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Concise guidance: diagnosis and management of the epilepsies in adults

Author: Margaret J Jackson[A]

ABSTRACT

This concise guidance comprises a distillation of recommendations for the diagnosis and management of epilepsies for non-specialists and is based on updated clinical guideline 137 published by the National Institute of Health and Care Excellence (NICE). It is intended to provide the generalist at the front line (particularly but not exclusively in the acute hospital setting) with an accessible and up-to-date outline of key guidance on assessment, clinical management, communication and referral. Recommendations abstracted verbatim from the guideline are highlighted. Brief explanatory or supporting comment is given where appropriate.

KEYWORDS: Diagnosis, epilepsies, management

Introduction

The epilepsies are a group of neurological disorders characterised by recurrent, (usually) unprovoked epileptic seizures. They can (broadly) be divided into focal and generalised categories, each defined by the types of seizures experienced, the age of onset and the results of investigations (primarily electroencephalography [EEG] and imaging). Epilepsies are a significant cause of unscheduled and emergency care. Much urgent care of epilepsy is undertaken by emergency departments and acute care physicians. In contrast, particularly in teaching hospitals, long-term care of people with epilepsy is mostly undertaken by neurologists and specialist nurses.

Recent guidance from the National Institute of Health and Care Excellence (NICE) (clinical guideline [CG] 137)[1] on diagnosis and treatment of epilepsies assists non-specialists in the management of epilepsy by signposting pathways of care and advising on treatment when specialist expertise is not immediately available. A related NICE guideline on transient loss of consciousness (CG109)[2] is relevant, especially in highlighting the importance of close links between cardiology and neurology in the management of suspected epilepsy.

Epilepsy is a long-term condition for many people. Optimal management is based on accurate classification of the epilepsy and appropriate choice of anti-epileptic medication, taking into account the specific needs of the individual. Despite numerous new anti-epileptic drugs, about 25% of people with epilepsy remain refractory to treatment.[3]

Managing epilepsy includes addressing patients' social and psychological needs. Epilepsy nurses provide a valuable resource for advice, support and information for patients and should be available to people with epilepsy. People with epilepsy have a high prevalence of depression and psychological difficulties[4] and should have ready access to psychological therapy and, in the case of more severe mental health difficulties (eg psychoses associated with epilepsy), an appropriately trained psychiatrist.

People with epilepsy should be helped to live their lives as normally as possible within the inevitable restrictions that a disorder associated with unprovoked episodes of loss of consciousness entails. Helping people with epilepsy to fulfil their potential by managing their condition well is not easy, but it is a very rewarding task.

Scope and purpose

This concise guidance is intended to highlight those areas of CG137 that are particularly relevant to non-specialists. Of the total 286 recommendations in the guideline, 24 are abstracted for this purpose, focusing particularly on the management of first seizures, early assessment and investigation of seizures, and status epilepticus. These are highlighted in bold. Text commentary draws on other CG137 recommendations, as appropriate.

Recommendations

First seizures

The differential diagnosis of a first convulsive seizure is wide and includes acute symptomatic seizures caused by metabolic disturbance, intoxication with drugs or alcohol, infections such as encephalitis or meningitis, acute intracranial events (eg intracerebral haemorrhage or venous sinus thrombosis), convulsive syncope, cardiac syncope and functional/dissociative seizures. It is usually the work of emergency medicine to triage patients with a first seizure into those likely to have acute symptomatic seizures and those with a first unprovoked seizure.

Author: [A]consultant neurologist, Royal Victoria Infirmary, Newcastle upon Tyne, UK

- **Children, young people and adults** *['people' or 'person' are hereinafter assumed to encompass children, young people and adults, except where specified]* **presenting to an accident and emergency department following a suspected seizure should be screened initially. This should be done by an adult or paediatric physician with onward referral to a specialist** *[defined as a medical practitioner with training and expertise in epilepsy]* **when an epileptic seizure is suspected or there is diagnostic doubt.**
- **Protocols should be in place that ensure proper assessment in the emergency setting for children, young people and adults presenting with an epileptic seizure (suspected or confirmed).**

Such protocols enable optimum immediate management and inform subsequent referral for further investigation and management (see, for example, Fig 1).

