

CLINICAL REVIEW

First seizures in adults

Heather Angus-Leppan *consultant neurologist and epilepsy lead*¹ *honorary senior lecturer*²

¹Clinical Neurosciences, Royal Free London NHS Foundation Trust and Barnet Chase Farm Hospitals NHS Trust, London, UK; ²Institute of Neurology, University College London and Centre for Restorative Neuroscience, Imperial College London

A seizure is a clinical manifestation of presumed or proved abnormal electrical activity in the brain. A first seizure can range from a fleeting subjective experience such as déjà vu or a twitch (myoclonic jerk) through to a tonic-clonic convulsion. Some seizure manifestations overlap with normal phenomena. A single seizure may be provoked (with an acute precipitant that may or may not recur) or unprovoked (idiopathic or of unknown cause). Epilepsy is defined as more than one seizure.

This article focuses on the diagnosis of first seizures and differentiation from their “mimics” in adults. The diagnosis is correct in only two thirds of cases or less and relies almost exclusively on the clinical history.¹⁻⁹ Information for patients, particularly regarding risks of recurrence, investigation and treatment, driving, and mortality, will be discussed.

This review uses older seizure terminology,¹⁰⁻¹¹ as this is better understood by most readers and succinctly conveys important clinical concepts. Where the revised terminology differs, this is noted in the text and the supplementary table.¹²

How common are first seizures?

Few data about the frequency of minor (non-convulsive) first seizures exist. Many minor first seizures are unrecognised. The recorded incidence of first seizure (provoked and unprovoked) in Europe is approximately 70 per 100 000 per year,¹³⁻¹⁴ with twice that incidence in poorer countries.¹⁵⁻¹⁷ Febrile seizures are the “first seizure” with the highest worldwide incidence (50 per 100 000 per year), usually occurring in the first three years of life.¹⁸

The cumulative lifetime incidence of single seizures and recurrent epileptic seizures (including febrile seizures) is estimated as 5-10%.¹⁹⁻²⁰ The prevalence of epilepsy is between 0.5% and 1% of the population.²⁰ Epileptic seizures are responsible for 1% of hospital admissions and 3% of emergency department attendances.²¹

First seizures are not always declared in epidemiological questionnaires,²²⁻²³ because of social stigma, fears about losing the driving licence, and concerns about employment.²⁴⁻²⁵ Few epidemiological studies of provoked seizures have been done, as episodes are often indexed under their provocation (for

example, alcohol withdrawal or head injury) rather than seizure and may not reach neurological attention.²⁶

Transient loss of consciousness is the most commonly recorded and studied presentation of “first seizure.” In 2005-06 100 000 hospital attendances in the United Kingdom were for transient loss of consciousness.²⁷ The table[↓] summarises the causes of transient loss of consciousness from several descriptive studies. These include epileptic seizure, syncope, and non-epileptic attack disorder.

Diagnosing a first seizure: how do people present?

In addition to the patient’s history, an eyewitness account is very important and should be sought whenever possible. The patient’s and eyewitness’s histories are not only critical for diagnosis of the event. The “first seizure” may be a major event after other missed minor epileptic events, so that the diagnosis is epilepsy rather than a single seizure.⁸⁻⁹ Clinically, clarifying whether the first seizure occurred with or without loss of awareness or consciousness is useful.

Seizures without loss of consciousness

The brief duration and a clear description of the experience define these seizures, which patients often do not recognise as important. If patients present, it is often to primary care. Early recognition allows for correct management and may change the diagnosis from a single seizure to epilepsy.

Myoclonus

Myoclonus is a sudden irregular jerk caused by involuntary muscle activity, involving the trunk or one or more limbs. Many causes of myoclonus exist—it may be physiological or pathological. In primary care, it is important to be aware of hypnic myoclonus (physiological) and acute causes related to drugs and to refer other patients with myoclonus (including seizures). Myoclonus in the awake state usually requires specialist assessment. Hypnic (night time) myoclonus is the most common form of myoclonus, experienced as a jolt, which

Correspondence to: H Angus-Leppan, Royal Free Hospital, Pond Street, London NW3 2QG heather.angus-leppan@nhs.net

Extra material supplied by the author (see <http://www.bmj.com/content/348/bmj.g2470?tab=related#webextra>)

Summary points

- First seizures range from a brief subjective experience (aura) to a major tonic-clonic seizure
- Up to 10% of people living to 80 years of age have one or more seizures; half of these are febrile convulsions
- In 85% of patients, the diagnosis comes from the history; blood tests, electrocardiography, electroencephalography, and sometimes magnetic resonance imaging are important for classification and risk prediction
- 50% of patients with an apparent “first seizure” have had other minor seizures, so their diagnosis is epilepsy
- Low risk patients with first seizures have no neurological deficits, normal magnetic resonance imaging and electroencephalography, and a 35% risk of recurrence at five years; they are not usually offered treatment
- High risk patients with first seizures have neurological deficit, magnetic resonance imaging and/or electroencephalography abnormalities, and a 70% risk of recurrence at five years; they are offered treatment

Sources and selection criteria

I consulted my personal archive of references and searched Medline and the Cochrane Collaboration and Clinical Evidence databases, using “seizure”, “first seizure”, and specific topics. I also consulted the National Institute for Health and Care Excellence’s guidelines. I carefully examined randomised controlled trials, systematic reviews, and meta-analyses. Ranges of results are used in preference to averages, because pooling results from methodologically diverse studies is not accurate

may be dramatic and awaken the person, on drifting into sleep. Most of us have experienced this at least once, and patients can be reassured that this is a normal phenomenon.

