What Is Epilepsy?

CHAPTER 1

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WHEN IT IS EPILEPSY

Epilepsy is an ongoing predisposition to recurrent, unprovoked epileptic seizures in a person, resulting from many underlying neurological or somatic conditions.[1] Unprovoked paroxysmal seizures often coexist with a range of psychological, psychiatric, psychosocial and somatic comorbidities.[2] People with epilepsy are at an increased risk of premature mortality.[3,4] The interaction of individual-specific factors, including seizures, frequently multiple comorbidities, and an increased premature death risk, forms their experience and creates a complex reality for them.

Epileptic seizures are, in effect, a paroxysmal disruption of the brain's physiological activity.[5] Seizures manifest as transient clinical or sub-clinical events resulting from abnormal neuronal activity. A clinical seizure is an event discernible by the concerned individual and/or observable by a witness. Typically, seizures are stereotyped, with similar sequences and symptomatology during each event. Some people may have more than one seizure type, each one with its own stereotyped presentation. In contrast, subclinical seizures do not manifest observable behavioural changes and are only identifiable on electroencephalographic (EEG) recordings.

The International League against Epilepsy (ILAE) established diagnostic criteria, providing a standardised framework stressing the risk of recurrence and the unprovoked nature of the seizures.[1,6]

There are three diagnostic criteria.

1. The occurrence of at least two unprovoked seizures on separate days, as seizures occurring within 24 hours are regarded as a single event.
2. An unprovoked seizure with an enduring predisposition for recurrence, defined as a minimum of 60% recurrence risk over the next ten years.
3. The presence of a specific epileptic syndrome, characterised by distinct clinical features such as age of onset and EEG features.[1]

At the other end of the pathway, there is the concept of 'resolved epilepsy' which applies mainly to people with age-dependent epileptic syndromes and who have exceeded the relevant age of the syndrome.[1] This also applies to

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people who have been seizure-free for ten years, with at least the last five years off antiseizure medication (ASM).

The natural history of epilepsy is remarkably diverse, ranging from spontaneous remission in some self-limited syndromes to a chronic, debilitating condition in others.[5,7,8] This heterogeneity arises from many factors influencing the presentation of epilepsy. There are many risk factors for epilepsy, different seizure semiologies, varying severities, a spectrum of comorbidities, and variable outcomes.

Epilepsy is a symptom, not a disease, highlighting that seizures are a manifestation of underlying brain or systemic problems, like anaemia, which is a symptom of various blood-related disorders.[9] Just as anaemia may underlie a range of blood or somatic-related problems, epilepsy should be viewed as a manifestation of broader health concerns. This perspective is critical in considering Developmental and Epileptic Encephalopathies, of which seizures are part of a complex phenotype, not the defining or the index condition.

The impact of epilepsy extends far beyond individual experiences, having a significant burden on society and global health, as it impacts heavily on people living in low to middle-income countries (LMIC).[8–10] Over 70 million people are estimated to be affected worldwide, most living in LMIC. In high-income countries (HIC), the incidence is also higher in people in more deprived areas. This increased prevalence and incidence among less affluent populations suggests a role of social determinants of health in the risk of developing epilepsy.[5,10–12]

The Global Burden of Disease Project provides stark statistics, estimating that epilepsy contributes to over 13 million disability-adjusted life years (DALY) worldwide.[10] DALY are a measure of overall disease burden, combining years of life lost due to premature mortality (YLL) and years lived with disability (YLD). Every year, epilepsy results in over 150,000 years of life lost (YLL) globally, emphasising the risk and burden of premature mortality.

Seizures, while the defining characteristic of epilepsy, rarely exist in isolation and frequently coexist with a range of physical, cognitive, socioeconomic and mental health challenges.[2–5] This often-complex picture requires a holistic approach to medical care, recognising that effective management extends beyond simply controlling seizures. Identifying and treating co-occurring conditions and proactive strategies to mitigate the heightened risk of premature death are part of the approach to improve seizure control and provide an appropriate quality of life to the person.

WHEN IT IS NOT EPILEPSY

Several paroxysmal disorders can mimic epileptic seizures and may be misdiagnosed as epileptic events.[13–15] The differential diagnosis of epileptic seizures is broad, including cardiovascular, functional dissociative and neurological disorders. Distinguishing these seizure mimics is crucial for accurate diagnosis and appropriate management. Most but not all of the mimicking events are due to paroxysmal neurological disorders. A wide range of medical and psychological conditions can mimic epilepsy, presenting with symptoms that closely resemble epileptic seizures. In addition, some apparent epileptic seizures, if provoked by an acute insult to the brain or an evident metabolic or somatic disturbance, are not considered epileptic, even if recurrent, and they are termed acute symptomatic seizures.

