A practical guide to managing epilepsy

Approaches to treating epilepsy are being increasingly refined as more is understood about the different syndromes and their response to drugs. Aiming medication and counselling at the specific epilepsy syndrome will lead to best management.

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Epilepsy is a common condition, affecting one in 300 of our population. Its impact on psychosocial function varies from very mild to severe, and knowledge of the underlying epilepsy syndrome and its prognosis is essential in guiding a patient and his or her family. Lifestyle disciplines remain an essential component of management, although the number of antiepileptic drugs available is increasing. New information regarding the role of medications and their long term effects, interactions and teratogenicity is expanding and will naturally inform counsel. Overall, the great majority of people with epilepsy will continue to lead a normal social and occupational life, yet there remains a minority who will require the specialist input of epilepsy services in the major neurology centres of Australia.

Diagnosis

A diagnosis of epilepsy is usually made on the basis of a careful history. Witnessed accounts of events are invaluable in discriminating seizures from a variety of other conditions. EEG is helpful because specific syndromes are partially identified by their electrical patterns, but a normal interictal EEG does not exclude epilepsy. Other investigations include MRI (Figure 1), to look for underlying structural causes in focal (partial) epilepsies, and occasionally chromosomal or genetic studies, which are helpful in rare syndromes.

The precise syndrome is generally diagnosed by a neurologist. An epilepsy syndrome is the association of particular seizure types with particular EEG findings. For example, juvenile myoclonic epilepsy is the primary generalised syndrome in which myoclonic jerks and occasional tonic–clonic seizures are found together with generalised spike, polyspike and slow wave discharges at a frequency of 3.5 to 5 Hz on a normal background EEG (Figure 2). However, not all syndromes have constant or specific EEG changes – some of the focal epilepsies, such as those of frontal or occipital lobe origin, may not show anything diagnostic on the resting EEG. In these cases, syndrome identification rests largely with the clinical data.

Usually, the neurologist initiates medication and begins the educative process with the patient and family. This aspect of diagnosis is essential because the prognosis of epilepsy syndromes varies widely, from being self-limiting and relatively

IN SUMMARY

- **The prognosis of epilepsy varies widely and depends on the specific epilepsy syndrome.**
- **Some self-limiting syndromes do not demand treatment.**
- **Lifestyle counselling should be complemented by input from local epilepsy support associations.**
- **Driving restrictions often have the greatest impact on psychosocial function.**
- **Knowledge of the most commonly used antiepileptic medications is essential in guiding therapy.**
- **There are special needs according to age and gender.**
- **A small group of refractory patients will benefit from referral to specialist epilepsy clinics.**

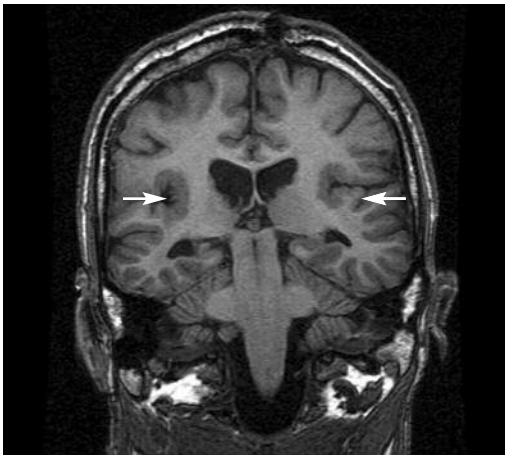

Figure 1. MRI. Coronal section of a young woman with a secondary generalised epilepsy due to a cortical malformation. Note the thickened irregular cortex in the perisylvian regions (arrows).