Drugs (including some narcotics, antidepressants, and antipsychotics) cause myoclonus, as can drug toxicity or withdrawal. Secondary causes include epileptic seizure. A myoclonic seizure varies from a subtle unrecognised jerk, presenting as “clumsiness” or dropping of an object, to a violent jolt causing a fall. It may be the first feature of juvenile myoclonic epilepsy, the most common form of myoclonic epilepsy, classically with myoclonic jerks or clumsiness occurring in the first hours after awakening, especially after sleep deprivation. Recognition, referral, and treatment of these may prevent a full tonic-clonic seizure. Other causes include post-hypoxic brain damage (such as after cardiac arrest), encephalopathy, encephalitis, and neurodegeneration (which will present with other clinical features such as cognitive change) and spinal myoclonus due to injury or disease.²⁸

Aura (simple partial subjective seizure)

Epileptic auras are brief (seconds only) and should be distinguished from migraine auras, which usually last several minutes. They can be autonomic, usually a rising epigastric sensation, lasting seconds. Psychic epileptic auras such as *déjà vu* are often unpleasant and out of the realm of any normal experience, sometimes intensely so; they may involve distortions of time or a feeling of separation or depersonalisation. *Déjà vu* (already seen) and *jamais vu* (never seen) refer to a false impression that a present experience is familiar. They refer to something heard, experienced, or seen. These are common auras of a temporal lobe seizure. They need to be distinguished from normal experience (such as occasional bland *déjà vu*), psychiatric illness (usually prolonged and with persistent behavioural or personality change), and migrainous auras (lasting many minutes in the setting of other features of migraine). Sensory epileptic auras are often simple, unformed elementary hallucinations (such as metallic taste, coloured spots, tinnitus, tingling), are usually positive (as opposed to the loss of function seen in stroke), and last seconds (as opposed to migraine and stroke). Complex hallucinations, such as formed objects or scenes or formed words or sentences, are very unlikely to be epileptic.²⁹ An aura is designated as a “focal seizure without impairment of consciousness or awareness involving subjective sensory or psychic phenomena only” in the revised classification.¹²

Simple partial motor seizure

These are clonic (regular shaking), tonic (stiffening), or dystonic (spasm), usually in a distal limb, and are usually brief (lasting seconds). They must be distinguished from spasticity due to cortical or spinal disease (such as occurs in about 30% of patients with multiple sclerosis or stroke, in which other clinical features and characteristic disabilities will indicate the diagnosis) or focal dystonia (such as writer’s cramp, which is situation specific). Rigors can be mistaken for a first seizure, particularly in children.³⁰ A simple partial motor seizure is designated as a “focal motor seizure without impairment of consciousness or awareness” in the revised classification.¹²

Seizures with loss of consciousness

Absences

Previously referred to as “petit mal,” these last seconds or less, with disruption of awareness, activity, and sometimes learning. They may happen many times a day. A motionless stare, sometimes with eyelid fluttering, may be observed. They start in childhood but continue into adulthood in 7-80% of cases. They are more likely to persist to adulthood if onset is in later childhood or in adolescence, if they are difficult to treat, and if they are associated with other types of seizures.³¹ Absences may present late, with the person being unaware of them or having tolerated them for decades.³² They must be distinguished from daydreaming, cognitive difficulties, hearing or visual loss, autism, and psychological difficulties, as well as from complex partial seizures (see below). A decline in academic performance at school should alert family, teachers, and healthcare professionals to the possibility of absence seizures. The electroencephalogram is diagnostic in more than 90% of cases.⁹ If electroencephalography is unavailable, hyperventilation may induce a typical event.

Complex partial seizure

Some impairment of awareness, consciousness, and/or memory of the event occurs during a complex partial seizure.¹⁰ These sometimes evolve from an aura (simple partial seizure). They may be a motionless stare or automatisms (automatic involuntary movements) such as lip smacking, fiddling, and rubbing or pseudo-purposeful movements. Objects in the immediate vicinity may be used; movements may include dressing and undressing, hitting out, or vocalisations. Tasks involving detailed cognition, such as loading a gun, finding a key and unlocking a cabinet, or typing in a password, would not be expected. Episodes last

for seconds to minutes, and communication is usually impaired. These are designated as “focal seizures with impairment of consciousness or awareness” in the revised terminology.¹²

Tonic-clonic seizure (convulsion)

Tonic-clonic seizures may have no warning (if generalised from onset) or may start with an aura (if focal with secondary generalisation) before consciousness is lost. Often an initial cry is followed by a loss of tone and a fall, then a phase of tonic rigidity followed by regular rhythmic shaking in all limbs, trunk, and face, lateral tongue biting, and cyanosis. Eyes are usually open.^{33 34} The usual duration is 1-2 minutes, and postictal confusion (a period usually longer than 10 minutes characterised by disorientation, poor concentration, poor short term memory, and decreased verbal and interactive skills) occurs.¹⁰

Differential diagnosis of transient loss of consciousness

Up to 35% of people will experience at least one episode of transient loss of consciousness by the age of 60 years.³⁵ The differentiation of tonic-clonic seizures from syncope and non-epileptic attack disorder is discussed below. This may be difficult, particularly if no eyewitness account is available. No single clinical feature or investigation is pathognomonic.

Postictal confusion,^{7 34 36} cyanosis,³⁶ lateral tongue biting,³⁶ preceding *déjà vu* or *jamais vu*,³⁶ confirmed unresponsiveness,³⁶ head or eye turning to one side,^{7 36} and rhythmic limb shaking or unusual (dystonic) posturing are strong seizure markers.^{34 36} Seizure is five times more likely than syncope if the patient has postictal confusion characterised by disorientation ($P<0.001$).⁷ Patients themselves are poor judges of their own postictal confusion, and the eyewitness account is crucial for this information.⁷ Incontinence and injury do not discriminate between seizure, syncope, and non-epileptic attack disorder.⁷

