EVIDENCE FOR INVOLVEMENT OF CARBONIC ANHYDRASE (CA) IN RENAL SULFATE EXCRETION IN THE SHARK, *SQUALUS ACANTHIAS*

Erik R. Swenson[1], Christina Zeien[2], Thomas H. Maren[2], J. Larry Renfro[3]
[1]Department of Medicine, University of Washington, VA Medical Center, Seattle, WA, 98108,
[2]Department of Pharmacology and Therapeutics, University of Florida, Gainesville, FL 32610,
[3]Department of Physiology and Neurobiology, University of Connecticut, Storrs, CT 06269

We have recently demonstrated in vitro and in vivo a functional role of renal carbonic anhydrase in sulfate excretion by the marine teleost (Renfro et al. *Am. J. Physiol.* 1999; in press). Although CA inhibiting sulfonamides have no effect on renal bicarbonate reabsorption and urinary acidification in marine elasmobranchs and teleosts (Swenson and Maren, *Am J Physiol* 253:F288-F293, 1986; Maren et al., *Am. J. Physiol* . 263:F49-F55, 1992), the much higher rates of sulfate excretion in the teleost likely require CA catalysis in the operation of apical and basolateral membrane sulfate-anion exchangers (Renfro, *Fish Physiology*, Academic Press, New York, Vol. 14:147-172, 1996). Given the obligatory large sulfate secretion also of marine elasmobranchs, we studied whether renal CA in the spiny dogfish, *Squalus acanthias*, plays an equivalent role as in the teleost.

Male dogfish, (n = 8; wt 1.8 - 2.2 kg) were studied 12-16 hours after caudal artery and urinary catheter placement (Swenson and Maren, *ibid.*). After catheter placement, 150 mg/kg inulin was given intramuscularly to permit GFR calculation. To determine renal clearances, plasma and urine were sampled for acid-base parameters as well as sulfate, phosphate and inulin, during a 2-4 hour control period, and then 4-6 hours following an intra-arterial administration of 50 mg/kg methazolamide. Inorganic phosphate and sulfate were measured by anion chromatography (Renfro et al., 1999, *ibid.*), inulin by the indole acetic acid colorimetric method (Benyajati and Dantzler, *Am. J. Physiol.*. 250:R712-R720, 1986) and pH by glass electrode. The results with CA inhibition (CAI) are shown below.

	ml x kg^{-1} x hr^{-1}				umol x kg^{-1} x hr^{-1}	
	GFR	Urine flow	Plasma pH	Urine pH	Phosphate secretion	Sulfate
Control	2.77 ± 0.55	0.64 ± 0.25	7.64 ± 0.04	5.9 ± 0.1	23.1 ± 8.2	31.5 ± 9.9
CAI	2.52 ± 0.52	0.55 ± 0.21	7.44 ± 0.03*	5.9 ± 0.1	27.1 ± 7.2	19.8 ± 8.4*

Values are mean ± SEM, * $p < 0.05$ vs. Control

Methazolamide caused systemic pH to fall indicative of red cell CA inhibition and a respiratory acidosis. There were no significant changes in GFR, urine output, urine pH or phosphate excretion, but sulfate excretion was reduced by roughly one third. With CA inhibition plasma sulfate rose from 1.1 to 1.26 mM ($p < 0.05$) consistent with a reduction in secretion. These data confirm an importance of carbonic anhydrase in the renal function of sea-going fish apart from systemic acid-base balance, its major and dominant function in all other vertebrates.

Supported by the following grants: NIH # HL-45571 to ERS, NSF IBN 9604070 and a Salsbury Cove Research Fund Senior Fellowship to JRL, and a University of Florida Summer Fellowship to CZ.