



# Drugs Used in Epilepsy-I

1<sup>st</sup> Lecture

By

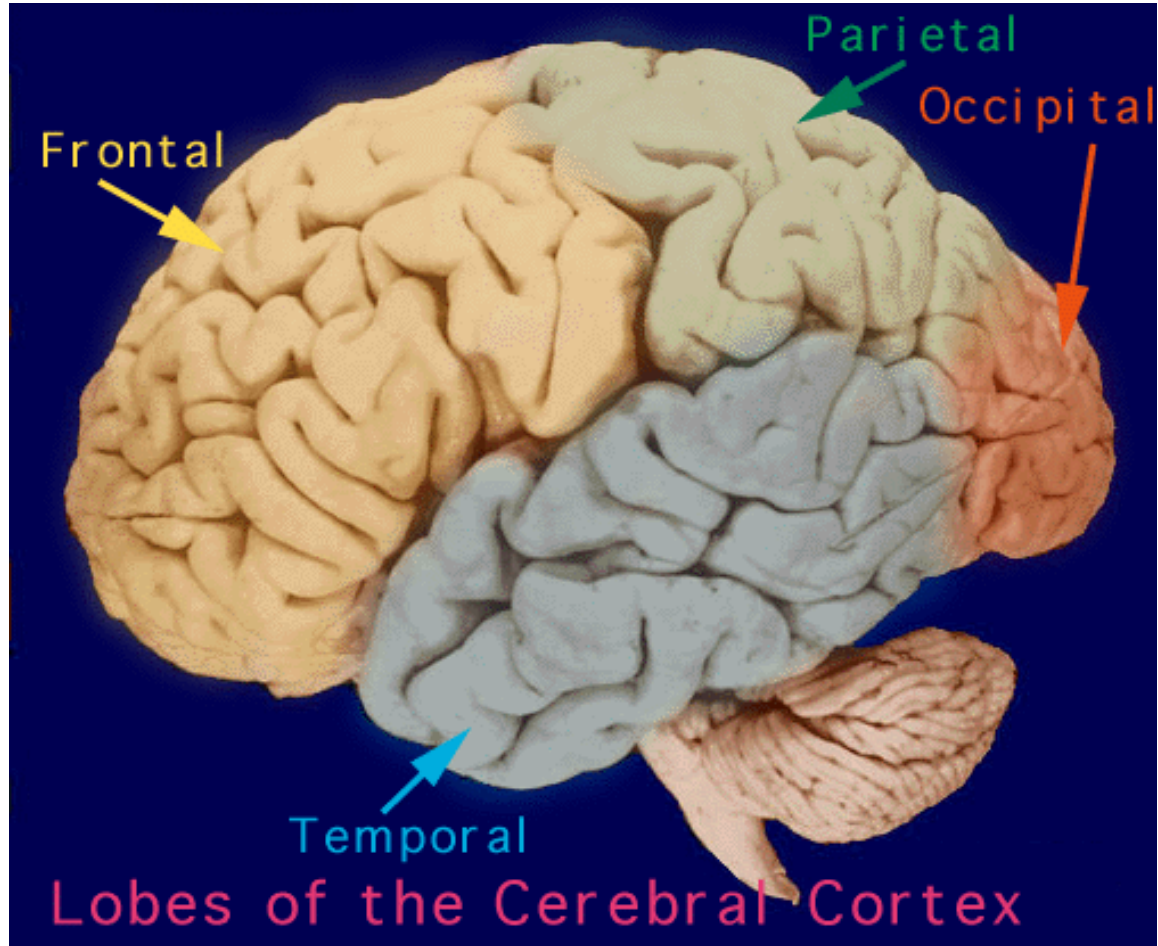
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Slides adopted from Dr. Yeldez Bassiouni

