

**Epilepsy** refers to a group of chronic neurologic disorders characterized by recurrent seizures, brought on by excessive excitability of neurons in the brain.

**Symptoms:**

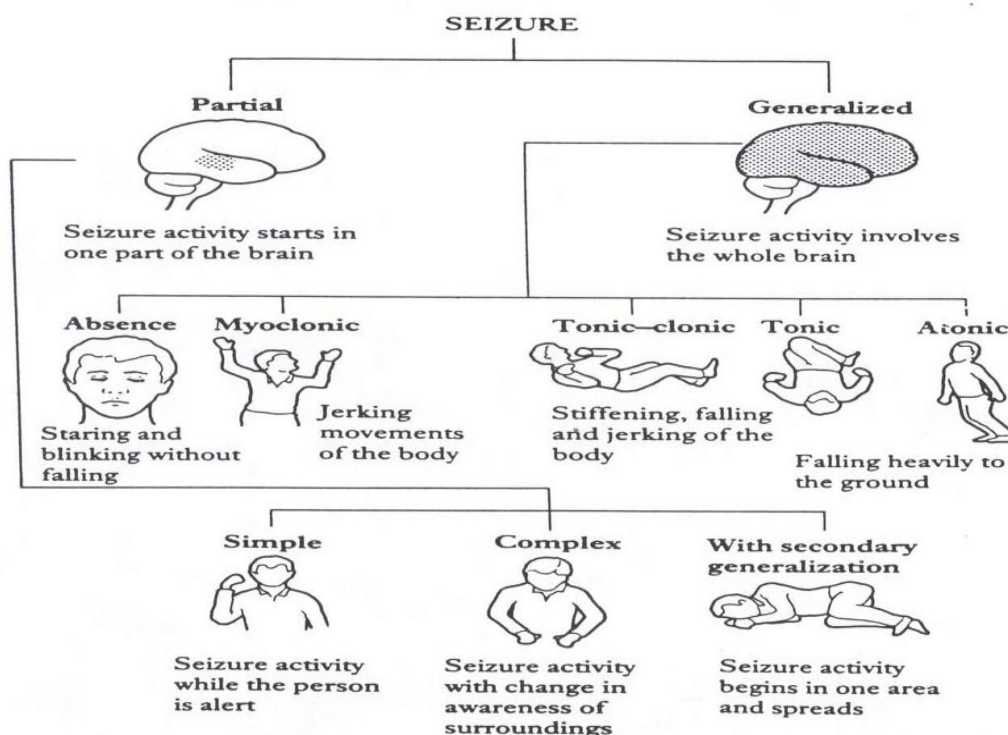
1. Range from brief periods of unconsciousness to violent convulsions.
2. Patients may also experience problems with learning, memory, and mood, which can be just as troubling as their seizures.

**Seizure** is a general term that applies to all types of epileptic events. Seizures are initiated by synchronous, high-frequency discharge from a group of hyperexcitable neurons, called a *focus*.

**convulsion** has a more limited meaning, applying only to abnormal motor phenomena, for example, the jerking movements that occur during a tonic-clonic attack.

**Etiology**

1. Idiopathic
2. Congenital defects
3. Head injuries, trauma, hypoxia
4. Infection (meningitis, brain abscess, encephalitis)
5. Brain tumors (including tuberculoma), vascular occlusion
6. Drug withdrawal (CNS depressants)
7. Fever in children (febrile convulsion)
8. Hypoglycemia, hypocalcemia

**Types of seizures:-****Classification of anti-epileptics drugs (AEDs) : (generally)**

1. Suppression of sodium influx.
2. Suppression of calcium influx.
3. Promotion of potassium efflux.
4. Blockade of receptors for glutamate.
5. Potentiation or increase of gamma-aminobutyric acid (GABA).

**A. The older AEDs****1. Phenytoin (Dilantin)****M.O.A:**

At the concentrations achieved clinically, phenytoin causes selective inhibition of sodium channels. entry of sodium into neurons is inhibited, and hence action potentials are suppressed. Blockade of sodium entry is limited to neurons that are hyperactive. As a result, the drug suppresses activity of seizure-generating neurons while leaving healthy neurons unaffected.

### Therapeutic Uses

Phenytoin can be used to treat all major forms of epilepsy except absence seizures. The drug is especially effective against tonic-clonic seizures, and is a drug of choice for treating these seizures in adults and older children.

