Today's Treatment

Diseases of the central nervous system

Epilepsy

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British Medical Journal, 1975, 4, 270-272

Epilepsy is an abnormal paroxysmal discharge of neurones which is sufficiently extensive to cause clinical manifestations. These will depend on the neurones involved. The more common types of epilepsy include grand mal with loss of consciousness and convulsions, petit mal, in which there is transient loss of consciousness, and focal epilepsy, especially of the temporal lobe. The various types can usually be distinguished by the history but the examination and special investigations such as electroencephalography may make this easier. This article discusses the treatment of epileptic attacks rather than their diagnosis and investigation.

Except in status epilepticus the treatment of epilepsy is prophylactic. Before starting treatment the doctor must have concluded that the patient has a continuing liability to epilepsy. This conclusion is easily reached if the patient has had recurrent attacks, but after a single episode it is less easy. If there was a clear precipitating factor such as prolonged hypoglycaemia then avoiding or correcting the circumstance may be all that is required. If there is persistent disease such as a tumour, then treatment should be given even after a single fit. Sometimes antiepileptic treatment is given after brain surgery even when no fit has occurred. Other factors which might influence a decision whether to give treatment for a single fit are the nature of the seizure, the electroencephalographic findings, and the certainty of the diagnosis. Most physicians would feel that a single attack without evidence of any other brain disease does not warrant treatment.

The aim of treatment should be to stop all clinical attacks of epilepsy but unfortunately the dose of drugs which might achieve this will often cause unwanted effects. Mild unwanted effects would be acceptable in return for control of frequent epilepsy and the prescriber will have to judge the drugs and dose level for each patient individually. Many different antiepileptic drugs are available with varying properties, advantages, and side effects.[1] All antiepileptic drugs should initially be given in small doses and the dose gradually increased to the maximum permitted or until unacceptable unwanted effects begin to develop. If the drug is then found to be of no value it should be stopped completely and a different drug tried. This means that there must be a careful assessment of the fit frequency and of the patient's condition. During the establishment of the regimen frequent consultations may be required, but later regular but not frequent reviews should be undertaken. Twice-daily dosage is nearly always sufficient because of the long biological half life of the drugs. Blood levels of the drugs should be measured in patients who are developing unwanted effects at ordinary doses or whose attacks continue in spite of carefully controlled treatment. Patients may have great difficulty in remembering to take their tablets. The interest of the doctor supervising the treatment and the counting of returned tablets to see how many have been taken since the last visit will often encourage the patient to persist with the tablets.[2]

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Age of patient

One may classify the types of epilepsy in many ways, but it is easier to discuss the management in terms of the age of the patient.

BIRTH TO THREE MONTHS

Attacks within the first two days of birth are often due to birth injury or hypoglycaemia. If the latter is suspected intravenous glucose should be given. Epilepsy due to brain damage or anoxia at birth may start at any time during childhood but if it is severe the epilepsy usually begins within the first three months. Attacks occurring several days after birth but within the first month may be due to hypocalcaemia if the child is being bottle-fed. This is due to the high phosphate content of the cows' milk and is treated with calcium gluconate initially intravenously in a dose of 30 mg/kg and then by mouth. Very occasionally pyridoxine deficiency causes epilepsy and may be corrected by pyridoxine 10 mg twice a day. Metabolic disturbances, secondary to gastroenteritis or pneumonia, may also lead to epilepsy. At this age barbiturates are probably the best treatment for the epileptic seizures if the attacks continue. Phenobarbitone 10 mg eight-hourly is usually adequate and can be given orally or intramuscularly.

THREE TO NINE MONTHS

Meningitis can be difficult to diagnose during the first year of life and if it is not treated quickly may lead to a permanent liability to epilepsy. Convulsions associated with meningitis should be treated with phenobarbitone. Infantile spasms (salaam attacks), which tend to present between the third and ninth month, may be a manifestation of prenatal or neonatal brain damage and are usually associated with mental retardation. Unlike other forms of epilepsy most patients improve on corticotrophin, tetracosactrin, or corticosteroids such as prednisolone. Treatment should be continued for at least four months. The benzodiazepines, especially nitrazepam, also decrease the frequency of the seizures.[3] Unfortunately permanent mental retardation occurs in a large proportion of these patients and responds less well to treatment than the convulsions.

