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.,

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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.,

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REFERENCE

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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.,

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⁴ Hall, P., *Lancet*, 1963, **1**, 752.
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⁶ Korsakoff, S. S., 1889, translated by M. Victor, P. I. Yakovlev, in *Neurology*, 1955, **5**, 1396.

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