CHANGES IN SERUM CHOLESTEROL AND LIPOPROTEIN CONTENT IN DOGS ON APPLICATION OF PROLONGED FUNCTIONAL STRESS TO THE NERVOUS SYSTEM

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The principal factor in the development of atherosclerosis is now usually assumed to be a disruption of cholesterol metabolism [1-4, 9].

In previous investigations [5-7] we showed that the cholesterol content of the blood decreases and its β-globulin and β-lipoprotein content increases in rabbits subjected to prolonged (1.5-2 years) functional stress on the nervous system. We detected adiposis of the aortic intima, which developed without addition of cholesterol to the diet, at a blood cholesterol content of 40-80 mg-%.

In the present investigation we studied the cholesterol and lipoprotein content of the blood of dogs subjected to prolonged functional stress on the nervous system.

EXPERIMENTAL METHOD

Eight yound dogs were used in the experiment. In 4 of them (Beglets—3 years, Medved'—2 years, Tyulen'—1.5 years, and Zhuchka—1.5 years) we developed a protective conditioned- reflex respiratory inhibition, reinforcing the conditioned stimulus (a 120 beat-per-min metronome) with gaseous ammonia. Over a period of 25 months the nervous systems of the experimental dogs were subjected to stress by induction of the conditioned reflex. The "working" periods, which lasted 15-60 days, alternated with rest periods (7-90 days). During the "working" and rest periods we determined the content of cholesterol (by the digitonin method) and lipoprotein fractions (by paper electrophoresis) no less than once a month. The nervous system of each experimental dog was subjected to stress for 9 periods (250-280 experiments lasting 60 min each). The conditioned-reflex reaction was induced 12 times during the experiment, at intervals of 5 min. The initial (control) determination of the cholesterol and lipoprotein content of the blood was made while the animals were being familiarized with the laboratory bench and experimental setup before induction of the conditioned reflex. The cholesterol and lipoprotein content of the blood of the control dogs was determined over a 7-month period under ordinary laboratory conditions.

EXPERIMENTAL RESULTS

Figure 1 presents the results of our experiments, in the form of averaged data for the 4 dogs. During the first 10 days of induction of the conditioned reflex (period A) the cholesterol content of the blood was elevated, while its β-lipoprotein content was somewhat reduced. After 20 days of work to establish the conditioned reflex the cholesterol content began to drop and the β-lipoprotein content remained at a low level. During the 7 day rest period the serum cholesterol and β-lipoprotein contents reverted to their initial levels.

On subsequent application of functional stress to the central nervous system, in 6 of the 9 "working" periods, during which the conditioned reflex was displayed in response to application of the conditioned stimulus in 60-80% of all cases, the cholesterol content was less than at the end of the preceeding rest period. During 2 "working"

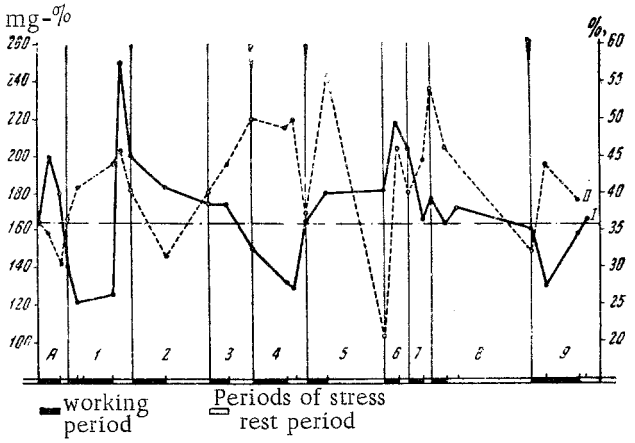

Fig. 1. Change in serum cholesterol (I) and lipoprotein (II) contents in dogs subjected to prolonged functional nervous stress (averaged data for 4 animals). A) Period of establishment of conditioned reflex; 1-9) periods of nervous stress;

