Contraindications to Oral Contraception

SIR,—In connexion with your annotation (August 4, p. 315) it must be emphasized that there is absolutely no evidence that women using oral contraceptives are more liable to thrombophlebitis than women who are not. You refer to a private conference held in the United States. This was arranged by the Searle medical department so that independent experts might review the evidence. You appear to have been misinformed about the conclusions arrived at by the experts. None of the experts present expressed the opinion that oral contraception increases the risk of thrombophlebitis to the level associated with pregnancy. You state correctly: "These cases do not establish cause and effect"; but this is precisely the assumption in your statement: "It must be asked whether even this risk should be run just for contraception." The pseudo-pregnancy effects of oral contraception were discussed at the conference, but in another context. The Searle medical department have been keeping a close watch on the side-effects of oral contraception for many years (since 1952). Our literature draws attention to the fact that oral contraception mimics the hormonal effects of pregnancy, as this is important in relation to definite known effects, including nausea, breast changes, and transient fluid retention at the start of medication. There is, however, no evidence that the risk of thrombophlebitis in pregnancy is in any way related to the female sex hormones. It is likely that the connexion is related to local effects upon the venous return due to changes in the circulation in the pelvis.

The conference reviewed the data on possible hormonal influences on the thrombotic process, and the following considered statement has been authorized by Dr. Sol Sherry (Professor of Medicine, Washington University), a world authority on coagulation and fibrinolysis:

> "Though preliminary data suggests that some patients on Enovid might develop abnormally high levels for those clotting factors involved in the later stages of clotting (prothrombin or proconvertin or Stuart Power factor), this point remains to be established. Were it established its true significance would still remain obscure."

(In my opinion the only connexion between sex hormones and thrombosis which rests upon any secure foundation is the well-known immunity from coronary thrombosis enjoyed by women with normal ovarian function. While no claim is made that oral contraception provides any beneficial action of this type there is no evidence of any contrary effect.)

It was pointed out at the conference that in view of our existing comments on the pseudopregnancy effects of oral contraception there appeared to be no need for any additional warning in our literature. It was in this context that the opinion was expressed that oral contraception carries no greater risk of thrombophlebitis than normal pregnancy. The conference did not make any suggestion that the use of oral contraceptives leads to an increased risk of thrombophlebitis such as exists in pregnancy. The writer of your annotation is definitely incorrect in making this assumption.

Apart from this there are many aspects of the problem not even considered in your annotation; some should at least be mentioned. Short[1] found pulmonary embolism to be commoner than pneumonia in a general hospital, and it is now increasingly becoming realized that thromboembolic disease may occur without known precipitating factors,[2] even among premenopausal women.[3] A very conservative estimate of the incidence of thrombophlebitis in women aged 15 to 45 is 1,000 cases per million women per annum. Less than 30 reports have been received from among a million women using norethynodrel. While there are probably a number of unreported cases the data certainly provide no evidence of increased risk. As, however, the matter has received wide publicity in the lay press throughout the world as a result of your annotation we recommend that oral contraception should not normally be advised for women with a history of thromboembolic disorders in pregnancy. It should, however, be pointed out that these women run a real risk if they become pregnant again, and this should be weighed against the hypothetical risk of oral contraception.—I am, etc.,

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REFERENCES

1 Short, D. S., *Brit. med. J.*, 1952, **1**, 790.
2 Stevens, A. E., *Lancet*, 1961, **2**, 1005.
3 Searle Conference on Thrombophlebitis, Philadelphia, U.S.A., April 12, 1962.

SIR,—Your annotation (August 4, p. 315) on contra-indications to oral contraception was indeed timely. You state that in America there have been apparently a number of examples of women on "enavid" developing thromboembolic complications, some of them fatal; and that in Britain four cases are known, all with a previous history of thromboembolic episodes in pregnancy, but that clinical details of these have not yet been published.

I have already described (*Lancet*, 1961, **2**, 1146) the first case reported in Britain of severe pulmonary embolism and infarction produced by treatment with enavid. My patient had never been pregnant, had no previous history of thrombophlebitis, and had no varicose veins in the legs. She had none of the proposed contraindications to oral contraeeption, but only suffered from endometriosis, which was the indication for which enavid was prescribed by her gynaecologist. A daily dose of 20 mg. caused continued vomiting and bilateral pulmonary embolism, with the typical clinical, radiographic, and electrocardiographic features of this disease.

This dreaded and sometimes fatal complication to treatment with enavid can occur without warning in patients with no previous history of thrombophlebitis. The risk of provoking pulmonary embolism should be considered before enavid is prescribed for therapeutic, or "conovid" for contraceptive, purposes.—I am, etc.,

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SIR,—I read with interest the letter on this subject by Dr. A. R. Hill (July 7, p. 52).

There is a great deal of anxiety associated with the problem of contraception, and its easy solution is everywhere desirable. Oral contraceptives are the cheapest, the easiest, and most relatively certain means of contraception, and consequently have had a great welcome both by the medical profession and the public.