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GUIDELINES UPDATE

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Current Guidelines For Management Of Seizures In The Emergency Department

In this issue of *EM Practice Guidelines Update*, 3 practice guidelines that address the management of seizures are reviewed. The recommendations within the 3 documents focus on decisionmaking around the patient with seizures refractory to first-line therapy, the management of patients with an unprovoked first seizure, and options for anticonvulsant drug delivery.

Status epilepticus complicates up to 7% of seizures in the emergency department (ED), with a significant mortality rate.[1] Patients with ongoing seizures demand immediate general resuscitative and specific therapeutic maneuvers; good evidence exists to direct clinicians in managing these dangerous presentations. Stable seizure patients commonly seek emergency care for first-time seizures, breakthrough seizures, or unrelated complaints that affect their ongoing anticonvulsant therapy. High-quality trials examining issues that arise in the care of these patients are few; however, consensus-based recommendations offer guidance to clinicians navigating controversial testing and treatment scenarios.

Practice Guideline Impact

- Intravenous (IV) lorazepam is first-line therapy for active seizures. Patients who continue to seize after 2 benzodiazepine doses should be treated with propofol or barbiturates.
- Diagnostic lumbar puncture is indicated in immunocompromised patients with an unprovoked first seizure.
- EEG monitoring is indicated to rule out nonconvulsive status epilepticus in patients receiving aggressive therapy for generalized convulsive status epilepticus.

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Prior to beginning this activity, see "Physician CME Information" on page 7.

Editor's Note: To read more about this publication and the background and methodologies for practice guideline development, go to: http://www.ebmedicine.net/introduction

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Practice Parameter: Evaluating An Apparent Unprovoked First Seizure In Adults (An Evidence-Based Approach).[2]

Neurology. 2007;69:1996-2007.
Link to this: http://www.neurology.org/cgi/reprint/69/21/1996

This document was developed by a group of neurologists organized by the American Academy of Neurology (AAN) in collaboration with the American Epilepsy Society; the methodology is adapted from the AAN Clinical Practice Guideline Process Manual.[3] The group identified 5 questions based on a literature search from 1966 to 2004, and it was carried out according to explicit criteria. Article inclusion and exclusion criteria are specified and selected details around the review process are described.

Evidence was evaluated for quality according to predefined, specified criteria and assigned to 1 of 4 classes (I, II, III, IV). Recommendations were graded at 4 levels: A, B, C, U, based primarily on the strength of evidence for each question. Level A: established as true; Level B: probably true; Level C: possibly true; Level U: data inadequate or conflicting. The target provider population is not defined. The Practice Parameter applies to adults 18 years of age and older presenting with a first unprovoked seizure (ie, excluding patients with diagnosed seizure disorders and seizures resulting from an obvious cause such as trauma and stroke).

The Conflict of Interest statement notes "Drafts of the guidelines have been reviewed by at least 3 AAN committees, a network of neurologists, *Neurology* peer reviewers, and representatives from related fields," and "The AAN forbids commercial participation in, or funding of, guideline projects." The authors report no conflicts of interest. The following questions and recommendations are abstracted from the Practice Parameter. To view the original document in its entirety, click here: http://www.neurology.org/cgi/reprint/69/21/1996

In an adult presenting with an apparently unprovoked first seizure, should an EEG be ordered routinely?

Recommendation 1 (Level B): For an adult with an apparent unprovoked first seizure, the EEG should be considered as part of the neurodiagnostic evaluation, because it has a substantial yield.

Recommendation 2 (Level B): For an adult with an apparent unprovoked first seizure, the EEG should be considered as part of the neurodiagnostic evaluation because it has value in determining risk of seizure recurrence.

For an adult presenting with an apparent unprovoked first seizure, should a brain imaging study (CT, MRI) be routinely ordered?

Recommendation 3 (Level B): For an adult presenting with an apparent unprovoked first seizure, brain imaging studies using CT or MRI should be considered as part of the neurodiagnostic evaluation.

For an adult presenting with an apparent unprovoked first seizure, should blood counts, blood glucose, and electrolyte panels be routinely ordered?

Recommendation 4 (Level U): There are insufficient data to support or refute routine recommendation of laboratory tests such as blood glucose, blood counts, and electrolyte panels for an adult presenting with an apparent unprovoked first seizure, though they may be helpful in specific clinical circumstances.

For an adult presenting with an apparent unprovoked first seizure, should lumbar puncture be routinely performed?

Recommendation 5 (Level B): There are insufficient data to support or refute recommending routine lumbar puncture in the adult initially presenting with an apparent unprovoked first seizure; however, in special clinical circumstances (eg, febrile patients), it may be helpful.

In an adult presenting with an apparent unprovoked first seizure, should toxicologic screening be routinely ordered?

