ceptualisation and psychoanalytic treatment of psychosis in French psychiatry throughout the 1960s and 1970s.

The questionnaire survey showed that British and French psychiatrists also differed over the management of schizophrenia. Although opinion should be distinguished from behaviour, the difference in views probably affects clinical practice. Thus the same patient might be treated very differently in the two countries, even if they happened to have received the same diagnostic label.

Conclusion—In psychiatry there is a need for further collaborative projects within the European Community to promote mutual understanding, facilitate communication, and arrive at a consensus for the diagnosis and management of schizophrenia and other psychiatric disorders. In a dialectical Europe different psychiatric traditions should be able to learn from each other but talk in a common language.

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Epilepsy and pregnancy

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The prevalence of recurrent epilepsy is about 0·5-1·0%, and slightly less than half of those affected are women. The possibility of pregnancy should be considered in any woman of childbearing age with epilepsy because treatment is likely to be necessary for a minimum of two years and maybe indefinitely. This certainly applies to any girl over the age of 15. Withdrawal of antiepileptic drugs well before a planned pregnancy should be considered because neural tube defects occur before 28 days, but if a patient requires antiepileptic drugs treatment should be continued throughout pregnancy.

In this article we answer the questions commonly asked by epileptic patients regarding contraception and pregnancy. Patients may ask only a few of the questions at one time, but most will appreciate a discussion of other potential problems.

Summary of main points

- Women taking enzyme inducing antiepileptic drugs should take higher doses of oral contraceptives
- Progesterone concentrations should be measured on day 21 of the first or second cycle to ensure that ovulation is being suppressed
- Risk of fetal abnormalities, especially cleft lip and palate and congenital heart abnormalities, is raised in women taking antiepileptic drugs
- Women taking antiepileptic drugs should all have α fetoprotein concentrations measured at 18 weeks and high resolution ultrasonography
- Impaired absorption of antiepileptic drugs during pregnancy and increased blood volume may make it necessary to adjust the dose, particularly in women with poorly controlled epilepsy
- Vitamin K_1 supplements in the last week before delivery help raise fetal plasma concentrations. Infants should also be given vitamin K_1 at birth
- Breast feeding is relatively contraindicated only in women taking phenobarbitone or primidone

Contraception

COMBINED CONTRACEPTIVE PILL

There is no reason why women with epilepsy taking antiepileptic drugs should not take combined oral contraceptives, which act by giving a sufficient dose of oestrogen to inhibit ovulation. In most women this requires an oral dose of oestrogen above 20 μg and the most widely prescribed drugs contain 30 μg of oestrogen (Microgynon 30, Eugynon 30, Ovran 30, Ovranette, and Marvelon), giving some measure of safety. The induction of microsomal liver enzyme activity by some antiepileptic drugs (phenytoin, carbamazepine, phenobarbitone, and primidone) increases the rate of metabolism of both oestrogen and progesterone, thereby lowering the blood concentrations of these drugs, often by 50% or more. It is therefore usual to recommend a combined oral contraceptive preparation containing at least 50 μg of oestrogen (Ovran) for women taking enzyme inducing antiepileptic drugs. Sodium valproate, the benzodiazepines (clobazam, clonazepam), vigabatrin, and lamotrigine do not have this effect.

If breakthrough bleeding occurs contraception cannot be assured and the dose of oestrogen should be

