REVIEW

Epilepsy: a review of reports, guidelines, recommendations and models for the provision of care for patients with epilepsy

Rebecca LM Aylward

Rebecca LM Aylward DM FRCP, Consultant Neurologist, Department of Neurology, Torbay District Hospital, Torquay

Clin Med 2008;8:433–8

ABSTRACT – Epilepsy is common and has a variety of causes and associated pathologies. Increased understanding of the pathophysiology underlying the epilepsies and advances in classification, diagnostic imaging and drug treatments have led to a reduction in stigma and growing demand for services to be improved for patients. A number of important reports and guidelines have emerged in the UK in recent years, which are summarised here. Diagnosis, classification, management and models of care are discussed as well as the management of drug intractable seizures, status epilepticus, and approaches to special patient groups: women in the fertile years, the elderly and those with learning difficulties.

KEY WORDS: epilepsy, guidelines, seizures, antiepileptic drugs

Epilepsy, meaning a tendency to have recurrent seizures,[1] is the most common serious neurological condition,[2] with a prevalence of 0.5–1% in the developed world and an incidence of 25–80/100,000 per year.[3] Epilepsy and 'funny turns' are the most common problem presenting to an acute neurology service in the UK and a major part of the work of casualty departments.[4] The condition has a wide variety of causes. It is therefore more helpful to think in terms of 'the epilepsies' rather than 'epilepsy'.[5] It is a long-term condition, which may exist alone or in association with other chronic conditions such as learning disability.

Historically, epilepsy has been stigmatised and neglected. Recent improvements include better classification, and the development of useful new medical and surgical treatments. The refinement of imaging techniques and molecular genetics has vastly improved understanding of the epilepsies. As awareness of the condition has grown so the stigma has reduced, laws have been enacted to protect the rights of people with epilepsy and there have been calls for its management to be improved and standardised.[2,6,7]

The past decade has seen the publication of useful guidelines for the medical management of epilepsy, in adults and children, as well as publications on the organisation of epilepsy services and the problem of epilepsy-related deaths (Box 1).[1–3,7–9] The National Service Framework for long-term conditions provides a basis for the establishment of effective care for patients with epilepsy.[10]

What do the guidelines say?

In view of the high rate of misdiagnosis, all patients with suspected seizures should be referred quickly, preferably within a fortnight, to an epilepsy specialist, defined for adults as a 'medical practitioner with training and expertise in epilepsy'.[3,8] This is not happening in most parts of the UK and there is a need for casualty officers, general practitioners (GPs) and specialist nurses to be able to identify patients with epilepsy early so that a provisional diagnosis can be made and adequate information and advice given.[2]

Diagnosis and classification

The diagnosis is primarily clinical, based on a clear history from the patient and from an eyewitness.[3,8] Syncope and non-epileptic attacks are the most common alternatives in a wide differential diagnosis (Table 1).[3]

The history should include details of the attacks themselves, of any warning or prodrome and of the aftermath. The context of attacks is important. Those occurring from standing or following exercise and

Box 1. Some of the most influential recent guidelines.

SIGN 21 – adults, 1997
SIGN 70 – adults, 2003
SIGN 81 – children and young people, 2005
NICE 20 – adults and children, 2004
National Service Framework for long term conditions, 2005
CSAG report, 2000
National Sentinel Audit on epilepsy-related deaths, 2002

CSAG = Clinical Standards Advisory Group; NICE = National Institute for Health and Clinical Excellence; SIGN = Scottish Intercollegiate Guidelines Network.

preceded by a warning are likely to be syncopal. Epilepsy is more likely if attacks occur when sitting, lying or sleeping, if they come in clusters with little or no warning and are stereotyped. Frequent attacks of long duration, with normal intellectual function in between, are likely to be non-epileptic. This should also be suspected where the attacks are very variable in semiology.

Investigations are not used to make a diagnosis of epilepsy, but rather to confirm the diagnosis and establish a cause.[3,8] Serum prolactin levels are not recommended to distinguish between epileptic and non-epileptic attacks.[8]

An electroencephalogram (EEG) should not be used 'to exclude epilepsy'.[3,8] It should be ordered only if there is a strong clinical suspicion of epilepsy based on a careful history.[8] The rate of false positive 'non-specific' EEG abnormalities is high, particularly in the elderly, and this may lead to misdiagnosis. The main value in an EEG is to assist in classification and to confirm a clinical suspicion of epilepsy.[3,8] EEGs are not generally useful for monitoring the condition.[8] Video-EEG recording is used either where the diagnosis of epilepsy is in doubt (most commonly where non-epileptic attacks are suspected), or as part of the detailed work-up for epilepsy surgery.[3,8]

Accurate classification is important to determine prognosis and to choose appropriate medication.[3,8] Seizure may broadly be classified as focal, generalised or unclassifiable (Table 2).[11] Under these three headings there are multiple sub-classifications, but these have minor relevance to the generalist.

