

THE EFFECT OF NEUROPLEGIC AGENTS ON RAT'S LIVER ALKALINE PHOSPHATASE ACTIVITY UNDER CONDITIONS OF BURN SHOCK

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According to modern pathophysiological theory, shock cannot be considered only a circulatory disturbance. Soviet researchers [1, 2, 3, 6, 7 et al.] were primarily responsible for the discovery that the nervous system in general and the higher nervous activity in particular play a decisive role in the development of traumatic shock. In shock, the neurohumoral regulation is disturbed, upsetting the equilibrium of almost all the vital processes in the organism and causing thereby serious disturbances of the metabolic processes [4, 17, 21]. The liver's importance in the metabolism suggests that it is involved in these pathologic processes. According to F. Engel, the liver sustains hypoxic injuries even during the early stages of shock. Engel and other authors believe that the increased blood sugar content observed in shock is due to intensified decomposition of liver glycogen. According to the observations of D. Cordier and M. Touze [see 13], the rate of glycogen phosphorylation in rat's liver decreases considerably in traumatic shock, and the inorganic phosphorus content increases. G. Le Page discovered that, under conditions of shock, there is a greater decrease in the adenosine triphosphate of the liver than in that of the other organs; the data of P. F. Minaev, show that the administration of ATP prevents the development of shock.

A series of laboratory-experimental and clinical data indicate that neuroplegic agents (derivatives of the phenothiazine group) alleviate the course of traumatic and hemorrhagic shock, as does artificial hibernation [9, 21, 15, 16, 18 et al.]. However, the question of the changes caused in the metabolism by the administration of phenothiazine preparations (chlorpromazine) or artificial hibernation under conditions of shock has not yet been solved.

On this background, we believed it expedient to study the changes in the alkaline phosphatase activity in liver tissue under conditions of burn shock, in the first place, and in the second place, to what extent these changes are affected by the administration of chlorpromazine or a hibernation mixture under the same conditions.

METHOD

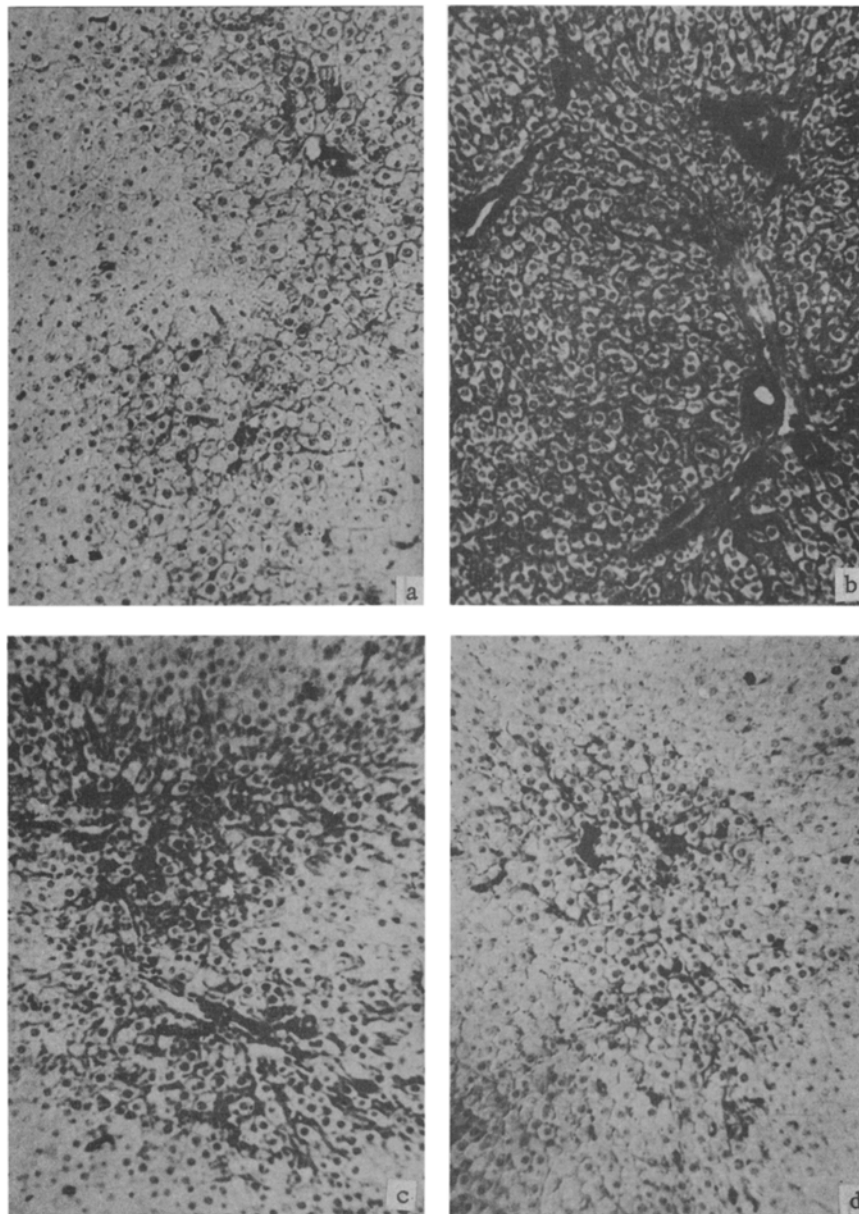
Experiments were performed on 42 male white rats weighing 100-120 g each. Shock was induced by the in-

