Critical Care in the Pediatric Emergency Department

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KEYWORDS

• TBI • Seizure • Respiratory failure • Metabolic • Cardiac • Critical care

KEY POINTS

- Acute respiratory failure and pediatric acute respiratory distress syndrome must be identified and precisely managed in the emergency department.
- A large number of patients with congenital heart disease, either before or after surgery, will return to emergency department with both cardiac and medical illnesses requiring specific and aggressive attention.
- Management of pediatric traumatic brain injury may include intracranial pressure monitor placement and management of intracranial hypertension with hyperosmolar therapy, sedation and analgesia, ventilator management, and consultation with pediatric neurosurgery.
- After the initial 1-hour management in pediatric status epilepticus, general anesthesia with midazolam infusion is recommended as next-tier therapy.
- Presentation of inborn errors of metabolism may be severe yet vague and require time-sensitive and specific management.

INTRODUCTION

The pediatric intensive care unit (PICU) shares a symbiotic and complementary relationship with the pediatric emergency department (ED). Efficient management on one end will inevitably benefit efficient care and throughput on the other. This is particularly relevant for ED patients being transported to a PICU at another institution and/or if high census in the receiving PICU requires a transient delay in the ED to PICU transfer. Accordingly, many clinical practice guidelines for some of our most common diagnoses involve phases of care that greatly benefit from critical care management that commences in the ED.

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This article is broken down into critical illness categories based on primary organ system involved (respiratory, neurologic, cardiovascular, and metabolic) and focuses on "beyond the first hour" strategies in selected disease processes for each category. The management of septic shock is covered in the Raina Paul's article, "Recognition, Diagnostics and Management of Pediatric Severe Sepsis and Septic Shock in the Emergency Department," elsewhere in this issue of *Pediatric Clinics of North America*. Basics of resuscitation are not covered.

ACUTE RESPIRATORY FAILURE

Respiratory emergencies account for a great proportion of all ED visits. The vast majority of patients will be evaluated and managed without need for critical care interventions; however, a significant minority will require advanced respiratory care before transfer to a PICU can be accomplished. For patients in overt respiratory failure, intubation and mechanical ventilation are required. There has been a dramatic increase in the use of noninvasive respiratory support such as continuous positive airway pressure/biphasic positive airway pressure and heated high-flow nasal cannula (HHFNC) with data supporting these modalities decreasing the need for intubation.[1] The availability of these technologies coupled with the expertise of our pediatric respiratory therapists in the manipulation of these modalities has allowed expanded use in ED environments.[1–3]

HEATED HIGH-FLOW NASAL CANNULA

HHFNC have been successfully implemented in all age groups: from neonate through adulthood.[4,5] This success is multifactorial. The added humidity of the flow provides excellent mucolysis. HHFNC provides improved ventilation and "wash out" of physiologic dead space in the upper airways. The increased flow provides support to the increasing minute ventilation needs of the pediatric patient with increasing respiratory distress. Usual HHFNC rates often supply a bit of end-expiratory pressure that can stent the closing airway. This feature can be the biggest liability to this modality as well, because the provider must be clear to assess whether the patient is "flow starved" and therefore will respond nicely to HHFNC, or whether the patient is "pressure starved" in which case use of HHFNC will be inappropriate and the provider risks delaying the needed transition to positive pressure strategies such as continuous positive airway pressure/biphasic positive airway pressure or invasive mechanical ventilation. The HHFNC "dose" required to reduce the effort of breathing has been recently determined to be approximately 1.5 to 2.0 L/kg/min.[6] Flows are not usually greater than 8 LPM in infants with variable rates used in children but usually less than 20 LPM, and up to 50 LPM in adults.[4] Research predicting patients at increased risk of HHFNC failure is limited, but some authors have identified failure to have improvement in oxygenation indices (SpO_2/Fio_2 ratio of <200) within 1 hour after initiation portends the need for more invasive support.[7]

HHFNC systems that experience acute increases in pressure from a kinking of the tubing, for example, will "pop-off" with cessation of forward flow to the patient. Unless the system is reset with this occurrence, the patient will have nasal prongs in place with no flow of gas, resulting in partial occlusion of the airway. Risks of delayed escalation of care or unidentified equipment failure can be best mitigated by the use of operationalized guidelines that include appropriate initiation strategies and distinct reassessment by qualified providers to ensure patient tolerance and improvement. Finally, some HHFNC systems are not portable, which may mean use of an alternate

modality of respiratory support when transferring the patient from the ED to a different location in the hospital.