Idiopathic generalised seizures tend to have a genetic basis, to be benign and relatively easy to control, and to have their onset in teenage years. Tonic-clonic seizures characteristically occur on wakening and are exacerbated by alcohol and sleep deprivation. Blank spells and/or myoclonic jerks may be a feature. Epilepsy of adult onset is most commonly focal and acquired. Here the semiology and prognosis is variable, depending on the cause. Seizures arising from sleep are most likely to be focal. In about a fifth of cases, a structural brain lesion can be identified. Other cases are considered cryptogenic as a structural cause is presumed. Genetic focal epilepsies are exceptional (Table 3).

Imaging (magnetic resonance imaging unless contraindicated or unavailable) should always be performed if the epilepsy starts in the first two years of life or after the age of 20.[3,8] Older children and young people should be scanned if the history suggests that they have focal seizures. Anyone presenting with new-onset seizures should have a 12-lead electrocardiogram and screening blood tests to exclude metabolic causes of fits.[3,8]

Treatment

Drugs are the mainstay of treatment, but should be used only once the diagnosis is secure.[3,8] Underlying structural or metabolic causes should be treated as appropriate. Patients whose seizures are infrequent and do not interfere with life may prefer not to take medication.[8] Table 4 shows the most commonly used drugs. If the epilepsy is unclassifiable, a broad-spectrum drug such as sodium valproate should be chosen. Drugs should always be tailored to take account of the epilepsy classification, the lifestyle and possible side-effects.[8]

Monotherapy should be the aim, starting with a low dose and increasing slowly until either the seizures remit, or adverse effects emerge.[8] A single drug should be increased to the maximum tolerated level before abandoning it for another. The routine measurement of serum levels is necessary only for phenobarbital and phenytoin. Levels should also be measured if non-compliance is suspected or if there are signs of toxicity.[3,8]

Table 1. Differential diagnosis of epilepsy.

Syncope	Panic attacks
Non-epileptic attack disorder	Drop attacks
Migraine	Narcolepsy
Daydreaming	Transient global amnesia
Vertigo	Movement disorder

Table 2. Classification of seizures.

Focal	Focal sensory, focal motor, other focal seizure types Secondary generalisation
Generalised	Absence, myoclonic, clonic, tonic, tonic/clonic, atonic and other generalised seizure types

Table 3. Aetiologically based classification of epilepsy.

Symptomatic epilepsy	Identified structural cause
Cryptogenic epilepsy	Structural cause likely but not identified
Idiopathic epilepsy	Cause not known and structural cause clinically unlikely
Genomic	Specific genetic mutation identified

Table 4. Drugs used in epilepsy.

Most commonly used drugs	
Primary generalised epilepsies	**Focal epilepsies**
Sodium valproate	Carbamazepine
Lamotrigine	Lamotrigine
	Sodium valproate
Phenytoin (in the developing world)	Phenobarbitone and phenytoin (in the developing world)
New antiepileptic drugs	
Levetiracetam	Levetiracetam
Topiramate	Topiramate
	Gabapentin
	Oxcarbazepine
	Tiagabine
	Pregabalin
	Zonisamide

Failure to respond to two or three successive drugs in therapeutic doses and with adequate compliance may indicate drug-resistant epilepsy (or misdiagnosis). In this case, combinations of two drugs may be tried.[3,8] Sodium valproate and lamotrigine work well in combination, but evidence for the effectiveness of other specific combinations is lacking. Polypharmacy can be counterproductive, sometimes producing exacerbations in seizures and worsening side-effects.

Precipitating factors such as alcohol, sleep deprivation, and, for some patients, photosensitive triggers, should be minimised. Some drugs such as antidepressants may exacerbate seizures, and should be used with care. Alternative therapies, eg acupuncture, cannot replace drug treatment, but may have a role in reducing stress and improving wellbeing. This in turn may reduce seizure frequency.

