First seizure in the adult: management in the emergency department

This article provides an up-to-date evidence-based framework for the management of first presentation of an adult seizure in the emergency department. It reviews current guidelines and outlines a patient pathway from decisions to admit to discharge in the emergency department.

Seizures account for 0.5 (Reuber et al, 2000) to 1% (McKee et al, 1990) of emergency department attendances and first seizure for around half such cases (McKee et al, 1990). However, the management of first seizures is quite variable (Reuber et al, 2000; Dunn et al, 2005). Dunn et al (2005) reviewed first seizure management and developed a clinical pathway to improve consistency in emergency department practice. Other clinical reviews have helped reinforce best practice, but their conclusions vary (McLachlan, 1993; Pellegrino, 1994; Smith and Cossburn, 2004; Dunn et al, 2005; Pohlmann-Eden et al, 2006; Adams and Knowles, 2007; Stephen and Brodie, 2008; Wiebe et al, 2008; Seneviratne, 2009; Jagoda and Gupta, 2011) and few are focused on the emergency department (Pellegrino, 1994; Smith and Cossburn, 2004; Jagoda and Gupta, 2011). Furthermore, most reviews are focused on health-care systems outside the UK where the function of the emergency department and resource availability differs (Pellegrino, 1994; Smith and Cossburn, 2004; Adams and Knowles, 2007; Stephen and Brodie, 2008; Wiebe et al, 2008; Seneviratne, 2009; Jagoda and Gupta, 2011).

The Guidelines in Emergency Medicine Network subcommittee of the UK College of Emergency Medicine published guidelines in 2009 on the management of a first seizure to further improve practice (Turner and Benger, 2009). The Scottish Intercollegiate Guidance Network updated guidelines on epilepsy management in 2005 and the National Institute for Health and Clinical Excellence updated their epilepsy guidelines in 2012.

Aim

Personal experience from working in the emergency department revealed uncertainty about best clinical practice. This article provides an up-to-date, evidence-based discussion focused on practical problems faced by junior doctors in the emergency department when managing first seizures in the NHS. It addresses specific questions pertinent to the emergency department management of first seizure (*Table 1*), such as differential diagnosis and the management of important complications.

Method

A literature search was conducted on Medline for 'first seizure' and 'new seizure'. Clinical and systematic review articles were selected if the title and abstract showed a focus on the management of first seizure presentations. Particular focus was given to articles considering seizures in the context of the emergency department. Specific searches were later conducted to address focused questions on topics shown in *Table 1* including 'seizure diagnosis', 'seizure investigation', 'seizure treatment', 'alcohol-related seizure' and 'status epilepticus management', again identifying articles with a focus on the emergency department. References in articles were followed if the articles addressed the clinical questions. Emphasis is placed on randomized control trials where available.

National Institute for Health and Clinical Excellence and Scottish Intercollegiate Guidance Network guidance was specifically sought. Relevant clinical policy and consensus statements from specialty groups were also identified, e.g. the International League Against Epilepsy, the UK College of Emergency Medicine, the American

Table 1. Questions pertinent to the emergency department management of first seizure

Is this an epileptic seizure?
What are the most important differential diagnoses?
What is the seizure type?
What treatment should be given?
How should status epilepticus be treated in the emergency department?
What investigations are appropriate in the emergency department?
Should seizure prophylaxis (antiepileptic drugs) be started?
Who is safe to discharge home?
What advice should the patient be given?
What follow up is appropriate?

Dr Pamela Sarkar* *is Core Medical Trainee in the Department of Infectious Diseases/Genito-Urinary Medicine, St George's Hospital NHS Trust, London SW17 0QT,* **Dr Richard T Ibitoye*** *is Core Medical Trainee in the Department of Neurology, Royal Preston Hospital, Fulwood, Preston,* **Dr Steve Sturman** *is Consultant in the Department of Neurology, and* **Dr Prabodh K Sarkar** *is Consultant in the Department of Elderly Care, City Hospital, Birmingham*

Correspondence to: Dr P Sarkar (pam524sarkar@hotmail.com)
**Dr P Sarkar and Dr RT Ibitoye are joint first authors*

College of Emergency Physicians and American Association of Neurologists.

