NEUROLOGICAL MANAGEMENT

Epilepsy

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Epilepsy is the most common of chronic neurological disorders and it imposes the biggest burden on health care systems. It varies greatly in its clinical features, aetiology, severity, and prognosis and its association with other neurological disabilities. For this reason, many different disciplines may be responsible for supplying care, including neurologists, paediatricians, geriatricians, psychiatrists, and specialists in mental handicap, and in all spheres, the professions allied to medicine have an important input.

Unfortunately, services for people with epilepsy in the United Kingdom are poorly developed, and vary considerably from region to region. The quality of care they offer is varied but often quite poor. A number of reasons are apparent for this, the prime being that British neurology has remained a small specialty and one in which few British neurologists have epilepsy as a major interest. This has meant that many patients with epilepsy are managed by clinicians without appreciable neurological training.

Definition

Epilepsy is most easily defined in physiological terms, being "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. Two major types are recognised—namely, epilepsy with focal or generalised seizures.

The international classification of epileptic seizures (ICES) was proposed in 1981² and table 1 summarises this. It makes use of both clinical and EEG information. Similar seizures may occur at different ages and have very different implications. Conversely, patients may experience differing seizures during the course of their lives so that a classification of different epileptic syndromes based on seizure types occurring within the syndrome, age of onset, and aetiology will also be of vital importance in the management of patients with epilepsy. Table 2 presents a proposed classification of epilepsy.³

Epilepsy must be regarded as a symptom complex rather than a disease entity. The causes of epilepsy are many and varied and include purely genetic disorders (for example, the idiopathic generalised epilepsies), as well as those that result from any type of acquired cerebral insult.

Epidemiology

Despite problems with differing definitions of epilepsy and case ascertainment methods, there is remarkable agreement about the epidemiology of epilepsy in different populations.⁴ Incidence rates vary in an age-specific way between about 20 and 70 per 100 000 per year, whereas the prevalence for active epilepsy is in the range of 4–10 per 1000. Figure 1 gives age-specific incidence, prevalence, and cumulative incidence for a population in Rochester, Minnesota. It can be seen that the incidence of epilepsy is highest at the extremes of life but there are significant differences between the cumulative incidence and prevalence of epilepsy, indicating that most patients who develop epilepsy do not have a chronic disorder.

Most seizures and epilepsies developing in adult life will be regarded as symptomatic but significant numbers of patients may be investigated without a cause becoming apparent. In the National General Practice Study of Epilepsy, 60% of all patients had no identifiable cause of epilepsy, although a proportion of these will have had a specific (genetically determined) epileptic syndrome.⁵

It may be useful to differentiate causes of

Table 1 Classification of seizures

Partial seizures (seizures beginning locally):
Simple (consciousness not impaired)
With motor symptoms
With somatosensory or special sensory symptoms
With autonomic symptoms
With psychic symptoms
Complex (with impairment of consciousness):
Beginning as simple partial seizures (progressing to complex seizure)
Impairment of consciousness at onset
Partial seizures becoming secondarily generalised
Generalised seizures:
Absence seizures
Typical (petit mal)
Atypical
Myoclonic seizures
Clonic seizures
Tonic seizures
Tonic-clonic seizures
Atonic seizures

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Table 2 International classification of epilepsies, epileptic syndromes, and related seizure disorders (ICE) (adapted from ref³)

Localisation-related (focal, local, partial)	Generalised
Idiopathic (primary) Benign childhood epilepsy with centrotemporal spike Childhood epilepsy with occipital paroxysms Primary reading epilepsy	Benign neonatal familial convulsions Benign neonatal convulsions Benign myoclonic epilepsy in infancy Childhood absence epilepsy (pyknolepsy) Juvenile absence epilepsy Juvenile myoclonic epilepsy (impulsive petit mal) Epilepsies with grand mal seizures on awakening Other generalised idiopathic epilepsies Epilepsies with seizures precipitated by specific modes of activation
Cryptogenic Defined by: seizure type (see ICES), clinical features, aetiology, anatomical localisation	Cryptogenic or symptomatic West's syndrome (infantile spasms, Blitz-Nick-Salaam Krämpfe) Lennox-Gastaut syndrome Epilepsy with myoclonic-astatic seizures Epilepsy with myoclonic absences
Symptomatic (secondary) Temporal lobe epilepsies Frontal lobe epilepsies Parietal lobe epilepsies Occipital lobe epilepsies Chronic progressive epilepsia partialis continua of childhood Syndromes characterised by seizures with specific modes of precipitation	Non-specific aetiology Early myoclonic encephalopathy Early infantile epileptic encephalopathy with suppression bursts Other symptomatic generalised epilepsies Specific syndromes Epileptic seizures may complicate many disease states
Undetermined epilepsies With both generalised and focal seizures Neonatal seizures Severe myoclonic epilepsy in infancy Epilepsy with continuous spike-wave during slow-wave sleep Acquired epileptic aphasia (Landau-Kleffner syndrome) Other undetermined epilepsies Without unequivocal generalised or focal features	Special syndromes Situation-related seizures Febrile convulsions Isolated seizures or isolated status epilepticus Seizures occurring only when there is an acute or toxic event due to factors such as alcohol, drugs eclampsia, non-ketotic hyperglycaemia

seizures and epilepsy into acute symptomatic seizures occurring in response to metabolic or cerebral insult, and remote symptomatic epilepsies in which epilepsy develops in relation to a persisting cerebral lesion or damage. Some aetiologies—for example, head injury, stroke, and intracranial infections—may cause both acute symptomatic seizures and remote symptomatic epilepsy. The presence of the first does not necessarily result in the second.

Sander *et al*⁵ found that the commonest remote symptomatic causes of epilepsy were vascular disease (15%) and tumour (6%).⁵ Remote symptomatic epilepsy was commonest in the elderly patients, in whom vascular disease accounted for 49% of cases. Tumour was a rare cause of epilepsy below the age of 30 (1%), but accounted for 19% of cases aged between 50 and 59. Trauma caused 3%

of cases and infection 2%. Acute symptomatic seizures occurred in 15%, and alcohol was the commonest single cause (6%), the incidence being highest between 30 and 39 years of age (27%).

The cost of epilepsy to the NHS was around £110 million in 1988.⁶ In a recent pilot survey of five general practices in the Mersey Region, the overall prevalence for active epilepsy was 0.8% (225 adults and 48 children) of the population, of whom about a third had attended hospital services on at least one occasion within the previous 12 months. Fifty seven per cent had been free of seizures since the previous year and 14% had more than one seizure per month; 8% had some additional neurological, mental, or psychiatric handicaps; 60% of children and 11% of adults had had at least one EEG during the previous 12 months, 26% and 8% some form of scanning, and 82% and 94% respectively were receiving at least one antiepileptic drug.

Diagnosis

The diagnosis of epilepsy is clinical, and is based on a detailed description of events experienced by the patient before, during, and after a seizure and, more importantly, on an eye witness account. In view of the social and economic implications diagnostic errors need to be avoided at all costs. Thus the first basic rule about diagnosing epilepsy is never to make the diagnosis without incontrovertible clinical evidence. If there is any doubt, the clinician should resist the temptation to

Figure 1 Incidence, prevalence, and cumulative incidence rates for epilepsy in Rochester, Minnesota 1935–74 (reproduced from Anderson *et al*^{2a} with permission).

Table 3 Differential diagnosis of epilepsy

Syncope
Reflex syncope:
Postural
Psychogenic
Carotid sinus syncope
Micturition syncope
Valsalva
Cardiac syncope:
Dysrhythmias (heart block, tachycardias, etc)
Valvular disease (especially aortic stenosis)
Cardiomyopathies
Shunts
Perfusion failure:
Hypovolaemia
Syndrome of autonomic failure
Psychogenic attacks:
Pseudoseizures
Panic attacks
Hyperventilation
Night terrors
Breath holding
Transient ischaemic attacks
Migraine
Narcolepsy
Hypoglycaemia

attach a label and should rely on the passage of time and the further description of symptomatic events to reach a firm conclusion. Hardly anyone with epilepsy will come to any harm from a delay in diagnosis whereas a false positive diagnosis is gravely damaging.

IS IT EPILEPSY?

The first test will be to differentiate *seizures* from other transient symptoms (table 3). Syncope and pseudoseizures are most often mistaken for epilepsy. Both are common in young adults. Pseudoseizures may account for anything up to 20% of apparently intractable epilepsies in this age group.⁷ Once it is accepted that seizures have occurred, it is important to determine whether they are acute symptomatic events (not necessarily requiring antiepileptic drug treatment) or spontaneously occurring seizures indicating a truly epileptic disorder. Causes of acute symptomatic seizures include alcohol and other drugs, fever in children aged between 1 and 5 years, and metabolic disturbance. The hallmark of almost all of these types of seizures is that they usually occur in patients with an acute encephalopathy who have an associated confusional state or systemic disturbance that often outlasts the seizures themselves. The presence of other associated symptoms and signs commonly indicates the correct diagnosis for which specific treatment will be required.

