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Emergency Department Management Of Seizures In Pediatric Patients

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Abstract

Seizures account for 1% of all emergency department visits for children, and the etiologies range from benign to life-threatening. The challenge for emergency clinicians is to diagnose and treat the life-threatening causes of seizures while avoiding unnecessary radiation exposure and painful procedures in patients who are unlikely to have an emergent pathology. When treating patients in status epilepticus, emergency clinicians are also faced with the challenge of choosing anticonvulsant medications that will be efficacious while minimizing harmful side effects. Unfortunately, evidence to guide the evaluation and management of children presenting with new and breakthrough seizures and status epilepticus is limited. This review summarizes available evidence and guidelines on the diagnostic evaluation of first-time, breakthrough, and simple and complex febrile seizures. Management of seizures in neonates and seizures due to toxic ingestions is also reviewed.

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CME Objectives

Upon completion of this article, you should be able to:

1. Identify life-threatening secondary causes of pediatric seizures.
2. Assess which patients require emergent neuroimaging.
3. Predict when laboratory investigations are likely to change patient management.
4. Identify options for treatment of status epilepticus that is unresponsive to benzodiazepines.

Prior to beginning this activity, see "Physician CME Information" on the back page.

Case Presentations

You are working a busy morning shift with a new medical student. You are reviewing the nursing notes for the 12-year-old boy who had a 2-minute generalized tonic-clonic seizure just after waking up. Just then, a 7-month-old girl is rushed in by panicked parents who say they were driving near the hospital when their daughter became unresponsive and was shaking in all her extremities for 1 minute. By the time you see her, she is awake and alert, and only wants to be held by her mother. Her temperature in triage is 40.5˚C. Your charge nurse comes to tell you that an ambulance is bringing in a 6-year-old boy with a known seizure disorder who is actively seizing. You ask the triage nurse to give the 7-month-old acetaminophen while you prepare for the 6-year-old patient. As you are running through medication dosing in for the 6-year-old, the medical student asks what laboratory tests you would order for each patient and if he should call for a CT scan for any of the patients…

Introduction

Seizures account for 1% of all emergency department (ED) visits for patients aged < 18 years and account for an even higher percentage of visits in some tertiary referral hospitals.[1,2] Each year, approximately 25,000 to 40,000 children in the United States experience their first nonfebrile seizure.[3,4] Seizures are especially common in infants and children aged < 5 years.[1] Infants aged < 1 year have the highest incidence of new unprovoked seizures in any age group.[5]

Seizures present special diagnostic and treatment challenges because the etiologies of seizures range from benign to life-threatening. Evaluation and treatment of seizures must be individualized based on the patient's presentation and the likely etiology. Management of a patient in status epilepticus requires simultaneous attention to respiratory and circulatory status, vascular access, and investigation into and treatment of reversible or life-threatening causes of seizure. However, well-appearing patients with self-resolved recurrent seizures or simple febrile seizures may not require any further investigation after a reassuring history and physical examination is completed. Unnecessary laboratory testing and radiation exposure should be avoided in these patients.

Critical Appraisal Of The Literature

A literature search was performed in PubMed using combinations of the search terms *pediatric, child, children, neonatal, neonate, seizure, febrile seizure, complex febrile seizure, status epilepticus, neuroimaging*, and *anticonvulsant*. The references of articles were reviewed to identify relevant publications. The National Guideline Clearinghouse and the Cochrane Library were also searched.

Searches of the clinical policies and guidelines of the American Academy of Pediatrics (AAP), the American College of Emergency Physicians (ACEP), the American Academy of Neurology (AAN), the Child Neurology Society, and the American Epilepsy Society were conducted. The only relevant ACEP clinical policy was a 2014 policy on evaluation and management of seizures in adults. Applicable AAP clinical policies dealt only with febrile seizures. Available guidelines do not address many questions that arise in the evaluation and treatment of seizures. Specific issues not addressed in published guidelines are the appropriate evaluation of complex febrile seizures and the role of newer anticonvulsants (such as levetiracetam) in the ED setting.

Etiology And Pathophysiology

Seizures can be either provoked or unprovoked. Provoked seizures occur in the context of a brain insult and may not recur when the underlying cause is resolved.[6] Triggers include head trauma, toxins, fever, electrolyte abnormalities, hypoglycemia, and other causes. Unprovoked seizures may be cryptogenic or may be the result of a brain malformation, disturbance of neuronal migration, or a genetic syndrome.

The most frequent provoked seizure in pediatric patients is a febrile seizure. According to the 2011 AAP guideline, febrile seizures are seizures associated with fever without central nervous infection, occurring in 2% to 5% of children.[7] Febrile seizures may be simple or complex. Simple febrile seizures occur in neurologically normal children aged 6 months to 5 years, last < 15 minutes, have no focal features, and do not recur within 24 hours. Febrile seizures not meeting all of these criteria are defined as complex febrile seizures. The differentiation between febrile seizure and seizure with fever due to intracranial infection is made after careful evaluation of the patient, and intracranial infection should be carefully considered in patients with multiple, prolonged, or focal seizures.

Although most seizures will self-resolve, a subset of patients will progress to status epilepticus and require anticonvulsant medication. Neuronal damage can occur with prolonged seizure activity, but the timing of damage is complex, multifactorial, and difficult to predict.[8] Morbidity and mortality from seizures are often due to hypoxemia or other systemic derangements, rather than direct neuronal damage from prolonged seizure activity. Although the International League Against Epilepsy defines status epilepticus as 30 minutes of continuous seizure activity or a series of seizures without return to baseline for 30 minutes, this definition is most appropriate for the purposes of epidemiologic studies.[9] One study of 407 children with a first-time unprovoked seizure found that if a seizure had not

resolved in 5 to 10 minutes, then it was unlikely to terminate in the following few minutes.[10] Therefore, an operational definition of status epilepticus as continuous seizure activity or a series of seizures, without return to baseline, lasting > 5 minutes is more appropriate for use in clinical settings to guide treatment of prolonged seizures.[8]

Differential Diagnosis

In order to identify the diagnosis, the emergency clinician must first determine whether the event was truly a seizure. Multiple diagnoses may mimic seizure activity. **(See Table 1.)** One life-threatening seizure mimic that may be seen in children is syncope due to cardiac disease (either a dysrhythmia or structural heart disease).[11]

Historical and physical examination findings consistent with seizure activity include the presence of a postictal period, bite marks to the side of the tongue, urinary incontinence, and stereotyped movement.[11]

The differential diagnosis of seizure etiologies is broad and includes multiple life-threatening etiologies that require time-sensitive diagnosis. **Table 2** lists potentially life-threatening causes of seizure.

The differential diagnosis for seizures in children varies from the differential in adults, and it also varies by the age of the child. Febrile seizures are generally seen in children between the ages of 6 months and 5 years. While head trauma is always a possibility in patients with active seizures or altered mental status, nonaccidental head trauma is an important consideration in infants and young children. In cases of abuse, the history given by caregivers is likely to be unreliable, so emergency clinicians must consider the possibility of occult head trauma even when a history of trauma is denied.

While patients of any age can have seizures due to electrolyte abnormalities, this is an especially important consideration in infants with seizure activity. Infants can develop seizures due to hyponatremia or hypernatremia if their formula is not properly prepared. Metabolic disorders can present at any age, but metabolic disorder is higher on the differential in a young infant presenting with a new-onset seizure.

Table 1. Seizure Mimics

- Psychogenic nonepileptic attacks (pseudoseizures)
- Breath-holding spells
- Movement disorders (eg, tics)
- Syncope
- Cardiac syncope due to dysrhythmia or structural heart disease
- Migraine variants
- Sleep disorders
- Gastroesophageal reflux disease
- Hypertonicity in a patient with cerebral palsy or anoxic brain injury
- Myoclonus while falling asleep or waking up or with startle (other types of myoclonic activity may represent seizure activity)

Prehospital Care

Seizures account for 10% to 12% of emergency medical services (EMS) calls for children.[12,13] As with all EMS transports, attention should be directed toward assessment and stabilization of the patient's airway, breathing, and circulation. Because hypoglycemia is a reversible cause of status epilepticus, blood glucose levels should be checked in patients with active seizures or altered mental status.

Patients with ongoing seizures are generally placed on oxygen by nonrebreather mask for transport. Apnea or shallow respirations seen in the atonic phase of a seizure are of particular concern in seizing patients, and EMS providers must be prepared to assist ventilation as necessary. This concern is compounded by the fact that the first-line treatment, benzodiazepines, can increase the risk of apnea. Bosson et al studied the risk factors for apnea in children transported by EMS for seizures. The rate of apnea was 4.5%, and, while administration of midazolam was a risk factor for development of apnea, prolonged seizure activity was associated with an even greater risk of apnea.[14] The authors concluded that, while benzodiazepines can increase the risk of apnea, the risk is outweighed by the benefits of early seizure termination. A randomized trial by Alldredge et al found that adults with status epilepticus who received benzodiazepines in the prehospital setting had a lower rate of respiratory or circulatory complications than those who received placebo.[15] Both of these studies support early treatment of status epilepticus with benzodiazepines by EMS providers.

Obtaining intravenous access in a seizing child can be challenging, and other routes of administration of medication may be necessary. In a large,

Table 2. Life-Threatening Causes Of Seizure

- Hypoglycemia
- Electrolyte disturbances (glucose, sodium, calcium, or magnesium)
- Inborn errors of metabolism
- Head injury (including nonaccidental trauma)
- Atraumatic intracranial bleed (such as ruptured arteriovenous malformation)
- Ischemic stroke
- Brain tumor
- Infection (including meningitis, encephalitis, and brain abscess)
- Toxins (including illicit drugs, medications, organophosphates, lead, and others)
- Withdrawal syndromes
- Hypoxemia
- Hypertensive encephalopathy
- Eclampsia

well-designed, noninferiority trial, intramuscular injection of midazolam was found to be at least as effective as intravenous lorazepam for termination of seizures in the prehospital setting.[16,17] Unfortunately, only 16% of patients in this study were aged ≤ 20 years. Another study performed in an ED setting compared the use of intranasal and intravenous lorazepam and found that intranasal lorazepam was not inferior in termination of seizure activity in children.[18] A small study in healthy adults found that intranasal lorazepam was absorbed faster than intramuscular lorazepam.[19] The use of intramuscular or intranasal routes of administration is a reasonable alternative to intravenous administration of benzodiazepines, especially when intravenous access is challenging and may delay transport and treatment.

Emergency Department Evaluation

History

The urgency and timing of obtaining the patient's history depends on the patient's presentation. A patient with active seizures or altered mental status requires immediate attention. Initial priorities are the assessment and maintenance of respiratory and circulatory status, the identification of potential causes of the seizure, and the establishment of vascular access. Key questions to ask caregivers immediately include any history of trauma, medical issues, medications, potential toxic exposures, and fever or illness prior to the seizure. Caregivers of young infants should be asked whether the infant has been fed tea, rice water, overly diluted formula, or other sources of free water. Powdered formula (with rare exceptions for specialty medical formulas) should be prepared in a ratio of 2 ounces of water to 1 scoop of formula. In infants and young children, inconsistencies in the history, the presence of other injuries or suspicious bruises, or a history of previous ED visits for injuries may be clues to inflicted injury and nonaccidental trauma. In adolescents, ingestions (either recreational or suicidal) must be considered. After stabilization, a more detailed developmental, past medical, and family history should be taken.

