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# Epileptic seizures and their classification

Epileptic seizures are numerous and diverse in their presentation, pathophysiology, age relationships, prevalence and triggering factors (Tables 2.1–2.3).

## The definition of epileptic seizures

Epileptic seizures are transient paroxysmal events, characterised by clinical symptoms, signs or both, which are generated by abnormal excessive and synchronous electrical discharges of brain networks. The most recent formal definition of epileptic seizures reflects consensus discussions held by representatives of the ILAE and the IBE (2005).[1]

*An epileptic seizure* is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.[1]

Other ILAE definitions are:

*Epileptic seizure:* Manifestation(s) of epileptic (excessive and/or hypersynchronous), usually self-limited activity of neurones in the brain.[2]

*Epileptic seizure:* A clinical manifestation presumed to result from an abnormal and excessive discharge of a set of neurones in the brain. The clinical manifestation consists of a sudden and transitory abnormal phenomena, which may include alterations of consciousness, or motor, sensory, autonomic or psychic events perceived by the patient or an observer.[3,4]

All three essential elements of the definition of an epileptic seizure should be present before it is decided that a paroxysmal event is an epileptic seizure and not something else:[1]

1. transient, with an onset and termination of usually brief duration
2. clinical manifestations
3. ictogenesis due to abnormal enhanced synchrony in the brain

*Mode of onset and termination:* An epileptic seizure is 'transient', demarcated in time, with a start and finish of usually brief duration. In practice, onset and termination are assessed by clinical and EEG changes. However, it should be realised that an ictal electrical discharge may start in a set of neurones and networks before it becomes evident on surface EEG (either in the same or different brain locations) and clinical manifestations appear. Furthermore, clinical changes may be more apparent than EEG changes or vice versa and there may be a significant time lag between their onsets (on video EEG), with the EEG changes often appearing first (Figures 1.2, 12.3, 12.5). There are plenty of illustrative cases in this book emphasising that some epileptic seizures, such as hypermotor seizures, may manifest with severe clinical symptoms and/or signs but without visible changes in surface EEG (Figure 15.8).

Conversely severe ictal EEG abnormalities may be associated only with subtle clinical manifestations that may not be apparent to the observer (Figure 15.4) and/or the patient, such as phantom absences. These facts are even more striking when one attempts to determine precisely the onset of clinical and EEG ictal events.

See also onset of focal versus generalised seizures on pages 33 and 57.

Termination of an epileptic seizure is often less evident than is the onset, because EEG and clinical post-ictal abnormalities can blur its end. The duration of a seizure varies significantly from seconds or minutes (usually 1–3 min) to lengthy periods of status epilepticus, when self-sustaining processes prevail over self-terminating mechanisms (see chapter 3, page 65).

*Clinical manifestations:* Clinical symptoms and signs are an essential part of defining an epileptic seizure. 'Ictal-like' EEG-only patterns are not defined as epileptic seizures.

## Subclinical and/or electrographic seizures

'EEG only' ictal patterns that resemble those seen during epileptic seizures, but not perceived subjectively or objectively either by the patient or by the observer, are not defined as epileptic seizures.[1] They are called 'subclinical' or 'electrographic' seizures, which manifest with paroxysmal rhythmic epileptiform discharges that evolve in time and space in the absence of objective and subjective clinical manifestations. However, it is often difficult to determine the lack of subtle clinical manifestations during 'ictal-like' EEG paroxysms and their boundaries with truly ictal seizures (see for example phantom absence seizures or electrographic seizures in neonates and comatose patients).

An epileptogenic discharge may start in or invade any cortical or subcortical brain area and network. Therefore any type of function controlled by the affected brain regions may be disturbed, producing abnormal symptoms and signs that may be sensory, motor, autonomic, cognitive, behavioural, mnemonic or psychological and/or affect alertness, awareness and responsiveness. An epileptic seizure may affect only one or many brain functions with a varying degree of severity and a shifting sequence. Symptoms may be entirely subjective or objective or both. They may be so mild that they are barely perceived by the patient, observer or recording device or very severe and massive.

Seizure semiology depends on location of onset in the brain, patterns of propagation, maturity of the brain, confounding disease processes, sleep–wake cycle, medications and a variety of other factors.[1]

Detailed specification of subjective and objective clinical phenomena during an epileptic seizure is difficult because of the wide range of possible manifestations.[1] Tables 2.1, 2.2 and 2.3 show the classification of seizures according to their predominant symptoms and localisations.

*Motor manifestations* may be clonic, tonic, myoclonic, dystonic, atonic or hypermotor and may be limited to a small group of muscles or involve the entire voluntary musculature.

*Sensory manifestations* can affect the somatosensory, auditory, visual, olfactory, gustatory or vestibular senses. Again, they may be entirely localised or widely spread, and may occur alone or in combination with other sensory or other manifestations.

*Autonomic manifestations* of any type are often encountered in seizures, whether focal or generalised, in adults or children, and they are implicated in occurrences of sudden death. They are sometimes the most difficult symptoms and signs to detect without, for example, ictal ECG or polygraphic recordings (see neonates and figures 1.2; 8.1; 12.5). They usually appear together with symptoms from other modalities but they may also occur alone for brief or lengthy periods (see autonomic status epilepticus in Panayiotopoulos syndrome, page 347).

*Effects on cognition, perception, attention, emotion, memory, execution, praxis, speech, consciousness, awareness, responsiveness, behaviour, psychology and other related functions* are common, may occur alone or in combination, and may appear as the first ictal symptom or occur later in the course of a seizure. These symptoms are often referred with various terms that need to be clarified. 'Complex internal

sensations',[1] 'dreamy states', 'psychic or mental symptoms', 'intellectual aura' and 'experiential phenomena' are the terms most commonly used to denote symptoms of seizures that uniquely relate to the patient's personality, identity, experience, emotion, thought and memory. These terms are not necessarily synonymous, because they are used in the relevant literature to encompass either limited or much wider ictal manifestations (see Chapter 15 page 438). Dyscognitive is a term that is widely used to denote impairment of cognition, which is the process of knowing, including aspects such as awareness, perception, reasoning and judgement (see chapter 3 page 78). "Memory distortions can be either negative or positive, in the sense of interruption of memory formation or retrieval as a negative symptom, or intrusion of inappropriate memories as a positive symptom."[1] "Emotional state is difficult to specify but must be considered in the definition, because some seizures manifest as fear, elation, satisfaction, anxiety or other subjective sensations that cannot be ascribed to the primary senses".[1] For 'impairment of consciousness', see blue box on this page.

*Ictogenesis:* This is the most difficult element of the definition of an epileptic seizure to assess in practice because the electrical discharge may not be visible even in long EEG recordings and some patients may have consistently normal EEGs. "Nevertheless, the definition assumes that such an abnormal electrical discharge could be ascertained under ideal circumstances....Without the electrical discharge criteria, many other clinical events that are not epileptic seizures would meet the other definition criteria".[1] Consider for example the galaxy of clinical imitators of epileptic seizures in listed chapter 4, such as migraine with aura, that may be clinically near-identical to epileptic seizures but without a causative relation to ictogenesis. Further, "definition of an epileptic seizure becomes operationally difficult without ascribing it to the brain. Trigeminal neuralgia, for example, can result from an abnormal enhanced synchrony of neurones in the trigeminal ganglion or the fifth cranial nerve, but would not be considered an epileptic seizure. Nor would hyperactive spinal reflexes resulting in an excessive discharge of anterior horn cells and tonic stiffening of a limb".[1]

The book *Epileptic Seizures*, edited by Hans Luders and Soheyl Noachtar, is highly recommended for its in-depth insight into pathophysiology and clinical semiology.[9]

## Impairment of consciousness, unresponsiveness, awareness

There is no precise definition of 'consciousness' and therefore 'impairment of consciousness' cannot be exactly defined either. Components of consciousness include perception, cognition, memory, affect, and voluntary motility. In epileptic seizures 'loss or impairment of consciousness' often reveals that only some components of consciousness are impaired. Responsiveness and awareness are frequently disturbed during ictal 'impairment of consciousness' but to a varying degree of severity, and in some seizures the patient may be entirely responsive but unaware (amnesic) of the events or vice versa. Further, unresponsiveness may be due to aphasia, inability to perform voluntary movements, ictal or postictal amnesia (sometimes with preservation of memory during the ictus itself), or to diversion of attention by a hallucinated experience.[5,6]

See also 'altered content of consciousness' in fully alert patients with absence status epilepticus (page 73).

Impaired consciousness according to the 1981 ILAE report is the inability to respond normally to exogenous stimuli by virtue of altered awareness and/or responsiveness. Aberrations of behaviour (automatisms) may occur in patients with impaired consciousness.[7]

The precise brain mechanisms for control of consciousness are not fully understood but emerging data show that conscious information processing depends on the activation of certain networks in the brain and that the impairment of consciousness is related to abnormal activity in these systems.[8]

# Other useful or ILAE seizure-related terminology

*Aura:* A subjective ictal phenomenon that, in a given patient, may precede an observable seizure; if alone, it constitutes a sensory seizure.[2]

*Prodrome:* A preictal phenomenon, i.e. a subjective or objective clinical alteration (e.g. unlocalised sensation or agitation), that heralds the onset of an epileptic seizure but does not form part of it.[2]

*Ictus:* A sudden neurological occurrence, such as a stroke or an epileptic seizure.[2]

*Ictal:* The seizure period or events due to a seizure.

*Inter-ictal:* The interval between seizures.[2]

*Post-ictal:* A transient clinical abnormality of CNS function that appears or becomes accentuated when clinical signs of the ictus have ended.[2]

*Single or isolated seizure:* One or more epileptic seizures occurring in a 24 hour period.[3,4]

*Symptomatogenic zone:* the brain region that corresponds with the ictal symptoms and signs of an epileptic seizure as detected by clinical means. Ictal symptoms may happen long after the onset of the electrical discharges and may appear from areas that are different from the epileptogenic zone.

*Epileptogenic zone or focus:* the brain region that corresponds with the onset of ictogenesis as detected with surface and more accurately invasive EEG (see also page 224). This frequently extends beyond the structural lesion visualised on neuroimaging (called *epileptogenic lesion*) or the epileptogenic cortical area generating inter-ictal spikes (called *irritative zone*).

### Important clinical notes

Prodrome should not be confused with aura

Aura is not synonymous with prodrome; aura is a seizure itself, and is brief, lasting seconds or minutes. Prodrome is a non-epileptic symptom preceding the onset of an epileptic seizure by several hours (page 99).[10]

# Classification of epileptic seizures

## Epileptic seizures in accordance with the 1981 ILAE classification[11]

The currently valid ILAE *Classification of Epileptic Seizures* was made in 1981.[11] This is an updated version of the classification proposed by Gastaut in 1970,[12] with a full description of each seizure in his classic book[13] and the WHO dictionary of epilepsies.[10]

The 1981 ILAE seizure classification is based on clinical and EEG (ictal and inter-ictal) manifestations (Tables 2.1 and 2.2). Seizures are principally divided into the following types:

I. *Partial (focal or local) seizures* (with great variation in clinical expression and severity).

II. *Generalised seizures (tonic, clonic or tonic–clonic, myoclonic and typical or atypical absences).*

III. *Unclassified epileptic seizures*, which cannot be classified because of inadequate or incomplete data and some that defy classification in hitherto described categories. This includes some neonatal seizures, e.g. rhythmic eye movements, chewing and swimming movements.[11]

IV. *Prolonged or repetitive seizures (status epilepticus).*

'Focal seizures' are synonymous and exchangeable with, but preferred to, 'partial seizures'.[14]

The dichotomy between focal and generalised seizures was considered to be necessary 'because an abnormal paroxysmal discharge of cerebral neurones may be localised (partial seizures) or simultaneously affect the whole cerebral cortex from onset to termination (generalised seizures)'.[11]

See page 31 for the recent debate on this dichotomy.

## ILAE classification of partial (focal, local) seizures

| Clinical seizure type | EEG seizure type | EEG inter-ictal expression |
|---|---|---|
| **A. Simple partial seizures (consciousness not impaired)** | Local contralateral discharge starting over the corresponding area of cortical representation (not always recorded on the scalp) | Local contralateral discharge |
| 1. With motor signs<br>a. Focal motor without march<br>b. Focal motor with march (jacksonian)<br>c. Versive<br>d. Postural<br>e. Phonatory (vocalisation or arrest of speech) | | |
| 2. With somatosensory or special-sensory symptoms (simple hallucinations, e.g. tingling, light flashes, buzzing)<br>a. Somatosensory<br>b. Visual<br>c. Auditory<br>d. Olfactory<br>e. Gustatory<br>f. Vertiginous | | |
| 3. With autonomic symptoms or signs (including epigastric sensation, pallor, sweating, flushing, piloerection and pupillary dilation) | | |
| 4. With psychic symptoms (disturbance of higher cerebral function). These symptoms rarely occur without impairment of consciousness and are much more commonly experienced as complex partial seizures<br>a. Dysphasic<br>b. Dysmnesic (e.g. déjà vu)<br>c. Cognitive (e.g. dreamy states, distortions of time sense)<br>d. Affective (e.g. fear, anger)<br>e. Illusions (e.g. macropsia)<br>f. Structured hallucinations (e.g. music, scenes) | | |
| **B. Complex partial seizures (with impairment of consciousness; may sometimes begin with simple symptomatology)** | Unilateral or, frequently, bilateral discharge, diffuse or focal in temporal or frontotemporal regions | Unilateral or bilateral, generally asynchronous focus; usually in the temporal or frontal regions |
| 1. Simple partial onset followed by impairment of consciousness<br>a. With simple partial features (A1 to A4) followed by impaired consciousness<br>b. With automatisms | | |
| 2. With impairment of consciousness at onset<br>a. With impairment of consciousness only<br>b. With automatisms | | |
| **C. Partial seizures evolving to secondarily generalised seizures (this may be generalised tonic–clonic, tonic or clonic) (above discharges become secondarily and rapidly generalised)** | | |
| 1. Simple partial seizures (A) evolving to generalised seizure | | |
| 2. Complex partial (B) evolving to generalised seizure | | |
| 3. Simple partial seizures evolving to complex partial seizures evolving to generalised seizure | | |

**Table 2.1** *Adapted with permission from the Commission of Classification and Terminology of the ILAE (1981).*[11]

**ILAE classification of generalised seizures (convulsive and non-convulsive)**

| Clinical seizure type | EEG seizure type | EEG inter-ictal expression |
|---|---|---|
| **A1. Absence seizures**<br>a. Impairment of consciousness only<br>b. With mild clonic components<br>c. With atonic components<br>d. With tonic components<br>e. With automatisms<br>f. With autonomic components<br>*(b–f may be used alone or in combination)* | Usually regular and symmetrical 3 Hz, but may be 2–4 Hz spike–slow-wave complexes and may have polyspike–slow-wave complexes. Abnormalities are bilateral | Background activity usually normal, although paroxysmal activity (such as spikes or spike–slow-wave complexes) may occur. This activity is usually regular and symmetrical |
| **A2. Atypical absence seizures**<br>May have:<br>a. Changes in tone that are more pronounced than in A1<br>b. Onset and/or cessation that is not abrupt | EEG more heterogeneous, may include irregular spike–wave complexes, fast activity or other paroxysmal actions. Abnormalities are bilateral but often irregular and asymmetrical | Background usually abnormal paroxysmal activity (such as spikes or spike–slow-wave complexes) frequently irregular and symmetrical |
| **B. Myoclonic seizures**<br>Myoclonic jerks (single or multiple) | Polyspike and wave or sometimes spike and wave or sharp and slow waves | Same as ictal |
| **C. Clonic seizures** | Fast activity (⩾10 cycles/s) and slow waves or occasional spike–wave patterns | Spike and wave or polyspike and wave discharges |
| **D. Tonic seizures** | Low-voltage, fast activity or a fast rhythm 9–10 cycles/s, decreasing in frequency and increasing in amplitude during tonic phase. Interrupted by slow waves during clonic phase | Polyspike and wave or spike and wave or, sometimes, sharp- and slow-wave discharges |
| **E. Tonic–clonic seizures** | Rhythm at ⩾10 cycles/s decreasing in frequency and increasing in amplitude during tonic phase. Interrupted by slow waves during clonic phase | Polyspike and waves or spike and wave or, sometimes, sharp- and slow-wave discharges |
| **F. Atonic seizures (astatic)** | Polyspikes and wave or flattening or low-voltage fast activity | Polyspikes and slow wave |
| *Combinations of the above may occur, e.g. B and F, B and D* | | |

Table 2.2 *Adapted with permission from the Commission of Classification and Terminology of the ILAE (1981).*[11]

## Partial (or focal) seizures (Table 2.1)

> Partial (focal) seizures are those in which, in general, the first clinical and EEG changes indicate initial activation of a system of neurones limited to a part of one cerebral hemisphere.[11]

Partial seizures are further subclassified chiefly on the basis of (1) whether or not consciousness is impaired during the attack and (2) whether or not progression to generalised convulsions occurs.

