32) Testosterone regulates the mechanisms of hypertensinogenesis. Yoshiko Masubuchi, Toshio Kumai, Taiichiro Ohno and Masanao Hirai. Department of Pharmacology, St. Marianna University School of Medicine, Kawasaki, Kanagawa 213

Dimorphism of spontaneous hypertension and gonadectomy inhibited the onset and maintenance of spontaneous hypertension in both male and female SHR have been reported previously. We have also found that pressure response to exogenous nor-epinephrine (NE) was sensitized by gonadectomy in Wistar Kyoto normotensive rat (WKY) and the effect can be reversed by testosterone treatment suggesting the hormonal factor modulate NE ontogeny in sympathetic synaps and indicate the pre-synaptic up regulation of androgen and postsynaptic sensitization of estrogen. It seemed feasible to consider also that endogenous androgen could modulate blood pressure by regulating the release of NE at the level of sympathetic synaps.

Male and female SHR originated from WKY were kept in our Research Animal Bulding where temperature ($23 \pm 1^\circ\text{C}$), humidity ($55 \pm 5\%$) and lighting (06:00~18:00) were controlled for 24 hours, and supplied with water and regular commercial rat chow (CLEA-CE-2) which has a regulating low fat content (less than 3.8%) ad libitum. In the first experiment, SHR were castrated at 5 weeks old (W) and testosterone (T, $500 \mu\text{g}/\text{rat}$ in oil, s.c.) was given twice in a week from 15 W of those rats. The blood pressure (BP) was measured from 4 W to 28 W by tail-cuff technique in concious rats. In male, BP of intact rat (no-castrated Int.) was $112.8 \pm 3.16 \text{ mmHg}$ at 5 W and the BP was increased with aging ($186.3 \pm 3.33 \text{ mmHg}$ at 28 W). There was no significant difference between Int. and Int.+T in BP, but the BP of castrated rat (Cast.) was significantly increased from 8 to 28 weeks after the treatment of T as compared with Cast. only. In female, BP of Int. was $118.2 \pm 3.54 \text{ mmHg}$ at 5 W and the BP was increased with aging ($156.9 \pm 2.45 \text{ mmHg}$ at 28 W). The BP was significantly increased by the treatment of T in both Int. (from 8 to 13 weeks after T) and Cast. (from 4 to 13 weeks after T) rat as compared to Int. or Cast., respectively (Int.+T>Int., Cast.+T>Cast.), and further, the BP of Cast.+T was significantly enhanced over that of Int. at 13 weeks (28W) after the T (Cast.+T>Int.). In the second experiment, SHR were castrated at 5 W and during treatment of T as above mentioned, prazosin $30 \mu\text{g}/\text{kg}$, i.p. or captopril $5 \text{ mg}/\text{kg}$, i.p. was given at 25~32 W, 33~34 W, respectively. Prazosin significantly lowered the BP in male and female Int., Cast., Int.+T and Cast.+T as compared to those of non-treated each groups, respectively. Captopril significantly lowered the BP in male and female Int. and Int.+T and in female Cast. and Cast.+T, however didn't change it in male Cast. and Cast.+T. There is limited information on the interrelationships of sympathetic nervous system activity and renin-angiotensin system with BP reduction during gonadal hormone effect or gonadectomy. The autonomic nervous system has important function in the hemodynamic and hormonal adaptation of BP to sexual behavior. Thus, the reduction in BP associated with gonadectomy may result from at least two effects of catecholamines through gonadal hormone activated: a direct effect on vascular adrenergic receptors, and a decrease in the production of angiotensin II. The effect of estrogen on BP appears to be different in the male from that in the female rat. It should be noted that testosterone act on pre-synaptic membranes to release of NE and estradiol act on the catecholamine receptor of post-synaptic membrane to stimulate the sensitivity to catecholamines.

Present result demonstrate that actions of antihypertensive drugs involment in reduction on hypertensive BP disappear coincident with the removal of gonadal organs, such as captopril in male Cast. and Cast.+T, and further unusual drop in BP of prazosin was induced by the castration. These results indicates that androgen play of indispensable role in the ethiology of spontaneous hypertension in SHR and raise the possibility that mechanisms of action of α_1 -blocker and angiotensin converting enzyme inhibitor was involved in mediating the regulatory influence of androgen.