If there was a witness, a detailed description of the event is helpful. In the event of a partial seizure, the child may be able to provide this history. Specifically, this would include the behavior just prior to the event, whether there was loss of consciousness, a detailed description of the type of movement (including the body parts involved), whether the movements were bilateral, a history of incontinence, and behavior after the event.

Physical Examination

The emergent examination of an actively seizing patient includes complete vital signs (including core temperature), examination for evidence of trauma, and evaluation of respiratory status and blood pressure. A complete examination, with a detailed neurologic examination, should be completed as soon as possible. A glucose level should be obtained immediately in all actively seizing or mentally altered patients. Adolescent females should be assessed for pregnancy due to the possibility of seizures caused by eclampsia, which necessitates immediate delivery, and changes management drastically. An electrocardiogram (ECG) is warranted for first-time seizures if there is a possibility that the event was due to a dysrhythmia. Patients with a known seizure disorder should be asked about any recent changes in medication and missed or extra doses. Other common causes of breakthrough seizures in patients with epilepsy include fever, acute illness, and sleep disruption.

An important distinction in the evaluation is whether the seizure was generalized or partial. Generalized seizures occur when both hemispheres of the brain are involved. If motor activity is present with a generalized seizure, the motor activity is bilateral. Because both hemispheres are involved, there is loss of consciousness at the onset of the seizure. Focal, or partial, seizures occur when abnormal brain activity is restricted to one area of the brain. Depending on the location of the activity, consciousness may be intact (simple partial seizure) or impaired (complex partial seizure). Seizures may begin as focal seizures, but can then generalize.

Diagnostic Studies

Simple Febrile Seizures

In 2011, the AAP updated their clinical practice guidelines for the neurodiagnostic evaluation of a child with a simple febrile seizure. These, along with other national guidelines and literature reviews, recommend minimal routine testing in an otherwise healthy, well-appearing child presenting with a simple febrile seizure.[7,20-23]

Lumbar Puncture

What Are The Current Guidelines For Performing A Lumbar Puncture For A Febrile Seizure?

The AAP guidelines have changed since the 1996 version and no longer recommend routine lumbar puncture in well-appearing, fully immunized children presenting with a simple febrile seizure.[7] These changes are partly due to the significant decline in the overall incidence of bacterial meningitis in young children since the introduction of the *Haemophilus influenzae* type b (Hib) and pneumococcal conjugate vaccines.[24-26]

Current AAP guidelines state that a lumbar puncture should be performed in any child who presents with a seizure and a fever and has meningeal signs and symptoms or in any child whose

history or examination suggests the presence of meningitis or intracranial infection.[7] In an otherwise healthy appearing infant aged 6 to 12 months, a lumbar puncture is an option if the child is deficient in Hib or *Streptococcus pneumoniae* immunizations or if immunization status cannot be determined. A lumbar puncture is also an option if the child is pretreated with antibiotics, because antibiotic treatment can mask the signs and symptoms of meningitis. The decision to perform a lumbar puncture in a child who is underimmunized or pretreated with antibiotics will depend on many factors including the patient's age, ability to follow up, duration of antibiotic therapy, duration of fever, the emergency clinician's comfort assessing young children, and, potentially, parental preference. While a lumbar puncture is not required in all cases, there should be a lower threshold to perform a lumbar puncture in children who are underimmunized or pretreated with antibiotics.

A simple febrile seizure is almost never the sole manifestation of bacterial meningitis in children. A retrospective review by Green et al of 503 children diagnosed with meningitis found that 115 children (23%) presented with seizures.[27] The remaining children had other concerning signs and symptoms. Of the children in the study, 91% were obtunded or comatose after the seizure. Other children had nuchal rigidity, petechial rashes, or prolonged, focal, or multiple seizures. No child who presented with only a simple febrile seizure was found to have bacterial meningitis.

There is no current evidence that children presenting with their first simple febrile seizure have an increased risk for meningitis when compared to febrile children without seizures.[28-31] Lumbar punctures are not routinely necessary for simple febrile seizures, and should only be performed if there are signs and symptoms concerning for meningitis or other pathologies.

Other Testing For Serious Bacterial Illness

The most recent AAP guidelines recommend evaluation to identify the underlying cause of the fever in simple febrile seizures; however, in the absence of abnormal findings on history or physical examination, routine laboratory studies are of limited value.[7,22]

Routine complete blood cell count and blood culture are not recommended unless otherwise indicated by history and physical examination. Children with first-time simple febrile seizures carry the same rate of bacteremia and serious bacterial illness as febrile children without seizures.[28,32] Teran et al studied 182 children with simple febrile seizures. Of these children, 93% had blood cultures performed, and only 1 was positive for *Salmonella*.[33]

A chest x-ray, urinalysis, and urine culture may be helpful in determining the cause of the fever. The presence of urinary tract infections in children with first-time simple febrile seizures is similar to that of febrile children without seizures, with an incidence of 5.9% in one retrospective study.[28] Emergency clinicians are encouraged to follow the AAP guidelines for diagnosis and management of urinary tract infections based on patient sex and age. In the same cohort, approximately half of the patients received chest x-rays, of which 12.5% were consistent with pneumonia. In another study, 6.9% of patients grew pathogenic organisms on urine culture, and chest x-rays were abnormal in 9.5% of patients in the study.[33] Not all patients in these studies had a chest x-ray, and, presumably, chest x-rays were ordered in children with other signs and symptoms of lower respiratory tract infection. The decision to order a chest x-ray should be based on signs and symptoms of lower respiratory tract infection, and not solely because the child had a febrile seizure.

Electrolyte Panels

Metabolic and electrolyte profiles should not be performed routinely for children presenting with their first febrile seizure.[7,34] A retrospective study of 108 children with first and repeat febrile seizures found no abnormal test values that were thought to have caused the seizure.[35] The most common abnormality was an elevated potassium level in 7% of patients, which was attributed to the venipuncture technique. Serum hyponatremia occurred in 3% of patients, but this did not change management. No patient had hypoglycemia. Other studies found no significant electrolyte abnormalities.[33,36,37] In the absence of clinical evidence of electrolyte abnormalities, routine electrolyte testing is not required in well-appearing children with simple febrile seizure who have returned to baseline mental status.

Neuroimaging

The AAP guidelines state that neuroimaging should not be performed in the routine evaluation of the child with a simple febrile seizure.[7] Most of the evidence for this recommendation comes from retrospective studies. Al-Qudah et al reviewed head computed tomography (CT) scans of 38 patients who presented with simple febrile seizures, and 14 had no abnormalities.[38] Warden et al also found no abnormalities on imaging studies of children meeting criteria for simple febrile seizures.[39] Garvey et al studied 99 children who presented with a simple or complex first febrile seizure. Seven had findings on CT scan that required further intervention.[40]

One prospective cohort study evaluated magnetic resonance imaging (MRI) brain abnormalities within 1 week of a first febrile seizure in children aged 6 months to 5 years.[41] They found definite abnormalities in 11.4% of children presenting with simple febrile seizures, but no findings changed clinical management. Abnormalities consisted mostly of subcortical focal hyperintensities, abnormal white

matter signaling, or focal cortical dysplasias. Although neuroimaging may provide earlier diagnosis of structural lesions, it rarely changes acute management in patients with simple febrile seizures.

Electroencephalography

An electroencephalogram (EEG) should not be performed in the evaluation of a neurologically healthy child with a simple febrile seizure.[7,42] The reported incidence of EEG abnormalities in children with febrile seizures is quite varied, but abnormal EEG findings have not been found to be predictive of an increased risk for recurrence of febrile seizures.[43-45] There is some controversy on the usefulness of EEG in predicting development of future epilepsy, but this is unlikely to alter management in the emergency setting.[46,47]

Complex Febrile Seizures

Approximately one-third of febrile seizures are classified as complex.[48] There are currently no consensus recommendations for the evaluation and management of complex febrile seizures. Given the lack of national guidelines and the lack of heterogenicity of patient presentations, extensive variability in management of children with a complex febrile seizure was found among pediatric emergency clinicians.[49] Unfortunately, the available studies combine patients with focal febrile seizures, prolonged febrile seizures, and multiple febrile seizures. In most studies, the majority of children present with multiple febrile seizures, but all the studies were small enough that the possibility of significant pathology in any one subset could not be excluded. A review of available data is presented here, but caution must be maintained in management, as patients with complex febrile seizures must be closely evaluated, and a lower threshold for diagnostic evaluations, such as lumbar puncture and neuroimaging, is wise. Factors such as patient age, details of presentation, immunization status, and pretreatment with antibiotics are especially important in these cases.

Lumbar Puncture

The majority of febrile seizures associated with bacterial meningitis are complex.[27,34] However, complex febrile seizures are rarely the only presenting sign of acute bacterial meningitis.[34,50] Multiple retrospective reviews have analyzed the incidence of acute bacterial meningitis in children presenting with a complex febrile seizure. In a study by Kimia et al, lumbar puncture was performed in 340 out of 526 patients, and 3 were diagnosed with acute bacterial meningitis. Two of these children had other signs or symptoms; however, 1 child appeared well. That patient's cerebrospinal (CSF) sample was contaminated with blood. The CSF culture was without growth, but her blood culture grew S*treptococcus pneumoniae*, and she was treated for suspected acute bacterial meningitis.[50] According to a study of 366 total patients by Seltz et al, out of 146 patients who underwent lumbar puncture, 6 patients were found to have bacterial meningitis, and 1 was diagnosed with herpes simplex virus encephalitis. They were all noted to have decreased responsiveness.[51]

Boyle and Sturm reported on 199 patients diagnosed with complex febrile seizures, of whom 37% underwent lumbar puncture.[52] No abnormal CSF findings were noted. The data from this and other retrospective studies suggest that the incidence of acute bacterial meningitis in children presenting with complex febrile seizures is low, and routine lumbar puncture is likely unnecessary. The need for a lumbar puncture should be based on clinical suspicion and signs and symptoms suggestive of meningitis or encephalitis, with a lower threshold to perform lumbar puncture if the patient has any other risk factors for meningitis.[32,50,53-55]

Other Testing For Serious Bacterial Illness

Retrospective data also suggest that bacteremia, urinary tract infection and pneumonia are rare in an otherwise healthy-appearing child presenting with a complex febrile seizure.[33,52,53] The incidence of urinary tract infections and pneumonia in children presenting with complex febrile seizures appears to be similar to that of children with simple febrile seizures and fevers without seizures.[52,53] In Teran et al's study, 32 of 37 patients had chest x-rays, and 4 (12%) were read as abnormal.[33] The authors of that study did not state if there were other indications for ordering the chest x-ray.

