

The management of chronic epilepsy

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About one in 40 people will have two or more non-febrile seizures at some time and one in 200 people endure chronic epilepsy. Despite the availability of potent antiepileptic drugs (AEDs), many of these patients with a chronic seizure disorder are likely to remain intractable and present a challenge to the physician. These notes are intended to provide a strategy for dealing with such patients. Accompanying chapters (Section Six) give details on the range of medical and surgical treatments.

Antiepileptic drug treatment in patients with chronic epilepsy

About 70% of patients developing epilepsy may expect to become seizure free with optimal AED therapy. The remaining 30% are the most difficult to treat satisfactorily. Approximately 80% of all patients will be best controlled with a single drug, and 10–15% with a combination of two agents. Poor adherence to therapy, drug interactions and long-term toxicity are all more likely to occur if more than one drug is prescribed^{1,2,3}. The goal of therapy should be complete seizure control with a single drug taken once or twice a day, and without side effects. Precise classification of the types of seizure and of the epilepsy, from clinical and EEG data, and careful recording of seizures and side effects are essential if rational management decisions are to be made.

If control is difficult to achieve, the maximally tolerated dose of each drug used should be explored, but a balance needs to be struck between side effects and control of seizures, and drugs that do not contribute to seizure control should be discontinued. In patients in whom treatment appears to be ineffective, the diagnosis of epilepsy and adherence to therapy should be reviewed. Consideration should also be given to the presence of a progressive cerebral disorder, such as a tumour or metabolic defect, and the patient investigated accordingly.

The general principles are as follows:

1. Review diagnosis and history of the epilepsy. This will usually necessitate obtaining and reviewing old records, in addition to interviewing the patient and a witness to the seizures. The types of seizure and the epilepsy syndrome should then be classified on the basis of clinical features and the EEG. In addition, two specific questions should be addressed. Is there evidence for non-epileptic attacks? Is there an identifiable aetiology? In many series of patients with supposed chronic epilepsy, 10–15% have non-epileptic attacks⁴. The aetiology of a seizure disorder may be identified in 40–50% of patients. Imaging of the brain with high quality MRI scanning is appropriate at this time, looking for an underlying structural lesion⁵ (Chapter 21).

2. *Check serum concentrations* of AEDs and question adherence.
3. *Review past and present AED treatment* for efficacy and side effects. Has the patient had a good trial with a maximally tolerated dose of all the major AEDs⁶?
4. *Select the AED that is most likely to be efficacious and with the least side effects.* This information needs to be determined from a detailed drug and seizure history. The drug to be retained will usually be chosen on the grounds that it has not been used to its full potential, and/or that it appears to have had a definite beneficial effect. In some cases, e.g. patients with idiopathic generalised epilepsy, there is a clear indication to use particular agents, and to avoid others.⁷
5. *Adjust the dose of the selected drug to the optimum,* with increments made if seizures continue and side effects do not occur and, for some agents, being guided by assay of serum drug concentrations. Zealous adherence to quoted therapeutic ranges of serum AED concentrations is not appropriate. These data should always be subordinate to the clinical picture of whether or not the patient continues to have seizures and/or dose-related side effects from AEDs. When employed as a guide to dosing, measurements of serum concentrations of phenytoin are particularly useful. Assay of concentrations of carbamazepine, the monohydroxy derivative of oxcarbazepine, phenobarbitone and ethosuximide are moderately helpful, but vigabatrin, gabapentin, lamotrigine, sodium valproate and primidone concentrations are of little utility. There are insufficient data on topiramate, pregabalin, tiagabine and levetiracetam to judge the usefulness of measuring the serum concentrations of these drugs.
6. *Attempt to reduce and discontinue the other AEDs,* particularly if their prescription has not aided seizure control and they are suspected of giving rise to adverse effects; remember that seizures may worsen at this time. Frequently, however, reduction of the number of AEDs results in the patient feeling better and improved seizure control^{3,8-9}. The rate at which AEDs should be withdrawn in this situation is controversial. Some AEDs may be safely withdrawn fairly rapidly but conventionally this is carried out over a period of weeks. This is particularly important in withdrawal of benzodiazepines and barbiturates, which may precipitate status epilepticus if withdrawn too rapidly¹⁰. Although it takes longer, it is preferable to make only one drug change at a time. It is then possible to determine cause and effect, if there is any improvement or deterioration.
7. *If seizures continue* despite a maximally tolerated dose of a first-line AED, *check adherence* to the prescription with tablet counts, measurement of the serum drug concentration and counselling.
8. *Another first-line drug* (if there is one that has not been used to its optimum) *should then be commenced,* and increased to an optimal dose. If there is a marked improvement, withdrawal of the first drug should be considered and, if not, the second drug should be tapered and stopped.
9. *If seizures continue* despite a maximally tolerated dose of all the individual first-line drugs, *try a combination of two first-line drugs* for that seizure type. The chances of duotherapy controlling seizures when monotherapy has been unsuccessful is of the order of 10–15%^{1,2,11}.

10. If a combination of two first-line AEDs is unhelpful, the drug which appears to have the most effect and fewest side effects should be continued, and the other AED replaced with a second-line drug. The chances of the addition of a second-line drug resulting in a 50% reduction of seizures is 20–50%, the chances of the patient becoming seizure free is less than 10%.

11. If the second-line drug is effective, withdrawal of the initial agent should be considered. Prescription of an unhelpful second-line drug should not be continued.

12. Consider using a novel AED. As a general rule, the use of such drugs should only be as part of a formal organised trial, with very accurate documentation of seizures and side effects. Drug trials are demanding for patients and should not be entered into lightly.

13. The above scheme may take months to years to work through. However, if satisfactory seizure control cannot be obtained with drugs then consideration should be given to evaluation for epilepsy surgery. This is especially indicated if there is a lesion evident on MRI with concordant clinical features, but should be considered in anybody with a focal onset epilepsy with ongoing seizures despite optimal doses of 2–3 AEDs in monotherapy or combination.

Holistic issues

In addition to the pharmacological aspects, it is important to consider the implications and consequences of intractable epilepsy, which are often more devastating than the seizures themselves. Not least, people with intractable epilepsy benefit enormously from somebody taking a personal interest in them and their problems, and from advice on practical issues, such as safe cooking with a microwave oven, safe bathing and discussion of reasonable expectations and limitations with regard to the prognosis and the prospects for independent living, leisure and social life, and employment. For such patients and their families, the support of an epilepsy specialist nurse¹² and of the voluntary organisations (see Chapter 58) are invaluable.

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