Drugs used in epilepsy

- Main text
- Male slide
- Female slide
- Important
- Dr, notes
- Extra info

EDITING FILE

Objectives

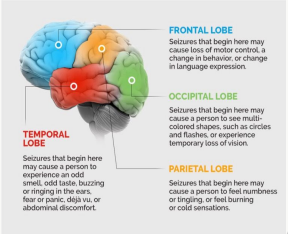
- Define & distinguish between seizure & epilepsy.
- Classify different types of epilepsy.
- Identify the possible mechanisms that antiepileptic drugs act through.
- Classify different types of antiepileptic agents.
- Discuss the effect of antiepileptic drugs in pregnancy.
- Recognize the non-pharmacological interventions that can be used to treat epilepsy.

Dr.Foda videos (highly recommended)

Epilepsy

Definition

- A chronic medical condition characterized by **2 or more unprovoked seizures** occurring **> 24 h** apart (within 6-12 months).
- It is a **syndrome**, not a disease.
- A person will experience different symptoms depending on where a seizure starts in their brain.



Epilepsy vs Seizures

Epilepsy: a group of related disorders characterized by a tendency for recurrent seizures.

Seizures: abnormal movements or behavior due to unusual electrical activity in the brain. Are a symptom of epilepsy, but not all people with seizures have epilepsy.

Syndrome vs Disease

Syndrome: a set of medical signs & symptoms that occur together and suggest the presence of a certain disease or an increased chance of developing a disease.

Disease: the actual diagnosed impairment of health or a condition of abnormal functioning.
(Distinguished cause, symptoms & treatment)

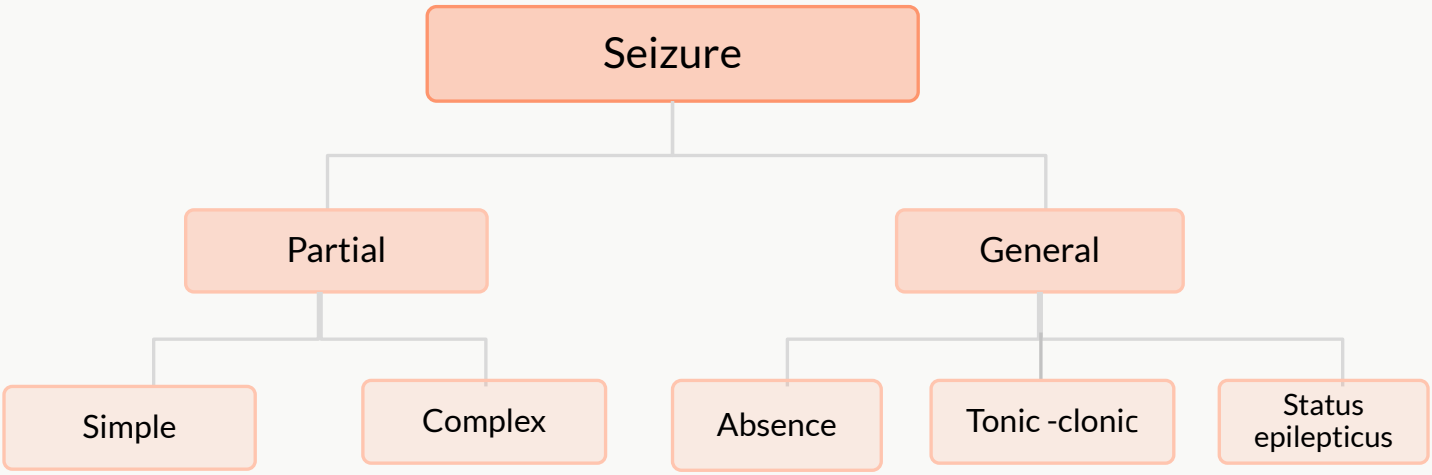
Etiology of seizures

- **Drug withdrawal** (e.g. CNS depressants)
- Alcohol or drug abuse
- Drug overdose (e.g. Penicillin)
- **Poison (e.g. lead)**
- Fever in children (febrile convulsion)
- Hypoglycemia decreases the threshold of epilepsy
- Phenylketonuria (PKU):
  Accumulation of Phenylalanine causes direct damage to the brain
  ↑ Phenylalanine —(Phenylalanine hydroxylase)—✕→ Tyrosine
- Photo epilepsy due to flashing lights of video games [439]
- Congenital defects
- Head injuries, trauma & hypoxia
- Concussion, depressed skull & fractures
- Bacterial or viral infection (e.g. meningitis, brain abscess, viral encephalitis) fever increases the sensitivity of the brain for neurotransmitters
- Brain tumors (including tuberculoma)
- Vascular occlusion & stroke

Triggers

Fatigue | Sleep Deprivation | Stress | Poor nutrition | Alcohol

Old Classification of Seizures



1. Partial (focal) seizure

Arise in one cerebral hemisphere.