Syncope

Transient loss of consciousness is much more commonly caused by syncope, particularly reflex (vasovagal) syncope, than by seizure. Many cases will not reach medical attention. Prodromal blurred vision, sweating, dizziness, dyspnoea, nausea, or palpitations,^{7 36 37} precipitation by prolonged sitting or standing,³⁶ and pallor during the episode are common.³⁴ If movements occur, they are usually brief, often myoclonic jerks. However, syncope can sometimes be convulsive with tonic-clonic movements, owing to cerebral hypoxia, particularly if the patient is not able to assume the horizontal position.³⁸ Eyes are usually open in both syncope and epileptic seizures but not in non-epileptic attacks.^{33 38 39} Nausea or sweating before the event make seizure much less likely than syncope.⁷ Cardiac syncope may be an apparently bland event, with no prodrome, brief loss of consciousness, and pallor, sweating, or clamminess, followed by rapid recovery. Cyanosis strongly suggests cardiac rather than reflex syncope.⁷ Cardiac syncope due to arrhythmia or structural abnormality of the heart doubles the standardised mortality ratio and needs urgent investigation.³⁷

Non-epileptic attack disorder

These are episodes resembling seizures but caused by psychological or psychiatric illness. They are also called non-epileptic seizures, dissociative seizures, or psychogenic non-epileptic seizures and were previously called pseudo-seizures or hysterical seizures (but they are not seizures). Sometimes the term “non-epileptic attack” is misused for any

event that is not epilepsy (including syncope, psychiatric or psychological events, and migraine)

Non-epileptic attack disorder occurs in about 12-18% of people with transient loss of consciousness,⁴⁰ can be difficult to diagnose and manage, and presents in many forms. A successful outcome is more likely when the diagnosis is made early.⁴¹ Key features are prolonged apparent loss of consciousness with normal colour or oxygen saturation on room air, fluctuating motor activity, asynchronous movements, pelvic thrusting, side to side head or body movements, ictal crying, some responsiveness such as resistance to eye opening, memory recall, and rapid post-event recovery. If the event is one of prolonged shaking and apparent loss of consciousness (more than 10 minutes) and the patient retains normal colour, the event is almost never an epileptic seizure.

Should first status epilepticus and seizure clusters be considered first seizure or epilepsy?

A cluster of seizures or status epilepticus within 24 hours is defined as a form of first seizure,⁴² but this is controversial and not solidly supported by data.⁴³ Strong grounds exist for revising the inclusion of seizure clusters and first status epilepticus in the definition of first seizure.

In children, the risk of recurrence for multiple seizures in one day is double that for a single seizure, strongly supporting the argument for calling this epilepsy.⁴⁴ In adults, the recurrence rate after discharge from hospital is unclear. Some series suggest no increased risk of subsequent seizures if the patient presented with multiple seizures in the first 24 hours.⁴⁵ However, 16% of first status epilepticus patients die during their inpatient stay, whereas the immediate mortality from a single seizure is negligible.⁴⁶ Of those surviving the first 30 days, the long term standardised mortality rate for first seizure status epilepticus is more than double that for a brief single first seizure.⁴⁷ Management of first status epilepticus and seizure clusters is very different from that of a single seizure. Early management of “first status epilepticus” will be the same as for status epilepticus in patients with known epilepsy.

Who is most at risk?

Worldwide, social deprivation is closely associated with first seizures and epilepsy.⁴⁸ Young people and older people are at the highest risk for first seizure (as well as for epilepsy).^{18 49} The frequency and cause of first seizures also vary in different economic and geographical settings.

Provoked seizures in early life are usually febrile convulsions,⁵⁰ caused by viral infection in 80%, with 8% due to meningitis (viral or bacterial).⁵¹ Unprovoked remote symptomatic seizures in children are more commonly due to prenatal than postnatal factors.¹³ An unprovoked idiopathic (presumed genetic) first seizure occurs in childhood or teenage years, commonly with a family history of idiopathic epilepsy.⁵²

Worldwide, in adults, infections such as acute meningitis, encephalitis, malaria, HIV related disease, and cysticercosis are common causes of first seizures.⁵³ Provoked seizures due to intoxication and withdrawal from alcohol are also frequent.^{13 54} In later life, vascular disease becomes the most common cause.⁵⁵ Brain tumours, including metastases, are responsible for about 4% of first seizures.¹³ Paradoxically, lower grade primary tumours are more likely to present with a seizure than are higher grade ones.⁵⁶

How should first seizure be managed?

Following a first seizure of any kind, all patients should be referred to a specialist for investigation. In the UK, patients with a first seizure see a wide range of health professionals including paramedical officers, emergency department nurses and doctors, primary care doctors, neurologists, other physicians, and specialist nurses, or none at all in at least 25% of cases.⁴⁸ If a tonic-clonic seizure is witnessed then stabilisation, removal of surrounding dangers, and examination for acute factors (including blood glucose, metabolic disturbance, sepsis, toxins and withdrawal states, acute stroke, and brain injury) are the starting points. If the tonic-clonic seizure lasts longer than two minutes, benzodiazepines (such as rectal diazepam, buccal midazolam, or intravenous lorazepam) are usually given as rescue medication. Admission is needed if the seizure recurs or continues, an underlying cause requiring acute treatment exists, level of consciousness is reduced, a neurological deficit is present, or social support for discharge is inadequate.⁵⁷ A provoked (acute symptomatic) first seizure with a trigger may need urgent treatment (such as for infection, encephalitis, metabolic disturbance, toxicity, haemorrhage). Remote or progressive symptomatic causes (such as chronic cerebrovascular disease or brain tumour) may also need treatment. A single seizure without loss of consciousness does not usually need any first aid.

Why is investigation after first seizure important?

When the history has not clarified whether the event was a seizure, the investigations are unlikely to do so. Retaking the history from the patient and from eyewitnesses is often more useful. Clinical assessment contributes more than 85% of the diagnostic yield in transient loss of consciousness.^{1 4} Warning patients that investigations are unlikely to change the clinical diagnosis and may all be normal, even with a firm diagnosis of an epileptic seizure, is important.⁴

After a first seizure, further seizures (that is, epilepsy) occur in between 6% and 82% of patients.^{18 58} Averaging these figures does not allow prediction of the risk for an individual. Thorough clinical assessment and investigations help to establish the type of seizure, cause, and recurrence risk. Provoked seizures are more common in people with an underlying genetic or other tendency to epilepsy,⁵² and a single trigger (such as alcohol) should not be assumed to be the only cause.