Neuroimaging

Complex febrile seizures are rarely the only sign of intracranial pathology. Emergent neuroimaging should be based on signs and symptoms suggestive of a hemorrhage, brain abscess, or increased intracranial pressure. All available studies are small, but suggest a low yield from routine neuroimaging for all complex febrile seizures. Kimia reported on 526 patients with complex febrile seizures, and 268 patients underwent head CT scans, 6 had MRI scans, and 8 had both studies.[56] Only 4 patients had findings on neuroimaging, which included frontoparietal hematoma, subdural hematoma, encephalomyelitis, and a low-density lesion in the cerebellum. These patients had other signs of intracranial pathology, including multiple days of emesis, abnormal mental status, multiple bruises concerning for nonaccidental trauma, multiple days of fever and vomiting, nystagmus, photophobia, stiff neck, residual hemiparesis, and sleepiness. Other studies have shown that findings of imaging abnormalities, including subcortical focal hyperintensities and abnormal white matter signaling, did not change management.[33,41,52,57]

These studies and others suggest that routine neuroimaging is not necessarily indicated in otherwise healthy, neurologically normal, and well-appearing children who present with prolonged or multiple febrile seizures.[40,58] However, emergency clinicians should be aware that there are no clinical guidelines and only limited evidence on this topic. Focal febrile seizures were relatively uncommon in these studies, and, because neuroimaging is recommended in first-time afebrile focal seizures, neuroimaging is probably prudent in focal febrile seizures.

Electroencephalography

Similar to simple febrile seizures, the utility of an EEG in well-appearing children with complex febrile seizures is limited. The reported incidence of EEG abnormalities in children with febrile seizures is quite varied.[43,45] One study reported normal postictal sleep EEGs in 33 patients with complex febrile seizures and predicted the rate of EEG abnormalities in otherwise normal children with complex febrile seizures to be ≤ 8.6%.[59] However, abnormal EEG findings have not been found to be predictive of an increased risk for recurrence of febrile seizures, and their value in predicting the subsequent development of epilepsy is still controversial.[42,44,45] There is no convincing evidence for an emergent EEG in an otherwise healthy appearing child presenting with a complex febrile seizure.[60]

First Nonfebrile/Unprovoked Seizure

After stabilizing the patient, assessment for provoking factors such as trauma or toxic ingestion should be undertaken. If no provoking factors are present, then it may be a first unprovoked nonfebrile seizure. In the year 2000, the AAN released practice parameters addressing the evaluation of first nonfebrile seizures in children. The AAN practice parameters and other literature reviews and proposed guidelines recommend individualized assessment for determining further diagnostic management.[3,61,62]

Lumbar Puncture

There is very little evidence regarding the yield of a routine lumbar puncture after a first nonfebrile seizure; and, in the otherwise healthy appearing child, lumbar puncture is likely of limited value. In a retrospective review, 33 out of 134 infants presenting with a nonfebrile seizure underwent a lumbar puncture.[37] No CSF abnormalities were reported. The decision to perform a lumbar puncture should be based on signs and symptoms suspicious for meningitis, meningoencephalitis, or subarachnoid hemorrhage. In children too young or developmentally delayed to clinically evaluate mental status or depending on the clinician's comfort in assessing the patient, the threshold to perform a lumbar puncture should be lower.

Electrolyte Panels

The AAN practice parameters state that laboratory tests should be ordered based on individual clinical circumstances.[3] Routine serum chemistries in children presenting to the ED with a first nonfebrile seizure are of extremely low yield, and the clinical history and physical examination should be used to direct testing.[63,64] In a prospective study, Turnbull et al reported on 136 patients (16 children and 120 adults) who presented with a new-onset nonfebrile seizure. Eleven adult patients (but no children) were found to have correctable laboratory abnormalities that were felt to have contributed to or caused the seizure; however, all but 2 cases were suspected based on history or physical examination.[64]

Studies on laboratory testing in new-onset afebrile seizures have shown minimal metabolic or electrolyte abnormalities.[35,36,65] Scarfone identified 70 infants with a first nonfebrile seizure (including status epilepticus). Fifty-one infants underwent laboratory testing, and 8 were found to have clinically significant abnormalities, 4 with hyponatremia, and 4 with hypocalcemia. These abnormalities were found most commonly in infants who were actively seizing in the ED, had a temperature < 36.5°C, or who were aged < 1 month.[37] Although routine laboratory studies in a well-appearing child with a first nonfebrile seizure are unlikely to change management, clinically significant abnormalities are more likely in certain subgroups of patients. Laboratory testing (including sodium, magnesium, calcium, phosphorous, and glucose levels) should be strongly considered in infants, especially neonates, and in any child with repeated or continuing seizures in the ED.

Toxicology Screening

The AAN practice parameters recommend toxicology screening only if there is any suspicion of drug exposure or substance abuse.[3] The ACEP clinical policy for management of adult patients with seizures also does not recommend routine toxicology screening.[66] One caveat for pediatrics is that, in young children, illicit drug ingestion can imply neglect or abuse. In young children, if illicit drug ingestion is suspected, a toxicology screen or drug level could change management and disposition.

Neuroimaging

As the long-term risks of radiation in children are now better appreciated, it is important to determine which patients with first-time seizures require emergent neuroimaging. Abnormalities on neuroimaging are seen in about one-third of children with a first seizure, but most abnormalities do not influence treatment. Guidelines published in 2009 from the International League Against Epilepsy state that 2% to 4% of children with new-onset seizures have

neuroimaging findings that could alter immediate management; however, significant imaging abnormalities were rare in the absence of a focal seizure, abnormal neurological examination, or focal EEG abnormalities. Children aged > 2 years with generalized seizures, normal examinations, and normal EEGs, or only generalized EEG abnormalities were unlikely to benefit from neuroimaging.[67] An evidence-based review in 2007 found abnormalities that could change acute management in 3% to 8% of head CT scans, with an even higher yield in patients with focal seizures, predisposing history, abnormal neurologic examination, or age < 6 months.[68]

In a prospective study of 411 children with a first nonfebrile seizure, 218 patients had imaging studies performed.[69] Forty-five of the 218 children (21%) had abnormal imaging studies, with the most common abnormalities being focal encephalomalacia and cerebral dysgenesis. Four children (2 with brain tumors and 2 with neurocysticercosis) required intervention. The 2 children with neurocysticercosis presented in status epilepticus and 1 clearly had focal seizure onset. One child with a medulloblastoma presented with staring and respiratory arrest and had an abnormal neurological examination. The other child with a brain tumor presented with a focal seizure.[69] Stroink et al prospectively followed 156 children aged 1 month to 16 years, and 112 had head CT scans.[70] Twelve were found to have abnormalities (mostly atrophy), but none required further management.

Sharma et al reported on 500 patients of whom 38 had significant abnormalities on neuroimaging, 3 requiring urgent operative interventions. They found that children were at low risk of clinically significant abnormal neuroimaging if they were aged > 33 months, did not have a focal seizure, and lacked predetermined predisposing conditions (eg, sickle cell disease, bleeding disorders, cerebrovascular disease, malignancy, human immunodeficiency virus, hemihypertrophy, hydrocephalus, exposure to cysticercosis, and closed head injury).[2] In a prospective study, Hsieh et al investigated the yield of neuroimaging in infants aged 1 to 24 months with new-onset afebrile seizures. Of the 317 patients, 298 had head CT scans, and 105 (35.2%) showed abnormal findings, with 27 abnormalities (9%) that changed acute management. In that cohort, younger patients were more likely to have abnormalities on neuroimaging.[71]

A complete history and thorough examination—including a detailed neurologic examination—is necessary in any child presenting with a new-onset seizure. Patients with abnormal neurologic examinations, signs of increased intracranial pressure, altered mental status, or suspicion of trauma require emergent imaging. The AAN practice parameters suggest emergent neuroimaging for any child who exhibits a postictal focal deficit that does not resolve quickly or who has not returned to baseline within several hours after the seizure.[3] The practice parameter does not give exact guidance on how long clinicians should wait for a child to return to baseline before obtaining imaging, and emergency clinicians must make a judgment based on the complete clinical picture, including the patient's level of responsiveness, whether or not the patient's mental status is improving, and whether medications were given that could have contributed to the altered mental status.

The AAN practice parameters also suggest that an MRI scan within several days should be seriously considered in any child with a significant cognitive or motor impairment of unknown etiology, unexplained abnormalities on neurological examination, a partial-onset seizure, an abnormal EEG not consistent with a benign partial epilepsy of childhood or primary generalized epilepsy, or in children aged < 1 year.

While the AAN does not recommend emergent neuroimaging for children with new-onset focal seizures, the literature suggests that neuroimaging is more likely to be abnormal in these cases. Since focal seizures are more likely to be associated with abnormalities on neuroimaging, many clinicians choose to order head CT scans on patients with new-onset focal seizures. However, in otherwise well-appearing patients with normal neurological examinations who can receive a timely outpatient MRI, it may be reasonable to defer neuroimaging. Compared to head CT, MRI has superior resolution, versatility, and does not expose patients to ionizing radiation. MRI can be helpful in establishing an etiology and determining prognosis, but rarely alters acute management.

Electroencephalography

The AAN practice parameters recommend an EEG as part of the neurodiagnostic evaluation of a child with an apparent first unprovoked seizure. An EEG is helpful in determining the seizure type, epilepsy syndrome, and risk for recurrence, and its results, therefore, may affect further management decisions.[72,73]

The optimal timing for the EEG is unclear. Doescher et al prospectively performed EEGs on 181 neurologically normal school-aged children within 3 months of a first-time seizure. Fifty children had normal EEGs, and the remaining 131 had epileptiform activity or slowing noted.[74] Stroink et al performed at least one EEG on 156 patients (aged 1 month to 16 years) with a first unprovoked seizure. Eighty-eight children (56.4%) were found to have epileptic discharges.[70] Although EEG abnormalities are common in children with seizures, there is no evidence that the EEG must be completed before discharge from the ED. An EEG can be performed as an outpatient along with consultation or follow-up with a pediatric neurologist.

Status Epilepticus

As in all presentations to the ED, the evaluation will depend on the clinical status of the patient. The patient who was in status epilepticus but quickly stopped seizing after treatment by paramedics or by clinicians in the ED and who has returned to baseline may demand significantly less workup than the patient who cannot be evaluated due to continued seizure activity, altered mental status, or intubation. The AAN published practice parameters for the diagnostic assessment of a child with status epilepticus in 2006.

Lumbar Puncture

The AAN practice parameters state that there are insufficient data to support or refute routine lumbar puncture in children for whom there is no clinical suspicion of a central nervous system (CNS) infection,[75] and our search revealed limited evidence regarding the yield of a routine lumbar puncture in children with status epilepticus. According to a prospective study by Chin et al of 226 children with status epilepticus, 95 had a first episode of febrile status epilepticus.[76] Among these children, 11 (12%) were diagnosed with acute bacterial meningitis, and 7 (8%) were diagnosed with a viral CNS infection. In another study of 144 children with seizures lasting ≥ 20 minutes, 89 children (including 59 febrile children) had a lumbar puncture.[77] All cultures were negative, but 13 were diagnosed with a primary CNS infection based on clinical symptoms, CSF pleocytosis, and EEG and imaging findings.

Emergency clinicians should maintain a high level of suspicion for meningitis or meningoencephalitis in children with otherwise unexplained status epilepticus, particularly in febrile patients and patients with ongoing seizure activity or altered mental status. In patients with a clinical suspicion for meningitis or encephalitis, antibiotics and, possibly, acyclovir should be given immediately. The lumbar puncture should be performed as soon as is feasible once the patient is stabilized.

Other Testing For Serious Bacterial Illness

The value of routine blood cultures in children presenting with status epilepticus is unknown and is inadequately reported in the literature. The AAN practice parameters concluded that there were insufficient data to support or refute routine blood cultures in children with no clinical suspicion of infection. Systemic infections can lower the seizure threshold, and bacterial infection should be considered in children with unexplained status epilepticus. Chin's study of 226 children with status epilepticus identified 21 children with a previous neurologic abnormality whose status epilepticus was attributed to a febrile intercurrent illness.[76] Bassan et al prospectively evaluated 60 children with febrile seizures lasting > 15 minutes and identified 1 case of bacteremia.[78] A blood culture should be obtained if there is clinical suspicion for a systemic infection.