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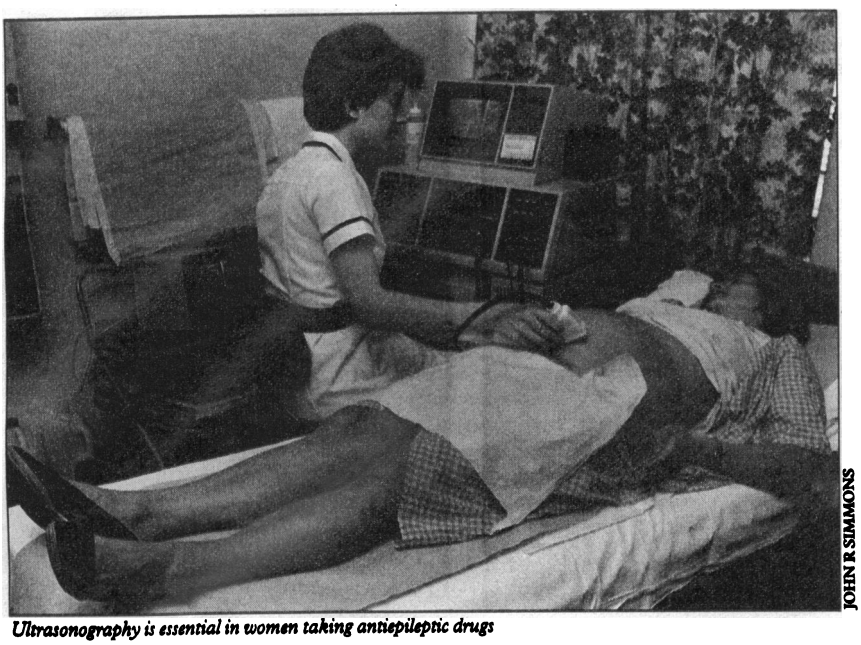

JOHN R SIMMONS

Ultrasonography is essential in women taking antiepileptic drugs

increased, but even a regular menstrual cycle without breakthrough bleeding is not an entirely reliable guide to effective contraception. To ensure that ovulation is inhibited the blood progesterone concentration can be measured on day 21 of the first cycle if the combined pill was started on days 1-3, or in the second cycle if the pill was started on days 3-5. The synthetic progestogens in the combined oral contraceptive pill (norethisterone, desogestrel, levonorgestrel, gestodene, norgestimate, and norgestrel) do not interfere with the assay of human progesterone (M D O'Brien *et al*, unpublished observations). The serum progesterone concentration should clearly indicate suppression of the luteal phase progesterone. Progesterone concentration normally rises tenfold by day 21 if ovulation has taken place. Patients taking enzyme inducing antiepileptic drugs should therefore be given a combined oral contraceptive pill containing 50 μg of oestrogen initially; this can be conveniently increased to 60 μg by taking two 30 μg pills, and if necessary to 80 μg (30 μg plus 50 μg). Some patients will need up to 100 μg of oestrogen to inhibit ovulation. As both oestrogen and progestogen metabolism is affected, the higher doses of oestrogen should be accompanied by higher doses of progestogen. Effective contraception should not be assumed until ovulation has been shown to be inhibited. The incidence of side effects with this larger dose given in combination with liver enzyme inducing antiepileptic drugs is comparable with that associated with 30 μg preparations on their own because of the reduced oestrogen blood concentration.[1]

PROGESTOGEN ONLY PILL

Progestogens are also affected by liver enzyme inducing antiepileptic drugs. The progestogen only pill is likely to be associated with a higher contraception failure rate when used in combination with liver enzyme inducing antiepileptic drugs and patients should take at least double the usual dose.[2] This problem does not apply to the use of parenteral preparations (medroxyprogesterone acetate) because the usual dose is probably more than sufficient.

POST PARTUM CONTRACEPTION

The combined pill reduces the secretion of milk, but the progestogen only pill may be used and should be started two to four weeks post partum. If the woman is not breast feeding either preparation can be used from four weeks. Contraception before this is unnecessary.

Fertility

Antiepileptic drugs do not cause infertility in women, but women with epilepsy may be less fertile than normal.[3] Antiepileptic drugs may have some effect on fertility in men, probably by altering sperm motility and reducing circulating testosterone concentrations.[4] These factors should be considered in the investigation of infertility.

