INTRODUCTION

Epilepsy is the most common of neurological disorders and it imposes a large burden on health care systems. The clinical features, aetiology, severity, prognosis and its association with other neurological disabilities vary greatly, and for this reason, many different disciplines may be responsible for supplying care including neurologists, paediatricians, psychiatrists, and very importantly too, the family doctor.

Epilepsy is most easily defined as the name for occasional sudden, excessive, rapid and local discharges of grey matter. (1) An epileptic seizure can be defined clinically as an intermittent, stereotyped, disturbance of consciousness, behaviour, emotion, motor function, or sensation that on clinical grounds is believed to result from cortical neuronal discharge. Epilepsy can then be defined as a condition in which seizures recur, usually spontaneously. (2) These seizures may be partial or generalised.

The International League Against Epilepsy (ILAE) has proposed two classification schemes, both of which are in current use. An understanding of these classifications is essential for proper management and communication among clinicians. The International Classification of Epileptic Seizures (ICES) in 1981, makes use of clinical and EEG information. (3) Table 1. A second classification was formulated by the ILAE in 1989, as it was recognised that patients may experience similar seizure types within a syndrome with similar age of onset and aetiology. This is termed The International Classification of the Epilepsies and Epileptic Syndromes. (4) Classifying epilepsies into a syndrome where possible may be of vital importance in the management of patients with epilepsy.

EPILEPMIOLOGY

In most studies, the overall incidence of epilepsy (excluding febrile convulsions and single seizures) has been found to be around 70 cases per 100,000 persons per year (with a range of 20-120 per 100,000). The usual prevalence figure given is about 5-10 cases per 1000 persons (excluding febrile convulsions, single seizures and inactive cases). The lifetime prevalence of seizures (the risk of having a non-febrile epileptic seizure at some point in an average lifetime) is between 2 and 5%. The difference between lifetime prevalence and the prevalence of active epilepsy shows that in most patients developing epilepsy, the condition remits. The course of the condition in its early years is an important predictor of its prognosis; the longer the epilepsy remains active the poorer the long-term prognosis. (5) Approximately 70-80% of people with epilepsy have well-controlled seizures on conventional treatment and are cared for mainly within general practice. The remainder will need continuing access to secondary care. (6)

AETIOLOGY

Epilepsy must be regarded as a symptom complex rather than a disease entity. The causes of epilepsy are many and varied and include the idiopathic and purely genetic disorders, as well as those resulting from any type of acquired cerebral insult. In a recent community based survey of epilepsy in the United Kingdom, 60% of all patients had no identifiable cause of epilepsy, although a proportion of these may have had a specific genetically determined syndrome. The remote symptomatic causes included: vascular disease (15%), tumour (6%), post-traumatic (2%), alcohol related (6%). (7)

DIAGNOSIS

Epilepsy is a clinical diagnosis, and there are no tests that can substitute for the clinical history. As the patient is often unaware of what happens during an attack, it is imperative to obtain an account from a first-hand witness as well as details from the patient about events experienced before, during, and after the seizure. In view of the social and economic implications, diagnostic errors need to be avoided. If there is any doubt, the clinician should delay until further evidence is forthcoming to reach a firm diagnosis.

Is it epilepsy? The first step will be to differentiate seizures from other transient symptoms. Table 2. Syncope and pseudoseizures are most often mistaken for epilepsy. Pseudoseizures may account for up to 20% of apparently intractable epilepsies. (8) Accurate diagnosis of non-epileptic seizures is further complicated by the fact that sometimes patients may have both the organic and non-organic seizures.
Once it is accepted that seizures have occurred, the next step would be to classify the seizure disorder according to seizure type and aetiology.

First and foremost, acute symptomatic events have to be ruled out, such as alcohol related seizures, a metabolic or toxic encephalopathy, in which case treatment should be primarily directed at the cause and may not necessarily require antiepileptic drug therapy.

Clinical information to be obtained should include a history of perinatal events and milestone development, severe head injury (including prolonged post-traumatic amnesia, depressed skull fractures, and intracerebral haematoma), infections of the CNS. A history of febrile convulsions in infancy has an association with hippocampal sclerosis. A family history of seizures may suggest a genetic cause.

Clinical information together with age of onset of seizures, may suffice to allow a presumptive classification of the epilepsy into a specific epileptic syndrome where possible.

For example a history of nocturnal focal motor seizures involving the face or upper limb in a child below the age of 12 may suggest the diagnosis of Benign Childhood Epilepsy with Centro-Temporal Spikes. The development of myoclonic jerking on awakening in an adolescent together with tonic-clonic seizures point to Juvenile Myoclonic Epilepsy. A specific aura indicates a localised onset and therefore a greater likelihood of the epilepsy being symptomatic caused by a localised cerebral lesion.

