HYPERTENSIVE AND HYPERCHOLESTEREMIC REACTIONS IN EXPERIMENTAL CEREBRAL ISCHEMIA

L. A. Myasnikov and V. V. Suchkov

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Unilateral ligation of the external and internal carotid arteries in rabbits caused an increase in arterial pressure and in the serum cholesterol concentration.

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The frequent association of essential hypertension and of atherosclerosis and the multiplicity of factors influencing their onset, development, and course are evidence of the close pathogenetic relationship between two diseases [6, 10, 11].

The nervous origin of many hypertensive reactions is now firmly established. Changes in lipid metabolism may also result from neurogenic action [2, 16], and from administration of neurotropic pharmacological agents [9, 17]. A conditioned-reflex hypercholesteremia [5] has been obtained and hypercholesteremia has also been found during conditioned-reflex catecholamine, renal, and reflexogenic hypertension [3]. Cerebral anoxia is one of the pathogenic agents concerned in both vasomotor and metabolic regulation. Partial or complete cerebral ischemia is known to lead to acute hypertensive [1, 9] and to chronic hypertensive states [13, 20]. Meanwhile, not only the various types of hypertension but also atherosclerosis are accompanied as a rule by a disturbance of oxido-reductive processes in nerve tissue [4, 7].

It can therefore be postulated that a chronic disturbance of the cerebral circulation constitutes a pathogenetically valid model for studying the unity of vasomotor and metabolic reactions in the living organism.

EXPERIMENTAL METHOD

The external and internal carotid arteries and the small branches above the carotid sinus were ligated on the right side in 20 rabbits under local anesthesia. During ligation the large nerve trunks and the nerve to the carotid sinus were carefully spared. In 5 rabbits a control mock operation was performed with dissection of the vessels and insertion of the ligature, but the vessels were not tied. One month before the operation and at intervals of 6-7 days during the 9-12 months after the operation the mean arterial pressure was measured by McGregor's method [19]. The cuff was applied to the abdominal aorta and the pulse auscultated in one of the iliac arteries. In the experiments with parallel measurement of the arterial pressure in the abdominal aorta and the carotid artery exteriorized into the cuff, and by the direct method in the aorta, the difference did not exceed 5-10 mm Hg. The serum cholesterol concentration in blood taken from the marginal vein of the ear was determined systematically by Bloor's method over a period of two months.

EXPERIMENTAL RESULTS

Despite the fact that the external and internal carotid arteries were ligated unilaterally and the cerebral anoxia was by no means complete, all 20 animals developed a hypertensive response after 7-10 days, reaching a maximum between the 35th and 45th day, and falling slowly thereafter to reach the initial level of the arterial pressure on the 90th-150th day after operation.

In 13 of the 20 experiments (65%) the increase in arterial pressure was accompanied by a considerable increase in the serum cholesterol concentration. In some cases these changes were parallel,

A. L. Myasnikov Institute of Therapy, Academy of Medical Sciences of the USSR, Moscow (Presented by Active Member of the Academy of Medical Sciences of the USSR I. A. Kassirskii). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 65, No. 6, pp. 39-41, June, 1968. Original article submitted February 24, 1967.

but sometimes the highest cholesteremia was found either at the time of the initial increase in arterial pressure or at the height of the hypertension. By the 9th-14th day after the operation the arterial pressure had risen from 130.4 ± 7.4 to 180 ± 11 mm Hg, and the blood cholesterol had increased by 71% (from 105.3 ± 10.75 to 180.1±21.49 mm%). In some experiments the cholesterol concentration was 380-400 mg%. After 30-34 days, when the arterial pressure had reached its maximum (193±13.1 mm Hg), the cholesterol level had fallen almost to its initial value (116.7±10.7 mg%). On the 60th-65th day of the experiment, while the hypertension continued (143 ± 10.8 mm) the hypercholesteremia had disappeared (96 ± 10.5 mg%). In 4 of the 5 control animals undergoing the mock operation, hypercholesteremia did not develop. Only in one case was a transient increase in the cholesterol concentration found on the 9th-14th day. The hypertensive reaction in these animals was very slight and of short duration.

The results described show the presence of a connection between vasomotor reactions and the state of the cholesterol metabolism. This connection can be shown by producing a moderate degree of cerebral anoxia.

When attempting to explain the mechanism of onset of the hypercholesteremia, the fact must be remembered that of the total sterol content about half is present in the brain tissue, and cholesterol accounts for 98% of the sterols. It may be postulated that the hypercholesteremia which was produced is due to changes in the processes of formation and accumulation of lipids in the brain and to an increase in the liberation of cholesterol into the blood stream, as during central disturbances [14, 18]. However, the situation is evidently not due entirely to a direct change in lipid metabolism in the nerve tissue as a result of anoxia. Cerebral anoxia affects a wide group of nervous structures, causing excitation of various parts of the diencephalon and other regions participating in regulation of vascular tone and intermediate metabolism. The increased blood cholesterol level may therefore be the result of changes in the activity of structures concerned in nervous regulation. The simultaneous hypertensive reactions confirm the centrogenic mechanism of the hypercholesteremia. If hypertension during cerebral ischemia is regarded as an adaptive reaction, compensating for the inadequacy of the cerebral circulation [12], the hypercholesteremia may be regarded in the same light. The considerable lability of the blood cholesterol level in patients with atherosclerosis in general, the appearance of experimental hypercholesteremia only in periods of modification of the stereotype [15], its rapid onset during cerebral ischemia, and the rapid restoration of the normal cholesterol level in the experiments described above are all evidence in support of the adaptive character of this reaction.

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