THE PROBLEM OF THE THROMBOPLASTIN ACTIVITY OF THE BLOOD

V. P. Baluda and V. V. Chernaya

Department of Pathological Physiology (Director: Professor I. A. Oivin) and Department of Obstetrics and Gynecology (Director: Prof. E. S. Akopyan), Kuban Medical School, Krasnodar
(Presented by Academician V. N. Chernigovskii)
Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 51, No. 4, pp. 39-42, April, 1961
Original article submitted April 26, 1960

The increased coagulability of the blood in various conditions (in the post-operative period, after childbirth, in case of haemorrhage after painful stimuli in stenocardia and myocardial infarction) is one of the factors enhancing the formation of thromboses and their spread over the vascular system. The acceleration of blood coagulation in the conditions mentioned above is due to an increase in the thromboplastin activity of the blood [2-5, 11, 17]. The mechanism responsible for the increase in the thromboplastin activity of the blood however is still unknown.

In the present paper we report findings concerning the mechanism responsible for the increase in the thromboplastin activity of the blood after acute haemorrhage and in the post-operative period.

METHOD

One hundred patients who had been operated upon under general ether narcosis for fibroid of the uterus were observed. The duration of the narcosis varied between one and two hours. The age of the patients varied between 27 and 68 years. The functional state of the blood coagulation system was established before the operation and two and a half hours, three days, five days, eight days and eleven days after the operation.

Besides, 25 experiments were carried out on dogs to study the influence of an acute loss of blood up to 40% upon the coagulability of the blood and its thromboplastin activity.

The acute loss of blood was caused by rapid bleeding from the femoral artery. The functional state of the blood coagulation system was investigated before the bleeding, at the time of bleeding and 10, 20, 30 and 60 mins after the bleeding. The blood coagulation time was estimated by the method of S. Ts. Bazaron [1], the silicone coagulation time of the blood by the method of Jaques, Fiedler, Feldsten and McDonald [14], the heparin tolerance of the plasma was established by the method of Poller [18] the thromboplastin activity of the blood was estimated by the modified method of Graham, Langdell and Brinkhouse [13] the antithromboplastin activity of the blood by the method of V. P. Baluda and V. V. Chernaya and the thrombocytes were counted by the method of Fonio. To establish the significance of the results the findings were subjected to statistical evaluation according to the usual method.

RESULTS

The findings obtained after statistical evaluation are set forth in Table 1 and 2.

Table 1 shown that the coagulability of the blood increases on the average in the post-operative period by 34%, the heparin tolerance of the plasma increases three times and the thromboplastin activity increases one and

TABLE 1

The Influence of Operative Interventions upon the Indices Characterizing the Coagulation System of the Blood

Indices characterizing the coagulation system of the blood	Statistical indices	Before the operation	Time elapsed since the operation				
			in hours	in days			
			2.5	3	5	8	11
Blood coagulation time (in seconds)	*M*	360	300	240	260	320	350
	m±	6	5	4	4	5	5
	P	—	<0,02	<0,001	<0,001	<0,001	<0,02
Silicone coagulation time of the blood (in seconds)	*M*	885	790	580	665	840	880
	m±	9	10	9	18	11	11
	P	—	<0,02	<0,001	<0,001	<0,01	=0,5
Heparin tolerance of the plasma (in seconds)	*M*	640	320	210	250	530	630
	m±	11	10	4	15	16	14
	P	—	<0,001	<0,001	<0,001	<0,001	=0,2
Thromboplastin activity of the blood (in %)	*M*	50	73	79	79	58	51
	m±	1,1	1,4	1,3	2,9	1,7	1,5
	P	—	<0,001	<0,001	<0,001	>0,05	=0,5
Antithromboplastin activity of the blood (in %)	*M*	127	72	47	59	99	130
	m±	7,1	4,3	3,0	2,3	5,6	2,1
	P	—	<0,001	<0,001	<0,001	<0,01	>0,05
Thrombocytes (in thousand/ mm³)	*M*	254	246	218	—	308	258
	m±	69	72	106	—	81	83
	P	—	=0,5	=0,1	—	<0,01	=0,5

Note: M—arithmetical mean; m—standard deviation; P—probability of deviation calculated on the basis of the original findings.

