SCOPE OF THE PROBLEM
Epilepsy is common. About 3% of individuals develop epilepsy during a lifetime of 70 years, and about 0.5–0.9% of the population have epilepsy at any given time. For the majority, the prognosis is favourable: about two-thirds of those who develop epilepsy will - at some stage - attain freedom from seizures for at least 5 years, and about one-third will become free of seizures for 5 years or more, and off medication (Cockerell et al. 1997). While these figures predate the ‘new’ antiepileptic drugs (AEDs) and the vagal nerve stimulator, there is no evidence that any of these interventions have diminished the proportion of patients with medically refractory seizures, somewhat arbitrarily defined as the recurrence of seizures despite a trial of two or more AEDs.

Given the estimate that about 1 in 1000 of the population have monthly seizures, and about 60% of patients have partial seizures, approximately 6 per 10 000 (600 per million) of the population have monthly partial seizures, worthy of consideration for surgery. If, for example, 10% of these patients are suitable, then about 60 per million of the population may benefit from resective surgery. A United Kingdom population-based study estimated that about 1.5% of patients with newly diagnosed epilepsy will ultimately require surgery (Lhatoo et al. 2003). In other words, about 7 per million of the population are added every year to the pool of patients with prevalent epilepsy requiring surgery.

WHY ALL THE FUSS ABOUT EPILEPSY?
Compared to someone without epilepsy, an individual experiencing epileptic seizures has an increased morbidity and mortality. And for patients with medically refractory seizures, health-related quality of life is often markedly impaired. They may have to endure many hardships, including: prohibition from driving, stigmatization, mood disorders, fear of seizures, adverse effects of AEDs, a sense of losing control, social isolation, relationship problems, low self-esteem, low rates of employment, and the conse-
quences of injuries such as burns, fractures and dislocations (Kellett et al. 1997). For women, AEDs during pregnancy increase the risk of congenital malformations, some of which can be very serious (Holmes et al. 2001).

Although the ‘here and now’ may be uppermost in the mind of an individual with epilepsy and the attending doctor, an understanding of the long-term aspects of epilepsy should be incorporated into therapeutic decision-making. In particular:

- Epilepsy and its treatment may have a profound impact on the psychosocial and neuro-developmental aspects of an individual, especially a child. In a study with over 30 years of follow-up of a cohort of children followed into adulthood, compared with their age-matched peers in the general population, those with epilepsy were disadvantaged with respect to educational level, vocational training, marriage or cohabitation, having children, having a driver’s license, employment and socio-economic status (Sillanpaa et al. 1998).
- There is some evidence that epileptic seizures may adversely affect the cognitive development of children who have a higher prevalence of behavioural disorders than healthy children (Lendt et al. 2000). It is unclear whether intermittent epileptic seizures in adults, short of status epilepticus, cause enduring neurological dysfunction.
- Population-based studies indicate that patients with epilepsy have a higher risk of dying than those without epilepsy (Cockerell et al. 1997). Much of this excess risk is due to the underlying cause of the epilepsy. In addition, epilepsy-related deaths may occur as a result of accidents, drowning, overdose, status epilepticus or sudden unexplained death in epilepsy (SUDEP).
- The cost of having epilepsy, especially intractable epilepsy, is considerable. Most of the costs are indirect (mainly loss of income), while medications and hospitalizations appear to consume the bulk of the direct costs. If all these consequences of epilepsy are to be minimized, remission from seizures should clearly be achieved as soon as possible.

**WHEN IS EPILEPSY LIKELY TO BECOME REFRACTORY?**

Prognostication for individuals with epilepsy is an imperfect science. More than a half of all patients who enter remission do so during the first year after diagnosis (Cockerell et al. 1997).

However, late spontaneous remission does occur in a few patients and, until such time as there are means of identifying them, there will be some uncertainty about the early identification of patients with a poor prognosis.

