1) Age-related Changes in Platelet Aggregation Activity and Some Drug Modification on Platelet Function. Makoto Kumode, Hideaki Higashino, and Aritomo Suzuki. Department of Pharmacology, Kinki University School of Medicine, Osaka-fu 589.

The blood platelet which is necessary for clot formation is known to keep vascular endothelium healthy and act as the sealing of injured vessels. In these regards, it is interesting to study the relationship between thrombosis and secondary apoplexy which is most likely to occur in hypertension. We have focused on the age-related changes in platelet aggregation activities in SHRSP and compared with those of WKY, and examined the properties of platelet, using the agents which inhibit platelet aggregation such as Aspirin and ONO-3144 (a TXA synthetase inhibitor and hydroperoxidase stimulator: 2-amino-methyl-4-tert-buty1-6-protonylphenol hydrochloride).

The age-matched male SHRSP and normotensive WKY of 2-to 12-months old being bred in our laboratory were used for the experiment of age-related platelet aggregation (n=8-10). Aspirin (30mg/kg/day) was mixed with powdered chow to administer orally to age-adjusted female SHRSP for 1, 2, 4 and 16 weeks respectively until they were 10 months old (n=3-4). ONO-3144 at the doses of 10, 20, 40mg/kg/day was administered to the 2 month old male SHRSP (n=8) for 4-5 months. Under anesthetized by pentobarbital, the whole blood was drawn by plastic syringes with plastic needle in cardiocentesis and platelet rich plasma (PRP) and platelet poor plasma (PPP) were separated. The activities of platelet aggregation induced by various amounts of ADP (Sigma, 0.3-10uM) and collagen (Norm, 10-100ug/ml) were determine by measuring the initial velocity and maximum aggregation rate in 2.5x10^7/mm^3 platelets using a aggregation meter (Niko Bioscience). The platelet count was measured by Coulter Counter.

Aging Effect: The ADP-mediated aggregation activity was lower in SHRSP than WKY even at 2 months old and the differences in value at 6 and 12 months old were larger. It was found that the aggregation activity had age-dependently low or lower tendency in both rat groups. The decreasing activities of collagen-mediated were not found in 2, 6, 12 month old WKY and 2, 6 month old SHRSP, which didn't refer to any significant difference between groups. However, 12 month old SHRSP showed apparently lower activities. The higher platelet count was noted in 2 month old SHRSP compared with the age-matched WKY, but in 6 and 12 month old SHRSP the opposite results were obtained.

The effect of Aspirin: Both ADP- and collagen-mediated aggregation activities were lowered in 1-2 weeks after administration of Aspirin (30mg/kg/day). However, longer administration periods of 4-16 weeks made the results reversed. And, the collagen-mediated effects were more marked than the ADP-mediated ones. Regardless of how long the agent was given, platelet count was always higher in Aspirin treated rats than in non-treated ones, and this difference was most marked in the rats given for 4 weeks.

The effect of ONO-3144: With administration of ONO-3144 (40mg/kg/day) for 4-5 months, there was no difference in ADP-mediated aggregation activity, but in collagen-mediated one the initial velocity of the treated groups was found higher in value than that of the non-treated ones. The decrease in platelet count with age was apparently kept minimum with this agent.

From these results, it is considered that the decrease in platelet count and the lowered aggregation activity found in older SHRSP might be due to the accelerated consumption of the intact platelet, and under such condition, the effects of these agents such as Aspirin or ONO-3144 on platelet function appear to be exerted in association with some circulatory systems, which might lead to the prevention of the occurrence of apoplexy.