Activity of Megakaryocytes in the Postoperative State

By A. A. Kerhulas, M.D., Robert L. Ohler, M.D., Richard Warren, M.D. and John S. Belko, M.S.

VENOUS THROMBOSIS with its threat of pulmonary embolism is a constant danger following major surgical procedures. Of the three factors which may predispose to this event, namely, venous stasis, injury to the intima of the vein wall and alterations in the factors of the blood which participate in the coagulation process, the latter is at the moment perhaps the least well described.

In a study of several of the coagulation factors of the blood in postoperative patients[1] it was found that an alteration in the numbers of platelets circulating in the peripheral blood was the most constant and reproducible observation. The characteristic of this alteration, originally described by Dawbarn, et al.[2] and observed by nearly all subsequent workers in the field, was that a thrombocytopenia occurred in the early postoperative period, becoming maximal on about the third day, and then gives over to a thrombocytosis, becoming maximal on about the tenth postoperative day. The height of the platelet "tide" nearly coincides with the time in the postoperative period traditionally considered as showing the highest incidence of pulmonary embolism.

This variation in the number of platelets in the peripheral blood has led us to inquire further into underlying mechanisms. The early thrombocytosis might be due to decreased platelet production, increased "peripheral" loss, destruction or utilization, or to increased storage. The two most appealing of these theories are loss by hemorrhage resulting from the surgical procedure, which is not replaced by platelet poor bank blood,[3–5] and utilization of platelets in the white thrombi of the arterioles and venules of the operative field as suggested by Wright[6] and Zucker.[7] Decreased production should be evident in a decreased megakaryocytic activity of the bone marrow, whereas an increased disappearance of platelets from the circulation should cause no alteration other than a possible slight increase in this activity.

The later thrombocytosis might be due to a compensatory reaction to the earlier thrombocytopenia, which would be evidenced by increased megakaryocytic activity in the marrow, or to the liberation of platelets from stores, in which case no increased megakaryocytic activity would take place.

The present investigation was undertaken in order to throw light on the above points by correlating the response of platelets in the peripheral blood with the production of platelets by megakaryocytes in the bone marrow during the postoperative period.

From the Veterans Administration Hospital, West Roxbury, Mass., and Harvard Medical School, Boston, Mass.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Submitted October 20, 1950; accepted for publication April 3, 1951.

Plan of Study

Fourteen patients were studied. They were individuals undergoing operations of comparable magnitude involving comparable degrees of blood loss, trauma, intravenous replacement therapy and chemotherapy (table 1).

Table 1.—*Comparison of the Peripheral Platelet Counts and Percentage of Active Megakaryocytes in the Pre- and Postoperative Major Surgical Cases Studied*

Patient	Name of Operation	Preoperative Levels		Third Day Postoperative Levels		Tenth Day Postoperative Levels	
		Peripheral Platelet Count	Active Megakaryocytes %	Peripheral Platelet Count	Active Megakaryocytes %	Peripheral Platelet Count	Active Megakaryocytes %
A. B.	Subtotal gastrectomy, Billroth #1	284,000	26%	230,000	20%	410,000	58%
R. D.	Subtotal gastrectomy, Billroth #1	158,000	32%	138,000	58%	259,000	61%
J. F.	Subtotal gastrectomy, Omentectomy, excision polyp of colon	168,000	51%	148,000	27%	272,000	64%
V. P.	Transthoracic gastrectomy, splenectomy	242,000	45%	150,000	54%	650,000	68%
T. R.	Left colectomy	150,000	59%	96,000	13%	214,000	69%
J. R.	Thoracotomy, biopsy lymph node, biopsy tumor right upper lobe	260,000	50%	296,000	61%	320,000	63%
L. S.	Appendectomy, lysis of adhesions, biopsy of inflammatory mass	194,000	47%	162,000	22%	210,000	49%
L. T.	First stage gastrectomy, Hofmeister type	254,000	28%	156,000	50%	320,000	70%
R. K.	Subtotal gastrectomy	134,000	40%	94,000	20%	246,000	61%
C. J.	Subtotal gastrectomy	184,000	55%	124,000	35%	204,000	59%
J. C.	Subtotal gastrectomy	186,000	50%	94,000	43%	244,000	45%
M. K.	First stage subtotal gastrectomy	216,000	51%	130,000	21%	232,000	64%
F. S.	Subtotal gastrectomy	154,000	66%	150,000	58%	192,000	67%
N. C.	Thoraco-abdominal incision and drainage splenic abscess	208,000	39%	68,000	43%	198,000	56%
Mean		199,428	45.64%	145,428	37.5%	283,642	61%
Standard Deviation		46,3	11.5	58,7	16.9	38,4	7.2
Standard Error		12,3	3.07	15,6	4.51	10,24	2.08

