Seizures and Epilepsy

S. Nizam Ahmed, MD, FRCPC
Associate Professor – Neurology
University of Alberta
snahmed@ualberta.ca

What is an epileptic seizure?

An epileptic seizure is a paroxysmal hyper synchronous discharge of the cerebral neurons. The clinical manifestation depends on the location and extent of the area involved.

How do you define epilepsy?

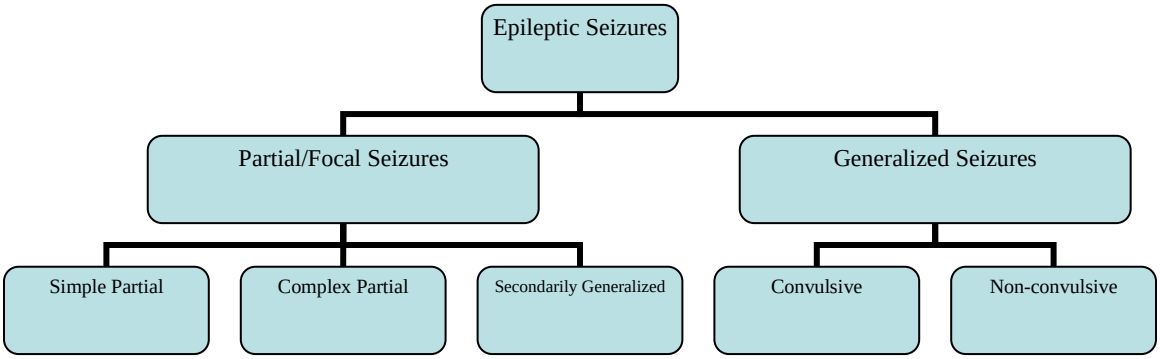
The tendency to have recurrent unprovoked seizures is defined as epilepsy. In clinical practice if a patient has 2 or more unprovoked seizures he/she is diagnosed with epilepsy.

How do you classify epileptic seizures?

Epileptic seizures are broadly classified as partial and generalized.

Partial/Focal seizures are so named because they originate from a focal area of the brain. These usually originate from areas with focal pathology. Seizures that follow strokes, brain tumors, cerebral abscess and cerebral contusions are examples of partial seizures. Partial seizures that are confined to a very small area may not be associated with a loss of consciousness or awareness. These are termed as *simple partial seizures*. Partial seizures that are associated with loss of awareness are called *complex partial seizures*. Partial seizures that spread to bilateral motor areas leading to tonic-clonic activity are called *secondarily generalized seizures*. A partial seizure may begin as a simple partial seizure and then evolve into a complex partial and secondarily generalized seizure.

Generalized seizures do not originate from an identifiable focal area and tend to involve both hemispheres simultaneously. Neuroimaging such as MRI and CT scans of the head in these patients are normal. Generalized seizures can be classified as convulsive or non convulsive. Tonic-clonic, clonic, tonic and myoclonic seizures are examples of generalized convulsive seizures whereas absence (also known as petit-mal) seizure is an example of non-convulsive generalized seizure.



Common Terminology when Describing Seizures and Epilepsy

AURA: Aura is the warning that precedes a seizure. It may consist of an unusual smell, taste, visual or tactile sensation or déjà vu. Aura actually is a simple partial seizure. Eliciting history of a specific aura helps localizing the seizure onset.

ICTAL: The term "Ictus" refers to the actual seizure. *Ictal* basically describes the occurrences during the seizure such as lip smacking, eyelid fluttering, tonic clonic activity, facial twitching, tongue bite and urinary incontinence.

POSTICTAL: Refers to the events that may follow the seizure such as disorientation, sleep, lateralized weakness and numbness.

TODD'S PARALYSIS: Refers to lateralized weakness that may follow a partial/focal seizure.

AUTOMATISMS: These are automatic behaviors that are often seen with seizures that originate from the temporal lobes. Fidgeting of hands, chewing movements and lip smacking, are all examples of automatisms.

What is the clinical presentation of a complex partial seizure (CPS)?

Complex partial seizures may start with an aura of an abnormal smell, taste or déjà vu sensation followed by a relatively prolonged (30-40 seconds) episode of spacing-out. These may be associated with seemingly automated movements of the hands (automatisms), such as repeatedly picking on the clothes or other objects. Witnesses may describe stiff (dystonic) posturing of one of the upper extremity along with repeated lip smacking or swallowing movements. Patients appear disoriented (confused) for 2-5 minutes after the episode. Complex partial seizures most frequently originate from the temporal lobes.

Is there a difference between absence/petit mal seizures and complex partial seizures? What is the clinical presentation of a typical absence seizure?