A. *Simple partial seizures (when consciousness is not impaired).*

B. *Complex partial seizures (when consciousness is impaired).* Impairment of consciousness may be the first clinical sign or simple partial seizures may evolve into complex partial seizures.

A partial seizure may not terminate, but instead progress to a generalised motor seizure.

C. *Partial seizures (simple or complex) evolving to secondarily generalised (tonic–clonic or tonic or clonic) seizures.*

## Generalised seizures (Table 2.2)

> Generalised seizures are those in which the first clinical changes indicate initial involvement of both hemispheres. Consciousness may be impaired and this impairment may be the initial manifestation. Motor manifestations are bilateral. The ictal EEG patterns initially are bilateral and presumably reflect neuronal discharge, which is widespread in both hemispheres.[11]

Generalised seizures may be convulsive or non-convulsive and vary considerably: mild or severe myoclonic jerks, inconspicuous or severe typical and atypical absences and generalised clonic, tonic or tonic–clonic convulsions.[11]

In this[11] and the newer[7,14] ILAE epileptic seizure classifications, there is a main "distinction between seizures that are generalized from the beginning and those that are partial or focal at onset and become generalized secondarily",[11] with significant differences in their epileptogenesis, clinical and EEG features, aetiology and management.

### Important note

**The terminology of primarily and secondarily generalised seizures**

The terms primarily and secondarily GTCSs should not be confused with the now obsolete terms of primary (= idiopathic) and secondary (= symptomatic or cryptogenic) epilepsy, which either have not been used or have been rightly abandoned by the ILAE and most physicians. These terms are also not used in the current ILAE glossary.[2] Idiopathic (from the Greek words *idios* = self, own and personal, and *pathic* = suffer; see also pathology and pathological)[16] usually refers to genetically determined aetiology.[7] In the USA idiopathic is traditionally considered to signify cases of unknown aetiology and pathogenesis, which is the reason why American physicians prefer the term 'primary' to 'idiopathic'.[17] Of the dictionary definitions of 'primary', the following are relevant to its use in the classification of epilepsies:

1. Preceding all others in time: earliest, first, initial, maiden, original, pioneer, prime, primordial. This definition would apply to primarily GTCSs (PGTCSs).
2. Not derived from something else: original, prime, primitive. This definition would apply to idiopathic GTCSs.

In ILAE classifications and guidelines, as well as other formal recommendations, the frequency and inconsistency with which the words primary and primarily, secondary and secondarily are used are confusing; for instance, why use 'primary reading epilepsy' instead of 'idiopathic reading epilepsy'?

A major issue is that the term 'primary GTCS', which etymologically means and implies 'idiopathic GTCS', is in fact used for GTCSs of idiopathic, symptomatic and cryptogenic epilepsies, particularly in randomised controlled trials of AEDs (see pages 190–193).[18]

Another issue to clarify is that the PI and SmPC of an AED may indicate that it is licensed for focal epileptic seizures with or without "secondary generalisation", meaning secondarily GTCS only. Tonic, clonic or absence seizures and possibly epileptic spasms may also result from secondarily generalisation (Table 2.1 and 2.3).

1. *Generalised-onset seizures.* They are often called primarily or primary generalised seizures, although this is not a formal term used in the ILAE nomen-

clature. 'Generalised-onset seizures' are synonymous with 'generalised epileptic seizures' in the ILAE classifications.

2. *Focal-onset generalised seizures (is synonymous to 'secondarily generalised seizures' used in the ILAE terminology).* They are partial (focal) at onset but do not remain localised. They spread and trigger a generalised epileptic seizure.

A significant and continuing problem of confusion may result from the inappropriate use of the terms 'primary' or 'secondary' for the characterisation of epileptic seizures and epileptic syndromes (see important note in chapter 5 page 140).[15] In idiopathic generalised epileptic syndromes, seizures are likely to be of generalised onset, whereas in cryptogenic and symptomatic syndromes, generalised seizures are likely to be of focal onset (see important note on page 27).

The ILAE classification of generalised-onset seizures is presented in Table 2.2 with the following broad categories:[11]

A1. absence seizures
A2. atypical absence seizures
B. myoclonic seizures
C. clonic seizures
D. tonic seizures
E. tonic–clonic seizures
F. atonic seizures (astatic).

## Seizure classification in the new ILAE Task Force reports[7,14]

Table 2.3 lists the various types of epileptic seizures approved in the recent ILAE report,[7,14] which varies little from the original ILAE seizure classification.[11]

Significant changes in the ILAE Task Force reports are:

*I. The old term 'focal' is reintroduced to replace 'partial' and 'localisation-related' epileptic seizures,* which is an understandable and welcomed change.

However, this new scheme abandons the division of focal seizures into 'simple' (without impairment of consciousness) and 'complex' (with impairment of consciousness).[7] The reason given is that this 'inappropriately created the impression that impairment of consciousness had certain mechanistic implications related to limbic system involvement' (Figure 2.1) and that 'complex partial seizures' has been erroneously used as a synonym of 'temporal lobe epilepsy'.[7] Although these are correct, there are significant practical reasons (medicolegal cases, driving and job-related performance) for distinguishing seizures with or without impairment of consciousness. Therefore, I keep using the terms 'simple' and 'complex' focal seizures in this book, while emphasising that (1) ictal impairment of consciousness is a symptom of either neocortical or limbic seizures and (2) complex focal seizures may originate from any cerebral lobe and therefore they are not synonymous with temporal lobe epilepsy.

The newest ILAE report proposes to abandon the terms simple and complex partial seizures and their distinction.[19] An added argument is that "the distinction based on impairment of consciousness... was impossible to define in a precise scientific manner".[19] However, 'impairment of consciousness' is also a defining symptom of other seizures such as absence seizures. Therefore, it needs to be defined and clarified (see important clinical note on page 23) even if 'complex partial seizures' are eliminated from our glossary.

*II. The scheme introduced the terms 'self-limited seizure types' for brief seizures and 'continuous seizure types' for status epilepticus.*[7] These terms were unlikely to find any support and they were not used in the first edition of this book. Also, 'continuous seizure types' is etymologically incorrect because 'status epilepticus' is sometimes self-limited (see examples of absence, autonomic or febrile status epilepticus) and often discontinuous (see examples of myoclonic or complex focal status epilepticus). The terms 'self-limited' and 'continuous' seizure are both rightly abandoned in the new ILAE report.

*III. The ILAE Task Force has also introduced the term 'epileptic seizure type',* which 'represents a unique diagnostic entity or natural class which ought to be defined on the basis of a distinct pathophysiology and anatomical substrate'.[14]

## Epileptic seizures

### I. Generalised onset

**A. Seizures with tonic and/or clonic manifestations**
1. Tonic–clonic seizures
2. Clonic seizures
3. Tonic seizures

**B. Absences**
1. Typical absences
2. Atypical absences
3. Myoclonic absences

**C. Myoclonic seizure types**
1. Myoclonic seizures
2. Myoclonic–astatic seizures
3. Eyelid myoclonia

**D. Epileptic spasms**

**E. Atonic seizures**

### II. Focal onset (partial)

**A. Local**
1. Neocortical
   a. without local spread
      i. focal clonic seizures
      ii. focal myoclonic seizures
      iii. inhibitory motor seizures
      iv. focal sensory seizures with elementary symptoms
      v. aphasic seizures
   b. with local spread
      i. jacksonian march seizures
      ii. focal (asymmetrical) tonic seizures
      iii. focal sensory seizures with experiential symptoms
2. Hippocampal and parahippocampal

**B. With ipsilateral propagation to:**
1. Neocortical areas (includes hemiclonic seizures)
2. Limbic areas (includes gelastic seizures)

**C. With contralateral spread to:**
1. Neocortical areas (hyperkinetic seizures)
2. Limbic areas (dyscognitive seizures with or without automatisms [psychomotor])

**D. Secondarily generalised**
1. Tonic–clonic seizures
2. Absence seizures
3. Epileptic spasms (unverified)

### III. Neonatal seizures

Table 2.3 *Reproduced with permission from Engel (2006).*[14]

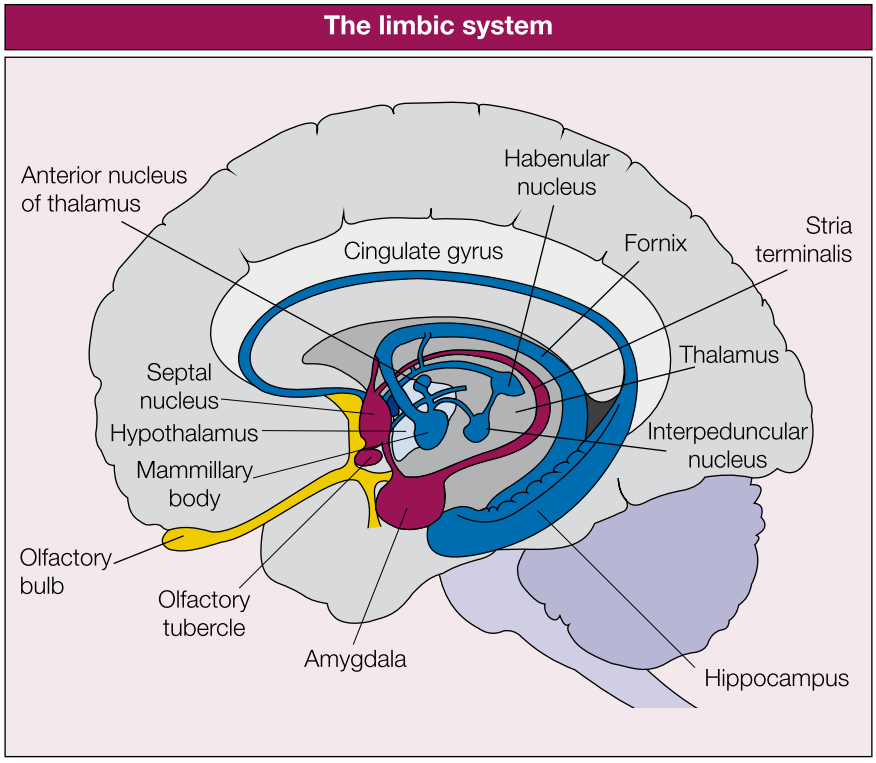


Figure 2.1

The following criteria were used to select specific seizure types as possibly unique diagnostic entities, for further hypothesis testing:

- *Pathophysiological mechanisms:* Including electrophysiological features, neural networks, neurotransmitter evidence if known (e.g. increased excitation and decreased inhibition for generalised tonic–clonic and some neocortical seizures versus increased excitation and increased inhibition, leading to hypersynchronisation for absences and some hippocampal seizures).
- *Neuronal substrates:* For these purposes, the neocortex is considered a single substrate regardless of exact location and function subserved, unless specific pathophysiological mechanisms differ. Thus, focal clonic movements caused by an epileptogenic abnormality in precentral cortex are not, in any essential way, different from unformed visual hallucinations caused by the same type of epileptogenic abnormality in the calcarine cortex if the pathophysiological mechanisms are the same, just as electrical stimulation induced after discharge of the neocortex represents the same epileptogenic mechanism, regardless of the area of neocortex stimulated and the behavioural signs and symptoms elicited. Other brain structures and networks should be included (e.g. thalamic reticular nucleus for absence seizures versus brain stem for GTCSs).
- *Response to AEDs:* Selective responsiveness to or exacerbation associated with specific drugs can suggest a specific mechanism of seizure generation.
- *Ictal EEG patterns:* Specific ictal EEG patterns can be necessary diagnostic features of specific seizure types (e.g. 3 Hz for absences). These should reflect specific pathophysiological mechanisms and anatomical substrates.
- *Propagation patterns and post-ictal features:* Patterns of propagation, or lack of propagation, and post-ictal features, or lack of them, help to define pathophysiological mechanisms and anatomical substrates (e.g. typical absences have no post-ictal dysfunction; contralateral propagation is

slow for hippocampal seizures versus fast for neocortical seizures; some seizures are strictly local, others more widespread).

The newest ILAE report makes no reference to "epileptic seizure type".[19] Therefore, it is assumed that this is no longer considered to be a diagnostic entity or natural class.

## Debate on the distinction between generalised and focal seizures

The dichotomy between generalised and focal seizures is rightly maintained in all ILAE classifications and their distinction has immense practical implications for the evaluation and management of patients. However, there has recently been significant debate on whether the differences between generalised and focal (partial) seizures are as sharp as was initially thought. This is well clarified in the newest ILAE report, which maintains the dichotomy between generalised and focal seizures.[19]

*Generalised epileptic seizures* are now considered to originate at some point within, and rapidly engage, bilaterally distributed networks. Such bilateral networks can include cortical and subcortical structures, but do not necessarily include the entire cortex. Although individual seizure onsets can appear localised, the location and lateralisation are not consistent from one seizure to another. Generalised seizures can be asymmetric. [19]

*Focal epileptic seizures* are now considered to originate primarily within networks limited to one cerebral hemisphere. These may be discretely localised or more widely distributed. Some lesions in subcortical structures may produce focal seizures (e.g. hypothalamic hamartomas). For each seizure type, ictal onset is consistent from one seizure to another with preferential propagation patterns, which can involve the contralateral hemisphere. In some cases, however, there is more than one epileptogenic network, and more than one seizure type, but each individual seizure type has a consistent site of onset. This also applies to cases in which focal seizures may arise independently in either hemisphere (e.g, bilateral mesial temporal lobe epilepsy or benign epilepsy with centrotemporal spikes).[19]

Focal seizures does not necessarily imply that the epileptogenic region is limited to a small circumscribed area, nor does generalised seizures imply that the entire brain is involved in initiation of the epileptogenic process.[14]

### Important clarification

In all previous and new ILAE classification the dichotomy between focal and generalised epileptic seizures is maintained. A significant deviation has occurred in the newest ILAE report in that although the distinction is maintained for epileptic seizures, it is stated that "for epilepsies, recent electro-clinical, imaging and genetic data do not support such a simple dichotomy".[19] Abolishing the distinction between focal and generalised epileptic syndromes creates significant problems of clinical and diagnostic significance, as detailed in Chapter 1, page 15.

The ILAE Task Force in justifying the decision to maintain the distinction between generalised and focal seizures states:

> Although the dichotomy of focal (partial) vs. generalized has been criticized, and we have recommended in an earlier report that these terms should eventually be discarded because no seizures or syndromes are truly generalized, nor is it likely that many, if any, seizures or syndromes are due to a discretely focal epileptogenic process, the Core Group has recognized the value of distinguishing epileptic seizures that begin in a part of one hemisphere, from those that appear to begin in both hemispheres at the same time. The Core Group, however, has been unable to come up with simple terms to describe these two situations. Given the prevalent usage, and the therapeutic implications, of the terms 'focal' and 'generalized,' we have decided to retain them, with the understanding that the former does not necessarily imply that the epileptogenic region is limited to a small circumscribed area, nor does the latter imply that the entire brain is involved in initiation of the epileptogenic process.[14]

The comments of Peter Wolf should also be considered:[17]

> The definition of generalised is very simple and straightforward. There are, however, serious problems with the term which the two subsequent commissions did not pay sufficient attention to. When generalised seizures are defined as those where the first changes indicate bilateral involvement, the concept of secondary generalisation which also is included in the 1981 seizure classification becomes meaningless, and a contradiction in itself. Then, in an unexplained way, secondary generalisation is not considered in the same way as bilateral spread of seizure activity which would seem logical. In complex partial seizures there is often bilateral involvement, but this seizure type is not considered as generalised but as partial. Both localisation-related and 'generalised' idiopathic epilepsies are about to be understood as related variants of system disorders of the brain, with an ictogenesis making pathological use of existing functional anatomic networks.[17]

The explanations given above for the use and boundaries of the terms generalised and focal epileptic seizures would be more than sufficient and the same applies to the distinction between generalised and focal epileptic syndromes (see important clarification in blue box on page 32 and chapter 1, page 15). It would be premature and confusing to discard or change these terms to something else that we may have to abandon again when new information emerges.Both pathophysiological and clinical factors render it important to retain the distinction between the focal and generalised epileptic seizures and syndromes.

