PMID: 10793592]

[67] Akin A, Bayram A, Esmaoglu A, *et al.* Dexmedetomidine *vs*. midazolam for premedication of pediatric patients undergoing anesthesia. Paediatr Anaesth 2012; 22(9): 871-6.
[http://dx.doi.org/10.1111/j.1460-9592.2012.03802.x] [PMID: 22268591]

[68] http://www.micromedexsolutions.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.DoIntegratedSearch#

[69] Jia JE, Chen JY, Hu X, Li WX. A randomised study of intranasal dexmedetomidine and oral ketamine for premedication in children. Anaesthesia 2013; 68(9): 944-9.
[http://dx.doi.org/10.1111/anae.12312] [PMID: 23848405]

[70] http://www.micromedexsolutions.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.DoIntegratedSearch#

[71] Altiparmak B, Akça B, Yilbaş AA, Çelebi N. All about ketamine premedication for children undergoing ophtalmic surgery. Int J Clin Exp Med 2015; 8(11): 21525-32.
[PMID: 26885101]

[72] Rodieux F, Wilbaux M, van den Anker JN, Pfister M. Effect of Kidney Function on Drug Kinetics and Dosing in Neonates, Infants, and Children. Clin Pharmacokinet 2015; 54(12): 1183-204.
[http://dx.doi.org/10.1007/s40262-015-0298-7] [PMID: 26138291]

[73] Allegaert K, van de Velde M, van den Anker J. Neonatal clinical pharmacology. Paediatr Anaesth 2014; 24(1): 30-8.
[http://dx.doi.org/10.1111/pan.12176] [PMID: 23617305]

[74] Gleich S, Nemergut M, Flick R. Anesthetic-related neurotoxicity in young children: an update. Curr Opin Anaesthesiol 2013; 26(3): 340-7.
[http://dx.doi.org/10.1097/ACO.0b013e3283606a37] [PMID: 23511038]

[75] Sun LS, Li G, Miller TLK, *et al.* Association Between a Single General Anesthesia Exposure Before Age 36 Months and Neurocognitive Outcomes in Later Childhood. JAMA 2016; 315(21): 2312-20.
[http://dx.doi.org/10.1001/jama.2016.6967] [PMID: 27272582]

[76] Davidson AJ, Disma N, de Graaff JC, *et al.* Neurodevelopmental outcome at 2 years of age after general anaesthesia and awake-regional anaesthesia in infancy (GAS): an international multicentre, randomised controlled trial. Lancet 2016; 387(10015): 239-50.
[http://dx.doi.org/10.1016/S0140-6736(15)00608-X] [PMID: 26507180]

[77] Zielinska M, Holtby H, Wolf A. Pro-con debate: intravenous *vs*. inhalation induction of anesthesia in children. Paediatr Anaesth 2011; 21(2): 159-68.
[http://dx.doi.org/10.1111/j.1460-9592.2010.03488.x] [PMID: 21210885]

[78] Jöhr M, Berger TM. Paediatric anaesthesia and inhalation agents. Best Pract Res Clin Anaesthesiol 2005; 19(3): 501-22.
[http://dx.doi.org/10.1016/j.bpa.2005.01.001] [PMID: 16013697]

[79] Boonmak P, Boonmak S, Pattanittum P. High initial concentration *versus* low initial concentration sevoflurane for inhalational induction of anaesthesia. Cochrane Database Syst Rev 2012; (9): CD006837.
[PMID: 22972100]

[80] Bai W, Voepel-Lewis T, Malviya S. Hemodynamic changes in children with Down syndrome during and following inhalation induction of anesthesia with sevoflurane. J Clin Anesth 2010; 22(8): 592-7. [http://dx.doi.org/10.1016/j.jclinane.2010.05.002] [PMID: 21109130]

[81] Holm-Knudsen RJ, Rasmussen LS. Paediatric airway management: basic aspects. Acta Anaesthesiol Scand 2009; 53(1): 1-9. [http://dx.doi.org/10.1111/j.1399-6576.2008.01794.x] [PMID: 19128325]

[82] Klučka J, Štourač P, Štoudek R, Ťoukálková M, Harazim H, Kosinová M. Controversies in Pediatric Perioperative Airways. BioMed Res Int 2015; 2015: 368761. [http://dx.doi.org/10.1155/2015/368761] [PMID: 26759809]

[83] Schmidt AR, Weiss M, Engelhardt T. The paediatric airway: basic principles and current developments. Eur J Anaesthesiol 2014; 31(6): 293-9. [http://dx.doi.org/10.1097/EJA.0000000000000023] [PMID: 24247412]

[84] Neuhaus D, Schmitz A, Gerber A, Weiss M. Controlled rapid sequence induction and intubation - an analysis of 1001 children. Paediatr Anaesth 2013; 23(8): 734-40. [http://dx.doi.org/10.1111/pan.12213] [PMID: 23763293]

[85] Rawicz M, Brandom BW, Wolf A. The place of suxamethonium in pediatric anesthesia. Paediatr Anaesth 2009; 19(6): 561-70. [http://dx.doi.org/10.1111/j.1460-9592.2009.03032.x] [PMID: 19645973]

[86] Neumann RP, von Ungern-Sternberg BS. The neonatal lung--physiology and ventilation. Paediatr Anaesth 2014; 24(1): 10-21. [http://dx.doi.org/10.1111/pan.12280] [PMID: 24152199]

[87] Tobias JD. Pediatric airway anatomy may not be what we thought: implications for clinical practice and the use of cuffed endotracheal tubes. Paediatr Anaesth 2015; 25(1): 9-19. [http://dx.doi.org/10.1111/pan.12528] [PMID: 25243638]

[88] Murat I, Constant I, Maud'huy H. Perioperative anaesthetic morbidity in children: a database of 24,165 anaesthetics over a 30-month period. Paediatr Anaesth 2004; 14(2): 158-66. [http://dx.doi.org/10.1111/j.1460-9592.2004.01167.x] [PMID: 14962332]

[89] Weiss M, Engelhardt T. Proposal for the management of the unexpected difficult pediatric airway. Paediatr Anaesth 2010; 20(5): 454-64. [http://dx.doi.org/10.1111/j.1460-9592.2010.03284.x] [PMID: 20337959]

[90] Fiadjoe JE, Nishisaki A, Jagannathan N, *et al.* Airway management complications in children with difficult tracheal intubation from the Pediatric Difficult Intubation (PeDI) registry: a prospective cohort analysis. Lancet Respir Med 2016; 4(1): 37-48. [http://dx.doi.org/10.1016/S2213-2600(15)00508-1] [PMID: 26705976]

[91] Society DA. Paediatric Difficult Airway Guidelines das.uk.com/guidelines/paediatric-difficult-airway-guidelines

[92] Bhananker SM, Ramamoorthy C, Geiduschek JM, *et al.* Anesthesia-related cardiac arrest in children: update from the Pediatric Perioperative Cardiac Arrest Registry. Anesth Analg 2007; 105(2): 344-50. [http://dx.doi.org/10.1213/01.ane.0000268712.00756.dd] [PMID: 17646488]

[93] Alalami AA, Ayoub CM, Baraka AS. Laryngospasm: review of different prevention and treatment modalities. Paediatr Anaesth 2008; 18(4): 281-8. [http://dx.doi.org/10.1111/j.1460-9592.2008.02448.x] [PMID: 18315632]

[94] Burgoyne LL, Anghelescu DL. Intervention steps for treating laryngospasm in pediatric patients. Paediatr Anaesth 2008; 18(4): 297-302. [http://dx.doi.org/10.1111/j.1460-9592.2008.02445.x] [PMID: 18315634]

[95] Ortiz AC, Atallah AN, Matos D, da Silva EMK. Intravenous *versus* inhalational anaesthesia for paediatric outpatient surgery. Cochrane Database Syst Rev 2014; (2): CD009015.

