mind on the subject. In the interim it is not justifiable to withhold such therapy from the normal informed patient requesting it provided that no contraindications exist, that the patient is properly re-evaluated at frequent intervals, and that appropriate selection of drug, dosage, and therapeutic regimen is considered. Ideally, all this can be accomplished, including the necessary research, through a menopause clinic.⁹

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¹ *British Medical Journal*, 1976, 2, 791.

² Mulvey, G, and Mitchell, J R A, *Lancet*, 1976, 1, 1397.

³ Utian, W H, PhD Thesis, University of Cape Town, 1970.

⁴ Utian, W H, *South African Medical Journal*, 1972, 46, 732.

⁵ Campbell, S, et al, in *Management of the Menopausal and Postmenopausal Years*, ed S Campbell, p 149. Lancaster, MTP, 1976.

⁶ Campbell, S, and Whitehead, M, in *Clinics in Obstetrics and Gynecology*, vol 4, No 1, ed R Greenblatt and J Studd. Philadelphia, Saunders, 1977.

⁷ Utian, W H, *South African Medical Journal*, 1972, 46, 1079.

⁸ Furuhielm, M, and Fedor-Freijbergh, P, in *Consensus on Menopause Research*, ed P A van Keep, R B Greenblatt, and M Albeaux-Fernez, p 84. Lancaster, MTP, 1976.

⁹ Utian, W H, *Obstetrical and Gynecological Survey*, 1977, 32, 193.

Depot tranquillisers for disturbed behaviour

SIR,—I was most interested to read the letter from Drs P J Perinpanayagam and R A Haig (26 March, p 835). I have for the past two years been using fluphenazine decanoate in an average dose of 25 mg monthly to treat explosive personality disorders in both sexes, in the first year in a large mental hospital and in the past year in a mental handicap setting. I must emphasise that there was no question of psychotic illness being present in the 16 adolescents nor in the 40 older patients (in their twenties), who displayed psychopathic instability of the usual varieties—for example, self-injury such as repeated drug overdosing or wrist slashing and/or antisocial behaviour such as unreasonable aggressiveness, destructiveness, etc. Alcohol acted as at least a precipitant in a third of the cases of "difficult" behaviour. One case in particular may be of interest to your readers. A delinquent boy of 14 years with a very disturbed family background who had been placed in the care of the social services because of his destructive and life-threatening activities has apparently responded extremely well over a period of a year to fluphenazine decanoate 12.5 mg fortnightly. He has had no further episodes of absconding or getting into mischief at school or at home since starting on the drug.

I agree wholeheartedly with your correspondents that a long-acting tranquilliser can stabilise disturbed behaviour and in many cases open the way to psychotherapeutic, occupational, and other forms of rehabilitation. Thus these individuals don't seem to feel tense enough any more to inflict damage on themselves or others. I would be inclined to generalise from my own and your correspondents' experience and say that a long-acting tranquilliser is a useful means of reducing anxiety in a group classically prone to abuse oral tranquillisers.

I am conducting a mirror image study of the use of fluphenazine in ameliorating difficult behaviours in approximately 100 non-psychotic residents in a mental handicap

hospital, the majority of whom had failed to respond to other types of psychotropic medication, including a variety of other phenothiazines. The institution of the drug has coincided with a dramatic reduction in such behaviour; it remains to be seen whether cessation of the drug, which is at present being effected, will result in a resurgence of "difficult" behaviour. I hope to publish the results in due course.

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Liver biopsy in "difficult" jaundice

SIR,—We feel that the short report by Dr P Lance and his colleagues (23 July, p 236) may give an inappropriate impression of the safety and value of percutaneous liver biopsy for obstructive jaundice. We would, of course, concur with the author's view on the hazards of operating inadvertently on patients with intrahepatic cholestasis. Of 43 such patients in their series, eight underwent a laparotomy, one as a result of an incorrect percutaneous liver biopsy result. This laparotomy rate (18.6%) in intrahepatic cholestasis is unacceptable by modern standards and the dangers are adequately borne out by the 37% mortality in these patients (3/8). With the use of the full range of modern diagnostic techniques available it should now rarely be necessary to perform such laparotomy.

