An Approach to the Evaluation of a Patient for Seizures and Epilepsy

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ABSTRACT
Epilepsy affects approximately 1 percent of the population and is characterized by recurrent unprovoked seizures. A careful clinical history is often helpful in diagnosis, classification of seizure and epilepsy types, selection of appropriate ancillary studies, selection of anti-epileptic drugs, and formulation of a long-term management plan. This article provides directions and guidelines both for the family practice physician and the specialist in evaluating this patient population in the clinics.

INTRODUCTION
A seizure is defined as an abnormal, excessive, paroxysmal discharge of the cerebral neurons. Epilepsy is a chronic condition characterized by recurrent, unprovoked seizures. In clinical practice, if a patient has 2 or more seizures, he/she is diagnosed as having epilepsy.

It is of the utmost importance for a clinician to be aware of other conditions and/or episodes that may simulate seizures. In short, the first question to be addressed is: Does the episode in question represent a seizure? The following section provides a brief overview of conditions that can masquerade as seizures.

DIFFERENTIAL DIAGNOSIS OF SEIZURES
A detailed discussion of the differential diagnosis of seizures and epilepsy is beyond the scope of this article. Some of the common conditions that present to the epilepsy clinics will be discussed (Table 1).

Syncope
A syncope refers to a transient loss of consciousness due to brief interruption of blood supply to the brain. Convulsive movements of the extremities may follow some prolonged episodes. Vasovagal syncope may be secondary to fear, pain or unpleasant sights such as blood or medical procedures. Reflex syncope can follow coughing, micturition, defecation or Valsalva’s maneuver. Other causes, especially in the elderly, include orthostatic hypotension and cardiac arrhythmias. Patients report feeling dizzy/light-headed, fullness in ears, nauseous and often gradual graying or blurring of the vision. Patients who fall tend to go down more “gracefully” than those with seizures. Careful history will elicit stereotypical provoking factors such as prolonged periods of standing in the heat, sight of blood, micturition, or abruptly assuming an erect posture after prolonged recumbence. The absence of an aura (described later), tongue bite, urinary incontinence and prolonged tonic-clonic activity in the presence of a provoking factor would be more suggestive of syncope.

Transient Ischemic Attacks and Migraines
Transient ischemic attacks (TIA) result from a temporary interruption of blood supply in the distribution of a cerebral vessel. It may be secondary to an embolic phenomenon or may result from a critically stenosed vessel. “Negative symptoms” such as numbness and weakness are more likely to manifest as compared to the “positive symptoms” (stiffness and twitching) seen with seizures. Symptoms appear in a vascular distribution and date back to a few months rather than several years. Patients will likely have risk factors for cerebrovascular disease such as hypertension, diabetes and/or coronary artery disease. However, there will be certain patients with a diagnostic dilemma and a detailed work up for TIA and seizures will be warranted.

A classic migraine with visual aura, nausea/vomiting and pounding hemricranial headache can be differentiated easily from a seizure based on history alone. However, migraines presenting with isolated symptoms such as vertigo, episodic vomiting (cyclic vomiting), vi-
Susal changes and aphasia with/without headaches can be a challenge. It is important to consider migraines in the differential diagnosis of paroxysmal episodes. A detailed history of previous attacks, certain triggers (caffeine, sleep withdrawal, chocolate), or family history of migraines may provide additional clues. Empirical treatment with antiepileptic/anti-migraine medications may clarify the diagnosis in some instances.

**Pseudoseizures and Hysterical Seizures**

Pseudoseizures are paroxysmal attacks of non-epileptic etiology. The clinical attacks may resemble different seizure types and at times are a challenge to the inexperienced. Certain clinical characteristics are suggestive of non-epileptic attacks:2 waxing and waning movements during a single attack, prolonged tonic-clonic activity without postictal disorientation, non-rhythmic pelvic thrusting, non-physiological evolution of symptoms such as motor activity spreading from one hand to the other without first affecting the ipsilateral face or leg.

Although several characteristics of pseudoseizures have been described in literature, this is not an easy diagnosis to make. It is strongly suggested that all such patients should be evaluated by clinicians experienced in dealing with epilepsy. A significant number of patients misdiagnosed with pseudoseizures may turn out to have epilepsy.3 Inpatient video electroencephalogram is one of the most useful tools in clarifying the correct diagnosis.4,5

**CLASSIFICATION OF SEIZURES AND EPILEPSY**

Some basic understanding of the classification of seizures and epilepsy is essential before more formal guidelines regarding history taking in epilepsy can be presented. Seizures can be classified as partial or generalized (Table 2).