[PMID: 24510622]

[96] Gallagher TM, Black GW. Uptake of volatile anaesthetics in children. Anaesthesia 1985; 40(11): 1073-7.
[http://dx.doi.org/10.1111/j.1365-2044.1985.tb10604.x] [PMID: 4073423]

[97] Taylor RH, Lerman J. Minimum alveolar concentration of desflurane and hemodynamic responses in neonates, infants, and children. Anesthesiology 1991; 75(6): 975-9.
[http://dx.doi.org/10.1097/00000542-199112000-00008] [PMID: 1741518]

[98] Cameron CB, Robinson S, Gregory GA. The minimum anesthetic concentration of isoflurane in children. Anesth Analg 1984; 63(4): 418-20.
[http://dx.doi.org/10.1213/00000539-198404000-00007] [PMID: 6703367]

[99] Lerman J, Sikich N, Kleinman S, Yentis S. The pharmacology of sevoflurane in infants and children. Anesthesiology 1994; 80(4): 814-24.
[http://dx.doi.org/10.1097/00000542-199404000-00014] [PMID: 8024136]

[100] LeDez KM, Lerman J. The minimum alveolar concentration (MAC) of isoflurane in preterm neonates. Anesthesiology 1987; 67(3): 301-7.
[http://dx.doi.org/10.1097/00000542-198709000-00004] [PMID: 3631603]

[101] Allegaert K, de Hoon J, Verbesselt R, Naulaers G, Murat I. Maturational pharmacokinetics of single intravenous bolus of propofol. Paediatr Anaesth 2007; 17(11): 1028-34.
[http://dx.doi.org/10.1111/j.1460-9592.2007.02285.x] [PMID: 17897267]

[102] McFarlan CS, Anderson BJ, Short TG. The use of propofol infusions in paediatric anaesthesia: a practical guide. Paediatr Anaesth 1999; 9(3): 209-16.
[PMID: 10320599]

[103] Neuromuscular blocking drugs in infants and children. Contin Educ Anaesth Crit Care Pain 2007; 7(5): 143-7.
[http://dx.doi.org/10.1093/bjaceaccp/mkm032]

[104] Meretoja OA. Neuromuscular block and current treatment strategies for its reversal in children. Paediatr Anaesth 2010; 20(7): 591-604.
[http://dx.doi.org/10.1111/j.1460-9592.2010.03335.x] [PMID: 20642658]

[105] Mason LJ, Betts EK. Leg lift and maximum inspiratory force, clinical signs of neuromuscular blockade reversal in neonates and infants. Anesthesiology 1980; 52(5): 441-2.
[http://dx.doi.org/10.1097/00000542-198005000-00015] [PMID: 6990835]

[106] Infants TFOPI. The assessment and management of acute pain in infants, children, and adolescents. Pediatrics 2001; 108(3): 793-7.
[http://dx.doi.org/10.1542/peds.108.3.793] [PMID: 11533354]

[107] Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. Anesthesiology 2012; 116(2): 248-73.
[http://dx.doi.org/10.1097/ALN.0b013e31823c1030] [PMID: 22227789]

[108] Russell P, von Ungern-Sternberg BS, Schug SA. Perioperative analgesia in pediatric surgery. Curr Opin Anaesthesiol 2013; 26(4): 420-7.
[http://dx.doi.org/10.1097/ACO.0b013e3283625cc8] [PMID: 23756911]

[109] Malviya S, Polaner DM, Berde C. Acute Pain. A Practice of Anesthesia for Infants and Children. 4th ed. 2008. pp. 939–978.

[110] Chidambaran V, Sadhasivam S. Pediatric acute and surgical pain management: recent advances and future perspectives. Int Anesthesiol Clin 2012; 50(4): 66-82.
[http://dx.doi.org/10.1097/AIA.0b013e31826f3284] [PMID: 23047447]

[111] Lönnqvist P-A, Morton NS. Postoperative analgesia in infants and children. Br J Anaesth 2005; 95(1):

59-68.
[http://dx.doi.org/10.1093/bja/aei065] [PMID: 15668207]

[112] Maitra S, Baidya DK, Khanna P, Ray BR, Panda SS, Bajpai M. Acute perioperative pain in neonates: An evidence-based review of neurophysiology and management. Acta Anaesthesiol Taiwan 2014; 52(1): 30-7.
[http://dx.doi.org/10.1016/j.aat.2014.02.004] [PMID: 24999216]

[113] Dahmani S, Michelet D, Abback P-S, *et al.* Ketamine for perioperative pain management in children: a meta-analysis of published studies. Paediatr Anaesth 2011; 21(6): 636-52.
[http://dx.doi.org/10.1111/j.1460-9592.2011.03566.x] [PMID: 21447047]

[114] Schnabel A, Reichl SU, Poepping DM, Kranke P, Pogatzki-Zahn EM, Zahn PK. Efficacy and safety of intraoperative dexmedetomidine for acute postoperative pain in children: a meta-analysis of randomized controlled trials. Paediatr Anaesth 2013; 23(2): 170-9.
[http://dx.doi.org/10.1111/pan.12030] [PMID: 23043461]

[115] Schultz-Machata A-M, Weiss M, Becke K. What's new in pediatric acute pain therapy? Curr Opin Anaesthesiol 2014; 27(3): 316-22.
[http://dx.doi.org/10.1097/ACO.0000000000000074] [PMID: 24709667]

[116] Polaner DM, Suresh S, Cote CJ. Regional Anesthesia. A Practice of Anesthesia for Infants and Children. 4th ed. 2008. pp. 867–884.

[117] Ivani G, Suresh S, Ecoffey C, *et al.* The European Society of Regional Anaesthesia and Pain Therapy and the American Society of Regional Anesthesia and Pain Medicine Joint Committee Practice Advisory on Controversial Topics in Pediatric Regional Anesthesia. Reg Anesth Pain Med 2015; 40(5): 526-32.
[http://dx.doi.org/10.1097/AAP.0000000000000280] [PMID: 26192549]

[118] Taenzer AH, Walker BJ, Bosenberg AT, *et al.* Asleep *versus* awake: does it matter?: Pediatric regional block complications by patient state: a report from the Pediatric Regional Anesthesia Network. Reg Anesth Pain Med 2014; 39(4): 279-83.
[http://dx.doi.org/10.1097/AAP.0000000000000102] [PMID: 24918334]

[119] Marhofer P, Ivani G, Suresh S, Melman E, Zaragoza G, Bosenberg A. Everyday regional anesthesia in children. Paediatr Anaesth 2012; 22(10): 995-1001.
[http://dx.doi.org/10.1111/pan.12003] [PMID: 22967158]

[120] Polaner DM, Taenzer AH, Walker BJ, *et al.* Pediatric Regional Anesthesia Network (PRAN): a multi-institutional study of the use and incidence of complications of pediatric regional anesthesia. Anesth Analg 2012; 115(6): 1353-64.
[http://dx.doi.org/10.1213/ANE.0b013e31825d9f4b] [PMID: 22696610]

[121] McClain CD, McManus ML. Fluid Management. A Practice of Anesthesia for Infants and Children. 4th ed. 2008. pp. 159–175.

[122] Pierro A, Eaton S. Metabolism and nutrition in the surgical neonate. Semin Pediatr Surg 2008; 17(4): 276-84.
[http://dx.doi.org/10.1053/j.sempedsurg.2008.07.006] [PMID: 19019296]

[123] Berleur M-P, Dahan A, Murat I, Hazebroucq G. Perioperative infusions in paediatric patients: rationale for using Ringer-lactate solution with low dextrose concentration. J Clin Pharm Ther 2003; 28(1): 31-40.
[http://dx.doi.org/10.1046/j.1365-2710.2003.00456.x] [PMID: 12605616]

[124] Lindahl SG. Energy expenditure and fluid and electrolyte requirements in anesthetized infants and children. Anesthesiology 1988; 69(3): 377-82.
[http://dx.doi.org/10.1097/00000542-198809000-00015] [PMID: 3415017]

[125] Gouyet L, Dubois MC, Murat I. Blood glucose and insulin levels during epidural anaesthesia in children receiving dextrose-free solutions. Paediatr Anaesth 1994; 4: 307-11.

[http://dx.doi.org/10.1111/j.1460-9592.1994.tb00393.x]

[126] Murat I, Dubois M-C. Perioperative fluid therapy in pediatrics. Paediatr Anaesth 2008; 18(5): 363-70. [http://dx.doi.org/10.1111/j.1460-9592.2008.02505.x] [PMID: 18312509]

[127] Paut O, Lacroix F. Recent developments in the perioperative fluid management for the paediatric patient. Curr Opin Anaesthesiol 2006; 19(3): 268-77. [http://dx.doi.org/10.1097/01.aco.0000192818.68730.9d] [PMID: 16735810]

[128] Larsson LE, Nilsson K, Niklasson A, Andreasson S, Ekström-Jodal B. Influence of fluid regimens on perioperative blood-glucose concentrations in neonates. Br J Anaesth 1990; 64(4): 419-24. [http://dx.doi.org/10.1093/bja/64.4.419] [PMID: 2334614]

[129] Holliday MA, Segar WE. The maintenance need for water in parenteral fluid therapy. Pediatrics 1957; 19(5): 823-32. [PMID: 13431307]

[130] Leelanukrom R, Cunliffe M. Intraoperative fluid and glucose management in children. Paediatr Anaesth 2000; 10(4): 353-9. [http://dx.doi.org/10.1046/j.1460-9592.2000.00536.x] [PMID: 10886690]

[131] Patel RI, Hannallah RS, Norden J, Casey WF, Verghese ST. Emergence airway complications in children: a comparison of tracheal extubation in awake and deeply anesthetized patients. Anesth Analg 1991; 73(3): 266-70. [http://dx.doi.org/10.1213/00000539-199109000-00006] [PMID: 1867418]

[132] von Ungern-Sternberg BS, Davies K, Hegarty M, Erb TO, Habre W. The effect of deep *vs*. awake extubation on respiratory complications in high-risk children undergoing adenotonsillectomy: a randomised controlled trial. Eur J Anaesthesiol 2013; 30(9): 529-36. [http://dx.doi.org/10.1097/EJA.0b013e32835df608] [PMID: 23344124]