Electrolyte Panel

It is common practice to obtain a chemistry panel in children presenting with status epilepticus. The AAN practice parameters did not make recommendations on this practice, but reported that electrolyte abnormalities or basic metabolic disorders were present in an average of 6% (range 1%-16%) of children with status epilepticus.[75] Studies have shown that patients presenting in status epilepticus can occasionally have an etiology of electrolyte abnormalities.[77,79] Since electrolyte abnormalities are easily identifiable and treatable causes of seizure and the available studies have reported patients with abnormalities, an electrolyte panel should be sent in patients with ongoing seizure activity or altered mental status.

Toxicology Screening

The AAN practice parameters suggest toxicology screening in children with status epilepticus when there is suspicion of drug exposure or substance abuse or when no apparent etiology is identified. Two literature reviews found the frequency of ingestion as a causative etiology in at least 3.6% of cases of status epilepticus.[75,80] Medications cited as causing status epilepticus (such as tricyclic antidepressants and theophylline) are currently less commonly prescribed, but ingestion is an important consideration in cases of unexplained status epilepticus.

Singh et al performed toxicology screens on 61 of 144 children with status epilepticus, and all were negative.[77] Dunn discovered 6 patients with toxic drug levels in a 1988 study of 97 patients with status epilepticus.[79] Routine urine toxicology screens test for a limited number of drugs of abuse, and these are less likely to be responsible for seizures in children compared to adults. Ingestion should be considered in cases of unexplained status epilepticus, and, if suspected, specific serum drug levels or other toxicologic testing should be performed.

Neuroimaging

Neuroimaging is indicated if there is any clinical evidence of emergent pathology, and it should be considered if the etiology of status epilepticus is unknown. Neuroimaging should be performed after the child is stabilized and seizure activity is controlled.[75] Neuroimaging has been reported to impact management in 24% of patients, but not all management changes were emergent.[77] At least 8% of children with convulsive status epilepticus are thought to have imaging abnormalities, but only a small percentage of these findings change ED management.[75] MRI is more sensitive and specific than head CT, but a CT scan should be performed emergently if there

are concerns for trauma, infarction, hemorrhage, or increased intracranial pressure.

Electroencephalography

The AAN practice parameters suggest that an EEG should be considered in a child presenting with new-onset status epilepticus.[75] Multiple studies have shown that a significant percentage of children presenting with status epilepticus have EEG abnormalities.[73,77-79,81] Singh et al prospectively followed 144 children presenting with status epilepticus, of whom 139 had EEGs within 24 hours of presentation. Five demonstrated electrographic seizures, with 4 cases showing nonconvulsive status epilepticus.[77] An emergent EEG should be considered for persistent seizure activity, persistently depressed level of consciousness after a prolonged seizure, or signs of nonconvulsive status epilepticus such as altered behavior, tachycardia, or eye deviation.[82]

Known Seizure Disorder/Epilepsy

There are currently no national guidelines for ED management and treatment of children with known epilepsy who present with a breakthrough seizure or increased seizure frequency.

Laboratory Testing

Routine laboratory studies in the otherwise well-appearing child with known epilepsy is likely of limited value; however, checking anticonvulsant drug levels may be helpful for management, as either low or toxic drug levels may lead to increased seizures. Three small studies did not identify any clinically significant laboratory levels in patients with recurrent seizures.[35,36,65] However, in a study by Eisner, 96 of 163 patients had subtherapeutic antiepileptic drug levels and received further treatment.[63] In one prospective study, antiepileptic medications levels were checked in 54 out of 107 patients, and 30 (60%) had subtherapeutic levels.[65] Eighty-seven percent of those patients reported being compliant with medications.

Based on the available data, electrolyte panels are unlikely to change management in patients with recurrent seizures in the absence of a suggestive history, or potentially young age. Anticonvulsant drug levels may provide important information for diagnosis and treatment. Unfortunately, rapid turnaround time for anticonvulsant drug levels is only available for a limited number of anticonvulsant medications. Drug levels should be sent if the result will be available during the ED visit or, potentially, if the patient's neurologist will be able to follow up on results with longer turnaround times.

Neuroimaging

The AAN found that the evidence is inadequate to support or refute the usefulness of emergency CT scan in patients with chronic seizures presenting with a recurrent seizure.[3] The majority of children who present to the ED with recurrent seizures should not require neuroimaging in the absence of new neurological abnormalities or clinical evidence of head trauma.

Table 3 (see page 11) summarizes the recommendations for diagnostic studies in seizures.

Treatment

Fortunately, the majority of seizures will have terminated by arrival to the ED, and many patients will not require any emergent interventions. Patients with persistent or recurrent seizures may require more aggressive management and intervention.

Airway

Airway management is a first priority in treating patients with ongoing seizure activity or altered mental status. Unfortunately, there is little evidence to guide the decision of when to intubate a patient with ongoing seizure activity, and available guidelines on treatment of status epilepticus often do not address the issue. Recommendations published in 1993 by the Epilepsy Foundation of America state only that assisted ventilation is likely to be needed when phenobarbital or pentobarbital is administered after benzodiazepines.[83] The ACEP published a clinical policy on management of seizures in adults and did not address advanced airway management.[66] A United Kingdom practice guideline on status epilepticus in children did recommend intubation if first- and second-line treatments fail to stop seizure activity,[84] but the authors were unable to find controlled studies to support this recommendation.

Abend and Dlugos published a literature review and proposed a treatment protocol for refractory status epilepticus that states that the airway should be supported as needed, but did not suggest routinely securing the airway until after failure of third-line medications and admission to the pediatric intensive care unit.[85] Not surprisingly, Lewena et al found wide practice variation in intubation rates for prolonged seizure activity between medical centers.[86] Emergency clinicians must make decisions about advanced airway management based on the patient's clinical status, including oxygen saturation, oxygen requirement, and the patient's ability to protect the airway. Patients who must leave the ED for emergent neuroimaging pose a special challenge, and the decision may be made to intubate a borderline patient who requires emergent imaging. For additional information on management of the pediatric airway, refer to the January 2013 issue of *Pediatric Emergency Medicine Practice* titled "Evidence-Based Emergency Management Of The Pediatric Airway," available at: www.ebmedicine.net/pediatricairway.

Table 3. Summary Of Recommendations For Diagnostic Studies For Seizure Disorders

Diagnostic Study	Recommendation
Simple Febrile Seizures	
Lumbar puncture	• Not recommended for well-appearing, fully immunized children. • Lumbar puncture should be performed if there are signs and symptoms of meningitis or encephalitis. • Maintain a lower threshold for lumbar puncture in children pretreated with antibiotics or with incomplete vaccination history.
Other testing for serious bacterial illness	• CBC and blood culture not recommended unless indicated by history and physical examination. • Urinalysis and urine culture may be helpful in determining the cause of the fever. • Chest x-rays should be ordered based on signs and symptoms of lower respiratory tract infection.
Electrolyte panels	• Not recommended for children with self-limited seizures who have returned to baseline mental status.
Neuroimaging	• Not recommended.
Electroencephalography	• Not recommended.
Complex Febrile Seizures	
Lumbar puncture	• Lumbar puncture should be performed if there are signs and symptoms of meningitis or encephalitis. • Maintain a lower threshold for lumbar puncture in children pretreated with antibiotics or with incomplete vaccination history.
Other testing for serious bacterial illness	• CBC and blood culture not recommended unless indicated by history and physical examination. • Urinalysis and urine culture may be helpful in determining the cause of the fever. • Chest x-rays should be ordered based on signs and symptoms of lower respiratory tract infection.
Neuroimaging	• Consider for focal or prolonged complex febrile seizures or persistent altered mental status. • Perform for signs and symptoms of brain abscess, increased intracranial pressure, or hemorrhage.
Electroencephalography	• Not recommended.
First Nonfebrile/Unprovoked Seizure	
Lumbar puncture	• Lumbar puncture should be performed if there are signs and symptoms of meningitis, encephalitis, or subarachnoid hemorrhage. • A lower threshold should be maintained for children too young or developmentally delayed to clinically evaluate mental status.
Electrolyte panels	• History and physical examination should be used to guide testing. • Strongly consider in infants (especially neonates) and in any child with repeated or continuing seizures.
Toxicology screening	• Consider only if there is suspicion of drug exposure or substance abuse.
Neuroimaging	• Recommended for patients with an abnormal neurologic examination, signs of increased intracranial pressure, altered mental status, or suspicion of trauma. • Recommended for patients who exhibit a postictal focal deficit that does not resolve quickly or for patients who have not returned to baseline within several hours after the seizure. • Consider head CT for patients with new-onset focal seizures or in patients aged < 2 y. • Imaging can be deferred in otherwise well-appearing patients with normal neurological examinations who receive a timely outpatient MRI.
Electroencephalography	• Recommended, but can be performed as an outpatient in consultation with a neurologist.
Status Epilepticus	
Lumbar puncture	• Not recommended for routine assessment. • Lumbar puncture should be performed if there are signs and symptoms of meningitis or encephalitis. • Maintain a lower threshold for lumbar puncture in children pretreated with antibiotics or with incomplete vaccination history.
Other testing for serious bacterial illness	• Should be considered if there is suspicion of a systemic infection.
Electrolyte panels	• Recommended.
Toxicology screening	• Consider if there is suspicion of drug exposure or substance abuse or if no apparent etiology is identified.
Neuroimaging	• Recommended for patients with first-time seizures with ongoing status epilepticus or altered mental status, unless there is a known etiology.
Electroencephalography	• Should be considered in a child presenting with new-onset status epilepticus, persistently depressed level of consciousness after prolonged seizure, or signs of nonconvulsive status epilepticus (eg, altered behavior, tachycardia, or eye deviation).
Known Seizure Disorder/Epilepsy	
Laboratory testing	• Recommended to check patient medication levels.
Neuroimaging	• Not recommended in the absence of new neurological abnormalities or clinical evidence of head trauma.

Abbreviations: CBC, complete blood count; CT, computed tomography; MRI, magnetic resonance imaging.

Anticonvulsant Medications

There are currently more than 20 medications available for the treatment of seizures. In the last decade, the United States Food and Drug Administration (FDA) approved 6 new anticonvulsants. New formulations and extended-release forms of older anticonvulsants are also available. However, there are few changes in the treatments available for acute management of seizures in the ED. Options for emergent treatment include benzodiazepines, hydantoins (phenytoin/fosphenytoin), barbiturates (phenobarbital/pentobarbital), levetiracetam, valproic acid, lacosamide, and general anesthetics such as propofol.

If the patient has a subtherapeutic anticonvulsant drug level, then the patient's home medication dose can be increased or a bolus can be given in the ED. This is preferably done with the guidance of a pediatric neurologist. The medications with easily checked drug levels (phenobarbital, phenytoin, carbamazepine, and valproic acid) all carry risk of hepatotoxicity and blood count abnormalities. This should be taken into consideration before medication changes are made. Emergency clinicians should remember that the use of intramuscular or intranasal routes of administration is a reasonable alternative to intravenous administration of some medications, especially when intravenous access is challenging and may delay treatment.

