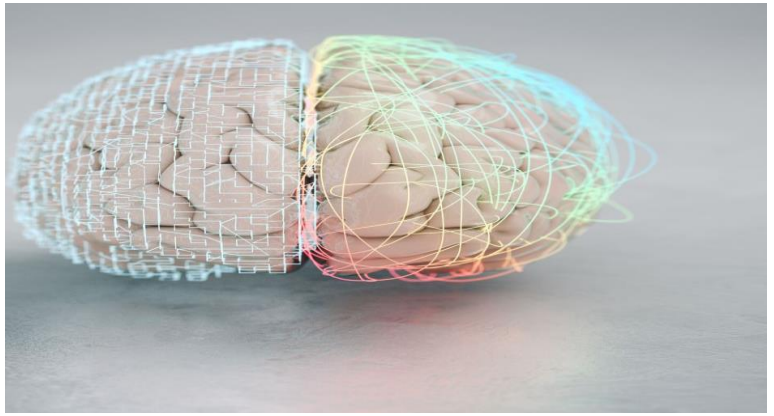
Semester 4

# Anti-epileptic Drugs

# Seizures



- **Episodes** of **abnormal electrical activity** in the **brain** that may lead to **involuntary** movements and sensations, which are accompanied by characteristic **changes on electroencephalography** (EEG).

According to the **focus** and **spread** of discharges, seizures may be classified into ways.

- **Partial (focal)**, which originate at **a specific focus** and **do not spread** to involve other cortical areas.
- **Generalized**, which arise in **both cerebral hemispheres**, and accompanied by **loss of consciousness.**

# Classification of anticonvulsant drugs

| | |
|---|---|
| ➢ **Drugs that inhibit Voltage-gated Na+ channels:** | ▪ Phenytoin & Fosphenytoin<br>▪ Carbamazepine & Oxcarbazepine<br>▪ Valproic acid<br>▪ Lamotrigine<br>▪ Topiramate<br>▪ Zonisamide |
| ➢ **Drugs that inhibit T-type Ca++ channels:** | • **Ethosuximide** |
| ➢ **Drugs that potentiate GABA activity:** | **A-Stimulate GABA/Cl- receptor complex:**<br>• Phenobarbital & Primidone<br>• Clonazepam, Diazepam & Lorazepam<br>**B-Block GABA reuptake:**<br>• Tiagabine<br>**C-GABA-mimetics:**<br>• Gabapentin<br>• Pregabalin<br>**D-Decrease GABA degradation:**<br>• Vigabatrin |

# Clinical uses of anti convulsant drugs

| Seizure type | 1st choice | 2nd choice |
|---|---|---|
| **Partial and generalized tonic-clonic seizures:** | • Carbamazepine<br>• Sodium valproate | • Lamotrigine<br>• Phenytoin<br>• Gabapentin<br>• Vigabatrin<br>• Phenobarbital |
| **Absence seizures:** | • Ethosuximide (children)<br>• Sodium valproate (adults)<br>• Lamotrigine | |
| **Status epilepticus:** | • Lorazepam<br>• Diazepam | • Phenytoin or fosphenytoin<br>• Phenobarbital |

# Status epilepticus

I. **Benzodiazepines : Treatment of choice**
   - The most used → **Lorazepam** or **diazepam** (IV).
   - Recently, **midazolam** (IM) is tried with equal effectiveness

II. **IV fosphenytoin or phenytoin**

A 2nd therapy if seizures continue.

III. **IV Phenobarbital**

An acceptable 2nd therapy if seizures continue.

# Antiepileptic drugs during pregnancy

- It is recommended to use the lowest possible doses of anticonvulsant drugs during pregnancy.
- **Lamotrigine and Levetiracetam** present the lowest level of risk to the fetus considered for use in pregnancy.
- If possible, **valproate, phenobarbital, and topiramate** should be **avoided**.


CASES

A 12-year-old girl has her first tonic-clonic seizure while at school. Her seizure was preceded by lip smacking and lasted about 1 minute during which she lost consciousness, she was started on carbmazepine.

a. What is the mechanism of action of carbmazepine?

b. What are the side effects of carbmazepine?

- The mechanism of action of carbmazepine :

They block the **voltage-gated $Na^+$ channels.**

- Side effects:
  - CNS : Nystagmus, ataxia, diplopia - sedation and vertigo.
  - ***Allergic*** reactions, e.g., ***rash***
  - Hematological effects, e.g., ***aplastic anemia***
  - Endocrine effects, e.g., ↑ ADH secretion → water retention and ***hyponatremia***
  - ***Teratogenic*** effects.

