Epilepsy

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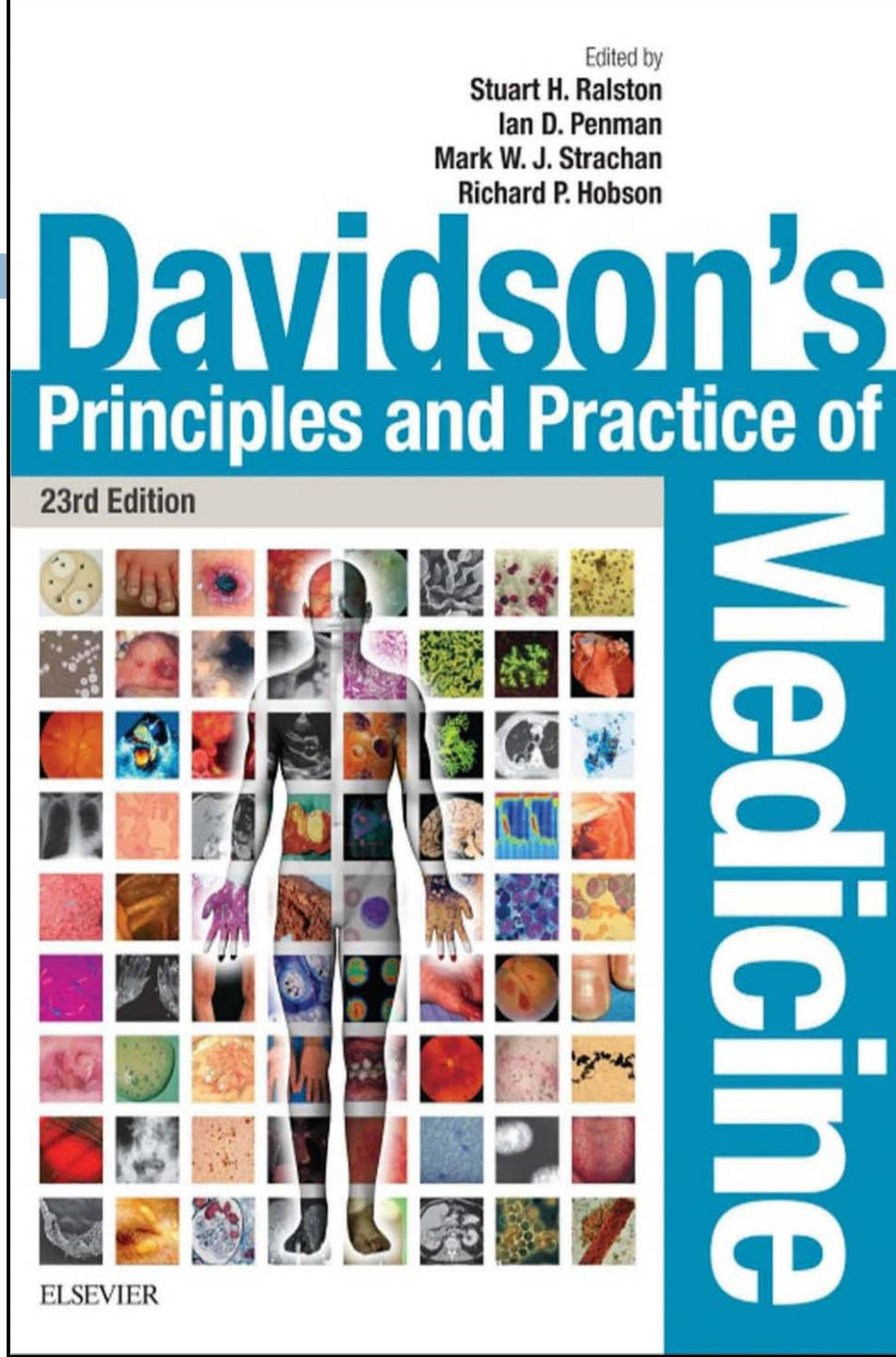
References :

- Davidson's Principles and practice of medicine-(22nd Edition)

- Davidson's Principles and practice of medicine-(23rd Edition)



What is seizure ??

- A seizure can be defined as the occurrence of signs and/or symptoms due to abnormal, excessive or synchronous neuronal activity in the brain.

- The lifetime risk of an isolated seizure is about 5%, although incidence is highest at the extremes of age.

What is epilepsy ??

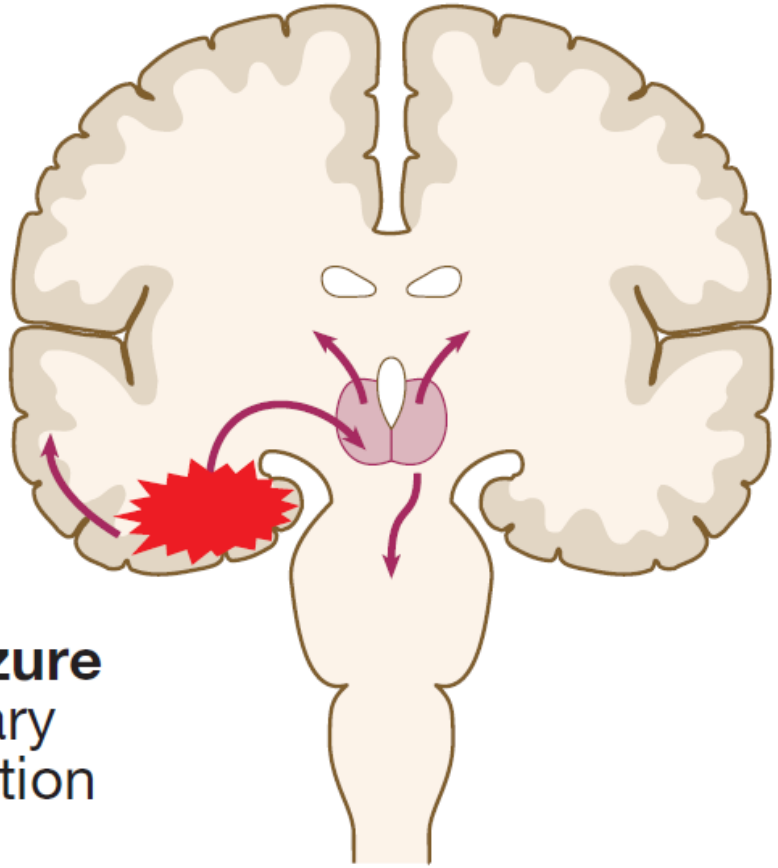
- ***Epilepsy is the tendency to have unprovoked seizures.***

- A recent change in definition allows the diagnosis of epilepsy to be made after a single seizure with a high risk of recurrence (e.g. a single seizure in the presence of a cortical lesion).

