sions when toxic buccal and gastrointestinal symptoms develop to mild or moderate severity.

One patient received an initial infusion of 11 g. in five days without any clinical benefit or toxic symptoms. Six weeks later infusion was repeated. A total of 31 g. was administered in 14 days. This was excessive, causing severe gastrointestinal and haematological effects, but recovery was rapid. The most recent case, a young British migrant, received 19 g. in nine days into the hepatic artery (not the coeliac axis). This infusion was deliberately terminated early because the patient intended to, and three weeks later did, return to Britain, with a patent catheter in situ.

The clinical course of these cases, and laboratory surveillance by Dr. W. Roman, of the Institute of Medical and Veterinary Science, North Terrace, Adelaide, showed that the dosage used was well tolerated systemically and by the liver parenchyma. Serial serum enzyme estimates by Dr. W. Roman revealed large increases in serum lactic dehydrogenase and very small increases in alanine aminotransferase, but minor changes in other liver-function tests. This was regarded as clear indication of breakdown of tumour cells in preference to parenchymal liver cells. These results have been reported in a paper presented to the Sixth International Congress of Clinical Pathology, with the result of confirmatory hepatic infusion in animals by Dr. S. T. Hopcraft. Full details of this work will be published in due course.—I am, etc.,

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Oestrogens and Thromboembolism

SIR,—I wish to take issue with you over your leading article on oral contraceptives and thromboembolism (27 April, p. 187). This article led recently to a minor panic in the popular press in Australia about the alleged dangers of oestrogens in oral contraceptives, a panic quite unjustified by the scientific evidence you have uncritically quoted.

It is true that the work of Drs. M. P. Vessey and R. Doll (27 April, p. 199) did not incriminate any particular kind of oral contraceptive, and it is also true that there is other evidence that oestrogens may have an effect on blood clotting. But then you go on to say that these findings suggest that it is the oestrogens rather than the progestogens which are responsible for thrombosis. This statement is quite unjustified on the evidence quoted, and so is your next statement that sequential preparations are therefore more dangerous than combined.

The first authority you quote is that of Daniel, Campbell, and Turnbull.¹ These authors used oestrogens in the form of diethylstilboestrol in doses of 30–60 mg. daily for three days and then 20 mg. daily for a final three days, and they reported that this regimen significantly increased the risk of embolism in the puerperium. However, when the doses used are considered, one begins seriously to wonder whether oestrogens, as used in the suppression of ovulation, are necessarily dangerous. Martindale² suggests doses of 5 mg. of diethylstilboestrol three times a day for three days and then 5 mg. daily for six days, for the suppression of lactation (a total of 75 mg. as opposed to the doses used by Daniel *et al.* of 150–240 mg.

given over a shorter period). Martindale quotes 1 mg. of diethylstilboestrol as being equivalent in potency to 0.05 mg. of ethinyloestradiol, so that in effect Daniel *et al.* were using doses, in six days, equivalent to up to 240 by 6 by 0.05 mg. (=72 mg.) of ethinyloestradiol. The dose of this drug for ovulation suppression over the same period would be 0.60 mg. This means that Daniel *et al.* were using doses 120 times higher than those used in ovulation suppression. This casts some doubt on your suggestions about the danger of oestrogens in more physiological doses as used in oral contraception.

The other authority you quote in support of your somewhat shaky arguments is Oliver,³ who found that unstated doses of ethinyloestradiol in men produced more episodes of thrombotic type than occurred in controls. The figures given are not analysed statistically. Oliver also suspects oestrogens and quotes in support of his argument the work of Wynn and Doar⁴ and Wynn, Doar, and Mills.⁵ These authors studied glucose metabolism and other factors of blood chemistry in women who had been on oral contraceptives and compared results with a control group. There were certainly significant changes in the test group, but neither Oliver nor the B.M.J. is entitled to draw any conclusions about the effects of oestrogens from this work, because the oral contraceptives studied, as pointed out by Wynn *et al.*, were almost exclusively of combined type (and in fact most of those used contained 19 nortestosterone derivatives, which are known to have certain androgenic and anabolic properties).