A. Simple:
consciousness is retained.

B. Complex (psychomotor):
Altered consciousness

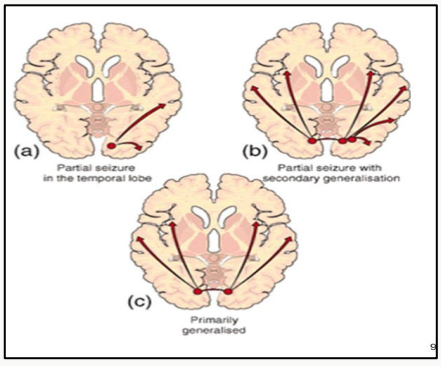
2. Secondarily generalized

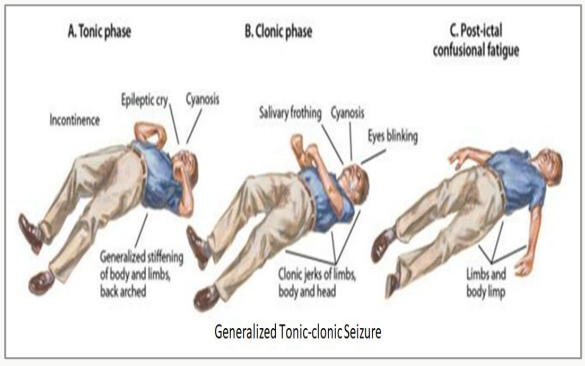
Begins as partial (simple or complex) and progress into tonic- clonic (grand mal) seizure.

3. Primary Generalized

Both hemispheres + loss of consciousness.

- **Tonic-clonic (Grand mal):** stiffness (15-30 s) followed by violent contractions & relaxation (1-2 m).
- **Tonic:** muscle stiffness.
- **Clonic:** spasms of contraction & relaxation.
- **Atonic (loss of tone/relaxation):** patient's legs give under him & drop down.
- **Myoclonic:** jerking movement of body.
- **Absence (Petit mal):** brief loss of consciousness with minor muscle twitches & eye blinking (no fall down).
- **Status epilepticus**: re-occurring (most dangerous; if not treated → death).



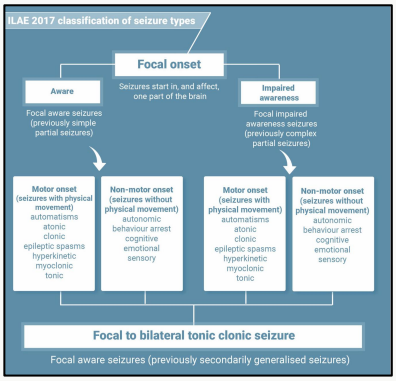


New Classification of Seizures

Seizures are now divided into groups depending on:

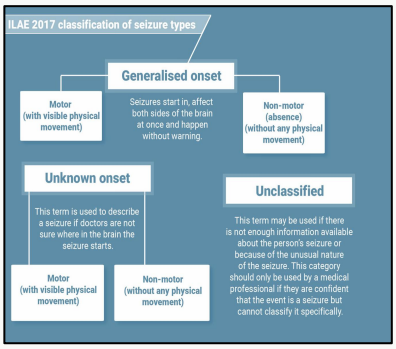
01

Where they start in the brain (onset): first seizure
-Focal onset
-Generalized onset
-Unknown onset when the family didn't notice the exact symptoms associated with the seizure



02

Whether or not a person's awareness is affected



03

Whether or not seizures involve other symptoms, such as movement

Focal motor onset Seizure

Focal to bilateral tonic-clonic seizure	Secondarily generalized
Focal tonic seizure	Muscle stiffness
Focal clonic seizure	Sustained rhythmic jerking
Focal atonic seizure	Sudden loss or diminution of muscle tone without apparent preceding myoclonic or tonic activity
Focal myoclonic seizure	Single or short cluster of brief muscle connections (Jerks)
Focal epileptic spasms	Sudden flexion, extension or mixed flexion-extension of proximal and truncal muscles
Focal automatism seizure	Coordinated, repetitive motor activity, often resembling a voluntary movement
Absence with eyelid myoclonia	Absence seizures accompanied by brief, repetitive, often rhythmic, myoclonic jerks of the eyelids

Pathophysiology of Epilepsy

Normal CNS function

Inhibition
-GABA

Excitation
-Glutamate
-Aspartate

Abnormal excitation

Inhibition
-GABA

Excitation
-Glutamate
-Aspartate

Other causes for imbalance → channelopathies (defects in ion channels)

Membrane depolarization leads to enhanced excitatory receptor function & reduced GABA receptor function. This pattern of 'voltage-dependence' leads to an even greater level of excitation (i.e. epilepsy results from ↑ **Glutamate** & ↓ **GABA**).

Mechanisms of Anti-Epileptic Drugs

three Main Mechanisms

1-Enhance **GABA** action GABA-A Receptors
→ ↑ permeability to Cl^-
→ ↓ neuronal excitability

Barbiturates - Benzodiazepines
Tiagabine - Topiramate
Vigabatrin - Valproate - Gabapentin

2-Inhibit **Na+ channel function**

Carbamazepine - Phenytoin - Lamotrigine - Oxcarbazepine - Topiramate - Valproate

3- Inhibit **Ca+2 T-channel function**

Valproate - Ethosuximide

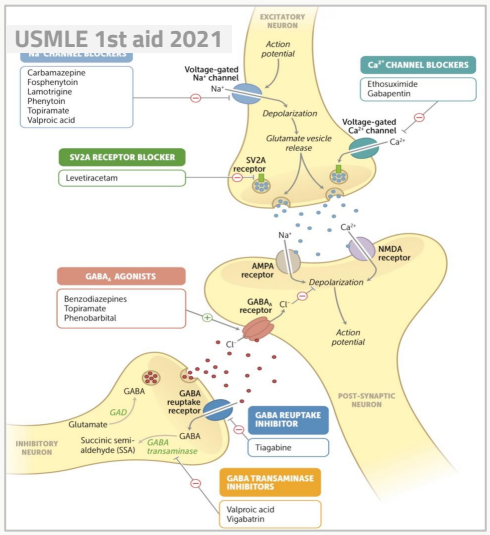
Other mechanisms

Inhibit **glutamate** release

Lamotrigine

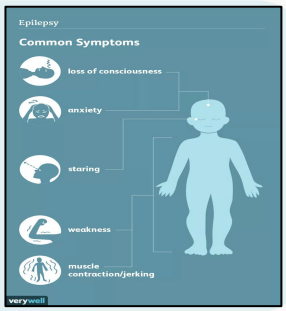
Block **glutamate** receptors

↑ Outward +ve current (**K+ channel**)