NINE MONTHS TO THREE YEARS

Meningitis is still an important cause of epilepsy, and epilepsy due to minor birth injuries may not occur until after the first year of life. Idiopathic epilepsy may first present at this age but in less severe cases it does not usually start until later. In this age group the common epileptic presentation is a febrile convulsion. Although the convulsion is usually precipitated by fever, other metabolic factors may also be responsible. The long-term prognosis is good if there is no evidence of brain damage, the child's physical and intellectual development is normal, there is a clear association between the fit and the fever, and the fit did not last for over 10 minutes. If the doctor is confident that the diagnosis is a febrile convulsion and that the child does not have meningitis special investigations are not usually needed.

The mother should be instructed that if the fever recurs the child should be cooled and if necessary sponged with tepid water. A cold bath may be used but may be dangerous if the child has a convulsion and is not being adequately supervised. Soluble aspirin 150 to 300 mg should be given as soon as a fever starts and continued every six hours until there has been no fever for two days. It is better to give the aspirin unnecessarily than late. If in spite of antipyretic treatment the child has another attack then anticonvulsants should be given. If the history suggests that there was more than a few hours between the child starting an illness and the fit then the anticonvulsants might be begun when the illness starts; otherwise they would need to be given continuously. Phenobarbitone 15 or 30 mg may be given initially followed by 15 mg every six or eight hours. The phenobarbitone should be given until at least two days after the child is well.

OVER THREE YEARS

By the age of 3 years the types of epilepsy that a child may develop are similar to those found in adults although the incidence of the different types alters with age. Occasionally febrile convulsions may not present until the fourth year.

Petit mal

Petit mal is much more common in children, although it may persist into adult life. Petit mal should not be confused with temporal lobe epilepsy, in which alterations of awareness rather than loss of consciousness are common. The treatment of the two is different. A single attack of petit mal is not of much account but often a child has many attacks which may considerably interfere with schooling.

The best treatment is ethosuximide, 250 mg capsules, starting with one a day and gradually increasing to a maximum of four a day or until there are unwanted effects, such as nausea, psychological changes, ataxia, or rashes. If there is no improvement the treatment should be stopped and 300 to 600 mg of troxidone given twice daily. This may cause leucopenia, although it is usually reversible if the drug is stopped. Akinetic seizures and some types of myoclonus can be treated in the same way as petit mal.

Grand mal

When grand mal starts after the age of 3 and before 30 it is usually idiopathic but specific causes of epilepsy should be excluded. So far as the treatment of the seizures is concerned, however, it is the same whether the attacks are idiopathic or due to other disease. During the attack those present should be advised not to restrain the patient but to place him in a position which allows easy breathing and which prevents the patient hurting himself.

Precipitating factors which may have triggered off the attack should be sought and if possible controlled. One of the more common precipitating factors is a flashing light or television. It is not reasonable to ban watching television, but the patient should never turn on the set, adjust it, or watch while this is being done. He should sit well back from the set and the background lighting in the room should be good. Anxiety may lead to hyperventilation and the ensuing alkalosis may precipitate epilepsy, although there are probably other mechanisms by which emotional stress can trigger an attack in someone liable to seizures. Occasionally vasovagal fainting (syncope) causes such severe anoxia of the brain that a fit occurs. This is more likely if well-meaning friends support a person who is fainting and prevent him lying down. Hormonal factors, especially menstruation and the contraceptive pill, may lower the threshold for epilepsy. If there is also excessive weight gain at the time of menstruation a diuretic for a few days may prevent attacks. Sometimes changing the method of contraception helps. Patients with epilepsy taking excessive alcohol or having attacks related to alcohol must be advised to become teetotal. Drugs, such as the tricyclic antidepressants or intravenous penicillin, may increase the risk of epilepsy.

