

exogenous estrogen, or estrogen plus a progestin, should be viewed in proper perspective. The abnormalities described in the New York City family planning study may be assumed to be due to the estrogen and progestin contained in the pill and have been described as "carcinoma in situ." But there is no proof that these changes are premalignant since none progressed to the point of invasive cancer. Furthermore, we don't even know they were carcinoma in situ. In 1954 Hellman and associates (Hellman, L. M., Rosenthal, A. H., Kistner, R. W., and Gordon, R., *Am. J. Obst. & Gynec.* 67:899, 1954) showed that similar changes to carcinoma in situ occurred spontaneously in the cervix of the pregnant human female, probably as the result of the endogenous levels of estrogen and progesterone, and even in the cervix of certain newborn females who were stillborn and then were autopsied and were shown to have exactly the same changes which could not be differentiated morphologically from carcinoma in situ obtained from biopsies of other women. The newborn cervix had this effect as a result of the mother's estrogen and progesterone which affected the baby's cervix.

It was assumed that these changes represented a response of reserve, these are the lining cells, cells toward the bottom of the cervix, response of these cells to the hyperhormonal, the excessive, progesterone and estrogen stimulation of pregnancy. These same changes were produced experimentally in postmenopausal females, by the work I did myself by the administration of extremely large doses of estrogen prior to hysterectomy. These workers concluded, workers Hellman, et cetera, "These estrogen induced changes show varying degrees of atypism" that is, "not exactly normal, or atypical," "varying degrees of atypism, which as demonstrated in pregnancy, can be so marked as to be histologically indistinguishable from carcinoma in situ. However, there is no evidence that they bear any direct relationship to human cervical carcinoma." And I would like to ask, in regard to the situation described earlier about the experiments of Dunn, giving the estrogen-progestin combination—which in this morning's newspaper was *Enovid* in the Anderson column—what dosage of estrogen-progestin was given to the mouse, how long was it given, and particularly whether these changes were the changes that we described 16 years ago; namely, were these changes the effects of estrogen and progesterone on the epithelium of the cervix or was this really cancer that metastasized and killed these animals.

At the Boston Hospital for Women during the interval 1964–69, there has not been an increase in the incidence of carcinoma in situ of the cervix among the patients screened, despite the annual increase of pill users because of the increased number of patients coming to our clinic who are on welfare, aid to dependent children, and so on. The type of patient who comes to our clinic is in the socioeconomic group where cancer of the cervix has a higher prevalence but we have not been able to show, it has not been shown that we have an increased incidence.

This fact, as I have just said, seems even more impressive since during these years, as increased number of patients were seen in whom socioeconomic and racial factors are known to increase the prevalence rate of carcinoma in situ.