Benzodiazepines

As a group, benzodiazepines are effective anticonvulsant agents that rapidly cross the blood-brain barrier and potentiate gamma amino-butyric acid (GABA) neurotransmission. The potency of each benzodiazepine is dependent on its affinity to the benzodiazepine-$GABA_A$–receptor complex. Lorazepam has the highest potency, followed by midazolam and diazepam.[87]

Intravenously administered lorazepam, midazolam, and diazepam cross the blood-brain barrier in seconds. Diazepam and lorazepam are completely absorbed when administered orally, but intramuscular administration results in slow and erratic absorption. Conversely, midazolam is less effective when administered orally due to high first-pass metabolism, but it is well-absorbed when administered intramuscularly because it is water-soluble. Intranasal and buccal administration of midazolam has also been reported to be effective in stopping seizures.[88-90] Diazepam is also commercially available in a rectal preparation for prehospital use.

Lorazepam and diazepam are highly lipid-soluble and can terminate seizure activity within 2 to 3 minutes of administration. Lorazepam has a much longer duration of anticonvulsant effect than diazepam, whose effects last approximately 30 minutes. **Table 4** shows typical dosing protocols for midazolam, lorazepam, and diazepam.

Hydantoins

Phenytoin and fosphenytoin are the primary hydantoins currently used in seizure management. They are thought to prolong the refractory period of voltage-dependent sodium channels in the cerebrum. Hydantoins cross the blood-brain barrier rapidly, with therapeutic drug levels reached within 10 minutes of completion of an intravenous infusion.[91] Fosphenytoin is a water-soluble prodrug of phenytoin delivered in a neutral pH solution. It is quickly converted to phenytoin through enzymatic conversion. Use of intravenous fosphenytoin rather than phenytoin is preferred in children, as it allows for faster infusion with fewer cardiovascular side effects and no local irritation or tissue destruction. Fosphenytoin is dosed in phenytoin equivalents and can be given intravenously or intramuscularly. Concerning side effects of the hydantoins include severe hypotension, cardiac dysrhythmias, agranulocytosis, and Stevens-Johnson syndrome. Rarely, phenytoin toxicity can cause seizures, but seizures would be preceded by other signs of toxicity such as nystagmus and confusion. In a patient chronically taking phenytoin or fosphenytoin, it would be prudent to check a phenytoin level or administer a different anticonvulsant if phenytoin toxicity is suspected.

Barbiturates

Barbiturates have been used in the management of seizures for over a century. They enhance the activation of $GABA_A$ receptors.[92] Phenobarbital is one of the most commonly used anticonvulsant medications in the developing world, but its use in higher-resource countries is declining due to concerns about potential cognitive and behavioral side effects.[93] When used as an emergency medication for treatment of seizures, potential side effects include sedation, hypotension, and respiratory depression potentially requiring intubation. However, it has a long half-life, averaging 1.5 days in children, with sustained efficacy.

Table 4. Benzodiazepine Dosing For Seizure Management

Drug	Route	Dose
Midazolam	Intranasal – use atomizer or drip into nares	0.2 mg/kg, max 10 mg
	Intramuscular	0.1-0.2 mg/kg, max 10 mg
Lorazepam	Intravenous	0.1 mg/kg, max 4 mg
	Intranasal (may have low/delayed absorption) – use atomizer or drip into nares	0.1 mg/kg
Diazepam	Intravenous	0.1-0.3 mg/kg, max 10 mg
	Rectal (max 20 mg)	Age 2-6 y: 0.5 mg/kg Age 6-12 y: 0.3 mg/kg Age > 12 y: 0.2 mg/kg

Valproic Acid

Valproic acid has a variety of mechanisms of action including increased GABA transmission, blockage of voltage-gated sodium channels, and dopaminergic and serotonergic transmission.[94] Intravenous valproic acid was approved by the FDA in 1996 for use in children aged > 10 years; however, it is not approved by the FDA for the management of status epilepticus. It is a broad-spectrum anticonvulsant used to treat almost all seizure types. Significant side effects include encephalopathic symptoms associated with hyperammonemia, thrombocytopenia or platelet dysfunction, pancreatitis, hepatotoxicity, and teratogenicity. The risk of fatal hepatotoxicity is greatest in children aged < 2 years, and it should not be used in this age group without the close supervision of a pediatric neurologist. Valproic acid should also be avoided in any child known or suspected to have a metabolic or mitochondrial disorder.

Levetiracetam

Levetiracetam has a novel mechanism of action. It binds to the synaptic vesicle glycoprotein, SV2A; inhibits presynaptic calcium channels, reducing neurotransmitter release; and acts as a neuromodulator. In 2006, the intravenous form was approved by the FDA for use in patients aged ≥ 16 years. It is not approved by the FDA for treatment of status epilepticus. Levetiracetam is effective in both generalized and focal epilepsy. It causes no significant cardiovascular or respiratory changes and has no appreciable pharmacokinetic drug interactions.[95] Common side effects include mood and behavioral changes and rarely, psychosis.

Lacosamide

Lacosamide is a new anticonvulsant medication with a unique mechanism of action. It selectively enhances the slow inactivation of voltage-gated sodium channels. Lacosimide was approved in 2008 for adjuvant treatment of refractory partial-onset epilepsy in patients aged ≥ 17 years and is available in both oral and intravenous formulations. Studies to evaluate its efficacy in younger children are ongoing. Several small prospective and retrospective studies suggest that lacosamide is effective and well tolerated in children with refractory epilepsy.[96-98] Lacosamide does not appear to have significant cardiovascular or respiratory side effects.

Carbamazepine And Related Drugs

This class of anticonvulsant medications includes carbamazepine, oxcarbazepine, and, more recently, eslicarbazepine acetate. None of these medications are available in an intravenous formulation and should not be loaded or given as bolus doses. The mechanism of action is blockage of fast-acting voltage-gated sodium channels. Carbamates are only indicated for focal or partial-onset epilepsy and can worsen generalized epilepsy. Additionally, these medications can cause serious and sometimes fatal dermatologic reactions, including toxic epidermal necrolysis and Stevens-Johnson syndrome, particularly in patients carrying the HLA-B 1502 allele, which is found almost exclusively in patients of Asian ancestry. Carbamates can also cause symptomatic hyponatremia, including hyponatremic seizures.

Carbamazepine is the only carbamate with drug levels that are easily checked; however, care needs to be taken before changing a patient's carbamazepine dose. Carbamazepine displays dose-dependent elimination pharmacokinetics, in which dose increases produce a less-than-proportional increase in steady-state total concentration. Carbamazepine metabolism also undergoes autoinduction so that drug clearance increases over time after initiation. An increase in the maintenance dose may result in further induction. In some children, plasma carbamazepine concentrations remain unchanged or even decline despite increasing doses, due to autoinduction. Carbamazepine metabolism can also be induced by phenytoin or phenobarbital.[87]

Propofol Infusion

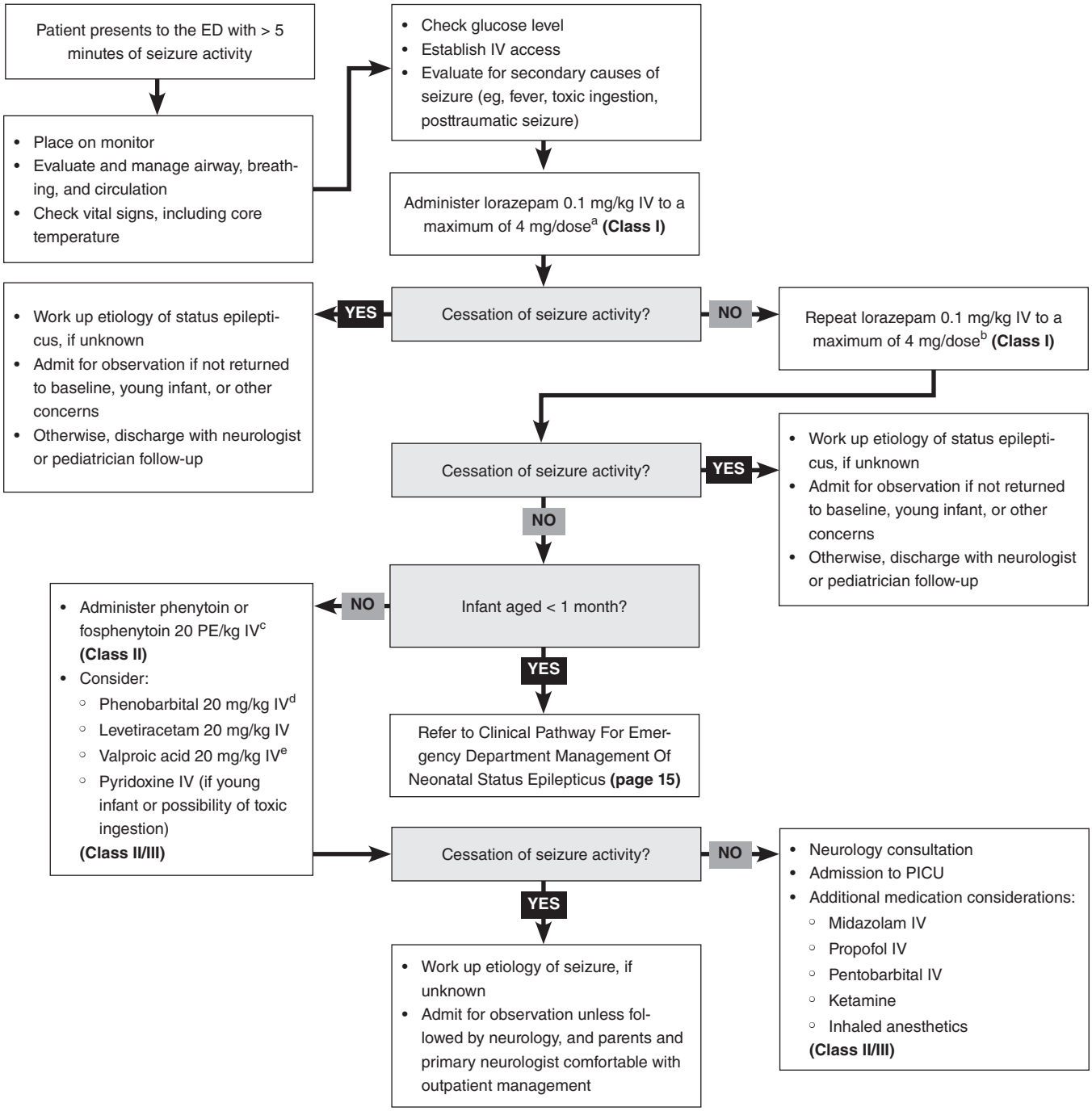
One treatment option for refractory status epilepticus is a continuous propofol infusion. Unfortunately, propofol is associated with significant side effects. Consideration should be given to intubation and continuous cardiovascular monitoring, and patients may require the use of vasopressors to maintain an adequate blood pressure.[99] A particular concern in children on prolonged treatment with propofol is propofol infusion syndrome, which can result in severe metabolic acidosis, rhabdomyolysis, heart failure, renal failure, hepatomegaly, and death.[100]

A 2012 guideline by the Neurocritical Care Society states that propofol is contraindicated in young children, but there is no lower age limit for safe use given in the guideline.[99] A survey published in 2013 found that experts in status epilepticus were reluctant to use propofol in children.[101] The Italian League Against Epilepsy 2013 guidelines for status epilepticus in children do list propofol as an option in children who have not responded to first- and second-line medications, but recommend limiting use to intensive care units with continuous EEG monitoring.[100] When possible, the decision about continuous infusions in patients with refractory status epilepticus should be made in conjunction with the neurologist and the intensivist who will be assuming care of the patient.

