PEDIATRIC ANESTHESIA:
A GUIDE FOR THE NON-PEDIATRIC ANESTHESIA PROVIDER - PART II

Editors:
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Part II

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FOREWORD

"Pediatric Anesthesia A Guide for the Non-pediatric Provider" edited by Bharathi Gourkanti, MD with Drs. Gratz, Dippo, Peiris and Choudhry is a worthwhile addition to the library of every anesthesia resident and anesthesia practitioner. It is a solid reference for common and uncommon encounters in pediatric anesthesia practice.

Pediatric anesthesia is a complicated and often intimidating subject for anesthesia trainees as well as non-pediatric trained anesthesia providers. This textbook gives a new light to various topics in a user-friendly format including pediatric emergencies inside and outside the operating room. It includes the most recent literature at the time of publication for evolving topics including anesthetic considerations for COVID 19. It also has a section on the current state of research in the pediatric population as well as updates on quality and patient safety in pediatric anesthesia. The authors have written and illustrated a resource with high yield charts, graphs and tables.

One of the primary goals of this book is to provide a user-friendly resource for the safe care of infants and children and this book meets this goal. It breaks down the current clinical practice into an approachable outline for all providers. I recommend it for anesthesia trainees, new and established practicing clinical anesthesiologists, anesthetists, pediatric dental, emergency medicine providers, and pediatric intensivists.

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PREFACE

Our second volume was added to focus on specific topics that reflect current issues in anesthesia practice. This volume was constructed to complement the first volume but can also stand alone. As always, our goal was to be a comprehensive and readily available resource that the busy practitioner can easily utilize. Many of the same authors contributed to this volume.

As the content of the text has grown, we made a concerted effort to ensure a coordinated approach and stay focused on topics relevant to the current practice of anesthesiology. Chapters have been added that focus on the ongoing changes that affect the current practice of pediatric anesthesia. The problems associated with the COVID-19 pandemic are discussed in a chapter. We also included some specialized chapters, such as Research in Pediatric Anesthesia and Quality Assurance and Patient Safety in Pediatric Anesthesia, in hopes of inspiring others to further improve the practice and advance the science.

WHO CONTRIBUTED TO THIS BOOK

Contributions to this book are made by different anesthesia providers from qualified pediatric anesthesiologists, researchers, general anesthesiologists who do occasional pediatric anesthesia, including anesthesia residents, pediatric anesthesia fellows, and certified registered nurse anesthetists. This book could serve as an invaluable source of knowledge for all who provide pediatric anesthesia because of the wide range of contributors and their diverse perspectives in the medical care of children.

THANKS

As in the first volume, I am extremely grateful to all the contributors who generously gave their time to bring their knowledge, points of view, and unique expertise to this book in order to provide this rich resource of information.

I thank my co-editors, Drs. Irwin Gratz, Grace Dippo, Nathalie Peiris, and Dinesh K. Choudhry for their knowledge, experience, patience, and scrupulous attention to detail to make this manuscript more meaningful.

SUMMARY

In summary, we designed this book for all practitioners who routinely or occasionally provide pediatric anesthetic care with a readily available source of reference. We sincerely hope this book will be of help to you in providing safe practice of pediatric anesthesia.

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CHAPTER 1

Anesthesia for Pediatric Patients with Common Comorbidities Part I

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Abstract: Children undergoing anesthesia have many considerations of disease processes that require careful attention to details and addressing specific needs. There are several comorbidities that are frequently encountered in a pediatric setting. A common scenario is a child with an upper respiratory tract infection presenting for elective surgery. We will discuss the criteria to be considered regarding when it is safe to proceed with elective surgery and when the risk is high. Asthma is common among children, and exacerbation can occur during an anesthetic. Anesthetic management of children with these respiratory illnesses is discussed. Children with Down syndrome frequently present for various cardiac and non-cardiac surgical interventions. Anesthetic issues relating to their non-cardiac surgeries will be discussed. Children with sickle cell disease is yet another group of patients frequently admitted to the hospital with sickle cell crisis. They warrant attention to specific details to ensure getting through surgery safely and require optimal pain management. Obstructive sleep apnea is increasingly encountered in children presenting for surgical procedures. Anesthetic challenges and risks they pose will be discussed.

Keywords: Acute chest syndrome, Apnea-hypopnea index, Asthma, Bronchospasm, Central sleep apnea, Cervical spine instability, Deep extubation, Down syndrome, Hemoglobin F, Laryngeal mask airway, Laryngospasm, Obstructive sleep apnea, Perioperative respiratory adverse events, Red blood cell transfusion, Short-acting beta2 agonist, Sickle cell disease, Sleep-disordered breathing, Upper respiratory tract infection, Vaso-occlusive crisis, Wheezing.

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UPPER RESPIRATORY TRACT INFECTION

Introduction

Upper respiratory tract infection (URI), the common cold, refers to infection limited to the upper respiratory tract airway and involves a runny nose, nasal congestion, cough, sneezing, sore throat, wheezing, low-grade fever and malaise as presenting symptoms. Most adults in the United States experience 2 to 4 URIs per year, while youngest children experience 6 to 8 episodes per year [1]. Ninety-five percent of URIs are secondary to acute viral causes, of which rhinovirus with >100 serotypes accounts for a large majority, 30%-50% [2]. Preschool children attending large daycare centers were reported to have more colds than children at home [3].

In the Anaesthesia Practice In Children Observational Trial (APRICOT) study, a large prospective observational study of 30,874 children from birth to 15 years of age in 261 hospitals located across 33 European countries, the incidence of perioperative severe critical events was 5.2%. Respiratory critical events were the most frequent (3.1%) followed by critical cardiovascular events (1.9%) [4].

Perioperative Respiratory Adverse Events

Current or recent URI in children undergoing surgery poses a higher risk of perioperative respiratory adverse events (PRAEs), which include laryngospasm, bronchospasm, coughing, airway obstruction, breath-holding, and arterial hypoxemia [5, 6]. Significant respiratory complications, such as atelectasis, aspiration, post-intubation croup, stridor, and pneumonia could result in unanticipated tracheal intubation or re-intubation, return to the emergency department or unexpected hospital admission [4, 6]. Twice the usual length of stay in the hospital and higher costs were associated in a prospective study of children with PRAEs undergoing non-cardiac surgery [7]. Complications are generally mild and managed easily and safely [8, 9] and do not have long-term sequelae [6, 10, 11]. Few reports of children with URI undergoing surgery resulting in death were related to unsuspected myocarditis [12].

URIs are generally self-limiting, but airway hyperactivity can persist for 6-8 weeks with increased secretions, mucosal inflammation, and altered neural reflexes. Anesthetic risks are greatest in the first few days after a URI but remain increased for up to 6 weeks [13].

Risk Factors

The relative risk of PRAEs doubled for children who had symptoms of URI

present or less than two weeks preceding surgery, particularly for laryngospasm [14]. The risk for PRAEs, however, was lower when URI symptoms were 2-4 weeks prior to procedures requiring anesthesia in this study. In the Pediatric Sedation Research Consortium database, 83,491 sedations were analyzed for complications. Risk of PRAEs was found to be greater than 22% in children undergoing procedural sedation with current URI with thick and/or green secretions [15]. A parental statement that the child has a 'cold' on the day of surgery is a good indicator of increased risk of PRAEs [16]. This study had eight variables associated with increased risk of PRAEs that included sputum production, nasal congestion, snoring, passive smoking, orotracheal intubation, choice of an induction agent, and whether muscle relaxant was reversed. With every additional year of age risk of occurrence of PRAEs decreased by about 8% in one study [11] and relative risk decreased by 11% in another [14]. Various factors that have been found to be associated with a greater risk of PRAEs are summarized in Table **1**.

Table 1. Factors associated with increased risk of perioperative respiratory adverse events.

