EFFECT OF EMOTIONAL STRESS ON BLOOD-CLOTTING SYSTEM INDICES IN MONKEYS

S. V. Chernigovskaya, G. M. Cherkovich, and L. A. Uzunyan

UDC 616.89-008.44-092.9-07:616.151.5-07

Prolonged emotional stress causes a marked rise in the blood fibrinogen level of healthy monkeys and of monkeys fed for a long time (3 years) with cholesterol. Changes in some other indices of the blood-clotting system are independent of the animal's emotional state and are possibly seasonal fluctuations.

Considerable attention has been paid in the recent literature to the role of neuropsychic stress in the pathogenesis of atherosclerosis and its complications, notably myocardial infarction [1, 8, 12].

The object of this investigation was to study the effects of emotional stress on certain indices of the blood-clotting system and of lipid metabolism in monkeys.

Spontaneous atherosclerosis is observed very rarely in monkeys living under natural conditions [2, 4]. In monkeys living in captivity, atherosclerosis is found in 2.6% of cases and is clearly dependent upon age, for it is found in 19.6% of cases in monkeys over 5 years old [2]. Figures for the experimental reproduction of atherosclerosis in monkeys are not consistent. Some workers found no atherosclerosis in monkeys fed with cholesterol [6, 10], while others found only hypercholesteremia and lipoidosis [14]. A third group, however, observed true atherosclerosis with the development of plaques in the vessels [11, 15].

At the Institute of Experimental Pathology and Therapy, Academy of Medical Sciences of the USSR in Sukhumi feeding monkeys with cholesterol added to the diet led to the development of certain biochemical changes in the blood [2] and also to the development of a certain number of plaques in the aorta, discovered after death of the monkeys.

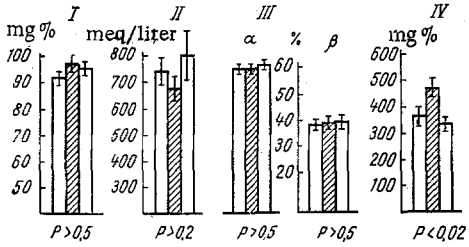


Fig. 1. Levels of cholesterol (I), NEFA (II), α- and β-lipoproteins (III), and fibrinogen (IV) in the blood of monkeys of group 1 exposed to stress. Shaded column corresponds to period of emotional stress.

EXPERIMENTAL METHOD

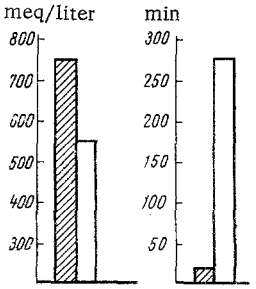
Two groups of monkeys were investigated: 1) control (6 animals) and 2) experimental, receiving cholesterol with the diet (7 animals). Both groups consisted of males aged from 6 to 8.5 years of the species Papio hamadryas. The monkeys of the experimental group each received 5 g cholesterol with the diet (porridge) daily for 3 years.

The fibrinogen level was determined by the method of Parfent'ev et al., the recalcification time by Howell's method, the prothrombin index by Quick's method, the adhesiveness of the platelets by the method of Moolten and Broman, the heparin time by Sirmai's method, the fibrinolytic activity of the blood by the method of Kowalsky et al., the cholesterol level by Sackett's method, the α- and β-lipoprotein levels by

Institute of Experimental Pathology and Therapy, Academy of Medical Sciences of the USSR, Sukhumi. I. P. Pavlov Institute of Physiology, Academy of Sciences of the USSR, Leningrad. (Presented by Academician V. N. Chernigovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 75, No. 3, pp. 29-32, March, 1973. Original article submitted December 16, 1971.

TABLE 1. Indices of Blood-Clotting System and Lipid Metabolism of Control Group of Monkeys (Papio hamadryas) and of Monkeys Receiving Cholesterol

Group of animals	Number of animals	Concentration				
		NEFA (meq/liter)	cholesterol (mg%)	α-lipoproteins (%)	β-lipoproteins (%)	fibrinogen (%)
1	6	740 ± 52.9	90 ± 2.69	61.03 ± 4.4	38.9 ± 4.40	367 ± 36.11
2	7	1002.2 ± 114.02	100 ± 5.4	59.1 ± 3.4	40.82 ± 4.02	340.7 ± 9.07
Group of animals	Number of animals	Recalcification time (sec)	Prothrombin index (%)	Index of adhesiveness of platelets	Heparin time (sec)	Fibrinolytic activity (min)
1	6	138 ± 18.8	91 ± 7.64	1.24 ± 0.1	14 ± 0.23	368 ± 66.35
2	7	191.4 ± 24.24	86.7 ± 3.62	1.12 ± 0.056	10.7 ± 1.21	362.8 ± 25.81



Effect of repeated blood taking from monkeys on NEFA level (left) and fibrinolytic activity (right). Shaded column corresponds to taking blood for the first time.

electrophoresis on paper, and the nonesterified fatty acids (NEFA) by Dole's method.