Drug withdrawal

Drug withdrawal should be discussed with patients who have been seizure free for at least two years.[3,8] Trial data show that drug withdrawal is associated with an increased risk of seizure recurrence overall, and extent of risk is influenced by the duration of seizure freedom, the history of seizure types (juvenile myoclonic epilepsy being high risk), the occurrence of one or more seizures after the start of treatment and whether the patient was on mono- or polytherapy. EEG abnormalities are a poor indicator of risk.[3,8]

The Driver and Vehicle Licensing Agency strongly advises that patients withdrawing from medication should stop driving during the period of withdrawal and for six months afterwards.[12] This matter should be discussed, as well as employment, fear of seizure recurrence and possible long-term effects of medication.[3] Drugs should be withdrawn slowly and one at a time.

Special situations

Severe intractable epilepsy and epilepsy surgery

Twenty per cent of patients fail to respond to medication. These cases should be referred to a neuroscience centre as the diagnosis or treatment may be incorrect and should be reviewed.[8] A minority will benefit from epilepsy surgery, which should always be carried out in a specialist setting.

Sudden unexpected death in epilepsy

Patients with epilepsy have a mortality rate two to three times greater than that of the population at large.[1] Of these deaths, 40% are directly related to the condition. Causes include death due to the underlying disease in symptomatic epilepsy, sudden unexpected death, status epilepticus, suicide, treatment, and accidents due to seizures. Sudden unexpected death in epilepsy (SUDEP) accounts for 8–17% of these deaths and is more likely to occur in those with frequent seizures. The overall risk of SUDEP is 1/1,000 rising to 1/100–300 in severe drug-resistant epilepsy. These findings suggest that some deaths might be avoided with better seizure control. These matters should be discussed with patients and their families so that they are fully informed and motivated to take treatment seriously.[3,8]

Status epilepticus and other emergencies

Convulsive status epilepticus, defined as a single seizure (or series of seizures without recovery) lasting 30 minutes or more, is a medical emergency. In individuals known to have epilepsy, warning signs are common in the hours and days leading up to the attack and should be heeded, since early treatment with benzodiazepines can abort the crisis. Status-prone patients should have protocols in place so that carers know how to act when seizures are more than usually frequent or prolonged. Rectal diazepam or buccal midazolam should be used before an ambulance is called. A protocol for treating status epilepticus in hospital is given in both Scottish Intercollegiate Guidelines Network and National Institute for Health and Clinical Excellence guidelines and should be followed (Table 5).

Single seizures or provoked seizures

Antiepileptic drugs (AEDs) should only be prescribed after a single convulsive seizure if there is a previous history of

Table 5. Treatment of status epilepticus in hospital.

Immediate measures	Secure airway Give oxygen Assess cardiac and respiratory function Secure iv access Give lorazepam 4 mg iv or diazepam 10 mg iv Repeat after 10 mins if no response
In hospital	Take blood for electrolytes, LFT, calcium, glucose, clotting, AED levels and storage for later analysis Measure blood gases Establish aetiology Give thiamine or 50% glucose solution if indicated
Within 30 minutes	In patients with established epilepsy: give usual AED orally, NG or iv In patients with new-onset epilepsy or if seizures continue: fosphenytoin (18 mg/kg phenytoin equivalent), up to 150 mg/min with ECG monitoring or phenytoin 18mg/kg, 50 mg/min with ECG or phenobarbital 15 mg/kg iv, 100 mg/min
Longer than minutes	ITU may be necessary Anaesthetise with EEG monitoring Midazolam, phenobarbital, propofol, or thiopentone most commonly used
Non-convulsive status	Augment or reinstate usual AEDs Consider lorazepam or diazepam iv

AED = antiepileptic drug; ECG = electrocardiogram; EEG = electroencephalogram; ITU = intensive treatment unit; iv = intravenous; LFT = left fronto-temporal.

myoclonic jerks or absences, if there are unequivocal epileptiform discharges on EEG or if there is a structural brain abnormality present.[3,8]

Provoked seizures are those caused by an acute metabolic disturbance, most commonly alcohol or drugs, or by an acute brain injury. Any metabolic disturbance should be corrected and short-term benzodiazepines used for alcohol withdrawal and delirium tremens. Prophylactic AED treatment is not indicated following an acute brain injury and provoked seizures should be treated for a short time only. Long-term treatment is indicated only for unprovoked seizures.