• URI within 2-4 weeks of surgery [4, 6, 14, 17]
• URI with green rhinorrhea, moist cough, and fever [14 - 16]
• Wheezing/reactive airway disease [4, 6, 14]
• Parental confirmation of URI [16, 18]
• Younger age group, infants at highest risk [6, 11, 17 - 20]
• Prematurity was associated with higher risk [4, 6]
• Obstructive sleep apnea/snoring [4, 16]
• Parental/environmental smoking [4, 6, 13, 14, 21]
• Family history of asthma or atopy [4, 14]
• Airway anomalies (subglottic stenosis and cysts, laryngeal papillomatosis, cleft palate, Pierre Robin syndrome, tracheal stenosis, vocal cord paralysis and laryngomalacia) [22]
• Ear, nose, and throat/airway procedure [4, 6, 11, 14, 18, 19]
• Urgent procedure [14]
• Lack of pediatric experience [4, 6, 11, 14, 18]
• Increasing ASA risk category is associated with significantly more PRAEs [4]

ASA = American Society of Anesthesiology

Preoperative Evaluation

Preoperative assessment begins with obtaining a thorough history. Special attention is given to the presence of current respiratory symptoms and those in the past 2-4 weeks. Symptoms, such as high fever (core body temperature higher than 100.4 °F or 38 °C) with dry or productive cough, clear or purulent nasal discharge, presence of wheezing, lethargy, poor oral intake, and general feeling of being unwell should be considered for postponement of surgery (Table **2**). Risk factors, such as airway endoscopic procedure, the urgency of surgery, presence of

CHAPTER 2

Anesthesia for Pediatric Patients with Common Comorbidities Part II

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Abstract: In this chapter, we will discuss the perioperative anesthetic concerns of children with autism, attention-deficit hyperactivity disorder (ADHD), cystic fibrosis, epidermolysis bullosa, and von Willebrand disease. Children with autism and ADHD are at high risk for having severe anxiety and distress when undergoing anesthesia due to difficulty in adjusting to the changes in daily routine and new environment. Careful planning to limit waiting time in the preoperative area and appropriate premedication are critical to minimizing distress. Children with cystic fibrosis may have involvement of pulmonary, gastrointestinal, and pancreaticobiliary organ systems. Due to the increasing longevity of this population, both children and adults may present for a variety of surgical procedures; pulmonary status is a key concern when formulating an anesthetic plan. Children with epidermolysis bullosa present special challenges when undergoing anesthesia because both airway devices and the equipment used to monitor vital signs can cause serious postoperative complications. Von Willebrand disease is the most common congenital bleeding disorder encountered in pediatric anesthesia. Safe perioperative management requires interdisciplinary coordination to create a plan for prophylaxis prior to surgery, intraoperative and postoperative management to maintain hemostasis.

Keywords: Aggressive child emergencies, Autism spectrum disorder, Asperger's syndrome, Attention-deficit hyperactivity disorder, Anxiety, Cystic fibrosis, Desmopressin, Dystrophic epidermolysis bullosa, Epidermolysis bullosa, Hemostasis, Perioperative care, premedication, Postoperative aggression, Von Willebrand disease.

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Bharathi Gourkanti, Irwin Gratz, Grace Dippo, Nathalie Peiris and Dinesh K. Choudhry (Eds.)

AUTISM

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder with impairment of communication and social skills. It is defined in the Diagnostic and Statistical Manual Edition 5 (DSM5) as a persistent deficit in social interaction and social communication across multiple contexts and restricted, repetitive pattern of behaviors, interests, or activities [1]. Autism spectrum disorder includes autism, Asperger syndrome, and pervasive developmental disorder. The prevalence worldwide is thought to be approximately 1% [4]. Boys are four times more likely to be diagnosed with ASD than girls [7]. The etiology is still unknown; genetic, immunologic, and environmental factors are thought to be involved [4].

Many autistic children will have other medical, developmental, psychiatric problems, or intellectual disability. Common comorbidities include epilepsy, Attention Deficit Hyperactivity Disorder, anxiety, oppositional defiant disorder, conduct disorder, and sensory processing disorder. Gastrointestinal disturbances such as malabsorption, maldigestion, food intolerance, and food allergies can often be seen [4]. Verbal and nonverbal communication can be limited in these children [4].

There are both pharmacological and nonpharmacological treatments used in ASD [5]. Nonpharmacological interventions include cognitive and behavioral therapy starting at an early age. Pharmacologic agents can be used to help manage the symptoms (Table **1**). The following table shows many of the commonly used medications [4 - 6]. Consultation with a psychiatrist is recommended before stopping long term medications [5].

Table 1. Medications used for Children With Autism.

Medications used for Children With Autism		
Medication	Mechanism of action	Potential adverse effects
Haloperidol Risperidone Aripiprazole	Antipsychotic drugs	Sedation, weight gain, extrapyramidal symptoms, hypotension with general anesthesia; risperidone → arrhythmia
Clozapine	Atypical antipsychotic	Agranulocytosis, cardiac conduction problems, hyperthermia, hypotension
Divalproex sodium	Anti-epileptic medication	Liver disease, coagulation abnormalities
Fluoxetine Citalopram	Selective Serotonin Reuptake Inhibitors	GI symptoms, agitation, reduced platelet aggregation and increased transfusion risk

(Table 1) cont.....

Medications used for Children With Autism		
Methyphenidate Amphetamines	Stimulants	May increase anesthesia requirement, increased risk of hypertension and arrhythmias, lower seizure threshold, interact with vasopressors
Melatonin		
Clonidine Guanfacine	Alpha-adrenergic agonists	

Preoperative Concerns and Premedication

In addition to surgical needs, autistic children will often need sedation for diagnostic procedures such as magnetic resonance imaging, echocardiogram, phlebotomy, or auditory brainstem reflex studies [2]. Autistic children have a difficult time coping with changes in their routine which can lead to a stressful perioperative experience. They may have difficulty expressing their anxiety in the new environment and progress to becoming inconsolable and disruptive. Premedication is very effective in reducing anxiety in most children. Autistic children are more likely to need a premedication to reduce distress and also more likely to receive a nonstandard premedication [3]. The following Table **2**, lists the most commonly used agents for premedication [4].

Table 2. Commonly used agents for premedication.

Medication	**Route**	**Dose**
Midazolam	Oral	0.5-1 mg/kg
	Intranasal	0.2 mg/kg
	Intramuscular	0.1-0.2 mg/kg
	Intravenous	0.01-0.1mg/kg
Ketamine	Oral	3-6 mg/kg
	Nasal	3 mg/kg
	Intramuscular	3-5 mg/kg
Dexmedetomidine	Oral	4 mcg/kg
	Intranasal	1 mcg/kg

Ideally, these children should be scheduled early in the day with minimal time in the waiting room and preoperative area. They are more sensitive to visual and auditory stimuli in the hospital, so a quiet and private preoperative area is essential. Child life specialists may be helpful in controlling anxiety in the preoperative area. Other helpful practices include allowing both parents to be

CHAPTER 3

Anesthesia for Pediatric Patients with Common Comorbidities Part III

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Abstract: There have been dramatic improvements in the survival of neonates and children with many diseases and disorders due to advancements in medicine over the past several decades. These advances are attributed to the better understanding of these disease processes, the advent of multidrug combinations, molecularly targeted therapies, critical care and various surgical interventions. In the wake of this rapidly developing wide range of treatment protocols, the anesthesiologist needs to have a clear understanding of these disorders and their comorbidities, and stay abreast of the various treatment modalities, including their safety and toxicity profiles. This review attempts to emphasize some of the clinical conditions unique to these patients and special considerations for the conduct of anesthesia in this population.

Some of the disease processes and comorbidities discussed here include anesthetic considerations for ex-premature infants, diabetes mellitus, obesity, childhood cancer, and children with congenital heart disease who present for non-cardiac surgery. The objective of this discussion is to provide an updated and comprehensive review of current perioperative anesthetic management of pediatric patients with these conditions. We also delineate the effects of anesthesia during the perioperative course, including major metabolic changes that may result in increased morbidity. We provide guidelines for any anesthesia provider involved in the care of these vulnerable patients. Special considerations need to be taken to promote the physical and mental wellbeing of these children and their families. Collaborative coordination with all providers involved in care is essential to provide safe and effective anesthesia to this subset of patients

Keywords: Apnea, Bronchopulmonary dysplasia, Cardiotoxicity, Chemotherapy, Congenital heart defects, Continuous glucose monitoring, Diabetes type 1, Diabetes type 2, Ex-premature, Fontan, Hyperglycemia, Hypoglycemia, Insulin, Insulin pumps, Left-to-right, Leukemias, Low birth weight, Lymphomas, Media-,

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stinal mass, Obesity, Prematurity, Pulmonary vascular resistance, Respiratory distress syndrome, Right-to-left, Systemic vascular resistance.

