

The changes in pregnancy are not exactly comparable. Factors I and VII invariably rise from the outset. Factors VIII and X rise during the second and third trimesters in almost all women. Factor IX increases in about half the patients and factor II shows a slight rise in somewhat less than half. Factors V and XII show no change, and factor XIII decreases.

The data on effect of progestins alone are very scanty, but it is noteworthy that they have not been shown to alter the levels of factors I, VII, and X, all of which are increased by oral contraceptives. There are essentially no data of this type on the effect of estrogens.

FIBRINOLYSIS

Data pertaining to fibrinolysis are summarized in Table 4. The effect of oral contraceptives appears somewhat uncertain and a clear pattern does not emerge. Activator levels rise in all women after several months of use of these drugs, and the euglobulin clot lysis time falls in about half, suggesting increased fibrinolysis. The associated fall in plasminogen expected in such a state does not occur, however. Instead, an increase in plasminogen is seen in about two-thirds of the patients.

The pattern in pregnancy is much clearer, demonstrating hypoactivity of the fibrinolytic system with long euglobulin clot lysis time, decreased activator, increased antiplasmins, and increased plasminogen levels.

The data on estrogens are so scanty and inconsistent that no conclusions are warranted.

Progestins clearly enhance fibrinolysis although additional data on the components of the fibrinolytic system would be helpful.

SUMMARY AND CONCLUSIONS

The data as a whole are presented in condensed form in Table 5. If these data are examined in the light of our initial assumptions about the roles of platelets, coagulation and fibrinolysis in thrombus formation, we may form some tentative conclusions. Pregnant women appear to be in danger of inappropriate intravascular clotting, in that coagulation rate and potential are increased while fibrinolysis is depressed. On the other hand, the women using oral contraceptives is in a more balanced state in that coagulability is increased, but so is fibrinolysis.

Clinical experience, however, suggests that the opposite is the case, that is, pregnant women have little problem with thromboembolic disorders, whereas users of oral contraceptives have excessive disease of this type. Perhaps the explanation lies in the platelets. Platelets are little affected by pregnancy, whereas the steroid contraceptives increase their number and possibly their tendency to adhere and clump. The increased arterial thrombosis with oral contraceptives could be explained on this basis, although the increased incidence of venous thrombosis might not be so explained. The answer may well lie elsewhere, for example, in changes in the endothelium and vessel wall and in slowing of blood flow.²

With regard to the relation of composition of the oral contraceptives to their effect, the estrogen appears to predispose to enhanced platelet function and the acceleration of clotting, while the progestin leads to increased fibrinolytic activity. The amount of each component does not clearly affect the outlook. A few studies comparing the effects of high-dose and low-dose oral contraceptives did not show any great differences in platelet function, coagulation, or fibrinolysis between the two groups (37, 46, 53). There do not appear to be any differences in the thromboembolic effects of sequential and oral contraceptives other than those reported by Sartwell (Appendix 2A).

The changes brought about by the oral steroids are not immediately reversible upon discontinuing the drugs (2, 8, 22). One to several weeks are required for return to the normal pattern.

Among the 1000 patients surveyed, two developed thrombotic episodes: one fatal pulmonary embolus (1) and one cerebral artery occlusion (8). It may be significant that the first patient was paraplegic, and that platelets in the second showed a greater alteration in reactivity than in all other patients studied.

² See Reference 68, Appendix 4.