women to thromboembolic reactions to the oral contraceptives. The O-type blood seems to be associated with a very low frequency of blood clots either spontaneously or in response to the oral contraceptives. And that is genetically determined.

The uneven susceptibility of women of various ethnic and familial groups to breast cancer suggests that such uniformity in response is not to be expected.

Women starting on the pill frequently complain of increased fullness and sensitivity of the breasts. In most instances this complaint subsides with more prolonged use, but in some women it persists and may be accompanied by actual increase in breast size. These phenomena indicate that some type of tissue reaction is taking place in the breast, but it is not practicable to ascertain the nature of this response by microscopic study except in those women in whom breast biopsies become otherwise clinically necessary while they are taking the medication. In such instances, the FDA has instructed physicians to indicate that such specimens are from women using oral contraceptives. This is in the package literature of every package of oral contraceptives sold, so that the pathologist should know when he is examining the tissue whether or not it comes from a patient who is on oral contraceptives.

This is well advised because it aids the pathologist in interpreting the minor deviations from normal structure sometimes encountered in such biopsies. Some observers have described several instances of more marked structural changes which are not malignant but which have not been previously encountered in nonpill users. These observations are too limited to establish any clear association between them and oral contraceptive use. However, such tissue effects demand detailed scrutiny and analysis.

Let us turn now to a consideration of the hormonal factors affecting cancer of the neck or of the body of the uterus. These cancers are termed respectively "cancer of the cervix" and "cancer of the endometrium." Cancer of the cervix is accessible on pelvic examination and its very earliest phases of development can be detected by microscopic study of material scraped from the neck of the womb. This type of microscopic examination is called a "Papanicolaou 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 1 to 7 years, depending upon the severity of the condition observed in the first smears. In this instance, as you see, we can give a definitive answer of this problem of the duration of the developmental effect of these tumors whereas we cannot do it in relation to the breast.

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