Pathophysiology

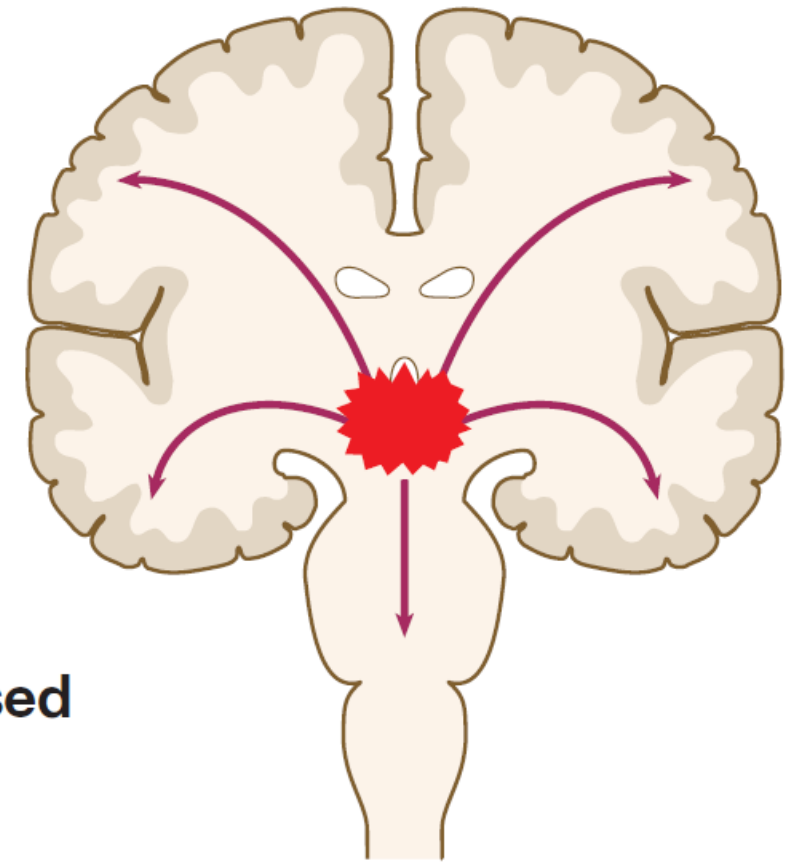
- To function normally, the brain must maintain a continual balance between excitation and inhibition, remaining responsive to the environment while avoiding continued unrestrained spontaneous activity.
- The inhibitory transmitter gamma-aminobutyric acid (GABA) is particularly important, acting on ion channels to enhance chloride inflow and reducing the chances of action potential formation. Excitatory amino acids (glutamate and aspartate) allow influx of sodium and calcium, producing the opposite effect.
- It is likely that many seizures result from an imbalance between this excitation and inhibition.

A focal seizure originates from a paroxysmal discharge in a focal area of the cerebral cortex (often the temporal lobe); the seizure may subsequently spread to the rest of the brain (secondary generalisation) via diencephalic activating pathways



Focal seizure
± secondary generalisation

In genetic generalised epilepsies (GGEs) the abnormal electrical discharges originate from the diencephalic activating system and spread simultaneously to all areas of the cortex.



Primary generalised seizure

Clinical features

- Patients can experience more than one type of seizure attack, and it is important to document each attack type and the patient's age at its onset, along with its frequency, duration and typical features.

- Any triggers should be identified.

What might trigger a seizure ??

- Sleep deprivation
- Missed doses of anti-epileptic drugs in treated patients
- Alcohol (particularly withdrawal)
- Recreational drug misuse
- Physical and mental exhaustion
- Flickering lights, including TV and computer screens (generalised epilepsy syndromes only)
- Intercurrent infections and metabolic disturbances
- Uncommon: loud noises, music, reading, hot baths
- Menstrual cycle (catamenial epilepsy)

EPILEPSY
TRIGGERS

- STRESS
- CHANGE IN MEDICATIONS
- CIGARETTES
- TV, COMPUTER
- ALCOHOL
- VIDEO GAMES
- BRIGHT LIGHT
- HORMONAL DISBALANCE

26.34 Classification of seizures (2010 ILAE Classification)

Generalised seizures

- Tonic–clonic (in any combination)
- Absence
  - Typical
  - Atypical
  - Absence with special features
- Myoclonic absence
- Eyelid myoclonia
- Myoclonic
  - Myoclonic
  - Myoclonic atonic
  - Myoclonic tonic
- Clonic
- Tonic
- Atonic

Focal seizures

- Without impairment of consciousness or awareness (was 'simple partial')
  - Focal motor
  - Focal sensory
- With impairment of consciousness or awareness (was 'complex partial')
- Evolving to a bilateral, convulsive seizure (was 'secondarily generalised seizure')
  - Tonic
  - Clonic
  - Tonic–clonic

Unknown

- Epileptic spasms

- Where activity remains focal, the classification will be obvious.

- With generalised tonic–clonic seizures, a focal onset will be heralded by positive neurological symptoms and signs corresponding to the normal function of that area. Occipital onset causes visual changes (lights and blobs of colour), temporal lobe onset causes false recognition (déjà vu), sensory strip involvement causes sensory alteration (burning, tingling), and motor strip involvement causes jerking.

Focal seizures

1 - Without impairment of consciousness or awareness (was 'simple partial'):

- Focal motor
- Focal sensory

Seizures arising from the anterior parts of the frontal lobe may produce bizarre behaviour patterns, including limb posturing, sleep walking or even frenetic, ill-directed motor activity with incoherent screaming.