Is this a seizure?

The International League Against Epilepsy and the International Bureau for Epilepsy define an epileptic seizure as: 'a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain' (Fisher et al, 2005). Epilepsy is an enduring predisposition to seizures and usually requires evidence of two seizures for diagnosis. Infrequently, epilepsy may be diagnosed after a single seizure in an appropriate context (e.g. electroencephalographic findings suggesting idiopathic epilepsy). In the following discussion the word seizure is used to infer 'epileptic seizure'.

Generalized convulsive tonic clonic seizures and focal seizures are most common. Generalized convulsive tonic clonic seizures predominate in the emergency department, accounting for 83% of cases in one study (McKee et al, 1990). Abrupt generalized increase in muscle tone (tonic phase) is followed by rhythmic contractions (clonus) in the head, trunk and limbs. Low amplitude, fast movements are seen initially and progress to high amplitude, slower movements. Drowsiness (post-ictal phase) and weakness follows and confusion is common (Manford, 2001).

In generalized seizure, the patient is unable to give an account of the ictal event in view of the implicit transient loss of consciousness. A witness history is key to evaluation but should be interpreted with care as reliability of accounts is quite variable (Mannan and Wieshman, 2003). In generalized convulsive tonic clonic seizures, typical features in the history thought discriminative for seizure are post-ictal confusion, tongue biting and urinary incontinence (Manford, 2001). In a single centre prospective study, Hoefnagels et al (1991) found post-ictal confusion predicts a seizure diagnosis.

The evidence for tongue biting predicting a seizure diagnosis is from observation studies of patients under investigation for transient loss of consciousness (Benbadis et al, 1995; DeToledo and Ramsay, 1996; Oliva et al, 2008), and for lateral tongue biting. No significant association has been found between urinary incontinence and a seizure diagnosis (Hoefnagels et al, 1991; Oliva et al, 2008).

Focal seizures (caused by focal onset of epileptiform activity) are characterized by abrupt onset of symptoms or signs such as tonic/clonic limb movement, sensory hallucination, strange thoughts, memories or experiences (e.g. déjà vu). The symptoms usually resolve but epileptic activity may progress to other cortical areas or spread diffusely leading to generalized convulsive tonic clonic seizures.

Where a seizure is suspected, possible provoking factors should be considered. The Commission on Epidemiology and Prognosis, International League Against Epilepsy (1993) identified common causes which are summarized in *Table 2*. Commonly, the first seizure presenting in the emergency department is idiopathic in aetiology. Structured questionnaires such as CAGE and Alcohol Use Disorders Identification Test (AUDIT) are reliable methods of assessing alcohol misuse (Rathlev et al, 2002).

Aside from factors leading to provoked or unprovoked seizure, additional contributors can trigger a seizure in the predisposed. Sleep deprivation, drugs (e.g. serotonin-selective re-uptake inhibitors) and alcohol consumption (rather than intoxication or withdrawal) are often implicated.

Is this epilepsy?

Although presenting with a 'first seizure', a history of previous seizure episodes should be sought. Absence, myoclonic jerks and drop attacks may not be volunteered by the patient but suggest idiopathic epilepsy. Generalized convulsive tonic clonic seizures occurring only at night may be noted by a witness.

What are the differential diagnoses?

Seizure is readily confused with other causes of true or apparent transient loss of consciousness. Syncope and psychogenic non-epileptic seizures account for the majority of misdiagnoses. Scheepers et al (1998) found a misdiagnosis of epilepsy in 23% patients in the community; Smith et al (1999) found a similar rate of 26% in a clinic population. Zaidi et al (2000) performed cardiovascular work-up on 74 patients with apparent treatment-resistant epilepsy and found 31 with a cardiovascular cause, reflecting the diagnostic difficulty in this subgroup.

