difference between the case and control subjects in the use of oral contraceptives.

This conclusion duplicates the results of many other studies as well. Worth and Boyes compared the use of oral contraceptives among 310 women, 20 through 29 years of age, who had carcinoma in situ of the cervix with 682 control subjects matched for age who had negative smears. Again, there was no significant difference in the use of oral contraceptives. Thomas compared 324 women who had positive cervical smears showing dysplasia or carcinoma in situ of the cervix with 302 women from the same locality. No difference was found in their use of the Pill.

Although there has been a significant increase in recent years in pre-invasive lesions of the uterine cervix, this increase has been found in both users and non-users of the Pill.

This brings out one of the more positive aspects of the Pill. Just think of the number of women who routinely see their physicians now and obtain a Pap smear because they are on the Pill. Women who are on the Pill have a much better chance for earlier diagnosis of changes in their cervical epithelium than those who are not — and that's certainly a plus factor in the relationship of cancer to oral contraception.

Editor: *You discount a link between oral contraceptives and uterine cervical cancer. But if a Pap test reveals cervical dysplasia in a patient, would you advise her to stop taking the Pill?*

Dr. Kretzschmar: No, I would manage the dysplasia with selective biopsies and appropriate treatment. I would not advise her to stop taking the Pill.

Editor: *Are oral contraceptives associated with endometrial cancer in your view?*

Dr. Kretzschmar: No, there is no relationship. The sequential tablets, which provided estrogen alone for 14 days, and then estrogen and progestogen in combination for seven more days, were taken off the market when controversial evidence linking estrogen with possible cancer of the uterus came to light. In 1975, 21 cases of endometrial cancer among Pill-taking women under the age of 40 had been recorded, but in eight of the cases, factors were found which militated against a close relationship between oral contraceptives and carcinoma, and of the remaining 13 cases, 11 had taken sequential agents. So, there is absolutely no evidence to link endometrial cancer with combination or progestin-only oral contraceptives. In fact, since only about eight percent of women taking oral contraceptives at that time used sequential agents, the unduly high incidence of sequential agent therapy in these 21 cases might suggest that women who are predestined to develop this tumor are actually protected against it by the combination pills.

If you wish to discuss replacement estrogen, exogenous long-term estrogen for menopausal women, that's controversial. According to an article published in the *New England Journal of Medicine* in 1975, the use of these exogenous estrogens in menopausal and post-menopausal women was associated with a 4.5 times greater risk of endometrial cancer. However, some physicians do not believe that there is a connection, and there are many knowledgeable people on both sides of the fence. Women taking estrogens should have frequent pelvic cancer-screening examinations and physicians should be on guard if abnormal bleeding develops. I would point out, in this respect, that the Pap smear is not a totally effective screening device for endometrial cancer; in fact, 40 to 60 percent of patients with adenocarcinoma of the uterus will have negative Pap results. An evaluation of the endometrial cavity with a suction curette, or an endometrial biopsy should be performed on all patients at high risk, or on those with a suspicious history. If a physician then feels he has not gotten a sufficient sampling, a dilation and fractional curettage should be done under local or general anesthesia. Our diagnostic procedures in this area should be further developed.

Editor: *Would you comment on the evidence linking oral contraceptive use to benign liver tumors?*

Dr. Kretzschmar: Yes, this was looked at carefully, and in April 1977, the American College of Surgeons released documented evidence on the increased incidence of benign hepatomas related to oral contraceptives. Their survey material consisted of 543 cases of primary liver tumors among both sexes; 378 in females and 165 in males. Among the males, 8.5 percent were benign, while among the females, 56.1 percent were benign. A positive history of oral contraceptive use was reported in 49.5 percent of the female patients, and in 29 percent the contraceptive history was unknown. However, it is reasonable to assume that a certain number of these "unknowns" included Pill-users; therefore, among the female patients in this study, more than 50 percent of primary liver tumors occurred in users of oral contraceptives.

The majority (73.8 percent) of the liver tumors diagnosed in Pill-users were benign. On the other hand, among non-users, the percentages of benign and malignant tumors were roughly equal. This difference in the proportion of benign to malignant tumors among users and non-users is substantial, and further supports the association between Pill use and the occurrence of benign liver tumors. Also, the frequency of malignant tumors in this study increased with age, and resembled the distribution of malignant liver tumors in the various age groups of the general population. But the distribution of benign liver tumors peaked in the age group of 26-30 years, and this parallels the age distribution of oral contraceptive use in the general population.

Editor: *What were the histologic types of these benign liver tumors?*

Dr. Kretzschmar: The survey showed that among non-users, the benign tumors were proportionately divided among four histologic types. But