Seizures and Epilepsy

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DEFINITION

- A chronic neurologic disorder manifesting by repeated seizures (attacks or fits) which caused by paroxysmal uncontrolled discharges of neurons within the central nervous system (gray matter disease).

- The clinical manifestations range from a major motor convulsion to a brief period of lack of awareness. The stereotyped and uncontrollable nature of the attacks is characteristic of epilepsy.

DEFINITION

- Seizure (Convulsion)
  - Clinical manifestation of synchronized electrical discharges of neurons

- Epilepsy
  - Present when 2 or more unprovoked seizures occur at an interval greater than 24 hours apart

DEFINITION

- Provoked seizures

  - Seizures induced by somatic disorders originating outside the brain (E.g. fever, infection, syncope, head trauma, hypoxia, toxins, cardiac arrhythmias)

- Status epilepticus (SE)

  - Continuous convulsion lasting longer than 30 minutes OR occurrence of serial convulsions between which there is no return of consciousness no regain consciousness

DEFINITION

- Idiopathic seizure:
  - Seizure develops in the absence of an underlying CNS lesion/insult

- Symptomatic seizure:
  - Seizure occurs as a result of an underlying neurological disorder or a metabolic abnormality

INTRODUCTION

- Incidence:

Approximately 45/100,000 per year

- Prevalence:

0.5-1% (2.5 million with epilepsy)

- 14 years or younger 13%
- 15 to 64 years most 63%
- 65 years and older 24%

- Cumulative risk of epilepsy: 1.3% - 3.1%
- Epilepsy refractory to AEDs: 20-30%

Aetiology of Seizures

1. Epilepsy
    - Idiopathic (70-80%)
    - Cerebral tumour
    - Neurodegenerative disorders
    - Neurocutaneous syndromes
    - Secondary to:
        - Cerebral damage: e.g. congenital infections, HIE, intraventricular haemorrhage
        - Cerebral dysgenesis/malformation: e.g. hydrocephalus

Aetiology of Seizures

2. Non-epileptic
   - Febrile convulsions
   - Metabolic
     - Hypoglycaemia, Hypocalcaemia,
     - Hypomagnesaemia, Hypernatremia and Hyponatremia
   - Head trauma
   - Meningitis
   - Encephalitis
   - Poisons/toxins

CNS infection

Pathogenesis

- The 19th century neurologist Hughlings Jackson suggested “a sudden excessive disorderly discharge of cerebral neurons“ as the causation of epileptic seizures.

- Recent studies in animal models of focal epilepsy suggest a central role for the excitatory neurotransmitter glutamate (increased) and inhibitory gamma aminobutyric acid (GABA) (decreased)

Pathophysiology

- Abnormal tissues — tumour, AVM, dead area

  only in CNS

  These regions of the brain may promote development of novel hyperexcitable synapses that can cause seizures

Pathophysiology

- Genetic factors
  - At least 20 %
    - Benign neonatal convulsions.
    - Juvenile myoclonic epilepsy.
    - Progressive myoclonic epilepsy.

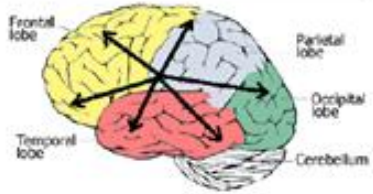
Classification of Seizures

Seizure Classification

Partial
Seizure activity starts in one area of the brain

1 area

Generalized
Seizure involves whole brain & consciousness is affected



Simple
Retains awareness

Complex
Altered awareness and behavior

Secondary generalisation (spreading from one area to the whole brain)

Tonic Clonic
"grand-mal" or convulsion
Loss of consciousness, stiffening of body then jerking of limbs

Absence
"petit mal" or staring fit or trance like state

Tonic or Atonic
"drop attack"
Abrupt fall, either with stiffening (tonic) or with loss of muscle tone (atonic or "astatic" attacks)

Myoclonic
Sudden muscle jerks

Classification

- The modern classification of the epilepsies is based upon the nature of the seizures rather than the presence or absence of an underlying cause.

- Seizures which begin focally from a single location within one hemisphere are thus distinguished from those of a generalised nature which probably commence in a deeper structures (brainstem) and project to both hemispheres simultaneously.