All seizures "start somewhere", but there are significant pathophysiological, clinical, EEG and therapeutic differences between focal and generalised seizures:

- Pathophysiologically, generalised seizures start within specific regions that rapidly engage bilaterally distributed networks while focal seizures begin in other brain areas that engage localised and unilateral network of epileptogenicity.
- Clinically, focal seizures start with symptoms and signs that can be ascribed to specific brain locations while generalised seizures do not (unless they are secondarily generalised).
- EEG, interictal and ictal patterns are predominantly different between focal and generalised seizures as illustrated on many occasions in this book
- Pharmacologically, certain AEDs beneficial for focal seizures may have deleterious effects on generalised seizures

The main types of generalised and focal seizures are described below.

# Generalised epileptic seizures

## Generalised tonic–clonic seizures[10,20]

A GTCS is the most dramatic seizure type. It is a symptom of many idiopathic, cryptogenic or symptomatic epilepsies. GTCSs occur in all ages except neonates.[21] Examples of GTCSs in children include most febrile seizures and GTCSs in idiopathic generalised epilepsies (IGEs), such as juvenile myoclonic epilepsy (JME). Almost all focal epilepsies manifest with secondarily (focal-onset) GTCSs (SGTCSs).

The ILAE[2] glossary provides the following definitions for GTCSs.

*Generalised tonic–clonic seizure* (synonym: bilateral tonic–clonic seizure [formerly 'grand mal' seizure]). Noun; bilateral symmetrical tonic contraction, then bilateral clonic contractions of somatic muscles usually associated with autonomic phenomena.[2]

*Generalised-onset tonic–clonic seizures* (= PGTCSs) are generalised from the onset without warning other than by a series of myoclonic jerks or absences that often herald GTCSs (Figure 2.2). This contrasts with SGTCSs of focal epilepsies in which seizures of focal onset do not remain localised but spread and trigger a GTCS (Figure 12.3).[25]

*Secondarily generalised tonic–clonic seizures* are often preceded by an aura, motor sensory or other symptoms of focal seizures.

The differentiation of PGTCSs from SGTCSs is of immense clinical significance and is usually easy using clinical, EEG and MRI findings (Table 2.4). In addition, single photon emission CT (SPECT) shows increased thalamic cerebral flow only after PGTCSs.[24]

Investigation of symptoms and precipitating factors immediately before the onset of a GTCS is a crucial part of the history taking, with significant diagnostic and management implications.

## Epidemiology of GTCS

PGTCSs are the most serious type of seizures in IGE. Their prevalence, frequency and prognosis markedly depend on the syndrome of IGE (see chapter 13).

SGTCSs occur in around 90% of patients with focal epilepsies with marked variability in their occurrence, frequency, severity and prognosis (see for example chapters 12, 14 and 15).

## Clinical manifestations

A GTCS, whether a PGTCS or SGTCS, manifests with:

- loss of consciousness from onset to the late phase of recovery
- generalised tonic–clonic convulsions
- significant autonomic disturbances.

The depiction of GTCSs in this chapter is largely taken from the classic text of Gastaut and Broughton,[7] which has not been surpassed (Figure 2.3). More recent contributions have been made with video-EEG analyses of PGTCSs and SGTCSs.

### Ictal events preceding the onset of a GTCS

These differ between the PGTCSs and SGTCSs; e.g. clusters of myoclonic jerks or absences or absence status epilepticus precede and herald PGTCSs in IGEs, whereas SGTCSs develop from focal seizures.

### Onset of GTCS proper

At the start of a GTCS, the eyes immediately open and remain open during the whole period of the attack (Figure 2.4). A GTCS may start with asymmetrical lateral tonic deviation of the head and eyes. This is of little practical diagnostic significance because it may occur in both PGTCSs and SGTCSs, and may be contralateral or ipsilateral to the epileptic focus in SGTCSs. Brief symmetrical or asymmetrical clonic movements may also occur at the start of a PGTCS or SGTCS, and immediately before the tonic phase. Asymmetrical clonic jerks are more common in SGTCSs and may last for 3–21 s.[25] However, lateralisation of SGTCSs is more likely when head turning is forceful and prolonged, usually in a clonic motion with the chin pointing upwards, and eye version to the same side as the head version allows.[26] The 'sign 4' (extension of the elbow on the side contralateral to the epileptogenic focus and with elbow flexion of the ipsilateral side; Figure 2.5) may also be of lateralising significance when it occurs at the onset of a GTCS.[27]

### Tonic phase of GTCSs

The tonic phase is a 10–20 s sustained contraction of all skeletal muscles, producing a succession of characteristic body postures. It usually consists of an initial brief phase of tonic flexion forwards, followed by a longer one of tonic extension backwards. In tonic flexion, the arms are in elevation, abduction and external rotation, with semiflexion of the elbows; the body is dorsiflexed, and the lower limbs are less involved, but there may be flexion, abduction and external rotation of the thighs and legs. This converts into tonic ventriflexion of the neck and trunk with extension of the limbs. The tonic extension phase is heralded by forced closure of the previously widely open mouth, which often causes tongue biting. The 'epileptic cry', a high, pinched, loud scream occurring at this stage, is caused by the tonic contraction of thoracic abdominal muscles, which forcibly emit air across the tightly closed vocal cords. The semiflexed arms slowly lower in adduction until the forearms are crossed in front of the chest. Their subsequent posture is of extension and pronation at the elbow, with the fists clenched and wrists extended, or with the fingers extended and wrists flexed. The legs are in extension,

**Video-EEG recording of a 23-year-old woman with IGE: numerous typical absences occurred on awakening and one progressed to a GTCS**

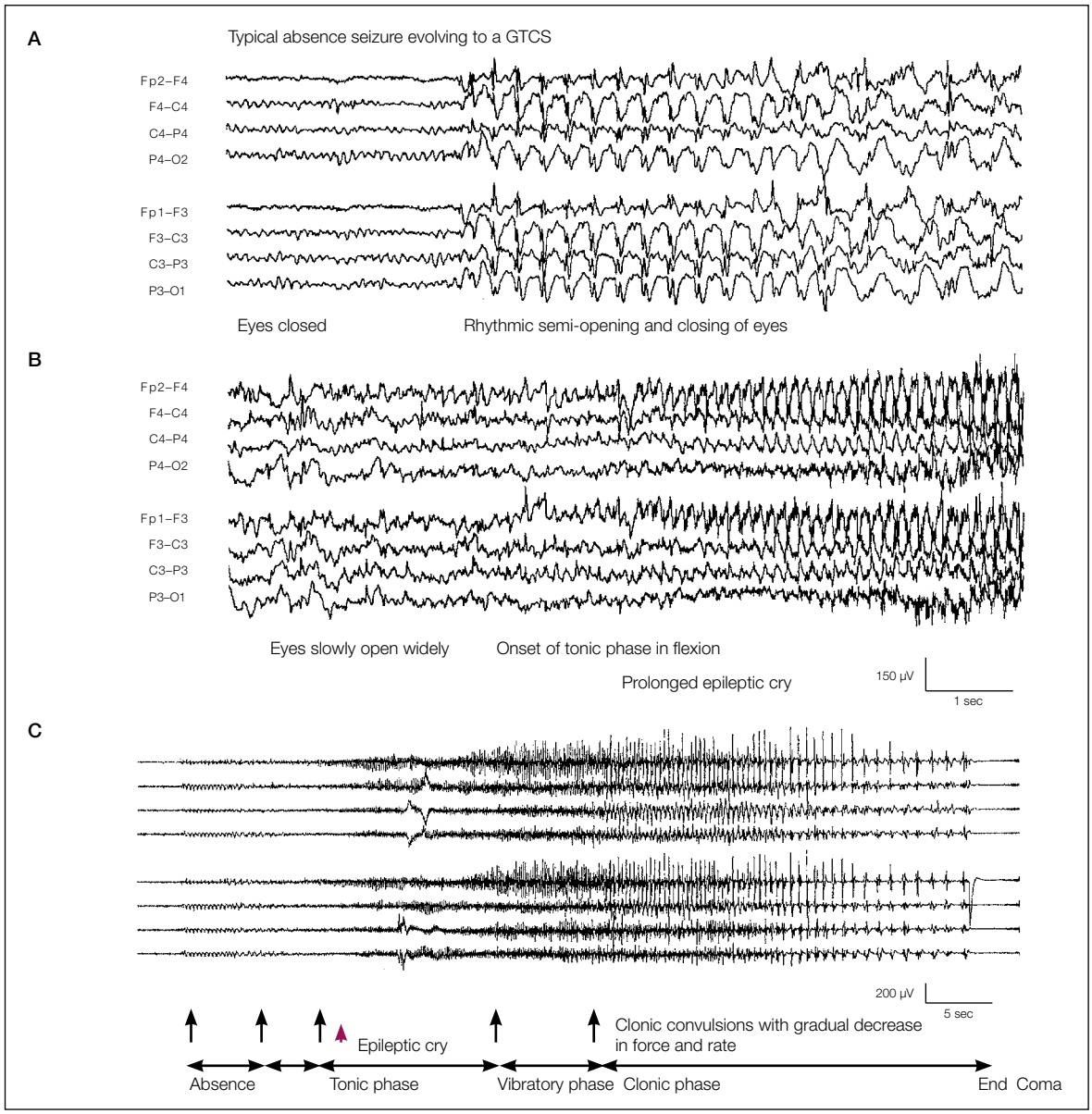


**Figure 2.2** Video-EEG recording of a 23-year-old woman with IGE. Numerous typical absences occurred on awakening, and one progressed to a GTCS (see details in Panayiotopoulos[22]). (**A**,**B**) Continuous recording from onset of the absence seizure to just before the onset of the vibratory phase of the GTCS. (**C**) The various phases of the whole seizure from onset to termination (duration approximately 1 min).
*Modified with permission from Panayiotopoulos (2000).*[22]

adduction and external rotation. Feet and big toes are also in extension (spontaneous Babinski sign). Tonic contraction of the diaphragm and chest wall muscles appears to be responsible for the cyanosis that results from inadequate alveolar ventilation. The tonic phase may be brief for 1–3 s, or last longer for 20 s.

**Differentiation of primarily versus secondarily GTCS**

| | Primarily GTCS | Secondarily GTCS |
|---|---|---|
| **GTCS in patients who also have other clinically evident seizures** | About 90% | About 90% |
| Typical absences | About 40% | None |
| Myoclonic jerks | About 60% | None |
| Focal seizures | None | About 90% |
| **GTCS in patients without other clinically evident seizures*** | About 10% | About 10% |
| Precipitating factors | >60% | <10% |
| Consistently on awakening | Common | Uncommon |
| Family history of similar epilepsies | Common | Uncommon |
| **EEG in untreated patients** | | |
| Generalised discharges | About 80% | Exceptional |
| Focal abnormalities alone | About 10% | About 60% |
| Generalised discharges and focal abnormalities | About 30% | Exceptional |
| **High-resolution brain imaging** | | |
| Focal abnormalities | Exceptional | About 60% |
| Normal | By definition | About 40% |

Table 2.4 *It is these patients, who make up about 10% of each category, that constitute the main problem in the differential diagnosis between primarily and secondarily GTCS. However, other features, such as precipitating factors, circadian distribution, EEG and brain imaging, are often of diagnostic significance.

### Intermediate transitory (vibratory) phase of GTCSs

The tonic phase ends gradually with fine clonus (vibratory tremor) initially superimposing on dominant tonic rigidity. The clonus is of waxing amplitude and waning frequency from 8 Hz down to 4 Hz. Distal muscles are affected before the proximal and facial masticatory muscles.

### Clonic phase of GTCSs

This is characterised by continuously repetitive, massive, symmetrical and synchronous flexor clonic convulsions of the facial, trunk and limb musculature. They last for 30 s to 1–2 min with progressively decreasing force, amplitude and frequency (to 1 Hz). They may finally restrict only in the facial muscles or end with a massive clonic convulsion. The tongue is often bitten repeatedly during this clonic phase and each convulsion may produce an epileptic cry. Towards the end of the clonic phase, the clonic convulsions may become asynchronous and asymmetrical, and side-to-side head and eye movements may also occur. Contraction of the bladder sphincter blocks urinary incontinence until the end of the clonic phase.

### Recovery phase of GTCSs

*Immediate post-ictal phase of GTCSs (comatose or stertorous phase):* Recovery starts with the cessation of clonic convulsions, although the patient remains in a coma, is unresponsive and markedly hypotonic. Respiration is restored with a deep inspiration, followed by usually noisy deep breathing associated with the secretion of frothy and bloodstained saliva. Urinary incontinence occurs only at this stage (Figure 2.4). Faecal incontinence or ejaculation is rare. Skin resistance and blood pressure return progressively to pre-seizure levels; the patient becomes pale.

Then, 5–8 s later, there may be a new phase of tonic contraction that mainly affects the facial and masticatory muscles: teeth are tightly clenched, and the limbs and trunk (when involved) take a decerebrate-like posture. Autonomic abnormalities include mydriasis, tachycardia, sometimes with marked cardiac arrhythmia, and intense tachypnoea. This state is associated with hypometabolism predominating in cortical structures.[46] It is of variable duration, from seconds to 3 or 4 min, or it may not occur. The patient remains unconscious throughout

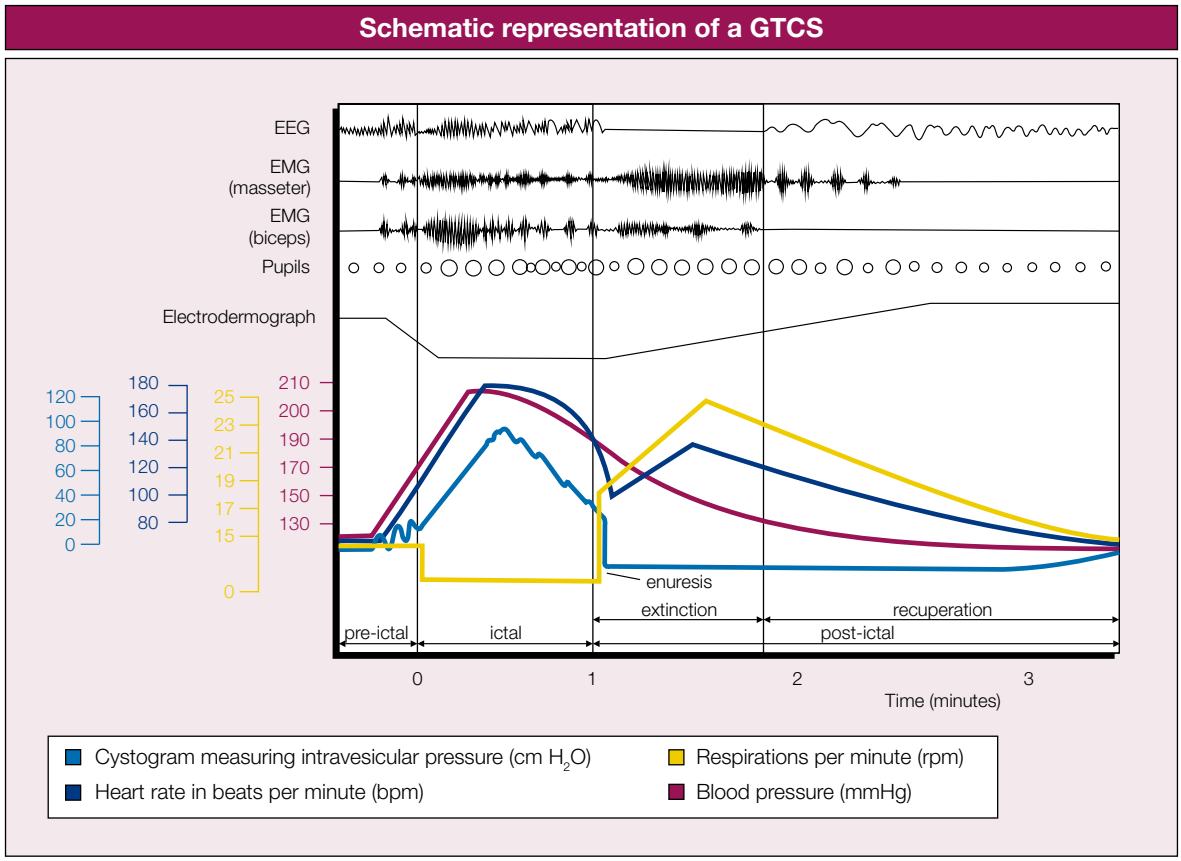


**Figure 2.3** *Modified with permission from the classic monograph of Gastaut and Broughton (1972).*[10]

this post-ictal state. Pupillary and cutaneous reflexes are absent, deep tendon reflexes are often exaggerated and the Babinski sign is elicited in half the patients. Unilateral pyramidal signs indicate SGTCSs of contralateral cortical onset.