Absolutely! Absence seizures are non-convulsive generalized seizures whereas CPS originate from a focal area of the brain, usually temporal lobes. Absence seizures typically present between 5-10 years of age. The duration is relatively brief, 5-10 seconds. Patients do not appear confused or disoriented after the episode (i.e relatively brief post-ictal state). There can be dozens of absence seizures in a day. Seizures may be associated with a brief stare with blinking/fluttering of the eyelids. Complex automatic movements (automatisms) are infrequent and unusual. There is no aura. Whereas CPS can occur at any age, it is extremely unlikely that a 50 year old man presents with new onset absence seizures.

What are myoclonic seizures?

Myoclonic seizures are a type of generalized seizures. These present with sudden, abrupt and brief jerks of both upper extremities or the axial musculature. Myoclonic seizures tend to occur more frequently on awakening or after sleep deprivation. On specific questioning patients may report flipping things out of their hands, spilling tea/coffee in the mornings or an excessive startling.

What are the clinical features of a generalized tonic-clonic (grand mal) seizure?

A generalized tonic-clonic (GTC) seizure often begins with a loud deep guttural sound, followed by tonic contraction of musculature of all 4 extremities and the axial musculature. Intermittent clonic movements follow the tonic contraction. A tonic clonic seizure typically lasts for 60-90 seconds. Once the motor activity stops, deep labored breathing ensues associated with hypersalivation and foaming from the mouth. After the seizure is over (postictally), patient may go into state of sleep lasting 30-60 minutes. Generalized tonic-clonic seizures are often associated with tongue bite and urinary incontinence.

What are the risk factors for developing generalized seizures?

The main risk factor for recurrent unprovoked generalized seizures is genetic susceptibility. Provoked generalized seizures can result from withdrawal of alcohol, certain medications, such as barbiturates and benzodiazepines, excessive sleep deprivation and metabolic derangements such as hyponatremia and hypoglycemia.

What are the risk factors for developing partial seizures with or without secondary generalization?

Partial seizures can develop following any kind of insult to the cerebral neurons. Stroke, brain tumor, cerebral abscess, meningitis, depressed skull fracture with cerebral contusion and congenital developmental malformations can all lead to partial seizures with or without secondary generalization. Patients who develop febrile seizures as a child are at a higher risk of developing epilepsy later in life.

What is the differential diagnosis of seizures?

Differential Diagnosis of Seizures
Benign positional vertigo
Breath holding spells of children
Cardiac arrhythmia
Hypoglycemia
Migraine
Narcolepsy/Cataplexy
Night terrors
Nightmares
Nocturnal myoclonus
Panic attacks
Periodic paralysis
Pseudoseizures/Hysterical seizures
Sleep apnea
Syncope
Transient ischemic attacks

Ahmed SN, Spencer S. Wisconsin Medical Journal 2004. Volume 103, No 1 Page 50.

What is Syncope?

Syncope is an abrupt loss of consciousness with associated loss in postural tone resulting from cerebral hypoperfusion. In lay terms it is referred to as a “faint”.

How do you classify Syncope? What conditions can cause syncope?

Syncope can be broadly classified as *cardiogenic* (resulting from a cardiac pathology) and *non-cardiogenic*. Any condition that compromises the hearts ability to adequately pump oxygenated blood to the brain can cause a cardiogenic syncope. Examples include conduction abnormalities leading to a third degree heart block, cardiac arrhythmias, valvular heart disease, cardiac tamponade, myocardial infarction and aortic stenosis. In young healthy individuals, cardiogenic syncope is less common than non-cardiogenic syncope.

Non-cardiogenic syncope can result from hypovolemia, medications that cause peripheral vasodilatation or an abnormal vasovagal response leading to neurocardiogenic syncope. *Vasovagal syncope*, is one of the commonest types. It can be provoked in susceptible individuals at the sight of blood, with needle sticks, during micturation or defecation or after sudden emotional excitement. The mechanism is probably a combination of parasympathetic over-stimulation and sympathetic under-stimulation.

What is the clinical description of Syncope?

Patients tend to feel hot, with a sense that they are going to pass-out, there may be buzzing/fullness in the ears followed by the black-out. Patients with syncope tend to fall down more "gracefully" than those with seizures. Usually patients recover immediately on assuming a recumbent position. A patient may appear white and pale before and during a syncope. The loss of consciousness is usually brief with a rapid recovery. Specific triggers can reproduce the symptoms. Brief clonic movements of the upper extremity follows if the syncope is prolonged, lasting more than 30 seconds. This is called "convulsive syncope" and should not be confused with an epileptic convulsion.

How do you clinically differentiate a seizure from syncope?

