principle be regarded as proof of the their role in the origin of the symptoms of that disease, for as a rule sensitivity rises in the case of a deficiency of endogenous effects of the corresponding factors.

LITERATURE CITED

1. L. M. Gol'ber and V. I. Kandror, Ter. Arkh., No. 5, 59 (1977).
2. L. M. Gol'ber, V. I. Kandror, and I. V. Kryukova, in: Current Problems in Diabetology and Diseases of the Thyroid Gland [in Russian], Kishinev (1977), pp. 19-20.
3. G. A. Bray, Endocrinology, 79, 554 (1966).
4. V. J. Cairoli and J. R. Crout, J. Pharmacol. Exp. Ther., 158, 55 (1967).
5. A. F. Debons and I. L. Schwartz, J. Lipid Res., 2, 86 (1961).
6. W. G. Duncombe, Clin. Chim. Acta, 9, 122 (1964).
7. V. Felt and J. Nedvidkova, Vnitrni Lek., 18, 374 (1973).
8. M. E. Hess and J. Shanfeld, J. Pharmacol. Exp. Ther., 148, 290 (1965).
9. V. I. Kandror and I. V. Kryukova, in: Abstracts of the 3rd International Congress of Pathological Physiology, Varna, Bulgaria (1978), p. 177.
10. G. S. Levey, Am. J. Med., 50, 413 (1971).
11. G. S. Levey, Med. Clin. N. Am., 59, 1193 (1975).
12. D. G. McDewitt, R. G. Shanks, D. R. Hadden, et al., Lancet, 1, 998 (1968).
13. S. Seifter, S. Dayton, B. Novic, et al., Arch. Biochem., 25, 191 (1950).
14. A. I. Vinik, B. L. Pimstone, and R. Hoffenberg, Metabolism, 19, 93 (1970).
15. L. T. Williams, R. J. Lefkowitz, A. M. Watanabe, et al., J. Biol. Chem., 252, 2787 (1977).

RELATIONS BETWEEN PLATELET AND PLASMA-COAGULATIVE COMPONENTS OF HEMOSTASIS IN HEALTH AND DISEASE

S. A. Pavlishchuk

UDC 612.115-08/612.111.7:612.124/+616.151.5-07:/616.155.25:616.153.96

The adhesive-aggregative activity of the platelets and the rate of blood clotting were compared in 125 healthy subjects during an emergency adaptation reaction (emotional stress, ACTH loading) and in 157 patients with heart and circulatory diseases during the period of crisis, and also during acute drug therapy. Changes in the platelets and plasma-coagulative components of hemostasis were found to be opposite in direction, and on this basis new ideas were put forward to explain the hemostatic function of the platelets.

KEY WORDS: blood clotting; adaptation; platelets.

The problem of the relationship between adhesive-aggregative properties of platelets and the clotting power of the blood have been studied chiefly in vitro and in model experiments. The results are contradictory and largely depend on the concentration of procoagulants and the number of platelets.

The aim of the present investigation was to determine relations between the platelet and plasma-coagulative components of hemostasis in an emergency adaptation reaction in healthy subjects and in patients with diseases of the heart and blood vessels.

EXPERIMENTAL METHOD

The following parameters were determined in one blood sample before and after external intervention: the aggregating power of the platelets by Born's method [7], recorded graphically by O'Brien's method [10], adhesion of platelets to glass by the method of Moolten and Vroman [9], the number of platelets (in a humid

Department of Internal Medicine, Kuban Red Army Medical Institute.

(Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Fedorov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 88, No. 12, pp. 669-672, December, 1979. Original article submitted January 19, 1979.

TABLE 1. Relations Between Some Indices of Platelet and Plasma-Coagulative Components of Hemostasis in an Emergency Adaptation Reaction

Group of subjects	Number of observations	Procedure	Time of investigation	No. of platelets, thousands/ μl	P	Area of ADP-aggregation, cm^2	P	T-Electrocoagulogram, sec	P	Plasma fibrinogen concentration, mg%	P
Healthy	10	Diurnal rhythm	8 h	221,8		4,9		406,5			
			14 h	144±8,9	<0,001	8,2±0,86	<0,01	489,5±11,16	<0,001	—	—
With ischemic heart disease	17	Injection of ACTH	Initial data	184		4,6		288,6			
			20 min	129,3±12,25	<0,001	7±0,6	<0,001	356,8±11,74	<0,001	—	—
			180 min	200±14,5	<0,5	2,4±0,69	<0,05	299,6±19,73	<0,05	—	—
Healthy	10	» »	Initial data	217		7,1		385,3			
			20 min	99,7±16,42	<0,001	13,4±1,98	<0,01	470,9±17,89	<0,001	—	—
			120 min	268,2±14,8	<0,01	5,7±1,77	<0,02	290,4±18,63	<0,001	—	—
»	25	Submaximal physical exertion	Initial data	195,8		6,7		392			
			Immediately after procedure	194±1,8	<0,2	4,3±0,9	<0,05	313±15	<0,2	—	—
»	28	Emotional stress	Initial data	228		5,7		385,5		310,5	
			120 min	164±13	<0,001	14,4±2,16	<0,001	575,1±16,79	<0,001	211,2±27,2	<0,001
»	25	Intravenous injection of 10% NaCl	Initial data	230		5,3		396		320	
			10 min	190±12,2	<0,05	9,1±1,82	<0,01	470±11,86	<0,001	280,3±16,4	<0,02
»	24	Injection of analgin	Initial data	238		5,9		318,9		318,9	
			30 min	260±13,72	<0,2	3,1±1,1	<0,05	—	—	360,7±21,9	<0,01
»	28	Injection of heparin (10,000 units)	Initial data	184,8		9,85				211,2	
			15 min	156±9,4	<0,1	33,7±0,69	<0,001	—	—	130±19,96	<0,001
With arterial hypertension	60	The same	Initial data	174		3,3				327	
			15 min	90±5,63	<0,001	16,77±1,89	<0,001	—	—	228,1±14,9	<0,001
The same	20	During crisis	Initial data	158		3,5		357		380	
		Outside crisis		185±10,09	<0,1	8,1±1,89	<0,01	411±30,11	<0,05	350±23,03	<0,05
With decompensated tonsillitis	60	Tonsillectomy	Initial data	202		4,1		384		275	
			Immediately after procedure	218±8,8	<0,5	1,9±0,4	<0,01	259±19,5	<0,001	370±10	<0,001
			60 min	186±6,9	<0,2	10,3±2	<0,001	390±14	<0,5	238±6	<0,02