Teratogenicity

The incidence of fetal abnormalities in the general population is less than 3%. There is a small increased risk of fetal abnormalities in children of mothers with epilepsy and this risk is further increased if they are taking antiepileptic drugs. The number of antiepileptic drugs taken concurrently seems to be important. The risk of fetal abnormality rises from about double the natural risk in women taking two antiepileptic drugs to nearly 10 times the risk in those taking four antiepileptic drugs,[5] but these patients would have less well controlled epilepsy. Risk of miscarriage is not increased by epilepsy or antiepileptic drugs.[6] Some reports have suggested a slight increase in the risk of fetal abnormalities if the father has epilepsy. Taking antiepileptic drugs during pregnancy seems to have no lasting effect on growth or intellectual development,[7] but this conclusion is based on rather limited data and excludes the so called fetal hydantoin and valproate syndromes, which are largely dose dependent and potentially avoidable.

COMMON ABNORMALITIES

The commonest malformations are cleft lip and palate and congenital heart disease, usually septal defects. These abnormalities may be caused by all the major antiepileptic drugs, especially when used in combination. Phenytoin has been particularly implicated and may cause minor defects in up to 30% of infants and more major defects in about 5%.[8] The incidence of cleft palate and heart defects with phenytoin is 1·8% compared with 0·7% in the general population.[9] The most important risk with sodium valproate is of neural tube defects, which occur in about 1·5% of pregnancies.[10] Carbamazepine is also associated with a small additional risk of neural tube defects, but this is probably less than 0·5%. Vigabatrin and lamotrigine, two recently introduced drugs, are not recommended for patients who might become pregnant because there is insufficient information at present about their effects in pregnancy.

It is therefore advisable that all women with epilepsy who are taking antiepileptic drugs and contemplating pregnancy be given a single drug and that the drug should be at the lowest possible dose. Present evidence suggests that carbamazepine is the safest drug. For patients with types of epilepsy that respond best to valproate and who have achieved good control with this drug, the risk of recurrence of fits in pregnancy may need to be balanced against the small increased risk of fetal abnormality. Parents can be reassured that there is a more than 90% chance that their infant will be entirely normal.[11]

FOLIC ACID

Folic acid supplements reduce the risk of neural tube defects in women at risk.[12] Enzyme inducing anticonvulsant drugs such as phenytoin and carbamazepine reduce serum folate concentrations[13] and are associated with an increased risk of neural tube defects. There is some evidence that folic acid reduces the risk in women taking these drugs.[13a] All women taking antiepileptic drugs who are contemplating pregnancy should be given a small folic acid supplement, perhaps twice a week, or a diet rich in folate. This should

preferably be started before pregnancy since neural tube defects occur in the first 28 days after conception, usually before the woman realises that she is pregnant.

Investigations during pregnancy

The antiepileptic drug concentrations in blood should be measured as soon as it is known that the patient is pregnant to establish a baseline and concentrations should be monitored as appropriate (see later).

After appropriate counselling all pregnant women taking antiepileptic drugs, particularly valproate and carbamazepine, should have serum α fetoprotein concentrations measured at 18 weeks since raised concentrations are a good indicator of neural tube defects. A high definition ultrasound scan is also important for identifying neural tube defects and congenital cardiac malformations.

Hyperemesis

Several antiepileptic drugs (phenytoin, primidone, and phenobarbitone) need to be taken only once a day and can therefore be taken at night or at a time when sickness is less severe. Carbamazepine and valproate should be taken twice a day, but the morning dose could be postponed by a few hours. It is reasonable to tell patients, "If you see the tablet when you are sick, take another."

Effects of fits on the fetus

Minor fits have no effect on the fetus, but major convulsive seizures associated with cyanosis can produce anoxia in the infant. If a fit results in a fall, the fetus could be injured or early labour or miscarriage be precipitated.

Effect of pregnancy on fits

Pregnancy does not usually have much effect on the control of epilepsy, but fits may become more frequent, particularly in patients with poorly controlled epilepsy. This is mainly because antiepileptic drug concentrations tend to fall as a result of several factors including poor compliance, impaired absorption, increased protein binding, increased blood volume, and increased liver activity. It may therefore be necessary to increase the dose during pregnancy and monitor blood concentrations of antiepileptic drugs. The dose may need to be reduced again after delivery.

