

basis of known supply figures (provided by Intercontinental Medical Statistics Ltd., personal communication, 1967). No indication was obtained that any one contraceptive formulation is more likely to be responsible for thromboembolic disease than the others, though only a marked effect would have been detectable with a few data. None of the affected women had been using sequential preparations; but this was to be expected as only about 2% of the oral contraceptives consumed during 1964-6 were of this sort.

Comparison of the duration of use of oral contraceptives was also handicapped by the small amount of data. We may note, however, that 42% of the women who developed thromboembolic disease (11 out of 26) had been using oral contraceptives for less than six months, and the corresponding proportion for the control patients was almost identical (4 out of 10).

Family history

All affected and control patients were questioned about the illnesses and causes of death of their parents and sibs. No significant differences were found between the numbers of relatives who had died from a variety of causes. There were, however, small differences in the reported frequency of morbidity from phlebitis among both mothers and sisters. Thus nine mothers and seven sisters of the affected women and nine mothers and two sisters of twice as many control women were reported to have suffered from non-fatal phlebitis. These differences may indicate family predilection for venous thromboembolism or they may be the result of preferential recall by the affected subjects. There was no suggestion that a positive family history might be more common among affected women who used oral contraceptives than among affected women who did not.

Estimate of incidence

Data provided by the North-West Metropolitan Regional Hospital Board indicates that the hospitals participating in the study include approximately 60% of the Board's female acute general medical and surgical beds. All but one of the affected patients resided within the Board's catchment area at the time of admission to hospital, so that we can reasonably relate our findings to the population of that area.

The total number of woman-years at risk can be estimated by reducing the size of the total female population aged 16-40 years for the Board's area in 1965 (Registrar General, 1967) by appropriate factors to allow for the proportion of single, widowed, pregnant, and puerperal women, and then multiplying the result by three. No adjustment can, however, be made for the other factors taken into account in this study, such as the number of women with relevant chronic diseases or in the postoperative or postmenopausal state; but the number is unlikely to be large (not more, we would think, than 10% of the population). An estimate of the years at risk for women who took oral contraceptives can be made from supply figures for the country as a whole, on the assumption that women resident in the Board's area were representative of the whole population with respect to their use of oral contraceptives; and an estimate of the number of affected patients who did and who did not use oral contraceptives can be obtained by multiplying the observed numbers by 1.67, on the assumption that the study covered 60% of the relevant hospital beds and that the one affected patient who was not resident in the area counterbalanced one affected resident who was treated elsewhere.

On this basis the annual attack rate of venous thromboembolic disease, without evident cause but of sufficient severity to require hospital admission, is about 5 per 100,000 (or 1 in 20,000) women who do not use oral contraceptives, and is about 10 times higher (47 per 100,000, or 1 in 2,000) in women of similar marital status who do. If the calculations are limited to women without previous venous thromboembolic disease the annual attack rate is reduced to about 1 in every 3,000 women who use oral contraceptives, but the relative risk is not materially altered. The two patients taking Metrulen-M have been omitted from these calculations as the use of this drug is not known for the estimated population at risk.

Relative risks can also be calculated directly from the hospital data given in Table IV. From these data the risk among women who use oral contraceptives is calculated to be about nine times that among women who do not (26/32 divided by 10/106). These two values for the relative risk, which use different