Salt Sensitivity and Insulin Resistance in Spontaneously Hypertensive Rats
Toshiaki Sato¹, Yasuo Nara², Yuzuru Kato¹, Yukio Yamori³, Department of Internal Medicine¹, Shimane Medical University, Izumo 693, and Otsuka Department of International Nutritional Medicine², Graduate School of Human and Environmental Studies³, Kyoto University, Kyoto 606, Japan

Introduction: Substantial epidemiologic evidence has indirectly implicated sodium intake in the pathogenesis of hypertension. Insulin resistance has been postulated to be responsible for enhanced sodium retention; therefore, insulin resistance may be critical to the pathogenesis of salt-sensitivity in individuals with hypertension. The aim of this study was to elucidate the effects of salt-loading and high calorie sucrose enriched diet (HD) on blood pressure (BP), insulin resistance and renal sodium handling in both SHR and normotensive control rats (WKY).

Methods: Male SHR and WKY were divided into four groups. The first group of rats were fed normal diet (ND) with tap water. Second group of rats were fed ND with 1 % sodium chloride. Third group of rats were fed HD with tap water. The last group of rats were fed HD with 1 % sodium chloride. After 8-week of experimental period, oral glucose tolerance test and insulin suppression test were performed. During the last 2 days, these rats were individually housed in metabolic cages. The consumption of diet for 24 hours were recorded and 24-hour urine samples were collected to estimate the renal sodium handling.

Results: Body weight (BW) in both strains was increased by HD, whereas BW was not affected by salt-loading. BP was consistently higher in SHR than in WKY. BP in SHR was elevated by both HD and salt-loading. Moreover, the BP in HD fed SHR was more elevated by salt-loading. In contrast, BP in WKY was not affected by HD or salt-loading. In normal diet groups, both integrated glucose, insulin levels and steady state glucose levels were higher in SHR than in WKY. In both strains, these values were much increased in HD groups than in ND groups. Moreover, HD resulted in more impaired glucose tolerance and insulin resistance in SHR than in WKY. Salt-loading alone did not affect glucose intolerance and insulin resistance in both strain. However, salt-loading more aggravated the glucose intolerance and insulin resistance in HD fed SHR, but not in WKY. Urinary sodium excretion rate in SHR was decreased by HD, whereas that in WKY was not affected by HD. Sodium balance in SHR was much more increased by HD, whereas that in WKY was not affected. Sodium retention induced by HD was found in only SHR. Salt-loading increased sodium balance despite increased urinary sodium excretion rate in SHR. Moreover, salt-loading more increased sodium retention in HD fed SHR, but not in same treated WKY.

Discussion: Insulin resistance in SHR was not so much greater than that in WKY. Sodium retention induced by salt-loading was not found in HD fed WKY, of which insulin resistance was almost same as that in SHR. Therefore, these findings in the present study suggest that slight insulin resistance such as SHR might not be the main metabolic link responsible for salt sensitivity in SHR. Salt-loading also more elevated BP in HD fed SHR, of which insulin resistance was more severe than that in ND fed SHR. In this situation, insulin resistance results in sodium retention, leading to plasma volume expansion and BP elevation. These findings indicate that insulin resistance may be involved in salt sensitivity in hypertension under HD condition.