

Objectives:

- ★ Definition of epileptic seizure, provoked seizure and epilepsy.
- ★ Status epilepticus.
- ★ Frequent causes of seizure and risk factors.
- ★ Triggers of seizures in epileptic patient.
- ★ Epilepsy classification and seizure semiology.
- ★ DDX of SZ
- ★ Seizure vs syncope
- ★ Approach to seizure disorder (Hx, Ex, inx)
- ★ Medical and surgical management of epilepsy.
- ★ How to select antiepileptic medications.
- \star When to stop antiepileptic medications.

Color index:

Original text Females slides Males slides Doctor's notes Textbook Important Golden notes Extra

Epilepsy

History Of Epilepsy :

- One of the earliest descriptions of a secondarily generalized tonic-clonic seizure was recorded over 3000 years ago in Mesopotamia.
- The seizure was attributed to the god of the moon
- Epileptic seizures were described in ancient cultures, including those of China, Egypt, and India.
- Hippocrates wrote the first book about epilepsy almost 2500 years ago.
- Hippocrates in his book On Sacred Disease described the first neurosurgery procedure referring that craniotomy should be performed at the opposite side of the brain of the seizures, in order to spare patients from "phlegma" that caused the disease.
- In 18th and 19th century, medicine made important advances and research on epilepsy was emancipated from religious superstitions such as the fact that epilepsy was a divine punishment









What is Epilepsy?

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Epileptic seizure

Transient occurrence of signs and symptoms of sudden changes in neurological function due to **abnormal excessive** and **synchronous** discharge of cortical neurons.



Provoked seizures

Occurs in the setting of acute medical and neurological illnesses¹ in people with no prior history of seizures



Recurrent (two or more) unprovoked seizures.

Seizure is a symptom of epilepsy, it's not a diagnosis.

1: Ex: hypoglycemia, hyponatremia, hypernatremia, fever, stroke, meningitis, intracerebral hemorrhage or sinus infection

Epilepsy



Danger of epilepsy

Main reason for road traffic accidents
 Drowning
 Admission to ICU (due to status epilepticus)
 Sudden death "SUDEP" (sudden unexpected death in epilepsy)

 How does it happen? When they are asleep they role on there face and suffocate themselves, or they get arrhythmia

Seizures



Classification of seizures¹



4: ex: epileptic spasm, usually affect pediatric pt (6m to 6 yo).

International classification of seizures 1981

Partial Seizure		 Any disturbance of cortical architecture and function can precipitate this, whether focal infection, tumour, hamartoma or trauma-related scarring. If focal seizures remain localised, the symptoms experienced depend on which cortical area is affected. An initial 'aura' may be experienced by the patient, depending on the cortical area from which the seizure originates. Simple (no loss of consciousness of memory) Sensory Motor Sensory-Motor Psychic (abnormal thoughts or perceptions), Autonomic (heat, nausea, flushing, etc.) Complex (consciousness or memory impaired (not lost)) With or without aura (warning) → depends on lobe involved. ex: deja vu, oral Automatism (chewing), hand movement, epigastric racing sensation or nausea. With or without automatisms. 	
Generalized Seizures	Absence (petit mal)	 Always start in childhood. The attacks are rarely mistaken for focal seizures because of their brevity. They can occur so frequently (20–30 times a day) that they are mistaken for daydreaming or poor concentration in school. Characterized by fast recovery from seizure (No post-ictal phase), and can be provoked by hyperventilation 	
	Tonic-clonic "grand mal"	 The patient then becomes rigid (tonic) and unconscious, falling heavily if standing ('like a log') and risking facial injury. During this phase, breathing stops and central cyanosis may occur. As cortical discharges reduce in frequency, jerking (clonic) movements emerge for 2 minutes at most. Afterwards, there is a flaccid state of deep coma, which can persist for some minutes, and on regaining awareness the patient may be confused, disorientated and/or amnesic. During the attack, urinary incontinence and tongue-biting may occur. Subsequently, the patient usually feels unwell and sleepy, with headache and myalgia. 	
	Atonic "drop seizures"	Involving brief loss of muscle ton e, usually resulting in heavy falls with or without loss of consciousness.	
	Myoclonic	Typically brief, jerking movement s, predominating in the arms.	
	Other Unclassifiable seizure	Tonic: Associated with a generalised increase in tone and an associated loss of awareness. They are usually seen as part of an epilepsy syndrome and are unlikely to be isolated. Clonic: Similar to tonic–clonic seizures but there is no preceding tonic phase.	