Phenytoin and phenobarbitone are the most commonly used drugs for the prophylaxis of grand mal. Phenytoin is given in a dose of 50 to 200 mg twice a day. The rate of metabolism varies and some patients can only tolerate a small dose. If too large a dose is given ataxia and nystagmus will develop and occasionally this occurs after many months on a steady dose. The ataxia and nystagmus cease if the dose is decreased sufficiently. For young women the increased hair growth with phenytoin is such a disadvantage that it is better to start their treatment with phenobarbitone. In children gum hyperplasia is frequent but the incidence is lower in adults. It may be prevented or curtailed by careful dental and gingival hygiene. Occasionally glandular enlargement or a rash may appear with phenytoin.

Other hydantoins, such as methoin and ethotoin, have actions similar to phenytoin. If phenytoin in full doses is ineffective phenobarbitone in doses of 30 to 90 mg twice a day should be tried. Phenobarbitone is not the best drug for children between the ages of 4 and 13 as it often causes irritability and hyperactive behaviour. In the elderly it may cause depression and in all patients it induces drowsiness when first used. Primidone, a desoxybarbiturate, and methylphenobarbitone have actions similar to phenobarbitone.

In a few patients on anticonvulsants folic acid deficiency and, very occasionally, megaloblastic anaemia occur and for these a low-dose folic acid supplement is necessary. Folic acid should be prescribed only when there is evidence of deficiency, as it has been suggested that folic acid in high doses might cause side effects. If a patient is given folic acid the blood level of B_{12} should also be estimated as very rarely this may also be low. Osteomalacia and changes in calcium metabolism may also occur during long-term treatment. All patients on high doses of anticonvulsants, especially if the attacks are poorly controlled or if there is a deterioration in the mental or physical health, should have occasional metabolic and haematological reviews and, if necessary, estimations of the blood level of the anticonvulsants.

If phenobarbitone or phenytoin alone does not control the attacks then the two may be given together. The dose of only one should be altered at a time, as the interaction of the two drugs may cause the blood level of the other to alter without any change in its dosage. If a hydantoin and a barbiturate together are unsuccessful then pheneturide up to 400 mg twice a day, sulthiame up to 300 mg twice a day, or carbamazepine up to 300 mg four times a day may be added. Carbamazepine needs to be given four times a day. The benzodiazepines, such as diazepam, are not helpful in the prophylactic management of epilepsy of the grand mal type, except in patients with alcohol-withdrawal fits.[3]

Focal epilepsy

Temporal lobe epilepsy is the commonest form of focal

epilepsy and is frequently due to a structural lesion which may require treatment in its own right. Nevertheless, as far as the treatment of the epileptic attacks is concerned, the drugs used are the same as for grand mal. Focal epilepsy responds less well to treatment than grand mal. Antiepileptic drugs may reduce the severity of the attacks or prevent them progressing to grand mal without actually stopping them.

One of the major problems in patients with temporal lobe epilepsy is the frequent association with behaviour disorders. The benzodiazepines are helpful but often adjustments have to be made in the patient's social life and occupation. If the temporal lobe attacks cannot be sufficiently well controlled to allow the patient to lead a fairly normal life then he should be considered for temporal lobectomy. The assessment would include electroencephalography and air encephalography as well as psychological studies. If the patients are carefully selected the results of operation are good.

Other forms of focal epilepsy are treated with the same anticonvulsants but are often associated with structural lesions which require special investigations and treatment.

Status epilepticus

Status epilepticus[4] is a medical emergency that may occur at any age. There is recurrent grand mal without intervening recovery. Although the brain damage that may follow status epilepticus is probably due to more factors than anoxia, the most urgent part of the treatment is to restore cerebral oxygenation. The airway should be kept clear but artificial respiration is of no value if the respiratory muscles are contracted, as the chest wall cannot be moved without fracturing the ribs. Antiepileptic treatment, with intravenous diazepam (10 mg for an adult), should be started at once.[5] Intramuscular diazepam is less effective. If intravenous diazepam is not available other treatment such as intramuscular paraldehyde, intravenous phenytoin, or intramuscular barbiturates should be given rather than nothing. Barbiturates should not be repeated as they may cause respiratory depression.