What investigations are needed after first seizure in acute setting?

The most important initial tests in the acute setting are blood glucose measurement (for hypoglycaemia or hyperglycaemia) and electrocardiography. Electroencephalography is mandatory in anyone with loss of consciousness, as syncope of any cardiac cause may present as a secondary hypoxic seizure, and potentially fatal arrhythmias, particularly long QT syndromes (Brugada syndrome), will otherwise be missed.⁵⁹ Cardiac disease is the most common cause of non-traumatic sudden death in young people, sometimes preceded by potentially treatable cardiac syncope.⁶⁰

Other blood tests will exclude hyponatraemia or hypernatremia, hypocalcaemia or hypercalcaemia, hypothyroidism, uraemia, liver failure, anaemia (which can trigger syncope), leucocytosis (suggesting infection, although mild leucocytosis can occur after a seizure), and eosinophilia (a clue to parasitosis, an

important cause of a first seizure in many parts of the world).⁴⁸ Although the yield of blood tests is low,^{1 4 59} they are needed to determine whether the seizure is provoked.⁵⁰

What investigations will be done at early specialist follow-up?

Early specialist assessment by a neurologist can reduce investigations, improve diagnostic accuracy, and save time for the patient.^{4 61} If, for example, the neurologist revises the diagnosis from seizure to reflex syncope, no further investigations are needed beyond the blood tests and electrocardiography.

Electroencephalography is useful in suspected first seizure for predicting recurrence and in classification of the seizure (idiopathic generalised or focal). Yield is highest in the first 24 hours after the seizure.⁹ Relevant abnormalities (spikes and/or slow waves)^{59 62} are found in 8-50% of cases.⁵⁹ The yield is increased by activation procedures (hyperventilation and photic stimulation)⁶³ and with electroencephalography after sleep deprivation (up to 80% yield, but also an increase to 4% in false positives).⁹ An electroencephalogram is unhelpful when the diagnosis is syncope, as it does not “rule out” epilepsy and has a false positive rate of 4%.⁶⁴

Is brain imaging needed in all first seizure patients?

Many guidelines advocate magnetic resonance imaging in all first seizure patients.⁵⁹ However, no sound justification exists in idiopathic epilepsy presenting at a young age. For example, in an 18 year old with a single convulsion, previous early morning myoclonic jerks, normal neurological examination, and an electroencephalogram with 3/second spike and wave discharges, the diagnosis of juvenile myoclonic epilepsy (idiopathic) is clear cut. Relevant lesions on magnetic resonance imaging are not found in patients with electroencephalogram proved idiopathic epilepsy. Magnetic resonance imaging can be safely restricted to first seizure patients without clinical or electroencephalographic evidence of idiopathic epilepsy.⁶⁵ Overall, magnetic resonance imaging has a yield of 10% in first seizures and is superior in resolution to computed tomography scanning, especially for temporal lobe epilepsy.⁵⁹

Computed tomography scanning is useful for first seizure patients with acute head injury or patients with reduced level of consciousness. It is safer and faster than magnetic resonance imaging for acutely unwell patients,⁶⁵ and it may influence acute management in 9-17% of patients.⁶⁶

Is this a first seizure and will it recur?

This is a critical question. The first step is to go back to the history. Up to half of people with a “first seizure” have historical evidence of non-convulsive seizures or nocturnal seizures (bed wetting, tongue biting, blood on the pillow, early morning headache, or “hangover” without alcohol), which suggests that the diagnosis is epilepsy.^{8 9 13 67}

Studies with varying methods and follow-up from two to 26 years estimate the risk of recurrence after a first seizure to be between 6% and 82%.^{68 69} Maximum recurrence risk is within the first 3-6 months.^{8 18} For the individual patient, predictive factors need to be examined. For example, after a febrile convulsion, the risk of developing epilepsy is 6%, reducing over time.⁶⁸ Neurological deficits (prenatal injury, neurological deficit, intellectual disability) or relevant magnetic resonance

imaging or electroencephalographic abnormalities (spikes, slow waves, or both) are the strongest predictors of recurrence across many studies.⁷⁰ For patients with one or both of these factors, the risk of recurrence is 70% over five years.⁷¹ For patients without these factors, recurrence is estimated at 35%.^{70 71}

To treat or not to treat?

After a first seizure, the default position is not to give antiepileptic drug treatment. We offer treatment to first seizure patients with a high risk of recurrence, because of known neurological deficit, a magnetic resonance imaging or electroencephalographic abnormality, or individual factors.⁷² These include risk of fracture or injury, social isolation, and the need to return to driving as soon as possible.

Does early treatment improve long term prognosis and prevent death?

Early treatment reduces the risk of recurrence but does not improve the long term prognosis.^{71 73} It has not been shown to reduce mortality due to epilepsy. These findings apply predominantly to low risk patients, as randomisation to early or delayed treatment occurs only when both doctor and patient are uncertain about whether to treat.

Should we treat if provocation is ongoing?

We have no solid evidence regarding treatment if the provocation continues (for example, ongoing alcohol or drug intake, brittle diabetes, or hypothyroidism or hypercalcaemia that is taking months to correct). The natural history of alcohol use and seizures suggests an increasing risk of further events with each recurrence, directly due to alcohol,⁷⁴ head injuries, or alcoholic brain damage. Hypoglycaemia causes neuronal damage, which predisposes to further seizures.⁷⁵ Although treatment is not proved, it may protect from further seizures and can be justified while the chronic provoking factors remain.

What follow-up is recommended after first seizure?

Specialist review and investigations are recommended for first seizure patients within four weeks.⁶⁵ Unless the diagnosis is revised to syncope, follow-up with results will usually occur after about three months, earlier if abnormalities are found. Further specialist follow-up depends on the estimated risk of recurrence, whether drug treatment has been started, and other individual factors. Many patients with a first seizure and normal investigations will be discharged to primary care, with specialist review if a further event occurs. Patients may remain concerned, even after explanation, when told that they have had a seizure and they cannot drive but their tests are normal and they do not need further specific treatment or specialist follow-up. Primary care physicians have an important role in further explanation, particularly in the significant minority of first seizure patients in whom the diagnosis may trigger depression and anxiety.⁷⁶

What should we advise with regards to driving?

