Notes on Epilepsy

Definition
Recurrent transient paroxysmal attacks of disturbed consciousness and sensorimotor function, resulting from abnormal electrophysiological discharges of cerebral neurons

Epidemiology
Incidence 500 / 100,000 of UK population (~37,000 people)
Age range extremes (congenital in kids / degeneration in elderly)
Sex distribution M:F → 1:1

Electrical activity spread of between cortical neurones is normally restricted. In seizures there is a failure of inhibitory synaptic contact between neurons → overall excitation of large groups of neurons. Each individual has a threshold for seizure activity. Some individuals have a low threshold → having seizures in response to flashing lights stimulus.

International League Against Epilepsy: Classification

1. GENERALISED
   a. TONIC CLONIC SEIZURES (GRAND MAL)
      • Vague warning → unconsciousness & generalised tonic-clonic convulsions
      • Tonic phase: body becomes rigid for up to a minute, pt utters a cry & then falls → serious injury sometimes, tongue usually bitten may be incontinence of urine or faeces
      • Clonic phase then begins: generalised convulsions, frothing at mouth and rhythmic jerking lasting secs → mins. Self-limiting → drowsiness, confusion or coma for several hrs
   b. TYPICAL ABSENCE SEIZURES (PETIT MAL)
      • Begins in childhood – developmental abnormality of neuronal growth
      • Brief episodes of unconsciousness with little or no motor component
      • Accompanied by 3Hz spike + wave ECG activity
      • Activity ceases, pt stares and is spaced out for a few secs. Interruption mid-sentence carries on as normal afterwards
      • Eyelids twitch, a few muscles may jerk
      • After attack, normal activity is resumed
      • Usually develop generalised tonic-clonic seizures in adult life.
   c. MYOCLONIC SEIZURES
      • Single/multiple sudden or uncontrollable isolated muscle jerking
      • JUVENILE MYOCLONIC EPILEPSY: Common, occurs b/t 8 & 26 yrs of age, but usually starts between 12 and 16. Girls > boys affected. 3 types of epilepsy can occur: Tonic-clonic (usually occurs AM within 1/2hrs of waking, lack of sleep), Myoclonic (soon after waking up & when getting dressed or at brekkie, can also occur in evening if tired), Absence (any time of the day, more in the morning)
   d. TONIC SEIZURES
      • Intense stiffening of body NOT followed by convulsive jerking
   e. ATONIC SEIZURES / AKINETIC SEIZURES / DROP ATTACKS
      • Sudden loss of tone with falling and LOC. May → severe injury from falls.

2. PARTIAL (FOCAL)
   An ‘aura’ describes effects of initial focal electrical events e.g. unusual smell, tingling in a limb or strange inner feeling usually recognised by pt as a WARNING SIGN
   a. SIMPLE PARTIAL SEIZURES (JACKSONIAN SEIZURES)
      • Originates in motor cortex
      • Typically begins at angle of mouth or in thumb & index finger spreading to the limbs on the side opposite epileptic focus (Jacksonian march pattern)
• Weakness of convulsive limbs for several hrs (Todd’s paralysis)
• No impairment of consciousness!

b. COMPLEX PARTIAL SEIZURES
• Impairment of consciousness
• Prodrome symptoms experiences: Changed hearing, Visual disturbances, Smell sensations, Mood changes, Muscle pain, Muscle tremor

TEMPORAL LOBE SEIZURES: simple or complex → feelings of unreality (jamais vu) or familiarity (déjà vu). May → absence attacks, vertigo, visual hallucinations
FRONTAL CORTEX: autonomic disturbances → piloerectin, flushing, overbreathing, strange smells
PARIETAL CORTEX: sensory disturbance. OCCIPITAL CORTEX: crude visual shapes

c. PARTIAL SEIZURES WITH 2º GENERALISED TONIC-CLONIC SEIZURES

3. UNCLASSIFIED
• Seizures that don’t fit in any of the categories

AETIOLOGY
A definite cause for the seizure is found in less than a third of patients

