15) 11Beta-Hydroxysteroid Dehydrogenase Activity in the Mesenteric Arteries of Spontaneously Hypertensive Rats. Yoshiyu Takeda, Takashi Yoneda, Isamu Miyamori and Ryoyu Takeda Second Department of Internal Medicine, School of Medicine, Kanazawa University, Kanazawa 920 Japan

11Beta-hydroxysteroid dehydrogenase (11-HSD) is present in many tissues, raising the possibility that the enzyme modulates access of corticosteroids to their receptors at extra-renal sites. Funder et al reported the conversion of corticosterone (B) to 11-dehydrocorticosterone (A) in minced tissue from rat mesenteric artery and aorta. More recently, Walker et al demonstrated mRNA expression of 11-HSD in vascular and cardiac tissues. The present study was undertaken to compare the activity of 11-HSD in mesenteric arteries of spontaneously hypertensive rats (SHR) to that of Wistar Kyoto (WKY) rats. We also intend confirming the expression of 11-HSD mRNA in the vascular smooth muscle cell (VSMC).

Materials and Methods: Mesenteric arteries from 4 and 9 week-old SHRs and WKY rats were used. Under pentobarbital anesthesia, the mesenteric artery was cannulated and isolated by cutting along the intestinal borders of the mesentery. The mesenteric artery was perfused with Krebs-Ringer solution containing ^3H -B at a temperature of 37°C , and a flow rate of 4 ml/min. The pH of the perfusion fluid was maintained at 7.4 by aerating with a 95% O_2 and 5% CO_2 mixture. The 11-HSD was extracted from the perfusate using Sep-pak C18 cartridge. ^3H -B and ^3H -A were separated by a gradient mobile phase of methanol-water of HPLC at a flow rate of 1.5 ml/min. The 11-HSD activity was calculated as the percentage conversion of ^3H -B to ^3H -A. Plasma B and aldosterone concentrations were measured by RIA after extraction using a Sep-pak C18 cartridge. Total RNA from the rat vascular smooth muscle cells was prepared with selective precipitation in 3M LiCl/6M urea. The expression of mRNA of 11-HSD was done with Northern blot analysis.

Results and Comments: 11-HSD activity was significantly decreased in mesenteric arteries of both 4 and 9 week-old SHRs compared with WKY rats ($p < 0.05$). There were no significant differences of plasma B and aldosterone between in SHR and WKY rats. The expression of 11-HSD mRNA was confirmed in the rat VSMC. These results indicate that 11-HSD in vascular wall may play a role in pathogenesis of hypertension in SHR.