

tice, we avoid the use of estrogens for fear of increasing the activity of existing disease or stimulating the growth of clinically latent foci of breast cancer.

Recent studies have shown that the incidence of breast cancer increases before the age 55 but remains constant beyond this age. These findings suggest that the risk from breast cancer is related to the quality of ovarian function.

The incidence of breast cancer in childless women is higher than in women who bear children. Even more important is the recent finding that a woman who has her first child under the age of twenty has a considerable protection against breast cancer. From epidemiological studies, it would seem that the decade following puberty (13-23) is a critical period in establishing the future risk of breast cancer.

The fact that breast cancer is common in women who have passed the menopause when the estrogen levels are lower can be readily explained on the basis that those cancers are the end-result of a process which began many years before.

The carcinogenic effect in humans and in lower animals is characterized by a long latent period of some 10 to 20 years or even longer. A carcinogenic agent exerting its effect over a relatively short period can induce biological changes in cells that progress slowly over a period of many years and end up as clinical cancer. One classical example related to workers in aniline factories who are exposed to the carcinogenic dyes for as short a period as 1 year and develop cancer of the bladder some 20 years later. Withdrawal of the carcinogenic agent did not arrest the progress of the latent lesions. Clinical, pathological and experimental evidence support the view that breast cancer follows a similar pattern.

Our studies of whole serial sections of the breast supported by clinical experience have shown that cancer of the breast is not a sudden event or an accident in a previously normal tissue, but rather the end-result of a series of changes which began many years before. Benign tumors change into precancerous lesions before ending up as fully established cancers. It is not inconceivable that the causative agents that result in breast cancer exert their initial effect at a young age, possibly in that critical postpuberty decade.

The tissues of the breast present a highly sensitive target for the ovarian hormones and have a great potential for the development of cancer. In all probability there is no direct etiological relationship between the estrogens and breast cancer. It is more probably that the carcinogenic effect of the hormones is to alter the biological state of the cells and thus render them vulnerable to the action of another agent—possibly, if not probably, a latent virus.

Recognizing the possible risk of breast cancer as a side effect of the oral contraceptive, the American Cancer Society, as early as 1961, supported research studies on this problem and a recent report of the Advisory Committee on Obstetrics and Gynecology referred to the need for well designed studies and long-term support for research on the breast and uterus.

Senator NELSON. May I interrupt a moment, Doctor. You are referring to the second FDA report on obstetrics and gynecology?