36.1

RENIN-ANGIOTENSIN SYSTEM IN CARDIOVASCULAR HOMEOSTASIS: USE OF NONMAMMALIAN MODELS. Hiroko Nishimura. Univ. of Tennessee, Memphis, TN 38163

I will present two nonmammalian models investigating the role of the renin-angiotensin system (RAS) in cardiovascular homeostasis and discuss their biomedical implications. The first model, the aglomerular toadfish (*Opsanus tau*) kidney, is for determining the signals for cellular control of renin release. This model offers 1) an anatomically simpler juxtaglomerular apparatus, and 2) a baroreceptor or stretch receptor for control of renin release. Renin release from toadfish renal slices is suppressed by treatments that increase Ca^{2+} influx or cytosol Ca^{2+} levels, whereas cyclic AMP has no stimulatory effect. Protein kinase C and calmodulin may be involved in cellular signal transduction. Thus, in this model, we can elucidate the role of the Ca signal pathway in the control of renin release that may underlie the renal arterial baroreceptor. The second model, fowl arteries that exhibit relaxation in response to angiotensin (ANG), is for examining the role of the RAS in the control of vascular tone. Many avian species show elevated blood pressure (BP). ANG causes vasocontraction by releasing catecholamines. ANG II also causes endothelium-dependent relaxation of the fowl aorta inhibited by hemoglobin and hydroquinone, but independent of arachidonate metabolism. ANG II receptors exist in the aortic endothelium, and relaxation may be mediated by cyclic GMP. ANG II-induced relaxation becomes more dominant as chickens mature, but decreases after atheromatous lesions develop. Thus, the fowl vascular system provides a useful model for investigating interactions among the vascular endothelium, smooth muscle, and RAS in the control of vascular function and BP.

REFERENCES:

1. Nishimura, H., and M.A. Madey. Signals controlling renin release in aglomerular toadfish. Fish Physiol. Biochem. 7: 323-329, 1989.

2. Yamaguchi, K., and H. Nishimura. Angiotensin II-induced relaxation of fowl aorta. Am. J. Physiol. 255: R591-R599, 1988.

3. Stallone, J.S., H. Nishimura, and A. Nasjletti. Angiotensin II binding sites in aortic endothelium of domestic fowl. Am. J. Physiol. 258: R777-R782, 1990.

36.2

COMPARATIVE STUDIES ON HORMONES, CELLULAR CALCIUM REGULATION AND CARDIOVASCULAR FUNCTION

Peter K.T. Pang
Department of Physiology, University of Alberta, Edmonton, Alberta, Canada T6G 2H7

Hormones are important in the maintenance of a stable plasma calcium level. Intestinal absorption, bone turnover and renal excretion all contribute to produce such an equilibrium. However, cells use calcium as an intracellular messenger. Plasma calcium is the source of intracellular calcium. Therefore, the use of calcium by the cells is part of the overall balance, as indicated by plasma calcium level. Hormones can affect the regulation of intracellular calcium balance. Our recent studies on the endocrine control of cellular calcium regulation in lower vertebrates reveal some interesting evolutionary findings, some of which have led to significant discoveries in mammals and humans.

REFERENCES:

1.

2.

3.

36.3

REPTILIAN MODELS FOR THE STUDY OF CARDIOVASCULAR HOMEOSTASIS. Harvey B. Lillywhite. Univ. of Florida, Gainesville, FL 32611

Reptilian cardiovascular systems exhibit wide variation in form and function attributable to phylogeny, variation in body architecture and ecological diversification. In addition, temporal instability of circulatory processes is imposed by variations of body temperature (related to ectothermy), activity and pH of body fluids. From a regulatory point of view, these unstable components, in addition to adaptive variation, provide useful experimental probes for discovering what properties of the cardiovascular system are regulated, the mechanisms involved, and how they interact with other aspects of integrated homeostasis. Comparative studies allow identification of those aspects of the circulation that are susceptible to perturbation and the range of adaptations that are employed to offset instability. Therefore, reptiles have provided useful models for understanding cardiovascular homeostasis and its attendant adaptations (e.g., 1-3). Because, in general, vertebrate cardiovascular systems have evolved in parallel with metabolic and respiratory requirements of tissues, knowledge of primary processes in reptilian systems is usually transferable to other vertebrates. For reasons related to practicality, availability and social or regulatory issues, in addition to advantages already mentioned, the value of reptilian models in cardiovascular research will likely continue to increase.