TABLE 2

Influence of Acute Loss of Blood upon the Indices Characterizing the Blood Coagulation System in Dogs

Indices characterizing the coagulation system of the blood	statistical indices	before the loss of blood	Time elapsed after the loss of blood in min			
			immediately after the bleeding	10	30	60
Blood coagulation time (in seconds)	*M*	260	200	160	120	160
	m±	4	5	4	5	5
	P		<0,001	<0,001	<0,001	<0,001
Silicone coagulation time of the blood (in seconds)	*M*	600	475	400	360	420
	m±	12	8	8	7	9
	P		<0,001	<0,001	<0,001	<0,001
Heparin tolerance of the plasma (in sec)	*M*	420	360	300	160	230
	m±	12	10	9	7	8
	P		<0,001	<0,001	<0,001	<0,001
Thrombocytes (in thousand/mm³)	*M*	400	380	380	300	320
	m±	8	8	8	6	6
	P		>0,05	>0,05	<0,001	<0,001
Thromboplastin activity of the blood (in %)	*M*	55	70	84	100	100
	m±	2,0	2,4	2,4	2,4	3,0
	P		<0,001	<0,001	<0,001	<0,001
Antithromboplastin activity of the blood (in %)	*M*	100	85	70	56	75
	m±	3,6	3,0	2,0	1,6	2,0
	P		<0,001	<0,001	<0,001	<0,001

a half times, the antithromboplastin activity decreases two and a half times. The changes enumberated above take place already within two and a half hours after the operation and are most marked on the third day. On the eleventh day the coagulability of the blood, the heparin tolerance of the plasma, the thromboplastin activity and the antithromboplastin activity of the blood returned to the original values. The number of thrombocytes in-

creases slightly only on the eighth day after the operation.

The data set forth in Table 2 show that acute loss of blood is accompanied by a shortening of the blood coagulation time to one half of the original level a more than twofold increase in the heparin tolerance of the plasma a twofold increase in the thromboplastin activity of the blood and an almost twofold decrease in the anti-thromboplastin activity of the blood. After acute haemorrhage the number of thrombocytes decreases on the average by 25%.

After acute loss of blood and after operative intervention the coagulability of the blood, the heparin tolerance of the plasma and the thromboplastin activity of the blood increase, and the antithromboplastin activity decreases. After acute loss of blood the number of thrombocytes decreases and in the post-operative period the number of thrombocytes shows a slight increase.

What is the basis for the increase in the thromboplastin activity of the blood? It is believed that the thromboplastin activity of the blood mainly depends on the concentration of the plasma factors of thromboplastin (antihaemophilic globulin A and B) and on the number of thrombocytes. In this context the rate of blood thromboplastin generation will depend on the concentration of the antihaemophilic globulins A and B and the quantity of thromboplastin will depend on the number of thrombocytes [6, 7, 16].

The low thromboplastin activity of the blood in haemophilia is due to the absence or marked decrease in the concentration of the antihaemophilic globulin A and B and in Werlhof's disease - to a decrease in the number of thrombocytes [8, 9, 12, 19]. There are however some reports according to which the disorders in the thromboplastin generation in case of haemophilia and the decrease in the thromboplastin activity of the blood are connected with the increase in the anti-thromboplastin activity of the blood in these patients [15, 21, 22].

From the data quoted above it appears that after acute loss of blood the thromboplastin activity of the blood increases twofold and the number of thrombocytes decreases. Consequently the increase in the thromboplastin activity of the blood after acute loss of blood is not connected with an increase in the number of thrombocytes. In the post-operative period the thromboplastin activity increases already within two and a half hours after the operation, the maximum increase can be observed on the third day and a slight increase in the number of thrombocytes can be observed only on the eighth day, i.e., at the time when the thromboplastin activity of the blood has almost returned to the original value. Consequently the post-operative increase in the thromboplastin activity of the blood is not connected with an increase in the number of thrombocytes.

