

COMPARISON OF INDICES OF PROTEIN METABOLISM WITH PATHOLOGICAL CHANGES IN THE LIVER TISSUE AFTER EXPERIMENTAL ADMINISTRATION OF DIPHTHERIA TOXIN

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The earliest manifestation of changes in the serum protein composition after experimental administration of diphtheria toxin is a decrease in the β -globulin and increase in the γ -globulin concentration. The appearance of embryo-specific α -globulins in the blood serum coincides with the development of proliferative changes in the liver. The decrease in serum albumin concentration takes place against the background of initial cirrhotic changes in the liver tissue.

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Certain hepatocellular lesions are accompanied by the appearance of embryospecific globulins in the blood [1, 4, 5]. In this investigation we compared changes in the serum protein composition with pathological changes in the liver tissue and the appearance of embryo-specific globulins (ES α -globulins) at various stages of development of experimental diphtheria toxicosis in dogs.

EXPERIMENTAL METHOD

Diphtheria toxin (batch No. 8, 1 MLD = 0.0032 ml) was injected as a single dose of 0.0005 ml/kg body weight into the femoral vein. The dogs were sacrificed at various times after injection of the toxin and a pathological investigation of the liver tissue carried out.

Total serum proteins were determined refractometrically, and protein fractions by electrophoresis on paper.

The appearance of ES α -globulins was judged from the results of titration in agar with a standard test system [6] for ES α_2 - and ES α_1 -globulins. The method of identification of these proteins was described previously by one of us, A. V. Afanas'eva [2, 3].

EXPERIMENTAL RESULTS

Pathological changes in the liver tissue during the first two days after injection of toxin consisted of marked degenerative changes in the liver cells. No changes were found in the blood protein formula and no ES α -globulins appeared.

From the 3rd to the 7th day after injection of toxin the dominant pathological changes as before were degenerative changes as necrosis of the liver cells, although large numbers of leukocytes appeared, the Kupffer cells were more numerous, and the PAS reaction revealed glycogen only in the Kupffer cells (Fig. 1). In the serum the β -globulin level was lowered and the γ -globulin level raised ($P < 0.02$), while ES α -globulins appeared in some animals.

Starting from the 8th day, proliferative changes became clearer in the morphological picture of the liver tissue. Large numbers of PAS-positive granules were found over the whole area of certain lobules, proliferation of PAS-positive reticuloendothelial cells was observed, and the leukocytes were more numerous. After 2 weeks, areas of periportal infiltration of lymphocytes and fibroblasts, with thin bands of connective tissue began to appear.

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TABLE 1. Change in Serum Proteins Composition in Dogs with Experimental Diphtheria Toxicosis (M ± m)

Time of observation after injection of toxin (in days)	Content of protein and protein fractions					Embryo-specific proteins		
	Total protein (in %)	Globulins (in %)				Number of observations	Frequency of detection	
		albumins (in %)	α_1	α_2	β	γ	total	α_2 -globulins
1-2	6.72 ± 0.21	40.0 ± 1.16	12.55 ± 0.82	12.3 ± 0.83	21.15 ± 0.9	10.0 ± 0.71	—	—
3-7	5.67 ± 0.47	40.0 ± 1.06	12.0 ± 0.64	15.0 ± 0.64	18.8 ± 0.67	14.2 ± 0.82	4	3
8-13	6.3 ± 0.21	39.4 ± 1.1	11.5 ± 0.72	16.6 ± 0.67	17.8 ± 1.02	14.7 ± 1.4	6	4
14 and over	6.67 ± 0.33	30.1 ± 2.07	12.1 ± 1.091	15.3 ± 1.4	20.3 ± 2.03	22.2 ± 2.2	5	5
Control	6.71 ± 0.23	40.45 ± 1.02	12.13 ± 0.42	14.7 ± 0.84	21.72 ± 1.04	11.0 ± 0.59	—	—

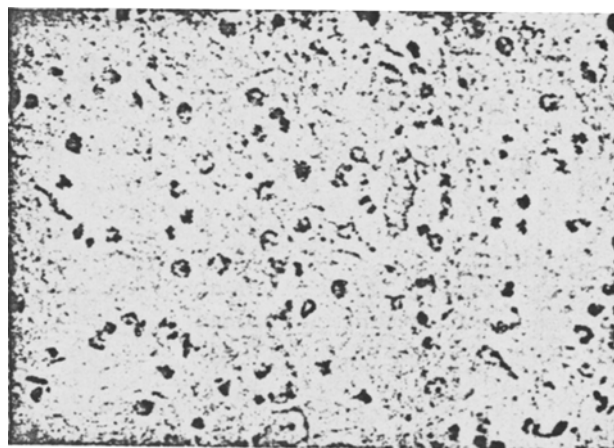


Fig. 1. Liver of dog with diphtheria toxicosis. Cloudy swelling of liver cells. Infiltration of the serous membrane. Areas of commencing necrosis. Increased number of leukocytes in capillaries. Hematoxylin - eosin, 400X.

Whereas during the first two weeks the increase in γ -globulins and decrease in β -globulins took place along with maintenance of the normal serum albumin level, on the following days the increase in the relative γ -globulin concentration ($P < 0.001$) was accompanied by a perceptible decrease in the serum albumin concentration ($P < 0.001$). The possibility of detection of embryo-specific globulins in the blood serum was increased at these times (Table 1).

In the control dogs receiving diphtheria toxin inactivated by heating to 70–80° for 1 h or receiving no injections whatever, the serum protein composition and pathological appearance of the liver tissue remained unchanged.

It may be concluded from analysis of these findings that the earliest manifestation of changes in the serum protein composition in experimental diphtheritic toxic hepatitis is a decrease in the concentration of β -globulins and an increase in that of γ -globulins.

The appearance of embryo-specific proteins in the blood serum coincides with the development of proliferative changes in the liver.

The decrease in serum albumin level in the blood takes place against the background of initial cirrhotic changes in the liver tissue.

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