Decreases in substance P and vasoactive intestinal peptide (VIP) concentrations in plasma of SHRSP. Kazuo Mori*, Shunji Asakura*, Norifumi Morikawa*, Masaharu Takeyama*, Hiroshi Ogawa**, Sukenari Sasagawa**. *Department of Clinical Pharmacy, Oita Medical University, Hasama-machi, Oita 879-55 Japan. **Department of Hygiene, Kinki University School of Medicine, Osaka-fu 589 Japan.

INTRODUCTION It is well known that vasomotor tone is mainly regulated by sympathetic vasoconstrictor. While, some peptide-containing non-adrenergic non-cholinergic nervous systems are considered to be involved in the regulation of vasomotor tone. The neuropeptides, substance P (SP) and vasoactive intestinal peptide (VIP) are widely distributed in the central and peripheral nervous system. SP and VIP are generated and contained in neural cell bodies, and perhaps released from the nerve endings. In the peripheral nervous system, SP- and VIP-immunoreactive nerves are found in connection with blood vessels in an innervation-like pattern. SP and VIP directly induce marked vasodilation, and they are considered to participate in the regulation of blood pressure. However, the precise roles of peripheral SP- and VIP-immunoreactive nerves in the regulation of vasomotor tone are still unclear. In the present study, the SP and VIP concentrations in plasma of stroke-prone spontaneously hypertensive rats (SHRSP) and Wistar-Kyoto rats (WKY) were measured, in order to study the alterations of the activities of SP- and VIP-immunoreactive nerves in the hypertensive state.

METHODS For hypertensive animals, male SHRSP (n=61) at the ages of 8, 12, 18, 28, 30, 35 and 48 weeks were used. For normotensive control animals, male WKY (n=58) at the ages of 8, 12, 18, 28, 30, 35 and 48 weeks were used. The animals were classified into young (8 weeks), adult (12, 18 weeks), prime (28, 30 weeks) and elder (35, 48 weeks) groups. Blood samples were obtained after overnight fasting, and 500 KIU/ml aprotinin and 1.2 mg/ml EDTA were immediately added. The plasma SP and VIP concentrations were measured using ELAs established by us.

RESULTS The mean SP concentrations of SHRSP and WKY were 4.9±1.2 fmol/ml and 6.6±1.9 fmol/ml, respectively. The value of SHRSP was significantly lower than that of WKY (P<0.01). The mean SP concentrations of young, adult, prime and elder SHRSP were 6.4±0.6 fmol/ml, 4.9±0.8 fmol/ml, 4.7±1.2 fmol/ml and 4.6±1.4 fmol/ml, respectively. The mean SP concentrations of young, adult, prime and elder WKY were 7.4±0.9 fmol/ml, 6.7±2.1 fmol/ml, 6.5±2.3 fmol/ml and 6.2±1.4 fmol/ml, respectively. The mean VIP concentrations of SHRSP and WKY were 0.80±0.25 fmol/ml and 1.01±0.32 fmol/ml, respectively. The value of SHRSP was significantly lower than that of WKY (P<0.01). The mean VIP concentrations of young, adult, prime and elder SHRSP were 0.82±0.13 fmol/ml, 0.77±0.17 fmol/ml, 0.78±0.21 fmol/ml and 0.85±0.35 fmol/ml, respectively. The mean VIP concentrations of young, adult, prime and elder WKY were 1.09±0.27 fmol/ml, 1.06±0.33 fmol/ml, 1.03±0.32 fmol/ml and 0.90±0.32 fmol/ml, respectively.

DISCUSSION The decreases in the plasma SP and VIP concentrations of SHRSP were revealed in the present study. Hypertensive state of SHR was reported to be due to the elevation of vascular resistance. Vascular resistance is considered to be modulated by the central and peripheral nervous system. SP- and VIP-immunoreactive cell bodies are variously found in the central nervous system, and some of them are considered to excite the sympathetic preganglionic neuron. However, it is difficult to consider that the alterations of SP and VIP levels in the central nervous system directly result in the fluctuations of the SP and VIP concentrations in circulating blood. The concentrations of these neuropeptides in circulating blood may depend on the peripheral releases of them from the nerve endings. Therefore, the significant decreases in the plasma SP and VIP concentrations of SHRSP were assumed to be due to the decreases in the peripheral releases of SP and VIP from the endings of peripheral SP- and VIP-immunoreactive nerves. The functional involutions of peripheral SP- and VIP-immunoreactive nerves of SHRSP were suggested in the present study. Whether the functional involutions of SP- and VIP-immunoreactive nerves of SHRSP were the causes or the results of hypertension was still unclear. Additionally, the age-related involutions of SP-immunoreactive nerves of SHRSP were suggested. The plasma VIP concentrations of SHRSP and WKY were not affected by aging. The alterations of central SP and VIP levels of SHRSP can not be explained from the present study, although central SP and VIP may indirectly affect the regulation of vasomotor tone.