Concerning the important question of identification of large-duct obstruction by liver biopsy, if we exclude the operative biopsies from the authors' series 15 out of 95 percutaneous biopsies in obstructive jaundice either failed or were incorrect or unhelpful (15.8%). This indicates the known difficulty in diagnosing large duct obstruction from a needle biopsy, and indeed interpretation was incorrect or unhelpful even in 6/18 operative liver biopsies from patients with obstructive jaundice (33%). This success rate of 84% is significantly below that which has been reported by the use of grey-scale ultrasonography (GSU)¹ or fine-needle percutaneous transhepatic cholangiography (PTC).^{2,3}

Although the availability of GSU and endoscopic retrograde cholangiography is limited, PTC using the Chiba needle is easily performed and readily available. Recent communications have shown that this procedure is now being widely performed both within and outside the major teaching centres.^{4,5} PTC also has the clear advantage of providing precise anatomical location of extrahepatic obstruction.

While fine-needle PTC carries a risk, it is unlikely, particularly with the facility for percutaneous drainage of a grossly dilated biliary tree, that the risk of biliary peritonitis will be as high as that following needle liver biopsy. In addition, the use of prophylactic antibiotics appears to minimise the risk of septicæmia.⁶ There can be few experienced biliary surgeons who have not had to operate for one of these complications following a percutaneous liver biopsy in obstructive jaundice. There is now a case for restricting the use of liver biopsy to patients in whom a non-dilated biliary tree has been demonstrated by other means.

Dr Lance and his colleagues have reported a series of patients collected over the years 1959-75, an era which predates the widespread use of GSU and the Chiba needle in Britain, and their results must be accepted with

caution. While the figures quoted may be acceptable for such a retrospective series, they do not necessarily reflect current views in the practice of biliary surgery.

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¹ McKay, A J, et al, *British Journal of Surgery*. In press.

² Elias, E, *Gut*, 1976, 17, 801.

³ Benjamin, I S, et al, *Gut*. In press.

⁴ Fraser, G M, et al, *British Medical Journal*, 1976, 2, 1321.

⁵ Hinde, G de B, and Smith, P M, *British Medical Journal*, 1976, 2, 1561.

⁶ Jain, S, et al, *British Journal of Radiology*, 1977, 50, 175.

Effect of abortion on obstetric patterns

SIR,—I read with interest the interview with Professor R W Beard (23 July, p 251) and in particular the remarks made by the interviewer, corroborated by Professor Beard regarding the effect of abortion on obstetric patterns. Professor Beard implies that in Sheffield the availability of easy terminations of pregnancy has reduced the number of low-birth-weight babies and he goes on to point out how very difficult it is to deal with a woman who comes in at 26 weeks with ruptured membranes.

Surely it is an established fact^{1,2} that one or more terminations of pregnancy are liable to result in more women coming in at 26 weeks with ruptured membranes, and this would exacerbate the precise problem mentioned by Professor Beard. I would suggest that the effect on living standards which is so reasonably desired, and which might be expected to reduce the number of small-for-dates babies, is more likely to be accomplished by a sensible sterilisation campaign rather than the potentially damaging short-term solution of termination of pregnancy in young women.

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¹ Jeffcoate, TNA, *Principles of Gynaecology*, 4th edn, p 641. London, Butterworths, 1975.

² Wright, C S W, Campbell, S, and Beasley, J, *Lancet*, 1972, 1, 1278.

More hydatidiform moles?

