disease, compared to persons not having the attribute, can be expressed very simply in the context of a 2 x 2 table constructed as follows:

Cases	Controls	
	Attribute present	Attribute absent
Attribute present	a	b
Attribute absent	c	d

The sum of the numbers in the four cells is the number of case-control pairs.

The relative risk of acquiring the disease (thromboembolism) for persons having the attribute (use of oral contraceptives) is the number in cell b divided by the number in cell c. A test of significance of the difference between the numbers in cells b and c, where b>c, with correction for continuity, is a χ^2 test in which $\chi^2 = (b-c-1)^2/(b+c)$, with one degree of freedom.

Table 9 shows the relative risks for various subdivisions of the material, computed in this way, together with an indication of the statistical significance of each difference. For the entire series of 175 case-control pairs the relative risk is 4.4 with confidence limits of 3.1 and 6.8. Since pairing was on so many factors, no statistical adjustments are needed. No material differences in the relative risk are seen according to age, race, or marital status, but the number of pairs of nonwhite subjects and for some other subdivisions is too small to be sure that a difference does not exist.

For each diagnostic group in which numbers were sufficiently large to allow any statement to be made, there was a higher risk for users than non-users of oral contraceptives.

The brand names of the products used within two years before admission were analyzed. There were 16 cases and 6 controls who had used more than one product during the interval. The respondents were shown samples of the various tablets, as well as a list of the names of 14 different products—in some cases, as many as four produced by a single manufacturer. For many of these products the combined number of case-users and control-users was too few to yield any evidence as to whether they differed in their capacity to produce thromboembolism.

A special situation exists with respect to the sequential formulations. Sequential is the term for oral contraceptive formulations in which tablets containing only an estrogenic compound are taken for 20 or 21 days of the cycle, followed by the administration for 5 days of estrogen plus a progestogen. Three of these products were used by one or more subjects. Altogether, 15 cases and no controls had used them within one month of hospitalization. Contrasting the ratios of cases to controls—15:0 for sequential users, 52:23 for users of all other products—the difference is statistically significant. Of the 15 sequential users, 7 had pulmonary embolism, without a known thrombophlebitis, while only 11 of the other 160 cases had pulmonary embolism. Appendix 2 gives the frequency of use of the different formulations by cases and controls.

DISCUSSION

When case reports began to appear linking the use of oral contraceptives with intravascular occlusive states, two features of the problem made it difficult to decide whether the association was genuine: the fact that millions of women were adopting the use of the method, and the fact that the illnesses often occurred long after beginning use of the product.

An ad hoc committee (1) in 1963, the advisory committee on obstetrics and gynecology of the F.D.A. (2) in 1966, and a WHO scientific group (3) in the latter year all found no definite evidence on which to incriminate these hormones in the production of thromboembolism, defined as venous thrombosis (exclusive of the veins of head and neck), or embolism of the pulmonary artery, or both. Beginning in 1967, however, there have appeared several reports, all from Britain, which strongly indicate a relationship. The first of