

spectro-enzymatic method as modified by Hashimoto. And for determination of Total-SH, DTNB method was used. Total-SH and glutathione contents in whole blood of patients with cholelithiasis and hepatitis were not different from those of healthy humans, while in obstructive jaundice by stones and cancers total-SH and GSH in whole blood were decreased. According to remission of jaundice by operative procedure, total-SH and GSH levels in whole blood were increased. In follow-up cases of hepatitis, at the time of remission, total-SH and GSH levels in whole blood were once decreased. In liver tissues of patients with obstructive jaundice, total-SH and GSH level were lower than those in controls containing gastric ulcer and gastric cancer. In dogs bile ducts of which were ligated, total-SH and GSH contents were slightly increased in the first week after operation, but decreased in the third week. Total-SH and GSH in liver tissues were not increased in the third week, compared with those in control. And GSSG content in whole blood and liver tissues was also increased in many cases. The difference between experimental and clinical results must be studied hereafter.

## 121. AN ENZYMOLOGICAL STUDY ON REMAINING STOMACH AFTER RESECTION (II) CHRONOLOGICAL CHANGES IN EACH ORGAN UPON THE USE OF EACH METHOD OF OPERATION

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We have already reported enzymological studies on the remaining stomach after resection especially on the remaining portion in the 54th Meeting of the Japanese Society of Gastroenterology and the 1st Meeting of the Japanese Society of Digestive Surgery. In the present study, the liver was taken up for similar study.

In the group of dogs in the initial stage of BI operation, scarcely any decrease of glycogen was noted in the liver. Moderately positive reaction was noted in LDH and SDH stain. In the liver of dogs in the same stage after operation with BII method, moderate hydrops-like degeneration and decrease of glycogen were noted, while mild decrease of activity was noted in LDH and SDH stain. In the group after a long interval from the operation, no marked difference was noted.

The liver cells in the group of dogs in the initial stage after cardiac resection were atrophic but without decrease of glycogen. In LDH and SDH stain, moderate or high grade of positive reaction was noted in many cases. In the liver of animals after a long interval following operation, advanced hydrops-like degeneration and marked decrease of glycogen were noted, along with a marked decrease of activity of LDH and SDH.

In dogs in which the corpus of the stomach was resected, no remarkable changes of LDH and SDH stain were noted in each stage.

In summary, in both groups of dogs subjected to operations according to BI and BII method, no difference in staining was noted after a long interval from the operation. In dogs in which the cardiac portion was resected, decrease of glycogen and marked decrease of enzymic activities were noted after a long interval. In dogs in which the corpus was resected, scarcely any changes of enzymic activities were noted in each stage.

## 122. EFFECTS OF LATHYROGENIC AGENTS ON EXPERIMENTAL HEPATIC INJURIES

—ELECTRON MICROSCOPIC AND HISTOCHEMICAL OBSERVATION—

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The formation and persistence of collagen rest on the equilibrium of formation and resorption. Lysosomal enzymes, mainly hydrolytic, have recently been regarded as important for the

understanding of the mechanism of fibrosis. In the present study, the number and activity of lysosomes were located with electron microscope and histochemical techniques demonstrating acid phosphatase, beta-glucuronidase and N-acetyl-beta-glucosaminidase in the liver tissue.

Each group of Wistar strain female rats was sacrificed 24 hours, 1 week, 3 weeks, 6 weeks and 8 weeks of experiment. 0.15 ml of carbon tetrachloride per 100 g of rat body weight were injected subcutaneously twice a week. Simultaneous daily administration of aminoacetonitrile (AAN) (10 mg/100 g of rat body weight, subcutaneous) was performed in one group. The activity of lysosomal enzymes decreases within hepatic cells and increases within mesenchymal cells in a few weeks. In 3 and/or 4 weeks, when apparent increase in hexosamine and acid mucopolysaccharides in the ground substance of injured liver and fibrosis would be reversible, the activity of the lysosomal enzymes within mesenchymal cells is most prominent and decreases thereafter as the fibrotic process appears to get irreversible. Simultaneous administration of AAN remarkably suppresses the degeneration of liver cells due to carbon tetrachloride intoxication as represented by the accumulation of fat droplets, dilatation of rough surfaced endoplasmic reticulum, depletion of Palade granules and disappearance of primary lysosomes, keeping the lysosomal enzymes active as a whole. AAN also suppresses the accumulation of mucopolysaccharides preceding to the hepatic fibrosis. The above findings would strongly support the important role of lysosomal enzymes in the metabolism of connective tissue.

### 123. STUDIES ON HEPATIC FIBROGENESIS (XXVI) ACTIVITIES OF ACID MUCOPOLYSACCHARIDE SULFOTRANSFERASES IN CHRONIC HEPATIC INJURY

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Previous report from our laboratory indicated that a remarkable increase of sulfated acid mucopolysaccharides (AMPS) occurred in the liver of rat with experimental hepatic damage. We also found chondroitin sulfate B was shown to have a close relationship with collagen in the damaged liver. In this report, in order to elucidate the abnormality of the formation of sulfated AMPS in damaged liver, the sulfation mechanism of AMPS was studied. Rats with chronic damage were induced by serial inhalation of carbon tetrachloride twice a week for 4, 6 and 10 weeks. The activities of AMPS sulfotransferases of whole homogenates and subcellular fractions of the liver were analyzed by the method of Suzuki and Strominger. As it is known, vitamin A influences on the AMPS sulfation, the effect of this vitamin on the enzyme activity was also examined. Desulfated chondroitin sulfate A and/or C and B were prepared for sulfate acceptors by the method of Kantor and Schubert, and [<sup>35</sup>S] 3'-phosphoadenosine-5'-phosphosulfate was used as a sulfate donor. Rats with hypervitaminosis A were given orally a daily dose of 2×10<sup>4</sup> I. U. of vitamin A acetate per 100 g of body weight for 4 days. The following results were obtained. (1) *Distribution pattern of the enzyme in healthy rat liver.* 62% of the enzyme activity in whole homogenate was found in the soluble fraction, and the specific activity per mg of protein was the highest in the microsomal fraction. (2) *Changes of the activities in the process of hepatic damage.* The activity of chondroitin sulfate (ChS) B sulfotransferase showed a remarkable increase in the liver in the 4th week of the hepatic injury and decreased thereafter. The activity in the liver with chronic hepatic injury showed higher level than that of healthy liver throughout the experimental period. The activity of ChS A and/or C sulfotransferase, also, increased in the 4th week of the experiment and maintained as high as the level of the 4th week, however, the increase was not so remarkable as seen in ChS B sulfotransferase. (3) *Effect of hypervitaminotic A on the enzyme activity.* The activity of AMPS sulfotransferase decreased significantly in the liver of hypervitaminosis A rats.