Driving is often a great concern to patients with a first seizure.⁷⁷ People with epilepsy have 40% more serious road traffic accidents than do other people.⁷⁸ Initial advice to the first seizure patient should be not to drive until medically advised otherwise, whether or not the diagnosis is certain. First seizures should be

reported to the Driver and Vehicle Licensing Agency (DVLA) in the UK or the equivalent body internationally.

Driving regulations vary considerably between, and sometimes within, countries. In the UK, decision making is centralised.⁷⁹ The regulatory body, the DVLA, gathers information from treating doctors, with the advantage of separating the therapeutic relationship and decision making about driving. New regulations allow some patients with only simple partial seizures to drive. If the first seizure is unprovoked, investigations are normal, and no neurological deficit is present, driving will usually be permitted after six months. Otherwise, driving is usually permitted after 12 months seizure free. Commercial licences are subject to more stringent regulation.⁷⁹

What advice should be given about safety at home and at leisure?

Patients should be advised to have showers rather than baths, ideally with a heat controlled system.⁸⁰ If this is not possible, an informed relative or carer should be present and available during bathing. Ideally, household members should be trained in first aid.

Swimming can be safe, with an informed lifeguard or another person trained in first aid. For some patients with intellectual disability or other medical needs, swimming guidelines are advisable and can be individually tailored to the need.⁸¹ The UK Sport Diving Medical Committee recommends that the person is off medication and seizure free for five years before scuba diving.⁸² For this and other potentially hazardous activities such as downhill skiing, abseiling, bungee jumping, cycling, parachuting, and gliding, no clear evidence base exists for our advice.

What advice should be given regarding sex following first seizure?

Little evidence exists on epilepsy and sexuality, particularly in women. No data are available on the risks of injury with a seizure during sexual activity. One study in patients with severe epilepsy estimated that 8% of seizures occurred during intercourse or masturbation and that 25% feared a seizure during sexual activity, but these figures cannot be extrapolated to patients with first seizures.⁸³ Hyposexuality and sexual concerns are common, but doctors, nurses, and patients are often uneasy about discussing them.^{84 85} In the absence of any firm evidence, we should tell patients to continue with their normal level of sexual activity and answer any specific questions.

Should we warn all patients about sudden unexpected death in epilepsy?

In the UK, specialists are mandated to discuss sudden unexpected death in epilepsy with all patients with epilepsy,⁶⁵ but not for first seizure patients. Only 5% of neurologists discussed sudden unexpected death in epilepsy with all patients; 60% discussed it with some, usually high risk, patients or those who specifically asked about it.⁸⁶ The standardised mortality rate after a first seizure is about 2.3,⁸⁷ which overlaps with the 2-4 described for epilepsy.⁸⁸ If we discuss sudden death with patients with epilepsy, we should also do so with patients with first seizures and those with cardiac syncope. Discussing sudden unexpected death in epilepsy at the first visit is not always appropriate, as there is much to discuss and sometimes a risk of information overload. Content and timing of this discussion

must be individualised to prevent a negative psychological effect.⁸⁹

I greatly appreciate the support of S Powis and the Royal Free Hospital research scheme, C Burghes and the Royal Free Charity, and my colleagues. I thank R J Guiloff for suggestions.

Contributors: HAL planned the organisation, content, and structure of the paper on the basis of the BMJ's guidelines for writing a clinical review.

Competing interests: I have read and understood the BMJ Group policy on declaration of interests and declare the following interests: none.

Provenance and peer review: Commissioned: externally peer reviewed.

