adhesion to a foreign surface precedes aggregation, tests in which aggregation is produced directly by chemical means, and electrophoretic responses of platelets exposed to aggregating agents. The bleeding time is an *in vivo* measurement of platelet adhesiveness and aggregability.

These data may be summarized as follows:

Short-term use of oral contraceptives appears to have little effect on platelate except for altering their electrophoretic mobility. The physiological significance of this observation is unknown. Long-term use, in addition to changing the electrophoretic mobility, produces a rise in the platelet count in two-thirds of the users, and may increase the ability of the platelets to adhere to foreign surfaces.

Pregnancy seems to have little effect on platelets except, however, some studies demonstrate increased aggregability.

Administration of estrogens, particularly the synthetic forms, increases the responsiveness of platelets to aggregating agents. Capillary resistance, on the other hand, is increased by natural (Premarin) but not by the synthetic estrogens.

Progestins have no effect on platelet count or function.

The number of observations on platelet function is too small to permit any definite conclusions. The estrogenic component of oral contraceptives, however, may have an effect on platelets that favors the development of platelet aggregates *in vitro*, and presumably *in vivo* also.

CLOTTING

There is a considerable quantity of data pertaining to clotting in patients receiving oral contraceptives, as presented in Tables 2 and 3. For comparison, data are presented on clotting in pregnancy and in persons receiving estrogens or progestins alone.

The clotting tests fall into three groups: those that measure the unaided coagulation of the blood (clotting time, prothrombin consumption test, and thromboplastin generation test); those that measure coagulation in the presence of an excess of a procoagulant (the prothrombin and partial thromboplastin times); and those that measure activity of specific factors (the P & P test and the factor assays). The first two groups measure the speed at which blood clots and they might, therefore, shed some light on the question whether thrombosis is a result of rapid clotting. The factor assays, on the other hand, measure amount of potential coagulant activity. It has not yet been shown that an increase above usual levels in concentration of a procoagulant factor makes blood clot with greater ease or that it causes thrombosis.

Examination of the data on oral contraceptives shows that some changes from normal are evident soon after initiation of treatment with these agents. Other changes appear or become prominent only after several months of treatment. Early changes indicate an increased rate of clotting: the clotting time (and its variants) and the Prothrombin Consumption tests show rapid coagulation in about 20 to 25 per cent of the patients. With prolonged treatment the proportion of patients showing rapid clotting increases to about 35 per cent in these tests. A similar acceleration of clotting is seen in the Prothrombin and Partial Thromboplastin Times. The TGT, a more sensitive test, detects rapid clotting in about 66 per cent of the patients early in treatment. This number does not change with prolonged use of oral contraceptives.

The changes in pregnancy must be more subtle, since they are detected only in the TGT and PTT but also indicate increased rate of clotting. Data on the estrogens and progestins are scanty, but they suggest that progestins and natural estrogens do not accelerate clotting, whereas synthetic estrogens do.

Data pertaining to concentration of clotting factors during use of oral contraceptives show that some factors begin to increase promptly. A rise in concentration of fibrinogen occurs in about one half of the women. About one fourth show an increase in factor VIII, about three fourths in factors II and IX, and all in factor XII. Long-term use does not change in the proportion of patients showing these increases. With factors VII and X the rise in activity is slower. Both factors are increased in only one half of women early in therapy but after more than 3 cycles, virtually all women have high levels of activity. The levels reached do not appear to exceed those seen in pregnancy (28, 47). Factors XI and XIII and probably V are not affected by use of oral contraceptives. Once these changes have occurred there is no cyclic fluctuation.