HYPERHAEMOLYSIS DURING THE PREMENSTRUAL PERIOD (PRELIMINARY REPORT)

BY

RAGNAR BERLIN

From the Medical Clinic, University Hospital, Uppsala, Sweden

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Winifred Ashby (1921), in her transfusion studies by means of differential agglutination, claimed that there was a definite periodicity in the elimination of transfused red cells in women in connexion with the menstrual flow. She suggested that this phenomenon was probably due to hormonal influences, but she gave no further explanation of these irregularities as a whole. Several later workers, using the same method, have failed to show this periodicity (Wearn, Warren, and Ames, 1922), but they based their conclusions on only two patients who were in the menopausal period. Since that time, the reports on this subject have been very scarce, only one paper (Callender, Powell, and Witts, 1947) dealing with this problem in any detail. These investigators followed the survival of transfused red cells in the circulation of four normal women and found that the cells disappear discontinuously and that the blood loss in women exceeds that in men by 400 ml. per month. It is not clear, however, from their curves exactly where, on the elimination curve, the cell disappearance is most pronounced; it is only apparent that it may occur in connexion with menstruation. The data obtained in their cases are relatively few, and it is thus impossible to analyse the detailed relationships in these respects. The authors emphasize that the actual blood loss during the menstrual period is much more than can be expected from a normal menstruation.

In this study the differential agglutination method was used to study the survival of red cells in one 5-year-old girl, five normal young women, and two women over 60 years of age. The girl showed a disappearance curve of the same linear type as that found in boys and men. This type of curve was also obtained in the two elderly women. The survival curves in the young women, on the other hand, differed in a significant manner from those just mentioned. In accordance with earlier observers a more rapid drop in the curve was found in connexion with menstruation, but the drop begins about ten to six days before menstruation and goes on until the period begins or, in some instances, one or two days earlier. This premenstrual change appears simultaneously with the progesterone phase of the menstrual cycle, i.e., parallel with the well-known premenstrual increase in body temperature. These changes could be due to a simple dilution of the blood at this time, but in this case the curve would then revert to the extrapolated

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elimination curve before the drop began. This is not the case, however; at the beginning of the menstrual bleeding the curve bends more horizontally but is still falling. The fact that there is no change in the total plasma protein (Van Slyke method) during this period also makes a premenstrual dilution

of the blood unlikely. The simplest explanation seems to be that there is an increased blood destruction during the progesterone phase of the cycle, and this could explain the excessive blood corpuscle disappearance in women beyond the actual flow during menstruation. This belief receives strong support from the fact that there is a considerable reticulocytosis, beginning about ten days before menstruation and increasing day by day until the start of menstruation

(10,000 cells counted on every slide; error 5-8%). On that day there is a rapid drop in the reticulocyte count, which remains within normal limits in spite of the menstrual blood loss. This view is partially in opposition to the observation made by C. M. Plum (1942) and R. Plum (1947) in their work on the reticulocyte ripening factor, where they claim that there is a reticulocyte increase due to menstruation but that the peak occurs one or two days after the onset

of menstruation. In the graphs here shown all curves are smoothed according to successive means, and the original observations are based on determinations made every third day during the first half of the menstrual cycle and every second day during the premenstrual period of unagglutinated cells remaining after differential agglutination.

By a closer analysis of the survival curve in these menstruating women it can be observed that the curve has a flatter course from menstruation to the beginning of the progesterone phase, thus indicating a less rapid destruction during this period, corresponding to a considerably longer survival time than normal. The normal survival time is about 120 days, and the daily destruction of red cells is calculated to be about 0.83% in a normal man. Table I shows the different values

TABLE I
CALCULATED DAILY RED CELL DESTRUCTION VALUES IN THREE CASES

	Daily Red Cell Destruction (%) during Premenstrual Period	Mean
Case 1— α_2 α_3	1.56 1.28	1.42
Case 2— α_2 α_3	1.56 1.73	1.55
Case 3— α_2 α_3	2.77 1.96	2.36

obtained for the calculated daily destruction of R.B.C. in three women in the two middle premenstrual periods, these two being probably the most reliable ones. The two other women show similar values. It is of special interest to point out that the angle α , between the two parts of the curve in each period, seems to be correlated to the height of the reticulocyte peak, i.e., the greater the angle the greater the haemolysis, therefore the more pronounced is the reticulocyte response.

These observations indicate the presence of a considerably increased blood destruction during the last ten to six days before the beginning of normal menstruation and explain the findings of earlier workers of an increased blood loss during the menstrual period. The nature of this hyperhaemolysis is obscure, but it is probably due to hormonal influences. The spleen plays no part in this haemolysis, as a similar curve has been obtained in a woman who had undergone splenectomy.

Further experiments on the elimination curve in young oophorectomized women before and after progesterone treatment are in progress.

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