Symptoms

- Range from a brief lapse of attention to convulsion (several minutes)
- Depends on the function of the region of the brain that affected



Barbiturates

CNS depressants

Drugs	Phenobarbital	Mephobarbital	Pentobarbital
M.O.A	Enhance the GABA-A receptor activity by increasing **the <u>duration</u>** of GABA-A receptor opening time		
Important P.K.	• Metabolised by CYP2C9 • Induce **CYP2C** and **CYP3A** subfamilies by any drug induce or inhibit CYP2C9 يتأثر CYP2c and CYP3A يأثر على		
Uses	• Generalized tonic-clonic seizures • focal seizures		
ADRs	• Sedation • Nystagmus and ataxia at excessive dosage • Tolerance and addiction		

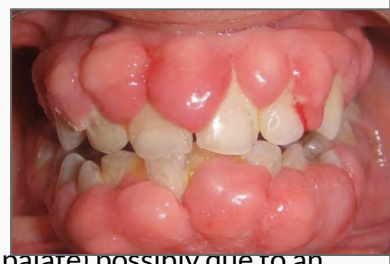
Benzodiazepines

CNS depressants

Drugs	Midazolam	Diazepam	Lorazepam	Clobazam	Clorazepate	Clonazepam
M.O.A	Enhance the GABA-A receptor activity by increasing the **<u>frequency</u>** of opening GABA-A receptors					
Important Uses	• **Clonazepam** use for absence seizures and myoclonic seizures in children • **Focal seizures** and **status epilepticus**					
ADRs	• Drowsiness and lethargy • Hypotonia and dizziness • Seizures if the drug is discontinued abruptly • Tolerance and addiction					

Important

When we talk in general Almost all CNS drugs are CNS depressant . but in case of antiepileptic drugs, we talk about different situation so there are two drugs which Classified as **CNS depressant: Benzodiazepine & Barbiturates**

Drugs	Phenytoin	Fosphenytoin
M.O.A	• Block **Na+** & **Ca2+** influx into neuronal axon • Inhibit the release of excitatory transmitters (glutamate & aspartate) • Potentiate **GABA**'s action	
P.K.	• Given orally + well-absorbed from GIT [t1/2 ≈ 20h] • **Enzyme inducer;** ↑ metabolic activity of enzymes → drug-drug interactions →↓bioavailability • t1/2 ≈ 20 h **Never given IM!** because it can cause tissue damage & necrosis so we use Fosphenytoin in emergency cases	• **A prodrug** means need to be activated through metabolism → parenteral form of Phenytoin (IV & IM). • Rapidly converted to Phenytoin in the body.
Uses	• Partial & generalized tonic-clonic seizures • Status epilepticus (IV) **(Fosphenytoin)**	
C.I	**Absence seizures**	
ADRs	• **Neurological:** headache, vertigo, ataxia, diplopia, nystagmus & sedation • **Gum (gingival) hyperplasia** • Vitamin D deficiency → osteomalacia •Acne & **Hirsutism** (Hirsutism: excessive male pattern hair growth) • Folic acid deficiency → megaloblastic anemia • **Fetal Hydantoin Syndrome (FHS):** growth retardation, **microencephaly** & **craniofacial** abnormalities (e.g. cleft palate) possibly due to an **epoxide metabolite** of Phenytoin. Imp:the metabolite itself cause malformation so when the phenytoin not metabolized for any reason will not cause this malformation	

Drugs	Carbamazepine (CBZ)	Oxcarbazepine
M.O.A	• Block **Na+** & **Ca2+** influx into neuronal axon • Inhibit the release of excitatory transmitters (glutamate & aspartate) • Potentiate **GABA**'s action	
P.K.	• **Strong enzyme inducer** including its own metabolism (may cause drug-drug interaction with others enzyme inducer drugs) • Available only orally , well-absorbed • Metabolized by the liver to active & inactive metabolites • t1/2 = 18-35 h	• A prodrug similar to Carbamazepine • Short t1/2 of 1-2 h • Coated tablet w/layers → extended release
Uses	• **Drug of choice in complex partial seizures** • Tonic-clonic seizures (1ry & 2ry generalized)	
C.I.	**Absence seizures**	
ADRs	• GIT upset • Drowsiness, ataxia, headache & diplopia • **Water intoxication & hyponatremia** (water retention due to ↑ ADH) • **Idiosyncratic** (drug reactions that occur rarely and unpredictably) blood dyscrasias & severe rash • Teratogenicity	• Fewer adverse effects than CBZ, phenytoin

Broad-spectrum Antiepileptics

(they have more than one mechanism and act on different types of epilepsy so they are more effective)

1- Sodium Valproate (VPA: valproic acid)

M.O.A.