Oral contraceptives are not an entity, but vary widely in their qualities. Conclusions drawn about combined oral contraceptives give information about the effect of combined oral contraceptives—not the relative parts played by different components.—I am, etc.,

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REFERENCES

- ¹ Daniel, D. G., Campbell, H., and Turnbull, A. C., *Lancet*, 1967, 2, 287.
- ² *Extra Pharmacopoeia: Martindale*, 25th ed., 1967. London.
- ³ Oliver, M. F., *Lancet*, 1967, 2, 510.
- ⁴ Wynn, V., and Doar, J. W. H., *Lancet*, 1966, 2, 715.
- ⁵ Wynn, V., Doar, J. W. H., and Mills, G. L., *Lancet*, 1966, 2, 720.

Disappearing Drain

SIR,—A recently encountered complication from the use of closed suction drainage may be of interest to your readers.

A 42-year-old man was submitted to a left medial meniscectomy. As he had had previous femoral artery disease which had required surgery a tourniquet was not employed for this procedure. After routine haemostasis had been secured the wound was closed over a perforated plastic closed suction drain. Six hours after the operation the drain was removed, as there had been virtually no return in the suction bottle. The drain came out with some difficulty, and it was therefore strongly suspected that a segment of the drain had in fact broken off within the joint. Multiple x-rays of the joint were taken without revealing any foreign body within the joint. The knee was then x-rayed with the catheter lying on the skin. Under these latter conditions with the catheter filled with air the plastic showed up clearly. The knee was then re-explored through the original operation wound and a 2 cm. segment of plastic drain was removed

which matched exactly to the end of the major fragment, the plastic having broken through one of the perforations. Under the particular circumstances encountered the fragment of drain could not be demonstrated by x-ray examination.

There seems to be a case for having this type of appliance impregnated with radio-opaque material.—I am, etc.,

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Organic Brain Dysfunction

SIR,—The clarification of the questions which Drs. P. Graham and M. Rutter (21 September, p. 695) brought to the combination of organic brain dysfunction and childhood psychiatric disorder was well served by a deliberately restrictive methodology, such as applied in their valuable investigation. They excluded non-current neurological disorder and "minimal brain damage." Important as their findings are for this whole field, they should not, by their acknowledged weight, overshadow the existence of further possibilities and problems which are present in the same field.

This field clearly comprises two sectors: the "coexistence" sector, and the "sequels" sector. They both stand in their own right, but connecting points may be lost to sight if mutual exclusion should become a rule. There is much to be said for the "longitudinal" (or life-developmental) aspect, which brings out further facts relevant to psychiatry. For instance, some children who have suffered from chorea or one of the post-infectious encephalopathies of the encephalitic or meningitic type or even severe concussion (and some like these must have been among the nearly 12,000 Isle of Wight schoolchildren) may in the long run become even more productive of psychiatric symptoms or developments than the children highlighted in the survey.

As one who has applied some endeavour to the investigation of the "sequels" sector,¹ I venture to hope and to plead that research developments may bring about a combination and integration of the two possible aspects.—I am, etc.,

STEPHEN KRAUSS.

Reading.

REFERENCE

- ¹ Krauss, S., in *Proc. 8th Internat. Congr. Neurology*, Vienna, 1965, Vol. 5, p. 145.

"Sniffing" and Addiction

SIR,—The paper by Dr. J. Merry,¹ and your leading article,² on the subject of addiction to "glue sniffing," have prompted me to report another case of addiction to a volatile organic substance.

Not long ago I encountered a young man who had decided to try for fun the effect upon him of inhaling carbon tetrachloride, a liquid much used in industry and to which he had easy access. Liking the feeling of light-headedness (and other sensations) produced when a small quantity of carbon tetrachloride was poured on a handkerchief and inhaled, he could not resist the temptation to repeat the experiment with ever-increasing frequency.