Nervous System Disease

Epilepsy

Introduction / Epidemiology

- Epilepsy is a chronic neurological disorder characterized by a predisposition to generate recurrent, unprovoked seizures.
- A seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.
- **Epidemiology:**
    - **Global prevalence:** Approximately 50 million people worldwide have epilepsy (WHO).
    - **Incidence:** 30–50 cases per 100,000 population per year in high-income countries; higher in low- and middle-income countries due to increased risk factors such as infections and trauma.
    - **Age distribution:** Bimodal; more common in children and the elderly.
    - **Gender:** Slightly more common in males.
    - **Risk factors:** Genetic predisposition, birth trauma, infections (e.g., neurocysticercosis, meningitis), traumatic brain injury, stroke, and tumors.

Etiopathogenesis

Etiology (Causes):

Epilepsy is classified into:

1. **Genetic:** Idiopathic epilepsy syndromes (e.g., Juvenile Myoclonic Epilepsy)
2. **Structural:** Cortical dysplasia, brain tumors, trauma, stroke, hippocampal sclerosis
3. **Metabolic:** Hypoglycemia, hyponatremia, uremia, hepatic encephalopathy
4. **Infectious:** Neurocysticercosis, tuberculosis, HIV, encephalitis
5. **Immune-related:** Autoimmune encephalitis
6. **Unknown causes**

Pathophysiology:

- Epileptic seizures arise due to abnormal electrical discharges from a group of neurons.
- Mechanisms include:
    - Imbalance between excitatory neurotransmitters (e.g., glutamate) and inhibitory neurotransmitters (e.g., GABA)
    - Altered ion channel function (Na^+, Ca^{2+}, K^+ channels)
    - Synaptic reorganization, gliosis
    - Failure of inhibitory mechanisms leading to hypersynchronous discharges

Clinical Features / Symptoms

Seizure types (per ILAE classification):

1. **Focal onset seizures:**
   - With preserved awareness: e.g., focal motor/sensory
   - With impaired awareness
2. **Generalized onset seizures:**
   - Tonic-clonic (grand mal)
   - Absence (petit mal)
   - Myoclonic
   - Atonic
3. **Unknown onset seizures**

Symptoms:

- Sudden loss of consciousness (in generalized seizures)
- Convulsions, jerking movements
- Aura (e.g., strange smell, taste, déjà vu)
- Post-ictal confusion, lethargy, headache
- Injuries from falls or biting tongue
- Incontinence

Diagnosis & Investigations

Clinical History:

- Detailed description of seizure (from patient and witness)
- Duration, aura, post-ictal state, triggers

Neurological Examination:

- Usually normal interictally

Investigations:

1. **EEG (Electroencephalogram):**
   - Interictal spikes, sharp waves
   - 24-hour or video EEG for unclear cases
2. **Neuroimaging:**
   - **MRI brain**: Preferred for structural lesions
   - CT head: Acute cases or emergencies

3. Blood Tests:

- Electrolytes, glucose, calcium, magnesium, LFTs, RFTs

4. Other:

- Toxicology screen (if substance-related seizure is suspected)
- Lumbar puncture if infection suspected

Treatment Goals / Therapeutic Objectives

- Prevent recurrence of seizures
- Minimize adverse effects
- Improve quality of life
- Address underlying cause (if identifiable)
- Restore psychosocial functioning
- Educate and empower patient for self-care and safety

Non-Pharmacological Therapy

- **Lifestyle modifications:**
  - Adequate sleep
  - Avoid alcohol, recreational drugs
  - Avoid known triggers (e.g., flashing lights, stress)
- **Ketogenic diet:** Especially in drug-resistant childhood epilepsies
- **Vagus Nerve Stimulation (VNS):** For refractory cases
- **Epilepsy surgery:** Resective surgery in focal epilepsy with identifiable focus
- **Psychological counseling:** For anxiety, depression, stigma

Pharmacological Therapy

First-line Drugs

Seizure Type	First-line AED	Dose	Mechanism of Action	Rationale
Focal	Carbamazepine, Lamotrigine	CBZ: 200–1200 mg/day	Na^+ channel blocker	Effective in focal discharges
Generalized tonic-clonic	Valproate	600–2500 mg/day	↑ GABA	Broad-spectrum, effective across seizure types
Absence	Ethosuximide	500–1500 mg/day	T-type Ca^{2+} channel blocker	Specific for absence seizures

Myoclonic	Valproate	See above	See above	Effective in JME

Alternative Drugs

- Levetiracetam: Broad-spectrum, favorable side-effect profile
- Topiramate
- Zonisamide
- Clobazam, Clonazepam (benzodiazepines)
- Lacosamide

Duration of Therapy

- First seizure with normal imaging/EEG: May not start AED unless high-risk
- Recurrent seizures: Long-term therapy (usually 2–5 years seizure-free before tapering)
- Some cases may require lifelong therapy

Individualized Patient-Specific Therapeutic Plan

- **Age:** Children may benefit from ketogenic diet; some drugs not approved (e.g., valproate caution in young girls)
- **Pregnancy:** Valproate is **teratogenic** – avoid if possible; use lamotrigine or levetiracetam
- **Renal function:** Adjust levetiracetam, gabapentin
- **Hepatic dysfunction:** Avoid valproate
- **Comorbidities:** Depression → avoid levetiracetam; Obesity → avoid valproate
- **Allergies:** Rash with lamotrigine → discontinue
- **Occupation:** Avoid sedating AEDs in drivers, machine operators

Controversies / Special Considerations

- **Valproate in women of childbearing age:** Major concern due to teratogenicity (neural tube defects, cognitive impairment)
- **Generic substitution of AEDs:** Some guidelines warn against switching brands due to bioavailability concerns
- **Early withdrawal of therapy:** Risk of relapse; debate exists on when to taper
- **Newer AEDs vs. Older AEDs:** Newer drugs have better tolerability, but higher cost and less long-term data

Guidelines:

- **ILAE 2022 update:** Emphasizes individualized therapy and shared decision-making
- **NICE guidelines:** Favor lamotrigine for focal epilepsy; valproate only when other drugs are ineffective in women of childbearing age

Monitoring Therapy

Clinical Parameters:

- Seizure frequency
- Adverse effects (sedation, rash, mood changes)
- Adherence

Laboratory Monitoring:

- Liver function tests (for valproate)
- CBC (for carbamazepine, valproate)
- Sodium (for carbamazepine, oxcarbazepine)
- Drug levels: May be used in valproate, phenytoin

Time-course of Response:

- Initial seizure control usually within weeks of therapeutic dose
- Full assessment of efficacy after 6–8 weeks

Adverse Effects & Management

Drug	Common Adverse Effects	Management
Valproate	Weight gain, tremor, hair loss, hepatotoxicity	Monitor LFTs; dose adjust
Carbamazepine	Hyponatremia, rash, leukopenia	Monitor CBC, Na^+; discontinue if severe
Lamotrigine	Rash (SJS)	Titrate slowly; discontinue if rash appears
Levetiracetam	Mood changes, irritability	Consider switch if psychiatric issues

Follow-up and Patient Counseling

Follow-up Schedule:

- Initial: Every 1–3 months until stable
- Later: Every 6–12 months if well-controlled

Counseling Topics:

- Importance of **medication adherence**
- Avoiding **triggers**
- Safety precautions: Not swimming alone, avoiding heights

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