Recommendation 6 (Level B): There are insufficient data to support or refute a routine recommendation for toxicology screening; however, it may be helpful in specific clinical circumstances. ■

Clinical Policy: Critical Issues In The Evaluation And Management Of Adult Patients Presenting To The Emergency Department With Seizures.[1]

Annals of Emergency Medicine. 2004;43:605-625.
Link to this: http://www.acep.org/WorkArea/DownloadAsset.aspx?id=8820

This document was developed by a committee and subcommittee organized and funded by the American College of Emergency Physicians (ACEP). Panel members are listed; their affiliations/qualifications are not. The group identified 6 critical questions and utilized an explicit strategy for their literature search and review. Evidence was evaluated for quality according to predefined criteria and sorted into 4 classes (I, II, III, or X-fatally flawed). Recommendations were graded based on the strength of evidence for each question. A: high degree of certainty; B: moderate degree of certainty; C: based on preliminary, inconclusive, or conflicting evidence or panel consensus. Disclosures were reported for the subcommittee for this policy. The policy targets clinicians working in hospital-based EDs. The guidelines presented in the policy apply to adult patients presenting to the ED with seizures. Pediatric patients are excluded.

What laboratory tests are indicated in the otherwise healthy adult patient with a new-onset seizure who has returned to a baseline normal neurologic status?

Recommendation 1 (Level B): Determine a serum glucose and sodium level on patients with a first-time seizure with no comorbidities who have returned to their baseline.
Recommendation 2 (Level B): Obtain a pregnancy test if a woman is of childbearing age.
Recommendation 3 (Level B): Perform a lumbar puncture, after a head computed tomography (CT) scan, either in the ED or after admission, on patients who are immunocompromised.

Which new-onset seizure patients who have returned to a normal baseline require a head CT scan in the ED?

Recommendation 4 (Level B): When feasible, perform a neuroimaging of the brain in the ED on patients with a first-time seizure.
Recommendation 5 (Level B): Deferred outpatient neuroimaging may be used when reliable follow-up is available.

Which new-onset seizure patients who have returned to normal baseline need to be admitted to the hospital and/or started on an antiepileptic drug?

Recommendation 6 (Level C): Patients with a normal neurologic examination can be discharged from the ED with outpatient follow-up.
Recommendation 7 (Level C): Patients with a normal neurologic examination, no comorbidities, and no known structural brain disease do not need to be started on an antiepileptic drug in the ED.

What are effective phenytoin or fosphenytoin dosing strategies for preventing seizure recurrence in patients who present to the ED after having had a seizure with a subtherapeutic serum phenytoin level?

Recommendation 8 (Level C): Administer an intravenous or oral loading dose of phenytoin or intravenous or intramuscular fosphenytoin, and restart daily oral maintenance dosing.

What agent(s) should be administered to a patient in status epilepticus who continues to seize after having received benzodiazepine and phenytoin?

Recommendation 9 (Level C): Administer 1 of the following agents intravenously: “high-dose phenytoin,” phenobarbital, valproic acid, midazolam infusion, pentobarbital infusion, or propofol infusion.

When should EEG testing be performed in the ED?

Recommendation 10 (Level C): Consider an emergent EEG in patients suspected of being in nonconvulsive status epilepticus or in subtle convulsive status epilepticus, patients who have received a long-acting paralytic, or patients who are in a drug-induced coma. ■

EFNS Guideline On The Management Of Status Epilepticus.[4]

European Journal of Neurology. 2006;11:577-581.

Link to this: http://www.efns.org/fileadmin/user_upload/guidline_papers/EFNS_guideline_2006_management_of_status_epilepticus.pdf

This document was developed by a task force comprised of 7 neurologists organized by the European Federation of Neurological Societies (EFNS), a consortium comprised of 43 European national neurological societies based in Austria. The development process was carried out in accordance with a preparation document generated by the EFNS in 2004.[5] The group designated a single member to carry out the literature search according to reported parameters. Evidence was evaluated for quality based on criteria specified in the preparation document and sorted into 4 classes (I, II, III, IV). Recommendations were graded (A-established as effective; B-probably effective; C-possibly effective, GPP - the opinion of the panel reported as good practice points "where there was a lack of evidence but consensus was clear") based on the strength of evidence for each question.

A funding source is not identified. Panelists' conflicts of interest were reported as none declared. The target is identified as adults with status epilepticus "in critical care situations." Debate around the definition of status epilepticus is described; studies on patients with seizures lasting 5, 10, and 30 minutes were included. Recommendations in this document are reported in narrative style; those recommendations that pertain to emergency medicine are summarized here.

General initial management

Recommendation 1 (Level GPP): Support airway and ventilation; monitor blood pressure and ECG waveform; perform blood gas analysis; supplement glucose and thiamine as required; measure serum antiepileptic drug levels, electrolytes (including magnesium), blood counts, hepatic and renal function tests. Identify and treat the underlying cause.

Initial pharmacological treatment of generalized convulsive status epilepticus (GCSE)

Recommendation 2 (Level A): Treat partial status epilepticus and GCSE with lorazepam 4 mg IV; repeat in 10 minutes if seizures persist. Phenytoin 15 to 18 mg/kg or equivalent fosphenytoin is recommended "if necessary." An alternate regimen is diazepam 10 mg IV followed by phenytoin 15 to 18 mg/kg or equivalent fosphenytoin; repeat diazepam in 10 minutes if seizures persist.

