Studies on the Metabolism of Acetone Bodies in Alloxan Diabetic Rabbits

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Previous studies from our laboratory revealed that acetone bodies eliminated into bile and the concentration of acetone bodies in bile is approximately 1.4 times higher than that in serum.

The present study was designed to clarify the fate of acetone bodies excreted into bile and the metabolism of acetone bodies with notmal and alloxan diabetic rabbits.

1. Ethyl-acetoacetate-3-^{14}C injected into the duodenum of both normal and alloxan diabetic bile fistula rabbits was absorbed from the intestine and excreted into bile. Most of ^{14}C in biliary acetone bodies of both animals were rapidly excreted within first 6 hours. Thus the evidence of the enterohepatic circulation of ^{14}C-Acetone bodies was demonstrated.

2. Acetate-1-^{14}C was administered intravenously to normal and alloxan diabetic fistula rabbits. The total ^{14}C recovered as ^{14}C-Acetone bodies in bile was 2 times greater in alloxan diabetic than in normal 24 hours after injection. Blood and bile levels of acetone bodies and radioactive acetone bodies in diabetics were much greater than in normal. The specific activities in serum and bile of normal rabbit decreased rapidly in the first 6 hours, while those of diabetics decreased slowly over 24 hours. This result indicates that the conversion of ^{14}C-Acetate to ^{14}C-Acetone bodies will be delayed markedly in diabetics.

3. Radioactive acetone bodies were kept much greater in muscle than in other tissues of alloxan diabetics 24 hours after injection of ^{14}C-Acetate. These findings indicate that acetone bodies are significantly accumulated in the muscle of alloxan diabetic rabbit.

Studies of Fatty Acid Metabolism with Incorporation of ^{14}C into Lipids of Human Whole Blood and Bone Marrow (Report 1) Normal Subjects and Patients with Aplastic Anemia

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Numerous studies of fatty acids metabolism with animals and plants. Awai and Hennes have described RI incorporation into lipids of human blood, particularly from normal Americans and patients with diabetes mellitus.

We have incubated whole blood and bone marrow from Japanese normal subjects and five patients with aplastic anemia one non-treated and four under treatment. We have followed the procedure of Awai and Adams; five ml. of whole blood and two ml. of bone marrow plus three ml. of his own blood plasma was obtained and five μc of 1-^{14}C-Acetate sodium was added to it. After four hours of shaking incubation at 37°C, lipids were extracted according to the method of Folch et al. Saponification by Bjorntorp, and methyl esterification were performed in this order.

The methyl esters were then separated by gas liquid chromatography, using a 2250 mm. 20 percent diethylen glycol succinate column. The fatty acid methyl esters in each peak were trapped by the specially prepared defatted siliconized cotten plug and the radioactivity of each fatty acid was measured by the liquid scincillation spectrometer (Shimadzu L S G-3 type).

Wakil et al. had found that fatty acid

synthesis ocurs by two separate pathways; one, the malonyl CoA pathway yields primarily palmitic, the other yields primarily 18 carbons also some longer chain fatty acids. We have therefore, analyzed the data in terms of 3 groups of fatty acids; 1) myristic and palmitic (14:0, 16:0). 2) stearic and oleic (18:0, 18:1). 3) those fatty acids with retention time corresponding to arachidic acid (20:0) or longer.

1)) In normal or iron deficiency anemia
1) 40.51~48.66% (normal Americans 36.04 ±2.45)
2) 16.97~25.18% (20.43±4.41)
3) 22.52~32.50% (39.15±6.98) are obtained from whole blood.

2)) A significant increase in radioactivity in the peak of myristic and palmitic (14:0, 16:0) (49.97%) and, on the contrary a remarkable decrease in 20:0 and longer (15.48%) are found in the case of aplastic anemia who is not treated, however, it is interresting that the group 1) is 30.05~47.39% and group 3) 39.10~27.60% in cases which are under treatment of steroid and ACTH. These are explainable by the steroid effect which appears to depress the malonyl CoA pathway more severely than mitochondrial pathway.

3)) Percentage of each group of bone marrow is different from that of whole blood in normal subjects and aslo in aplastic anemia.

To clarify this problem, more cases are to be studied later.

Body Distribution of Orally Administered ^{35}S-BTDS and ^{35}S-B_1 HCl in Rats

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S-O-Benzoyl Thiamine Disulfide (^{35}S-BTDS) and ^{35}S-B_1HCl were orally given to Wistar rats in a dose of 5mg per kg body weight, and the rats were killed 24, 48, 72, 96, 108 hours later in order to study the body distribution of the vitamines. Radioactivity was counted with GM counter in the blood, liver, kidney, intestinal content, cardiac musle, calf muscle and sciatic nerve.

Cpm per gram was then calculated in each specimen and compared with others. The following results were obtained.

Fifty to sixty % of ^{35}S-BTDS and ^{35}S-B_1HCl was excreted in the stool in 24 hours. At the 24th hour, cpm of B_1-HCl was higher than that of BTDS in the caecal content and in the wall of jejunum, whereas it was the other way around in the blood, liver, kidney, cardiac and calf muscles.

At the 72nd hour, cpm of ^{35}S-BTDS was lower than that of ^{35}S-B_1HCl in all specimens.

At the 108th hour, cpm of ^{35}S-BTDS was less than one third of the count at the 24th hour in the liver.

In the sciatic nerve, the radiation count from ^{35}S-BTDS was obtained at the 48th and 72nd hour after the administration, whereas that from ^{35}S-B_1HCl was obtained only at the 48th hour.

The followings may be speculated from the above results; The ^{35}S-BTDS adsorbed by the intestine are rather quickly carried to the liver, kidney, cardiac muscle, and to the calf muscles. After 48 hours, it will be taken even in the peripel nerve.

The radiation count in the wall of ileum, blood, and calf muscle were constant after 72 hours, while it was not before 96 hours in the liver.

The intestinal adsorption of ^{35}S-B_1HCl is less than ^{35}S-BTDS in the first 24 hours, then less amount of the former taken in the various organs, especially in the cardiac muscles in that duration.

The fact, that the residual radiation count was obtained from the wall of jejunm in all cases administered B_1-HCl, suggests the quicker transfer of BTDS into the portal circulation than B_1-HCl.