In each patient the platelets in the peripheral blood were counted and the megakaryocytic activity of the bone marrow examined preoperatively and on the third and tenth postoperative days.

Methods

In order to avoid the possible liberation of platelets into the peripheral blood venipunctures for peripheral platelet counts were made in the anticubital vein before bone marrow

aspirations. The platelets were counted by the direct counting chamber method using capillary blood diluted 200 times with a solution containing 20 Gm. of sucrose, 5 Gm. sodium citrate, 0.1 Gm. of brilliant cresyl blue to 250 cc. of water. This was modified after the method of Rees and Ecker[8] in that sucrose was used instead of formaldehyde.

Bone marrow was obtained by aspiration from the spinous process of the lower thoracic and upper lumbar vertebrae. Smears of marrow were made on slides and cover slips. They were stained with Wright's and counterstained with Giemsa's stains[9] and studied in the following manner. Consecutive fields were observed, the low power objective was used to detect the megakaryocytes within the microscopic field. The cells were then examined under the oil immersion objective for structural details. The activity of the megakaryocytes was determined by performing a differential count based on the recent classification reported by De La Fuente.[10] This classification is as follows: Amitotic Forms, Mitotic Forms, Megakaryoblasts (A, B, C), Promegakaryocytes (A, B, C) Megakaryocytes (A, B, C, D) Asynchronic Megakaryocytes.

The subdivisions of the classifications in "A," "B," "C," "D" cells are based on the presence of platelets near or at the margin of the cytoplasm and hence the degree of activity of the cell is definitely determined.

"A" cells do not exhibit platelets in the cytoplasm. "B" cells are those whose cytoplasm contains one to ten marginal or juxtamarginal platelets. "C" cells are those whose cytoplasm contains more than ten marginal or juxtamarginal platelets. "D" cells are those whose cytoplasm is wholly converted into platelets.

One hundred megakaryocytes were studied in each differential. The results obtained are expressed as per cent of active megakaryocytes. Of 5 normal individuals studied by De La Fuente the average per cent of active megakaryocytes was 74.2. This is a higher per cent than that obtained by us which was 45.64.

Results

Of the 14 patients studied 13 showed a thrombocytopenia on the third postoperative day and all a thrombocytosis on the tenth postoperative day (table 1).

Nine of the 14 patients showed a decrease in the activity of the megakaryocytes on the third postoperative day while the remaining 5 showed an increase. Thirteen of the patients showed an increase in the activity of the megakaryocytes on the tenth postoperative day (table 1). The mean activity of the megakaryocytes on the third postoperative day was depressed by 8 per cent below the mean preoperative value. On the tenth postoperative day the mean activity was elevated by 15.5 per cent over the preoperative mean.

When analyzed statistically the change on the third day is not significant, whereas that of the tenth day is.

Summary and Discussion

Simultaneous bone marrow smears and platelet counts on the peripheral blood were made preoperatively and on the third and the tenth days after operation in 14 patients. Observations of the activity of the megakaryocytes of the bone marrow on the third day were inconclusive and require further observation. There was, however, a significant increase in activity on the tenth day.

It is postulated that the thrombocytosis which occurs on the tenth postoperative day is the result of increased activity of the megakaryocytes of the bone marrow induced by the attempt of the body to replenish depleted platelet reserves.

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