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Pediatric Status Epilepticus

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Core Objectives

At the end of the module the PALS provider will be able to

- Define pediatric status epilepticus (PSE) and list common causes
- Describe different types of pediatric seizures
- Describe initial assessment, support, and therapy for PSE
- List indications for intubation in PSE

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Case 1

A 3-year-old child with a history of a seizure disorder is brought to the Emergency Department by his parents. He developed tonic-clonic seizure activity that persisted during the 30-minute drive to the hospital.

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Case 1

- History of 3 previous seizures, takes valproic acid
- Vomiting for the past 24 hours, including medications
- Received rectal diazepam (5 mg) at home

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Video of generalized tonic-clonic seizure

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Case 1

What information do you need?

Rapid cardiopulmonary assessment:

- Appearance: active tonic-clonic movements involving all extremities
- Airway clear; RR 25/minute
- HR 160 bpm, BP 90/62 mm Hg, capillary refill 2 seconds, good distal pulses, extremities warm

Temperature (rectal) 102.3°F

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Case 1

What are your management priorities?

- Assess and support the ABCs
- Prevent hypoxia
- Assess blood glucose; treat hypoglycemia
- Control seizure
- Control temperature

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Definition of Status Epilepticus

- A single seizure ≥30 minutes
- A series of seizures ≥30 minutes without full recovery
- Some experts believe shorter time definitions (eg, 10 to 15 minutes) are more appropriate
- Alternative definition: Continuing seizure lasting ≥5 minutes or ≥2 seizures with incomplete recovery

Data from Lowenstein DH, Alldredge BK. *N Engl J Med.* 1998;338:970-976.

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Many Types

- Partial seizures
  - Simple partial
    - Focal motor activity without loss of consciousness
  - Complex partial
    - Alteration of consciousness without major motor activity
  - Partial seizures evolving into generalized seizures

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Many Types

- Generalized seizures
  - Absence
    - Alteration of consciousness without major motor activity
  - Myoclonic
    - Brief localized or generalized jerks; may be single or repetitive
  - Tonic-clonic (most common)
    - General bilateral major motor activity
  - Others: tonic, clonic, atonic, unclassified

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Many Causes

- Fever
- Insufficient anticonvulsant levels
  - May be due to abrupt discontinuation of or interference from other medications
- Electrolyte abnormalities
  - Including but not limited to hypoglycemia, hypocalcemia, and other electrolyte abnormalities
- Infections
  - Consider central nervous system, but seizures may also be associated with systemic infections

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Many Causes (continued)

- Congenital malformations
- Degenerative diseases
- Drugs, toxins
- Anoxia
- Trauma
- Vascular events

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Caveats of Therapy

The longer status epilepticus persists,

- The more difficult it is to stop
- The greater the potential for morbidity and mortality
  - Mortality rate: 3% to 15%
  - Long-term morbidities
    - Neurodevelopmental problems
    - Chronic seizures

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Management Priorities

- Assess and support airway, monitor respiratory rate and effort
- Ensure adequate oxygenation and ventilation
- Assess circulation
- Evaluate neurologic status: evaluate eyes for movements (may be only evidence of ongoing seizures), pupillary responses
- Assess blood glucose; treat hypoglycemia
- Control temperature (in this case reduce fever)

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Case Progression

- During your initial assessment, the seizure stops; the child gradually returns to normal over the next hour
  - Rectal diazepam may take time to reach peak activity but will maintain therapeutic levels because of continued absorption
- Rectal acetaminophen given
  - Fever may reduce seizure threshold in children with epilepsy; treatment of fever should be a priority
- Patient is admitted to the hospital for neurologic evaluation

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Case 2

- EMS arrives at the home of a 6-month-old infant. The infant is found lying in his crib. He has generalized tonic-clonic seizures and grunting respirations.
- The initial targeted history is notable for an infant with no other healthcare needs who was doing well until 3 days ago, when he developed diarrhea.

What should you do next?

