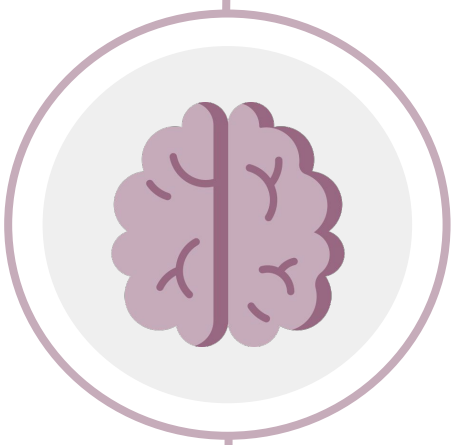
Epilepsy



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.
- ★ When to stop antiepileptic medications.

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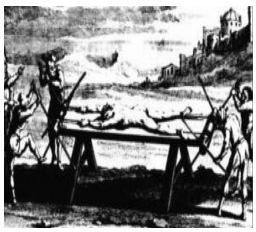
Epilepsy

◄ 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?

Very important to differentiate between provoked and epiliptic seizure because the management differs.

1

Epileptic seizure: Every word of the definition is important

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

2

Provoked seizures: (Acute symptomatic seizure) It’s not epilepsy

Occurs in the setting of acute medical and neurological illnesses [1] in people with no prior history of seizures. تشنج مستثار بعامل معين مهما كان السبب

3

Epilepsy [2]**:**

Recurrent (two or more) **unprovoked** seizures.

Unprovoked seizure: a seizure that occurs in the absence of an identifiable cause.

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

1: Ex: hypoglycemia, hyperglycemia, electrolytes imbalance (hyponatremia, hypernatremia), fever, stroke, CNS infections (meningitis, encephalitis) , intracerebral hemorrhage or sinus infection

2- A single unprovoked seizure or multiple provoked seizures or triggered seizures (e.g. febrile seizures) without an underlying predisposition to seizures is not sufficient for the diagnosis of epilepsy

Epilepsy

◀ Epidemiology and Course:

5% — Suffer a single **seizure** at some time. (seizure whatever cause not conditionally epilepsy)

0.5-1% — Have recurrent seizures = **EPILEPSY**

30% — Of epilepsies are at least **resistant** to drug treatments = INTRACTABLE EPILEPSY.

70% — Of epilepsies are well **controlled** with drugs (prolonged remissions)

◀ Pathophysiology EXTRA

- The inhibitory transmitter gamma-aminobutyric acid (GABA) is particularly important, acting on ion channels to enhance chloride inflow and reducing the chances of action potential formation.
- Excitatory amino acids (glutamate and aspartate) allow influx of sodium and calcium, producing the opposite effect. It is likely that many seizures result from an imbalance between this excitation and inhibition.

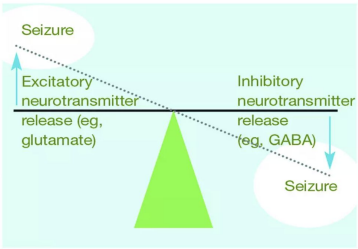
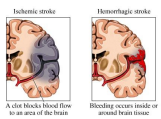


Figure 1: Seizures occur when there is an imbalance in excitatory and inhibitory neurotransmitter release

◀ Risk Factors for Epilepsy:

1. Perinatal insult (intrauterine infection e.g. TORCH[1] infection toxoplasmosis, rubella)
2. Family history
3. Abnormal gestation or delivery (Birth asphyxia: Hypoxic insult during delivery leading to ischemic encephalopathy)
4. Febrile convulsion — Recurrent febrile seizures seen in children. Needs 2 conditions to cause epilepsy: prolonged and recurrent febrile seizure.
5. CNS infection (E.g. Meningitis and encephalitis)
6. CNS mass lesion (Tumor)
7. Head injury (Studies stated that it's usually frontal penetrating injury)
8. Developmental delay
9. Stroke (ischemic or hemorrhagic)



65% of epilepsy cases have an **unknown cause** (Usually has genetic predisposition)

◀ Danger of epilepsy

- Main reason for road traffic accidents that's why epiliptic patients are banned from driving.
- 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.