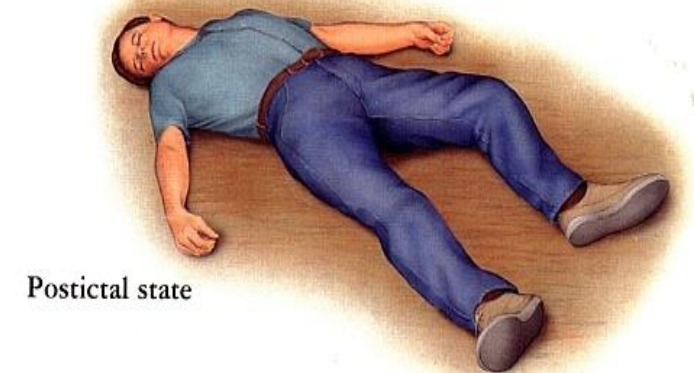
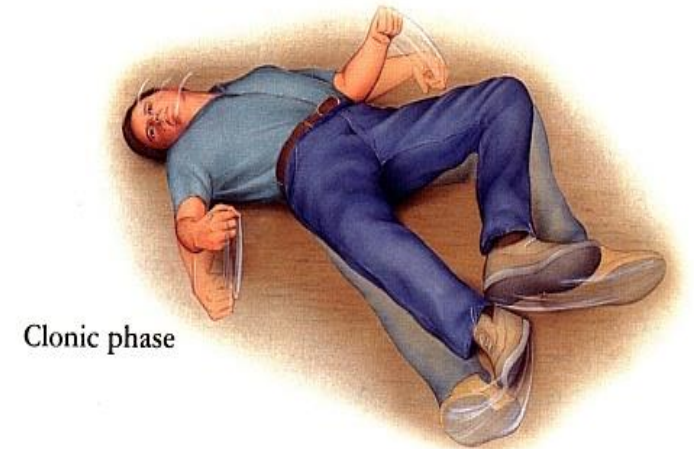


# Objectives

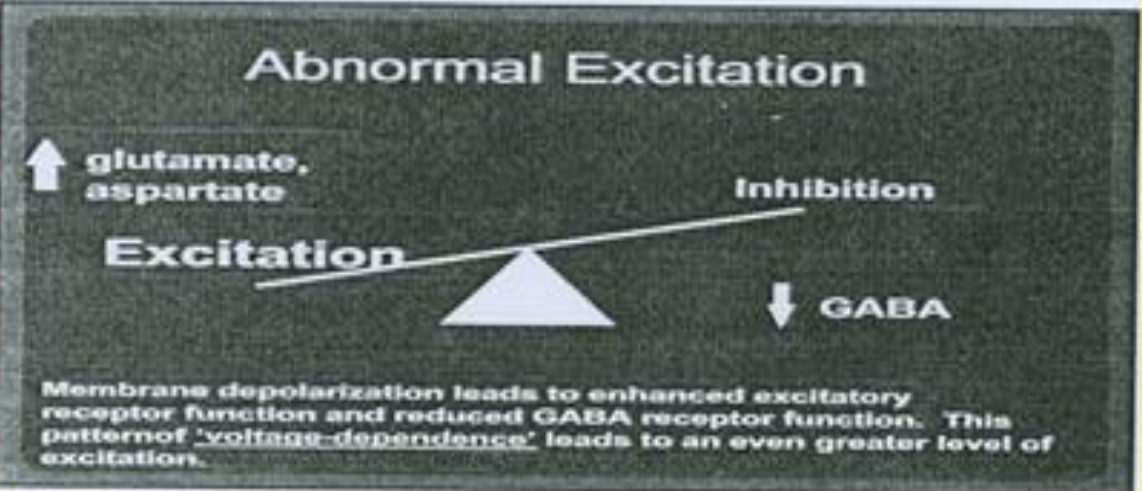
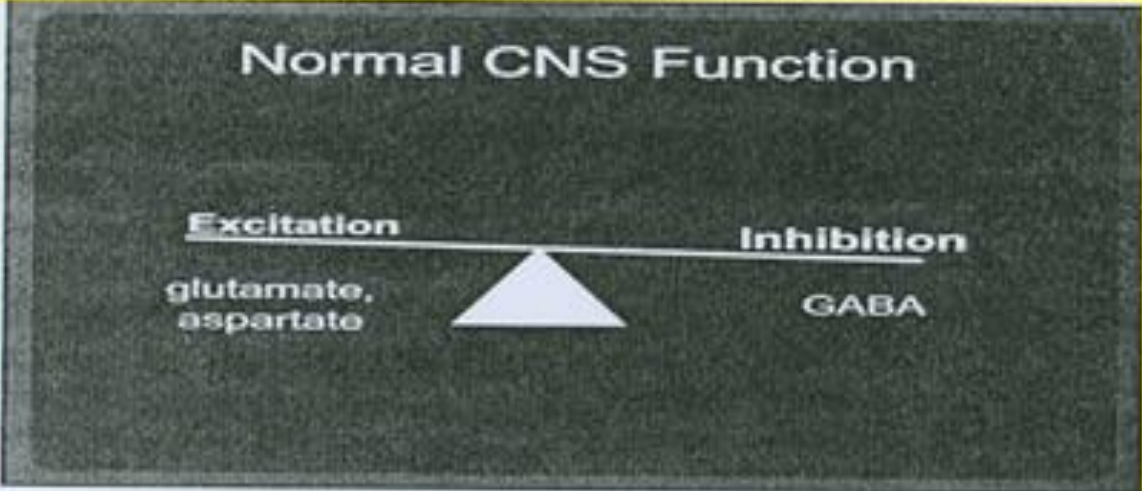
- **At the end of the lectures, students should**
  1. Describe types of epilepsy
  2. List the antiepileptic drugs
  3. Expand on pharmacokinetic and dynamic patterns of first and second generation antiepileptic drugs
  4. Specify their mechanism of action
  5. Therapeutic indications and adverse effects
  - 6- Describe treatment of status epilepticus