Seizures (cont.)

Seizure Semiology



happen during sleep.

Differential Diagnosis for Seizure attacks:



Approach to Seizures

Clinical history

Questions that help clarify the type of seizure include the following :



3: important for surgery, for ex: if seizures happening in left temporal lobe with impaired function and there is intact function of right temporal lobe, we may remove the affected area as a management if the function of left lobe (affected lobe) intact we can't do surgery.

Approach to Seizures (cont.)

Video EEG

- Video EEG may be necessary to differentiate these from psychogenic attacks (which are more common) but abruptness of onset, stereotyped nature, relative brevity and nocturnal preponderance may indicate a frontal origin.
- An EEG performed immediately after a seizure may be more helpful in showing focal features than if performed after a delay.
- Seizure activity is usually apparent as spike and wave discharges.

Summary on the typical signs of video EEG

VEM



Typical EEG Sign	Localizes to	Typical EEG Sign	Localizes to
Oral Automatismes	Temporal lobe	Tonic arm elevation	Supplementary motor area
Hypermotor automatism	Frontal lobe	Epigastric Aura	Temporal lobe
Manual picking automatismes	Temporal lobe	Throat tightening Sensation	Insula
Visual Hallucinations	Occipital lobe	Ictal pain	Parietal lobe
Auditory Hallucinations	Temporal neocortex (Heschl's Gyrus)	Somatosensory sensations	Postcentral gyrus or Supplementary motor area
Olfactory Hallucinations	Mesial temporal lobe	Clonic activity	Precentral gyrus
Nystagmus, eye blinking, eye pulling sensation	Occipital lobe	De-ja-vu or jamais vu aura	Mesial / Medial temporal lobe
Ictal amaurosis	-	Fear	Most often temporal, but also frontal lobe



→ might be helpful to localize seizure.



How to administer first aid for seizures



Lifestyle

- People with epilepsy (the term 'epileptic' is no longer used) should be encouraged to lead lives as unrestricted as reasonably possible, though with simple, safety measures such as:
 - avoiding swimming and dangerous sports such as rock-climbing.
- Advice at home includes:
 - leaving bathroom and lavatory doors unlocked
 - taking showers rather than baths.
- Epilepsy triggers such as sleep deprivation, excess alcohol and drugs should be avoided, and strobe lighting where there is EEG evidence of a photo-paroxysmal response.

Epilepsy and driving

- Patients should be asked to **stop driving** after a seizure and to **inform the regulatory authorities if they hold a driving licence**.
- After a seizure, a temporary driving ban until seizure free is usual but regulations vary from country to country.
- Many driving regulatory bodies also suggest refraining from driving while withdrawing from AEDs.



Treatment

First: Medical

Drugs	 Phenytoin, Ethosuximide, Carbamazepine, Valproate, Lamotrigine, Oxcarbazepine, Bromide salt, Phenobarbital, Primidone, Clonazepam, Felbamate, Gabapentin, Topiramate, Tiagabine, Levetiracetam, Zonisamide, Pregabalin, Rufinamide, Lacosamide, and Ezogabine. Phenytoin is no longer considered a first-line AED; it is now principally used in emergency control of seizures. Levetiracetam is increasingly used in most types of epilepsy. Carbamazepine can worsen absence seizure and myoclonic epilepsy. 		
MOA	 Current antiepileptic drugs are thought to act mainly by two main mechanisms: 1. <u>Reducing electrical excitability of cell membranes.</u> by inhibition of sodium channel. 2. <u>Enhancing GABA.</u> O By inhibiting GABA-transaminase O By drugs with direct GABA-agonist properties. 		
Clinical uses of Antiepileptic drugs	 Tonic-clonic (grand mal) seizures: phenytoin or valproate (drug of choice) Use of single drug is preferred when possible because of risk of pharmacokinetic interactions. 70% of patients will have good seizure control with a single AED. Partial (focal) seizures: carbamazepine (drug of choice) valproate; clonazepam or phenytoin are alternatives. Absence seizures (petit mal): ethosuximide (drug of choice) or valproate Myoclonic seizures: valproate or clonazepam 		
Basic rules for drug treatment	 Drug treatment should be simple, preferably using one anticonvulsant (monotherapy). "Start low, increase slow" → titrate upwards until the seizures are controlled or side effects become unacceptable. Add-on therapy is necessary in <u>some patients</u> (If seizures not controlled with first AED, gradually introduce second agent and then slowly withdraw the first AED. If still not seizure free then combination therapy is required). If patient is seizure-free for three years, withdrawal of pharmacotherapy should be considered. Should be performed very carefully and <u>slowly!</u> 20% (50%) of pts will suffer a further seizure within 2 years. 		
Seizure freedom with AED use	1st drug \rightarrow seizure free (47%)2nd drug \rightarrow seizure free (14%)3rd drug \rightarrow seizure free (3%)		
Side effects of AEDs	 Intoxication with most AEDs causes unsteadiness, nystagmus and drowsiness. Side effects are commoner with multiple AEDs. Skin rashes are seen particularly with lamotrigine, carbamazepine and phenytoin. A wide variety of idiosyncratic drug reactions may occur, e.g. blood dyscrasias with carbamazepine. 		
Drug resistant epilepsy	 Medication resistant → (36%) Failure of at least TWO antiepileptic medications to completely control seizures Appropriately chosen for seizure type . Taken as prescribed Well tolerated (not failed due to side effects) 		