periods the cholesterol level was elevated and during one it remained unchanged. The changes in cholesterol content proved to be statistically reliable during only 2 periods; however, since serum cholesterol content decreased in the majority of cases, it must be assumed that it has a tendency to decrease when the nervous system is subjected to prolonged functional stress. The statistical unreliability of the differences probably resulted from the great discrepancy among the changes in serum cholesterol content in the different animals. The serum cholesterol content was elevated at the end of the 5th "working" period. The elevated cholesterol content during these periods resulted from the increased level during the rest periods. Thus, when the serum cholesterol content was determined during the 1st 3 weeks of rest it was elevated in 5 of 6 periods. During the 7 day rest period after the 1st "working" period the serum cholesterol content increased, on the average, from 130.7 to 250 mg-%, i.e., endogenous hypercholesterolemia was observed (cholesterol content increased from 117 to 192 mg-% in Beglets, from 134 to 227 mg-% in Medved', from 127 to 242 mg-% in Tyulen', and from 145 to 338 mg-% in Zhuchka). When the "working" period was prolonged the cholesterol level increased only during prolonged rest. Prolonged rest (60-90 days) led to normalization of the serum cholesterol level. On alternating functional nervous stress and rest we thus noted periodic changes in serum cholesterol content, ranging from hypercholesterolemia to a normal cholesterol level. It may be assumed that a disruption of the dynamic stereotype of nervous activity and formation of a new stereotype are of special importance in the increase in cholesterol content which occurs in transition conditions.

Serum Cholesterol and Lipoproteins Content of Control Dogs

Date of determination (1962)	Cholesterol content (mg	P	Lipoprotein content (%)	P
5/VI	142±10,0	—	42,5±2,9	—
28/VI	148±12,8	>0,05	40,1±1,6	>0,05
11/VII	147±12,6	>0,05	41,6±1,4	>0,05
4/IX	140±10,0	>0,05	39,1±2,6	>0,05
4/X	143±5,3	>0,05	37,0±2,8	>0,05
3/XI	157±4,4	>0,05	36,8±4,0	>0,05
14/XII	155±7,0	>0,05	35,8±2,1	>0,05

Note: P represents the reliability of the differences with respect to the preceding index.

During the majority of the "working" periods of (6 of 9) the content of β-lipoproteins and neutral fat* in the blood was greater than at the end of the preceeding rest period (see Fig. 1). Their content was reduced during 2 periods and remained unaltered during 1 period. In 8 of the 9 "working" periods the content of β-lipoproteins and neutral fat was elevated. The quantity of β-lipoproteins and neutral fat frequently increased to 60-80% in individual animals (Fig. 2), as against a mean initial value of 36.6%. In certain cases the quantity of β-lipoproteins and neutral fat also increased during the 1st week of the rest period. Their content was normalized after prolonged rest (60-90 days). Although the increase in β-lipoprotein and neutral fat content was frequently independent of the serum cholesterol level, the changes in these indices were found to be inversely proportional in the majority of cases. The β-lipoprotein content varied in parallel with the change in cholesterol content only when hypercholesteremia was present.

Determination of the serum cholesterol and β-lipoprotein contents of the 4 control dogs over a 7 month period did not reveal any substantial changes; the β-lipoprotein content decreased somewhat as the animals became familiar with the blood-taking procedure (see Table).

* The lipoproteins and neutral fat (the colored spot in vicinity of the γ-globulins) were not separated in interpreting the electrophoregrams.