Partial seizures originate from a discrete or localized area of the brain, and may or may not spread to other areas. If a patient maintains awareness during a partial seizure he/she is diagnosed with simple partial seizures. If awareness is lost, the event is classified as a complex partial seizure. A simple partial seizure may evolve into a complex partial and/or secondary generalized seizure.

A generalized seizure does not have a focal onset, and awareness is lost immediately. There are several recognized kinds of generalized seizures: absence (brief lapse of awareness), petit mal; grand mal (tonic clonic activity), myoclonic (sudden massive jerk, usually of upper body), atonic (sudden loss of tone), and tonic (brief generalized stiffening). The term epilepsy incorporates the kind(s) of seizures and other information about presentation and electroencephalogram (EEG). It is broadly classified as localization-related if the seizures have a focal onset, and generalized when they begin all over at once. The term idiopathic denotes that the etiology is unknown, while symptomatic means that a structural cause has been identified and cryptogenic implies that a structural abnormality is suspected but could not be identified.6 One example is that a 6-year-old, otherwise normal child who presents

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**Table 1. Differential Diagnosis of Seizures**

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Benign positional vertigo</td>
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<td>Breath holding spells in children</td>
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<td>Cardiac arrhythmia</td>
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<tr>
<td>Hypoglycemia</td>
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<td>Migraine</td>
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<tr>
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<tr>
<td>Night terrors</td>
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<tr>
<td>Nightmares</td>
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<td>Nocturnal myoclonus</td>
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<td>Panic attacks</td>
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<td>Periodic paralysis</td>
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<tr>
<td>Pseudoseizures/Hysterical seizures</td>
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<tr>
<td>Sleep apnea</td>
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<tr>
<td>Syncope</td>
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<tr>
<td>Transient ischemic attacks</td>
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</table>

**Table 2. Classification of Seizures and Epilepsy**

**Seizure**

Partial (seizures with a focal or localized onset)

- Simple partial (awareness* is not lost)
- Complex partial (loss of awareness)

Generalized (Generalized seizures affect both hemispheres simultaneously, without a focal onset.)

- Absence seizures
- Myoclonic seizures
- Tonic seizures
- Clonic seizures
- Atonic seizures
- Tonic-clonic seizures

**Epilepsy**

Examples of localization-related epilepsies

- Frontal lobe epilepsies
- Temporal lobe epilepsies
- Parietal lobe epilepsies
- Occipital lobe epilepsies

Examples of generalized epilepsies

- Juvenile absence epilepsy
- Juvenile myoclonic epilepsy
- Infantile spasms (West syndrome)
- Lennox-Gastaut syndrome

* The patient may appear awake but is unable to interact with his surroundings in a meaningful way, therefore the term “loss of awareness” rather than “loss of consciousness” is used.
with absence seizures (a kind of generalized seizure) would be diagnosed with idiopathic generalized epilepsy. A 70 year old who presents with focal seizures after left middle cerebral artery stroke is said to have localization-related epilepsy symptomatic of the stroke. A patient who is developmentally challenged with generalized seizures but normal cerebral imaging will be classified as having cryptogenic generalized epilepsy.

HISTORY OF PRESENTING COMPLAINTS
A witness who can supplement the history should accompany the patient. Collateral history from observers can also be obtained over the telephone if necessary. Ask the patient to describe what happens preceding, during, and following the episode. Let them answer this open-ended question in as much detail as they can without interruption. With a good historian, this question alone may provide all the important details. However, in most instances, further history and details will be required. These questions are presented to the patient and the witness.

1. *When did you experience the first seizure in your life?* The age of onset may shed some light on the classification and etiology of seizures. Seizures starting in the early neonatal period are usually secondary to perinatal insults, metabolic disorders, and congenital malformation. Generalized seizures tend to present in early childhood or teenage years. A 70 year old who presents with new onset seizures is likely to have structural pathology such as a stroke or brain tumor. Sometimes a patient cannot answer this question reliably, and it is important to have input from a parent or other close family member.