PEDIATRIC ACUTE RESPIRATORY DISTRESS SYNDROME IN THE EMERGENCY DEPARTMENT

Acute respiratory distress syndrome (ARDS) was first described by David Ashbough in 1966[8] in a case series of 12 patients with a syndrome consisting of acute hypoxemia, poor lung compliance, and bilateral infiltrates on chest radiograph. Interestingly, 4 of those 12 patients were between 11 and 19 years of age. Since that time, definitions have changed and included hypoxemia assessments based on oxygen saturation rather than arterial blood gas.

The *1994 American European Consensus Conference*[9] determined the minimal oxygenation defect required for the diagnosis of ARDS to be a Pa_{O_2}/Fi_{O_2} of less than 300. Biomarker studies in children, as in adults, have confirmed alveolar epithelial and vascular endothelial injury even in the earliest days of hypoxemia and, in about 25% of cases, before invasive mechanical ventilation was started.[10] The mission of the National Institutes of Health–funded Prevention and Early Treatment of Acute Lung Injury network (available from: http://petalnet.org) includes partnering intensive care units (ICUs) with EDs for earlier diagnosis and initiation of supportive measures.

In 2015, the Pediatric Acute Lung Injury Consensus Conference[11] determined new, specific definitions for patients with pediatric ARDS (PARDS) (**Table 1**). Patients who are invasively mechanically ventilated or on full face mask biphasic positive airway pressure may qualify for PARDS. Further, patients with comorbidities, such as cyanotic heart disease, chronic lung disease, and left ventricular dysfunction, now have specific criteria enabling a PARDS diagnosis. The Pediatric Acute Lung Injury Consensus Conference also defined an at-risk group as those patients with a milder acute hypoxemia, acute pulmonary disease on chest radiography—whether unilateral or bilateral—and an associated diagnosis within 7 days of this clinical presentation. The preferred assessment of oxygenation defect for PARDS should be oxygenation index if arterial blood gas available or oxygenation saturation index if no arterial blood gas available.

- Oxygenation index = (Fi_{O_2} * Mean airway pressure * 100)/Pa_{O_2}
- Oxygenation saturation index = (Fi_{O_2} * Mean airway pressure * 100)/Sa_{O_2}

Why is earlier diagnosis, even when in the ED, relevant? Mechanistic studies in both adults and children have indicated that ARDS pathophysiology starts far before

Table 1
2015 PALICC definition of PARDS

Age	Excludes Perinatal Lung Disease
Timing	Within 7 d of known ARDS risk factor
Pulmonary edema etiology	Not cardiac or fluid overload based
Oxygenation defect: mild PARDS	4≤ OI <8 or 5≤ OSI <7.5
Oxygenation defect: moderate PARDS	8≤ OI <16 or 7.5≤ OSI <12.3
Oxygenation defect: severe PARDS	OI ≥16 or OSI ≥12.3

Abbreviations: ARDS, acute respiratory distress syndrome; OI, oxygenation index; OSI, oxygenation saturation index; PALICC, Pediatric Acute Lung Injury Consensus Conference; PARDS, pediatric acute respiratory distress syndrome.

mechanical ventilation is initiated.[10] Even recent studies indicate that many patients with ARDS are not identified as such early in their course and sometimes are never properly diagnosed. Although therapies do not exist to reverse existing ARDS, it is well-known that improperly applied mechanical ventilation, fluid resuscitation, and/or sedation that results in improper patient/ventilator synchrony can quickly result in worsened ventilator-induced lung injury physiology. To date, randomized, controlled trials in adults and large observational studies in children have endorsed lung protective mechanical ventilation,[12] attainment of a euvolemic fluid balance (after shock has been reversed),[13–15] and goal-directed, nurse-implemented sedation.[16] Some of the recent Pediatric Acute Lung Injury Consensus Conference recommendations for ventilation in patients with PARDS[11] include physiologic tidal volume 3 to 8 mL/kg, increased positive end-expiratory pressure (PEEP) (up to 15 in severe ARDS) limiting plateau pressure to 28 cm H_2O, targeting saturations of 88% to 97%, targeting pH 7.15 to 7.30, and use of cuffed endotracheal tubes to maintain mean airway pressure and PEEP.

NEUROLOGIC EMERGENCIES

Pediatric neurocritical care focuses on timely recognition and stabilization of conditions that threaten central and peripheral nervous function. The recognition process begins in the ED. This section focuses on the advances in evaluation and management of pediatric traumatic brain injury and status epilepticus (SE). Routine ABCs and Advanced Trauma Life Support guidelines are not covered.

