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Textbook Corrections are Required: Electro osmosis Causes Epithelial Fluid Transport, Not Osmosis

Jorge Fischbarg *

University of Buenos Aires, Investigador Superior, at ININCA Institute, Buenos Aires, Argentina

The words (osmosis, electro osmosis) may be similar, but this hides a profound difference in mechanisms. In electro osmosis [1], an electric current carried by ions drives the fluid. In osmosis [2], a difference in concentrations of salt across a semipermeable membrane results in diffusion of the liquid in the direction of equilibrium.

In the world of epithelia, the "driving force" for the mechanism of epithelial fluid transport always constituted one of the major mysteries. Towards the turn of the 20th century, all the other epithelial functions had been finally solved, except for fluid transport.

The leading conception was that some convenient mélange of modified standing gradients along paracellular channels [3], plus local osmosis through newly-discovered aquaporins [4], formed part of the driving mechanism. AAdding to that the relatively high osmotic permeabilities (Pf) of cell membranes of gall bladders: [5], 550, and 1,200 μm/s for the apical and basolateral membranes and kidney proximal tubule [6], 300 μm/s, both laboratories suggested that a few milliosmoles of osmotic pressure difference across the cell boundaries would suffice to drive the transported fluids through the cells. Some textbook writers picked up on this explanation [7], which has been termed "normal science" [8].

Actually, however, there was no general consensus for "local osmosis". In fact, at the same time there had been experimental evidence published all along for the diverging view that fluid transport took place via paracellular, transjunctional water flow. That contrary evidence came from the laboratories of Adrian Hill [Hill, 1978 #2224; Hill, 1978 #2225], John Pappenheimer using intestine [Madara, 1987 #1600], and Whittembury and Malnic using kidney proximal tubule [Whittembury, 1988 #687]. Objections against local osmosis were also raised from a different quarter [9-12].

A detailed description of these events has been given in a recent review of ours [10]. We will now analyze the crux of the matter, with the benefit of recent elaborations.

For this, we will use as an example the transfer of fluid and electrolytes that occurs in corneal endothelium, a typical fluid-transporting epithelium of simple geometry. It consists of a single layer of hexagonal cells, each one with sides 11 μm long (68 μm in perimeter). It covers the corneal stroma (basal side of cells facing outside), and on the opposite side it is bathed by the anterior chamber of the aqueous humor (apical side of the cells facing inside).

The cells are separated by anfractuous intercellular channels. The cells are only 4.5 μm thick, but as the intercellular channels are convoluted,their length extends to 12 μm. At the posterior last 1 μm of length, the intercellular channels narrow into 40 Å wide spaces, the leaky tight junctions. Thus, the spaces between cells are open for water passage from one end to the other.

In addition, as a result of the electrical field created by the cell, a stationary electrical current from base to apex circulates along the intercellular channels and junction. It is carried by Na^+ ions that are secreted by the Na^+ pumps located at the lateral cell membranes [11] .

At the level of the leaky tight junctions, a special phenomenon occurs. There is electroosmotic coupling between the stream of Na^+ ions and the column of water in the junction. As a result, the column of fluid rushes into the aqueous humor. We will quantify this phenomenon.

The hexagonal network of junctions, if made into a line, would measure 1.2×10^3 cm (for 1 cm^2 of tissue area). Given a junctional width of 40 Å, the cross-sectional area of the junctions is 4.076×10^{-4} cm^2 (for 1 cm^2 of tissue area). The density of the electrical current of Na^+ ions circulating across the junctions is 34 μA (per cm^2 of tissue area). If one considers instead the area of the junctions, that intensity increases to 83.4 mA (per cm^2 of tissue area). For an epithelium, that is a comparatively large value, and that gives an indication of the importance of the electroosmotic process. As a detail, since the current is pulsating with periods of 9 s [12], the peak intensity becomes 166.8 mA (per cm^2).

Furthermore, there is wide open paracellular communication between the basal and apical compartments bathing the cells. The lateral spaces are some 200 Å wide, but the junctions are only 40 Å. Under these conditions, If there would be any increase in the hydrostatic pressure of the fluid inside the paracellular space (due, for instance, to osmosis), the fluid would obligingly exit towards the basal end. However, that direction of flow happens to be exactly opposite to the one experimentally observed, which is from basal to apical. The physics are such that a flux of fluid from basal to apical can only be due to electro osmosis. The alternative could only be peristaltic contractions of the spaces, but such have never been observed.

This is the current state of affairs as of 2015. Recently, authors in the Eye field [13,14] have already cautiously agreed to consider electro osmosis a possible mechanism, The future may bring further interesting developments, that ought to eventually close this fundamental question of epithelial fluid transport.

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***Corresponding author:** Jorge Fischbarg, University of Buenos Aires, Investigador Superior, at ININCA Institute, Buenos Aires, Argentina, E-mail: jf20@columbia.edu

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