REFERENCES:

1. Johansen, K. & W. Burggren (eds.)
Cardiovascular Shunts: Phylogenetic, Ontogenetic and Clinical Aspects.
Alfred Benzon Symposium 21 (1985)
Munksgaard, Copenhagen
review for all vertebrates, including reptiles

2. Jackson, D.C.
Cardiovascular function in turtles during anoxia and acidosis: in vivo and in vitro studies.
Amer. Zool.
27 (1987):49-58
summarizes key findings on cardiac function

3. Lillywhite, H.B.
Circulatory adaptations of snakes to gravity.
Amer. Zool.
27 (1987):81-95

synthesis of integrated adaptations

36.4

Hereditary Nephrogenic Diabetes Insipidus in Domestic Fowl: A Model for Basic Studies. Eldon J. Braun. Dept. of Physiol., Col. of Med.,Univ. of Arizona,.Tucson AZ. 85724.

Nephrogenic diabetes insipidus is the excessive intake of water caused by a failure of the kidneys to respond to antidiuretic hormone (ADH). The physiologically appropriate response of the kidneys to ADH is to excrete solutes in excess of water. Much of what is known of HNDI has been learned from one animal model, a strain of domestic mice described by Falconer et al.('64). The present paper describes a second animal model-a strain of domestic chickens that can be exploited to study HNDI. In these birds, the males drink water at a rate of 24.0% of their body mass (BM) per day (controls 5.4%) and the females drink at the rate of 51.4% (controls 11.7%) of BM per day. The plasma osmolality of the HNDI birds tends to be higher than that of normal controls (males 319 vs. 311; females 323 vs. 310), and the urine osmolality is substantially lower than that of controls (males 90 vs. 524; females 70 vs. 245). The basal ADH levels were markedly higher in the HNDI birds than in normal controls (males 9.9 μU/ml vs. 1.73; females 2.45 vs. 7.04). Additional data will be presented to support the idea that these birds indeed can serve as a model to study HNDI.

REFERENCES:

1. Braun, E.J. and J.N. Stallone.
The occurrence of nephrogenic diabetes insipidus in domestic fowl.
American Journal of Physiology.
256, 1989, F639-F645
This paper contains a clear description of the water metabolism defect that occurs in this strain of domestic fowl.

2. Jackson, B.A., R.M. Edwards, H. Valtin and T.P. Dousa.
Cellular action of vasopressin in medullary tubules of mice with hereditary nephrogenic diabetes insipidus.
Journal of Clinical Investigation.
66, 1980, 110-122.
This paper discusses the cellular action of ADH and the possible cellular defect causing the NDI.

3. Benoff, F.H. and E.G. Buss.
Water consumption and urine volume in polydipsic and normal white leghorn chickens.
Poultry Science.
55, 1976, 1140-1142.
The original description of NDI in domestic fowl.

36.5

CONTROL OF RENAL HEMODYNAMICS: THE AVIAN RENAL PORTAL CIRCULATION AS A MODEL. R.F. Wideman, The Pennsylvania State University, University Park, PA 16802.

