EFFECT OF SEVERE STRESS ON THE β-LIPOPROTEIN CONTENT OF BLOOD SERUM AND OF SOME ORGANS

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Determination of the content of certain conjugated proteins in blood serum, in particular lipoproteins, is widely applied in clinical practise for diagnostic, differential diagnostic, and prognostic purposes. The β-lipoprotein fraction (β-LP) is the easiest to determine chemically, and its content varies most widely in pathological conditions. For this reason special interest attaches to its study.

β-LP is an unstable adsorption complex of β-globulin (21%) with lipids (79%) [2, 9]. Not enough is known about the biological function of β-LP. It is supposed that it serves for the transport of lipids and fat-soluble substances (including those of dietary origin) to the organs and tissues. β-LP serves for the transport of vitamins (A, D, E) and hormones (corticosteroids, sex hormones). It has recently been shown that some serum enzymes (transaminases, lactic dehydrogenase, phosphatase, choline esterase, and others) may enter into the composition of β-LP, in an inactive form, and that they are activated when the complexes enter the cells [13]. The permeability of cell membranes and of structural cell elements to various substances is determined by tissue lipoproteins.

A special enzyme, called lipoproteinase [11] has been found to catalyze cleavage of fats from β-LP, followed by their transfer to other proteins (α-globulin, albumin). This enzyme is activated by heparin [7]. Liver diseases are associated with a deficiency in this enzyme, and with a rise in serum β-LP content [10]. According to G. V. Troitskii [2], under physiological conditions, with normal mutual proportions of lipoproteinase activity and β-LP content, the latter contributes to protection of the intima of blood vessels from imbidition of colloidal lipid particles (atheromatous plaques). There is evidence that β-LP participates in unspecific defense mechanisms of organisms [14]. β-LP plays a certain part in immune reactions, and, as a component of properdin, it contributes to the neutralization of some viruses, such as that of influenza [1].

It has been found [3] that the content of β-LP rises in the serum in a wide variety of pathological states (viral and bacterial infections, myocardial infarct, diabetes, nephrosis, the Schwartzman phenomenon, after surgery, and in experimental hypoproteinemia). Severe physical and emotional stresses have also been shown to cause elevation of serum β-LP [4]. It was concluded, on this basis, that raising of the blood β-LP level is one of the manifestations of the unspecific reaction of the organism to severe stress.

In order to test this hypothesis we examined the effect on the β-LP content of the serum and of various organs (liver, heart, and brain) of a number of powerfully stressful factors, some of which were known to give rise to the unspecific adaptive syndrome [15], while others could be expected to do so. For these experiments we used white rats of body-weight 150-300 g. Blood samples for analysis were taken from exposed cervical vessels, and transferred to test-tubes. Portions of organs were taken for analysis immediately after the death of the animals. The experimental details are presented in the legend to Fig. 1.

The β-LP content of serum and organ homogenates was determined by the micromethod of Burstein and Samaille [5]. The tissues were homogenized in 9 volumes of physiological saline. The β-LP contents of serum and tissue homogenates are expressed as arbitrary extinction units.

Figures 1 and 2 represent the changes found in β-LP content of serum and organs (mean values and standard error of means at $P = 0.05$) under the various experimental conditions. These data show that not all the stressful factors

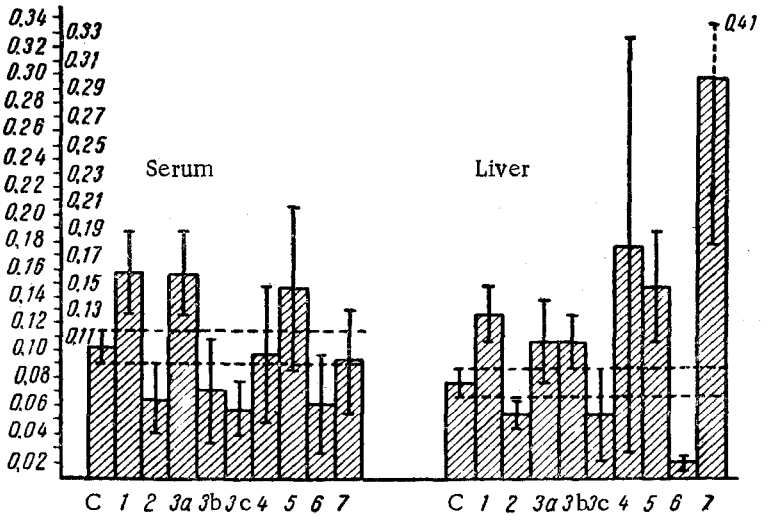

Fig. 1. Changes in the β-LP content of serum and liver tissue of white rats following application of powerfully stressful factors (mean values and standard error of means at P = 0.05). C) Control group: 1) hypoxia ("ascent" in a pressure chamber to 4000 m for 2 hr); 2) asphyxia (maintenance in a sealed vessel of capacity 12 liters for 15 hours); 3a) hypothermia (immersion in a water bath at 1° for 15 minutes); 3b) hypothermia (water bath at 15-20° for ½-1½ hours); 3c) hypothermia (maintenance in a refrigerator at 8-10° for 20 hours); 4) sterile inflammation (injection of 0.2 ml of formalin into a foot pad); 5) scald shock (immersion in water at 65° for 10 seconds); 6) convulsions (subcutaneous injection of Bemigride, at a dose of 20 mg/kg); 7) septicemia (intraperitoneal injection of living Escherichia coli suspension, at a dose of 3 milliard cells).

affect the β-LP content of serum and organs in the same way. Violent and acute stresses (hypoxia, immersion in very cold water (1°), and scalding) appear to cause a pronounced rise in the β-LP content of the serum (although the mean β-LP content of the serum of scalded animals was clearly higher than for the control group, the standard error of the mean is very large, because of the insufficient number of animals taken).

