Seizure disorders, epilepsy, and status epilepticus

Objectives (regarding the Blueprint):

1. Understand the definition of seizure, epilepsy and status epilepticus.
2. Differentiae between a seizure and syncope using semiology and historical clues.
3. Know the subtypes (generalized, partial, etc) and causes of seizures.
4. Know the role of investigations (EEG, MRI, etc) in a patient with a seizure.
5. Master the steps in the management of status epilepticus.
6. Know how to counsel a patient with a seizure (including triggers, precautions, etc).

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Understand the definition of seizure, epilepsy and status epilepticus.

Clinical seizures

Definition: are caused by an excessive, synchronous, abnormal discharge of cortical neurons that produces a sudden change in neurologic function.

Acute symptomatic seizure (provoked seizure)

Definition: a seizure that occurs at the time or soon after the onset of an acute systemic or CNS condition. Examples include:

- Within 1 week of stroke, traumatic brain injury (TBI), anoxic encephalopathy, or intracranial surgery.
- Subdural hematoma.
- Acute CNS infection.
- Exacerbation of multiple sclerosis or other autoimmune diseases.
- Metabolic disturbances.
- Drug/alcohol intoxication or withdrawal.

Unprovoked seizure

Definition: a seizure that occurs in the absence of an identifiable cause or beyond the specified interval after an acute CNS condition.

Reflex seizure

Definition: a seizure constantly evoked by a particular stimulus (trigger) that lowers seizure threshold. (e.g, flashing lights, see "Seizure triggers")

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Epilepsy

Definition: a **chronic** neurologic disorder characterized by a predisposition to seizures as defined by one of the following:

1. Two or more unprovoked seizures **separated by more than 24 hours.**
2. One unprovoked seizure in an individual with high risk of subsequent seizures (after traumatic brain injury, stroke, CNS infections).

Causes:

- **Genetic**.[1]
- **Chromosomal abnormalities** (e.g, Angelman syndrome, Prader-Willi syndrome, Rett syndrome).
- **Genetic metabolic disorders** (e.g, PKU, congenital disorders of glycosylation, lysosomal storage diseases, peroxisomal biogenesis disorders).
- **Mitochondrial diseases** (e.g, MELAS).
- **Structural**: chronic cerebral lesion or abnormality.
- **Perinatal injury** (e.g, hypoxic-ischemic injury).
- **Brain tumors and metastases**.
- **Traumatic brain injury (TBI).**
- **Hippocampal sclerosis.**
- **Tuberous sclerosis.**
- **Congenital cerebral or arteriovenous malformations.**
- **Microcephaly, megalocephaly, cortical dysgenesis.**
- **Cranial radiation therapy.**
- **Metabolic.**
- **Inborn errors of metabolism** (e.g, organic acidemias, phenylketonuria).
- **Porphyrias**
- **Immune**: autoimmune encephalitides (e.g, anti-NMDA receptor encephalitis), Rasmussen encephalitis.
- **Infectious**: chronic CNS infection (e.g, toxoplasmosis, malaria, neurocysticercosis) or complication of acute CNS infection (e.g, viral or bacterial meningitis or encephalitis).

Status epilepticus[2]

- **Definition:** 5 minutes or more of **continuous** clinical and/or electrographic seizure activity or recurrent seizure activity **without recovery** between seizures.
- Status epilepticus is a seizure that lasts ≥ 5 minutes or a series of seizures in rapid succession without full neurological recovery in the interictal period, which increases the **risk of long-term consequences such as neuronal injury and functional deficits.**
- The time threshold after which a seizure is considered status epilepticus differs according to the type of seizure:

1. Tonic-clonic seizures: ≥ 5 minutes
2. Focal seizures with impaired consciousness: ≥ 10 minutes
3. Absence seizures: 10–15 minutes

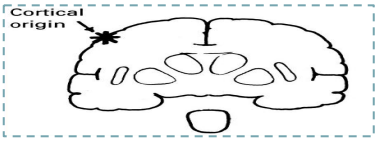
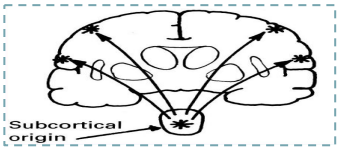
- **Refractory status epilepticus:** SE that does not respond to the standard treatment regimens, such as initial benzodiazepine followed by another antiepileptic medication.