- 1 Day SC, Cook EF, Funkenstein H, Goldman L. Evaluation and outcome of emergency room patients with transient loss of consciousness. *Am J Med* 1982;73:15-23.
- 2 Leach JP, Lauder R, Nicolson A, Smith DF. Epilepsy in the UK: misdiagnosis, mistreatment, and undertreatment? The Wrexham area epilepsy project. *Seizure* 2005;14:514-20.
- 3 Smith D, Defalla BA, Chadwick DW. The misdiagnosis of epilepsy and the management of refractory epilepsy in a specialist clinic. *GJM* 1999;92:15-23.
- 4 Angus-Leppan H. Diagnosing epilepsy in neurology clinics: a prospective study. *Seizure* 2008;17:431-6.
- 5 Forsgren L. Prospective incidence study and clinical characterization of seizures in newly referred adults. *Epilepsia* 1990;31:292-301.
- 6 Zaidi A, Clough P, Cooper P, Scheepers B, Fitzpatrick AP. Misdiagnosis of epilepsy: many seizure-like attacks have a cardiovascular cause. *J Am Coll Cardiol* 2000;36:181-4.
- 7 Hoefnagels W, Padberg G, Overweg J, Van der Velde E, Roos R. Transient loss of consciousness: the value of the history for distinguishing seizure from syncope. *J Neurol* 1991;238:39-43.
- 8 Hauser WA, Rich SS, Annegers JF, Anderson VE. Seizure recurrence after a 1st unprovoked seizure: an extended follow-up. *Neurology* 1990;40:1163-70.
- 9 King MA, Newton MR, Jackson GD, Fitt GJ, Mitchell LA, Silvapulle MJ, et al. Epileptology of the first-seizure presentation: a clinical, electroencephalographic, and magnetic resonance imaging study of 300 consecutive patients. *Lancet* 1998;352:1007-11.
- 10 Angeles DK. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. *Epilepsia* 1981;22:489-501.
- 11 Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989;30:389-99.
- 12 Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde Boas W, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009. *Epilepsia* 2010;51:676-85.
- 13 Jallon P, Goumaz M, Haeggeli C, Morabia A. Incidence of first epileptic seizures in the canton of Geneva, Switzerland. *Epilepsia* 1997;38:547-52.
- 14 Loiseau J, Loiseau P, Guyot M, Duche B, Darigues JF, Aublet B. Survey of seizure disorders in the French southwest: I. Incidence of epileptic syndromes. *Epilepsia* 1990;31:391-6.
- 15 Placencia M, Suarez J, Crespo F, Sander JW, Shorvon SD, Ellison RH, et al. A large-scale study of epilepsy in Ecuador: methodological aspects. *Neuroepidemiology* 1992;11:74-84.
- 16 Meinardi H, Scott RA, Reis R, Sander JW, for the ILAE Commission on the Developing World. The treatment gap in epilepsy: the current situation and ways forward. *Epilepsia* 2001;42:136-49.
- 17 Lavados J, Germain L, Morales A, Campero M, Lavados P. A descriptive study of epilepsy in the district of El Salvador, Chile, 1984-1988. *Acta Neurol Scand* 1992;85:249-56.
- 18 Hart Y, Sander J, Shorvon S, Johnson A. National general practice study of epilepsy: recurrence after a first seizure. *Lancet* 1990;336:1271-4.
- 19 Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984. *Epilepsia* 1993;34:453-68.
- 20 Hauser WA, Annegers JF, Rocca WA. Descriptive epidemiology of epilepsy: contributions of population-based studies from Rochester, Minnesota. *Mayo Clin Proc* 1996;71:576-86.
- 21 All Party Parliamentary Group on Epilepsy. Wasted money, wasted lives: the human and economic cost of epilepsy in England. Stationery Office, 2007.
- 22 Zielinski JJ. Epidemiology and medicosocial problems of epilepsy in Warsaw: final report on research program. Psychoneurological Institute, 1974.
- 23 Beran RG, Michelazzi J, Hall L, Tsimnadis P, Loh S. False-negative response rate in epidemiologic studies to define prevalence ratios of epilepsy. *Neuroepidemiology* 1985;4:82-5.
- 24 Jacoby A, Baker G, Smith D, Dewey M, Chadwick D. Measuring the impact of epilepsy: the development of a novel scale. *Epilepsia Res* 1993;16:83-8.
- 25 Bellon M, Walker C, Peterson C, Cookson P. The "E" word: epilepsy and perceptions of unfair treatment from the 2010 Australian Epilepsy Longitudinal Survey. *Epilepsy Behav* 2013;27:251-6.
- 26 Bellon M, Walker C, Peterson C. Seizure-related injuries and hospitalizations: self-report data from the 2010 Australian Epilepsy Longitudinal Survey. *Epilepsy Behav* 2013;26:7-10.
- 27 National Institute for Health and Clinical Excellence. Transient loss of consciousness ("blackouts") management in adults and young people. NICE, 2010.
- 28 Caviness JN, Brown P. Myoclonus: current concepts and recent advances. *Lancet Neurol* 2004;3:598-607.
- 29 Angus-Leppan H. Migraine: mimics, borderlands and chameleons. *Pract Neurol* 2013;13:308-18.
- 30 Cross JH. Pitfalls in the diagnosis and differential diagnosis of epilepsy. *Paediatr Child Health* 2009;19:199-202.
- 31 Panayiotopoulos C, Chroni E, Daskalopoulos C, Baker A, Rowlinson S, Walsh P. Typical absence seizures in adults: clinical, EEG, video-EEG findings and diagnostic/syndromic considerations. *J Neurol Neurosurg Psychiatry* 1992;55:1002-8.
- 32 Marini C, King M, Archer J, Newton M, Berkovic S. Idiopathic generalised epilepsy of adult onset: clinical syndromes and genetics. *J Neurol Neurosurg Psychiatry* 2003;74:192-6.
- 33 Chung SS, Gerber P, Kirlin KA. Ictal eye closure is a reliable indicator for psychogenic nonepileptic seizures. *Neurology* 2006;66:1730-1.
- 34 Thijs RD, Wagenaar WA, Middelkoop HA, Wieling W, van Dijk JG. Transient loss of consciousness through the eyes of a witness. *Neurology* 2008;71:1713-8.
- 35 Ganzeboom KS, Mairuhu G, Reitsma JB, Linzer M, Wieling W, Van Dijk N. Lifetime cumulative incidence of syncope in the general population: a study of 549 Dutch subjects aged 35-60 years. *J Cardiovasc Electrophysiol* 2006;17:1172-6.
- 36 Sheldon R, Rose S, Ritchie D, Connolly SJ, Koshman M-L, Lee MA, et al. Historical criteria that distinguish syncope from seizures. *J Am Coll Cardiol* 2002;40:142-8.