Milder and more slowly acting stresses (immersion in moderately cold water, sterile inflammation, septicemia) did not cause any appreciable variations in the β-LP content of serum.

Finally, stresses leading to development of acidosis (asphyxia, hypothermia in a closed refrigerator, Bemigride convulsions) caused a fall in the level of blood β-LP.

It is noteworthy that the changes in β-LP found in experiments involving factors leading to acidosis coincide with those observed in infectious hepatitis patients in hepatic coma. Acidosis usually develops in such patients, and the raised β-LP level usually encountered in Botkin's disease then falls to subnormal levels.

In most cases, a correlation is evident between the changes in serum β-LP content and in that of the liver. It can be seen from Fig. 1 that factors which cause an increase in serum β-LP content also give this effect in the liver (hypoxia, extreme hypothermia, scalding). Conversely, those factors which lower the serum β-LP level (asphyxia, hypothermia, in the refrigerator, and convulsions) also lower the liver β-LP content. On the other hand, the β-LP content of the liver rose sharply (to over three times the control level) in E. coli septicemia (whereas there was no change in serum β-LP content in this condition), and in sterile inflammation (data not statistically significant).

The mechanism whereby the changes in liver β-LP content observed in convulsive states (a fall to an eighth of the normal level) and in septicemia (an 8-fold rise above normal) are effected is of particular interest, and merits special study. The hypothesis might tentatively be advanced that acidosis developing in convulsed animals causes disturbances in synthesis or dissociation of β-LP, while in septicemia septic hepatitis rapidly develops, the early stages of which are usually associated with raised liver β-LP content (due perhaps to lipoproteinase deficiency).

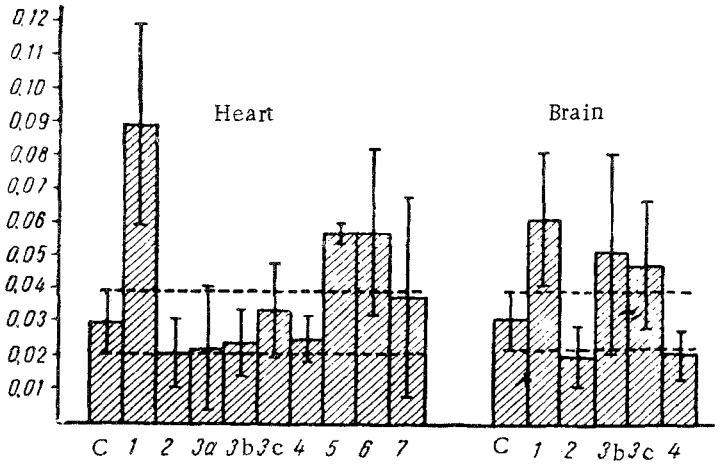

Fig. 2. Changes in the β-LP content of heart and brain tissues of white rats subjected to violent stresses (mean values and their standard deviations at P = 0.05). Designations as in Fig. 1.

The observed changes in β-LP content of heart and brain tissue are represented in Fig. 2. With the exception of a slight fall in β-LP content of the brain in the sterile inflammation group, in no case did the β-LP level fall below that of the control group. Only for some of the factors was there a moderate rise in the β-LP content of the liver and brain. Even convulsions, which so drastically lowered liver and blood β-LP, not only did not lower the β-LP content of heart tissue, but, on the contrary, somewhat raised it. It seems probable that, in such vitally important organs as are the heart and the brain, the mechanisms regulating homeostasis are particularly effective, and hence that changes in the contents of their cell components are the longest deferred.

We have shown that there exists a considerable degree of parallellism between the changes in β-LP content and in the activity of some of the enzymes concerned in carbohydrate and protein metabolism (aldolase, transaminase), observed following the application of violent stresses. This parallellism points indirectly to the possibility of the existence of some common mechanism of these changes, and indicates the need for the investigation of this mechanism.

In this connection, interest attaches to the findings of Järnefelt [12], that serum β-LP may form loose complexes with enzymes, in which form the latter enter cells, where they participate in oxidation-reduction reactions.

It is possible that hyperlipoproteinemia constitutes a response to heightened activity of serum enzymes induced by the action of violent stresses.

Our present knowledge of the subject does not permit of an adequate explanation of the mechanism and biological significance of the observed changes in β-LP content of the serum and of organs. It might, in accordance with the above-cited data, be supposed that a rapid rise in β-LP levels following application of violent acute stresses is related to mobilization and transport to the tissues ofphysiologically active substances. The fall in serum and liver β-LP content observed in acidosis is probably related to enhanced dissociation of the β-lipoprotein complex, or else to inhibition of its synthesis.

Our experiments have thus shown that the subjection of rats to violent stresses causes changes in the β-LP contents of the serum and of various organs. It cannot be concluded from our findings that raising of the β-LP content of organs and tissues is necessarily an attribute of the adaptation syndrome developing in the organism as a result of the action on it of violent stresses.

SUMMARY

Subjection of rats to violent stresses causes appreciable changes in the β-lipoprotein contents of their serum and of some of their organs. Violent acute stresses (hypoxia, scalding, immersion in cold water) cause rises in the β-lipoprotein levels of the serum and the liver. Acidosis developing following application of some of the stressful factors is regularly associated with a fall in the content of liver and serum β-lipoproteins.

Application of violent stresses either does not affect the β-lipoprotein contents of the brain and the heart, or it raises them.

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