Traumatic Brain Injury

Traumatic brain injury (TBI) is the leading cause of death and disability in children in the United States, accounting for nearly 500,000 ED visits annually. The rate of injury after a fall is increasing and there remains a paucity of evidence on improving long-term neurologic outcomes.[17] For this reason, we prioritize immediate stabilization to prevent secondary injury—the primary goal of ED and ICU care. This begins and continues with ongoing vigilance of airway, breathing, and circulation. Secondary insults like hypoxia and hypotension have devastating effects on the injured brain.

Airway

Neuroprotective goals of airway management include prevention of hypoxia and hypercarbia. To accomplish this goal, ensure the patient has a patent airway and adequate level of consciousness to allow for adequate respiration. An experienced provider should intubate any patient with a Glasgow Coma Score of 8 or less, unstable facial fractures, and/or hemodynamic instability. Field intubations should be avoided unless performed by experienced personnel.[18] Oral intubation should be performed with attention to maintaining alignment of the cervical spine. Modified rapid sequence induction is recommended with additional support immediately available.

Evidence on optimal rapid sequence induction agents for trauma patients remains lacking.[19] Etomidate and a short-acting nondepolarizing agent such as rocuronium remain safe options for minimizing effects on hemodynamics and intracranial pressure (ICP), but concerns regarding the potential for adrenal insufficiency with repeated use remain. A narcotic with benzodiazepine plus neuromuscular blockade remains another option with the risk of hypotension, but the benefit of analgesia and anxiolysis. Ketamine is relatively contraindicated[20] out of concern for elevating the ICP, but recent evidence suggests this may be unfounded. Propofol should be avoided owing to dose-related hypotension,[19] with resultant hypoperfusion related secondary brain injury.

Breathing

Patients with TBI are at risk for lung injury from aspiration, pulmonary contusion, or neurogenic pulmonary edema after injury, requiring vigilance in ventilation and oxygenation strategies. Further, disordered control of breathing is common after TBI. The following are recommendations for neuroprotective strategies when mechanically ventilating patients with TBI.

- The use of end-tidal carbon dioxide capnometry is the standard of care in trauma resuscitation. Goal-directed ventilation aims for $Paco_2$ of 35 to 40 mm Hg, using end-tidal carbon dioxide as a surrogate.[21] Values of greater than 40 are associated with increased cerebral blood volume and resultant increases in ICP. Values of less than 35 increase the risk for long-term cerebral ischemia.
- Pulse oximetry should be used to achieve SpO_2 of 90% to 98%. Hyperoxia can cause additional free radical damage to the injured brain and should be avoided.
- The use of PEEP is controversial owing to increased intrathoracic pressure causing increased ICP. Generally, PEEP of 5 to 10 cm H_2O is safe.[22]
- Tidal volumes of 6 to 8 mL/kg are recommended.
- There is no evidence supporting superiority or inferiority of any single mode of ventilation.

Circulation

The primary aim in TBI resuscitation is to provide adequate blood supply to the injured brain by balancing cerebral blood volume with ICP. Hypotension should be addressed rapidly with crystalloid in 20 mL/kg aliquots. Once a patient has received 40 to 60 mL/kg of crystalloid, consider colloid resuscitation to prevent crystalloid toxicity. Targeted blood pressure (BP) management is aimed at maintaining an adequate cerebral perfusion pressure (CPP; **Table 2**). If vasoactive agents are needed to maintain CPP, norepinephrine remains the first-line agent.[23] Beware of hypotension without an increase in the heart rate, which is concerning for neurogenic shock and spinal cord injury; imaging should be obtained and neurosurgery contacted immediately.

Cerebral perfusion pressure

CPP is based on arterial BP monitoring or central venous pressure and ICP. Until the ICP monitor is placed, however, clinicians must rely on noninvasive BP and estimation of ICP. Discussions are ongoing regarding the appropriate CPP for age in children because the cerebral metabolic rate and cerebral blood flow vary from infancy to adolescence and adult standards may be inappropriate. Most pediatric trauma centers use an age-based guideline (see **Table 2**).

Table 2
Cerebral perfusion pressure goals by age

Age	mm Hg
0–5 y	>40
6–17 y	>50
>18 y	50–60

Data from Allen BB, Chiu YL, Gerber LM, et al. Age-specific cerebral perfusion pressure thresholds and survival in children and adolescents with severe traumatic brain injury*. Pediatr Crit Care Med 2014;15(1):62–70.

