

THE BLOOD-PLATELETS IN PREGNANCY AND IN THE PUERPERIUM

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IN SEVERAL recent papers^{1, 2, 3} dealing with the morphology of the blood in pregnant women, it was shown that a moderate to a severe grade of secondary anemia and a rapid sedimentation rate are usually present. The deficiency of the blood is early overcome after labor without special treatment, and the sedimentation rate returns to normal within two to six months after delivery.

In a further study of the blood in pregnancy, we have made determinations of the number of platelets (thrombocytes) in pregnancy and in the puerperium. This investigation was undertaken because comparatively little is known of the behavior of the platelets in pregnancy, and because of the important relation these elements are thought to bear to blood clotting. It was hoped that this study would throw some light on the coagulability of the blood in pregnant women.

It is definitely known that the process of coagulation is dependent on three essential elements: the blood-platelets, fibrinogen, and calcium salts. Modern theories in general agree that fibrin is formed by the action of thrombin on fibrinogen. Intravascular clotting does not occur because thrombin exists only in its inactive form of prothrombin. Morawitz (1904)⁴ believes that in shed blood a coagulating agent is liberated by the disintegration of the blood-platelets and by the extravascular tissues which in the presence of calcium salts converts prothrombin into active thrombin.

It has been pointed out by several investigators^{5, 6} that a pronounced increase in fibrinogen occurs in pregnancy. Greisheimer⁷ working in conjunction with others has recently pointed out a correlation existing between the fibrin content of the blood and sedimentation, namely: that as the fibrin content increases, the sedimentation rate becomes more rapid. The excessive production of fibrinogen is probably an expression on the part of the body to control hemorrhage during labor by increasing the elements necessary for hastening blood coagulation.

Investigations of the calcium content of the blood in the gravid state have recently been reported in the literature. DeWesselow,⁸ Krebs and Briggs,⁹ Bogert and Plass,¹⁰ and Kehrer,¹¹ found the content lessened in the latter half of pregnancy. Meigs, Blatherwick and Cary¹² could find no significant lowering of the calcium in the whole blood or in the serum of pregnant cows. Denis and King,¹³ taking 9 to 11 mg. per c.c. as a standard for normal serum calcium, discovered significant changes in pregnant women.

Hueper¹⁴ found experimentally in dogs that the increased calcium content of the blood produced by injections of parathyroid extract augments the coagulability of the blood and favors the formation of thrombi.

From the results of the studies of these investigators, it is obvious that any increased coagulability of the blood encountered in pregnancy cannot be attributed to a hypercalcemia, and that the calcium content of the nongravid state is usually sufficient for the proper coagulation of the blood during labor.

The existence of blood-platelets has been known since 1882 when Bizzozero¹⁵ isolated the platelets and described their morphology. Numerous hypotheses have been suggested for their histogenesis. On morphologic grounds, Wright¹⁶ claimed that platelets are detached particles of the cytoplasm of the giant cells of the bone marrow (megakaryocytes) which are thrown into the blood stream.

The blood-platelet determinations for the normal as reported by various authors are indicated in Table I. The marked variations noted are due in part to the use of different methods of examination and to the fact that the number of platelets is altered by various physiologic states and changes from day to day.^{17, 18}

REVIEW OF THE LITERATURE

Our knowledge concerning the number of blood-platelets in different pathologic conditions, as well as in pregnancy, is incomplete, owing largely to different methods of enumeration. Only a few meager studies have been made of the variations of these bodies in pregnancy and in the puerperium.

TABLE I. NORMAL PLATELET COUNTS

AUTHOR	NUMBER OF PLATELETS PER C.MM.
Thomsen ²⁷	250,000-300,000
Wright and Kinnicutt ¹⁶	226,000-367,000
Hayem*	250,000
Zeller*	500,000-750,000
Emden*	200,000-300,000

*Quoted from Gram.⁶

Bizzozero¹⁵ was the first to contend that the platelets increased in pregnancy.

