

MORPHOLOGICAL CHANGES IN RABBITS PRODUCED BY PROLONGED ADMINISTRATION OF TRYPSIN

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UDC 615.355:577.156.3] .015.4:616-091

Morphological changes arising in the organs of rabbits during prolonged intravenous injection of trypsin were studied. After 7 injections of 5 cc of 2% trypsin solution collections of plasma cells and histiocytes were found between the glomeruli and around the blood vessels of the kidneys and also around the vessels and along the course of the bile ducts in the liver. No changes were found in the heart or brain. After 23 intravenous injections of trypsin severe degenerative changes developed in the liver and kidneys, while tissue edema, vasodilatation, and accumulation of plasma cells and histiocytes in the tissues were found in the heart and brain. The immunologic character of the changes developing in the tissues after trypsin injection is postulated.

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It has been suggested [4, 7, 9] that proteolytic enzymes may play a role in the development of autoimmune processes. In a previous communication [5] we described immunologic changes developing as a result of repeated injections of trypsin into rabbits. We found that with an increase in number of intravenous injections of trypsin the titer of antibodies against autologous and homologous kidney, liver, heart, and brain tissues increases. An increase in the thermostability of these antibodies compared with normal antibodies also is observed.

In this paper we describe the results of morphological investigations of certain organs of these animals.

After 7 intravenous injections (5 cc on alternate days) of 2% trypsin solution mild changes were found in the kidneys and liver. In some glomeruli Bowman's capsule was filled with pink homogeneous fluid, and the epithelium of the convoluted tubules showed cloudy swelling. Around the vessels and between the renal tubules were collections of plasma cells and histiocytes (Fig. 1). Similar collections of histiocytes and lymphocyte-like cells were also found along the course of blood vessels and bile ducts in the liver. No changes were found in the heart and brain.

After 23 intravenous injections of trypsin the morphological changes in the organs were more marked. Most glomeruli of the kidneys were enlarged, and collections of erythrocytes could be seen in the lumen of many of them. The epithelium of the convoluted tubules showed diffuse necrobiosis with considerable desquamation. Between the glomeruli and around the vessels areas of hemorrhages and multiple collections of lymphocyte-like cells and histiocytes could be seen (Fig. 2). In the liver extensive areas of necrobiosis and necrosis were present. In other fields of view there were numerous islands consisting of collections of lymphocytes, plasma cells, and occasional polymorphs. Foci of accumulation of cells of this type were found in large numbers around the blood vessels and bile ducts (Fig. 3).

In the heart, considerable loosening of the fibers and edema of the cells were found in the stroma, mainly around the vessels. The vessel walls were thickened and loose in structure. In the brain, the pia was edematous and infiltrated in some places with plasma cells and histiocytes.

The results show that with an increase in the number of intravenous injections of trypsin, morphological changes in the organs increase in severity. In the first stage these changes consist mainly of vascular

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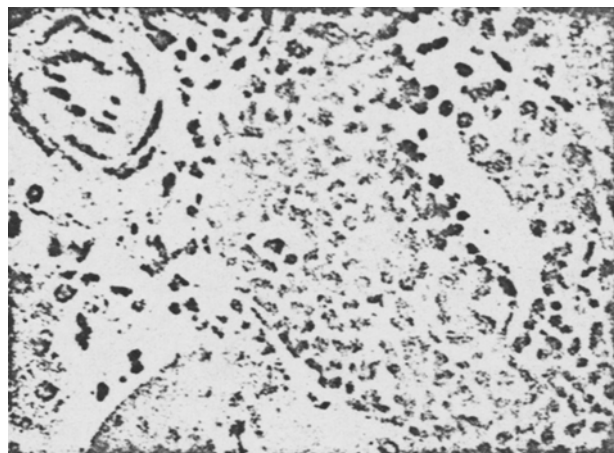


Fig. 1. Kidney of rabbit after 7 intravenous injections of 2% trypsin solution. Perivascular collections of histiocytes and plasma cells. Looseness and edema of vessel walls. Hematoxylin-eosin. 400 \times .

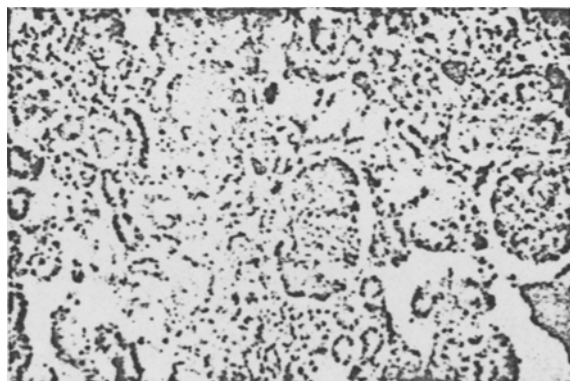


Fig. 2. Kidney of rabbit after 45 intravenous injections of 2% trypsin solution. Marked dilatation of glomeruli. Diffuse necrobiosis of tubular epithelium. Hemorrhages in glomeruli and between tubules. Hematoxylin-eosin. 80 \times .

reactions (tissue edema, increased permeability of the vessel walls, and formation of foci of infiltration consisting of plasma cells and histiocytes).

It is an interesting fact that the morphological changes were to some extent correlated with the accumulation of antibodies against the organs in the serum of these animals. The results of the previous investigation [5] showed that after 23 intravenous injections of trypsin the titer of antibodies against liver and kidney tissue antigens rose to 1:160-1:320. Antibodies against heart and brain tissues also were found. The results of the present investigation show that corresponding changes developed in the organs. Many authors [1-3] stress the similarity between antigen-antibody reactions in the tissues and allergic reactions. In its mildest form this reaction consists of increased permeability of the blood vessels, migration of the blood cells, and tissue edema [6, 8].

Interdependence of these two processes can be assumed on the basis of comparison of the immunologic changes detected in animals after repeated intravenous injections of trypsin and the pattern of the morphological changes developing in the organs in these animals.

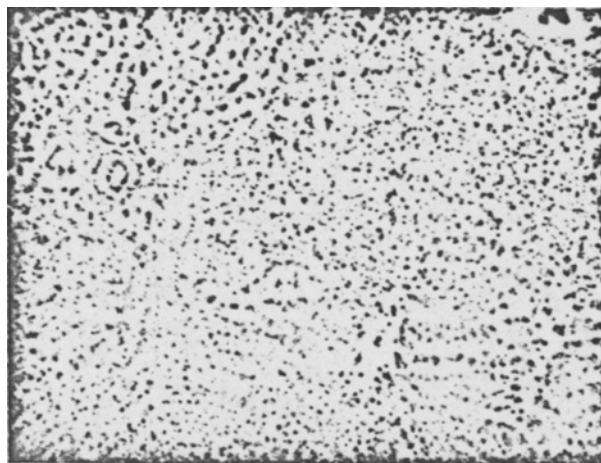


Fig. 3. Liver of rabbit after 23 intravenous injections of trypsin. Necrobiosis and necrosis of liver tissue. Hematoxylin-eosin. 80 X.

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