WHAT KIND OF EPILEPSY?

Although the diagnosis of a specific epileptic syndrome may require confirmation from interictal or ictal EEG recordings, clinical information will often be sufficient to allow a presumptive diagnosis. Thus a history of occasional nocturnal focal motor seizures involving face or upper limb in children below the age of 12 may strongly suggest benign Rolandic epilepsy, whereas in an adolescent the development of myoclonic jerking on awakening with occasional tonic-clonic seizures points to juvenile myoclonic epilepsy. Seizures associated with a specific epileptic

aura indicate a localised onset and therefore imply a greater likelihood of symptomatic epilepsy caused by a localised cerebral lesion.

WHAT IS THE AETIOLOGY OF THE EPILEPSY?

The cause may be readily apparent from clinical information alone. A previous neurological disorder may often be the cause of the seizures. Thus the history must include direct questions about early perinatal events and development, severe head injury (especially those that are complicated by longlasting post-traumatic amnesia, depressed skull fracture, or intracerebral haematoma), and infection of the CNS. A family history of epilepsy may suggest a genetic cause when seizure disorders develop in persons aged 5 to about 25 years.

THE EEG

The EEG provides valuable information that may (a) add weight to the clinical diagnosis; (b) aid the classification of epilepsy; and (c) show changes that may increase the suspicion of an underlying structural lesion.

EEG as a diagnostic aid

Routine interictal EEG recording is one of the most abused investigations in clinical medicine and is unquestionably responsible for great human suffering. The diagnostic value of an interictal EEG is widely misunderstood. EEGs are often requested either to exclude or to prove a diagnosis of epilepsy—something that can seldom, if ever, be done. Between 10 and 15% of the population may have an “abnormal” EEG; most such abnormalities are mild and of no diagnostic importance. By the use of more rigid definitions of focal or generalised spike or polyspike and slow wave abnormality in the EEG, probably only 1% of a non-epileptic population have such abnormalities. Waking interictal EEGs of patients with epilepsy show that about 35% consistently have specific epileptiform discharges and 50% do so on some occasion with repeated recording; about 15% never do. A single routine EEG is likely to show an epileptiform abnormality in about 50% of patients with epilepsy.

Continuous ambulatory EEG monitoring or videotelemetry may be helpful in the diagnosis of frequent events that can be captured. Such facilities will only be available in specialist centres.

Classification of epilepsy

The EEG is especially important in two clinical settings. In patients with seizures occurring without an aura that are characterised by a brief period of absence with or without automatism, it may be difficult to differentiate absence seizures from complex partial seizures. The finding of generalised spike wave or focal spike activity, respectively, will clarify the diagnosis. The differentiation has important implications for treatment and prognosis. In patients with tonic-clonic seizures without an aura, especially when these occur during sleep, the EEG can again

differentiate between primary generalised epilepsies characterised by generalised spike wave activity and seizures with a focal onset in which there may be localised abnormalities.

Detection of structural brain lesions

The EEG may, by showing the presence of focal slow-wave abnormalities, suggest the presence of a structural lesion as a cause for a patient's epilepsy. This use of the EEG is of diminishing value with the increasing availability of imaging.

NEUROLOGICAL IMAGING IN THE DIAGNOSIS OF EPILEPSY

In practical terms imaging means computed tomography (CT) or magnetic resonance imaging (MRI). The frequency of abnormalities in CT scans of patients with epilepsy varies greatly. In surveys of patients with established epilepsy from specialist centres, 60%–80% may have abnormal CT scans but most of these abnormalities are atrophic in nature. Tumours may be identified in about 10% of patients. In patients who present with either a first seizure or early epilepsy the frequency is lower—abnormalities are detected in less than 20% of cases—but again atrophic abnormalities predominate. Abnormalities on CT scan are very strongly predicted by the presence of focal rather than generalised seizures, focal neurological signs, and focal EEG abnormalities. When all three are present, abnormalities on CT scan may be found in up to 70% or 80% of cases.⁸ CT is most clearly indicated in patients with onset of epilepsy after the age of 20 who have focal seizures.

MRI is increasingly important in epilepsy. In particular it is sensitive in detecting hippocampal and mesial temporal atrophy and sclerosis, which are important causes of drug resistant temporal lobe epilepsy. It can also show dysplastic and developmental extratemporal lesions. It may be more important to offer MRI to patients whose epilepsy is unresponsive to antiepileptic drug treatment than to pursue a policy of indiscriminate MRI of all patients at the presentation of their epilepsy.

Prevention

A role for primary prevention in epilepsy has yet to be clearly identified. Inevitably the incidence of some of the causes of epilepsy in the community may be reduced. Stroke is a common cause of epilepsy in later life and a reduction in its incidence should be accompanied by a decline in the incidence of epilepsy (see earlier). Road traffic accidents represent a major cause of head trauma, some of which will be complicated by post-traumatic epilepsy. Reduced perinatal morbidity and an improved genetic understanding of rare genetic disorders that can be associated with epilepsy could reduce the incidence of epilepsy in early life.

Secondary prevention is of much greater

importance in epilepsy. For many patients the aim of medical or surgical management is a complete cure or control of seizures. It remains controversial whether early intervention with antiepileptic drugs is able to influence the longer term outcome of epilepsy and clinical trials to establish this are of considerable importance. It is important that adequate counselling concerning provocative factors is given to patients and their families. This is particularly the case with febrile seizures where the main arm of management may well be early intervention to control temperature during episodes of infection. Equally, many tonic-clonic seizures occurring in the idiopathic generalised epilepsies may be avoided if subjects are aware of the importance of sleep deprivation and alcohol in provoking seizures. Counselling about alcohol and drug abuse may reduce the recurrence of acute symptomatic seizures.

Seizures contribute to disability by interrupting normal activities of everyday life and by producing forms of behaviour that may be hazardous or be misinterpreted by observers. Of greatest concern to patients and their families is the risk of accidental injury or even death.⁹ Information needs to include sensible counselling to reduce the risks to people with epilepsy from accidental injury from seizures.

MORTALITY FROM EPILEPSY

All available studies show an increased mortality ratio for epilepsy of between two and three times the expected.¹⁰ A number of factors seem to contribute to this. The greatest excess seems to occur in the first decade of life¹¹ or follows soon after diagnosis and is more obvious in the males: the risk is highest for patients with tonic-clonic seizures and seizures that recur often.

Considerable controversy surrounds the contribution of sudden unexpected death in people with epilepsy. Some studies have highlighted cases in which people with epilepsy are found dead, usually in bed.^{12,13} It is assumed that deaths are related to seizures and possibly to associated cardiac dysrhythmias. Accidental death is more common in epilepsy than would be expected, drowning being the commonest cause. Whereas status epilepticus continues to be associated with mortality its rarity means that it does not contribute significantly to the excess mortality associated with epilepsy.

ACCIDENTAL INJURY

Injuries due to falling are not uncommon in people with epilepsy but most injuries are not severe. Intuitively, these are more likely to occur in patients whose epilepsy involves frequent loss of consciousness with or without falls. Unfortunately, very few systematic analyses have been performed.

Hauser *et al*¹⁴ have shown that patients with epilepsy are over-represented ($\times 3$) in a study of non-fatal head trauma, accounting for 7.4% of admissions with such trauma to five New York hospitals. Accidents were significantly more likely to be due to falls and

less likely to be sustained in a road traffic accident than non-epileptic trauma victims. Russell-Jones and Shorvon¹⁵ found that 2.7% of seizures at the Chalfont Centre for Epilepsy resulted in a head injury requiring some medical intervention, but only one in over 9000 seizures was complicated by skull fracture or intracranial haematoma.

There have been no studies of the incidence of burns in unselected populations of patients with epilepsy. It is suggested, however, that epilepsy is over-represented as a cause of burns. Bhatnagar¹⁶ in a retrospective review of presentations to an Indian burns unit, identified epilepsy as the cause of 2.6% of all burns, and 8.4% of those requiring admission. In a study of patients attending an epilepsy clinic 38% of patients had a history of burns with 13% seeking hospital treatment, 4% requiring admission, and 1% needing skin grafts. Those who sustained burns were older, had a longer history of epilepsy and were more likely to have complex partial seizures than those who had no history of burns.¹⁷

EPILEPSY AND PSYCHOSOCIAL HANDICAP

The social, psychological, and emotional problems encountered with epilepsy are considerable and may be complicated by the effects of associated neurological impairments and the effects of anticonvulsant therapy.¹⁸⁻²⁰ Psychosocial problems may be the result of the unpredictability and the severity of seizures, rather than their frequency.²¹ The fear evoked by the unpredictable nature of the seizures may lead to social withdrawal, with loss of existing friendships and an inability to form new relationships. Loss of employment or inability to compete in the job market may lead to loss of self-esteem and financial hardship. These factors often result in anxiety, depression, and a loss of sense of control. This loss of control may have serious psychological consequences, including feelings of helplessness and low self-esteem.^{20, 22}

EPILEPSY AND PSYCHIATRIC DISORDERS

The relation between epilepsy and psychiatric disorders has evoked much discussion. Studies on unselected populations of patients have shown an increased incidence of psychiatric illness in patients with epilepsy.^{23, 24} These show that, in both adults and children, having epilepsy rather than other chronic conditions is associated with increased psychopathology. A recent general practice survey²⁵ has shown that psychiatric morbidity (especially anxiety and non-psychiatric depression) occurs more commonly in people with epilepsy than would be expected by chance and is particularly common in patients with focal epilepsy as opposed to primary generalised epilepsy.