Special patient groups

Women: epilepsy, fertility, and pregnancy

Fertility may be reduced in patients with epilepsy for social as well as medical reasons. Enzyme-inducing drugs (eg carbamazepine, phenytoin and, to a small extent, lamotrigine) may reduce the efficacy of combined oral contraceptives.

Advice on contraception and pregnancy should be given before young women become sexually active and pregnancies should be planned.[3,7,8] Folic acid, 5 mg per day, is given prior to conception and continued at least until the end of the first trimester.[3,8] Anticonvulsant polypharmacy and high-peak doses should be avoided.[3] Women on carbamazepine require oral vitamin K in the third trimester of pregnancy to minimise the risk of haemorrhagic disease of the newborn and all women on AEDs should have intramuscular vitamin K in the delivery room.[3,8] Women should be warned of the risks to the foetus and to themselves of uncontrolled seizures, as some will be tempted to withdraw from medication when planning a pregnancy.[3,8]

Antiepileptic drugs are associated with an increased risk of foetal abnormalities, especially with polytherapy and high-drug doses. Table 6 shows figures from the UK epilepsy and pregnancy register.[13] All pregnancies should, with the woman's consent, be reported to the UK pregnancy register.[14] Doses of AEDs should not be increased routinely in pregnancy but should be monitored clinically. Routine measurement of drug levels is not indicated. All patients should have their epilepsy and drug treatment reviewed post-partum.

Breastfeeding should be encouraged.[3,8] Women who have convulsive seizures will need to breastfeed in a safe position, such as on the floor with cushions, and should be supervised when bathing the baby. SIGN 70 contains detailed guidance on managing fits during labour, the genetic risks of inheriting epilepsy and advice on the use of hormone replacement therapy.[3]

Teenagers

The transition from paediatric to adult services can be difficult and should be carefully managed.[8,15] It is useful to have a named contact, most commonly a specialist nurse. Issues such as fertility, sexual health and employment should be discussed and it may not always be appropriate for parents to be present. There may be particular difficulties with drug compliance as some rebel against their diagnosis and boys in particular have a tendency to engage in high-risk activities. A clinic attended by other teenagers allows for the formation of friendships and peer-support networks.

Patients with learning disability

Epilepsy and learning disability are commonly associated with up to 60% of patients with severe learning disability having epilepsy.[8,15] The hospital outpatient department may be intimidating for these patients. They should be accompanied by a carer who knows them well otherwise the visit will be wasted. It is helpful for carers to receive a checklist of things that the specialist or nurse needs to know about the patient so that they can come to the consultation well prepared.[8] Patients may need to be given extra time as communication might be difficult and stress needs to be minimised. Information should be presented in a clear form. It is desirable for patients to be seen in or close to their own homes if possible.

Patients at risk of status should have a clear protocol in place and carers should be trained so that rescue treatment can be given at home, minimising the need for hospital admissions. Where admissions are necessary, patients benefit from being admitted to the same ward each time so that they can build relationships with staff.

Patient information

The provision of written information and advice for patients is currently very poor.[3] Patients should have access to a named person whom they can contact by phone or email at times of crisis, and this may be a nurse or field worker.[8] They need information on a range of issues including driving, employment,

Table 6. Mothers with epilepsy: rates of foetal malformation.

	Rates of foetal malformation (%)
No AED	3.5**
Monotherapy	3.7**
Polytherapy	6.0**
Total	4.2**
	Foetal malformation rate associated with individual drugs (%)
Background rate	1.2
Carbamazepine	2.2*
Lamotrigine	3.2*
Sodium valproate	6.2*
Phenytoin	3.7**
Gabapentin	3.2**

*narrow confidence intervals; **wide confidence intervals; AED = antiepileptic drug.

medication, first aid, sport and leisure, benefits, contraception, pregnancy and fertility (Table 7). Much of this information is widely available from the different epilepsy charities in leaflet form or online. Clinicians should ensure that patients have access to this information and have enough time to discuss it.

Models of care

A structured management system with annual review should be in place in primary care with a register allowing patients to be easily identified.[3,8] A shared-care system is desirable, with close liaison between GPs, specialist nurses, learning disability services, field workers, pharmacists, the charitable sector and hospital services. GPs should make a provisional diagnosis and provide adequate support and information, but an epilepsy specialist should make the definitive diagnosis and initiate treatment.

Annual review should include a check on the diagnosis, discussion of seizure frequency and type and date of last seizure. Written patient information should be provided and this should be documented in the notes. Issues such as driving and contraception can be discussed as well as the patient's medication, compliance and drug side effects.