Seizures

Partial	Generalized
• Electrical discharges in a relatively small group of dysfunctional neurons in one cerebral hemisphere	• Diffuse abnormal electrical discharges from both hemispheres
• Aura may reflect site of origin hear - smell - visual warning	• No warning
• + / - LOC	• Always LOC

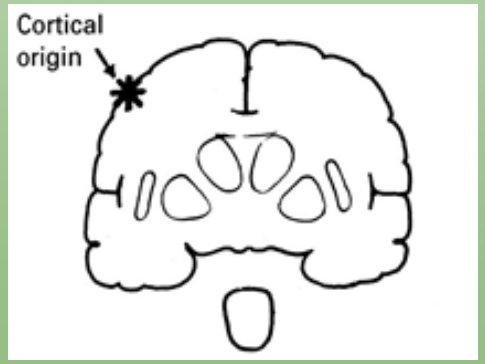
Partial Seizures

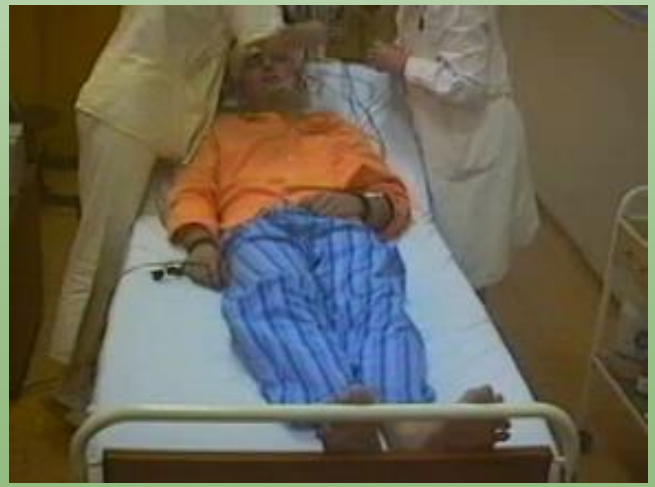
Simple	Complex	Secondary generalized
1. motor		
2. sensory	Simple partial --> altered consciousness	Simple partial --> complex partial --> generalized
3. autonomic		
4. psychic		