Treatment (cont.)

Guidelines for Antiepileptic drug therapy

01	Start with one first-line drug, at a low dose; gradually increase dose until effective control of seizures is achieved or side-effects develop and optimise adherence.
02	If first drug fails (seizures continue or side-effects develop), start second first-line drug, followed if possible by gradual withdrawal of first
03	If second drug fails (seizures continue or side-effects develop), start second-line drug in combination with the preferred baseline drug at maximum tolerated dose (beware interactions)
04	If this combination fails (seizures continue or side-effects develop), replace second-line drug with alternative second-line drug
05	If this combination fails, check adherence and reconsider diagnosis (Are events seizures? Occult lesion? Treatment adherence/alcohol/ drugs confounding response?)
06	Consider alternative, non-drug treatments (e.g. epilepsy surgery, vagal nerve stimulation) and Use minimum number of drugs in combination at any one time

Epilepsy Type	First Line	Second Line	Third Line
Focal onset and/or secondary GTCS	 Lamotrigine 	 Carbamazepine Levetiracetam Sodium valproate Topiramate Zonisamide Lacosamide 	 Clobazam Gabapentin Oxcarbazepine Phenobarbital Phenytoin Pregabalin Primidone Tiagabine
GTCS ¹	 Sodium valproate Levetiracetam 	LamotrigineTopiramateZonisamide	 Carbamazepine Phenytoin Primidone Phenobarbital Acetazolamide
Absence	• Ethosuximide	 Sodium valproate 	LamotrigineClonazepam
Myoclonic	Sodium valproate	LevetiracetamClonazepam	LamotriginePhenobarbital

Treatment (cont.)

Second: Surgical

Hemispherectomy

Definition

Hemispherectomy is a surgical treatment for epilepsy in which one of the two cerebral hemispheres is removed.

Hemispherotomy

Definition

A hemispherotomy is an operation that disconnects the cortex of a hemisphere from the other without removing it by cutting the corpus callosum. it is done so seizure won't start focally on one hemisphere and travel to the other hemisphere to become generalized



Temporal lobectomy will result in seizure freedom in 50–70% of selected patients with uncontrolled seizures caused by hippocampal sclerosis (defined by imaging and confirmed by EEG).

If my patient is not a good candidate for surgery?

. . . .

Vagus Nerve Stimulation (VNS)















Status epilepticus

Definition

Defined as <u>recurrent</u> convulsions that last for more than **30 minutes** (5 min in the last update)¹ and are interrupted by only brief periods of partial relief².

- It's serious, potentially life-threatening, has a mortality of 10–15%.
 - The longer the duration of status, the greater the risk of permanent cerebral damage.
- Any type of seizure can lead to SE:
 - the most serious form of status epilepticus is the generalized tonic-clonic type.
 - **Over 50% of cases occur without a previous history of epilepsy**. Some 25% with apparent refractory status have pseudostatus (non-epileptic attack disorder).
 - Focal status also occurs.
 - Epilepsia partialis continua is continuous seizure activity in one part of the body, such as a finger or a limb, without loss of consciousness. This is often due to a cortical neoplasm or, in the elderly, a cortical infarct.
- Not all status is convulsive. In absence status, for example, status is non-convulsive the patient is in a continuous, distant, stuporous state.
- **Rhabdomyolysis** is a complication of SE that may lead to acute kidney injury in convulsive status epilepticus.