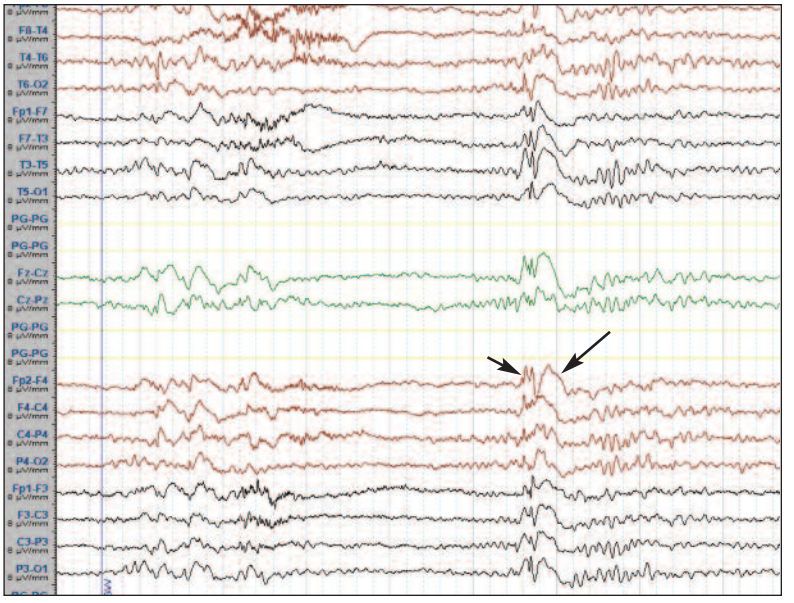

Figure 2. EEG of an adolescent girl who presented with a tonic–clonic seizure at school. The EEG shows bisynchronous spike, polyspike (short arrow) and slow wave (long arrow) discharges at 3 to 4 Hz, erupting from a normal backgound rhythm. This is typical of juvenile myoclonic epilepsy, one of the primary generalised epilepsy syndromes.

benign (in conditions such as childhood absence epilepsy) to severe and refractory (in generalised types such as Lennox–Gastaux syndrome).

Lifestyle counselling

Sleep on it

All people with epilepsy – regardless of the syndrome – benefit from having a regular sleep pattern and avoiding sleep deprivation. This may affect those with occupations that require shiftwork or very early morning starts. This 'early to bed' advice is, of course, not usually welcomed by young people with an active social life. Often people have to learn the hard way, with provoked seizures after a late night out or long strenuous day.

This principle pertains regardless of whether a patient is taking medication or not. Even optimal drug treatment cannot make the brain immune to the effects of sleep deprivation.

'Party fuels'

Excessive alcohol is a provocative factor in all sorts of seizures, as are stimulant recreational drugs (cannabis is the only exception). The combination of a late night and alcohol is a potent provocative situation for 'day after' seizures.

Other medications

A host of prescribed medications can occasionally lower seizure threshold, and this must be taken into account when prescribing and counselling patients about the use of these drugs. The effect is not predictable. Antidepressants and antipsychotic agents are the most common offenders.

You are your work

Occupational considerations are important because a diagnosis of epilepsy will restrict or even exclude an individual from working in some areas – these include the military and police forces and occupations that involve driving heavy articulated trucks, taxis and buses. In the case of some trucks, restricted licensing can be obtained for specific situations when epilepsy control is secure – this is arranged through communication with medical review panels of the licensing authority in each State or Territory. (Readers are also referred to the 2003 edition of the Austroads publication, *Assessing Fitness to Drive*.) The issue of licensing is complex, and input from the neurologist is usually required.

Driving prohibition or restriction is an agonising experience for professional drivers, with some being left in difficult financial situations. Anxiety and depression can arise in these circumstances – awareness and vigilance will allow early treatment.

When an employee is diagnosed with epilepsy, a letter of medical clearance to work may be appreciated by his or her employer; a declaration outlining duties to avoid and the duration of

avoidance may also be helpful. It is helpful to encourage communication between the patient and employer early on, and to emphasise the good prognosis of epilepsy treatment. A rule of thumb in the case of potentially dangerous work duties is 'if cleared for driving then cleared for work'.

Students' concerns

Students may need letters supporting requests for extra time for study or examinations if their epilepsy or medications affect their concentration. Usually, however, it is the time lost in investigations and clinic visits that concern students and their parents most, so allowance for this is important when scheduling appointments. Input from local epilepsy support associations can be vital in helping young people and their families and schools come to terms with the condition (see the box below).

Medical management

When should medication be started?

The common teaching has been not to treat the first seizure. Like most generalisations, however, this has exceptions, such as juvenile myoclonic epilepsy (which is known to commonly persist throughout life). An example would be a young patient who presents with a tonic–clonic seizure, a history of myoclonic jerks (particularly after waking) and EEG showing the typical spike and polyspike wave discharges. In such a case, the likelihood of seizure recurrence is high and medication should be withheld only if the patient is not keen for it at that stage.

In patients with focal epilepsies, the history may not reveal a cause (such as trauma or stroke) and there may be no underlying structural abnormality detected on MRI. In such cases, it is usually appropriate to wait for a second seizure of any sort before starting medication because 40% of these patients will not have another. Sometimes, however, the presenting seizure will have had such injurious consequences that patients do not want to risk another and are prepared to commit to medication for 12 to 24 months before reviewing that position.