There have been some conflicting studies investigating the incidence and prevalence of interictal as opposed to postictal psychosis in patients with epilepsy. Pond and Bidwell found that 29% of a general practice population of people with epilepsy had a history of

psychiatric illness but none of psychosis.²³ By contrast, studies on outpatients have reported a prevalence of between 2% and 5% for psychosis.^{26, 27} In an earlier study of 69 patients with schizophrenia-like psychosis, 80% were found to have focal temporal lobe EEG abnormalities,²⁸ leading the authors to conclude that the characteristics of the psychoses accompanying epilepsy were distinct from functional psychosis. This finding has not, however, been confirmed in subsequent prospective studies.²⁹

A review of studies of mortality and suicide in epilepsy by Barraclough³⁰ confirmed that there was an increased risk of suicide in persons with epilepsy. Barraclough estimated a fivefold increase in incidence of those with temporal lobe epilepsy. Feelings of helplessness, lack of control, low self-esteem and anxiety were important risk factors in the aetiology of suicide.

Prognosis

Most studies have been hospital based; this has an adverse effect on apparent outcome because patients with refractory epilepsy are more likely to be referred to specialist centres. In this respect the study of Annegers *et al*³¹ is of particular importance in being community rather than hospital based. Four hundred and fifty seven patients identified in Rochester, USA, with a history of two or more non-febrile seizures, were followed up for at least five years, and in the case of 141 for 20 years. The probability of being in a remission lasting for five years or more was 61% at 10 years, and as high as 70% at 20 years (fig 2). Results of this large study are supported by those of a smaller one of 122 patients drawn

Figure 2 Actuarial percentage of patients in remission after a diagnosis of epilepsy (reproduced from Annegers *et al*³¹ with permission).

from a general practice population.³² By 15 years after the onset of seizures, 80% of these patients had achieved a two year remission, and only 38% were still taking antiepileptic drugs. Further support for such high rates of remission has been obtained from studies of patients followed up prospectively from diagnosis and the commencement of treatment, which show that between 50% and 77% of such patients are "controlled", depending on how control is defined.^{33 34}

FACTORS INFLUENCING PROGNOSIS

Age of onset of epilepsy seems the most important. Seizures beginning within the first year of life (when they are usually symptomatic of cerebral pathology), carry an adverse prognosis,³⁵ but this aside, Annegers *et al*³¹ found that both partial and generalised epilepsies had a better prognosis if they started before the age of 20.

Whatever the age of onset, the duration of the epilepsy before treatment seems to be an important prognostic factor. Annegers *et al*³¹ showed that most patients who achieve remission do so early during the course of treatment. With continuing seizures it becomes progressively less likely that an individual patient will enter remission.³⁴ Thus there is a plateau in the proportion of patients in remission 15–20 years after the onset of epilepsy. Similar findings have been reported with shorter term follow up in children.³⁵

Seizure classification is of importance in determining outcome. Remission rates range from around 60% to 80% for patients with only tonic-clonic seizures, and between 20% and 60% in patients with complex partial seizures.^{33 36} The combination of complex partial seizures with secondary generalised tonic-clonic seizures carries an adverse prognosis, tonic-clonic seizures coming under good control with anticonvulsant therapy, whereas partial seizures remain resistant to drug treatment.^{33 37} Generalised epilepsies of childhood carry varying prognoses. Between 70% and 80% of patients with simple absences (petit mal) are likely to enter remission.^{35 35a} Complex absences show a lesser remission rate (33%–65%), and in patients with the West or Lennox-Gastaut syndromes remission rates may be as low as 35% to 65%.

Epilepsy of unknown aetiology has a better prognosis than symptomatic epilepsy.^{31 36} In keeping with this, epilepsy complicated by an

associated neurological or psychiatric deficit carries an adverse prognosis.³⁵

There is no clear indication that any specific abnormalities on EEG either in historical EEGs or at a particular point in time when prognosis is to be predicted are of any great value.^{37 38}

The evidence about the factors affecting the prognosis of epilepsy does not allow any satisfactory quantification and assessment of the varying weights that prognostic factors carry. The prognosis of 306 patients diagnosed between 1935 and 1978 was studied³⁹ using Cox's proportional hazards model to investigate those factors determining the likelihood of achieving a five-year seizure-free period and a five-year seizure-free period off drugs. It can be seen (table 4) that no single factor is strongly predictive of remission, but those that are include the absence of early brain damage, never having had a tonic-clonic seizure, and the absence of generalised spike-wave activity from a number of EEGs. Similar factors were also predictive of five-year seizure-free periods off antiepileptic drugs.

Communication and counselling

DIAGNOSIS

The diagnosis of epilepsy is often frightening and disconcerting for patients and their families. There remains a considerable misunderstanding of the nature of epilepsy and it is one of the few organic neurological diagnoses associated with considerable stigma. For this reason patients need a careful explanation of the basis of epilepsy; an emphasis that it is an organic disorder and that it is not a primary psychiatric disorder or stroke. Patients and their families need time to assimilate this information and to ask any relevant questions. Supplementary written information is extremely valuable and the epilepsy associations are good sources of this. Often, doctors are poor information givers and patients may feel unable to ask the questions that they want answered. As clinical time is often limited, intervention by knowledgeable counselors or specialist nurse services probably represent a better way of addressing these issues.

EFFECTS OF PROGNOSIS AND TREATMENT

At the time of diagnosis patients need to be given a clear indication of the likely outcome of their epilepsy and in particular whether treatment with antiepileptic drugs is necessary, and if so for how long it may need to be maintained. Failure to provide satisfactory information is bound to complicate the problems of poor compliance.

IMPLICATIONS OF EPILEPSY AND LIMITATION OF SOCIAL DISADVANTAGE

The unpredictable nature of epileptic seizures and the stigmatisation and concealment that often comes with the diagnosis creates particular problems that must be considered at an early stage. There can be a considerable fear

Table 4 Factors affecting prognosis of epilepsy (from Shaffer *et al*³⁹)

Factor	Five years seizure free Relative risk (95% CL)*	Five years seizure free and off medication Relative risk (95% CL)
Age < 16 at first fit	1.09 (0.82–1.44)	1.88 (1.23–2.8)
No early brain damage	2.15 (1.22–3.78)	4.27 (1.35–13.47)
No known aetiology	1.50 (1.05–2.13)	2.64 (1.45–2.84)
Never had a tonic-clonic fit	1.37 (1.03–1.82)	2.19 (1.48–3.24)
No generalised spike-wave in third year EEG	3.47 (1.37–8.8)	2.36 (0.56–10.16)

*Univariate Cox regression estimate of relative risk from 298 patients.
CL = Confidence limits.

of accidental injury or death as a result of seizures. Any counselling about these risks needs to be put clearly in context. Although sensible avoidance of higher risk situations needs to be emphasised, overprotection and limitation should be avoided except in the most severe of the epilepsies.

For most, reassurance about the low risks of serious injury by accident seems appropriate, perhaps with advice to avoid climbing to appreciable heights, to use microwave cooking in preference to gas or electric hobs, and to ensure that fires are adequately guarded. Showers are to be preferred to baths, and swimming in open water best avoided. For most people a full range of leisure activities should be possible although perhaps with some accompanying supervision where appropriate (for instance, swimming in a pool or cycling on a busy road).

For patients with frequent seizures complicated by falls more supervision and attendance may be necessary and occasionally protective helmets may be worn although these can be regarded as unduly stigmatising by some.

For children, liaison with schools concerning the diagnosis of epilepsy is important and teaching staff need to be reassured and advised about the child usually being able to fulfil a full pattern of school activity with the likely exception of climbing. Epilepsy itself is rarely a reason for special education and most children will be in main stream schooling. Special education is usually necessary for those children with associated mental and neurological handicap.