1: TORCH" is an acronym meaning (T)oxoplasmosis, (O)ther Agents, (R)ubella (also known as German Measles), (C)ytomegalovirus, and (H)erpes Simplex.

Seizures

◄ Triggers for seizures:

1. Poor compliance to anti-epileptic medication (most common in SA)
2. Stress
3. Alcohol. particularly withdrawal
4. Infection. URTI & Tonsillitis
5. Menstrual cycle
6. Sleep deprivation & metabolic disturbances
7. Flickering lights, including TV and computer screens
8. Recreational drug misuse

◄ Classification of seizures

Seizure classification is important as it will guide in the management. For example, focal epilepsy may benefit from surgery, but those with generalized seizure are not candidate for surgery.

Important to differentiate between focal and generalized seizures from the perspective of:

1. **Level of consciousness (LOC)**
2. **Aura "same as the one presented in migraine"** (epigastric rising sensation as if the stomach goes up and down with a nauseated feeling, numbness (parital), flash (occipital lobe seizure)(the type of aura is based on the location of the focus)

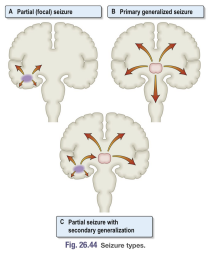


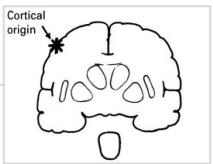
Fig. 26.44 Seizure types.

Types of Seizures

Focal Seizures [1] تشنج بؤري

Focus discharge which produces electricity.
(Account for **80%** of adult epilepsies)
preceded by warning "Aura"

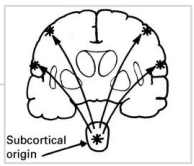
- **Simple partial seizures**
  (called aware in the new classification)
  → **Preserved** consciousness, complete awareness (LOC is intact)
- **Complex partial seizures**
  (called Impared in the new classification)
  → **Altered** consciousness **but not** complete loss nor completely preserved
- **Partial seizures secondarily generalised**
  (Starts as focal then the focus gets bigger and goes to the corpus callosum where it goes to the other hemisphere then its converted into generalized)(Both hemispheres involved)



Generalized seizures [2]

All parts of brain fires at the same time.
Comes with **no aura** (no warning) and leads to **complete loss of consciousness**.

- **Tonic Clonic Seizure** (Most common)
- **Atonic Seizure** (falls down)
- **Myoclonic Seizure** (jerks)
- **Absent Seizure** (staring)



Unclassified seizures [3]

1: One place in the brain produce discharges
2: Whole brain wil fire at same time. Patient describe it as light off-on.
3: Ex: epileptic spasm, usually affect pediatric pt (6m to 6 yo).

Seizures *(cont.)*

◀ International classification of seizures 1981

Partial Seizure
(Starts at one place)

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 or memory)**
  1. Sensory
  2. Motor
  3. Sensory-Motor
  4. Psychic (abnormal thoughts or perceptions)
  5. Autonomic (heat, nausea, flushing, etc.)
- **Complex (consciousness or memory impaired (not lost))**
  1. With or without aura (warning) → depends on lobe involved. ex: deja vu, oral Automatism (chewing), hand movement, epigastric racing sensation يحس كأن المعدة ترقى وتنزل""or nausea.
  2. With or without automatismes.
     Automatism: (e.g., lip smacking, blinking, tapping, exploratory movements with hands)
- **Secondarily generalized**

Generalized Seizures (Apparent starts over wide areas of brain)

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.
- Interrupted motion or activity, **blank stare**, **unresponsiveness**
- Characterized by **fast recovery** from seizure (No postictal phase), and can be **provoked by hyperventilation**
- EEG shows spike and slow wave pattern

Tonic-clonic
"grand mal"

- The patient starts with an epiliptic cry.
- 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, disoriented and/or amnesic.
- During the attack, **urinary incontinence and tongue-biting** may occur.
- Subsequently, postictal the patient usually feels unwell and sleepy, with headache and myalgia.

Atonic
"drop seizures"

- Involving **brief loss of muscle tone**, usually resulting in heavy falls with or without loss of consciousness.

