pregnancies or by cyclic administration of ENOVID-E or ENOVID delays the onset of the menopause or prolongs it. In patients taking ENOVID cyclically, as in the grand multipara, there is no reason to doubt that the natural aging process, with eventual total suppression of ovulation and replacement of primordial follicles with fibrosis, proceeds at its normal pace. It should be noted that when ENOVID is given cyclically to a woman approaching, or already in, the menopause, she may be expected to respond with regular cycles. It is necessary to discontinue ENOVID to determine whether spontaneous ovulation and menstruation have ceased in a menopausal woman.

Whenever a progestin is prescribed for long periods, the question of possible androgenic effect is of importance. It is worth recalling that one reason ENOVID was chosen to be tested as the first oral contraceptive[2] was that "it is neither androgenic nor antiestrogenic." Kistner[38], in a review of progestational steroids, notes that while the antiestrogenic activity of norethindrone is about nine times greater than that of progesterone, "Norethynodrel actually is estrogenic, having 3 to 7 per cent of the estrogenic activity of estrone. . . ." In a recent discussion of oral contraception, Jackson[26] stressed "the essential clinical oestrogenicity of products containing norethynodrel" as opposed to the "heavy overlay of progestogenic and even of mild androgenic activity" with norethisterone tablets. In view of this, it is not surprising that the author[39] of the one report of fetal masculinization associated with ENOVID administration later declared that the occurrence was probably coincidental.

It is apparent that with ENOVID-E, as with ENOVID, when cyclic use is discontinued, the effects on reproductive organs and on the pituitary are rapidly reversed; there is no harm to subsequent children, and no delay or extension of the menopause. As to fertility, there is no evidence that it is in any way impaired in women who have used ENOVID-E or other oral contraceptives. Instead, as it is pointed out[40] in the *British Medical Journal*, "there is some evidence that it might be increased."

Factors enhancing acceptance: A paucity of complaints. "Acceptability is the most critical factor in the effectiveness of a contraceptive method."[41]

A woman's acceptance of an oral contraceptive is, of course, heavily influenced by the incidence and severity of side effects. Physicians familiar with ENOVID-E agree that the relatively few side effects encountered are for the most part mild and transient. Naturally, there are differences in the incidences of the various side effects reported by different investigators. But every study shows that after the first cycle, as medication is continued, there is a sharp decline in the incidence and severity of virtually every type of complaint. After the third cycle of therapy the incidence of side effects is very low.

Indeed, one investigator[16] with long experience in the study of oral contraceptives has said: "The decrease in the incidence of side effects to practically nil after the third cycle of medication in this group is remarkable."

The short duration of the nausea that is sometimes encountered is indicated in the accompanying graph. Pullen's comment[23] is typical: "Whatever the degree, as estimated by the patient, it had cleared considerably by the second cycle, and all were free of it by the fourth cycle." In the experience of Andrews and Andrews[18] with ENOVID-E, nausea is "seldom significant," and "has rarely been encountered after the first cycle."

Nausea during the initial cycles of ENOVID-E administration is believed to be another manifestation of the pseudopregnancy produced by ENOVID-E. It has been suggested that women who have experienced nausea during pregnancy are more likely to have some degree of nausea during the initial cycles of ENOVID-E medication. If nausea occurs—or seems likely to occur—it can often be controlled by taking the tablet with meals or with a glass of milk at bedtime, or by prescribing an antacid or antinauseant with the ENOVID-E tablet during the first two or three cycles.

The pattern for breakthrough bleeding is similar to that occurring with nausea. Like the other investigators, Binks, Cambourn and Papworth[9] found that the incidence of breakthrough bleeding "was highest in the first cycle, and dropped during the succeeding two cycles." Spotting and breakthrough bleeding are usually controlled by increasing the daily dosage of ENOVID-E. The in-