- Blocks activated **Na^+** channels
- ↑ **GABA** synthesis & ↓ degradation
- Suppress **glutamate** action
- Blocks T-type **Ca^{2+}** channels

P.K.

- **Enzyme inhibitor** (drug-drug interactions → ↑ toxicity)
- Available as capsules, syrup & I.V.

Uses

Important

- **Effective for all forms of epilepsy**
  - 1ry or 2ry generalized tonic-clonic seizures
  - Absence seizures
  - Complex partial seizures
  - Myoclonic seizures
  - Atonic seizures
  - Photosensitive epilepsy
  - Status epilepticus **(but not as the 1st choice)**
- **Other uses:**
  - **Bipolar disorder & mania**
  - Migraine prophylaxis
  - Lennox-Gastaut syndrome: a childhood epileptic encephalopathy which is usually caused by early brain injury or congenital malformations. Patients with LGS can have different kinds of seizures.

ADRs

Mnemonic for ADRs [439]: "VALPROATE"
Vomiting - Appetite - ↑ Liver toxicity - Pancytopenia - Regrowth of curly hair
Oedema - Aspirin contraindication - Teratogenicity - Enzyme inhibitor

- **Weight gain** (↑ appetite)
- **Transient hair loss with re-growth of curly hair**
- Thrombocytopenia
  (↓ platelets → ↑ bleeding risk)
- Hepatotoxicity (Rx caution in pts taking Paracetamol or other hepatotoxic drugs)
- Bone loss
- Teratogenicity:

2- Lamotrigine

Male's Dr: May cause cardiac problems

M.O.A.

- Blocks **Na^+** channels
- Inhibits excitatory amino acid release (**glutamate** & **aspartate**)
- **★Does not induce or inhibit CYP-450 isozymes**

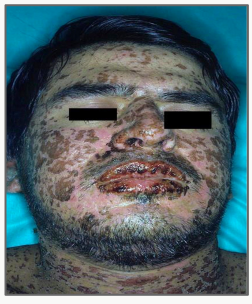
(Extra)
Cardiac Rhythm and Conduction Abnormalities ? (FDA – EMA – ILAE)
In vitro testing showed that lamotrigine exhibits Class IB antiarrhythmic activity at therapeutically relevant concentrations 2

Uses

- As add-on therapy or as monotherapy in partial seizures
- Lennox-Gastaut syndrome

ADRs

- Influenza-like symptoms
- Skin rash → may progress to Steven–Johnson Syndrome
  (rare but serious disorder that affects the skin, mucous membrane, genitals & eyes)
- Somnolence (drowsiness)
- Blurred vision
- **Diplopia**
- Ataxia



3- Topiramate

M.O.A.	• Blocks **Na^+** channels → membrane stabilization • Potentiates **GABA**'s inhibitory effect
Uses	• Can be used alone for **partial, generalized tonic-clonic, & absence seizures** • **Lennox-Gastaut syndrome** (or Lamotrigine, or Valproate) • Adjunct therapy
ADRs	• Psychological or cognitive dysfunction (nervousness) • **Weight loss** (can be a desirable effect) • Sedation, dizziness & fatigue • ★**Urolithiasis** (renal stones) • ★**Paresthesias** (abnormal sensation) It's specific ADR for topiramate • Teratogenicity **(in animal but not in human)**

4- Zonisamide

Sulfonamide derivative

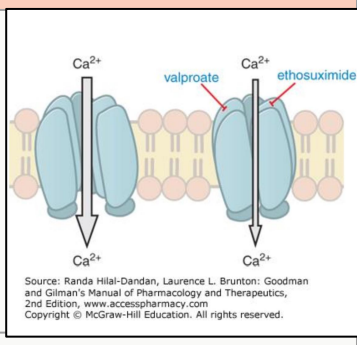
M.O.A.	• **Na^+** channel inhibitor • Inhibits T-type **Ca^{2+}** currents • Binds to **GABA** receptors • Facilitates **dopaminergic** & **serotonergic** neurotransmission they have modulatory activity in GABA and Glutamate NTs so indirectly control them
Uses	Approved for adjunct treatment of partial seizures in adults.
ADRs	• Weight loss • **Abnormal thinking** • Nervousness, agitation & irritability

5- Felbamate

Broad spectrum of anticonvulsant action

M.O.A.	• Blocks voltage-dependent **Na^+** channels (weak). • Competes with the glycine-coagonist binding site on the **NMDA** receptor. • Blocks **Ca^{2+}** channels. • Potentiates **GABA** actions.
Uses	**Refractory epilepsies** that are unresponsive to other drugs. (particularly Lennox-Gastaut syndrome) **-Important : Temporal lobe is the most common type of epilepsy and 30% of them are refractory**
ADRs	• **Aplastic anemia** that's why we don't commonly use it • Hepatic failure