Further information at this stage is then to be obtained by investigation, mainly electroencephalography (EEG) and neuroimaging.

**THE EEG IN EPILEPSY**

The electroencephalogram (EEG) was developed in the late 1920's and has continued to play a major role in the diagnosis and investigation of epilepsies. Scalp EEG represents a summation of excitatory or inhibitory potentials at synapses in the cortex, but deep generators may produce little or no change at the surface.

Routine interictal EEG may provide valuable information that confirms the diagnosis, or helps in the classification of the
type of seizure disorder, or raises
the suspicion of a focal underlying structural lesion.

Of patients with epilepsy, 35% consistently have specific epileptiform discharges, 50% do so on some occasion after repeated recording, and 15% never show any discharges. A single routine EEG in the wakeful state will show an epileptiform abnormality in 50% of epileptic patients. Repeated EEG recordings and/or sleep EEG’s (sleep deprived or drug induced) increases this figure to about 70-80%. Activating techniques such as hyperventilation and photic stimulation also increases the yield of epileptiform features. In patients with persisting attacks of uncertain cause, prolonged EEG monitoring with video will lead to definite diagnosis in a significant proportion of cases.

Video-telemetry allows the EEG to be recorded for long periods of time, and combined with synchronised video recording of the patient will allow correlation of clinical and electrographic events. As mentioned, one of the main indications for video telemetry is diagnosis, where the nature of the attacks is uncertain. The second main indication is evaluation of the epilepsy with determination of seizure type, quantity of epileptiform activity, documentation of unrecognised attacks, and assessment of presurgical cases. Sleep disorders can also be studied by video-telemetry. Sometimes it is necessary to reduce anti-epileptic medication to increase the chances of recording an attack. Patients with pseudoseizures very often will have attacks soon after the recording commences. Intracranial electrode placement is also used in a selected number of patients undergoing pre-surgical assessment.

NEUROIMAGING IN EPILEPSY

In patients with a clear diagnosis of epilepsy, neuroimaging is performed in order to identify any underlying structural pathology that would merit specific treatment, particularly if there is evidence of partial onset from the clinical history or from EEG, at any age.

The frequency of abnormalities on computed tomography (CT) scans of patients with epilepsy varies greatly. Tumours may be identified in about 10% of cases. Other abnormalities may include: vascular malformations, post-traumatic lesions, or strokes.

Magnetic resonance imaging (MRI) is becoming increasingly important in epilepsy especially in the assessment of patients whose epilepsy is unresponsive to antiepileptic drug medication. It is superior to CT in the identification of small lesions such as hippocampal sclerosis (with the possibility of volumetric analysis in specialised centres), cavernomas, hamartomas, and dysembryoplastic neuroepithelial tumours. MRI is also superior in identification of abnormalities of the cerebral cortex and other neuronal migration defects, and would be particularly indicated in infants with intractable seizures. MRI is of course essential in the pre-surgical evaluation of patients.

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If seizures continue and no side-effects occur, the doses can be increased gradually. If seizures continue despite maximally tolerated doses of first-line drugs, the diagnosis should be reviewed, and it must be ensured that the patient has received the appropriate drug for their seizure type and syndrome. Secondly, drug-compliance must be ascertained. Non-compliance is an important cause of poor seizure control, and the reasons may include poor communication, problems with understanding or remembering of instructions, dissatisfaction with side-effects, or inconvenient regimens.

Once this has been done, an add-on first-line drug can be introduced, and doses increased gradually until seizure control is achieved. If satisfactory control is achieved with the add-on drug, gradual withdrawal of the initial drug may be considered. Usually 70% of patients respond to monotherapy alone.

If a combination of two first-line drugs is unsuccessful, one of the newer or second-line drugs should be considered, and again seizure type should be taken into consideration. These drugs include: Vigabatrin, Lamotrigine, Gabapentin, and Topiramate. Clobazam and Clonazepam are also used as add-on drugs. In the treatment of partial seizures, Vigabatrin and Topiramate show a trend towards better efficacy, while Lamotrigine and Gabapentin show a trend towards better tolerability. (10) Vigabatrin should not be used in the treatment of primary generalised epilepsies. It is the treatment of choice especially in West Syndrome and in symptomatic epilepsies such as that associated with Tuberous Sclerosis. Myoclonus is sometimes worsened by Gabapentin and Lamotrigine, and absence seizures may be worsened by Gabapentin. Lamotrigine may also be used as monotherapy for partial seizures and generalised tonic-clonic seizures.