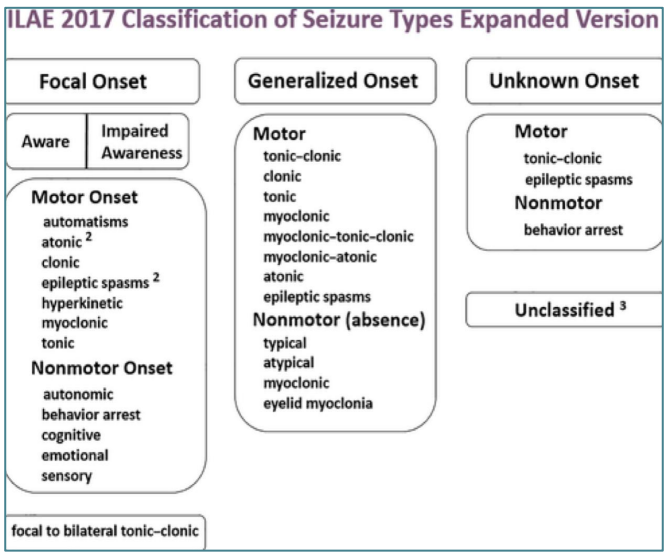
- **Causes of SE:** Prior epilepsy - Idiopathic - Anticonvulsant withdrawal - Alcohol withdrawal - Metabolic - Cerebrovascular - Trauma - Drugs - CNS infection - Tumor - Congenital.

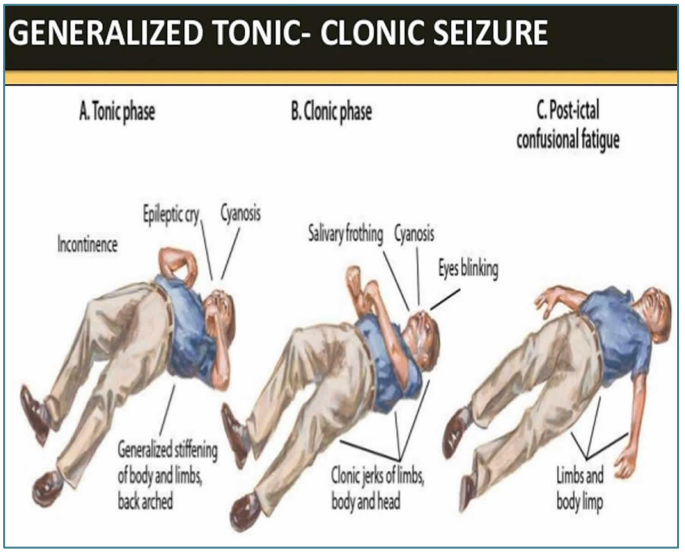
1. Genetic mutations affecting ion channels or transmitter receptors.
2. Any type of seizures may lead to status epilepticus.

Know the subtypes (generalized, partial, etc) and causes of seizures.

Seizure Classification

	Focal Seizures	Generalized Seizures	Unclassified
Definition	Seizures that involve a single brain region, causing limited dysfunction. Usually preceded by Aurea	Seizures that involve the whole brain, leading to loss of consciousness and convulsions. Not preceded by an Aura	-
Types	**Partial Seizures** - **Simple focal aware:** no loss of consciousness (sensory, motor, sensory-motor, psychic,autonomic). - **Complex impaird aware:** impaired level of consciousness (with or without Aura or automatisms) - **Secondary generalized.** 	- Absence (petit mal) - Tonic-clonic (grand mal) - Atonic (drop seizures) - Myoclonic 	-





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Causes of Seizures

VITAMINS

1. **V** (vascular): Stroke, Intracranial hemorrhage, acute or chronic ischemic infarction, subarachnoid hemorrhage, arteriovenous malformation, venous sinus thrombosis.
2. **I** (Infectious): meningitis or abscess.
3. **T** (traumatic): new or old head injury with subdural hematoma.
4. **A** (autoimmune): systemic lupus erythematosus or vasculitis.
5. **M** (metabolic): hypo/hypernatremia, hypo/hypercalcemia, hypomagnesemia, hyperthyroidism, uremia, hyperammonemia, ethanol toxicity or withdrawal, drugs cocaine or amphetamines.
6. **I** (idiopathic/iatrogenic).
7. **N** (neoplastic).
8. **S** (structural) (sycitaric).

Seizure Triggers

Seizure triggers are stimuli that can precipitate seizures both in people with and without epilepsy.