Recurrent psychogenic non-epileptic seizures can be very difficult to differentiate from epilepsy – in a prospective video-electroencephalography study King et al (1982) found neurologists misdiagnosed over 20% of these.

Syncope is defined as transient loss of consciousness as a result of global cerebral hypoperfusion (Moya et al, 2009). Features differentiating this from seizure are short

Table 2. Common provoking factors for seizures as identified by the International League Against Epilepsy

Factor	Description
Head injury	Within 7 days of traumatic brain injury
Cerebrovascular accident	Within 7 days
CNS infection	In the course of disease such as meningitis, encephalitis or abscess
CNS tumour	Presenting symptom of tumour
Intracranial surgery	Immediate postoperative period
Toxic	Examples include recreational drugs (e.g. cocaine), ethanol intoxication, drug overdose, poisoning (e.g. carbon monoxide) and prescription drugs (e.g. tricyclic antidepressants)
Withdrawal	Typically benzodiazepines or alcohol (in context of intoxication or chronic excess)
Metabolic	Examples include uraemia, anoxia, hypoglycaemia and eclampsia
Fever	In children, leading to febrile convulsions
Multiple	Combination of factors
Undefined	In context of an acute, not otherwise defined condition

From Commission on Epidemiology and Prognosis, International League Against Epilepsy (1993)

duration (usually less than 20 seconds), loss of postural tone and spontaneous complete recovery. Reflex syncope (inappropriate activation of cardiovascular reflexes by common triggers) and syncope secondary to structural heart disease are the two most common aetiologies. In the context of syncope, such as dysrhythmia or neutrally mediated ('vasovagal'), the episode of collapse may be accompanied by some form of clonic or other positive motor phenomena, termed 'convulsive syncope'; this is thought to be provoked by the period of cerebral hypoperfusion, rather than true epileptic seizure, and is an important differential to bear in mind when assessing a patient in the emergency department (Donaghy, 2009). A careful history can help delineate the aetiology of syncope and may identify triggers (e.g. micturition and exercise). Focused examination should exclude dysrhythmia, valvular heart disease and heart failure.

Psychogenic non-epileptic seizures are episodes resembling epileptic seizures, without epileptiform activity but with positive evidence of psychogenic factors which may have caused the 'seizure' (Bodde et al, 2009). Avbersek and Sisodiya (2010) systematically reviewed 34 prospective video telemetry studies of characteristics differentiating seizure and psychogenic non-epileptic seizures. Psychogenic non-epileptic seizures were predicted by asynchronous movements, pelvic thrusting, side-to-side head and body movement, forceful eye closure and a fluctuant course.

What investigations are appropriate?

Diagnosis of an epileptic seizure is made on clinical grounds. Investigation are required to evaluate potential causes and exclude differential diagnoses.

Full blood count, urea, electrolytes and creatinine are common investigations in the emergency department. The value of blood investigations in first seizure has been questioned. Studies looked at abnormalities in full blood count, urea, electrolytes, calcium and magnesium (Eisner et al, 1986; Turnbull et al, 1990; Sempere et al, 1992; Tardy et al, 1995). Significant abnormality was infrequent (16 cases in a total of 639 patients), mainly unexpected hypoglycaemia, hyperglycaemia and hyponatraemia.

In light of this, the American College of Emergency Physicians (2004) recommends serum sodium and blood glucose measurements. National Institute for Health and Clinical Excellence guidelines recommend that electrolyte, glucose and calcium measurements should be considered. Scottish Intercollegiate Guidance Network guidelines make no comment on blood investigations. Neither guidance is focused on first seizure presentations in the emergency department, where the frequency of provoked seizure is higher. Routine full blood count, urea and electrolytes, and glucose may thus be appropriate. During a seizure blood glucose should be measured to rule out hypoglycaemia as a provoking factor.

Pregnancy is an important consideration in first seizure, especially in the third trimester where eclampsia should be considered. The American College of Emergency Physicians (2004) recommend pregnancy testing in all women of childbearing age presenting with suspected first seizure as this alters antiepileptic drug choices.