If a second-line drug proves to be unhelpful in controlling seizures, it should be gradually withdrawn.

**ANTIEPILEPTIC DRUG MONITORING**

Serum level monitoring of antiepileptic drugs should be performed with clear indications. The main reasons for carrying out these tests are to detect non-compliance, and to identify dose-related drug toxicity. It is routinely necessary to monitor concentrations only for phenytoin, as this drug undergoes saturable hepatic metabolism, and small changes in doses can result in large changes in serum concentration with loss of efficacy or toxicity. Measurements of carbamazepine and phenobarbitone are necessary in certain clinical situations where dose-related toxicity is suspected on clinical grounds. Drug concentration is a useful guide to optimising doses, but should never be taken as the sole criterion on which to base clinical decisions.

**ANTIEPILEPTIC DRUG WITHDRAWAL**

With good management, about 70% of patients should achieve long-term remission. In patients who achieve remission for two, three or more years, a potent argument for drug withdrawal may be the many associated adverse reactions. However against this are the dangers of the recurrence of seizures, with important consequences on driving and employment in the adult patient. Advice offered to patients varies widely. In paediatric practice, concern over the drug side-effects on cognitive function and learning abilities, seems to be the more prominent deciding factor in attempting drug withdrawal. With adults, concern over the issue of recurrence of seizures with their effect on driving and employment, renders the decision more complicated. The consequences of seizure recurrence may outweigh possible benefit in the patient’s opinion. On the other hand most young women contemplating pregnancy with a seizure-free period of more than two or three years, may see this as reason enough for contemplating drug withdrawal.

Few studies have been carried out to determine the success of drug withdrawal. The Medical Research Council Antiepileptic Drug Withdrawal Group studied the relative risk of recurrence on withdrawal of drugs compared to continued treatment. The risk of relapse on continued treatment was 10% per annum, but was two to three times greater in the drug withdrawal group within two years of starting to withdraw treatment. (11) Detailed assessment of the study has proposed seven prognostic factors for increased risk of seizure recurrence: Age 16 years and over, taking more than one antiepileptic drug, history of seizures after starting treatment, history of tonic-clonic seizures (primary or secondarily generalised), a history of myoclonic seizures, an abnormal EEG in the previous year. Risk of seizure recurrence decreases with increasing seizure-free period.

It should be emphasised that the decisions to be made about stopping antiepileptic drugs lie with the patient because social factors such as the possession of a driving license are often of greater importance.

**SURGICAL TREATMENT**

Surgical treatment of epilepsy was pioneered in the United Kingdom over 100 years ago. However it was never made widely available to patients with epilepsy. With increasing sophistication of neurophysiological
(EEG) investigation, neuro-imaging, and neuropsychology, this form of treatment is becoming successful in a large number of patients. To be considered for epilepsy surgery, patients must have a history of medically refractory epilepsy, and be sufficiently disabled by the frequency of their seizures to warrant the risks associated with the procedure.

The philosophy of surgical treatment is basically of two types.

The first is the accurate identification and excision of a localised site of seizure onset. Temporal lobe surgery for mesiotemporal sclerosis or slow growing glioma in the temporal lobe, is no doubt the procedure that yields best results, with in some centres even a 60-70% chance of complete control of a previously intractable epilepsy in the ideal candidate.

The second philosophy of surgical treatment is palliative with disconnection of epileptogenic zones and interruption of seizure spread. Callosotomy is performed in uncontrolled secondary generalised seizure disorders. Hemispherectomy may be suitable for patients with intractable epilepsy and an infantile hemiplegia, or the rare Ramussen’s focal encephalitis. Multiple sub-pial resections, is also another technique developed by Morrell in 1989, where the principle is to interrupt horizontal connections and therefore spread of epileptogenic activity throughout the cortex, while maintaining vertical connections important for cortical function.

MENSTRUATION, CONCEPTION AND PREGNANCY

Many women link the occurrence of their seizures to the perimenstrual period. Changes in hormonal levels, premenstrual tension and fluid retention may be contributing to this catamnial exacerbation of seizures. There have been various approaches to this treatment, including giving intermittent clobazam, which has been reported to be useful in about 78% of women without developing benzodiazepine tolerance. (12)

Enzyme inducing anti-epileptic drugs, such as Phenytoin, Carbamazepine, Barbiturates, Topiramate and Lamotrigine, increase the metabolism of oestrogen, and therefore reduce the efficacy of oral contraceptive preparations, causing breakthrough bleeding during a cycle. Women who wish to rely on oral contraceptive pills, should have preparations containing at least 50g of oestradiol, or if breakthrough bleeding occurs, up to a maximum dose of 100g of oestrogen.