Myoclonic

- Juvenile myoclonic epilepsy usually provoked by flashing lights.
- Typically **brief, jerking movements**, 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.)*

I don't want you to know all these details but as medical student I want you to know what's focal and generalized seizure and their classification in general without detailed classification

◀ New ILAE classification (2017)

Dr: I won't ask you about the new classification

Focal onset

Further classified into:

- Aware (simple partial)
- Impaired awareness (complex partial)

1 Motor onset

- Automatism
- Atonic
- Clonic
- Epileptic spasms
- Hyperkinetic
- Myoclonic
- Tonic

2 Non-motor onset

- Autonomic
- Behavioral arrest
- Cognitive
- Emotional
- Sensory

3 Focal to bilateral tonic-clonic

Generalized onset

1 Motor onset

- Tonic-Clonic
- Tonic
- Clonic
- Myoclonic
- Myoclonic-Tonic-Clonic
- Myoclonic-atonic
- Atonic
- Epileptic spasms

2 Non-motor (absence)

- Typical
- Atypical
- Myotonic
- Eyelid myoclonia

Unknown onset

1 Motor onset

- Tonic-Clonic
- Epileptic spasms

2 Non-motor

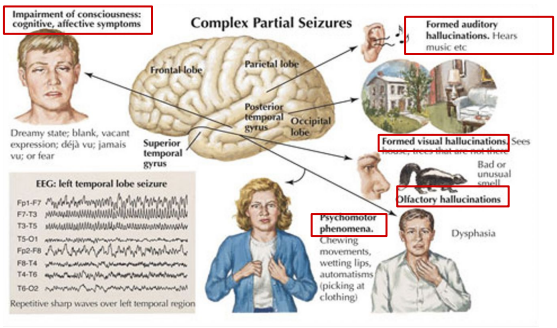
- Behavioral arrest

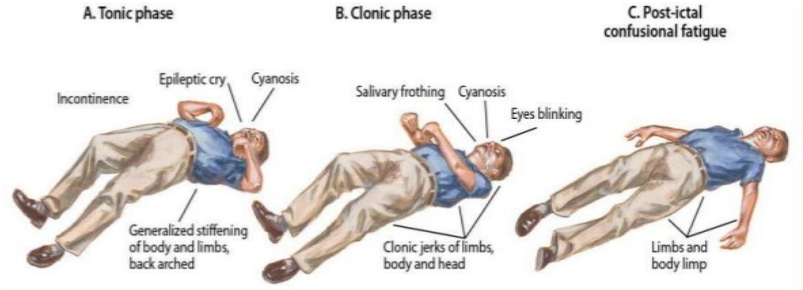
Unclassified

Seizures *(cont.)*

◀ Seizure Semiology

(Seizure semiology = Seizure description which is important for management and locating the focus)





★ To know which lobe of the brain we're dealing with, and the type of the seizure and to choose the appropriate Anti-epileptic medication

- **Parietal lobe:** usually sensory ex: pain, tingling.
- **Temporal lobe:** which is provoked by sleep deprivation with stress ex: epigastric rising sensation, memory impairment, manual picking, oral and hand automatism or deja vu (which means familiar or similar situation), left arm dystonia.
- **Occipital lobe:** symptoms related to vision (e.g. flashlight or decreased vision, right field blindness "ictal amaurosis" a feeling similar to a curtain where vision is loss temporary then comes back happens in TIA, visual hallucination, etc).
- **Frontal lobe:** hypermotor or hyperactive seizure described as bizarre like movements. ex: **bicycling** leg movement, frontal lobe seizure usually happen during sleep "nocturnal" where he can wake up and start hitting. (hard to differentiate between it and psychogenic seizure "Pseudoseizure" which cause eyes to close tightly with arching back)

◀ Differential Diagnosis for Seizure attacks:

Anything transient and gets better is a differential for seizure

1. **Migraine** Because patients experience an aura ex: nausea and flashes.
2. **Syncope**
3. **TIA** Patients experience weakness of a part of their body relieved after minutes.
4. **Panic attack**
5. **Movement disorders**
6. **Psychogenic seizure** Always down in the list

◀ Seizure vs Syncope:

Comparison of clinical features in cardiogenic syncope versus seizure disorders

Clinical features	Cardiogenic syncope	Seizure disorders
Loss of consciousness	Typical	Common
Episode duration	Seconds	Minutes
Involuntary movements	Common	Typical
Amnesia	Yes	Yes
Arrhythmia	Common	Rare*
Electroencephalogram	Slow waves Flattening	Focal or general spike activity
Responsive to AEDs	No	Often
Short term mortality†	High	Low

Approach to Seizures

1 Non invasive tests

- Clinical history then clinical history then clinical history (it's very important to select the most appropriate antiepileptic medication)
- MRI
- Neuropsychological evaluation
- Video EEG
- Nuclear medicine

2 invasive tests

i 25.34 Investigation of epilepsy

From where is the epilepsy arising?

- Standard EEG
- Sleep EEG
- EEG with special electrodes (foramen ovale, subdural)

What is the cause of the epilepsy?

Structural lesion?
- CT
- MRI

Metabolic disorder?
- Urea and electrolytes
- Liver function tests
- Blood glucose
- Serum calcium, magnesium

Inflammatory or infective disorder?
- Full blood count, erythrocyte sedimentation rate, C-reactive protein
- Chest X-ray
- Serology for syphilis, HIV, collagen disease
- CSF examination

Are the attacks truly epileptic?
- Ambulatory EEG
- Videotelemetry

(CSF = cerebrospinal fluid; CT = computed tomography; EEG = electroencephalography; HIV = human immunodeficiency virus; MRI = magnetic resonance imaging)

1 Clinical history

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

1. Was any warning (aura) noted before the spell?
   → Differentiate between focal and generalized seizures
2. What did the patient do during the spell?
   → For type of seizure + Lobe involved
3. Was the patient able to relate to the environment during the spell?
   → For consciousness (simple partial, complex partial or generalized)
4. How did the patient feel after the spell? Post-ictal
5. How long did it take for the patient to get back to baseline condition?[1]
6. How long did the spell last? → >5 min = status epilepticus
7. How frequent do the spells occur? → For management
8. Are any precipitants associated with the spells?

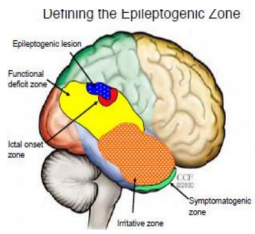
2 MRI[2] Most important type of imaging

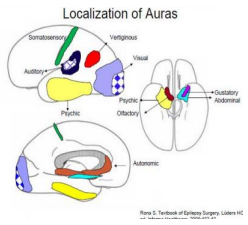
- **Lesional:** Tumor , cyst, Vascular, Trauma, Developmental, Mesial Temporal Sclerosis
- **Non Lesional**

Imaging cannot establish a diagnosis of epilepsy but identifies any structural cause.

Indications for brain imaging in epilepsy:

- Epilepsy starting after the age of 16 years
- Seizures having focal features clinically
- Electroencephalogram showing a focal seizure source
- Control of seizures difficult or deteriorating





3 Cognitive testing[3] (neuropsychology)

- **Intelligence**
- **Memory** Frequent temporal lesion might lead to memory decline so we need to assess the memory
  - **Verbal**
  - **Visual**
- **Language**

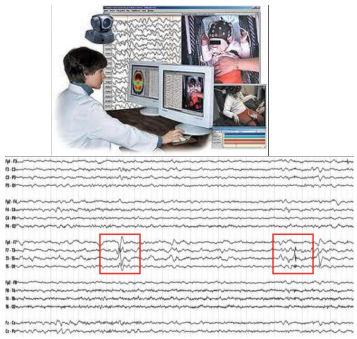
1: No post-ectal phase → Absence seizures. Prolonged post-ectal → complex partial and generalized .
2: Most patients experience seizure should do MRI to rule out focal lesion
3: Important for surgery, for ex: if seizures happening in left temporal lobe with impaired function and there is intact function 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.)*

4 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.
- Typical generalized spike wave is seen with absent seizure.

VEM



patient with temporal lobe epilepsy. Tracings of the left cerebral hemisphere show anterior temporal spikes and sharp waves (examples in red boxes). These findings indicate a possible epileptogenic source in the left anterior temporal lobe.

