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Seizures are an important and frequent reason for an emergency department (ED) visit. Childhood epilepsy has an overall incidence of 40 per 100,000 children per year, with many more children having underlying neurologic abnormalities that predispose to seizure activity.[1]

Both the appearance of epileptic activity and etiologies of seizures vary with age. Anticonvulsant drug (ACD) therapy optimally should both stop seizure activity and prevent further brain injury that may later manifest as repeat spontaneous seizures or other neurodevelopmental injury. Since not all types of recurrent or persistent seizure activity are known to cause brain injury, the decision to treat must be individualized. Both knowledgeable parents of children with known underlying disease and their pediatric neurologists can provide valuable information that can be integral in management decisions. Once a seizure type that warrants therapy is identified, therapy needs to be rapidly administered.

— The Editor

Tremors vs. Seizures: Recognizing and Managing Seizures in Children

Authors: **William E. Novotny, MD,** Associate Professor of Pediatrics, Pediatric Critical Care Medicine, Brody School of Medicine, East Carolina University, Greenville, NC; **Ronald M. Perkin, MD, MA,** Professor and Chairman of Pediatrics, Brody School of Medicine, East Carolina University, Greenville, NC.

Peer Reviewer: **Steven M. Winograd, MD, FACEP,** Attending Physician, Emergency Department, EMH Regional Medical Center, Elyria, OH.

Introduction

Seizure activity confers no recognized health benefit.[2] To the contrary, enduring seizures in the newborn[3] or older child are viewed as medical emergencies that predict death, neurologic injury, or later occurrence of epilepsy. Numerous data collected in both human and animal studies strongly suggest that early administration of ACD therapy in certain seizure types reduces seizure-related adverse outcomes. Some seizure types or epilepsy syndromes, however, appear to have negligible acute and chronic adverse effects. Since ACD therapy carries a certain degree of inherent risk, the decision to treat or not to treat should be considered carefully. Understanding details of seizure type, duration, and underlying illness will help direct needed therapies.

Seizure Types

Epileptic seizures are sudden abnormal discharges of neurons in the brain and are classified by electroencephalogram (EEG) and clinical findings.[4] Focal and generalized EEG discharges define

partial and generalized seizures, respectively. The clinical finding of intact consciousness occurs during simple seizures, but consciousness is impaired during complex seizures. (Note that consciousness also is impaired during generalized seizures.) Further clinical categorization relies upon motor manifestations. Generalized tonic clonic (GTC) seizures often begin with sustained (10-30 seconds) extension or flexion of trunk or limbs that transition into a tremor. The tremor slows to massive jerks of the extremities and trunk; clonic jerks decrescendo in frequency in 30-60 seconds. As the seizure prolongs, the clonus becomes less evident. Clonic seizures are characterized by rapid, rhythmic jerks. Each rapid jerk is followed by a relatively prolonged motion in the opposite direction. Myoclonic seizures are very brief, shock-like muscle contractions that are single or slowly repetitive, erratic, or irregular. Spasms are myoclonic-like movements followed by a sustained tonic phase. Spasms may recur in clusters. Automatisms are preservative ongoing behavior or de novo behavior reactive to external stimuli that occur during complex seizures.[5] Examples include chewing, swallowing, clapping, scratching, ambulating, emotional displays, or utterances.

Nonconvulsive (NC) seizures most often have altered consciousness as the primary manifestation. Motor findings may be present but are nominal findings in comparison with altered consciousness, which is the primary seizure manifestation. Absence seizures are NC seizures with generalized EEG discharges associated with clinical findings of sudden onset confusion or drowsiness; minor motor findings include blinking or automatisms. Altered consciousness usually lasts fewer than 30 seconds, with sudden return to consciousness. Atypical absence seizures clinically are similar to absence seizures but have longer duration and a more gradual onset and resolution. Complex partial (focal) seizures are NC seizures that present with behavioral arrest with eye/head deviation or an aura that is followed by altered consciousness. Minor tonic, clonic, GTC, or automatic activity may occur during this portion of the seizure, with eye blinking occurring less commonly than in absence seizures. Although the ictal period ranges from 60-90 seconds, the postictal period may last minutes to hours.[6]

GTC seizures are rare in the neonatal period (< 44 weeks gestation), while focal or multifocal clonic; focal and symmetric tonic; myoclonic events; and spasms are more typical occurrences.[7] Clonic activity may remain localized to an extremity, both limbs on one side or the facial region. Clonus may shift in unpredictable patterns or alternate sides of the body. Focal tonic seizures of eye gaze, trunk or extremity are less frequent occurrences. Spasms are rare. Myoclonic jerks may or may not represent seizure activity, and differentiation may or may not be possible at the bedside. The jerks may be isolated or recurrent; unlike clonic activity, myoclonic activity generally is slower, less rhythmic, and irregular. If tactile or proprioceptive stimulation provokes myoclonus (or other types of movement) similar to spontaneous movements, or if spontaneous or evoked movements are suppressed by restraint or repositioning, then the spontaneous events most likely are not seizures.[7] Automatisms and generalized tonic activity also most often are not epileptic events.[8]

Convulsive disorders in infants younger than 6 months are difficult to diagnose. Initial symptoms may mimic airway obstruction, vagal hyperactivity, cardiac or digestive problems, or present as apnea or apparent life-threatening events (ALTE).[9-11] Apnea rarely occurs as the sole seizure phenomenon in infants, but also is a common symptom in preterm and sick newborns with various underlying disorders. Admission for EEG monitoring is mandatory to rule out seizure, although some associated symptoms such as staring may suggest convulsive apnea.[10] Seizures may be associated with hypoxemia and have been shown to occur in up to 7% of infants with ALTE, and such infants have a particularly high risk of sudden death.[11]

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Editorial Group Head: Valerie Loner
Managing Editor: Allison Mechem
Marketing Manager: Schandale Kornegay

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Please call **Allison Mechem,** Managing Editor, at (404) 262-5589, or e-mail allison.mechem@ahcpub.com.

