

males was greater than for females; in the other three age classes the female slopes were steeper than the male, and the differences were somewhat larger. However, statistical significance at the conventional level ( $p < .05$ ) was not reached for any age class (Table 2).

The use of oral contraceptives has rapidly increased since 1960 having become extensive around 1962. Therefore the data were examined to ascertain whether there had been a change in the slope at that time. Two periods were chosen: one of six years, 1956-1961; and one of five years, 1962-1966 (designated 1 and 2 respectively). Regression coefficients were calculated separately for each period in the same fashion as for Table 1 (Table 3).

For males, the slope increased in the second period in two of the five age classes, and for females, in four of the age classes (all except the oldest). The magnitude of the increases among females in the second time period is greater than that for males (and greater than that for the first time period), for the three age classes between 25 and 54. Although all the coefficients are positive, they are not significantly different from zero except in the oldest age classes (because of the short periods over which the regressions were computed), and most of the differences by sex are nonsignificant.

Mortality data for pulmonary embolism (I.C.D. 465) were examined separately by the same method for the period 1960-1966. As Tables 4 and 5 will show, these rates also increased significantly over the seven-year span, for both sexes. The rate of increase was greater for females than for males in all age classes studied except the youngest, but most of the differences were not statistically significant. Since the number of deaths from this one cause in the younger age classes is quite small, the failure to show a significant difference could be a consequence of the large sampling error.

In our opinion, these findings are consistent with the hypothesis that oral contraceptives have produced a small increase in the mortality from thromboembolism, but they do not add any great support to it.

Grounds for deciding whether the increases are wholly the result of changes in certification practice by physicians are lacking at the present time. If the increases are in part real, we should be looking for changed environmental factors that may be producing them.

In an endeavor to see whether they are related to oral contraceptives, two analyses of mortality trends have been published. The first, by Vessey and Weatherall (2), examined British statistics for deaths from peripheral, venous thrombophlebitis and pulmonary embolism. There has been an upward trend in both sexes, with a distinct suggestion of an acceleration in females at reproductive ages since these agents came into wide use. They concluded that this evidence was consistent with the hypothesis.

Markush and Seigel (1) have published a detailed analysis of mortality trends within the United States. Their conclusions also substantiate a possible association between oral contraceptive usage and increased mortality from thromboembolism. Both the British and American groups of researchers employed techniques of study similar to those described in this report.

In summary, recorded mortality rates for thromboembolic diseases in the United States at ages 15-64 have been increasing among both white males and white females. The rate of increase is greater for females than males. The increase was accelerated in the period 1962-1966 as contrasted with 1956-1961. These facts are consistent with the hypothesis that an increasing use of oral contraceptives is responsible for some of the thromboembolic mortality. However, because of the difficulty in diagnosis of these diseases and the possibility of changes in the practice of certifying underlying causes of death, we do not regard these findings as strong evidence for the hypothesis.