[133] Baijal RG, Bidani SA, Minard CG, Watcha MF. Perioperative respiratory complications following awake and deep extubation in children undergoing adenotonsillectomy. Paediatr Anaesth 2015; 25(4): 392-9. [http://dx.doi.org/10.1111/pan.12561] [PMID: 25370474]

[134] Mathew PJ, Mathew JL. Early *versus* late removal of the laryngeal mask airway (LMA) for general anaesthesia. Cochrane Database Syst Rev 2015; (8): CD007082. [PMID: 26258959]

[135] Wallace IF, Berkman ND, Lohr KN, Harrison MF, Kimple AJ, Steiner MJ. Surgical treatments for otitis media with effusion: a systematic review. Pediatrics 2014; 133(2): 296-311. [http://dx.doi.org/10.1542/peds.2013-3228] [PMID: 24394689]

[136] Finkel JC, Cohen IT, Hannallah RS, *et al.* The effect of intranasal fentanyl on the emergence characteristics after sevoflurane anesthesia in children undergoing surgery for bilateral myringotomy tube placement. Anesth Analg 2001; 92(5): 1164-8. [http://dx.doi.org/10.1097/00000539-200105000-00016] [PMID: 11323340]

[137] Phillips ML, Willis BC, Broman AJ, Lam HV, Nguyen TT, Austin TM. Bimodal analgesia *vs*. fentanyl in pediatric patients undergoing bilateral myringotomy and tympanostomy tube placement: a propensity matched cohort study. J Clin Anesth 2016; 32: 162-8. [http://dx.doi.org/10.1016/j.jclinane.2016.03.003] [PMID: 27290968]

[138] Dewhirst E, Fedel G, Raman V, *et al.* Pain management following myringotomy and tube placement: intranasal dexmedetomidine *versus* intranasal fentanyl. Int J Pediatr Otorhinolaryngol 2014; 78(7): 1090-4. [http://dx.doi.org/10.1016/j.ijporl.2014.04.014] [PMID: 24814231]

[139] Pestieau SR, Quezado ZMN, Johnson YJ, *et al.* The effect of dexmedetomidine during myringotomy and pressure-equalizing tube placement in children. Paediatr Anaesth 2011; 21(11): 1128-35. [http://dx.doi.org/10.1111/j.1460-9592.2011.03615.x] [PMID: 21575102]

[140] Hippard HK, Govindan K, Friedman EM, *et al.* Postoperative analgesic and behavioral effects of intranasal fentanyl, intravenous morphine, and intramuscular morphine in pediatric patients undergoing bilateral myringotomy and placement of ventilating tubes. Anesth Analg 2012; 115(2): 356-63.
[http://dx.doi.org/10.1213/ANE.0b013e31825afef3] [PMID: 22669347]

[141] Subramanyam R, Varughese A, Willging JP, Sadhasivam S. Future of pediatric tonsillectomy and perioperative outcomes. Int J Pediatr Otorhinolaryngol 2013; 77(2): 194-9.
[http://dx.doi.org/10.1016/j.ijporl.2012.10.016] [PMID: 23159321]

[142] Lerman J. A disquisition on sleep-disordered breathing in children. Paediatr Anaesth 2009; 19 (Suppl. 1): 100-8.
[http://dx.doi.org/10.1111/j.1460-9592.2009.03011.x] [PMID: 19572849]

[143] Tait AR, Bickham R, O'Brien LM, Quinlan M, Voepel-Lewis T. The STBUR questionnaire for identifying children at risk for sleep-disordered breathing and postoperative opioid-related adverse events. Paediatr Anaesth 2016; 26(7): 759-66.
[http://dx.doi.org/10.1111/pan.12934] [PMID: 27219118]

[144] Sanders JC, King MA, Mitchell RB, Kelly JP. Perioperative complications of adenotonsillectomy in children with obstructive sleep apnea syndrome. Anesth Analg 2006; 103(5): 1115-21.
[http://dx.doi.org/10.1213/01.ane.0000244318.77377.67] [PMID: 17056942]

[145] Batra YK, Ivanova M, Ali SS, Shamsah M, Al Qattan AR, Belani KG. The efficacy of a subhypnotic dose of propofol in preventing laryngospasm following tonsillectomy and adenoidectomy in children. Paediatr Anaesth 2005; 15(12): 1094-7.
[PMID: 16324030]

[146] Mihara T, Uchimoto K, Morita S, Goto T. The efficacy of lidocaine to prevent laryngospasm in children: a systematic review and meta-analysis. Anaesthesia 2014; 69(12): 1388-96.
[http://dx.doi.org/10.1111/anae.12788] [PMID: 24992191]

[147] Lalwani K, Richins S, Aliason I, Milczuk H, Fu R. The laryngeal mask airway for pediatric adenotonsillectomy: predictors of failure and complications. Int J Pediatr Otorhinolaryngol 2013; 77(1): 25-8.
[http://dx.doi.org/10.1016/j.ijporl.2012.09.021] [PMID: 23063385]

[148] Sierpina DI, Chaudhary H, Walner DL, *et al.* Laryngeal mask airway *versus* endotracheal tube in pediatric adenotonsillectomy. Laryngoscope 2012; 122(2): 429-35.
[http://dx.doi.org/10.1002/lary.22458] [PMID: 22252780]

[149] Goldstein NA. Evaluation and Management of Pediatric Obstructive Sleep Apnea.Cummings Otolaryngology – Head and Neck Surgery. 6th ed., Philadelphia: Elsevier, Inc 2015.

[150] Hollis LJ, Burton MJ, Millar JM. Perioperative local anaesthesia for reducing pain following tonsillectomy. Cochrane Database Syst Rev 2000; (2): CD001874.
[PMID: 10796831]

[151] Møiniche S, Rømsing J, Dahl JB, Tramèr MR. Nonsteroidal antiinflammatory drugs and the risk of operative site bleeding after tonsillectomy: a quantitative systematic review. Anesth Analg 2003; 96(1): 68-77.
[http://dx.doi.org/10.1213/00000539-200301000-00015] [PMID: 12505926]

[152] Lewis SR, Nicholson A, Cardwell ME, Siviter G, Smith AF. Nonsteroidal anti-inflammatory drugs and perioperative bleeding in paediatric tonsillectomy. Cochrane Database Syst Rev 2013; (7): CD003591.
[PMID: 23881651]

[153] Brown KA, Laferrière A, Lakheeram I, Moss IR. Recurrent hypoxemia in children is associated with increased analgesic sensitivity to opiates. Anesthesiology 2006; 105(4): 665-9.
[http://dx.doi.org/10.1097/00000542-200610000-00009] [PMID: 17006062]

[154] Bolton CM, Myles PS, Nolan T, Sterne JA. Prophylaxis of postoperative vomiting in children undergoing tonsillectomy: a systematic review and meta-analysis. Br J Anaesth 2006; 97(5): 593-604. [http://dx.doi.org/10.1093/bja/ael256] [PMID: 17005507]

[155] Elhakim M, Ali NM, Rashed I, Riad MK, Refat M. Dexamethasone reduces postoperative vomiting and pain after pediatric tonsillectomy. Can J Anaesth 2003; 50(4): 392-7. [http://dx.doi.org/10.1007/BF03021038] [PMID: 12670818]

[156] Fields RG, Gencorelli FJ, Litman RS. Anesthetic management of the pediatric bleeding tonsil. Paediatr Anaesth 2010; 20(11): 982-6. [http://dx.doi.org/10.1111/j.1460-9592.2010.03426.x] [PMID: 20964765]

[157] Collins CE. Anesthesia for pediatric airway surgery: recommendations and review from a pediatric referral center. Anesthesiol Clin 2010; 28(3): 505-17. [http://dx.doi.org/10.1016/j.anclin.2010.07.008] [PMID: 20850081]

[158] Kramer RE, Lerner DG, Lin T, *et al.* Management of ingested foreign bodies in children: a clinical report of the NASPGHAN Endoscopy Committee. J Pediatr Gastroenterol Nutr 2015; 60(4): 562-74. [http://dx.doi.org/10.1097/MPG.0000000000000729] [PMID: 25611037]

[159] Zur KB, Litman RS. Pediatric airway foreign body retrieval: surgical and anesthetic perspectives. Paediatr Anaesth 2009; 19 (Suppl. 1): 109-17. [http://dx.doi.org/10.1111/j.1460-9592.2009.03006.x] [PMID: 19572850]

[160] Liu Y, Chen L, Li S. Controlled ventilation or spontaneous respiration in anesthesia for tracheobronchial foreign body removal: a meta-analysis. Paediatr Anaesth 2014; 24(10): 1023-30. [http://dx.doi.org/10.1111/pan.12469] [PMID: 24975102]

[161] Chai J, Wu X-Y, Han N, Wang L-Y, Chen W-M. A retrospective study of anesthesia during rigid bronchoscopy for airway foreign body removal in children: propofol and sevoflurane with spontaneous ventilation. Paediatr Anaesth 2014; 24(10): 1031-6. [http://dx.doi.org/10.1111/pan.12509] [PMID: 25145573]

[162] Palmer LS, Palmer JS. Management of Abnormalities of the External Genitalia in Boys.Wein AJ, Kavoussi LR, Partin AW, Peters CA, Peters. 11th ed., Philadelphia: Elsevier, Inc 2016.