Unfortunately intravenous diazepam may be effective for only 15 minutes. If a further attack occurs a continuous intravenous infusion of diazepam should be given in an increasing dose up to 10 mg/h in an adult until the attacks are controlled. The treatment should be continued until the patient has recovered and for at least 12 hours after the last fit; otherwise they may recur. Diazepam prepared for intravenous injections is not very soluble in water and if given in an infusion with saline must be sufficiently diluted to keep the solution clear and prevent clouding. Diazepam may rarely be associated with apnoea, but this is less likely to occur when it is given by infusion than when it is given as a single bolus.

If diazepam is not effective paraldehyde should be given by intramuscular injection (0·1 mg/kg). It is safe but may cause abscesses. Rectal paraldehyde is absorbed but it is difficult to give to a patient having a fit. Intravenous phenytoin may also be tried. If all these regimens fail the patient will probably require an anaesthetic with a muscle relaxant and positive pressure respiration. Unfortunately this does not stop the cerebral epileptic activity but it does ensure cerebral oxygenation. A patient recovering from status epileticus must be given prophylactic antiepileptic treatment.

Recurrent fits in eclampsia should be treated in the same way as status epilepticus.

Cessation of treatment

Theoretically treatment should stop if the liability to seizures has ceased. There is no definite way, however, of telling whether the attacks have stopped because the treatment is being continued or whether the liability to epilepsy has become negligible.[6] The following factors would be against stopping treatment:

(*a*) The underlying cause in symptomatic epilepsy is still present.

(*b*) The attacks occurred over a long period. A patient who had epilepsy in childhood, adolescence, and in early adult life is more likely to have further attacks than a person who had had all his attacks over a period of a year or two.

(*c*) There is a strong family history of epilepsy.

(*d*) The electroencephalogram continues to show epileptic activity.

(*e*) When a single attack of epilepsy would considerably disrupt a patient's way of life. For example, a patient in Britain who has had no attacks while awake for three years may have a licence to drive a car if he satisfies certain conditions. One attack could prevent him driving for at least a further three years.

(*f*) Previously stopping treatment was associated with renewed epilepsy.

(*g*) An attack within about the last three to five years. For children this could be shorter, for adults sometimes longer.

There is no clear rule to help decide when to stop treatment, but treatment should always be stopped slowly, as withdrawal of antiepileptic drugs can precipitate an attack. At least six months should be taken and the patient advised about the dangers of a convulsion. Driving a car should be forbidden. For this reason it is usually better for a patient who has been free of attacks for several years to stop treatment during adolescence rather than wait until a solitary fit would be a greater inconvenience.

There is a slightly increased incidence of fetal abnormalities in children born to women taking antiepileptic drugs but the risk is small. Treatment should not be stopped if epilepsy is still continuing especially as the fit frequency may increase during pregnancy. Nevertheless, the danger of fetal abnormalities is a reason for stopping treatment fairly readily in women free of attacks who may later wish to become pregnant.

A doctor should also realise that to continue prescribing treatment for any patient for more than six years after the last attack is tantamount to deciding to continue treatment for ever, as withdrawal of antiepileptic treatment after that length of time becomes more difficult rather than easier.

Social management

This article is not intended to cover the social and psychological problems of adults and children with epilepsy but often these are worse than the disturbances due to the attacks themselves. Normal activities such as sport should whenever possible be allowed and it is preferable to take some risks (and accept the consequences) if it allows the person to enjoy a more normal life. Sympathetic but authoritative advice by doctors, teachers, and social workers towards the patients, their relatives, and employers will often alleviate some of the emotional disturbances which the chronic liability to epilepsy brings with it.

The monthly MIMS index of proprietary preparations available in Britain includes the following trade names for the main drugs mentioned in this article (other than broad groups such as corticosteroids): carbamazepine—Tegretol; diazepam—Valium; ethosuximide—Capitus, Emeside, Zarontin; methylphenobarbitone—Prominal; nitrazepam—Mogadon; pheneturide—Benuride; phenobarbitone—Gardenol, Luminal; phenytoin—Epanutin; primidone—Mysoline; sulthiame—Ospolot; and troxidone—Tridione.

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