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Status epilepticus (SE) exists when self-sustained seizure discharges sufficiently are prolonged or repeated so as to produce persistent alterations in neurologic function.[12] Historically, 30 minutes of GTC seizure, continuous or interrupted, without full recovery of consciousness was a traditional definition of GTC SE.[13] This definition was based on the concept of injury; healthy animals that seized more than 30 minutes tended to suffer brain injury.[14,15] Statistically, childhood new-onset GTC convulsions that last longer than 5-10 minutes tend to persist.[16] Based upon this information, treatment of GTC seizures has been suggested once seizure duration exceeds 10 minutes in a child younger than 5 years of age, or seizure duration exceeds five minutes in an older child.[16,17]

Refractory generalized convulsive SE (RGCSE) is defined as SE that continues despite administration of two or more ACDs in appropriate doses.[18] Other criteria require seizure duration of more than 1-2 hours.[19,20] Simple partial SE occurs when focal seizures persist for at least 30 minutes, whereas epilepsia partialis continua is present when the condition lasts for hours.[21] Descriptons of other seizure types, including nonconvulsive SE (NCSE), often use seizure duration of 30 minutes to designate occurrence of SE. Distinguishing NCSE from undiagnosed nonepileptic conditions that reduce consciousness can be a special challenge that requires EEG evaluation.[22,23] Four types of NCSE can result in altered consciousness: absence SE (ASE), complex partial SE (CPSE), myoclonic SE, and subtle SE.

In newborns, SE is defined by convention; clinical observation of seizures that are prolonged or recur during a 10-15 minute period are considered to require therapy.[3] In newborns, seizures may be clinically evident or clinically subtle. In either case, the duration of EEG abnormal discharges (with or without clinical seizures) is a somewhat arbitrary gold standard for neonatal SE. Neonatal SE has been rather arbitrarily defined to be either continuous seizure activity for 30 minutes or more, or intermittent activity for 50% of recording time.[4]

Epidemiology of SE

Neonatal seizures occur with an incidence of 1.8-3.5 per 1000 live births, with 26% occurring after discharge from the nursery.[24,25] Clinical paroxysms lasting more than 30 minutes were present in 5% of neonates with seizures.[26] Hypoxic-ischemic encephalopathy, infections, metabolic abnormalities, low birth weight, congenital cerebral anomalies, and intraventricular hemorrhage are frequent risk factors for neonatal seizures.[25-28]

In children age 30 days to 16 years, SE was estimated to occur with an average incidence of 38 per 100,000 per year.[29] Infants younger than 1 year had the greatest incidence of seizures within the pediatric age group. Acute symptomatic and febrile seizures were the most common causes of SE in this age group.[30] Acute symptomatic causes distributed similarly across all pediatric age groups: central nervous system (CNS) infection, 29%; metabolic, 25%; trauma, 17%; and anoxia, 12%.[31] In the second year of life, seizures associated with fever (> 38.4°C) as "the sole acute provocation" accounted for two-thirds of all SE. Hyperthermic/febrile seizures affect 2-4% of children in the United States and 5% of these last more than 30 minutes.[32] Cryptogenic (without condition predisposing to seizure) and remote symptomatic (prior CNS abnormality predisposing to seizure) categories dominated as causes of SE in children older than 4 years of age.[31,33]

Cerebral palsy has been reported to increase the risk for SE; 16% of children with cerebral palsy vs. 1.7% of controls developed SE.[34] Genetic predisposition for seizures also has been demonstrated. Monozygotic twins have a greater concordance rate for SE when compared to dizygotic twins.[35]

SE typically is more prolonged when caused by acute symptomatic etiologies and in infant age groups.[36] Hyponatremia is a common cause of seizures in infants with normal development.[37,38] It frequently is due to water intoxication. Acute symptomatic hyponatremia is characterized by signs of neurologic dysfunction, typically including generalized tonic-clonic seizures with progression to SE, respiratory insufficiency, and hypothermia.[37] Respiratory failure can develop and require intubation/mechanical ventilation. Because hyponatremia usually is identified by means of laboratory evaluation rather than on the basis of clinical findings, recognition of hyponatremia and seizures often is delayed. Patients with hyponatremia are refractory to ACD for seizure control; correction of the underlying electrolyte is more effective than the use of anticonvulsants in infants with seizures and hypothermia in the absence of findings suggesting other causes. The morbidity among children with this type of seizure is high.[37,39] Although it is unlikely that the majority of children who have hyponatremic seizures have been abused, hyponatremia may be a marker of abuse.[39,40]

It is known that many drugs may lead to SE in childhood. Some of the prescribed drugs described as causing SE include carbamazepine, theophylline, baclofen, dimenhydrinate, and isoniazid.[41] The need for a complete history and perhaps a drug screen should be considered in children with SE.

Children with absence epilepsy typically are otherwise normal children with onset in the 5-9 year age group. ASE has been estimated to occur in 3% of these children though presentations to the ED are reported uncommonly.[29,42,43] Most children who present with atypical absence NCSE often have underlying epilepsies, including Lennox-Gastaut syndrome (LGS) or myoclonic-astatic epilepsy.[42] In a case series of 50 children with NCSE, ASE was diagnosed in only 6-12% who had underlying complex partial seizures.[42] Temporal lobe epilepsy, which may underlie CPSE, may occur from brain malformations, cysts, dysplasia, sclerosis, preceding trauma, or hypoxic event.[44] Tonic SE can develop in children diagnosed with LGS especially after treatment with benzodiazepines (BZD). Myoclonic status (MS) may erupt in any primary generalized epilepsy, but probably occurs even less commonly than ASE.[24] Multiple syndromes are associated with both convulsive and NC forms of SE.

