

Epilepsy

- ‘paroxysmal alteration of intellectual, sensory, motor, autonomic, or affective activity, which is time limited (usually under one hour) and presumably associated with neuronal hypersynchronous activity’ (Alter *et al.* 1972)

Epidemiology

- prevalence of active epilepsy = 5 per 1000
- approximately 5 % of the population will have a fit of some sort during their lifetime
- equal sex ratios, although males at increased risk of post-traumatic epilepsy
- age of onset shows highest rate in the first year of life
- 25 % of cases begin before the age of 5, and 50% by school leaving age
- in the first 20 years of life generalized tonic-clonic seizures are the most common; after this age, focal epilepsies increase

Aetiology

- post-traumatic 7 %
- cerebrovascular 9 %
- other 9 %
- unknown 75 %

Genetics of epilepsy

- twin studies have shown greater concordance between MZ twins than DZ twins
- family concentrations occur with:
 - ‘idiopathic’ epilepsy
 - febrile convulsions
 - in those below the age of 12
 - non-focal EEG abnormalities

Epilepsy of unknown aetiology

- 2/3 of cases are in this category
- M:F = 1:1
- most are generalized from the start
- a focal component strongly indicates some form of structural brain lesion
- in most cases, no neurological abnormality is found between attacks
- the incidence of psychiatric illness is lower in this category

Epilepsy due to birth injury or congenital malformation

- most often, the seizures will be declared in infancy or very early childhood
- common causes include:
 - anoxia
 - direct trauma leading to cerebral haemorrhage
 - CVA (e.g. Intraventricular haemorrhage, Periventricular leucomalacia)
 - cardiorespiratory disorders

- infection (e.g. meningitis)
- metabolic disorders (e.g. hypoglycaemia, kernicterus)
- a large proportion of children with cerebral palsy suffer from seizures
- congenital causes include:
 - porencephaly
 - microgyria
 - tuberous sclerosis (chromosome 9 malformation)
 - AV malformation (Sturge-Weber and Lindau's diseases)

Post-traumatic epilepsy

- higher incidence among men than women
- overall incidence after closed head injury is 5 %
- more than 50 % have their first fit within one year of injury
- 75 % have their first fit within 3 years of injury
- temporal lobe epilepsy accounts for 20 % of cases
- factors increasing the risk of epilepsy (incidence in brackets):
 - fit in the 1st week after injury (25 %)
 - depressed skull fracture (15 %)
 - intracranial haematoma (31 %)
 - depressed fracture with post-traumatic amnesia longer than 24 hrs (32 %)
 - depressed fracture with post-traumatic amnesia longer than 24 hrs and a fit in the 1st week (57 %)
 - penetrating injury (30-50 %) - risk higher with wounds in the central regions of the brain:
 - parietal (65 %)
 - motor and premotor cortex (55 %)
 - prefrontal (39 %)
 - temporal (38 %)
 - occipital (38 %)

Post-infective epilepsy

- encephalitis is more likely to be followed by epilepsy than meningitis, cerebral abscess, or venous sinus thrombosis
- any systemic infection may result in **febrile convulsions**, presumably due to the lowered seizure threshold induced by the effect of toxins or pyrexia
 - there is a genetic predisposition to febrile convulsions - siblings of affected children are more likely to respond to pyrexia with convulsions
 - the predisposition appears to fade after the age of 3 or 4
 - when severe, febrile convulsions may be responsible for the genesis of anoxic brain lesions which underlie TLE

Epilepsy due to cerebrovascular disease

- cerebral atherosclerosis
- hypertensive encephalopathy
- a cerebral embolus is more likely to lead to a fit than a thrombosis or haemorrhage
- any cerebral infarct may leave behind a focal source for seizures

Epilepsy due to cerebral tumour

- in approximately 20 % of tumours, a fit will be the first sign

Epilepsy due to degenerative disorders

- in childhood:
 - the lipoidoses - Kufs disease
 - tuberous sclerosis
- in adulthood:
 - multiple sclerosis
 - dementia

Epilepsy due to drugs and toxins

- alcohol and drug withdrawal
- seizures induced by:
 - amphetamines
 - ergot alkaloids
 - steroids
 - phenothiazines
 - tricyclic antidepressants
 - lead
 - chlorinated hydrocarbons found in insecticides

Metabolic causes

- in infancy:
 - galactosaemia
 - pyridoxine deficiency
- uraemia
- hypocalcaemia
- hypoglycaemia
- electrolyte disturbance
- porphyria

Other

- Huntington's disease
- Mitochondrial myopathy
- Wilson's disease
- Klinefelter's syndrome
- Leigh disease