Focal (partial) seizures

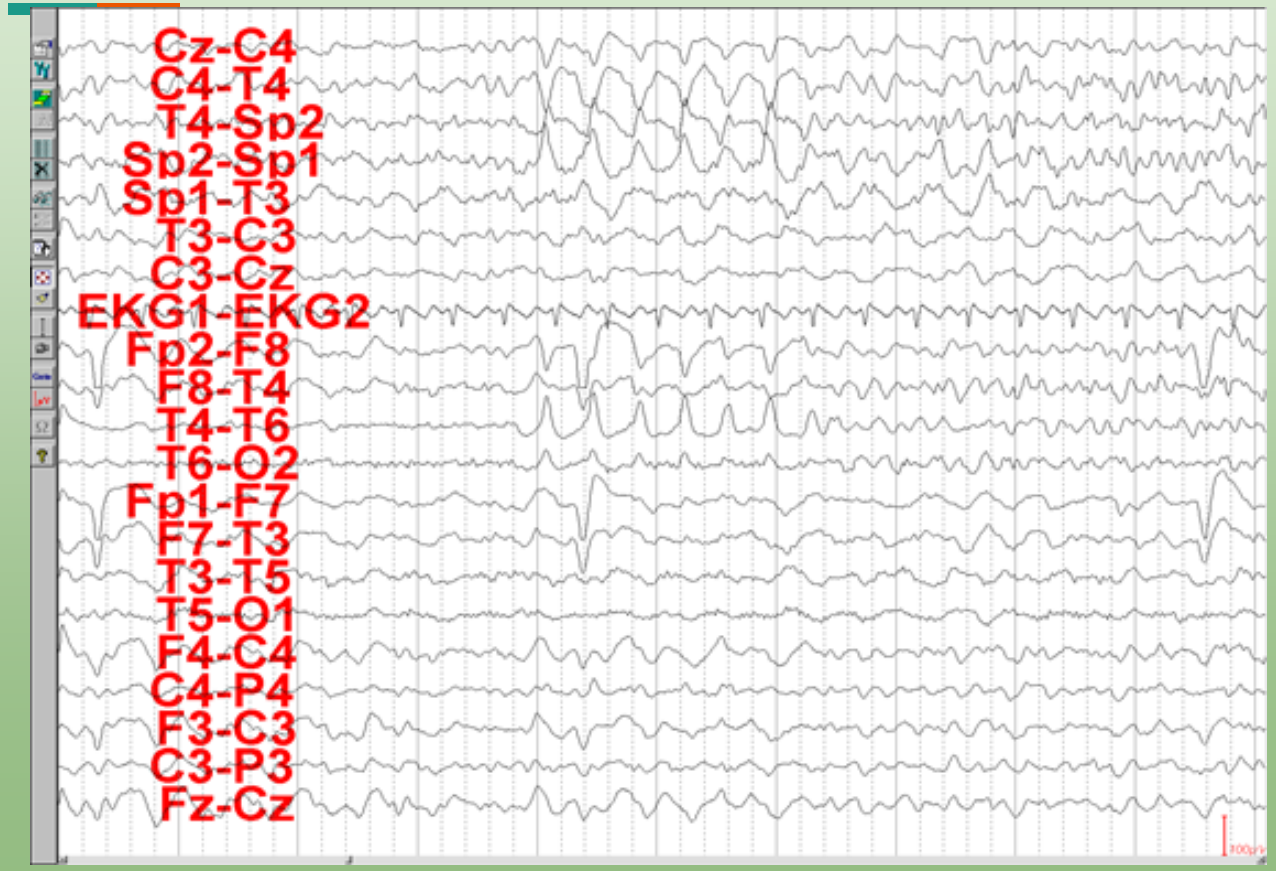
- Simple partial seizures

  Motor, sensory, vegetative or psychic symptoms *Typically consciousness is preserved*





EEG: Partial Seizure



Right temporal seizure with maximal phase reversal in the right temporal lobe

Simple partial seizures with motor signs

- Focal motor without march
- Focal motor with march

Simple partial seizures with sensory symptoms

- Visual
- Auditory
- Olfactory
- Gustatory
- Vertiginous

Simple partial seizures with autonomic symptoms

- Vomiting
- Pallor
- Flushing
- Sweating
- Pupil dilatation
- Piloerection
- Incontinence

Simple partial seizures with psychic symptoms

- Dysphasia
- Dysmnesic
- Cognitive
- Affective
- Illusions
- Structured hallucinations

- Dysmnesic symptoms “déjà-vu”
- Affective symptoms
  - fear and panic
- Cognitive
- Structured hallucination
  - living through a scene of her former life again

Complex Partial Seizures

- Simple partial onset followed by impaired consciousness

Partial seizures evolving to secondarily generalized seizures

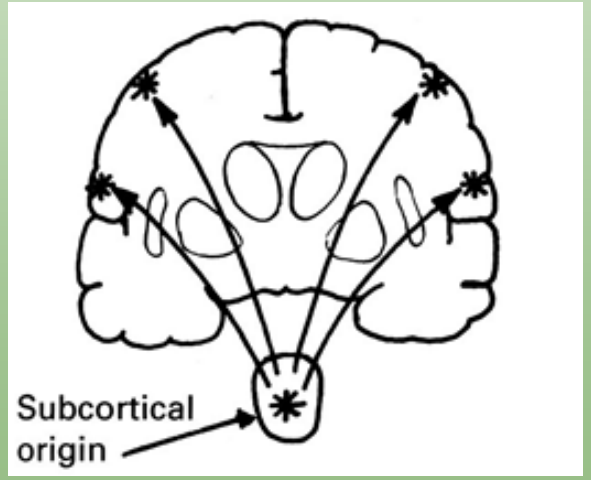
- Simple Partial Seizures to Complex Partial Seizures to Generalized Seizures

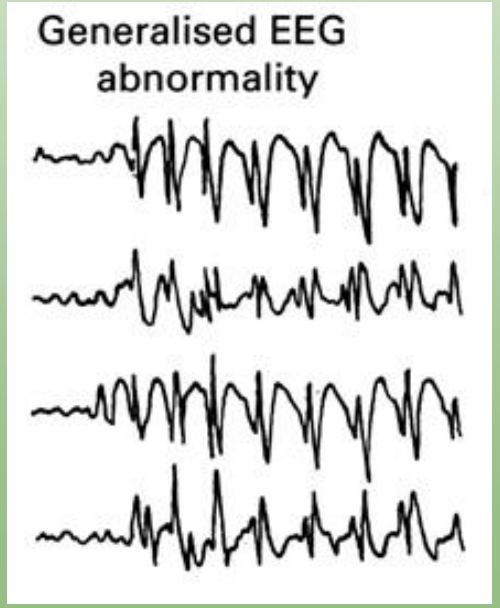
Generalized Seizure

- Absence
- Myoclonic
- Clonic
- Tonic
- Tonic-clonic
- Atonic

Generalized Seizures (convulsive or non-convulsive)

- Absences
- Myoclonic seizures
- Clonic seizures
- Tonic seizures
- Atonic seizures





Absence seizures

- Sudden onset
- Interruption of ongoing activities
- Blank stare
- Brief upward rotation of eyes
- Few seconds to 1/2 minute
- Evaporates as rapidly as it started
- Stops hyperventilating
- Mild eyelid clonus
- Slight loss of neck muscle tone
- Oral automatisms

Myoclonic seizures

- Sudden, brief, shock-like
- Predominantly around the hours of going to or awakening from sleep
- May be exacerbated by volitional movement (action myoclonus)
- Symmetrical myoclonic jerks
- Family history
- Photo convulsion