An understanding of aetiology and syndromic classification is useful for prognostication, and for treatment. For example, a child with Benign Rolandic Epilepsy of Childhood can be expected to enter remission during teenage years and need never be considered for surgery; while someone with a malformation of cortical development and seizures for 5 years, despite the use of AEDs, is unlikely to become seizure-free and should be considered for surgery. An epilepsy syndrome can be diagnosed at first-seizure presentation in nearly half of all patients, and those with seizures due to a pre-existing brain lesion have a lower likelihood of attaining long-term remission than patients with genetic forms of epilepsy (Sillanpaa et al. 1998).

Kwan and Brodie found that after the first AED proved ineffective for controlling epilepsy, only 11% of patients became seizure-free for 1 year or more when subsequent medications were tried, and only 4% of patients responded to a third drug or multiple drugs situation in nearly half of all patients, and those with seizures due to a pre-existing brain lesion have a lower likelihood of attaining long-term remission than patients with genetic forms of epilepsy (Sillanpaa et al. 1998).

**WHO SHOULD BE REFERRED FOR POSSIBLE SURGERY?**

Seizure frequency is less important than quality of life in deciding about surgery. Therefore, in principle, any patient with medically refractory seizures – and whose quality of life is impaired by having seizures – should be considered for surgery. For example, just four seizures per year may prevent someone from driving or working, cause embarrassment when seizing in view of the family, and stigmatize the person. Perhaps one should ask who should not be evaluated for surgery? Patients with idiopathic generalized epilepsy are usually not candidates for surgery. Also those with seizures that originate multifocally are unlikely to benefit from surgery, with the exception of some with independent bitemporally originating seizures.

Circumstances that particularly merit referral include patients with known structural lesions and those with partial seizures, especially where the symptomatology suggests temporal lobe
WHAT ABOUT THE EEG?

Intercital EEG findings, while useful, cannot be relied upon to predict the suitability of surgery. A normal EEG does not exclude epilepsy or epilepsy surgery. Nor are patients with multifocal epileptiform discharges (or spikes) on interictal recordings necessarily excluded from having epilepsy surgery. Patients with spikes over both temporal regions may have seizures originating on one side and hence patients with bi-temporal spikes are not excluded from consideration either. Those with seizures of extra-temporal origin not infrequently have epileptiform discharges over the temporal region. Therefore, someone with temporal and frontal spikes, or occipital and temporal spikes, is again not necessarily excluded from having successful surgery.

WHAT ABOUT BRAIN MRI?

An MR brain scan reported as normal does not always preclude epilepsy surgery; in part because scans on patients with epilepsy are frequently performed in the same manner as for other neurological illnesses. Unless epilepsy-specific protocols are followed and the MR unit is capable of producing images of high quality, lesions such as hippocampal sclerosis (Fig. 1) and malformations of cortical development may be missed. It should be self-evident that the quality of both the images and the interpreter need to be of a high standard. MR lesions have an unpredictable spatial relationship to seizures, as seizures may originate within, adjacent to or remote from such lesions. Also, some patients with lesions may have non-epileptic seizures. When multiple lesions are present on MR (e.g., tuberous sclerosis), epilepsy surgery may sometimes still be considered because only one lesion may be responsible for generating all, or most of, the seizures. Localization of such an origin is often obtained from combinations of clinical, scalp EEG, intracranial EEG and ictal SPECT data (Engel 1993). Intercital PET may sometimes be a useful adjunctive investigation while MR spectroscopy is a research tool that shows much promise.

WHAT IS DONE DURING THE PREOPERATIVE EVALUATION?

Evaluation is aimed at defining the issues illustrated in Fig. 2. The history is supplemented...
by video-EEG monitoring to understand the physiology of the seizures, including the region(s) of seizure onset. MRI may identify the site and nature of the causative lesion. If there is doubt about the region of seizure onset or the proximity to eloquent brain function, intracranial electrodes may have to be surgically implanted (Fig. 3). Concordance of clinical, EEG, MRI and functional imaging (SPECT, PET) data best predict the likelihood of freedom from seizures. Before performing a temporal lobectomy, the functional reserves of the remaining temporal lobe may be assessed by neuropsychological testing and/or the intracarotid sodium amytal test. When resections are in close proximity to eloquent function, cortical stimulation may demonstrate the location of language, primary motor and primary visual cortex. Resection of these areas and consequent loss of function can then be avoided.