[163] Snodgrass WT, Bush NC. Hypospadias.Campbell-Walsh Urology. 11th ed., Philadelphia: Elsevier, Inc 2016.

[164] Barthold JS, Hagerty JA. Diagnosis and Management of the Undescended Testis. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. Campbell-Walsh Urology. 11th ed. Phildalephia: Elsevier, Inc; 2016.

[165] Verghese ST, Hannallah RS, Rice LJ, Belman AB, Patel KM. Caudal anesthesia in children: effect of volume *versus* concentration of bupivacaine on blocking spermatic cord traction response during orchidopexy. Anesth Analg 2002; 95(5): 1219-23. [http://dx.doi.org/10.1097/00000539-200211000-00019] [PMID: 12401597]

[166] Londergan TA, Hochman HI, Goldberger N. Postoperative pain following outpatient pediatric urologic surgery: a comparison of anesthetic techniques. Urology 1994; 44(4): 572-6. [http://dx.doi.org/10.1016/S0090-4295(94)80062-6] [PMID: 7941199]

[167] Cyna AM, Middleton P. Caudal epidural block *versus* other methods of postoperative pain relief for circumcision in boys. Cochrane Database Syst Rev 2008; (4): CD003005. [PMID: 18843636]

[168] Silvani P, Camporesi A, Agostino MR, Salvo I. Caudal anesthesia in pediatrics: an update. Minerva Anestesiol 2006; 72(6): 453-9. [PMID: 16682915]

[169] Martindale M, Worsley M. Caudal additives in children-solutions or problems? Br J Anaesth 2003; 91(2): 300-1.

[http://dx.doi.org/10.1093/bja/aeg598] [PMID: 12878639]

[170] Apfelbaum JL, Silverstein JH, Chung FF, Connis RT, Fillmore RB, Hunt SE. Practice Guidelines for Postanesthetic Care: An Updated Report by the American Society of Anesthesiologists Task Force on Postanesthetic Care. 18(2):291–307.

[171] Hackel A, Badgwell JM, Binding RR, *et al.* Guidelines for the pediatric perioperative anesthesia environment. American Academy of Pediatrics. Section on Anesthesiology. Pediatrics 1999; 103(2): 512-5.
[http://dx.doi.org/10.1542/peds.103.2.512] [PMID: 9925855]

[172] Taenzer A, Cravero J. The Postanesthesia Care Unit and Beyond. A Practice of Anesthesia for Infants and Children. 4th ed. 2008. pp. 1009–1021.

[173] Aldrete JA. The post-anesthesia recovery score revisited. J Clin Anesth 1995; 7(1): 89-91.
[http://dx.doi.org/10.1016/0952-8180(94)00001-K] [PMID: 7772368]

[174] Aldrete JA, Kroulik D. A postanesthetic recovery score. Anesth Analg 1970; 49(6): 924-34.
[http://dx.doi.org/10.1213/00000539-197011000-00020] [PMID: 5534693]

[175] White PF, Song D. New criteria for fast-tracking after outpatient anesthesia: a comparison with the modified Aldrete's scoring system. Anesth Analg 1999; 88(5): 1069-72.
[PMID: 10320170]

[176] Moncel JB, Nardi N, Wodey E, Pouvreau A, Ecoffey C. Evaluation of the pediatric post anesthesia discharge scoring system in an ambulatory surgery unit. Paediatr Anaesth 2015; 25(6): 636-41.
[http://dx.doi.org/10.1111/pan.12612] [PMID: 25581378]

[177] Awad IT, Moore M, Rushe C, Elburki A, O'Brien K, Warde D. Unplanned hospital admission in children undergoing day-case surgery. Eur J Anaesthesiol 2004; 21(5): 379-83.
[http://dx.doi.org/10.1097/00003643-200405000-00005] [PMID: 15141796]

[178] Blacoe DA, Cunning E, Bell G. Paediatric day-case surgery: an audit of unplanned hospital admission Royal Hospital for Sick Children, Glasgow. Anaesthesia 2008; 63(6): 610-5.
[http://dx.doi.org/10.1111/j.1365-2044.2008.05438.x] [PMID: 18477272]

[179] da Silva PSL, de Aguiar VE, Fonseca MCM. Risk factors and outcomes of unplanned PICU postoperative admissions: a nested case-control study. Pediatr Crit Care Med 2013; 14(4): 420-8.
[http://dx.doi.org/10.1097/PCC.0b013e3182720fab] [PMID: 23439460]

[180] Gibson AR, Limb J, Bell G. Retrospective audit of unplanned admissions to pediatric high dependency and intensive care after surgery. Paediatr Anaesth 2014; 24(4): 372-6.
[http://dx.doi.org/10.1111/pan.12343] [PMID: 24417703]

[181] Kurowski I, Sims C. Unplanned anesthesia-related admissions to pediatric intensive care - a 6-year audit. Paediatr Anaesth 2007; 17(6): 575-80.
[http://dx.doi.org/10.1111/j.1460-9592.2006.02154.x] [PMID: 17498021]

[182] Barry N, M Miller K, Ryshen G, Uffman J, Taghon TA, Tobias JD. Etiology of postanesthetic and postsedation events on the inpatient ward: data from a rapid response team at a tertiary care children's hospital. Paediatr Anaesth 2016; 26(5): 504-11.
[http://dx.doi.org/10.1111/pan.12874] [PMID: 26972832]

[183] von Ungern-Sternberg BS, Boda K, Chambers NA, *et al.* Risk assessment for respiratory complications in paediatric anaesthesia: a prospective cohort study. Lancet 2010; 376(9743): 773-83.
[http://dx.doi.org/10.1016/S0140-6736(10)61193-2] [PMID: 20816545]

[184] von Ungern-Sternberg BS. Respiratory complications in the pediatric postanesthesia care unit. Anesthesiol Clin 2014; 32(1): 45-61.
[http://dx.doi.org/10.1016/j.anclin.2013.10.004] [PMID: 24491649]

[185] Mamie C, Habre W, Delhumeau C, Argiroffo CB, Morabia A. Incidence and risk factors of perioperative respiratory adverse events in children undergoing elective surgery. Paediatr Anaesth

2004; 14(3): 218-24.
[http://dx.doi.org/10.1111/j.1460-9592.2004.01169.x] [PMID: 14996260]

[186] Koka BV, Jeon IS, Andre JM, MacKay I, Smith RM. Postintubation croup in children. Anesth Analg 1977; 56(4): 501-5.
[http://dx.doi.org/10.1213/00000539-197707000-00008] [PMID: 560135]

[187] Voepel-Lewis T, Malviya S, Tait AR. A prospective cohort study of emergence agitation in the pediatric postanesthesia care unit. Anesth Analg 2003; 96(6): 1625-30.
[http://dx.doi.org/10.1213/01.ANE.0000062522.21048.61] [PMID: 12760985]

[188] Banchs RJ, Lerman J. Preoperative anxiety management, emergence delirium, and postoperative behavior. Anesthesiol Clin 2014; 32(1): 1-23.
[http://dx.doi.org/10.1016/j.anclin.2013.10.011] [PMID: 24491647]

[189] Sikich N, Lerman J. Development and psychometric evaluation of the pediatric anesthesia emergence delirium scale. Anesthesiology 2004; 100(5): 1138-45.
[http://dx.doi.org/10.1097/00000542-200405000-00015] [PMID: 15114210]

[190] Dahmani S, Delivet H, Hilly J. Emergence delirium in children: an update. Curr Opin Anaesthesiol 2014; 27(3): 309-15.
[http://dx.doi.org/10.1097/ACO.0000000000000076] [PMID: 24784918]

[191] Kain ZN, Caldwell-Andrews AA, Maranets I, *et al.* Preoperative anxiety and emergence delirium and postoperative maladaptive behaviors. Anesth Analg 2004; 99(6): 1648-54.
[http://dx.doi.org/10.1213/01.ANE.0000136471.36680.97] [PMID: 15562048]

[192] Dahmani S, Stany I, Brasher C, *et al.* Pharmacological prevention of sevoflurane- and desflurane-related emergence agitation in children: a meta-analysis of published studies. Br J Anaesth 2010; 104(2): 216-23.
[http://dx.doi.org/10.1093/bja/aep376] [PMID: 20047899]

[193] Höhne C. Postoperative nausea and vomiting in pediatric anesthesia. Curr Opin Anaesthesiol 2014; 27(3): 303-8.
[http://dx.doi.org/10.1097/ACO.0000000000000073] [PMID: 24722005]

[194] Gan TJ, Diemunsch P, Habib AS, *et al.* Consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2014; 118(1): 85-113.
[http://dx.doi.org/10.1213/ANE.0000000000000002] [PMID: 24356162]

[195] Eberhart LHJ, Geldner G, Kranke P, *et al.* The development and validation of a risk score to predict the probability of postoperative vomiting in pediatric patients. Anesth Analg 2004; 99(6): 1630-7.
[http://dx.doi.org/10.1213/01.ANE.0000135639.57715.6C] [PMID: 15562045]

[196] Bourdaud N, Devys J-M, Bientz J, *et al.* Development and validation of a risk score to predict the probability of postoperative vomiting in pediatric patients: the VPOP score. Paediatr Anaesth 2014; 24(9): 945-52.
[http://dx.doi.org/10.1111/pan.12428] [PMID: 24823626]

CHAPTER 9

Pediatric Trauma

Dheeraj Goswami and **R. Blaine Easley***

Baylor College of Medicine/Texas Children's Hospital, Houston, Texas, USA

Abstract: Trauma is the leading cause of death between ages 1-44. The "Golden Hour" represents the need for quick, accurate, and efficient response which can lead to the improved morbidity and mortality. Even in the community hospital setting, practitioners should be current in BLS, ACLS and PALS. Common categories of injury are traumatic brain injury, and penetrating injuries. After the primary survey, stabilization, and secondary survey; prompt decisions should be made for the need to transfer the pediatric patient to a pediatric hospital and trauma center or to maintain care in the community hospital setting.

