

these (4) was carried out by selected members of the College of General Practitioners who reported on 147 women from their practices with thromboembolic disease (mostly superficial venous thrombosis) and 294 controls. The risk of venous thrombosis was estimated to be increased nearly three-fold among users of oral contraceptives.

A study of women who had fatal attacks of pulmonary, coronary and cerebral thrombosis and embolism in the year 1966 was made by Inman and Vessey (5). Among 26 idiopathic cases of pulmonary embolism, there was a clear excess of users of oral contraceptives over the number expected from the experience of control women; in 49 cases where predisposing conditions existed, there was a small, statistically insignificant excess. Findings for coronary thrombosis were conflicting. For cerebral thrombosis, there was again an association with the drugs, limited to patients without predisposing conditions.

The most significant study has been that of Vessey and Doll, a second report on which has recently been published (6). Although their study and the one reported in this paper are quite similar in design, they were planned and conducted entirely independently. The main differences are that Vessey and Doll excluded patients with only superficial thrombophlebitis but included those who had had previous attacks of thrombophlebitis. They interrogated 87 married cases of idiopathic deep vein thrombosis or pulmonary embolism, 19 of cerebral thrombosis, and 17 of coronary thrombosis. For 84 of the thromboembolism cases they interviewed two matched controls per case, or altogether 168 controls with other diseases. The subjects had been treated between 1964 and 1967 in 19 hospitals in the northwest region of metropolitan London. Large differences between cases and controls in the proportions having used oral contraceptives within one month before onset (or in the case of controls, entry to hospital) were found for the thromboembolism and cerebral thrombosis series, but none for the coronary thrombosis series. Little difference was seen between thromboembolism cases and controls according to type of contraceptive combination; none of the cases or controls had used the sequential preparations, but this is not remarkable, as only 3% of the oral contraceptives supplied in Britain during this period were sequentials. Duration of use was similar for thromboembolism cases and those controls who had used the hormones. The association was stronger for patients who had never had a previous attack of thromboembolism than for those who had, but interpretation of this observation is considered by the authors as impossible without further knowledge of the interaction between use of oral contraceptives and the predisposing factors associated with a history of previous disease. The thromboembolism cases tended to weigh more than controls, and to be above standard weight, a relationship that held irrespective of use of oral contraceptives. The authors consider that a suggestion in the preliminary report of their findings of an interaction between heavy smoking and use of oral contraceptives in the pathogenesis of thromboembolism is not supported by the complete figures. However, our examination of their data still seems to show an association of at least borderline significance between heavy smoking and thromboembolism.

They conclude that the relative risk of hospital admission for deep vein thrombosis or pulmonary embolism among married women who are oral contraceptive users appears to be 6.3, with confidence limits of 3.4 and 11.6. They also state that their estimate of the annual risk of hospital admission for these conditions plus cerebral thrombosis is about 0.5 per 1,000 for married women who are using oral contraceptives, and 0.06 for those who are not.

Drill and Calhoun (7) have reviewed the evidence linking oral contraceptives to thromboembolic disease, and have concluded that the incidence of thrombophlebitis is not increased when these drugs are employed. Their paper, published when only the preliminary report by Vessey and Doll had appeared, deals with a considerable number of complex issues. It has led to a vigorous correspondence in the columns of the *Journal of the American Medical Association*; the reader's attention is invited especially to the response by Doll, Inman and Vessey (8) and the reply by Drill and Calhoun, as well as the comments of Seltzer, and of Frederiksen and Ravenholt, in the same issue.

In view of the importance of the paper by Drill and Calhoun, its major points will be re-examined. Firstly, it placed emphasis on the disparity between the incidence rates of thrombophlebitis in nonpregnant women of child-bearing age as estimated by Vessey and Doll (.05 admissions per thou-