Among the non-neurological imitators, syncope and cardiac arrhythmias are prominent. Syncope, or fainting, is common in the population and can mimic seizures, typically with clear triggers and rapid recovery. Characterised by a brief loss of consciousness due to reduced cerebral blood flow, syncope usually has a discernible trigger, often with jerky movements, that may be mistaken for convulsions. The main subtypes include vasovagal syncope, reflex anoxic seizures, especially in children, and cardiac syncope. Cardiac arrhythmias can also cause sudden loss of consciousness, potentially with convulsive activity.

Brain-related imitators include migraine, sleep disorders, movement disorders, transient ischemic attacks, stroke, functional events and psychiatric disorders. Migraine, particularly with aura, can present with visual, sensory, or motor symptoms resembling focal seizures. Sleep disorders such as parasomnias (e.g. somnambulism, night terrors), hypnic jerks, and sleep enuresis can be mistaken for seizures, especially in children. Cataplexy may mimic atonic seizures.

While 'basal ganglia epilepsy' is sometimes mentioned, it is not true epilepsy. Unusual seizure-related movements during seizures, such as posturing, might prompt this term due to their similarity to basal ganglia paroxysmal movement disorders. Seizure symptoms can mimic these movements; seizures elsewhere can affect the basal ganglia. However, events primarily resulting from basal ganglia dysfunction are considered non-epileptic movement disorders, not epilepsy of basal ganglia origin.

Transient ischaemic attacks and stroke can cause sudden neurological deficits, but these typically last longer than most seizures, often lack motor activity, and do not have the frequency of focal seizures.

Functional dissociative seizures are another critical consideration, as they are common, particularly amongst people labelled as having drug-resistant epilepsy. Often triggered by psychological stress, they lack the typical EEG correlates of epileptic seizures (see Chapter 24).

Acute symptomatic seizures or provoked seizures, unlike epilepsy which is defined by unprovoked seizures, are triggered by an identifiable and often reversible cause, either by an acute systemic or brain insult.[16–18] The typical time window for these seizures includes the first week after acute brain insults such as a stroke, brain injury, anoxic encephalopathy, intracranial surgery, during active CNS infection/inflammation (encephalitis, meningitis, MS), and within 24 hours of severe metabolic derangements.[16] These seizures usually require urgent investigation and management of the underlying cause and are common in neonates and older adults. Long-term ASM is generally not recommended unless unprovoked seizures subsequently occur.

Controversies exist regarding acute symptomatic seizures.[16] Challenges in their identification in epidemiological studies have led to data inconsistencies due to their potential inclusion under epilepsy or failure to differentiate them from unprovoked seizures.[8] While generally carrying a lower recurrence risk than unprovoked seizures, conditions such as severe traumatic brain injury or autoimmune encephalitis can blur this distinction, with many people developing epilepsy later. The ILAE's 'enduring predisposition' in the epilepsy definition lacks clear boundaries, particularly with structural brain lesions or ongoing CNS insults.[1] A relevant example is whether neurocysticercosis-related seizures are acute symptomatic seizures, given the potentially long evolution of the condition before 'acute' seizures occur, posing challenges for treatment

PRACTICE POINTS

- **Epilepsy as a Symptom Complex:** Epilepsy is a manifestation of various underlying neurological or somatic conditions requiring a broader diagnostic and management perspective.
- **Diagnosis Based on Recurrence Risk and Syndrome Recognition:** The ILAE diagnostic criteria include at least two unprovoked seizures on separate days, a single unprovoked seizure with ≥60% risk of recurrence over 10 years or identifying a specific epilepsy syndrome.
- **Comorbidities and Premature Mortality Risk:** Frequently there is coexistence of comorbidities in people with epilepsy and an increased risk of premature mortality. Care should be taken to proactively identify and manage these associated challenges.
- **Other Causes for Seizures:** Always consider and actively rule out common epilepsy-mimics such as syncope, cardiac arrhythmias, migraine, sleep disorders, and functional dissociative seizures through careful history taking.
- **Provoked and Unprovoked Events:** Seizures occurring in the context of acute brain insults or metabolic disturbances are distinct from epilepsy and require addressing the underlying cause rather than routine long-term anti-seizure medication unless unprovoked seizures subsequently occur.

recommendations. A new classification based on evolutionary stages could better guide treatment for this condition.[19]

A thorough clinical history, including a detailed description of the events, triggers, duration, associated symptoms, and post-event state, is vital in distinguishing epilepsy from its mimics. The presence or absence of warning signs, loss of bladder or bowel control, tongue biting and post-ictal confusion provide valuable clues. The EEG remains fundamental for confirming an epilepsy diagnosis by showing characteristic epileptiform discharges during or between seizures. However, a normal EEG does not exclude epilepsy, and some non-epileptic conditions can show nonspecific abnormalities.[20] In complex cases, video-EEG monitoring, cardiac investigations, neurological imaging, and psychological evaluations may be necessary for accurate diagnosis and to ensure appropriate treatment.

FURTHER READING

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