Keywords: Blunt force injury, Pediatric trauma, Penetrating injury, Primary survey, Secondary survey, Traumatic brain injury.

INTRODUCTION

Trauma is the leading cause of death from the age of 1 through 44 [1]. The "golden hour" has been discussed in both pediatrics and adult literature as a quick and efficient response to severe injury that can lead to improved mortality and morbidity [2, 3]. The role of the anesthesiologist can vary during this time period and can include intubation and resuscitation both in the emergency and operating rooms. Many of these patients are initially treated at community hospitals where the capabilities and resources of each hospital can further influence patient management during this critical period. Therefore, the community anesthesiologist must utilize good clinical judgment and excellent situational awareness to promote an optimal patient outcome.

A quick assessment of stability in a patient is important, regardless of cause and type of injury. The assessment includes taking a quick history, evaluating the injury, and monitoring the patient's vital signs. If the patient is stable, a thorough evaluation can occur before a disposition is made.

* **Corresponding author R. Blaine Easley:** Baylor College of Medicine/Texas Children's Hospital, Houston, Texas, USA; Tel: 832-876-5471; Fax: 832-875-1903; E-mail: rbeasley@texaschildrens.org

Amballur D. John (Ed.)

The disposition could include transfer to a center that has a higher level of care or to the operating room for surgery. Occasionally, further imaging or tests may be warranted to assist in deciding the best location for the patient. Finally, though the patient may be suitably cared for pre- and intraoperatively in the community setting, recognition of the need for additional resources and/or limitation of the current environment to provide ongoing care is important. Optimally, a plan for transition of trauma or unstable patients to a tertiary-care facility is already in place. However, prior to transfer/transport, the acute trauma patient presenting to the community hospital will require quick and thoughtful management for the best interest of the patient.

An unstable trauma patient requires both a quick assessment and treatment. BLS, ACLS, and PALS have been shown to improve mortality in patients treated in an in-hospital setting [4, 5]. However, there are multiple studies that show that many providers are either not certified or do not have an adequate understanding of the material [6, 7]. An important first step in preparation for these emergencies is to establish a criteria that the community anesthesiologist not only be familiar with up-to-date guidelines in emergency patient care, but establishing and maintaining current certification in BLS, ACLS, and potentially PALS, if their patient population includes children. This will help insure familiarity with changing recommendations and guidelines on managing patients in cardiac and respiratory arrest.

While a trauma patient may be unstable, but does not require an ACLS or PALS algorithm, the principles of management and communication can be utilized. Implicit to an "emergency situation" the management of a trauma patient in the community setting has no specific guidelines or algorithms to help a practitioner. Simultaneous with the primary trauma assessment, if blood products are available, then a type and screen should be obtained immediately as type-specific blood is safest and a plan for secondary labs established. The secondary labs (*i.e*. complete blood count, basic electrolyte panel, coagulation profile, *etc*.) can vary, depending on the cause and type of injury as well as the resources of the facility. Multiple imaging modalities are utilized in trauma assessment and care. From focused assessment with sonography, to plain radiographs to evaluate fractures and line positions, and potential thoracic injuries, imaging is an important aspect of the "secondary" assessment of the trauma patient. FAST (focused assessment with sonography in trauma) ultrasound has even become part of the primary evaluation in abdominal trauma [8]. Computed tomography (CT) may be required for further evaluation or injuries in other parts of the body.

PRIMARY ASSESSMENT CONSIDERATIONS

Airway Evaluation for difficulty, equipment including adjunctives, Difficult airway algorithm.

Access Large bore access, central and arterial line consideration, I/O if access unable to be immediately obtained

Labs T&S, CBC, coagulation panels, electrolytes

Imaging Plain films, neck films, FAST (Ultrasound) CT, MRI

An unstable patient can test the capabilities of a community hospital. They may be too unstable to transfer leading to surgeries and therapies not commonly performed at the institution. Unstable patients can also stress the critical judgment of physicians regarding the timing and need for transfer to a larger institution. The specific type of injury is a key component in this decision making process.

HEAD TRAUMA

The majority of head injuries are minor and rarely require medical treatment. However, severe head injury is a cause of long-term morbidity and contributes to 30% of all deaths related to injury [9]. The physiology in head trauma can be separated into the primary injury occurring immediately after the trauma and secondary injury occurring with cellular death, swelling, and the release of neurochemicals. Minimizing secondary injury is must be a goal of all anesthesiologists. Therefore, it is important to have an understanding of the severity of the head injury.

The Glascow Coma Scale (GCS) was created in 1974 as an assessment tool for patients suffering from head injuries [10]. The GCS is a scoring scale of three systems, eyes, verbal and motor response. A score of 14-15 is normal while a scale of 3 is comatose. Consensus statements consider intubation to be necessary at a GCS of 8 or lower (Table **1**) [11].

Given the potential complexity of trauma patient airway, management should take into consideration the most experienced personnel, and often includes having available anesthesiologist and surgeons to participate in the intubation. First, intubation in the emergency setting can be more difficult, and failure rates have been reported to be as high as 1:100 [12]. Facial and neck trauma are often seen with head trauma and may make intubation more difficult. These issues must be balanced with the risks from delays in intubation which is often the episodes of hypoxia [12]. This can complicate the overall care as single episodes of hypotension and hypoxia are associated with increases in mortality for traumatic

brain injury (TBI) [13]. Therefore, it is important to quickly assess the likelihood of a difficult airway in the patient, to have secondary and tertiary options available if intubation is unsuccessful, and to quickly recognize and treat any episodes of hypotension and hypoxia.

Table 1. Glascow Coma Scale (GCS).

Glascow Coma Scale (GCS)		
Eyes Open	Spontaneously	4
	To Voice	3
	To Pain	2
	No response	1
Verbal Response	Oriented	5
	Confused	4
	Inappropriate words	3
	Incomprehensible words	2
	No response	1
Motor Response	Obey command	6
	Localizes pain	5
Flexion to Pain	Withdrawal	4
	Abnormal	3
	Flexion	2
	No response	1
Total:		**3-15** ©2018 A.D. JOHN

Imaging may be necessary after a decision for intubation is made but before transport to the operating room. Anesthesiologists often play the role of transport personnel and primary resuscitator during this time. The decision of type of imaging will rarely be up to the anesthesia team, but there should be an understanding of the considerations and length of the imaging before one commits to a procedure that may last 1-2 hours. Magnetic resonance imaging (MRI), due to its limited availability and acquisition times, is not recommended in the acute trauma patients outside of tertiary care centers. While MRI may be useful in prognosis or less severe trauma, these images can often be obtained after stabilization in severe head trauma [14, 15]. Head CT is the most common test obtained for both mild and severe head trauma as it is easy to obtain and often takes less than 1-2 minutes [15]. It is still essential that the anesthesiologist continues closely monitoring vital signs and cognitive function during the

imaging procedure. Imaging can quickly reveal the need of surgery and may benefit the anesthesiologist by evaluating the severity and type of injury.

There are a wide number of urgent procedures that an anesthesiologist must be familiar with after a head injury. The goal during these procedures is similar to all other anesthetics but is complicated by the management of cerebral perfusion pressure (CPP). CPP is defined as mean arterial pressure (MAP) – the intracranial pressure (ICP) or central venous pressure (CVP) if that happens to be higher. In a healthy adult, **CPP** is usually between 70-90 mmHg; **autoregulation**, or the ability to keep a constant flow despite changes in blood pressure, is thought to occur at a CPP of 50-150 mmHg. Though the true limits likely vary from patient to patient, it is important to attempt to remain within these limits as it may effect patient outcomes [16, 17]. The overall goal is to attempt to optimize CPP, and an anesthesiologist must be familiar with the mechanisms to both regulate the MAP and ICP. An arterial line can be placed for measurement of MAP, but many TBI patients do not have a monitor for ICP during their initial surgery.