Focal seizures

2 - Awareness may become impaired if spread occurs to the temporal lobes (previously 'complex partial seizure'). Patients stop and stare blankly, often blinking repetitively, making smacking movements of their lips or displaying other automatisms, such as picking at their clothes. After a few minutes consciousness returns but the patient may be muddled and feel drowsy for a period of up to an hour. The age of onset, preceding aura, longer duration and post-ictal symptoms usually make these easy to differentiate from childhood absence seizures .

Generalized seizures

- Tonic - clonic seizures (Grand Mal)
- Absence seizures (Petit Mal)
- Myoclonic seizures
- Atonic seizures
- Tonic seizures
- Clonic seizures

Tonic - clonic seizures

- An initial ‘aura’ may be experienced by the patient, depending on the cortical area from which the seizure originates .The patient then becomes rigid (tonic) and unconscious, falling heavily if standing (‘like a log’) and risking facial injury. During this phase, breathing stops and central cyanosis may occur.

- As cortical discharges reduce in frequency, jerking (clonic) movements emerge for 2 minutes at most.

- Afterwards, there is a flaccid state of deep coma, which can persist for some minutes, and on regaining awareness the patient may be confused, disorientated and/or amnesic.

Tonic - clonic seizures

- During the attack, urinary incontinence and tongue-biting may occur.

- A severely bitten, bleeding tongue after an attack of loss of consciousness is pathognomonic of a generalised seizure but less marked lingual injury can occur in syncope.

- Subsequently, the patient usually feels unwell and sleepy, with headache and myalgia.

Witnesses are usually frightened by the event, often believe the person to be dying, and may struggle to give a clear account of the episode. Some may not describe the tonic or clonic phase and may not mention cyanosis or tongue-biting. In less typical episodes, post-ictal delirium, or sequelae such as headache or myalgia, may be the main pointers to the diagnosis.

Absence seizures

- Rare after age 10 years.
- F > M.
- Brief loss of awareness many times a day. Triggered by hyperventilation.
- Remits in adulthood.
- EEG characteristic—3 Hz spike and wave, no photosensitivity.

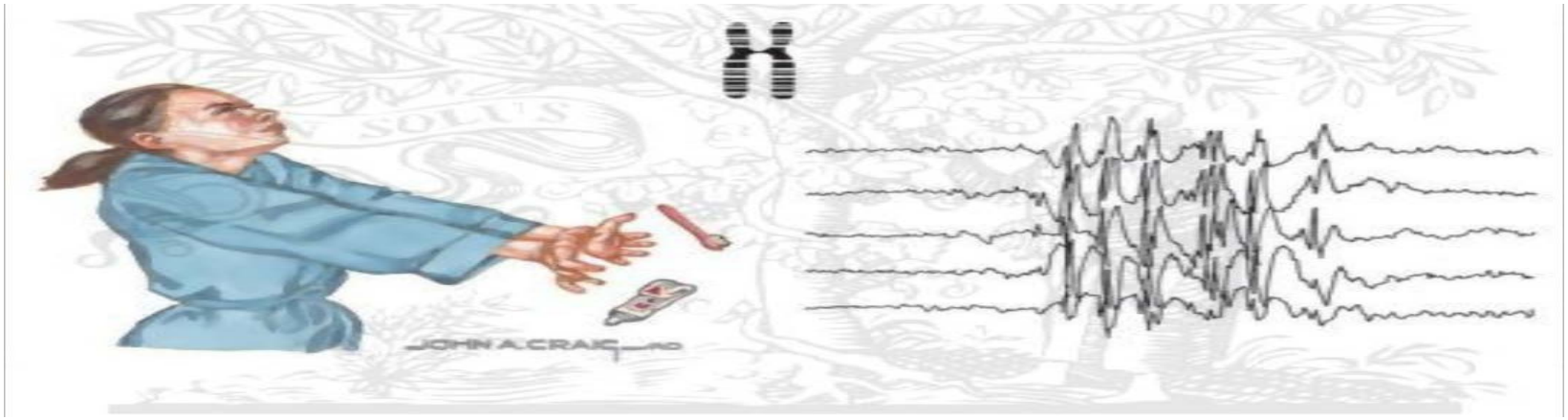
The attacks are rarely mistaken for focal seizures because of their brevity. They can occur so frequently (20–30 times a day) that they are mistaken for daydreaming or poor concentration in school.

Absence seizure

Myoclonic seizures

These are typically brief, jerking movements, predominating in the arms.

- In epilepsy, they are more marked in the morning or on awakening from sleep, and tend to be provoked by fatigue, alcohol, or sleep deprivation



Atonic seizures

- These are seizures involving brief loss of muscle tone, usually resulting in heavy falls with or without loss of consciousness. They occur only in the context of epilepsy syndromes that involve other forms of seizure.

Tonic seizures

- These are associated with a generalised increase in tone and an associated loss of awareness. They are usually seen as part of an epilepsy syndrome and are unlikely to be isolated.

Clonic seizures

- Clonic seizures are similar to tonic–clonic seizures.

- The clinical manifestations are similar but there is no preceding tonic phase.


Epilepsy
Syndromes
Lennox-Gastaut
Landau-Kleffner
Doose
Juvenile-Absence
Glut1-Deficiency
Lafora
Infantile-Spasms
Myoclonic-Absences
Dravet
Childhood
Ring-Chromosome-20
LGS
PCDH19
West's
Ohtahara
Rasmussen's
Myoclonic-Encephalopathy
Spike-and-Wave-During-Sleep
Juvenile-Myoclonic
TBCK
Hypothalamic-Hamartoma
Absence
Angelman
Frontal-Lobe-Epilepsy
EME
Rolandic
CDKL5
Panayiotopoulos
Temporal-Lobe

Epilepsy syndromes

- Many patients with epilepsy fall into specific patterns, depending on seizure type(s), age of onset and treatment responsiveness: the so-called electroclinical syndromes.

