# MORPHOLOGICAL CHANGES IN THE LUNGS AND KIDNEYS DURING CHRONIC CARBON TETRACHLORIDE POISONING

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During prolonged administration of carbon tetrachloride to rabbits, leading to development of cirrhosis of the liver with ascites, the animals developed toxic edema of the lungs accompanied by pleural effusion, and combined tubular and glomerular changes in the kidneys, expressed as cloudy swelling, necrosis, and necrobiosis of the epithelium of the convoluted and straight tubules, interstitial edema, and the presence of protein masses in the capsules of the glomeruli. Changes in the lungs and kidneys were persistent and were still present 4 months after the end of administration of the carbon tetrachloride.

The object of this investigation was to study morphological changes in the lungs and kidneys of animals with cirrhosis of the liver developing as the result of prolonged administration of carbon tetrachloride ($CCl_4$).

The basic assumption was that the functions of the liver, lungs, and kidneys, under both normal and pathological conditions, are closely interdependent.

## EXPERIMENTAL METHOD

Cirrhosis of the liver was induced in 25 male rabbits by daily injections of 50% $CCl_4$ solution in peach oil for 3-4 months, in a dose of 0.12 ml solution per kilogram body weight.

Paraffin and celloidin sections were stained with hematoxylin and eosin, by Van Gieson's method, with iron-hematoxylin, and with silver nitrate by Karupu's method.

## EXPERIMENTAL RESULTS

From 3-4 months after the beginning of $CCl_4$ administration the rabbits developed marked atrophic cirrhosis of the liver with ascites. In histological sections of the liver marked proliferation of coarse connective tissue was observed both along the course of the portal tracts and around the central and collecting veins. The architectonics of the sinusoids was severely disturbed, they ran haphazardly, and their lumen was constricted because of swelling of the hepatocytes. The vessels of the portal tracts were considerably dilated, whereas the lumen of the sinusoids and of the central and collecting veins was reduced through their compression by connective tissue and by nodules of regeneration. Desse's spaces and internal Eck's fistulas were found. The Kupffer cells were large in size. The argyrophilic skeleton was greatly increased and very coarse in structure. The volume of ascitic fluid in the animals reached 120 ml.

Against the background of these changes in the liver and lung tissue, thickening of the interalveolar septa was observed as the result of their infiltration by cells, a high percentage of which were lymphocytes and plasma cells. The interalveolar septa were saturated with protein-containing fluid. The epithelium of the alveoli was very swollen and high, and frequently the cells were round in outline; the cytoplasm of the alveolar epithelium was vacuolated. The lumen of the alveoli contained a fibrinous ecudate, a

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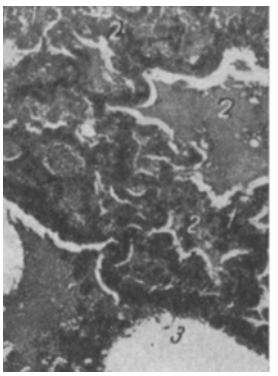

Fig. 1

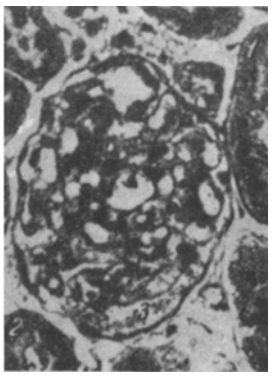

Fig. 2

Fig. 1. Section through lungs of rabbit at height of experimental cirrhosis: interalveolar septa thickened (1), exudate present in lumen of alveoli (2), alveoli free from exudate and bronchioles are dilated (3). Hematoxylin-eosin, 90 ×.

Fig. 2. Sections of kidney tissue of a rabbit at the height of experimental cirrhosis: cloudy swelling of convoluted (1) and straight (2) tubules, protein masses in lumen of glomerular capsule (3), and interstitial edema. Hematoxylin-eosin, 200 ×.

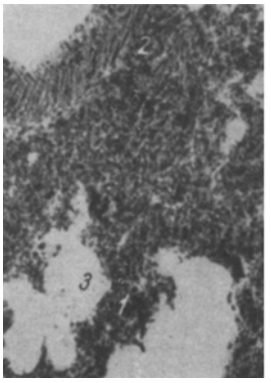

Fig. 3

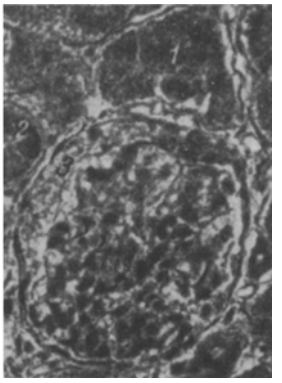

Fig. 4

Fig. 3. Section through lung tissue four months after end of administration of $CCl_4$: interalveolar septa thickened (1), periarteritis (2), lumen of alveoli free from exudate (3). Staining and magnification as in Fig. 1.