Rebaudi¹⁹ claimed that the number of platelets at any period of gestation is always greater than normal (300,000 per c.mm.), though it is subject to very noticeable fluctuations. He noted an increase during the first, second, and third months with a maximum of 630,000 per c.mm. in the first half of the fourth month. The total number declined slowly and gradually during the fifth and first half of the sixth month, reaching the maximum average of 950,000 per c.mm. at term, and a maximum average of 1,500,000 per c.mm. in the last stage of labor. Rebaudi observed a rapid diminution in the number of platelets within twenty-four hours after delivery, these falling to a minimum average of 560,000 per c.mm. He found an increase on the third day which continues during the fourth and fifth days until a maximum average of 930,000 per c.mm. is reached. After this peak is obtained, the number decreases in the following week until by the twelfth day of the puerperium it falls to an average of 670,000 per c.mm.

Dawborn, Earlam, and Evans²⁰ studied the blood-platelets in 28 unselected cases of parturition and 5 cases of cesarean section. They observed that these bodies

began to multiply in number on the fourth day postpartum, reaching a maximum representing a 100 per cent increase on the tenth to twelfth day. The platelets then gradually diminished in number, the counts made after three weeks being approximately normal. In two cases of severe hemorrhage the curves slightly exceeded the average. In 6 patients the rise was insignificant, whereas in 14 others the count was doubled or more than doubled. In 5 cases of cesarean section, the average rise was approximately 200 per cent, while the lowest was 146 per cent. The count reached a maximum in from nine to thirteen days and fell rather more slowly than in the normal parturition series.

Louros²¹ examined the blood of 66 women and found that platelets in the same individual varied from time to time. In 15 young nonpregnant women, he found an average of 350,000 platelets, ranging from 250,000 to 500,000 per c.mm. In 10 cases of pregnancy in the second month, he noted counts ranging from 370,000 to 600,000. In one case of parturition with fever, 420,000 platelets were present. In 14 gravid women in the eighth month, the count ranged from 500,000 to 650,000.

TECHNIC OF PLATELET COUNTING

The direct method of counting blood-platelets was employed in this study. By this method the blood is mixed according to the ordinary hemocytometric principle, using a diluting fluid which fixes and stains the platelets.

The diluting fluid of Rees and Ecker was found altogether satisfactory for our purpose as it affords one the opportunity of counting the red cells at the same time.²² The technic is essentially simple.

The diluting fluid is drawn to near the 1 mark in the ordinary pipette used for counting red blood corpuscles. Blood from a freely bleeding puncture is then drawn exactly to the 0.5 mark, and finally the diluting fluid is again drawn to the 101 mark. This gives a blood dilution of 1 in 200. In order that clumping of the platelets may be avoided, special care must be taken to draw the blood into the pipette immediately after puncture. The Levy-Hausser counting chamber is filled and ten minutes allowed for the platelets to settle to the bottom of the chamber before counting.

The platelets appear as sharply outlined, round, or oval glistening bodies.

The diluting fluid consists of:

Sodium citrate—3.8 per cent aqueous solution	100.0 c.c.
Formaldehyde—40 per cent	0.2 c.c.
Brilliant cresyl blue	0.1 gm.

With a dilution of 1 to 200, the platelets are counted in 400 small squares, and the number multiplied by 2,000. Thus, if 120 platelets are enumerated in 400 squares, the count would be 240,000 for each cubic millimeter.

The platelet determinations in this study were made under the direct supervision of Dr. Baxter L. Crawford, Pathologist of the Jefferson Medical College Hospital.

TABLE II. BLOOD-PLATELET DETERMINATIONS IN 50 NONPREGNANT WOMEN

THOUSANDS PER C.M.M.	NUMBER OF PATIENTS	PERCENTAGE
150-200	3	6
201-250	13	26
251-300	15	30
301-350	12	24
351-400	4	8
401-450	3	6
Total	50	100

Table II indicates the results of blood-platelet determinations in 50 nonpregnant women made according to the method herewith described. Dr. Crawford believes that a variation of 50,000 in the count is of no significance and may be due either to unavoidable error in enumeration, or to some alteration in the physiologic state of the patient examined. This adds to the difficulty of properly evaluating the rise or fall in the platelet count in any condition studied.

