Hertz and Bailar (23) have estimated the size of the sample required to answer this question as well as to provide other pertinent epidemiological data.

A survey of women attending the clinics of Planned Parenthood of New York City revealed a higher prevalence of epithelial abnormalities, diagnosed as carcinoma in situ, among women using oral contraceptives compared with those using the diaphragm (32a). These women had never been subject to systematic cytologic screening prior to this study, but some of them may have had Papanicolaou smears done in other cancer detection programs. The diagnosis was made in each case on the basis of a biopsy, examined by two pathologists without knowledge of the contraceptive used.

Women who had used oral contraceptives for one year or more were individually matched against diaphragm users with respect to five variables: age (5 classes), parity (2 classes), age at first pregnancy (3 classes including nulligravida), ethnic group (4 classes), and family income (2 classes). Because more women had used oral contraceptives (6,331) than the diaphragm (3,874) and because the distributions of the two groups of women in terms of the five variables were quite different, three matchings were performed: (1) one woman who had used the diaphragm against one who had used oral; (2) one diaphragm user against two pill users; and (3) one diaphragm user against three pill users. The three matchings produced, respectively, 2,351 pairs, 1,831 triplets, and 1,471 groups of four matched cases. In each matching the prevalence of epithelial abnormalities, diagnosed as carcinoma in situ, was about twice as high among those who used oral contraceptives as among those who used the diaphragm, and in each instance the difference was significant at the 5 per cent level of confidence.

Whereas these findings emphasize the urgent necessity of further research in this area, they do not, in the opinion of either the Task Force or the investigators, establish that oral contraceptives have a carcinogenic effect. Several important questions remain unanswered.

1. The prevalence of epithelial abnormalities diagnosed as carcinoma in situ, was higher among the 6,331 women who had used oral contraceptives for one year or more (9.8 per 1,000) than among the 21,177 women who were using other methods at the time of their first clinic attendance (5.6 per 1,000). There appears to be no further increment with duration of use of the pill. This finding is at variance with what would be expected in the case of a causal relation.

2. How do diaphragm users differ from pill users with respect to age at first coitus, frequency of coitus, number of sexual partners, and previous screening, all of which may contribute to the observed level of prevalence? It appears likely that all or most of these factors are correlated with one or more of the variables used in matching, but important residual differences may remain.

3. Finally, if there is a significant difference in the prevalence and, presumably, incidence of carcinoma in situ, is the reason for this difference a carcinogenic effect of hormonal contraception or a protective effect of the diaphragm, which may shield the cervix from coital trauma and possibly from infection?

Accordingly, the Task Force urgently recommends prospective studies of the effect of sustained oral contraception on the immediate and ultimate response of the cervical epithelium in a carefully observed and representative population of women.

ENDOMETRIAL CANCER

The demonstrated regression of endometrial cancer in response to large doses of progestin clearly indicates that this is a hormone-sensitive lesion (26, 28). Moreover, retrospective histological studies indicate a prolonged pathogenetic phase in the development of endometrial carcinoma (18, 19, 21, 42) Because this tumor is more occult, less is known about its incipient phases than about those of cervical cancer. For the same reason interpretation of epidemiological findings in relation to the pathogenesis of cancer of the corpus is difficult and conclusions are of limited value.

Accordingly, the Task Force does not regard studies relating specifically to endometrial cancer as a practical basis for evaluation of the carcinogenic potential of oral contraceptives.