2. *Do you experience some kind of a warning or unusual feeling at the onset, or immediately preceding the seizure?* The warning symptoms that are perceived at the onset of a seizure are called “aura.” An aura actually represents a simple partial seizure, and thus indicates that the seizure is focal in origin. A particular aura may help localize a seizure. Patients with temporal lobe epilepsy may report a déjà vu and/or a rising epigastric sensation, paresthesias may be reported in parietal lobe epilepsy, and visual distortions or transient blindness may be experienced in occipital lobe epilepsy. Generalized seizures are not preceded by auras since they involve the whole brain at onset and there is no awareness of any component. If auras are reported at the onset of generalized seizures, a focal pathology should be sought and the generalized classification reconsidered.

3. *What happens during the seizure?* Unless a patient has simple partial seizures with preserved awareness, he/she will not be able to answer this question. A witness should be interviewed and specific information sought that may help classify the seizure type. Is there head or eye deviation to one side? Does the motor activity start on one side of the body? Is the patient able to talk during the seizure? Is there excessive eye blinking at the onset? If automatisms (defined by Lüders as involuntary, organized sequences of movement that are not causally related to the external environment) occur, are these more pronounced on one side? Is there a posturing of an extremity? Does the patient bite his tongue or lose control of the bladder function? Seizures originating from the frontal eye fields may cause head and eye deviation to the contralateral side. Temporal lobe seizures are often manifested with lip smacking and other oral and alimentary automatic behavior (automatisms), which are most pronounced in the ipsilateral extremity, along with dystonic posturing of the contralateral arm. Occipital lobe seizures can present with excessive blinking at the onset, negative visual symptoms or visual distortions. Tongue biting and urinary incontinence, although more often seen with generalized seizures, can also be present in complex partial seizures.

4. *What happens immediately following the seizure?* The immediate period following a seizure is known as the postictal period. Following a generalized tonic-clonic seizure (convulsion), the patient may go into a period of postictal sleep. Periods of disorientation and lack of awareness of the surroundings may follow some complex partial seizures. Hemiparesis or hemiplegia following a seizure (Todd’s paralysis) is suggestive of a focal onset. Aphasia with otherwise normal awareness is suggestive of involvement of the language areas in the dominant hemisphere. Absence seizures are typically associated with brief or no postictal disorientation.

5. *Is there a diurnal variation?* Certain seizures are more commonly seen during different times in the 24-hour daily cycle. Tonic-clonic and myoclonic seizures seen in primary generalized epilepsies are more common on awakening or in early morning. Temporal lobe seizures occur any time. Certain frontal lobe seizures have nocturnal presentation, occasionally exclusively.

6. *Are there any known triggering factors?* Seizures can be precipitated by sleep deprivation, flickering lights, menses, alcohol consumption, medication
non-compliance, use of antihistamines, stress, fever, or exercise. Identification of a risk factor may help with preventive counseling.

7. **What is the seizure frequency?** This information is helpful in establishing the response to treatment in the subsequent visits.

8. **What has been the maximum seizure-free period since the seizure onset?** This question is especially helpful in trying to determine if any specific antiepileptic drug was more efficacious than the others. Once the maximum seizure-free period is identified, try to determine what medications were being used at that time. This medication may be re-tried if other medications fail.

9. **Is there more than one kind of seizure?** Inquire about different seizure types, and describe each type in detail.

10. **Has the patient sustained injuries related to the seizures?** This is a very important practical question. Patients who are injured either do not have auras or do not have enough time after the aura to take preventive measures. The presence of falls in itself does not help classify the seizures, but the information may prompt recommendations for wearing a helmet and modifying the home environment to minimize injuries.

11. **What is the frequency of visits to the emergency department?** The answer to this question may shed light on the degree of seizure control, as well as the comfort level of the caregivers in dealing with this condition. Information should be obtained regarding the specific situation with each hospital visit, such as non-compliance, changes in the medication, and concurrent medical illnesses. If certain precipitants are identified, appropriate measures can be taken. If frequent hospital visits result from the poor comfort level of the caregivers, proper education may help rectify the situation.

**PAST MEDICAL HISTORY**

Past medical history, when combined with seizure semiology, can provide useful information in terms of etiology. In localization-related epilepsy, knowledge of the underlying etiology/pathology can help make useful decisions with regard to medical and surgical options.

1. **Was the patient the product of a normal full-term pregnancy, labor, and delivery?**

2. **Was there any asphyxia or respiratory distress at birth?**

3. **Were the developmental milestones age-appropriate?**

4. **Any history of febrile seizures?** The risk of developing epilepsy in the presence of simple and complex febrile seizures is approximately 2% and 13%, respectively.  

5. **Any history of central nervous system infections such as meningitis, encephalitis, and Lyme disease?** In endemic regions, obtain history of known cysticercosis.