Tonic-clonic seizures (grand mal)

Tonic_Phase

- Sudden sharp tonic contraction of respiratory muscle: stridor / moan
  - Falls
  - Respiratory inhibition cyanosis
  - Tongue biting
  - Urinary incontinence

Clonic_Phase

- Small gusts of grunting respiration
- Frothing of saliva
- Deep respiration
- Muscle relaxation
- Remains unconscious
- Goes into deep sleep
- Awakens feeling

Tonic-clonic seizures

- Tonic stretching of arms and legs
- Twitches in his face and body
- Purses his lips and growls
- Clonic phase

Atonic seizures

- Sudden reduction in muscle tone (drop attack)
- Atonic head drop

Epilepsy Syndrome

- Epilepsy syndromes may be classified according to:
  - Whether the associated seizures are partial or generalized
  - Whether the etiology is idiopathic or symptomatic/ cryptogenic
  - Several important pediatric syndromes can further be grouped according to age of onset and prognosis

- EEG is helpful in making the diagnosis

- Children with particular syndromes show signs of slow development and learning difficulties from an early age

Three most common epilepsy syndromes

1. Benign childhood epilepsy
2. Childhood absence epilepsy
3. Juvenile myoclonic epilepsy

Three devastating catastrophic epileptic syndromes

1. West syndrome
2. Lennox-Gastaut syndrome
3. Landau Kleffner Syndrome

Benign Childhood Epilepsy with Centrotemporal Spike (Benign Rolandic Epilepsy)

1. Typical seizure affects mouth, face, +/- arm. Speech arrest if dominant hemisphere, consciousness often preserved, may generalize especially when nocturnal, infrequent and easily controlled
2. Onset is around 3-13 years old, good respond to medication, always remits by mid-adolescence

West’s Syndrome (Infantile Spasms)

Triad:

1. infantile spasms
2. arrest of psychomotor development
3. hypsarrhythmia

- Spasms may be flexor, extensor, lightning, nods, usually mixed. Peak onset 4-7 months, always before 1 year.

Lennox-Gastaut Syndrome

- Characterized by seizure, mental retardation and psychomotor slowing

Three main type:

- tonic
- atonic
- atypical absence

Landau- Kleffner Syndrome (acquired aphasia)

Diagnosis in Epilepsy

Aims:

- Differentiate between events mimicking epilepsy (syncope, vertigo, migraine, psychogenic non-epileptic seizures)

- Confirm the diagnosis of seizure (or possibly associated syndrome) and the underlying etiology

Differential Diagnosis

- Syncope attacks
- Cardiac arrhythmias
- Migraine
- Hypoglycemia
- Narcolepsy
- Panic attacks
- PSEUDOSEIZURES

Diagnosis in Epilepsy

Approach:

- History (from patient and witness)
- Physical examination
- Investigations

History

- Event
  - Localization
  - Temporal relationship
  - Factors
  - Nature
  - Associated features

- Past medical history
- Developmental history
- Drug and immunization history
- Family history
- Social history

Physical Examination

- General
  - esp. syndrome or non-syndromal dysmorphic features, neurocutaneous features
- Neurological
- Other system as indicated
  - E.g. Febrile convulsion, infantile spasm

Investigation

- Routine investigation: Haematology, biochemistry chest X-ray and toxicology
- electroencephalogram (EEG).Neuroimaging (CT/MRI) should be performed in all persons aged 25 or more presenting with first seizure and in those pts. with focal epilepsy irrespective of age.
- Specialised neurophysiological investigations: Sleep deprived EEG, video-EEG monitoring.
- Advanced investigations): Semi Invasive or invasive EEG recordings, MR Spectroscopy, Positron emission tomography (PET) and ictal Single photon emission computed tomography (SPECT)

Electroencephalography (EEG)

- EEG indicated whenever epilepsy suspected
- Uses of EEG in epilepsy
  - Diagnostic: support diagnosis, classify seizure, localize focus, quantify
  - Prognostic: adjust anti-epileptic treatment