A stress situation was created by disturbing the normal relationships within the group of monkeys and the hierarchy of the group by the method of Miminoshvili [3] and also by disturbing the normal 24-hourly routine of light and darkness and of feeding by Cherkovich's method [7]. The animals' emotional reaction during this period was aggressive and restless in character.

EXPERIMENTAL RESULTS

The indices of the blood-clotting system of the monkeys were almost indistinguishable from those for man, in agreement with observations in the literature [9, 13].

As Table 1 shows, in monkeys kept on a cholesterol-enriched diet the NEFA level was significantly higher than in the control group ($P < 0.05$), while the cholesterol and lipoprotein levels and the indices of the blood-clotting system were practically indistinguishable from the control. During the period of stress no significant changes were found in the levels of cholesterol, NEFA, and α- and β-lipoproteins in the monkeys of group 1. Only an increase in the fibrinogen level in the period of emotional stress from 363 ± 36.11 to 470 ± 37.26 mg% ($P < 0.02$) could be observed (Fig. 1). The remaining indices of the blood clotting system in the monkeys of group 1 during the period of stress showed no significant change. In 4 animals of group 2 exposed to the stress situation the concentrations of cholesterol, NEFA, and α- and β-lipoproteins were not significantly changed. The fibrinogen concentration was increased, the recalcification time slightly reduced, and fibrinolytic activity lowered. However, similar changes in the recalcification time and fibrinolytic activity were observed in 3 animals of group 1, so that they were most probably due to seasonal fluctuations in the level of these indices.

The procedure of taking blood from certain animals not previously accustomed to such events was accompanied by brief stress, during which the NEFA level increased and considerable activation of fibrinolysis took place (the time of lysis of the clot was shortened to 15-30 min (Fig. 2). Repeated taking of blood was no longer accompanied by such a marked response of the indices of lipid metabolism and the fibrinolytic system. A similar reaction in monkeys unaccustomed to experimental situations as regards the white cell count, the blood cholesterol, and various other physiological indices has been described previously and is regarded as an autonomic component of the defensive reaction which is gradually extinguished when these procedures are repeated [5].

To judge from the results of these experiments prolonged emotional stress led to a marked increase in the blood fibrinogen concentration in the monkeys of both groups.

The increase in the fibrinogen level accompanying emotional stress in the absence of changes in the indices of lipid metabolism and other indices of the clotting system was probably connected with hormonal changes taking place in the period of stress, and it requires further study. It must not be forgotten that a prolonged increase in the fibrinogen concentration may lead to changes in the vessel wall disturbing its permeability and contributing to the development of atherosclerosis, and under unfavorable conditions it may also play a role in thrombosis.

LITERATURE CITED

1. I. E. Ganelina, I. N. Komarova, I. V. Krivoruchenko, et al., Lipid Metabolism and Atherosclerosis [in Russian], Moscow-Leningrad (1965).
2. B. A. Lapin, G. M. Cherkovich, and L. A. Yakovleva, Vestn. Akad. Med. Nauk SSSR, No. 4, 73 (1966).
3. D. I. Miminoshvili, in: Theoretical and Practical Problems in Medicine and Biology in Experiments on Monkeys [in Russian], Moscow (1956), p. 46.
4. A. P. Savinov and A. V. Tyufanov, Abstracts of Proceedings of the 1st Scientific Session of the Institute for the Study of Poliomyelitis [in Russian], Moscow (1957), p. 36.
5. I. A. Utkin, in: The Physiology and Pathology of Higher Nervous Activity of Monkeys [in Russian], Sukhumi (1960), p. 7.
6. E. I. Chazov, A. F. Ushkalov, and A. I. Klembovskii, Arkh. Pat., No. 11, 29 (1963).
7. G. M. Cherkovich, Byull. Éksperim. Biol. i Med., No. 8, 21 (1959).
8. F. Dreyfuss, Am. J. Cardiol., 3, 590 (1959).
9. C. Hawkey and C. Symons, Symp. Soc. Zool. (London), 17, 213 (1966).
10. W. Hueper, Am. J. Path., 22, 1287 (1946).
11. M. Malinow, C. Maruffo, and A. Perley, J. Path. Bact., 92, 491 (1966).
12. H. Russek, Geriatrics, 22, 84 (1967).
13. A. J. Seaman and M. Malinow, Lab. Animal Care, 18, 80 (1968).
14. J. Strong, J. Rosal, and R. Deupree, Exp. Molec. Path., 5, 82 (1966).
15. C. Taylor, C. Cox, P. Manalo-Estrella, et al., Arch. Path., 74, 16 (1962).