Management of a first fit in pregnancy

It is rare for a first fit to occur during pregnancy without obvious cause. These women should be referred for a specialist neurological opinion about the appropriate investigations and management. There is a higher incidence of underlying structural lesions in these patients. Patients with toxaemia may present with epilepsy, but they will all have proteinuria and usually hypertension, though the blood pressure settles if the baby dies in utero.

Epilepsy during delivery

All pregnant women with epilepsy taking antiepileptic drugs should have their babies delivered in hospital. The increased risk of epilepsy at delivery is usually due to failure to take antiepileptic drugs, lack of sleep, or impaired drug absorption. The risk of status epilepticus is low—about 1%.

Some antiepileptic drugs, particularly primidone, phenobarbitone, and the benzodiazepines, are sedating and some infants show withdrawal symptoms from these drugs in the first few days of life. Withdrawal fits are rare but are most common with phenobarbitone.

VITAMIN K

The liver enzyme inducing antiepileptic drugs cause a reduction in vitamin K dependent clotting factors. Although giving vitamin K to women in the last few weeks of pregnancy does raise the fetal vitamin K_1 concentration appreciably, it remains an order of magnitude lower than maternal levels because of poor placental passage and low concentrations of transport lipoproteins in fetal plasma. To reduce the risk of bleeding in the perinatal period, pregnant women taking enzyme inducing antiepileptic drugs should be given oral phytomenadione (vitamin K_1) 20 mg daily for at least one week before delivery and vitamin K_1 should be given to the baby immediately after delivery.[14]

Breast feeding

All the antiepileptic drugs are excreted in breast milk but only in low concentrations and, with the possible exception of phenobarbitone, there is no reason why mothers taking antiepileptic drugs should not breast feed. The concentration received by the infant is much less than that received by the fetus during pregnancy.[15] For example, calculations of the largest amount of drug likely to be received daily in breast milk expressed as a percentage of the lowest recommended daily therapeutic dose for an infant give the following figures: carbamazepine $< 5\%$, phenytoin $< 5\%$, valproate $< 3\%$, and phenobarbitone $> 50\%$. Only phenobarbitone and primidone might be contraindications for breast feeding. Fetal hepatic immaturity results in a considerable increase in the blood half life of phenobarbitone, which can be up to 300 hours.

Epilepsy after the birth

Mothers with uncontrolled major epilepsy should not be left alone with small children. Maternal epilepsy probably presents a greater risk to infants and toddlers than to the fetus. The child could be injured if held by the mother at the start of a fit or if left unattended during the mother's fit. Mothers should seek advice about appropriate precautions—for example, changing nappies on the floor and only bathing infants when somebody else is present.

Hereditary risks

A child inherits its epileptic liability from both parents. If the father and his first degree relatives have no history of epilepsy the risk of a child of an epileptic mother having epilepsy before the age of 20, excluding febrile convulsions, is about 4% compared with 0·5-1·0% in the general population. The risk is the same if the epilepsy is only on the father's side. If there is already one sibling with epilepsy the risk rises to about 10% and if both parents have epilepsy the risk is 15-20%.[16] These figures exclude the inherited conditions which may be associated with epilepsy, such as tuberous sclerosis and neurofibromatosis, and the genetically determined epilepsies, such as juvenile myoclonic epilepsy.

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Grand Rounds—Hammersmith Hospital

A case of chylous ascites

Chylus may be mistaken for mucus

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Chylous ascites is a rare clinical presentation of several intra-abdominal conditions, mainly lymphomas. It is often forgotten in the differential diagnosis of a milky transudative ascites. We present a case of chylous ascites with an unusual pathology.

