Symposium on Allergy and Liver*

Hepatitis and Auto-Allergy

Kiyoshi ISHII and Sukeo YAMAMOTO

Department of Internal Medicine, Osaka City
University Medical School, Osaka, Japan

As for the reason why the clinical conditions of hepatitis patients shift in their course to acute malignant type, chronic type, cirrhosis, or to some other various types, it may be possible to say that there is a marked intervention of bodily reactions of patient, that is, immunologic reaction and allergy. Since 1952 the author has continued his study on this problem from the point of view of auto-allergy.

Detection of allergic condition caused by liver auto-allergy

1) Various antigens were made of liver tissues and complement fixation test or sensitized hemagglutination test was performed in the serum of hepatitic patients. The positive rate of liver phosphatide antigen was seventy per cent in acute hepatitis, sixty per cent in chronic hepatitis, eighty per cent in hepatic cirrhosis, and ten per cent in other diseases.

2) When the hepatitis serum with liver auto-antibody was injected into the abdominal cavity of guinea pig, and its intestine was immersed in Schutz-Dale Bath, with the addition of liver antigen, there occurred almost instantly the contraction of the intestinal tube and when antigen was added a second time, de-sensitization was noticed (Fig. 1).

* Held at the 59th Annual Meeting of Japanese Society of Internal Medicine, April 3, 1962, in Tokyo.

Fig. 1.

Fig. 2.

3) According to Prausnitz-Kuestner method, serum of hepatitis containing liver-auto-antibody was transferred passively subcutaneously and then liver tissue was used as a antigen. There were noticed stasis of capillary vessels, congestion, thrombosis, and furthermore, swelling degeneration of connective tissue, round cell infiltration and development of necrosis.

4) A serum of hepatitis containing liver-auto-antibody was injected into the lymphatic sac of a toad and liver tissue antigen was made to act under the microscopic observation of mesenteric capillary vessels. By this procedure contraction and dilation of blood vessels were noticed; agglutination of blood corpuscle, change in blood circulation and irregularity of capillary vessels became remarkable at mesenteric capillary vessels, and with the lapse of time exudation of plasma and local edema were observed (Fig. 2).

5) When liver tissue antigen was added to hepatitis blood in a test tube by means of Favour's method, observations were made after one hour as well as after three hours, and leucopenia was seen on both occasions; it was chiefly granular leucocytes that collapsed and decreased in number and if complement was added, the destruc-

Fig. 3.

tion was further accelerated (Fig. 3).

The above mentioned results of our experiments would show that owing to the development of liver auto-antibody some patients with hepatitis are in the state of liver-auto-allergy.

Experimental allergic cirrhosis of the liver

For the purpose of causing liver-auto-allergy in experimental animals, Freund's adjuvant mixed with homogeneous liver powder was intramuscularly injected in rabbits or rats 5-6 times at intervals of 5 days.

Histological findings of the sensitized animals showed enlargement and phagocytosis of sinusoidal cells and of Kupffer cells. At the time prominent plasma cell reaction and the specific interstitial hepatitis was noticed. But where this sensitization alone was performed, there were simply noticed congestion and vacuolar degeneration of hepatic cells, and there was no marked degeneration nor necrosis, and proliferation of connective tissue was slight, if any.

What is most important is that if sterilized tuberculous bacilli are injected into mesenteric veins of the sensitized rabbits, cirrhosis with pseudo-lobules will be caused in the course of 2-3 months.

Five days after the reinjection, there was observed a formation of tubercles of various sizes around the lobule. In about 30 days, an infiltration of epitheloid cells and monocytes was observed, mostly around the portal veins. Fibrosis was found around the tubercles, as well as in Glisson's capsule.

In about 60 days, fibrosis around the tubercles became more pronounced, the tubercles and Glisson's capsule being connected with fibrous tissue. The portal area showed evidence of a proliferation of bile ducts. Pseudolobules were formed, accompanied by an intensive fibrosis. Macroscopically the surface of the liver was finely granulated, showing its marked consistency.

These findings seem to indicate that there exists an allergic factor in the production of cirrhosis of the liver and in the progression of hepatitis to cirrhosis.

Fig. 4. Sensitized animal: Prominent plasma cell reaction and interstitial hepatitis.

Fig. 5. Granuloma formation around the portal field.

Fig. 6. No increase in reticulin fibers within and around the granuloma.

Fig. 7. Plasmotaxis of one of the branches of the portal vein.

Fig. 9. Fibrosis with marked cellular infiltration in the interlobular area.

Fig. 11. Pseudolobule formation due to active fibrosis.

Fig. 8. Broadening and invasive proliferation of the interlobular interstitium with moderate cellular exudate.

Fig. 10. Definite encapsulation of the granuloma with giant cells and epithelioid cells within.