It is seen from Table II that 40 (80 per cent) of the 50 nonpregnant women examined had counts varying from 200,000 to 350,000 per c.mm.

PLATELET DETERMINATIONS IN PREGNANCY

The platelets have been studied in 230 gravid women and in 100 of these further studies were made during the puerperium. The counts were made on all patients registering in the Antenatal Clinic of the Jefferson Medical College Hospital. The results of the examinations in the 230 patients at different periods of gestation are described in Table III. Complete data disclose that 177 (77 per cent) had from

TABLE III. BLOOD-PLATELET DETERMINATIONS IN PREGNANCY

THOUSANDS OF PLATELETS PER C.MM.	NUMBER OF PATIENTS	PERCENTAGE
150 to 200	11	4.8
201 to 250	50	21.7
251 to 300	64	27.8
301 to 350	63	27.4
351 to 400	20	8.7
401 to 450	12	5.2
451 to 500	6	2.6
Over 500	4	1.8
Total	230	100.0

200,000 to 350,000 platelets per c.mm., whereas 42 (18.2 per cent), had over 350,000 platelets per c.mm. No noteworthy relation between the platelet count and the length of gestation was found. A comparison of the platelet count in the nonpregnant and pregnant individual (Tables II and III) reveals that the number of platelets is not appreciably altered in pregnancy.

The average level of platelets is apparently not influenced by the diminished number of erythrocytes, nor by the rapid sedimentation rate ordinarily occurring in pregnancy.

PLATELET DETERMINATIONS IN THE PUERPERIUM

Platelet determinations of 100 unselected patients were performed within twenty-four hours after labor, on the third to fourth day, and on the eighth to the tenth day of the puerperium. The results of these examinations are depicted in Tables IV, V, and VI and in Fig. 1.

In this study only variations of more than 50,000 platelets were considered of importance. A count which did not vary by 50,000 in either direction during the puerperium was considered as "unchanged."

Table IV lists the counts of 100 women made within twenty-four hours after delivery. In this table it is noted that 27 per cent of the patients gained over 50,000 platelets per c.mm. Included in this group are 9 women with an increase of over 100,000 per c.mm.

Table V indicates the counts made three to five days after delivery. This table reveals that 55 women gained more than 50,000 platelets within five days after labor. Of this number, 20 gained between 50,000 and 100,000 whereas 35 gained over 100,000.

TABLE IV. PLATELET COUNTS WITHIN TWENTY-FOUR HOURS AFTER DELIVERY

THOUSANDS PER C.MM.	NUMBER OF PATIENTS	UN-CHANGED*	REDUCED OVER 50,000	INCREASED 50-100,000	INCREASED 100-200,000	INCREASED OVER 200,000
150-200	1	0	0	1	0	0
201-250	26	18	0	3	4	1
251-300	26	21	0	5	0	0
301-350	32	17	3	9	3	0
351-400	5	3	1	0	0	1
401-450	6	2	4	0	0	0
451-500	1	0	1	0	0	0
Over 500	3	0	3	0	0	0
Total	100	61	12	18	7	2
Percentage			73			27

*Increase or Reduction Less than 50,000.

TABLE V. PLATELET COUNTS THREE TO FIVE DAYS AFTER DELIVERY

THOUSANDS PER C.MM.	NUMBER OF PATIENTS	UN-CHANGED	REDUCED OVER 50,000	INCREASED 50-100,000	INCREASED 100-200,000	INCREASED OVER 200,000
150-200	1	0	0	0	1	0
201-250	26	2	0	7	11	6
251-300	26	12	0	8	5	1
301-350	32	15	5	4	7	1
351-400	5	2	0	0	2	1
401-450	6	3	2	1	0	0
451-500	1	1	0	0	0	0
Over 500	3	0	3	0	0	0
Total	100	35	10	20	26	9
Percentage			45			55

