

to 39 years, however, were recorded as having a deep vein thrombosis or pulmonary embolism when neither pregnant nor puerperal (Crombie, personal communication, 1967); three used oral contraceptives and three did not, and two in each category were admitted to hospital. The resultant annual hospital admission rates (approximately 60 per 100,000 women who used oral contraceptives and 5 per 100,000 women who did not; are subject to large standard errors, but are none the less similar to those calculated in the present study (47 and 5 per 100,000 respectively).

In the second study (Inman and Vessey, 1968) the data relate only to deaths and, in the case of pulmonary embolism, women who had suffered a previous thromboembolic episode were classified with women who had other predisposing conditions. Again, however, it may be noted that the relative risk among women who used oral contraceptives was increased about eight times, whereas in our study the relative risk of pulmonary embolism was increased approximately 12 times.

In any disease which is as rare as "idiopathic" deep vein thrombosis or pulmonary embolism it is always possible that the condition reflects an idiosyncratic reaction due to the patient's genetic constitution. Our data do not rule out this possibility, but neither do they provide any strong support for it. In particular there is no suggestion, either in this study or in that of the Committee on Safety of Drugs, that venous thromboembolism tends to occur shortly after beginning the use of oral contraceptives—as might be expected if the reaction was idiosyncratic.

The data are also too few to give any clear answer to the question of the relative effect of the different combinations of oestrogen and progestogen, but neither study provides any indication that there is likely to be much difference between them.

Cerebral and coronary thrombosis

Our data contribute little new information relating to the occurrence of cerebral and coronary thrombosis. Only nine previously healthy women who were married and aged 40 years or under were treated for "cerebral thrombosis" and 16 (including three who died) from coronary thrombosis in 16 large hospitals in a three-year period. The diagnosis of cerebral thrombosis is difficult to establish with certainty, and it is possible that the majority of patients in our small series suffered from some other intracranial condition. It is notable, however, that five of the nine patients had been using oral contraceptives when their disease began. This finding in itself implies little, but taken in conjunction with the similar findings of the Committee on Safety of Drugs (Inman and Vessey, 1968), of Bickerstaff and Holmes (1967), and of Illis *et al.* (1965), it justifies the conclusion that oral contraceptives can be a cause of episodes of cerebrovascular insufficiency. Only Jennett and Cross (1967), who studied 26 non-pregnant women suffering from "ischaemia in the carotid territory" during 1961-5, failed to find any evidence of an association.

Most of the nine patients in the present study suffered a mild illness followed by a good recovery. At the time of interview several of the patients complained of minor residual disabilities, but only one was still severely incapacitated by a slowly recovering left hemiplegia. She had suffered bilateral internal carotid artery thrombosis in September 1966, demonstrated by angiography, and had previously taken an oral contraceptive for several months.

Despite the fact that changes have been demonstrated in carbohydrate metabolism and the pattern of serum lipids in women taking oral contraceptives, which might be regarded as conducive to coronary thrombosis (Wynn and Doar, 1966; Wynn, Doar, and Mills, 1966), epidemiological studies have as yet provided very little confirmatory evidence. A few case histories have been reported—for example, Hartveit (1965)—and a number of other studies have shown an excess mortality from coronary thrombosis in men treated with oestrogens for various reasons (see Schrogie and Solomon, 1967). The study of the Committee on Safety of Drugs (Inman and Vessey, 1968) is compatible with some increased risk under 35 years of age, but the 13 patients with non-fatal coronary thrombosis in our study (only five of whom were under 35 years of age) offer no further support. We conclude that the existence of a risk of coronary thrombosis is not proved. If, as our data suggest, women who use oral contraceptives are somewhat heavier smokers than average, this factor will need to be taken into account in interpreting future findings (Dorken, 1967).