Radiologic evaluation

Emergent neuroimaging is indicated in all TBI.[24] Computed tomography scanning is the preferred modality because it will identify fracture, blood, midline shift, and cerebral edema. MRI is not indicated emergently, because most lesions with an acute intervention can be identified on computed tomography scans, which can be obtained more rapidly without need for anesthesia.

Invasive neuromonitoring

ICP monitoring is indicated for all patients with Glasgow Coma Score of 8 or less. Different types of monitors are available with the ultimate determination residing in the hands of the neurosurgeon. Externalized ventricular drains have the added benefit of cerebral spinal fluid drainage in addition to monitoring, whereas parenchymal monitors can only transduce pressure. Goal-directed management targets an age-based ICP and CPP (see **Table 2**).[25] A CPP of less than 40 mm Hg is associated with increased mortality and worse functional outcomes. Because not all systems are compatible, if the patient is to be transferred to another facility after monitor placement, it is imperative to ensure that the receiving facility can transduce ICP using the chosen modality.

Acute management of intracranial hypertension

The diagnosis of ICH is based on vital signs (bradycardia, hypertension, irregular respirations, pupillary examination, posturing) until invasive monitoring in place. As shown in **Fig. 1**, early management options including elevation of the head of the

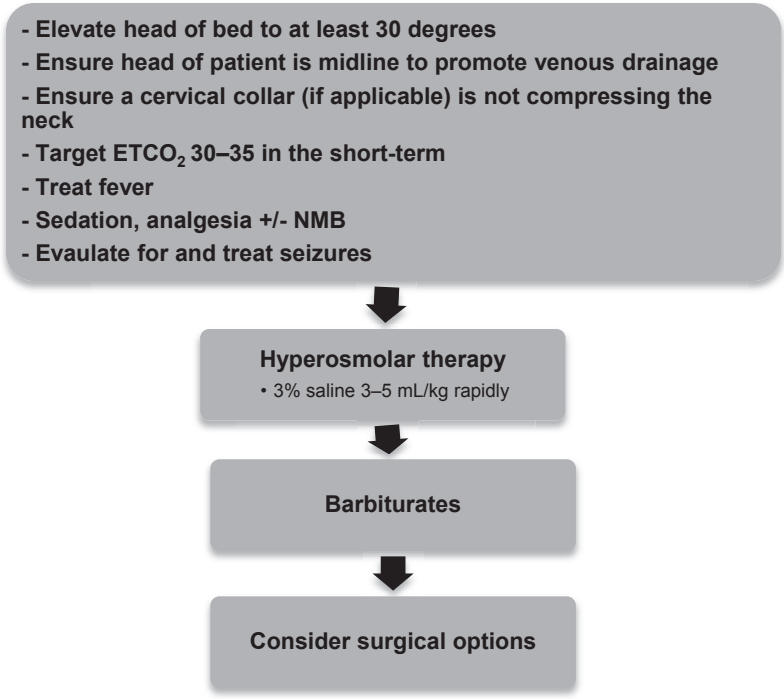

Fig. 1. Acute management of intracranial hypertension. $ETCO_2$, end-tidal carbon dioxide; NMB, neuromuscular blockade.

bed, placing the head midline, avoiding neck compression from a cervical collar, and mild hyperventilation. All can be performed at the bedside with minimal assistance and yet are brain saving. Other management options are vital, but require some coordination and planning and are reviewed herein.

Temperature regulation

Fever should be prevented in all patients with TBI. Normothermia is the goal, because hypothermia has no proven benefit. Begin with antipyretics, if no contraindication is present; however, cooling devices may be required.[26] If so, invasive temperature monitoring is needed and neuromuscular blockade should be used to prevent shivering. If your unit is unfamiliar with the use of cooling devices, seek an expert opinion.

Sedation

Adequate sedation and analgesia are the standard of care in trauma. Not only does this measure control symptoms associated with trauma, but also appropriate level of sedation will reduce cerebral metabolic rate and reduce ICP. Neuromuscular blockade should be used if ICP remains elevated despite adequate sedation and analgesia.

Seizures

Patients should be evaluated with electroencephalography (EEG) as clinically indicated. Seizures should be treated aggressively because they increase the cerebral metabolic rate and elevate the ICP. Prolonged seizures are associated with poor outcomes.

