Epilepsy

- A seizure is a transient disturbance of consciousness, behaviour, emotion, sensation or motor function due to abnormal electrical activity in the brain.
- Epilepsy is the tendency to recurrent unprovoked seizures: the WHO defines it as a “chronic brain disorder of various aetiologies characterised by recurrent seizures due to excessive neuron discharge”
- Neurotransmitters are activated repetitively and hypersynchronously as inhibitory synaptic activity fails
- Abnormal excitation can spread and become generalised
- 1000 people die each year (to rule out cardiac syncope)
- 70% of sufferers will be free from seizures on appropriate treatment

**Causes include:**
- Idiopathic ➔ light, lack of sleep, alcohol
- Genetic disorders e.g. NF, tuberous sclerosis
- Trauma/surgery/hypoxia
- Pyrexia
- Intracranial mass lesion
  - Cancer
  - Haematoma
  - Abscess/encephalocoele
- Neurodegenerative disorders
  - Dementia: Alzheimer’s, MD
  - Hippocampal sclerosis (temporal atrophy)
  - Neurosyphilis, HIV

**Classification:**
- Grand mal/tonic-clonic
  - Prolonged
  - Tonic phase ➔ stiffening and cyanosis
  - Clonic phase ➔ high frequency low amplitude clonus
  - May injure self, bite tongue laterally, or have incontinence, should last <4 minutes
  - Aftermath with amnesia, headache, weakness, confusion, drowsiness
- Petit mal/absence
  - Common in children: activity stops for about 10 seconds before picking up where left off
  - Patient stares and goes pale, may have eyelid twitching or muscle jerks
  - 3Hz spike-and-wave EEG activity
- Myoclonic: isolated sudden muscle jerking
- Tonic: intense stiffening and fall, no subsequent clonic convulsions
- Atonic/akinetic: sudden loss of tone with fall and LOC

**Classification:**
- Simple partial
  - Patient remains aware
- Complex partial
  - Awareness is impaired, may progress to 2: generalised with automatisms, pallor, staring
- Jacksonian: simple partial seizures of motor cortex
  - Contralateral jerking movement spreading from mouth/face
  - May have Todd’s paresis afterwards
- Temporal
  - Dèjà vu/jamais vu, unusual smells or tastes, vertigo, autonomic symptoms, psychosis
- Frontal
  - Bizarre stereotyped movements, often at night, little residual confusion
- Occipital: coloured visual disturbances, may have visual loss afterwards
- Parietal: migrating sensory phenomena e.g. electric shocks

**Investigations**
- Detailed history, need witness account for full story
- Full examination including monitoring of conscious level and cognitive function
- Bloods: FBC, U+E, LFT, glucose, calcium, CRP/ESR
- ECG to rule out cardiac syncope
- EEG: interictal/EEG video telemetry (normal EEG ≠ absence of epilepsy)
- MRI/CT brain if indicated (to rule out epileptic focus, and/or any head trauma from seizure)

**Drugs used to treat Epilepsy**

1) Carbamazepine (Tegretol) + oxcarbazepine
- Stabilises inactivated voltage-gated Na⁺ channels to decrease membrane excitability
- Potentiates GABA receptors
- Indications: epilepsy, neuropathic pain, and bipolar disorder (manic phase)
- Contraindications: AV conduction abnormalities, history of bone marrow depression, porphyria
- Side effects: drowsiness, N+V, dizziness, headache, confusion, dry mouth, blurred vision, diplopia, reduced coordination, bone marrow suppression, thromboembolism, hepatitis
- Suicidal ideations, SIADH, ↓Na⁺, hepatic enzyme induction (increases metabolism of itself → start at low dose then increase in increments every few weeks until stable), teratogenesis

2) Lamotrigine
- Thought to inhibit and stabilise Na⁺ channels
- Indications: epilepsy, bipolar disorder (depression)
- Contraindications: no absolute contraindications
- Side effects: rash, hypersensitivity, GI upset, headache, dizziness, sleep disturbance, movement disorders, agitation, confusion, hallucinations, bone marrow suppression, teratogenesis