• Trauma / hypoxia / surgery: Post traumatic epilepsy in 2%. Perinatal trauma & fetal anoxia are common in childhood seizures. Hypoxic damage to hippocampi → childhood epilepsy. May get early epilepsy within a week of brain injury, or late epilepsy months / yrs later. 10% of neurosurgical ops on cerebral hemispheres → seizures.
• Genetic / developmental abnormalities: ~30% → 1st degree relative with seizure Hx. Inheritance mode uncertain. Generalized typical absence seizures: autosomal dominant with variable penetrance. Developmental abnormalities e.g. harmatomas, neuronal migration abnormalities.
• Pyrexia: can → febrile convulsions in pyrexic kids <5. Tend to be isolated cases NOT classed as epilepsy.
• Brain tumours / abscesses: cerebral tumours → 6%. Mass cortex lesions → epilepsy, (partial / secondary generalized seizures). Hydrocephalus also lowers the seizure threshold.
• Vascular: may follow cerebral infarctions (esp elderly) ~ 15% of seizures. A brain arteriovenous malformation may present with a seizure.
• Alcohol / drugs / drug withdrawal: Alcohol → ~ 6% - drinking heavily, withdrawal or alcohol induced hypoglycaemia. Phenothiazines, MAO inhibitors, tricyclic antidepressants, amfetamines, lignocaine, & nalidixic acid can → fits, (overdose/therapeutic levels). Anticonvulsant withdrawal.
• Encephalitis and inflammatory conditions: often presenting feature of encephalitis, cerebral abscess, cortical venous thrombosis, neurosyphilis, chronic meningitis (e.g. TB) & rarely bacterial meningitis.
• Metabolic abnormalities: hypoglycaemia, hypocalaemia, hyponatraemia, acute hypoxia, porphyria, uraemia, hepatocellular failure, mitochondrial disease.
• Degenerative brain disorders: e.g. Alzheimers, 3 times more common in MS
• Provoked seizures (e.g. photosensitivity): e.g. flashing lights, flickering TV, music
• Sleep deprivation: missing a nights sleep → seizure in susceptible people

DIAGNOSIS
• Confirm pt has epilepsy based on Hx and examination
• Do FBC, glucose, U & E’s LFT, ESR, CRP ? metabolic, infective or inflammatory cause
• EEG to investigate suspected epilepsy: ambulatory EEG, video telemetry → ? nature of attacks. Standard EEG, sleep EEG with special electrodes → ? type of epilepsy
• CT/MRI indications: if epilepsy after 20, EEG shows focal seizure type, seizures have focal features, difficult to control seizures → ? intracranial masses
DIFFERENTIAL DIAGNOSIS

1. HYPERVENTILATION & PANIC ATTACKS:
   - During stress periods
   - Altered awareness, dizziness and LOC
   - May get chest pain, dyspnoea, blurred vision, paraesthesia
   - Hyperventilation & palpitations, sweating, abdo discomfort
   - Occasionally similar pattern to TEMPORAL LOBE SEIZURES

2. BREATH-HOLDING ATTACKS
   - Occurs when child is angry
   - Period of crying → cessation of breathing
   - Cyanosis and child becomes limp & unresponsive
   - Trembling & few clonic movements
   - Persists for 2 mins → rapid recovery

3. DAY DREAMING
   - Can be mistaken for ABSENCE SEIZURES
   - Child however can be easily altered here

4. MIGRAINE
   - Syncope may occur when vomiting
   - Basilar Migraine may → LOC followed by headache. Differentiated on FH & brainstem symptoms
   - Migraine preceded by visual or sensory disturbance may be mistaken for PARTIAL SEIZURES

5. TIA
   - Weakness & sensory symptoms
   - TIA's usually last longer & there's rarely LOC
   - Sensory phenomenon may spread like Jacksonian march, not seen in TIA

6. TRANSIENT GLOBAL AMNESIA
   - Usually an isolated episode lasting several hrs
   - Pt unable to remember
   - Pt alert & communicative during the episode but may repeatedly ask the same question
   - Recovery afterwards normally complete

7. MOVEMENT DISORDERS
   - Tics and chorea sometimes confused with MYOCLONUS
   - Paroxysmal choreoathetosis → no LOC

8. HYPOGLYCAEMIA
   - Uncommon: pts with DM on insulin or oral hypoglycaemics, very rarely due to insulinoma
   - Usually pt gets warning signs of autonomic changes e.g. pallor, sweating, tachycardia
   - Loss of hypoglycaemic awareness / no warning signs → coma ensues → genuine seizures

9. VERTIGO
   - Often paroxysmal → epilepsy
   - Very occasionally is a symptom of an epileptic seizure particularly PARIETAL LOBE EPILEPSY

10. SYNCOPE / VASOVAGAL ATTACKS
    - LOC < 2 mins, recovery rapid
    - May → jerks
    - Cardiac arrhythmias e.g. Stokes-Adams attacks

11. NON-EPILEPTIC ATTACK (PSEUDOZEURSES)
    - Often resembles grand mal seizures
    - PROLACTIN levels however are normal here (↑ in a true grand mal)

12. FEBRILE CONVULSIONS
    - Occurs in children when there is a rapid ↑ in body temp.
TREATMENT

Seizure <5-10 minutes:
- Clear surrounding area
- Put into recovery position once it is over
- Observe for signs of breathing, aspiration, injury

1st seizure:
- If not confused or injured, no immediate action required Seek medical attention → Investigation
- If confused / injured: wait with them and reassure them; do not attempt to give fluids/food/drug
- Call ambulance

Known epileptic:
- If they recover from seizures: Wait with them until fully recovered, May be worth noting any triggers, patterns etc, ?Consider meds review
- If they don’t: MEDICAL EMERGENCY

Seizure >5-10 minutes:

IMMEDIATE TREATMENT
Treat and investigate source.

