39) Changes in Platelet Functions due to Hypertension in The Rat VI. Comparison of Experimental Hypertension with Spontaneous Hypertension. Keizo Umegaki, Kazuki Nakamura, Takako Tomita and Eiichi Hayashi. Department of Pharmacology, Shizuoka College of Pharmaceutical Sciences, 2-2-1 Oshika, Shizuoka, Japan, 422.

Although a leading cause of death in patients with hypertension is thrombosis of coronary and cerebral arteries, the effects of hypertension on platelet function is not fully understood. We have observed that thrombin-, collagen- and ADP-induced aggregation, and thrombin-induced secretion were markedly reduced in SHRSP with the development of hypertension compared with normotensive WKY (Tomita et al. Stroke 15-1 1984). In this study, effects of experimental hypertension on platelet functions (aggregation, secretion, MDA formation and serotonin contents) were compared with those of spontaneous hypertension in the rat. Washed platelets were used throughout.

DOCA-salt hypertension was induced by injecting 15 mg/kg of DOCA twice a week into uninephrectomized male Wistar rats (150 g) and giving 1% NaCl in place of drinking water. Sham-operated control rats were given 1% NaCl for 5 week experimental period. Renal hypertension (one-clip one-kidney) was induced by clipping (0.3 mm I.D.) the left renal artery of male Wistar, following contralateral nephrectomy one week after. They were killed 7 weeks after nephrectomy. As spontaneously hypertensive rats and their control male SHR, SHRSP, and WKY at ages of 15 and 23 weeks were used in this study. Platelet aggregation, secretion, MDA formation and the content of serotonin were measured as described in the preceding papers.

The blood pressure (mm Hg, mean $\pm$ S.D.) of DOCA-salt hypertensive rats was $215 \pm 14.6(9)$ vs $151 \pm 8.12(9)$ in the control, while that of renal hypertensive rats was $190 \pm 23.1(10)$ vs $139 \pm 11.8(6)$ in the control. In DOCA-salt hypertension aggregation responses to thrombin and collagen were significantly reduced by 25 - 35 % and by 13 %, respectively, in the hypertensive group compared with the control. Serotonin release from the granules of platelets was also significantly less in the hypertensive group. In addition, MDA formation reflecting the release of arachidonic acid and the function of cyclo-oxygenase system were inhibited due to hypertension. There was a significant decrease of serotonin contents in platelets from the hypertensive group, suggesting the presence of degranulated platelets in the circulation. Analogous results were obtained with renal hypertension. Aggregation, MDA formation and serotonin contents were all significantly reduced in hypertensive groups. In spontaneously hypertensive rats at the age of 15 weeks aggregation was significantly reduced by 42 - 50 % in SHRSP compared with that of WKY but not in SHR, whereas at the age of 23 weeks, SHR platelets showed a 33 % decrease in aggregability as well as SHRSP platelets (a 55 - 75 % decrease). Despite severe hypoaggregability of SHRSP at 15 and 23 weeks, and SHR at 23 weeks there was no change in MDA formation between hypertensive rats and age-matched WKY. Additionally, the content of serotonin was not different between SHRSP and WKY at 15 weeks and between SHR and WKY at 23 weeks.

In conclusion, hypertension despite the ethiology resulted in a reduction of aggregation and secretion responses. Changes in other functions, however, differ between experimental and spontaneous hypertension in 1) that a decrease in MDA formation parallel to a reduction in aggregation was observed in experimental hypertension but there was no substantial decrease of MDA in spontaneous hypertension, and 2) that a decrease in the contents of serotonin was observed in the former but not in SHRSP at younger ages than 20 weeks. Therefore, all these results suggest that hypoaggregability observed in experimental hypertension is ascribed to the presence of exhausted platelets due to an exposure to the damaged endothelium and so forth. On the other hand, the presence of exhausted platelets is not a cause of hypoaggregability of spontaneous hypertension. Other unknown mechanism appears to be functioning.