One of the most important implications of the diagnosis of epilepsy in adults is the effect on driving. In the United Kingdom the diagnosis results in an immediate disqualification from all forms of driving, which will continue until a seizure-free period lasting two years has been attained, or until only seizures beginning during sleep have occurred for at least three years. Where a single seizure has occurred, a seizure-free period of one year is usually required unless the seizure is associated with some form of structural brain disease, such as a stroke or cerebral tumour. In these circumstances, and where an EEG shows the presence of classical three cycle spike-wave activity indicative of an absence epilepsy, the usual two year period of disqualification will apply. Drivers with epilepsy must be informed of the legal requirement to inform the Driver and Vehicle Licensing Agency of recent seizures.

Employment issues also demand discussion. It is unwise for people with a recent history of epilepsy to work at heights or close to large volumes of water that might present a risk. The risks of working with machinery require more selective evaluation as now most factory machinery should be adequately protected. Unfortunately, the diagnosis of epilepsy inevitably leads to significant employment problems. There are statutory limitations that affect the driving of public service or heavy goods vehicles and employ-

ment as an airline pilot, taxi driver, train driver, etc. People with epilepsy also experience considerable unwarranted job discrimination and they need careful counselling about how and when to declare a history of epilepsy to a prospective employer.

For women it is important to explain the relevance of epilepsy and its drug treatment to contraception (interaction with oral contraceptives), pregnancy (risks of teratogenicity), and the genetic risk of epilepsy in the offspring.

SHARING CARE

Because of the variable nature and severity of epilepsy no single system of care is appropriate for all patients and many different agencies will come into contact with many people with epilepsy. For this reason effective systems of liaison should exist between the agencies that may be involved and the primary aim must be to offer continuity of care with a single clearly identified clinician having the prime responsibility for the medical management of the individual patient.

The diagnosis and initiation of treatment of the epilepsy will usually require specialist skills. Most patients with newly diagnosed epilepsy, however, quickly enter a remission and at this stage the patient's general practitioner can usually assume responsibility. Rereferral to specialist services may be required after two to three years of remission for counselling about withdrawal of antiepileptic drugs. Patients with poorly controlled seizures may also benefit from specialist referral for reconsideration of the diagnosis, second line or newer drug treatment, or where appropriate, consideration of surgical treatment. There is no doubt that standards of care could often be improved by better liaison between primary care and specialist services. The use of liaison cards for epilepsy is poorly developed and would seem highly appropriate. Shared care systems for people with diabetes have made extensive use of nurse practitioners as "key workers". This model would also be of particular benefit in epilepsy where a specialist liaison nurse working between specialist services and general practice could improve communication, not only with general practitioners but also with other community teams dealing with learning disability and psychiatric disorder.

One area where communications often break down is in the transfer of people with epilepsy from paediatric to adult services. This is a particularly traumatic time in that the state guarantees the individual patient a place in society with his or her peer group up until the age of 16, but after leaving school no such guarantee is extended to further education, training, and employment. At the same time the young person with epilepsy is often discharged from the well integrated paediatric services and has to cope with forming relations with a new clinician dealing with adults, and who is less well equipped to provide a comprehensive system of clinical and social support. Here there seems to be a clear role

for joint specialist clinics run by paediatricians and neurologists who work with adults to facilitate the process of the handing over of care.

Management

STARTING TREATMENT

Antiepileptic treatment has, in the past, been advocated before seizures occur. Such prophylactic treatment has been undertaken in patients with a high prospective risk of epilepsy after head injury and craniotomy for various neurosurgical conditions.⁴⁰ Because no clear evidence exists that antiepileptic treatment is effective in preventing late epilepsy,^{41 42} it seems better to delay treatment until seizures have occurred rather than to adopt a policy of treatment of all those at risk—particularly as there may be a high incidence of side effects with prophylactic treatment⁴³ and poor compliance.⁴⁴

When two or more unprovoked seizures have occurred within a short interval, antiepileptic treatment is usually indicated. Problems do, however, arise in defining a short interval. Most would include periods of six months to one year within the definition. Even where seizures occur in a close temporal relation, the identification of specific precipitating factors may make it more important to counsel patients than to commence drug treatment. The most common examples are febrile convulsions in children and alcohol withdrawal seizures in adults. Less commonly, seizures may be precipitated in photosensitive subjects by television, visual display units, or other photic stimuli.

CHOICE OF DRUG

There is now considerable evidence⁴⁵ that patients with newly diagnosed epilepsy should be treated with a single drug. The major factors that influence the choice of antiepileptic drug are comparative efficacy and toxicity.

Although many clinicians have been persuaded that one drug is likely to be most effective against particular seizure types and epileptic syndromes, it is difficult to identify satisfactory clinical trials that support this contention.⁴⁶ Table 5 summarises conventional practice. In children the differences in efficacy between sodium valproate and etho-

suximide on the one hand, and phenytoin and carbamazepine on the other in the treatment of absence seizures seem too obvious to demand confirmation in a prospective clinical study. Studies do not, however, differentiate between the efficacy of sodium valproate and ethosuximide in absence epilepsy.^{47 48} Similarly, the preferential response of juvenile myoclonic epilepsy to sodium valproate seems to identify this as the drug of choice in this syndrome.⁴⁹ It is much more doubtful whether there are major differences in efficacy between carbamazepine, phenytoin, barbiturates, and sodium valproate in the treatment of partial epilepsies.^{46 50–52}

Where differences in efficacy are marginal, the importance of comparative drug toxicity becomes a major consideration in the choice of antiepileptic agent. Antiepileptic drugs possess four distinct types of toxicity: acute dose-related toxicity, acute idiosyncratic toxicity, chronic toxicity, and teratogenicity.

ACUTE DOSE RELATED TOXICITY

Most antiepileptic drugs, including phenytoin, carbamazepine, barbiturates, and benzodiazepines, give rise to a non-specific encephalopathy associated with high blood concentrations. Patients exhibit sedation and nystagmus and, with increasing blood concentration, ataxia, dysarthria, and ultimately confusion and drowsiness.⁵³ In some instances frequency of seizures may increase with high blood concentrations and occasionally involuntary movements are seen, particularly with phenytoin.⁵⁴ Phenytoin is especially likely to result in dose-related toxicity because of its unusual pharmacokinetics (see later). Carbamazepine may cause similar symptoms if the dose is not built up slowly. This is probably related to autoinduction of liver microsomal enzymes. Sodium valproate does not seem to be associated with this typical syndrome of neurotoxicity, but some patients with high blood concentrations may exhibit restlessness and irritability (sometimes with a frank confusion state). Postural tremor is a common accompaniment.⁵⁵

All antiepileptic drugs have adverse effects on cognitive function of behaviour at therapeutic concentrations that become more apparent both with polytherapy and with increasing blood concentrations. Agents such as carbamazepine and sodium valproate have fewer adverse effects in this respect and this is one argument for preferring these agents to longer established antiepileptic drugs.

Toxicity may occur because of drug interactions. Thus valproate may potentiate the sedative effects of phenobarbitone and greatly prolong the half life of lamotrigine, making dosage reduction necessary during comedication.

ACUTE IDIOSYNCRATIC TOXICITY

Most antiepileptic drugs, particularly phenytoin, carbamazepine and lamotrigine, may cause a maculopapular erythematous eruption which, in more severe cases, may be associated with fever, lymphadenopathy, and

Table 5 Choice of antiepileptic drugs (adapted from Chadwick^{46a})

	First line drugs	Second line drugs
Generalised epilepsy		
Idiopathic		
Simple absence	VPA, ESM	BZPs, LTG
Juvenile myoclonic	VPA	PHB, LTG
Awakening tonic-clonic	VPA	CBZ, PHT, LTG
Symptomatic	VPA, BZPs	CBZ, PHT, PHB
Partial epilepsy	CBZ, VPA	PHT, PHB, VGB
Unclassified epilepsy	VPA	LTG

VPA = sodium valproate; CBZ = carbamazepine; PHT = phenytoin; PHB = phenobarbitone; ESM = ethosuximide; BZPs = benzodiazepine; LTG = lamotrigine; VGB = vigabatrin.

hepatitis.⁵³ The incidence of allergic skin reaction with phenytoin may be as high as 10% and with carbamazepine up to 15%.⁴³ It may be possible to avoid such reactions with a cautious build up of initial doses. Marrow aplasia is a rare complication of carbamazepine. Reports of fatal liver failure in association with sodium valproate treatment largely concern children under the age of two years who often have multiple handicaps and receive many different antiepileptic drugs. It may be that they have an underlying error of metabolism that predisposes them to liver failure.⁵⁶ Vigabatrin has been associated with behaviour disorders and psychosis, particularly in patients with a psychiatric history.⁵⁷ The potential for rare idiosyncratic side effects of lamotrigine and gabapentin is currently uncertain.

CHRONIC TOXICITY

Antiepileptic drugs are unusual in that they may be given to patients over long periods as treatment for chronic epilepsy. This may lead to the development of a wide variety of syndromes of chronic toxicity (table 6). A number of factors seem to predispose to the development of these disorders—namely, the use of polypharmacy, the dosage, and the duration of treatment. Although it seems that sodium valproate and carbamazepine may have fewer chronic toxic effects than barbiturates and phenytoin, the time that elapsed before common chronic toxic effects were recognised with the older agents should warn us that continued vigilance is needed in the use of the newer antiepileptic drugs.