MEDICAL EMERGENCY:
- Immediate → resuscitative measures ABC: Airway maintained, oxygen given
- Control of seizure – anticonvulsant medication given
- Identification of underlying cause - ? hypoglycaemia, electrolyte/cardiac/biochemical monitoring

1. Premonitory phase
   - Diazepam (10-20mg iv or rectally) – can be repeated once 15 mins later if status still dangerous
   OR iv bolus clonazepam (1-2mg)

2. Early status
   - Lorazepam bolus (4mg iv) – repeat once if necessary, after 10 mins

3. Established status
   - Phenobarbitone bolus (10mg/kg 100mg/min) and/or phenytoin infusion (15mg/kg 50mg/min – ECG monitoring) – small risk of respiratory depression but can help obtain control

4. Refractory status
   - If seizures continue for >30 mins despite tx then general anaesthesia is given ( thiopentone iv bolus then infusion) – artificial ventilation is likely to be necessary – the anaesthetic dose shouldn’t be tapered until >12 hrs after last seizure – EEG monitoring must be done as ventilated pt will be paralysed with muscle relaxants so may not have observable seizures

LONG TERM MANAGEMENT

Anti-epileptic drugs (AEDs) – generally recommended after 2nd seizure
- Monotherapy where possible
- Review medication – aim to use minimum dose to maintain control and ideally seizure-free
- It may be possible for patients to come off medication (epilepsy remits in 70%) – obviously they need to have been well-controlled and seizure-free for some time
- Important to consider the implications for the patient – depends on individual, their lifestyle, needs etc – i.e. someone who relies on driving may not wish to risk losing their license etc.
THERE ARE 3 BASIC MECHANISMS FOR THE ACTION OF ANTIEPILEPTIC DRUGS:

1. **SUPPRESSION OF SODIUM INFLUX.** The AED binds to sodium channels when they are in the inactive state, thus prolonging the inactive state → ↓ ability of neurons to fire at high frequency. Seizures that depend on high frequency discharge are therefore suppressed. **Carbamazepine, phenytoin & lamotrigine** exert their main action in this way & are effective in limiting the spread of a discharge from a focus → Rx of partial & 2nd generalised seizures.

2. **SUPPRESSION OF CALCIUM INFLUX.** The AED acts by inhibiting influx of calcium ions through T-type Ca channels. These calcium channels generate T-currents which usually play a minimal role in action potential generation, but in some neurons in the hypothalamus, T-currents cause action potentials. **Absence seizures** are caused by ↑ firing of hypothalamic neurons &, thus, drugs that act by this mechanism are preferred for absence seizures. **Sodium valproate & ethosuximide** act in this way.

3. **POTENTIATION OF GAMMA-AMINOBUTYRIC ACID (GABA).** GABA is an inhibitory neurotransmitter that is widely distributed in the brain & causes a general ↓ in neuronal excitation. AEDs potentiate GABA, either by acting directly on GABA receptors (**Barbiturates e.g. phenobarbital**), by promoting GABA release (e.g. gabapentin) or by inhibiting the enzyme that degrades GABA (e.g. vigabatrin), **Benzodiazepines e.g. diazepam** (IV/rectal to control individual fits) & clonazepam (orally for prophylaxis usually taken with other drug) ↑ affinity of GABA for its receptor

---

### VALPROATE
- 1st line if unable to classify type of epilepsy
- Broad spectrum
- Recommended esp. for **generalised onset seizures**
- Fewer pharmacokinetic problems
- Fewer adverse effects
- CONCERNS – foetal damage

### CARBAMAZEPINE
- Good general choice
- Recomm. esp. for **partial seizures**
- But acts on P450 system - → interacts with OCP etc → many drug interactions
- Fewer side-effects than phenytoin
- Monitoring of levels helps determine optimum dose

### PHENYTOIN
- Narrow therapeutic window
- Significant variation in individual response
- Many drug interactions
- Zero order kinetics
- Monitoring of levels ESSENTIAL
- Avoid where possible

### LAMOTRIGINE
- Best-established of the newer generation drugs
- Broad spectrum
- Works for almost all forms of epilepsy
- Reasonable safety profile but:
  - Severe skin reactions in children
  - Blood disorders
  - Interaction with valproate
- Good choice for girls (i.e. re: pregnancy etc)
Surgery
Surgery is an option in pts where there is a definite site of seizure onset with highly localised focus. Occasionally it can be used to reduce symptoms is patients with intractable epilepsy. Only beneficial to a limited group of carefully selected patients:

- **focus** – surgery can only help where there is a specific site at which seizures always start
- **nature** – surgery always carries risk therefore the benefits need to be significant – usually patients with frequent, severe seizures, impacting on their QoL, despite treatment
- **area** – tests will be performed to accurately assess the area of brain involved and its function

<table>
<thead>
<tr>
<th>PROCEDURE</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective amygdalohippocampectomy</td>
<td>Removal of 2 structures in temporal lobe which are the sites of seizure activity. Sometimes only hippocampus is removed.</td>
</tr>
<tr>
<td>Temporal lobectomy</td>
<td>A larger part of the temporal lobe is removed - usually the right side as the left side of the temporal lobe controls speech</td>
</tr>
<tr>
<td>Sub-pial resection</td>
<td>Fine cuts are made in the motor areas of the brain -they don’t affect motor function but do prevent the spread of seizures</td>
</tr>
<tr>
<td>Hemispherectomy</td>
<td>Sometimes used to treat very severe epilepsy in children with damage to one whole side of the brain - the damaged side of the brain is removed</td>
</tr>
<tr>
<td>Corpus callosotomy</td>
<td>Also sometimes used to treat children with very severe epilepsy (Atonic drop attacks) - the operation involves sectioning the fibres that connect the two halves of the brain</td>
</tr>
<tr>
<td>Removal of a lesion e.g. tumour, cyst</td>
<td></td>
</tr>
</tbody>
</table>

**COMPLICATIONS OF EPILEPSY:**

- **Status Epilepticus** (recurring seizures, w/o pt regaining consciousness b/t attacks, for 30 mins or more. May → permanent brain damage & death due to prolonged hypoxia) A MEDICAL EMERGENCY!
- Injury: falls, bumps, self-inflicted bites, seizure while driving or operating machinery.
- Inhaling fluid into the lungs → aspiration pneumonia
- Permanent brain damage / Difficulty with learning.
- Many anti-epileptic medications cause birth defects - women wishing to become pregnant should alert their doctor in advance in order to adjust medications

**LIFESTYLE AND SOCIAL ISSUES**

- **Driving:** must inform DVLA when diagnosed. Generally → 1 year ban following a seizure (regardless of whether it occurs in the day or at night). Pt is then reviewed, & if they have been seizure free & are believed to be under good control then they will be allowed to drive again. If a person only has night seizures, they may be allowed to drive again even if they continue to have seizures. If a pt is withdrawing from AEDs, they are **advised** not to drive during the withdrawal period or for the next 6 months and if they do have a seizure, they will be banned for 1 yr again.
- **Employment** – UK Disability Discrimination Act – only the Armed Forces are completely banned (by law). Other jobs may be restricted due to health & safety regulations (e.g. pilots, drivers, work that could be hazardous to the person or risk harm to others etc) – advisable to disclose epilepsy although there is no legal obligation to do so – if it is not disclosed, employers will not be liable for any harm should the employee have a seizure
Leisure – being active does not provoke seizures and may even be beneficial – safety is the important consideration – people with epilepsy should never swim alone (or be around water), should not perform activities e.g. climbing while epilepsy is uncontrolled – most activities are ok as long as person is sensible & always has a companion who knows what to do should they have a seizure – potential hazards include television (photosensitive epilepsy), computers (rarely), video games, theme parks, night clubs and of course water, heights etc.

Pregnancy – many AEDs reduce the efficiency of the pill → need to consider type of medication & potentially other methods of contraception – also, when considering pregnancy, beneficial to have epilepsy under control before becoming pregnant (ideally) – need to think about medication/risks of malformation (give oral vit K a wk before deliver to preventneonatal haemorrhage causd by inhibition of transplacental transport) – after birth → breastfeeding is usually not a problem

Other – free prescription charges – exemption certificate FP92A (England)
Counselling – diagnosis of epilepsy can have substantial psychological impact – important to discuss with pt & family
Alcohol can provoke seizures so it may be necessary to provide advice and support on this
Epileptics shouldn’t be alone e.g. when having a bath, bathing/looking after a baby so it really can impact greatly upon everyday life

Please Note
These notes were compiled by Mona Zaky as a medical student in 2007. They are presented in good faith and every effort has been taken to ensure their accuracy. Nevertheless, medical practice changes over time and it is always important to check the information with your clinical teachers and with other reliable sources. Disclaimer: no responsibility can be taken by either the author or publisher for any loss, damage or injury occasioned to any person acting or refraining from action as a result of this information.

Please give feedback and report any inaccuracies or ambiguities to support@askdoctorclarke.com