Common generalized epilepsy syndromes

25.33 Common generalised epilepsy syndromes

Syndrome	Age of onset	Type of seizure	EEG features	Treatment	Prognosis
Childhood absence epilepsy	4–8 years	Frequent brief absences	3/sec spike and wave	Ethosuximide Sodium valproate Levetiracetam	40% develop GTCS, 80% remit in adulthood
Juvenile absence epilepsy	10–15 years	Less frequent absences than childhood absence	Poly-spike and wave	Sodium valproate Levetiracetam	80% develop GTCS, 80% seizure-free in adulthood
Juvenile myoclonic epilepsy	15–20 years	GTCS, absences, morning myoclonus	Poly-spike and wave, photosensitivity	Sodium valproate Levetiracetam	90% remit with AEDs but relapse if AED withdrawn
GTCS on awakening	10–25 years	GTCS, sometimes myoclonus	Spike and wave on waking and sleep onset	Sodium valproate Levetiracetam	65% controlled with AEDs but relapse off treatment

(AED = antiepileptic drug; GTCS = generalised tonic–clonic seizure)

Investigations

- All patients with transient loss of consciousness should have a 12-lead ECG.

- Where seizure is suspected or definite, patients

should have cranial imaging with either MRI or CT, although

the yield is low unless focal signs are present.

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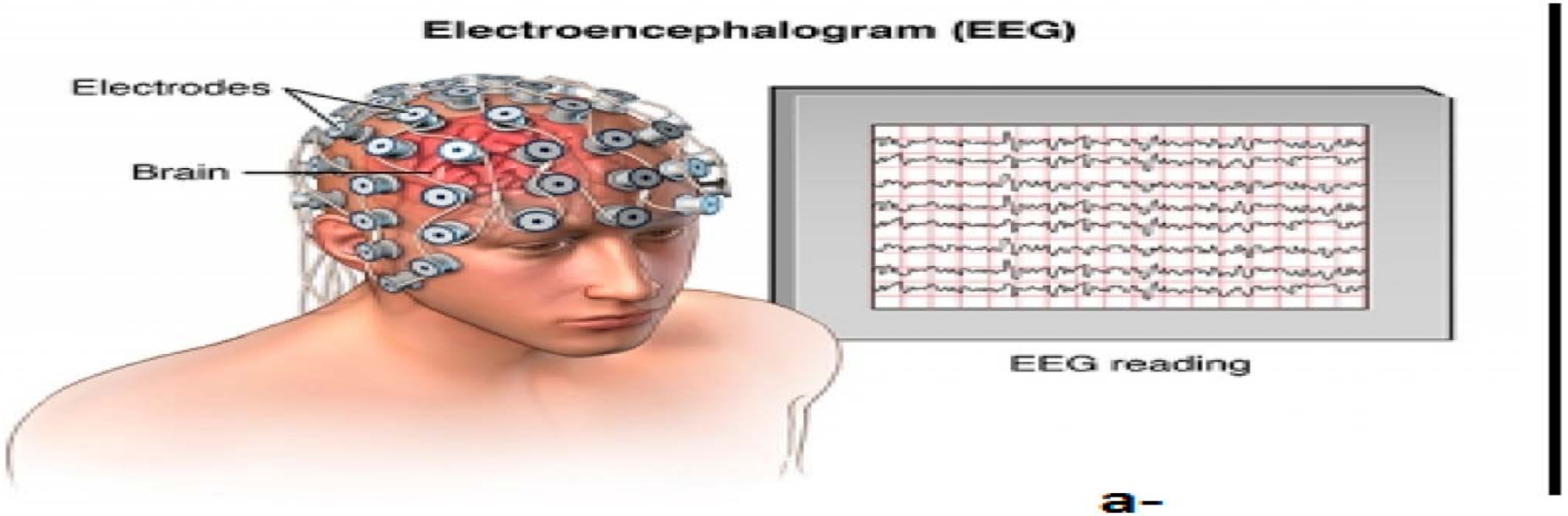
EEG

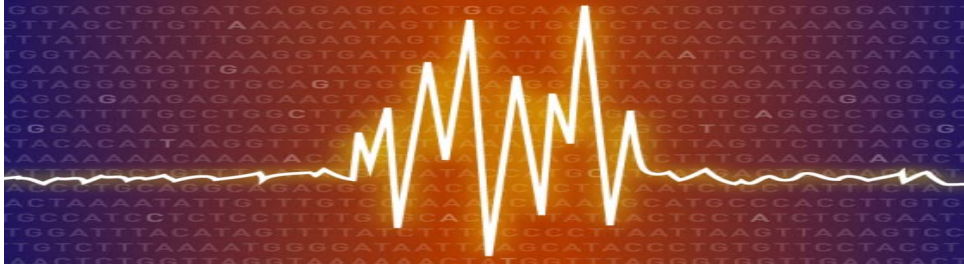
- The EEG may help to establish the type of epilepsy and guide therapy.

- An EEG performed immediately after a seizure may be more helpful in showing focal features than if performed after a delay.