Outcomes

The etiology of a neonatal seizure is a major factor that influences outcome.[7,45] A population-based mortality of newborns with seizures is 9%.[26] Mortality historically has been greatest with asphyxia, infections, and inborn errors, with smaller risk associated with other metabolic causes.[7] In the neonate with underlying encephalopathy, mortality may range up to 55%.[46] Epilepsy and neurodevelopmental delay frequently are seen in newborns with documented EEG seizures.[27,47] The contribution of seizure activity to brain injury is not known in these situations.[45,48,49]

Overall mortality in pediatric SE (any type) was only 3.6%, and all deaths occurred in the acute CNS insult or progressive encephalopathy groups.[35] Death uncommonly is associated with prolonged febrile convulsions.[50] By comparison, pediatric RGCSE was linked to mortalities of 16% overall, 20% in symptomatic cases, and 4% in idiopathic cases.[51] A recent pediatric case series reported mortality of refractory SE (RSE) at 31%.[52] A review of 1686 SE events that included 12 case studies of children and adults revealed that 2% of all SE deaths were due to SE, vs. 89% that were secondary to the etiology of SE.[24]

The causal relationship of SE to development of subsequent epilepsy currently is inadequately researched.[53] In children who presented with first seizure as SE, 34-43% developed subsequent unprovoked seizures, and 10-34% developed neurodevelopmental deterioration.[36] Memory, concentration, fine motor, and linguistic disabilities may follow SE.[54,55] Children with prolonged febrile convulsions had an increased risk of epilepsy compared to children without seizures (6-7 per 1000 vs 0.4-0.5 per 1000, respectively).[50] Shinnar recently reported that febrile SE was not followed by new cognitive or motor deficits.[56] Recurrent SE occurs in 15-20% of children with convulsive SE.[57]

Whether mortality or permanent brain injury results from NCSE remains controversial.[58,59] Children with underlying epilepsies (e.g. LGS) who present with NCSE (often atypical ASE) prove difficult to treat and intellectual deterioration occurs subsequent to NCSE.[42,60]

Seizures, Brain Injury, and Epilepsy in the Experimental Model

In the animal model, even brief seizures either can cause neuronal death or can trigger gene expression that may influence neuronal activities.[61,62] The brain regions recognized to be most vulnerable to seizure-induced neuron injury are the hippocampi and the serpiginous cortical regions of the brain located on the medial temporal lobes. These regions are important for memory, learning, and behavior. Animals rescued from SE with diazepam within 30 minutes have less neuronal damage and fewer exhibit spontaneous seizures.[63,64]

Important systemic changes in airway, breathing, circulation, and metabolic balance occur during experimental generalized convulsive SE (GCSE). In animal models, assurance of airway/breathing by mechanical ventilation and decreasing muscle activity with muscle paralysis can reduce GCSE-related mortality.[65] Furthermore, treatment of metabolic acidosis with bicarbonate in the experimental model can decrease occurrence of hypotension.[66] During GCSE, airway patency may be threatened by airway secretions or emesis caused by seizure-related increases of autonomic discharge. Hypoxia accompanies seizure activity in approximately two-thirds of the seizures in children, often during breathing pauses.[67] During or after SE, neurogenic pulmonary edema may appear and contribute to hypoxia.[68,69] Arterial carbon dioxide concentrations in excess of 60 torr commonly are recorded during GCSE, but may be normal or decreased.[70] Guaranteed oxygenation by use of mechanical ventilation and muscle paralysis unfortunately does not guarantee prevention of neuronal loss.[15] Severe lactic acidosis often develops within early minutes after seizure onset; as noted, acidosis may promote occurrence of hypotension.[71] Glucose utilization increases by more than 200% during the first hour of GCSE.[71] In the newborn brain, glucose utilization increases by six-fold, making for special vulnerability to depletion of glucose levels and energy reserves.[65,72] With RSE lasting hours, cerebral edema can develop.[73] Hyperthermia increases risk of neuronal damage, especially to cells in the cerebellum.[74] Relative hypo-thermia may be preventative of neuronal injury. Temperatures recorded during SE in humans often are elevated only modestly (< 102.5°F).[70]

Bedside Evaluation and Testing for Possible Seizure Activity

Physical examination is a crucial tool in identification of neonatal seizures.[7,75] In this age group, look for generalized tonic activity and automatisms including roving eye movements, nystagmus, sucking, chewing, tongue protrusions, rowing, swimming, pedaling, or bicycling movements, which usually are not epileptic. Tremors resolve with restraint, whereas clonic activity (with a rate typically at 1-3 per second) will persist during restraint attempts. Remember that myoclonic movements may be either epileptic or nonepileptic. Try to evoke myoclonic movements by stimulus; evoked myoclonus often is not epileptic. Check the eyes; tonic gaze deviation often is caused by seizure. Examine for truncal tone and symmetry of tone in extremities. Include infantile reflexes—Moro, root, suck, palmar and plantar grasp, and asymmetric tonic neck reflex—in the exam. Determining the presence of altered consciousness related to seizure can be a challenge; obtain an EEG if necessary. Look for heart rate changes, particularly during focal clonic or myoclonic seizures. Monitor breathing pattern, especially during multifocal clonic or tonic seizures; apnea usually is accompanied by other seizure activities. Characterize the arousal state as alert, lethargic, irritable, obtunded, or comatose. Palpate the fontanelle for swelling and inspect the scalp for injury. Needle marks may indicate inadvertent injection of local anesthetic at delivery. Auscultate the head for bruits which may be seen with arteriovenous malformations. Perform a funduscopic exam to detect retinal hemorrhage that might suggest trauma. Retinal abnormalities or cataracts may accompany inborn errors, intrauterine infections, or chromosomal

defects. Examine the skin for angiomas (Sturge-Weber), café-au-lait spots (neurofibromatosis), ash leaf spots (tuberous sclerosis), or vesicles (herpes, incontinentia pigmenti). Smell for an unusual odor: musty (phenylketonuria), maple syrup (branch chain ketonuria), or sweaty feet (isovaleric acidemia). Continuously monitor pulse oximeter saturations, electrocardiogram rhythms, and perfusion.

