Carbonic Anhydrase Inhibition in the Gill and Erythrocyte of the Dogfish

Alfred P. Fishman,*J. E. Hodler,** and Jerome Block
Columbia University and New York University

Previous investigations from this laboratory (W. W. Smith) have demonstrated: 1) fixity of urinary pH in the dogfish despite induced variations in blood pH, and 2) lack of a carbonic anhydrase sensitive renal mechanism (Hodler and Heinemann). However, the latter studies suggested that such a system might exist elsewhere than in the kidney. The present study extended these earlier observations and have shown, in accord with them, that following the intravenous administration of the carbonic anhydrase inhibitor, Diamox, there is no significant change in urinary pH, titratable acidity, phosphate, sodium, potassium, or ammonia. Despite the lack of urinary changes, arterial pCO_2 increased rapidly, pH fell and serum bicarbonate increased gradually. These changes suggested an action of Diamox on some extra-renal organ. Three possible sites of carbonic anhydrase inhibition were investigated: gut, erythrocyte and gills. Carbonic anhydrase in these tissues was demonstrated by direct tissue analysis (Maren). No evidence of impaired bicarbonate excretion could be demonstrated in either the stomach or intestine after the administration of bicarbonate and Diamox. Inhibition of a carbonic anhydrase dependent system in the gills was investigated by means of a box designed to separate the gills from the caudal end of the fish. It was demonstrated by this device that following intravenous bicarbonate and Diamox, bicarbonate excretion by the gills was reduced. This evidence for inhibition in excretion of sodium was further supported by in vitro carbon dioxide dissociation curves which reflected the increase in alkali reserve following Diamox administration. These findings suggest that Diamox in the dogfish inhibits two carbonic anhydrase sensitive systems: 1) in the nucleated erythrocytes, manifested by the high blood pCO_2 and 2) in the gills manifested by decreased excretion of bicarbonate. The latter findings, in conjunction with the studies of the carbon dioxide dissociation curves, suggest inhibition of a hydrogen ion exchange mechanism in the gills.

The details of these experiments are published elsewhere: Amer. J. Physiol. **183**: 155, 1955.

* Aided by a grant from the New York Heart Association.
** Permanent address: Genossenschaft fur Biologisch-medizinische, Basel, Switzerland.