Calcium Channel Blockers

Drugs	Ethosuximide (ETSM)	Gabapentin (Neurontin) Pregabalin (Lyrica)
Overview	• Antiseizure drugs, induced reduction of current through T-type Ca^{2+} channels • Inhibit low-threshold (T-type) Ca^{2+} currents, especially in thalamic neurons that **act as pacemakers to generate rhythmic cortical discharge**	
M.O.A.	**Inhibit T-type Ca^{2+} channels in thalamo-cortical neurons**	Initially designed as an analogue of GABA, then found out to bind to P/Q type Ca channels instead of GABA receptors
P.K.	• Absorption is complete • Syrup & capsule forms • Not bound to plasma proteins or tissues • Metabolized in liver (Incomplete) • t½ = 52-56 h • 10-20% of a dose is excreted unchanged in urine *from 441 slides	**Pregabalin:** • A pro-drug of Gabapentin • More potent than gabapentin
Uses	★**Absence seizures**	• **Gabapentin: adjunct** therapy in adults and children with partial & secondarily generalized seizures . • as **monotherapy**. • **Neuropathic pain,Fibromyalgia:** a syndrome characterized by chronic pain in muscles of soft tissues surrounding joints, fatigue, & tenderness at specific sites in the body
ADRs	• Gastric distress • ★**hiccups** • Drowsiness, fatigue & headaches	• Weight gain with **ankle edema** • Irritability • Behavioral problems in children • Movement disorders

Other Mechanisms

	Levetiracetam	Brivaracetam Newly approved in KSA
M.O.A.	**Act on synaptic vesicle protein 2A (SV2A) → slow synaptic** vesicle mobilization → slow NT release but synthesis + storage are normal **Brivaracetam:** same mechanism as Levetiracetam but **more potent**	
Uses	• Adjunct therapy for adults with partial seizures. • Some patients have success with monotherapy.	Adjunctive therapy for **partial seizures with or without secondary generalization** in patients aged 4 years or older.
C.I	**Renal dysfunction** as 66% of the drug is excreted by the kidney	Hypersensitivity to brivaracetam
ADRs	• Asthenia (physical weakness) • Infection • Behavioral problems in children	• Somnolence & dizziness • Infection (influenza) • Convulsion • **Suicidal ideation & psychotic disorder**

Cannabidiol "CBD" (Epidiolex)

It is the first FDA-approved (June 25,2018) drug that contains a purified drug substance derived from *marijuana*.
Not yet approved in KSA

M.O.A.	Activation of **CB1** receptors → **inhibition of glutamate release**
Uses	• The first FDA approval of a drug for the treatment of Dravet syndrome • Lennox-Gastaut syndrome
ADRs	• Somnolence • ↑ Hepatic enzymes **CBD does NOT cause intoxication or euphoria that comes from tetrahydrocannabinol (THC).** It is THC (and not Cannabidiol) that is the primary psychoactive component of marijuana.

Other Mechanisms

Fenfluramine (Fintepla)

Overview	• First approved by FDA in June 25, 2020. • In is an amphetamine derivative.
M.O.A	• Stimulate 5-HT1D and 5-HT2C → Inc GABA release • Antagonize σ1 R → modulate NMDA responses
Uses	Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) in patients 2 years of age and older.
ADRs	Decreased appetite, diarrhoea, pyrexia, fatigue, upper respiratory tract infection, lethargy, somnolence, and bronchitis
C.I	• Aortic or mitral valvular heart disease. • Pulmonary arterial hypertension • Within 14 days of the administration of MAOIs due to an **increased risk of serotonin syndrome.**

Status Epilepticus

- **Most seizures last from few seconds to few minutes.**
- **Seizures that follow one another without recovery of consciousness**
- **Has a high mortality rate.**
- **Death is from cardiorespiratory failure.**