Please refer to the article on the following website:

http://stacommunications.com/journals/cme/2004/September/pdf/072.pdf

What is a pseudoseizure?

Pseudoseizure refers to an episode that may simulate an epileptic seizure but on detailed history and investigations identified as non-epileptic. Pathological entities such as narcolepsy and cataplexy, cardiac syncope, night terrors, nightmares can simulate epileptic seizures but are not labeled as pseudoseizures. The term is more often used synonymously with psychosomatic, factitious and hysterical disorders. The diagnosis of pseudoseizures can be quite challenging even for neurologists and should best be made by experts in the field. Some features of pseudoseizures are presented here. These can be considered when suspecting pseudoseizures but by no means are pathognomic of the diagnosis (table 1).

TABLE 1. Clinical Features Suggestive of Pseudoseizures
1. Waxing and waning motor activity during same episode
2. Clinical characteristics and duration varies from episode to episode
3. Often a dramatic presentation
4. Tends to happen when patient suspects being watched
5. May respond to suggestions
6. Most often refractory to medications
7. Serious injuries are uncommon
8. Progression of motor symptoms do not follow expected anatomic features

What is Epilepsy?

Epilepsy is the tendency to have recurrent unprovoked seizures. In clinical practice if a person has had 2 or more unprovoked seizures a diagnosis of epilepsy can be made.

What is Status Epilepticus?

If a person has one seizure lasting more than 30 minutes or two seizures without fully recovering consciousness in between he/she is diagnosed with status epilepticus.

What is the urgency in treating status epilepticus (SE)?

SE is a medical emergency which if left untreated can cause irreversible cerebral injury. This condition responds best to medications when treated early.

Briefly describe the management of a patient with status epilepticus.

Immediately check for airway, breathing and circulation (ABC). Turn the patient to a lateral decubitus position to prevent aspiration. Obtain a quick history from friends and family regarding history of epilepsy or coexisting medical problems. Check for blood sugar, CBC, Electrolytes and renal functions. Arrange for a CT scan if suspecting head injury.

Intravenous benzodiazepines such as lorazepam and diazepam are usually the first line agents followed immediately by an intravenous load of phenytoin. Number of other agents can be used subsequently such as midazolam, phenobarbital, pentobarbital and propafol. It is best to consult the neurology service if patient continues to seize despite the use of benzodiazepines.

How do you investigate a patient with a new onset seizure?

The first and foremost task is to establish the diagnosis with a detailed clinical history (1). You can start with basic laboratory investigations such as complete blood count (CBC), electrolytes and renal functions (Na, K, Mg, PO, BUN, Cr and glucose). If CNS infection is suspected based on a high fever or elevated white cell count spinal; tap is indicated. Gross structural abnormalities (subdural hematoma, abscess, brain tumor) can be excluded with a computed tomography (CT) scan. Magnetic Resonance Imaging (MRI) is the neuroimaging of choice. Electroencephalogram (EEG) can demonstrate epileptiform activity and help classify the seizures/epilepsy. Presence of epileptiform activity is supportive of the diagnosis of epilepsy. Table 2 lists the common investigations typically employed in the evaluation of the first seizure.

TABLE 2. INVESTIGATIONS FOR THE FIRST SEIZURE

1. Good history
2. Thorough neurological examination
3. Electrolytes and blood glucose
4. CBC
5. EEG
6. Spinal tap
7. CT scan
8. MRI

What are the restrictions that you advise to a patient with newly diagnosed epilepsy?

Patients with a new diagnosis of epilepsy are instructed not to drive. Driving restrictions can vary between different provinces. In Alberta a patient who is seizure free for 6 months can operate a private vehicle (Class 5 license), after favorable recommendation from his/her neurologist. Patients are instructed to abstain from any activity that can endanger them or others in the event they lose consciousness. Patients whose jobs involve climbing ladders, driving school buses, working on roof tops require counseling for job modification.

What are some of the commonly used antiepileptic/antiseizure medications and their use according to seizure types?

ANTIEPILEPTIC DRUG	SPECTRUM OF USE
1. Phenytoin	Partial and generalized seizures. Ineffective against myoclonic and absence seizures
2. Carbamazepine	Partial and generalized seizures. Ineffective against myoclonic and absence seizures
3. Valproic acid (VPA)	Very effective against all types of generalized seizures including absence and myoclonic seizures. Also effective against partial seizures.
4. Lamotrigine	Effective against partial and generalized seizures. Not as potent as VPA in the control of generalized seizures.
5. Topiramate	Effective against partial and generalized seizures.
6. Gabapentin	Add on therapy for partial seizures only.
7. Ethosuximide	Only effective against absence seizures.
8. Clobazam	Effective against partial and generalized seizures.
9. Phenobarbital	Effective against partial and generalized seizures.
10. Levetiracetam	Effective against partial seizures. Shows promise in the treatment of generalized seizures.

