Epilepsy and pregnancy

The treatment of epilepsy with drugs has been greatly improved since the introduction of monitoring of the serum concentrations of antiepileptic drugs and with more general awareness that epilepsy is not a homogeneous entity.

The distinction between three-per-second spike-wave absences (petit mal) and other primary generalised epilepsies, on the one hand, and the partial or focal epilepsies including temporal lobe epilepsy, on the other, has important therapeutic implications. The first may be treated effectively with ethosuximide or sodium valproate and the second with carbamazepine, though tonic-clonic and other grand-mal seizures are often best controlled with phenytoin. Phenytoin or primidone is also effective in some cases. Other antiepileptic drugs are now prescribed much less often in Britain, and combined preparations containing two or more drugs are no longer acceptable. Patients who have only a single type of epileptic attack are ideally treated with a single drug. Measuring the serum concentrations helps the clinician to determine the optimum dosage of the drug when attacks are difficult to control and may also provide evidence of non-compliance or drug toxicity. Furthermore, if seizures are not controlled adequately with one antiepileptic drug at an optimum serum concentration that should be taken as an indication for changing to a different drug, rather than for adding a second (and possibly later a third); as was common practice in the past. More than one antiepileptic drug may be required in some cases, but the aim should be to obtain optimum control of the seizures without side effects using the fewest possible drugs.

All these points, together with the increase in our knowledge of pharmacokinetics and drug interactions, must be taken into account by doctors looking after women with epilepsy who wish to have a baby. There is no evidence that antiepileptic drugs interfere with fertility, but they may occasionally be responsible for failure of oral contraception. This interaction may be of special importance in women whose epilepsy is not well controlled and who require fully effective contraception because of the difficulties they would be likely to have in looking after a baby.

Usually the first question prospective parents with epilepsy ask is about the risk for their children. The prevalence of epilepsy (excluding febrile convulsions) varies from four to seven per 1000, and it may occur with a negative family history. If one parent has epilepsy, the risk for offspring depends on the cause; for example, if due to brain trauma, there is only a slightly increased risk; if due to idiopathic epilepsy the risk is a little higher but is still small and not prohibitive; but if the other parent also has idiopathic epilepsy (or a family history of the disorder) the risk for the children is appreciably greater.

What about the teratogenic risks of antiepileptic drugs? The diorides—though seldom used now—may have serious effects and are best avoided during pregnancy. Congenital malformations in man have not been reported with sodium valproate, though in animals it has induced teratogenic effects. The risk that the fetus will develop hare lip, cleft palate, or congenital heart lesions is increased by two or three if the mother is treated during pregnancy with phenytoin, either alone or in combination with phenobarbitone, primidone, or carbamazepine. This risk of major and minor malformations may also be related in part to the maternal epilepsy and to other variables, including maternal age, diabetes, and social class, the family history of malformations, the incidence of twins, and obstetric complications. On balance, the teratogenic risk of antiepileptic drugs seems small and does not justify discouraging a woman who needs treatment with them from having a child or changing a satisfactory drug regimen when the epilepsy is well controlled. Genetic and other factors influencing the risk of malformations must also be taken into account when the risks are assessed.

The effect of pregnancy on the frequency of fits in a woman with idiopathic epilepsy is difficult to predict: the findings in several studies have been inconsistent and the frequency fluctuates naturally irrespective of pregnancy. Knight and Rhind reported that the frequency of fits was increased in 45%, of 84 pregnancies in 34 patients with idiopathic epilepsy, was unchanged in 50%, and was decreased in 5%. Those who before pregnancy had had more than one fit a month were likely to deteriorate, especially during the first trimester, whereas only one in four of those who had intervals greater than nine months between convulsions deteriorated during pregnancy. The effect of subsequent pregnancies was the same in some cases but inconsistent in others. An increase in frequency seemed more likely during pregnancy with a male than a female fetus.