- **It is recommended that all people having a first seizure should be seen as soon as possible by a specialist in the management of the epilepsies to ensure precise and early diagnosis and initiation of therapy as appropriate to their needs.**

An interval of 2 weeks is stipulated for this recommendation. The diagnosis of epilepsy is clinical and can have major implications, such as loss of driving licence and employment.

Many units now provide 'first seizure' clinics to fast-track patients to specialist care. These clinics should provide access to nurse specialists who can advise patients and their relatives on safety, first aid, driving and other issues.

- **Essential information on how to recognise a seizure, first aid, and the importance of reporting further attacks should be provided to a person who has experienced a possible first seizure, and their family/carer/parent as appropriate. This information should be provided while the person is awaiting a diagnosis and should also be provided to their family and/or carers.**

A first seizure can be a frightening event to witness, so support for family and friends is important. A care plan with advice on what to do in the event of further seizures (eg similar to that of 'Epilepsy Action')[5] should be provided.

Diagnosis and investigation

Metabolic and toxic disorders should be excluded in an individual presenting acutely with an apparent seizure. Every adult with an episode of loss of consciousness should have a 12-lead electrocardiogram (ECG), as cardiac arrhythmias with convulsive syncope can easily be mistaken for epileptic seizures.

- **The clinical decision as to whether an epileptic seizure has occurred should [then] be based on the combination of the description of the attack and different symptoms. Diagnosis should not be based on the presence or absence of single features.**

Use of the electroencephalography

- **An EEG should be performed only to support a diagnosis of epilepsy in adults in whom the clinical history suggests that the seizure is likely to be epileptic in origin.**

Referral from A&E for adults with uncomplicated first generalised seizure (copy to GP).

Inclusion criteria	Patients ≥ 16 years Clear history of first generalised epileptic seizure OR patients with several seizures but no diagnosis of epilepsy	Name DOB Address Tel no
Exclusion criteria	> Patients with non-epileptic attacks > Those with symptomatic seizures, eg hypoglycaemia, acute trauma, eclampsia > People more suited to elderly care review	Attach address label

History: (continue onto second page if needed)	Temp:
	Pulse:
	BP:
	BM:

Investigations table (enter results or attach results sheet)

ECG	(send photocopy with form)			Indications for CT scan prior to disposition > Persistent new focal neurtological deficits > Persistent altered mental status > Fever or persistent headache > Recent head trauma > History of cancer or HIV infection > Patients with focal onset seizure > Anticoagulation or bleeding diathesis > Past history of stroke/TIA > Patients whose follow up cannot be ensured (discuss with senior) PLEASE ENSURE ALL FILMS ARE TRANSFERRED TO.....
Urea		AlkPh		
Creat		ALT		
Na		Bil		
K		Alb		
CO_2		Hb		
Ca		MCV		
GGT		WBC		
Gluc		Plat		
CXR				
CT				

Discharge table: instructions in all sections must be fulfilled before referral made

Patient has fully recovered with no persistent neurological symptoms or signs (including headache)
Normal observations and investigations (including temperature)
Consider social circumstances prior to discharge (will the patient be safe?)
Patient has been given departmental written advice sheet > including driving and lifestyle changes
Patient suitable for First Seizure Clinic follow up > copies of form and all notes* forwarded FAO Neurology - First Seizure Clinic > *NB if you do not do this you may delay your patient's follow up > fax number
Copy referral form to GP
Retain original form in A&E notes

Hospital/department referring patient.....
Signature/name (in capitals and contact phone number of person faxing referral).....

Fig 1. Example of first seizure referral form. A&E = accident and emergency; AlkPh = alkaline phosphatase; Alb = albumin; ALT = alanine transaminase; Bil = bilirubin; BP = blood pressure; Ca = calcium; Creat = creatinine; CT = computed tomography; CXR = chest X-ray; DOB = date of birth; ECG = electrocardiogram; FAO = for the attention of; GGT = gamma-glutamyl transferase; Gluc = glucocorticoids; GP = general practitioner; Hb = haemoglobin; HIV = human immunodeficiency virus; K = potassium; MCV = mean corpuscular volume; Na = sodium; Plat = platlets; Temp = temperature; TIA = transient ischaemic attack; WBC = white blood cell.