Some epilepsy syndromes may be relatively mild, such as childhood absence epilepsy or benign rolandic epilepsy. If the seizures are brief and not interfering with school or social function then parents may be prepared to wait for the condition to remit naturally.

Which medication?

Medications used in the treatment of epilepsy are listed in the Table. The box on page 51 lists treatment recommendations for various epilepsy syndromes. As a guideline, the generalised epilepsies – both primary and secondary – are best treated

Epilepsy Associations

Epilepsy Australia*

National Office
826 Burke Road
CAMBERWELL VIC 3124
Phone: 03 9805 9111
Helpline: 1300 852 853
website: www.epilepsyaustralia.org

Epilepsy Association Australia*

National Office
Suite 8, 44-46 Oxford Street
EPPING NSW 2121
Phone: 02 9856 7090
Action line: 1300 366 162
Website: www.epilepsy.org.au

* Contact the national office of each association for respective details of State and Territory offices.

Table. Drugs used in the treatment of epilepsy

Drug	Generalised epilepsy syndromes	Focal epilepsy syndromes
Carbamazepine (Tegretol, Teril)	No	Yes
Ethosuximide (Zarontin)	Yes (for absence seizures)	No
Gabapentin (Gantin, Neurontin, Pendine)	No	Yes
Lamotrigine (Lamictal)	Yes	Yes
Levetiracetam (Keppra)	No	Yes
Oxcarbazepine (Trileptal)	No	Yes
Phenytoin (Dilantin)	No	Yes
Sodium valproate (Epilim, Valpro)	Yes	Yes
Tiagabine (Gabitril)	No	Yes
Topiramate (Topamax)	Yes	Yes
Vigabatrin (Sabril)	Yes (for secondary generalised epilepsies)	Yes
Clobazam (Frisium)	Yes	Yes
Clonazepam (Paxam, Rivotril)	Yes	Yes
Diazepam (Antenex, Ducene, Valium, Valpam)	Yes	Yes
Midazolam (Hypnovel)	Yes	Yes

with sodium valproate (Epilim, Valpro), while the focal epilepsies can be treated by any of the other antiepileptic drugs. Carbamazepine (Tegretol, Teril) has become by common use the drug of first choice for focal epilepsies, but there is little evidence that it has any advantage over the others. It is, however, probably an easier drug to use and has slightly fewer interactions than its traditional predecessor, phenytoin (Dilantin).

Initiation of therapy should follow the 'start low and go slow' principle. Naturally, a patient needs to be warned about common allergic side effects as well as those that are dose related. Rashes usually mean intolerance to the medication – in such cases the drug should be withdrawn and a substitution made. Routine blood counts and liver function tests are not necessary when initiating medication unless there is an underlying concern such as liver disease. If the patient feels unwell or develops a sore throat or infection while taking the medication then clinical review and investigations would be warranted. Between 70 and 80% of people who start one medication are able to remain on it happily; the remainder will need a change at some stage, either because of side effects or lack of efficacy.

The information leaflets in packs of antiepileptic medications usually list a complete range of side effects that manage to frighten most patients – I forewarn people of this and mention only the common reactions. I also assure them that at any time they can discuss any concerns with their GP or neurologist.

How much should I give?

Dosing will be determined by the age and size of the patient, and some weight-based guidelines for children are given in *MIMS*. The overarching principle, however, is to give the minimum required to prevent seizures and avoid side effects. These clinically appropriate doses may be associated with the so-called therapeutic range of serum drug levels; for some, however, such as sodium valproate and lamotrigine (Lamictal), the relationship between the serum level and seizure control is less clear. I measure serum drug levels only to check compliance (if necessary), to look at the effect of a potential drug interaction, or to examine the relationship between symptoms and suspected drug toxicity. 'Fitness to drive' forms may benefit from recording 'therapeutic levels', to confirm compliance.

If seizures persist, the dosage can be increased judiciously. Some knowledge of the underlying pharmacokinetics is necessary because drugs with zero order kinetics, such as phenytoin, can show profound increases in serum levels with a relatively modest increase in dosage.

When should medication be changed?

When the side effects are persistent or intolerable or if the medication is not working or even making the epilepsy worse (the so-called paradoxical effect) then a change must be made. If allergic side effects are occurring, the medication can be stopped relatively quickly, but if there is any fear of a drug withdrawal seizure then short term cover with a benzodiazepine such as clobazam (Frisium) or clonazepam (Paxam, Rivotril) should be considered. Otherwise, I usually overlap the drugs, reducing the first while gradually increasing the second. However, seizure control is sometimes possible only with the combination of medication rather than with one medication alone. During the change-over period, a written dosage schedule giving clear guidance is essential for the patient and family.

