

incorporation liver ribosome and albumin biosynthesis was investigated in the operated mice. The liver protein fraction, which was soluble in 96% ethanol including 1% TCA, was extracted by Korner's procedure. The specific activity of these fraction showed biphasic peaks, the initial peak was situated between 1 and 3 hours, and the second peak between 6 and 10 hours after injection. The second peak might be the liver albumin. Although Korner described that the procedure might be the liver albumin. Although Korner described that the procedure might be the simple method of liver albumin extraction, it is still doubtful whether these ethanol fraction is purely composed of albumin or not. Therefore,  $^{14}\text{C}$ -specific activity of albumin was studied chiefly in plasma protein of the venous blood which was collected from vena cava under ether anaesthesia. Plasma protein fraction of mice, separated by cellulose acetate membrane electrophoresis, was composed of albumin in 52%, alpha-globulin in 14%, beta-globulin in 34%. In mice plasma the separation between beta- and gamma-globulin was difficult in this procedure. Albumin fraction

was slightly decreased after operation.  $^{14}\text{C}$ -specific activity of plasma protein fraction, separated by the filter paper electrophoresis, was measured by the paper strip counting method using the liquid scintillator. The composition of the scintillator was similar as mentioned in the ribosome (the counting efficiency was between 60 and 70%). It has been recognized that, the peak labelling of plasma protein was between 6 and 8 hours after injection both in albumin and globulin fraction in the control group. On the other hand the rapid increase of incorporation into globulin and the gradual increase of albumin incorporation were revealed in the early stage after operation. The meaning of the difference in the labelling speed, observed between albumin and globulin in operated mice, should be solved by the further investigation. However, it is interesting that in the durabolin-treated mice the rapid incorporation of globulin after operation was moderately suppressed and the more definite increase of albumin incorporation has been recognized in this series of our experiment.

## Studies on Protein Metabolism by RI

### II. The Albumin Metabolism in Liver Diseases

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By administering  $^{131}\text{I}$  RISA to 10 cases of the control group, 35 cases of chronic hepatitis, and 18 cases of liver cirrhosis a study was carried out on the albumin metabolism. As for the methods de scription is omitted as they were mentioned in the first report. The results of this study are briefly summarized as follows.

In contrast to the control group, in the cases of liver cirrhosis the half-life ( $T_{1/2}$ ) is prolonged to  $16.8 \pm 2.49$ ; the serum albumin concentration (SA) is decreased to  $3.58 \text{ g} \pm 0.712$  ( $P < 0.01$ ); and the total albumin contents (TEA/kg) decline to  $5.25 \text{ g} \pm 2.0$  ( $P < 0.01$ ), indicating a high direct correlation ( $r=t$ ) between SA and the amount of metabolites (Deg). In the cases of ascites of non-

compensatory liver cirrhosis, when SA is decreased to 2.98 g/dl and TEA to 2.65g/kg, there is found a mechanism working to maintain the level of SA by lowering the amount of metabolites (Deg). In the liver cirrhosis of ABA' type there is a slight tendency of the decrease in TEA to  $4.92 \text{ mg} \pm 0.74$  and Deg to  $243 \text{ mg} \pm 29.9$  and also a similar tendency can be observed in B and B' types of liver cirrhosis, but there is no significant difference between the two types.

In our study on the albumin metabolism in chronic hepatitis of various types following the type classification established by Kosaka and Ohta, there can be recognized not any appreciable differences among the control groups and among various types themselves.

However, there is observed a slight acceleration in the metabolism in IV type (precirrhosis of the liver) as Deg to be 297.5 mg/kg and TEA 5.058 g/kg. Furthermore, in those cases of acute hepatitis in early stage, i.e. within 3-4 weeks and the stage at which jaundice is present, there is revealed a decline in the albumin metabolism including the decrease of SA.

We make it a rule to administer prednisolone and 6MP for the treatment of liver disease on our clinic, and when we compare the albumin metabolism before and after the treatment we find that by the intermittent administration of 40-20 mg prednisolone the half-life ( $T_{1/2}$ ) is shortened by 10-20% while the rate of decomposition ( $\lambda$ ) is accelerated by 11.6-19%, resulting in the increase of 5-10% of Deg. With 7 cases of chronic hepatitis

and liver cirrhosis when we administer 50 mg and 75 mg of 6MP intermittently for the period over 4 weeks and compare the albumin metabolism before and after the administration, we find that the decomposition rate ( $\lambda$ ) is decreased by  $-23.9 \sim +8.9\%$ , TEA by  $-12 \sim -27\%$ , and also Deg to  $-29.2 \sim -5.5\%$ . While by 75 mg 6MP Deg is decreased by  $-5 \sim -29\%$ , by 50 mg the decrease is by  $+2.3 \sim -17.5\%$ . It is obvious from this fact that the albumin metabolism is inhibited by 6MP. However, as for the inhibition of albumin synthesis the extent of its change is distributed mostly within the range of  $\pm 2\sigma$  of the control group. There can be recognized no difference in the extent of the inhibition of the metabolism by 6MP caused by the type of disease and by the methods of intermittent administration.

## Studies on Fatty Acid Metabolism by Using $^{14}\text{C}$ Incorporation

### Report III: Pattern of Incorporation of Radioactivity into Fatty Acid from Patients in Hypelipidemia

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As a part of a series of investigations of formation of lipids by blood cells from normal and arteriosclerotic subjects, we have studied the distribution in certain major lipid fractions of fatty acids formed by white blood cells and effect of linoleate on incorporation of  $^{14}\text{C}$  acetate into lipids. Method: After 4 hours incubation at  $37^\circ\text{C}$  with  $5 \mu\text{Ci } ^{14}\text{C}$  acetate Na, lipids were extracted and separated by silicic acid column chromatography. (Hanahan). Finally, we have got fatty acids methyl esters of major lipid fractions—non-esterified, glyceride, sterol and phospholipid fatty acids due to Borgstrom, Metcalf and Hennes.

They were separated by gas liquid chromatography. Peaks were trapped separately and radioactivity was determined. In order to observe effect of linoleate on incorporation of  $^{14}\text{C}$  into lipids, two samples of 5 ml. whole blood which were obtained simultaneously, were prepared; the one was control and the

other was incubated with 5 ul. of linoleate.

Results: 1. Most cases of arteriosclerotics with hypercholesterolemia incorporated less  $^{14}\text{C}$  into fatty acids than control did, and myristic and palmitic acid synthesis was also suppressed. On the other hand, percentage of radioactivity in peaks of stearic, oleic, 20 carbons, fatty acids increased significantly, relatively. 2. Female subjects, though those serum cholesterol might demonstrate high value, incorporated more radioactivity into fatty acid and percentage of  $^{14}\text{C}$  incorporation into myristic and palmitic acid increased significantly. 3. Radioactivity in total cholesterol had a tendency to be higher in diabetics than arteriosclerotics or in control. 4. The fatty acids of neutral lipids consistently contained more radioactivity than did the phospholipids. The greatest percentage of  $^{14}\text{C}$  was usually in non-esterified fatty acid ( $50 \sim 70\%$ ). 5. The pattern of fatty acid radioactivity in each fraction was strikingly