What are the common mode of action of antiepileptic drugs AEDs?

The main mechanisms of action of the available AEDs are thought to be

1. blockading voltage-dependent ion channels (sodium, potassium and calcium channels).
2. increasing the activity of the inhibitory GABA-ergic system and
3. decreasing the activity of the excitatory glutamatergic system

The following table provides the main mode of action of the AEDs

AED	Main mode of action
Carbamazepine	Blocks voltage-dependent Na^+ channels ($\downarrow Na^+$)
Clobazam	Increases inhibition by $GABA_A$ ($\uparrow GABA_A$)
Clonazepam	Increases inhibition by $GABA_A$ ($\uparrow GABA_A$)
Ethosuximide	Blocks T-type Ca^{++} channels ($\downarrow Ca^{++}$)
Gabapentin	Multiple (modifies Ca^{++} channels and neurotransmitter release)
Lamotrigine	Blocks voltage-dependent Na^+ channels ($\downarrow Na^+$)
Levetiracetam	Novel. Binds to synaptic vesicle protein SV2A
Oxcarbazepine	Blocks voltage-dependent Na^+ channels ($\downarrow Na^+$)
Phenobarbitone	Multiple ($\downarrow Na^+$; $\downarrow Ca^{++}$; $\uparrow GABA_A$; $\downarrow$ Glutamate)
Phenytoin	Blocks voltage-dependent Na^+ channels ($\downarrow Na^+$)
Tiagabine	Increases inhibition by $GABA_A$ ($\uparrow GABA_A$)- potent inhibitor of GABA uptake into neurons and glial cells
Topiramate	Multiple ($\downarrow Na^+$; $\downarrow Ca^{++}$; $\uparrow GABA_A$; $\downarrow$ Glutamate)
Valproate	Multiple ($\downarrow Na^+$; $\downarrow Ca^{++}$; $\uparrow GABA_A$; $\downarrow$ Glutamate)
Vigabatrin	Increases inhibition by $GABA_A$ ($\uparrow GABA_A$)-selective and irreversible $GABA_A$-transaminase inhibitor thus increasing whole-brain levels of $GABA_A$
Zonisamide	Multiple ($\downarrow Na^+$; $\downarrow Ca^{++}$)
	CP Panayiotopoulos. In: The Epilepsies – Seizures, Syndromes and Management. Bladon Medical Publishing. 2005. page 70

www.neurophysiology.ca

References:

1. Ahmed, S.N, Spencer S.S. An approach to evaluating patients for seizures and epilepsy. (Review article). Wisconsin Medical Journal 2004. Volume 103, No. 1. 49-55.

http://www.wisconsinmedicalsociety.org/uploads/wmj/ahmed.pdf

2. Ahmed SN, Siddiqi Z. Seizure or Syncope – differentiating. Review article. The Canadian Journal of CME. September 2004, 83-87.

http://stacommunications.com/journals/cme/2004/September/pdf/072.pdf

3. Kandel ER, Schwartz JH and Jessel TM. 2000. Seizures and Epilepsy. In: Kandel ER (ed) Fourth Edition. Principles of Neural Science, pp. 910-935. McGraw Hill.

4**.** Warren T. Blume. Diagnosis and management of epilepsy. Can. Med. Assoc. J., Feb 2003; 168: 441 – 448 (CMAJ is available on the net free of charge).

CASE 1:

A 25-year-old female school bus driver presented to the emergency room after a single vehicle accident. She was unresponsive with no obvious external injuries. She recovered in 30 minutes and had no recollection of the accident.

When she was 4 years old she had a febrile convulsion that lasted for 10 minutes. She had a few episodes of loss of consciousness once 2 years ago at home and another 3-4 years ago while donating blood. She also reports that her "heart races" funny especially when she is in a lot of stress.

She further reports that twice over the last 5 years she found having bitten her tongue in sleep with blood drooling on her pillow. Family history is significant for her mother and sister "passing-out" while getting the flu shots. General medical and neurological examination is normal.

QUESTIONS:

1. What is your differential diagnosis?
2. What is the significance of this woman's history of "febrile convulsion"?
3. What is the significance of her family history?
4. Is there a significance of tongue bites in sleep?
5. Can this lady continue with her current job?
6. What are some of the risk factors for developing epilepsy?
7. Based on clinical history how do you differentiate seizure from syncope?
8. What are common triggers for syncope?
9. What investigations will you conduct?
10. If you do conclude that this lady has had a seizure what antiepileptic drug would you consider?