The new patient with a first seizure

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BACKGROUND First seizures are common, with one in 20 people suffering a seizure at some time in their life.
OBJECTIVE This article aims to outline the assessment of patients with a first seizure, including making an accurate diagnosis of both seizure type and an epilepsy syndrome, if present.
DISCUSSION Seizures are classified into generalised and partial (arising from a focal region in the brain) based on clinical and electroencephalogram findings. However, as a partial seizure may proceed to a tonic clonic phase, differentiation may be difficult. Inquiring directly about 'minor' epileptic symptoms before the episode such as absences, myoclonic jerks, visual or auditory hallucinations or feelings of déjà vu, is needed to attempt to make a epilepsy syndrome diagnosis, as this has practical implications for treatment, prognosis and genetic counselling. Generalised epilepsies should be treated initially with valproate, while partial epilepsies should be treated with carbamazepine and switched to newer agents if intolerance occurs.

Case history

An ambulance arrives at the emergency department one Sunday morning with a postictal man aged 19 years of age. Housemates had witnessed a tonic clonic seizure half an hour previously. He is healthy, does not take drugs or medications and there is no history of seizures. Over the previous two nights he had been out late, drinking and celebrating the end of semester exams. He is drowsy but rousable, with no neck stiffness or fever; the finger-prick glucose is 4 mmol/L. There is a bite laceration on one side of his tongue. He complains of a headache and vomits. You draw blood for routine tests and order a brain CT. All results are normal. Over the next hour he becomes more alert and you learn that he went to bed around 3 am and he had only five hours of sleep, with about the same amount of sleep the night before. You observe him for another few hours and then discharge him to the care of his parents, with the usual advice not to drive and what to do in the event of another seizure. You refer him to a neurologist. A month later, the neurologist writes that an initial EEG was nondiagnostic but a sleep deprived EEG showed generalised spike-wave discharges of idiopathic generalised epilepsy. The neurologist obtained a history of absences and morning myoclonic jerks and diagnosed juvenile myoclonic epilepsy. A brain MRI was not thought necessary. Treatment with sodium valproate was recommended.

The first seizure is a common medical problem, one that represents a diagnostic challenge for both the general practitioner and the neurologist. At least 5% of the population will suffer a non-febrile seizure at some time in their life.[1] Although a seizure may turn out to be a solitary event, more often another seizure will follow days, weeks or months later. It is usually only then that the doctor begins to consider a diagnosis of epilepsy. However, in many cases it is possible to confirm the diagnosis and to consider treatment much earlier, soon after the initial presentation.

Table 1. Differential diagnosis of seizures

- Cardiac syncope
  - arrhythmias: bradycardia, heart block, tachycardia
  - aortic stenosis
  - cardiomyopathy
- Noncardiac syncope
  - vasovagal (vasodepressor) syncope
  - postural (orthostatic) hypotension
- Migraine
- Narcolepsy-Cataplexy
- Tremors
- Tics
- Movement disorders
- Psychological and psychiatric
  - pseudo seizures
  - hyperventilation
  - panic attacks
  - disassociative reactions

Table 2. Causes of acute reactive seizures

- Metabolic derangements
  - hypoglycaemia
  - hypoxia
  - severe acid base disturbances
  - febrile illness, hyperthermia
  - respiratory, liver and renal failure
  - intoxications and poisonings
  - drug and alcohol withdrawal
- Head injury
  - acute concussive convulsions
  - extradural, subdural haematoma
  - raised intracranial pressure, by any other cause
- Cerebral infections
  - bacterial meningitis
  - viral encephalitis
- Stroke
  - cortical infarction; embolism or thrombosis
  - subarachnoid haemorrhage
  - intracerebral haemorrhage

Most first seizure patients present with a convulsion (or tonic clonic seizure) and are assessed acutely in a hospital emergency department. A GP in a metropolitan practice will seldom encounter a new patient who is recovering from a recent tonic clonic seizure. However, the GP is likely to be involved from the outset when the patient presents subacutely; when the seizure occurred during sleep, was unwitnessed, occurred some time ago, or the details of just what happened are unclear. General practitioners play an important role in distinguishing seizures from nonepileptic events (Table 1) and in selecting patients with possible seizures who may need to be further assessed by a neurologist. General practitioners are also called upon to diagnose nonconvulsive epileptic symptoms in patients who have not yet had a convulsion or complex partial seizure.