### Adverse effects

- Gingival hyperplasia.
- hypersensitivity reactions (measles like rash)
- megaloblastic anaemia
- foetal hydantoin syndrome (teratogenic effects)
- ❖ hypoplastic phalanges
- ❖ cleft palate
- ❖ microcephaly
- **Cardiovascular Effects.** When phenytoin administered by IV injection, cardiac dysrhythmias and hypotension may result. **These dangerous responses can be minimized by injecting phenytoin slowly and in dilute saline solution.**

## 2. Carbamazepine (TEGRETOL)

### M.O.A:

Carbamazepine suppresses high-frequency neuronal discharge in and around seizure foci. The mechanism appears to be the same as that of phenytoin: delayed recovery of sodium channels from their inactivated state.

### Therapeutic uses:

Effective against tonic-clonic, simple partial and complex partial seizures. Most effective drug for partial seizures.

### Adverse effects:

- ❖ Neurotoxicity
- ❖ Vomiting & diarrhoea
- ❖ Hypersensitivity reactions
- ❖ Hyponatremia & water intoxication
- ❖ Craniofacial anomalies & neural tube defects

### 3. Valproic acid (Depakene)

#### M.O.A:

Valproic acid appears to act by three mechanisms:

1. First, it shares the same mechanism as phenytoin and carbamazepine: suppression of high-frequency neuronal firing through blockade of sodium channels.
2. Second, it suppresses calcium influx through T-type calcium channels.
3. Third, it may augment the inhibitory influence of GABA.

#### Therapeutic Uses:

Valproic acid is considered a first-line drug for all partial and generalized seizures. As mentioned previously, this drug is also indicated for management of bipolar disorder and migraine headache prophylaxis.

#### Adverse Effects:

1. Hepatotoxicity and pancreatitis are rare but serious.
2. Teratogenic effects, valproic acid should be avoided during pregnancy.
3. Rash
4. Obesity

### B. Newer antiepileptic drugs

1. **Oxcarbazepine** ( It is a derivative of carbamazepine; therefore, they share some of the same features.

#### Mechanism of Action

Anti-seizure effects result from blockade of voltage-sensitive sodium channels in neuronal membranes, an action that stabilizes hyper-excitable neurons and thereby suppresses seizure spread. The drug does not affect neuronal GABA receptors.

#### Therapeutic Uses

Oxcarbazepine is indicated for both monotherapy and adjunctive therapy for management of partial seizures. It is approved for use in both adults and children.

### 2. Gabapentin

#### Mechanism of Action

Gabapentin [Neurontin] is an analog of GABA but does not directly affect

GABA receptors. Its precise mechanism of action is unknown, but it may enhance GABA release, thereby increasing GABA-mediated inhibition of neuronal firing.

### **Therapeutic Uses**

Gabapentin has a broad spectrum of antiseizure activity. However, its only FDA-approved use in epilepsy is adjunctive therapy of partial seizures (with or without secondary generalization). prophylaxis of migraine.

## **3. Pregabalin**

### **Mechanism of Action**

Pregabalin [Lyrica], an analog of GABA, is much like gabapentin. pregabalin can bind with calcium channels on nerve terminals, and can thereby inhibit calcium influx, which in turn can inhibit release of several neurotransmitters, including glutamate, norepinephrine, and substance P. Reduced transmitter release may underlie seizure control and relief of neuropathic pain.

### **Therapeutic Uses**

- ❖ seizures and neuropathic pain.
- ❖ neuropathic pain associated with diabetic neuropathy.
- ❖ postherpetic neuralgia.
- ❖ adjunctive therapy of partial seizures.
- ❖ fibromyalgia.

## **4. Topiramate**

### **Mechanism of Action**

Topiramate [Topamax]

- (1) Potentiation of GABA-mediated inhibition
- (2) Blockade of voltage-dependent sodium channels.
- (3) Blockade of calcium channels.
- (4) Blockade of receptors for glutamate, an excitatory neurotransmitter.

## **5. Zonisamide**

### **Mechanism of Action:**

The underlying mechanism appears to be a blockade of neuronal sodium channels and calcium channels.

**Therapeutic uses:**

Zonisamide approved only for adjunctive therapy of partial seizures in adults.

**Common Causes Of Failure Of AEDs:**

- ❖ Improper diagnosis of the type of seizures
- ❖ Incorrect choice of drug
- ❖ Inadequate or excessive dosage
- ❖ Poor compliance