Management:

Early status (up to 30 min)

General measures

- Administer oxygen, monitor ECG and blood pressure, perform routine blood tests (include glucose, calcium, drug screen, magnesium, FBC, anticonvulsant levels urgently).
- Secure a venous access through a large vein (some anticonvulsants cause phlebitis)
- Seizure control
 - Give **lorazepam IV**, Repeat once if necessary. **Buccal midazolam and rectal diazepam** are alternatives if no IV access is available.
 - Lorazepam may cause respiratory depression and hypotension, resuscitation facilities should be available.

Established status (30-90 min)

- **Phenytoin or fosphenytoin** (a prodrug of phenytoin and can be given faster than phenytoin).
 - Both drugs could cause cardiac dysrythmias, ECG monitoring is essential.

If ongoing seizures

• Phenobarbital, and Valproate are the third-line therapy.

Refractory status (>90 min) – general anaesthesia

- Only In Intensive Care Setting; intubation and ventilation usually required
- Propofol Bolus, Thiopental and Midazolam Infusions may also be used
- Use continuous EEG monitoring to assess efficacy of treatment –aim for EEG burst suppression pattern
- Reinstate previous AED medication via nasogastric tube
- Establish Diagnosis: CT or MRI may reveal an underlying cause
- Remember: 25% of apparent status cases turn out to be pseudostatus

Epilepsy in women

Birth defects



The overall risk of birth defects in babies of mothers who take one AED is around 7%, as compared with 3% in women without epilepsy.



Counselling before conception is essential

Contraception

- AEDs inducing hepatic enzymes (e.g. carbamazepine, phenytoin and phenobarbital) reduce efficacy of oral contraceptives.
- A combined contraceptive pill containing a higher dose of oestrogen or the progesterone only pill provides greater contraceptive security.
- An IUCD or barrier methods of contraception are often used in preference to oral contraceptives.

Epilepsy treatment in pregnancy

The risk of teratogenicity is well known (~5%), especially with valproates , but <u>withdrawing</u> drug therapy in `			
pregnancy is <u>more risky</u> than continuation ² (risk to the fetus of uncontrolled seizures).			
 All antiepileptic medications are not safe, however <u>lamotrigine</u> is the <u>safest</u>. 			
• Preconception treatment with folic acid (5 mg daily) before conception and throughout the first			
trimester, along with use of the smallest effective doses of as few AEDs as possible, may reduce the			
risk of fetal abnormalities. The risks of abrupt AED withdrawal to the mother should be stressed.			

- **Vitamin K** 20 mg orally should also be taken during the month before delivery to prevent neonatal haemorrhage.
- Epileptic females must be aware of this problem and thorough family planning should be recommended (Antenatal screening is necessary).
- Over 90% of pregnant women with epilepsy will deliver a normal child

Breastfeeding

• Mothers taking AEDs need not in general be discouraged from breastfeeding, though manufacturers are often hesitant in assuring that there is no risk to the baby.

1: Sodium valproate is associated with a higher rate of serious malformations (e.g. neural tube defects) and should be stopped or substituted if possible 2: we can decrease doses or shift to safer medication before pregnancy, but No change of medication should be considered during pregnancy.

Seizures vs Syncope:

	Cardiogenic Syncope	Seizure Disorders
Definitiondue to sudden reflex bradycardia with vasodilation of both peripheral and splanchnic vasculature		sudden synchronous discharge of cerebral neurons causing symptoms or signs.
Loss of Consciousness Typical		Common
Aura -		+
Cyanosis -		+
Episode Duration Seconds		Minutes
Involuntary movements	Common	Typical
Amnesia Yes		Yes
Post-ictal delirium -		+
Post-ictal headache	-	+
Arrhythmia Common		Rare
Electroencephalogram Slow waves Flattening		Focal or General Spike
Responsive to AEDNo(anti-epileptic medications)No		Often
Short Term Mortality High		Low
Recovery	Rapid , usually taking place over seconds, but may be followed by a feeling of general fatigue	Postictal drowsiness and confusion following a seizure

An area for your notes

Summary

Epilepsy

- Epileptic seizure: transient occurrence of signs and symptoms of sudden changes in neurological function.
- Provoked seizures: occurs in the setting of acute illnesses in people with no Hx of seizures.
- Epilepsy: recurrent (two or more) unprovoked seizures.