Assessing the patient

After making an initial assessment of the airway, breathing and circulation, the doctor's first priority in a patient presenting with a presumed first fit is to consider a possible neurological or metabolic emergency as the cause. Seizures can arise as a complication of numerous medical disorders and acute brain insults (Table 2). Bacterial meningitis, viral encephalitis, head injury, stroke due to haemorrhage or thromboembolism, tumour, raised intracranial pressure, hypoglycaemia, drug overdose and poisonings all demand urgent diagnosis and treatment.

Commonly however, the patient with a first seizure has been well in the past and the seizure was a sudden, unexpected event. Seldom are there neurological signs, apart from postictal drowsiness or confusion that gradually resolves. The general physical examination is usually normal, apart from a bitten tongue. The standard blood tests are also usually normal. It is essential in all cases to rule out hypoglycaemia but rarely do other blood tests determine the cause of the seizure. Liver function tests sometimes identify alcohol abusers. Blood alcohol and urine drug screen for opiates and amphetamines can be useful in selected cases. Brain computerised tomography (CT) is often done routinely in the acute setting but has a low diagnostic yield in the recovering postictal patient who lacks neurological signs.

In the majority of cases where the cause of the seizure is unknown, the most likely explanation for

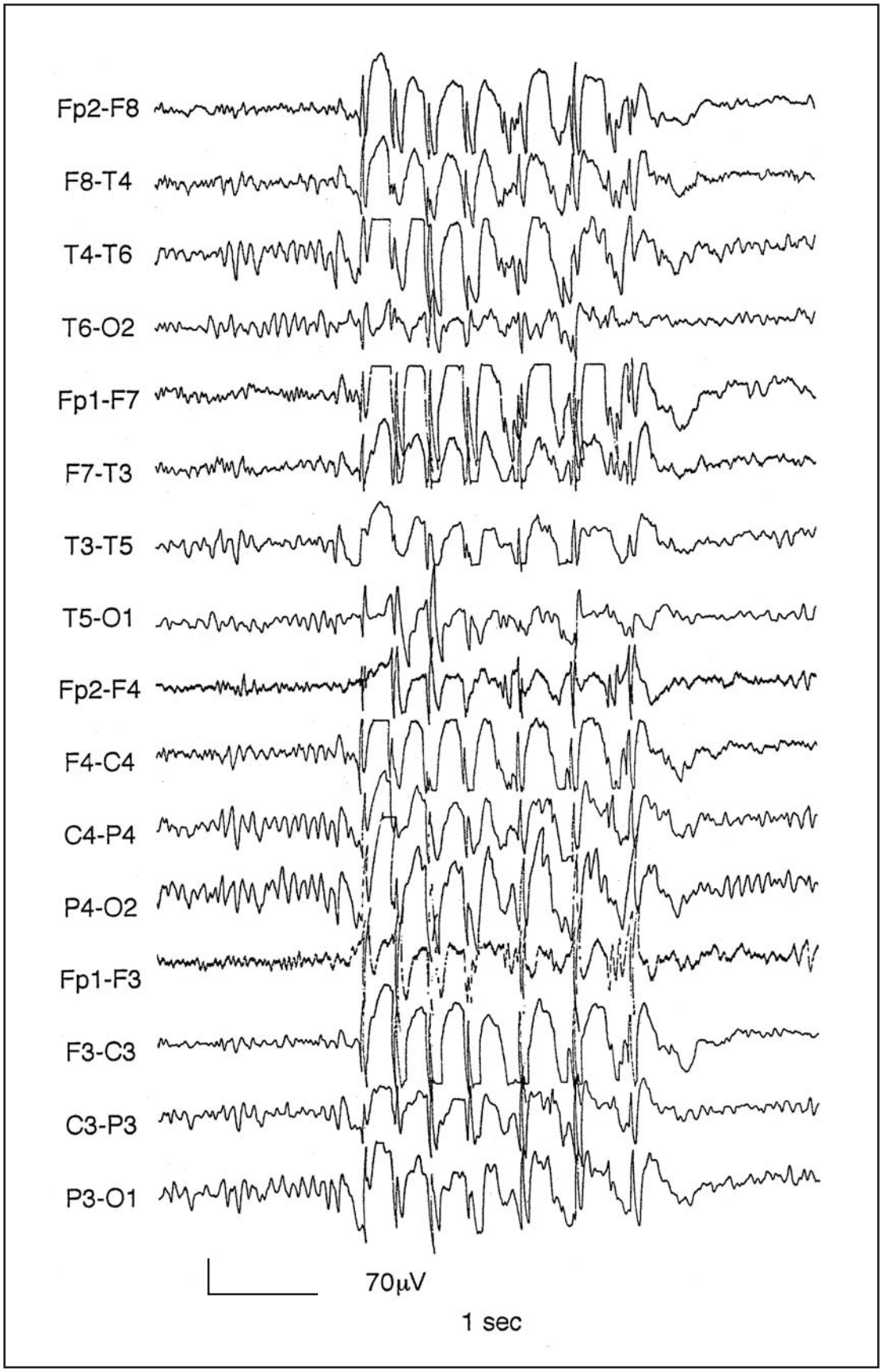

Figure 1. Generalised spike wave discharges

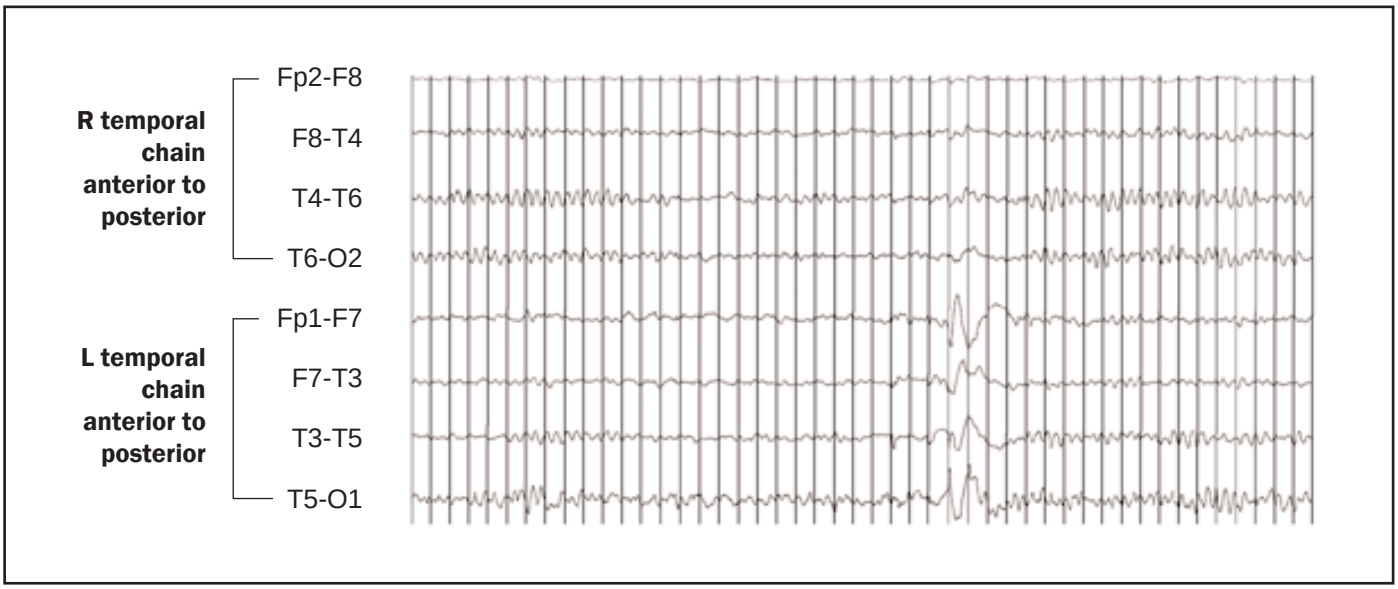

Figure 2. Focal epileptiform discharge in left temporal region