In older infants and children, documentation of altered consciousness more readily is accomplished but still may be challenging. In the neurologically impaired child, start by obtaining a detailed description of abnormal behaviors or movements. Parents are invaluable sources of information. In all children, perform and repeat Glasgow coma scores (as well as a more comprehensive examinations) during and after treatment. Pseudoseizures may be over-represented in teenage girls who suffer from mood disorders or sexual abuse.[76] As always, determine symmetry of posture, tone, movement, and reflexes. Document sequence of abnormal behaviors and movements as the seizure progresses. While examining the head in the obtunded child, always stabilize the neck when trauma may have occurred.[77] Examine for pupillary dilation, which is sometimes present during SE. Perform a funduscopic examination for retinal hemorrhages or blunted disc margins. Watch for changes in airway patency or protection. Continuously monitor air exchange and oxygenation. Consider hypertension as a cause of SE if extremely high; otherwise it likely is secondary to seizure. If dehydration is evident, vigorously pursue electrolyte results and monitor physical examination for hemodynamic insufficiency. Poor perfusion may obscure presence of a fever; check the temperature.

Common Considerations in Seizure Evaluation. Head computerized tomography (CT) has been helpful in children with SE. Abnormalities were present in 20% when seizure duration exceeded 15 minutes and in 30% when focal findings were identified clinically during or after seizure activity.[78,79] Seizures, apnea, and retinal hemorrhages may suggest head trauma; perform a head CT if suspected.[80-82] Strokes in childhood can be associated with trauma, heart defects, vascular abnormalities, coagulopathies, malignancies, infections, HIV, post organ transplantation, or cocaine exposure.[83,84] Maintain an appropriate level of suspicion. A magnetic resonange image (MRI) may offer greater detail for tumor or other foreign tissue pathology when a CT is unrevealing.[85]

Lumbar puncture is indicated when meningitis or encephalitis is suspected, but should not be performed if the risk for brain herniation has not been assessed. Antibiotic therapy should never be delayed unnecessarily. Cerebrospinal fluid (CSF) white blood cell counts (WBCs) may increase to 10-28 $\times$ 10^6/L as a direct result of SE.[86,87] Remember that non-bacterial encephalitis also may elevate CSF WBCs; enteroviral RNA in CSF can be assayed in children with SE suspected from enteroviral infections.[88]

Children with neurodevelopmental delays and baseline altered consciousness may require an EEG to detect ongoing SE.[89]

Differential Diagnosis

Differential diagnosis of neonatal seizures includes jitteriness and generalized rigidity to noise or touch (hyperekplexia).[90,91] In older infants, gastroesophageal reflux may cause abnormal posturing of the neck, trunk, and limbs (Sandifer syndrome). Shuddering attacks are characterized by behavioral arrest with consciousness maintained, tonic posturing, and flexion/extension of head or neck. In spasmus nutans asymmetric nystagmus, head nodding and abnormal head position are present. Dystonic reactions are characterized by sustained simultaneous contraction of opposing muscles; twisted postures or neck extension are not uncommon. Causes include a multitude of medications (e.g., mood stabilizers, antihistamines, some ACDs, metoclopramide, and street drugs), carbon monoxide exposure, head trauma, encephalitis, or inborn errors. In older children, the history is essential to helping distinguish seizure from nonepileptic events (NEE). Migraines in children can occur in association with "alternating hemiplegia of childhood" (not SE), in which choreoathetosis, ocular motor dysfunction, and autonomic disturbances may occur.[92] Staring may represent inattention or daydreaming. Psychoseizures may be provoked by suggestion or psychosocial stress, may have atypical clinical seizure features, and lack urinary incontinence or postictal changes. Hand-wringing in Rett syndrome or hand-flapping in autistic patients usually is nonepileptic. Underlying cardiac arrhythmia, structural abnormality, or functional disturbance may result in altered consciousness or even cause SE.

Therapy—General Measures

Initial interventions that frequently apply to GCSE and may apply to children with selected other types of SE include:

Airway—Suction increased secretions or vomitus with large diameter tubing and position head to optimize air exchange. Rotate head and body to the side if emesis occurs. Place on supplemental oxygen. Intubation is facilitated by use of a short-acting agent with which the operator is familiar and practiced (e.g., vecuronium, and mivacurium).[93]

Breathing—Immediately apply supplemental oxygen and pulse oximeter, and assemble equipment needed for manual ventilatory assistance. Rapid sequence intubation commonly is performed in SE when the following conditions are present: respiratory failure; raised intracranial pressure; RSE; or extreme hyperthermia.[93] Hypopnea is not uncommon for 1-3 minutes after SE and manual assistance with bag mask breaths may be needed.[93]

Circulation—Hypotension at presentation may be due to prolonged SE but should prompt consideration of other causes of shock. Watch for hypotension during ACD therapy. Infuse fluid for volume expansion or vasoactive agents, as indicated. Treat significant hypertension, if it persists, after resolution of seizure activity. Throughout ACD administration, monitor for arrhythmias or blood pressure changes.

Dextrose—Serum glucose of less than 50 mg/dL for the neonate and less than 60 mg/dL for the older infant should be considered for treatment with IV/IO D_{10} (1-2 mL/kg) in newborn and

D_{25} (2-4 mL/kg) in child.[73] If the initial glucose is low, include dextrose in the IV fluid and frequently repeat bedside glucose. Consider glucagon or steroid if hypoglycemia persists in neonate.

Seizure Therapy—Initiate ACD within 10 minutes of GTC seizure recognition in children younger than 5 years of age and within five minutes in those older than 5 years of age.[16,17] This may decrease seizure duration and limit possible associated brain injury. EEG monitoring/interpretation can be initiated. If indicated, begin to arrange for transfer to a medical center with comprehensive assessment and management capabilities. Metabolic and infectious causes should be pursued after initial stabilization.