Status Epilepticus

Status epilepticus is a neurological and medical emergency. Prompt recognition and management

Clinical Pathway For Emergency Department Management Of Pediatric Status Epilepticus



Abbreviations: ED, emergency department; IV, intravenous. PE, phenytoin sodium equivalents; PICU, pediatric intensive care unit.
For Class of Evidence definitions, see page 15.

[a]Do not delay medication administration for difficult IV access. Alternate routes include intranasal, rectal, intramuscular, and intraosseous.

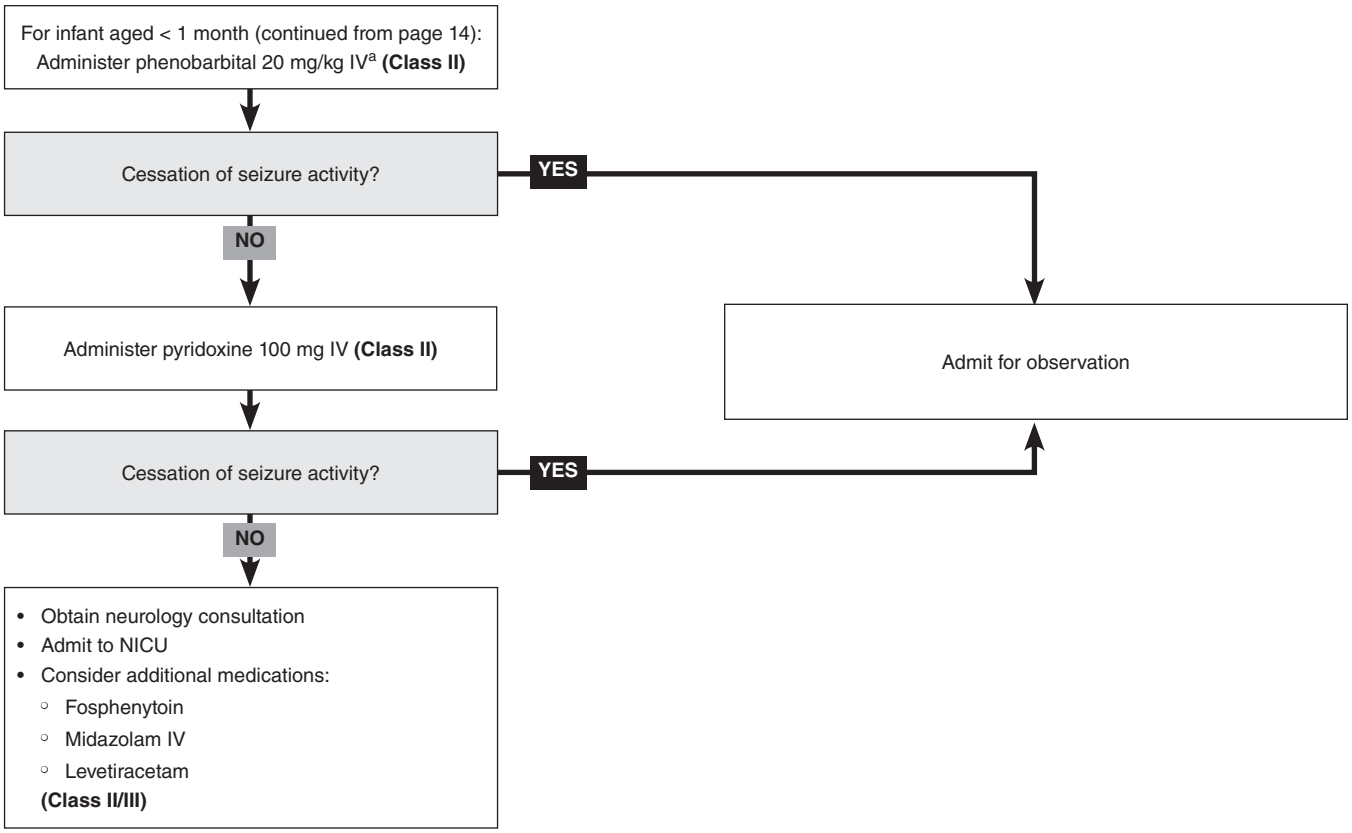
[b]Administer 2 total doses of parenteral benzodiazepines (including any prehospital doses).

[c]Avoid phenytoin in patients with toxic ingestions. Administer phenobarbital instead.

[d]Re-evaluate airway and breathing at every step. Intubation is likely required when giving phenobarbital after benzodiazepines. If the patient is not already intubated, secure the airway when starting a continuous infusion.

[e]Avoid valproic acid in children aged < 2 years, children with a possible metabolic or mitochondrial disorder, and children with hepatic disease.

Clinical Pathway For Emergency Department Management Of Neonatal Status Epilepticus



Abbreviations: IV, intravenous; NICU, neonatal intensive care unit.

[a]Reevaluate airway and breathing at every step. Intubation is likely required when giving phenobarbital after benzodiazepines. If the patient is not already intubated, secure the airway when starting a continuous infusion.

Class Of Evidence Definitions

Each action in the clinical pathways section of *Pediatric Emergency Medicine Practice* receives a score based on the following definitions.

Class I
- Always acceptable, safe
- Definitely useful
- Proven in both efficacy and effectiveness

Level of Evidence:
- One or more large prospective studies are present (with rare exceptions)
- High-quality meta-analyses
- Study results consistently positive and compelling

Class II
- Safe, acceptable
- Probably useful

Level of Evidence:
- Generally higher levels of evidence
- Nonrandomized or retrospective studies: historic, cohort, or case control studies
- Less robust randomized controlled trials
- Results consistently positive

Class III
- May be acceptable
- Possibly useful
- Considered optional or alternative treatments

Level of Evidence:
- Generally lower or intermediate levels of evidence
- Case series, animal studies, consensus panels
- Occasionally positive results

Indeterminate
- Continuing area of research
- No recommendations until further research

Level of Evidence:
- Evidence not available
- Higher studies in progress
- Results inconsistent, contradictory
- Results not compelling

leads to the best chance of successful outcome. The goals of emergency management should be to ensure adequate brain oxygenation and cardiorespiratory function while terminating clinical and electric seizure activity as rapidly as possible, and diagnosing and treating the underlying cause.

Data to guide optimal treatment of status epilepticus are limited. Benzodiazepines appear to be the most effective first-line treatment for status epilepticus, but there are insufficient data to conclusively determine the best second- and third-line therapies if benzodiazepines do not terminate seizure activity.[17,99,102,103] There are limited randomized controlled trials in children comparing treatment options for status epilepticus that is refractory to benzodiazepines. Without data or clinical guidelines to guide treatment decisions, there is wide practice variation in treating refractory status epilepticus.[104,105]

A 2014 Cochrane review of anticonvulsant therapy for status epilepticus evaluated both the adult and pediatric literature. Diazepam and lorazepam were both found to be superior to placebo for cessation of seizures. Lorazepam was better than diazepam or phenytoin and carried a lower risk of continuation of status epilepticus requiring further treatment.[17] However, a double-blind randomized prospective study published in 2014 by Chamberlain at al found that intravenously administered diazepam and lorazepam were equally effective in terminating pediatric status epilepticus and had similar rates of severe respiratory depression.[106] Lorazepam did have a higher rate and duration of sedation in that study.

Several randomized prospective studies in the pediatric population indicate that appropriately dosed intravenous lorazepam is successful in at least 70% of cases.[106-108] A recent large randomized prospective study also suggested that intramuscular midazolam may be just as effective as intravenous lorazepam.[16] This may be a good alternative when there is difficulty placing an intravenous line.

There is limited evidence to guide the choice regarding commonly used second- and third-line treatment options for pediatric status epilepticus. Phenytoin or fosphenytoin are chosen by most experts as the second-line agent for treatment of status epilepticus.[101] In a small randomized study of 62 adults and 38 children, intravenous phenytoin and valproic acid were both highly effective, controlling status epilepticus in 84% and 88% of patients, respectively.[109] Success rates with phenytoin are lower in other, mostly adult, studies.[110-112]

If a child's status epilepticus is refractory to treatment with 2 anticonvulsant agents, there are a variety of options for third-line treatment. Phenobarbital was the traditional third-line agent, but with the advent of newer anticonvulsant medications, it is being used less routinely due to frequent side effects such as respiratory depression.[113,114] There are increasing data that valproic acid is well tolerated as a rapid infusion and effective in controlling status epilepticus, but this is currently considered to be off-label use.[109,113,115] Since the approval of intravenous levetiracetam in 2006, it is also being increasingly used for refractory status epilepticus due to its safety profile.

After attempts to control status epilepticus with intermittent medication boluses fail, a continuous infusion is needed to suppress seizure activity. In children, most experts opt for a continuous midazolam infusion, but there are insufficient data to support one particular agent over another.[99,101]

Special Populations

Neonatal Seizures

The neonatal period is one of the highest-risk periods for new-onset seizures.[116,117] Neonatal seizures can be challenging to diagnose, and clinical evaluation is insensitive for the diagnosis of neonatal seizures.[118,119] Neonatal seizures are often subtle, unusual, or multifocal-appearing due to the relatively limited degree of cortical and subcortical myelination. Certain automatisms, such as tongue thrusting, lip smacking, and bicycling of the legs, may all represent seizure activity. Furthermore, normal neonatal behaviors, such as jitteriness and the Moro reflex, may be mistaken for seizure activity.

Even when the diagnosis of seizure is obvious, optimal management is not always clear. There are no convincing data that anticonvulsant treatment is superior to placebo in decreasing morbidity or rates of neurodevelopmental impairment in neonates.[120] A 2004 Cochrane review found insufficient evidence to support the use of one particular anticonvulsant over another for treatment of neonatal seizures.[120] Authors of a more recent meta-analysis suggested phenobarbital as a first-line agent in neonates with seizures without an easily correctable etiology (such as hypoglycemia).[121] The authors of that analysis suggested a second load of phenobarbital for continued seizure activity, and an option of levetiracetam, phenytoin/fosphenytoin, or lidocaine for persistent seizures. One prospective study of 38 newborns who were given levetiracetam as first-line treatment for seizures found that 30 out of 38 patients were seizure-free after 1 week with no serious adverse side effects.[122]

Available data on diagnostic evaluation of neonatal seizures are also limited. Neonates are excluded from the imaging guidelines published by the International League Against Epilepsy.[67] One small study of new-onset seizures in infants aged < 6 months found that more than one-third had abnormal neuroimaging.[123] Another study of new onset afebrile seizures in infants aged > 1 month by Hsieh

et al also found high rates of abnormal neuroimaging.[71] Although MRI had a higher yield of abnormal findings than CT, MRI abnormalities were unlikely to alter emergent management, while 9% of head CTs did alter acute management. Although little data exist to guide management of neonatal seizures, when considering the high rates of imaging abnormalities in infants aged > 1 month with seizures, imaging should be strongly considered in neonates with seizures.