Women with epilepsy should be offered counseling and advice even if they are not immediately planning a pregnancy. About 90% of women with epilepsy will deliver healthy children. Studies about the effects of epilepsy on pregnancy have varied in their results, from no increased risk to a 1.5-3 fold increase in common obstetric complications, such as toxoaemia, pre-eclampsia, bleeding or premature labour. (13) Tonic clonic seizures can lead to injury of the foetus by virtue of hypoxia, or blunt trauma with resultant abruptio placentae.

The teratogenic potential of anti-epileptic drugs should be put into perspective. The background risk of foetal malformation in developed countries is about 3%. This increases to 7% if one anticonvulsant drug is taken, and to 15% if two drugs are taken. Larger doses are also associated with an increased risk. Sodium Valproate is associated with spina bifida (1% risk) and hypospadias. Phenytoin and phenobarbitone are associated with cardiovascular malformations (2% risk) and cleft lip or palate (1.8% risk). (14-19) The risks associated with the newer anti-epileptic drugs (vigabatrin, lamotrigine, gabapentin, and topiramate) cannot yet be reliably determined because of the lack of data.

If a woman with epilepsy and taking anti-epileptic medication, presents for pre-pregnancy planning, the following steps should be taken. Therapy should be tailored to have the best protection against seizures with the lowest doses of the least possible number of drugs, preferably with a change to monotherapy if possible. Peak plasma levels of valproate should be avoided by dividing the required daily dose over two or more administrations and use of slow release formulations. All women of child bearing age on anti-epileptic treatment should be prescribed Folic Acid 5mg/day. Folic acid before and during the first 12 weeks of pregnancy helps protect against neural tube defects in the general population. (20) Although no studies have yet been performed to determine this protection in women on anti-epileptic drugs, it is advisable to prescribe the vitamin in particular with valproate and carbamazepine.

Changes of medication during pregnancy should be made on clinical grounds, and monitoring of plasma levels only indicated where there is increase in seizure frequency or concern about compliance or toxicity.

Vitamin K 20mg/day can be administered prophylactically to women on enzyme inducing anticonvulsants during the last month of pregnancy, to help protect the infant against haemorrhage caused by deficiency of vitamin K dependant coagula-
tion factors. In addition intramuscular Vitamin K may be given to the infant.

All the main anti-epileptic drugs pass in small quantities into breast milk. However this is not a contraindication to breast feeding although care should be taken with phenobarbital and benzodiazepines which may have a sedative effect with withdrawal syndromes on the baby. General advice should be given to mothers with poorly controlled seizures about safe baby care. (21)

**DRIVING AND EMPLOYMENT**

When a person with epilepsy wishes to obtain a driving license, this could be issued providing all normal requirements are fulfilled and a one-year period free of seizures has passed. When a person already holding a license has a seizure, he cannot drive until the one year fit-free period requirement is fulfilled. From the driving point of view, an aura, partial seizure or myoclonic jerk when due to epilepsy are all significant events. Patients are not exempted from these requirements if seizures have occurred because of non-compliance or change in medication. A patient with a well-established pattern of nocturnal-only seizures observed for at least three years may be granted a temporary license. In order to drive large vehicles or vehicles carrying passengers, a patient must not have a continuing liability to seizures.

The occurrence of seizures at any age is likely to effect employment prospects, and advice should be sought in career guidance for school-leavers and in cases of employment difficulties in adults with active epilepsy. Many factors are likely to effect employment prospects, and it is dangerous to generalise. It would be appropriate to ask what the patient's wishes and ambitions are and assess the relevance of the epilepsy to this. Assessment should include: employee-related factors, including age, motivation, work experience, seizure-related and drug-related effects, as well as other handicaps. Job-related factors should also be considered including health and safety requirements and availability of special employment provisions. Lastly assessment should also include employer-related factors, such as knowledge and attitude towards epilepsy, the recruitment policies and practices, and access to occupational health services. Patients may choose not to declare their epilepsy to their employer. Two proposals to improve this situation include: using driving license regulations as a standard, and passing on the information to suitably qualified personnel rather than include it on an application form.

**STATUS EPILEPTICUS**

Status epilepticus is defined as serial seizures without recovery of full consciousness between them. It is a medical emergency and even in modern hospital settings may reach a mortality of 30%. It can be the first manifestation of epilepsy, or complicate chronic epilepsy especially with changes in medication. It can also be precipitated by alcohol, infections, intracranial trauma or tumour. Treatment should be instituted acutely and when resistant, with admission to intensive care, propofol infusion or general anaesthesia with thiopentone.

**REFERENCES**