Temperature—Treat with rectal acetaminophen 15 mg/kg up to 650 mg in case non-seizure related causes of fever are present. Haafiz has suggested that if the child's temperature is higher than 103°F after first line ACD, then cooling with wet towels or ice blankets is indicated.[93] Watch for development of hypothermia in the small exposed infant.

Bedside Approach to Neonatal Seizure Activity

Newborns with should be treated aggressively with ACD. *(See Table, "A Bedside Approach to Neonatal Seizure Activity," on enclosed Rapid Reference Card.)* Administer IV phenobarbital as the first-line ACD to achieve levels of 40 mcg/mL and then phenytoin, if needed, thereafter. Phenobarbital that achieves levels 25-40 mcg/mL or phenytoin at free levels of 3 mcg/mL (approximately 15-20 mcg/dL total) will control 40-50% of newborn seizures.[94-96] Combining phenobarbital and phenytoin will control 57-62% of neonatal seizures.[94,96] Phenobarbital usually is not increased beyond 40 mcg/mL because levels up to 100 mcg/mL only control an additional 5% of SE.[95] When seizures continue, administer either diazepam or lorazepam; carefully monitor cardiorespiratory function. Consider first-line therapy with longer acting BZD as a nontraditional therapy.[8] Start midazolam infusions if seizures are refractory to first- and second-line therapy; midazolam infusions have been used up to 6.6 mcg/kg/minute.[97] Valproate also has been described to be effective in intractable neonatal seizures.[98,99] Consider lidocaine infusions[100] for control of RSE when avoidance of cardiorespiratory depression is of particular concern; monitor carefully for arrhythmias or recurrent seizures.[101,102] For ongoing seizures, pyridoxine and folinic acid supplementation may be helpful.[103]

Pyridoxine-dependent seizures are a recognized, though rare, cause of intractable seizures in neonates.[104,105] Patients with this autosomal recessive disorder have recurrent seizures that are resistant to conventional anticonvulsants but respond dramatically to intravenous administration of pyridoxine (vitamin B_6). The initial intravenous dose of pyridoxine should be 100 mg. If the patient responds to pyridoxine, all anticonvulsants should be discontinued and a daily oral pyridoxine dose should be started.[104] In the absence of a biological marker for this disease, clinical diagnosis often is delayed and severe neurological sequelae are common.[105]

Exchange transfusion/peritoneal dialysis are potential therapies that may be instituted in the pediatric intensive care unit to treat some urea cycle disorders that may have high arterial ammonia levels on laboratory testing. Arginine infusions can be initiated in the ED setting, as metabolic consultants indicate is necessary. Methylmalonic acidemia is a ketotic hyperglycinemia associated with seizures that may respond to vitamin B_{12}.[106] Remember to initiate treatment of underlying etiologies as seizure treatment is in progress. Most importantly, pursue glucose therapy vigorously once hypoglycemia is identified or an inborn error of metabolism is suspected. Follow up of hypoglycemia by bedside testing with laboratory blood glucose is advisable.

Bedside Approach to Pediatric GCSE

Pre-hospital BZD Treatment. In infants and children, IV BZD terminates SE but causes unacceptable respiratory depression in many children.[107-109] Therefore, consider rectal BZD, which is equieffective with IV therapy at stopping seizures and has less respiratory compromise.[110] *(See Table 1.)* Pre-hospital rectal diazepam (DZP) reaches ACD levels within five minutes of administration.[111] If an IV has been established and airway support is readily available, IV DZP may be a reasonable alternative. DZP therapy of SE has been demonstrated to shorten the duration of SE (32 vs 60 minutes) and prevent recurrence of seizures after arrival at ED (58% vs 85%).[112] Consider the use of rectal lorazepam (LZP) as untested therapy that may become a recognized alternative in pediatric therapy.[113] Another alternative for controlling seizures in the prehospital setting is IM midazolam (0.15mg/kg/dose).[114] Midazolam has been shown to be at least as effective as rectal or intravenous DZP in the control of seizures.[115]

ED First-line Therapy. Children who are seizing at time of arrival to the ED are assumed to need emergent therapy for SE.[73] Appropriately dosed IV DZP or LRZ will stop convulsions in 50-75%, respectively,[116] in children within 2-3 minutes of administration.[116-118] Benzodiazepines may be administered via IV or intraosseous route at time of arrival to the ED; if needed, the rectal route for dosing DZP is a ready alternative. Repeating DZP if the first dose was ineffective often will not control SE and may cause respiratory insufficiency.[117] LRZ now is preferred to DZP because it causes less respiratory depression and is associated with a lower rate of seizure recurrence.[117-119] Duration of effect on controlling seizures is longer with LRZ than DZP (12-24 hours vs 20 minutes to four hours).[118,120] IM midazolam also may be considered.[115]

ED Second-line Therapy. Phenytoin or fosphenytoin is routine treatment when SE continues or recurs following treatment with first-line agents. Due to the brief duration of effect of DZP, coadminister a second line therapy if this BZD is used. Adult GCSE responded to diazepam + phenytoin in more than 55% of cases.[121] Fosphenytoin is a water-soluble phosphate ester of phenytoin that is converted to phenytoin by serum phosphatases. Though infusion time of fosphenytoin is more rapid, time to peak concentration is nearly identical.[122] Advantages associated with fosphenytoin include less frequent phlebitis/soft tissue injury and possible IM administration, but the cost is 20 times that of pheny-

Table 1. A Bedside Approach to Pediatric Status Epilepticus

1st

Airway – suction/position/secure
Breathing – supplemental oxygen to ensure pulse oximeter saturation of > 95%
Circulation – electrocardiographic monitor
Dextrose – bedside glucose and if low administer 2 mL/kg of 25% dextrose up to maximum dose of 25 grams
Seizures → observe and record awareness/responsiveness & motor activity and **vital signs**