International 10-20 System of Electrode Placement in EEG

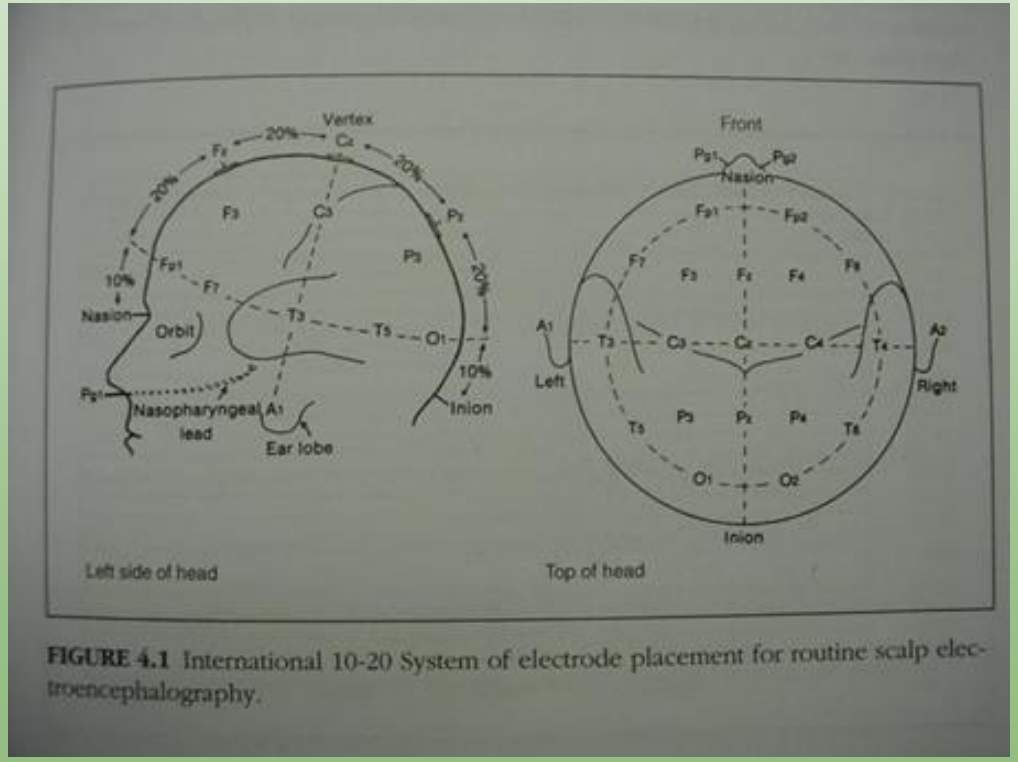


FIGURE 4.1 International 10-20 System of electrode placement for routine scalp electroencephalography.

Electroencephalography (EEG)

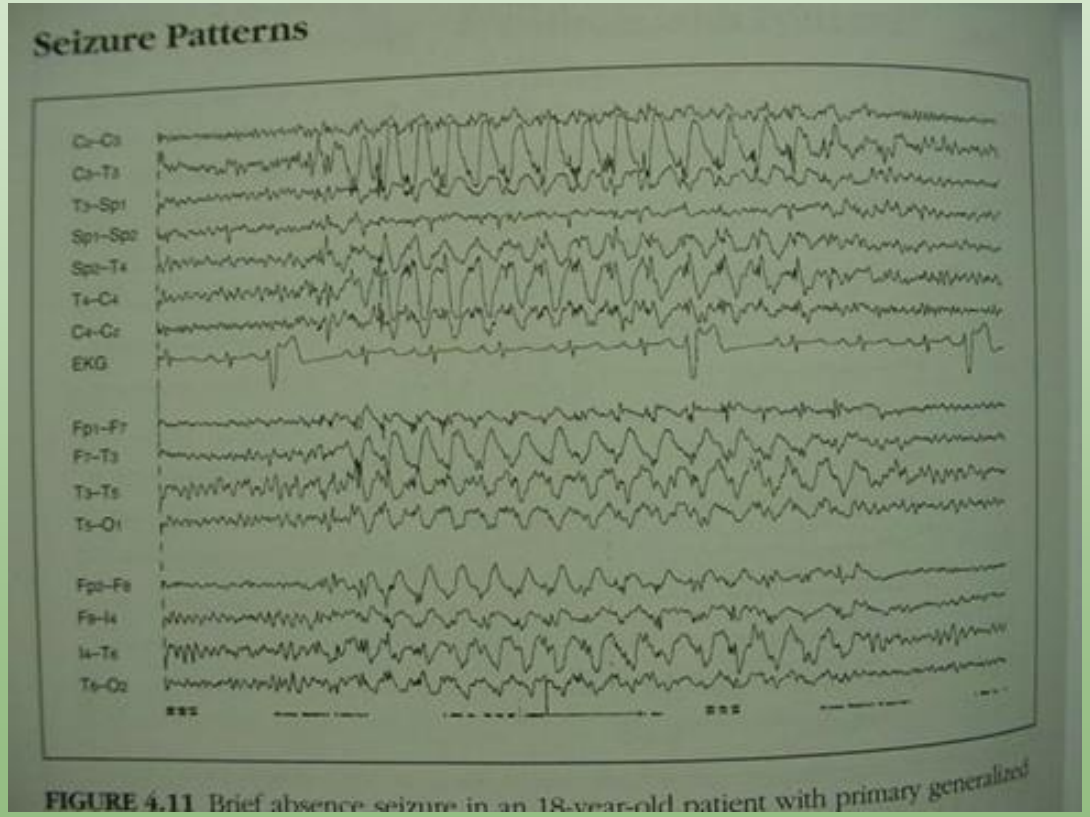


FIGURE 4.11 Brief absence seizure in an 18-year-old patient with primary generalized