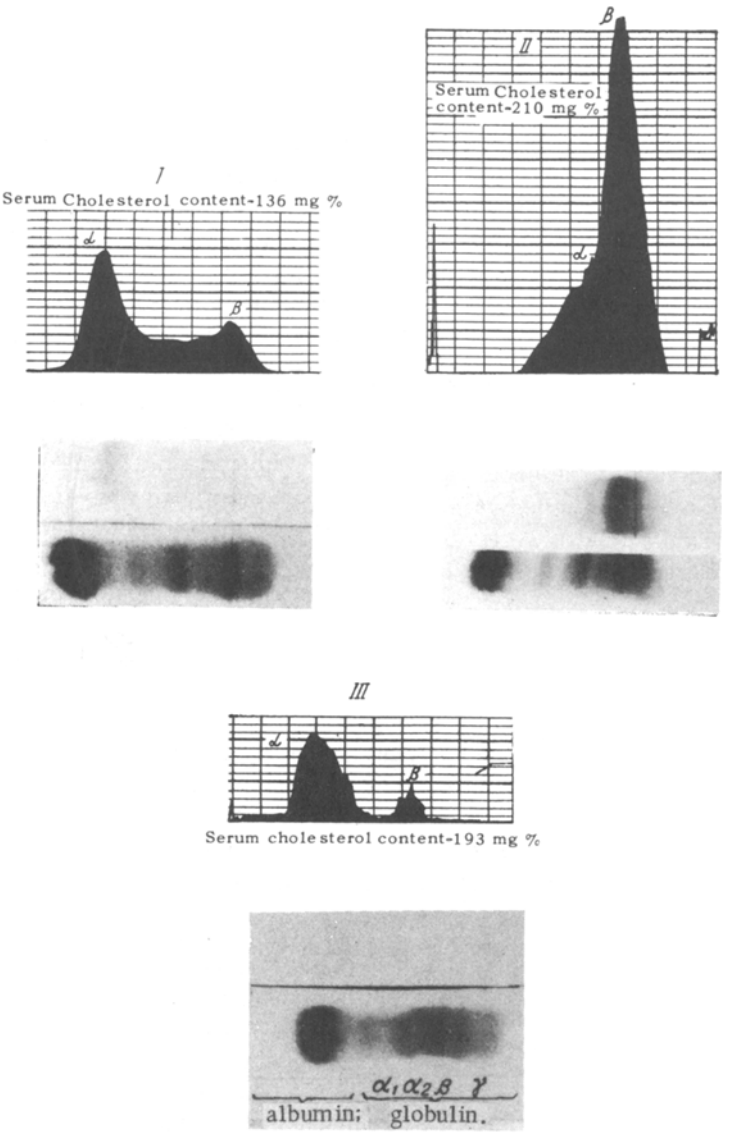

Fig. 2. Change in content of lipoprotein fractions in the dog Medved' during the 6th period of nervous stress. I) Electrophoregram of lipoproteins and proteins and lipoprotein-content curve after 20 days of rest; II) after 21 days of nervous stress; III) after 55 days of rest.

There is thus a tendency toward a decrease in serum cholesterol content and an increase in serum β-lipoprotein content under prolonged functional nervous stress. The cholesterol content increases during the transition from the "working" period to the rest period. We previously observed similar changes in serum cholesterol and β-lipoprotein content in rabbits [7] and humans [9]. The rabbits exhibited deposition of lipids in the aortic wall.

The periodic changes in serum cholesterol and β-lipoprotein content in the experimental dogs were similar to the fluctuations observed in atherosclerosis. It may be assumed that the variation in serum cholesterol content is based on a change in cholesterol synthesis under the influence of the disruption of thyroid function which occurs while the dynamic stereotype of central nervous activity is being destroyed and the varying extent to which cholesterol is converted in the adrenals when stress is applied to the nervous system and in transition states. The increase in β-lipoprotein and neutral fat content which takes place under functional nervous stress is apparently caused by the intensified mobilization of free fatty acids resulting from secretion of adrenaline and the intensification of β-lipoprotein synthesis [10-13].

SUMMARY

Functional CNS strain was provoked in experiments on dogs for 25 months; this was done by reproducing the protective conditioned reflex to respiratory inhibition. Working periods lasting 15-60 days were alternated by rest periods of the same duration. In nervous functional strain the majority of experimental animals exhibited a reduction in the blood cholesterol level and a rise in the β-lipoprotein and the neutral fat content. During the rest periods (7-21 days) blood cholesterol increased; cholesterol, β-lipoproteins and neutral fat approximated the initial level only after a 30-90 day rest period.

Hypercholesterolemia during rest, hypocholesterolemia in prolonged straining and a rise in β-lipoproteins in the experimental dogs are similar to oscillating changes in patients with atherosclerosis. It is emphasized that passing from prolonged work to rest, and conversely, is of significance in the development of cholesterol metabolic disturbances.

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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.
