8) Fluctuation of Lipid Peroxides and Related Enzyme Activities accompanying the Development of Stroke in Stroke-Prone Spontaneously Hypertensive Rats. Isao Tomita, Mitsuaki Sano, Kunio Ohta, Masaru Kikuchi and Kazuo Shinji. Shizuoka College of Pharmaceutical Sciences, Shizuoka (422).

We have reported in previous papers that the levels of lipid peroxides (determined as thiobarbituric acid reactive substances, TBARS) increased in the brain and serum of SHRSP with advancing age and markedly with the development of the stroke. The activities of glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) were concomitantly changed. In the present study, TBARS and the enzyme activities were monitored daily for about 24 to 30 days in the blood from 35 male SHRSPs which were given 1% NaCl in drinking fluid ad libitum to induce stroke in a shorter period of time.

Experimentals :

SHRSPs were kindly provided by Dr. K. Okamoto of Kinki University and raised in our laboratory. Each of the rats was kept in a metabolic cage and given a CE-2 powder diet (Japan Clea) and 1% NaCl ad libitum during the experimental period. Most rats developed stroke symptoms within 2 to 3 weeks after the start of the experiment. The samples of blood (0.1ml) were taken from the tail artery daily or every other day starting one week after the NaCl loading. TBARS and GSH-Px activities were determined as described in the previous paper (I. Tomita et al. : *Igaku no Ayumi* 107:518, 1978) and SOD activity according to the method of T. Imanari et al. (*Igaku no Ayumi* 101: 496, 1977).

Results and Discussion :

The earliest development of the stroke was observed as early as 9 days after the loading of 1% NaCl and 63% of the rats used suffered from the stroke by the end of the experimental period. Until 2 days before the onset of the stroke, the TBARS levels of most of the rats (86.4%), which later developed the stroke symptoms, remained almost constant (6.10 ± 1.64 n moles of malon aldehyde/ml blood) and were not significantly different from those developed no symptom. A marked increase of TBARS levels, however, were observed immediately before and after the development of the stroke [8.01 ± 2.15 (14 rats) at -1 day, 9.42 ± 2.73 (13 rats) at 0 day, 10.92 ± 2.82 (13 rats) at 1 day, 12.07 ± 4.00 (24 rats) at 2~3 days after the stroke]. It must be noted that TBARS levels in some animals (13.6% of the all) began to increase for the first time on the 2nd day after the development of the stroke symptoms. Accompanying the sharp increase of TBARS levels in SHRSP after the stroke, the activities of GSH-Px and SOD decreased significantly after the symptoms and the activities were not restored to the original level afterwards. In order to analyze the relationship between the changes of TBARS, the enzyme activities and the stroke, 15 animals which developed the stroke symptoms were divided into 2 groups, A and B; A is the group of 7 rats which survived more than 8 days and B that of 8 rats which died within 8 days after the development of symptoms. While TBARS levels of group A were not significantly different from those of group B, the activity of GSH-Px ($8.22 \pm 1.21 \times 10^3$ units/ml blood) in group A was significantly ($P < 0.02$) different from that of group B ($6.77 \pm 0.68 \times 10^3$ units/ml blood) in the immediate examination after the stroke. SOD activities of group A ($20.08 \pm 4.67 \times 10^2$ units and $17.79 \pm 4.81 \times 10^2$ units/ml blood, 1 and 2 to 3 days after the stroke respectively) were significantly ($P < 0.05$) different from those of group B ($15.35 \pm 2.41 \times 10^2$ units and $13.27 \pm 2.64 \times 10^2$ units/ml blood 1 and 2 to 3 days after the stroke respectively). The GSH-Px activity of group B, however, was significantly ($P < 0.01$) higher than that of group A at least 2~5 days before the onset of stroke. The sharp decrease of GSH-Px activity of group B might result in the death of rats due to the accumulation of lipid peroxides. The examination of TBARS levels in liver, brain, kidney, spleen, heart, lung and pancreas from SHRSPs revealed that TBARS levels in the liver from NaCl loaded rats with the stroke lesion were significantly ($P < 0.01$) higher (216.94 ± 30.49 n moles of malon aldehyde/g tissue, 5 rats) than those from NaCl loaded healthy rats (147.80 ± 16.54 , 4 rats). TBARS levels in the brain from the rats with the stroke were also higher than those without stroke lesion though they were not significant.

* ; Mean $\pm$ SD