28-year-old man is being treated with phenytoin for tonic-clonic seizures. His drug plasma concentration is in the low therapeutic range, and he is still having occasional seizures. His dose is increased slightly. Within 2 weeks he is ataxic, lethargic, and has nystagmus. A repeat of his plasma concentration shows that he is now slightly above the upper limit of the therapeutic range. The reason for the dramatic rise in his plasma concentration following a modest increase in his dose is most likely because of:

A. renal failure.

B. liver failure.

C. zero order elimination.

D. metabolic acidosis.

E. poor Gl absorption of Ca.

**Answer: C**

A 29-year-old woman is being treated with valproic acid for simple partial seizures. She is at risk for developing a rise in her plasma:

A. calcium.
B. hepatic transaminases.
C. blood urea nitrogen (BUN).
D. potassium.
E. glucose.

**Answer: B**

A 32-year-old woman is being treated with vigabatrin because her complex seizures have been refractory to all other therapies. Vigabatrin is reserved for use in patients such as this although its availability is restricted due to:

A. renal failure.
B. liver failure.
C. heart failure.
D. vision loss.
E. hearing loss.

**Answer: D**

A 16-year-old boy is brought to the urgent care clinic after suffering an episode of lip smacking followed by stiffness and convulsions. His mother explains that this is the third such attack in the past 2 years and that each attack has lasted about a minute. The pediatrician prescribes carbamazepine control his seizures. What is the mechanism of action of this agent:

A. Inhibition of calcium channels.
B. Inhibition of potassium channels.
C. Inhibition of sodium channels.
D. Potentiation of GABA receptors.
E. Stimulation of chloride channels.

**Answer: C**

An 8-year-old boy presents to the emergency department after seizure-like activity. During class, the teacher noted that the boy stare off for about 45 s. He has done this three times in the past. He would not respond to her during the episode and was confused for about 1 min following it. What is the most appropriate first-line therapy for this child?

A. Carbamazepine.
B. Ethosoximide.
C. Lamotrigine.
D. Phenytoin.
E. Valproic acid.

**Answer: B**

B. what is the mechanism of action of this drug?

C. what are the adverse effects of this drug?

- the mechanism of action of Ethosoximide :

  Blocks the low-threshold T-Type **Ca++ channels** in the thalamus

- the adverse effects of this drug:

  1- Gastrointestinal upset.

  2- Drowsiness and mood swings.

  3- Rarely, it causes serious bone marrow depression.

A 15-year-old boy presents to clinic for follow-up for his tonic-clonic seizures. He reports that he has not had a seizure in the past 6 months. A complete blood count is performed and shows megaloblastic anemia. The physician told the patient that this was most likely a side effect of his antiseizure medication. What is the must likely medication he was taking:

A. Lamotrigine.
B. Ethosuximide.
C. Phenobarbital.
D. Phenytoin.
E. Valproic acid.

**Answer: D**

33-year-old woman with seizure disorder, Bipolar disorder, and trigeminal neuralgia presents to her primary care physician for follow-up and treatment She has no new complaints. Which of the following medications may serve to treat all of her earlier mentioned problems?

A. Carbamazepine.
B. Ethosuximide.
C. Fellsamate.
D. Gabapentin.
E. Lacosamide.

**Answer: A**

Which antiepileptic drug is most likely to elevate the plasma concentration of other drugs administered concomitantly ?

A. Carbamazepine.

B. Clonazepam.

C. Phenobarbital.

D. Phenytoin.

E. Valproic acid.

**Answer: E**

With chronic use in seizure states, the adverse effects of this drug include coarsening of facial features, hirsutism, and gingival hyperplasia:

A. Carbamazepine.
B. Zonisamide.
C. Ethosuximide.
D. Tiagabine.
E. Phenytoin.

**Answer: E**

A 45-year-old man with a history of alcohol abuse was brought to the emergency department after having a seizure. The patient had a witnessed seizure lasting approximately 10 minutes. Upon arrival, he was found to be in status epilepticus. What is the first drug of choice?

A . Phenobarbital.

B. Lorazepam.

C. Lamotrigine.

D. Valproate.

**Answer: B**


THANK YOU