23) The Contents of Urinary and Plasma Catecholamine Conjugate in SHR and SHRSP. *Shunichi Maemura, Masami Niwa, and Masayori Ozaki. 2nd Department of Pharmacology, School of Medicine, Nagasaki University, Nagasaki 852, *Tsumura Research Institute for Pharmacology, Ibaragi 300-11.

INTRODUCTION A considerable proportion of catecholamines in plasma and urine is conjugated as sulfates or glucuronates, but the role of these conjugates has never been clarified. The main urinary and plasma catecholamine conjugates of rats have been considered to be glucuronates. We previously reported a new method of measuring catecholamine glucuronates by enzymatic hydrolysis. In this report we measured the contents of free and conjugated catecholamines in rat urine and plasma and compared them with Wistar-Kyoto strain (WKY), spontaneously hypertensive rat strain (SHR), and SHR-stroke prone strain (SHRSP).

METHODS Rats were housed in glass metabolic cages for 24 hours and urine was collected in glass bottles containing 0.4 N PCA with antioxidants. Blood samples were collected during normal daily activities by inserting a catheter in the jugular vein for an extended period of time. Free catecholamine contents were measured by HPLC with electrochemical detection. Conjugated catecholamines were hydrolyzed by partially purified β -glucuronidase from the preputial glands of female rats. After an incubation period of 18 hours at 37° C total catecholamine contents were measured similarly.

RESULTS and DISCUSSION In urine, at every age measured (4, 10, 15, and 25 weeks of age) and in any strains, 80-90 % of dopamine (DA), about a third of both norepinephrine (NE) and epinephrine (E) were glucuronide conjugates.

In hypertensive stage (10, 15, and 25 weeks of age), the urinary excretion levels of both free and conjugated NE were higher in hypertensive rat strains (SHR and SHRSP) than WKY. Especially at 25 weeks of age these differences were distinct.

At every age measured, the urinary excretion levels of free E in SHR were significantly higher than those in both WKY and SHRSP. Similarly, at 4 and 10 weeks of age, the levels of conjugated E in SHR were significantly higher than those in both WKY and SHRSP. However, the levels of conjugated E in SHRSP after the development of hypertension, increased and were significantly higher than those in both WKY and SHR. These results suggest that in SHRSP the facilitation of the activity of adrenal medulla occurred after the development of hypertension, supporting our previous observation (Jpn. Heart J., 23, 593-602). As a result of the increase of conjugated E content in SHRSP the levels of conjugated E in three rat strains were correlative to their blood pressure, seen at 15 and 25 weeks of age. These correlations were observed also between the levels of conjugated NE and the blood pressure. Between the 10 weeks and 15 weeks period the hypertensive rat strains developed hypertension. Therefore, the levels of conjugated NE and E may be correlative with maintenance of hypertension.

At the hypertensive stage, the levels of free DA in the hypertensive rat strains were slightly higher than WKY. However, there was not a significant difference in conjugated DA between these hypertensive rat strains and WKY.

In plasma, almost all of DA, about a half of NE, and about a third of E were glucuronide conjugate. At 25-40 weeks of age, plasma levels of both free and conjugated NE were significantly higher in SHRSP than those in both WKY and SHR.