what has happened is that the patient has new onset epilepsy, either idiopathic or due to an as yet undiscovered brain lesion. The seizure has occurred just now, through the influence of a trigger factor such as:

- sleep deprivation
- overuse of alcohol
- fever
- intercurrent illness
- severe sustained stress, or
- a combination of factors.

Whether or not a trigger factor can be identified, further investigations are required to diagnose an underlying epilepsy syndrome, if present, and determine the aetiology. It is inadequate to simply attribute the seizure to 'stress' alone.

Minor epileptic symptoms and diagnosis of epilepsy syndromes

Patients who have ostensibly had their 'first' seizure, have commonly experienced 'minor' seizure symptoms in the past. Such patients already have an epilepsy at the time of presentation with a first tonic clonic seizure. Minor epileptic symptoms are often not volunteered, especially in the aftermath of a convulsion, but inquiring directly about them is necessary to make an epilepsy syndrome diagnosis. Absences, myoclonic jerks and photosensitivity are features of generalised epilepsies. Temporal lobe epilepsies can produce rising sensations, déjà vu, detached feelings, hallucinations of smell and taste, and other unusual sensations. These are auras, due to simple partial seizures. Occipital epilepsies can produce unformed visual hallucinations such as coloured balls. Parietal epilepsies produce sensory and experiential auras. Frontal epilepsies are complex and difficult to diagnose even for experts, with motor and verbal phenomena being two characteristics. Complex partial seizures (blank outs) and automatisms should also be sought when taking the history from patients and those close to them.