2nd

Rapid bedside history:
Prior seizures ± ACD therapy, baseline neurocognitive function, allergies or adverse reactions to medications
Chief complaint acute illness, medications, trauma, description of event

3rd

If likely diagnosis = status epilepticus:

Then → **Vascular access/initial blood for stat analysis (as indicated)**
electrolytes, Ca^{2+}, Mg^{2+} PO^{4-}, urea, creatinine, liver function tests,
complete blood count, arterial blood gas, toxicology panel, ACD levels, blood culture

Begin **ANTI:**
→ -**Convulsant** – as indicated – see below
→ -**Biotic** – consider systemic/nervous system infection
→ -**Pyretic** – consider for fever
METABOLIC THERAPY – as indicated

Type of SE	Sequencing ACD therapy	ACDs	Doses	Other information
Generalized Tonic-clonic Tonic Clonic	Pre-hospital therapy	**diazepam rectal gel** or **parenteral form**	0.5 mg/kg PR (2-5 yrs) 0.3 mg/kg (6-11 yrs) 0.2 mg/kg (≥12 years)	max dose 10mg
		OR		
		[midazolam intranasal]	[0.2 mg/kg with doses up to 5 mg in child < 50 kg and doses up to 10 mg if > 50 kg]	½ dose given into each nostril over 30 seconds (use 5 mg/mLsolution); clear secretions before delivery
		[midazolam IM]	0.15 mg/kg	
	1st tier ED ACD therapy	**lorazepam**	0.1mg/kg IV/IO (max 4 mg/dose)	over 3-5 minutes (in 10 minutes repeat dose x1 PRN)
		OR		
		[diazepam with phenytoin]	>30 days of age 0.05-0.3 mg/kg IV/IO and repeat PRN for < 5y/o-q3-5 min, ≥5y/o-q15-30min	max total dose < 5y/o 5 mg ≥ 5y/o 10 mg

(Continued on next page)

toin.[118] In pediatric patients, conventional therapy fails in 10-15% of seizure episodes.[123]

ED Refractory SE. IV phenobarbital has been a traditional initial agent used for RSE. Administer phenobarbital if the child is not critically ill with severe systemic disturbances (including extreme hyperthermia) or if SE has not already prolonged beyond 60 minutes.[19] Crawford achieved control of RSE using 10 mg/kg dosage increments every 30 minutes; median levels at time of control were 114 mcg/mL.[124] Watch for respiratory depression and/or hypotension, especially if phenobarbital has been coadministered

Table 1. A Bedside Approach to Pediatric Status Epilepticus (Continued)

Type of SE	Sequencing ACD therapy	ACDs	Doses	Other information
	2nd-line ED ACD therapy	**phenytoin** *OR* **fosphenytoin**	15-20 mg/kg IV/IO (No max dose) 15-20 mg/kg phenytoin equivalents IV/IO/[IM]	1 mg/kg/min IV/IO (max 50mg/min) 3 mg/kg/min IV/IO (max 150 mg/min)
	3rd tier ED ACD therapy interventions to consider	**phenytoin** OR **phenytoin equivalents**	Additional 5 mg/kg IV/IO Additional 5 mg/kg IV/IO/[IM]	
		phenobarbital	15-20 mg/kg	≤ 50 mg/minute *be ready to intubate
	RSE^			
		pentobarbital	10-15 mg/kg IV then infusion 0.5-1.0 mg/kg/hour	bolus over 1-2 hours goal is burst suppression(therapy used in partial complex SE
		Midazolam	0.15 mg/kg IV bolus then 1mcg/kg/min	titrate drip upward q 5 minutes until seizures controlled or max of 18 mcg/kg/min

with a BZD. More rapid control of RSE can be achieved with short-acting barbiturate infusions (e.g., thiopental), but EEG, intubation/mechanical ventilation, neuromuscular blockade, invasive hemodynamic monitoring, and pressor support often are required.[125-127] Short-acting barbiturates can be adjusted until clinical convulsions abate or until an EEG suppression-burst or isoelectric pattern is achieved.[128] A prolonged intensive care stay needs to be anticipated with this treatment.

Continuous midazolam infusions are equieffective when compared to thiopental in stopping RSE, but fewer than half of children required mechanical ventilation or develop hypotension.[125,129] On the downside, mean time for seizure control with midazolam infusion was 47 minutes.[130]

Inhalational anesthesia using isoflurane is similarly a rapidly titratable ACD, but fluid and dopamine responsive hypotension frequently occurs.[93,131] Clear advantage of any specific agent used in control of refractory GCSE on subsequent mortality currently is not known.[132,133]

Since the risk-benefit ratio of aggressive therapy in CPSE has yet to be established, consult a pediatric neurologist, as a tempered approach to therapy may be appropriate. In contrast, treat NCSE-in-coma that follows GCSE or severe CNS insult and that is associated with electrographic seizures, whether or not subtle motor activity is present.[26,134] Establish and continue EEG monitoring during treatment.[22,135]

Use caution in treating atypical ASE with a BZD because tonic SE may be induced to occur; treat with oral valproic acid, lamotrigine, or topiramate, if needed.

Conclusions

SE is the most common neurological medical emergency and continues to be associated with significant morbidity and mortality.[122] Neuronal injury/loss and prolonged seizure activity, under certain circumstances, likely are co-dependent processes.[136] Both SE and underlying diseases should be diagnosed rapidly so that appropriate treatment can begin. Simultaneous management of airway, breathing, circulation, seizure activity, and underlying disease processes in GCSE are important to limiting brain injury. Although the outcome from an episode of GCSE mainly is determined by its cause, the duration of GCSE also is important. In addition, the longer the duration of the episode, the more difficult it is to terminate.[122] In NCSE and neonatal seizures, ongoing seizure activity can be difficult to determine. Management in a step-wise fashion will terminate the majority of seizures.