*Late post-ictal phase of GTCSs:* This period of recovery is characterised by a gradual return to normality. Autonomic nervous system function normalises and pupillary, cutaneous and tendon reflexes reappear, but muscle atonia persists. Reactivity to pain stimuli returns. Cognitive functions also return to normal, but confusion and automatisms may initially be marked (post-ictal epileptic automatisms). The patient is extremely tired and drowsy and goes into a deep and lengthy sleep if left undisturbed. On awakening the patient feels exhausted, usually complaining of severe throbbing headache and with complete retrograde amnesia. The usual duration of the late post-ictal phase (not including the sleep period) is 2–10 min.

Upon full recovery, the patients are totally amnesic of what happened during the GTCS and most of the post-ictal state. However, they are aware that something happened to them mainly because of the memory gap, aching muscles and traumas.

## Autonomic changes of GTCS

Significant autonomic changes occur from the onset of a GTCS; they reach their peak at the end of the tonic phase and progressively improve with the onset of the clonic phase. Some continue in the immediate post-ictal phase and return to baseline normal function in the late post-ictal phase (see Figure 2.3 for their sequence). Apnoea is prolonged,

## Onset and sequence of a GTCS

Pre-ictal: In this example the patient is relaxing in bed and eyes are closed

Initial stage of tonic phase in flexion

The eyes open immediately after the onset and remain open during the whole period of a GTCS. They usually close post-ictally. Asymmetrical postures may occur both in PGTCS and SGTCS

Second stage of tonic phase in extension

Immediate post-ictal stage with urinary incontinence

Urinary incontinence occurs in the immediate post-ictal stage and not during the convulsions

Figure 2.4

starting immediately after the epileptic cry, and lasts throughout the entire tonic and clonic phases and, occasionally, into the initial post-ictal period. Heart rate and blood pressure increase markedly to double their pre-seizure values (Figure 2.3). Bladder (intravesicular) pressure increases sixfold, but urinary incontinence is prevented during the convulsions because of tonic contraction of the bladder sphincter muscles.

Urinary incontinence occurs only in the immediate post-ictal phase (Figure 2.4) because of relaxation of the urinary sphincter muscles. It does not occur earlier in the attack.

> It may be doubted whether they [the loss of urine and faeces] are due to epileptic spasm; they may occur after the fit and be due to loss of control.
>
> John Hughlings Jackson (1878)[3]

Pupils dilate in the tonic phase and become unresponsive to light. Hippus (rhythmic pupillary contraction and dilatation) occurs in the clonic phase. Unvarying pupil dilatation occurs again in the immediate post-ictal phase. Skin-colour changes are profound. Cyanosis caused by apnoea-induced hypoxia is apparent in the convulsive stages, whereas pallor becomes apparent in the immediate post-ictal phase. Piloerection is common. Glandular hypersecretion produces marked sweating, hypersalivation and tracheobronchial secretions.

### Post-ictal metabolic and hormonal changes[28]

Post-ictal metabolic and hormonal changes occurring immediately after a GTCS last for approximately 1 hour. The most consistent changes are lactic acidosis and the elevation of prolactin and serum creatine kinase levels. Rise of prolactin peaks 20 min post-ictally to 5–30 times the baseline levels and remains significantly elevated for 1 hour.[29]

**Important note**

Serum prolactin levels are normal in GTC status epilepticus.[29]

### Variants of GTCS

It should be emphasised that GTCSs often vary in severity, duration of the tonic and clonic phases, and duration and symptoms of the recovery period. Either the clonic or tonic phase may predominate,

**The 'sign 4' position**

Figure 2.5

recovery may be very slow or relatively fast, and post-ictal symptoms may be severe or relatively mild. The tonic phase may be brief followed by lengthy clonic convulsions. In children the tonic phase may be longer than the clonic phase. These variants of GTCS are sometimes difficult to differentiate from a genuine tonic or clonic seizure.[10]

### Complications of GTCSs[28]

The complications of a GTCS are either from a direct effect of the GTCS manifestations on the body or by accidents occurring as a result. Trauma of differing types and severity is the most likely complication. Skin lesions, aspiration pneumonia, pulmonary oedema and death may occur.

*Oral lacerations* involving the tongue, lip and cheek occur probably in one out of ten GTCSs.[20] These are more often unilateral than bilateral.

> Placing an object in the patient's mouth to prevent tongue biting is erroneous and causes more harm than good. Mouth closure is so forceful that it can amputate a finger placed between the teeth or break the teeth if the object is metallic.

*Craniocerebral trauma* is caused by falls. Severe burns may occur while cooking or when falling into a fire. *Stress fractures* as a direct consequence of a GTCS without direct trauma occur in 0.3% of cases and are more common in elderly people. They mainly affect the thoracic and lumbar vertebrae and are usually asymptomatic. More serious fractures may occur. Vertebral compression and other fractures are the main complications during epilepsy monitoring when AEDs are withdrawn.

> An astute orthopaedic surgeon referred a young patient to me with recurrent dislocation of the shoulder during sleep. He was not known to have epileptic seizures but EEG confirmed the diagnosis of IGE.

*Skin abrasions* and lacerations are caused by external trauma during a GTCS. Skin petechial haemorrhages over the face, neck and chest, as well as conjunctival haemorrhage, are due to capillary bleeding.

*Aspiration pneumonia* is an uncommon (around 4 of 1600 patients)[30] but potentially life-threatening complication caused by the aspiration of saliva, tracheobronchial secretions or vomiting. It occurs in the post-ictal rather than the ictal phase (when oral secretions are not usually increased and there is cessation of respiratory movements) of a GTCS. The risk for aspiration pneumonia is higher in institutionalised patients and those with swallowing difficulties, increased oral secretions,[30] lowered resistance to infection or depressed airway reflexes from drug or alcohol abuse.

> Positioning the patient in a lateral decubitus position in the immediate post-ictal phase significantly decreases the risk of aspiration.[30]

*Pulmonary oedema* is rare, but potentially life threatening if untreated. It is usually misdiagnosed as aspiration pneumonia. Its exact pathophysiology is unknown. Pulmonary oedema usually resolves rapidly with oxygen, independent of diuretic use. It is associated with high mortality mainly of older patients.

*Death:* Accidental (falls, drowning) and non-accidental deaths (aspiration, pulmonary oedema, cardiac arrhythmias, cardiac asystole) may occur during and immediately after a GTCS. Furthermore, the risk of sudden unexplained death in epilepsy (SUDEP) is significantly higher in patients with GTCS than in patients with other types of seizure.[31]

## Ictal EEG of GTCSs[10,28]

In routine EEGs the electrical signature of GTCSs is usually masked by muscle artefacts in all derivations, except those from the vertex. Accurate EEG description has been mainly derived from patients who were pharmacologically paralysed at the time of the GTCS.[10]

The ictal EEG discharges of GTCSs are diffuse and generalised with approximately synchronous and symmetrical amplitude on the corresponding areas of both sides.

The patterns of PGTCSs and SGTCSs are virtually indistinguishable from the onset of the tonic phase to the end of the seizure. GTCSs during sleep have EEG patterns that are virtually identical to those of a diurnal attack; they interrupt the electrical activity of the ongoing sleep.

*Tonic phase:* The ictal EEG onset of the GTCSs is marked by a brief (1–3 s) period of flattening or with low-voltage fast rhythmic activity at about 20 Hz or fast spiking. This gradually becomes more synchronised, increases in amplitude and slows in frequency to a sustained 10 Hz rhythm ('epileptic recruiting rhythm' is the preferred term of Gastaut). See Figure 2.2.

*Intermediate phase and clonic phase:* Slow waves of increasing amplitude and decreasing frequency superimpose and gradually rhythmically interrupt the 10 Hz fast rhythms of the tonic phase. Finally, the EEG assumes a pattern of repetitive, high-amplitude polyspike–slow-wave complexes that increase in amplitude and slow down to 1 Hz. The clonic convulsions correspond to the polyspikes, whereas the periodic muscle atonia corresponds to the slow waves. See Figures 2.2 and 12.3.

*The post-ictal period* is characterised by diffuse background suppression (flat or isoelectric EEG) or a burst-suppression or triphasic wave pattern of several seconds to 2 or 3 min (longer in children). This is followed by diffuse slow waves that gradually increase in frequency and amplitude. The periods of coma and confusion and the return to normality correlate fairly well with dominant delta activity, theta activity and the return of a normal alpha rhythm after several minutes. See Figures 2.2 and 12.3.

*Surface electromyography (EMG)* shows sustained and continuous muscle contraction at around 50 Hz, which corresponds to the tonic phase of GTCSs and is concurrent with the EEG recruiting rhythms. This is followed by repetitive EMG bursts–EMG paucity at the frequency of the slow waves of the intermediate phase and spike–wave complexes of the clonic phase. The EMG bursts correspond to the clonic convulsions. Each slow wave is associated with decrease, then abolition, of muscle tone. See Figure 2.2.

The variants of tonic–clonic seizures have the EEG patterns expected based on clinical grounds. Those with relatively prolonged tonic or clonic phases have correspondingly longer periods of recruiting rhythm or polyspike–wave discharges.

## Aetiology of GTCS

Any structural or functional brain abnormality can generate a GTCS, which may be a one-off event or a cause of epilepsy with recurrent GTCSs. GTCSs occur:

- in nearly all types of focal or generalised epileptic syndromes (idiopathic, symptomatic and cryptogenic)
- are the most common type of 'situation-related epileptic seizures', acute symptomatic seizures and often occur in 'diseases frequently associated with epileptic seizures or syndromes'.

### GTCSs in epileptic syndromes

PGTCSs are the most serious seizure type of IGEs, and SGTCSs are the most serious seizure type of focal (idiopathic, symptomatic or cryptogenic) epilepsies.

### GTCSs in 'situation-related epileptic seizures' and acute symptomatic seizures

PGTCSs and SGTCSs are the most common types among the situation-related epileptic seizures,[13] such as febrile seizures (see Chapter 5), which are a separate category of acute symptomatic seizures.

Acute (provoked, occasional, reactive) symptomatic seizures are epileptic seizures that occur in close temporal association with a transient CNS insult or transient systemic disturbance.[32,33]

These seizures are presumed to be an acute manifestation of the insult. The definition of 'close' varies with the insult.[32,22]

Most of the acute symptomatic seizures are PGTCSs or SGTCSs, and their major causes are:

- structural CNS lesions due to any type of infection, brain trauma, cerebrovascular disease, primary or metastatic CNS tumour
- metabolic or toxic systemic dysfunction, such as acute toxic insults due to poisoning or drug overdose, alcohol or drug withdrawal, eclampsia, metabolic disorders or an electrolyte imbalance (such as uraemia, hyponatraemia, hypocalcaemia, ketoacidosis and hypoglycaemia).

In certain brain disorders, such as encephalopathies, there is a combination of metabolic dysfunction and structural abnormalities.

Each type of acute symptomatic seizure has age, gender and time period patterns that reflect the occurrence of the underlying cause. Meningitis, encephalitis, dehydration and toxic encephalopathy predominate in children. Stroke, brain haemorrhage, infection, trauma and degenerative disease, such as dementia, are the main causes in the elderly.[34]

The aetiological spectrum of acute symptomatic seizures in resource-poor countries (CNS infections, dehydration and acute diarrhoea account for a significant number of cases) is different[35] from that described in developed countries (cerebrovascular disorders predominate).

## Pathophysiology

The pathophysiology of GTCSs is not precisely known, as also indicated by the ILAE Core Group report,[14] which raises more questions than answers:

GTCSs involve brain stem, possibly prefrontal, and basal ganglia mechanisms. Ictal initiation of primarily bilateral events are predominantly disinhibitory, but other mechanisms are responsible for ictal evolution to the clonic phase, involving gradual periodic introduction of seizure-suppressing mechanisms. Several discrete types might be identified – future investigation is needed to determine which of these types represent unique phenomena:

- reactive GTCSs (acutely provoked seizures)
- GTCSs of idiopathic epilepsies
- GTCSs of symptomatic epilepsies
- GTCSs evolving from myoclonic seizures (e.g. clonic–tonic–clonic seizures in JME and epilepsy with myoclonic–astatic seizures)
- GTCSs evolving from absence seizures.

And several questions can be raised:

Do patients with idiopathic focal epilepsies have primarily as well as secondarily seizures? Some data suggest that GTCSs in benign childhood epilepsy with centrotemporal spikes are secondarily, although some patients with this condition may have PGTCSs as well.

What are clonic–tonic–clonic seizures? Are GTCSs that evolve from myoclonic seizures the only form, or are there also true clonic–tonic–clonic seizures (as may be seen in forms of progressive myoclonus epilepsy)?

How should we regard hemi-seizures that manifest unilaterally in the immature brain owing to poor myelinisation of the corpus callosum? In this case, the disorder is bilateral, but the onset is clearly unilateral. Do these only occur in infants, or do they also occur in children and adults? In some infants, hemi-seizures have focal onset.

Some experimental evidence suggests that the mechanisms of ictal initiation could be different for some or even all of these subtypes of GTCSs, and that there may even be more than one mechanism of initiation within each of the subtypes.[14]

### The pathophysiology of the various stages of GTCSs

Gastaut attributed 'the entire GTCS to be a diffuse subcortical reticular discharge which leads to activation of inhibitory systems and, at the end of the seizure, to a transient post-ictal state of cortical depression'.[10]

### Theories of the synchronous and bilateral nature of generalised discharges associated with absence seizures and GTCSs (Figure 2.6)

The centrencephalic, corticoreticular and cortical theories that have been proposed explain the synchronous and bilateral nature of the generalised discharges associated with absence seizures, GTCSs and loss of consciousness. The analysis of these theories by their main protagonists can be found in the classic book *The Physiopathogenesis of the Epilepsies*.[36] See also more recent reviews in the literature.[37,38]

Animal and human data suggest that the various types of generalised epileptic seizures involve selective networks (while sparing others) that engage in abnormally synchronous and high-frequency neuronal oscillation.