➔ Summary on the typical signs of video EEG

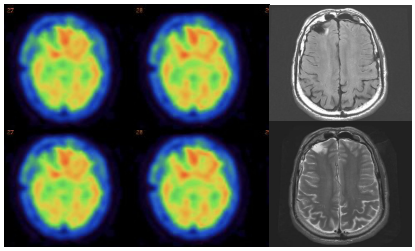
Dr: Very important never enter the exam without knowing it because I usually bring a scenarios and ask about the focus and localization of the seizure.

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

Management

5 Nuclear medicine

➔ Might be helpful to localize seizure.



◀ How to administer first aid for seizures

1 Move from danger	2 After convulsions	3 Airway	4 non-resolving	5 When to leave the patient?
Move the person away from danger (fire, water, machinery, furniture)	After convulsions cease, turn the person into the 'recovery' position (semi-prone)	Ensure the airway is clear but do NOT insert anything in the mouth (tongue-biting occurs at seizure onset and cannot be prevented by observers)	If convulsions continue for more than 5 mins or recur without the person regaining consciousness, summon urgent medical attention	Do not leave the person alone until fully recovered (drowsiness and delirium can persist for up to 1 hr)

◀ 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.**

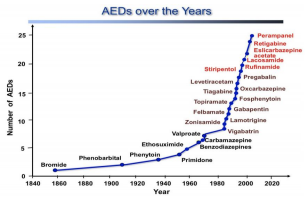
Treatment

First: Medical

Concept of treatment is to rise the seizure threshold that is pathologically lowered in individuals with epilepsy. Selection of the appropriate antiepileptic is very important that's why we need to understand the history and semiology very well

Drugs

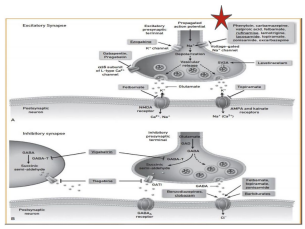
Phenytoin, Ethosuximide, Carbamazepine, Valproate, Lamotrigine, Oxcarbazepine, Bromide salt, Phenobarbital, Primidone, Clonazepam, Felbamate, Gabapentin, Topiramate, Tiagabine, Levetiracetam, Zonisamide, Pregabalin, Rufinamide, Lacosamide, and Ezogabine.



- 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 juvenile myoclonic epilepsy.

MOA

Current antiepileptic drugs are thought to act mainly by two main mechanisms:



1. **Reducing electrical excitability of cell membranes.**
   - **by inhibition of sodium channel.** (90% of antiepileptic medications works on sodium channels)
2. **Enhancing GABA** (GABA is an inhibitory)
   - By inhibiting GABA-transaminase
   - By drugs with direct GABA-agonist properties.
3. **SV2A protein receptor** Keppra (Levetiracetam) medication "this question came in the SMLE)
4. **AMPA receptor** Topiramate

Clinical uses of Antiepileptic drugs

1. **Generalized 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.
2. **Partial (focal) seizures: carbamazepine** (drug of choice)
   - valproate; clonazepam or phenytoin are alternatives.
3. **Absence seizures (petit mal): ethosuximide** (drug of choice) or valproate (valproic acid)
4. **Myoclonic seizures: valproate** or clonazepam

Valproic acid acts like broad spectrum antibiotics as it works on different epilepsy types but not preferred in female because contraindicated in pregnancy and it causes obesity, hair loss and hirsutism pancreatitis and polycystic ovaries.

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 some patients (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 two to three years, withdrawal** of pharmacotherapy should be considered.
  - Should be performed very carefully and **slowly!**
  - 20% (50%) of pts will suffer a further seizure **within 2 years**.

