reflected increased phospholipase A2 activity and alternations in the availability of renal fatty acids might be related to increased prostaglandin biosynthesis in SHR.

-92-  RENAL KIDNEY FATTY ACID BINDING PROTEIN INCREASED BINDING ACTIVITY IN SPONTANEOUSLY HYPERTENSIVE RATS-

Satohi Fujii, Hiroshi Okamoto, Hideaki Kawaguchi, Hisakazu Yasuda
Department of Cardiovascular Medicine, Hokkaido University School of Medicine

To clarify the mechanism of increased renal prostaglandins (PGs) synthesis in spontaneously hypertensive rats (SHR), fatty acid binding protein (FABP), which is abundantly present in rat liver and intestine and involved in the uptake and transport of fatty acids, was purified from rat kidney and its binding activity for arachidonic acid (AA), the major substrate for PGs, was measured. This protein was purified 21-fold by sequential chromatography of Sephadex G-75 and DEAE cellulose. The binding of palmitate to this protein was saturable and the molecular weight determined by SDS-PAGE was 13,500. Binding activity for AA was greater in young SHR (2weeks) (cortex 6.34±0.71, medulla 8.23±0.43 nmol/mg protein, mean±SD, n=6) than in age-matched Wistar-Kyoto rats (WKY) (2.09±0.35, 1.96±0.25). However in old SHR (40 weeks), FABP activity was reduced (1.51±0.20, 1.61±0.29) and similar to that in age-matched WKY (1.46±0.27, 1.54±0.16). AA amount in total homogenate phopholipids determined by gas chromatography was also greater in young SHR (14.4±0.5%, 27.3±4.4% mg/mg protein) than in age-matched WKY (9.7±0.5, 2.9±0.2). In old SHR, AA amount was reduced (10.1±0.5, 10.6±1.4%) and similar to that in age-matched WKY (10.1±0.1, 4.1±0.2). In conclusion, fatty acid metabolism in kidney may be regulated by FABP, whose increased activity for AA with age may be related to the development of hypertension through increased PGs synthesis in the kidney.

*p<0.001, **p<0.05, ***p<0.01

-93-  PROSTAGLANDINS AND LIPIDS METABOLISM IN THE KIDNEY OF HYPERTENSIVE RATS  

Hideaki Kawaguchi, Hiroshi Okamoto and Hisakazu Yasuda
Department of Cardiovascular Medicine, Hokkaido University School of Medicine

Renal prostaglandins participate in blood pressure regulation. In SHR, a renal prostaglandin synthesis increased with age but it is not evident in WKY. We have reported that renal phospholipase A2 activity increases in SHR and it may have an important role to develop and maintain hypertension in SHR. Recently it is reported that phospholipase C is rate-limiting step in prostaglandin synthesis in many tissues. In this report we determined phospholipase C activity in SHR. Prostaglandins were determined in 0.1 M Tris-HCl pH 8.0. Renal microsomes were incubated with [14C] arachidonic acid for 10 min at 37°C. PGs were extracted with ethyl acetate and separated on TLC. Phospholipase C (PLC) was determined in SHRSP (10 and 40 weeks old) and age-matched WKY. Renal cortex and medulla were separated and homogenized, then subcellular fractions were prepared by centrifugation. Each fraction was incubated with [14C] arachidonic acid labeled phospholipids in 0.1M Tris-HCl pH 7.0 for 2 min at 37°C. The released diglyceride and free arachidonic acid was extracted by the method of Folch. Chloroform phase was pooled and evaporated under vacuum. The residues were applied to TLC and analyzed. PGE2, PGF2α, PGD2 and thromboxane were synthesized in renal microsomes and increased with age. The ratios of PGE2/PGF2α and PGD2/PGF2α were lower in SHRSP in all ages. It shows that vasodilator activity of SHRSP, Cytosomal PLC was highest activity in subcellular fractions and had substrate specificity toward phosphatidylinositol. In SHRSP, PLC activity increased more than 2-fold at 40 weeks comparing 10 weeks. In WKY there was no difference in PLC between 10 and 40 weeks.

The results suggest that PLC may have an important role to regulate blood pressure in SHRSP.

-94-  RENAL HEMODYNAMICS IN EXPERIMENTAL NEPHRITIS-

- PARTICULARLY IN RESPONSE TO PHARMACEUTICAL LOAD-

Yoshifumi Matsumoto, Ryoji Kunotani, Masazumi Okabayashi, Takuo Tsujimura, Masafumi Hayashi, Soichiro Kitaoka, Naoyuki Shimizu, Hideo Nonaka and Koie Ishikawa
The First Department of Internal Medicine, Niigata Medical University

A comparative study has been made on the response to a given pharmaceutical load shown by blood circulation of kidney between dogs contracting Masugi nephritis and controls. Both prior and subsequent to the application of norepinephrine (NE), angiotensin II (AngII) under denervation, and of NE and AngII under continuous infusion of SQ14225 (SQ), calcium output, total peripheral resistance, renal blood flow, renal vascular resistance, Ccr, GFR, urinary sodium excretion rate, fractional excretion of filtered sodium, plasma renin activity and plasma AngII concentration, all these were measured.

Results: The nephritis group showed a more sensitive reactivity of renal vascular system and renal tubules against application of NE in contrast to the control. An excessive reaction of K-A system and endogenous All-reactive sthenia has been established as underlying mechanism in the nephritis group, particularly those of K-A system were convincingly observed also through Sq-infusion. In addition to endogenous and exogenous All-reactive sthenia was verified in the nephritis group. Both groups showed an elevated All-reactivity upon infusion of SQ, but loss of Ccr was found to be more distinctive in the nephritis group, which suggests gain of glomerular All receptor in nephritis for the most likely explanation of All reactive sthenia involved.

-95-  CALCIUM ENTRY BLOCKER (DILTIAZEM) INDUCED NATRIURESIS - ROLE OF THE RENAL KININ-PROSTAGLANDIN SYSTEM-

The Second Department of Internal Medicine, Tohoku University School of Medicine

The renal microcirculatory function was studied in SHR exposed to diltiazem infusion. There was no significant difference in the renal tissue blood flow among the control and diltiazem infusion groups. The plasma renin activity was significantly increased in diltiazem infusion group as compared to control group. The urinary sodium excretion was significantly increased in diltiazem infusion group as compared to control group in the presence of denervation. The urinary sodium excretion was also significantly increased in diltiazem infusion group as compared to control group in the presence of sodium loading. The renal renin activity was significantly increased in diltiazem infusion group as compared to control group. The renal renin activity was significantly increased in diltiazem infusion group as compared to control group. The renal renin activity was significantly increased in diltiazem infusion group as compared to control group. The renal renin activity was significantly increased in diltiazem infusion group as compared to control group. The renal renin activity was significantly increased in diltiazem infusion group as compared to control group. The renal renin activity was significantly increased in diltiazem infusion group as compared to control group.

Japanese Circulation Journal Vol. 50, June 1986