When the medication is taken in doses of 10 milligrams from day 5 to 25 as directed, the cycle length is unchanged. A condition known as breakthrough bleeding may occur despite regularity in taking the tablets (6 percent on 10 milligrams of Enovid and 18 percent on 5 milligrams of Enovid daily). Breakthrough bleeding is manifested by the appearance of bleeding sometime in the menstrual cycle other than at the usual menstrual period. The incidence is highest in the first treatment cycle and declines to lower levels by the fifth cycle. After that time, it is a rare occurrence. The amount of bleeding with menses is unchanged although Dr. John Rock of Brookline, Mass., states that after 4 or 5 successive cycles, the duration and amount of flow tends to diminish.

(3) Side effects or reactions.

Side effects such as nausea, dizziness, vomiting, headaches, and gastralgia occur in from 6.3 to 18.3 percent of the subjects in the various series. However, the side effects last only 2 to 3 weeks at the most. There were no apparent changes in weight, well-being, or libido. Any objection by the patient to the side effects, of course, would result in voluntary discontinuances of the use of the product and therefore are of no serious concern.

(4) The effect on fertility when medication stopped.

Altogether in the entire series of clinical cases, 897 women representing 801.6 women-years and 10,427 cycles have been studied. However, only 66 patients have taken Enovid for 24 cycles or more to 38 and an additional 66 women have continued medication for 12 or more cycles to 21. In one of the series in San Juan, Puerto Rico, there were 86 women on Enovid from 1–20 months; 83 percent (54) of those not using other contraceptives became pregnant after a mean exposure time of 6 months after discontinuing use of the drug. Dr. Rock did follicle counts on the ovary to be sure that the potential for production of the egg was left intact on 15 women taking Enovid for 2–20 months and found no change from normal controls.

(5) Possible malignant changes.

Robert Kistner, M.D., Harvard Medical School, administered Enovid to 7 patients; 4 with endometrial hyperplasia, 2 with endometrial carcinoma and one patient with adenocanthoma. Six of these patients were administered daily dosages from 14 to 80 days. The seventh patient with adenocanthoma received 2 other preparations, Delalutin and an estrogen antagonist in addition to Enovid. With one exception, reversal of the malignant endometrial changes occurred and a beginning or fully developed pseudodecidual endometrial response was obtained. The one exception continued to have "carcinoma in situ" remaining. The conclusion here was that "cystic and adenomatous hyperplastic glands may undergo regression and actively growing stroma may be converted into decidus by the action of potent progrestins." However, this in no way implies that this product would be of therapeutic value for malignancy of the female generative tract.

In order to obtain some additional assistance in determining safety for use of this product for this particular indication, conception control, a letter of inquiry was sent to 61 professors and associate professors of obstetrics and gynecology at the medical schools in the United States. We were pleased to receive a 100-percent response. The answers we received were as follows: 14 of the professors felt that they did not have sufficient data to reach a conclusion and said that because of lack of knowledge they did not know whether or not this product should be allowed for this indication; 26 said yes, it should be allowed for contraceptive purposes; 21 of the professors said that even though they could give no specific reason for reaching this conclusion they must say no; however, 2 of the noes were based on religious grounds, and others may have been. Some were based on cost and what was felt to be impracticality so that safety was not a factor.

We asked in our letter of inquiry 7 questions of these professors so that we could determine if there were any side effects or potential dangers of which we were not cognizant. The questions were as follows:

1. Do the side effects such as nausea and break-through bleeding proscribe the use of this product for contraception?
2. Would the fertility of women on this product be effected after the medication is stopped?
3. Is there any concern about the possible carcinogencity after longterm use?
4. Would there be any concern about premature menopause?
5. Would abortion be any higher in these women than usual?