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Case 2

Rapid cardiopulmonary assessment:

- Airway is patent, but mouth is clenched shut; copious secretions present
- Breath sounds are coarse, RR 66/minute
- Capillary refill 3 seconds; HR 170/minute; BP 100/60 mm Hg
- Temperature 37°C

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The infant's size falls in the pink zone on the length-based tape; estimated weight: 7 kg

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Case 2

What are your initial interventions?

- Turn infant on his side; suction oropharynx
- Protect from injury; do not force bite blocks
- Administer oxygen; be ready to support with bag-mask ventilation
- Attach cardiorespiratory monitor, pulse oximeter
- Consider IV access, check glucose, and give an anticonvulsant (per local protocol)

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Initial Anticonvulsant Choices

Benzodiazepines

- Lorazepam:
  - Advantages: rapid onset, duration of action 4 to 6 hours
  - Disadvantages: requires refrigeration
  - Dose: 0.1 mg/kg IV/IO (maximum single dose 4 mg)

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Initial Anticonvulsant Choices

Benzodiazepines (continued)

- Diazepam (Valium®)
  - Advantages: inexpensive, requires no refrigeration, widely available, rapid IV onset, may be given rectally
  - Disadvantages: short duration of anticonvulsant action (15 to 20 minutes); apnea common when given IV; irritating to veins
  - Dose: 0.2 to 0.6 mg/kg rectally (maximum dose 10 mg) or 0.1 to 0.3 mg/kg IV

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Initial Anticonvulsant Choices

- Midazolam (Versed®):
  - Advantages: may be given by multiple routes (IV, IM, and intranasal) with rapid onset of action; requires no refrigeration
  - Disadvantages: shorter duration of action than lorazepam (about 1 hour)
  - Dose: 0.1 mg/kg IV/IO; 0.2 mg/kg IM; 0.2 to 0.3 mg/kg intranasal (maximum single dose of 4 mg any route

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Case Progression

- Rectal diazepam 0.5 mg/kg given
- Generalized tonic-clonic seizure activity continues during the 7-minute transport
- Seizure activity persists on arrival at the ED

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Case 2

What should you do now?

- Give an additional anticonvulsant from these choices:
  - Benzodiazepines
  - Phenytoin/fosphenytoin (be aware of potential for apnea)
  - Phenobarbital (be aware of potential for apnea)
- Perform additional studies
  - Electrolytes; consider sodium, calcium, phosphorus, magnesium, BUN, creatinine

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Case 2

- Stat electrolyte results
  - Sodium: 118 mEq/L
  - Chloride: 83 mEq/L
  - Potassium: 3.9 mEq/L
  - CO_2: 17 mEq/L
- *What next?*
  - 4 to 6 mL/kg 3% NaCl (provides 2 to 3 mEq/kg Na+) over 3 to 5 minutes if seizures persist

OR

  - 20 mL/kg normal saline provides 3 mEq/kg sodium – give rapidly to control seizures

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Case 2

- Seizures stop within 3 minutes of administration of NaCl
- Further history: infant formula had been improperly mixed and was quite dilute
- Infant admitted to the hospital for further monitoring and correction of electrolytes
- Social work referral was made

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Metabolic Abnormalities Resulting in Status Epilepticus

- Hypoglycemia
- Hyponatremia (first year of life)
- Hypocalcemia (more common in early infancy)
- Hypomagnesemia (rare)
- Uremia
- Inborn errors of metabolism
- Hyperammonemia

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Case 3

- A 3-month-old infant reportedly stopped breathing at home; during parent transport to the hospital he developed rhythmic jerking of his right arm
- On arrival in the Emergency Department he is breathing and continues to have tonic-clonic movements of the right arm
- He has been healthy; he ate well today.

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Infant appears pale with bruises on the forehead and abdomen.

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Case 3

Rapid cardiopulmonary assessment:

- Appearance: pale with bruises on the forehead and abdomen
- Airway patent; RR 44/minute (unlabored); SpO_2 95%
- HR 155 bpm, BP 85/56 mm Hg, capillary refill and pulses normal

Temperature 37°C

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Case 3

What are your initial management priorities after assessment?

- Maintain airway and administer oxygen
- Check blood glucose; treat hypoglycemia
- Establish IV access, check electrolytes
- Control temperature (maintain normothermia)

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Case 3: Progression

- Occipital area bruising, scalp swelling noted
- Seizure persists after 0.1 mg/kg lorazepam IV

What should you do now?