TABLE VI. PLATELET COUNTS EIGHT TO TEN DAYS AFTER DELIVERY

THOUSANDS PER C.MM.	NUMBER OF PATIENTS	UN-CHANGED	REDUCED OVER 50,000	INCREASED 50-100,000	INCREASED 100-200,000	INCREASED OVER 200,000
150-200	1	1	0	0	0	0
201-250	26	5	0	7	12	2
251-300	26	9	3	4	9	1
301-350	32	6	5	3	5	3
351-400	5	0	0	4	1	0
401-450	6	5	1	0	0	0
451-500	1	1	0	0	0	0
Over 500	3	1	2	0	0	0
Total	100	38	11	18	27	6
Percentage			49			51

Table VI lists the counts of the same group of women within eight to ten days after delivery. It is observed that 51 per cent of the group had a gain over 50,000. Of these 51 women, 18 gained 50,000 to 100,000, 27 gained 100,000 to 200,000, while only 6 gained over 200,000 per c.mm.

It is particularly noted that no patient with a count of over 400,000 per c.mm. showed a gain in the puerperium.

A comparison of the alterations in the platelet count in the course of the puerperium is shown in Fig. 1. This reveals that 18 to 20 per cent of the patients had a rise of 50,000 to 100,000 during the various stages of the puerperium. Only 9 per cent, however, had the large increase

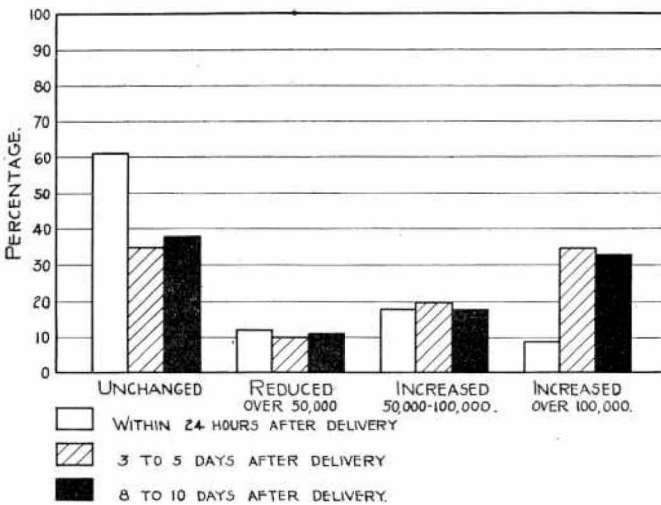


Fig. 1.—Variations in blood-platelet count of 100 patients in puerperium.

of over 100,000 within twenty-four hours, whereas 33 to 35 per cent showed this excessive increase within three to ten days after child-birth. The gain of over 100,000 represents in many cases a rise of 30 to 100 per cent above the original count in pregnancy.

DISCUSSION

From the results of our study it is apparent that no marked variation in the number of blood-platelets occurs in pregnancy. The significance of the failure of the blood-platelets to increase in pregnancy remains undetermined. It seems, however, that a rise in the platelets is not essential in increasing the blood coagulability in pregnancy. The added power of the blood to clot in pregnancy may be explained entirely on the basis of an increased fibrinogen content of the blood. A low platelet count encountered in pregnancy, however, may be an indication of the presence of a hemorrhagic diathesis, especially when the deficiency in platelets is associated with a severe grade of anemia. In such a contingency it may be of value to stimulate platelet forma-

tion by the use of the ultraviolet light or by irradiation with small doses of either radium or the roentgen ray as suggested recently by Cramer and Bannerman.^{23, 24}

Factors Concerned in the Platelet Rise in the Puerperium.—It is difficult to render an exact explanation of the rise of the platelet count in the third to the tenth day of the puerperium. According to Dawborn, Earlam and Evans, it appears that hemorrhage as ordinarily encountered is not the dominant factor, but that the destruction of tissue and its subsequent absorption may be the cause of the elevation.

