

these changes: Roughly 35 years for dysplasia, 40 years for carcinoma in situ, and 47 years for invasive cancer.

The data from the various study groups using contraceptive pills were difficult to analyze for the following reasons:

1. Patients with suspicious smears were admitted to the study or in other instances the initial cytologic status was not stated.
2. The various methods of collecting cytologic specimens and the subjective factors in reading and reporting any changes make standardization of data difficult.
3. The frequent failure to record histologic followup after suspicion has been created on cytologic examination.
4. The concentration of contraceptors in age group below 35 yields such a low incidence of malignancy that very large samples are necessary.
5. The relatively small number of patients followed regularly and thoroughly for 4 years or more.

It is to be emphasized that all known human carcinogens require a latent period of approximately one decade. Hence any valid conclusion must await accurate data on a much larger group of women studied for at least 10 years. Furthermore, there is not sufficient evidence to support the contention that contraceptive pills may protect against the development of carcinoma of the cervix.

One possibly significant study showed an appreciable increase of coccoid bacteria, trichomonads, and fungi in women using contraceptive pills. This alteration in the microorganisms of the genital tract might be related to the use of the pills and could account for some of the changes in cytologic reports.

Endometrial Malignancy:

Endometrial carcinoma is primarily a disease of postmenopausal women and only 5 to 8 percent of the cases of this cancer occur before the age of 40.

In the data submitted the paucity of endometrial biopsies as a routine followup procedure, the limited number of women more than 40 years of age, and the short duration, do not permit any conclusions relative to the effect, either adverse or beneficial, of these contraceptive pills on endometrial cancer.

There are numerous studies that suggest an effect of a preponderance of estrogen, either endogenous or exogenous, in women who subsequently develop endometrial adenocarcinoma. While a precise etiologic relationship has not been established, nevertheless, all women receiving estrogen therapy must be followed with care. Administration of a progestogen periodically to women receiving estrogen, in order to allow periodic "withdrawal" bleeding on the basis that it "prevents" endometrial cancer, is invalid both theoretically and on the basis of the very limited number of postmenopausal patients so treated. It must be remembered, furthermore, that carcinolytic agents may also be potentially carcinogenic. Recent reports indicate that progestational compounds may exert a palliative effect on cancer, and adenomatous hyperplasia of the endometrium. While this matter is under study at several centers, there is no evidence, at present, that these compounds are curative. It must be remembered, furthermore, that cancer-suppressing agents may also be carcinogenic.

Breast Cancer

The relationship of the oral contraceptives to breast cancer in the human being is unknown. The solution to this problem is made difficult for several reasons as follows:

- (a) Contraceptors are predominantly in the lower age groups in which breast carcinoma is sufficiently infrequent as to necessitate very large samples for studies of early effects.
- (b) There are few long-term followup studies and none of sufficient duration to overcome the long latent period necessary to produce cancer in the human being.
- (c) Many studies simply do not state whether the breasts have been routinely examined.

There are data that give contributory, although not very strong evidence to both sides of the question.

For:

There is experimental and clinical evidence that indicate a relationship between both endogenous and exogenous estrogen.

There is experimental evidence that estrogens closely related to those used in the oral contraceptives currently marketed will, when continuously