- Second dose of lorazepam given
- Infant becomes apneic

What are your next steps?

Should you obtain arterial blood gases?

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Rapid Sequence Intubation (RSI)

- Bag-mask ventilation with oxygen
- Select appropriate RSI medications for possible increased intracranial pressure:
  - Atropine
  - Lidocaine
  - Thiopental or etomidate
  - Rocuronium

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Arterial Blood Gases in Pediatric Status Epilepticus

- Ensuring oxygenation is important to avoid hypoxia
- Most patients with seizures will have some component of metabolic and respiratory acidosis (ABG not routinely needed)

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Arterial Blood Gases in Pediatric Status Epilepticus (continued)

- Treatment of acidosis should be directed at the primary cause
- STOP THE SEIZURE
- Intubation is probably overused during treatment of seizures
  - It should NOT be performed simply to treat blood gas anomalies
  - Blood gas analysis is rarely indicated

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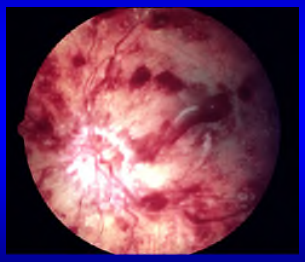
Funduscopic Exam



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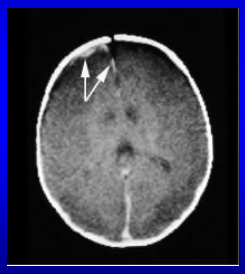
Head CT



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Medications for Persistent Seizures

- Fosphenytoin (Cerebyx®)
  - IV form less less irritating than phenytoin
  - Dose: 20 phenytoin equivalents (PE) per kilogram over 6 to 10 minutes
  - May cause hypotension
  - If unavailable give phenytoin 20 mg/kg over 20 minutes (IV infusion must not exceed 1 mg/kg per minute); monitor HR and BP during infusion

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Medications for Persistent Seizures

Phenobarbital

- Dose
  - 15 to 20 mg/kg IV or IO given over 15 to 20 minutes
  - May repeat doses of 5 mg/kg every 30 minutes
  - Monitor levels
- Side effects/complications
  - Respiratory depression common when combined with benzodiazepines
  - Can cause hypotension

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Indications for Intubation

- Respiratory arrest after anticonvulsants if no response to a few minutes of bag-mask ventilation
- Concern for increased intracranial pressure after seizure stopped (eg, persistent posturing, asymmetric pupils)
- Status epilepticus requiring continuous infusions of anticonvulsants
- Hemodynamic compromise

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Nonconvulsive SE

- Definition: continued seizure activity on EEG with alteration in consciousness (electrographic seizures) in absence of clinical motor activity
- May occur after convulsive SE

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Nonconvulsive SE

- Consider when patient does not respond to painful stimuli within 20 minutes of termination of seizure; diagnosis requires urgent EEG
- If present, treat with additional anticonvulsants
- Morbidity is lower than convulsive SE

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Drug Choices for Refractory Status Epilepticus

- IV midazolam infusion
- IV pentobarbital infusions
- IV valproic acid
- All patients requiring this level of support should be intubated and admitted to a pediatric intensive care unit

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Critical Concepts

- Assess and support ABCs
- Ensure adequate oxygenation
- Ensure adequate blood glucose
- Control seizure with anticonvulsants
- Control temperature
- Assess for etiology based on history, age, and clinical examination

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End of Module

- Supplemental material follows

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Myoclonic Seizure

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Absence Seizure

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Partial Seizure

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Tonic Clonic

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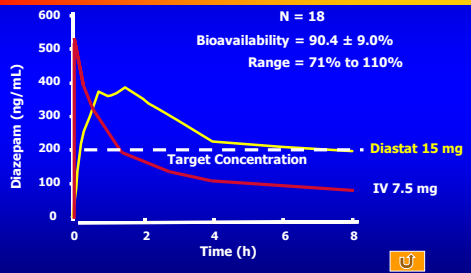
Bioavailability of Diazepam

Diastat® vs IV diazepam



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Data from Cloyd et al. *Epilepsia.* 1998;39:520-526.