TERATOGENICITY

All antiepileptic drugs must be regarded as potentially teratogenic. Phenytoin, and probably barbiturate antiepileptic drugs, seem to increase the risk of major fetal malformation

by two to three times: the most common malformations are hare-lip, cleft palate, and cardiovascular anomalies. The risks are higher with polytherapy than with monotherapy. There seems to be an association between neural tube defects and exposure to sodium valproate or carbamazepine. Estimates of this risk suggest it is 1% to 2% of pregnancies on these drugs.^{58,59} Patients should be advised to take folate supplements. Early screening for neural tube defects, by ultrasound and amniocentesis, and testing for α -fetoprotein, therefore, seem to be indicated in women becoming pregnant while taking these drugs.

LONG-TERM MANAGEMENT OF DRUG TREATMENT

Most patients developing epilepsy achieve a long-lasting remission soon after the start of treatment. For these patients drug withdrawal may be considered after two, three, or more years (see later). Some 20% of patients developing epilepsy have a chronic disorder uncontrolled by drugs. In patients receiving, and complying with, optimal doses of a single antiepileptic drug, the addition of further agents is likely to result in a significant (> 75%) improvement in seizure control in only about 10% of patients.⁶⁰ Such a policy, however, inevitably increases the risks of dose-related, idiosyncratic, and chronic toxicity. In essence, a law of diminishing returns applies. Thus for this group of patients an appropriate aim may not be complete remission of seizures but a compromise of reduced seizure frequency with less severe seizures, to be achieved with one, or at most two, drugs.

Some patients may continue to have seizures but are not disabled by them; they may have very infrequent seizures or seizures that are minor in their symptomatology or confined to sleep. In such patients, assuming that a single drug appropriate to the seizure type and epilepsy syndrome has been used, there is usually little to be gained from alternative or additional drugs.

Patients who continue to be disabled by the occurrence of seizures despite treatment with a single drug in optimal dosage demand further careful consideration. In particular it is important to consider whether there are factors that would explain an unsatisfactory response to treatment—for example, unidentified structural pathology, the presence of complex partial seizures, poor compliance, or pseudoseizures. If this is not the case, then it is important to review the diagnosis: a common reason for failure of treatment is that the patient does not have epilepsy.

Where none of these conditions apply, it may be reasonable to try alternative drugs as monotherapy, and in some instances to undertake a trial of the addition of a second drug. This demands careful discussion with the patient, however, and the understanding that the second drug will be withdrawn in the absence of a satisfactory sustained response. Patients with intractable partial seizures despite adequate drug treatment may benefit from surgical treatment (see later).

Table 6 Chronic toxicity of anticonvulsant drugs (adapted from ref ^{57a})

Nervous system:
Memory and cognitive impairment
Hyperactivity and behavioural disturbance
Pseudodementia
Cerebellar atrophy
Peripheral neuropathy
Skin:
Acne
Hirsutism
Alopecia
Chloasma
Liver:
Enzyme induction
Blood:
Megaloblastic anaemia
Thrombocytopenia
Lymphoma
Immune system:
IgA deficiency
Drug-induced systemic lupus erythematosus
Endocrine system:
Decreased thyroxine concentrations
Increased cortisol and sex hormone metabolism
Bone:
Osteomalacia:
Connective tissue:
Gum hypertrophy
Coarsened facial features
Dupuytren's contracture
Pregnancy:
Obstetric complications
Teratogenicity
Fetal hydantoin syndrome

Table 7 Pharmacokinetics of anticonvulsant drugs (adapted from ref 57a)

Drug	Absorption (time to peak serum conc (h) after oral dose)	Protein binding (%)	Active metabolites	Metabolism	
				Half life (h)	Doses/ day
Phenytoin	4–12	90	—	9–140	1
Phenobarbitone	1–6	45	—	50–160	2
Primidone	2–5	20	Phenobarbitone: phenylethyl- malonamide	4–12	2
Carbamazepine	4–24	75	10,11-Epoxyde	8–30	2 or 3
Valproate	1–4	90	—	8–20	2 or 3
Ethosuximide	1–4	—	—	40–70	2 or 3
Vigabatrin	1–2	—	—	5–7	1 or 2
Lamotrigine	2–3	50	—	12–48	2

ADMINISTERING AND MONITORING DRUG TREATMENT

Pharmacokinetic data (table 7) defines drug absorption, distribution, metabolism, and elimination, but it does not describe the mode of action of drugs in the CNS. One clinical application of pharmacokinetics is therapeutic drug monitoring in serum or plasma, but this technique samples a physiological pool that can be remote from the site of drug action.

Phenytoin has a non-linear relation between the dose and the serum concentration.⁶¹ This results in a narrow therapeutic window, and monitoring is necessary to avoid neurotoxicity in patients whose dosage is being increased. The concept of the “therapeutic” or “optimal” range for phenytoin has been extended to other antiepileptic drugs, and many laboratories now routinely estimate serum concentrations of drugs other than phenytoin. This is seen increasingly as a questionable practice.

A single measurement will give a good approximation of the steady state concentration for drugs with long half lives (phenytoin and phenobarbitone) but not for drugs with short half lives. Measurements of sodium valproate concentrations from specimens taken at random during the day are virtually uninterpretable as they may represent unpredictable peak, trough, or intermediate concentrations. Collecting early morning specimens for measuring troughs is, however, rarely practicable.

It is important to be aware of what is measured during routine estimations of blood concentrations of antiepileptic drugs and, perhaps more importantly, what is not measured. Some drugs have metabolites that contribute to the therapeutic effect but which are not routinely assayed. These include the 10,11-epoxide of carbamazepine and phenylethylmalonamide derived from primidone. Most laboratories in the United Kingdom determine the drug concentration in whole plasma or serum. Phenytoin, carbamazepine, and sodium valproate are heavily protein-bound, but only the free drug fraction is in equilibrium with the brain and pharmacologically active. Measurement of free drug concentrations by equilibrium dialysis or ultrafiltration techniques are expensive and not readily available.

Even when concentrations of free drugs and their metabolites in the blood are known, important pharmacodynamic considerations may alter the relation between the blood concentration and the therapeutic effect. Thus for sodium valproate the onset of action is slower and longer lasting than can be explained by the pharmacokinetics of the drug.⁶² Similarly, tolerance to the neurotoxicity and therapeutic effects of benzodiazepines and barbiturate drugs is unexplained by pharmacokinetic changes and must be due to drug-receptor interaction.

There are further fundamental biological reasons for doubting the value of routine monitoring of blood concentrations of antiepileptic drugs. The upper limit of a therapeutic range may be defined as the concentration of the drug at which toxic effects are likely to appear. The most consistent relation between the serum concentration and toxic effect is for phenytoin, but even with this drug some patients may tolerate, and indeed require, serum concentrations above 20 µg/ml.⁶³ For sodium valproate, phenobarbitone, and carbamazepine there is a wide variation in individual tolerance of serum concentrations.

The lower limit of the therapeutic range is even more difficult to define, and most patients have epilepsy that is controlled by antiepileptic serum concentrations well below the optimal range.³³ Unquestioning acceptance of therapeutic ranges creates problems: patients with satisfactory control of seizures and low blood concentrations of drugs may have their doses needlessly increased, and patients who tolerate and need high blood concentrations may have their doses reduced. Treating patients is much more important than treating blood concentrations.

Routine monitoring should increasingly be restricted to certain categories of patients: firstly, those receiving phenytoin or multiple drug treatment in whom dosage adjustment is necessary because of dose-related toxicity and poor seizure control; secondly, mentally retarded patients in whom the assessment of toxicity may be difficult; thirdly, patients with renal or hepatic disease; and fourthly, perhaps pregnant patients⁶⁴ in whom monitoring of free drug concentrations may be indicated; and, finally, patients who may not be complying with treatment.

ANTIEPILEPTIC DRUG WITHDRAWAL

The fact that antiepileptic drugs have been associated with many adverse reactions is a potent argument for exploring the possibility of withdrawing drugs in patients who achieve remissions lasting two, three, or more years. Against this are the dangers of a recurrence of seizures, which may have important consequences for driving and employment as well as self-esteem.

