36) Bile Acid Metabolism and Patterns in Spontaneously Hypertensive Rats. Nobuko Iritani*, Eiko Fukuda*, Yasuo Nara** and Yukio Yamori**. *Tezukayama Gakuin College, Osaka 558, **Japan Stroke Prevention Center, Department of Pathology, Shimane Medical University, Izumo 693.

INTRODUCTION

Spontaneously hypertensive rats (SHR) and stroke-prone SHR are regarded as good models for studies on hypertension and cerebrovascular diseases. In search of the better models for atherogenesis in rats, Yamori started a selective breeding of SHR which showed a greater reactive hypercholesterolemia when fed on a hypercholesterolemic diet and finally established arterio-lipidosis-prone rats (ALR) which quickly develop reactive hypercholesterolemia and arterial fat deposits in mesenteric, cerebral, renal and even coronary arteries within a few weeks (Yamori: JAP HEART J 18:602, 1977). We studied cholesterol metabolism in ALR in comparison with SHR and normotensive Wistar-Kyoto rats (WK), and clarified that intestinal cholesterol absorption was increased when labelled cholesterol was given through a stomach tube, while cholesterol catabolism determined by the disappearance of labelled cholesterol from circulating plasma was delayed (Yamori et al: JAP HEART J 20 Suppl I:349, 1979). Since cholesterol absorption and catabolism can be influenced by the amount and pattern of bile acids, we analyzed bile acid metabolism in SHR, and ALR compared with WK.

MATERIALS AND METHODS

SHR, ALR and WK at the age of 12 weeks with blood pressure 182 ± 10 , 194 ± 12 and 126 ± 9 mmHg, respectively, were used. Under Nembutal anesthesia (40mg/kg), bile ducts were cannulated for the measurement of bile flow and bile acid secretion for 24 hours and cholesterol turnover into bile acids was determined by counting the radioactivities of the bile collected for 24 hours after the intraperitoneal injection of $[4-^{14}\text{C}]$ cholesterol ($0.1 \mu\text{Ci}/100\text{g}$, New England Nuclear, Boston). During the collection of bile acids rats were restrained in cages but accessible to saline containing 10% glucose to drink ad libitum. The biliary radioactivity was extracted separately into sterols and bile acids (Iritani et al: J ATHEROSCLER RES 10:207, 1969), evaporated to dryness and dissolved in the scintillator solution for counting by a Packard Type 3385 scintillation counter. Bile acids were extracted from bile and analyzed by chromatography (Uchida, K. et al: ENDOCRINE JAPON 17:107, 1970).

RESULTS WITH DISCUSSION

Bile flow, bile acid secretion and cholesterol turnover into bile acids for the first one hour are summarized in Table. Bile flow and bile acid secretion decreased in order of WK, SHR and ALR. Bile flow remained to be significantly lower especially in ALR for the first one hour and the following 23 hours. After labelled cholesterol injection, biliary radioactivity secretion was significantly slow in ALR in comparison with WK, while the specific activities (cpm/mg cholesterol) were similar among 3 strains. As far as the composition of biliary bile acids was analyzed, cholic acid was significantly lower in ALR ($54.1 \pm 3.3\%$) than in WK ($65.2 \pm 2.8\%$). SHR showed the intermediate value ($60.0 \pm 2.7\%$) between them. Hyodeoxycholic acid was increased in order of WK ($2.7 \pm 0.5\%$), SHR ($4.9 \pm 1.2\%$) and ALR ($13.9 \pm 3.2\%$). Chenodeoxycholic acid was significantly increased in ALR ($10.6 \pm 2.2\%$) than in WK ($6.1 \pm 1.2\%$) and SHR ($4.6 \pm 1.1\%$).

These changes of bile acid pattern, especially since the ratio of cholic acid to hyodeoxycholic acid is affected by intestinal microflora, might be due to the secondary alteration of intestinal microflora. However, reduced bile flow, biliary bile acid secretion and/or cholesterol turnover to bile acids may be pathogenically related to reactive hypercholesterolemia in ALR.

	Bile volume ml/h/rat	Biliary bile acids $\mu\text{mole}/\text{h}/\text{rat}$	Bile acid radioactivity in bile	Specific activities of bile acids in bile
WK	0.86 ± 0.14	26.1 ± 7.79	2.91 ± 0.51	0.09 ± 0.03
SHR	$0.52 \pm 0.07^*$	20.7 ± 1.05	2.35 ± 1.04	0.11 ± 0.07
ALR	$0.57 \pm 0.08^*$	18.4 ± 2.96	$1.50 \pm 0.56^*$	0.08 ± 0.01

M $\pm$ SD * : Significant difference from WK ($p < 0.05$)