EX-PREMATURE PATIENTS

Introduction

Anesthesia for ex-premature and term infants has undergone enormous change during the past several decades. There has been steadily improved survival and quality of life in preterm and very low birth weight infants since the 1980s due to advances in prenatal, obstetric, and neonatal care. These advances in care affect a subset of the premature patient population who present with distinctive illnesses and pose unique challenges for surgical procedures and their anesthesia care. As patients with these diseases live longer, the morbidity in these surviving infants has also increased. Many of them develop acute or chronic organ dysfunction, which can require surgical attention and add to the anesthetic risk.

The impact of premature birth is life-long, affects multiple organ systems, and is associated with reduced life expectancy. Preterm newborns and ex-premature infants who present for surgery are uniquely challenging due to the immaturity of all organ systems and associated congenital defects. They have ongoing complex medical needs in addition to the urgent reasons for any surgical procedures.

Every year, an estimated 15 million babies are born preterm (before 37 completed weeks of gestation), and this number is rising [1]. The improved care and survival of the premature babies of decreasing gestational age over the last four decades have been attributed to advances in medicine, improvement in healthcare, and the advent of the neonatal intensive care unit (NICU).

Definitions

The American Academy of Pediatrics (AAP) defines gestational age (GA) as time elapsed between the first day of the last menstrual period and the day of delivery. Postconceptional age (PCA) is defined as gestational age (in weeks) plus the number of weeks since birth. A full-term neonate is born between 37 to 42 weeks' gestation and aged less than 1 month. The World Health Organization (WHO) defines preterm birth as babies born alive before 37 weeks of pregnancy have been completed. Further, preterm birth babies are sub-categorized based on their gestational age (GA) into:

Moderate to Late preterm (32 to 37 weeks)

Very Preterm (28 to 32 weeks)

Extremely Preterm (less than 28 weeks)

Preterm birth infants are also classified based on their birth weight as [2]:

Low birth weight (LBW) of <2500 grams

Very low birth weight (VLBW) of <1500 grams, or

Extremely low birth weight (ELBW) of <1000 grams

Morbidity and Mortality

Preterm birth is associated with high perinatal morbidity and mortality. Prematurity affects multiple systems in the body as important aspects of organ development are not complete. The clinical consequences of prematurity ultimately depend on the gestational age at birth and any underlying abnormalities that may have caused the preterm birth [3]. Babies that are more premature have increased severity of disabilities in later life [4]. Low gestational age at birth is an independent risk factor for increased mortality from respiratory, cardiovascular, endocrine, and congenital disorders in childhood through early adulthood [5]. The data from the perioperative cardiac arrest registry (POCA) suggest that the incidence of cardiac arrest in ex-premature infants is much higher than in older children. A similar high incidence of perioperative severe critical events in pediatric anesthesia (APRICOT Trials) was found in the European prospective multicenter observational study in 261 hospitals. They reported an overall incidence of 5.2%, with an incidence of respiratory critical events in 3.1% of patients and cardiovascular instability in 1.9%. An immediate poor outcome occurred in 5.4% of their cases [6]. Prolonged hospital stay after birth and multiple readmissions to the hospital in the first year of life increase morbidity in these fragile children. Many of the surviving babies face a lifetime of learning disabilities, visual problems, or hearing difficulties.

Consequences of Prematurity

The consequences of premature birth are life-long. Although the risk of many of the acute complications declines throughout infancy and early childhood, long-term morbidity remains high. Ex-premature infants remain at a higher risk for postoperative complications than term infants even after minor surgical procedures and interventions. Some of the problems that a preterm infant may present in subsequent years of growth include the following:

- Neurological disability (including cerebral palsy)
- Intraventricular hemorrhage (IVH)

CHAPTER 4

Anesthetic Considerations for the Critically Ill Pediatric Patient

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Abstract: In comparison to adults, critical illness is relatively uncommon in the pediatric population. Many facilities may be unprepared or ill-equipped for treating these rare conditions. The conventional anesthesiologist may not be familiar with the common pathologies of critical illness in children. These patients may need complex and life-saving urgent procedures to stabilize them. It is logistically challenging to have pediatric trained personnel readily available at all hospitals and care centers. These patients have special perioperative needs that the anesthesiologist should consider. They may potentially present to the operating room, emergency department, or pediatric intensive care unit. Here, we offer a direct and practical approach to managing the care of these younger patients.

Keywords: Acute sickle cell crisis, Acute respiratory distress syndrome, Cardiac shunts, Cerebral edema, Congenital cardiac diseases, Critical illness myopathy, Diabetic ketoacidosis, Enteral feeding and nutrition, Increased intracranial pressure, Propofol related infusion syndrome, Patent ductus arteriosus, Respiratory distress in tracheostomy patients, Sepsis, Septic shock, Seizure disorders, Status epilepticus, Sickle cell disease, Status asthmaticus.

INTRODUCTION

As medical advancements continue, an increase in the survival of neonates and children with congenital disorders and pathology can be challenging and often unfamiliar to the conventional anesthesia provider. Often, these patients undergo procedures that require general anesthesia, sedation, and analgesia. These patients differ significantly in their clinical response to anesthetics compared to adult patients.

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Many procedures differ in their degree of stimulation and invasiveness, which can affect the appropriate anesthetic technique. Sedation techniques are very institutionally dependent. In the United States, the most common sedative technique in critically ill children utilizes midazolam and fentanyl [1]. Although most modern-day anesthetic techniques are straightforward and safe, adverse events related to "under-sedation" and "over-sedation" are still common and must be promptly diagnosed and treated [2]. Caregivers should appreciate anatomic and physiologic differences unique to the pediatric population, including congenital disorders. Recognition of these differences and adjustment of the anesthetic technique is necessary to avoid potential complications. Airway management, medication choice and dosing, and sedation levels should always be individualized based on the child's needs and performed procedure.

Studies have shown that inadequate sedation and analgesia for critically ill pediatric patients are not uncommon. These patients experience sleep disturbances, increased risk for delirium, and prolonged hospital stays [3]. These stress factors also increase parental anxiety and can result in a traumatic and unpleasant experience for these patients. The implications for neurocognitive development due to adverse environmental factors and inadequate analgesia have yet to be fully discovered. Prolonged hypoxia in critically ill pediatric patients may be one of the most significant causes of long-term impairment in cognitive function [4].

INFECTIOUS DISEASE

Sepsis in Children

Infectious disease is common in children. A prematurely developed immune system puts these patients at risk. The majority of infections in children are mild, resolve quickly, and usually do not require extensive care. Patients with stable vital signs can be monitored and discharged home with observation [5]. The treatment of sepsis in children is different from adult treatment in terms of clinical diagnosis and management. Sepsis is uncommon in children, accounting for 0.56 cases per 1,000 people each year; however, the associated mortality remains high [6]. Although sepsis can occur at any time, the incidence tends to occur at a peak at the age of 2 months. Infections peak seasonally for pediatric patients in the colder winter months. Interestingly, the incidence is about 15% greater in boys than in girls.[7] The cost burden of treating sepsis has been documented to be about 5 billion dollars yearly in the United States [7].

Diagnosis

Sepsis is defined as systemic inflammatory response syndrome (SIRS) combined

with a suspected or identified infection. Pediatric SIRS criteria are age-dependent and differ from the diagnostic SIRS criteria for adults [7]. In sepsis, a complex and widespread immune-mediated response involves overwhelming inflammatory cytokines, resulting in systemic vasodilation. This leads to overall decreased cellular tissue perfusion and end-organ dysfunction. SIRS criteria include the following: core body temperature greater than 38.5 degrees C or less than 36 degrees C, tachycardia, tachypnea, and abnormal leukocyte count or greater than 10% neutrophils. Two out of the four criteria with one abnormal temperature or leukocyte count are diagnostic of pediatric SIRS [8, 9].

The most common pathogens are specific to certain age groups. Neonates with sepsis are typically infected with Group B streptococci, E.coli, or HSV. The symptoms of sepsis can be nonspecific. The difficulty of obtaining a history from the pediatric patient can pose an obstacle to diagnosing and treating sepsis promptly. It is essential to receive a comprehensive history from the child and their parents or caregivers and perform a thorough physical exam. Early but nonspecific signs of infection include decreased oral intake, fever, and symptoms of dehydration such as sunken fontanelles [10]. Pediatric patients are susceptible to decompensating more rapidly than adults. Most importantly, early recognition and treatment of sepsis have been shown to decrease mortality [10].