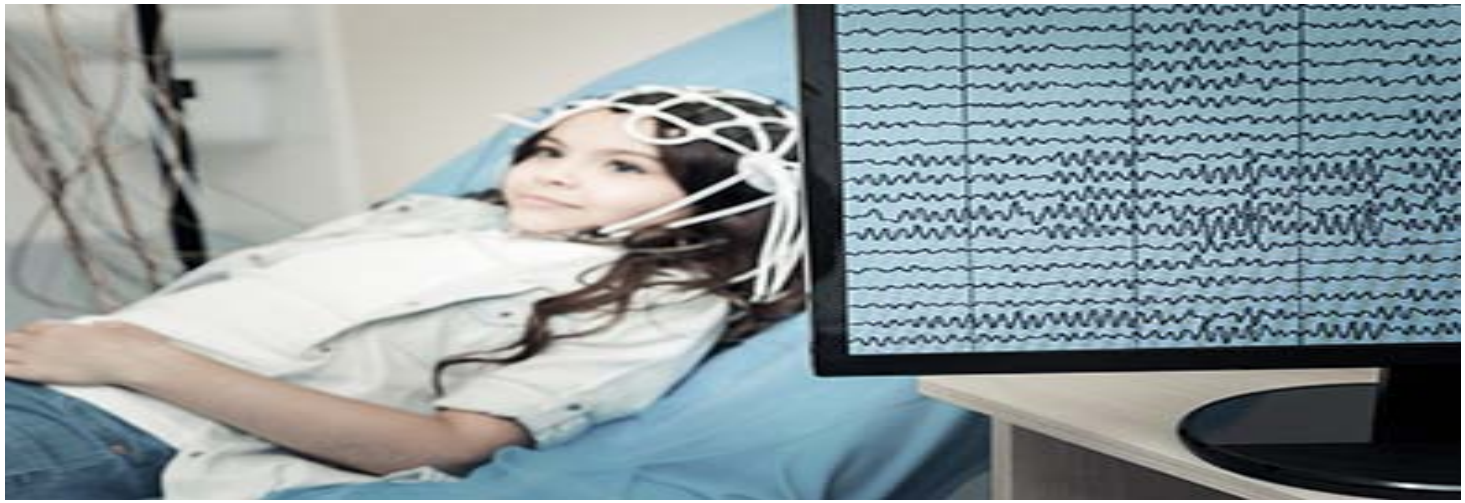
- Inter-ictal EEG is abnormal in only about 50% of patients with recurrent seizures, so it cannot be used to exclude epilepsy.



EEG



- Ambulatory EEG recording or video EEG monitoring may help with differentiation of epilepsy from other disorders if attacks are sufficiently frequent.



25.34 Investigation of epilepsy

From where is the epilepsy arising?

- Standard EEG
- Sleep EEG
- EEG with special electrodes (foramen ovale, subdural)

What is the cause of the epilepsy?

Structural lesion?

- CT
- MRI

Metabolic disorder?

- Urea and electrolytes
- Liver function tests
- Blood glucose
- Serum calcium, magnesium

Inflammatory or infective disorder?

- Full blood count, erythrocyte sedimentation rate, C-reactive protein
- Chest X-ray
- Serology for syphilis, HIV, collagen disease
- CSF examination

Are the attacks truly epileptic?

- Ambulatory EEG
- Videotelemetry

(CSF = cerebrospinal fluid; CT = computed tomography; EEG = electroencephalography; HIV = human immunodeficiency virus; MRI = magnetic resonance imaging)

Imaging

- Imaging cannot establish a diagnosis of epilepsy but identifies any structural cause.

- While CT excludes a major structural cause of epilepsy, MRI is required to demonstrate subtle changes such as hippocampal sclerosis, which may direct or inform surgical intervention.

25.35 Indications for brain imaging in epilepsy

- Epilepsy starting after the age of 16 years
- Seizures having focal features clinically
- Electroencephalogram showing a focal seizure source
- Control of seizures difficult or deteriorating

Management

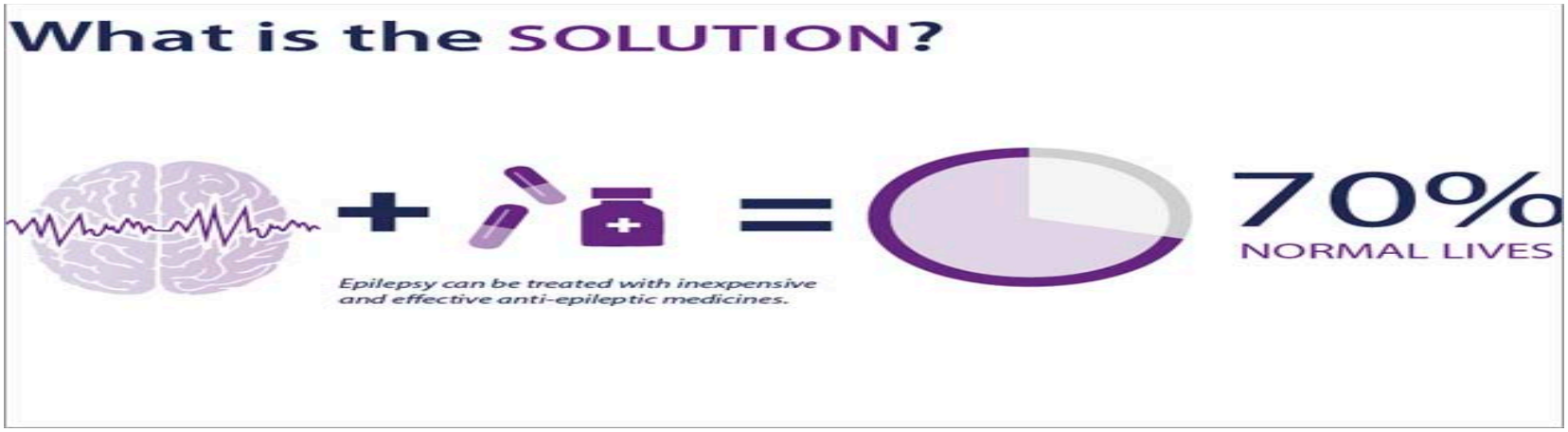
Management

- It is important to explain the nature and cause of seizures to patients and their relatives, and to instruct relatives in the first aid management of seizures.

- Many people with epilepsy feel stigmatized and may become unnecessarily isolated from work and social life.

Management

- It is important to emphasize that epilepsy is a common disorder that affects 0.5–1% of the population, and that full control of seizures can be expected in approximately 70% of patients.



