Definition, etiopathogenesis, clinical manifestations, nonpharmacological and pharmacological management of the diseases associated with Central Nervous System

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Epilepsy

Definition:

- Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures.
- A seizure is a transient occurrence of signs/symptoms due to abnormal, excessive, or synchronous neuronal activity in the brain.

Diagnosis is made when:

- Two or more unprovoked seizures occur >24 hours apart, OR
- One unprovoked seizure with a high probability of recurrence

Etiopathogenesis:

- Epilepsy results from a disturbance in the normal balance between excitatory and inhibitory neurotransmission in the brain.

Causes:

1. **Genetic:**
   - Channelopathies (mutations affecting ion channels)
   - Familial epilepsy syndromes (e.g., juvenile myoclonic epilepsy)
2. **Structural (Acquired):**
   - Head injury/trauma
   - Stroke
   - Brain tumors
   - Infections (e.g., meningitis, encephalitis)
   - Congenital malformations
3. **Metabolic:**
   - Hypoglycemia
   - Hypocalcemia
   - Uremia
   - Hepatic encephalopathy

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4. Unknown (Idiopathic):

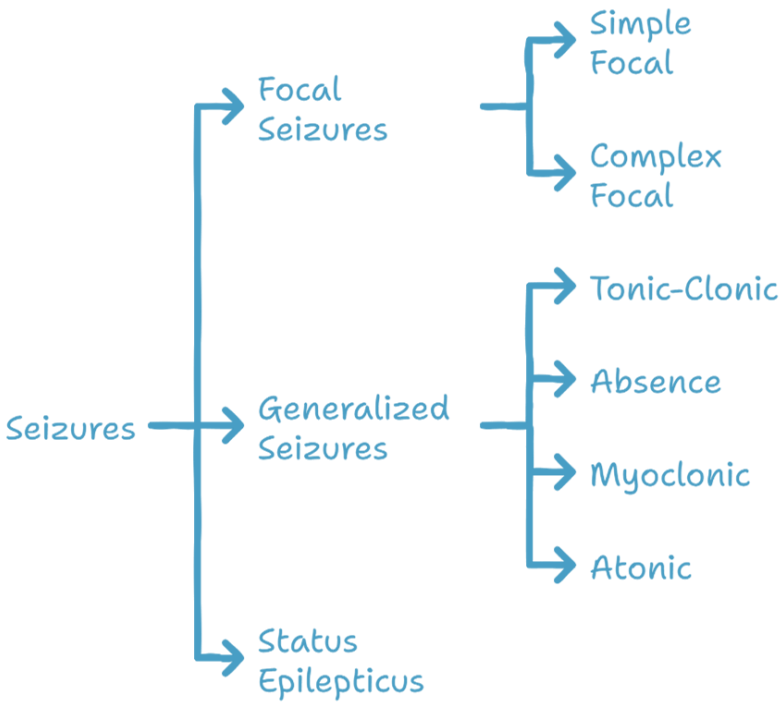
- In many cases, the cause remains unidentified.

Pathophysiology:

- A seizure begins with a focus of hyperexcitable neurons.
- Disruption in ion channels or neurotransmitter systems (glutamate ↑, GABA ↓) leads to neuronal hyperexcitability.
- Electrical activity spreads to adjacent neurons (focal seizures) or entire brain (generalized seizures).

Clinical Manifestations:

Types of Seizures:



1. Focal (Partial) Seizures:

- **Simple focal:** No loss of consciousness, motor/sensory/autonomic symptoms.
- **Complex focal:** Altered consciousness, automatisms (e.g., lip smacking).

2. Generalized Seizures:

- **Tonic-clonic (Grand mal):** Muscle stiffening (tonic), followed by jerking (clonic), post-ictal confusion.
- **Absence seizures:** Brief lapses in consciousness (common in children).
- **Myoclonic:** Sudden brief jerks.
- **Atonic:** Sudden loss of muscle tone (drop attacks).

