

lactation is less likely, however, if medication is delayed²¹ six to eight weeks post partum, when lactation is well established.

Central Nervous System. An occasional woman receiving Enovid may experience psychic depression, although the relationship of Enovid administration to such a response is by no means clear.

Epileptiform convulsions have been reported to occur in women receiving Enovid. Since Enovid may cause salt and water retention an exacerbation of the epileptic state might be expected from this cause. Conversely, some epileptic patients whose attacks primarily occur^{31, 32} premenstrually have been relieved of their attacks.

Fibroids. There is no evidence that Enovid is etiologic in the production of uterine fibroids, although pre-existing fibroids frequently increase in size while Enovid is being given. Discontinuance of therapy ordinarily results in a regression.

Thrombophlebitis. Considerable attention has been given to the several hundred instances of peripheral thrombophlebitis and embolism (including fatalities due to embolic phenomena) occurring in women receiving Enovid. The possible causal relationship of Enovid administration to these incidents has received much study and has been reviewed by four committees of recognized authorities.

Any relationship between a state of "hypercoagulability" and thromboembolic disease still remains undetermined. In any event, presently available data do not establish — or exclude — the possibility that Enovid produces hypercoagulability as defined by increases in clotting components or acceleration of clotting kinetics. A number of blood coagulation factors are known to be modified during normal pregnancy. These include fibrinogen, fibrinolysin, prothrombin, factors VII, VIII and X, and other complicated measurements of the blood coagulation mechanism. Enovid also produces³³⁻⁵¹ changes in these factors in the same directions as those observed during pregnancy. Although the significance of these changes is presently unknown, additional studies are in progress.

Enovid was first distributed commercially in June 1957. As