

therapy is usually prolonged; thus a woman for whom a twenty-eight-day cycle is usual might not menstruate for thirty-five days or longer. Ovulation in such prolonged cycles may occur correspondingly later in the cycle. Succeeding cycles, however, are usually typical for the individual woman prior to therapy with Enovid-E. Occasionally amenorrhea or menstrual irregularities persist.

Endometrial Effects. The characteristic action of Enovid-E on the endometrium is of considerable importance when biopsies are taken during or after therapy. As discussed in the section on *Human Pharmacology*, a biopsy taken late in the cycle when Enovid-E is given from the fifth through the twenty-fourth day of the cycle will reveal a definitely edematous stroma containing pseudodecidual cells (similar in appearance to the decidual cells in the endometrium of early pregnancy), increased vascular development and relatively sparse glands with scanty secretion. Because of this pseudodecidual activity, mention of Enovid-E therapy should accompany biopsy specimens when sent to the pathology laboratory for examination.

Androgenic Effects. The question of androgenic effects of a progestin is of importance whenever the drug is prescribed for long-term use. One case of fetal masculinization has been reported²⁵ in connection with Enovid administration, but the author²⁶ later stated that the incident was probably coincidental. Clinically, Enovid-E has manifested no evidence of androgenicity and, in fact, is estrogenic and progestational in its actions. Nevertheless, the physician should take this report into account when prescribing the drug.

Cervical Erosion. Early reports that cervical erosion was worsened by Enovid therapy have not been substantiated²⁷ by subsequent investigation. However, women receiving Enovid-E should receive periodic vaginal examinations and any cervical erosion found should be treated by accepted means.

Thyroid Function. Women on Enovid-E therapy may show an increase in protein bound iodine^{21, 28} and butanol extractable iodine and a decrease in T³ values. These results do not