3) Sodium valproate
- Blocks and stabilises Na⁺ channels and T-type Ca²⁺ channels
- Increases GABA
- Indications: epilepsy, bipolar disorder
- Contraindications: active liver disease, family history severe liver disease, porphyria
- Side effects: GI upset, weight gain, hyperammonaemia, thrombocytopenia, transient hair loss, psychomotor agitation, liver damage, hepatic enzyme inhibition, significant teratogenesis

4) Phenytoin
- Stabilises inactivated voltage-gated Na⁺ channels to decrease membrane excitability
- Indications: epilepsy, neuropathic pain
- Contraindications: vitamin D deficiency, history of bone marrow suppression, porphyria
- Side effects: N+V, constipation, anorexia, insomnia, anxiety, tremor, paraesthesiae, dizziness, headache, painful gingival hypertrophy, rash, acne, hirsutism, drug-induced lupus, folate deficiency, hepatic enzyme induction, narrow therapeutic index ➔ toxicity, teratogenesis

5) Gabapentin + pregabalin
- Stabilises voltage-gated Na⁺ and Ca²⁺ channels, increase GABA synthesis
- Indications: epilepsy, neuropathic pain, management of addiction/withdrawal, GAD
- Caution: diabetes mellitus, elderly patients, may interfere with urinary protein tests
- Side effects: GI upset, dry mouth, flatulence, loss of appetite, gingivitis, weight gain, ↑BP, vasodilatation, oedema, SOB/cough, sensorimotor disturbances, leucopenia, joint and muscle pains, urinary incontinence, rashes and acne

6) Ethosuximide
- Blocks T-type Ca²⁺ channels ➔ effective specifically on absence seizures
- Caution: porphyria
- Side effects: GI upset, headache, fatigue, dizziness, hiccups, ataxia, impaired concentration, irritability/aggression, psychiatric disturbance, bone marrow suppression, lupus

NB! Use all antiepileptic drugs with caution in renal/hepatic impairment, pregnancy and breastfeeding.

It is vital to educate all patients about features of side effects and the importance of concordance.
Status Epilepticus

- Seizures lasting for >30 minutes, or repeated seizures (>3 in 1hr) with no intervening consciousness
- Mortality and risk of permanent brain damage increase with the length of the attack so aim to terminate seizures lasting more than a few minutes as soon as possible i.e. within 20 minutes
  - Total mortality is 5-10% in adults, 3% in children, will recur in a third of patients
  - Requires review of current anti-epileptic therapy to prevent further seizures

- Risk factors
  - History of epilepsy
  - Aged under 5 or elderly
  - Genetic predisposition
  - Mental handicap
  - Structural brain pathology (>50% chance of this if first presentation with status epilepticus)

- Potential precipitants: intercurrent illness, alcohol, withdrawal, hypoglycaemia, stroke

- Emergency seizure management should start as soon as the seizure starts: usually patients are before any action is taken

1) Make the patient comfortable
   - Ensure head is protected and there is no risk of falling objects
   - Carefully remove false teeth
   - Start treatment after a second seizure if seizures persist after repeated attempts with monotherapy

2) Open and maintain airway
   - e.g. oral or nasopharyngeal airway, intubation if necessary
   - Give oxygen if possible, start pulse oximetry monitoring

3) Assess cardiorespiratory function and start blood pressure monitoring
   - FBC, U+E, LFT, glucose, calcium, ABG, beta-hcG (could be eclampsia)
   - Tox screen if indicated
   - Anticonvulsant levels
   - Consider the possibility of non-convulsive status e.g. absence or continuous partial seizures

4) Establish IV access and take blood
   - First line: carbamazepine, lamotrigine, valproate, topiramate
   - Second line: clobazam, levetiracetam, oxcarbazepine, gabapentin, phenytoin
   - Anticonvulsant levels
   - Consider combination therapy if seizures persist after repeated attempts with monotherapy

