Since Enovid-E exerts estrogenic activity, the presence of carcinoma in either of these areas should be ruled out before therapy is instituted.

2. *Pre-existing Liver Disease, Dysfunction or Jaundice.* In suspected or overt liver dysfunction or disease Enovid-E should not be used. The status of liver function in these patients treated with Enovid-E must be followed closely.

3. *Previous Thrombophlebitis or Pulmonary Embolism.* Enovid-E is contraindicated in these patients unless the reason for its use in the judgment of the physician is overwhelming.

PRECAUTIONS

THE maximal patient exposure to Enovid-E, as of May 1963, was forty-six cycles and a significant number of women were well into their third year of continuous cyclic medication. In one study[12], however, 234 women received other dosage forms of Enovid before taking Enovid-E and more than one-half of these women were in their fourth year or more of Enovid medication at the end of April 1963. Nevertheless, since the bulk of clinical experience with Enovid-E does not extend beyond three years and owing to any unanticipated effect on the ovaries, uterus, pituitary and adrenal glands or other body organs, duration of use longer than thirty-nine cycles (three years) must await the results of continuing studies.

Multiple detectable functional changes in the endocrine system with particular reference to the thyroid, adrenal and pituitary glands and perhaps the ovary occur in women treated with Enovid-E. The long-term effect on the pituitary, adrenal and thyroid glands and on liver metabolism is not yet clearly established although observations made of long-term users of Enovid-E reveal some changes (discussed later). The present experience indicates that endocrine function typical for the individual woman prior to treatment with Enovid-E usually returns promptly when medication is stopped.

Prolongation of First Post-Treatment Intermenstrual Interval. The first intermenstrual interval after discontinuing Enovid-E