- **An EEG should not be performed in the case of probable syncope because of the possibility of a false-positive result.**
- **The EEG should not be used to exclude a diagnosis of epilepsy in a person in whom the clinical presentation supports a diagnosis of a non-epileptic event.**

The specificity of a single EEG is high but the sensitivity is low. An EEG should never be used 'to exclude epilepsy'. The EEG may point to a particular type of epilepsy (epilepsy syndrome) and can give useful information on the risk of recurrence after a single seizure. Definite epileptiform changes in the EEG increase the likelihood of recurrent seizures, but a normal EEG does not exclude epilepsy.

Other investigations

- **MRI [magnetic resonance imaging] should be the imaging investigation of choice in people with epilepsy.**

This recommendation applies when causal structural abnormalities are being considered and should be implemented soon after the event, with computed tomography (CT) reserved for urgent investigation and those in whom MRI is contraindicated.

- **Measurement of serum prolactin is not recommended for the diagnosis of epilepsy.**

Diagnostic uncertainty

- **It may not be possible to make a definite diagnosis of epilepsy. If the diagnosis cannot be clearly established, further investigations and/or referral to a tertiary epilepsy specialist should be considered. Follow up should always be arranged.**

Treatment

- **Anti-epileptic (AED) therapy should only be started once the diagnosis of epilepsy is confirmed, except in exceptional circumstances that require discussion and agreement between the prescriber, the specialist and the person and their family and/or carers as appropriate.**
- **The decision to initiate AED therapy should be taken between the person, their family and/or carers (as appropriate) and the specialist after a full discussion of the risks and benefits of treatment. This discussion should take into account details of the person's epilepsy syndrome, prognosis and lifestyle.**

Treatment is not usually given after a first seizure unless the individual regards the risk of a further seizure as unacceptable or further seizures are likely. High-risk groups for further seizures include those with a neurological deficit, a learning disability, an abnormality on imaging or unequivocal epileptic activity on EEG.

Anti-epileptic medication has to be tailored to the needs of the individual, and the risks and benefits must be balanced against the risk of ongoing seizures, including the risk of sudden unexplained death in epilepsy (SUDEP). Choice of medication will depend on the epilepsy syndrome and characteristics of the individual – for example, the risk of teratogenicity in women of childbearing potential. A brief guide for choice of AED is given in Table 1.[6]

Failure to respond to the first appropriate well-tolerated medication is a marker for refractory epilepsy but can also indicate misdiagnosis with functional non-epileptic seizures, seizures associated with alcohol or drugs, and an undetected brain tumour.

Stopping treatment for epilepsy

- **The decision to continue or withdraw medication should be taken by the person, their family and/or carers as appropriate, and the specialist after a full discussion of the risks and benefits of withdrawal. At the end of the discussion, the person, and their family and/or carers as appropriate, should understand their risk of seizure recurrence on and off treatment. This discussion should take into account details of the person's epilepsy syndrome, prognosis and lifestyle.**
- **Withdrawal of AEDs must be managed by, or be under the guidance of, the specialist.**

Withdrawal of AED can lead to recurrence of seizures, with major implications for an individual's driving licence and livelihood. An estimate of risk of recurrence can be made from the type of epilepsy and other factors, and these should be shared with the patient, as well as the risk of seizures, including SUDEP.

Status epilepticus

Convulsive status epilepticus is a medical emergency, which has high mortality if allowed to persist. Status epilepticus often emerges from an increase in background seizure activity; if this pattern is recognised and treated with oral benzodiazepines (oral clobazam or diazepam), status epilepticus can be prevented,[7] so recognition of 'pre-status' is important, as are personal care plans to treat it.

Community-initiated treatment of prolonged convulsive seizures and early status epilepticus with buccal midazolam can be effective and prevent recurrent admission to hospital.[8] A protocol for administration of buccal midazolam should be arranged for patients who have had an episode of status epilepticus, and their family and carers should be instructed in its implement, administration of buccal midazolam, and when to call emergency services if treatment fails.

Non-convulsive status epilepticus can be difficult to recognise, as it may manifest as confusion or a subtle alteration in cognitive function. Diagnosis is by EEG, which should be considered in anyone with a diagnosis of epilepsy who develops such altered mental states. Treatment with oral benzodiazepines is usually effective.