Hyperosmolar therapy

Hyperosmolar therapy is a mainstay in management of ICH, but the agent of choice is controversial. Hypertonic (3%) saline is more proven and recommended in the 2012 TBI guidelines.[27] Dosing for 3% saline is 3 to 5 mL/kg given rapidly, aiming for a goal sodium of 145 to 155 mmol/L. Patients may only require bolus dosing, but infusions are also helpful.[28] Mannitol is as effective, but carries significantly more risk, especially acutely. Mannitol has been associated with abrupt hypotension, which is increased in the presence of hypovolemia in trauma patients and can cause renal crystallization and acute kidney injury.[28]

Barbiturates

Barbiturates are extremely effective in decreasing the cerebral metabolic rate and ICP.[27] They carry significant risk, however. Barbiturates can cause diminished cardiac output, hypotension, and increased intrapulmonary shunting. They should not be used without invasive BP and ICP monitoring and expert consultation.

Surgical options

Decompressive craniectomy (DC) has been suggested for ICH refractory to maximal medical management. However, the utility remains controversial. Recently, 2 randomized controlled trials proved that early DC improves ICP and ICU duration of stay, but results in worse functional outcomes. The DECRA trial showed DC resulted in lower ICP, fewer interventions to control ICP, and a duration of shorter ICU stay, but increased mortality and worse functional outcomes.[29] The RESCUEICP trial showed that DC resulted in reduced mortality but increased incidence of vegetative state.[30]

STATUS EPILEPTICUS

SE is a continuous seizure for greater than 5 minutes or 2 or more discrete seizures between which there is incomplete recovery of consciousness. After 30 minutes

without recovery of consciousness, the brain suffers irreversible excitotoxicity.[31] Thus, it is within this window where we focus treatment efforts. The basics of management, including airway, breathing, and circulation, are not reviewed herein.

Etiology

SE is one of the most common neurologic emergencies in children. It is encountered in nearly 20 per 100,000 children-years[32] and more common in children less than 12 months of age.[33] In first-time seizures, 12% present in SE.[34] The most common causes of SE in children are infection with fever, low medication levels, and remote symptomatic causes.[35] Mortality of SE is less than 10%, but higher in cases of bacterial meningitis, metabolic disorders, and progressive neurodegenerative conditions.[32] If left untreated, cases of refractory SE carry the highest morbidity and mortality (16%–32%).[36]

Neurologic Monitoring

EEG is recommended for all patients in SE. For patients with refractory SE and other select patients, continuous EEG is preferred. Nearly one-half of patients who no longer have clinical seizures remain in nonconvulsive SE, so prolonged EEG should be considered.[37]

Imaging is deferred until seizures are controlled.[38–40] Once stable for imaging, MRI is preferred unless seizures are related to trauma. Cytotoxic edema from seizure can mimic acute stroke on MRI, so neuroradiology should be consulted. Emergent neuroimaging is reserved for patients with histories and physical examinations consistent with trauma or intracranial mass, but cessation of seizure activity takes priority.

Management

Antiepileptic drugs

A summary guideline is found in **Fig. 2**. For antiepileptic drug dosing and side effects, see **Table 3**. Children on existing antiepileptic drugs may not follow a traditional guideline because they may be dosed with medications they are already on, because they have been effective for these children in their past. Consult your pediatric neurologist for assistance.

The initial treatment of SE with benzodiazepines at 5 minutes remains the mainstay of treatment.[41] The dose may be repeated at 10 minutes (see **Fig. 2**). No single benzodiazepine has been found to be more effective than others, so give what is available by any mode available (intravenous, intramuscular, per rectum, etc). Intramuscular midazolam is as effective as intravenous for the cessation of seizures, preventing hospitalization, and preventing ICU admission.[42]

Refractory status epilepticus

After seizure has persisted for 20 to 30 minutes without return to baseline, 10% to 25% of SE becomes refractory.[43] This is also when disordered control of breathing becomes apparent. Early intubation is warranted if apnea, desaturation, or the inability to protect one's airway is present. The most commonly used agents in refractory SE are phenobarbital, fosphenytoin, valproic acid, and levetiracetam (see **Table 3**). Phenobarbital has falling out of favor in children less than 1 year of age owing to concerns for long-term cognitive impairment. Fosphenytoin is effective, but not without risk. It can cause arrhythmia, hypotension, and apnea. Additionally, to avoid cardiovascular collapse, it needs to be run over 30 to 60 minutes. Valproic acid is effective in aborting seizures but contraindicated in patients less than 2 years of age, those with hepatic dysfunction, and those with mitochondrial disorders. Levetiracetam

