

then begun, and BALB/c mice were given Enovid in Metrecal continuously. All 6 mice receiving the mixture for 518–721 days and 2 mice born to a mother on Enovid and continued on Enovid for 599 days had lesions of the uterine cervix, diagnosed as early cancer or infiltrating cancer. None of the mice on Metrecal alone developed cervical lesions. Previous reports on the induction of carcinoma of the cervix in mice by estrogens are reviewed, and the histology of the lesions induced by Enovid is described. The need for further studies is discussed.—*J Nat Cancer Inst* 43: 671–692, 1969.

Senator NELSON. Please proceed, Doctor.

Dr. HERTZ. Moreover, chemicals which are known to produce cancer in man usually require about a decade for the full expression of their carcinogenic effect. This latent period often follows the complete cessation of earlier exposure to the cancer-producing substance. Hence any investigation aimed at determining the carcinogenic potential of a given chemical in man may be expected to yield incomplete answers during less than a decade of observation and followup.

Turning now to more direct clinical observations concerning the role of estrogens in certain cancers in women—and this I think will come to your question—it is appropriate to focus our attention on cancer of the breast and uterus since we know most about hormonal relationships of these two cancers in women.

It has been known since 1896 that in young women with breast cancer, the removal of the ovaries will result in an improvement in about half the cases. Also, women who undergo ovariectomy before reaching 40 years of age have a reduced risk of breast cancer. May I say as I read this that each statement is documented in the bibliography and subject to your affirmation by direct reference to the scientific articles indicated so that the numbers in the text indicate a specific reference to the medical literature in which the statement can be documented.

These effects are thought to be due to the reduction in estrogens produced by the patient's ovaries because the administration of estrogens to such women will produce chemical indications of an exacerbation of their disease in most cases. Paradoxically, an occasional young woman and about half of our older, postmenopausal women with breast cancer will show improvement when receiving estrogens.

Because of these opposing effects of ovariectomy and of estrogens in young women, it is universally accepted practice to refrain from giving estrogens to young women with previously identified breast cancer. Still, we know from X-ray studies and in addition from mammographic, xerographic, and thermographic studies, that breast cancer exists in some cases for years before it can be clinically detected. However, since one woman in about 20 will at some time in her life develop a breast cancer, it is obvious that in using the pill we are exposing at least this portion of women to a substance known to stimulate pre-existing breast cancer in women. We have no data concerning the effect of such medications on breast cancer during the developmental or preclinical phase of the disease.

Senator NELSON. May I interrupt for just one question.

On your sentence, "Still we know from X-ray studies that breast cancer exists in some cases for years before it can be clinically detected," I don't quite understand the sentence. Do you mean that—

Dr. HERTZ. You can see the tumor in the X-rays, but cannot feel it.

Senator NELSON. "Clinically" does not include an X-ray?