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Physician CME Questions

91. Which of the following is true regarding symptomatic hyponatremia in children?
    A. It rarely is seen in water intoxication.
    B. Tonic-clonic seizures are an uncommon characterization.
    C. Morbidity is low.
    D. It is a common cause of seizures in infants of normal development.

92. Regarding status epilepticus (SE), which of the following is true?
    A. There have been no increased risk of SE in children with cerebral palsy.
    B. The lowest incidence of seizures is seen in children younger than 1 year.
    C. SE typically is more prolonged when caused by acute symptomatic etiologies and in infant age groups.
    D. Memory, concentration, fine motor, and linguistic disabilities have not been seen following SE.

93. Regularly prescribed, safe, and efficacious initial treatment of generalized tonic-clonic SE in children included which of the following?
    A. Prehospital IM fosphenytoin
    B. Prehospital IM midazolam

CME Objectives

The CME objectives for *Pediatric Emergency Medicine Reports* are to help physicians:

a.) Quickly recognize or increase index of suspicion for specific conditions;

b.) Understand the epidemiology, etiology, pathophysiology, historical and physical examination findings associated with the entity discussed;

c.) Be educated about how to correctly formulate a differential diagnosis and perform necessary diagnostic tests;

d.) Apply state-of-the-art therapeutic techniques (including the implications of pharmacologic therapy discussed) to patients with the particular medical problems discussed;

e.) Provide patients with any necessary discharge instructions.

C. Prehospital IV lorazepam
D. Prehospital rectal diazepam

94. Risk of brain injury from generalized tonic-clonic SE is most associated with which of the following?
A. Prolonged seizure activity
B. Fever during seizure activity
C. Hypertension during seizure activity
D. Hyperglycemia during seizure activity

95. Which of the following therapy choices for refractory generalized tonic-clonic SE is *least* likely to need mechanical ventilation and hemodynamic support?
A. Thiopental infusion
B. Propranolol infusion
C. Midazolam infusion
D. Isoflurane anesthesia

96. An EEG most likely would be immediately helpful in assessment in which of the following circumstances?
A. A neonate with tremors that stop with applied restraint
B. An infant with prolonged neck extension following a dose of antihistamine
C. A 3-year-old girl who arouses from staring episodes with tactile stimulation
D. A 6-year-old with nonconvulsive status epilepticus (NCSE) and acute alteration of mental status

97. Neonatal movements most likely to represent underlying seizure activity are:
A. sucking and tongue protrusion that are provoked by stimulation.
B. tonic eye deviation not intensified by tactile stimulation.
C. myoclonic movement suppressed by restraint.
D. nystagmus intensified by tactile stimulation.

98. Children with underlying epilepsies who present with nonconvulsive status epilepticus prove difficult to treat and face subsequent intellectual deterioration.
A. True
B. False

CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge.

To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this activity, you must complete the evaluation form that will be provided at the end of the semester and return it in the reply envelope provided to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you.

99. The first issue to assess in the management of a seizing child is:
A. bedside glucose.
B. airway patency.
C. history of head trauma.
D. cardiac rhythm.

100. In infants and children, IV benzodiazepines terminate status epilepticus but cause unacceptable respiratory depression in many children.
A. True
B. False

Answer Key:

91. D; 92. C; 93. D; 94. A; 95. C; 96. D; 97. B; 98. A; 99. B; 100. A

Audio Conference Clarifies Final EMTALA Regulations

The final version of the recently proposed changes to the Emergency Medical Treatment and Labor Act (EMTALA) takes effect on Nov. 10.

To provide you with critical information on the updated regulations from the Centers for Medicare and Medicaid Services, Thomson American Health Consultants offers *New EMTALA Regulations: Are They Too Good to be True?*—an audio conference on Tuesday, Oct. 21, from 2:30-3:30 p.m., EST.

Ensure that you and your staff are prepared with straightforward advice from a panel of EMTALA experts. The program will be presented by **James R. Hubler, MD, JD, FACEP, FAAEM, FCLM**, attending physician and clinical assistant professor of surgery, Department of Emergency Medicine, OSF Saint Francis Hospital and University of Illinois College of Medicine in Peoria, IL; and **Robert A. Bitterman, MD, JD, FACEP**, director of risk management and managed care, Department of Emergency Medicine, Carolinas Medical Center in Charlotte, NC.

Each participant can earn 1 FREE nursing contact hour or AMA Category 1 CME credit for one low facility fee of $249. The conference package also includes handouts, additional reading, a free 48-hour replay of the live conference, and a CD recording of the program.

For more information, or to register, call (800) 688-2421 or (404) 262-5476, or e-mail customerservice@ahcpub.com.

In Future Issues:

Pediatric Migraines and Headaches

PEDIATRIC Emergency Medicine Reports
The Practical Journal of Pediatric Emergency Medicine

Tremors and Seizures

A Bedside Approach to Neonatal Seizure Activity

1st

Airway—suction/position/secure
Breathing—oxygen to maintain oxygen saturations > 95%-97% (if without congenital heart disease)
Circulation—electrocardiographic monitor
Dextrose—bedside glucose: < 50 mg/dL treat with 2 mL/kg D10 *(See below—definitions of "low" may vary.)*
Seizures → observe responsiveness, abnormal movements/tone, motor abnormalities and changes with tactile stimulus or application of gentle restraint and **vital signs**

2nd

Rapid history:

Prior	Seizure activity or ACD therapy, baseline posture/movements/level of consciousness, pertinent gestational/delivery/postnatal issues, past adverse drug reactions
Chief complaint	Description of ongoing event, acute illness, medications, trauma

3rd

Do clinical findings indicate seizure activity that warrants treatment with ACDs?