WHAT IS DONE AT SURGERY?
Surgery entails either resection of the part of the cortex deemed to be responsible for generating seizures (i.e. onset), or disconnection of pathways responsible for propagation of seizures (i.e. spread). Resections vary in size from small corticectomies and selective amygdalohippocampectomies to antero-mesial temporal lobectomies (the most commonly performed procedure) and hemispherectomies. Disconnection procedures, which are less commonly performed, include corpus callosotomies and multiple subpial transections. Disconnection procedures are intended to diminish seizure frequency and/or severity and only infrequently render patients seizure-free. Usually the anterior two-thirds of the corpus callosum is sectioned in order to avoid the risks of a disconnection syndrome. Multiple subpial transections are typically done in eloquent cortex and, if complicated by haemorrhage, may produce clinically important neurological dysfunction, such as aphasia or paralysis of a limb.

IS EPILEPSY SURGERY EFFECTIVE?
There is very compelling evidence that temporal lobectomy is an effective procedure, and reasonable evidence for the effectiveness of various other epilepsy surgery procedures. A randomized controlled trial (RCT) demonstrated that, for patients presenting to a tertiary care epilepsy service with medically refractory temporal lobe seizures, 58% of operated patients were free of seizures with loss of awareness 1 year later compared with only 8% of patients continuing on medical management. Compared to continuing with medical therapy, one needs to operate on about two patients to render one patient free of seizures with loss of awareness, and about three patients to render one patient free of all seizures.
Concluding auras (Wiebe et al. 2001). One may contrast, indirectly, this effect with the results of the RCTs of levetiracetam and vagal nerve stimulation as add-on therapy for medically refractory epilepsy. Compared to placebo, about seven patients need to be treated with 1000 mg levetiracetam daily for one to experience a 50% reduction in seizures at about 3 months. Compared to 'low-intensity' stimulation, about eight patients need to have vagal nerve stimulators implanted and set to 'high-intensity' for one patient to have a 50% reduction in seizures at about 3 months (note the much more lenient outcome measures and shorter follow-up in these studies).

In the RCT of temporal lobectomy, patients had a better quality of life and were more likely to be working or at school one year after surgery than those continuing with medical therapy (Wiebe et al. 2001) and a report of a cohort of 79 patients followed up for 10 years after temporal lobectomy demonstrated that the benefits are sustained (Foldvary et al. 2000). There is some evidence that temporal lobectomy may reduce but not normalize the excess mortality associated with epilepsy. Using available data and modelling, economic evaluations assessing the costs and consequences of surgery for patients with medically refractory temporal lobe epilepsy, suggest that surgery is more effective than continued medical therapy and cheaper in the medium and long-term (a ‘win-win’ situation).

There are a plethora of case-series reporting the efficacy of various neocortical resections, generally with seizure-free rates of between 30 and 50% (Engel 1996). Corpus callosotomy appears to produce worthwhile improvement in about half of patients with epileptic drop attacks (e.g. in Lennox–Gastaut syndrome).

Is surgery not risky?

Because the goal of surgery is to improve quality of life, it should not be attempted unless the potential benefits considerably outweigh the potential risks (Behrens et al. 1997). Apart from the small anaesthetic risk, the general risks of neurosurgery include a low risk of strokes (about 1%) and infections (about 2–3%). Other risks have to be individually determined, depending on the region of cortex to be resected. In the RCT of temporal lobectomy, a clinically important deterioration in memory was observed in about 5% of patients (Wiebe et al. 2001). Varying degrees of word-finding difficulties occur after dominant temporal resections, depending on the extent of surgery. Contralateral peripheral superior quadrant visual field dysfunction following a temporal lobectomy is usually asymptomatic. As the majority of patients have a substantial improvement in quality of life following a temporal lobectomy (Kellett et al. 1997; Wiebe et al. 2001), this means that the untoward consequences of surgery are, at most, modest and outweighed by the benefits.

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