Metabolic derangements (such as electrolyte disturbances, acidosis, or hypoglycemia) are well documented causes of neonatal seizures and their presence affects ED management. Most studies examining the yield of laboratory tests in children with seizures exclude young infants. Scarfone et al studied the utility of laboratory testing in infants with seizures, and 10 of the 80 included patients were aged < 1 month.[37] Three of the 10 neonates had hypocalcemia, and the authors concluded that laboratory testing was recommended for neonates with seizures.

Neonatal sepsis and meningoencephalitis are often accompanied by seizures. A lumbar puncture and workup for bacteremia should be performed in any neonate presenting with a seizure associated with fever or hypothermia and should be strongly considered in cases of prolonged altered mental status. Herpes simplex encephalitis is an important consideration in a neonate with seizures, particularly focal seizures, and a herpes simplex polymerase chain reaction test should be ordered in addition to the usual cerebrospinal fluid studies. Suspected meningoencephalitis should be treated with acyclovir and antibiotics. For additional information on management of herpes simplex encephalitis in pediatric patients, refer to the January 2014 issue of *Pediatric Emergency Medicine Practice* titled "Pediatric Herpes Simplex Virus Infections: An Evidence-Based Approach To Treatment," available at: www.ebmedicine.net/PediatricHSV.

Multiple rare metabolic and genetic disorders cause neonatal seizures. One of the best-described disorders is pyridoxine-dependent epilepsy. Neonates with this disorder have seizures that are refractory to traditional anticonvulsants but respond to 100 mg of pyridoxine administered intravenously. This diagnosis should be in the differential for any neonate with continued seizure activity despite treatment with anticonvulsant medications.

In Hsieh et al's study, infants were found to have high rates of recurrent seizures.[71] There are a few benign genetic neonatal epilepsies, but these are diagnoses of exclusion. Most neonatal seizures are thought to be symptomatic or secondary to a provoking factor, and admission is recommended for any neonate with new-onset seizures.

Seizures Due To Toxic Ingestions

Although toxin-induced seizures are relatively uncommon in children, toxins are important to consider because the seizures are managed somewhat differently. Similar to treatment of other seizure types, benzodiazepines are the first-line treatment for drug-induced seizures. Although the evidence base is limited, barbiturates (rather than phenytoin) are generally recommended as second-line treatment for toxin-induced seizures.[124-126] Similar to all other seizures, a rapid bedside glucose level should be checked, as multiple ingestions can lead to hypoglycemia.

A number of toxins have the potential to cause seizure in overdose. In a recent study of poison center consultations for toxin-induced seizures in children, Finkelstein et al found that the most com-

Time- And Cost-Effective Strategies

- **Routine electrolyte panels are unlikely to change management in patients with brief self-resolved seizures unless the history and physical examination are suggestive of an electrolyte abnormality.**
  Risk management caveat: Young infants are more likely to have significant electrolyte abnormalities, and testing should strongly be considered. Electrolyte panels should be performed on older patients if the history or physical examination reveals an increased risk of electrolyte abnormalities.

- **Lumbar punctures are not required in all patients with febrile seizures.**
  Risk management caveat: All patients with seizure and fever must be evaluated for signs of meningitis and encephalitis. Lumbar puncture should be performed if there is any clinical evidence of meningitis or encephalitis. Lumbar puncture should be more strongly considered in children pretreated with antibiotics, those who have incomplete vaccination status, and in complex febrile seizures.

- **Many patients with self-resolved first-time seizures can be discharged home.**
  Risk management caveat: Patients must have a thorough history and physical examination to evaluate for evidence of a life-threatening cause of seizures. Infants aged < 1 year have a higher incidence of recurrent seizures and should be admitted for evaluation and observation. Patients should have follow-up with a neurologist or pediatrician, and patients with unprovoked seizures will need an outpatient EEG.

Risk Management Pitfalls In The Management Of Seizure Disorders In Pediatric Patients

1. **"I didn't think to check the patient's blood sugar. The patient isn't diabetic, and I was focused on stopping the seizure and managing the airway."**
   Hypoglycemia is a dangerous but reversible cause of seizures. Children may be hypoglycemic for a number of reasons such as ingestion of oral hypoglycemic medications and undiagnosed metabolic disorders. A bedside glucose level should be checked immediately in patients with active seizures or altered mental status.

2. **"I didn't consider eclampsia as a cause of seizures. The patient is only 14 years old."**
   While rare in pediatric patients, eclampsia cannot be missed, as this diagnosis changes patient management drastically. For additional information on management of this condition, refer to the January 2015 *Emergency Medicine Practice* issue titled "Clinical Decision Making In Seizures And Status Epilepticus," available at: www.ebmedicine.net/EMPseizures.

3. **"The 3-month-old girl had a single, brief, self-resolved generalized seizure. She looked great, so I diagnosed her with a simple febrile seizure."**
   Febrile seizures are seen in children aged 6 months to 5 years. A fever and seizure in a younger infant is concerning for infections such as meningitis and encephalitis.

4. **"I thought febrile seizures were a benign entity, so I didn't work up the 18-month-old child for meningitis."**
   While simple febrile seizures are generally a benign entity, not all seizures associated with fever are febrile seizures. Encephalitis, brain abscess, and meningitis may all present with fever and seizure. While the vast majority of children with simple febrile seizures do not require a lumbar puncture, a careful history and physical examination is needed to evaluate for signs and symptoms of serious infection or other serious pathology.

5. **"Witnesses said the patient had a seizure at school. I worked him up for a first-time seizure, but didn't see any reason to get an ECG."**
   Dysrhythmia leading to syncope is a dangerous seizure mimic. Patients with a dysrhythmia may have twitching motions that are mistaken for seizure activity.

6. **"I know chemistries are generally normal in seizure patients, so I didn't order one for the seizing 3-week-old."**
   While electrolytes are likely to be normal in an older infant or child with a self-resolved seizure, status epilepticus in any child, or even a resolved seizure in a neonate, warrants further investigation. A neonate may have hypocalcemia due to undiagnosed DiGeorge syndrome or hyponatremia or hypernatremia from improper formula preparation.

7. **"The pediatric neurologist said I should have given pyridoxine to the neonate with status epilepticus. I'd never even heard of pyridoxine-dependent seizures."**
   Pyridoxine-dependent seizures are a diagnosis unique to pediatric patients. Pyridoxine should be administered to infants with seizures that do not resolve with first-line treatments.

8. **"The pediatric intensive care unit attending just told me that I should have treated the 2-year-old in status epilepticus with pyridoxine because it turned out the child ingested isoniazid. I never thought to ask about isoniazid in the home."**
   Isoniazid overdose and several other ingestions can cause seizures that are unlikely to be controlled with other treatments. Pyridoxine should be considered for difficult-to-control and otherwise unexplained seizures.

9. **"I asked about a history of trauma in the baby, but the family denied it. They seemed trustworthy."**
   Unfortunately, one diagnosis that must always be a consideration in pediatric patients is nonaccidental trauma, and caregivers are unlikely to volunteer this information or provide a reliable history.

10. **"I'm being sued because a teenager I saw for a first-time seizure was in a car accident during a second seizure and injured several people. I always report adults with seizures to the Department of Motor Vehicles, but I didn't know this teenager even had a driver's license."**
    Clinicians must report patients with seizures in some states. It is prudent to understand the laws of the state and remember that older teenagers are of driving age.

monly responsible class of drug was antidepressants.[127] Other drug classes found to be responsible for seizures in that study were antihistamines/anticholinergics, anticonvulsants, psychoactive drugs, and antituberculosis medications.

In cases in which accidental ingestion or suicide attempt is suspected as a possible etiology of status epilepticus, emergency clinicians should ask caregivers about the availability of the antituberculosis drug, isoniazid, in the home, as a specific antidote is available. Isoniazid leads to functional deficiency of pyridoxine, resulting in impaired production of GABA and seizures that are often resistant to treatment with typical anticonvulsants.[128] If isoniazid overdose is suspected to be the cause of status epilepticus, appropriate treatment includes administration of pyridoxine. A pediatric dose of 70 mg/kg of pyridoxine is commonly recommended; however, this dose may be insufficient.[128] When possible, dosing should be based on the amount of isoniazid ingested. Recommended dosing is 1 gram of pyridoxine for every gram of isoniazid ingested, even in pediatric patients. One problem that has been described in treating isoniazid-induced status epilepticus is that not all hospitals stock pyridoxine, and even those that do may not have sufficient supplies to treat large ingestions.[129-131] Pyridoxine may also be beneficial in seizures due to overdoses of ginkgo seeds and Gyromitra, or false morel mushrooms.[124,132]

Antidepressants are commonly prescribed medications that are potentially available in the home to young children who may ingest them in accidental overdoses and older children and adolescents who may ingest them in suicide attempts. Because some caregivers may not recognize the risk of ingestion of antidepressants and other psychiatric medications and may not volunteer that these drugs are present in the house, in unexplained seizures, it would be prudent to ask about access to these medications in particular. Bupropion has a particularly high potential to cause seizures in overdose,[133,134] and, although most cases of bupropion-induced seizures have been described in adults and adolescents after suicide attempts, there is a case report of bupropion-induced seizures in a child.[135]

Baclofen is a medication commonly prescribed for spasticity that can also cause seizures when overdosed or discontinued too rapidly. In children taking baclofen who present with new or increasing seizures, baclofen dosing should be reviewed.

Posttraumatic Seizures

Another somewhat controversial topic is the management of children with posttraumatic seizures. Any child with a head injury who has altered mental status on arrival to the ED requires a head CT.[136] Less clear is the appropriate workup of a child with a history of a brief posttraumatic seizure who has a normal mental status and normal examination by the time of ED evaluation. The literature provides little guidance on this topic. Haydel et al studied patients with minor head injury and a normal neurologic examination in the ED and found that a history of posttraumatic seizure was associated with a positive head CT scan.[137] However, that study included both adults and children and only included 24 patients with posttraumatic seizure. A large prospective, multicenter study developed a prediction rule to identify children at very low risk of clinically important traumatic brain injuries.[136] Although posttraumatic seizure was not a variable in the prediction rule that was derived, it is not clear how many patients had a posttraumatic seizure. United Kingdom guidelines published in 2014 recommend CT for all patients with a posttraumatic seizure.[138]

Available data, though limited, do support discharge of children who have had an immediate posttraumatic seizure provided that the neurologic examination and neuroimaging are normal. Multiple studies have demonstrated that children with immediate posttraumatic seizures and normal CT scans have good outcomes and do not develop delayed neurologic deterioration.[139,140] In a study of 63 pediatric patients with posttraumatic seizures, Holmes et al found that 10 of the 62 patients (16%) undergoing neuroimaging had a traumatic brain injury.[140] All patients with a traumatic brain injury evident on CT scan had an abnormal Glasgow Coma Scale score. Of the patients without traumatic brain injury on CT, none had further seizure activity or neurologic deterioration.