*The pathophysiology of absence seizures* is better understood than that for any other type of generalised seizures (Figure 2.6).[38–41] It appears that the generalised discharges of spikes and waves associated with absence are generated and sustained by highly synchronised abnormal oscillations between thalamic and cortical networks, which mainly involve neocortical pyramidal cells of predominantly mesial frontal cerebral cortex, the reticular thalamic nucleus and the relay nuclei of the thalamus. Neither the cortex

nor the thalamus alone can sustain these discharges, indicating that both structures are involved in their generation. However, their primary neurocellular and neurochemical abnormality is still debated, with evidence and arguments for the primary role of either the cortex[42] or the thalamus.[43] More recently, it has been suggested that seizure activity from an epileptic focus within the perioral region of the somatosensory cortex generalises rapidly over the cortex. During the first cycles of the seizure, the cortex drives the thalamus, whereas thereafter the cortex and thalamus drive each other, thus amplifying and maintaining the rhythmic discharge.[37]

The basic intrinsic neuronal mechanisms involve low-threshold T-type calcium currents. $GABA_B$ receptors play the most prominent role by eliciting the long-standing hyperpolarisation needed to drive low-threshold calcium channels for the initiation of sustained burst firing. Thus, the generation of absences is due to a predominance of inhibitory activity (mainly $GABA_B$), in contrast to generalised or focal convulsive seizures in which an excess of excitatory activity is present.[44]

*The pathophysiology of GTCSs* is different to that of absence seizures, but there may be a similar interplay of oscillations in networks intensely involving, not the whole brain homogeneously, but rather the focal bilateral regions most intensely, especially the frontal and parietal association cortex, thalamus, basal ganglia and brain stem.[40,51,52] Some other cortical regions appear to be relatively spared, or at least less intensely involved.[47] The cerebellum may also play a role in GTCS termination and post-ictal suppression.[53]

In mammals, there are two sets of convulsive seizure circuitry: the forebrain and brain-stem seizure circuitry. In humans, focal seizures correspond with

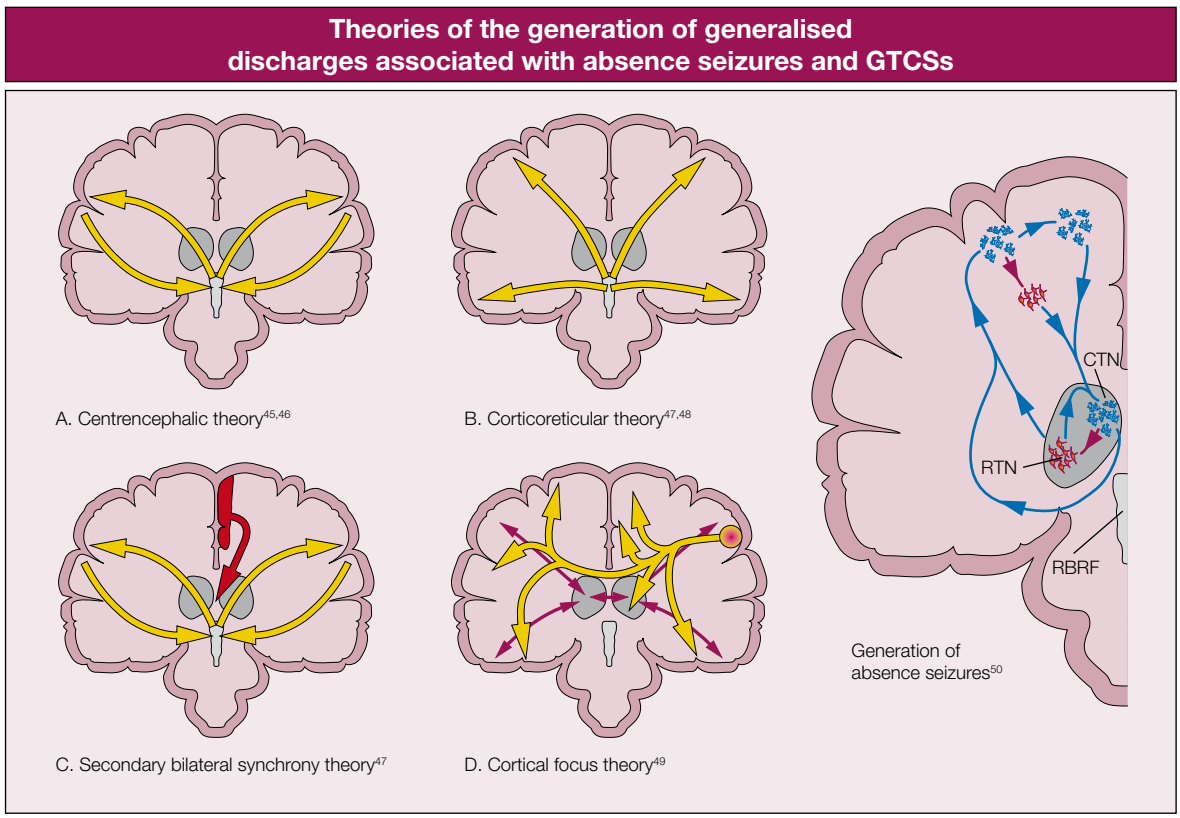


Figure 2.6 CTN, corticothalamic neurones; RTN, reticular thalamic nucleus; RBRF, rostral brain-stem reticular formation.

those of the forebrain circuitry, GTCSs with those of the brain-stem circuitry and SGTCSs with forebrain seizures that secondarily evoke brain-stem seizures.[54] The clinical and electrophysiological manifestations of GTCSs (including initiation, continuation and termination) in humans closely resemble generalised brain-stem seizures in genetically epilepsy-prone rats (GEPR) and *Papio papio*.[54]

Advanced functional neuroimaging techniques have been used in the study of spontaneous GTCSs of patients with epilepsy[51,55] or GTCSs induced by electrotherapy in psychiatric patients.[51] On the basis of their findings, Blumenfeld, *et al*[51] proposed a model in which GTCSs involve the cortical regions of seizure onset and selective bilateral regions of seizure propagation. Corresponding subcortical networks are also involved, whereas other cortical regions may be relatively spared or even inhibited during seizures. The behavioural manifestations of GTCSs can be explained by selective abnormal regional cortical excitation and inhibition, together with the involvement of brain-stem networks.[51]

## Generalised tonic seizures

Generalised tonic seizures are convulsive attacks of sustained muscular contractions only, without clonic components. They usually last a few seconds (>2 s to 10 s) but sometimes minutes and thus they are of longer duration than myoclonic jerks (under a tenth of a second) and epileptic spasms (0.2–2 s). The tonic seizures differ from the tonic convulsions of GTCS, which occur in continuity with the subsequent clonic convulsions. In addition, the mechanism responsible is probably different to that of the tonic phase of GTCS.

*Prevalence* is high, because generalised tonic seizures frequently occur in a variety of common epileptic syndromes affecting neonates, infants and children.

*Aetiology:* The aetiology of generalised tonic seizures is mainly symptomatic.

### Clinical manifestations

Tonic seizures usually have an abrupt onset, may be symmetrical or asymmetrical, and may be inconspicuous or violent. Concurrent autonomic manifestations including apnoea may be prominent. Consciousness is impaired. Focal and asymmetric signs of head or eye deviation may occur. In Lennox–Gastaut syndrome, tonic seizures occur more often during slow non-rapid eye movement (REM) sleep (hundreds of times in some patients) than in states of wakefulness; they do not occur during REM sleep.

Tonic seizures are descriptively classified as:

*Axial tonic seizures* affect the facial, neck, trunk, paraspinal, respiratory and abdominal muscles, either alone or in combination. Symptoms include raising the head from a pillow, elevation of the eyebrows, opening of the eyes, upward deviation of the eyeballs, opening of the mouth and stretching of the lips to a fixed smile. An 'epileptic cry' is common at the onset of attacks.

*Axorhizomelic tonic seizures* are axial seizures that also involve the proximal (rhizomelic) muscles of the upper and less often the lower limbs. Elevation and abduction or adduction of the upper limbs and shoulders occur together with the other symptoms of axial tonic seizures.

*Global tonic seizures* are axorhizomelic seizures that also involve the distal part of the limbs. The arms are forced upwards, abducted and semiflexed with clenched fists. The lower limbs are forced into triple flexion at the hip, knee and ankle or into extension. Global tonic seizures often cause forceful falls and injuries.

*Tonic seizures* are precipitated/facilitated by sleep. Startle-induced tonic seizures may be of focal origin.

### Aetiology

The aetiology of generalised tonic seizures is mainly symptomatic. Tonic seizures are the most common type of seizure (80–100%) in Lennox-Gastaut syndrome. They are exceptional or do not occur in epilepsy with myoclonic–astatic seizures or IGE.

### Diagnostic tests

*Interictal EEG* is grossly abnormal with frequent runs of fast rhythms and spikes mainly in non-REM sleep and also slow spike–wave discharges.

*Ictal EEG* comprises low-voltage accelerating fast paroxysmal activity that may be: (a) very rapid (20 ± 5 Hz) and progressively increasing in amplitude from low to 50–100 μV; and (b) rhythmic discharge

of around 10 Hz similar to that of the tonic phase of GTCS. Generalised tonic seizures usually correlate with the burst component of the burst-suppression pattern. *Brain imaging and other tests* are necessary, because most tonic seizures are symptomatic.

### Differential diagnosis

Generalised tonic seizures should be differentiated from epileptic spasms, myoclonic attacks, other seizures manifesting with combined tonic, clonic and other symptoms, and focal tonic seizures. Conditions that may mimic tonic seizures include hyperekplexia, dystonia and repetitive sleep starts in neurologically impaired patients, and benign non-epileptic myoclonus in infancy.

### Management

Treatment with any AED is often disappointing (see Lennox-Gastaut syndrome). Callosotomy may be the last resort.

## Generalised clonic seizures

Generalised clonic seizures, by definition, manifest with bilateral rhythmic clonic convulsions only. Their duration varies from minutes to hours but each clonic event lasts < 100 ms at a rate of 1–3 Hz (Figure 12.3). The generalised clonic seizures differ from the clonic convulsions of GTCS, which occur in continuity with the preceding tonic convulsions. They also differ from other types of seizure that manifest with tonic components mixed with myoclonus (e.g. eyelid myoclonia) or absence (e.g. myoclonic absence seizures in which the myoclonic component is rhythmic at 2.5–4.5 Hz, is clonic rather than myoclonic and has a tonic component). The mechanisms responsible for generalised clonic seizures (rhythmic excitatory discharges) are probably different from those in the clonic phase of GTCS (phasing in of seizure-suppressing mechanisms). Clonic seizures should also be distinguished from myoclonic seizures; clonic seizures are rhythmic at 1–5 Hz, whereas myoclonic seizures are singular or irregular recurrent events. Thus, the ILAE defines clonic seizures as 'rhythmic myoclonus' at a frequency of about 2–3 Hz.[11]

According to the ILAE Task Force,14 generalised clonic seizures are: "fast rhythmic events (1–2 Hz), associated, or not, with impaired consciousness" and proposes that their "mechanisms are different from those of the clonic phase of GTCS. In the latter, the clonic phase represents the phasing in of seizure-suppressing mechanisms, whereas in clonic seizures, the repetitive discharges appear to be due primarily to rhythmic excitatory discharges."[14]

*Prevalence:* Isolated generalised clonic seizures (without the preceding tonic phase of GTCS, or the clonic-absence or clonic/tonic complex) are rare. They are reported in neonates and infants (but are often of focal onset), progressive myoclonic epilepsies (but may be myoclonic jerks with rhythmic or pseudo-rhythmic occurrence) and hemiconvulsions (which are not generalised seizures).

### Clinical manifestations

Clonic seizures may cause:

- repetitive rhythmic flexion and extension
- repetitive rhythmic contraction and relaxation of the affected muscles.

In neonates and infants, generalised clonic seizures may appear as more or less rhythmically repeated, bilateral clonic contractions, distributed more or less regularly throughout the entire body and associated with loss of consciousness and massive autonomic symptoms and signs. Clonic seizures are associated with the loss, or severe impairment, of consciousness. Exceptionally, bilateral clonic convulsions of the upper extremities may occur without clouding of consciousness; however, in these cases, there are no EEG generalised spike–wave discharges and the seizures originate in the supplementary motor area. Also, some children with benign myoclonic epilepsy of infancy may have generalised clonic seizures exclusively during sleep or on awakening, which are prolonged (up to 15–20 min) and can cause cyanosis without loss of consciousness.

### Aetiology

The aetiology is usually symptomatic. Generalised clonic seizures alone are not specific to any syndrome.

### Diagnostic tests

*Interictal EEG* can range from normal to grossly abnormal.

*Ictal EEG:* Each clonic convulsion corresponds to a generalised discharge of spike and multiple spikes or, more rarely, a mixture of rapid rhythms and slow waves.

*Brain imaging and other tests* are needed to detect the underlying pathology.

### Differential diagnosis

The main problem is to differentiate clonic seizures from myoclonic seizures and from seizures manifesting with clonic convulsions in continuity or together with tonic, absence and myoclonic manifestations. In early childhood and the epileptic encephalopathies, GTCS may appear only as generalised clonic convulsions, in which the preceding tonic phase is brief and inconspicuous.

### Management

Pure generalised clonic seizures probably require AEDs that are suitable for generalised seizures. Phenobarbital may be preferred in neonates.

## Epileptic spasms[56,57]

*Synonyms:* infantile spasms, salaam spasms.

Epileptic spasms are seizures that may be generalised, focal, or of unclear onset.[19]

Epileptic spasms are sudden and brief bilateral tonic contractions of the axial and proximal limb muscles with abrupt onset and termination (Figure 10.1). They usually last for around 1 s (range 0.2–2 s) and thus they are of longer duration than myoclonic jerks (<0.1 s) but of shorter duration than tonic seizures (usually 2–10 s) (Figure 2.8).

*Prevalence* of epileptic spasms must be higher than that of West syndrome (which is around 0.5/1000 babies), because they also have other aetiologies.

### Clinical manifestations

The most common and characteristic form of epileptic spasms is with West syndrome but epileptic spasms may also occur in older children with epileptic encephalopathies (see Chapter 10).

Epileptic spasms are usually symmetrical and may involve widespread muscle groups or only the neck (bobbing of the head or grimacing), abdomen (mild bending) or shoulders (a shrug-like movement). Lateralising features may occur. Subtle epileptic spasms may appear as episodes of yawning, gasping, facial grimacing, isolated eye movements and transient focal motor activity. The more common form manifests with moderate flexion of the hips, the upper trunk and the head. The arms are almost always involved, being abducted, elevated and in a semi-flexed position. The force is usually violent but may also be mild or intermediate. Falls are common. Alteration and pauses of respiration during the spasms are common (60%) while changes in heart rate are rare. The end of the attack is often followed by a cry or laughter. Post-ictally, there may be a brief (< 90 s) arrest of motion and responsiveness. On rare occasions, this 'arrest' constitutes the entire seizure. Epileptic spasms usually occur in clusters, often on awakening.

Spasms may be flexor, more often flexor-extensor and less frequently extensor (see West syndrome page 276).

Epileptic spasms are precipitated by the half-awake state before sleep or after waking, sudden loud noises, tactile stimulation and feeding, but not by light.

### Aetiology

Epileptic spasms may be idiopathic or cryptogenic, but is mainly symptomatic. Epileptic spasms are seen in West syndrome and young children with epileptic encephalopathies. Reversible causes include drugs such as theophylline and ketotifen.

### Diagnostic tests

*Interictal EEG* shows hypsarrhythmia, modified hypsarrhythmia or the slow waves of the epileptic encephalopathies.

*The ictal EEG* is heterogeneous. The most common pattern is an electrodecremental event. A high amplitude, biphasic, slow wave or spike and wave activity may occur.[58,59]

*Brain imaging and other tests* are usually necessary.

### Differential diagnosis

Includes exaggerated startle responses, 'colic and abdominal pain', non-epileptic episodic disorders, gastro-oesophageal reflux and benign myoclonus of early infancy or Fejerman syndrome (See Chapter 4).

### Management

Treatment comprises vigabatrin, adrenocorticortricotrophic hormone and corticosteroids. See also West syndrome (Chapter 10, page 283).

## Myoclonus

There is no generally accepted, precise definition of 'myoclonus' and there is a long-standing source of confusion and debate about the term and concept of epileptic and non-epileptic 'myoclonus'.[60–62] 'Myoclonus' is a descriptive term for heterogeneous phenomena such as 'sudden brief jerk caused by involuntary muscle activity', 'quick muscle regular or irregular jerks', 'a sudden brief, shock-like muscle contraction arising from the central nervous system', and 'abrupt, jerky, involuntary movements unassociated with loss of consciousness'.

*Myoclonus* is probably best defined as sudden jerks typically lasting 10–50 ms, with the duration of movements rarely longer than 100 ms (Figure 2.7).[63]

The ILAE definition for myoclonus[2,14] is:

> *Myoclonic (adj.); myoclonus (noun):* sudden, brief (<100 ms), involuntary, single or multiple contraction(s) of muscles(s) or muscle groups of variable topography (axial, proximal limb, distal).[2]

### Description of myoclonus

Myoclonic jerks are shock-like, irregular and often arrhythmic, unidirectional, clonic, twitching movements that are singular or occur in irregular clusters. They are of variable amplitude, force, location, duration, precipitating factors and circadian distribution.