- Excessive physical exertion.
- Alcohol consumption.
- Fever (febrile seizures).[1]
- Sleep deprivation.
- Flashing lights (e.g., strobe lights, video games).
- Music.[2]
- Hormonal changes (e.g., at different phases of the menstrual cycle, after menopause).
- Medication-related issues in **patients with known epilepsy**: e.g., poor adherence, recent changes in drug doses or formulation, new medication interactions.

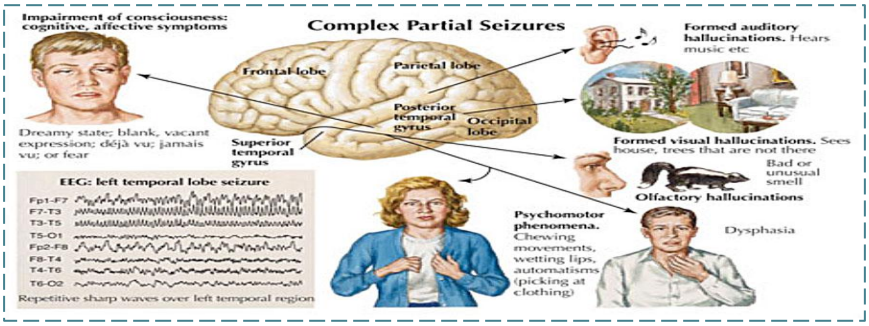
DDx of Seizure Attacks

- TIA.
- Syncope.
- Migraine. Both are preceded by an aura.
- Movement disorder. e,g, tick disease
- Panic attack.
- Sleep disorders. Frontal lobe seizure.

1. Commonly affects children between six months and five years of age.
2. The pathogenesis of music-induced seizures is unclear; emotional response to music rather than the sound itself is suggested to provoke seizures, although pure tones have also been reported as seizure triggers.

Differentiae between a seizure and syncope using semiology and historical clues.

Seizure Semiology (Very IMP)



-Frontal lobe: presents with nocturnal symptoms.
-Occipital lobe: Visual symptoms.
-Parietal lobe: Sensory symptoms.

Typical EEG sign	Localizes to
Oral automatisms	Temporal lobe
Hypermotor automatisms	Frontal lobe
Manual picking automatisms	Temporal lobe
Visual hallucinations	Occipital lobe
Auditory hallucination	Temporal lobe (Heschl's Gyrus)
Olfactory hallucination	Mesial Temporal lobe
Nystagmus, Eye blinking , Eye pulling sensation	Occipital lobe
Ictal amaurosis (loss of vision)	Occipital lobe
Tonic arm elevation	Supplementary motor area
Epigastric Aura	Temporal lobe
Throat tightening sensation	Insula
Ictal pain	Parietal lobe
Somatosensory sensation	Postcentral gyrus or supplementary motor area
Clonic activity	Precentral gyrus
De-ja vu	Mesial temporal lobe
Fear	Most often temporal but may be frontal

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Historical clues

Questions that help clarify the type of seizure: imp OSCE

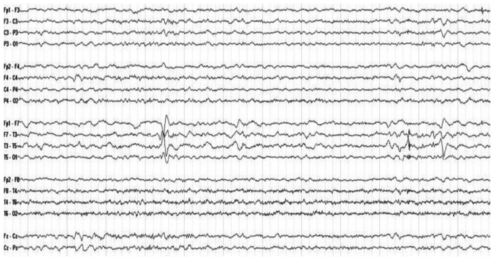
- Was any warning noted before the spell?
- What did the patient do during the spell?
- Was the patient able to relate to the environment during the spell?
- How did the patient feel after the spell?
- How long did it take for the patient to get back to baseline condition?
- How long did the spell last?
- How frequent do the spells occur?
- Are any precipitants associated with the spells?

Seizure vs Syncope[1]

Clinical Features	Cardiogenic syncope	Seizure
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

1. Cyanosis with seizures, while pallor with syncope.

Know the role of investigations (EEG, MRI, etc) in a patient with a seizure.



Diagnostic workup

1 All patients

If the patient history is not clear, or if this is the patient's first seizure:

- Laboratory screening: to identify metabolic disorders, or infectious diseases if suspected: Blood glucose, CBC, BMP, Electrolytes (Ca, MG…), LFT, RFT, urinalysis.
- Monitor vital signs.
- EEG monitoring

EEG findings

- Performed in individuals who present with first seizure, with insufficient information for seizure classification, and/or treatment refractory seizures.
- Although the EEG is the most helpful diagnostic test in the diagnosis of seizure disorder, an abnormal EEG pattern **alone is not adequate** for diagnosis of seizures.
- A **normal** EEG in patient with first seizure is associated with a **lower risk of recurrence**.