Pharmacological treatment for refractory GCSE and subtle status epilepticus

Recommendation 3 (Level GPP): Infuse anesthetic doses of midazolam, propofol, or barbiturates titrated against an EEG burst suppression pattern. Initiate treatment with non-sedating antiepileptic agents simultaneously. Thiopental: 100 to 200 mg bolus over 20 seconds with 50 mg boluses every 2 to 3 minutes until seizures are controlled, then infusion 3 to 5 mg/kg/hr. Pentobarbital: 10 to 20 mg/kg bolus followed by an infusion of 0.5 to 3 mg/kg/hr. Midazolam: 0.2 mg/kg bolus followed by an infusion of 0.1 to 0.4 mg/kg/hr. Propofol: 2 mg/kg bolus followed by an infusion of 5 to 10 mg/kg/hr.

Pharmacological treatment for non-convulsive status epilepticus (NCSE)

Recommendation 4 (Level GPP): Ongoing NCSE is less dangerous than GCSE; therefore, non-anesthetizing anticonvulsants may be tried initially. Phenobarbital: 20 mg/kg IV. Valproic acid: 25 to 45 mg/kg IV infused at a maximum rate of 6 mg/kg/min. ■

Editorial Comment

The patient in status epilepticus presents an immediate resuscitative challenge to the emergency clinician, as efforts to terminate seizures must be carried out simultaneously with measures to support the airway, breathing, and circulation as well as diagnostic maneuvers directed at identifying dangerous underlying disorders. Emergency providers should not be distracted by definitions of status epilepticus that vary across sources and treat as status epilepticus any patient who arrives seizing or any patient who has a seizure in the ED that does not self-terminate or respond to initial therapies. When confronted with a patient in status epilepticus who does not respond to benzodiazepine treatment, the clinician should consider underlying causes that require specific therapies, such as hypoglycemia, hyponatremia, eclampsia, and toxic exposures amenable to antidotes (eg, isoniazid, heterocyclic antidepressants, cyanide, carbon monoxide). Most patients with refractory status should be intubated and started on a barbiturate or propofol infusion with or without high-dose phenytoin and/or intravenous valproate. Hypotension should be anticipated and managed in these cases.

If the seizure has terminated and ABCs are stable, the emergency clinician must determine whether the patient had a seizure or another episodic disorder such as syncope or complex migraine. If a presumptive diagnosis of seizure is made in a patient not known for seizures, management is directed at finding dangerous and reversible causes. A non-contrast brain CT is indicated in most patients with first seizure to rule out structural causes. In younger patients where radiation concerns are more prominent, MRI is an alternative. Although laboratory studies are of low yield in patients whose symptoms have resolved, serum chemistry analysis in the ED is prudent. Lumbar puncture should be performed on immunocompromised patients and patients for whom central nervous system infection is a significant concern. Although toxicologic causes of seizures can be life-threatening, undirected toxicology testing such as a urine drug screen is unlikely to alter ED management. It is worth special mention that alcohol-related or alcohol-withdrawal seizure is a diagnosis of exclusion; alcoholics are at particular risk for several other dangerous causes of seizures.

Another AAN Practice Parameter published in the same issue as the guideline abstracted here looked specifically at the utility of brain CT in the ED in various populations of patients who present with seizure.[6] Their conclusions are similar to the recommendations made in the abstracted report on evaluating the first seizure; in addition, the panel makes a class II recommendation that patients who present with chronic seizures are more likely to have an abnormal brain CT if there is an abnormal neurologic examination, a predisposing history of neurologic disease, or a focal seizure onset.

The EEG provides important information regarding prognosis and seizure classification; however, it is not required in the ED when dangerous etiologies of seizure have been ruled out and the patient has returned to clinical baseline. The chief indications for performing an emergent EEG are to assess the patient paralyzed and intubated for status epilepticus, and to rule out nonconvulsive status epilepticus in the patient with altered mentation, especially in patients who do not return to baseline after a generalized seizure. The emergency clinician is not compelled to initiate anticonvulsant therapy in uncomplicated cases; however, this decision is ideally made in collaboration with the neurologist who will see the patient in follow-up.

Although fosphenytoin can be infused more quickly than phenytoin, it does not work faster or cause fewer adverse effects than phenytoin and should not be routinely used in place of its much less expensive parent.[7,8] Fosphenytoin is preferred in cases where the patient cannot complain of pain if extravasation occurs (eg, a comatose patient) or when intramuscular delivery is required. In patients who will not be quickly discharged from the department, oral phenytoin loading is underutilized; in uncomplicated patients at low risk for immediate recurrent seizure, oral loading is effective and offers benefits of convenience, cost, and safety.[8,9] ■

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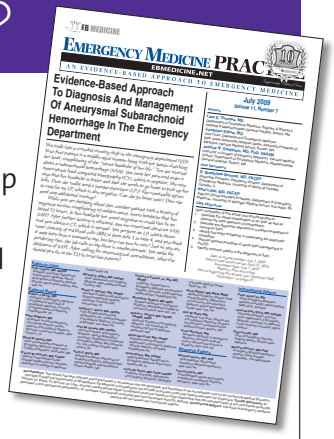

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