Electroencephalography (EEG)

- Normal in 10-20% of epileptic patients
- Background slowed by:
  - AED, diffuse cerebral process, postictal state
- Artifact from:
  - Eye rolling, tremor, other movement, electrodes

False positive reading

Neuroimaging

- Structural neuroimaging
- Functional neuroimaging

Structural Neuroimaging

- Who should have a structural neuroimaging?

  - Status epilepticus or acute, severe epilepsy
  - Develop seizures when > 20 years old
  - Focal epilepsy (unless typical of benign focal epilepsy syndrome)
  - Refractory epilepsy
  - Evidence of neurocutaneous syndrome

Structural Neuroimaging

- Modalities available:
  - Magnetic Resonance Imaging (MRI)
  - Computerized Tomography (CT)
- What sort of structural scan?
  - MRI better than CT
  - CT usually adequate if to exclude large tumor
  - MRI not involve ionizing radiation
    - I.e. not affect fetus in pregnant women (but nevertheless avoided if possible)

Functional Neuroimaging

Principles in diagnosis of epilepsy

- When a region of brain generates seizure, its regional blood flow, metabolic rate and glucose utilization increase
- After seizure, there is a decline to below the level of other brain regions throughout the interictal period

Functional Neuroimaging

- Modalities available:
  - Positron Emission Tomography (PET)
  - Single Photon Emission Computerized Tomography (SPECT)
  - Functional Magnetic Resonance Imaging (fMRI)
- Mostly used in:
  - Planning epilepsy surgery
  - Identifying epileptogenic region
  - Localizing brain function