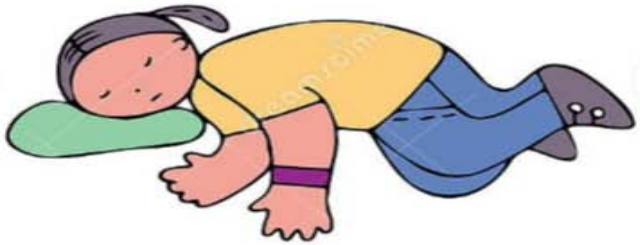
25.36 How to administer first aid for seizures

- Move the person away from danger (fire, water, machinery, furniture)
- After convulsions cease, turn the person into the 'recovery' position (semi-prone)
- Ensure the airway is clear but do **NOT** insert anything in the mouth (tongue-biting occurs at seizure onset and cannot be prevented by observers)
- If convulsions continue for more than 5 mins or recur without the person regaining consciousness, summon urgent medical attention
- Do not leave the person alone until fully recovered (drowsiness and delirium can persist for up to 1 hr)

SEIZURE FIRST AID

DONT HOLD

BLOCK HAZARDS



CUSHION THE HEAD

TIME THE SEIZURE

SPEAK CALMLY

EXPLAIN TO OTHERS

Antiepileptic drugs

- Antiepileptic drugs (AEDs) should be considered where risk of seizure recurrence is high.

- A diagnosis of two or more seizures is justification enough but a prolonged inter-seizure interval may deter some patients and physicians.

- Treatment decisions should always be shared with the patient, to enhance adherence. enhance adherance

Mechanism?

. These drugs either increase inhibitory neurotransmission in the brain or alter neuronal sodium channels to prevent abnormally rapid transmission of impulses ..

25.40 Guidelines for choice of antiepileptic drug[1]

Epilepsy type	First-line	Second-line	Third-line
Focal onset and/or secondary GTCS	Lamotrigine	Carbamazepine Levetiracetam Sodium valproate Topiramate Zonisamide Lacosamide	Clobazam Gabapentin Oxcarbazepine Phenobarbital Phenytoin Pregabalin Primidone Tiagabine
GTCS[2]	Sodium valproate Levetiracetam	Lamotrigine Topiramate Zonisamide	Carbamazepine Phenytoin Primidone Phenobarbital Acetazolamide
Absence[2]	Ethosuximide	Sodium valproate	Lamotrigine Clonazepam
Myoclonic[2]	Sodium valproate	Levetiracetam Clonazepam	Lamotrigine Phenobarbital

AED	Dose	Side-effects
Carbamazepine (SR form)*	Start 100 mg/day. ↑ at 2-week intervals 100–200 mg until control achieved. Usually 400–1600 mg/day	Rash, neutropenia, conduction defects, SIADH, numerous drug interactions. May make myoclonus worse. Liver enzyme inducing. Note COC
Sodium valproate	Start 200 mg bd, ↑ at 2-weekly intervals. Max 2.5 g/day. CR form available for od use	Rash, tremor, weight gain, hair loss, pancreatitis, menstrual changes (PCOS), ↓ platelets. ↑ NH_3, encephalopathy, hepatotoxicity, teratogenicity. ↓ IQ in offspring
Lamotrigine*	Start 25 mg/day as monotherapy; ↑ 50 mg 2–weekly. If adjunct to valproate, start 25 mg alternate days for 2 weeks, ↑ 25 mg 2-weekly. Maximum dose, 400 mg/day	Rash, especially with valproate. Multisystem allergic disorder, liver failure, aplastic anaemia
Topiramate	Start 25 mg/day; ↑ 25 mg 2-weekly. Maximum dose 400 g/day	Weight loss, memory problems, renal calculi, paraesthesiae
Levetiracetam	Start 250 mg/day, ↑ 2–weekly. Maximum dose 3 g/day	Weakness, irritability, mood swings. Rare: ↑ seizures
Phenytoin	Start 100 mg/day, then monitor levels to ↑ dose 2-weekly. Note: First-order kinetics—small dose increase → large changes in levels	Gum hypertrophy, acne, hirsutism, coarse facies, osteomalacia, ataxia

- ***Carbamazepine and valproate*** are accepted as first-line recommendations for partial (with or without 2° generalization) generalized seizures, respectively and

Lamotrigine is used for both types of seizures in women of child-bearing age

Withdrawing antiepileptic therapy

- Withdrawal of medication may be considered after a patient has been seizure-free for more than 2 years. Childhood-onset epilepsy, particularly classical absence seizures, carries the best prognosis for successful drug withdrawal.

- Other epilepsy syndromes, such as juvenile myoclonic epilepsy, have a marked tendency to recur after drug withdrawal.

- Focal epilepsies that begin in adult life are also likely to recur, especially if there is an identified structural lesion.