Alcohol withdrawal is a common cause of seizure, usually evident from the history. A European Federation of Neurological Societies review concluded carbohydrate deficient transferrin or gamma glutamyl transferase may play a role where the history is not available, but are limited by poor sensitivity (Bråthen et al, 2005). Blood alcohol levels may also be useful (Rathlev et al, 2002).

An electrocardiogram is important in considering syncope as the cause of transient loss of consciousness. The European Society of Cardiology, American College of Emergency Physicians, American Association of Neurologists and UK College of Emergency Medicine, National Institute for Health and Clinical Excellence and Scottish Intercollegiate Guidance Network all recommend routine electrocardiography in patients presenting with a seizure. The actual rate of significant abnormality of electrocardiograms in first seizure presentations is not known as no prospective studies have addressed this.

Lumbar puncture is useful in the evaluation of CNS infection, especially in the immunocompromised. No randomized control trial or controlled study has addressed its utility in first seizure presentations. An American Association of Neurologists practice parameter found no evidence to support routine lumbar puncture in unprovoked seizures (Krumholz et al, 2007). National Institute for Health and Clinical Excellence and Scottish Intercollegiate Guidance Network do not comment on lumbar puncture in the assessment of first seizure.

Neuroimaging should be performed immediately when an intracranial lesion is suspected (Turner and Benger, 2009). There is particular emphasis on imaging in patients with new focal deficit, fever, persistent headache and focal onset of seizures (Turner and Benger, 2009). Neuroimaging is also essential in patients with a history of malignancy, immunocompromise, HIV infection, alcoholism or bleeding diathesis, where the seizure may be the presenting symptom of underlying structural CNS pathology (Turner and Benger, 2009). The key questions are the modality – computed tomography or magnetic resonance imaging – and timing. The UK College of Emergency Medicine suggest imaging can be deferred, provided reliable follow up is arranged, in patients who have fully recovered without a clearly identifiable cause (Turner and Benger, 2009). Otherwise imaging needs to be performed in the emergency department (American College of Emergency Physicians, 2004; Turner and Benger, 2009).

Magnetic resonance imaging is preferable, if available within an acceptable timeframe (Turner and Benger, 2009). It is more sensitive, and identifies lesions not seen on computed tomography such as mesial temporal sclerosis. However, UK College of Emergency Medicine, National Institute for Health and Clinical Excellence and Scottish Intercollegiate Guidance Network guidelines highlight that computed tomography is preferred in the acutely ill patient.

Electroencephalography is useful for identifying focal lesions, diagnosis of idiopathic epilepsy and quantification of seizure recurrence risk (Turner and Benger, 2009). There is no evidence for its use in decision making in an emergency department patient having fully recovered from a seizure. American College of Emergency Physicians and UK College of Emergency Medicine guidelines recommend that electroencephalography is not routinely requested in the emergency department. National Institute for Health and Clinical Excellence and Scottish Intercollegiate Guidance Network guidance do not address the role of electroencephalography in the emergency department.

Investigations such as drug toxicity screens and chest X-rays should be considered if clinically indicated (Turner and Benger, 2009).

Should antiepileptic drugs be started?

Provoked seizures do not tend to recur once the acute cause has resolved. Multiple studies have demonstrated that abnormal neurological status, abnormal electroencephalography, previous seizures, focal seizure and a remote symptomatic cause (abnormal neuroimaging) all predict seizure recurrence. In this light, risk stratification is often used to guide treatment (Chadwick, 2008).

The emergency department is not an appropriate setting for starting antiepileptic drugs. The rate of non-specialist seizure misdiagnosis is high, and key tools in assessing recurrence risk (e.g. electroencephalography) are not routinely performed. Antiepileptic drugs have significant side effects and drug reactions which must be discussed with the patient. Patients with abnormal neurology and at high risk of seizure recurrence need further work-up beyond the emergency department.

