ORAL CONTRACEPTION AND BLOOD COAGULABILITY

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Recent reports on thromboembolic episodes associated with the use of oral contraceptives (*Brit. med. J.*, 1962) have raised the problem of a possible causal relationship between hormonal therapy and the risk of thrombosis. Several factors are known to predispose to thrombosis, such as lesions of the vascular intima, changes in the velocity of the local blood flow, changes in platelet count and adhesiveness and in the coagulation properties of the blood. The fact that oral contraception mimics the hormonal effects of pregnancy, which is associated with high levels of certain clotting factors, prompted us to investigate whether changes in blood coagulability might be induced by oral contraception. The drug tested was "enavid" (norethynodrel + ethinyloestradiol 3-methyl ether), and results show that this drug in recommended contraceptive dosage produced an increased coagulability of the blood.

Materials and Methods

Ten normal healthy women aged 22 to 42, with regular menstruation and no previous hormonal therapy, served as volunteers. Five of these received oral enavid medication in the standard contraceptive dosage of 5 mg. a day from the fifth menstrual day to be applied for 20 days. The other five served as controls for analysing possible physiological variations in blood coagulability during the menstrual cycle. Plasma samples were prepared according to a standardized technique as described for the methods used, and stored at −20° C. until assayed.

The following methods were used: Plasma cephalin time (partial thromboplastin time) (Egeberg, 1961). Plasma thromboplastin time (prothrombin time) (Waaler, 1959). Antihaemophilic A factor (A.H.A.=VIII), B factor (A.H.B.=IX, Christmas factor), and C factor (A.H.C.=XI, P.T.A.) (Egeberg, 1961). Proconvertin (factor VII) (Aas, 1952). Proaccelerin (factor V) (Owren, 1947). Prothrombin (factor II) (Hjort, Rapaport, and Owren, 1955). Fibrinogen (Jacobsson, 1955, modified by Blombäck and Blombäck, 1956).

Results

Four women used enavid as prescribed for 20 days, and one woman discontinued medication after 12 days because of nausea and vomiting. Three of the four experienced moderate side-effects, including nausea and transient fluid retention during the first days of medication. After discontinuation of therapy the consecutive menstrual bleeding appeared at about the expected time in all cases.

The results of the coagulation study are illustrated in Figs. 1–4. No definite changes occurred in the coagulation activities of the blood samples from non-treated women, neither for the "global" tests (the cephalin time and the thromboplastin time) nor in the activities of separate clotting factors (Figs. 1 and 2).

Plasma samples from the women on enavid medication showed a shortening of the cephalin time and a definite increase in the activity of the antihaemophilic A factor (Fig. 3). Further, the measured proconvertin activity increased slightly but significantly (Fig. 4). These changes developed during the first and second weeks of therapy, and the values showed a tendency to return to pretreatment levels soon after the drug was discontinued.

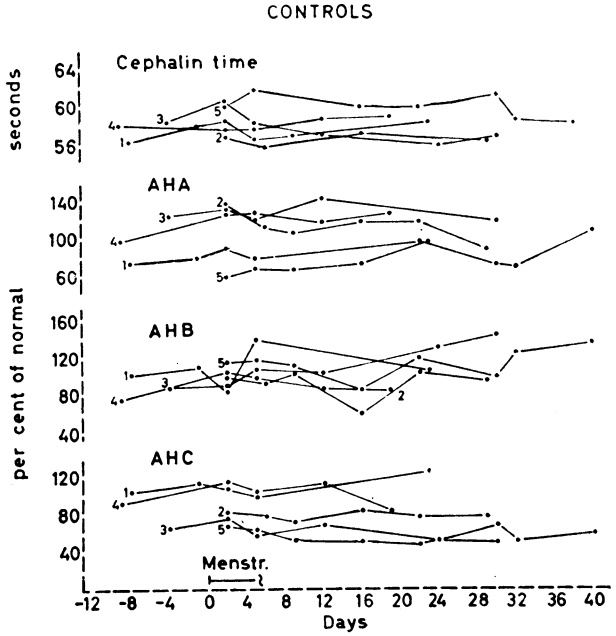

FIG. 1.—Plasma cephalin time and levels of antihaemophilic A, B, and C factors in control women.

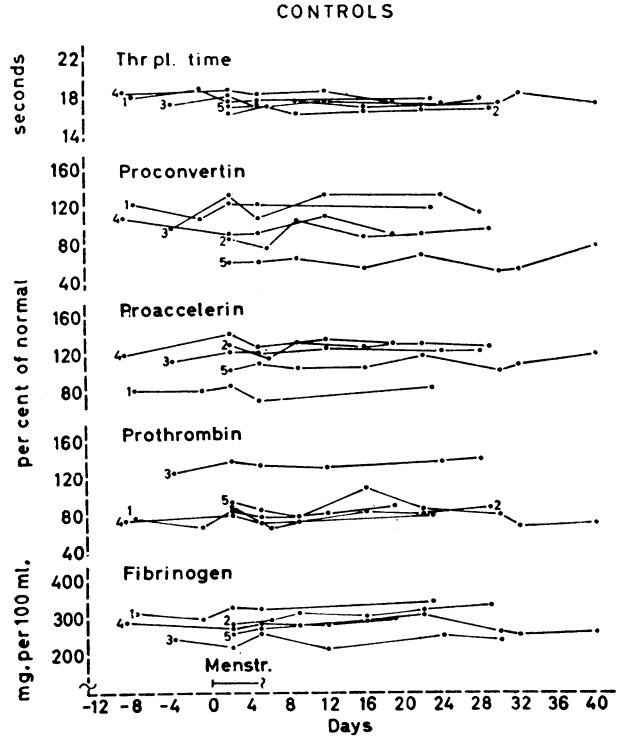

FIG. 2.—Plasma thromboplastin times and levels of factors influencing the extrinsic clotting systems in control women.