6. **Any history of head injuries, especially associated with depressed skull fracture, intracerebral hemorrhage, loss of consciousness and prolonged amnesia?**

7. **History of brain tumor?**

8. **History of cerebrovascular accident?**

**SOCIAL HISTORY**

Some social aspects directly pertaining to the seizures and epilepsy are an important part of the history and evaluation.

1. **What is your level of education?** In patients with a long-standing diagnosis of epilepsy, the level of education may be a reflection of how well the condition has been managed. It also helps to determine the level of community support the individual will require and the potential of educating the patient to cope with his/her chronic illness.

2. **Are you employed? What is your job description?** Patients whose epilepsy is well-controlled can lead a productive and normal life. Many of these patients are employed full-time or part-time. If seizures are poorly controlled, getting and maintaining employment may be a challenge. The physician can provide guidance regarding welfare plans and other kinds of community support. If the patient is employed, the nature of the job should be addressed. A person who is mainly involved with an office job, as a cashier, or other sedentary tasks may not be at risk. However, if you are dealing with a construction worker, heavy equipment mechanic, or someone responsible for supervising others in high-risk areas, detailed education with some job modification can be critical.
3. Do you drive? Patients with uncontrolled seizures who have altered awareness should not be driving. They carry a risk to their personal safety, and endanger other civilians. Each province and state has its own driving standards for patients with epilepsy. Treating physicians should be familiar with these sets of codes and advise their patients accordingly. According to the Wisconsin Department of Transportation, to be eligible for a driver’s license, a person must be episode-free for at least 3 months.

4. Are you sexually active? Do you use contraception? Are you planning pregnancy in the near future? Female patients should be educated about the teratogenicity of antiepileptic drugs, the lower efficacy of oral contraceptives with enzyme-inducing medication (phenytoin, carbamazepine, and phenobarbital), and the need for using more than one form of contraception. The above information is also helpful for patients who are planning pregnancy. Any female patient who is of childbearing age and is or may become sexually active should be on a daily supplement of folic acid to reduce the risk of neural tube defects in the newborn. Detailed discussion on the issues of pregnancy and epilepsy is beyond the scope of this article.

5. Do you drink alcohol? Alcohol use is a risk factor for a first generalized tonic-clonic seizure. Patients with epilepsy should be discouraged from the excessive use of alcohol. This may adversely interact with the metabolism of the antiepileptic drugs, or may directly result in seizure exacerbation, especially after continued or binge drinking.

FAMILY HISTORY
Family history is important to determine specific epilepsy syndromes or other genetically mediated neurological disorders that have seizures as one manifestation. Examples include juvenile myoclonic epilepsy (JME), familial neonatal convulsions, benign rolandic epilepsy, and the syndrome of generalized tonic clonic seizures with febrile seizures plus. Some of these are age-limited while others are known to be associated with a lifetime seizure risk (JME).

ALLERGY
Precise information should be obtained regarding allergies to antiepileptic drugs. Distinction should be made between poorly tolerated gastrointestinal side effects versus a hypersensitivity reaction. If a rash is reported, try to distinguish between photosensitivity reaction (on sun exposed regions) versus hypersensitivity (more diffuse).

MEDICATIONS
Inquire about each antiepileptic drug used at any time, including strength of tablet, time of intake, duration of therapy, maximum dose, side effects, and efficacy.

PREVIOUS WORK UP
Detailed information should be obtained with regard to EEGs and neuroimaging such as computed tomography (CT) scans of brain and magnetic resonance imaging (MRI).

REVIEW OF SYSTEMS
Information should be obtained about potential side effects of antiepileptic drugs. Excessive drowsiness is common with early use of phenobarbital, gabapentin, and primidone but can also be seen with carbamazepine, phenytoin, and levetiracetam. Gastrointestinal side effects can be related to any medication but are more common with carbamazepine. Weight gain, hair loss, and postural tremors can be seen with valproic acid, whereas weight loss and paresthesias are more common with topiramate. Blurry vision, diplopia, and incoordination can be a dose-related side effect with phenytin, carbamazepine, and lamotrigine. Gingival hyperplasia and hirsutism are associated with phenytoin.