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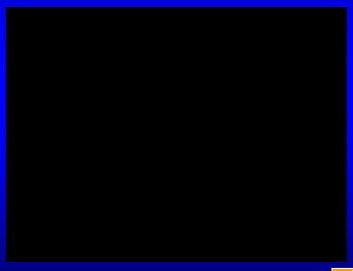
Capillary Refill



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Crit Care Med. 1991 Jun;19(6):758-62.
Management of hyponatremic seizures in children with hypertonic saline: a safe and effective strategy.
Sarnaik AP, Meert K, Hackbarth R, Fleischmann L.
Department of Pediatrics, Children's Hospital of Michigan, Detroit 48201.
OBJECTIVE: To study efficacy and safety of hypertonic saline administration in the management of hyponatremic seizures. DESIGN: Retrospective, observational, cross-sectional study with factorial design. SETTING: In-patient population in a university hospital. PATIENTS: All children admitted with serum sodium concentrations less than 125 mmol/L. Sixty-nine episodes of severe hyponatremia in 60 children were reviewed. Forty-one of these children presented with seizures. INTERVENTIONS: Twenty-five of 41 seizure patients received an iv bolus of 4 to 6 mL/kg body weight of 3% saline. Twenty-eight patients were treated with a benzodiazepine and/or phenobarbital with or without the subsequent administration of hypertonic saline. MEASUREMENTS AND MAIN RESULTS: Thirteen treatment failures and ten instances of apnea occurred among the 28 patients treated with benzodiazepine/phenobarbital. Administration of hypertonic saline resulted in resolution of seizures and apnea in all cases. Those patients receiving 3% saline had a higher serum sodium increase rate from 0 to 4 hrs than the remaining patients (3.1 +/- 1.3 vs. 1.7 +/- 1.2 mmol/L/hr, p less than .01). None developed subsequent neurologic deterioration or clinical manifestations of osmotic demyelination syndrome. CONCLUSION: Treatment of hyponatremic seizures with routine anticonvulsants may be ineffective and is associated with a considerable incidence of apnea. A rapid increase in the serum sodium concentration by 5 to 5 mmol/L with the use of hypertonic saline is safe and efficacious in managing acute symptomatic hyponatremia.
PMID: 2055051 [PubMed - indexed for MEDLINE]
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J Child Neurol. 2002 Dec;17 Suppl 3:3S3-7; discussion 3S8.
Classification of infantile seizures: implications for identification and treatment of inborn errors of metabolism.
Nordli DR Jr, De Vivo DC.
Department of Pediatrics, Lorna S. and James P. Langdon Chair of Pediatric Epilepsy, Children's Memorial Hospital, Northwestern University, Chicago, Illinois 60614-3394, USA. DNordli@childrensmemorial.org
Metabolic disorders constitute an important cause of neurologic disease, including infantile epilepsy. The inability to characterize seizures and epilepsy syndromes precisely in infants impedes the recognition of features suggestive of specific underlying metabolic and neurodegenerative etiologies. Classification systems using simple descriptions of ictal behaviors can be reliably applied and may aid in the recognition of these disorders. Myoclonic seizures in infancy in particular suggest an inborn error of metabolism. In addition, certain epileptic syndromes are known to be associated with metabolic disorders, including some forms of neonatal seizures, West's syndrome, early myoclonic encephalopathy, and early infantile epileptic encephalopathy. Occasionally, there are distinctive electroencephalographic patterns that may suggest a specific metabolic disease. Earlier recognition of metabolic disorders may be accomplished by careful study of clinical and electrographic characteristics. There are important treatment considerations associated with these disorders.
