progesterone combinations. But so far as the combined preparations are concerned, my findings fail to confirm her hypothesis that depression and loss of libido is dose-specific. With the seven different products in use in the Croydon clinic from 1962 to 1967, the incidence varied from 12.4 to 23.8% over an average of 21.9 cycles, compared with Dr. Grant's range of from 10 to 34% over an average of 14.9 cycles with the same preparations. For the strongly progestogenic tablets with ethinyl-oestradiol the incidence was 17.2% compared with Dr. Grant's 28%, and with mestranol 16.7% (Dr. Grant 17%), and for the intermediate combined tablets with ethinyl-oestradiol 23.8% (Dr. Grant 20%) and with mestranol 18.8% (Dr. Grant 16%).

As in the case of headache, a change from one preparation to another with a different oestrogen/progesterone combination only occasionally resulted in sustained relief, and I had one patient who developed a psychotic depression on Volidan (megestrol acetate, ethinyl-oestradiol), who later found that her identical twin sister had had a similar reaction on a different compound. That the response is specific there seems little doubt, but, as with the development of migraine, is the specificity as much in the patient as in the pill?—I am, etc.,

Cheam, Surrey.

JOY WEST.

SIR,—Drs. Ellen C. G. Grant and J. Pryse-Davies (28 September, p. 777) show that the highest incidence of depression together with a concomitant rise in endometrial monoamine oxidase occurs with the use of those oral contraceptives with high progestogenic content. I have been using injection of progesterone in premenstrual tension with depression, obtaining excellent results over a number of years. This is equally effective in both reactive and endogenous types of depression in which there is an exacerbation during the intermenstrual phase and when monoamine oxidase inhibitor drugs are not in use. This would appear to contradict the conclusions reached.—I am, etc.,

London W.1.

DAVID WAXMAN.

E.C.G. Changes in Amitriptyline Poisoning

SIR,—The paper by Dr. R. J. Barnes and colleagues (27 July, p. 222) and the letter from Dr. R. G. Brackenridge (10 August, p. 377) prompt me to report another case of amitriptyline poisoning in which E.C.G. abnormalities were recorded.

A 34-year-old European housewife was admitted to hospital nine hours after swallowing 2,450 mg. (44.2 mg./kg.) of the drug. She was deeply comatose, with flaccid paralysis and dilated pupils unresponsive to light. The E.C.G. showed regular rhythm at 110 beats/min., with widening of QRS (to 0.16 sec.) in leads III, aVL, and aVF, sagging depression of ST segment not suggestive of ischaemia in leads I, III, aVL, aVF, and V2-4, and T-wave flattening in all leads, without recognizable U or P waves. She regained consciousness after eight hours, without chemotherapeutic interference, as recommended by Steel *et al.*,¹ but remained confused for a further 24 hours. At no time was she hypotensive, and serum electrolytes were normal. The E.C.G. pattern did not return to normal until the seventh day.

An abnormal E.C.G. in a comatose patient may well be a pointer to amitriptyline or imipramine ingestion, though as Dr. G. R. Burston (24 August, p. 500) points out similar changes occur in poisoning by other agents, but its real value would appear to be the caution it indicates in the management of such cases.—I am, etc.,

W. M. ROBINSON.

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Recovery from Subacute Encephalitis

SIR,—I found your leading article (21 September, p. 693) "Recovery from Subacute Encephalitis" most interesting, particularly the suggestion that so-called subacute sclerosing panencephalitis may be due to measles virus (27 April, p. 189) and that recovery may occur.¹ It is perhaps worth adding that the characteristic clinical picture of progressive spasticity and dementia of this type of subacute encephalitis described by your article is not the only type of subacute encephalitis known.^{2,3} Patients with a presumptive subacute virus encephalitis who recovered, and where the clinical features were of lengthy retrograde amnesia with parietic Lange patterns in the cerebrospinal fluid, were described as long ago as 1960,² and I reported two cases^{1,5} where there was presumptive evidence that herpes zoster and perhaps respiratory syncytial virus may have been the causal agents. In these, subacute encephalitis was associated with a clinical picture of minimal general intellectual deficit, a pronounced Korsakoff dysmnnesia,⁶ abnormal electroencephalogram signs principally in the temporal regions, a mildly parietic Lange curve, and profound retrograde amnesia, with eventual recovery.