A simplified avian kidney model has been developed and validated (1). This model permits independent manipulation of renal arterial perfusion pressure (RAPP) and renal portal flow. Avian GFR is autoregulated between 60 and 120 mmHg RAPP. The autoregulatory profile is unaltered by large differences in dietary sodium. As RAPP is reduced below 60 mmHg, reductions in GFR are not associated with sustained glomerular intermittency. Positive correlations exist between RAPP and sodium excretion (pressure natriuresis), while RAPP and urine osmolality are negatively correlated (2,3). Effective renal plasma flow, estimated by PAH clearance, remains constant over the entire RAPP range tested (30-120 mmHg). Constant PAH clearances could reflect RAPP-induced alterations in PAH extraction efficiency, or co-autoregulation by the portal system. Renal plasma flow (RPF) was assessed at normal (100-110 mmHg) or reduced (40-50 mmHg) RAPP in birds with ambient or restricted portal flow. PAH extraction efficiency was unaffected by RAPP. RPF was perfectly autoregulated in birds with ambient portal flow, but RPF decreased along with RAPP in birds with restricted portal perfusion. The avian renal portal system contributes to overall RPF autoregulation, maintaining constancy of renal blood flow after RAPP is reduced well below the GFR autoregulatory limit. "Perfect" RPF autoregulation may subserve cell maintenance during glomerular intermittency.
KEY WORDS: Autoregulation, Pressure Natriuresis.

REFERENCES:

1. Gregg, C.M., and Wideman, R.F.
Morphological and functional comparisons of normal and hypertrophied kidneys of adult domestic fowl, (Gallus gallus).
Am. J. Physiology 258:F403-F413, 1990.

2. Wideman, R.F., and Gregg, C.M.
Model for evaluating avian renal hemodynamics and glomerular filtration rate autoregulation.
Am. J. Physiology 254:R925-R932, 1988.

3. Vena, V.E., Lac, T.H., and Wideman, R.F.
Dietary sodium, glomerular filtration rate autoregulation, and glomerular size distribution profiles in domestic fowl (Gallus gallus).
J. Comp. Physiology 160:7-16, 1990.

36.6

FISH ADAPTATION TO CHANGES IN SALINITY: A MODEL FOR UNDERSTANDING THE PHYSIOLOGICAL ROLE OF VASOACTIVE PEPTIDES. Sara M. Galli. Deptx of Physiology, University of Florida, Gainesville, FL.

Lower vertebrates offer useful models for the study of hormonal control of body fluid and Na+ excretion. We have studied peptide hormones in Na+ balance in fish. The shark, Ginglymostoma cirratum was used after the removal of the rectal gland as a model to study the effect of Na+ load in fish. It was found that plasma angiotensin II levels rises in parallel with the increase of Na+ in the plasma. The effect of Na+ depletion, by adapting the fish to 50% SW caused a 100% increase in pAng II levels (1). Since euryhaline fish move between sea water and fresh water, they present a biological model to study hormonal interactions with Na+ changes. Atrial natriuretic peptide (ANP) was measured by RIA and HPLC in Fundulus heteroclitus Opsanus tau, Mugil cephallus and Tilapia mosambicus. Each species showed a significant decrease in plasma ANP but a pronounced increase in brain and pituitary ANP levels as they were moved from sea water to fresh water. These effects were reversible. The results demonstrated that ANP plays a physiological role in the control of Na+ excretion in fish. This ancient function may have been conserved throughout evolution as an adaptive mechanism in response to changes in Na+ intake. Further studies also point out an independent role for ANP in the brain and pituitary, where ANP may serve as a neurotransmitter controlling dopamine and other peptides involved in Na+ balance such as angiotensin and prolactin. Lower vertebrates can revel fundamental osmoregulatory functions which have been preserved. They have unique features which can be used to advantage for physiological research.

REFERENCES:

1. Galli, S.M. and K. Qian.
Angiotensin II-like immunoreactivity in sharks: response to hemorrhage and sodium depletion.
FASEB, Vol. 4, No. 4:4000, 1990

2. Galli, S.M., K. Qian, M. Trolliet, and B. Kimura.
Brain and Pituitary ANP in euryhaline fish: its role in adaptation to different salinities.
Neuro Sc. Abstracts, Vol. 15, No. 138.8, 1989

3. Price, D.A., K.E. Doble, T.D. Lee, S. Galli, B.M. Dunn, B. Parten, and D.H. Evans.
The sequencing, synthesis, and biological actions of an ANP-like peptide isolated from the brain of the killifish fundulus hetroclitus.
Biol. Bull, 178:1-7, June 1990.