Treatment of Shock

Septic shock is defined as sepsis with hypotension requiring the use of vasopressors to maintain a MAP > 65 or serum lactate > 2 mmol/L despite adequate fluid resuscitation. These patients are typically intravascularly depleted, in addition to being systemically vasodilated. Septic shock is associated with significantly higher mortality than sepsis alone. It is essential to recognize shock quickly and start fluid resuscitation as soon as possible. Prompt intravenous (IV) or emergency intraosseous (IO) access should be initiated.

Fluid resuscitation should begin with a 10-20 cc/kg bolus with isotonic crystalloid or colloid. Empiric broad-spectrum antibiotics should be started as soon as possible to treat the underlying disease, as delays in treatment have been shown to increase mortality. Antibiotic coverage should be narrowed once the pathogen and sensitivities have been identified. If shock is not adequately treated with fluids and hypotension persists, vasoactive should be utilized [11].

Cold shock is characterized by cold, clammy extremities, weak pulses, and narrow pulse pressure and should be treated with IV dopamine at 5 μg/kg/min and titrated up to 10 μg/kg/min as needed. If shock persists, consider adding IV epinephrine at 0.05–0.3 μg/kg/min, to a maximum of 1 μg/kg/min. This syndrome is seen more commonly in pediatrics, with increased systemic vascular resistance

CHAPTER 5

Anesthesia-Related Genetic Disorders

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Abstract: Numerous pediatric genetic disorders have anesthetic implications; however, the ones that should be familiar to all anesthesiologists are those associated with malignant hyperthermia, pseudocholinesterase deficiency, and opioid prescribing. Genetic defects leading to ryanodine receptor mutations in malignant hyperthermia require attention in both anesthetic technique and pre-induction preparation. Pseudocholinesterase deficiency associated with rare mutations of pseudocholinesterase may be encountered by all anesthesiologists and has specific operative and postoperative considerations. Finally, opioids are a common modality for pain control throughout surgical care. Awareness of genetic differences in activation and metabolism for different opioids, as illustrated with codeine usage in pediatrics, is necessary for safe pain management prescribing.

Keywords: Butyrylcholinesterase, Central Core disease, Codeine, CYP enzyme, King-Denborough syndrome, Malignant hyperthermia, Native American myopathy, Opioids, Pediatric anesthesia, Pediatric, pseudocholinesterase deficiency, Pediatric analgesia.

INTRODUCTION

Pediatric genetic diseases with anesthetic implications are numerous, each disorder with a unique phenotype and pathology. The entirety of these defects would be too numerous to cover in this chapter, and many would be unlikely to be encountered in general practice. Genetic variabilities that should be familiar to all anesthesiologists are those that carry significant morbidity and mortality with anesthesia administration. The focus in the following pages will be on those disorders with strong genetic associations. Malignant hyperthermia, a condition every anesthesiologist is intimately familiar with, will be reviewed, along with

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associated genetic syndromes and management. Pseudocholinesterase deficiency is also discussed and its anesthetic management. Finally, genetic variations and pediatric opioid responses are discussed, focusing on codeine and the clinical impact seen in America last decade.

MALIGNANT HYPERTHERMIA

The unexpected sudden death of a patient is one of a clinician's greatest fears, and despite all the advances to make anesthesia safer, a child with malignant hyperthermia (MH) may be left with severe multiorgan dysfunction or death if not recognized or treated promptly.

As a brief review, during normal muscle contraction, sarcolemma depolarization causes a cascade of intracellular events to activate the ryanodine receptor, which regulates calcium efflux from the sarcoplasmic reticulum. Calcium then binds to troponin, and this combination links actin and myosin, resulting in muscle contraction. During repolarization, calcium is taken back into the sarcoplasmic reticulum by the enzyme SERCA, leading to muscle relaxation [1].

With MH muscle physiology, there is typically a mutation in the ryanodine receptor, where exposure to anesthetic drugs, such as volatile agents or succinylcholine, leads to calcium dysregulation. This unregulated calcium elevation results in sustained muscle contraction and increasing metabolic demand [2].

Inheritance

Malignant hyperthermia is typically an autosomal dominant inheritance pattern [3]. In other words, if a patient has MH there is about a 50% chance of passing the mutation to their offspring. Over 300 DNA changes have been implicated in MH susceptible patients; however, not all identified mutations are specific to the ryanodine receptor, but to other channels working alongside the receptor in controlling normal muscle contraction and calcium regulation [3].

Clinical Features

The majority of MH cases are associated with volatile agents or succinylcholine [4]. The most reliable initial clinical sign of an MH crisis is an unexplained increase in end-tidal CO^2. Continued muscle contraction results in increased anaerobic metabolism and lactate production, leading to metabolic and respiratory acidosis. Prolonged cellular stress ends in cell lysis and intracellular content

release. Increased potassium and myoglobin in the serum is indicative of this cell death. The increased metabolic demand leads to hyperthermia and ultimately causes further organ and coagulation failure [4].

The timing of clinical features varies from patient to patient and can occur at any time during the anesthetic or post-operative unit. Furthermore, not every patient will exhibit all the clinical manifestations. Sometimes these patients in the post-operative unit may only present with arrhythmias from hyperkalemia as end-tidal carbon dioxide is not frequently monitored in the recovery unit [5].

Generalized muscle rigidity despite nondepolarizing neuromuscular blockade is almost always indicative of MH, and an anesthesia provider should promptly check potassium, carbon dioxide, and temperature with this presentation [6]. Masseter Muscle Rigidity (MMR) is a sustained contraction of the jaw muscles following succinylcholine administration and is associated with malignant hyperthermia in up to 20% of instances [6]. The general opinion is that rigidity lasting less than one minute does not carry the same MH risk, but the decision to cancel the case and monitor these patients should be discussed with the proceduralist and evaluated on a case-by-case basis.

Management of an MH Crisis

The first steps after recognizing an MH crisis are to immediately stop all triggering agents, notify the surgeon and staff, and call for help. Several things must happen rapidly; having multiple providers in the room allows these tasks to be completed in a timely fashion. The United States Malignant Hyperthermia Association (MHAUS) has created an emergency algorithm to cover all aspects of MH management and can be easily accessible at www.mhaus.org (Figs. **1** and **2**).

CHAPTER 6

Pediatric Pain Management and Regional Anesthesia

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Abstract: Inadequate pain management in children not only leads to immediate stress and suffering, but it can also influence long-term psychological, physiological, and emotional outcomes for the patient and family. It is well-established that neonates not only feel pain, but also have an exaggerated perception due to immaturity of the descending inhibitory pathways. In addition, various physiologic differences influence the effect and duration of various medications. Despite the existence of many validated tools and pain scales, the assessment of pain in children is challenging. Successful acute pain management targets various elements in the complex system of pain transduction, transmission, modulation, and perception. A multimodal approach targeting multiple steps in the nociceptive pathway is more effective than those involving a single target. Regional analgesic techniques supplemented with opiates and nonopioid medications have proven to be effective in controlling postoperative pain. Traditionally, caudal and epidural analgesia have an established record of safety and are popular regional techniques in children. However, advances in ultrasound-guided techniques have encouraged pediatric anesthesiologists to perform more regional blocks in children. Additionally, application of the enhanced recovery after surgery (ERAS) protocol for major surgeries and concern about the opioid epidemic has led to increasing awareness about the benefits of regional anesthesia. In this chapter, we will discuss the fundamentals of pain perception in children, the assessment of pain and the multimodal approach to manage it, relevant pharmacology, and various regional techniques in routine and complex pediatric surgical patients.

Keywords: Caudal epidural, Central neuraxial blocks, Cerebral palsy, Chronic postsurgical pain, Developmental pharmacology, Enhanced recovery after surgery, Lower extremity nerve blocks, Lumbar epidural, Multimodal approach, Neonates, Nonopioid analgesics, Opioid analgesics, Opioid-induced hyperalgesia, Pain assessment, Pain neurobiology, Peripheral nerve blocks, Pharmacotherapy, Spinal fusion surgery, Spinal in neonates, Upper extremity nerve blocks.

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INTRODUCTION

Inadequate pain management in children not only leads to immediate undue stress and suffering, but it can also influence long-term psychological, physiological, and emotional outcomes for the patient and family [1, 2]. A successful pain management strategy in the pediatric population warrants consideration of age-related changes in neurobiology, pain processing, age-appropriate pain assessment tools, and developmental pharmacokinetics.