Temporal lobe epilepsy

- '**mesial temporal lobe sclerosis**' is the commonest lesion found at operation
 - occurs in 50 % of cases
 - commonest single finding in any epileptic patient who dies a natural death
 - consists of dense glial infiltration of Ammon's horn and adjacent structures such as the amygdala
 - usually unilateral

- 20% have small hamartomas, probably of congenital origin – ganglioglioma lesions with an early age of onset of first fit are strongly associated with the development of schizophrenia-like psychoses
- a history of severe febrile convulsions, often with status epilepticus is common

The international classification of epileptic seizures

Partial seizures, or seizures beginning focally

1. Simple motor or sensory (without impaired consciousness)
2. Complex partial (with impaired consciousness)
 - a) simple partial features followed by brief clouding of consciousness or more prolonged automatism
 - b) impaired consciousness at onset:
 - i) clouding of consciousness only
 - ii) automatism
3. Partial seizures with secondary generalization
 - a) simple partial seizures evolving to generalised seizures
 - b) complex partial seizures evolving to generalised seizures
 - c) simple partial seizures progressing to complex partial seizures and then generalised seizures

Generalized seizures

1. Absence (petit mal)
2. Myoclonic
3. Clonic
4. Tonic
5. Tonic-clonic (grand mal)
6. Atonic

Unclassified

- gelastic epilepsy = laughing during seizure
- cursive epilepsy = running during seizure

Partial (Focal) seizures

- discharge begins in some part of the cortex
- focal symptoms in the form of an **aura** therefore usher in the seizure - the symptomatology depends on the area of the brain in which the discharge originates and the direction of its spread

Simple / Elementary seizures

- includes Jacksonian motor seizures and a variety of sensory seizures in which the phenomena are relatively unformed
- the motor 'march' may sometimes spread along a limb and then recede
- the grand mal convulsions which may occur are often asymmetrical in origin and may be followed by longer lasting focal functional defects such as dysphasia or transient weakness of the affected limb (**Todd's paralysis**)

Complex partial seizures

- sometimes, and particularly in temporal lobe epilepsy, the focal discharge spreads to the limbic system rather than to the centrencephalic system, impairing consciousness
- complex behaviour can still be carried out
- clinical features:
 1. *Autonomic and visceral*
 - a) 'epigastric aura'
 - b) dizziness
 - c) flushing
 - d) tachycardia
 2. *Perceptual*
 - a) distorted perceptions
 - b) déjà vu
 - c) visual, auditory, olfactory, and somatic hallucinations
 3. *Cognitive*
 - a) disturbances of thought, speech, and memory
 4. *Affective*
 - a) fear
 - b) anxiety
 5. *Psychomotor*
 - a) automatisms
 - b) grimacing and other bodily movements e.g. lip-smacking
 - c) repetitive or more complex stereotyped behaviour

EEG abnormalities

- any variety of:
 - rhythmic spikes
 - sharp waves
 - spikes and slow waves
 - rhythmical runs of θ and δ
- the abnormality may remain localized, or spread widely over one or both hemispheres
- in occasional cases, such as Jacksonian epilepsy when the focus is discrete and not large enough to reach the electrodes, the EEG may remain normal
- once the attack has ceased normal rhythms may return at once, or after a period of random low voltage slow activity
- in the interseizure record, the commonest evidence of a cortical epileptogenic lesion is a spike and sharp wave focus, or paroxysmal θ and δ

- there may be a ‘mirror focus’ over the homologous area of the contralateral hemisphere
- in TLE, the record can be normal until sleep activation is employed – the spikes or sharp waves often appear only during light sleep

Generalized seizures

- originate in subcortical structure, most probably the brain stem reticular formation and the nuclei of the diffuse thalamic projection system
- can occur in the basal frontal cortex, and spread to involve the subcortical structures
- discharges spread rapidly to involve all areas of the cortex at the same moment
- an aura is lacking, although occasionally the patient may experience ill-defined malaise for a few seconds before the seizure

Absence seizures

- seen most commonly in children
- attacks often cease in adolescence
- always of primary subcortical origin
- simple absences are virtually always without evidence of any gross brain lesion
- without warning, the patient loses contact with his environment for between 5 seconds and a minute
 - the face is pale, the eyes are glazed, and the pupils may be fixed and dilated
 - posture and balance are usually well maintained
 - the patient usually is unaware of the break and continues exactly at the point the seizure occurred
 - there are usually no after-effects
- **EEG abnormalities:**
 - during attacks the record is suddenly interrupted by bilateral synchronous spike and wave complexes of high amplitude, occurring at approximately 3 Hz
 - the interseizure record may show brief bursts without accompanying attacks - their incidence is considerably increased with overbreathing