The gold standard for ICP measurement is an invasive intracranial catheter that will measure the pressure of the brain itself. The ICP is often thought to be at least 20 mmHg in a patient without an ICP monitor who is showing signs of elevated ICP. The ICP can be reduced *via three different mechanisms: **1)** ventilation/ oxygenation, **2)** Osmotic therapies and **3)** sedation/anesthesia/temperature [18].*

Ventilation is an easy and effective means for an anesthesiologist to affect ICP. Carbon Dioxide ($CO_{2)}$ has a significant effect on cerebral vasoconstriction by altering cerebral blood flow and pressure. Hyperventilation by decreasing CO_2 increases cerebral vasoconstriction which reduces cerebral blood flow and ICP.Acutely, this may prevent an episode of cerebral herniation, but cerebral ischemia can occur at CO_2 levels below 25. Routine hyperventilation is no longer recommended, and all attempts should be made to keep CO_2 levels between 35-40. Hypoxia and hyperoxia can both lead to secondary injury and further edema. Oxygen saturations greater than 96% are preferred as are PaO_2 levels between 80 and 120 mm Hg. Oxygen delivery should be optimized while minimizing the potential side effects of transfusion with a hemoglobin goal of 8-9 [18].

For head trauma patients, IV fluid therapy can alter ICP by altering cerebral volume/edema. Normal saline (0.9%) is the maintenance fluid of choice for maintenance IV fluids. However, if available hypertonic saline and other osmotic medications such as mannitol can be used if there are concerns for an acute change in ICP. **Typical dosing** for 3% saline is 3-5 mg/kg and 0.25 mg/kg-1 mg/kg for mannitol. The most acute effect of mannitol is likely an effect on red cell rheology and viscosity rather than a true osmotic effect. Boluses can be

repeated but hypotension and intravascular volume depletion must be strictly avoided as their likelihood is increased with the use of these agents [19, 20].

Sedation and anesthesia is an immediate and readily accessible method for an anesthesiologist to improve ICP. The primary effect is reduction in the cerebral metabolic rate of oxygen (CMR02) and in the case of analgesics, the reduction of stress hormones and the sensation of pain. Many medications can be used, including all opioid analgesics, though fentanyl use is common due to its immediate effect and short half-life. Propofol is another commonly used medication and can immediately effect ICP by lowering CMRO2. The concerns with propofol are hypotension and propofol infusion syndrome with prolonged use. There is still a debate on the optimal regimen for maintenance of anesthesia in patients with elevated ICPs. There is evidence of higher CPP values with IV infusions in comparison to inhalant anesthetics, but there have yet to be any studies that show an improvement in outcome [21, 22].

Temperature management has become a performance measure for all anesthesiologists. Generally, hypothermia is avoided with the use of convection devices. Hyperthermia in the setting of TBI increases CMR02 and is associated with worse outcomes [23]. An anesthesiologist should consider the use of cooling blankets, anti-pyretics (*e.g.,* intravenous acetaminophen) and intravascular intra-compartmental devices (*e.g.,* Foley catheter/NG tube) for temperature control [24].

In summary, head trauma is a common presenting complaint to emergency departments around the country. The severity can be broad but some of these patients may need an immediate surgical intervention and stabilization. Anesthesiologists can have an important role in improving outcomes and optimizing their care.

BLUNT TRAUMA AND PENETRATING TRAUMA

Blunt trauma is a broad term defined by injury to the body without penetration. Unintentional injury is the leading cause of death in patients age 1-44 and the fourth most common cause of death in any age group [24]. Motor vehicle collisions and falls accounted for over 64,000 deaths in 2013 alone [26]. The majority of these deaths are from blunt force trauma causing significant organ injury. It is important that an anesthesiologist know the level trauma center of their institution as this will set the expectations for the facility and physicians. Regardless of center designation, there may be times where an anesthesiologist must be involved in the stabilization and care of a trauma patient. The variance in type and severity in the injuries of these patients will test the skills and knowledge of any anesthesiologist.

Penetrating trauma is similar to blunt trauma in many ways. However, severe trauma by blunt injury often requires a large amount of force while penetrating trauma can often be more benign in nature. It is defined when an object pierces the skin and causes damage to the underlying tissue. The most common type of penetrating trauma in the United States are firearm injuries, causing over 11,000 deaths a year [25]. The point of injury can often easily be seen, though the tissue injury can be much more extensive then what is visualized externally. The severity and surgical urgency depend on location of injury, and imaging is often required to elucidate the exact area and depth of injury. Thoracic penetrating traumas are the most concerning and can be associated with a significant amount of blood loss. The use of imaging and potential need for the OR are based on stability and type of injury to the patient [36].

The focus of treatment for the early period after trauma is often referred to as the "**Golden Hour**" [38]. An anesthesiologist's role during this time can vary from stabilization and transfer to management of the patient from the trauma bay to the operating room. The initial assessment of these patients is often completed in the trauma bay or in the emergency department, depending on severity. The **primary survey** is focused on the airway, breathing, circulation and any obvious injuries causing severe vital sign abnormalities. During this evaluation, depending on the hospital structure, many anesthesiologists are called to intubate the patient. Blunt injuries to the neck and face are often missed in the primary survey and can complicate airway management. Inspection and visualization of the airway may show a neck hematoma, crepitus, hoarse voice or facial fractures that are associated with a difficult intubation [12, 27]. Penetrating injuries are usually much more obvious but no less difficult in terms of securing the airway [37]. The American Society of Anesthesia difficult airway algorithm should be used, though there are a number of modifications applied in a trauma situation. The most important are that a surgical airway may be the first and best option in certain situations, awake intubations should be used if possible, and that waking up the patient and "cancelling" the procedure is usually not possible [28]. Intubation is often complicated by a highly stressful situation, hemodynamic instability and significant time constraints. It is once again important to have a secondary and tertiary plan to minimize any further injury due to a prolonged time period without ventilation or oxygenation.

The **secondary survey** is completed soon after or during the primary survey. The secondary survey should go through all body parts and better define the injuries to the patient and give valuable information for the anesthesiologist. Imaging is often required as few blunt injuries are obvious to the eye. Chest films and chest CT are the most common studies used for thoracic injuries and can delineate injuries such as pulmonary contusion, pneumothorax, great vessel injuries and rib

fractures among others [29]. Most of these non-vascular injuries will not require immediate OR intervention, but may be concomitantly found in patients requiring surgery for another injury [30]. Management of these patients can be extremely complicated as ventilation strategies for lung injures may be in direct contraindication for injures to the head or other parts of the body.

The vascular injuries can be separated in abdominal vascular injuries and thoracic vascular injuries. The thoracic aortic injuries are the most severe of these as a majority of these patients will die before being seen in the trauma bay, and the few who do will often die within the first 24 hours of admission [31]. Few hospitals in the community have the staffing to manage these patients, but many centers will participate in stabilization of a patient until transfer to a facility with resources to manage this patient. Acute management should proceed with a dual focus for the patients. First, the patients should be actively resuscitated with fluids and blood products to stabilize the patient while reducing risk for further injury or rupture to the aorta. This is achieved by control of the heart rate and blood pressure down with beta-blockers, and calcium channel blockers, among other medications. Ongoing fluid resuscitation and control of physiologic parameters for the patient may be ongoing even though care will be transferred to another center.

Major abdominal vascular injures usually involve either the abdominal aorta or the inferior vena cava. The aortic injuries are slightly more benign and can occasionally be observed with no surgical management [32]. They can also be repaired endovascularly though this is usually only done at major trauma centers [33]. Immediate transfer if no stabilization is needed would be appropriate for these patients after discussion with the accepting trauma center.

Abdominal organ and smaller vessel damage can be much more insidious but just as concerning as trauma to the larger vessels. The difficulty in the direct visualization of bodily injury can be falsely comforting. The FAST exam (focused assessment with sonography in trauma) is completed in the trauma bay on both stable and unstable patients. If concerning, an unstable patient will need surgical management, potentially without any further imaging [8]. The FAST exam is very sensitive and specific test in detecting intra-abdominal injuries in adults, but its use is limited in pediatric abdominal trauma as it has low sensitivity and specificity. Therefore, **CT**, remains the imaging modality of choice for pediatric patients [34, 35]. CT is the test of choice to follow up on a positive FAST exam with a stable patient. CT can be important to assess surgical urgency and also to give information on the severity of injury.

The most severe of these injuries can cause a large amount of blood loss and

hemorrhagic shock, which are a leading cause of death in this patient population [39]. Many of these deaths could potentially be prevented by adequate preparation and appropriate equipment [36]. A rapid infuser should either be in the room or quickly located and assembled. There should be a process in place to obtain trauma blood units (O negative), and depending on frequency of events, to have the blood available in the trauma bay or operating suite. A convection warmer and aggressive temperature control of the room can prevent hypothermia and coagulopathies.

