11) Lower scavenge ability for free radicals in SHR myocardium. Mikinori Torii, Hiroyuki Ito and Tsuneyuki Suzuki. 1st Department of Pathology, Kinki University School of Medicine, Osaka-fu 589.

We have previously reported the membrane abnormalities in SHR myocardium such as enzyme abnormalities, increase of the membrane permeability, and enhancement of lipid peroxidation following doxorubicin administration. In order to elucidate the causative factors behind the proness of myocardial lipid peroxidation by the various oxidative stress, we examined the age-related changes of free radical scavengers such as superoxide dismutase (SOD), glutathione peroxidase (GSH-PX) and α -tocopherol in SHR myocardium in comparison with normotensive Wistar-Kyoto rat and further examined the SOD activity after doxorubicin administration.

Male SHR and age-matched WKY were used at young and mature age. After sacrificing rats under ether anesthesia. Hearts were thoroughly cleaned of blood in Krebs-Henseleit buffer (pH 7.5). Left ventricle and septa were used for various scavenger assays as follows. 1) Tocopherol was extracted with n-hexan after homogenization and was assayed by the method of Abe et al. 2) After homogenization in 0.25 M sucrose-10 mM Tris-HCl buffer (pH 7.5), the homogenate was centrifuged at 1,000 Xg for 10 min. and then 10,000 Xg for 10 min. Using the final supernatant, GSH-PX was assayed by modified Whanger's method. 3) The mitochondrial rich fraction and soluble fraction were collected from same homogenate as described before (Jpn Circ J. 56:688, 1990). SOD activity was assayed colorimetrically for each fraction by the nitrite method of Oyanagui (Anal. Biochem. 142:290, 1984). 4) Twenty mg/kg of doxorubicin was given intravenously to 24-week-old SHR and age-matched WKY and both mitochondria and cytosol SOD were also assayed as described above at the 4th day after administration.

α -tocopherol was significantly lower in both 6- and 16-week-old SHR than that in age-matched WKY and was also significantly lower in both strains at 16 weeks of age than it had been at 6 weeks of age ($P<0.01$). In normotensive WKY, GSH-PX was significantly higher at 16 weeks than at 6 weeks of age ($P<0.01$). However, SHR showed significantly lower activity at 16 weeks than at 6 weeks of age ($P<0.01$). GSH-PX activity was higher in 6-week-old SHR, but it was lower in 16-week-old SHR than those in age-matched WKY. Most of mitochondrial SOD was Mn-SOD and it was significantly higher in 4-week-old SHR than that in age-matched WKY ($P<0.01$), but no significant difference was found between SHR and WKY at 24 weeks of age. On the contrary, most of cytosol SOD was Cu, Zn-SOD and it was significantly lower in SHR than that in WKY at both 4 and 24 weeks of age ($P<0.01$). At the 4th day after doxorubicin administration, no significant difference was found in between mitochondrial SOD in treated-WKY and control WKY, whereas it was lower in treated-SHR compared to control SHR. Thereby it was significantly lower in treated-SHR than that in treated-WKY ($P<0.01$). Cytosol SOD was significantly higher in treated-WKY compared to control WKY ($P<0.01$), showing the possible protective response for free radical. However, no significant difference was found between treated SHR and control SHR, thereby SOD in treated-SHR was lower in comparison with that in treated-WKY.

In comparison with WKY, SHR myocardium showed lower level of SOD, α -tocopherol and GSH-PX even in prehypertensive stage. These results indicate the lower scavenge ability for free radicals may relate to membrane fragility via lipid peroxidation in SHR myocardium.