Case history

A 46 year old woman presented to her local hospital with a six month history of weakness, abdominal distension, flatulence, and diarrhoea. She had lost 15 kg and was wheezy and breathless on exertion. On examination she had a right sided pleural effusion and ascites but no evidence of congestive cardiac failure. Full blood count, urea and electrolyte concentrations, and liver function test results were all normal. The ascites had a low protein content but a normal serum albumin concentration, which excluded cirrhosis or the nephrotic syndrome as the cause. Chest radiography confirmed the pleural effusion but otherwise gave normal results. Abdominal ultrasonography showed a normal liver with patent hepatic and portal veins. A right sided ovarian cyst measuring 2×4 cm was noted. Abdominal computed tomography showed a thickened small bowel wall and a possible caecal mass. Barium enema confirmed the caecal filling defect, which was thought to be highly suggestive of a lymphoma or carcinoma. Laparotomy was therefore done, and mucinous ascites reported. Multiple liver, ileal, and caecal plaques were biopsied as were the ovaries. Caecotomy was performed but there was no abnormality. Histological examination showed reactive changes only. The ovarian cyst was found to be a degenerating corpus luteum. Pseudomyxoma peritonei was diagnosed clinically and she was referred to the Hammersmith Hospital for further investigation.

On arrival further exploration of her history found no systemic symptoms, foreign travel, or exposure to tuberculosis. Her father had died of pancreatic carcinoma. The ascites and pleural effusions were again aspirated and were found to be milky. No mucin was found, thus ruling out pseudomyxoma. However, the triglyceride concentration of the aspirate was higher than that in the serum (table) and chylous ascites was diagnosed. Further non-invasive investigations did not find the cause.

A small bowel enema showed diffusely thickened mucosal folds and the caecal filling defect was again seen. A digital lymphangiogram appeared entirely normal. Repeat computed tomography showed an ill defined, irregular, soft tissue mass arising from the root of the mesentery with oedema and thickening of the mesentery (fig 1). At laparotomy a mid-ileal tumour invading the mesentery was identified with lymphatic engorgement of the entire small bowel. The tumour was partly obstructing the mid-ileum and third part of the duodenum. The caecum was adherent to a mass of lymph nodes.

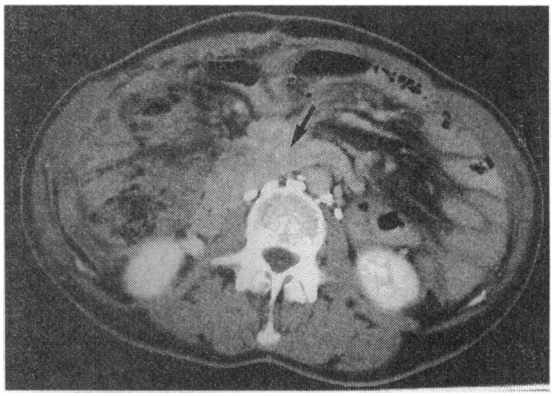

FIG 1—*Enhanced abdominal computed tomogram showing tumour mass arising from root of small bowel mesentery (arrow)*

The obstructed ileal segment was resected and a gastrojejunostomy done. Debulking of the tumour was not attempted. Histological examination showed nests of monomorphic cells separated by a fine fibrovascular stroma, typical of a carcinoid tumour (fig 2). Furthermore, dilatation of the lymphatics of the resected small intestine was noted, establishing a diagnosis of secondary lymphangiectasia caused by obstruction of the mesenteric lymph by the tumour. Silver staining of the resected specimen by Grimelius technique showed numerous secretory granules within the tumour cells, but a Masson silver stain (which is specific for serotonin) was only weakly positive (fig 3). The tissue was positive for substance P and neurokinin A but

Biochemical markers in ascitic and pleural fluids and serum

	Ascites	Pleural effusion	Serum (normal range)
Protein (g/l)	9	15	40 (35-55)
Glucose (mmol/l)	5·9	5·4	5·4 (3·5-5·5)
Cholesterol (mmol/l)	0·5	1·1	3·9 (4·1-6·5)
Triglyceride (mmol/l)	2·37	4·85	0·84 (<2·1)
Carcinoembryonic antigen (μg/l)			5 (0-9)
CA 125 (U/ml)			759 (0-34)