Publication Types:
• Review
• Review, Tutorial
PMID: 12597050 [PubMed - indexed for MEDLINE]
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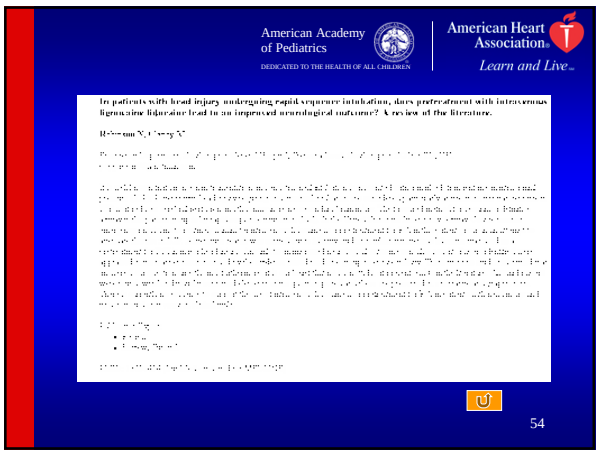
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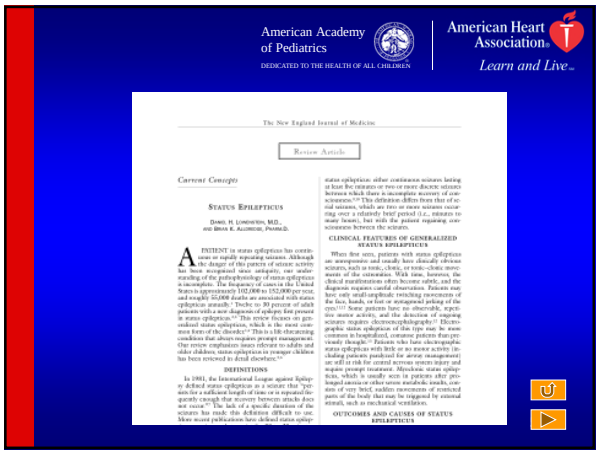
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The New England Journal of Medicine
Review Article
Current Concepts
STATUS EPILEPTICUS
DAVID M. LOWENSTEIN, M.D., AND BRIAN K. ALLDREDGE, PHARM.D.
A PATIENT in status epilepticus has continuous or rapidly repeating seizures. Although the danger of this pattern of seizure activity has been recognized since antiquity, our understanding of the pathophysiology of status epilepticus is incomplete. The frequency of cases in the United States is approximately 102,000 to 152,000 per year, and roughly 50,000 deaths are associated with status epilepticus annually.[1] Twelve to 30 percent of adult patients with a new diagnosis of epilepsy first present in status epilepticus.[2,3] This review focuses on generalized status epilepticus, which is the most common form of the disorder.[4,5] This is a life-threatening condition that always requires prompt management. Our review emphasizes issues relevant to adults and older children; status epilepticus in younger children has been reviewed in detail elsewhere.[5,6]
DEFINITIONS
In 1981, the International League against Epilepsy defined status epilepticus as a seizure that "persists for a sufficient period of time or is repeated frequently enough that recovery between attacks does not occur".[7] The lack of a specific duration of the seizures has made this definition difficult to use. More recent publications have defined status epilepticus as either continuous seizures lasting at least five minutes or two or more discrete seizures between which there is incomplete recovery of consciousness.[8,9] This definition differs from that of serial seizures, which are two or more seizures occurring over a relatively brief period (i.e., minutes to many hours), but with the patient regaining consciousness between the seizures.
CLINICAL FEATURES OF GENERALIZED STATUS EPILEPTICUS
When first seen, patients with status epilepticus are unresponsive and usually have clinically obvious seizures, such as tonic, clonic, or tonic–clonic movements of the extremities. With time, however, the clinical manifestations often become subtle, and the diagnosis requires careful observation. Patients may have only subtle twitching or stereotyped jerking of the face, head, or limbs, or they may seem strangely confused. Some patients have no observable, stereotypic motor activity, and the detection of ongoing seizures requires electroencephalography.[10] Electrographic status epilepticus of this type may be more common in hospitalized, comatose patients than previously thought.[11] Patients who have electrographic status epilepticus with little or no motor activity (including patients paralyzed for airway management) are still at risk for central nervous system injury and require prompt treatment. Myoclonic status epilepticus, which is usually seen in patients after prolonged anoxia or other severe metabolic insults, consists of very brief, sudden movements of restricted parts of the body that may be triggered by external stimuli, such as mechanical ventilation.
OUTCOMES AND CAUSES OF STATUS EPILEPTICUS

