RESEARCH OVERVIEW

THEORY OF SOLUTE AND WATER TRANSPORT ACROSS EPITHELIA

The primary objective of this laboratory is the development of a mathematical models of the renal epithelia. A mathematical model of the mammalian collecting duct will be developed, comprised of cellular models of cortical, outer medullary and inner medullary segments. The model will represent Na, K, and acid/base transport under normal and pathological conditions, and will predict their renal excretion, given distal delivery. The initial focus will be parameter assignment for normal collecting duct function and during hormonal stimulation. Particular attention will be paid to cell volume regulation, especially in inner medullary collecting duct, which can vary its Na transport rate from brisk reabsorption to secretion, and which faces a wide range in luminal fluid tonicity. The second focus will be simulation of collecting duct dysfunction. In experimental models (ureteral obstruction, amiloride or lithium administration), specific segmental transport defects have been identified.The model will assess the adequacy of known defects to rationalize observed solute excretion patterns. Finally, the model will simulate clinical tests of distal nephron function (e.g. transtubular K gradient; use of diuretics and impermeant anions to depress urinary pH) in order to assess their applicability to infer specific transport defects.

A second aspect of this project is investigation in the theory of cell volume regulation during fluctuations of net transport. In simulations of principal cells and proximal tubule cells, we examine the feasibility of several cellular signals in the control of cell volume. Such signals include pH-dependent K-channels, ATP-dependent K-channels, volume dependent cation and anion channels, and pH-dependent Na/H exchange.The question posed is whether such mechanisms are adequate for the variety of volume challenges encountered by the cell. A theoretical aspect of this work is the development of tools for comparing the efficacy of homeostatic mechanisms in epithelial model systems. e-mail: alan@nephron.med.cornell.edu Furhter Information: http://physiology.med.cornell.edu/faculty/aweinstein/index.html

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