- **For people with ongoing generalised tonic–clonic seizures (convulsive status epilepticus) who are in hospital, immediately: secure airway, give high-concentration oxygen, assess cardiac and respiratory function, check blood glucose levels and secure intravenous access in a large vein.**
- **Administer intravenous lorazepam as first-line treatment in hospital in people with ongoing generalised tonic–clonic seizures (convulsive status epilepticus). Administer intravenous diazepam if intravenous lorazepam is unavailable, or buccal midazolam if unable to secure immediate intravenous access. Administer a maximum of two doses of the first-line treatment (including pre-hospital treatment).**

Table 1. Pharmacological management of epilepsy (excluding status epilepticus): anti-epileptic drug (AED) options by seizure type.[6]

Seizure type	First-line AEDs	Adjunctive AEDs	Other AEDs that may be considered on referral to tertiary care	Do not offer these AEDs (may worsen seizures)
Generalised tonic–clonic	> Carbamazepine > Lamotrigine Oxcarbazepine* > Sodium valproate	> Clobazam* > Lamotrigine > Levetiracetam > Sodium valproate > Topiramate		> (If there are absence or myoclonic seizures, or if JME suspected) avoid: > Carbamazepine > Gabapentin > Oxcarbazepine > Phenytoin > Pregabalin > Tiagabine > Vigabatrin
Tonic or atonic	> Sodium valproate	> Lamotrigine*	> Rufinamide* > Topiramate*	> Carbamazepine > Gabapentin > Oxcarbazepine > Pregabalin > Tiagabine > Vigabatrin
Absence	> Ethosuximide > Lamotrigine* > Sodium valproate	> Ethosuximide > Lamotrigine* > Sodium valproate	> Clobazam* > Clonazepam > Levetiracetam* > Topiramate* > Zonisamide*	> Carbamazepine > Gabapentin > Oxcarbazepine > Phenytoin > Pregabalin
Myoclonic	> Levetiracetam* > Sodium valproate > Topiramate*	> Levetiracetam* > Sodium valproate > Topiramate*	> Clobazam* > Clonazepam > Piracetam > Zonisamide*	> Carbamazepine > Gabapentin > Oxcarbazepine > Phenytoin > Pregabalin
Focal	> Carbamazepine > Lamotrigine > Levetiracetam > Oxcarbazepine > Sodium valproate	> Carbamazepine > Clobazam* > Gabapentin* > Lamotrigine > Levetiracetam > Oxcarbazepine > Sodium valproate > Topiramate	> Eslicarbazepine acetate* > Lacosamide > Phenobarbital > Phenytoin > Pregabalin* > Tiagabine > Vigabatrin > Zonisamide*	

*At the time of publication of CG137 (January 2012), this drug did not have marketing authorisation in the UK for this indication or population. Informed consent should be obtained and documented.
†Note restrictions on use of vigabatrin due to high risk of visual failure.
AED = anti-epileptic drug; JME = juvenile myoclonic epilepsy.

Table 2. Emergency anti-epileptic drug (AED) therapy for convulsive status epilepticus (published in 2004).[9]

Status	Therapy
Premonitory stage (pre-hospital)	> Midazolam 10 mg given buccally or diazepam 10–20 mg given rectally, repeated once 15 minutes later if status continues to threaten
	> If seizures continue, treat as below
Early status	> Lorazepam (intravenous) 0.1 mg/kg (usually 4-mg bolus, repeated once after 10–20 minutes; rate not critical)
	> Give usual AED if already on treatment
	> For sustained control or if seizures continue, treat as below
Established status	> Phenytoin infusion (15–18 mg/kg at rate of 50 mg/minute) or fosphenytoin infusion (15–20 mg phenytoin equivalents (PE)/kg at rate of 50–100 mg PE/min) and/or phenobarbital (bolus of 10–15 mg/kg at a rate of 100 mg/min)
Refractory status	> General anaesthesia, with one of:
	– propofol (1–2 mg/kg bolus, then 2–10 mg/kg/hr) titrated to effect
	– midazolam (0.1–0.2 mg/kg bolus, then 0.05–0.5 mg/kg/hr) titrated to effect
	– thiopental sodium (3–5 mg/kg bolus, then 3–5 mg/kg/hr) titrated to effect; after 2–3 days, infusion rate needs to be reduced, as fat stores are saturated
	– anaesthetic continued for 12–24 hours after last clinical or electrographic seizure, then dose tapered

In above scheme, refractory stage (general anaesthesia) is reached 60/90 minutes after initial therapy. AED = anti-epileptic drug.

