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PILL EXPERTS PERPLEXED BY DATA ON PAP SMEARS

Investigators studying the cervical epithelium in women taking oral contraceptives find themselves on the horns of an anguishing dilemma. They now have data—much of it sketchy and none of it conclusive—suggesting that there is a significant increase in Class III Pap smears and possibly cervical carcinoma in situ in women who have used the pill for several years.

The scientists are reluctant to publish their preliminary findings, partly because they don't want fear of the slow-developing, nonlethal in-situ carcinoma to set off unnecessary panic among pill using women. But since the information now on hand is the best available, some of the investigators feel it ought not be suppressed.

In Chicago, editors of JAMA have put a bright red "rush" label on a controversial report by two Sloan-Kettering cancer researchers who found significantly more cervical carcinoma in situ among pill users than among diaphragam users. JAMA may publish the paper late this month—or not at all.

The controversial study, conducted by pathologist Myron Melamed and gynecologist Hilliard Dubrow, is one of at least four independent investigations. One is still incomplete, and one shows no change in incidence between controls and test women. But one, conducted by Dr. George Wied at the University of Chicago, reportedly shows a sixfold increase in positive Pap smears among women who have taken oral contraceptives. The Melamed and Wied studies both have the unusual distinction of being branded "inconclusive" by FDA Commissioner Herbert Ley before publication.

Dr. Melamed based his study on 35,000 to 40,000 Planned Parenthood clients who had been screened for cervical carcinoma in situ by Pap smears and biopsies. Excluding the positives, he matched pill takers with diaphragm users retrospectively, on the basis of age, ethnic group, parity, age at first pregnancy, and family income. Since pill users predominated in the study population, they were matched with the diaphragm users two to one. After three years, Dr. Melamed reportedly found a statistically significant higher incidence of cervical carcinoma in situ in the pill taking women.

Dr. Wied and his colleagues began their study by screening more than 40,000 women at Planned Parenthood clinics for cervical carcinoma in situ by means of Pap smears and biopsies, according to an article published in MWN's British sister publication, WORLD MEDICINE. This yielded them a prevalence rate of three per thousand for the premalignant change. Five years later, when the number of pill users in the study population had dwindled to 509, Dr. Wied found nine cases of carcinoma in situ among them. Extrapolating from this finding, he reported that the incidence was 18 per thousand—six times the anticipated rate.

Dr. Wied denies that he ever released any information about his on-going work except in a confidential memo to a grant-giving agency. "Naturally, I was shocked at this breach in confidence. Moreover, the nine 'atypical' smears have to be verified. We are now studying 2,100 women who have been pill users for five years or more. It will take at least three more years before we have any answers."

The third study, begun in 1961, is a prospective one with a homologous population of 8,000 to 10,000 Puerto Rican women randomly divided into pill users and controls. Dr. David D. Rutstein, chief of the department of preventive medicine at Harvard, designed the study and is analyzing the data. So far, he has not been able to support or refute the hypothesis of a link between the pill and cervical cancer.

Dr. Rutstein says the Wied and Melamed papers "have not convinced me because the controls do not permit a precise and comparable measure of the expected incidence of the disease. The expected incidence varies widely, depending on such factors as age at first intercourse, age at marriage, economic level, number of pregnancies, feminine hygiene practices, and whether the consort is circumcised."

Dr. Rutstein believes an adequately controlled study would be very hard to do and would require a prospective approach in which a homogeneous study population was divided randomly into pill users and controls.

Discussions with colleagues in Chicago led Dr. Wied to postpone his earlier plan to publish his report in the *Journal of Reproductive Medicine*. At JAMA,