

all, no significant association has been found between death from this disease and the use of oral contraceptives, a finding in keeping with that of Vessey and Doll (1968), though in that study there were few patients with coronary disease and in some the diagnosis was uncertain. There are, however, some subgroups in the present study among whom a significant association between oral contraception and death from coronary thrombosis has been found, in particular among young women of low parity. The work of Wynn and Doar (1966), and of Wynn *et al.* (1966) has shown that a proportion of women using oral contraceptives develop abnormalities of carbohydrate and lipid metabolism similar to those of steroid diabetes. The association between diabetes mellitus and coronary thrombosis is well established.

It is important to estimate the risk of a fatal outcome to oral contraception and also to identify any groups of women at special risk. Unfortunately this investigation can provide no information about the risk among women suffering from predisposing conditions. It is, however, possible to form some estimate of the risk for women without predisposing conditions in two broad age groups, and this has been done in Table VII.

TABLE VII.—ESTIMATES OF RISK OF DEATH FROM PULMONARY EMBOLISM OR CEREBRAL THROMBOSIS IN USERS AND NONUSERS OF ORAL CONTRACEPTIVES COMPARED WITH RISK OF DEATH FROM CERTAIN OTHER CAUSES

|                                                                                                                    | Age in years |       |
|--------------------------------------------------------------------------------------------------------------------|--------------|-------|
|                                                                                                                    | 20-34        | 35-44 |
| Estimated annual death rate per 100,000 healthy married nonpregnant women from pulmonary cerebral thromboembolism: |              |       |
| Users of oral contraceptives.....                                                                                  | 1.5          | 3.9   |
| Non-users of oral contraceptives.....                                                                              | 0.2          | 0.5   |
| Annual death rate per 100,000 total female population from: <sup>1</sup>                                           |              |       |
| Cancer.....                                                                                                        | 13.7         | 70.1  |
| Motor accidents.....                                                                                               | 4.9          | 3.9   |
| All causes.....                                                                                                    | 60.1         | 170.5 |
| Death rate per 100,000 maternities from: <sup>1</sup>                                                              |              |       |
| Complications of pregnancy (List Nos. 640-649).....                                                                | 7.5          | 13.8  |
| Abortion (List Nos. 650-652).....                                                                                  | 5.6          | 10.4  |
| Complications of delivery (List Nos. 660-678).....                                                                 | 7.1          | 26.5  |
| Complications of the puerperium:                                                                                   |              |       |
| Phlebitis, thrombosis and embolism (List Nos. 682-684).....                                                        | 1.3          | 2.3   |
| Other complications (List Nos. 681, 683, 685-689).....                                                             | 1.3          | 4.6   |
| All risks of pregnancy, delivery, and puerperium.....                                                              | 22.8         | 57.6  |

<sup>1</sup> Register General for England and Wales for the year 1966.

When an adverse reaction to a drug is itself a spontaneously occurring disorder with a "natural" incidence it is important to distinguish between the relative and absolute risks of the drug. The results shown in Table VII suggest that, irrespective of age, the risk of death from pulmonary embolism or cerebral thrombosis was increased seven to eight times in users of oral contraceptives. In absolute terms, however, the attributable mortality was substantially lower among those aged 20-34 than among those aged 35-44, there being an excess of 1.3 and 3.4 deaths per 100,000 users per annum respectively.

These estimates exclude deaths from coronary thrombosis because the evidence that oral contraceptives can cause this disease is weaker than that for pulmonary embolism and cerebral thrombosis. If it is thought justifiable to include deaths from coronary thrombosis the mortality attributable to oral contraceptives may be recalculated as 2.2 per 100,000 users per annum for women aged 20-34 and 4.5 per 100,000 users per annum for women aged 35-44.

The risks associated with the use of oral contraceptives in these two age groups have been compared in Table VII with some other risks to which women of similar age are exposed. It will be seen that, although the mortality attributable to oral contraceptives in women aged 35-44 is greater than that in younger women, the general mortality, including that associated with child-bearing, it also substantially increased in this age group. If the risk attributable to the use of oral contraceptives is expressed in terms of the total risk of death, it can be seen that in both age groups this risk amounts to about 2% of the total mortality.