Tonic-Clonic seizures

- subcortical origin
- no aura, but ill-defined prodromata may build up for hours or days, such as malaise, tension, nausea, or headache
- the seizure consists of tonic and clonic phases which involve all parts of the body symmetrically and from the same moment
- the fit is then followed by deep sleep, which may be succeeded by nausea, vomiting, and headache
- if sleep does not occur, confusion is usually seen before full consciousness is regained

- **EEG abnormalities:**

- for a few seconds before the fit there is a crescendo of low voltage fast activity
- with the tonic phase, this gives way to a generalized discharge of high amplitude spikes at 8-12 Hz
- after some 15-30 seconds the spikes become grouped and separated by slow waves as the clonic phase begins
- when the fit is over, low amplitude δ waves predominate the record

Myoclonic seizures

- sudden shock-like movements lasting for only a fraction of a second and mainly affecting the neck, arms, and shoulders
- balance may be affected if the legs are involved
- they are characteristic of subacute encephalitis, the cerebral lipoidoses, and Creutzfeldt-Jakob disease
- the rare progressive myoclonic epilepsy of Unverricht consists of increasingly frequent myoclonic jerks in association with progressive dementia

Aggravating and precipitating factors in epilepsy

1. Lowering of physical health:
 - a) sleep deprivation
 - b) extreme fatigue
 - c) starvation
 - d) mild degrees of hypoglycaemia
 - e) transient states of anoxia
 - f) in women, attacks sometimes increase in the premenstrual phase
2. Precipitants:
 - a) emotional disturbance
 - b) startle, shock, or surprise
 - c) interpersonal stresses and tensions
 - d) reflex seizures (esp. light, but all sensory modalities have been implicated) occur in 1-6%
3. Psychogenic seizures
 - i) generated by an act of will or by the mind without any external stimulus - e.g. thinking or calculating, attending to a particular point in the visual field
 - ii) may account for 15 % of seizures

Epileptic auras (and prodromata)

- auras:
 - last for seconds only

- associated with spike and wave on EEG
- experiences tend to be recalled when memory returns
- indicate a focal, structural lesion
- prodromata (different from auras):
 - are commoner in children than adults
 - build up slowly for hours or days
 - consist typically of psychological manifestations

Frontal seizures

- posterior parts:
 - ‘adversive aura’ in which the head and eyes turn away from the side of origin
 - ‘intrusion’ or ‘crowding’ of thoughts
- pre-rolandic cortex:
 - classical Jacksonian ‘march’, dysphasia
- orbital parts:
 - involve the limbic system (c.f. TLE)

Parietal seizures

- ‘sensory Jacksonian march’
 - paraesthesiae, numbness, tingling, feelings of hot and cold
- posterior parts:
 - disturbances of body image e.g. limbs appear to be larger, smaller, missing, heavier, etc.

Medial surface seizures

- supplementary motor area, anterior to the Rolandic fissure:
 - tonic postural movements
 - epigastric sensations
- posterior foci:
 - paraesthesiae in the contralateral foot and leg
 - rectal sensations
 - genital sensations, including orgasm

Occipital seizures

- visual disturbances, localized in the opposite half-field of vision
- scotoma or hemianopic field defect may occur

Other epileptic phenomena

Epileptic automatism

- a state of clouding of consciousness which occurs during, or immediately after, a seizure during which the individual retains control of posture and muscle tone, and

performs simple or complex movements and actions without being aware of what is happening

- i.e. **action without awareness**
- environmental cues may to some extent determine the detailed patterns of behaviour
- accompanied by continuous electrical disturbance of the EEG
- aura are common
- majority are brief, lasting from a few seconds to several minutes
- associated with psychomotor epilepsy originating in the medial temporal lobes
- violence is rare
- amnesia is common

Epileptic fugue

- less common than automatisms
- less impairment of consciousness than automatism, and abnormal behaviour is more complex, extended and integrated
- lasts longer than automatism - may last hours or days
- associated with a tendency to wander away

Twilight states

- commonly last from one to several hours, but can last for weeks
- consciousness is always impaired
- generally organic in origin
- characterized by:
 1. abrupt onset and end
 2. variable duration
 3. unexpected violent acts or emotional behaviour
- may present as dream-like absent-minded behaviour, or slowness of reaction and muddling of comprehension
- psychomotor retardation is commonly profound, with marked perseveration in speech and action
- affective (panic, terror, anger, ecstasy) and perceptual (hallucinations, usually visual and vivid and complex) phenomena are common
- tend to terminate in a tonic-clonic seizure more commonly than automatisms
- ECT is able to terminate twilight states of long duration
- memory is often fragmented, but a vivid recollection of the hallucinations may be retained
- associated with the Ganser state

Associations between epilepsy and psychiatric illness

Prevalence

- in general practice, 30 % of epilepsy patients had conspicuous psychological difficulties