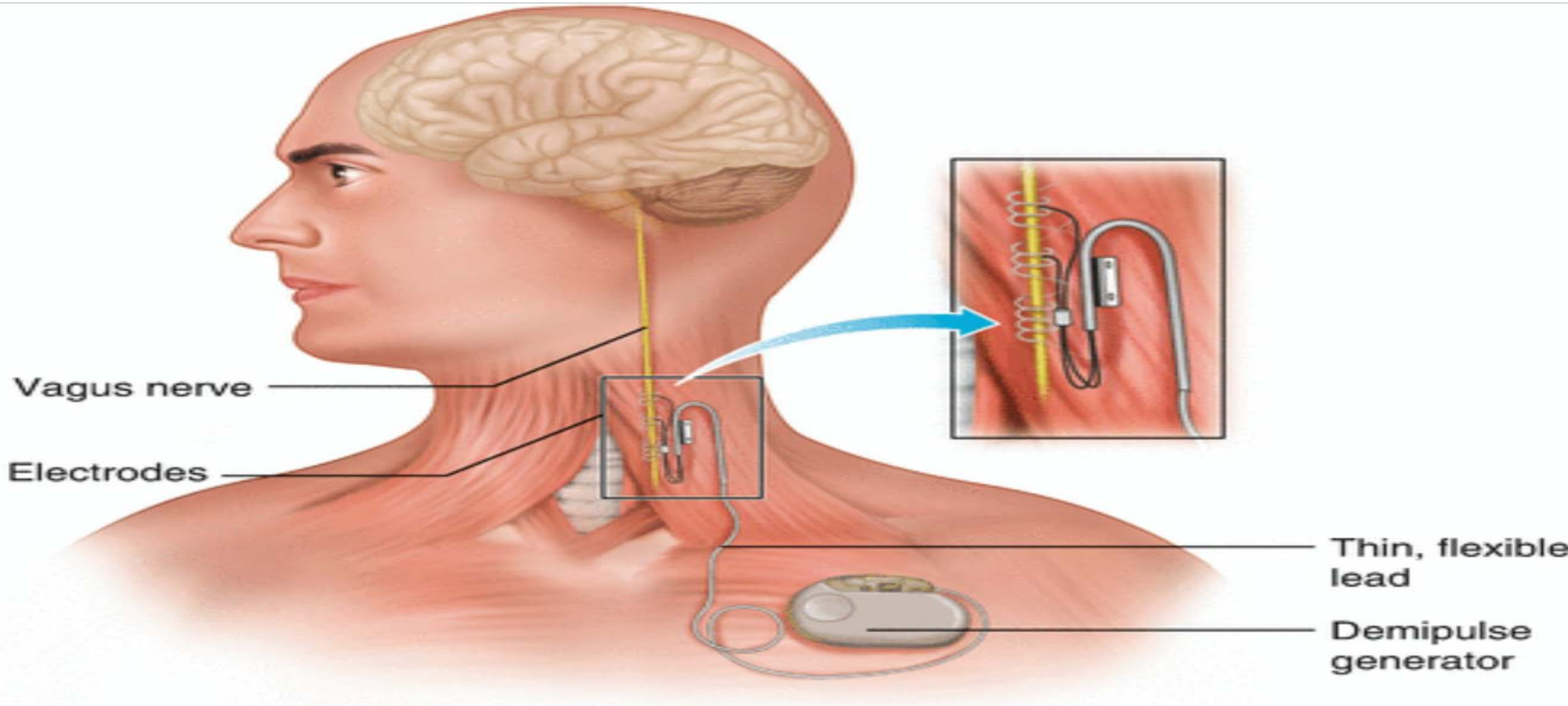
Surgery

Should be considered, and patients referred to a specialist centre, in cases with:

- surgically resectable lesion.
- temporal lobe seizures where there is evidence of mesial temporal sclerosis

Vagus nerve stimulation

- An option with no serious side-effects in those with refractory epilepsy, and unsuitable for surgery.

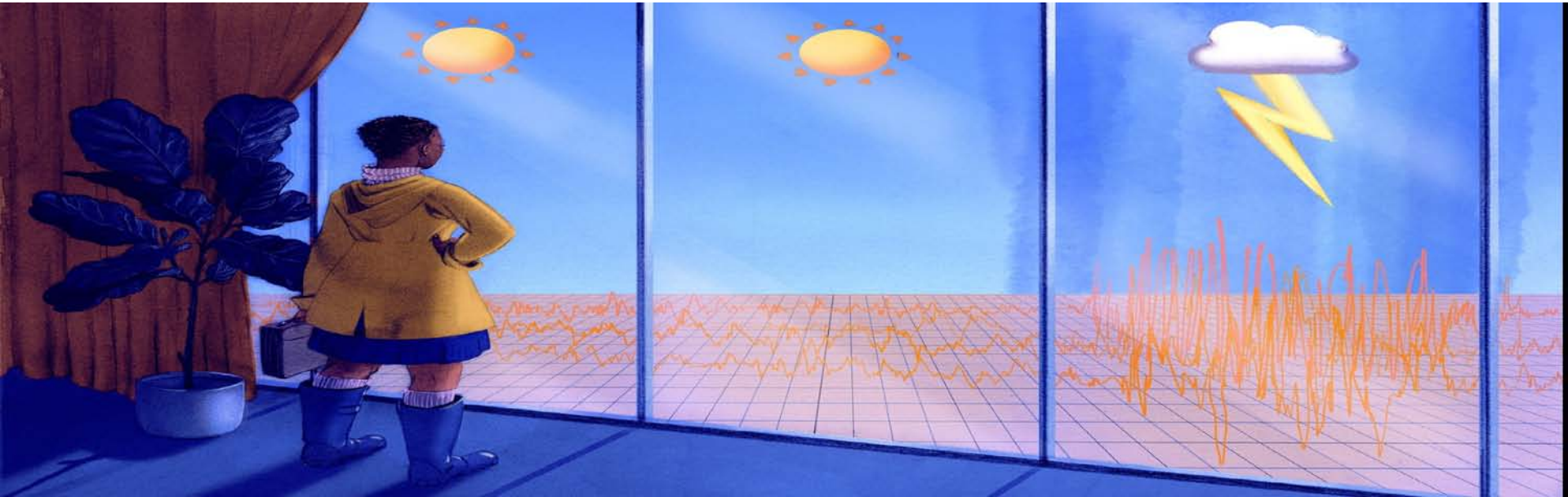


Status epilepticus

- A life-threatening neurological condition defined as ***5 minutes or more of either:***

1-continuous clinical and/or electrographic seizure activity; or

2-recurrent seizure activity without regaining consciousness in between.



Presentation

- More common in those with mental handicaps or structural lesions, especially children.

- In established epilepsy, recent medication reduction/withdrawal, intercurrent illness, metabolic derangement, or progressive disease should be considered.

- Ensure any withdrawn/reduced AEDs are restarted.

If no history of epilepsy consider the following:

- Febrile illness (children).
- Cerebral infections (e.g. encephalitis, meningitis).
- Space-occupying lesion (e.g. tumour, haematoma).
- Subarachnoid haemorrhage.
- Cerebrovascular disease—haemorrhagic/ischaemic infarcts.
- Metabolic derangement: d glucose, d Na, diCa++.
- Alcohol intoxication/withdrawal.
- Toxicity (e.g. cocaine, carbon monoxide, tricyclic antidepressants).
- Pseudo-status epilepticus—may have a previous history/normal EEG.

