

no complete assurance as to the ultimate nature of the final tissue response can as yet be had, because tissues exposed to known carcinogens frequently have an essentially normal microscopic appearance during the decade of latency we have already discussed. Moreover, in a few instances the drug-induced atrophy of the endometrium persists for prolonged periods of time and this is accompanied by a period of infertility and lack of menses.

It is important to appreciate that the renewed uterine lining is generated from 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 4-year followup of women 20 to 39 years of age would require a sample of 15,000 to 20,000 women to reliably detect an early twofold 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 FDA and the National Institute of Child Health and Human Development—and this answers your previous questions—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 followup. The few statistical studies available in this area, even when combined—and I have cited them in my documentation—even when combined, provide an inadequate sample drawn from a selected population of older women, and they give us no guidance as to what we should expect from larger numbers of younger 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 lifespan.

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