SIR,—In the eight months from November 1976 to June 1977 nine cases of hydatidiform mole have been seen at this hospital. This is an incidence of six to seven per 2000 pregnancies where normally only one would be expected.¹

The condition is said to be more common in elderly patients of high parity and in the lower socioeconomic groups. Carr has demonstrated a high incidence of triploidy in both hydatidiform moles² and in aborted conceptions of patients who have recently used oral contraceptives.³ Thus the increase in polyploidy resulting from hormonal imbalance consequent upon recent oral contraception might be expected to give rise to an increase in the incidence of hydatidiform mole. The nine patients were questioned closely about their medical history and contraceptive habits and none had recently used oral contraceptives, nor had they any age group, blood group,

parity, social class, or medical history in common.

All the molar pregnancies were conceived after the severe drought of last summer and it is known that the nitrate concentration in the drinking water in this area rose significantly at the time.¹ Nitrates have been implicated in methaemoglobinaemia in neonates and in gastric carcinoma in adults, but neither they nor any other constituent of drinking water are known to promote the development of trophoblastic tumours.

I wonder whether any other areas have experienced a similar increase.

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¹ Dewhurst, C J, in *Integrated Obstetrics and Gynaecology for Postgraduates*, 2nd edn, p 253. Oxford, Blackwell Scientific, 1976.

² Carr, D H, *Obstetrics and Gynecology*, 1966, 33, 333.

³ Carr, D H, *Lancet*, 1967, 2, 830.

⁴ Wild, A, *Nature*, 1977, 268, 197.

Preventing prematurity in twins

SIR,—In your leading article on this subject (25 June, p 1618) you say that "there seems to be no effective prophylaxis that can be offered to women expecting twins." You say further that no study of the use of β -sympathomimetic drugs in twin pregnancies has been reported. You do not refer to Continental studies—for example, the trials which began in Germany in 1972 and which were reported to the annual meeting of the German Society for Gynaecology in Wiesbaden in September 1974. Only 80 cases were reported, but up to that time no undesirable side effects had been reported in these trials. There were four perinatal deaths but in all four cases the twin pregnancy was diagnosed only after the beginning of labour. The paper concluded: "By a combination of bed rest and the use of β -sympathomimetic drugs it is possible to achieve a lengthening of gestation and a reduction in the incidence of preterm birth and perinatal mortality, doubtless as a consequence of the better perfusion of uterus and placenta."¹

The prophylactic use of the β -sympathomimetic drugs is stated now to be a central feature of the management of twin pregnancies in West Germany and also in East Germany.² The drug used for prophylaxis is in oral form. The German experience of the use of these drugs for preventing preterm birth now covers 10 years, but the results as published of German trials in twin pregnancies are not adequate and are no substitute for British trials.³

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¹ Scholtes, G, *Archiv für Gynäkologie*, 1975, 219, 337.

² Sachs, H, and Kühl, H O, *Zentralblatt für Gynäkologie*, 1977, 99, 552.

³ Wynn, M, and Wynn, A, *The Prevention of Preterm Birth*. London, Foundation for Education and Research in Childbearing, 1977.

Campylobacter enteritis

SIR,—We were interested in Dr M B Skirrow's account of campylobacter enteritis (2 July, p 9). We have been using Dr Skirrow's selective medium for the past three months and find that campylobacters similar to those described by him are prevalent in the Epsom area. Campylobacters were isolated from 19 (5.8%) of 330

faecal specimens from patients giving a history of diarrhoea and from only 1 of 120 specimens from patients without diarrhoea.

We confirm that abdominal pain is a common feature of the illness, and in one girl aged 11 years it resulted in admission to hospital and appendicectomy. She developed diarrhoea after operation and a profuse growth of campylobacters was obtained from her faeces. No abnormalities were found at operation and her appendix was histologically normal.

Two points of practical importance have emerged in our laboratory. Firstly, it is important to examine fresh specimens of faeces or to refrigerate the sample if there is likely to be delay. Aliquots of seven positive faecal specimens were kept at room temperature and at +4°C. After 24 hours' storage at room temperature two out of seven samples failed to yield growths of campylobacter on direct plating and only one out of seven remained positive after 48 hours' storage. All the samples kept at +4°C for 48 hours remained positive.