Randomized controlled trials have addressed the effects of immediate or delaying antiepileptic drug commencement after first seizures (First Seizure Trial Group, 1993). In the MRC Multicentre trial for Early Epilepsy and Single Seizures (MESS; Marson et al, 2005), 2-year recurrence rates were 39% in the untreated and 32% in the treated groups. Overall time to 2 years of remission was reduced, but by 5 years no significant difference was found in remission rates. Salient conclusions are that early treatment does not affect long-term seizure outcomes and seizure recurrence is uncommon – most patients had not experienced a recurrence at 2 years. These findings do not support the need for antiepileptic drug decision making in a 4-hour emergency department time window.

Status epilepticus

The International League Against Epilepsy defines status epilepticus where: 'a seizure persists for a sufficient length of time or is repeated frequently enough that recovery between attacks does not occur' (Commission on Classification and Terminology of the International League Against Epilepsy, 1981). There is no consensus on the minimum duration, but seizures lasting longer than 5 minutes are unlikely to spontaneously terminate (Jenssen et al, 2006). Such patients have a high risk of recurrence; they must be admitted and managed promptly, together with full work-up of investigations as outlined above, including urgent neuroimaging, to delineate the cause.

Prompt seizure control is needed to prevent or minimize neuronal injury, and reduce morbidity and mortality. Where available, departmental protocols should be followed.

Treatment should be started in any seizure lasting more than 5 minutes. Intravenous lorazepam 0.1 mg/kg is recommended first line (Meierkord et al, 2010). Per rectum diazepam is an alternative where no intravenous access has been secured. If this fails, a further dose of intravenous lorazepam is recommended.

Benzodiazepines are established in the initial treatment of status epilepticus: per rectum diazepam (Remy et al, 1992), intravenous diazepam (Leppik et al, 1983; Aldredge et al, 2001), intravenous diazepam followed by phenytoin infusion (Treiman et al, 1998), intravenous lorazepam (Leppik et al, 1983; Treiman et al, 1998; Aldredge et al, 2001; Silbergleit et al, 2012) and intramuscular midazolam (Silbergleit et al, 2012) have all been effective in randomized control trials.

Critical care colleagues should be involved early in any case failing to respond to first-line therapy, as the use of potent sedatives or anaesthetic agents requires cardiorespiratory monitoring and/or support.

There is no consensus on second-line treatments where seizures persist. Intravenous phenytoin at high dose or intravenous phenobarbital have been traditionally used, but the latter can lead to significant respiratory depression. Sodium valproate is similar in efficacy to phenytoin (Agarwal et al, 2007) and diazepam infusion (Chen et al, 2011) as second-line treatment. A continuous infusion of midazolam is an alternative. Anaesthetic agents, e.g. thiopentone and propofol, may also be used as second-line agents, or may be reserved for failure of other treatments. Although in common use, randomized controlled trial evidence for these agents is lacking. The European Federation of Neurological Societies recommends anaesthetic agents as second-line treatment to minimize the risk of neuronal damage (Meierkord et al, 2010).

Acute seizure management

Most seizures are self-terminating, so have resolved before arrival in the emergency department. If the patient arrives in the department with ongoing prolonged or recurrent seizure he/she should be managed as status epilepticus.

Where a patient having fully recovered from an earlier seizure develops a subsequent seizure in the emergency department, the episode should be managed as an acute seizure. Care should be taken to minimize the risk of injury from nearby apparatus. Drug treatment is not required unless the seizure is prolonged (e.g. >5 minutes). First-line treatment thereafter is with benzodiazepines: intravenous lorazepam is highly effective or per rectum diazepam can be used if there is no intravenous access.

Who should be discharged?

The cause of provoked seizures should be identified and managed. Alcohol-related seizures have a tendency to recur (Tardy et al, 1995) and inpatient management is required to minimize withdrawal-related complications. There are no prospective studies addressing emergency department discharge decisions. The American College of Emergency Physicians clinical policy concluded patients with a normal neurological evaluation can be discharged and UK College of Emergency Medicine extend this to include normal investigations, presence of a responsible adult at home (particularly to observe for the next 24 hours) and high likelihood of attending follow up (Smith and Cossburn, 2004; Turner and Benger, 2009). Admission should be considered if patients cannot be discharged with a responsible adult to observe them, and if they are unlikely to attend follow up. National Institute for Health and Clinical Excellence and Scottish Intercollegiate Guidance Network guidance do not address emergency department discharge decisions.