PATHOPHYSIOLOGY AND NEUROBIOLOGY

Pain is not simply a transmission of impulses from the peripheral neurons to the center but is a complex interplay of pain perception, amplification, and suppression. It results from the activation of sensory receptors specialized in detecting actual or impending tissue damage called the nociceptors. However, the correlation between activation of nociceptors and the sensory experience of pain is variable and is significantly influenced by emotional state; degree of anxiety; attention, distraction, and experiences; memories; and many other factors that can either enhance or diminish the pain experience. Tissue injury associated with surgery initiates a systemic reaction accompanied by inflammatory cytokines [3]. Inflammatory mediators (serotonin, bradykinin, histamine, prostaglandins, and leukotrienes) that are released in the wound and adjacent tissues lead to heightened synaptic transmission and reduction in pain threshold in the injured area called **primary hyperalgesia**. Tissue injury, nerve damage, and intense noxious stimuli generate a barrage of impulses from the site of injury leading to increased synaptic efficacy in somatosensory neurons in the dorsal horn of the spinal cord that is referred to as **central sensitization** (Fig. **1**). The action potential causes the presynaptic terminals of A-delta and C fibers to release a variety of pronociceptive substances such as glutamate, substance-p, and calcitonin gene-related peptide into the synaptic cleft. This heightened synaptic transmission leads to a reduction in pain threshold and central amplification of pain responses and a spread of pain sensitivity to non-injured areas. Spread of pain sensitivity to the surrounding non-injured areas is called **secondary hyperalgesia** and may lead to the occurrence of pain by stimuli that are normally not painful, such as touch, which is referred to as **allodynia** [5]. Presence of **allodynia** likely indicates amplified A-delta and C fiber activity, and activity in A-beta fibers that normally mediate touch begins to be interpreted as pain signals. In addition to nociceptive and inflammatory pain, a **neuropathic** component is likely due to surgical injury to local nerve tissue, leading to spontaneous firing of injured nerve endings that adds to increased pain sensitivity in the early postoperative period with a potential to become chronic postsurgical pain [6].

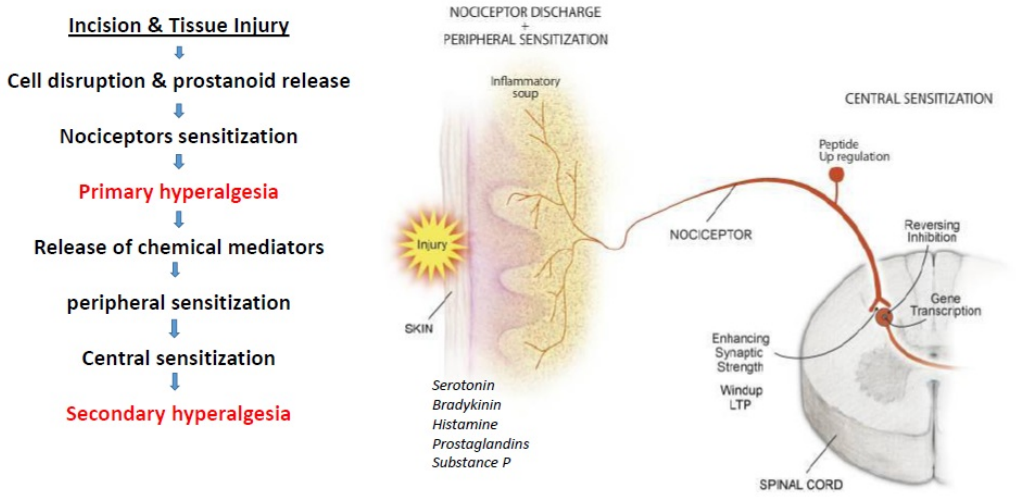

Fig. (1). Schematic diagram of major mechanisms involved in peripheral and central sensitization. Injury results in release of inflammatory mediators (inflammatory soup) that enhance the nociceptor discharge produced directly by the injury [4]. Reprinted with permission from Mendell LM. Computational functions of neurons and circuits signaling injury: Relationship to pain behavior. PNAS 2011; 108 (Supplement 3): 15596-601.

DEVELOPMENTAL PHARMACOLOGY

Children are not just miniature adults and differ physiologically and pharmacologically [7, 8]. It is during the first year of life that most maturational changes take place. There are significant pharmacokinetic differences that warrant consideration for dosage and timing of analgesic medications. High body water content in neonates and infants results in a larger volume of distribution for water-soluble drugs with a potential for longer duration of action. Since a higher percentage of cardiac output is delivered to the brain in neonates, brain concentration of drugs may be higher than in adults. Immaturity of the blood-brain barrier further facilitates drug delivery to the CNS. Lower levels of albumin and alpha-1 acid glycoproteins (to which highly protein-bound drugs such as opioids and local anesthetics bind) allow for greater availability of unbound plasma drug concentration with increased drug effect and toxicity [7]. Immaturity of hepatic enzyme systems and renal function results in reduced clearance of drugs necessitating adjustment in dose and interval. These organs reach adult function by 1 year of age. Drug clearance in children between 2 and 6 years of age may actually be greater than in adults because of the larger hepatic mass relative to body weight [9].

PAIN ASSESSMENT

Pain in children is poorly understood, underrecognized, and therefore,

CHAPTER 7

Research in Pediatric Anesthesia

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Abstract: In the United States and globally, governmental organizations have initiated programs to stimulate clinical research in the pediatric population. The most important reason for these programs is a lack of high-quality evidence to guide effective and safe treatment in children. In pediatric anesthesiology, physicians and scientists need to evaluate anesthetic drugs, medical equipment, and devices. Under improved global regulations, current and new anesthetic strategies will undergo a scientific evaluation of safety and effectiveness. Along these lines, the number of pediatric patients participating in anesthesiology research is expected to increase. Federal regulations deem minors to lack the required decision-making capacity to consent to participate in studies. In line with the Declaration of Helsinki, enrolling children in research should encompass legal guardian permission and assent of the child. Proxy consent and assent procedures should enable the legal representative to safeguard the child's interest while allowing the child to give meaningful agreement. Assent has been defined in detail by ethical scholars but is generally poorly defined legally. A specific challenge to appropriate proxy consent and a child's assent in pediatric anesthesiology research is the brief treatment interaction the pediatric anesthesiologist can have with patients. This challenge may require contacting potential research subjects well before admission to the hospital, depending on the risk and complexity associated with the study at hand.

Keywords: Assent, Consent, Ethical review, Institutional review board, Pediatric anesthesia, Quality improvement, Research, Risk.

INTRODUCTION

Pediatric anesthesiology is a dynamic discipline. Continuous advances in the development of anesthetic drugs, anesthesia equipment, and medical devices attempt to enhance the safety and quality of anesthesia provided to pediatric patients undergoing surgery. Research is needed to establish safe and effective clinical applications of new products and strategies. Traditionally, there was a

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lack of adequate research specifically in pediatric populations [1]. Leading national and international programs now stimulate clinical research in pediatric patients to improve the evidence basis for clinical practice in pediatric care [2].

IS IT IMPORTANT TO CONDUCT RESEARCH IN PEDIATRIC ANESTHESIOLOGY?

We highlight three primary reasons for research in pediatric anesthesia – and we discuss each of them within the pediatric anesthesia context as a specialty and with respect to the regulatory environment of the United States.

Pediatric Anesthesiologists Cannot Extrapolate Findings from Adult Research to Children

Most medications have never been investigated in pediatric patients, forcing pediatric anesthesiologists to resort to off-label use and estimate appropriate drug dosing. Compared with adults, randomized controlled trial data lacks for more than 50% of interventions used in children [1]. Thus, efficacy and safety information for medications is unavailable for the youngest children. Unfortunately, these children are also at the most significant risk. The Pediatric Exclusivity Program was passed by the US Food and Drug Administration (FDA) to minimize the risk of clinical use of non-approved medications causing adverse effects. Initiated in 1997 [3] and made permanent in 2012, this initiative grants 6 months of intellectual property protection to pharmaceutical companies who conduct pediatric clinical trials within the program. Several discoveries regarding pediatric drug efficacy and safety are the result of this program [2].