> **If seizures continue, administer intravenous phenobarbital or phenytoin as second-line treatment in hospital in people with ongoing generalised tonic–clonic seizures (convulsive status epilepticus).**

Because patients with convulsive status epilepticus present to emergency departments and are treated there by non-specialists in epilepsy, it is vital that locally agreed protocols for management are agreed and available for consultation. Clinical guideline 137 provides these (eg Table 2).[9] Randomised controlled trials for treatment of refractory status epilepticus do not exist, so treatment should be given in conjunction with local epilepsy specialists and access to EEG monitoring.

The possibility that 'refractory status epilepticus' is pseudo-status – that is, continuous functional non-epileptic seizures – should always be considered prior to intubation and ventilation.

> **If either the whole protocol or intensive care is required the tertiary service should be consulted.**

Special groups

Women with epilepsy

> **In order to enable informed decisions and choice, and to reduce misunderstandings, women and girls with epilepsy and their partners, as appropriate, must be given accurate information and counselling about contraception, conception, pregnancy, caring for children and breastfeeding, and menopause.**

> **In women of childbearing potential, the possibility of interaction with oral contraceptives should be discussed and an assessment made as to the risks and benefits of treatment with individual drugs.**

Many women with epilepsy require anti-epileptic medication in their childbearing years. Enzyme-inducing AEDs (carbamazepine, phenytoin and oxcarbazepine in particular) reduce oestrogen levels and make oral contraceptives and implants unreliable. Lamotrigine levels are reduced unpredictably by oestrogens. Levels of AEDs may change in pregnancy and levels of lamotrigine, in particular, can fall precipitously early in pregnancy, triggering seizures if not anticipated.

Anti-epileptic drugs taken in pregnancy have teratogenic potential. The risks are known for many established AEDs but not for the new drugs. Carbamazepine and lamotrigine increase the risk of a child having a major congenital malformation from a background of 1% to 2–3%.[10] Valproate (first choice for many generalised epilepsies) has a significantly higher risk (7% in the epilepsy pregnancy register in the UK).[10] Long-term effects on child development are uncertain, but there are concerns, particularly with high-dose valproate. The risks to the child need to be balanced with the risk to the mother (and unborn child) of uncontrolled convulsive seizures. Close collaboration between the epilepsy specialist and maternity services is advisable.

Individuals with a learning disability

> **It can be difficult to diagnose epilepsy in people with learning disabilities, and so care should be taken to obtain a full clinical history. Confusion may arise between stereotypic or other behaviours and seizure activity.**

> **Facilities should be available for imaging under anaesthesia, if necessary.**

Although the incidence of epilepsy is greatly increased in people with a learning disability, diagnosis can be challenging. Access to epilepsy services, investigations and treatment should be equal for these individuals, and appropriate time and adaptations should be made to allow for their care.

Older people

- **Pay particular attention to pharmacokinetic and pharmacodynamic issues with polypharmacy and comorbidity in older people with epilepsy. Consider using lower doses of AEDs and, if using carbamazepine, offer controlled-release carbamazepine preparations.**

The incidence of epilepsy increases in older people. Many have multiple comorbidities and are on numerous medications. Some older people seem to be more sensitive to the side-effects of AEDs, particularly sedative effects. The risk of hip fracture is increased with enzyme-inducing AEDs.[11] Social isolation is increased by inability to drive and perceived stigma.

Limitations of the guideline

Conducting randomised controlled trials (RCTs) in epilepsy presents self-evident difficulties. With the exception of some moderate-to-low quality evidence on AEDs from RCTs, many of the recommendations are based on descriptive studies and the experience and opinion of the guideline development group.

Implications for implementation

Detailed protocols for the management of status epilepticus are given as appendices to CG137. The particular challenges for AED in women of childbearing age are recognised in the coverage of alternatives. For quality monitoring and audit purposes, NICE have produced a quality standard for epilepsy (QS26).[12] ■

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Address for correspondence: Dr MJ Jackson, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne NE1 4LP.
Email: margaret.jackson@nuth.nhs.uk