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3. Status Epilepticus:

- A medical emergency defined as continuous seizure >5 minutes or multiple seizures without return to baseline.

Non-Pharmacological Management:

- **Education:** Avoid triggers (sleep deprivation, flashing lights, stress).
- **Lifestyle modification:** Regular sleep, hydration, exercise.
- **Diet:** Ketogenic diet (especially in refractory pediatric epilepsy).
- **Safety precautions:** No swimming alone, avoiding heights or dangerous machinery.
- **Psychological support:** Cognitive-behavioral therapy (CBT), counseling.
- **Surgery:** For drug-resistant epilepsy (e.g., temporal lobectomy).
- Vagus nerve stimulation (VNS) or responsive neurostimulation (RNS) in selected patients.

Pharmacological Management:

First-line antiepileptic drugs (AEDs) based on seizure type:

1. Generalized seizures:

- Valproic acid
- Lamotrigine
- Levetiracetam
- Topiramate

2. Focal seizures:

- Carbamazepine
- Phenytoin
- Lamotrigine
- Oxcarbazepine

3. Absence seizures:

- Ethosuximide
- Valproic acid

4. Myoclonic seizures:

- Valproate
- Clonazepam

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- Levetiracetam

Side effects vary widely—e.g., valproic acid can cause hepatotoxicity and weight gain; phenytoin can cause gum hypertrophy.

Parkinson’s Disease

Definition:

- Parkinson’s disease (PD) is a progressive neurodegenerative disorder primarily affecting movement, caused by the loss of dopaminergic neurons in the substantia nigra pars compacta of the midbrain.

Etiopathogenesis:

A. Primary (Idiopathic):

- Unknown exact cause; involves oxidative stress, mitochondrial dysfunction, protein aggregation (α-synuclein forming Lewy bodies).

B. Secondary (Parkinsonism):

- Drug-induced (e.g., antipsychotics like haloperidol)
- Vascular Parkinsonism
- Traumatic (e.g., repeated head injury)
- Toxins (e.g., MPTP)

Pathophysiology:

- Dopamine depletion in the nigrostriatal pathway → imbalance between dopamine (inhibitory) and acetylcholine (excitatory).
- This disrupts basal ganglia circuits, leading to motor symptoms.

Clinical Manifestations:

Motor symptoms (TRAP):

- **Tremor** (resting, “pill-rolling”)
- **Rigidity** (lead-pipe or cogwheel)
- **Akinesia/bradykinesia** (slowness of movement)
- **Postural instability**

Non-motor symptoms:

- Depression, anxiety

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- Sleep disturbances
- Autonomic dysfunction (e.g., constipation, orthostatic hypotension)
- Cognitive decline or dementia

Non-Pharmacological Management:

- **Physical therapy:** Improves flexibility, strength, balance.
- **Speech therapy:** For hypophonia and swallowing issues.
- **Occupational therapy:** Assist with daily activities.
- **Exercise:** Regular aerobic activity improves mobility.
- **Diet:** High-fiber diet for constipation; adequate hydration.
- **Support groups and counseling**

Pharmacological Management:

1. Levodopa + Carbidopa:

- Most effective, especially for bradykinesia.
- Long-term use associated with motor fluctuations, dyskinesias.

2. Dopamine agonists:

- Pramipexole, ropinirole, bromocriptine
- Used in younger patients or as add-on

3. MAO-B inhibitors:

- Selegiline, rasagiline
- Inhibit dopamine breakdown

4. COMT inhibitors:

- Entacapone, tolcapone
- Extend Levodopa’s action

5. Anticholinergics:

- Trihexyphenidyl (mainly for tremor in younger patients)

6. Amantadine:

- Mild benefit; used for dyskinesia

Surgical Options:

- **Deep Brain Stimulation (DBS)** for advanced cases not responding to medication.

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