Legend. Results subjected to variance analysis by difference method; initial data given as arithmetic mean (M), data after procedure as M ± m.

chamber), the electrocoagulogram of whole blood (using the N-333 apparatus), the plasma fibrinogen level after Gachev, the number of basophils (in a humid chamber) and the degree of their degranulation in films from Buffy coat. Observations were made on 307 subjects, including 150 healthy volunteers (mean age 21.5 years) and 157 patients (mean age 54 years) from the cardiological department. The distribution of the subjects by groups and the character of the procedures used are described in Table 1.

EXPERIMENTAL RESULTS

The results given in Table 1 show that different procedures and situations caused different changes in platelet activity. Emotional stress and acute pharmacological intervention (ACTH, heparin, 10% NaCl solution) caused platelet hyperfunction in the healthy subjects, and physical exertion (submaximal work on a bicycle ergometer) and injection of the antiaggregant analgin were accompanied by hypoaggregation of platelets. A hypertensive crisis in patients with an arterial hypertension syndrome also was characterized by platelet hypofunction. In some series, with long-term laboratory control (diurnal rhythm, injection of ACTH, effect of operative trauma), biphasic changes were observed in platelet adhesion and aggregation.

Whatever the direction of the initial deviations of the adhesive-aggregative properties of the platelets, and whatever the procedure used, the changes in clotting power of the blood were functionally opposite to changes in the platelet components of hemostasis. Hyperaggregation of platelets was accompanied by hypocoagulation, and a decrease in aggregative power by more rapid blood clotting. Similar relations between platelet activity and blood coagulability have been formed in certain pathological processes [1-3, 6], and they are regarded as a feature of the pathogenesis of these diseases or states. It can be concluded from the data showing dissociation between the platelet and plasma-coagulative components of hemostasis in the adaptation reaction that there is a certain biochemical agent which can induce hemostatic changes in opposite direction in the adaptation reaction or that substances with anticoagulant action are secreted into the plasma by activated platelets. The definite coincidence between the times of development of the hemostatic "scissors" and the peak of degranulation of basophilic leukocytes in the diurnal rhythm, and the greatest divergence between platelet activity and the rate of blood clotting after injection of heparin compared with the other procedures tested warranted the assumption that the adaptive hemostatic reaction is mediated through heparin. The probability of a heparin mechanism of adaptive hemostatic changes is confirmed by data on the very low plasma heparin concentration under normal conditions and its level in a period of stress, the view that heparin is a hemostatic factor, data on the reflex mechanism of its action on blood clotting [5], and ideas concerning heparin complexes as the main agents of the anticlotting system [4]. In recent years strong arguments have been put forward in support of the platelet aggregating action of heparin [8, 11, 12]. However, the present investigation did not confirm the view that heparin has a direct action on hemostasis: the anticoagulant action of heparin in a dose of 0.5 unit/ml is exhibited in vivo, and also after its addition to platelet-rich plasma, but is absent in platelet-deprived plasma. On the basis of these observations it can be postulated that the anticoagulant effect of endogenous and exogenous heparin is mediated through the platelets, and this suggestion is also confirmed by the data of Watanabe et al. [13], who showed that platelets have antithrombin activity which is not identical with the plasma antithrombin III.

There is thus reason to suppose that the role of platelets in hemostasis is much more complex than has traditionally been supposed. The range of their function is indeed great – from strengthening the endothelium and inhibiting hemocoagulation in the adaptation reaction to the trigger mechanism of thrombosis.

LITERATURE CITED

1. Z. S. Barkagan et al., in: Problems in Neurohumoral Regulation of Blood Clotting under Normal and Pathological Conditions [in Russian], Chita (1971), p. 25.
2. V. A. Germanov et al., in: Problems in Neurohumoral Regulation of Blood Clotting under Normal and Pathological Conditions [in Russian], Chita (1971), p. 38.
3. F. I. Komarov et al., Ter. Arkh., No. 11, 24 (1975).
4. B. A. Kudryashov, Biological Problems in Regulation of the Liquid State of the Blood and its Coagulation [in Russian], Moscow (1975).
5. A. A. Markosyan, The Physiology of Blood Coagulation [in Russian], Moscow (1966).
6. B. Boneu et al., Pathol. Biol., 20, Suppl. 71 (1972).
7. G. V. R. Born, Nature, 194, 927 (1962).
8. R. Landsay et al., Br. J. Haemat., 24, 377 (1973).
9. S. E. Moolten and L. Vroman, Am. J. Clin. Path., 19, 701 (1949).

10. J. R. O'Brien, Blood, 24, 309 (1964).
11. A. Rembaum et al., Mod. Dev. Art. Org., 1, 99 (1973).
12. J. Tew et al., Infect. Immun., 9, 179 (1974).
13. K. Watanabe et al., Thrombos. Diathes. Haemorrh. (Stuttgart), 34, 115 (1975).