Complications of status epilepticus

Cerebral	Cardiorespiratory	Systemic
Cerebral oedema + ↑ ICP	Hyper/hypotension	Dehydration
Cerebral damage secondary to hypoxia, seizure, or metabolic derangement	Cardiac arrhythmias	Electrolyte derangement (especially ↓ glucose, ↓ Na, ↓ Mg, ↑ K)
Cerebral venous thrombosis	Cardiogenic shock	Metabolic acidosis
Cerebral haemorrhage and infarction	Cardiac arrest	Hyperthermia
	Hypoxia (often severe)	Rhabdomyolysis
	Aspiration pneumonia	Pancreatitis
	Pulmonary oedema	Acute renal failure (often acute tubular necrosis)
	Pulmonary embolism	Acute hepatic failure
	Respiratory failure	Disseminated intravascular coagulation
		Fractures

25.12 Management of status epilepticus

Initial

- Ensure airway is patent; give oxygen to prevent cerebral hypoxia
- Check pulse, blood pressure, BM stix and respiratory rate
- Secure intravenous access
- Send blood for:
  - Glucose, urea and electrolytes, calcium and magnesium, liver function, antiepileptic drug levels
  - Full blood count and coagulation screen
  - Storing a sample for future analysis (e.g. drug misuse)
- If seizures continue for >5 mins: give midazolam 10 mg bucally or nasally or lorazepam 4 mg IV if access available or diazepam 10 mg rectally or IV if necessary; repeat *once only* after 15 mins
- Correct any metabolic trigger, e.g. hypoglycaemia

25.12 Management of status epilepticus

Ongoing

If seizures continue after 30 mins

- IV infusion (with cardiac monitoring) with one of:
  - Phenytoin: 15 mg/kg at 50 mg/min
  - Sodium valproate: 20–30 mg/kg IV at 40 mg/min
  - Phenobarbital: 10 mg/kg at 100 mg/min
- Cardiac monitor and pulse oximetry:
  - Monitor neurological condition, blood pressure, respiration; check blood gases

If seizures still continue after 30–60 mins

- Transfer to intensive care:
  - Start treatment for refractory status with intubation, ventilation and general anaesthesia using propofol or thiopental
  - EEG monitor

Once status controlled

- Commence longer-term antiepileptic medication with one of:
  - Sodium valproate 10 mg/kg IV over 3–5 mins, then 800–2000 mg/day
  - Phenytoin: give loading dose (if not already used as above) of 15 mg/kg, infuse at <50 mg/min, then 300 mg/day
  - Carbamazepine 400 mg by nasogastric tube, then 400–1200 mg/day
- Investigate cause

Epilepsy and pregnancy

Effects of epilepsy on pregnancy

3 times increase in complications (bleeding, pre-eclampsia, miscarriage and still birth, IUGR, low birth weight, premature labour).

Seizure frequency

No effect in most patients. seizures increase usually in those with severe epilepsy.

Causes:

- hormonal effects (oestrogen may be epileptogenic, progesterone convulsant and anticonvulsant properties)
- Dilutional effect of increased plasma volume.
- Increased metabolism by liver, fetus, placenta.
- Decreased drug absorption due to, e.g. antacids, nausea/ vomiting;
- Fatigue, sleep deprivation, anxiety.

New-onset seizures in pregnancy

- Incidence of epilepsy at child bearing age 20–30/100 000. Chance development occurs due to factors listed earlier.
- Increased size of meningiomas, AVM, stroke, SAH, cerebral venous thrombosis.
- CT contraindicated but MRI is safe.
- **Pre-eclampsia and eclampsia:**
- most common cause of new onset seizures; pre-eclampsia (hypertension, proteinuria, oedema, liver dysfunction, impaired clotting); eclampsia (confusion, focal signs, seizures, coma). May progress to status epilepticus,
- treatment: magnesium sulfate IV 4g, followed by 10g IM. Then 5g IM every 4 hours as required.

- *Management during pregnancy*:

- Measurement of drug levels and dose is increased as necessary.
- Folic acid 5 mg.

- *Management during labour*

- Continue AED (IV if required).
- If high risk of seizures—clobazam 10–20 mg.
- If seizures occur during labour then caesarean section.

- Post partum

- Enzyme inducing AEDs decrease vitamin K-dependent clotting factors with risk of ICH in neonate.
- Give neonate 1 mg vitamin K at birth and at 28 days.
- Gradually reduce AED levels to prenatal doses.

Non-epileptic attack disorder
('dissociative attacks')

- Patients may present with attacks that resemble epileptic seizures but are caused by psychological phenomena and have no abnormal EEG discharges.

- Such attacks may be very prolonged, sometimes mimicking status epilepticus.

- Epileptic and non-epileptic attacks may coexist and time and effort are needed to clarify the relative contribution of each, allowing more accurate and comprehensive treatment.

Non-epileptic attack disorder ('dissociative attacks')

- Non-epileptic attack disorder (NEAD) may be accompanied by dramatic flailing of the limbs and arching of the back, with side-to-side head movements and vocalising. Cyanosis and severe biting of the tongue are rare but incontinence can occur. Distress and crying are common following non-epileptic attacks.

- The distinction between epileptic attacks originating in the frontal lobes and non-epileptic attacks may be especially difficult, and may require videotelemetry with prolonged EEG recordings.

- Non-epileptic attacks are three times more common in women than in men and have been linked with a history of past or ongoing life trauma. They are not necessarily associated with formal psychiatric illness.

18.20 Typical features of cardiac syncope, vasovagal syncope and seizures

	Cardiac syncope	Neurocardiogenic syncope	Seizures
Premonitory symptoms	Often none Lightheadedness Palpitation Chest pain Breathlessness	Nausea Lightheadedness Sweating	Confusion Hyperexcitability Olfactory hallucinations 'Aura'
Unconscious period	Extreme 'death-like' pallor	Pallor	Prolonged (> 1 min) unconsciousness Motor seizure activity* Tongue-biting Urinary incontinence
Recovery	Rapid recovery (< 1 min) Flushing	Slow Nausea Lightheadedness	Prolonged confusion (> 5 mins) Headache Focal neurological signs

*__N.B.__ Cardiac syncope can also cause convulsions by inducing cerebral anoxia.

26.13 How to differentiate seizures from syncope

	Seizure	Syncope
Aura (e.g. olfactory)	+	–
Cyanosis	+	–
Tongue-biting	+	–/+
Post-ictal confusion	+	–
Post-ictal amnesia	+	–
Post-ictal headache	+	–
Rapid recovery	–	+


Thank
You
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