Admittedly, the inevitable difficulties of identifying the causative virus in patients who recover made the grounds for incriminating these particular viruses relatively slender, but the clinical picture in both my patients was almost identical with those described by previous workers,¹ and quite different from the kind of subacute encephalitis which your article seems to imply is the only type occurring. Certainly this seems also the impression one gains from most textbooks. It seems that the term "subacute virus encephalitis" should perhaps embrace a whole variety of subtypes, and it is interesting to speculate that the condition may perhaps be commoner in a mild form than is generally recognized, and that more than one of the common viruses may be responsible. If this were so, recovery may not be as exceptional as has hitherto been supposed.—I am, etc.,

PETER HALL.

Powick Hospital,
Near Worcester.

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⁴ Hall, P., *Lancet*, 1963, **1**, 752.
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Synthetic Isoquinoline in Acute Respiratory Disease

SIR,—Your leading article "Chemoprophylaxis of Influenza" (20 July, p. 137) referred to the efficacy of the isoquinoline derivative U.K. 2371 (Pfizer Ltd.) in preventing infection with myxoviruses.¹ The therapeutic efficacy of a related compound, 1-(4-chlorophenoxymethyl) 3, 4 dihydroisoquinoline hydrochloride (U.K. 2054, Pfizer Ltd.) in children up to 5 years of age with acute lower respiratory infection was tested by us in a double blind trial designed to encompass the usual early winter epidemic of respiratory syncytial virus infection in Glasgow.² Possible effects on both clinical illness and viral excretion were sought. Compound U.K. 2054 or placebo was given for seven days, and all patients were given ampicillin with or without cloxacillin. A clinical score was assigned to lower respiratory signs daily.

Comparison of daily median clinical scores (Fig. 1) showed no reduction in illness in the treated group compared with controls. Children with virologically proved respiratory syncytial infection were analysed separately; no difference in clinical response was found. Moreover, the duration of infectivity indicated by serial isolation of respiratory syncytial virus from throat swabs was not altered by the drug (Fig. 2).

FIG. 1.—Comparison of daily median clinical scores in treated and control groups. FIG. 2.—RS virus isolations on admission (D 0) and on subsequent three days (D+1, D+2, D+3).

The seriousness of respiratory syncytial virus infection of young children is well recognized, and its treatment and control present difficulty. There is doubt about the efficacy of antibiotic treatment³ and also about the feasibility of a protective vaccine

against this virus which can reinfect the same person and can attack infants despite the presence of antibodies of maternal origin.⁴ Indeed, in the present study, one child aged 1 year suffered two attacks of acute bronchiolitis separated by an interval of less than two months, during which she was quite well; respiratory syncytial virus was isolated in both attacks.

In most of these children the illness is caused directly by the virus rather than by bacterial secondary invaders, and the disease is thus a well-defined entity against which the efficacy of an antiviral drug might be assessed. In this study major clinical benefits from compound U.K. 2054 were not necessarily expected, and the trial was designed to measure slight effects both on clinical illness and on infectivity during treatment; irrespective of clinical benefit, curtailment of viral isolation would have encouraged further study of the antiviral efficacy of synthetic isouquinoline derivatives. In this trial compound U.K. 2054 was not effective in the treatment of respiratory syncytial virus infection in children, nor did it shorten the period of infectivity. No toxic effects attributable to the drug were observed.

We are grateful to Dr. A. K. Bannerjee, Dr. G. R. Crowe, Dr. J. B. Owens, Dr. J. C. Taylor,

and Dr. H. W. Thomson, and to the ward sisters and nurses for their co-operation in this study. We thank Dr. R. J. Fallon for bacteriological, biochemical, and haematological investigations, and the Medical Research Council Laboratories, Hampstead, and the Standards Laboratory of the Central Public Health Laboratories, Colindale, London, for certain cultures and reagents, and the Research Division, Pfizer Ltd., for supplying compound U.K. 2054 and placebo, making available the results of their preliminary experimental studies and providing a research grant to one of us (M.B.E.).

—We are, etc.,

J. A. SMITH.
MARGARET B. EADIE.
N. R. GRIST.
J. H. LAWSON.
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G.P. Obstetric Units

SIR,—The forthright criticism by Sir John Peel of your leading article (14 September, p. 678) must be assumed to represent the considered viewpoint of his College. This reveals certain inconsistencies which should be subjected to the fullest debate, since a pronouncement of this sort by one who is the acknowledged leader of his specialty will naturally carry considerable weight with the less well qualified planners of the Health Service.

The Royal College of Obstetricians and Gynaecologists awards the diploma in obstetrics to some 500 candidates annually. Many, if not the majority, of these doctors are destined for a career in general practice. Therefore college approval of general practitioner training for, and participation in, the practice of obstetrics can be presumed.

