51) Comparison of Platelet Aggregation Activities between SHRSP and WKY, with Special Reference to Aging. Hideaki Higashino, Makoto Kumode, and Aritomo Suzuki. Department of Pharmacology, Kinki University School of Medicine, Osaka-fu 589.

Tomita and Yamori et al. have reported that the platelets of SHR and/or SHRSP showed the lower aggregation activities than WKY platelets, which they assume would be due to the extreme consequences of hypertension developed with age. Although much effort has been made by many workers to clarify the physicochemical changes in SHR and/or SHRSP platelets, the defective role of platelet has not yet been satisfactorily explained. For some years we have been exploring the physiological differences of platelets between SHRSP and WKY, we reexamined the platelet aggregation activity using several aggregation reagents of different type.

The age-matched male SHRSP and normotensive WKY of 2- to 12-months old, being bred in our laboratory, were subjected to this experiment. Platelet rich plasma (PRP) and washed platelet, suspended in Hepes buffer containing 1mM CaCl_2 , each consisting of 2.5×10^5 platelet/ $\mu\text{l} \times 200 \mu\text{l}$, were used for measurement of platelet aggregation activity by means of an aggregometer (NKK hema tracer 1). Maximal light transmittance (600nm) at 5 min after addition of aggregation reagents such as ADP (1, 3 and $10 \mu\text{M}$), collagen (10, 30 and $50 \mu\text{g/ml}$), thrombin (0.1, 0.3 and 1.0U/ml), arachidonic acid (0.1, 0.3 and 1.0mM), A23187 (1, 3 and $10 \mu\text{M}$), and TPA (1, 3 and 10nM) indicated the aggregation activity, and values obtained were compared between two rat groups.

ADP-induced aggregation activities in WKY PRP were not changed from 2 to 12 months old, being sustained during this period. On the other hand, these activities in the SHRSP platelets tended to be less even at 2 months old, and when examined at three different concentrations of ADP significantly lower values were obtained with SHRSP of which age was older than 4 months after birth. The similar results were obtained with the washed platelet samples of SHRSP and WKY. Collagen-induced aggregation activities also showed the same results with ADP-induced ones. Thrombin-induced aggregation activities of SHRSP washed platelets from 2 to 10 months old decreased significantly as those compared with age-matched WKY. Arachidonic acid-induced aggregation activities of washed platelets showed no significant difference between SHRSP and WKY aged from 2 to 10 months. A23187-induced aggregation activities of washed platelets showed lower tendency in SHRSP compared with those of WKY, but there was no significant difference between two rat groups aged from 2 to 10 months. TPA-induced aggregation activities of washed platelets showed no significant difference between SHRSP and WKY aged 2 to 10 months.

From these results, the following conclusions were obtained. 1) Intracellular aggregation pathways involved in arachidonic acid metabolism, C-kinase system and free calcium ion utilization were rigid in both SHRSP and WKY. 2) We thought it likely that both phospholipase A_2 and C activities might be almost unchanged, as reported by Tomita et al.. 3) Receptor mediated aggregation assigned to SHRSP platelet even at younger ages may occur to the lesser extent compared with WKY platelet.

Taken together, on the plasma membrane levels some unknown defects present in SHRSP platelets may interfere the receptor mediated signals on the way to the intracellular second messengers, which may play etiologic roles in developing hypertensive state.