Advice offered to patients on this subject varies widely. Paediatricians and paediatric neurologists suggest a trial withdrawal of antiepileptic drugs in most children attaining remission, as they are concerned about the

impact of drugs on cognitive function and learning, and are impressed by the high expectation of success. Neurologists tend to be much more circumspect when dealing with adults, expressing concern over the possible effects of further seizures on driving and employment. In the United Kingdom, if not elsewhere, most patients attaining prolonged remission are unlikely to receive any advice from a neurologist or other physician with an interest in the treatment of epilepsy because they will have been discharged from regular follow up. Of 122 patients with a history of epilepsy drawn from general practice, 49 had stopped treatment, most of them on their own initiative.³²

The few studies that have been undertaken to determine the success of withdrawing drugs and the factors that identify patients likely to remain free of seizures have been reviewed.^{65,66} Comparison of the available studies is difficult because there is often little information about the patients, a lack of uniformity in the duration of remission before withdrawal of the antiepileptic drugs, and no information about the period over which withdrawal occurred and for how long patients were subsequently followed up.

One question that has not been widely considered is the relative risk of recurrence on withdrawal of antiepileptic drugs compared with continued treatment. The Medical Research Council Antiepileptic Drug Withdrawal Group⁶⁷ studied this in a randomised clinical trial. The risk of relapse on continued treatment was about 10% per annum, but was two to three times greater in the group withdrawing treatment for up to two years after commencing withdrawal.

A more detailed assessment of prognostic factors has also been undertaken in the Medical Research Council Antiepileptic Drug Withdrawal Study. Relatively few clinical factors influenced the risk of recurrence. A Cox's proportional hazard model selected seven prognostic factors for increased risk of seizures recurring: age 16 years and over (relative risk 1.75); taking more than one antiepileptic drug (1.83); a history of seizures after starting antiepileptic drug treatment (1.56); a history of tonic-clonic seizures (primarily or secondarily generalised) (1.56); a history of myoclonic seizures (1.84); and an

abnormal electroencephalogram in the previous year (1.32). The risk of recurrence also declined as the period without seizures increased, but in a complex way.

These factors have been used to generate a statistical model for everyday practical use (table 8).⁶⁸ The index can be used to obtain estimates of the probabilities of seizures recurring within one and two years of starting slow withdrawal of antiepileptic drugs or continuing treatment. The estimates can easily be calculated on a pocket calculator.

This model, derived from the only randomised study of withdrawal of antiepileptic drugs from patients in remission, provides the best available information for patients considering drug withdrawal. 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 licence are often as important or more important than the risk of recurrence of seizures.

SURGICAL TREATMENT OF EPILEPSY

Although the surgical treatment of epilepsy was pioneered in the United Kingdom over 100 years ago, it has never been made widely available to patients with epilepsy. The increasing sophistication of EEG investigation, neurological imaging, and neuropsychology, however, means that this form of treatment can be highly successful in large numbers of patients. It has been estimated that at least 75 000 patients in the United States may be suitable for surgical treatment⁶⁹ and in the United Kingdom there may be well over 12 000 patients who would benefit.

The philosophy of surgical treatment requires either the accurate identification and excision of the localised site of seizure onset or the disconnection of epileptogenic zones, so as to interrupt seizure spread in a palliative procedure (callosotomy or multiple sub-pial resections).

Engel⁷⁰ reviewed the varying procedures undertaken at centres worldwide. Sixty eight per cent of operations involve some form of temporal lobe surgery, whereas extratemporal cortical excisions accounted for 24% of operations; 2% were hemispherectomies and 6% corpus callosotomy. To be considered for any of these procedures, patients need to have a history of medically refractory epilepsy and be sufficiently disabled by their epilepsy to warrant the risks of surgical treatment and the necessary presurgical evaluation. There should be a high probability that an improvement in seizure control will lead to a significant improvement in the patient's quality of life. The evaluation of patients for surgical treatment requires a multidisciplinary specialist team (table 9).

Temporal lobe surgery

There is no doubt that patients with mesial temporal lesions experience the best results from epilepsy surgery. The ideal candidate for temporal lobe surgery has a history of seizures typical of a medial temporal onset, an initial

Table 8 Prognostic index for seizure recurrence by one and two years under policies of continued antiepileptic drug (AED) treatment and slow withdrawal

1	Starting score (all patients)	—	—175
2	Age 16 years or older	Add	45
3	Taking more than one AED	Add	50
4	Seizures after the start of AED treatment	Add	35
5	History of primary or secondarily generalised tonic-clonic seizures	Add	35
6	History of myoclonic seizures	Add	50
7	EEG in past year		
	Not available	Add	15
	Abnormal	Add	20
8	Period seizure-free in years(t)	Add	200/t
9	Total score		T
10	Divide total score by 100 and exponentiate (e^z) $z = e^{T/100}$		
Probability of seizure recurrence			
	By one year	By two years	
On continued treatment	1-0.89 ^z	1-0.79 ^z	
On slow withdrawal	1-0.69 ^z	1-0.60 ^z	

Table 9 Requirements for surgery for epilepsy

Expertise	Investigation/intervention	Role
Neurologist/epileptologist Neurophysiologist	Trial of antiepileptic drugs Interictal EEG Ictal EEG Surface electrodes Sphenoidal electrodes Foramen ovale* Subdural electrodes* Depth electrodes*	Selection of suitable patients Lateralisation and localisation of seizure onset
Neuroradiologist	MR imaging and volumetry SPECT and PET scanning*	
Neuropsychologist	Cognitive assessment Intracarotid amytal	Identification of foreign tissue lesions, dysplasia, and mesial temporal sclerosis. Identification of interictal hypoperfusion and hypometabolism
Neuropsychiatrist	Preoperative assessment Postoperative support and treatment	Lateralisation of functional deficits and predictive testing of effects of surgery
Neurosurgeon	Appropriate surgical treatment	Identification of high risk patients

*May not be essential in all centres.

epigastric aura being the most common mode of onset.⁷¹ The two pathological conditions with the best outcome are those of mesial temporal sclerosis (Ammon's horn sclerosis) or an indolent glioma of the medial temporal region,⁷² both of which may be defined by MRI. In the first a history of a prolonged febrile seizure before the age of 4 or 5 years is a particularly strong clinical indicator. Patients should usually be between the ages of 12 and 30 years, as psychosocial adjustment may be more difficult in patients having resective surgery after the age of 30.⁷³ Patients will show a unilateral anterior temporal interictal spike, and sphenoidal or other ictal surface recordings will confirm a temporal onset to seizures.

It must be recognised that many patients who do not conform to these criteria will, nevertheless, have a significant chance of benefiting from temporal lobe surgery, although they may require more detailed presurgical evaluation. All adolescents and young adults with refractory temporal lobe epilepsy should be offered appropriate presurgical evaluation.

The outcome of temporal lobe surgery and other operations is summarised in table 10. The most common surgical procedure is the en bloc anterotemporal lobectomy pioneered by Falconer *et al.*⁷⁴ More recently, amygdalo-hippocampectomy has been pioneered for patients in whom it can be shown that there is a definite medical temporal onset to seizures.⁷⁵ Potentially, this procedure may offer results as good as classical en bloc resection with, hopefully, a reduced morbidity.

Extratemporal cortical excisions

The outcome of such procedures is somewhat less satisfactory than temporal lobe surgery but extratemporal resections can reasonably be considered in patients with localised extratemporal lesions defined by imaging techniques and in patients where neurophysiological investigation reveals a consistent focal onset to seizures outside the temporal lobe. Complex partial seizures arising from frontal-orbital areas may be particularly helped by surgery.⁷⁶

Hemispherectomy

This procedure may be suitable for patients with intractable epilepsy and an infantile hemiplegia⁷⁷ with a useless hand and also in those children with rare chronic progressive focal encephalitis (Rasmussen's syndrome). Overall, 70% to 80% of patients become free of seizures after this operation, and behavioural abnormalities can also improve.

Callosotomy

Section of the corpus callosum and hippocampal commissure is an accepted palliative procedure for uncontrolled secondary generalised seizures.⁷⁸ The selection criteria for corpus callosotomy are more poorly defined than for other surgical procedures. The operation is most commonly considered in children and adolescents with very severe epilepsy, with a multifocal origin to seizures, or with seizures of sudden onset resulting in falls.

Clinical audit in epilepsy

It is generally accepted that health care systems should provide not only treatments of confirmed efficacy but that the provision should take place with the maximum effectiveness and efficiency. Donabedian⁷⁹ has defined three constituents of the quality of care: structure (the instruments of care of their organisation); process (the activities of care); and outcome (the end results of care). In the United Kingdom as elsewhere there has been an increasing emphasis in recent years on the need for medical audit, defined as "the systematic critical analysis of the quality of medical care . . .". Kessner *et al.*⁸⁰ have

Table 10 Survey results: outcome with respect to epileptic seizures (reproduced from Engel⁷⁰)

Classification	Hemispherectomy	Anterior temporal lobectomy	Extratemporal resection	Corpus callosum section
Total patients	88	2336	825	197
Total centres	17	40	32	16
No seizure-free	68	1296	356	10
Percentage (range)	77.3 (0-100)	55.5 (26-80)	43.2 (0-73)	5.0 (0-13)
No improved	16	648	229	140
Percentage	18.2	27.7	27.8	71.0
No not improved	4	392	240	47
Percentage (range)	4.5 (0-33)	16.8 (6-29)	29.1 (17-89)	23.9 (10-38)

listed a number of criteria that should be met if a condition is to be a useful tracer for an audit:

(1) It should have a definite functional impact (so conditions that are self-limiting and for which there is no specific treatment are not useful).