- 37 Soteriades ES, Evans JC, Larson MG, Chen MH, Chen L, Benjamin EJ, et al. Incidence and prognosis of syncope. *N Engl J Med* 2002;347:878-85.
- 38 Lempert T, Bauer M, Schmidt D. Syncope: a videometric analysis of 56 episodes of transient cerebral hypoxia. *Ann Neurol* 1994;36:233-7.
- 39 Lempert T. [Syncope: phenomenology and differentiation from epileptic seizures] [German]. *Nervenarzt* 1997;68:620-4.
- 40 Reuber M, Jamnadas-Khoda J, Broadhurst M, Grunewald R, Howell S, Koepp M, et al. Psychogenic nonepileptic seizure manifestations reported by patients and witnesses. *Epilepsia* 2011;52:2028-35.
- 41 Reuber M, Pukrop R, Bauer J, Helmstaedter C, Tessendorf N, Elger CE. Outcome in psychogenic nonepileptic seizures: 1 to 10-year follow-up in 164 patients. *Ann Neurol* 2003;53:305-11.
- 42 Commission on Epidemiology and Prognosis, International League Against Epilepsy. Guidelines for epidemiologic studies on epilepsy. *Epilepsia* 1993;34:592-6.
- 43 Haut SR, Shinnar S. Considerations in the treatment of a first unprovoked seizure. *Semin Neurol* 2008;28:289-96.
- 44 Camfield P, Camfield C. Epilepsy can be diagnosed when the first two seizures occur on the same day. *Epilepsia* 2000;41:1230-3.
- 45 Kho LK, Lawn ND, Dunne JW, Linto J. First seizure presentation: do multiple seizures within 24 hours predict recurrence? *Neurology* 2006;67:1047-9.
- 46 Rossetti A, Hurwitz S, Logroscino G, Bromfield E. Prognosis of status epilepticus: role of aetiology, age, and consciousness impairment at presentation. *J Neurol Neurosurg Psychiatry* 2006;77:611-5.
- 47 Logroscino G, Hesdorffer DC, Cascino GD, Annegers JF, Bagiella E, Hauser WA. Long-term mortality after a first episode of status epilepticus. *Neurology* 2002;58:537-41.
- 48 Crombie D. A survey of the epilepsies in general practice: a report by the Research Committee of the College of General Practitioners. *Br Med J* 1960;2:416-22.
- 49 Loiseau J, Loiseau P, Duche B, Guyot M, Darigues JF, Aublet B. A survey of epileptic disorders in southwest France: seizures in elderly patients. *Ann Neurol* 1990;27:232-7.
- 50 Beghi E, Carpio A, Forsgren L, Hesdorffer DC, Malmgren K, Sander JW, et al. Recommendation for a definition of acute symptomatic seizure. *Epilepsia* 2010;51:671-5.
- 51 Lewis HM, Parry JV, Parry RP, Davies HA, Sanderson P, Tyrrell D, et al. Role of viruses in febrile convulsions. *Arch Dis Child* 1979;54:869-76.
- 52 Panayiotopoulos CP. A clinical guide to epileptic syndromes and their treatment. Bladon Medical Publishing, 2002.
- 53 Carpio A, Hauser WA. Epilepsy in the developing world. *Curr Neurol Neurosci Rep* 2009;9:319-26.
- 54 Leone M, Tonini C, Bogliun G, Monaco F, Mutani R, Bottacchi E, et al. Chronic alcohol use and first symptomatic epileptic seizures. *J Neurol Neurosurg Psychiatry* 2002;73:495-9.
- 55 Szafarski JP, Rackley AY, Kleindorfer DO, Khoury J, Woo D, Miller R, et al. Incidence of seizures in the acute phase of stroke: a population-based study. *Epilepsia* 2008;49:974-81.
- 56 Van Breenen MS, Wilms EB, Vecht CJ. Epilepsy in patients with brain tumours: epidemiology, mechanisms, and management. *Lancet Neurol* 2007;6:421-30.
- 57 Dunn M, Breen D, Davenport R, Gray A. Early management of adults with an uncomplicated first generalised seizure. *Emerg Med J* 2005;22:237-42.
- 58 Hauser WA, Anderson VE, Loewenson RB, McRoberts SM. Seizure recurrence after a first unprovoked seizure. *N Engl J Med* 1982;307:522-8.
- 59 Krumholz A, Wiebe S, Gronseth G, Shinnar S, Levisohn P, Ting T, et al. Practice parameter: evaluating an apparent unprovoked first seizure in adults (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology* 2007;69:1996-2007.
- 60 Eckart RE, Scoville SL, Campbell CL, Shry EA, Stajduhar KC, Potter RN, et al. Sudden death in young adults: a 25-year review of autopsies in military recruits. *Ann Intern Med* 2004;141:829-34.
- 61 Angus-Leppan H, Leach JP. A new era in acute neurological consultations. *Eur J Neurol* 2010;17(4):e26-7.
- 62 Smith SJ. EEG in the diagnosis, classification, and management of patients with epilepsy. *J Neurol Neurosurg Psychiatry* 2005;76(suppl 2):ii2-7.
- 63 Angus-Leppan H. Seizures and adverse events during routine scalp electroencephalography: a clinical and EEG analysis of 1000 records. *Clin Neurophysiol* 2007;118:22-30.
- 64 Zivin L, Marsan CA. Incidence and prognostic significance of "epileptiform" activity in the EEG of non-epileptic subjects. *Brain* 1968;91:751-78.
- 65 National Institute for Health and Clinical Excellence. The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care. NICE, 2012.
- 66 Harden CL, Huff JS, Schwartz TH, Dubinsky RM, Zimmerman RD, Weinstein S, et al. Reassessment: neuroimaging in the emergency patient presenting with seizure (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2007;69:1772-80.
- 67 Shinnar S, Berg AT, Moshe SL, Petix M, Maytal J, Kang H, et al. Risk of seizure recurrence following a first unprovoked seizure in childhood: a prospective study. *Pediatrics* 1990;85:1076-85.
- 68 Neligan A, Bell GS, Giavasi C, Johnson AL, Goodridge DM, Shorvon SD, et al. Long-term risk of developing epilepsy after febrile seizures: a prospective cohort study. *Neurology* 2012;78:1166-70.
- 69 Berg AT, Shinnar S. The risk of seizure recurrence following a first unprovoked seizure: a quantitative review. *Neurology* 1991;41:965-72.
- 70 Kim LG, Johnson TL, Marson AG, Chadwick DW, for the MRC MESS Study Group. Prediction of risk of seizure recurrence after a single seizure and early epilepsy: further results from the MESS trial. *Lancet Neurol* 2006;5:317-22.
- 71 Marson A, Jacoby A, Johnson A, Kim L, Gamble C, Chadwick D, et al. Immediate versus deferred antiepileptic drug treatment for early epilepsy and single seizures: a randomised controlled trial. *Lancet* 2005;365:2007-13.

