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Letters to the Editor

Osmosis in Epithelial Membranes

The review of water flow in transporting epithelia which appeared recently in The Journal of Membrane Biology (Hill, 1980) is entertaining, if somewhat negative. The author holds cellular osmosis to be "a theory facing the gravest problems." It is my purpose here to call attention to a view of the problem presented elsewhere (Durbin & Helander, 1978) but not considered by Hill.

To begin, let me accept two major points of the author. (1) Unstirred layers are not likely to cause large deviations between measured osmotic permeability (P_{osm}) and that presented to actively transported solute. (2) The role of intercellular junctions in osmotic flow is dubious at best, since the area involved is small, and if the junctions are leaky, the corresponding reflection coefficient is less than unity.

Nature may have solved the problem by an appropriate adjustment of the area of cell membrane responsible for active transport. A clue here is provided by the finding that Na^+ pump sites are distributed over the entire basal-lateral surface of frog gallbladder cells (Mills & DiBona, 1978). In another tissue, the acid-secreting gastric mucosa, a striking increase in apical surface is known to occur upon stimulation: it seems likely that all of this surface functions to secrete acid.

To make the argument quantitative, it is necessary to make a reasonable estimate for P_{osm}. Fettiplace and Haydon (1980) review such values for erythrocyte membranes: these range from about 200 down to 20 $\mu m \cdot sec^{-1}$. The larger value suggests the presence of aqueous pores, while the smaller value is close to the diffusional permeability of water, and in the range of P_{osm} for artificial membranes of similar composition. I conservatively adopt the smaller value and change to the units favored by Hill, whence $P_{osm} = 3.6 \times 10^{-5}$ $cm \cdot sec^{-1}$ $osmolar^{-1}$.

Consider now absorption of water, accompanying NaCl, by rabbit gallbladder at a rate of 100 $\mu l \cdot hr^{-1}$ cm^{-2} (value taken from Hill, 1980). We have calculated elsewhere (Durbin & Helander, 1978) from stereological findings that the basal-lateral surface of this epithelium is 173 cm^2 per cm^2 macroscopic area. If net osmotic flow (and absorption of NaCl) is distributed uniformly over the basal-lateral surface, we need to account for a flow of 100/173, $=0.58$ $\mu l \cdot hr^{-1}$ cm_t^{-2}, with the subscript t denoting transporting area. Changing units, this is a net flow of 1.6×10^{-7} $cm \cdot sec^{-1}$. Such a flow requires a difference in osmolarity of $1.6 \times 10^{-7}/3.6 \times 10^{-5}$, $=4.4$ milliosmolar. This is 1.5% of plasma osmolarity, an osmotic excess which would be difficult to measure. Adoption of the larger value for P_{osm} would reduce the calculated osmotic excess by a factor of 10.

Stereological measurements have also been made in gastric mucosa. In the instance of maximally stimulated canine stomach, apical surface area was 350 cm^2 per cm^2 macroscopic area (Helander & Hirschowitz, 1972). In this connection it should be noted that water flow in stomach may present a special case of standing gradient (Diamond & Bossert, 1967), promoting a further equilibration between acid secretion and blood: the gastric tubule is long and narrow, and the site of transport (oxyntic cell) may be regarded as a point source deep within the tubule.

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Reply to: Osmosis in Epithelial Membranes

Durbin's letter raises a point which was not dealt with in my review because it refers, atavistically, to an era which has passed.

For a planar membrane transporting salt at a rate N with an osmotic permeability P_{osm}, the emergent osmolarity C_e is given as a function of the basal osmolarity C_o by

$$2C_e = C_o + \sqrt{C_o^2 + \frac{4N}{P_{\text{osm}}}}.$$

Although Durbin presents his calculation as a series of steps which pivot around the rate of flow, he has in fact made implicit use of this equation, as can easily be verified. His argument may be presented as follows: by greatly increasing the extent of membrane convolution θ per unit area of epithelium the effective permeability becomes θP_{osm}, and this can be high enough to reduce C_e to near C_o without requiring high values of P_{osm} for the membrane.

The membrane convolution however, will also affect the pumping term in the same way, which effectively becomes θN; the equation is therefore entirely independent of membrane area. As the membrane is now no longer planar, the equation cannot apply unless there is perfect internal stirring. The equation can represent a convoluted space only if there are no internal concentration gradients, and this obviously does not apply in general to interspaces. It was this very limitation, originally analyzed by Diamond, which finally gave rise to the standing-gradient theory and a step nearer to reality. Durbin's calculation is thus meaningless, and the extent of membrane convolution irrelevant.

Durbin is by no means alone in this, for in fact a general form of his argument is very widespread and shows that many people still apply the simplest osmotic theory to predict *rates* of flow when the essence of the problem is to predict emergent *osmolarities;* to do this there is no substitute for calculating the velocity and concentration profiles within the geometry of a particular system. Without high P_{osm}-values the results of such computations are never isotonic ones.

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