Serum concentrations of antiepileptic drugs tend to fall during pregnancy, and this may be one factor in fits recurring or increasing in frequency. The change in serum concentrations may be due to non-compliance or to the metabolic or hormonal changes of pregnancy. Clearance of the free
unbound fraction, which is responsible for the antiepileptic effect, may be increased, and serum protein binding is decreased later in pregnancy. Unfortunately, direct measurement of the free concentration of antiepileptic drugs is not yet generally available or reliable enough for routine use. The drug dosage should therefore be increased cautiously if major fits recur during pregnancy, and the patient's condition reviewed with the blood picture checked and serum concentrations of drugs measured monthly—or more frequently if fits are not controlled.

A woman having treatment for epilepsy who wants to embark on pregnancy should ideally be on a single drug with its serum concentration in the optimum range. Nevertheless, if control has been achieved with a combination of antiepileptic drugs the patient should be encouraged to continue with the same regimen, because the risks to the fetus and mother may be greater from uncontrolled fits—and particularly from status epilepticus—than from the drugs. Weight gain should be restricted, fluid retention prevented, and iron and low-dose folic acid supplements should be given to prevent or treat anaemia. Toxic effects of the antiepileptic drugs, including the haematological complications, should be prevented or treated promptly in both the mother and the newborn baby. Vitamin K should be given and expert neonatal care should be available. Careful follow-up post partum with serial measurements of serum drug concentrations is necessary, as it may take six to eight weeks for the pre-pregnancy state to be restored. Close collaboration with the obstetrician is important and further studies of the effects of pregnancy on epilepsy are required.

Fits occurring only in pregnancy or the puerperium with no evidence of toxoaemia have been described as gestational epilepsy. This is a term, however, that should be applied only in retrospect: no one can predict that fits will not recur unrelated to pregnancy, or that they will recur in subsequent pregnancies. In one series 159 out of 441 women developed epilepsy between the ages of 16 and 40; inevitably some women will have their first-ever fit during pregnancy. If it occurs without either toxoaemia or other cause antiepileptic treatment can be withheld unless there is a second fit. Investigations should include examination of the blood picture to see if there is anaemia, and electroencephalography. A normal electroencephalogram or one with non-specific abnormalities only is of no positive or negative help with the diagnosis, but generalised paroxysmal discharges on the electroencephalogram suggest idiopathic epilepsy. If there are clinical or electroencephalographic features suggesting a focal or structural cause—which is not uncommon in women who develop epilepsy in pregnancy—further investigations will probably be required if fits recur or if the neurological signs persist. Nevertheless, as radiography and computed tomography are done in pregnancy only if absolutely necessary, the timing will depend on several factors, including the stage of pregnancy and the likely cause. Driving must be stopped after a fit, in accordance with the advice given in Medical Aspects of Fitness to Drive.

Steroids in bronchitis

Corticosteroids have dramatically improved the treatment for bronchial asthma, but their value in chronic bronchitis remains a matter of dispute. While some trials have shown a favourable response, others have failed to show any improvement. Interpreting these findings is difficult, since most of the trials were not double blind and did not include controls.

Albert and his colleagues in Seattle, however, have recently reported a well-designed trial to investigate the effect of methylprednisolone in chronic obstructive airways disease. Patients were admitted to the study if they had evidence of chronic airflow obstruction (a forced expiratory volume in one second of 60%, or less than the predicted value of 60% or less than a simultaneous forced vital capacity). These measurements were taken after administration of a bronchodilator and at a time of clinical stability. Objective assessments made before and after treatment consisted of bedside spirometry (again after a bronchodilator) and measurement of the blood gases and arterial blood. Patients with a history of asthma or reversible bronchospasm were excluded. Methylprednisolone was given intravenously at a dose of 0.5 mg/kg every six hours (or an identical placebo) and added to a standard regimen of intravenous aminophylline, nebulised isoproterenol, antibiotics, and oxygen, thus avoiding the possibility that differences between the two groups could be attributed to omission of routine forms of treatment. Patients were allocated at random to either the placebo or the treatment group, and the study was performed double blind for 72 hours. A greater