# Definition

- *Epilepsy is **a chronic** medical condition characterized by 2 or more unprovoked seizures (within 6-12 months).*
- *It is not a disease, it is **a syndrome** (what is the difference ? )*
- *What is the difference between **seizure** & **epileptic syndrome**?*



**Generalized Tonic-Clonic Seizure**



# **Etiology**

- **Congenital defects, head injuries, trauma, hypoxia**
- **Infection ( bacteria or virus ) e.g. meningitis, brain abscess, viral encephalitis**
- **Concussion, depressed skull fractures**
- **Brain tumors (including tuberculoma), vascular occlusion, stroke.**

# Etiology, Cont.

- Drug withdrawal, e.g. CNS depressants, alcohol or drug abuse or drug overdose  
e.g. penicillin
- A poison, like lead
- Fever in children (febrile convulsion)
- Hypoglycemia
- PKU ( phenylalanine  $\xrightarrow{\text{Phenylalanine hydroxylase}}$  tyrosine )
- Photo epilepsy

# Triggers

- Fatigue
- Stress
- Sleep deprivation
- Poor nutrition
- Alcohol



# Classification of Epilepsy

## **A) Partial(focal)**

**Arise in one cerebral hemisphere**

*[1] Simple partial*

*consciousness is retained*

*[2] Complex partial*

*Altered consciousness*

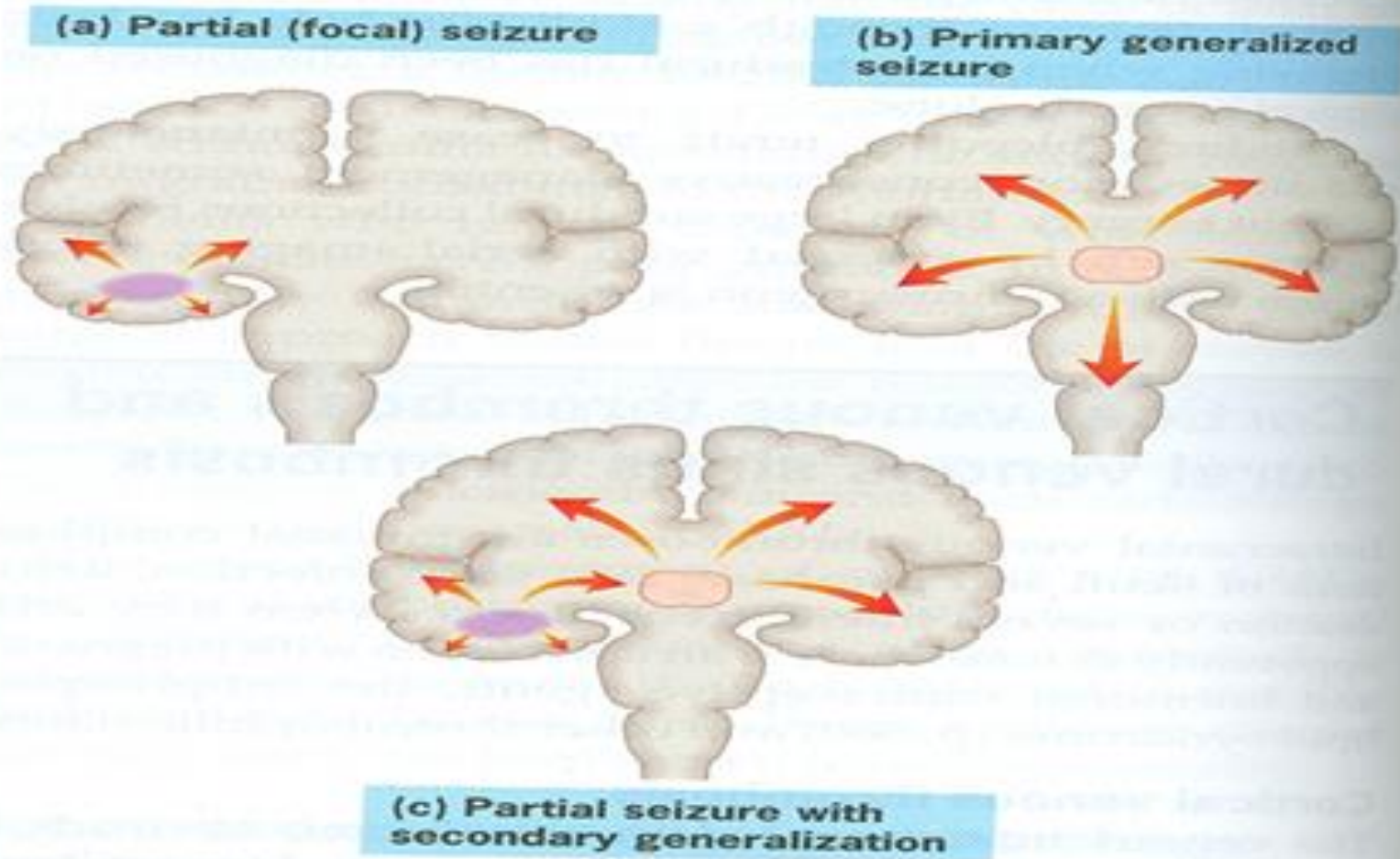
***Partial with secondary generalization***