Myoclonic jerks may be:

- focal, segmental, multifocal or generalised
- mild, causing minor and inconspicuous flickering, or massive with traumatic falls
- rhythmic, arrhythmic or oscillatory (often resembling a very fast tremor)
- spontaneous, reflex (photic, acoustic, somatosensory, reading) or action (movement or intention to move) induced
- related to sleep, awakening or alert stages
- brief bursts or repetitive and continuous for hours and sometimes for days.

### Classification of myoclonus[62–66]

Myoclonus may be:

- a normal (physiological) phenomenon such as hiccups (singultus) or hypnagogic jerks (sleep starts)
- an abnormal (epileptic or non-epileptic) symptom of a wide range of different disorders with regard to aetiology, semiology, nosology, pathophysiology and prognosis.

The two main classification systems of myoclonus are based on aetiology (Table 2.5) and physiology (Table 2.6).

### Epileptic myoclonus

There are various definitions of what epileptic myoclonus is: 'myoclonus is termed epileptic when it occurs in combination with cortical epileptiform discharges. In some cases, the latter may be demonstrated only by the technique of back-averaging'[64] or 'myoclonus is epileptic, when generated in the cortex, and non-epileptic, when generated in subcortical structures'. Others prefer indirect definitions such as 'epileptic myoclonus is the presence of myoclonus in the setting of epilepsy'[62] or 'myoclonic seizures are epileptic seizures in which the motor as well as the main manifestation is myoclonus'.[62]

I propose the following definition of epileptic myoclonus, which is in compliance with the current ILAE definition of an epileptic seizure:

> Epileptic myoclonus is a transient (<100 ms) involuntary single or multiple muscle jerk due to abnormal excessive or synchronous neuronal activity in the brain.[1]

Myoclonic seizures are briefer than tonic seizures and epileptic spasms (Figure 2.7). According to the recent ILAE report:[14]

## Myoclonus versus clonic, tonic, atonic seizures and epileptic spasms

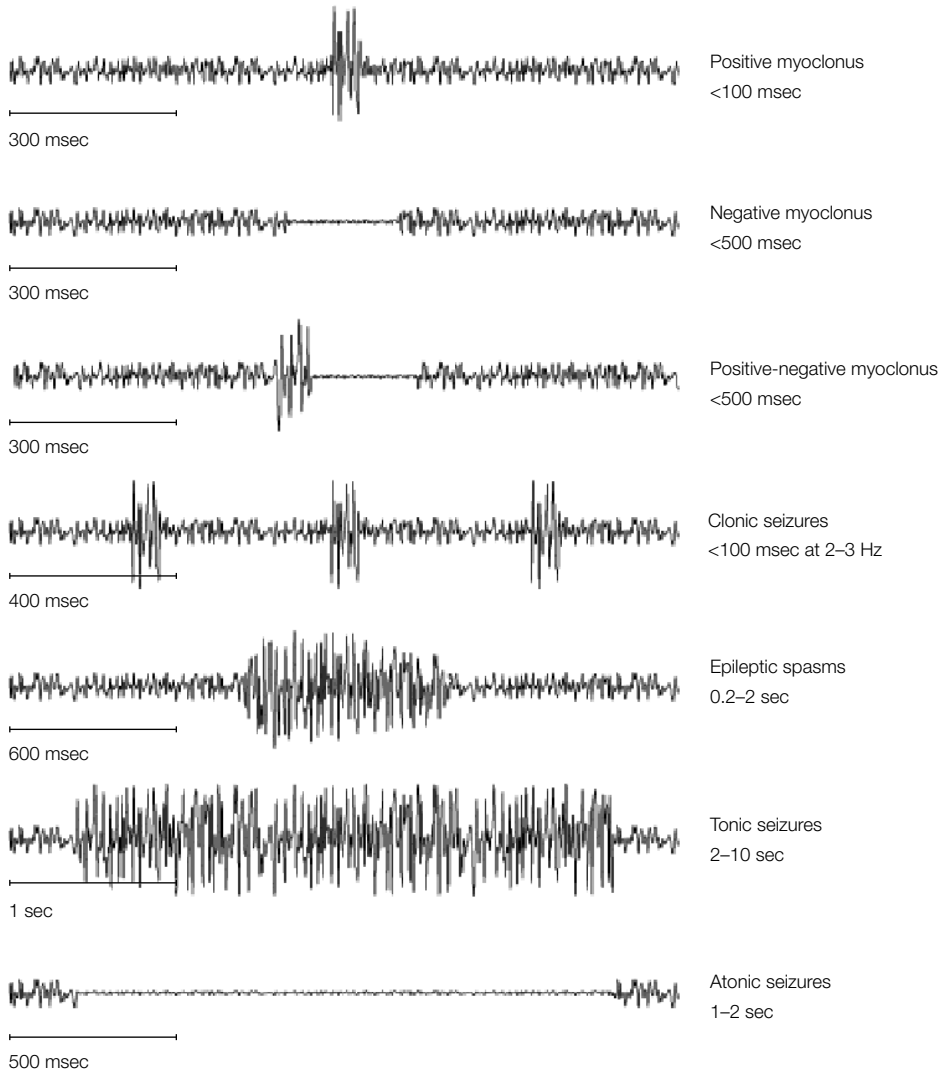


**Figure 2.7** Illustrative EMG presentation of positive and negative myoclonus, clonic, tonic and atonic seizures and epileptic spasms.
*Reproduced with permission from Panayiotopoulos (2006).*[23]

The distinction between myoclonic seizures and clonic seizures is not clear. Classically, clonic seizures are rapid rhythmically-recurrent events, whereas myoclonic seizures are single, or irregularly recurrent events. The prototype of generalized myoclonic seizures are those occurring with JME. These are typically bilateral and symmetrical, but localized reflex myoclonus can also occur. The slowly rhythmic events of subacute sclerosing panencephalitis (SSPE) used to be considered epileptic myoclonus but are more accurately epileptic spasms, those with biPEDs (bilaterally synchronous periodic lateriliziing epileptiform discharges) in comatose patients also are not necessarily epileptic, and their cause is usually not clearly defined. Differential

diagnosis between myoclonic and clonic seizures can be difficult because a single jerk can be a fragment of a clonic seizure.

Working groups will be convened to specifically evaluate myoclonic epileptic phenomena, including negative myoclonus and atonic seizures, compare them with non-epileptic myoclonic phenomena, and develop uniform criteria and terminology for these diagnoses.[14]

The epileptic myoclonus may be:

- generalised such as myoclonic jerks in JME (Figure 2.8)
- segmental such as eyelid myoclonia in Jeavons syndrome
- focal such as epilepsia partialis continua (EPC) of Kozhevnikov or jaw myoclonus of idiopathic reading epilepsy
- the only manifestation of an epileptic seizure, as in the above examples
- one component of an epileptic attack combining in continuity with another type of seizure such as myoclonic–atonic seizures, myoclonic absence seizures, myoclonic tonic–clonic seizures.

Epileptic myoclonus is commonly accompanied by generalised EEG discharges of mainly polyspikes, as in the generalised epilepsies. However, the ictal EEG may show focal abnormalities only (idiopathic reading epilepsy) or be entirely normal, requiring documentation with jerk-locked back-averaging techniques.

The cause of epileptic myoclonus may be idiopathic, cryptogenic or symptomatic.

## Epileptic negative myoclonus[2,64,68]

Most myoclonic jerks are caused by abrupt muscle contraction (*positive myoclonus*), but similar jerks are sometimes caused by sudden cessation of muscle contraction associated with a silent period in the ongoing EMG activity (*negative myoclonus*).

**Aetiological classification of myoclonus, including its multiple and heterogeneous causes[62,65]**

- Physiological myoclonus (normal myoclonus)
- Essential myoclonus (idiopathic and often of autosomal dominant inheritance)
- Epileptic myoclonus
- Symptomatic myoclonus

Symptomatic causes are more common and include post-hypoxia, toxic–metabolic disorders, reactions to drugs, storage disease and neurodegenerative disorders

Table 2.5

**Physiological classification of myoclonus based on presumed locations of its generators[63,66]**

- Cortical
- Subcortical*
- Spinal
- Peripheral

Table 2.6 *Some authorities also consider thalamocortical and reticular reflex myoclonus as belonging in this classification (see page 46).

Epileptic negative myoclonus, focal or generalised, is a motor symptom characterised by abrupt and brief (<500 ms) stoppage of muscular activity, not preceded by any enhancement of EMG activity (Figure 2.7).[68]

Negative myoclonus of cortical origin may be associated with an EEG spike or spike–wave complex but it is often difficult to establish exactly the temporal and spatial relationship between the EMG silent period and the associated EEG spike on conventional EEG/EMG recordings.

Epileptic negative myoclonus may originate from various brain areas, including the premotor cortex and the motor cortex, probably depending on aetiology.[64] It occurs in heterogeneous epileptic disorders of idiopathic, cryptogenic and mainly symptomatic origin. Patients may manifest with positive and negative myoclonus in various proportions, either independently or in combination.[63] When both forms of myoclonus occur in combination, the abrupt increase in muscle discharge (positive myoclonus) often precedes the onset of the silent period (negative myoclonus), but occasionally follows its offset.[63] In these cases it is often difficult to determine precisely whether the EEG spike is directly related to the activated or inhibited EMG phase.

**Violent myoclonic jerks of the hands associated with typical EEG manifestations**

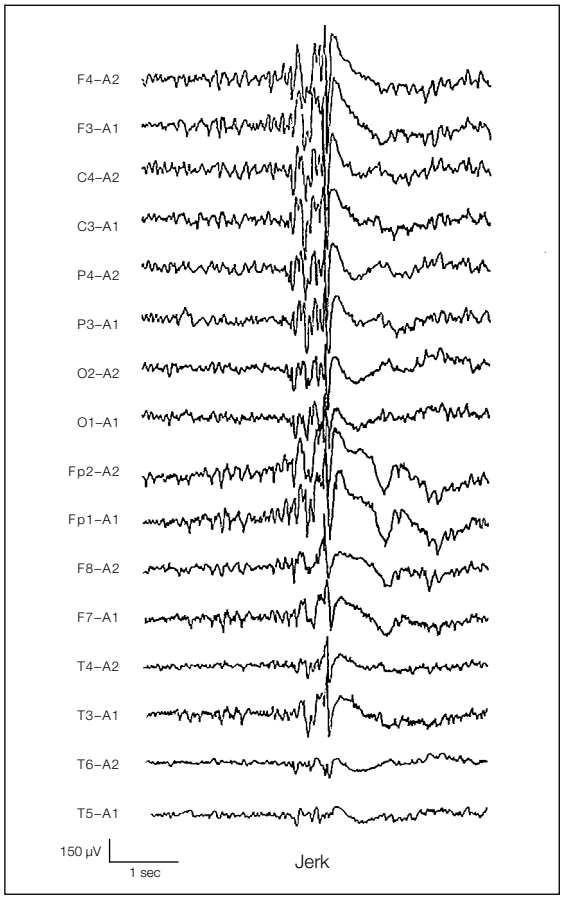


**Figure 2.8** *Figure reproduced with permission from Panayiotopoulos,* et al *(1994).*[67]

## ILAE classification of epileptic myoclonus

The ILAE classifies myoclonic seizures among generalised epileptic seizures (that simultaneously affect both cerebral hemispheres):[11] '*myoclonic seizures:* includes massive bilateral myoclonus, eyelid myoclonia, myoclonic–atonic seizures, myoclonic absence seizures, negative myoclonus'. Also, in tonic–clonic seizures they 'include variations beginning with a clonic or myoclonic phase'.[11] However, it is also recognised that other types of myoclonus are focal; for example, EPC or reading epilepsy.[7]

The new ILAE report[11] gives the following description for some types of myoclonic-related epileptic seizures:

*Myoclonic–atonic seizures:* These are characterised by a myoclonic–atonic sequence. Symmetrical myoclonic jerks of the arms or irregular twitching of the face precedes the more or less pronounced loss of tone.[2,69,70]

*Myoclonic–astatic seizures:* These seizures occur typically in epilepsy with myoclonic–astatic seizures. There is a question about whether the astatic component is an atonic seizure.[14]

*Eyelid myoclonia:* The degree to which these recurrent events (5 or 6 Hz) are associated with impairment of consciousness has not been adequately documented, but should be. In some patients they can be provoked by eye closure. Nonetheless, the seizure type does exist as a unique entity.[14] See, however, Chapter 16, page 514.

### Pathophysiological categorisation of epileptic myoclonus

The ILAE Commission on Pediatric Epilepsy categorised epileptic myoclonus, pathophysiologically, into:[64]

- cortical myoclonus
  - spontaneous cortical myoclonus[63]
  - reflex cortical myoclonus[63]
  - EPC[63]
- thalamocortical myoclonus
- reticular reflex myoclonus
- negative myoclonus.

Cortical myoclonus may be focal or multifocal. Patients with cortical myoclonus commonly have both positive and negative myoclonus, together or independently. Cortical myoclonus is usually more severe than myoclonus of other categories, and patients with cortical myoclonus often develop generalised convulsive seizures.

Myoclonus in progressive encephalopathies is of the cortical type, and EPC is a distinct form of cortical myoclonus.

Thalamocortical myoclonus occurs in:

- IGEs such as benign myoclonic epilepsy of infancy and JME[71]
- myoclonic absence seizures where a combination of positive and negative myoclonus exists; the muscle jerk is associated with the positive component of a spike that precedes its negative transient, whereas negative myoclonus follows the spike by 100 ms, and its onset is before the onset of the slow wave
- Dravet syndrome
- myoclonic–astatic epilepsy.

### Myoclonus and epileptic syndromes[64]

Epileptic myoclonus is a common symptom in the following epileptic syndromes:

- IGEs (see Chapter 13)[71,72]
- idiopathic focal epilepsies:[72] idiopathic reading epilepsy is a characteristic syndrome with focal jaw myoclonus (see Chapter 17)
- in idiopathic focal epilepsies such as rolandic epilepsy and Panayiotopoulos syndrome, positive and negative myoclonus may occur in either atypical evolutions or be induced by carbamazepine (see Chapter 12).[73,74] In these situations, atypical myoclonic status epilepticus may occur and consists of continuous unilateral or bilateral contractions of the mouth, tongue or eyelids, positive or negative subtle perioral or other myoclonia, dysarthria, anarthria or speech arrest, difficulties in swallowing, buccofacial apraxia and hypersalivation
- epileptic encephalopathies and congenital non-progressive encephalopathy of various causes (see Chapter 10)[64]
- progressive myoclonic epilepsies (see Chapter 17)[63,64]
- EPC (see Chapter 15).

## Atonic seizures[69,70,75,76]

*Atonic seizure:* A sudden loss or diminution of muscle tone without an apparent preceding myoclonic or tonic event, lasting approximately 1 or 2 s, involving the head, trunk, jaw or limb musculature (Figure 2.7).[2]

Atonic seizures are not synonymous with astatic seizures, which are defined as follows:

*Astatic seizure (synonym: drop attack):* A loss of erect posture that results from an atonic, myoclonic or tonic mechanism.[2,69]

Thus, an atonic seizure could also be called an astatic seizure, but not all astatic seizures are atonic as they may also be myoclonic or tonic-astatic. Furthermore, atonic seizures are not akinetic seizures. In akinetic seizures there is an inability to perform voluntary movements that is not caused by loss of consciousness (as, for example, in absence seizures) or by loss of muscle tone (as in atonic seizures).

Atonic seizures often occur in continuation with a preceding myoclonic seizure, so-called myoclonic–atonic seizures (see page 49).

Some atonic seizures may manifest solely with atonic symptoms. In others, there is a brief myoclonic or tonic component preceding the atonic manifestations. When these events are very short, they have been referred to as negative myoclonus. Also, a number of seizure types, such as typical and atypical absences, often manifest with atonic symptoms.[14]

Atonic seizures often occur in epilepsies with onset before the age of 5 years and predominate in 'epilepsy with myoclonic–astatic seizures' or epileptic encephalopathies such as Lennox–Gastaut syndrome.

### Clinical manifestations[77]

The manifestations of atonic seizures range from falls to only head nodding. Recovery is usually immediate, occurring within 1–2 s.