<table>
<tr><td colspan="2">1st Tier: Status Epilepticus
Within 5–20 min of seizure onset</td></tr>
<tr><td>If IV access:
• Lorazepam 0.1 mg/kg IV (Max 4 mg)
• Diazepam 0.2 mg/kg IV (Max 10 mg)
• Midazolam 0.2 mg/kg IV (Max 10 mg)
May repeat once after 5 min</td><td>If no IV access:
• Midazolam IN, buccal, or IM 0.2 mg/kg (Max 10 mg)
• Diazepam PR 0.2–0.5 mg/kg (Max 20 mg)
May repeat once after 5–10 min</td></tr>
<tr><td colspan="2">2nd Tier: Refractory Status Epilepticus
Within 20–30 min of seizure onset
Alert critical care team for ICU admission
Consult pediatric neurology and initiate EEG monitoring</td></tr>
<tr><td>Children 1–12 mo
• Phenobarbital 20–30 mg/kg IV
○ May repeat 10 mg/kg after 10 min
• Levetiracetam 60 mg/kg IV</td><td>Children > 12 mo
• Fosphenytoin 20 mg PE/kg IV or IM (Max 1500 mg PE)
○ May repeat 10 mg PE/kg after 10 min
• Levetiracetam 60 mg/kg IV (Max 2500 mg)
• Valproic Acid 20–40 mg/kg IV (No Max)</td></tr>
<tr><td colspan="2">3rd Tier: Super-refractory Status Epilepticus
Within 30–60 min of seizure onset
Proceed with endotracheal intubation</td></tr>
<tr><td colspan="2">Begin general anesthesia with a continuous infusion
Target cessation of seizure for 24–48 h
• Midazolam: Titrate infusion until cessation of seizure
○ Bolus 0.2 mg/kg IV (Max 10 mg)
○ Infusion start at 100–200 mcg/kg/hr
• If no cessation of seizure:
○ Repeat bolus 0.2 mg/kg (Max 10 mg) AND
○ Increase infusion by 50–100 mcg/kg/hr
• Dosing range 400–2000 mcg/kg/hr</td></tr>
<tr><td colspan="2">4th Tier: Super-refractory Status Epilepticus, continued
Beyond 60 min
If not intubated, intubate now</td></tr>
<tr><td colspan="2">Continue general anesthesia with a different agent
Target burst suppression for 24–48 h
• Pentobarbital
○ Bolus 5 mg/kg (No Max)
○ Infusion start at 0.5 mg/kg/hr
• If no burst suppression
○ Repeat bolus 2–5 mg/kg (No Max) AND
○ Increase infusion by 0.5 mg/kg/hr
• Monitor for bradycardia, hypotension, intestinal ischemia, and paralytic ileus</td></tr>
</table>

Fig. 2. Treatment Algorithm of Status Epilepticus in Children. EEG, electroencephalography; ICU, intensive care unit; IM, intramuscularly; IN, intranasally; IV, intravenously; PE, phenytoin equivalents; PR, per rectum.

has the best side effect profile and is becoming most providers' first agent after benzodiazepines.

Superrefractory status epilepticus

If seizure persists despite first- and second-line therapies, the child has superrefractory SE and general anesthesia is indicated.[44] Two commonly used agents to induce general anesthesia are administered intravenously—midazolam and pentobarbital. Both require a stable airway and continuous EEG monitoring. Arterial

Table 3
Antiepileptic agents for treatment of status epilepticus

Drug	Dose	Route	Side Effects
Lorazepam Diazepam Midazolam	0.1 mg/kg (maximum 4 mg) 0.2 mg/kg (maximum 10 mg) 0.2 mg/kg (maximum 10 mg)	IV IV, PR IV, IN, Buccal, IM	Respiratory depression Cardiovascular compromise
Phenobarbital	20–30 mg/kg	IV	Respiratory depression Cardiovascular compromise
Levetiracetam	60 mg/kg	IV	Somnolence
Fosphenytoin	20 mg PE/kg (maximum 1500 mg PE)	IV, IM	Respiratory depression Cardiovascular compromise Arrhythmia
Valproic Acid	20–40 mg/kg	IV	Contraindicated in patients <2 y and those with known hepatic failure or mitochondrial disease
Midazolam infusion	Starting dose 100–200 μg/kg/h	IV	Respiratory depression Cardiovascular compromise
Pentobarbital	Starting dose 0.5 mg/kg/h	IV	Respiratory depression Dose-related hypotension Bradycardia Paralytic ileus Intestinal ischemia
Propofol	Consult an expert	IV	PRIS Pain with injection Dose-related hypotension
Ketamine	Consult an expert	IV	Tachycardia Hypertension
Isoflurane	Consult an expert		Cardiovascular compromise Infection DVT Paralytic ileus

Abbreviations: DVT, deep venous thrombosis; IM, intramuscular; IN, intranasal; INH, inhaled; IV, intravenous; PE, phenytoin equivalents; PR, per rectum; PRIS, propofol infusion syndrome.