Scientists and physicians need to conduct research to increase safety and quality in pediatric anesthesiology

Quality improvement and safety research have been a focal point of anesthesiology practice in the United States. As a result, several national networks initiated registries specifically aimed at capturing adverse events related to the administration of anesthesia in pediatric patients. Examples of databases in the U.S. are Wake Up Safe [4], the Pediatric Perioperative Cardiac Arrest (POCA) Registry [5], as well as the Pediatric Regional Anesthesia Network (PRAN) [6]. These registries, and research using their data, provide important information about the potential prevention of rare but serious adverse events.

Research is an essential part of anesthesiology training

Clinical research is a key component of anesthesiology residency [7] and is also an essential part of pediatric anesthesiology fellowship training [8]. Practicing

anesthesiology requires the development of critical thinking skills and a commitment to learning throughout one's career. Clinical training programs that actively develop these competencies through engagement in clinical studies likely create more outstanding anesthesiologists who have an enduring commitment to education.

SPECIFIC CONSIDERATIONS FOR RESEARCH IN PEDIATRIC ANESTHESIA *VS.* RESEARCH IN ADULT ANESTHESIA

Ethical Justification

Pediatric anesthesia patients comprise a patient population that is more vulnerable because their emotional and intellectual capabilities are not mature. Therefore, a researcher needs to weigh the risks and discomfort involved in the planned research when proposing a pediatric anesthesia study. The researcher then should justify these risks against the expected benefits to the pediatric patient and future patients with the same condition.

Minimizing Risk

Every research study is associated with some risk to the enrolled child. The institutional review board that oversees the institution where the research will take place determines the risk of an investigation. In the U.S., studies in pediatric patients are generally only allowed when they represent minimal risk or a minor increase over minimal risk to the child. A definition of the concept of minimal risk is: "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests" [9]. The National Commission describes a minor increase over minimal risk as follows: "while [minor increase] goes beyond the boundaries of minimal risk, it poses no significant threat to the child's health or well being" [10]. Research procedures that have been considered a minor increase over minimal risk are skin or bone marrow biopsies, catheterized urine collections, MRI scans with sedation, and emotionally distressing surveys. The somewhat restrictive United States regulations on greater than minimal risk research in children have sometimes hampered scientific investigations compared to other countries [11].

Potential adverse events and study risks must be anticipated before a study starts, with the predefined possibility of study termination should unexpected related adverse events be found. A researcher should limit participant numbers and procedures to the expected number to allow scientifically valid conclusions based on a power calculation. When compared to clinical studies in adults, the efficacy

CHAPTER 8

Principles of Quality and Patient Safety in Pediatric Anesthesiology

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Abstract: The delivery of high-quality, safe patient care is fundamental to a successful outcome for pediatric patients undergoing anesthesia. Organizations rooted in a transparent culture where employees are encouraged to speak up for safety will often engage their staff and patients to design systems of care that are meaningful and effective. Successful healthcare organizations continuously analyze data and refine processes in search of opportunities for improvement. This chapter will discuss the core principles of quality and patient safety and review some ongoing national and international collaborative efforts to improve anesthesia care for children. Practical strategies for establishing a quality improvement program are explored, including incorporation of simulation for performance improvement.

Keywords: Adverse events, Checklists, Cognitive aids, Handoff communication, High reliability, Just culture, Medication error, Patient safety, Quality improvement, Simulation, System engineering.

INTRODUCTION

The pursuit of quality and patient safety is among the top priorities for every healthcare system in the United States today. Healthcare value is derived from patient outcomes in the context of cost, where outcomes are influenced by quality, safety, service, and patient and staff engagement. This is often referred to as the "quadruple aim" of healthcare [1], a framework for creating a positive clinical experience for both patients and providers. Paramount to the success of the quadruple aim is the delivery of optimum care. While the quadruple aim considers each of the domains equally, Fig. (**1**) below represents a model wherein quality and safety are represented as core drivers of health:

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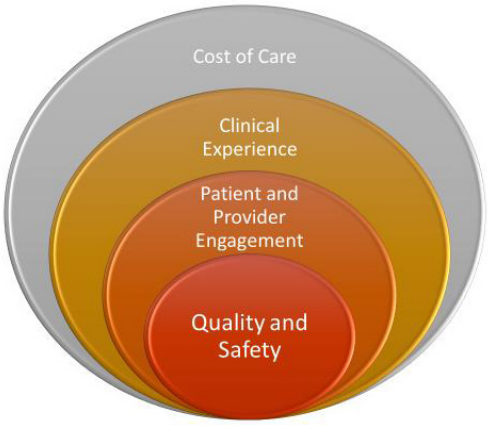

Fig. (1). Quality and Patient Safety Funnel.

In consideration of the principles examined in this chapter, the delivery of safe, high-quality care will be considered fundamental to the success of every healthcare system and pediatric anesthesiology department. Excellent quality outcomes result in improved clinical experience and satisfaction. Health care professionals and policymakers strive to provide the highest quality of care at the lowest cost to benefit the patient [2]. Anesthesiology as a specialty has been a historical leader in the adoption of reliable quality processes to ensure safety and value in the perioperative environment and beyond.

FUNDAMENTALS OF PATIENT SAFETY

The practice of anesthesiology is a key driver in the quality of care delivered to surgical patients [3]. In the Institute of Medicine's publication, **Crossing the Quality Chasm**, six domains of healthcare quality were introduced. These include safety, effectiveness, patient-centeredness, efficiency, equitability, and timeliness [4]. Efficient and equitable care refers to the provision of care that does not vary in quality due to personal characteristics of the patient (*e.g.*, race, gender, socioeconomic status), while efficiency refers to the elimination of waste in the system. Timeliness can help improve efficiency, which can ultimately drive down cost while maintaining the quality of care at a constant level [5]. A simple example of how timeliness can impact care stems from a common process in the care of the surgical patient: the administration of prophylactic antibiotics. During a relatively routine task, prophylactic antibiotics need to be administered at the right time in the perioperative period. If the antibiotic is not administered in time for it to reach effect in concert with surgical incision, the risk of surgical site infection increases. This can potentially lead to increased morbidity, increased

hospital length of stay, increased healthcare costs, and subpar outcomes for the patient.

In 1999, the Institute of Medicine produced a report titled "To Err is Human" [6]. This publication highlighted the failure of the U.S. healthcare system to keep patients safe from preventable harm. Between 40,000 and 98,000 patient deaths were estimated to be preventable due to a lack of standardized safety processes and human error. This report sparked what is now considered to be the modern patient safety movement. Yet despite significant investment of time, resources, and attention over the past 20 years, care delivery errors and preventable deaths remain unsolved issues in healthcare.

Just Culture

One of the outgrowths of the modern-day patient safety movement is the application of the "Just culture" concepts to healthcare. Just culture is aimed at improving patient safety by ensuring shared accountability between healthcare providers and their organizations [7]. Providers are held accountable for the quality of their choices, as they hold their colleagues accountable for theirs [8]. A just culture accomplishes shared accountability by empowering employees so that they feel comfortable monitoring the workplace and participating in safety efforts [7]. An open and honest reporting environment creates an opportunity to shift focus from shame and blame to system design for patient safety.

To achieve a just culture, departments must balance accountability between the organization, *i.e.*, the entity responsible for designing and improving workplace processes, and the provider, *i.e.*, the entity responsible for executing operations within that environment. Approaches to improving patient safety within a just culture are rooted in error analysis, tools to enhance safety, and outcomes engineering [7]. Error analysis includes a robust "deep-dive" into the factors that contributed to the error. This includes assessment of resources, equipment, staffing models and ratios, review of current processes and gaps, and any environmental conditions that may have altered the standard workflow. Specific safety tools can then be devised and employed based on the findings of the error analysis, and outcomes can be specifically engineered in support of human factors and behavior.

HIGH RELIABILITY ORGANIZATIONS (HROS)

In addition to just culture, the concept of high reliability enhances safe patient care in anesthesiology. High reliability organizations (HROs) are defined by their ability to maintain consistently safe and reliable operations in hazardous, high-risk environments. Examples of non-healthcare HROs include the nuclear power

CHAPTER 9

Anesthetic Considerations For Covid-19 (Year 2020)

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Abstract: In December 2019, patients clustered in Wuhan, China, were identified to have a novel virus now known as COVID-19, a virus from the coronavirus family. This virus has spread all across the world, with close to 8 million confirmed cases and over 432,000 confirmed COVID-19 deaths worldwide. This pandemic has rattled the modern era and presented with several new considerations that the anesthesiologist must be aware of. This chapter will cover several anesthetic concerns that involve this virus and all the precautions that one should take during this pandemic.