In falls from the standing position, the patient suddenly flexes at the waist and knees, followed by further knee flexion, and then drops straight down and lands on the buttocks. When sitting, the patient falls forward or backward depending on the position of the centre of gravity. Consciousness is usually intact. However, longer atonic seizures with loss of consciousness do occur; the patient falls down and remains mute and motionless.

### Aetiology

Aetiology may be idiopathic, cryptogenic and symptomatic. They predominate in 'epilepsy with myoclonic–atonic seizures' or epileptic encephalopathies such as Lennox–Gastaut syndrome. Atonic seizures also result from acquired central nervous system insults, including those of childhood cancer with uncontrolled seizures.

### Diagnostic tests

Interictal EEG is usually very abnormal, as in the epileptic encephalopathies. Ictal EEG reveals brief generalised 2–3 Hz spikes/polyspikes and slow waves. Atonic seizures associate with the slow wave and show sudden interruptions of EMG acivity in the affected musculature (EMG silence). Brain imaging and other testing is as for the epileptic encephalopathies.

### Differential diagnosis

The main difficulty is in differentiating atonic seizures from other types of seizure that may cause falls. This often requires polygraphic neurophysiological techniques.

### Management

Atonic seizures are very difficult to control. AED treatment usually involves rational polytherapy and may include any agent suitable for generalised epilepsies. Corpus callosotomy may be the only choice for devastating atonic seizures with traumatic falls.

## Typical absence seizures[39,71,78]

Typical absences (previously known as petit mal) are brief (lasting seconds) generalised epileptic seizures of abrupt onset and abrupt termination. They have two essential components:

1. a clinical component manifesting with impairment of consciousness (absence)
2. an EEG component manifesting with generalised spike–slow-wave discharges of 3 or 4 Hz (>2.5 Hz).[11,78]

The absence seizures are fundamentally different and pharmacologically unique compared with any other type of seizure, which also makes their treatment different.[78]

> The term 'typical' is used not to characterise them as 'classic', but to differentiate them from 'atypical' absence seizures.

The clinical and EEG manifestations of typical absences are extensive and syndrome related (Figure 2.9).

Impairment of consciousness may be severe, moderate, mild or inconspicuous (and special cognitive testing may be required to detect it). It is often associated with other concomitant symptoms, such as myoclonia, automatisms or autonomic disturbances. Myoclonia may be rhythmic or random, mild or severe, regional (mouth or eyes) or widespread (head, limbs and trunk).

Typical absences are predominantly spontaneous, although they are precipitated by hyperventilation in around 90% of untreated patients. Other specific modes of precipitation include photic, pattern, video games and thinking (reflex absences).

The ictal EEG consists of generalised discharges with repetitive and rhythmic 3 or 4 Hz single or multiple spike–slow-wave complexes. These generalised spike–wave discharges (GSWD) may be brief (sometimes <3 s) or long (≥30 s), and continuous

## Examples from video-EEG-recorded generalised discharges of 3-Hz spikes or polyspikes and waves of typical absence seizures

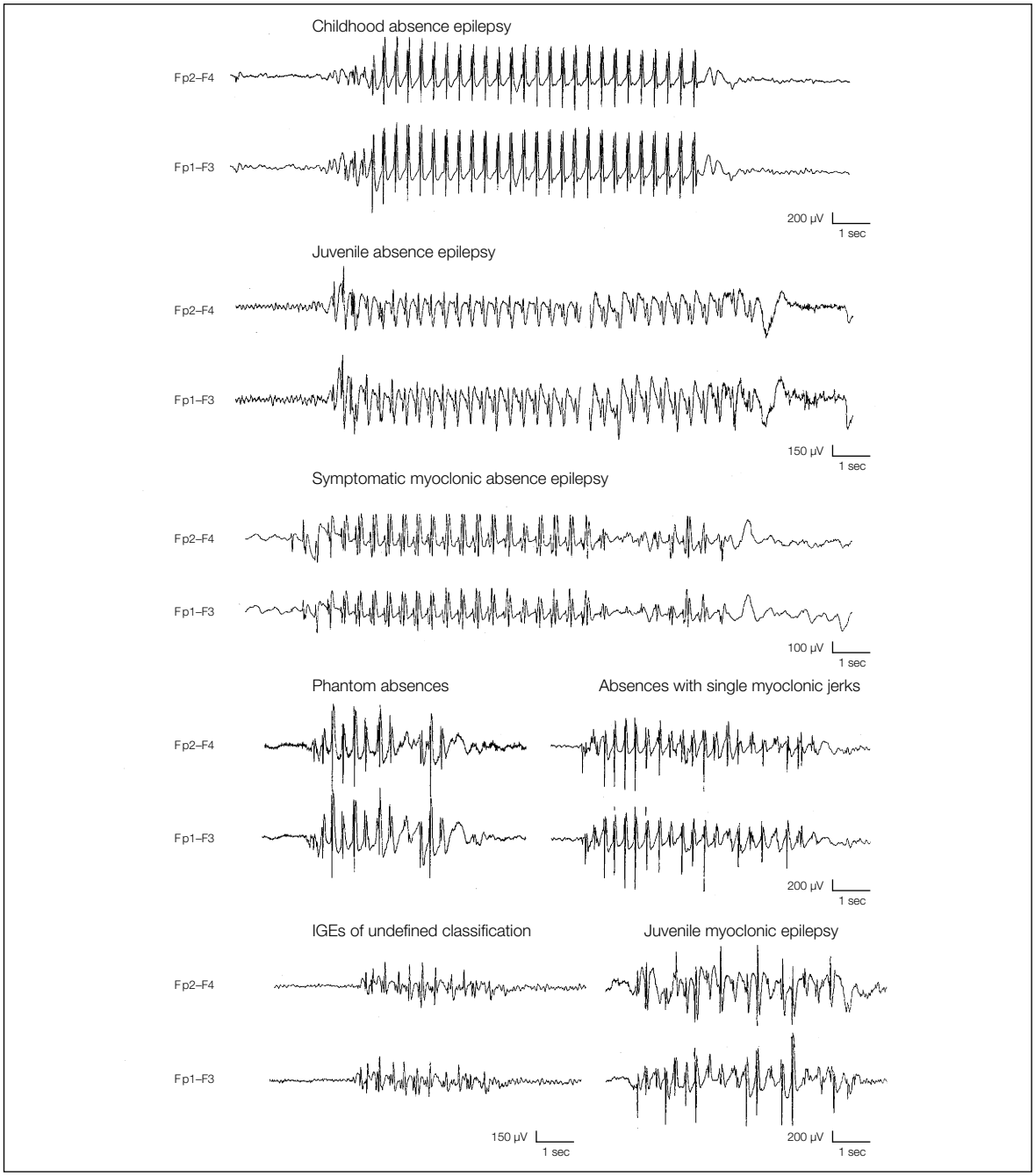


Figure 2.9 These seven patients had different syndromes of idiopathic and symptomatic absence epilepsies. Note that the GSWD may be brief or prolonged, with or without polyspikes and of regular or irregular sequence. Also, note that the intradischarge frequency of the spike–wave complexes may show marked diversity. Although there are significant variations between different syndromes, the GSWD is not itself pathognomonic of any syndrome. The syndromic diagnosis requires homogenous clustering of symptoms and signs.

or fragmented. The intradischarge frequency of the spike–wave may be relatively constant or may vary.

*Typical absence seizures in IGE syndromes:* Typical absences are severe in childhood absence epilepsy (CAE) and juvenile absence epilepsy (JAE), but mild or inconspicuous in other syndromes, such as JME. They may occur alone or in combination with other types of generalised seizures. IGEs with absences may remit with age or be lifelong.

Typical absence status epilepticus occurs in about a third of patients who have typical absence seizures.[79]

## Clinical manifestations[11,39,78]

The clinical manifestations of typical absence seizures vary significantly between patients. Impairment of consciousness may be the only clinical symptom, but it is often combined with other manifestations.

Typical absences are categorised as:

- simple absences with impairment of consciousness only
- complex absences when impairment of consciousness combines with other ictal motor manifestations.

Complex absences are far more frequent than simple absences in children. Simple absences are more common in adults. The same patient may have both simple and complex absences.

*Absence with impairment of consciousness only:* The classic[80] and ILAE[11] descriptions refer to absence seizures with severe impairment of consciousness, such as CAE and JAE:

> Transient loss of consciousness without conspicuous convulsions. A patient stops for a moment whatever he or she is doing, very often turns pale, may drop whatever is in the hand… There may be a slight stoop forward, or a slight quivering of the eyelids… The attack usually lasts only a few seconds. The return of the consciousness may be sudden and the patient after the momentary lapse, may be in just the same state as before the attack, may even continue a sentence or action which was commenced before it came on, and suspended during the occurrence.[80]

The hallmark of severe absence seizures is a sudden onset and interruption of ongoing activities, often with a blank stare. If the patient is speaking, speech is slowed or interrupted; if walking, he or she stands transfixed. Usually the patient will be unresponsive when spoken to. Attacks are often aborted by auditory or sensory stimulation.

In less severe absences, the patient may not stop his or her activities, although reaction time and speech may slow down.

In their mildest form, absences may be inconspicuous to the patient and imperceptible to the observer (*phantom absences*), as disclosed by video-EEG recordings showing errors and delays during breath counting or other cognitive tests during hyperventilation.

*Absence with clonic or myoclonic components:* During the absence, as described above, clonic motor manifestations, rhythmic or arrhythmic and singular or repetitive, are particularly frequent at the onset. They may be continuous. They may also occur at any other stage of the seizure. The most common manifestations are clonic jerking of the eyelids, eyebrows and eyeballs, together or independently, as well as random or repetitive eye closures. Fast flickering of the eyelids is probably the most common ictal clinical manifestation, and may occur during brief GSWD without discernible impairment of consciousness. Myoclonias at the corner of the mouth and jerking of the jaw are less common. Myoclonic jerks of the head, body and limbs may be singular or rhythmical and repetitive, and they may be mild or violent. In some patients with absence seizures, single myoclonic jerks of the head and, less often, of the limbs may occur during the progression of ictus.

In the so-called *myoclonic absences*, the myoclonic components of these seizures are rhythmic (2.5–4.5 Hz) clonic rather than myoclonic and have a tonic component. "The seizure type should be called something else, but there is no agreement on another name at this time."[14]

*Absence with atonic components:* Diminution of muscle tone is usual when absences are severe. This manifests with drooping of the head and, occasionally, slumping of the trunk, dropping of the arms and relaxation of the grip. Rarely, tone is sufficiently diminished to cause falls.

*Absence with tonic components:* Tonic seizures alone do not occur in IGEs. However, tonic muscular contractions are common concomitant manifestations during typical absence seizures. They mainly affect facial and neck muscles symmetrically or asymmetrically. The eyes and head may be drawn backwards (retropulsion) or to one side, and the trunk may arch.

*Absence with automatisms:* Automatisms are common in typical absences when consciousness is sufficiently impaired, and they are more likely to occur 4–6 s after the onset of GSWD. They do not occur in mild absence seizures irrespective of duration, as, for example, in absence status epilepticus. Automatisms of typical absence seizures are simple and void of behavioural changes. They vary in location and character from seizure to seizure. Perioral automatisms, such as lip licking, smacking, swallowing or 'mute' speech movements, are the most common. Scratching, fumbling with clothes and other limb automatisms are also common. Automatisms can be evoked; passive movements, postural repositioning or other stimuli can change their pattern and distribution.[81]

*Absence with autonomic components:* Autonomic components consist of pallor and, less frequently, flushing, sweating, dilatation of the pupils and urinary incontinence.

*Absences with focal motor components, hallucinations and other manifestations of neocortical or limbic symptomatology:* During a typical absence seizure, patients frequently manifest with concomitant focal motor components (tonic or clonic) imitating focal motor seizures. Hallucinations and other manifestations such as concurrent epigastric sensations[82] may occur; these are, in particular, more apparent during absence status epilepticus.[78]

## Electroencephalography

The ictal EEG is characteristic with regular and symmetrical 3 or 4 Hz GSWD (Figure 2.9). The intradischarge spike–wave frequency varies from onset to termination. It is usually faster and unstable in the *opening phase* (first 1 s), becomes more regular and stable in the *initial phase* (first 3 s), and slows down towards the *terminal phase* (last 3 s).[81] The intradischarge relationship between spike/polyspike and slow wave frequently varies. The GSWD are often of higher amplitude in the anterior regions.

Duration of the discharges commonly varies from 3 s to 30 s.

The background inter-ictal EEG is usually normal. Paroxysmal activity (such as spikes or spike–wave complexes) may occur. Focal spike abnormalities and asymmetrical onset of the ictal 3 to 4 Hz spike–wave discharges are common.

## Pathophysiology of absence seizures

See page 41 and Figure 2.6 for the pathophysiology of absence seizures.

The ILAE Task Force Core Group[14] considers that:

> Although the pyknoleptic manifestations of typical absences in CAE have been suggested to differ by shorter duration from the longer-duration, less frequent absences of JAE, based upon what we currently know, it seems likely that they do not represent two mechanisms, but merely the evolution of a single mechanism as the brain matures. Phantom absences also are likely to be a result of brain maturation. A working group will be convened to study whether absences of CAE and JAE represent two seizure types or a spectrum of the same seizure type, and to better define associated motor components.[14]

## Diagnosing absences and differential diagnosis

The brief duration of absence seizures, with abrupt onset and abrupt termination of ictal symptoms, daily frequency and almost invariable provocation by hyperventilation, makes the diagnosis easy.

The differential diagnosis of typical absence seizures with severe impairment of consciousness in children is relatively straightforward. The absences may be missed if mild or void of myoclonic components. Automatisms, such as lip smacking or licking, swallowing, fumbling or aimless walking, are common and should not be taken as evidence

**Differential diagnosis of typical absences from complex focal seizures**

| | Typical absences | Complex focal seizures |
|---|---|---|
| **Clinical criteria** | | |
| Duration <30 s | As a rule | Exceptional |
| Duration >1 min | Exceptional | As a rule |
| Non-convulsive status epilepticus | Frequent | Rare |
| Daily frequency | As a rule | Rare |
| Simple automatisms | Frequent | Frequent |
| Complex behavioural automatisms | Exceptional | Frequent |
| Simple and complex hallucinations or illusions | Exceptional | Frequent |
| Bilateral facial myoclonic jerks or eyelid closures | Frequent | Exceptional |
| Evolving to other focal seizure manifestations | Never | Frequent |
| Sudden onset and termination | As a rule | Frequent |
| Post-ictal symptoms | Never | Frequent |
| Reproduced by hyperventilation | As a rule | Exceptional |
| Elicited by photic stimulation | Frequent | Exceptional |
| **EEG criteria** | | |
| Ictal generalised 3 to 4 Hz spike and wave | Exclusive | Never |
| Inter-ictal generalised discharges | Frequent | Exceptional |
| Inter-ictal focal abnormalities of slow waves | Rare | Frequent |
| Normal EEG in untreated state | Exceptional | Frequent |

Table 2.7 The primary differences are shown in red.

of complex partial (focal) seizures, which require entirely different management.

The EEG or, ideally, video-EEG can confirm the diagnosis of typical absence seizures in more than 90% of untreated patients, mainly during hyperventilation. If not, the diagnosis of absences should be questioned.

The differentiation of typical absences from complex focal seizures may be more difficult when the motor components of the absence are asymmetrical and in adults in whom absences are often misdiagnosed as temporal lobe seizures (Table 2.7).[83]

## Atypical absence seizures[10,84]

Atypical absences are generalised epileptic seizures of inconspicuous start and termination with the following:

- clinical symptoms of mild-to-severe impairment of consciousness (absence), often significant changes in tone with hypotonia and atonia, mild tonic or autonomic alterations
- EEG discharges of slow spike–wave (1–2.5 Hz), which are often irregular and heterogeneous and may be mixed with fast rhythms.[11,78,84] They also innvade limbic areas.[85]

Their duration, determined by EEG changes rather than clinical manifestations, ranges from 5–10 s to minutes. A patient may have few or numerous atypical absences each day.

Atypical absences occur only in the context of mainly severe symptomatic or cryptogenic epilepsies of children with learning difficulties, who also suffer from frequent seizures of other types. They are common in Lennox–Gastaut syndrome, epileptic encephalopathy

with continuous spike and waves during sleep, and epilepsy with myoclonic–astatic seizures.