(2) It should have a prevalence sufficiently high to allow collection of adequate data.

(3) It should be well defined and easy to diagnose.

(4) Its natural history should vary with the utilisation and effectiveness of medical care.

(5) Techniques of medical management should be well defined for at least one of prevention, diagnosis, treatment, or rehabilitation.

(6) The effect on the condition of non-medical factors should be understood.

Epilepsy represents an appropriate condition for audit as it fulfils the first two of these criteria wholly and the next three partially. We know little about the last criteria in relation to epilepsy, but can assume that it is considerable.

There has been little systematic work in developing comprehensive means of assessing quality of care in epilepsy. In the United Kingdom, government reports on services for people with epilepsy have emphasised the importance of the primary health care services, specialist epilepsy clinics, and assessment centres in the management of epilepsy, in both its medical and psychosocial dimensions. The report of the working group on services for people with epilepsy⁸¹ stated that whereas general practitioners should normally refer all their patients with seizures to a hospital consultant for diagnosis, initial assessment and recommendations for treatment, patients should thereafter be cared for by the general practitioner, except in specific cases where problems persist, recur, or develop.

Assessments of the process of care in epilepsy should particularly focus on issues of communications and the interpersonal aspects of care. In this respect patient's satisfaction may be seen as representing one important outcome of care, and it also speaks to the measurement of the process of care.

Previous research suggests that patients' satisfaction makes a direct contribution to other important outcomes.⁸² Thus patients who are less satisfied with care are less likely to comply with treatment regimens and are less likely to reattend for treatment—both factors that are important in achieving good management and control of epilepsy. With this in mind a model for the audit of care in epilepsy can be proposed, particularly examining adequacy of diagnosis, ongoing care, information provision, and psychosocial adjustment. A structure should exist that provides primary care services with the specialist expertise, investigational, and treatment facilities necessary for the population in question. Assessment of the process and outcome of care may use some of the criteria in table 11.

Table 11 Audit of care

	Process measures	Outcome measures
Diagnosis	Is classification of seizures, epilepsy syndrome, and aetiology documented? Who made diagnosis? Were EEGs/CTs done? Are results available?	What is misdiagnosis rate?
Treatment	Use of drugs appropriate? Monotherapy Blood level monitoring Starting and stopping Are suitable patients considered for surgery? Is there a system for shared care? Is there continuity of care?	Remission rates Quality of life
Information and support	Counselling services available? Written informational materials? Appropriate referrals Education Employment Social services Patient organisations	Patient satisfaction Patient knowledge Adjustment Compliance

- Jackson JH. On the anatomical, physiological and pathological investigation of epilepsies. *West Riding Lunatic Asylum Medical Reports* 1873;3:3-5. Reprinted in: Taylor J, ed. *Selected writings of John Hughlings Jackson*. London: Hodder and Stoughton 1958:90-111.
- Commission on classification and terminology of the International League Against Epilepsy. Proposal for revised clinical and electro-encephalographic classification of epileptic seizures. *Epilepsia* 1981;22:489-501.
- Commission on classification and terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989;30:389-99.
- Sander JWAS, Shorvon SD. Incidence and prevalence studies in epilepsy and their methodological problems: a review. *J Neurol Neurosurg Psychiatry* 1987;50:829-39.
- Sander JWA, Hart YM, Johnson AL, Shorvon SD. National general practice study of epilepsy: newly diagnosed epileptic seizures in a general population. *Lancet* 1990;336:1267-71.
- Anderson VE, Hauser WA, Rich SS. Genetic heterogeneity in the epilepsies. *Adv Neurol* 1986;44:59.
- Griffin J, Wyles M. *Epilepsy towards tomorrow*. London: Office of Health Economics, 1991.
- Howell SJL, Owen L, Chadwick DW. Pseudostatus epilepticus. *Q J Med* 1989;266:507-19.
- Young AC, Bog Costanzi J, Mohr PD, Forbes W. Is routine computerised axial tomography in epilepsy worthwhile? *Lancet* 1982;ii:1446-7.
- Mittan R, Locke G. Fear of seizures: epilepsy's forgotten problem. *Urban Health* 1982;Jan/Feb:40-1.
- Hauser WA, Hesdorffer DC. *Epilepsy: frequency, causes and consequences*. New York: Demos Publications, 1990.
- Hauser WA, Annegers JF, Elverback LR. Mortality of patients with epilepsy. *Epilepsia* 1980;21:339-412.
- Neuspiel DR, Kuller LH. Sudden and unexpected natural death in childhood and adolescence. *JAMA* 1985;254:1321-5.
- Leestma JE, Kalelkar MB, Teas SS, et al. Sudden unexpected death associated with seizures: analysis of 66 cases. *Epilepsia* 1984;25:84-8.
- Hauser WA, Rich SS, Jacobs MP, Anderson VE. Patterns of seizure occurrence and recurrent risks in patients with newly diagnosed epilepsy. *Abstracts of 15th Epilepsy International Symposium*. Hartford, CT: American Epilepsy Society, 1983:16.
- Russell-Jones DL, Shorvon SD. The frequency and consequences of head injury in epileptic seizures. *J Neurol Neurosurg Psychiatry* 1989;52:659-62.
- Bhatnagar SK, Srivastava JL, Gupta JL. Burns: a complication of epilepsy. *Burns* 1977;3:93-5.
- Hampton KK, Peatfield RC, Pullar T, Bodansky HJK, Walton C, Feely M. Burns because of epilepsy. *BMJ* 1988;296:1659-60.
- Doddrill CB, Batzel L, Queisser HR, Temkin NR. An objective method for the assessment of psychological and social problems among epileptics. *Epilepsia* 1980;21:123-35.
- Masland RL. Psychosocial aspects of epilepsy. In: Porter EJ, Morselli PL, eds. *The epilepsies*. London: Butterworths, 1988:356-77.
- Betts TA. Depression, anxiety and epilepsy. In: Reynolds EH, Trimble MR, eds. *Epilepsy and psychiatry*. Edinburgh: Churchill Livingstone, 1981:60-71.
- Lechtenberg R. *Epilepsy and the family*. Cambridge, MA: Harvard University Press, 1984.
- Garber J, Seligman M, eds. *Human helplessness: theory and application*. New York: Academic Press, 1980.
- Pond D, Bidwell BH. A survey of epilepsy in fourteen general practices. *Epilepsia* 1959;1:285-99.
- Gudmundsson G. Epilepsy in Iceland. *Acta Neurol Scand* 1966;43(suppl 25):1-124.
- Edeh J, Toone B. Relationship between interictal psychopathology and type of epilepsy: results of a survey in general practice. *Br J Psychiatry* 1987;151:95-101.