Management in the trauma bay or the operating room is similar to any other surgical procedure. There are a few specific strategies that have been shown to be effective for patients with severe bleeding. Hypotensive fluid resuscitation has become a standard of care for trauma patients, as the fluid required to achieve higher blood pressures can cause further coagulopathies and also can disrupt clots that have already formed [40, 41]. The specific pressure goal has yet to be elucidated, but animal models indicate MAP between 60-100 mmHg are most appropriate [42, 43]. The CRASH-2 trial showed that a single bolus dose of 1 gm of tranexamic acid over 10 min followed by an infusion of 1 gm over 8 hours reduced death due to bleeding and all-cause mortality. Tranexamic acid reduces bleeding through the inhibition of fibrin breakdown. Clot stability is improved and bleeding is minimized [43].

Transfusion strategy is still one of the most controversial topics in trauma resuscitation. The combination of platelets, fresh frozen plasma and packed red cells is needed to prevent dilutional coagulopathy, but the exact ratio is still uncertain. Many practitioners believe in the 1:1:1 ratio during severe bleeding, but the PROPPR study showed there was no difference in mortality compared to a 1:1:2 ratios [44]. Many institutions have implemented massive transfusion protocols due to the large amount of blood products required by some of the patients. These protocols are usually a collaboration between the surgical, blood bank, anesthesia, and pharmacy teams to bring blood products, medications, and personnel to the operating room or trauma bay [45]. Anesthesiologists should be aware of any protocol at their hospital, and if none exists may advocate for its creation.

Blunt and penetrating trauma can be a high-pressure situation with potentially fatal outcomes. The variability and conspicuousness of the injuries can make diagnosis difficult, and major injuries can be missed. Anesthesiologists can improve their ability to handle these situations with established protocols and by understanding their hospital structure and their responsibilities in these traumas.

CONCLUSION

Trauma is a leading cause of morbidity and mortality across a variety of ages. The injuries can vary in severity and type and a community anesthesiologist must have good clinical judgment and an excellent understanding of their hospital structure and abilities. An anesthesiologist must complete a quick primary assessment of a trauma patient focusing on airway and access and consider laboratory values and further imaging that the patient may need before further management. The care for these patients is very dependent on the type and severity of injury and is an important consideration in the evaluation and management in the pre-operative and operative settings. Optimizing management may include a quick transportation to the operating room for surgery or further stabilization or transfer to a more appropriate facility. The community anesthesiologist plays an important role in all aspects of care for these patients and making quick and appropriate decisions can improve patient outcomes.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] http://www.cdc.gov/injury/overview/leading_cod.html

[2] McNicholl BP. The golden hour and prehospital trauma care. Injury 1994; 25(4): 251-4. [http://dx.doi.org/10.1016/0020-1383(94)90073-6] [PMID: 7605409]

[3] Stroud MH, Prodhan P, Moss MM, Anand KJ. Redefining the golden hour in pediatric transport. Pediatr Crit Care Med 2008; 9(4): 435-7. [http://dx.doi.org/10.1097/PCC.0b013e318172da62] [PMID: 18496407]

[4] Han YY, Carcillo JA, Dragotta MA, *et al.* Early reversal of pediatric-neonatal septic shock by community physicians is associated with improved outcome. Pediatrics 2003; 112(4): 793-9. [http://dx.doi.org/10.1542/peds.112.4.793] [PMID: 14523168]

[5] McEvoy MD, Field LC, Moore HE, Smalley JC, Nietert PJ, Scarbrough SH. The effect of adherence to ACLS protocols on survival of event in the setting of in-hospital cardiac arrest. Resuscitation 2014; 85(1): 82-7. [http://dx.doi.org/10.1016/j.resuscitation.2013.09.019] [PMID: 24103233]

[6] Heitmiller ES, Nelson KL, Hunt EA, Schwartz JM, Yaster M, Shaffner DH. A survey of anesthesiologists' knowledge of American Heart Association pediatric advanced life support resuscitation guidelines. Resuscitation 2008; 79(3): 499-505.

[http://dx.doi.org/10.1016/j.resuscitation.2008.07.018] [PMID: 18954934]

[7] Cline DM, *et al.* Physician compliance with advanced cardiac life support guidelines 1995. [http://dx.doi.org/10.1016/S0196-0644(95)70355-1]

[8] Gamanagatti S, Rangarajan K, Kumar A, Jineesh . Blunt abdominal trauma: imaging and intervention. Curr Probl Diagn Radiol 2015; 44(4): 321-36. [http://dx.doi.org/10.1067/j.cpradiol.2015.02.005] [PMID: 25801463]

[9] Faul M, Xu L, Wald MM, Coronado VG. Traumatic brain injury in the United States: emergency department visits, hospitalizations, and deaths. Atlanta, GA: Centers for Disease Control and Prevention, National Center for Injury Prevention and Control 2010. [http://dx.doi.org/10.15620/cdc.5571]

[10] Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974; 2(7872): 81-4. [http://dx.doi.org/10.1016/S0140-6736(74)91639-0] [PMID: 4136544]

[11] Gentleman D, Dearden M, Midgley S, Maclean D. Guidelines for resuscitation and transfer of patients with serious head injury. BMJ 1993; 307(6903): 547-52. [http://dx.doi.org/10.1136/bmj.307.6903.547] [PMID: 8400978]

[12] Sakles JC, Laurin EG, Rantapaa AA, Panacek EA. Airway management in the emergency department: a one-year study of 610 tracheal intubations. Ann Emerg Med 1998; 31(3): 325-32. [http://dx.doi.org/10.1016/S0196-0644(98)70342-7] [PMID: 9506489]

[13] Franschman G, Peerdeman SM, Andriessen TM, *et al.* Effect of secondary prehospital risk factors on outcome in severe traumatic brain injury in the context of fast access to trauma care. J Trauma 2011; 71(4): 826-32. [http://dx.doi.org/10.1097/TA.0b013e31820cebf0] [PMID: 21427618]

[14] Mechtler LL, Shastri KK, Crutchfield KE. Advanced neuroimaging of mild traumatic brain injury. Neurol Clin 2014; 32(1): 31-58. [http://dx.doi.org/10.1016/j.ncl.2013.08.002] [PMID: 24287384]

[15] Toyama Y, Kobayashi T, Nishiyama Y, Satoh K, Ohkawa M, Seki K. CT for acute stage of closed head injury. Radiat Med 2005; 23(5): 309-16. [PMID: 16342901]

[16] Czosnyka M, Pickard JD. Monitoring and interpretation of intracranial pressure. J Neurol Neurosurg Psychiatry 2004; 75(6): 813-21. [http://dx.doi.org/10.1136/jnnp.2003.033126] [PMID: 15145991]

[17] Brady KM, Shaffner DH, Lee JK, *et al.* Continuous monitoring of cerebrovascular pressure reactivity after traumatic brain injury in children. Pediatrics 2009; 124(6): e1205-12. [http://dx.doi.org/10.1542/peds.2009-0550] [PMID: 19948619]

[18] Brain Trauma Foundation. American Association of Neurological Surgeons, Congress of Neurological Surgeons, Joint Section on Neurotrauma and Critical Care Guidelines for the management of severe traumatic brain injury. II. Hyperosmolar therapy J Neurotrauma, 24 (2007), pp. S14-S20.

[19] Suarez JI. Hypertonic saline for cerebral edema and elevated intracranial pressure. Cleve Clin J Med 2004; 71 (Suppl. 1): S9-S13. [http://dx.doi.org/10.3949/ccjm.71.Suppl_1.S9] [PMID: 14964472]

[20] Bratton SL, Chestnut RM, Ghajar J, *et al.* Brain Trauma Foundation; American Association of Neurological Surgeons; Congress of Neurological Surgeons; Joint Section on Neurotrauma and Critical Care, AANS/CNS. Guidelines for the management of severe traumatic brain injury. II. Hyperosmolar therapy. J Neurotrauma 2007; 24 (Suppl. 1): S14-20. [PMID: 17511539]

[21] Hans P, Bonhomme V. Why we still use intravenous drugs as the basic regimen for neurosurgical anaesthesia. Curr Opin Anaesthesiol 2006; 19(5): 498-503.

[http://dx.doi.org/10.1097/01.aco.0000245274.69292.ad] [PMID: 16960481]

[22] Petersen KD, Landsfeldt U, Cold GE, *et al.* Intracranial pressure and cerebral hemodynamic in patients with cerebral tumors: a randomized prospective study of patients subjected to craniotomy in propofol-fentanyl, isoflurane-fentanyl, or sevoflurane-fentanyl anesthesia. Anesthesiology 2003; 98(2): 329-36.
[http://dx.doi.org/10.1097/00000542-200302000-00010] [PMID: 12552189]

[23] Saxena M, Young P, Pilcher D, *et al.* Early temperature and mortality in critically ill patients with acute neurological diseases: trauma and stroke differ from infection. Intensive Care Med 2015; 41(5): 823-32.
[http://dx.doi.org/10.1007/s00134-015-3676-6] [PMID: 25643903]

[24] Tokutomi, K. Morimoto, T. Miyagi, *et al*. Optimal temperaturye for the management of severe traumatic brain injury: effect of hypothermia on intracranial pressure, systemic and intracranial hemodynamics, and metabolismNeurosurgery, 52 (2003), pp. 102-111.