During the seizure (ictal):	After a seizure or between seizures (postictal or interictal):
- **Epileptiform discharges** (e.g. spikes, sharp waves) are usually detected. - If no epileptiform discharges are detected during a seizure, alternative diagnosis should be considered such as: psychogenic seizures.	- Often normal findings (even after provocation via sleep deprivation or visual stimuli). - May show epileptiform activity

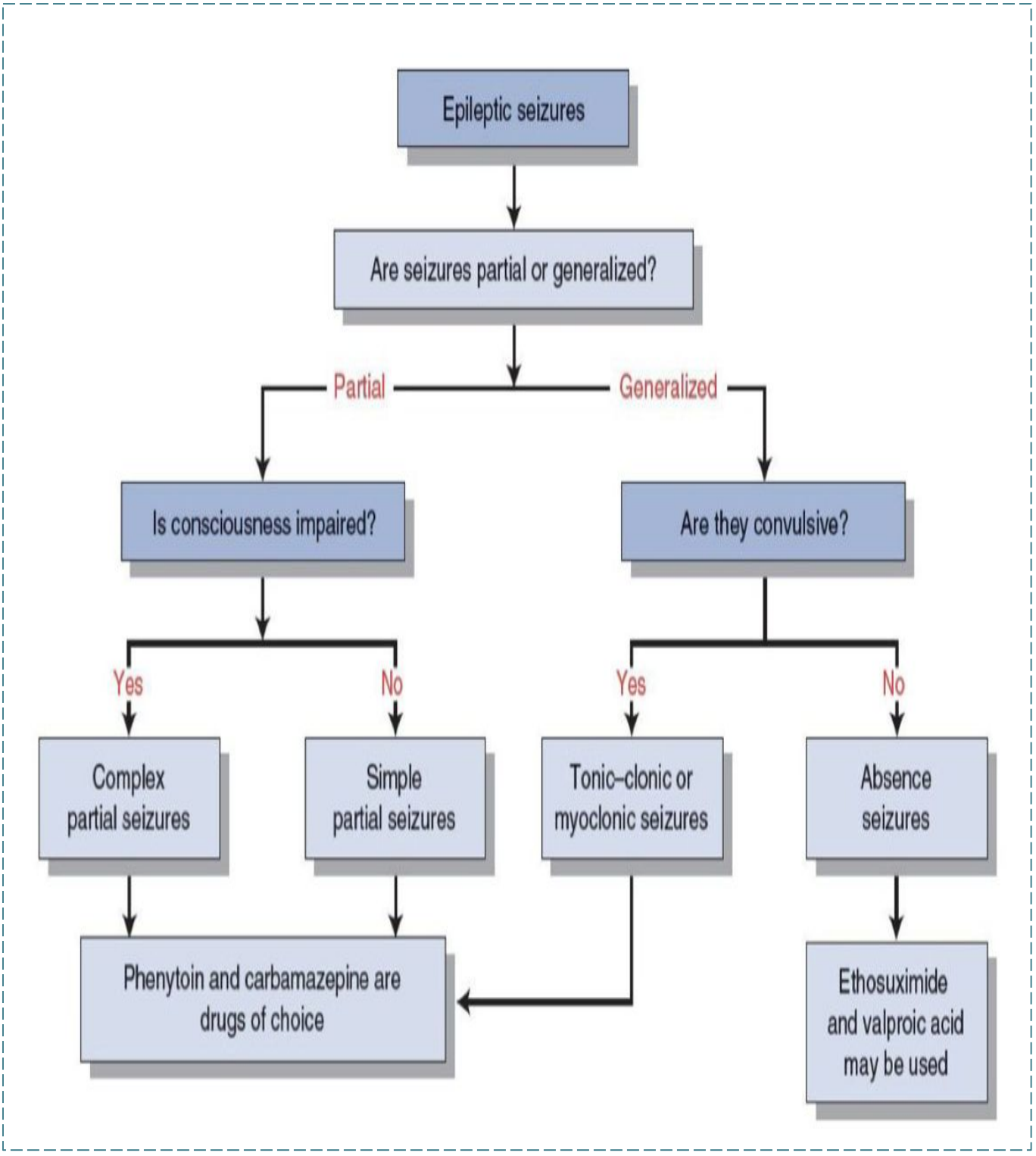
Consider based on clinical presentation

- CT scan of the head: to identify a structural lesion. (appropriate for most cases)
- Brain MRI , with or without gadolinium (initially without): modality of choice for investigating potential underlying structural abnormalities in all patients with first-time focal seizures (Exception: children with history and examination suggestive of benign seizure or characteristic epilepsy syndrome). More sensitive than CT scan in identifying structural changes. but not always practical (e.g, in unstable patients)
- Angiography: if vascular cause is suspected. (e.g, cerebral arteriovenous malformation)
- Lumbar puncture & blood culture: if patient febrile.
- Toxicology panel (isoniazid, TCAs, theophylline, cocaine, sympathomimetics, ETOH, organophosphates, cyclosporine).
- Other labs: LFTs, troponin, TSH, coagulation profile, ABG, AED levels, inborn errors of metabolism.

2

If the patient has a known seizure disorder (epileptic), **check anticonvulsant levels.** This is usually the only test that's needed.
Because therapeutic anticonvulsant level are variable, one dose may be toxic for one patient and therapeutic for another. Therefore, take the range given in laboratory reports as general guideline.

Management (EXTRA)



DO NOT treat patient with a single seizure. Antiepileptic drugs are started if **EEG is abnormal**, brain **MRI is abnormal**, patient is in **status epilepticus**.

Master the steps in the management of status epilepticus.

Management of status epilepticus

Management steps are determined by the time from seizure onset. Steps include:

- Patient stabilization.
- Identification.
- Treatment of reversible acute causes of seizures.
- Pharmacotherapy to terminate the seizure.

Step 1: ABCDE (Initial stabilization for acute seizures)

- Call for help and remove or control hazards (e.g, remove sharp objects in the patient's vicinity).
- Perform an ABCDE assessment; if needed, perform cardiopulmonary resuscitation.