Controversies And Cutting Edge

Intravenous Levetiracetam For Status Epilepticus

Intravenous levetiracetam is increasingly used for treatment of status epilepticus and acute repetitive seizures.[95,141-144] It seems to be an ideal agent because it is a broad-spectrum anticonvulsant, has a low risk of sedation and cardiorespiratory depression, is not hepatically metabolized, and has limited drug-to-drug interactions. Unfortunately, the evidence supporting this treatment is limited and mostly based on small retrospective case series. Multiple small studies have found intravenous levetiracetam to be well tolerated with a low risk of serious side effects.[95,141-145] A 2012 systematic review of levetiracetam in adults with status epilepticus found that the efficacy varied greatly between studies, and the authors of that review concluded that randomized data are needed.[146]

Although it would be ideal to have data from a large randomized clinical trial, the evidence base for treatment of pediatric status epilepticus, in general, is suboptimal. The use of intravenous levetiracetam

is a reasonable option when other therapies are contraindicated or do not terminate seizure activity. It is important to be aware that treatment of status epilepticus is an off-label use of this medication, and intravenous levetiracetam does not have an FDA indication for use in patients aged < 16 years. However, many drugs used in the treatment of pediatric patients are used off-label. If intravenous levetiracetam is chosen, a loading dose of 20 to 30 mg/kg with a 3-g maximum dose is recommended by expert opinion.[85]

Disposition

While seizures are frightening to parents, in most cases, pediatric patients can be safely discharged home. The 2014 ACEP clinical policy for seizures in adults states that patients with normal neurological examinations can be discharged from the ED with outpatient follow-up.[66] Although not addressed in guidelines, discharge of neurologically normal pediatric patients with a brief seizure is reasonable as well. Infants, however, have a higher rate of seizure recurrence. Unfortunately, there are insufficient data in the literature to support a particular age under which admission for new-onset seizures is advised. Consideration should be given to admitting children aged < 1 year with a first unprovoked seizure.

An outpatient EEG is recommended in the workup of a first-time unprovoked seizure. Patients who are discharged should receive outpatient follow-up with a neurologist. Parents can be reassured that a single seizure does not necessarily mean that the patient will have a seizure disorder. One study of 407 children with a first-time unprovoked seizure followed for a mean of 6 years found that fewer than half experienced a subsequent seizure.[73]

Once parents or caregivers have been reassured, children with simple febrile seizures can be discharged unless admission is necessary for treatment or evaluation of an associated infection.[20] Unfortunately, there is very little literature to guide disposition of children with complex febrile seizures. One recent study of febrile seizures found that seizure recurrence within 24 hours was more likely in patients with other complex features, such as focality or prolonged duration. Therefore, a longer period of observation is reasonable in patients with complex febrile seizures, particularly if parents are especially anxious about recurrent seizures.[147]

If the patient has an established neurologist, the neurologist can aid in the disposition of the patient. In a retrospective review by Landau et al, 29% of ED patients with seizures were discharged home. A neurologist was consulted in approximately 80% of those visits, but in only 32% of patients who were hospitalized.[148] Patients with status epilepticus are generally admitted for observation. In patients with known seizure disorders, if seizures terminate with benzodiazepines and parents are comfortable observing the patient at home, discharge is reasonable. Many pediatric patients with known seizure disorders have rectal diazepam prescribed by their neurologist. If caregivers administered rectal diazepam before ED arrival, the patient may need a prescription for a refill.

Seizure precautions should be given to patients who are discharged from the ED. Patients at risk of recurrent seizures should be advised not to swim alone. Showers are generally considered safer than baths for unsupervised patients with seizure disorders. When discharging teenage patients with seizures, it is important to counsel the patient on driving risk. The AAN recommends a 3-month seizure-free interval before resuming driving.[149] However, laws on required seizure-free intervals before driving vary from state to state.[150] While the AAN does not support mandatory physician reporting of medical conditions,[149] clinicians are mandated to report persons with seizures in some states.[151] Therefore, emergency clinicians must know the applicable laws in their state in order to advise patients and make a report, if required.

Summary

The etiologies of pediatric seizures range from benign to life-threatening, and a thorough history and physical examination is necessary for all patients to evaluate for secondary causes of seizures requiring emergent management. Diagnostic testing is not always necessary and should be guided by the history and physical examination. Patients with seizures lasting > 5 minutes should be treated with benzodiazepines to terminate seizure activity. Second-line treatment for refractory status epilepticus is more controversial, but fosphenytoin or phenytoin are reasonable options for most patients. Based on expert opinion, phenobarbital may be a better second-line treatment for neonatal seizures and toxin-related seizures. Disposition of the patient should be guided by the age of the patient, the length of the seizure, the type of seizure, and the ability of caregivers to provide appropriate follow-up.

Case Conclusions

When EMS brought in the 6-year-old boy, he was having a generalized tonic-clonic seizure. The paramedics had given 1 dose of midazolam en route without cessation of seizure activity. You ordered a bedside glucose level, which was 120 mg/dL, and administered intravenous lorazepam 0.1 mg/kg. The patient's mother told you that he has 1 seizure every 2 to 3 months, and he has had 3 prior ED visits for status epilepticus. He takes oral levetiracetam and hasn't missed any doses. The seizure activity

continued, and you loaded the patient with a second dose of lorazepam 0.1 mg/kg. The seizure stopped during the infusion, and, 30 minutes later, the patient was sleepy, but was easily aroused and had a normal neurologic examination. Since this was a typical seizure for the patient and the mother denied any recent trauma, illness, or neurologic changes, you determined that a head CT and routine laboratory testing were not necessary. After a discussion with the patient's neurologist, you decided to admit him for observation prior to discharge.

By the time you saw the 7-month-old infant with the febrile seizure, she was afebrile, smiling, and feeding well. Her examination was completely normal and her history was unremarkable. She had no evidence of meningitis, and you decided the only workup that was indicated was a catheterized urinalysis and culture. The urinalysis was negative, and you reassured the parents, educated them about febrile seizures, and discharged the patient home to follow up with her primary care physician.

The 12-year-old boy with a seizure on awakening had a normal mental status and neurologic examination. The history revealed no concerning features and no evidence that this was a provoked seizure. You discussed with his parents that a head CT was very unlikely to change management and that the risk of radiation was not warranted. Since the history and physical examination were otherwise unremarkable, you did not perform any laboratory testing. You contacted the boy's pediatrician who arranged an outpatient EEG and neurology follow-up.

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Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study will be included in bold type following the references cited in this paper, as determined by the author, will be noted by an asterisk (*) next to the number of the reference.

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1. Which of the following patients could be diagnosed with a simple febrile seizure?

a. A 4-month-old boy with several hours of fever to 40˚C and 2 minutes of generalized tonic-clonic seizure activity, who is now smiling, alert, and neurologically normal.
b. A 6-month-old boy with 1 day of fever with 1 minute of right leg twitching followed by 1 minute of generalized tonic-clonic seizure activity, who is now smiling, alert, and neurologically normal.
c. A 9-month-old girl without a history of fever at home, but was noted to have a fever of 41˚C in the ED, who had < 5 minutes of generalized tonic-clonic seizure activity and is now interactive, alert, and neurologically normal.
d. A 12-month-old boy with 1 day of fever with 2 episodes of generalized tonic-clonic activity in the last 2 hours, each lasting < 1 minute, who is now playful, laughing, and neurologically normal.

2. In which of the following patients would a chemistry panel be indicated?

a. An otherwise healthy 14-year-old girl who experienced a brief, self-resolved first-time generalized seizure, but now has normal mental status and no other medical complaints
b. A 15-month-old boy seen in the ED for 1 day of runny nose when he experienced a 1-minute generalized seizure, but is now back at baseline with a normal examination except for a temperature of 40˚C
c. A 3-year-old girl with a Glasgow Coma Scale score of 15 brought in to the ED after a brief generalized tonic-clonic seizure after falling down several stairs and hitting her head
d. A 2-month-old boy who is brought into the ED for vomiting and diarrhea after being fed rice water by the grandmother and subsequently he experienced a generalized seizure in the ED

3. According to the guidelines presented, an emergent head CT would be most appropriate in which of the following patients?

a. A previously healthy 9-month-old girl with a 1-minute generalized tonic-clonic seizure who is awake, alert, and found to have a temperature of 40.2˚C
b. An otherwise healthy 14-year-old boy who had a 2-minute generalized tonic-clonic seizure 30 minutes after awakening, but now has a Glasgow Coma Scale score of 15 and a nonfocal neurologic examination
c. A 2-year-old boy who had a generalized tonic-clonic seizure and a fingerstick glucose of 24 mg/dL after being found with his grandmother's pills in his mouth, who is awake and alert after receiving intravenous dextrose
d. A 10-year-old girl who had a 2-minute generalized tonic-clonic seizure immediately after being thrown from her bike and striking her head, who now has a Glasgow Coma Scale score of 14

4. Which of the following is thought to increase the risk of abnormal neuroimaging for a patient with a first-time seizure?

a. Age > 3 years
b. Fever
c. Focal seizure
d. Tonic-clonic activity

5. **Which of the following laboratory tests is most likely to be helpful in guiding management?**
   a. Serum chemistry in an otherwise healthy and well appearing 10-year-old girl with first-time self-resolved generalized seizure
   b. Phenobarbital levels in a 3-month-old boy on phenobarbital for a seizure disorder due to hypoxic-ischemic encephalopathy
   c. Cerebrospinal fluid studies in a smiling, well appearing, otherwise healthy 18-month-old girl with a brief generalized seizure associated with a fever of 40.5°C
   d. Serum chemistry in a well appearing 12-month-old girl with 1 day of mild cough and runny nose, 2 hours of fever, and 3 minutes of generalized tonic-clonic seizure activity

6. **Which of the following is TRUE?**
   a. Randomized controlled trials have demonstrated that fosphenytoin and phenytoin are the most effective second-line agents for treatment of status epilepticus.
   b. Fosphenytoin has a lower incidence of cardiovascular side effects and local skin irritation than phenytoin.
   c. Phenobarbital is the preferred medication for recurrent seizures in children because it has a low incidence of detrimental cognitive effects.
   d. A bolus loading dose of carbamazepine is indicated if carbamazepine levels are subtherapeutic.

7. **In which of the following patients would intravenous valproic acid be a reasonable third-line treatment?**
   a. A 2-week-old boy with status epilepticus that is unresponsive to intravenous lorazepam and phenobarbital
   b. A 5-year-old boy with a known seizure disorder and a mitochondrial disorder
   c. An 8-year-old girl with a known seizure disorder usually controlled with oral levetiracetam
   d. A 15-year-old girl with known liver disease who presents with new-onset status epilepticus

8. **Regarding neonatal seizures, which of the following is TRUE?**
   a. Neonates have a lower incidence of new-onset seizures than other pediatric age groups.
   b. Most neonates with a single seizure can be discharged home if an outpatient EEG can be arranged.
   c. Lip smacking, tongue thrusting, or bicycling movements with the legs can represent seizure activity in neonates.
   d. Fosphenytoin has been clearly demonstrated to be the most effective treatment for neonatal status epilepticus.

9. **In which of the following patients would intravenous pyridoxine be LEAST indicated?**
   a. A 1-week-old boy with status epilepticus that is unresponsive to intravenous lorazepam and phenobarbital
   b. A 2-year-old girl with status epilepticus after a witnessed single-agent ingestion of a sulfonylurea
   c. A 3-year-old girl with status epilepticus whose only past medical history is a recent diagnosis of latent tuberculosis
   d. A 14-year-old boy with status epilepticus whose sister states that "he tried to get high by eating some mushrooms he picked"

10. **Which of the following medications is most highly associated with seizures in overdose?**
    a. Bupropion
    b. Lorazepam
    c. Levetiracetam
    d. Acetaminophen

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