[25] http://www.cdc.gov/injury/wisqars/leadingcauses.html

[26] http://www.cdc.gov/injury/images/lccharts/leading_causes_of_injury_deaths_highlighting_ unintentional_injury_2013a.gif

[27] Pierre EJ, McNeer RR, Shamir MY. Early management of the traumatized airway. Anesthesiol Clin 2007; 25(1): 1-11, vii.
[http://dx.doi.org/10.1016/j.anclin.2006.11.001] [PMID: 17400151]

[28] Hagberg CA. Kaslow, O. Difficult Airway Algorithm Management in Trauma. ASA Newsl 2014; 78: 9.

[29] Peters S, Nicolas V, Heyer CM. Multidetector computed tomography-spectrum of blunt chest wall and lung injuries in polytraumatized patients. Clin Radiol 2010; 65(4): 333-8.
[http://dx.doi.org/10.1016/j.crad.2009.12.008] [PMID: 20338402]

[30] Langdor MI, Medak AJ, Hendey GW, *et al.* Prevalence and Clinical Import of Thoracic Injury Identified by Chest Computed Tomography but Not Chest Radiography in Blunt Trauma: Multicenter Prospective Cohort Study. Ann Emerg Med. 2015.

[31] Smith RS, Chang FC. Traumatic rupture of the aorta: still a lethal injury. Am J Surg 1986; 152(6): 660-3.
[http://dx.doi.org/10.1016/0002-9610(86)90444-7] [PMID: 3789291]

[32] Charlton-Ouw KM, DuBose JJ, Leake SS, *et al*.. Observation May be Safe in Selected Cases of Blunt Traumatic Abdominal Aortic Injury. Ann Vasc Surg 2015; (Aug): 5.
[PMID: 26253045]

[33] Azizzadeh A, Keyhani K, Miller CC III, Coogan SM, Safi HJ, Estrera AL. Blunt traumatic aortic injury: initial experience with endovascular repair. J Vasc Surg 2009; 49(6): 1403-8.
[http://dx.doi.org/10.1016/j.jvs.2009.02.234] [PMID: 19497498]

[34] Yoshii H, Sato M, Yamamoto S, *et al*.. Usefulness and limitations of ultrasonography in the initial evaluation of blunt abdominal trauma. J Trauma, 45 (1998), pp. 45–51.

[35] Scaife ER, Rollins MD, Barnhart DC, *et al.* The role of focused abdominal sonography for trauma (FAST) in pediatric trauma evaluation. J Pediatr Surg 2013; 48(6): 1377-83.
[http://dx.doi.org/10.1016/j.jpedsurg.2013.03.038] [PMID: 23845633]

[36] Sheffy N, Chemsian RV, Grabinsky A. Anaesthesia considerations in penetrating trauma. Br J Anaesth 2014; 113(2): 276-85.
[http://dx.doi.org/10.1093/bja/aeu234] [PMID: 24980427]

[37] Shiroff AM1, Gale SC, Martin ND, *et al*. Penetrating neck trauma: a review of management strategies and discussion of the 'No Zone' approach. Am Surg Jan;79(1):23-9.

[38] Cowley R. A total emergency medical system for the state of Maryland Md State Med J, 45 (1975), pp. 37-45.

[39] Tisherman SA, Schmicker RH, Brasel KJ, *et al.* Detailed description of all deaths in both the shock and traumatic brain injury hypertonic saline trials of the Resuscitation Outcomes Consortium. Ann Surg 2015; 261(3): 586-90.
[http://dx.doi.org/10.1097/SLA.0000000000000837] [PMID: 25072443]

[40] Morrison CA, Carrick MM, Norman MA, *et al.* Hypotensive resuscitation strategy reduces transfusion requirements and severe postoperative coagulopathy in trauma patients with hemorrhagic shock: preliminary results of a randomized controlled trial. J Trauma 2011; 70(3): 652-63.
[http://dx.doi.org/10.1097/TA.0b013e31820e77ea] [PMID: 21610356]

[41] Kowalenko T, Stern S, Dronen S, Wang X. Improved outcome with hypotensive resuscitation of uncontrolled hemorrhagic shock in a swine model. J Trauma 1992; 33(3): 349-53.
[http://dx.doi.org/10.1097/00005373-199209000-00003] [PMID: 1404501]

[42] Bai X, Yu W, Ji W, *et al.* Resuscitation strategies with different arterial pressure targets after surgical management of traumatic shock. Crit Care 2015; 19(1): 170.
[http://dx.doi.org/10.1186/s13054-015-0897-6] [PMID: 25927673]

[43] Shakur H, Roberts I, Bautista R, *et al.* Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet 2010; 376(9734): 23-32.
[http://dx.doi.org/10.1016/S0140-6736(10)60835-5] [PMID: 20554319]

[44] Holcomb JB, Tilley BC, Baraniuk S, *et al.* Transfusion of plasma, platelets, and red blood cells in a 1:1:1 *vs*. a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. JAMA 2015; 313(5): 471-82.
[http://dx.doi.org/10.1001/jama.2015.12] [PMID: 25647203]

[45] Waters JH. Role of the massive transfusion protocol in the management of haemorrhagic shock. Br J Anaesth 2014; 113 (Suppl. 2): ii3-8.
[http://dx.doi.org/10.1093/bja/aeu379] [PMID: 25498580]

SUBJECT INDEX

A

B

C

D

E

F

G

H

I

K

L

M

N

O

P

Q

R

S

T

U

V

W

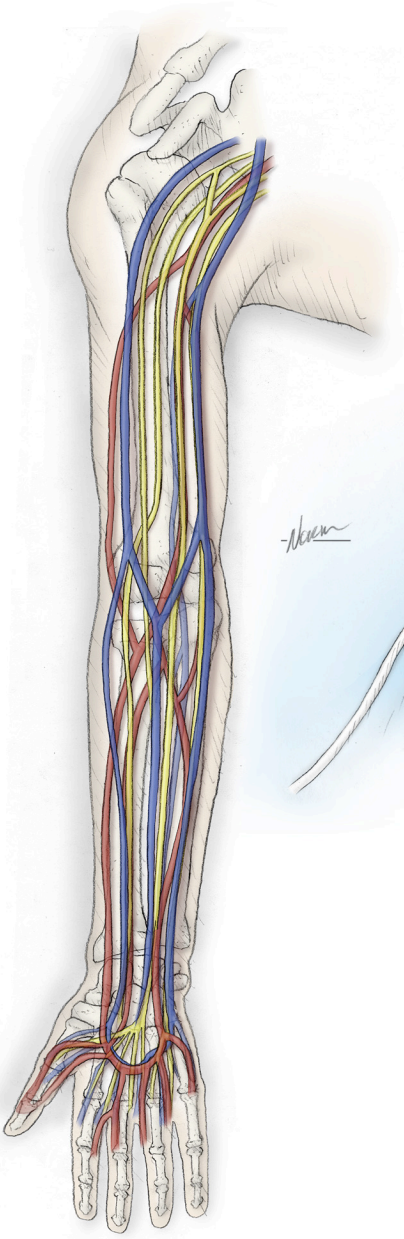
Recent Advances in Anesthesiology Volume 1

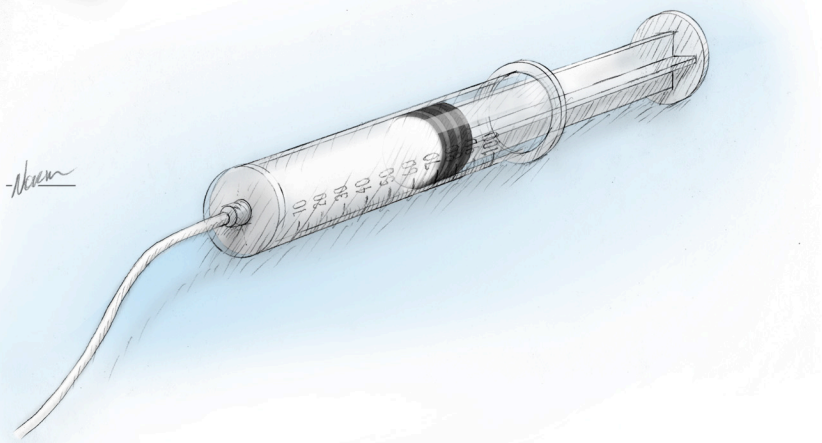
ANESTHESIA Essential Clinical Updates for Practioners

Regional, Ultrasound, Coagulation, Obstetrics, and Pediatrics

A.D. John

- A rapid refresher and resource for practitioners.
- Written for clinicians by preeminent clinicians from outstanding anesthesia training programs.
- Chapters/Themes are designed for a quick read – in minutes – to update practitioners on key topics in which they may not be fully facile.





Illustrations by Norm Myers