It should be noted that there is new research emerging rapidly about this novel virus, and one can always depend on World Health Organization, the American Society of Anesthesiologists, Anesthesia Patient Safety Foundation, and Centers for Disease Control and Prevention for updated COVID-19 resources for anesthesiologists. *This chapter was written in September 2020 and is the first textbook chapter that we know that is available at this time.*

Keywords: Axillary nerve block, COVID-19, Driving pressure, ELISA, HMEF, IgG and IgA immune response, Intubation, Lung protection strategies, Low tidal volume, Laryngoscopy, Leukopenia, Nasopharyngeal swab, Plateau pressure, RT-PCR, RBD-S protein, VFE.

PREOPERATIVE CONSIDERATIONS AND SYMPTOMOLOGY

Besides the normal comprehensive medical history, it is prudent that, as practitioners, we evaluate the patient for possible exposure to COVID-19 and specific anesthetic risks that may occur intraoperatively. All patients and their families should be screened for recent fevers, dry cough, diarrhea, headache, and/or loss of taste and smell. The most common initial symptom for COVID-19 is a fever [17]. In a systematic review in Europe, looking at 7480 children, symptoms were typically mild to moderate, with 51.6% of positive patients developing a fever, followed by cough (47.3%) and sore throat (17.9%). Less

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common symptoms included diarrhea and vomiting (<10% of cases). Neonates, on the other hand, were more likely to be severely ill with symptoms of dyspnea, fever, and feeding intolerance driving their illness. Looking at the pediatric population data published by the Center for Disease Control, the mortality rate is < 0.1% for children, which is strikingly different from the geriatric population, with a 32.4% mortality rate.

Although the mortality rate of COVID-19 is low in the pediatric population, there are reports of a rare severe hyperinflammatory syndrome in association with COVID-19 patients called Multisystem Inflammatory Syndrome in Children (MIS-C). This is thought to be a post-infectious immune dysregulation triggered by the virus. The CDC defines it as a fever lasting for more than 24 hours, laboratory evidence of inflammation, multisystem organ involvement (at least two systems), and a positive COVID test or exposure within four weeks of symptom onset. In June 2020, an article published in the New England Journal of Medicine stated that out of 186 patients diagnosed with COVID-19 infection, 80% required intensive critical care. Some individuals may fulfill all or some criteria for Kawasaki Disease. This disease is a vasculitis associated with preceding/active infection causing acute febrile illness of unknown etiology, typically affecting kids younger than five years, associated with fever, mucocutaneous changes, such as (conjunctival injection, rash, mucosal changes) and coronary artery aneurysms – the leading cause of acquired heart disease. A small subset of patients with MIS-C had developed macrophage activation syndrome – a life-threatening condition resulting in the proliferation of macrophage histiocytes and leading to Disseminated Intravascular Coagulation. Some of the most common laboratory findings associated with MIS-C include an elevated ESR, CRP, ferritin, LDH, IL-6, fibrinogen, CPK, and D-dimer.

When deciding whether a diagnostic test is warranted, studies revealed that in children with positive disease, a CT scan of the chest was normal a third of the time.

If a patient was recently treated for COVID-19, it is important to perform an EKG for QT prolongation. The use of azithromycin and hydroxychloroquine has gained traction, appearing in multiple guidelines. Although these medications are no longer recommended, it is likely that a child was prescribed these medications. The combination of these medications has been shown to cause a clinically evident prolongation of corrected QT (QTc) prolongation and possible myocardial injury [7].

Although the overall incidence of severe illness is low in the pediatric population, COVID-19 has brought concerns to public health issues. There has been a

significant decline in routine pediatric visits and immunizations. Various psychosocial and financial stresses from the pandemic have led to increased neglect and inability to care for children, along with a loss of adequate nutrition that many school services have provided to children. Mental health is also at risk given a loss of access to education. Children may not have reliable internet access at home to facilitate virtual learning, and the increase in online activity has opened up the potential for cyberbullying. All these considerations are important things to consider when a physician interacts with a child.

COVID-19 TESTING

The knowledge of diagnostic testing is still evolving; however, at this point in time, there are two commonly used tests, reverse transcriptase-polymerase chain reaction (RT-PCR) and ELISA IgM and IgG tests. The RT-PCR works by targeting one or more of the genes specific to COVID-19. Typically, these genes tested are the envelope, spike, or *ORF1* gene. All of the nasopharyngeal RT-PCR swabs have had similar sensitivities [1]. Typically, the RT-PCR test becomes detectable within one day of symptom onset and peaks within one week. By 3 weeks, the test is usually undetectable. Keep in mind that a positive RT-PCR indicates the viral RNA and does not necessarily mean that the virus is detectable. In a study, it was found that the RT-PCR test positivity was highest in the bronchoalveolar lavage specimens (93%), then sputum (72%), nasal sampling, and the lowest positivity was with a pharyngeal swab (32%) [2].

Rapid points of care (POC) detection of antibodies *via* ELISA are being widely developed. At a basic level, these tests measure a patient's immune response to COVID-19. At the current time, our institution's policy is that all patients receive a POC or PCR testing 72 hours before an elective procedure. A nasopharyngeal swab is preferred, however, if a child is non-compliant, then a substitution for a nasal or oral swab is recommended. If the case is an emergency and there isn't time to do COVID testing, then that patient will be assumed positive and must be placed in a negative pressure environment for the procedure, and all proper protective equipment must be available for all healthcare personnel.

Typically, IgM and IgG serology is observed by the 3rd week. After 5-7 weeks, IgM disappears, whereas IgG persists for a longer period [3]. In a recent study with 140 subjects, the combined sensitivity of RT-PCR and ELISA was 98.6% *vs*. 51.9% with just a solitary RT-PCR test [4]. The important point is that the most predominant antibody developed against the virus is the nucleocapsid antigen. Also, most tests that measure the antibody to nucleocapsid are sensitive. The virus attaches to human cells *via* the receptor-binding domain of S (RBD-S) protein, and antibodies against RBD S are considered to provide a stronger immune response

CHAPTER 10

Muscular Dystrophies and Mitochondrial Myopathies

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Abstract: Children with neuromuscular diseases have a broad range of presentation and anesthesia considerations. Muscle strength is reduced by degenerative nerve supply and affected neuromuscular junctions or by weakening of muscle fibers directly. Muscular dystrophies are an inherited group of disorders characterized by progressive muscle weakness. These children pose specific challenges related to anesthetic care due to skeletal muscle, pulmonary, and cardiac involvement. This chapter discusses the perioperative management of children with Duchenne, Becker, limb-girdle, Emery-Dreifuss, and myotonic muscular dystrophies. Also discussed are mitochondrial myopathies, a group of clinical conditions common to the pediatric population. Cerebral palsy (CP) is a nonspecific, descriptive term that encompasses a constellation of symptoms due to a neurologic lesion resulting from the insult to the developing brain sustained early in life. Although the neurologic lesion in CP is non-progressive, the motor dysfunction due to spasticity may be progressive, leading to spinal deformities, joint contractures, and dislocations requiring medical and surgical interventions. Anesthetic care for children with the above stated neuromuscular disorders requires understanding of their disease process and careful attention to all aspects of perioperative care. Thoughtful planning should include thorough preoperative assessment, attention to co-morbidities, management of chronic medications, and meticulous intraoperative care for these patients. Postoperative assessment of pain and its management are essential to facilitate recovery and uneventful perioperative course.

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MUSCULAR DYSTROPHIES

The muscular dystrophies are an inherited group of myopathic disorders due to the presence of dysfunctional proteins in the muscle fibers resulting in muscle weakness [1, 2]. The dysfunctional protein is due to a gene defect that is transmitted either as autosomal dominant or recessive or as an X-linked trait with sporadic de novo mutations also being reported [1, 2]. When the gene defect is expressed earlier in childhood, the phenotype is typically more severe. There is significant variability in presentation and involvement of organ systems, namely the musculature, heart, lungs, central nervous, and ophthalmic systems [3]. The perioperative management of Duchenne, Becker, limb-girdle, Emery-Dreifuss, and myotonic muscular dystrophies are discussed. Some of the characteristic features of these illnesses are displayed in Table **1**.

Table 1. Summary of muscular dystrophies [3, 4].

