

Getting back to the pregnancy question, it has often been the changes that we have seen in pregnancy that provides leads to metabolic alteration that were subsequently demonstrated for oral contraceptives. This doesn't make the complications more acceptable, just less frightening since one is mimicking changes seen in nature. As a matter of fact, I can think of no complication, described for the pill, that recently received so much publicity, actually no alteration, metabolic side effect of the pill, which has not already been reported in pregnancy at a higher incidence, including alterations in the cervix that mimic carcinoma-in-situ.

Of the many side effects of the pill, the risk of thromboembolism appears to be significantly increased and dangerous. We still have to remember that these are retrospective studies, not prospective studies. These are still going on. The combination of thromboembolic phenomena is shared with pregnancy but fortunately occurs at a lower level of incidence with the oral contraceptives. It will be important to try to determine whether lowering the estrogen component of the pill will reduce or remove this hazard.

The risk of inducing cervical or breast cancer with the pill cannot be predicted at this time. However, I think it has been the publicity about this which has frightened many patients, not only those taking the pill for contraceptive purposes, but women who are on estrogens, for instance, for replacement purposes in post-menopausal period. There are no convincing data for or against this possibility and only careful study will provide a definitive answer.

Aside from suspicions of the relationship of animal models to man, these were mentioned in the FDA report and quoted by, I believe, Dr. Davis in this committee, there is no evidence for steroid induction of breast cancer in humans or primates. Long-term clinical experience with estrogen thus far provides no obvious cause-and-effect relationship, but this is no substitute for careful epidemiological studies. There just is not any information on the subject one way or the other.

The reports indicating increased carcinoma-in-situ of the cervix in pill-users cannot be evaluated as yet since the patients did not routinely have cancer screening prior to being put on the contraceptives. Earlier short-term careful prospective studies did not demonstrate in-situ carcinoma as a consequence of pill use and only carefully controlled additional investigation will resolve these conflicting reports.

The pregnant state with which pill use has most often been compared does not in itself predispose to the cancers in question, and while experiences with estrogens in the past and knowledge of the effects of pregnancy cannot be equated with the current contraceptive medications, this does provide in my opinion a tempering balance to the cancer fears which can ultimately be resolved only by more study.

Finally, the occasional infertility that follows stoppage of the pill can fortunately be effectively treated in many cases with ovulation inducers, but it still presents a problem.

I would like to conclude these observations by saying that the on-going public drama of the pill should tell us more than anything