ABCDE:

1. Maintain airway. Initiate basic airway maneuvers, start oxygen therapy, and place the patient in the recovery position.
2. Breathing (be ready for intubation, benzo may cause respiratory distress).
3. Circulation (obtain IV access).
4. Dextrose (check POC glucose level).
5. Electrolytes (Na, Ca,Mg and anticonvulsant level).

- Check vital signs.

Pharmacotherapy (step 2,3,4,5)

Seizure phase (time from seizure onset)	Preferred agents	Alternatives
Early seizure (0–5 min)	Often self-limited; pharmacotherapy is usually not indicated.	-
Early status epilepticus (5–20 min): first-line therapy Administer push dose. Repeat every 5–10 min if no response.	• **IV benzodiazepine** (lorazepam OR diazepam). • IM midazolam if IV access is NOT available.	• Intranasal midazolam • Buccal midazolam • Rectal diazepam
Persistent status epilepticus (20–40 min): second-line therapy Administer loading dose.	• IV fosphenytoin • IV valproic acid • IV levetiracetam	IV phenobarbital
Refractory status epilepticus (40–60 min): Expert guidance is required.	Options include repeat second-line therapy or induction of coma (e.g., with IV propofol, thiopental, midazolam, or pentobarbital).	-

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Step 2: Benzodiazepine therapy *You must know the doses

	Diazepam	Lorazepam
Lipid solubility	Highly	Less
Duration of action	15-30 minutes	12-24 hours
Dose	<3 years (0.5 mg/kg) >3 years (0.3 mg/kg	0.05-0.1 mg/kg
Side effects	Sedation, decreased blood pressure, decreased respiration	Decreased LOC, decreased respiration, decreased blood pressure

Step 3: Administer Phenytoin/Fosphenytoin

- Administer phenytoin 15 to 20 mg/kg as a slow IV infusion.
- Always mix phenytoin with normal saline, never with dextrose because it causes thrombophlebitis.
- Rate of administration should not exceed 50 mg/min because it can cause cardiac arrhythmias, prolongation in the QT interval, and hypotension.
- ECG and blood pressure should be monitored during the infusion.
- Fosphenytoin is safer than phenytoin, and may be given as IM.

- **Approximately 70% of prolonged seizures will be brought under control, if the seizure lasts longer than 30 minutes, transfer the patient to ICU for probable intubation.**

Step 4: Administer phenobarbital

- Side effects: sedation, decreased respiration and BP.
- Be ready to intubate, give in ICU.
- Should be infused loading dose of 15 to 20 mg/kg.