fliction of a burn, for which purpose 36 of the animals were dipped into boiling water (65°) for ten seconds; 12 of the animals which received the burn were not given preliminary treatment. Forty minutes before the infliction of the burn, 12 animals were subcutaneously injected with chlorpromazine (Largactil preparation) in a dose of 20 mg/kg and 12 animals, with the hibernation mixture (20 mg/kg Largactil + 20 mg/kg Phenergan [promethazine] + 40 mg/kg Dolantin [Demerol]). After the injection, the animals were kept at room temperature (18-20°). The temperature of the animals (taken rectally) was 20-22°. The remaining six animals, which did not receive either the burn or an injection, served as the control. The animals were killed six hours after the burn. Pieces of the liver were fixed in cooled alcohol. The alkaline phosphatase activity was demonstrated according to Gomori's histochemical method. The sections were incubated for 6 and 12 hours.

RESULTS

The rats which had not received the preliminary treatment showed symptoms of acute excitation, then became quiet and sluggish, and their respiration was shallow and rapid. The treated animals were quite and drowsy after the burn.

We observed strongly increased alkaline phosphatase activity in the liver of the animals which had been burned without preliminary treatment (Figure). Well expressed enzymatic activity was noted throughout the liver lobes, in the bile capillaries and cell nuclei of the liver and even in the cytoplasm of the cells. The activity of the Kupffer's cells and the endothelial cells of the sinus increased to a like degree. In the animals which had received chlorpromazine before the burn, there was much less increase in the alkaline phosphatase activity. The bile capillaries, nuclei of the hepatic cells and Kupffer's cells only remained more or less active in certain parts of the sections. The phosphatase activity of the liver of the animals which had received the hibernation mixture before the burn shock hardly differed from the liver phosphatase activity in the control experiments; scattered active Kupffer's cells were observed, and the bile capillaries



Activity of rat's liver alkaline phosphatase. a) Normally; b) with burn shock; c) with burn shock after preliminary administration of chlorpromazine; d) with burn shock after preliminary artificial hibernation. Reaction according to Gomori's method. Magnification: ocular 7, objective 10.

and nuclei of the hepatic cells were somewhat more active than normally.

It should be mentioned that, in our previous investigations, the administration of these substances had no particular effect on the normal enzymatic activity of the liver.

The increased liver phosphatase activity observed after the burn shock indicates a process of intensive dephosphorylation of the substances. This corresponds to the literary data and throws new light on the process causing the loss of high-energy phosphoric acid esters. An increase in the activity of alkaline liver phosphatase has been observed in other cases besides the shock condition, for example, under conditions of hypothermia, anoxemia

and the administration of formalin. A. Meier [20] observed the same phenomenon, attended by loss of liver glycogen, under conditions of starvation. D. Cordier and M. Touze [13] discovered that phosphorylation of liver glycogen is retarded in traumatic shock. One can propose that retardation of the phosphorylation process must be attended by acceleration of the dephosphorylation process.

The mechanism of the protective effect exerted by chlorpromazine and artificial hibernation with respect to the increase in alkaline phosphatase activity is not yet sufficiently clear. E. Ciocatto and his coworkers [11] and Anselmo da Cruz et al. observed that Largactil decreases

the activity of blood serum phosphatase and cholinesterase. We believe that what occurred in our experiments, however, was not a peripheral effect acting directly on the enzyme, but a central effect excluding the reactivity of the autonomic nervous system. This is indicated by the fact that while these agents do not affect normal phosphatase activity, Largactil and artificial hibernation, in toxic injury of the liver induced by chloroform, do not decrease, but even increase alkaline phosphatase activity.

SUMMARY

The activity of the alkaline phosphatase of rat liver was found to be sharply increased under conditions of burn shock. This rise was considerably inhibited by largactyl and almost completely by the hybernation mixture (largactyl + phenergan + dolantin). The authors consider that the mentioned effect is central in origin and may play a certain role in the antishock effect of artificial hybernation.

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