62) Spontaneous Increase of Intracellular Ca^{2+} Level and Associated Active Tone in Aorta from Spontaneously Hypertensive Rats. Fumiko Sasaki, Kyoko Kaneko*, Kazuo Yamamoto*, Keiichi Shimamura* and Satoru Sunano. Faculty of Pharmaceutical Sciences, Kinki University, Higashi-Osaka 577 and *Research Institute of Hypertension, Kinki University, Osaka-Sayama 589.

Arterial smooth muscles of normotensive rat are quiescent and show no active tension unless they are stimulated. On the other hand, arterial smooth muscles of hypertensive rats exhibit spontaneous tension development (intrinsic active tone) in the absence of stimulations. The intrinsic active tone is extracellular Ca^{2+} dependent and can be blocked by the removal of extracellular Ca^{2+} or by the application of Ca-antagonists. The present study was performed to investigate the relation between the active tone and the degree of hypertension using various strains of spontaneously hypertensive rats. Level of intracellular free Ca^{2+} of aortic smooth muscle was also studied.

[Methods] Spontaneously hypertensive rats (SHR), stroke-prone SHR (SHRSP), malignant SHRSP (M-SHRSP) and control normotensive Wistar Kyoto rats (WKY) were used in the present experiment. SHR, SHRSP and WKY were sacrificed at the age of 16 weeks. Since M-SHRSP showed a high rate of stroke incidence already at 16 weeks of age, they were sacrificed at the age of 12 weeks. Ring preparations of 1 mm width were made from thoracic aorta of these rats. Endothelium was removed by rubbing the inner surface of the lumen with thin soft rubber band. The tension changes of the preparations were measured isometrically by a force-displacement transducer. Change in cytosolic Ca^{2+} level was observed by Fura-2 method.

[Results] The blood pressure of the animals used in the present experiments was higher in the following order: WKY<SHR<SHRSP<M-SHRSP.

Aortas of spontaneously hypertensive rats exhibited a spontaneously active tone even in the absence of stimulants and responded to the removal of extracellular Ca^{2+} showing a relaxation. The relaxation was greater in the order of preparations from SHR, SHRSP and M-SHRSP. The preparation from WKY, on the other hand, exhibited no relaxing response to the removal of extracellular Ca^{2+} . Thus, it was revealed that the active tone increased as the blood pressure of the animals increased, and a good correlation between these two parameters was demonstrated.

The removal of extracellular Ca^{2+} in the absence of stimulants induced decrease in intracellular Ca^{2+} level in the preparations from these rats. The decrease of intracellular Ca^{2+} level by the removal of extracellular Ca^{2+} was greater in the following order: WKY<SHR<SHRSP<M-SHRSP. The result indicates that the intracellular Ca^{2+} level under non-stimulated condition is elevated as the blood pressure of the rats increased and these two parameters are also in a good correlation.

[Discussion] The elevation of the active tone in aorta from spontaneously hypertensive rats was associated by the increase in intracellular Ca^{2+} level. The elevation in intracellular Ca^{2+} level is thought to be brought about by an influx of Ca^{2+} through voltage-dependent Ca channels, since it was blocked by the removal of extracellular Ca^{2+} and by the application of Ca-antagonist. It was also revealed that both the active tone and the level of the intracellular Ca^{2+} were elevated as the blood pressure of the rat increased, and a good correlation between blood pressure and the degree of these parameters was demonstrated. It can therefore be considered that the opening of the voltage-dependent Ca^{2+} channels is enhanced in the aortic smooth muscle from hypertensive rats depending on the degree of hypertension, and this is the cause of the development of the active tone.