In 1966 approximately 614,000 deliveries took place in hospitals and 200,000 in patients' homes. The total of obstetric beds available in hospitals was 22,500 of which 4,600 were under the care of general practitioner obstetricians.¹ At the present rate of hospital building it will be many years before obstetric beds in consultant-type units in district general hospitals are available to secure a 100% institutional confinement rate. Even then the geographical difficulty of general practitioners attending their patients in labour in a district general hospital some miles from their practice will prevent many of them from doing so. Their training will have been largely wasted.

The 1958 Perinatal Mortality Survey² showed that general-practitioner obstetric standards, as judged by attendance at labour, are raised by practising in a general-practitioner obstetric unit. And though this may be "one of the least safe places in which a patient could be delivered" it is still very much safer than the patient's home, which rarely contains the minima of communications, staffing, and facilities envisaged by your leading article.

That the Royal College of Obstetricians

and Gynaecologists should encourage general practitioners to train to practise obstetrics and now apparently wishes to limit their ability to do so requires further explanation. —I am, etc.,

Brecon.

A. J. M. CAVENAGH.

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SIR,—Your correspondent, Dr. Clement W. Walker (5 October, p. 54), surely puts his finger on the spot when he says it is "not institutions but midwives and obstetricians who make childbirth safe for the women of Britain," and it is time that we, the general practitioners, acknowledge the unpalatable fact that few of us see enough abnormal obstetrics to remain competent, however adequate our initial training may have been. Having obtained the diploma in obstetrics and gynaecology in 1960 and supervised 20 to 30 home deliveries per year for 15 years, I would be the first to admit that my experience is woefully inadequate and that in another 10 years I shall be downright incompetent.

Increased specialization within general practice is in my view inevitable and essential, and if obstetrics were undertaken by only a minority of general practitioners who would then have to devote a large amount of time to it and who could more readily be incorporated in a specialist's team then uniformity of care and greater safety would be achieved quite speedily. We have got to acknowledge the fact that the figures from a small number of general-practitioner units are quite appalling and, at the same time, make it plain that in the best general-practitioner units the figures are at least as good, if not better, than in average consultant units,

where the standard of care (due to chronic staff shortages) is far from optimal. Domiciliary midwifery is one of the great joys and rewards of general practice, but it is also wise to admit the financial stake which the general-practitioner obstetrician has in these discussions. Which of us can calmly contemplate the loss of 10 to 15% of our already inadequate income, without being just a little bit biased? The single-handed general practitioner is most concerned here, and it is only within the framework of a group practice where one of the four or six partners does all the obstetrics that it is possible to eliminate the bias of a vested interest. I submit, Sir, that any discussion which fails to take these unpalatable facts into account is unrealistic.—I am, etc.,

Dover, Kent.

R. J. L. DAVIS.

SIR,—Sir John Peel (14 September, p. 678) would appear to have missed the point with his comments on the excellent leading article (7 September, p. 567), which for the first time expressed what we have been trying to achieve.

Most are agreed that 100% hospital delivery is the ideal, and that as many 48-hour discharges as possible help towards the objective. There remains, however, a group of healthy women between the ages of 18 and 26 who have to be delivered in their own bedrooms, and there is nothing to suggest that this will not continue for a considerable time. No consultant is responsible for these cases, and to imply that it is safer for general practitioners and midwives to deliver these patients in their own homes instead of a unit with good lighting, firm beds, and drip equipment readily available is manifest nonsense. A midwife may have two or even three patients in labour at the same time who could be more easily managed under one roof.

Why these delivery units have to be near a consultant has always baffled us, as no consultant is at hand during domiciliary confinements and the flying squad is always 30 to 40 minutes away. We certainly are not interested in confining more difficult obstetric cases in such a unit than we already have to in this district.

If Sir John, as president, Royal College of Obstetricians and Gynaecologists, is expressing an official view, then we are condemned to continue what is literally "cottage obstetrics."—We are, etc.,

THOMAS FREW.

J. M. FREW.

Wickford, Essex.

R. G. ANDERSON.

SIR,—There are three general-practitioner maternity units in the Chelmsford group: at Maldon (17 beds), Braintree (11 beds), and Burnham-on-Crouch (5 beds). They are about 10, 10, and 20 miles (16, 16, and 32 km.) from the specialist unit at Chelmsford. Between 1963 and 1967 4,899 babies were born in the units, with a perinatal mortality rate of 4.9 per 1,000. During the same period 6,493 babies were born at home, with a perinatal mortality rate of 9.8. In 1967 the perinatal mortality rate for the units was 1.9 and that for home confinements was 11.5. Forty-six per cent. of the unit and 16% of the home births were to primi-