- 26 Currie S, Heathfield KWG, Henson RA, Scott DF. Clinical course and prognosis of temporal lobe epilepsy: a survey of 666 patients. *Brain* 1971;94:173-90.
- 27 Bruens JH. Psychoses in epilepsy. In: Vinken PL, Bruyn LW, eds. *Handbook of clinical neurology*. Amsterdam: North Holland, 1974;15:593-610.
- 28 Slater E, Beard AW, Glithero E. The schizophrenia-like psychoses of epilepsy. *Br J Psychiatry* 1963;109:5-150.
- 29 Perez MM, Trimble MR. Epileptic psychosis—diagnostic comparison with process schizophrenia. *Br J Psychiatry* 1980;146:155-64.
- 30 Barracough B. Suicide and epilepsy. In: Reynolds E, Trimble M, eds. *Epilepsy and psychiatry*. Edinburgh: Churchill Livingstone, 1980:72-6.
- 31 Annegers JF, Hauser WA, Elverback LR. Remission of seizures and relapse in patients with epilepsy. *Epilepsia* 1979;20:729-37.
- 32 Goodridge DMG, Shorvon SD. Epileptic seizures in a population of 6000: II—treatment and prognosis. *BMJ* 1983;287:645-7.
- 33 Turnbull DM, Howell D, Rawlins MD, Chadwick DW. Which drug for the adult epileptic patient: phenytoin or valproate? *BMJ* 1985;290:815-9.
- 34 Reynolds EH. Early treatment and prognosis of epilepsy. *Epilepsia* 1987;28:97-106.
- 35 Sofjanov NG. Clinical evolution and prognosis of childhood epilepsies. *Epilepsia* 1982;23:61-9.
- 35a Group for the study of the prognosis of epilepsy in Japan. Natural history and prognosis of epilepsy: report of a multi-institutional study in Japan. *Epilepsia* 1981;22:35-53.
- 36 Juul-Jensen P. Epilepsy. A clinical and social analysis of 1020 adult patients with epileptic seizures. *Acta Neurol Scand* 1964;40(suppl 5) 1-285.
- 37 Rodin EA. *The prognosis of patients with epilepsy*. Springfield, IL: Charles C Thomas, 1968.
- 38 Rowan AJ, French JA. The role of the electroencephalogram in the diagnosis and management of epilepsy. *Recent Advances in Epilepsy* 1988;4:63-92.
- 39 Shafer SQ, Hauser WA, Annegers JF, Klass DW. EEG and other early predictors of epilepsy remission: a community study. *Epilepsia* 1988;29:590-600.
- 40 Foy PM, Copeland GP, Shaw MDM. The incidence of postoperative seizures. *Acta Neurochir (Wein)* 1981;55:253-264.
- 41 Temkin NR, Dikmen SS, Wilensky AJ, et al. A randomized, double-blind study of phenytoin for the prevention of post-traumatic seizures. *N Engl J Med* 1990;323:497-502.
- 42 Foy PM, Chadwick DW, Rajgopalan N, et al. Do prophylactic anticonvulsant drugs alter the pattern of seizures following craniotomy. *J Neurol Neurosurg Psychiatry* 1992;55:753-7.
- 43 Chadwick D, Shaw MDM, Foy P, Rawlins MD, Turnbull DM. Serum anticonvulsant concentrations and the risk of drug induced skin eruptions. *J Neurol Neurosurg Psychiatry* 1984;47:642-4.
- 44 McQueen JK, Blackwood DH, Harris P, et al. Low risk of late post-traumatic seizures following severe head injury: implications for clinical trials of prophylaxis. *J Neurol Neurosurg Psychiatry* 1983;46:899-904.
- 45 Reynolds EH, Shorvon SD, Galbraith AW, et al. Phenytoin monotherapy for epilepsy: a long-term prospective study, assisted by serum level monitoring, in previously untreated patients. *Epilepsia* 1981;22:475-88.
- 46 Chadwick D, Turnbull EH. The comparative efficacy of antiepileptic drugs for partial and tonic-clonic seizures. *J Neurol Neurosurg Psychiatry* 1985;48:1073-7.
- 46a Chadwick D. Diagnosis of epilepsy. *Lancet* 1990;336:291-6.
- 47 Suzuki M, Maruyama H, Ishibashi Y, et al. A double-blind comparative trial of sodium dipropylacetate and ethosuximide in epilepsy in children with special emphasis on pure petit mal seizures. *Medical Progress* 1972;82:470-488. (In Japanese.)
- 48 Callaghan N, O'Hare J, O'Driscoll D, et al. Comparative study of ethosuximide and sodium valproate in the treatment of typical absence seizures (petit mal). *Dev Med Child Neurol* 1982;24:830-6.
- 49 Delgado-Escueta AV, Enrile-Bascal F. Juvenile myoclonic epilepsy of Janz. *Neurology* 1984;34:285-94.
- 50 Mattson RH, Cramer JA, Collins JF, et al. Comparison of carbamazepine, phenobarbital, phenytoin and primidone in partial and secondary generalised tonic-clonic seizures. *N Engl J Med* 1985;313:145-51.
- 51 Mattson RH, Cramer JA, Collins JF, et al. A comparison of valproate with carbamazepine for the treatment of complex partial seizures with secondarily generalized tonic-clonic seizures in adults. *N Engl J Med* 1992;327:765-71.
- 52 Heller AJ, Chesterman P, Elwes RDC, et al. Phenytoin, carbamazepine, or sodium valproate for newly diagnosed adult epilepsy. *J Neurol Neurosurg Psychiatry* 1994 (in press).
- 53 Schmidt D. *Adverse effects of antiepileptic drugs*. New York: Raven Press, 1982.
- 54 Chadwick D, Reynolds EH, Marsden CD. Anticonvulsant induced dyskinesias: a comparison with dyskinesias induced by neuroleptics. *J Neurol Neurosurg Psychiatry* 1976;39:1210-8.
- 55 Turnbull DM, Rawlins MD, Weightman D, Chadwick DW. Plasma concentrations of sodium valproate: their clinical value. *Ann Neurol* 1983;14:38-42.
- 56 Dreifuss FE, Santilli N, Langer DH, et al. Valproic acid fatalities: a retrospective review. *Neurology* 1987;37:379-85.
- 57 Sander JWAS, Trevisol-Bittencourt PC, Hart YM, Shorvon SD. Evaluation of vigabatrin as an add-on drug in the management of severe epilepsy. *J Neurol Neurosurg Psychiatry* 1990;53:1008-10.
- 57a Chadwick D, Cartledge A, Bates D. *Medical neurology*. Edinburgh: Churchill Livingstone, 1989.
- 58 Lindhout D, Schmidt D. In-utero exposure to valproate and neural tube defects. *Lancet* 1986;i:1392-3.
- 59 Rosa FH. Spina bifida in maternal carbamazepine exposure cohort data. *Teratology* 1990;41:587-8.
- 60 Crawford PM, Chadwick D. A comparative study of progabide, valproate and placebo as add-on therapy in patients with refractory epilepsy. *J Neurol Neurosurg Psychiatry* 1986;49:1251-7.
- 61 Richens A, Dunlop A. Serum phenytoin levels in the management of epilepsy. *Lancet* 1975;ii:247-9.
- 62 Rowan AJ, Binnie CD, Warfield CA, et al. The delayed effect of sodium valproate on the photoconvulsive response in man. *Epilepsia* 1979;20:61-8.
- 63 Gannaway DJ, Mawer GE. Serum phenytoin concentrations and clinical response in patients with epilepsy. *Br J Clin Pharmacol* 1981;12:833-9.
- 64 Knott C, Williams CP, Reynolds F. Phenytoin kinetics during pregnancy and the puerperium. *Br J Obstet Gynaecol* 1986;93:1030-70.
- 65 Chadwick D. Concentration effect relationships of valproate. *Clin Pharmacokinet* 1985;10:155-63.
- 66 Pedley TA. Discontinuing antiepileptic drugs. *N Engl J Med* 1988;318:982-4.
- 67 Medical Research Council Antiepileptic Drug Withdrawal Study Group. (Chadwick D, clinical co-ordinator). Randomized study of antiepileptic drug withdrawal in patients in remission. *Lancet* 1991;337:1175-80.
- 68 Medical Research Council Antiepileptic Drug Withdrawal Study Group. (Chadwick D, clinical co-ordinator). Prognostic index for recurrence of seizures after remission of epilepsy. *BMJ* 1993;306:1374-8.
- 69 Dreifuss FE. Goals of surgery for epilepsy. In: Engel J, ed. *Surgical treatment of the epilepsies*. New York: Raven Press, 1987:31-50.
- 70 Engel J. Outcome with respect to epileptic seizures. In: Engel J, ed. *Surgical treatment of the epilepsies*. New York: Raven Press, 1986:553-72.
- 71 Duncan JS, Sagar HJ. Characteristics, pathology and outcome after temporal lobectomy. *Neurology* 1987;37:405-9.
- 72 Oxbury JM, Adams CBT. Neurosurgery for epilepsy. *Br J Hosp Med* 1989;41:372-7.
- 73 Crandall PH. Cortical resections. In: Engel J, ed. *Surgical treatment of the epilepsies*. New York: Raven Press, 1987:377-404.
- 74 Falconer MA, Hill D, Meyer A, et al. Treatment of temporal lobe epilepsy by temporal lobectomy. A survey of findings and results. *Lancet* 1955;1:827-35.
- 75 Yasargil MG, Wieser HG. Selective amygdalohippocampectomy at the University Hospital, Zurich. In: Engel J, ed. *Surgical treatment of the epilepsies*. New York: Raven Press, 1987:653-8.
- 76 Quesney LF. Seizures of frontal lobe origin. In: Pedley TA, Meldrum BS, eds. *Recent advances in epilepsy*. Edinburgh: Churchill Livingstone, 1986:3:81-110.
- 77 Adams CBT. Hemispherectomy—a modification. *J Neurol Neurosurg Psychiatry* 1983;46:617-9.
- 78 Spencer SS, Gates JR, Reeves AR, et al. Corpus callosum section. In: Engel J, ed. *Surgical treatment of the epilepsies*. New York: Raven Press, 1987:425-44.
- 79 Donabedian A. Evaluating the quality of medical care. *Milbank Memorial Fund Quarterly* 1966;44(suppl):166-206.
- 80 Kessner DM, Kalk CE, Singer J. Assessing health quality: the case for tracers. *N Engl J Med* 1977;199:194.
- 81 Department of Health and Social Security. *Report of the working group on services for people with epilepsy*. London: HMSO, 1986.
- 82 Fitzpatrick R. Measurement of patient satisfaction. In: Hopkins A, Costain D, eds. *Measuring the outcome of medical care*. London: Royal College of Physicians, 1990.