The differentiation of typical from atypical absence seizures is shown in Table 2.8:

- patients with atypical absences usually have learning disabilities and also suffer from frequent seizures of other types, such as atonic, tonic and myoclonic seizures
- in atypical absences, onset and termination are not as abrupt as in typical absences, and changes in tone are more pronounced
- the ictal EEG of atypical absence has slow (<2.5 Hz) GSWD. These are heterogeneous, often asymmetrical, and may include irregular spike–wave complexes and other paroxysmal activity. Background inter-ictal EEG is usually abnormal.

## Clinical tip

In practical terms, a child suspected of typical absences should be asked to overbreathe for 3 min, counting his or her breaths while standing with hands extended in front. Hyperventilation will provoke an absence in more than 90% of those with typical absences. This procedure should preferably be videotaped to document the clinical manifestations. It may reveal features favouring a specific epileptic syndrome and, therefore, may determine the long-term prognosis and management. Video-EEG documentation may be particularly useful if absences prove resistant to treatment, if other seizures develop or for future genetic counselling. Focal spike abnormalities and asymmetrical onset of the ictal GSWD are common and may be a cause of misdiagnosis, particularly in resistant cases. If video-EEG is not available, documentation of absences using a camcorder or modern digital means of recording is recommended.

**Main differences between atypical and typical absence seizures**

| Clinical and EEG features | Atypical absences | Typical absences |
|---|---|---|
| Onset and termination | Usually gradual | Abrupt |
| Responsiveness | Decreased but not abolished | Varies from mild to severe |
| Changes in tone | Usually pronounced | Usually mild |
| Duration | Usually long sometimes for minutes | Usually brief; exceptionally >30–40 s |
| Post-ictal recovery | Cognitive impairment may persist | Immediately |
| Inter-ictal EEG | Background often abnormal with frequent discharges of various types and combinations | Background usually normal sometimes with typical IGE discharges |
| Ictal EEG | Slow (<2.5 Hz) spike and wave | Fast (>2.5 Hz) spike and slow wave |
| Normal neurological and mental state | Exceptional | As a rule |
| Other types of seizure | Commonly atonic and tonic seizures of symptomatic generalised epilepsies | Depend on IGE syndrome (myoclonic jerks, GTCS or both) |
| Prognosis | Commonly bad | Commonly good |

Table 2.8

# Focal epileptic seizures[9–11,86–88]

Focal epileptic seizures emanate from an epileptogenic focus anywhere within cortical and sometimes subcortical brain regions, leading to localisable and asymmetric semiology. 'Epileptogenic focus' or zone refers to a specific network within a circumscribed brain area, from which seizures are initiated; it can range in size from small to large or be widely distributed within one cerebral hemisphere (see page 24). This also applies when focal seizures arise independently in either hemisphere because of regional epileptogenicity, as for example in rolandic epilepsy (see below and chapter 12). Focal seizures may remain entirely localised within the initial epileptogenic focus or propagate and spread to involve (a) networks in other localisations within the same and/or contralateral hemisphere and (b) widespread networks of larger parts of the brain that are involved in the initiation of generalised seizures (secondarily or focal-onset generalised seizures.

Ictal symptoms, particularly at onset, are determined by localisation and not aetiology.

In practice, onset of focal seizures is determined by clinical and EEG manifestations (see page 22). Brain localisation can be identified from (a) an insightful clinical history and (b) skilful assessment of interictal and ictal EEG changes. This is often easy but in other cases can prove very difficult. Furthermore, (a) clinical manifestations may be very subtle in the presence of marked EEG changes and vice versa; (b) the syptomatogenic zone may not be concordant with the epileptogenic zone; and (c) onset of ictogenesis may be from clinically silent localisations.

Let us consider benign childhood focal seizures, which are also a good example of regional epileptogenicity (see also Chapter 12).[89]

- Interictal EEGs are disproportionally severe in relation to clinical manifestations
- Epileptogenicity involves bilateral regional cortical areas which are bi-rolandic in rolandic epilepsy, bi-occipital in idiopathic childhood occipital epilepsy of Gastaut (ICOE-G) and multifocal (bi-frontal, bi-parietal, bi-occipital and bi-temporal) in Panayiotopoulos syndrome (PS).
- Ictal EEG always starts from a localised area of the corresponding region of epileptogenicity; this may be on the right on one occasion or on the left on another occasion in the same patient
- Ictal clinical symptoms may appear shortly after the EEG onsets in rolandic and ICOE-G seizures or after a significant delay in PS.
- The symptomatogenic zone appears to correspond to the epileptogenic zone in rolandic epilepsy (sensory-motor symptomatology of the rolandic cortex) and the ICOE-G (occipital lobe symptomatology), while the autonomic clinical manifestations of PS are likely to be generated by variable and widely spread epileptogenic foci acting upon a temporarily hyperexcitable central autonomic network.
- Ictal clinical symptoms may be subtle and entirely localised (elementary visual hallucinations of ICOE-G, hemifacial sensory-motor symptoms of rolandic epilepsy), or may spread to involve other brain regions within the same or contralateral hemisphere, occasionally initiating a secondarily GTCS.
- Symptomatic focal epileptic seizures may manifest with identical clinical semiology, as exemplified by the visual seizures of ICOE-G and other occipital epilepsies of structural cause.

Focal epileptic seizures and syndromes have been extensively reviewed with regard to clinical manifestations, diagnostic procedures and management in a two-volume issue of "The educational kit on epilepsies". This publication includes numerous EEG and brain imaging illustrations as well as live video-EEG recordings of patients with focal seizures.[87,88]

## ILAE terminology and classification of focal seizures

The terminology and classification of focal seizures of the ILAE proposals has been described above and it is given in tables 2.1 and 2.3.

The ILAE Core Group considers that:[14]

(I). The anatomical substrates of a substantial number of focal seizure manifestations has now been sufficiently established to include this information in their description (see Table 2.3).

(II). As focal seizures represent dynamic events that usually involve propagation, and clinical manifestations can reflect discharges at the site of ictal onset, and/or sites of propagation, the organisation of focal seizures in their report takes into account the various patterns of ictal propagation (see Table 2.3).

(III). A number of factors will need to be investigated in order to develop more definitive criteria for distinguishing between different types of focal seizures. These include:

- Factors that might distinguish between focal seizures due to discretely localised lesions, as occur with focal symptomatic epilepsy, and focal seizures due to more distributed network disturbances, as might occur with some focal idiopathic epilepsies (e.g. those responsible for the transverse dipole of the centrotemporal spikes of rolandic epilepsy), or even in IGEs.
- Maturational factors.
- Modes of precipitation, as in reflex seizures.
- Pathology, i.e. focal seizures due to various malformations of cortical development may be different from each other and from those due to other lesions.
- Pathophysiological mechanisms (see pathophysiology below).[14]

The ILAE Core Group[14] provides the following information for the focal seizures listed in Table 2.3 with regard to the factors influencing seizure-induced progressive disturbances in neuronal function and structure at the site of, and downstream from, ictal onset:

**Focal onset (partial) seizures**

*A. Local*

*1. Neocortical*

a. Without local spread

i. *Focal clonic seizures* are brief focal motor events that are distinguished from focal myoclonic seizures by their rhythmic repetition. Localisation to the primary motor cortex is implied.

ii. *Focal myoclonic seizures* most likely consist of many types. These events, including multifocal myoclonus, will be discussed by the ILAE working group on myoclonus. There is no unanimity of opinion as to whether the myoclonic events in progressive myoclonic epilepsy, which have no EEG correlate, are epileptic. At least in Lafora disease, there is evidence to suggest a cortical site of initiation.

iii. *Inhibitory motor seizures* are not a unique seizure type. The clinical manifestation merely represents the function of the involved cortex, just as focal motor seizures and unformed visual hallucinations reflect seizures in precentral gyrus and calcarine cortex.

iv. *Focal sensory seizures with elementary* (visual, somatosensory, vestibular, olfactory, gustatory or auditory) symptoms manifest themselves as a variety of sensory phenomena that can be produced by activation of primary sensory cortices.

v. *Aphasic seizures* can consist of inability to speak when Broca's area is principally involved, or more complex disturbances of speech production or reception when other language cortical areas are principally involved.

b. With local spread

i. *Jacksonian march seizures* refers to the clinical manifestations of the slow ephaptic propagation of epileptic discharge along the motor cortex, although similar progression can sometimes be seen in other primary cortical areas as well.

ii. *Focal (asymmetrical) tonic seizures* can be associated with seizure origin from practically anywhere in the neocortex. In their purest form, focal tonic seizures are seen in the explosive motor seizures of supplementary motor area origin.

iii. *Focal sensory seizures with experiential symptoms* are those with complex, usually

formed, distorted and/or multimodal, sensory symptoms implying seizure initiation in association cortices, such as the temporo-parieto-occipital junction, with connections to multiple sensory areas.

2. *Hippocampal and parahippocampal* seizures almost always require local spread for clinical manifestation, which may involve insula, amygdala, hypothalamus and other limbic structures (Figure 2.1). Autonomic features such as a sensation of epigastric rising is common, as well as emotional experiences such as fear, dysmnesias, focal sensory seizures with olfactory or gustatory symptoms, and vague bilateral sensory phenomena such as tingling.

*B. With ipsilateral propagation to:*

1. *Neocortical areas (includes hemiclonic seizures)*
   a. Same manifestations as A.1.a and A.1.b.
   b. *Hemiclonic seizures* occur early in development before myelinisation of the corpus callosum and do not necessarily have localising value. They can alternately affect both hemispheres, as in Dravet syndrome and ischaemic encephalopathy, or only one hemisphere in the case of focal disturbances.
2. *Limbic areas*
   a. Same manifestations as A.2.
   b. *Gelastic seizures* are clearly unique ictal events when they are initiated in relation to structural abnormalities of the hypothalamus, which are usually hamartomas. The mechanism is unknown, but initiation, at least, is distinct from gelastic seizures arising from other areas, such as mesial temporal lobe and cingulate.

*C. With contralateral spread to:*

1. *Neocortical areas (hyperkinetic seizures):* also referred to by some as *hypermotor seizures*, involve bilateral forceful limb movements, sometimes with vocalisations. Frontal lobes are implicated in these behaviours.
2. *Limbic areas: dyscognitive seizures with or without automatisms (psychomotor)* are not exactly synonymous with the current term 'complex partial seizures', which were defined on the basis of impaired consciousness only and do not necessarily involve limbic areas. This new term, as well as the term 'psychomotor', conforms more to the original intent of the term 'complex partial seizures' in the 1970 *ILAE Classification of Epileptic Seizures*. It is implied that mesial temporal limbic areas and their immediate connections are involved in the clinical manifestations, although seizures may have been initiated elsewhere.

*D. Secondarily generalised*

1. *Tonic–clonic seizures* that are secondarily generalised probably consist of multiple types and may involve different pathophysiological mechanisms and anatomical substrates, at least initially, than GTCSs with generalised onset.
2. *Absence seizures* can rarely represent propagation from localised cortical areas, usually in the frontal lobe. There may be a continuum between these events and generalised atypical absences.
3. *Although epileptic spasms* can occur in infants with focal lesions, the mechanism by which these generalised events are generated is unknown.

## Epidemiology

In population-based studies, focal seizures predominate with a median incidence of 30.4 cases/100,000 population/year compared with an incidence of generalised seizures of 19.6 cases/100,000 population/ year. Also, focal seizures predominate in prevalence studies 55–60% (adults) and 36–66% (children).

## Clinical manifestations

The clinical manifestations of focal epileptic seizures are detailed in chapters 11, 12, 14 and 15, within focal epileptic syndromes and according to their site of origin and aetiology. It should also be noted that semiology, particularly at onset, is determined by localisation and not by cause.

## Aetiology

This may be symptomatic (21.7% of all epilepsies), cryptogenic (21.8%) or idiopathic (9.1%) (Figure 1.5). In children it is much more common for focal epileptic seizures to be idiopathic than symptomatic.

In the elderly, nearly all newly identified epileptic seizures are focal from a symptomatic cause.

## Pathophysiology[14,90–92]

Focal epileptogenesis is a multistep process. An initial precipitating injury may predispose to the development of the first seizure. During the latent phase, structural and functional changes occur that may ultimately lead to spontaneously recurrent epileptic seizures in some patients over the course of days to years. At each step of the process, biological and age- or gender-specific factors, and genetic, epigenetic or comorbid conditions, may interfere and modify the course of epileptogenesis.[90]

Neocortical[91] and limbic (mainly hippocampal)[92] seizures have some important differences in their pathophysiology. This reflects anatomical, functional and phylogenetic disparities between them, as well as all other factors involved in ictogenesis from elements within the neurones, synapses, interconnections and their modifications by age, exogenous and endogenous influences and causes of disease. These are beyond the remit of this clinical book.

As the ILAE Task Force emphasised:[14]

"Hypersynchronous ictal onsets most commonly occur in hippocampus while low voltage fast ictal onsets, most commonly occur in the neocortex. These electrophysiological features clearly reflect different pathophysiological mechanisms of seizure initiation, which may not be absolutely correlated with location, and there may be other ictal onset patterns indicative of other initiating mechanisms that have not yet been well described.[14] Also there are differences in neurophysiological properties and anatomical connections unique to specific areas of cortex, e.g. those that cause brief and clustered seizures with little or no postictal disturbances and nocturnal predilection typical of some frontal areas, compared with longer, less frequent events with profound postictal disturbances in other areas, and those that cause fast distant propagation from some areas and localised, slower propagation in others."[14]

## Diagnostic procedures

EEG and neuroimaging remain the cornerstones of investigation in the focal epilepsies, as detailed in chapter 7 and in the discussion of the individual focal epileptic syndromes. In view of the high incidence of symptomatic epilepsies, a high resolution structural MRI scan on a scanner with a field strength of at least 1.5 Tesla should now be considered standard practice. Other appropriate tests have been described in page 4 and these include molecular testing when genetic focal epilepsies are suspected (Chapter 14). More elaborate diagnostic procedures including functional neuroimaging, advanced MRI technologies, invasive EEG and magnetoencephalography are used to investigate patients with focal epileptic seizures that may benefit from neurosurgical interventions (page 222).

## Prognosis

This largely depends on aetiology and syndromic diagnosis. It varies from purely benign and age-limited (see examples in chapter 12) to very severe and progressive (Chapter 15).

## Management

When focal epileptic seizures have been unequivocally diagnosed, the decision of whether they need treatment depends on the underlying aetiology and syndrome and on factors relating to the individual. AED is the mainstay of treatment when the risk of recurrence is high. Currently there are more AEDs for the treatment of focal than generalised epilepsies (see Tables 7.1 and 7.12). These should be used according to the principles detailed in chapter 7 and chapter 15.

Surgical treatment is a life saving option for many patients with pharmaco-resistant focal epilepsy and this should be recommended as soon as possible (Page 222).

Socio-psychological support is part of good clinical practice in the management of all epilepsies.

# Reflex epileptic seizures

Reflex epileptic seizures and related syndromes are detailed in Chapter 16.

They are consistently precipitated by environmental or internal stimuli and are differentiated from spontaneous epileptic attacks in which precipitating factors cannot be identified. In individual patients, the precipitating stimuli are usually limited to a single specific stimulus or a limited number of closely related stimuli.

Reflex seizures have a prevalence of 4–7% among patients with epilepsies and may be of the same types as the spontaneous focal or generalised seizures:

- generalised, primarily or secondarily
- focal, simple or complex.

Visually induced seizures and epilepsies are the most common among reflex epilepsies.

In response to the same specific stimulus, the same patient may have absences, myoclonic jerks and GTCSs alone, or in various combinations. Usually, absences and myoclonic jerks precede the occurrence of GTCSs. Patients may have reflex and spontaneous seizures.

Focal seizures are exclusively seen in certain types of reflex focal epilepsy, such as visual seizures of photosensitive occipital lobe epilepsy or complex focal temporal lobe seizures of musicogenic epilepsy.

The role of the EEG is fundamental in establishing the precipitating stimulus in reflex epilepsies, because it allows subclinico-EEGs, or minor clinical ictal events, to be reproduced on demand by application of the appropriate stimulus.

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