Muscular Dystrophy	Inheritance	Natural History	Motor Function	Respiratory Impairment	Cardio Myopathy	Other Findings
Duchenne MD	X-linked R	Progressive	Ambulation present Lost at adolescence	Frequent	Common	CK levels high; cognitive & neurobehavioral problems
Becker MD	X-linked R	Variable but slower progression than DMD	Ambulation present	Not usually	Common	CK levels high; milder than DMD
Limb-girdle MD	AD, AR	Progressive	Ambulation present Some lose it in early adulthood or middle age	Variable and seen in advanced stages	Present in some forms	CK usually increased; intellectual disabilities seen

(Table 1) cont.....

Muscular Dystrophy	Inheritance	Natural History	Motor Function	Respiratory Impairment	Cardio Myopathy	Other Findings
Emery-Dreifuss MD	X-linked R, AD, AR	Progresses slowly	Ambulation present	Seen in adulthood	Yes, with conduction defects	CK moderately elevated with insulin resistance and rigid spine in some
Myotonic dystrophy	AD	Progresses slowly	Ambulation present	Sleep-disordered breathing	Yes, with conduction defects	CK increased slightly; intellectual disabilities; insulin resistance; cataracts; myotonia; increased sleepiness with circadian issues

MD = muscular dystrophy, R = recessive, AD = autosomal dominant, AR = autosomal recessive, CK = creatine kinase, DMD = Duchenne muscular dystrophy.

DUCHENNE MUSCULAR DYSTROPHY

Introduction

Duchenne muscular dystrophy (DMD) is associated with severe clinical symptoms at an earlier age of onset when compared with Becker muscular dystrophy (BMD), which typically has a mild clinical course and later onset. There is an intermediate phenotype with clinical symptoms between these two and DMD-associated dilated cardiomyopathy, which presents in adults with little or no skeletal muscle disease. Both DMD and BMD have an X-linked recessive inheritance pattern predominantly affecting males. Female carriers are usually asymptomatic but may have variable degrees of muscle weakness or cardiac involvement [5]. The worldwide incidence of DMD is an estimated 1:3500 live male births [6].

Clinical Manifestations

Clinical onset of weakness manifests by age 2-6 years, and affected boys are usually late walkers [7]. They have a waddling gait, difficulty running and climbing stairs, and a tendency to fall. Weakness affects the proximal hip and shoulder muscles and, therefore, children have to push down on the floor with the palms of their hands and slowly climb up on themselves, moving their hands up along the thighs/lower trunk to stand up (Gower's sign). Children usually have

CHAPTER 11

Anesthesia for Uncommon Pediatric Diseases

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Abstract: Several uncommon pediatric diseases encountered by non-pediatric anesthesiologists bear discussion because a failure to recognize unique issues relating to them could lead to significant morbidity and mortality. Anterior mediastinal masses share the same space as major pulmonary and cardiovascular structures, which, if compressed, can compromise the airway, heart and great vessels. Awareness of the potential for major physiologic derangement and a multidisciplinary approach to their diagnosis and management will ensure a safe perioperative course. Congenital pulmonary airway malformation is one of the most frequent pulmonary malformations in children that requires surgical intervention by thoracoscopic approach in the first year of life. Their anesthetic management is often challenging due to their small size, need for lung isolation and maintaining adequate oxygenation during surgery. Understanding lung isolation technique in infants is necessary for the safe administration of anesthetics in these children. Arthrogryposis multiplex congenita syndrome is a rare, non-progressive, and congenital heterogeneous group of disorders characterized by congenital joint contractures. These children require frequent surgeries during childhood to address various musculoskeletal abnormalities. Their anesthetic management is often challenging due to comorbidities related to musculoskeletal deformities, neurologic, cardiovascular and respiratory systems involvement. Understanding the disease with thorough evaluation and preparation prior to anesthetic management is essential for a good perioperative outcome. Pheochromocytoma is a rare neuroendocrine tumor in children that may present unexpectedly for the management by anesthesiologists. It secretes catecholamines which can cause life-threatening perioperative hemodynamic instability. The meticulous preoperative pharmacotherapy, intraoperative anesthetic management and postoperative monitoring are vital for a safe outcome.

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ANTERIOR MEDIASTINAL MASSES

Introduction

Although relatively rare in children, anterior mediastinal masses (AMM) are a common source of anxiety for pediatric anesthesiologists. Reports of the hazards of general anesthesia in AMM date back to a few decades [1]. This is because the location of the tumor shares the same space as major pulmonary and cardiovascular structures, leading to a greater potential for anesthesia-related complications (Fig. **1**). Awareness of the potential for major physiologic derangement and a multidisciplinary approach to the diagnosis and management will ensure a safe course for the patient.

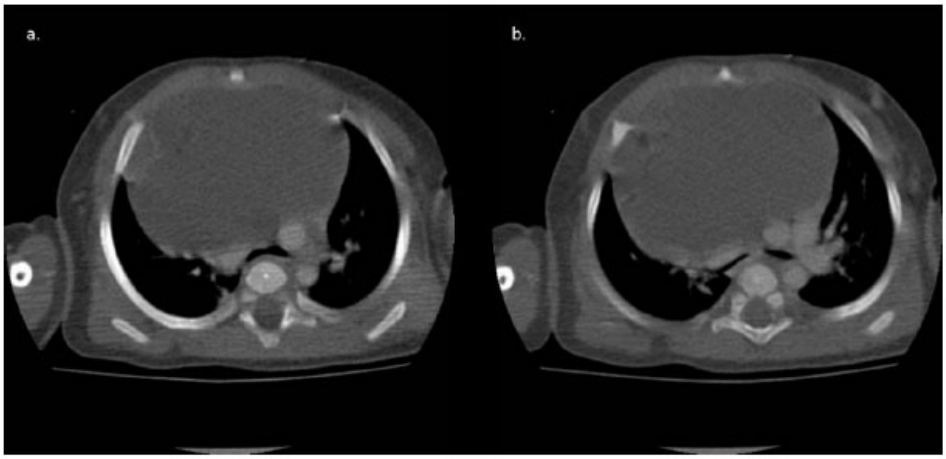

Fig. (1). Computerized tomography scan in an infant with anterior mediastinal masses believed to be a teratoma. As can be seen, the tumor occupies most of the thoracic cavity. At the level of the mid-distal trachea (a), just distal to the carina at the level of the mainstem bronchi (b). (Reproduced from the study of Brenn *et al*. Perioperative management of an anterior mediastinal teratoma in an infant: one more tool in the toolbox. BMJ Case Rep **2018**. with permission from BMJ Publishing Group Ltd.).

Prevalence

AMMs are represented by a variety of primary tumor types, but their specific prevalence is unknown. This is due to the fact that malignancy reporting is generally done by tumor type and that most cases are treated but not reported. It

must be remembered that AMM tumors are a problem of location regardless of tumor type.

Table 1. is a composite of several of the larger case series and shows the relative proportion of tumor types. Lymphomas are the most prevalent in pediatric patients. However, there are different tumor types that are present at different ages. Typically, the lymphomas occur in the early to late teens, while germ cell tumors such as teratomas may be present in infancy [1].

Case Series	N	Lymphoma	Germ Cell	Thymic	ALL	Other
**Mullen et al. 1986*	*179*	*80*	*43*	*30*	*0*	*26*
Anghelescu et al. 2007	*118*	*82*	*0*	*0*	*12*	*24*
Perger et al. 2008	*40*	*40*	*0*	*0*	*0*	*0*
Hack et al. 2008	*56*	*40*	*0*	*0*	*16*	*0*
Stricker et al. 2010	*45*	*28*	*4*	*3*	*0*	*10*
Garey et al. 2011	*26*	*16*	*0*	*0*	*4*	*6*
Acker et al 2015	*69*	*60*	*1*	*3*	*0*	*5*
Totals	*533*	*346*	*48*	*36*	*32*	*71*
Percent	*100%*	*64.92%*	*9.01%*	*6.75%*	*6.00%*	*13.32%*

Mediastinal Compartments

The mediastinal compartments contain the vital organs in close proximity to each other. While the mediastinum has been traditionally divided into the anterior, middle and posterior rather arbitrarily, most tumors do not respect these boundaries. A new, more functional and anatomic location system is being used to better describe and delineate tumors [2]. This classification system is shown in Fig. (**2**) and describes three sections, the prevascular, visceral, and paravertebral compartments.

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