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REGULATION OF UREA REABSORPTION IN THE ELASMOBRANCH KIDNEY

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These experiments on the spiny dogfish, Squalus acanthias, were designed to test the hypothesis that intrarenal hemodynamic factors may regulate the reabsorption of urea and certain other solutes, perhaps by controlling hydrostatic pressure in the peritubular vascular bed. Our earlier study showed that the renal clearances of urea and trimethylamine oxide could be remarkably elevated by exogenous epinephrine without necessarily affecting rates of glomerular filtration (Bull. MDIBL 9:14, 1969). It had been the generally accepted view that the normally high urea levels in body fluids dropped when elasmobranchs entered dilute habitats because an osmotic expansion of plasma volume would elevate glomerular filtration rates and urine flow, thereby increasing tubular luminal perfusion which would flush out of the tubules urea that normally is almost completely reabsorbed. (Sharks, Skates and Rays ed. by P. W. Gilbert, R. F. Mathewson and D. P. Rall. The Johns Hopkins Press, Baltimore, Chapter 11, p. 192, 1967.) Our current experiments involving volume expansion and environmental dilution, together with the earlier epinephrine studies, point instead to the control of tubular reabsorption by factors outside the glomeruli.

A protein-free balanced isotonic medium of the following composition was used to expand extracellular fluid (ECF) volume: NaCl, 280 m moles per liter; KCl, 6; $CaCl_2$, 5; $MgCl_2$, 3; Na_2SO_4, 0.5; NaH_2PO_4, 1; urea, 350, glucose, 5; and $NaHCO_3$, 8 m moles per liter. After two control clearance periods of 2 or 3 hour duration, the isotonic solution was slowly infused into the caudal vein in an amount calculated to expand ECF volume by 20 percent (4% of body weight), and urine collections were then continued for 2 or more experimental periods. Methods of handling the male dogfish and the chemical procedures used were similar to those previously described (J. Cell. Comp. Physiol. 49:281, 1957). Aortic blood pressure was monitored in parallel experiments before and after administration of the intravenous infusion. Direct manometric readings were taken from a 60 gauge polyethylene tubing that was advanced far into the dorsal aorta after insertion into the caudal artery at the mid-ventral line with the aid of a 16 gauge bent-tip "spinal" needle fitted with stylet. For the environmental dilution experiments renal clearance determinations were made on dogfish kept for 3 days in a large pool into which circulating seawater was being gradually diluted to 70% with freshwater.

Table 1 shows essential data from an experiment in which expansion of extracellular fluid (ECF) volume caused an 8-fold fractional increase in urea excretion over average control values. In this representative fish an average of 6.5% of the filtered load was excreted during the two control periods and this rose to an average of 52% following expansion of ECF. Inhibition of urea reabsorption was accompanied by a small increase in chloride excretion and by a slight diuresis. In 4 other similar experiments maximum increases obtained in the percentage of filtered urea load excreted following ECF expansion were: 3.8-, 1.2-, 6.4- and 4.4-fold, respectively. Corresponding values for chloride in the same animals were: 2.0-, 1.1-, 1.8- and 1.8-fold, respectively. Mean aortic blood pressures varied widely in various dogfish under control conditions (18-38 mm Hg) and, in contrast to the invariable hypertensive action of exogenous epinephrine, expansion of ECF did not appreciably affect pressure in the aorta.

Table 1

INCREASED FRACTIONAL UREA EXCRETION WITH ECF EXPANSION AND ENVIRONMENTAL DILUTION

Period	$\dot{V}$	GFR	Clearance (ml/kg x hr)		Percent excreted (of filtered load)	
	(ml/kg x hr)		Urea	Cl^-	Urea	Cl^-
1.85 kg Squalus						
Control 1	1.48	3.86	0.15	0.97	3.9	24.9
Control 2	1.41	3.30	0.30	1.07	9.1	32.3
4% of body wt balanced isotonic solution i.v.						
Experiment 1	1.75	4.61	2.01	1.64	43.5	35.3
Experiment 2	1.89	3.76	2.21	1.39	59.0	36.9
1.97 kg Squalus in 70% seawater						
1	2.80	5.30	1.97	1.33	37.4	25.1
2	3.30	5.49	2.34	1.62	42.7	29.6

Also included in Table 1 are data from a single dogfish after its "accommodation" to diluted (70%) seawater. The spiny dogfish is not truly a euryhaline fish and clearance values were found to vary widely in these animals which have a limited capacity to adapt to hypotonic conditions. However, the most consistent feature again was the striking rise in percentage of urea excreted, 37.4 and 42.7% of the filtered load in this instance. Corresponding values in 3 other dogfish under similar conditions averaged 42, 29 and 37%, respectively. Reductions in hemoglobin content of 35, 33, 25 and 34%, indicate appreciable expansion of fluid volume in the 4 fish maintained in this hypotonic environment.

Extraglomerular control mechanisms are indicated in these experiments involving exposure to a dilute environment, administration of epinephrine, and the expansion of extracellular fluid volume. Further direct micropuncture measurements are needed to confirm the indication that the tubular reabsorption of urea, water and electrolytes in these instances is controlled by variations in perfusion pressures of the peritubular vascular bed.

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UREA BIOSYNTHESIS AND EXCRETION IN FRESHWATER AND MARINE ELASMOBRANCH

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Urea concentration is markedly lower in the body fluids of freshwater elasmobranchs than in marine forms. Since the concentration of urea in the body fluids is the difference between