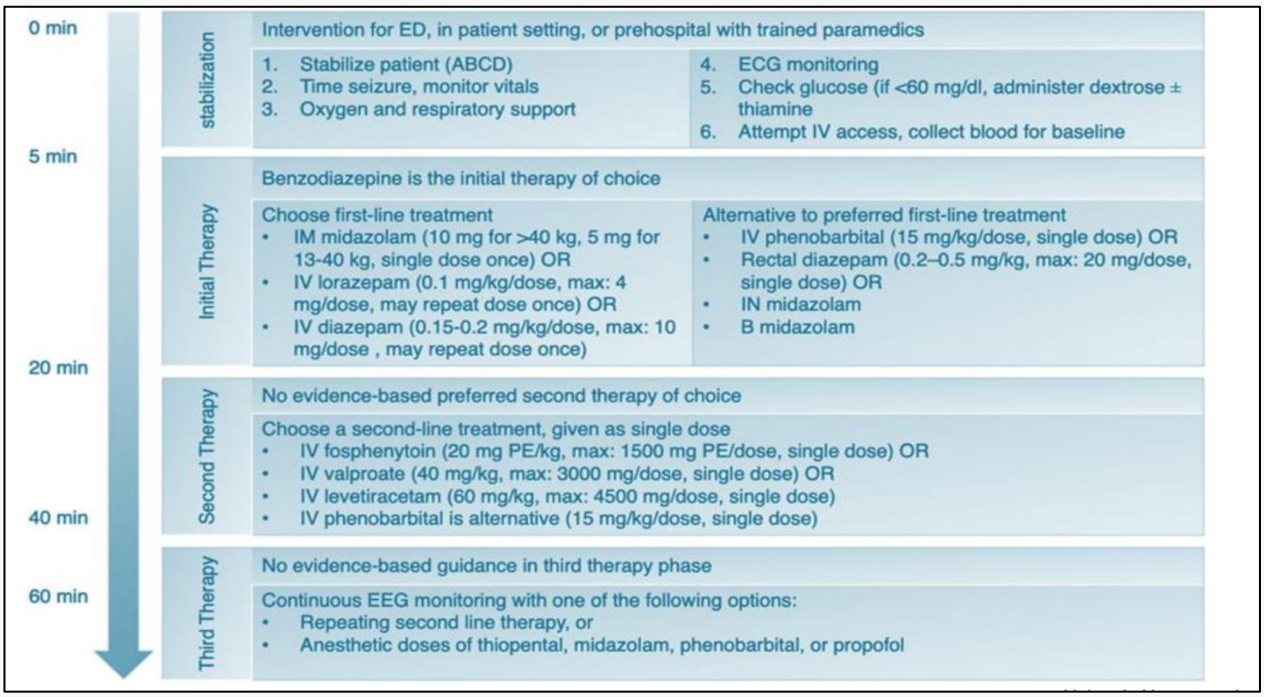
Management Of Status Epilepticus

Lorazepam (Rapid Acting) → **Diazepam** → **Phenobarbital** → **Midazolam** → **Fosphenytoin**

All given IV

Cont..

Just Read It



Pregnancy & Anti-Epileptic Drugs

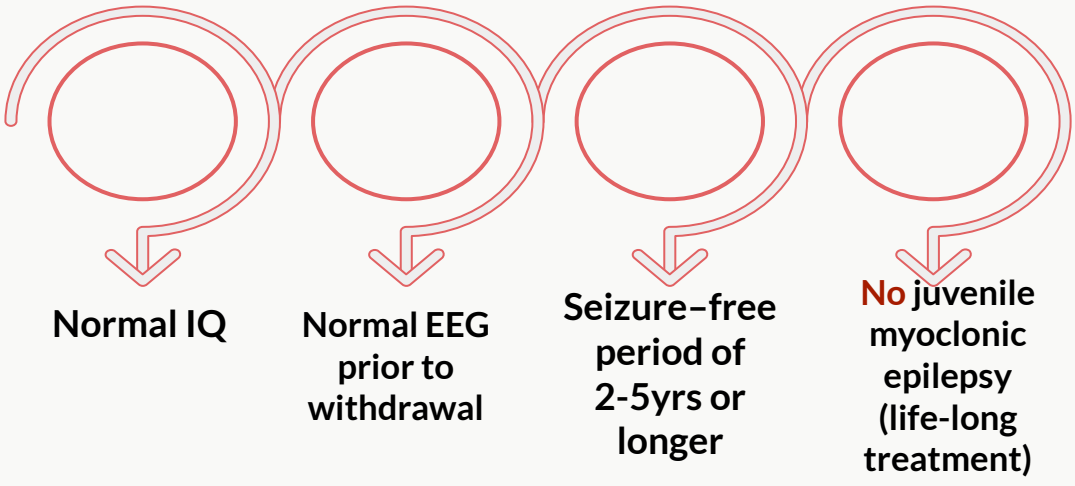
- Seizure is very harmful for pregnant woman.
- **Patient has to continue therapy.**
- **NO** antiepileptic drug is **safe** in pregnancy. The safest (Category C) are: **Lamotrigine** (best) & **Levetiracetam**. None belong to pregnancy categories A or B.
- **Monotherapy is usually better than drug combination.**
- Valproate & Phenytoin are **contraindicated** during pregnancy.

For your information:

According to ILAE:

- **Valproate** → associated with the *greatest* risks for malformations.
- **Lamotrigine** & **levetiracetam** → associated with the *lowest* risks for malformations.
- Woman planning to be pregnant should receive antiepileptic drugs with the *lowest* risk of malformation in addition to **folic acid**.

- **When** is withdrawal considered:



Relapse rate when antiepileptics are withdrawn is 20-40%.

- **How** is withdrawal considered:

01 — The treatment must be withdrawn gradually **over 2-3 months**

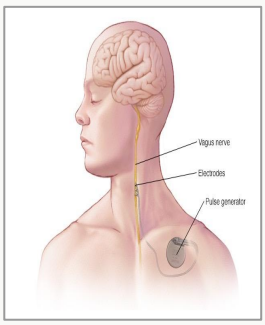
02 — The **benzodiazepines and barbiturates** must be withdrawn gradually **over 6 months or more.**

03 — The antiepileptics must be removed one by one

An agreement must be made that in the event of a seizure relapse, the patient must return to **taking the last dose before the dose in which the relapse was presented** and request assessment by clinical neurologist.

Non-pharmacological Treatment of Epilepsy

- **Vagal nerve stimulation**
  - An alternative for patients who have been refractory to multiple drugs or who are sensitive to the many ADRs of anti-epileptic drugs.
  - An expensive procedure.
- **Surgery** in refractory cases only
- **Ketogenic diet:**
  - A high-fat, adequate-protein, low-carbohydrate diet that in medicine is used primarily to treat refractory epilepsy in children.
  - When fat is the primary source of calories, ketones are formed.
  - **For your information**
  - Possible mechanisms of action of ketogenic diet:
    - Increase GABA -Decrease glutamate -Increase neuropeptide Y

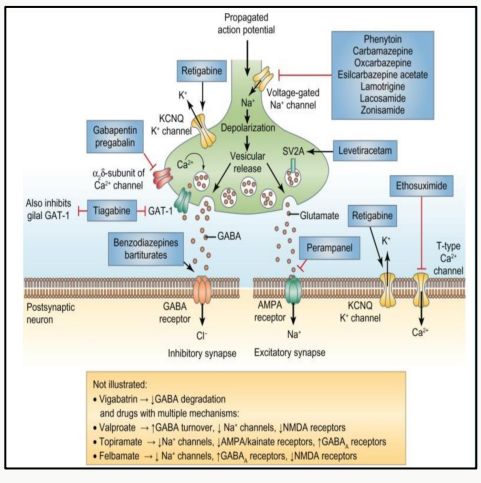


Summaries (From the slides)