PHYSICAL/NEUROLOGICAL EXAMINATION
Details about a neurological examination can be found in any standard book on clinical examination. Here are some key points with regard to patients with epilepsy:

- Look for stigmata of neurocutaneous syndrome such as café au lait spots and iris hamartoms with neurofibromatosis, Ash leaf spots, shahgreen patches, subungal fibromas, and adenoma sebaceum with tuberous sclerosis, or port-wine stain (capillary hemangioma) with Sturge-Weber syndrome.
- Look for asymmetries in the size of limbs or one half of the body (hemiatrophy), which may suggest perinatal cerebral insult.
- Check for marks or ulcerations on the side of tongue or oral mucous membranes as can be seen with seizures.
- Gingival hyperplasia can be seen with phenytoin.
- Diphytrens contractures can be seen with chronic use of barbiturates.
- Dystonic posturing of one arm on stressed gait, such as walking on the sides of the feet may suggest a remote insult to the corticospinal tracts.
- Multiple bruises or injuries may result from falls secondary to seizures.
End gaze nystagmus with reported diplopia and difficulty in tandem walking may suggest toxicity related to antiepileptic medications such as carbamazepine, phenytoin, and lamotrigine.

**INVESTIGATING THE FIRST SEIZURE**

A seizure is a symptom of an underlying pathology. Investigations are directed at identifying the precipitating etiology and conditions that can be arrested, reversed, or treated. A detailed history and physical examination can provide direction to the extent of investigations. The following work up is generally recommended.

**Laboratory Investigations**

Hyponatremia, hypoglycemia, hypomagnesemia, uremia and hepatic encephalopathy can all precipitate seizures. Checking serum electrolytes along with glucose, calcium, magnesium, blood urea nitrogen, creatinine, and liver function tests may provide useful clues to these etiologies. Serum and urine toxicology should be done when substance abuse or drug overdose is suspected. In newborns and young children appropriate metabolic screen can be requested.

**Neuroimaging**

CT scan will help to investigate subdural hematoma, subarachnoid hemorrhage, abscess, neoplastic processes, and other space occupying lesions. CT scan of the brain is recommended if the history or physical examination is suggestive of a focal pathology. MRI of the brain provides a better resolution of the normal and abnormal structure of the brain. It is recommended to look for pathologies commonly not clarified by the CT scan such as cerebral dysplasia, mesial temporal scleroses or when history and physical examination is suggestive of focal pathology and the CT does not show the cause. MRI may be requested before the CT for a better resolution.

**Electroencephalogram (EEG)**

EEG tests the cerebral function rather than structure. Epileptiform discharges on the EEG can help classify the seizure types and are suggestive of an increased risk of recurrent seizures. Focal and generalized slowing is reflective of focal and generalized disturbance of cerebral function respectively. Focal disturbance can be seen in strokes, tumors, and abscess. Generalized disturbance is seen in toxic, metabolic, or diffuse structural abnormalities. An EEG should be performed in all patients presenting with seizures with the understanding that a normal EEG does not rule out a clinical seizure disorder, whereas an abnormal EEG in isolation does not confirm the diagnosis of epilepsy.

**TREATMENT**

The treatment of seizures and epilepsy is an extensive topic and beyond the scope of this article. A few general principles are summarized.

- A single generalized seizure in the absence of abnormalities on the physical examination, EEG, and imaging studies may not require treatment.
- The risks and benefits of treatment versus observation should be discussed with the patients and tailored according to each individual case.
- Selection of pharmacotherapy should involve consideration of the efficacy, tolerability, side effect profile, mechanism of action, and cost.
- Baseline liver function tests, complete blood count, and electrolytes should be tested.
- Potential teratogenic effects should be discussed with female patients.
- Interactions with oral contraceptives should be realized.
- Female patients should be placed on folic acid.
- Drug levels should be monitored when compliance or toxicity is in question.
CONCLUSION
Seizures and epilepsy are classified based on the clinical history, physical examination, and ancillary studies, and treatment decisions follow. Patient education with regard to diagnosis, prognosis, and indications for medications is important. In patients with normal intellect, the decision to treat and the choice of antiepileptic drug are mutually agreed on by the patient and the doctor. Issues regarding work, driving, pregnancy, and other limitations should be addressed in detail. If a patient presents with first seizure, ancillary studies such as EEG and MRI for localization-related epilepsy should be arranged. A complete blood count, liver function tests, electrolytes, and renal function tests should be arranged before initiating the antiepileptic drugs.

For a patient with newly diagnosed seizures, at least one consultation should be obtained from a neurologist to address the need for further investigations and for the choice of antiepileptic medications. The classification of seizures and epilepsy are critical in decisions about treatment and prognosis.

REFERENCES
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