BP monitoring is recommended because they both can cause cardiovascular compromise.

Midazolam is generally accepted to be the first-line anesthetic agent. It works by enhancing the affinity at the gamma-amino butyric acid A ($GABA_A$) receptor, causing opening of chloride-gated channels. Once channels are open, the postsynaptic membrane is hyperpolarized, which renders the postsynaptic neuron resistant to excitation.[45] Midazolam at anesthetic doses is as effective in aborting SE as other intravenous anesthetic agents, yet has a lower mortality.[46] High-dose infusions control seizures in more than one-half of patients with refractory SE.[47,48] The use of high-dose infusions carries a similar side effect profile as low-dose infusions, but are superior in the cessation of seizure activity. Side effects include dose-related hypotension but at a lesser incidence (8%) than with other agents (71%).[49] Vasopressors are occasionally needed and epinephrine is the preferred agent.

Pentobarbital acts by binding the $GABA_A$ receptor and potentiating activity at chloride-gated channels, hyperpolarizing the postsynaptic membrane and making

the postsynaptic neuron less excitable—similar to midazolam. It is as effective at aborting seizures as midazolam,[45] but has a worse side effect profile. In addition to a higher incidence of hypotension, patients on pentobarbital require more days of mechanical ventilation and have an increased incidence of ventilator-associated pneumonias, bowel ischemia, and intestinal ileus.[50]

Other agents used to treat SE include propofol and ketamine infusions and inhaled anesthetics. These agents should not be used without consultation with anesthesia and intensive care. Propofol is a general anesthetic with direct activity at $GABA_A$ receptors. It is a potent anticonvulsant with a rapid onset and metabolism.[51,52] Dose-related hypotension is a known side effect and vasopressors are often needed. Propofol infusion syndrome is a life-threatening complication associated with prolonged propofol use. Propofol infusion syndrome was first described in children and is caused by mitochondrial dysfunction. Clinically, it presents as lactic acidosis, rhabdomyolysis, renal failure, and cardiovascular collapse. If present, propofol should be stopped immediately. Owing to the risk profile of propofol, it is not commonly used to manage SE in children.

Ketamine is an *N*-methyl D-aspartate antagonist that inhibits glutamate and limits neuronal excitation,[52] thus treating SE. Onset is rapid and patients suffer less hemodynamic instability than with other agents. Owing to its effect on the sympathetic nervous system, hypertension can occur. However, data on long-term exposure are limited and evidence on efficacy is lacking, so it is not commonly used.[53]

Inhaled anesthetics require consultation with pediatric anesthesia, the use of specialized equipment and personnel, and the presence of an endotracheal tube and arterial line. Although effective in controlling seizures, the impact of prolonged exposure is unknown and significant cardiovascular compromise can occur. Additionally, there remain logistical issues with administration and scavenging of gas, so it must be delivered in an operating room or the ICU.[54–56]

CARDIOVASCULAR EMERGENCIES IN PATIENTS WITH CONGENITAL HEART DISEASE

The Centers for Disease Control and Prevention report that congenital heart disease (CHD) affects 1% of births per year in the United States.[57–59] Twenty-five percent of patients born with CHD require surgery or other procedures in their first year of life. Prenatal diagnosis has drastically decreased the number of infants presenting to the ED in cardiogenic shock after closure of ductal-dependent lesions. However, nearly 1.5 million children are living in the United States with CHD and more than 20,000 patients with CHD are operated on annually; 55% are infants and 38% are children less than 18 years of age. The tremendous volume of CHD births, and those patients undergoing surgery, inherently results in these patients coming to EDs for intercurrent illnesses, and/or complications or worsening of their underlying disease processes. It is imperative for pediatric ED clinicians to accurately identify these patients, and to initiate and maintain appropriate care until the patient can be admitted to their destination PICU.