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

## B) Primary Generalized

### Both hemispheres + loss of consciousness

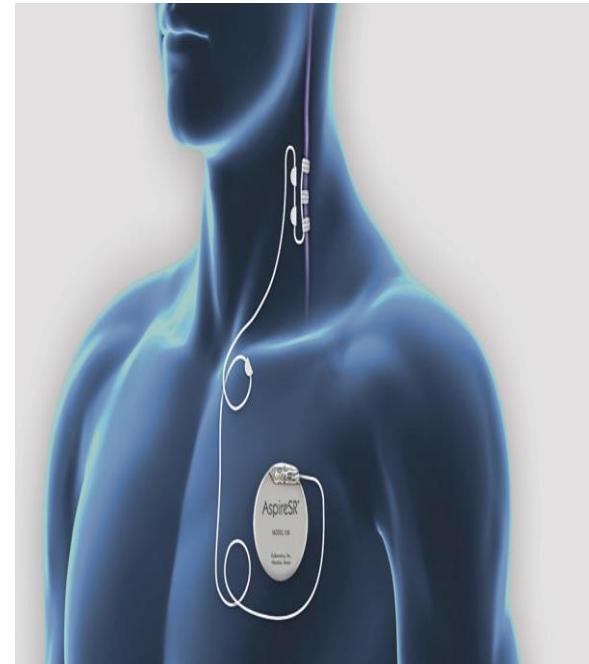
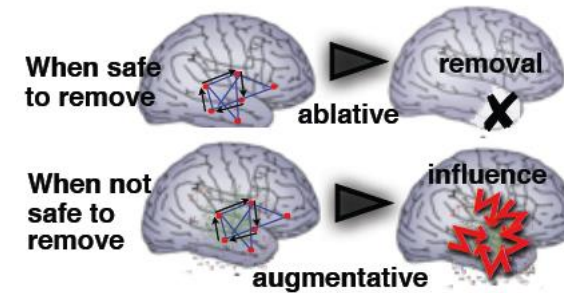
<i>Tonic-clonic</i>	<i>Stiffness followed by violent contractions &amp; relaxation (1-2 min).</i>
<i>Status epilepticus (Dangerous)</i>	Re-occurring tonic-clonic seizure (30 min or more)
<i>Tonic</i>	<i>Muscle stiffness</i>
<i>Clonic</i>	<i>Spasms of contraction &amp; relaxation</i>
<i>Atonic (loss of tone)</i>	<i>Pt's legs give under him &amp; drop down</i>
<i>Myoclonic</i>	<i>Jerking movement of the body</i>
<i>Absence</i>	<i>Brief loss of consciousness with minor muscle twitches. Eye blinking (no fall down).</i>



**Fig. 20.23** Seizure types. (a) Partial (focal) seizure. (b) Primary generalized seizure. (c) Partial seizure with secondary generalization.

# Treatment of Epilepsy

- **Drugs\*\*\***
- **Surgery**
- **Ketogenic diet**
- **Vagal nerve stimulation**



## How the Ketogenic Diet Works

The Ketogenic Diet is used to control epilepsy in children by forcing the body to burn fats instead of carbohydrates.

All foods are made up of:

- f fats
- c carbohydrates
- p protein

This diet is based off of a ratio of these foods:



This ratio of food produces a source of energy, called ketone bodies, that

**fuel cells** in the heart and brain.

Fueling these cells means more brain energy, which

**protects the brain** from future seizures.

Learn more: [luriechildrens.org/ketogenic](http://luriechildrens.org/ketogenic)

# General rules for treatment of epilepsy

- Epilepsy is usually controlled but not cured with medication
- Up to 80% of patients can expect partial or complete control of seizures with appropriate treatment
- Antiepileptic drugs are indicated when there is two or more seizures occurred in short interval (6 m -1y)
- An initial therapeutic aim is to use only one drug (mono therapy)