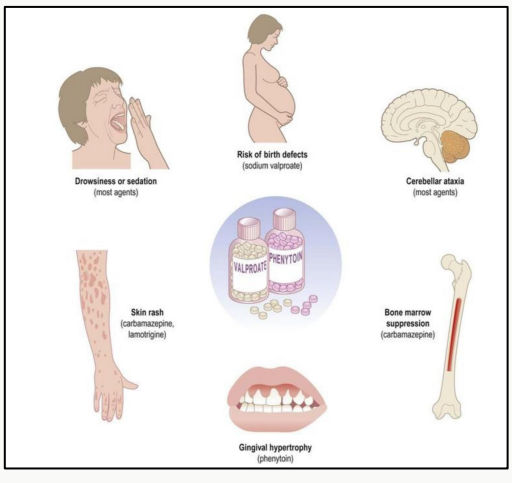
1.Enhancing GABA synaptic transmission	• Barbiturates, benzodiazepines, gabapentin, tiagabine, vigabatrin, topiramate, valproate. • Increased permeability to chloride ion, which reduces neuronal excitability. • Valproate, vigabatrin, and topiramate block GABA transaminase and tiagabine blocks reuptake of GABA
2.Inhibiting excitatory neurotransmitter glutamate	• Lamotrigine
3.Reducing cell membrane permeability to voltage-gated Na channels	• Carbamazepine, lamotrigine, oxcarbazepine, phenytoin, topiramate, valproate
4.Reducing cell membrane permeability to Ca T-channels	• Valproate, ethosuximide; the result is diminishing of the generation of action potential.

- Epilepsy is characterized by ≥ 2 unprovoked seizure [>24 h apart] (within 6-12 m).
- The symptoms of epilepsy depend on the affected area in the brain.
- Different molecular targets are used to manage epilepsy.
- Antiepileptic drugs need to be withdrawn gradually
- Antiepileptic drugs are not safe in pregnancy.
- some can cause teratogenicity.
- Different non-pharmacological interventions can be used in refractory epilepsy.

Mechanism of Action of Antiepileptic Drugs:



Side effects of antiepileptic drugs:



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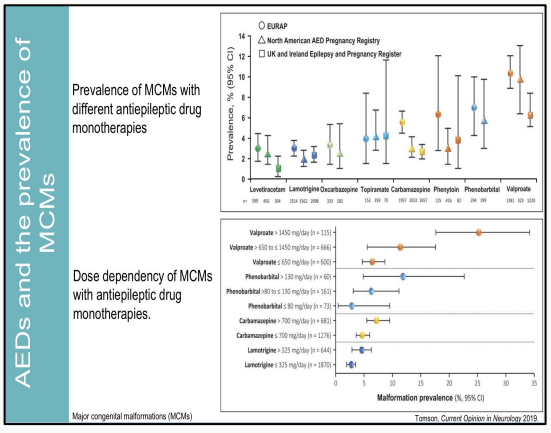

Summary

Drug	MOA	Uses	ADRs
Barbiturates	Enhance the GABA-A receptor activity by increasing **the duration** of GABA-A receptor opening time	• Generalized tonic-clonic seizures • focal seizures	• Sedation • Nystagmus and ataxia at excessive dosage • Tolerance and addiction
Benzodiazepines	Enhance the GABA-A receptor activity by increasing the **frequency** of opening GABA-A receptors	• **Clonazepam** use for absence seizures and myoclonic seizures in children • **Focal seizures** and **status epilepticus**	• Drowsiness and lethargy • Hypotonia and dizziness • Seizures if the drug is discontinued abruptly • Tolerance and addiction
Phenytoin	• Block **Na+** & **Ca2+** influx into neuronal axon • Inhibit the release of excitatory transmitters • Potentiate **GABA**'s action	• Partial & generalized tonic-clonic seizures • Status epilepticus (IV) Fosphenytoin	• **Neurological:** headache, vertigo, ataxia, diplopia, nystagmus & sedation • **Gum (gingival) hyperplasia** • Vitamin D deficiency → osteomalacia •Acne & Hirsutism • Folic acid deficiency → megaloblastic anemia • **Fetal Hydantoin Syndrome (FHS):** growth retardation, **microencephaly** & **craniofacial** abnormalities (e.g. cleft palate) possibly due to an **epoxide** metabolite of Phenytoin.
Fosphenytoin			
Carbamazepine		• **Drug of choice in complex partial seizures** • Tonic-clonic seizures (1ry & 2ry generalized)	• GIT upset • Drowsiness, ataxia, headache & diplopia • **Water intoxication & hyponatremia** • **Idiosyncratic** blood dyscrasias & severe rash • Teratogenicity
Oxcarbazepine			• Fewer adverse effects than CBZ, phenytoin