Venn Diagram

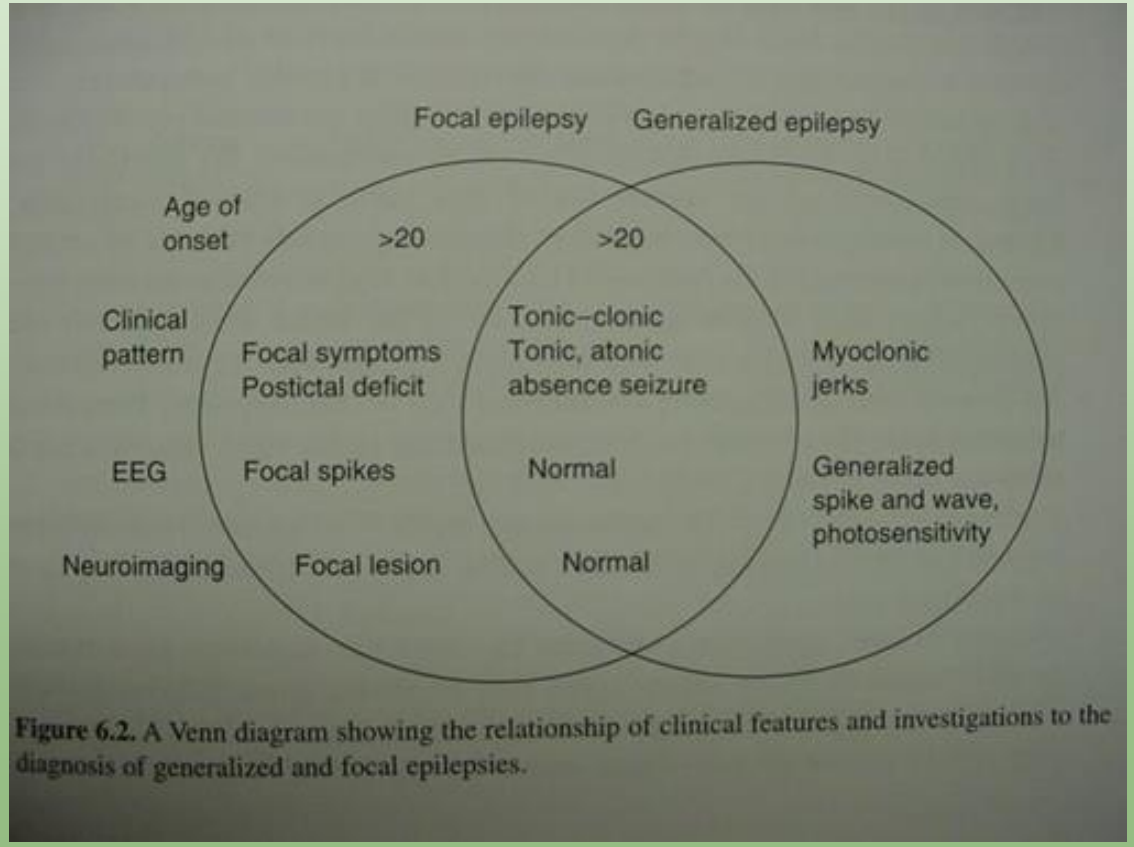
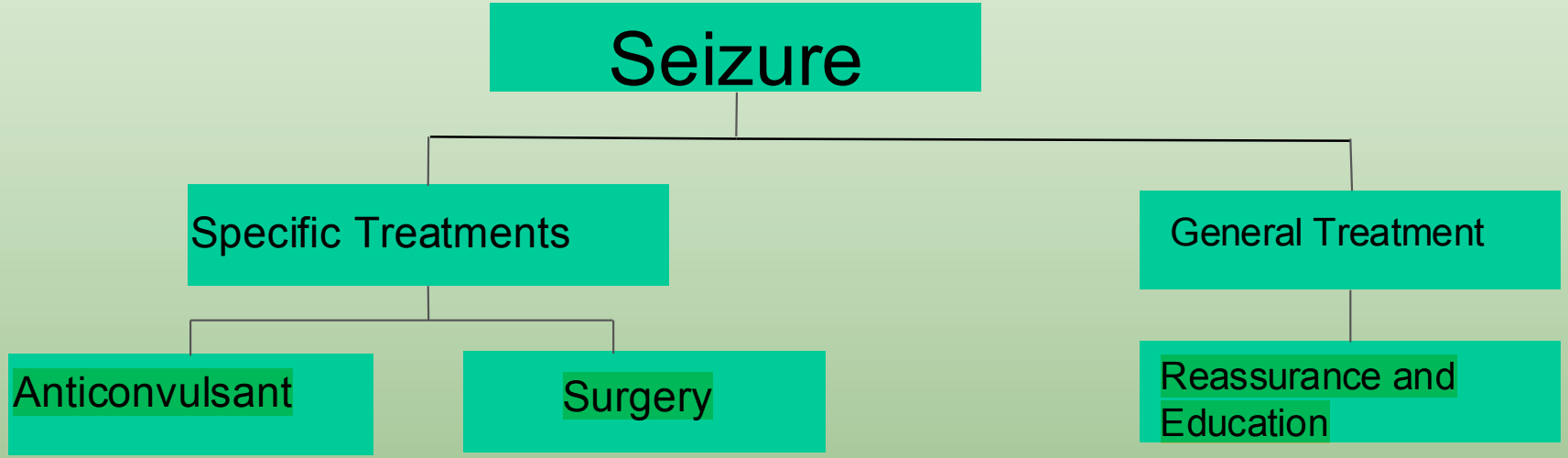


Figure 6.2. A Venn diagram showing the relationship of clinical features and investigations to the diagnosis of generalized and focal epilepsies.

Seizure Therapy



Education & Support

- Information leaflets and information about support group
- Avoidance of hazardous physical activities
- Management of prolonged fits
  - Recovery position
  - Rectal diazepam relive attack
- Side effects of anticonvulsants

Treatment

- The majority of pts respond to drug therapy (The treatment target is seizure-freedom and improvement in quality of life)
- The commonest drugs used in clinical practice are: Carbamazepine, Sodium valproate, Lamotrigine (first line drugs) Levetiracetam, Topiramate, Pregabaline (second line drugs)
- Basic rules for drug treatment: Drug treatment should be simple, preferably using one anticonvulsant (monotherapy). “Start low, increase slow“. Add-on therapy is necessary in some patient

