the persistent remnants of the same lining which has previously undergone these profound changes. Hence the impact of these earlier cellular changes is transmitted to the subsequently developed tissues for the remainder of the patient's life.

The paucity of definitive data concerning the effect of the pill on cancer of the breast, cervix and endometrium is comparable to the situation with respect to the pill's effect on thromboembolic phenomena just a few years ago. Appropriately controlled epidemiological studies are lacking. Indeed, we are just approaching the time when an adequate number of patients would present a sufficient duration of exposure and latency to provide essential data for such an investigation. Short term studies on limited numbers of women have thus far proven to be inconclusive. A study of the incidence of breast cancer with even only a four year follow-up of women 20 to 39 years of age would require a sample of 15,000 to 20,000 women to reliably detect an early two-fold increase in risk. Requirements for a study in relation to cancer of the cervix would be of this same order. To date we have no data even approaching this order of magnitude or duration. However, the F.D.A. and the National Institute of Child Health and Human Development have projected such studies and their representatives will undoubtedly outline these investigations for you as these hearings proceed.

Lacking such definitive studies we must rely on the anecdotal accounts of the vast number of physicians who have employed the estrogenic component of the pill for the past 25 years. The prevailing clinical impression among them is that they have not encountered a carcinogenic effect of estrogens in their patients. Epidemiologic experience shows that such anecdotal accounts are misleading and frequently totally inapplicable to the problem at hand. For the most part, these physicians have treated older, menopausal women for relatively short periods of time and with no significant follow-up (20) (32) (33) (34) (35). The few statistical studies available in this area, even when combined, provide an inadequate sample drawn from a selected population of older women. Such data shed little light on the problem as it affects an unselected population of much younger women to be treated for a major portion of their life-span.

Actually, our inadequate knowledge concerning the relationship of estrogens to cancer in women is comparable with what was known about the association between lung cancer and cigarette smoking before extensive epidemiologic study delineated this overwhelmingly significant statistical relationship.

Much that has been stated above applies to the estrogenic component of the pill. It is held that the combined or sequential application of the progestagen contained in the pill may be expected to neutralize some of the these effects of the estrogens. This view is based on the fact that estrogens and progestagens do antagonize each other in many of their respective biological effects. However, we do not know the optimal blend of each component required to yield a completely balanced result. Similarly recent British studies indicate that for the thrombophlebitis effect the estrogenic component seems to be critical and it exerts its effect independently of the progestagenic component. In the case of chemically induced cancer of the uterus in rabbits, progestagens have been shown to neutralize the cancer-stimulating effect of the estrogens. Moreover, progestagens will suppress pre-malignant changes in the endometrium of women and will induce regression of pre-existing endometrial cancer in women. The proponents of the pill state that the progestagenic content of the oral contraceptives is therefore to be relied upon to suppress the potential carcinogenic action of the estrogenic component of this type of medication, while paradoxically the very existence of such a carcinogenic potential is categorically denied (36). In actuality, for each type of tissue response the result of the interaction between estrogen and progestagen must be determined by actual test. That the estrogen-progestagen combinations do produce tumors in dogs and mice indicates that the hoped-for neutralization effect for carcinogenesis simply does not occur with these specific mixtures in these species. The unanswered question is whether or not such neutralization effects will occur in the breast and uterus of women.

Advocates of the pill also state that since women using the oral contraceptives will have regularly repeated Pap smears, the use of this medication favors the early detection of cancer of the cervix in its curable stage (36). Why must a woman be expected to assume this additional burden when she should be having regularly repeated Pap smears whether or not she is using any form of contraception?

In closing, a few general remarks seem to be in order.