International data indicate that patients with CHD seeking ED care most often present sub acutely with acute respiratory illness, dysrhythmia, worsening cyanosis or heart failure, and other less frequent conditions.[59,60,61] For patients with palliated conditions, such as cavopulmonary anastomoses or Fontan physiology, any respiratory illness can be life threatening. These physiologies are predicated on passive return of venous blood flow to the right heart and, therefore, any condition that would increase transpulmonary pressure can result in severe cyanosis and death. These patients require aggressive, inpatient management of any pneumonic

process, pleural effusions, and pulmonary edema. Similarly, these patients do not tolerate a supine position or positive pressure ventilation. For patients with cyanotic heart disease, the hemoglobin should be checked because excessive hypoxemia may be mitigated with transfusion. Patients presenting with worsening cyanosis with underlying history of shunt physiology require immediate echocardiography to identify obstruction to blood flow that may also require urgent surgical or procedural attention. The patient and family should be queried about anticoagulation use at home and possible lapses in dosing, as well as intercurrent risk factors for acute dehydration that may also place the patient at risk for a hypercoagulable state.

Older children with a history of CHD surgery may often present to EDs with syncopal-type events owing to arrhythmias—whether heart block or, more commonly, atrial tachyarrhythmias, such as atrial flutter, because atrial enlargement over time after these surgeries may result in distortion of the conduction systems.

Finally, patients with CHD may have altered immune function,[61] whether asplenia (especially in complete atrioventricular canal and pulmonary atresia) or polysplenia (seen most commonly in interrupted inferior vena cava and total anomalous pulmonary venous return) as well as altered lymphocyte function in patients with DiGeorge syndrome or similar genetic abnormalities. Therefore, all ED clinicians managing patients with a history of CHD and presentation consistent with sepsis, even in its mildest forms, must have a high index of suspicion for the risk of bacterial sepsis and should aggressively diagnose and presumptively apply broad spectrum antibiotics until culture results are ascertained and an accurate history of the potential immunocompromised state is determined.

METABOLIC EMERGENCIES

The acute presentation of neonates and children with inborn errors of metabolism remains an important and anxiety-provoking consideration for both ED and PICU providers.[62,63] Certain inborn errors present most prominently in the neonatal period (amino acid disorders, organic acidemias, urea cycle defects, mitochondrial defects, peroxisomal defects, etc), whereas other patients who retain residual activity of deficient enzymes may present at a later age. Many of these diagnoses are autosomal recessive in inheritance. Fortunately, there are increasing numbers of treatment opportunities available, including but not limited to enzyme replacement therapy, special diets, substrate inhibitors, and even organ transplantation.

These patients often have an acute-on-chronic course heralded by recurrent "attacks" precipitated by fever, fasting, medications, and so on. Each inborn error can present with a variety of vague symptoms such as altered level of consciousness, seizures, hypoglycemia, sepsis, liver failure, and cytopenias, that can lead the practitioner down a primary pathway appropriate for that presentation (ie, antibiotics and cultures for presumed sepsis) but without prompt diagnosis of the underlying cause—the inborn error itself.

Common red flags on laboratory studies include an anion gap metabolic acidosis, presence or absence of lactic acidosis, presence or absence of ketosis, and hyperammonemia in some. If missed, persistent hyperammonemia can be a life-threatening complication soon after the ED presentation, because these patients must be quickly triaged to a PICU that can offer immediate hemodialysis and have access to metabolic disease specialists and pharmacies that can supply alternate hyperammonemia management such as sodium benzoate. In addition, sending blood and urine for quantitative amino acids and qualitative urine organic acids while in the ED is often imperative

for proper diagnosis of the patient because these derangements will be less evident as the patient convalesces.

Fortunately, more advanced diagnostics are also becoming standard of care, as is the newborn screening process,[64] so more of these patients are diagnosed before their first catastrophic presentation. More centers are being established as Pediatric Metabolic Disease Centers of Excellence providing structured programs and ED based guidelines for more efficient management. The family may be able to arrive to the ED in crisis but with their specific disease documentation in hand to quickly triage these patients to their appropriate therapeutic regimen.[65]

Management

- Manage the overt presentation (ie, antibiotics and cultures for presumed sepsis).
- Diagnose and manage the inborn error itself (as discussed).
  - NPO pending further deterioration.
    - Enteral feeds may be contributing to metabolic toxicity.
    - Start intravenous glucose and electrolytes.
- Contact a metabolic disease specialist and the PICU immediately.

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