The patient with an unprovoked seizure with low seizure recurrence risk, no neurological deficit and who is likely to attend follow up can be safely discharged.

What advice should be given?

Key concepts that should be communicated to the patient include the clinical impression, follow-up plan, likelihood of recurrence, recognizing recurrence, hazards arising from recurrence and how they can be managed. Driving and lifestyle consequences must be discussed. Prospective studies are sparse in this area.

College of Emergency Medicine, National Institute for Health and Clinical Excellence and Scottish Intercollegiate Guidance Network guidelines emphasize the need to refer to a specialist (neurologist or epileptologist) for further management of suspected seizures. The clinical uncertainty and need for further evaluation should be communicated; the patient may otherwise interpret a suspected seizure as epilepsy. Follow up should be arranged as per local policies.

KEY POINTS

- A witness history is key to evaluation of seizures, but should be interpreted with care.
- When seizure is suspected, provoking factors should be considered.
- Syncope and psychogenic non-epileptic seizure account for most misdiagnoses.
- Neuroimaging is necessary in patients in whom an intracranial lesion is suspected, especially in focal onset of seizure, acute head trauma, fever, alcoholism, immunocompromise or malignancy.
- Antiepileptic drugs should not be started without involvement of an epilepsy specialist.
- Factors predicting low risk of seizure recurrence are a first seizure, no focal neurological deficit and no abnormality on neuroimaging.
- Patients with an unprovoked seizure, low risk of recurrence and likely to attend follow up can be safely discharged from the emergency department. A responsible adult should be available at home.
- Early neurologist or epileptologist review is recommended post-discharge, ideally within 2 weeks.

Current Driver and Vehicle Licensing Agency guidance for single unprovoked seizures in group 1 licence holders is not to drive for 6 months. If no further seizures occur and after review by a specialist the risk of seizure is deemed to be less than 20%, driving can resume. Group 2 licence holders must not drive for 5 years and require specialist review before returning to driving. Lifestyle advice entails avoiding potentially hazardous activities such as swimming without supervision, handling heavy machinery and working at heights. Alcohol, illicit drugs and sleep deprivation are known triggers of seizures and patients should be advised to avoid these.

What follow up should be arranged?

UK College of Emergency Medicine, American College of Emergency Physicians, Scottish Intercollegiate Guidance Network and National Institute for Health and Clinical Excellence guidelines recommend specialist review after a first seizure. National Institute for Health and Clinical Excellence Guideline Development Group considers first seizure to be an urgent indication for review, thus recommend the patient is seen within 2 weeks. Early neurologist or epileptologist review is the gold standard. All documentation of the circumstances of attendance in emergency department, account of seizure(s) and details of investigations should be forwarded to the specialist on referral. Any witness to the seizure should also be encouraged to attend the follow-up appointment. Studies suggest this standard may not always be achieved.

Conclusions

First seizures remain a challenging clinical problem with many reviews approaching the problem from different perspectives and arriving at different conclusions. The clinician needs to evaluate literature with care and select studies focused to the specific clinical setting. The emergency department is particularly challenging in view of the prevalence of provoked seizures, the diagnostic uncertainty that surrounds what is often a single witness account and time-critical decision making.

The College of Emergency Medicine are refreshing in their focus on this. The Scottish Intercollegiate Guidance Network (2005) and National Institute for Health and Clinical Excellence (2012) guidance address some but not all the issues pertinent to emergency department first seizure management. Further study is needed to address questions such as the cost-effectiveness of blood investigations, seizure recurrence rate after discharge and outcomes of patients after emergency department discharge. Such work would help provide the evidence needed to harmonize guidelines and improve patient outcomes. BJHM

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