Some adverse reactions of the newer drugs have limited their use, such as retinal toxicity with vigabatrin (Sabril) and precipitation of absence status epilepticus with tiagabine (Gabitril). It should be remembered also that carbamazepine and oxcarbazepine (Trileptal) can exacerbate seizures in some secondary generalised syndromes.

Benzodiazepines have a limited place in the long term because of tolerance and increasing doses required. As mentioned above, they are best used in the short term while other medications are being introduced. For emergency use in successive seizures, midazolam (Hypnovel) can be given intranasally, via the intrabuccal space, intravenously or intramuscularly. Clonazepam and diazepam (Antenex, Ducene, Valium, Valpam) are best given intravenously, but they can be given rectally; absorption from intramuscular injection is poor.

What are the important drug interactions?

Carbamazepine and phenytoin are potent inducers of the P450 hepatic enzyme system, and can reduce the efficacy of many other drugs, including contraceptive hormone preparations. Higher ethinyloestradiol doses will be necessary for women on these antiepileptic medications, but even then irregular menses can occur, indicating insufficient cycle regulation and the possibility of 'pill failure'. The newer antiepileptic medications, oxcarbazepine and topiramate (Topamax), act similarly.

Treatment of specific epilepsy syndromes

Benign focal epilepsy of childhood
Carbamazepine, if treatment is necessary

Absence epilepsy of childhood
Sodium valproate or ethosuximide, if treatment is necessary

Generalised epilepsy
First choice: sodium valproate
Second choice: lamotrigine or topiramate

Focal epilepsy
First choice: carbamazepine. Second choice: any other agent listed in Table 1. After failure of three drugs singly or in combination, presurgical evaluation is necessary.

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Sodium valproate impairs the metabolism of lamotrigine (these drugs are commonly used in combination for secondary generalised epilepsies or refractory primary generalised syndromes). Therefore, a little lamotrigine goes a long way with valproate.

Given the large number of interactions recorded with antiepileptic medications, it is prudent to check the literature before prescribing.

Gender, epilepsy and medication

Long term studies are revealing the effects of antiepileptic medications on women's reproductive and bone health. These should be discussed with patients, especially women planning a family and those who will be on lifelong treatment. The most common adverse effect is menstrual irregularity, but the relationship between these drugs and polycystic ovary syndrome (irregular menses, polycystic ovaries, obesity and hirsutism) remains controversial. Teratogenicity is a feared side effect, and daily folic acid (to prevent spina bifida and perhaps other defects) is recommended for all fertile women on these medications if they are planning to conceive or if they miss a period. Valproate appears to be the most teratogenic and if it must continue to be used throughout the pregnancy, the lowest effective dose is desirable as some studies have revealed a dose-related fetal malformation rate.

Ideally, a woman who needs antiepileptic medication and is planning a family should be on the lowest effective dose of a single drug. However, increased doses will be needed as pregnancy progresses to maintain adequate levels. Long term use of some antiepileptic medications may be associated with reduced bone mineral density, and regular DEXA scans will be needed to monitor this.

Men, having a simpler reproductive system, have fewer concerns regarding use of antiepileptic medications. However, impotence is occasionally seen, and their skeletal system may also be vulnerable in the long term.

Epilepsy in children and the elderly

Children and elderly patients with epilepsy require special consideration given their different metabolic states and changing cerebral physiology at either end of life. In particular, older patients will often be taking other medication and may have altered drug clearances due to renal or hepatic impairment, so they can be more susceptible to the physical and cognitive side effects of antiepileptic medications.

Summary

The management of epilepsy is being increasingly refined as more is understood about the different syndromes and their response to an increasing range of drugs. In addition, there is more information about the long term effects of antiepileptic medications in relation to patient gender and age. Aiming treatment and counselling at the specific epilepsy syndrome will lead to best management. Support for patient and families from local epilepsy associations (see the box on page 51) remains an invaluable resource. MT

Further reading

1. Assessing fitness to drive: commercial and private vehicle drivers. Sydney: Austroads; 2003 (www.austroads.com.au/aftd.html)
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4. Guerrini R, Arzimanoglou A, Brouwer O. Rationale for treating epilepsy in children. Epileptic Disord 2002; 4 Suppl 2: S9-S21.
5. Australian Adverse Drug Reactions Bulletin 2003; 22(5): 19-20.

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