Epilepsy

Epilepsy can be defined as a jerky movement of hands, feet and body due to repeated hyper synchronous discharge of cerebral neurons.

Types of Epilepsy:

1. Partial Seizure

a. **Simple Partial**: No loss of consciousness.
b. **Complex Partial**: Altered consciousness, preceded by aura, also known as "Temporal lobe epilepsy"
c. **Partial with secondary Generalisation**: Loss of consciousness, preceded by aura

2. Generalised Seizure

a. **Tonic-clonic (grand mal)**: Sudden onset, loss of consciousness, no aura.
b. **Absence seizure (petit mal):** Sudden, brief interruption of consciousness, no aura
c. Myoclonic

Antiepileptic Drugs

According to the mechanism of actions:

1. **Na+ channel inhibitors :**
    a. Phenytoin
    b. Fosphenytoin
    c. Carbamazepine
    d. Lamotrigine
2. **T-type Ca++ channel inhibitors:**
    a. Ethosuximide
    b. Valproic acid / Valproate
3. **GABA modifiers-**
    a. GABA receptor antagonist
        i. Gabapentin,
        ii. Benzodiazepines
        iii. Phenobarbitone
    b. GABA reuptake inhibitor
        i. Tiagabine
    c. Increase synthesis of GABA
        i. Valproate
        ii. Valproic acid
4. **Glutamate blockers:**
    a. Topiramate
    b. Felbamate

Principles of antiepileptic therapy:

- The selection of monotherapy depending on age, sex, associated disease, and economic status of the individual.
- Complete prevention of seizure with minimum possible dose and least side effects.
- Gradual increase in dose until cessation of seizure or appearance of side effects.
- Addition of another drug if required, should also be adjusted following the above principles.
- Once the control of seizures is achieved, the drug(s) should be continued for 2-3 years after the last seizure.
- Then gradual withdrawal (taking several weeks or months) should be planned.
- Treatment restarted, if relapse during withdrawal.
- Some patients may need treatment indefinitely.

Kinetics of antiepileptic:

- Route- oral and intravenous (in case of emergency).
- Bioavailability varies from 80-100%
- High plasma protein binding
- Chiefly cleared by hepatic mechanism
- Most of drugs produce active metabolites
- Most of drugs are teratogenic
- Some drugs are potent hepatic microsomal —
    - Enzyme inducer — Phenytoin, Carbamazepine, Phenobarbital
    - Enzyme inhibitor — Valproate.

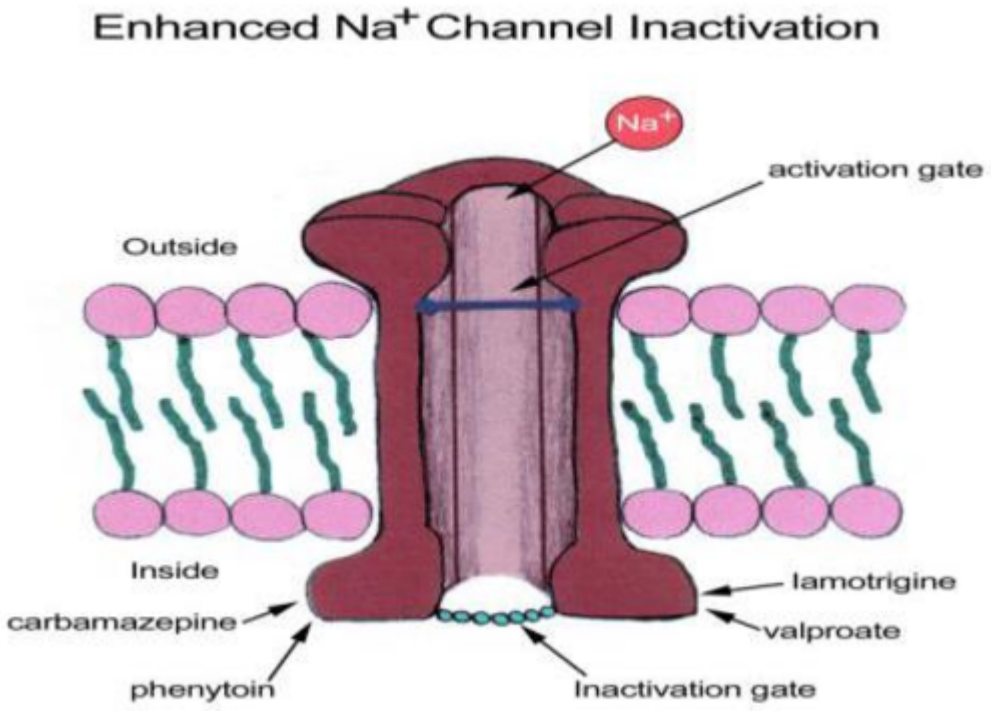
Mechanism of antiepileptic:

Na+ channel inhibitors:

- They block the Na+ channel in an inactivated state, slow the channel recovery and inhibit the generation of repetitive action potential.
- They prevent the rapid spread of seizure activity to other neurons

T-type Ca++ channel inhibitors:

- Reduce activity of low threshold T-type Ca++ channel
- Prevent paroxysmal hyperpolarization (that activate the channel in
- the awake state to initiate seizure)



Mechanism of action:

GABA modifier:

- Gabapentin may act by increasing the release of GABA.
- Benzodiazepines act on GABA receptors and potentiate its action increasing influx of Cf through GABA channels.
- Phenobarbitone binds to GABA receptor and potentiates the activates endogenous GABA by increasing Cl influx.

Valproic acid

Valproic acid / Sodium valproate have multiple mechanisms:

- Slows the Na+ channel recovery from inactivated state
- Limits the activity of the T-type Ca++ channel
- Increases synthesis & inhibit breakdown of GABA

Drugs used in different seizures

Partial seizures:

- Carbamazepine
- Phenytoin
- aLamotrigine
- Valproic acid

Absence seizures:

- Ethosuximide
- Lamotrigine

Tonic-clonic seizures:

- Valproate
- Lamotrigine
- Carbamazepine
- Topiramate

Status epilepticus:

- Diazepam followed by phenytoin

Adverse effect

Common:

Ataxia, diplopia, drowsiness, teratogenicity, hypersensitivity reactions.

Phenytoin:

Nystagmus, gum-hyperplasia, hirsutism, osteomalacia, megaloblastic A. teratogenicity.

Carbamazepine:

GI upset, Hyponatremia, Aplastic anaemia.

Lamotrigine:

Nausea, rash, headache, somnolence

Sodium valproate:

GI upset, heartburn, weight gain, hepatotoxicity, tremor, teratogenicity.

Pregnancy & Epilepsy:

- Women of child baring age should take folic acid 5mg/d. Valproate should be avoided.
- Valproate and carbamazepine can appear in breast milk.
- Pre-conception counselling of foetal abnormality is important.
- Non enzyme inducing antiepileptic can't do any problem with oral contraceptive pills.
- Lamotrigine is safe for pregnant and nursing mothers.

Caution during use:

Antiepileptic drugs have teratogenic potential-

- Phenytoin- foetal hydantoin syndrome
- Carbamazepine- cleft lip/palate
- Sodium valproate- spina bifida, neural tube defects, CVS abnormality

Management of status epilepticus:

Early status:

- IV Lorazepam 4mg repeat after 10 minutes if necessary.
- IV Diazepam 10-20mg over 2-4 min repeat after 30 minutes if necessary.

Establish status:

- IV Phenytoin 15-18 mg/kg at the rate of 50 mg/min

Refractory status:

- Thiopental (or)
- Propofol (or)

Drug interaction:

- Most of the antiepileptic hepatic microsomal enzyme inducers increase the metabolism of other drugs.
- Highly protein bound drugs may displace Phenytoin from its protein binding site.
- In hypo-proteinaemia, concentration of free antiepileptic drugs increased.