As regards effect on lactation there are no objective studies made of this so far as I am aware: I do know that in the various papers quoted by Dr. Venning there are figures based on the patients' impressions. I would certainly agree that this is something which must be explored with a view to using oral contraceptives in countries where prolonged lactation is common. This will have to be done for each population group, for it appears that women in these countries need a smaller dose of oral contraceptive than is used in this country and the smaller doses seem to have less effect on lactation.

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[2] —— *Family Planning*, 1963, **12**, No. 3.

Diethylpropion and Addiction

SIR,—It is perplexing that the otherwise excellent research report of Drs. I. Oswald and V. R. Thacore ("Amphetamine and Phenmetrazine Addiction," August 17, p. 427) concluded with the sweeping generalization, "These drugs, and drugs with comparable actions, such as diethylpropion,[1] are dangerous drugs in fact if not yet in law." Whatever else, the reference to diethylpropion hydrochloride, not one of the drugs studied by the authors, on the basis of a single published report is difficult to view as justified by the facts presented.

The problems of addiction are not identical with those of misuse and certainly not, *per se*, the equivalent of danger. Do the authors really believe that the abuse of a chemical compound by an emotionally disturbed individual indicates that the chemical is addictive and therefore dangerous? The inclusion of diethylpropion hydrochloride in the report depends upon such data in a single reported case. In fact, some hundreds of millions of tablets of diethylpropion hydrochloride have been issued for prescription. If the compound were indeed addictive and dangerous, reports of this kind would occur with much greater frequency than this.

The weight of presently available evidence indicates that the amphetamines, phenmetrazine, and diethylpropion hydrochloride are safe, effective, and useful when given under proper medical supervision according to the manufacturers' directions. The occasional report of addiction for these, or indeed for any compound, has much wider implications than merely the nature of the chemical substance involved. Certainly the sociological and psychological considerations should not be neglected.

The conscientious research worker must certainly warn his practising colleagues of dangerous reactions to the drugs he investigates. This writer has himself published such reports.[2] Warnings of this kind, supported by factual data, are of great value. Interpretations of them, to be of like worth, should not omit consideration of the total situation.

The observed misuse of a drug in even a hundred cases of a series of a million (0.0001%), let alone one such case (0.000001%), scarcely warrants the conclusion that it is addictive and certainly does not provide convincing evidence that it is dangerous.—I am, etc.,

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REFERENCES

[1] Clein, L. J., and Benady, D. R., *Brit. med. J.*, 1962, **2**, 456.
[2] Roebuck, B. E., *J. nerv. ment. Dis.*, 1956, **124**, 248.

Side-effects of Meprobamate

SIR,—I was surprised to see in the *British Medical Journal* of July 20, 1963, on page 163 in the article entitled "To-day's Drugs," the following statement related to meprobamate: ". . . serious toxic effects including agranulocytosis have been reported."

This statement is incorrect. Up to the present, not a single case of agranulocytosis has been described in patients receiving only meprobamate. There were three cases of agranulocytosis in patients who in addition to meprobamate also received a drug of the phenothiazine or imipramine group, which are known to produce agranulocytosis.

Dr. L. Meyer *et al.*[1] described a case of aplastic anaemia after meprobamate. The patient, as is apparent from the hospital records, was also receiving sulphonamide nose drops, "coricidin" (containing chlorpheniramine maleate, aspirin, phenacetin, and caffeine), as well as various hormones which may well have been responsible for the occurrence of the aplastic anaemia. This opinion is supported by the fact that no other case of aplastic anaemia was reported in the literature or came to my knowledge since then. Meprobamate has been widely prescribed since 1955 and during this period serious toxic effects have occurred only very exceptionally. The incidence of side-effects with meprobamate appears to be lower than with any other widely used tranquillizer.

I find it difficult to understand how a journal of your standing and reputation could publish such an irresponsible remark about a drug without first checking the facts.—I am, etc.,

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REFERENCE

[1] *New Engl. J. Med.*, 1957, **256**, 1232.

[On Dr. Berger's own showing it was not incorrect to write that serious toxic effects had been reported, and we cannot agree that it is irresponsible to quote results reported in reputable American scientific journals. Moreover, the Registry on Blood Dyscrasias of the A.M.A. (*J. Amer. med. Ass.*, 1963, **185**, 289) reports one case of agranulocytosis with meprobamate alone, as well as quite a number of cases when other drugs had been taken.—ED., *B.M.J.*]

Collapse after Pethidine and Promethazine

SIR,—Referring to Mr. A. G. Amias and Mr. D. Fairbairn's report of foetal death following pethidine and promazine by intravenous injection (August 17, p. 432), I wish to mention two cases of collapse following intramuscular injection of pethidine 100 mg. with levallorfan 1.25 mg. ("pethilorfan") 100 mg. and promethazine hydrochloride ("phenergan") 25 mg. Both patients were young women who had passed their expected dates of delivery by 14 days, and were given the above medication preparatory to artificial rupture of the forewaters for induction of labour.

The first, a primigravida aged 24 years, became pale and pulseless with an unrecordable blood-pressure approximately five minutes after the injection. She was given oxygen by mask and by the time an intravenous infusion was started (about five minutes) a rapid feeble pulse could be felt and the blood-pressure recorded as 60 mm. Hg systolic. The foetal heart rate, previously 140 beats per minute, had risen to 180 beats per minute. Her condition gradually improved and an hour later the blood-pressure was 120/80 mm. Hg systolic and pulse 90 per minute. The foetal heart rate remained around 160 beats per minute. Nothing further was done; the patient commenced labour spontaneously two days later and delivered a healthy female baby weighing 7 lb. 4 oz. (3.3 kg.).

The second patient was a healthy para-one aged 28 years. The medication and sequence of events was the same as in Case 1. The blood-pressure fell from 110/70 mm. Hg systolic to 80/50 mm. Hg systolic and returned to normal within 10 minutes. The foetal heart rate rose from 136 to 150 beats per minute. Rupture of the forewaters was proceeded with and a living male baby was delivered after a total labour of 11 hours.

Both these babies were healthy and cried immediately after delivery. Although the combination of pethilorfan and phenergan has been used for sedation and analgesia in well over 200 cases before and during labour, no ill effects have been observed apart from the cases described. The foetus survived in both cases. The fact that their patient was two weeks past the expected date of delivery and had a rise of blood-pressure with albuminuria must have contributed significantly to death of the foetus in the case described by Mr. Amias and Mr. Fairbairn.—I am, etc.,

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Reactions to Tranylcypromine

SIR,—We would like to report a further instance of a reaction to tranylcypromine, causing in this case definite subarachnoid haemorrhage.