# General rules for treatment of epilepsy

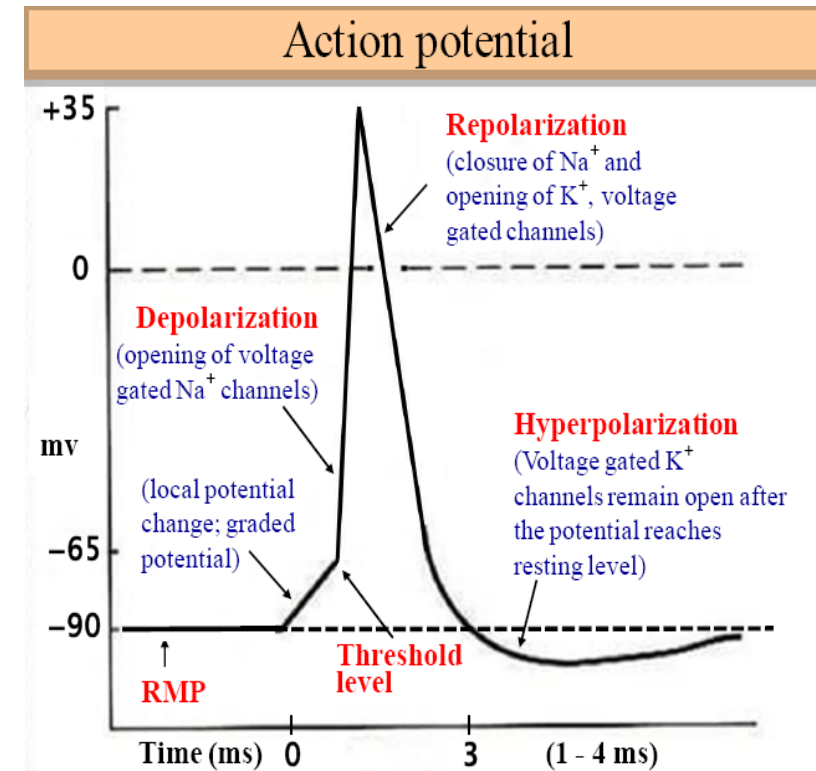
- Drugs are usually administered orally
- Monitoring plasma drug level is useful
- Triggering factors can affect seizure control by drugs
- Sudden withdrawal of drugs should be avoided

# Withdrawal considered

- ❖ Seizure – free period of 2-5 yrs or longer
  - Normal IQ
  - Normal EEG prior to withdrawal
  - NO juvenile myoclonic epilepsy
- ❖ Relapse rate when antiepileptics are withdrawn is 20-40%.

# Mechanism of Anti-Epileptic Drugs

- Antiepileptic drugs inhibit depolarization of neurons by following mechanisms:
  - Inhibition of excitatory neurotransmission  
**(Glutamate)**
  - Enhancement of inhibitory neurotransmission  
**(GABA)**
  - Blockage of voltage-gated positive current  
**(Na<sup>+</sup>)**  
**(Ca<sup>2+</sup>)**
  - Increase outward positive current  
**(K<sup>+</sup>)**





# Classification of antiepileptic drugs:

## First-generation

- ❖ Phenytoin
- ❖ Carbamazepine
- ❖ Valproate
- ❖ Ethosuximide
- ❖ *Phenobarbital and Primidone*
- ❖ *Benzodiazepines*  
(e.g. Clonazepam, lorazepam and diazepam)

## Second-generation

- ❖ Lamotrigine
- ❖ Topiramate
- ❖ Levetiracetam
- ❖ Gabapentin
- ❖ Felbamate
- ❖ Zonisamide
- ❖ Pregabalin

# Phenytoin

## ❖ Pharmacokinetics:

- Given orally, well absorbed from GIT.
- Also available i.v. and i.m. (fosphenytoin)
- **Enzyme inducer**
- Metabolized by the liver to inactive metabolites
- Half life approx. 20 hrs
- Excreted in urine

# Fosphenytoin

- **Parenteral form of phenytoin**
- **A Prodrug**
- **Given i.v. or i.m. and rapidly converted to phenytoin in the body**
- **Lower local tissue and cardiac toxicity than phenytoin**
- **Less pain and phlebitis at injection site than phenytoin**

# Phenytoin

## Mechanism of action:

- Blockade of  $\text{Na}^+$  &  $\text{Ca}^{++}$  influx into neuronal axon
- Inhibit the release of excitatory transmitters
- Potentiate the action of GABA

## Therapeutic uses:

- Partial and generalized tonic-clonic seizures **Not** in **absence seizure**.
- In status epilepticus, IV

# Phenytoin Side effects

- Nausea or vomiting
- Headache, vertigo, ataxia, diplopia , nystagmus
- Sedation
- Gum (gingival) hyperplasia
- Hirsutism
- Acne
- Folic acid deficiency (megaloblastic anemia)
- Vitamine D deficiency (osteomalacia)
- Teratogenic effects



## Phenytoin-induced gum hyperplasia



Questions ???

10/15/2019