Tips for first contact doctor

- After stabilisation of a patient with a first seizure, take a careful history from the patient and eyewitness(es)
- Blood tests and electrocardiography are important, especially for hypoglycaemia and arrhythmias
- Advise the patient not to drive and not to bath alone; give details of educational resources (see box)
- Refer to a specialist for early review (further assessment, tests, and antiepileptic drugs if indicated)

Additional educational resources*Resources for healthcare professionals*

- National Institute for Health and Care Excellence, UK (guidance.nice.org.uk/Topic)—Free guidelines, no registration needed; recommendations and references on initial assessment
- Scottish Intercollegiate Guidelines Network (sign.ac.uk/guidelines/published/index.html)—Free guidelines, no registration needed; recommendations and references on initial assessment
- Epilepsy.com (www.epilepsy.com)—Links and information pages, including links to videos with examples of different seizure types

Resources for patients and healthcare professionals

- Epilepsy Action (epilepsy.org.uk)—Free site with information for patients; no registration needed; explanations, descriptions, useful links, literature
- Epilepsy Society (epilepsysociety.org.uk; 01494 601 400)—Free site and helpline; no registration needed; information on important topics, links, brochure, helpline
- International League Against Epilepsy (ilae-epilepsy.org)—No registration needed; information and links to other sites; information pages on important topics

Questions for future research

- What are the recurrence rates of defined seizure types analysed by their cause?
- What is the optimal management strategy for first seizure patients, particularly regarding antiepileptic drugs?
- When should we treat provoked seizures with antiepileptic drugs?
- Are first status epilepticus and multiple seizures a “first seizure” or epilepsy?
- What causes sudden unexpected death in epilepsy and what prevents it for first seizure patients?
- How can we improve the way we advise first seizure patients on lifestyle and safety?

- 72 Cole C, Pointu A, Wellsted DM, Angus-Leppan H. A pilot study of the epilepsy risk awareness checklist (ERAC) in people with epilepsy and learning disabilities. *Seizure* 2010;19:592-6.
- 73 Leone MA, Solari A, Beghi E. Treatment of the first tonic-clonic seizure does not affect long-term remission of epilepsy. *Neurology* 2006;67:2227-9.
- 74 Ng SK, Hauser WA, Brust JC, Susser M. Alcohol consumption and withdrawal in new-onset seizures. *N Engl J Med* 1988;319:666-73.
- 75 Burns CM, Rutherford MA, Boardman JP, Cowan FM. Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycemia. *Pediatrics* 2008;122:65-74.
- 76 Velissaris SL, Saling MM, Newton MR, Berkovic SF, Wilson SJ. Psychological trajectories in the year after a newly diagnosed seizure. *Epilepsia* 2012;53:1774-81.
- 77 Sander JW. Ultimate success in epilepsy—the patient’s perspective. *Eur J Neurol* 2005;12(suppl 4):3-11.
- 78 Taylor J, Chadwick D, Johnson T. Risk of accidents in drivers with epilepsy. *J Neurol Neurosurg Psychiatry* 1996;60:621-7.
- 79 Driver and Vehicle Licensing Agency. 2014. www.dvla.gov.uk/medical/ata glance.
- 80 Seneviratne U. Management of the first seizure: an evidence based approach. *Postgrad Med J* 2009;85:667-73.
- 81 Burt J, Cole C. Swimming guidelines for adults with epilepsy: Jennifer Burt and Christine Cole describe how guidelines designed to ensure the safety of swimmers with epilepsy were researched, consulted on and distributed. *Learning Disability Practice* 2008;11(10):12-6.
- 82 Almeida Mdo R, Bell GS, Sander JW. Epilepsy and recreational scuba diving: an absolute contraindication or can there be exceptions? A call for discussion. *Epilepsia* 2007;48:851-8.
- 83 Fenwick PB, Toone BK, Wheeler MJ, Nanjee MN, Grant R, Brown D. Sexual behaviour in a centre for epilepsy. *Acta Neurolog Scand* 1985;71:428-35.
- 84 Lambert MV. Seizures, hormones and sexuality. *Seizure* 2001;10:319-40.
- 85 Duncan S, Blacklaw J, Beasall G, Brodie M. Antiepileptic drug therapy and sexual function in men with epilepsy. *Epilepsia* 1999;40:197-204.
- 86 Morton B, Richardson A, Duncan S. Sudden unexpected death in epilepsy (SUDEP): don’t ask, don’t tell? *J Neurol Neurosurg Psychiatry* 2006;77:199-202.
- 87 Hauser WA, Beghi E. First seizure definitions and worldwide incidence and mortality. *Epilepsia* 2008;49(suppl 1):8-12.
- 88 Sander JW. Comorbidity and premature mortality in epilepsy. *Lancet* 2013;382:1618-9.
- 89 Ng YS, Davenport R, Duncan S, Derry C. Complications of the SUDEP (sudden unexpected death in epilepsy) discussion. *J Neurol Neurosurg Psychiatry* 2013;84(11):e2-e.
- 90 Eagle KA, Black HR, Cook EF, Goldman L. Evaluation of prognostic classifications for patients with syncope. *Am J Med* 1985;79:455-60.

Accepted: 25 March 2014

Cite this as: *BMJ* 2014;348:g2470

© BMJ Publishing Group Ltd 2014

Table

Table 1 | Causes of transient loss of consciousness. Values are numbers (percentages)

Cause	Eagle, 1985—?syncope; emergency department*	Day et al, 1982—first episode (LOC); emergency department†	Angus-Leppan, 2008—first and recurrent episode (LOC); neurology clinic‡	Angus-Leppan, 2013; emergency department§
Syncopal—all	—	—	40 (25)	—
Syncopal—vasovagal	64 (35)	57 (29)	—	30 (35)
Syncopal—orthostatic	16 (10)	7 (3)	—	—
Syncopal—cardiac	15 (9)	17 (9)	—	10 (12)
Epilepsy	2 (1)	58 (29)	68 (43)	20 (23)
Non-epileptic attack disorder	3 (1)	14 (7)	19 (12)	10 (11)
Other	7 (5)	20 (10)	11 (7)	—
Unknown	69 (39)	25 (13)	20 (13)	16 (19)
Total	176	198	158	86

LOC=loss of consciousness.

*Patients with first and recurrent events.⁹⁰

†Patients with first events only.¹

‡Patients with first and recurrent events.⁴

§Patients with first events only (unpublished).