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OSMOTIC DIURESIS AND ELEVATED UREA CLEARANCES IN Squalus acanthias: EFFECT OF EPINEPHRINE

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These studies were undertaken to test the possibility that expansion of blood volume and corresponding increases in glomerular filtration rates (GFR) might explain our earlier observation that reductions occurred in fractions of filtered urea and chloride reabsorbed when the elasmobranch skate, Raja erinacea, was adapted to dilute sea water (Goldstein et al, Bull. MDIBL 8:29, 1968). Current experiments unexpectedly disclosed a remarkable action of exogenous epinephrine (Adrenalin, Park, Davis and Co.) in producing osmotic diuresis and elevated renal clearances of urea and trimethylamine oxide (TMAO) without necessarily affecting GFR. This observation supports a very early study by Clarke (Bull. MDIBL 3:38, 1933) that demonstrated adrenalin diuresis in Squalus through the use of parenterally administered sucrose to estimate GFR and also a confirmation of this finding by McCrory et al (Bull. MDIBL 4:38, 1956) employing inulin clearances.

The action of epinephrine administered intramuscularly as Adrenalin chloride 1-1000 in doses of 1 mg per kg was noted in 28 clearance periods on 3 male (1.6, 1.45 and 2.0 kg) and 4 female (3.4, 3.8, 3.0 and 3.6 kg) dogfish. Increased urine flow rates that usually doubled control values were observed in every instance following administration of the drug. Glomerular filtration rates increased slightly, or in some cases were actually reduced. Urea, chloride and TMAO clearances increased sharply in every instance. Table 1 contains representative data on a 3.4 kg female dogfish in which GFR dropped somewhat while there were 15-, 2.6- and 3.8-fold increases in the percentages of filtered load excreted for urea, chloride and TMAO respectively.

Table 1

OSMOTIC DIURESIS INDUCED BY ADRENALIN IN Squalus

Hours	$\dot{V}$	GFR	Clearance (ml/kg x hr)			% Excreted (of filtered load)		
	(ml/kg x hr)		Urea	Cl^-	TMAO	Urea	Cl^-	TMAO
0-2.8	.435	2.48	.06	.60	.05	2.0	23.5	3.0
4 mg adrenalin i.m. at 2.8 hrs								
2.8-5.8	1.03	1.95	.46	1.01	.22	23.5	52.0	11.0
5.8-7/8	1.15	2.05	.89	1.46	.25	36.0	71.0	12.4

The mechanism of adrenalin's inhibitory action on tubular reabsorption remains obscure. Emphasis has been placed on the hemodynamic role epinephrine might play in increasing GFR by augmenting renal blood flow and recruitment of resting glomeruli (Silverman et al, Bull. MDIBL 6:36, 1968) but, as in Table 1, we have noticed the typical diuretic response without a concomitant increase in filtration rates. Similarly, McCrory et al (1956) reported the diuretic

effect in every instance whereas GFR rose in only 3 of 5 dogfish tested. This, in turn, corresponded with Clarke's (1933) original demonstration of a doubling of the urine volume characterized by marked increase in urine/plasma ratios with no change in the sucrose (glomerular) clearance.

To test the notion that intrarenal hemodynamic factors may affect tubular reabsorption by raising hydrostatic pressure in peritubular blood, we infused intravenously massive volumes of dogfish plasma (100 ml into a 4 kg dogfish). Urea excretion was slightly elevated by this procedure but hemolysis occurred and enough trauma seemed to be involved to render the results inconclusive. Angiotensin amide (Hypertension-CIBA) was not tested since it was found to have only a transitory, insignificant effect on blood pressure in Squalus. Norepinephrine (levarterenol), which in contrast to teleost species appears to predominate over epinephrine in elasmobranchs (E. M. Stabrovskii, Zh. Evol. Biokhim. Fiziol. 5:38, 1969), was found to have no effect on urine flow in one dogfish and transitory antidiuretic effect in another. In the clearance periods immediately following administration of 0.5 mg per kg intramuscularly, the GFR dropped markedly, but this was accompanied by either a fall or no rise in urea, Cl^- and TMAO clearances, in contrast to the characteristic adrenalin response in Squalus.

In preliminary experiments p-aminohippuric acid (PAH), tubular transfer rates (Tm), and glucose reabsorption were found not to be affected by adrenalin when the simultaneous clearances of urea, Cl^- and TMAO were typically augmented.

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Na^+ AND Cl^- TRANSPORT ACROSS THE MUCOSA OF FLOUNDER INTESTINE

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Experiments with mammalian small intestines have shown there is a potential difference (PD) across the mucosal membrane with the serosa being the positive (Curran, Fed. Proc. 24: 993, 1965). This PD is interpreted as being due to the active transport of the Na ion from mucosal to serosal side. Glucose can increase the potential difference. Ouabain can inhibit it. Little is known regarding the ion transport in fish intestine. Our previous report (PSEBM 118:933, 1965) showed that flounder intestine did not transport D-glucose transmucosally against a concentration gradient. The question arises, in what process are the ion(s) transported across the flounder intestine, and can this process be affected by glucose?

Winter flounders (Pseudopleuronectes americanus) were kept in a live car more than 7 days after being caught. A piece of small intestine, about 2 cm distal from pylorus, was cut and mounted in a lucite Ussing flux chamber. Seven ml of fish Ringer medium was pipetted into the chamber on each side of the mounted section of intestine and was bubbled with 5% CO_2-95% O_2. PD was measured through two calomel electrodes attached to agar-NaCl bridges. As shown in Figure 1, a negative PD ranging from 1-5 mV and a short circuit current (I_{sc}) ranging from 10 to 30 μAmps with respect to the serosal side were observed, when Forster Fish Ringer (NaCl-HCO_3^- Ringer) was used as a bathing fluid. In Na_2SO_4 Ringer, the PD and I_{sc} shifted from negative to positive, with respect to serosal. In choline methylsulfate Ringer, either a low negative