Step 5: Consider IV Valproic acid, levetiracetam IV Load

EXTRA

Management of refractory status epilepticus

- Intubation, IV access.
- Continuous EEG monitoring.
- Medication Coma (phenobarbital, midazolam, propofol).
- General anesthesia with halothane and neuromuscular blockade (to avoid rhabdomyolysis).

General recommendations:

- Benzodiazepines should be given as emergent initial therapy.
- Lorazepam is the drug of choice for IV administration, while midazolam for IM administration.
- Rectal diazepam is available when there is no IV access or IM midazolam is contraindicated.
- Urgent control AED therapy recommendations include IV fosphenytoin/phenytoin, valproate. sodium, or levetiracetam.

Complications

- Cardiac: HTN, tachycardia, arrhythmia.
- Pulmonary: apnea, hypoxia, respiratory failure.
- Hyperthermia.
- Metabolic derangement.
- Cerebral: neuronal damage.
- Death.

Major threat to life

- Aspiration of gastric content if the airway is not protected.
- Head injury.
- Lactic acidosis, hypoxia, hyperthermia, rhabdomyolysis, cerebral edema, or hypotension from a prolonged seizure.
- Patient should be positioned in the lateral decubitus position, to prevent aspiration of gastric contents

Cont..

Maintenance treatment of epileptic patients

IMP to know the major side effects

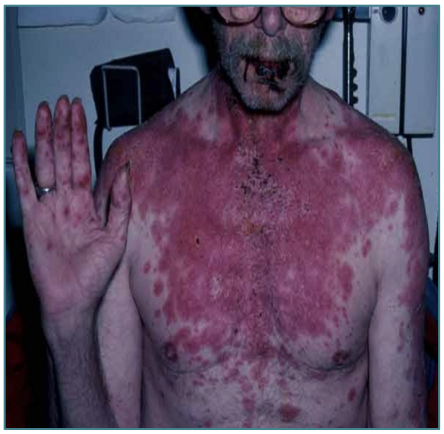
AED	Major side effect	Minor side effect
phenobarbital	Hepatotoxicity, Steven's johnson syndrome , connective tissue disorder	Sedation, depression, behavioral effects, osteopenia
phenytoin	Pancytopenia, hepatotoxicity, Steven's johnson syndrome	Dizziness, ataxia, gum hyperplasia, hirsutism, neuropathy, osteopenia
Carbamazepine	Agranulocytosis, aplastic anemia,hepatotoxicity, Steven's johnson syndrome	Dizziness, ataxia, hyponatremia, osteopenia
Valproate	Hepatotoxicity, thrombocytopenia, pancreatitis	Weight gain, alopecia, tremor, GI upset, osteopenia
Felbamate	Aplastic anemia, hepatotoxicity	Anorexia, insomnia
Gabapentin	none	Sedation, weight gain
Lamotrigine	Steven's johnson syndrome	Dizziness, ataxia, insomnia
Topiramate	Kidney stones, oligohidrosis, glaucoma	Paresthesias, cognitive impairment, weight loss
Tiagabine	Spike-wave stupor	Tremor, sedation, impaired concentration
Levetiracetam	none	Sedation, behavioral changes
Oxcarbazepine	Steven's johnson syndrome	Ataxia, diplopia, hyponatremia

Cont..

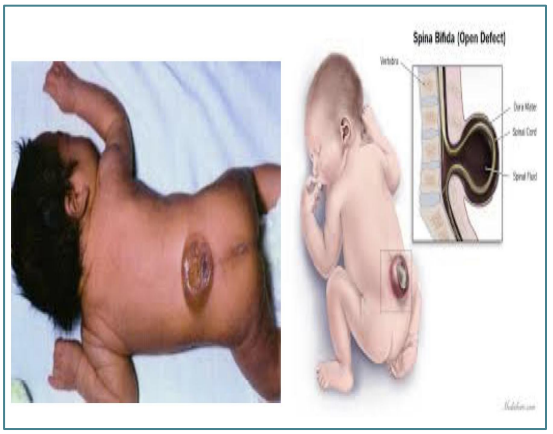
AED	Major side effect	Minor side effect
Zonisamide	Kidney stones, oligohidrosis, rash	Paresthesias, weight loss.
Pregabalin	none	Sedation, weight gain.
Lacosamide	none	Dizziness, nausea, fatigue.
Rufinamide	none	Somnolence, dizziness, nausea
Vigabatrin	Peripheral visual field defect	Anemia, neuropathy, weight gain.