District hospitals and intermediate care facilities should have systems in place to ensure that patients are seen quickly following a first seizure and that they can respond quickly and appropriately at times of crises. Written patient information should be available in all these settings as should access to epilepsy specialist nurses. Patients have suggested drop-in centres and educational programmes.[7] Very successful GP specialist epilepsy services run in some areas.[16]

The neuroscience centre should have a specialist multidisciplinary epilepsy service where the complex epilepsies can be treated and patients assessed for epilepsy surgery. A first-fit clinic should be set up so that patients can be seen within a fortnight of first presentation. Special clinics should be available for special groups of patients (learning disabled, teenagers, those needing contraceptive and pregnancy advice, and epilepsy surgery candidates). All clinics should have an epilepsy specialist nurse available, and all patients should have access to a specialist nurse.[8]

Communication between primary, secondary and tertiary services is important.[7] Specialists at the centre have a responsibility to educate, and should be available to offer advice to practitioners in all settings including learning disability services. In all settings patients should be treated with consideration, and information presented to them in an accessible fashion. All patients should have a structured care plan. They should be aware of the Expert Patients' Programme, which will empower them to manage their condition optimally.[17]

References

1 National Institute for Health and Clinical Excellence. *National clinical audit of epilepsy related death.* London: NICE, 2002.
2 Royal College of Physicians of Edinburgh. *Consensus conference on better care for children and adults with epilepsy. Final consensus statement.* Edinburgh: RCPE, 2002.
3 Scottish Intercollegiate Guidelines Network. *Scottish Intercollegiate Guidelines Network (70): diagnosis and management of epilepsy in adults, a national clinical guideline.* Edinburgh: SIGN, 2003.
4 Williams A. Western General Hospital Edinburgh. Internal Audit. Personal communication, 2004.

Table 7. Information for patients. Reproduced with permission from NICE.[8]

- epilepsy in general
- diagnosis and treatment options
- medication and side effects
- seizure type(s), triggers and seizure control
- management and self-care
- risk management
- first aid, safety and injury prevention at home and at school or work
- psychological issues
- social security benefits and social services
- insurance issues
- education and healthcare at school
- employment and independent living for adults
- importance of disclosing epilepsy at work, if relevant (if further information or clarification is needed, voluntary organisations should be contacted)
- road safety and driving
- prognosis
- sudden death in epilepsy
- status epilepticus
- lifestyle, leisure and social issues (including recreational drugs, alcohol, sexual activity and sleep deprivation)
- family planning and pregnancy
- voluntary organisations, such as support groups and charitable organisations, and how to contact them

5 Aylward RLM. *Epilepsy*. Edinburgh: Royal College of Edinburgh, 2006.www.rcpe.ac.uk/fellows/CME/neurology/neurol-index.html
6 Disability Discrimination Act 1995 (Ch 50). www.opsi.gov.uk/acts/acts1995/1995050.htm
7 Shorvon S *et al.* Clinical Standards Advisory Group. A report on services for NHS patients with epilepsy. 1999.
8 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.* London: NICE, 2004.
9 Scottish Intercollegiate Guidelines Network. *Scottish Intercollegiate Guidelines Network (81): diagnosis and management of epilepsies in children and young people.* Edinburgh: SIGN, 2005.
10 Department of Health. *The National Service Framework for long term conditions.* London: DH, 2005.
11 The Commission of Classification and Terminology of the International League against Epilepsy. Classification: proposal for revised clinical and electroencephalographic classification of epileptic seizures. *Epilepsia* 1981;22:489–501.
12 Driver and Vehicle Licensing Agency. www.dvla.gov.uk/media/pdf/medical/aagv1.pdf
13 Morrow J, Russell A, Guthrie E *et al.* Malformation risks of antiepileptic drugs in pregnancy: a prospective study from the UK Pregnancy Register. *J Neurol Neurosurg Psychiatry* 2006;77:193–8.
14 British Epilepsy and Pregnancy Register. www.epilepsyandpregnancy.co.uk
15 Giles A, Smith P. Adolescent neurology. *Practical Neurol* 2004;4;2–5.
16 Bradford Community Neurology Service www.nyx.org.uk/modernprogrammes/patientaccess/goodpractice/may2001/epilepsy.html
17 Department of Health. *The expert patient: a new approach to chronic disease management for the 21st century.* London: DH, 2001.