The central, diagnostic role of EEG

Electroencephalogram (EEG) remains an indispensable investigation for diagnosing epilepsies but is sometimes forgotten in patients with a first seizure. It is best done early (within 24 hours) in all acutely presenting cases for maximal diagnostic yield.[2] Delayed, or routine EEG studies have a lower yield of diagnostic focal or generalised (interictal) epileptiform discharges. If generalised 3–4 cycle per second discharges are present, the diagnosis is idiopathic generalised epilepsy (Figure 1). If focal discharges are shown, the patient is likely to have a partial epilepsy (Figure 2). Where the initial EEG is nondiagnostic, a sleep deprived EEG should be obtained if possible. Sleep deprivation and sleep itself (recorded during the EEG study) can 'activate' epileptiform discharges that were not seen during an earlier study. The proper role of EEG in first seizure cases is for diagnosis of epilep-

sies, not for prognosis, or identifying which patients may be at increased risk for seizure recurrence.

Brain imaging with CT and MRI

Computerised tomography (CT) remains a useful investigation in first seizure cases, but is often normal in the recovering postictal patient whose medical history is unrevealing and who lacks physical or neurological signs. However, patients and families dread the possibility of a brain tumour and a normal CT scan will quickly put minds at ease. Computerised tomography is of course mandatory in any patient with trauma, focal seizure onset, diseases that may lead to seizures (such as malignancy) and in all cases where there is fever, meningism or neurological signs. However, magnetic resonance imaging (MRI) is the superior brain imaging test.

Magnetic resonance imaging can detect small or subtle lesions that are below the resolution of CT, and it demonstrates clearly the temporal lobe anatomy which is not well shown by CT. Small tumours, especially benign or low grade missed by CT may be revealed by MRI. First seizure patients with partial epilepsy diagnosed on the clinical and EEG data and unclassified cases (those with no other seizure symptoms and negative EEG studies) will show an epileptogenic lesion in up to 20% of cases on MRI.[2] The idiopathic epilepsies are nonlesional and MRI images are almost always normal. As a working rule, all adult first seizure patients should be considered for MRI, except those who have generalised epilepsy based on clinical and EEG data.

Epileptic seizure classification

The ancient French terms 'grand mal' and 'petit mal' have long been abandoned by neurologists as vague and misleading, but unfortunately they continue to be used by some doctors and patients. These terms translate into English merely as: 'big bad' and 'little bad' and as such, they are almost meaningless.

A first seizure is generally thought of as a convulsion or a tonic clonic seizure, but there are a variety of seizure types. Seizures are classified into generalised and partial based on their clinical and EEG features. Generalised seizures are generalised at onset clinically and on EEG; while partial seizures arise in a focal brain region and usually produce focal symptoms and signs. Partial seizures may then spread to adjacent areas of cortex or more widely to produce loss of consciousness or a secondarily generalised tonic clonic seizure. The latter can be indistinguishable clinically from a primary generalised tonic clonic seizure. An EEG (if there are interictal epileptiform abnormalities) and MRI (if a lesion is demonstrated) may provide the answer, but not always. Because of the difficulty in knowing whether a tonic clonic seizure was generalised or partial in onset, it is best to use the term 'tonic clonic seizure' or 'convulsion' to cover both possibilities.

Generalised seizures for the most part comprise:

- tonic clonic
- absence, and
- myoclonic (muscle jerk) seizures.

The remaining three generalised seizure types: tonic, clonic and atonic (akinetic) seizures are rare and mainly affect children with very severe epilepsies such as Lennox-Gastaut syndrome. They do not occur among neurologically normal children (or rarely so) or adults with new onset seizures. Therefore, it is usually incorrect to postulate tonic or atonic seizures in an adult with falls.

Partial seizures are divided into simple and complex according to whether or not consciousness is affected. Simple partial seizures are further classified into:

- motor (eg. repetitive jerking of one hand)
- sensory (eg. a fizzing sensation in one foot)
- psychic (eg. a feeling of intense déjà vu)
- special sensory (a visual or auditory hallucination), and
- autonomic (an epigastric rising up sensation).

An aura is a simple partial seizure that may occur alone or herald the arrival of a complex partial or secondarily generalised (tonic clonic) seizure.

Epilepsy syndromes

An epilepsy syndrome is a set of clinical and EEG characteristics shared by patients having similar age of seizure onset, seizure type or types, EEG findings and aetiology where known. A syndrome diagnosis is a summary of many elements pertaining to the patient's epilepsy, and it carries practical implications for treatment, prognostication and genetic counselling.

