

APPENDIX V

WRIGHT COMMITTEE REPORTS ON ENOVID

REPORT ON ENOVID BY THE AD HOC COMMITTEE FOR THE EVALUATION OF A POSSIBLE ETIOLOGIC RELATION WITH THROMBOEMBOLIC CONDITIONS

SUBMITTED TO THE COMMISSIONER OF THE FOOD AND DRUG ADMINISTRATION
OF THE DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
AUGUST 4, 1963

For centuries man has been interested in mechanisms and factors affecting the normal menstrual cycle, as well as those believed to be effective in either increasing or decreasing fertility. The artifacts of many civilizations attest to this. Therefore it should arouse no surprise that when a preparation which suppresses ovulation became available in tablet form it should be rapidly accepted and widely used. Such a tablet consisting of norethynodrel with ethinylestradiol 3-methyl ether (Enovid) has now been used by well over 1.5 million women for either contraception or for the treatment of disturbances of gynecologic endocrinology. It is believed that this substance acts by inhibiting the synthesis of gonadotropin by the anterior pituitary gland and in this manner suppresses ovulation in a high percentage of users.

It was soon recognized that Enovid produced a variety of side effects, including nausea and vomiting (sufficient to require discontinuation of the treatment in about 25% of the cases) and there have been reports of edema, weight gain, changes in thyroid or adrenal function, thyroiditis or toxicosis, hair loss or growth, dermatitis, cholestatic jaundice, chloasma, toxemia of pregnancy like syndromes and others. Except for nausea and vomiting the proof that these have been a direct result of the use of Enovid is in most instances open to question and is not within the scope of this report.

Beginning in 1961 reports began to appear from numerous sources of thromboembolic conditions, including thrombophlebitis and pulmonary embolism, occurring in women who had taken or were taking Enovid. Some of these patients died. While the index of suspicion was raised it was also recognized by the scientific community that a very large number of young and middle-aged females were involved, that such conditions do occur with and without obvious explanation, and that the 'coincidental factors involved' in such situations are not necessarily etiological. One solution would have been to scrutinize carefully each case history in detail, select those which appeared to be idiopathic in all other aspects, but who had the common denominator of exposure to Enovid, and compare these with a proper sampling from the population as a whole to determine whether there was evidence of an increase in the incidence of thromboembolism and deaths in the exposed series. Unfortunately the incidence of thromboembolism in the United States in this or any other population group is not known despite efforts in a few areas to obtain such figures. This type of condition is not reportable so that most of the patients which are not hospitalized are never recorded at all or the records remain in the physician's files. Once the attention of the medical profession and the general population was drawn to a possible relationship with Enovid, reporting of all types and severity of thromboembolic conditions in patients who had taken this drug was inevitably accentuated and comparable statistics became even more difficult. The death rate from thromboembolism in females of a comparable age group during the same period was not known, although this was obtained in the course of the present investigation.

In January of 1963 the Commissioner of the Food & Drug Administration, of the Department of Health, Education & Welfare established an ad hoc Com-