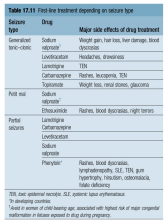
Seizure freedom with AED use

- 1st drug → seizure free (47%)
- 2nd drug → seizure free (14%)
- 3rd drug → seizure free (3%)

So there is no benefit adding 3rd drug because the chance to get free seizure is only 3% and it will cause only side effects and drug drug interaction without much benefit so we should choose the best 2 medications

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

1	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.
2	If first drug fails (seizures continue or side-effects develop), start second first-line drug, followed if possible by gradual withdrawal of first
3	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)
4	If this combination fails (seizures continue or side-effects develop), replace second-line drug with alternative second-line drug
5	If this combination fails, check adherence and reconsider diagnosis (Are events seizures? Occult lesion? Treatment adherence/alcohol/ drugs confounding response?)
6	Consider alternative, non-drug treatments (e.g. epilepsy surgery, vagal nerve stimulation) and Use minimum number of drugs in combination at any one time

Medication line	Generalized onset tonic-clonic	Focal	Typical absence	Atypical absence, Myoclonic and Atonic
First line	- Valproic acid - Lamotrigine - Topiramate	- Lamotrigine - Carbamazepine - Oxcarbazepine - Phenytoin - Levetiracetam[1]	- Valproic acid - Ethosuximide	- Valproic acid - Lamotrigine - Topiramate
Alternatives	- Zonisamide[a] - Phenytoin - Carbamazepine - Oxcarbazepine - Phenobarbital - Primidone - Falbamate	- Topiramate - Zonisamide[a] - Valproic acid - Tiagabine[a] - Gabapentine[a] - Lacosamide[a] - Phenobarbital - Primidone - Falbamate	- Lamotrigine - Clonazepam	- Clonazepam - Felbamate

[a] As adjunctive therapy

1: an advantage of levetiracetam treatment is that uptitration is not necessary.

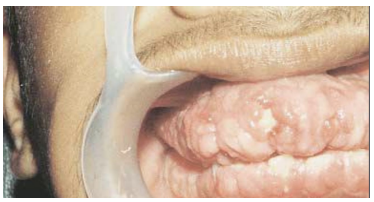
Treatment *(cont.)*

Dr: Don't memorize the table in detail I just want you to know that:

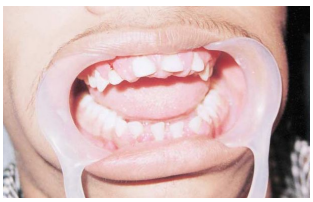
- Topiramate causes kidney stone
- Phenytoin causes reversible gum hyperplasia
- Stevens - Johnson Syndrome is caused by Lamotrigine, Phenytoin and Carbamazepine

AED	Major or potentially life threatening	Minor side effects
Phenobarbital	Hepatotoxicity, Stevens - Johnson Syndrome and connective tissue disorder	Sedation, depression, behavioral effects and osteopenia
Phenytoin (Dilantin)	Pancytopenia, hepatotoxicity and Stevens - Johnson Syndrome	Dizziness, ataxia, gum hyperplasia, hirsutism, neuropathy and osteopenia
Carbamazepine (Tegretol)	Agranulocytosis*, Aplastic anemia*, hepatotoxicity and Stevens - Johnson Syndrome	Dizziness, ataxia, hyponatremia and osteopenia
Valproate (Depakote)	Hepatotoxicity*, Thrombocytopenia and pancreatitis*	Weight gain, alopecia, tremor, GI upset and osteopenia
Felbamate (Falbatol)	Aplastic anemia* and hepatotoxicity*	Anorexia and insomnia
Gabapentin (Neurontin)	None	Sedation and weight gain
Lamotrigine (Lamictal)	Stevens - Johnson Syndrome*	Dizziness, ataxia and insomnia
Topiramate (Topamax)	Kidney stones, oligohydrosis and glaucoma	Paresthesias, cognitive impairment and weight loss
Tiagabine (Gabatril)	Spike - wave stupor	Tremor, sedation and impaired concentration
Levetiracetam (Keppra)	None	Sedation and behavioral changes
Oxcarbazepine (Trileptal)	Stevens - Johnson Syndrome	Ataxia, diplopia and hyponatremia
Zonisamide (Zonegran)	Kidney stones, oligohydrosis and rash	Paresthesias and weight loss
Pregabalin (Lyrica)	None	Sedation and weight gain
Lacosamide (Vimpat)	None	Dizziness, nausea and fatigue
Rufinamide (Banzel)	None	Somnolence, dizziness and nausea
Vigabatrin (Sabril)	Peripheral visual field defect	Anemia, neuropathy and weight gain