Fig. 4. Section through kidney tissue four months after end of $CCl_4$ administration: cloudy swelling of convoluted (1) and straight (2) tubules, protein masses in lumen of glomerular capsule (3). Staining and magnification as in Fig. 3.

characteristic feature of which was the almost total absence of neutrophils. Sometimes desquamated alveolar epithelium could be seen in it. In some alveoli the protein-containing exudate was very thick. Alveoli free from fluid and the terminal bronchii were dilated (Fig. 1). The walls of the blood vessels were edematous. The fibers of the media, the smooth-muscle coat, were loosely arranged. The intima

was thickened and uneven in outline and the lumen of the vessels was constricted. The adventitia was loose in structure. The vessels of the alveolar septa and the capillaries were congested with blood. Leukocytes accumulated around the vessels.

In the lungs of some rabbits, besides the changes described above, suppurative bronchitis with necrosis and purulent liquefaction of the bronchial mucous membrane, with diffuse infiltration of the bronchial wall with leukocytes, were observed. The bronchitis frequently developed into focal bronchopneumonia, when an exudate containing numerous leukocytes was found in the lumen of the bronchii and the adjacent alveoli.

In 29 rabbits fluid collected in the pleural cavity, while in some animals there were petechial hemorrhages on the surface of the lungs.

The morphological changes described above in the lung tissue were evidently associated with toxic injury to the lungs, resulting in increased permeability of the pulmonary capillaries and the development of toxic edema of the lung. At the same time the animals became more vulnerable to intercurrent infections, presumably because of a decrease in the protective properties of the lung tissue.

In the kidneys of these same animals the cells of the tubular epithelium were enlarged and the lumen of the tubules was completely closed in some places. The kidney tissue was edematous. Cloudy swelling and vacuolar degeneration of the epithelium of the convoluted and straight tubules were observed. Some cells of the tubular epithelium had no nuclei and some of them were destroyed. The lumen of the tubules contained protein.

The capsule and capillaries of the glomeruli were dilated. Protein masses were present in the lumen of the capsule. A protein exudate was found outside the glomeruli and between the tubules. Interstitial edema was marked (Fig. 2). Some glomeruli were destroyed.

These combined tubular and glomerular changes are evidence of severe toxic damage to the organ, leading to the development of toxic nephrosis.

The changes in the liver, lungs, and kidneys still remained clearly defined 1, 1.5, and 4 months after the end of $CCl_4$ administration. The liver structure of the animals sacrificed 4 months after the end of $CCl_4$ administration was disturbed as a result of the presence of compact bands of coarse connective tissue. The hepatocytes were hypertrophied, the sinusoids were chaotically arranged, and their lumen was constricted. The argyrophilic skeleton remained coarse.

Exudation in the lung tissue was reduced, the alveolar septa remained thickened because of infiltration, predominantly with lymphocytes and plasma cells, and the perivasculitis and peribronchitis became more marked (Fig. 3).

Cloudy swelling and vacuolar degeneration of the tubular epithelium appeared in the kidney tissue, the cells remained swollen, the interstitial edema diminished slightly, and protein masses appeared in the lumen of the capsule (Fig. 4). Sclerotic changes were marked in the kidneys of some rabbits.

Definite changes in the lungs and kidneys were thus found in rabbits with experimental cirrhosis of the liver.

The pathology of the kidneys and lungs in rabbits with experimental cirrhosis is evidently the result of the toxic action of metabolic by-products, not detoxicated by the damaged liver, on the lung tissue and on the structures of the tubules and glomeruli. Some of these by-products may possess antigenic properties and lead to the development of immunological conflicts in these organs (the plasma-cell response in the lungs).

A common feature of all the changes in the organs examined was increased permeability of the blood vessels, resulting in a considerable loss of protein from the body. This facilitates the development of ascites and hyperhydration. Changes in the lungs and kidneys in rabbits with experimental cirrhosis of the liver were persistent and were still present 4 months after the end of $CCl_4$ administration.