Teratogenic risk profiles of antiepileptic medication:

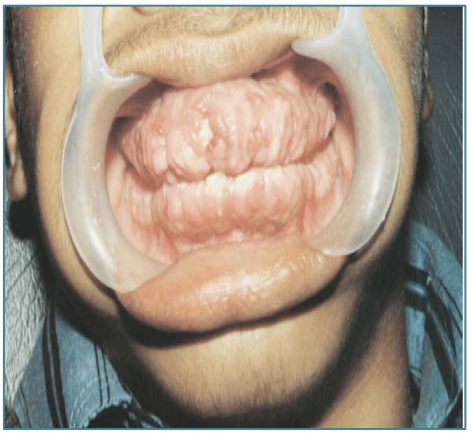
1. Valproic acid
2. Phenytoin, phenobarbital, topiramate
3. Carbamazepine
4. Lamotrigine (first line), Levetiracetam (second lime)



Steven's Johnson syndrome



Spina bifida (NTD) caused by valproate



Gingival hyperplasia induced by phenytoin

Know how to counsel a patient with a seizure (including triggers, precautions, etc).

1. Acknowledging the event.
2. Explanation of what a seizure is (and is not).
3. Possible etiology and prognosis.
4. Purpose and limitations of tests.
5. Lifestyle considerations (safety, occupation, seizure threshold).
6. Driving.
7. Seizure first aid.
8. Role of medication.
9. Medication action and side effects (if appropriate).
10. Psychological implications.
11. Next steps and when to call for help.

Life style

We must encourage people who experience a first seizure to **avoid the triggers.** As we mentioned before

While people with epilepsy should be encouraged to lead lives as unrestricted as reasonably possible, though with simple safety measures, such as:

1. Avoiding swimming and dangerous sports such as rock climbing.
2. Leaving bathroom and lavatory doors unlocked.
3. Taking showers rather than baths.
4. Avoid epilepsy triggers such as: sleep deprivation, excess alcohol and drugs.
5. Patients should be asked to stop driving after a seizure, and inform the regulatory authoroties if they hold a driving licence.

Epilepsy in women

- The overall risk of birth defects in babies with mothers who takes AED is around 7%.
- Counselling before conception is essential.
- The risk of teratogenicity is well known 5% especially with valproates, but withdrawing drug therapy in pregnancy is more risky than continuation.
- All antiepileptic medications are not safe, however lamotrigine is the safest.

OnlineMedEd

Introduction

Seizures are **uncontrolled synchronous firing of neurons** in the brain. There are many different types of seizures with many different presentations. As such, they should be considered **a symptom** of an underlying disease. For the disease and appropriate intervention consider **epilepsy** (usually only with a history of this disease) and the **VITAMINS** mnemonic. Generally, go through the Section marked "Seizure/Vitamins" for a 1st time seizure, and then the section marked "Epilepsy" for repeat offenders.

Seizure/Vitamins

On the boards, a new onset seizure will classically present as a grand mal. A grand mal seizure presents with **tonic clonic convulsions**, **bowel/bladder incontinence**, and **tongue biting**. Yet, all of these are very nonspecific. There's a **loss of consciousness**, but it's the **post-ictal confusion** that separates a seizure from alternative causes of loss of consciousness. A patient who has a seizure but is now normal requires observation, VITAMINS workup, and an **EEG**. However, when patients are actively seizing, are post-ictal, or have entered **Status Epilepticus**, they need to be **treated** as a **medical emergency**. The goal of treating a seizure acutely is to **reverse the underlying cause**. To do that the patient has to be alive - so the #1 priority is to **control ABCs** (Intubation, oxygenation, ventilation, IVF). Before drawing labs to investigate VITAMINS the **seizure must be aborted**. Do so by following this cascade: (1) **IV/IM Benzos** (lorazepam / diazepam) → (2) **FosPhenytoin** → (3) **Midazolam** and **Propofol** → (4) **Phenobarbital**. Then **draw labs** and reverse any underlying defects.

