Chronic Nitric Oxide Synthesis Inhibition Developed Stroke in Normotensive Wistar Kyoto Rats. IKEDA.K*, GU.D+, NARA.Y*+, TAGAMI.M** and YAMORI.Y. Shimane Institute of Health Science*, Department of Pathology Shimane Medical University+, Izumo 693, SANRAKU Hospital**, Tokyo and Graduated School of Human and Environmental Studies, Kyoto University, Kyoto JAPAN

Introduction In our previous report, we observed chronic inhibition of nitric oxide(NO) synthesis induced hypertension in normotensive Wistar Kyoto rats(WKY). To observe the detailed effect of hypertension, a risk factor for stroke, on cerebral vascular system in this hypertension model, NO synthesis was chronically inhibited in WKY through life.

Materials and Methods 1). Twenty WKYs at 10 weeks of age were given 0.023%(w/w) NG-nitro-arginine(L-NNA), a nitric oxide synthesis inhibitor, in a commercial (Funabashi SP) diet to observe blood pressure by a photoelectric cscillometric tail cuff method (UR-1000 UEDA Japan) and pathology. Twenty age-matched WKYs on the plain SP diets were used as the control. 2). Platelet aggregation was examined on the first and 28th days of L-NNA diet feeding in another set of the experiment using 15 male WKYs at 10 weeks of age. Blood was collected from inferior vena cava into a syring containing sodium citrate, and platelet rich and platelet poor-plasmas were separated by centrifugation at 1100rpm for 10 minutes and at 3000rpm for 10 minutes. Platelet numbers were counted by a Coulter counter (Coulter U. S. A), to adjust the platelet number. Platelet aggregation in response to 2.5 uM adenosine diphosphate was measured with a NKK HEMA TRACER(Nikko Bioscience Japan).

Results WKYs fed on L-NNA containing diet developed severe hypertension and died from 126 to 241 days of age(mean life span $\pm$ SE: 174 ± 8 days, n=20). Cerebral ischemic and hemorrhagic infarctions were observed in WKY given L-NNA without exception(20/20) while no control died during the experimental period. Contracted kidneys were observed macroscopically and renal vascular complications of malignant hypertension were confirmed. Platelet aggregation was not accelerated on the first and 28th days of the feedings of L-NNA containing diet.

Conclusion Our results clearly showed that the chronic inhibition of NO synthesis by L-NNA in normotensive WKY induced severe hypertension, nephrosclerosis and stroke. We could establish a new stroke model from normotensive WKY by the chronic dietary inhibition of nitric oxide synthesis that would hopefully contribute to our understanding of stroke mechanism mainly due to thrombosis caused by the impairment of local NO synthesis.