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The NEW ENGLAND JOURNAL of MEDICINE
REVIEW ARTICLE
MECHANISMS OF DISEASE
Epilepsy
Bernard S. Chang, M.D., and Daniel H. Lowenstein, M.D.
EPILEPSY IS ONE OF THE MOST COMMON NEUROLOGIC PROBLEMS worldwide. Approximately 2 million persons in the United States have epilepsy, and 3 percent of persons in the general population will have epilepsy at some point in their lives.[1] In recent years, important advances have been made in the diagnosis and treatment of seizure disorders.[2] However, our understanding of the cellular and molecular mechanisms by which epilepsy develops, or epileptogenesis, is still incomplete.
In this overview, we highlight some of the prevailing ideas about epileptogenesis by presenting examples of epilepsy syndromes and theories of their mechanisms of origin. Several recent reviews offer more specialized and comprehensive discussions of this topic.[3-5]
From the Comprehensive Epilepsy Center, Department of Neurology, Beth Israel Deaconess Medical Center, and Harvard Medical School — both in Boston (B.S.C.); and the University of California San Francisco Epilepsy Center, Department of Neurology, University of California San Francisco, San Francisco (D.H.L.).
N Engl J Med 2003;349:1257-66.
Copyright © 2003 Massachusetts Medical Society
CLASSIFICATION OF EPILEPSY
The term "epilepsy" encompasses a number of different syndromes whose cardinal feature is a predisposition to recurrent unprovoked seizures. Although specific seizures can be classified according to their clinical features (e.g., complex partial seizures and generalized tonic–clonic seizures),[6] epilepsy syndromes can also be classified according to the type of seizure, the presence or absence of neurologic or developmental abnormalities, and electroencephalographic (EEG) findings.[7] For example, the syndrome of juvenile myoclonic epilepsy is characterized by the onset of myoclonic seizures, generalized tonic–clonic seizures, and less frequently absence seizures in adolescents who have normal intellectual function, with EEG findings of rapid, generalized spike-wave and polyspike-wave discharges.[8]

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A COMPARISON OF FOUR TREATMENTS FOR GENERALIZED CONVULSIVE STATUS EPILEPTICUS
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ABSTRACT
Background and Methods Although generalized convulsive status epilepticus is a life-threatening emergency, the best initial drug treatment is uncertain. We conducted a five-year randomized, double-blind, multicenter trial of four intravenous regimens: diazepam (0.15 mg per kilogram of body weight) followed by phenytoin (18 mg per kilogram), lorazepam (0.1 mg per kilogram), phenobarbital (15 mg per kilogram), and phenytoin (18 mg per kilogram). Patients were classified as having either overt generalized status epilepticus (defined as easily visible generalized convulsions) or subtle status epilepticus (indicated by coma and ictal discharges on the electroencephalogram, with or without subtle convulsive movements such as rhythmic muscle twitches or tonic eye deviation). Treatment was considered successful when all motor and electroencephalographic seizure activity ceased within 20 minutes after the beginning of the drug infusion and there was no return of seizure activity during the next 40 minutes. Analyses were performed with data on only the 518 patients with verified generalized convulsive status epilepticus as well as with data on all 570 patients who were enrolled.
STATUS epilepticus is a life-threatening emergency that affects 65,000[1] to 150,000[2] people in the United States each year. Generalized convulsive status epilepticus is the most common and most dangerous type.
Phenobarbital,[3,4] phenytoin,[4-6] diazepam plus phenytoin,[4,7,8] and lorazepam[7,9,10] have been advocated for the initial treatment of generalized convulsive status epilepticus, and each is used by a substantial number of physicians.[3] There are few data from controlled trials, however, to document the efficacy of these treatments, and they have not been directly compared. We therefore undertook this study to compare the efficacy of standard doses of these four drugs in the treatment of generalized convulsive status epilepticus.
METHODS
Study Design
In a double-blind study conducted at 16 Veterans Affairs medical centers and 6 affiliated university hospitals between July 1, 1998, and June 30, 1999, patients with generalized convulsive status epilepticus were randomly assigned to receive intravenous
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