- 7 % had had in-patient psychiatric care
- 10 % were educationally subnormal
- in the Isle of Wight study (Rutter 1968), psychiatric disorder was diagnosed in:
 - 7 % of non-epileptic children
 - 30 % with uncomplicated epilepsy
 - 60 % with epilepsy complicated by evidence of brain damage/ lesions above the brain stem

Psychiatric disorders of epilepsy: classification (Fenton 1981)

1. Psychiatric disorder associated with the underlying cause
 - a) mental handicap
 - b) epileptic syndromes
 - i) West's syndrome
 - ii) Unverricht-Lundberg disease
 - iii) SSE
 - iv) Lennox-Gastaut syndrome
 - c) organic brain syndromes
 - i) Alzheimer's disease
 - ii) multi-infarct dementia
 - d) focal brain disease
 - e) psychotic syndromes
2. Behavioural disturbance associated with the seizure
 - a) Pre-ictal:
 - i) prodromal states
 - ii) mood disturbance
 - b) Ictal:
 - i) complex partial seizures
 - ii) absence status
 - iii) complex partial status
 - c) Post-ictal:
 - i) automatisms
 - ii) impaired consciousness
3. Inter-ictal disorders (disorders unrelated in time to the seizure occurrence):
 - a) Cognitive
 - b) Personality
 - c) Sexual behaviour
 - d) Depression and emotional disorder
 - e) Suicide and deliberate self harm
 - f) Crime
 - g) Psychoses
 - h) Neurosis

Behavioural disturbance associated with the seizure

- increasing tension, irritability, and depression are sometimes apparent as prodromata for several days before a seizure

- transient confusional states and automatisms may occur during seizures (especially complex partial) and after seizures (usually those involving generalized convulsions, and complex partial seizures)
- occasionally, non-convulsive seizures may continue for days or even weeks (absence status and complex partial status)
- automatic behaviour is most commonly due to abnormal electrical discharge originating in the periamygdaloid region

Cognitive function

- relatively few people with epilepsy show cognitive changes
- when intellectual changes do occur, the significant aetiological factors are likely to be:
 - brain damage
 - poor concentration and memory during periods of abnormal electrical activity
 - adverse effects of antiepileptic drugs
- learning problems are more common in children with epilepsy than in non-epileptic children

Personality

- the ‘epileptic personality’ was said to be characterized by egocentricity, irritability, religiosity, quarrelsomeness, and ‘sticky’ thought processes
- later studies have shown that only a minority of people have serious personality problems
- there is little evidence to support an association between epilepsy and aggressiveness
- it has been suggested that abnormalities of personality are mainly associated with TLE – characterised by ‘viscosity’, hyperemotionality, and hyposexuality
 - thought to be due to limbic system kindling with enhanced affective labelling of previously neutral stimuli

Sexual dysfunction

- lack of libido and sexual dysfunction are probably more common in the epileptic population
 - possibly a reflection of poor social skills in immature, dependent persons, who have had little chance to develop adult relationships due to excess medication/ sheltered or restricted lives/ parental overprotection
- more likely to occur with TLE
- anticonvulsants induce liver enzymes which results in rapid metabolism of testosterone
- an association between fetishism and transvestitism, and TLE has been reported

Depression and other emotional disorder

- depressed mood is more common in people with epilepsy than in the general population - it is usually of a moderate severity
- no evidence of increased risk of bipolar affective disorder
- depression is most common in those with adverse social factors

Suicide and deliberate self harm

- suicide is 4x more frequent
- DSH is 6x more frequent

Epilepsy and crime

- the incidence of epilepsy in prison is 7-8 per 1000, slightly higher than that of the general population – reasons may include:
 - brain damage causes fits and uninhibited antisocial behaviour
 - stigmatisation of epilepsy results in retaliatory offending
 - a deprived early environment may result in brain damage and aggressive behavioural responses
 - the brain damage may be a consequence of the criminal lifestyle
- no relationship between epilepsy and the type of crime
- crimes committed during epileptic automatisms are extremely rare

Inter-ictal psychoses

- some people have suggested that psychotic disorder is less common in people with epilepsy (the *antagonism hypothesis*)
- others have argued the opposite view (the *affinity hypothesis*)
- some patients with TLE develop ‘chronic paranoid hallucinatory psychosis’
 - the clinical picture resembles schizophrenia, except that affective responses are preserved
 - usually a lack of family history of schizophrenia
- it is likely that there is an association between TLE and epilepsy
- schizophrenia-like psychosis is more common among patients with foci in the temporal lobes than in those with primary generalized seizures
 - paranoid delusions and mystical delusional experiences are frequent
 - visual hallucinations, often mystical, are more common
 - affect is more commonly retained, and the progress is more benign than in schizophrenia