YES: Focal tonic or clonic movements if prolonged and recurrent
Improbable: Movements that are suppressed by restraint or provoked by stimulation and those same movements occur spontaneously

Then if indicated: → **Vascular access/Initial blood for stat analysis**
electrolytes, Ca^{2+}, Mg^{2+} PO^{4-}, urea, creatinine, liver function tests, complete blood count, arterial blood gas, toxicology panel, ACD levels, blood culture (as indicated)

Begin **ANTI:**
→ **Convulsant** – see below
→ **Biotic** – consider systemic/nervous system infection
→ **Pyretic** – consider for fever

METABOLIC THERAPY *(See below)*

Types of therapy	Medication*	Dose	Infusion time	Other information
1st-line seizure therapy ↓	**phenobarbital** ↓	20 mg/kg IV	> 10 minutes	May repeat 10 mg/kg to max of 40 mg/kg
2nd-line seizure therapy ↓	**phenytoin* IV *OR* fosphenytoin* IV (IM)** ↓	20 mg/kg IV (IO) 20 mg/kg IV (IO, IM) phenytoin equivalents	> 40 minutes >13 minutes	Goal serum level 15-20 mcg/mL
3rd-line seizure therapy	diazepam	0.25 mg/kg IV(IO) 0.5 mg/kg (PR)	> 3 minutes	Contains benzyl alcohol that may induce "gasping syndrome" (acidosis, cardiovascular collapse); benzoic acid may displace bilirubin
OR	lorazepam	0.05-0.1 mg/kg IV	over 10-15 minutes	same as for diazepam
AND	**pyridoxine** 10%	**0.5 to 1 mL IV, IM**		Respiratory compromise possible
	valproate	**25 mg/kg**	> 30minutes	
hypoglycemia < 20 mg/dL preterm < 30 mg/dL term < 40 mg/dL after three days of age at any gestational age	**dextrose 10%** for blood glucose	**2 mL/kg IV (IO)**		use overhead warmer if needed
hypocalcemia	**calcium gluconate** 10% for blood ionized calcium < 3 mg/dL serum total calcium: < 7.5 mg/dL (preterm) < 8.0 (term)	**2 mL/kg**	infuse over 15 to 30 minutes	monitor for bradycardia; recheck glucose frequently

* Traditional therapy – bold
Therapy sporadically reported in the literature – regular print

A Bedside Approach to Pediatric Status Epilepticus

1st

Airway – suction/position/secure
Breathing – supplemental oxygen to ensure pulse oximeter saturation of > 95%
Circulation – electrocardiographic monitor
Dextrose – bedside glucose and if low administer 2 mL/kg of 25% dextrose up to maximum dose of 25 grams
Seizures → observe and record awareness/responsiveness & motor activity and **vital signs**

2nd

Rapid bedside history:
Prior seizures ± ACD therapy, baseline neurocognitive function, allergies or adverse reactions to medications
Chief complaint acute illness, medications, trauma, description of event

3rd

If likely diagnosis = status epilepticus:
Then → **Vascular access/initial blood for stat analysis (as indicated)**
electrolytes, Ca^{2+}, Mg^{2+} PO^{4-}, urea, creatinine, liver function tests,
complete blood count, arterial blood gas, toxicology panel, ACD levels, blood culture

Begin **ANTI:**
→ -**Convulsant** – as indicated – see below
→ -**Biotic** – consider systemic/nervous system infection
→ -**Pyretic** – consider for fever
METABOLIC THERAPY – as indicated

Type of SE	Sequencing ACD therapy	ACDs	Doses	Other information
Generalized Tonic-clonic Tonic Clonic	Pre-hospital therapy	**diazepam rectal gel** or **parenteral form** *OR* [midazolam intranasal] [midazolam IM]	0.5 mg/kg PR (2-5 yrs) 0.3 mg/kg (6-11 yrs) 0.2 mg/kg (≥12 years) [0.2 mg/kg with doses up to 5 mg in child < 50 kg and doses up to 10 mg if > 50 kg] 0.15 mg/kg	max dose 10mg ½ dose given into each nostril over 30 seconds (use 5 mg/mLsolution); clear secretions before deliver
	1st tier ED ACD therapy	**lorazepam** *OR* [diazepam with phenytoin]	0.1mg/kg IV/IO (max 4 mg/dose) >30 days of age 0.05-0.3 mg/kg IV/IO and repeat PRN for < 5y/o-q3-5 min, ≥5y/o-q15-30min	over 3-5 minutes (in 10 minutes repeat dose x1 PRN) max total dose < 5y/o 5 mg ≥ 5y/o 10 mg
	2nd-line ED ACD therapy	**phenytoin** *OR* **fosphenytoin**	15-20 mg/kg IV/IO (No max dose) 15-20 mg/kg phenytoin equivalents IV/IO/[IM]	1 mg/kg/min IV/IO (max 50mg/min) 3 mg/kg/min IV/IO (max 150 mg/min)
	3rd tier ED ACD therapy interventions to consider	**phenytoin** OR **phenytoin equivalents**	Additional 5 mg/kg IV/IO Additional 5 mg/kg IV/IO/[IM]	
		phenobarbital	15-20 mg/kg	≤ 50 mg/minute *be ready to intubate
	RSE^			
		pentobarbital	10-15 mg/kg IV then infusion 0.5-1.0 mg/kg/hour	bolus over 1-2 hours goal is burst suppression(therapy used in partial complex SE
		Midazolam	0.15 mg/kg IV bolus then 1mcg/kg/min	titrate drip upward q 5 minutes until seizures controlled or max of 18 mcg/kg/min

Supplement to *Pediatric Emergency Medicine Reports*, October 2003: "Tremors vs. Seizures: Recognizing and Managing Seizures in Children." *Authors:* **William E. Novotny, MD,** Associate Professor of Pediatrics, Pediatric Critical Care Medicine, Brody School of Medicine, East Carolina University, Greenville, NC; **Ronald M. Perkin, MD, MA,** Professor and Chairman of Pediatrics, Brody School of Medicine, East Carolina University, Greenville, NC.