It may be that the increased formation of platelets is in the nature of a defensive act of the body against infection, analogous to the physiologic leucocytosis in gestation. Evidence that the thrombocytosis is a defensive mechanism is found in the work of Téoumine.²⁵ This investigator believes a low platelet count in the puerperium is indicative of poor resistance on the part of the patient. The fluctuation in the number of platelets in puerperal infection probably reflects the relationship between the defensive forces of the organism and the aggressive forces of the infection. In cases of puerperal sepsis ending in recovery, Téoumine found the number of platelets was much higher than in those ending fatally. Nine of 11 fatal cases of puerperal septicemia had counts below 200,000 per c.mm., and toward the end the counts decreased still further. A gross increase in the number of platelets may probably be regarded as a favorable prognostic sign, while a continuous fall may signify a failure of the defensive forces of the body and possibly point to a fatal determination.

There were no puerperal infections or other serious complications in our series of 100 patients, so that we are unable to correlate the platelet fluctuations with any pathologic condition of the patient. It is our belief, however, that the platelet rise is a reaction of the body against invasion by pathogenic organisms.

It has been recently suggested that a relationship exists between the number of platelets and thrombosis. It was observed by Dawborn, Earlam and Evans²⁰ that the tendency to thrombosis increases when the platelets are augmented in number. These authors suggest that with a retarded flow of blood, thrombosis is more likely to occur in blood rich in, rather than poor in, platelets. In 2 cases, high platelet counts were found in association with thrombosis. The underlying cause of the slow regular swing of the thrombocytes appearing so regularly after operation and parturition could not be determined. They conclude that this late rise of platelets is a natural phenomenon—a physiologic response on the part of the bone marrow—comparable to the early leucocytosis which occurs in pregnancy.

Dawborn cites the following interesting case: A woman, para ii, aged thirty-three, was anemic before delivery. On the morning of the tenth day, postpartum, examination showed 1,270,000 platelets.

On the night of the tenth day she developed a thrombosis of the left internal saphenous vein, extending to the middle of the leg. On the following day examination showed 540,000 platelets. The count continued to fall for the next few days. On the twenty-second day, a rise was again noticed, and on the twenty-third day, the clot extended to the femoral vein in the groin. The platelet count continued to rise until the forty-sixth day, when the patient left the hospital much improved.

A similar case was reported by Evans²⁶ who observed a high platelet count in a patient with splenic anemia who died of mesenteric thrombosis.

No definite conclusion can be reached regarding the relation of thrombocytosis (increased number of platelets) to thrombosis or phlebitis. Further clinical and pathologic studies may enlighten us regarding this connection.

SUMMARY AND CONCLUSIONS

1. The blood-platelet count for the nonpregnant woman was found to vary from 200,000 to 350,000 per c.mm.

2. Platelet determinations were made in 230 women in various stages of gestation, and in 100 of these after delivery.

3. It was found that 177 (77 per cent) of the 230 gravid women had from 200,000 to 350,000 platelets per c.mm. of blood, while 42 (18.2 per cent) gave a count of over 350,000. Therefore, it may be stated that the blood platelets are not appreciably increased in pregnancy.

4. Twenty-seven per cent of the 100 women gained over 50,000 platelets per c.mm. within twenty-four hours after labor, whereas 63 per cent had either a gain of less than 50,000 platelets or had a lower count than in pregnancy.

5. Counts made three to five days after delivery reveal that 55 women (55 per cent) gained more than 50,000 platelets. Of this number, 35 gained over 100,000 platelets.

6. Fifty-one per cent of the counts made on the group of 100 women eight to ten days after delivery showed a gain of over 50,000. Twenty-seven of these 51 women gained 100,000 to 200,000, whereas 6 gained over 200,000 per c.mm.

7. The cause of the rapid rise in the number of the platelets in the puerperium is undetermined. It has been suggested that the multiplication of platelets may be physiologic, a natural response of the body to safeguard against possible infection. Further investigation is necessary to ascertain the reason for the postpartum increase in the platelets and to determine if any relation exists between the increase and the occasional occurrence of thrombophlebitis in the lying-in period.

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