The antithromboplastin activity of the blood is caused by the presence of antithromboplastin and heparin in the body. The activity of the antithromboplastin is usually related to the effect upon the lipoid components of blood thromboplastin and tissue thromboplastin which leads to the decrease of thromboplastin and a decrease of the thromboplastin activity [22]. The antithromboplastin activity of heparin is apparently connected with the suppression of the thromboplastin generation in the final stage. Some reports suggest that heparin inhibits particularly the activation of blood thromboplastin probably by blocking the slowly proceeding reaction between the thrombocytic factor and the plasma factor [11]. Besides heparin also destroys the thromboplastin which has formed during the coagulation of blood [20].

As a result of the decrease in the antithromboplastin activity of the blood arising after operative intervention and loss of blood, conditions arise which are favorable for an increased rate of thromboplastin generation and consequently for an increase in the thromboplastin activity of the blood. This enhances the rapid formation of thrombin and leads to an increase in the coagulability of the blood.

An increase in the thromboplastin activity which accelerates the coagulability of the blood must be regarded as one of the manifestations of the "stress reaction" which arises under the influence of such extreme stimuli as loss of blood and operative intervention. It is well known that in the first five-nine days after operation the activity of the anterior lobe of the pituitary gland increases and the secretion of ACTH increases and that the corticoid and medullar activity of the adrenal glands becomes more intensive [10].

SUMMARY

The mechanism of increased thromboplastin activity of the blood was studied on 100 patients operated on in connection with fibromyoma of the uterus and in 25 experiments with acute blood loss in dogs. The thromboplastin activity increased during the postoperative period by one and a half times, antithromboplastin activity by two and a half times. These changes occurred as soon as 2.5 hours after the operation, being most pronounced

on the third day. The number of blood platelets increased insignificantly and only on the eighth postoperative day. Acute blood loss is associated with increased thromboplastin activity, reduction of antithromboplastin activity and a drop of the platelet count. The rise of the blood thromboplastin activity after the operations and blood losses are associated with reduced blood antithromboplastin activity. Increased blood thromboplastin activity, leading to accelerated blood coagulation, should be regarded as one of the manifestations of "stress" reaction.

LITERATURE CITED

1. Bazaron, S. Ts., Sov. med., 3, 36 (1954).
2. Baluda, V. P., Pat. fiziol. i éksper. ter., 6, 41 (1957).
3. Baluda, V. P., Pat. fiziol. i éksper. ter., 5, 79 (1959).
4. Markosyan, A. A., Abstracts of Proceedings of the 9th Congress of the All-Union Association of Physiologists, Biochemists and Pharmacologists [in Russian] (Moscow-Minsk, 1959) Vol. 1, p. 292.
5. Chernaya, V. V., Abstracts of Proceedings of the Scientific Session of Kuban Medical School [in Russian] (Krasnodar, 1959) p. 87.
6. Briggs, R., Douglas, A. S. and MacFerlane, R. G., J. Physiol. 122, 538 (1953).
7. Briggs, R., Douglas, A. S. and MacFerland, R. G., J. Physiol. 122, 554 (1953).
8. Brinkhous, K. M. and Graham, J. B., Blood 9, 254 (1954).
9. Brinkhous, K. M., Sang 25, 738 (1954).
10. Goller, F. A., Job, V. W., Conn, J. W. et al. Ann. Surg. 132, 374 (1950).
11. Cormsten, J., Koagulationsproblemer ved acut coronartrombose med experimentelt supplement (Copenhagen, 1957).
12. Gouttas et. al., Acta haemat. 12, 203 (Basel, 1954).
13. Graham, J. B., Langdell, R. D. and Brinkhous, K. M., in the book: The Coagulation of Blood, p. 117 (New York, 1955).
14. Jaques, L. B., et al., in the book: The Coagulation of Blood, p. 26 (New York, 1955).
15. Johnson, S. A., Am. J. Clin. Path. 23, 875 (1953).
16. MacFerlane, R. G., Physiol. Rev. 36, 479 (1956).
17. Nicola, P., Rev. Hemat. 9, 536 (1954).
18. Poller, L., Angiology 5, 21 (1954).
19. Quick, A. J., Am. J. med. Sci. 214, 272 (1947).
20. Shanderge, J. N., Sarelis, A. and Regan, E. E., J. Lab. clin. Med. 54, 501 (1959).
21. Tocantins, L. M., Carroll, R. T. and Holburn, R. H., Blood 6, 720 (1951).
22. Tocantins, L. M., Blood 9, 281 (1954).

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