Epilepsy syndromes are divided into:

- generalised, and
- partial (other terms are focal, or localisation related)

and are further classified into:

- idiopathic (presumed genetic)
- symptomatic (where a lesion is known to be present), and
- cryptogenic (where there is no demonstrable focal lesion but one is suspected).

Most of the generalised epilepsies are idiopathic, while the majority of partial epilepsies are either symptomatic or cryptogenic. Only three idiopathic partial epilepsies are recognised at present, and in practice we simply divide the majority of cases of partial epilepsy into frontal, temporal, parietal and occipital lobe epilepsies, according to clinical features, EEG findings and the site of a lesion if present.

Seizure recurrence and choice of treatment

Recurrence after a first unprovoked seizure is generally high. Studies of heterogeneous groups of patients have provided widespread figures from less than one in four to more than four in every five patients who will suffer a further seizure within the following 2–3 year period.[3,4] Metaanalysis puts the overall figure at around 50% of patients who will suffer seizure recurrence within a few years of a first seizure.[5] The greatest risk lies within the first 3–6 months and by 12 months, most patients destined to relapse have already done so.

If the history and EEG and possibly the MRI, indicate the presence of an underlying epilepsy, then treatment to prevent seizure recurrence would seem prudent, especially given the moderate to high risk of recurrence for first seizure cases. Studies of treatment following first seizures show indisputable benefit in terms of reduced seizure recurrence.[6] However, the long term prognosis for eventual seizure freedom off medications, is not altered by provision of early treatment.[6] Unfortunately, antiepileptic drug treatment has no curative effect.

The new antiepileptic medications lamotrigine (Lamictal), gabapentin (Neurontin), topiramate (Topamax), oxcarbazepine (Trileptal), tiagabine (Gabatril) are all very effective and can be better tolerated than the older established drugs such as phenytoin (Dilantin), carbamazepine (Tegretol) and sodium valproate (Epilim). However, many patients do tolerate the older agents when commenced at a low dose and increased gradually to the desired maintenance dose and they remain first line medications. There is no significant difference in efficacy between phenytoin, carbamazepine and valproate in preventing tonic clonic seizures. However, only valproate properly controls absence seizures and myoclonic jerks in generalised epilepsy. Carbamazepine and phenytoin can sometimes exacerbate these seizure types, or cause them to emerge in the first place. This is one reason why it is important to attempt to make an epilepsy syndrome diagnosis in first seizure patients and not leave the diagnosis at the basic level of seizure type alone. In partial epilepsies, carbamazepine is superior to the other two drugs in controlling simple partial seizures. Phenytoin is being used less often as a first line agent because of the cosmetic and dental side effects of long term use. However, it remains a useful first line drug in elderly patients, given as a single dose at night.

Newly diagnosed patients with generalised epilepsy should be commenced on valproate and later changed to lamotrigine or topiramate if intolerant. Patients with partial epilepsy should be commenced on carbamazepine (Tegretol CR is preferred) and switched to one of the newer agents if necessary.

The question of how long to continue treatment in a patient whose seizures are controlled is a vexing one for neurologists and researchers. Most experts would advocate treatment for at least two years after seizures come under complete control, before considering a trial of drug withdrawal. All such decisions are of course highly individualised and depend on multiple factors including the underlying epilepsy syndrome and aetiology.

Conflict of interest: none declared.

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SUMMARY OF IMPORTANT POINTS

- First seizures are common; at least one in 20 of us will suffer a seizure at some time.
- Recurrence after a first seizure is likely with the risk being 40-50% or higher over the next two years.
- EEG is a crucially important but often overlooked test and should be carried out urgently (within 24 hours) in acutely presenting patients for maximal diagnostic yield of generalised or focal epileptiform discharges.
- Brain CT is useful, but MRI is superior and should be considered in all adult first seizure patients, unless generalised epilepsy is diagnosed clinically and with EEG.
- Most new patients actually have new onset epilepsy that can be diagnosed clinically with EEG and brain imaging, preferably MRI. In most cases, the seizure has occurred at this time through the influence of a trigger factor such as sleep deprivation, fever, over indulgence in alcohol, sustained stress or a combination of factors.
- Epilepsy syndromes can be diagnosed in first seizure patients and attempts to do so should be made. Generalised epilepsies should be treated initially with valproate (Epilim) while partial epilepsies should be treated initially with carbamazepine (Tegretol CR).
- We should abandon the outmoded and misleading labels of ‘grand mal’ and ‘petit mal’ seizures and epilepsy!

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