Cholesterol Metabolism in Spontaneously Hypertensive Rats

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In search of better animal models for atherosclerosis researches SHR and other normotensive rats were selected for a greater reactive hypercholesterolemia. When they were fed on hypercholesterolemic diet for only 1 week, selected SHR quickly developed hypercholesterolemia, 500–600 and 800–900 mg/100 ml in males and females, respectively. In these selected SHR not only hypercholesterolemia but also marked arterial fat depositions were noted in cerebral, mesenteric and other small arteries. Therefore, they were named "arteriolipidosis-prone rats (ALR, Yamori, 1976)" (Yamori: Jap Heart J 18: 602, 1977).

ALR have been used for analyzing various contributory factors such as hypertension, lipidemia, and genetic disposition to acute arterial fat deposition (Yamori et al: Stroke 7: 120, 1976, Clin Exp Pharmacol Physiol 3 (Suppl 3: 199, 1976). We have studied lipid metabolism in SHR and ALR and proved a marked reduction of cholesterol synthesis in the liver and some other abnormalities in lipid metabolism in ALR (Iritani et al: Atherosclerosis 28: 217, 1977). SHR, especially selected ALR show a significantly lower serum cholesterol level when they are fed on a normal protein diet and develop a marked hypercholesterolemia only when they are fed on a hypercholesterolemic diet. Therefore, hypercholesterolemia in this model is presumed to be due to the increased absorption of cholesterol and or to the decreased catabolism in the liver. In the present studies, absorption and catabolism of cholesterol were studied by using labelled cholesterol.

Materials and Methods:

Experiment 1 The time course of cholesterol absorption was determined in normotensive WK rats, 20 in total, after the peroral administration of cholesterol [4-¹⁴C] (2 µ Ci/100 Gm) and 3-month-old male ALR, SHR, and Wistar-Kyoto rats (WK), 5 rats of each strain were sacrificed 6 hours after the labelled cholesterol administration and the radioactive cholesterol in the serum and the liver was extracted and measured by a liquid scintillation counter.

Experiment 2 Five of ALR, SHR, and WK at the age of 3 months were injected cholesterol—³H (10 µ Ci/100 Gm) intraperitoneally and the decay of labelled cholesterol in the serum and the liver was determined 6, 12, 24, 36, and 48 hours after the injection.

Results and Discussion:

Experiment 1 The radioactive cholesterol in the serum as well as in the liver increased sharply up to 9 hours after the peroral administration and gradually in-

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creased from 9 to 15 hours. Therefore, ALR, SHR, and WK were sacrificed for the determination of the absorbed radioactive cholesterol in the serum and the liver. The radioactive cholesterol both in the serum and the liver was highest in ALR as compared with those in SHR and WK, although the difference was not statistically significant (see the table).

Experiment 2  The decay of radioactive cholesterol in the serum after the intraperitoneal injection of 14C-cholesterol was delayed in ALR and SHR as compared with WK (see the table). The residual radioactivity in the liver was highest in ALR among 3 strains and significantly higher in ALR than in WK until 24 hours after the injection. These data indicate there is a possible impairment of cholesterol catabolism in the liver of the ALR that have been selected for a greater reactive hypercholesterolemia. As the impairment of cholesterol catabolism is noted in old animals, ALR may be a good model for hypercholesterolemia commonly observed in aged people.

Summary:
The absorption of radioactive cholesterol tended to be increased, and the catabolism of cholesterol detected by the decay of radioactive cholesterol in the serum after the intraperitoneal injection was delayed in ALR in comparison with normotensive WK rats. The reactive hypercholesterolemia in the ALR which had been selectively bred for a greater hypercholesterolemia was ascribed to the decreased cholesterol catabolism.

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