Gingival hyperplasia

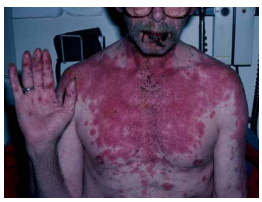


Induced by Phenytoin



After withdrawal of Phenytoin

Stevens - Johnson Syndrome

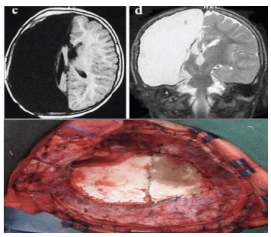


Treatment *(cont.)*

◀ Second: Surgical

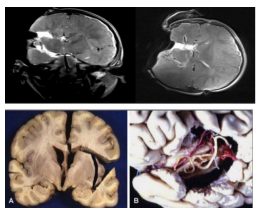
We perform surgery if we had a drug resistant focal seizure where we can remove the focus. We can't perform surgery on generalized seizure because the whole brain is firing.

Hemispherectomy



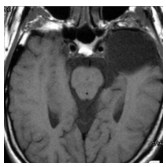
Hemispherectomy is a surgical treatment for epilepsy in which one of the two cerebral hemispheres is removed.

Hemispherotomy



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

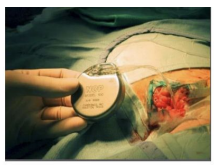


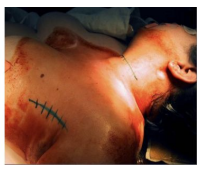
Temporal lobectomy will result in seizure freedom in 50–70% of selected patients with uncontrolled seizures caused by hippocampal sclerosis (defined by imaging and confirmed by EEG).

Selective Amygdalectomy

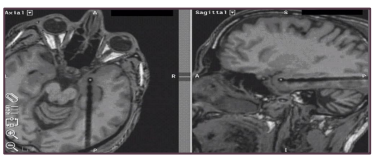
A more selective procedure

◀ If my patient is not a good candidate for surgery?





1. **Vagus Nerve Stimulation (VNS)**
   - Reduce seizure by 12-50%
   - Chosen if the patient is not a candidate for surgery.



2. **Deep Brain Stimulation (DBS)**

Status epilepticus

◄ Definition:

Defined as recurrent convulsions that last for **more than 30 minutes (more than 5 min in the last update)**[1] and are interrupted by only brief periods of partial relief [2].

- **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.

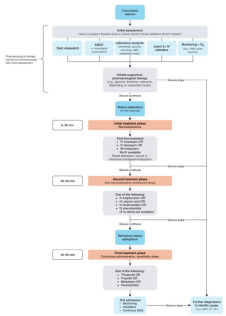
◄ Management:

Early status (up to 30 min) Concurrently manage rapidly reversible causes of seizure (hypoglycemia, hyponatremia, hypocalcemia without any delay

- **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 dysrhythmias, 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.

1: Time is brain, if seizure is prolonged, millions of neurons will be lost.
2: Patient won't be conscious.

Seizures VS syncope

◀ Seizures vs Syncope:

	Cardiogenic Syncope	Seizure Disorders
Definition	Due 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 because some types doesn't have complete loss of consciousness
Aura	-	+
Cyanosis	-	+
Episode Duration	Seconds (short)	Minutes
Involuntary movements	Common	Typical (more)
Amnesia	Yes	Yes
Post-ictal delirium	-	+
Post-ictal headache	-	+
Arrhythmia	Common (Asystole that lasts for 5-6 secs detected by ECG)	Rare
Electroencephalogram	Slow waves Flattening	Focal or General Spike
Responsive to AED (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

Epilepsy in women

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.

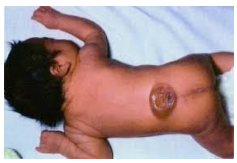
Birth defects

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.