Secondly, alkaline peptone water (pH 8.4) incubated at 43°C in an atmosphere of 5% oxygen, 10% carbon dioxide, and 85% hydrogen appears to be a satisfactory enrichment medium. Preliminary investigations showed that it supported the growth of a small inoculum of campylobacters (1-10 organisms) and allowed campylobacters to multiply in the presence of much larger numbers of *Escherichia coli* and *Streptococcus faecalis*. Two samples of faeces which were negative on direct plating yielded campylobacters after enrichment in alkaline peptone water and subsequent plating on selective medium.

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Plasma drug levels on once-daily dosage

SIR,—Previous correspondence (Drs A J Marshall and D W Barritt (14 May, p 1278) and Dr D A Persoff and Miss Elaine Mason (9 July, p 125)) has suggested that once-daily drug dosage may lead to better compliance. Although the plasma steady-state levels achieved may apparently be similar with once-daily and divided-dose regimens, considerable fluctuation of plasma drug concentration may occur between doses and it cannot be assumed that the therapeutic effects will be the same.

As part of a larger study we have recently examined¹ between-dose plasma level profiles of nortriptyline in the same subjects after receiving either a three-times-daily nortriptyline preparation (10 mg nortriptyline, 0.5 mg fluphenazine) or a once-daily preparation (30 mg nortriptyline, 1.5 mg fluphenazine). With each preparation the plasma level studies were carried out after seven days' medication. Although the two preparations gave similar before-dose plasma nortriptyline levels in the individuals studied, once-daily dosing produced a slow peaking effect in five out of six subjects which was not evident on the three-times-daily regimen. In two subjects the nortriptyline concentration increased after four hours to a maximum of 300% of the pre-dose concentration.

Routine monitoring of plasma nortriptyline levels has recently been advocated by Dr S A Montgomery and others (16 July, p 166), who provided further evidence that plasma nor-

triptyline concentrations above about 150 µg/l inhibit recovery. In the light of our findings single sampling for determination of so-called "steady-state" concentrations may not be appropriate with once-daily regimens, and studies of peak levels between doses may be required in addition to reveal the full implications of a change to a once-daily dose regimen. Furthermore, lower than customary doses of a tricyclic antidepressant, if given once daily, may be adequate for many patients since peak plasma concentrations within the recommended steady-state therapeutic range may be sufficient to produce a satisfactory antidepressant effect. This would avoid the risk of a poor response, as well as toxicity, associated with the high steady-state plasma concentrations, which Dr Montgomery and his colleagues found in 61% of their patients on standard doses of nortriptyline.

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¹ Stevenson, I H, and Schiff, A A, *Neuropharmacology*. In press.

Hygiene in NHS hospitals

SIR,—We were interested to see Dr G A J Ayliffe and Mr B J Collins's further letter (2 July, p 48) on this topic as their position now seems even more isolated. The Department of Health and Social Security has just issued HC(77)24 which reminds health authorities that they should comply with the provisions of the Food Hygiene (General) Regulations 1970 and that environmental health officers should be given "open access" to catering departments and food handling areas in health premises. The DHSS says that recommendations contained in environmental health officers' reports should be immediately considered for appropriate action.

Furthermore, the BMA at the recent Annual Representative Meeting resolved that crown property should be included within the scope of all public health regulations.

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Training programmes

SIR,—Commenting generally, your leading article on medical genetics (30 July, p 279) pointed out the worrying trend in British medicine caused by "the rigidity of the training programmes which have been set out by the royal colleges." You state that they are supposed to be flexible but they may be destroying the ability of young doctors to pursue their career in an unorthodox way.

This view is shared by very many people and in fact many physicians would like to see the whole concept of training programmes abolished. Those of us with considerable experience in training and advising aspiring consultants feel that the whole exercise in drawing up training programmes has been unnecessary