Discussion

The results show that enavid in the recommended contraceptive dosage of 5 mg. a day might produce definite changes in the blood-coagulation system in the direction of "hypercoagulability." The number of women treated is small, but the change in coagulability is marked and uniform.

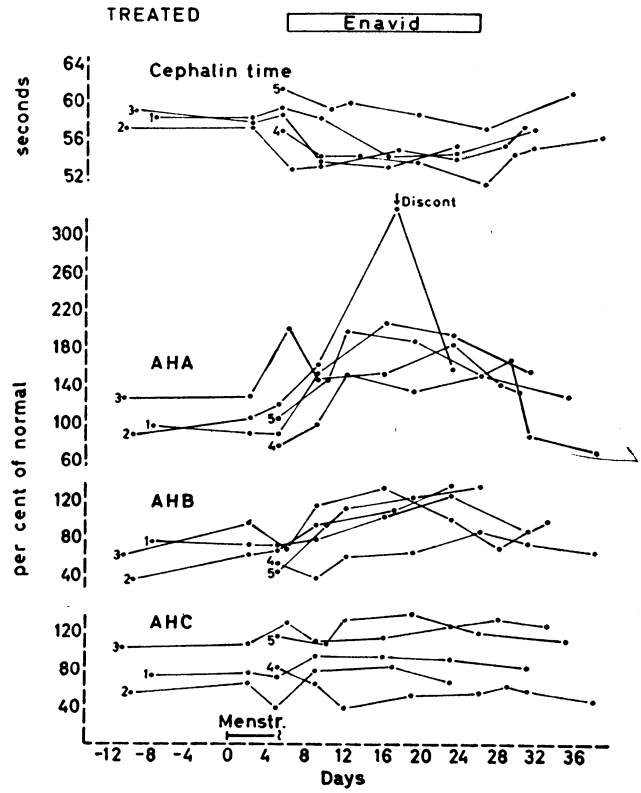

FIG. 3.—Plasma cephalin times and levels of antihaemophilic A, B, and C factors in women on enavid.

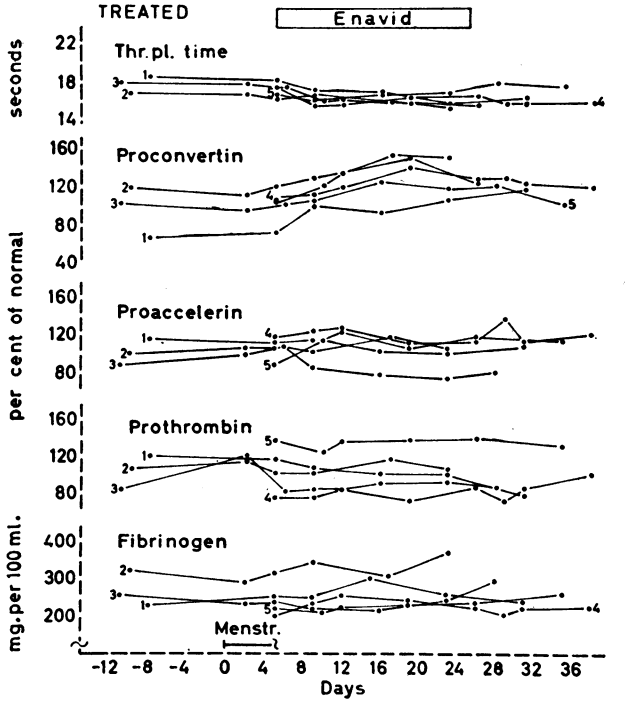

FIG. 4.—Plasma thromboplastin times and levels of factors influencing the extrinsic clotting system in women on enavid.

Summary

Anticonceptive therapy with enavid in five healthy women was followed by increased blood coagulability, as evidenced by shortened plasma cephalin time, marked increase in the activity of the antihaemophilic A factor (factor VIII), and a slight increase in proconvertin (factor VII) activity. No significant changes were observed in blood samples collected at intervals during one menstrual cycle in five non-treated normal women.

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CHLORINATED INSECTICIDE CONTENT OF HUMAN BODY FAT IN SOUTHERN ENGLAND

BY

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Chlorinated insecticides have been used for the control of insect pests of medical and agricultural importance for the past 20 years. Surveys which have been carried out in West Germany and in the United States have demonstrated that one of them (D.D.T.; 2,2-bis(*p*-chlorophenyl)-1,1,1-trichloroethane) is present in the body fat of the general population. No information is available concerning the presence or absence of this material in the body tissues of the population of England. As sensitive modern techniques are available we have carried out a limited survey of the general population of Southern England and analysed samples of human fat for the presence of D.D.T.-derived material. We have also determined the amounts of the active constituent of the insecticide dieldrin in the specimens of human fat; dieldrin is the common name for the product containing not less than 85% of the compound 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,-7,8,8a-octahydro-exo-1,4 - endo - 5,8 - dimethanonaphthalene; this compound is abbreviated as H.E.O.D. in the remainder of this report.

Materials and Methods

Specimens of body fat were obtained from consecutive necropsies carried out at two centres in the South of England; in all, 131 specimens were obtained in the winter of 1961–2. One of the centres was in a semi-rural area, the other was in an urban area. As