

smear". Such smears can detect minimal deviations from normal, which require confirmation by more detailed microscopic study of tissue removed from the cervix. When confirmed, these early changes, called dysplasia, indicate that a cancer will almost surely develop in time. Recent studies indicate that this process of very early cancer development requires on the average about 4 years, with a range of from one to 7 years, depending upon the severity of the condition observed in the first smears.

As previously mentioned, the first reports of Pincus and Garcia suggested an ameliorative effect of the pill on this process of early cancer-like changes in the cervix. However, their more extended observations in collaboration with Dr. Rocamora suggested that no significant alteration of these processes could be identified in pill-users. The small number of women involved and the limited extent of their follow-up rendered these studies virtually useless.

Similarly, Dr. Wied (25) reported no significant change only after a one to two year period of observation of women on the pill. More recently, Dr. Melamed and his colleagues at Memorial Hospital in New York found a "small but statistically significant difference between the population choosing and using the diaphragm and the population choosing and using oral steroids for contraception." Because of the multiplicity of social and economic factors which affect the incidence of cancer of the cervix these authors correctly conclude that: "The reason for the difference is not apparent from these data." Similarly, the second F.D.A. pill report (27) states that: "these findings do not establish that oral contraceptives have a carcinogenic effect" but they serve to "emphasize the urgent necessity for research in this area."

From the clinical reports just cited together with the observed qualitative changes in the lining of the cervix in women on oral contraceptives, it is clear that this tissue is exhibiting distinct changes under hormonal stimulus. We do not know the prognostic significance of these changes. Accordingly, the F.D.A. has advisedly included in its package literature the instruction that women on the pill are to be carefully monitored by Papanicolaou smears. We have already mentioned that the F.D.A. has also instructed doctors to clearly identify any tissue or smears coming from a patient who is on the pill. This is presumed to aid in the interpretation of marginal changes which may be seen on microscopic examination. In some instances these changes in the tissues of the cervix are grossly visible and assume the appearance of wart-like growths, called polyps, or they may be smaller and are clinically regarded as "erosions" (28) (29). Microscopic examination permits the pathologist to identify a deviation from normal but he can usually differentiate this condition from cancer. Nevertheless, we do not know what the future behavior of such abnormalities would be if the stimulating effect of the oral contraceptives were to be continued.

For these reasons, the optimal management of the pill-user would require a Pap smear each six to 12 months. Quite obviously the existing clinical and laboratory facilities for such examinations even in our highly developed country can accommodate only a small fraction of those women given the bill. In less developed parts of the world, this elementary precaution is almost completely unattainable.

Cancer of the endometrium or of the body of the uterus is less readily discernible by pelvic examination but can be detected in some cases by the smear technique. This cancer arises in a tissue which is delicately controlled by the hormonal balance in women. That the oral contraceptives disturb this balance is readily observable on microscopic examination of samples of this tissue. This effect is also reflected in the menstrual changes noted in pill users such as progressively scant menses, intermenstrual bleeding and failure of menses between courses of medication or after cessation of therapy (31). The features of these structural and functional abnormalities have been documented extensively in the world medical literature (37).

Limited reassurance as to the meaning of these tissue changes is derived from microscopic studies showing that the structural changes usually disappear fairly promptly after the pill is stopped (30). However, 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 appearances 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 (31).

It is important to appreciate that the renewed uterine lining is generated from