Treatment

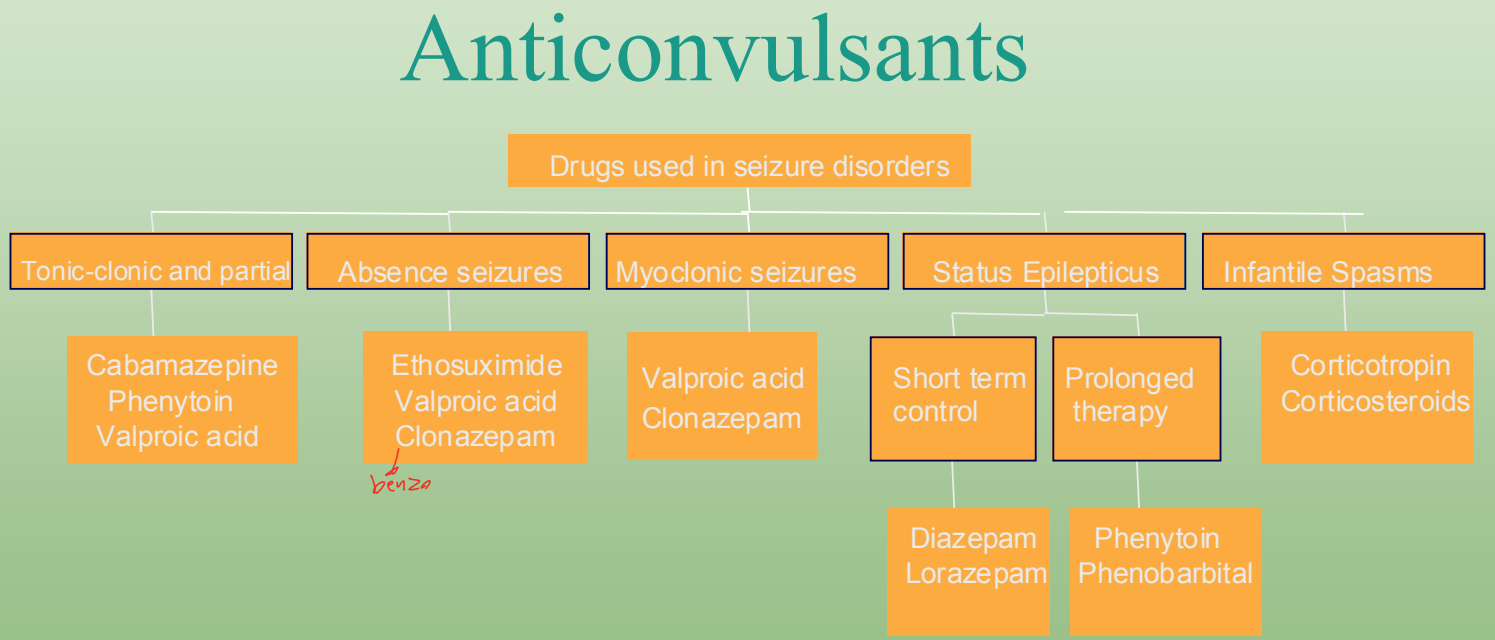
- If patient is seizure-free for three years, withdrawal_of_pharmacotherapy should be considered. Withdrawal should be carried out only if patient is satisfied that a further attack would not ruin employment etc. (e.g. driving license). It should be performed very carefully and slowly! 20% of pts will suffer a further sz within 2 yrs.
- The risk of teratogenicity is well known (~5%), especially with valproates, but withdrawing drug therapy in pregnancy is more risky than continuation. Epileptic females must be aware of this problem and thorough family planning should be recommended. Over 90% of pregnant women with epilepsy will deliver a normal child.

Anticonvulsants

Suppress repetitive action potentials in epileptic foci in the brain

- Sodium channel blockade
- GABA-related targets
- Calcium channel blockade
- Others: neuronal membrane hyperpolarisation

Anticonvulsants



Adverse Effects

- Teratogenicity
  - Neural tube defects
  - Fetal hydantoin syndrome
- Over dosage toxicity
- Life-threatening toxicity
  - Hepatotoxicity
  - Stevens-Johnson syndrome
- Abrupt withdrawal → seizure

Medical Intractability

- No known universal definition
- Risk factors
  - High seizure frequency
  - Early seizure onset
  - Organic brain damage
- Established after adequate drug trials
- Operability

Surgery

- Curative (Resection)
- Palliative
  - Vagal nerve stimulation

Aetiology of Status Epilepticus

- Idiopathic status epilepticus
  - Non-compliance to anticonvulsants
  - Sudden withdrawal of anticonvulsants
  - Sleep deprivation
  - Intercurrent infection
- Symptomatic status epilepticus
  - Anoxic encephalopathy
  - Encephalitis, meningitis
  - Congenital malformations of the brain
  - Electrolyte disturbances, drug/lead intoxication, extreme hyperpyrexia, brain tumour

Status Epilepticus

- A condition when consciousness does not return between seizures for more than 30 min. This state may be life-threatening with the development of pyrexia, deepening coma and circulatory collapse. Death occurs in 5-10%.

- Treatment: AEDs intravenously ASAP, event. general anesthesia with propofol or thiopentone should be commenced immediately.

Medication Used in Status Epilepticus

- Stop Seizure

Benzodiazepine

- Prevent Recurrence

Epanutin, Valproate and Levetiracetam

THANK YOU