Sodium Valporate	• Blocks activated **Na^+** channels
	• ↑ **GABA** synthesis & ↓ degradation
	• Suppress **glutamate** action
	• Blocks T-type **Ca^{2+}** channels
		• Effective for **all forms** of epilepsy
		  ○ 1^{ry} or 2^{ry} generalized tonic-clonic
		  ○ Absence
		  ○ Complex partial
		  ○ Myoclonic
		  ○ Atonic
		  ○ Photosensitive epilepsy
		  ○ Status epilepticus **(but not as the 1^{st} choice)**
			• **Weight gain** (↑ appetite)
			• **Transient hair loss with re-growth of curly hair**
			• Thrombocytopenia
			• Hepatotoxicity
			• Bone loss :
			• Teratogenicity

Summary

Drug	MOA	Uses	ADRs
Lamotrigine	• Blocks **Na^+** channels • Inhibits excitatory amino acid release (**glutamate** & **aspartate**) • **Does not induce or inhibit CTP-450 isozymes**	• As add-on therapy or as monotherapy in partial seizures • Lennox-Gastaut syndrome	• Influenza-like symptoms • Skin rash → may progress to **Steven–Johnson Syndrome** • Somnolence • Blurred vision • **Diplopia** • Ataxia
Topiramate	• Blocks **Na^+** channels → membrane stabilization • Potentiates **GABA**'s inhibitory effect	• Can be used alone for **partial, generalized tonic-clonic, & absence seizures** • **Lennox-Gastaut syndrome** • Adjunct therapy	• Psychological or cognitive dysfunction (nervousness) • **Weight loss** • Sedation, dizziness & fatigue • Urolithiasis • **Paresthesias**(abnormal sensation) • Teratogenicity (in animal but not in human)
Zonisamide	• **Na^+** channel inhibitor • Inhibits T-type **Ca^{2+}** currents • Binds to **GABA** receptors • Facilitates **dopaminergic** & **serotonergic** neurotransmission	adjunct treatment of partial seizures in adults.	• Weight loss • **Abnormal thinking** • Nervousness,agitation & irritability
Felbamate	• Blocks voltage-dependent **Na^+** channels (weak). • Competes with the glycine-coagonist binding site on the **NMDA** receptor. • Blocks **Ca^{2+}** channels. • Potentiates **GABA** actions.	Refractory epilepsies (particularly Lennox-Gastaut syndrome)	• **Aplastic anemia** • Hepatic failure

Summary

Drug	MOA	Uses	ADRs
Ethosuximide (ETSM)	**Inhibit T-type Ca^{2+} channels in thalamo-cortical neurons**	**Absence seizures**	• Gastric distress & hiccups • Drowsiness, fatigue & headaches
Gabapentin Pregabalin	Initially designed as an analogue of GABA, then found out to bind to P/Q type Ca channels instead of GABA receptors	• as **monotherapy**. • Neuropathic pain • Fibromyalgia	• Weight gain with **ankle edema** • Irritability • Behavioral problems in children • Movement disorders
Levetiracetam	Act on synaptic vesicle protein 2A (SV2A) → slow synaptic vesicle mobilization	• Adjunct therapy for adults with partial seizures. • Some patients have success with monotherapy.	• Asthenia (physical weakness) • Infection • Behavioral problems in children
Brivaracetam	same mechanism as Levetiracetam but **more potent**	Adjunctive therapy for **partial seizures with or without secondary generalization** in patients aged 4 years or older.	• Somnolence and dizziness. • Infection (influenza) • Convulsion • ★Suicidal ideation & psychotic disorder
Cannabidiol "CBD" (Epidiolex)	Activation of CB1 receptors → inhibition of glutamate release	• Dravet syndrome • Lennox-Gastaut syndrome	• Somnolence • ↑ Hepatic enzymes
Fenfluramine (Fintepla)	• Stimulate 5-HT1D and –HT2C → Inc GABA release •Antagonize σ1 R → modulate NMDA responses	Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) in patients 2 years of age and older.	Decreased appetite, diarrhoea, pyrexia, fatigue, upper respiratory tract infection, lethargy, somnolence, and bronchitis

MCQ

1.what do we use to treat an epileptic with bipolar disorder?			
A.Ethosuximide	B.fluoxetine	C.Valproate	D.Phenytoin
2.Adverse effect of Phenytoin?			
A.hypersensitivity	B.hair loss	C.gum hyperplasia	D.weight gain
3.What is the safest antiepileptic drug for pregnant woman?			
A. Valproate	B.phenytoin	C.Lamotrigine	D.Felbamate
4.increasing the activity of the neurotransmitter GABA in the brain is a therapeutic trigger for which of the following disease?			
A.Depression	B.Alzheimer	C.Epilepsy	D.Parkinson
5.which of the following drugs is considered the first choice for the management of absence seizures?			
A.Phenytoin	B.Ethosuximide	C.Valproate	D.Diazepam
6.patient who has seizures that follow one another without recovery of consciousness, what the best treatment?			
A.Ethosuximide	B.Carbamazepine	C.Valproate	D.Lorazepam
7.which one of the following is the likely mechanism of action of Lamotrigine?			
A.blockade of Cl channel	B.blockade of k+ channel	C.reduce the level of GABA content	D.reduce the release of glutamate

1: C ,2: C ,3: C ,4: C ,5: B ,6:D ,7:D

SAQ

01

9 years old boy was playing and suddenly he stopped and started staring and blinking and then he got back to normal.
A) What is the type of seizure that he had?
B) Which drug would be most appropriate for this patient?

a)Absence seizure, b)Ethosuximide

02

Which of the Antiepileptic drugs considered as CNS depressant

Barbiturates - Benzodiazepines

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Special thanks to norah almania for the amazing logo