Risk of in utero antiepileptic drug exposure:

- Major Congenital Malformation (MCM)
  - 1.6 - 2.1% in general population
  - Studies comparing to WWE on no AEDs
    - Increased with AEDs in class II studies (OR 3.9 (1.29 - 11.9))
    - No increased risk with AEDs in class I study.
- Minor anomalies
- Small for Gestational Age (SGA)
- Developmental Disability
- Microcephaly
- Spina bifida is a neural tube defect (NTD) involving incomplete formation of the spine
- Cleft lip



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.
- Phenobarbital is not recommended during breastfeeding and there is some medications that comes with the milk and cause sleepiness to the baby.
- Continue the medication while breastfeeding unless you've noticed poor sucking and floppy baby we check the drug level in blood but we don't stop the medications during breastfeeding.

Epilepsy in women

Epilepsy treatment in pregnancy

The **risk of teratogenicity** is well known (~5%), especially with **valproates**[1], but withdrawing drug therapy in pregnancy is more risky than continuation [2](risk to the fetus of uncontrolled seizures) so its better to change the medication to a safe one and in case she was taking the medication for a long duration we lower the dose and add folic acid to reduce the risk of neural tube defect .

- All antiepileptic medications are not safe, however **lamotrigine** is the **safest**. .
- 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

Teratogenic risk profiles of antiepiliptic drugs

Dr: Important and comes in the MCQ questions

	First line	Second line	Third line	Fourth line
More safe	Lamotrigine Safest	Oxcarbazepine*	Phenytoin, Topiramate*	
Less safe	Levetiracetam	Carbamazepine	Phenobarbital	Valporic acid
* = Neurodevelopmental outcomes are not yet known				

Increasing risk

Epilepsy (Kaplan)

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.

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

- Febrile convulsions
- Family History
- CNS mass/infection
- Trauma
- Stroke

Triggers

- Poor compliance
- Stress
- Infection

Classification

Generalized

- Absence (petit mal)
- Atonic (drop seizure)
- Tonic-clonic (grand mal)
- Myoclonic

Focal

- Simple partial seizures (no change in LOC)
- Complex partial seizures (impairment of LOC)

Seizure semiology

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

Seizures vs Syncope

Syncope

- Episode Duration (Seconds)
- Amnesia
- **NOT** Responsive to AED

Seizures

- Episode Duration (Minutes)
- Amnesia
- Oftenly Responsive to AED

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
- **N.B: all AEDs are teratogenic, BUT lamotrigine is the safest**

Take Home Messages

- Important to differentiate between focal and generalized seizures from the perspective of:
  1. Level of consciousness (LOC)
  2. Aura)
- **Epiletic seizure: Transient** occurrence of signs and symptoms of sudden changes in **neurological function** due to **abnormal excessive** and **synchronous** discharge of cortical neurons.
- Simple partial seizure: (no loss of consciousness or memory)
- **Complex partial seizure: (consciousness or memory is impaired)**
- **Absence seizure:** are mistaken for daydreaming or poor concentration in school. EEG shows spike and slow wave pattern
- Focal seizures with altered awareness or responsiveness are usually arise from the temporal lobe (60%) or the frontal lobe.
- **Seizure semiology:**
  1- Parietal lobe: usually sensory ex: pain, tingling.

  2- Temporal lobe ex: epigastric rising sensation, memory impairment, manual picking, oral and hand automatism or deja vu (which means familiar or similar situation), left arm dystonia.

  3- Occipital lobe: symptoms related to vision (e.g. flashlight or decreased vision, right field blindness “ictal amaurosis” a feeling similar to a curtain where vision is loss temporary then comes back happens in TIA, visual hallucination, etc).

  4- Frontal lobe: hypermotor or hyperactive seizure described as bizarre like movements. ex: bicycling leg movement.

  Frontal seizure can look like a Pseudoseizure due to odd motor activity that may occur
- IAEDs should be introduced at low dose and slowly titrate upwards until the seizures are controlled or side-effects become unacceptable.
- If seizures are not controlled with the first AED, gradually introduce a second agent and then slowly withdraw the first AED. If the patient is still not seizure-free, then combination therapy is required.
- Ethrouxismide is the first line treatment of absence seizure
- Best AEDs in pregnancy: **Levetiracetam** and **Lamotrigine**
- Status epilepticus can cause irreversible brain damage without treatment

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

Answers: Q1:D | Q2:B | Q3:A | Q4:B | Q5:A | Q6:D | Q7:D |

GOOD LUCK !

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