5) Stabilise patient
   - Fluids for hypotension
   - Treat acidosis if severe
   - Unless blood glucose is known to be normal give 50ml IV glucose 50%
   - If alcoholism or malnourishment is suspected give IV thiamine (B1)
   - Give IV pyridoxine (B6) if caused by pyridoxine deficiency

6) Emergency drug therapy
   - Slow IV bolus lorazepam 4mg over 2min repeat once after 10-20 minutes
     - Effective and relatively long-lasting
     - Easy to administer if IV access has been established
   - Risk of cardiorespiratory arrest during last part of injection, causes CNS depression
   - Slow IV bolus diazepam (Diazemuls) 10mg over 2min repeat once after 15 minutes
     - Less long-lasting than lorazepam but stops seizures in 80-80%
     - Risk of significant respiratory depression
   - Buccal midazolam (Epistatus)
     - An easy to use oral alternative to lorazepam
   - Rectal midazepam or paraldehyde
     - Less socially acceptable, more effective in premonitory phase than in established seizures
     - May be the only option if IV access is not possible

7) If seizures continue...
   - IV/intraosseous phenytoin infusion 15mg/kg or fosphenytoin 15-20mg/kg
     - Requires blood pressure and ECG monitoring, don't give if already on phenytoin
     - and/or IV/intraosseous phenobarbitone 10-15mg/kg and PR paraldehyde if not used yet
     - (less preferred alternative: IV diazepam infusion 100mg in 500ml 5% dextrose)

8) If seizures continue >60-90mins → REFRACTORY status epilepticus → general anaesthesia
   - Thiopentone, propofol or midazolam titrated to effect
   - Anaesthesia maintained for 12-24hrs then dose tapered off

Management Strategies

<table>
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<th>WHAT WORKS?</th>
<th>tonic-clonic</th>
<th>absence</th>
<th>myoclonic</th>
<th>tonic</th>
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- Start treatment after a second seizure within 12 months of the first
  - Unless there is a structural brain lesion, neurological deficit, or unequivocal epileptic EEG
- The decision to start treatment should be made after a full discussion of the risks and benefits of treatment with the patient and their families/carers, allowing for symptoms, lifestyle and preference
- Use monotherapy wherever possible
  - If side effects become a problem, alter dose timings or try modified release preparations
  - If monotherapy with one drug fails, try monotherapy with another drug
  - Consider combination therapy if seizures persist after repeated attempts with monotherapy
- Avoid abrupt withdrawal of ineffective/intolerable drugs: start replacement drug and build it up to effective dose, then slowly taper off the unwanted drug
- Use of the newer anti-epileptic drugs may be considered if
  - Older anti-epileptic drugs are ineffective
  - Older anti-epileptic drugs are poorly tolerated/contraindicated or may interact with other drugs
  - The patient is a woman of childbearing age
- Drug interactions are common and many drugs have narrow therapeutic index → ALWAYS CHECK BNF
- Generalised tonic-clonic seizures
  - First line: carbamazepine, lamotrigine, valproate, topiramate
  - Second line: clobazam, levetiracetam, oxcarbazepine
- Absence seizures
  - First line: ethosuximide, valproate, lamotrigine
  - Second line: clobazam, clonazepam, topiramate
- Myoclonic seizures
  - First line valproate, consider lamotrigine, clobazam, clonazepam, levetiracetam, topiramate
- Focal +/- 2 generalisation
  - First line: carbamazepine, lamotrigine, valproate, oxcarbazepine, topiramate
  - Second line: gabapentin, phenytoin, clobazam, levetiracetam, tiagabine
- Follow-up
  - Make appropriate contraceptive arrangements for women of childbearing age
  - Regular medication reviews: effectiveness, side effects, concordance!
  - Blood tests every 2-4yrs: FBC, U+E, LFT, calcium, vitamin D; clotting if need surgery
  - Discuss potential of withdrawing treatment after 2 seizure-free years → patient decision
- Social implications of epilepsy
  - Driving: cannot drive for 1 year after first seizure (unless seizures only in sleep for last 3 years), cannot drive during treatment withdrawal or for 6 months thereafter
  - Work: implications for jobs that involve driving, manual jobs, dangerous jobs etc…