et al., J. Pharm. and Exptl. Therap., 144, Feb. 1964). It is a powerful carbonic anhydrase inhibitor ($K_I = 5 \times 10^{-9}$ M), which enables its detection at very small concentrations (J. Pharm. and Exptl. Therap., 130:269, 1960) and allows an assessment of the physiological consequences of the distribution pattern.

One mg (3 μmoles) per kg was injected intravenously. Two hours later, the plasma pCO_2 had risen from 8 to 23 mm Hg—the typical effect of carbonic anhydrase inhibition in this species (Hodler et al., Am. J. Physiol., 183:155, 1955; Maren, Comp. Biochem. Physiol., 5:201, 1962). This lasted for 24 hours. The following gives mean (n = 3) tissue concentrations (μM) and renal clearances (ml/min) during the peak effect.

Time, hrs.	Plasma	RBC	Gill	Kidney	Urine	Clearance
2	1.0	3.3	0.5	11	300	4
6	0.4	3.6	0.2	2	1500	15

The drug is excreted nearly quantitatively by the kidney in 24 hours. U/P ratios reflect the high rates at which the fish can secrete such an anion. They are much higher than previously measured for PAH (Forster and Berglund, J. Cell. Comp. Physiol., 49:281, 1957) because the plasma concentrations of CL 11,366 are far below saturation of the renal transport system. Uptake into kidney is similar to that observed in the dog.

CL 11,366 is relatively excluded from the gill. From the known carbonic anhydrase concentrations of red cell (0.55 μM) and gill (0.63 μM), the K_I of the drug, and its concentrations in the tissues, it may be calculated that inhibition in the red cell is 99.8% complete but that in the gill it is negligible. The pCO_2 elevation is then a reflection of the red cell effect; it does not seem necessary to invoke the gill in establishment of CO_2 equilibria. Gill carbonic anhydrase may have another function; as in the nasal gland of sea gulls and the rectal gland of S. acanthias, it may be involved in NaCl secretion.

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1963 #21

THE PHARMACOLOGY OF THE GILL CIRCULATION IN Squalus acanthias

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The present study extends the previous observations of Burger and Bradley (J. Cell. Comp. Physiol., 37:389, 1951) on the regulation of the gill circulation of the dogfish. For this purpose, blood pressures were simultaneously recorded from the dorsal and ventral aortas of more than 30 spontaneously respiring dogfish following the administration of atropine sulfate (25 to 50 μg/Kg), norepinephrine (4 to 16 μg/Kg), acetylcholine (30 to 80 μg/Kg), or the infusion of whole blood or Ringer's solution into the caudal vein or ventral aorta. Pressures were transduced with Statham gauges and recorded with a direct-writer apparatus.

The control ventral and dorsal aortic pressures in 13 dogfish averaged 36/23,29 and 28/19,24 mm Hg, respectively; the average heart rate was 22 beats per min. After atropine, the heart rate

increased by 15 to 17 beats per minute; pulse pressure decreased in both the ventral and dorsal aortas without change in the pressure gradient across the gills, presumably reflecting the passive response of the gill circulation to an increase in heart rate. Acetylcholine produced cardiac arrest and a precipitous decline of blood pressure in both aortas; resumption of the heart beat was associated with a rise in the ventral aortic pressures to above control levels and an increase in dorsal aortic pressures toward control values; the "overshoot" of ventral aortic pressures was attributed to the re-expansion of the blood volume of the gill and of its vascular bed. With infusion of blood or Ringer's solution, dorsal and ventral aortic pressures increased with a widening of the pressure gradient across the gill. Norepinephrine increased dorsal aortic pressure more than ventral aortic pressure, thereby narrowing the pressure gradient across the gills; this response was presumably due to "back pressure" on the gill circulation from systemic vasoconstriction. These observations provide no evidence for independent vasomotor regulation of the gill circulation. Instead, they suggest that the circulation through the dogfish gills is regulated passively by the heart rate and by the systemic circulation.

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1963 #22

URIC ACID TRANSPORT BY THE AGLOMERULAR KIDNEY OF Lophius americanus

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Recently reported data indicate that uric acid may be secreted as well as reabsorbed by the nephron of the mammalian kidney. The possibility of bidirectional movement of uric acid across the tubule cells in the glomerular kidney hampers interpretation of specific effects of substances upon uric acid excretion mechanisms. The aglomerular kidney of the goosefish, Lophius americanus, has served as a classic model for tubule transport mechanisms since the absence of filtration-reabsorption decreases the variables to be considered. Uric acid concentrations of goosefish urine (U) and ultrafiltrates (UF) of goosefish plasma were determined in 13 fish. U/UF exceeded 1.1 in 11 of the 13 fish and averaged 1.75. The value 1.1 was used instead of 1.0 since 9% of uric acid was restricted in UF of uric acid standards of concentrations equal to goosefish plasma uric acid concentrations. After the intravascular administration of sodium salicylate or probenecid the urine uric acid concentrations decreased to or below plasma UF uric acid concentrations. These findings suggest that uric acid can be secreted by the renal tubule of the goosefish, and that both sodium salicylate and probenecid can inhibit uric acid secretion.

1963 #23

THE HYPOUREMIC DOGFISH

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Marine elasmobranchs utilize two major substances for the maintenance of extracellular fluid