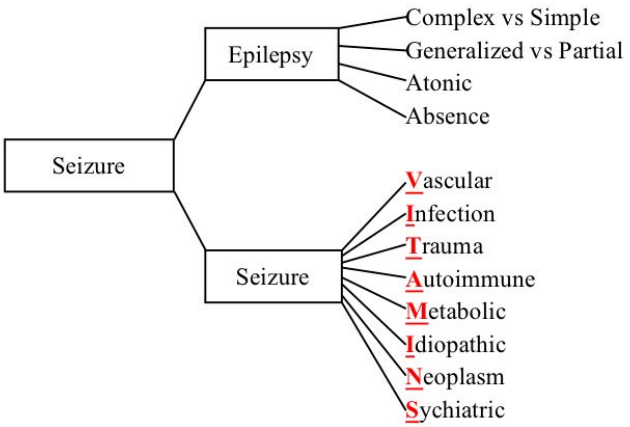
Epilepsy

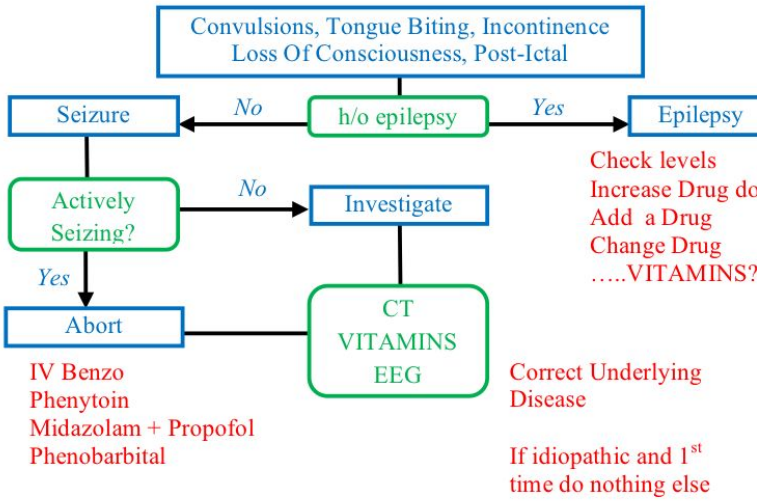
A patient with **epilepsy** (any history of seizure, repeat seizure in an idiopathic cause, etc) is treated a little different. If they are **actively seizing** treat them as above - **ABCs** and **Abort Seizure**. But an epileptic also requires chronic therapy to decrease the risk of another seizure. What to give is dependent on the type of seizure. **Valproate, lamotrigine**, and **levetiracetam** are broad spectrum and generally considered first line. As you dose patients it's important to reach **therapeutic levels** and **switch** if they **seize while therapeutic**. Diagnose the seizure and the location of origination with **EEG** by looking for **spike and waves** indicative of organized neuronal firing (abnormal for an awake adult). **24hr video monitoring + EEG** may be required to catch the seizure and its manifestations.

For the test, you'll need to be able to identify certain types of seizure and link them with their treatment. See to the right

Nonconvulsive Status

The altered person, intubated, but no seizure activity. Get an EEG.





VITAMINS

Vascular	Stroke, AVM, Hemorrhage	FND + Risk Factors
Infxn	Encephalitis, Meningitis	Seizure + Fever
Trauma	MVA, TBI	h/o Trauma
Autoimmune	Lupus, Vasculitis, Arthritis	Rash, Purpura, ANA
Metabolic	Na, Ca, Mg, O_2, Glucose	CMP, ABG, Mg, Phos
Idiopathic	"Everybody Gets One"	1st Time Seize
Neoplasm	Mets vs Primary	h/o Cancer, headache
Sychiatric	Faking it, Iatrogenic	Faking it / Hand Drop

Partial vs Generalized

Partial = Specific Complaint — **Carbamazepine Phenytoin**

Generalized = Total Brain Involvement — **Valproate or Lamotrigine**

Complex Vs Simple

Complex = ⊕ LOC

Simple = ⊖ LOC

Specific Types

Atonic = ⊕ Loss of Tone, ⊖ LOC — **Valproate**

Absence = ⊖ Loss of Tone, ⊕ LOC — **Ethosuximide**

Myoclonic = Jerky Muscle — **Valproate**

Trigeminal Neuralgia

Lecture Quiz

1:B / 2:A / 3:C

Q1: Which of the following is the drug of choice in case of absent seizure?

A. Lamotrigine
B. Ethosuximide
C. Phenytoin
D. Sodium Valproate

Q2: A 45 years old epileptic patient comes to the hospital with peeling skin and painful blisters all over his body, which one of these epileptic drugs did he take?

A. Lamotrigine
B. Sodium Valproate
C. Phenytoin
D. Topiramate

Q3: A 17 year old girl is brought to 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 15L of oxygen and they gave her two doses of rectal diazepam, but she has not stopped fitting. What is the most appropriate next step in management?

A. Lorazepam
B. Phenobarbital
C. Phenytoin loading