Risk factors	Triggers	
 Febrile convulsions Family History CNS mass/infection Trauma Stroke 	 Poor compliance Stress Infection 	
Classification		
Generalized	<u>Focal</u>	
 Absence (petit mal) Atonic (drop seizure) Tonic-clonic (grand mal) 	 Simple partial seizures (no change in LOC) Complex partial seizures (impairment of LOC) 	

• Myoclonic

Seizure semiology

- Frontal:Abnormal behaviour
- Temporal: Deja vu, epigastric aura, olfactory hallucinations
- Parietal: Sensory involvement
- Occipital:Visual hallucinations

Seizures vs Syncope

	<u>Syncope</u>	<u>Seizures</u>
	Episode Duration (Seconds) Amnesia <u>NOT</u> Responsive to AED	 Episode Duration (Minutes) Amnesia Oftenly Responsive to AED
The share such		

Treatment

- Grand mal: **phenytoin or valproate.**
- Focal: Carbamazepine (first choice)
- Absence: Ethosuximide (drug of choice)
- Myoclonic: Valproate

Notes:

- Valproate can be used for all types.
- Carbamazepine can worsen absence seizure and myoclonic epilepsy
- <u>N.B: all AEDs are teratogenic, BUT lamotrigine is the safest</u>

Lecture Quiz

Q1: A 38 year old man is evaluated for seizures. He achieves partial control with the addition of a second antiepileptic medication. He drives to work each day.

A- Allow him to drive if he is seizure-free for 1 year.

- B- Allow him to drive as long as his seizure history is noted on his license
- C- Allow him to drive as long as he is accompanied.

D- Recommend that he find an alternate means of transportation.

Q2: A 15-year-old girl is brought to the emergency department by her mother after experiencing a first-time seizure. The thin-appearing girl has a heart rate of 55/min, signs suggestive of dehydration, and fine, velvety hair covering her arms and legs. The physician calculates her body mass index to be 16.4 kg/m2. When the patient's mother leaves the room for a moment, the patient admits to the physician that she has been feeling depressed recently and that for the past week she has been self-medicating with normal daily doses of one of her friend's antidepressant medications. What antidepressant is the patient most likely taking?

- A-Amitriptyline
- **B-Bupropion**
- C- Fluoxetine
- D- Selegiline

Q3: A 45 years old epileptic patient comes to the hospital with peeling skin and painful blisters all over his body. Which of these epileptic drug did he take?

- A- Lamotrigine
- **B- Sodium Valproate**
- C- Phenytoin
- **D-**Topiramate

Q4: Which of the following is the drug of choice in case of absent seizure?

- A- Lamotrigine
- B- Ethosuximide
- C- Sodium Valproate
- **D-Phenytoin**

Q5: A 17-year-old girl is brought into accident and emergency with generalized tonic-clonic seizure. Her mother had found her fitting in her bedroom about 20 minutes ago. The ambulance crew handover state that her sats are 96 per cent on 15 L of oxygen and they have given her two doses of rectal diazepam, but she has not stopped fitting. What is the most appropriate management?

- A- Phenytoin loading
- B-Lorazepam
- C-Intubation
- D- Phenobarbital

Q6:A 23-year-old woman is seen in clinic for recurrent funny turns. She is not aware of them, but her family and friends have noticed them. They say she looks around blankly, then starts picking at her clothes and sometimes yawns, then she comes back after a minute. She can get drowsy after these episodes. What seizure type does this patient describe? A- Absence.

- B-Generalized
- C- Tonic clonic
- D- Complex partial

Q7: 24-year-old female is seen in the clinic complaining that she suddenly finds herself walking around the house without control. on history the doctor found out that she has this episode during night and it last for 1-2 minutes, she feels oriented when these episodes happen and her family didn't notice any loss of consciousness. the doctor admitted her for monitoring and her EEG showed spikes at night, when she experiences the same episode, and she was diagnosed with epilepsy. Which lobe is the most likely affected in this lady?

A- Parietal lobe

- **B-Occipital lobe**
- C- Temporal lobe
- D- Frontal lobe



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Send us your feedback: We are all ears!

