In Defense of the Vocal Fold and Phonation

Kimberly V. Fisher
Northwestern University Department of Communication Sciences and Disorders
Evanston, IL. USA

We hypothesize that the stratified squamous epithelium of the vocal fold is an active tissue that detects and responds to biological threats in a manner consistent with a balanced defense of the vocal fold, phonation, and the airway. In support of this hypothesis we will present evidence of adaptive epithelial responses to osmotic, mechanical, and ionic stress, *in vitro*. Data from cells and native tissues lead us to propose a pluristratified model that treats vocal fold epithelium as a complex organ with specialized layers. The model includes: (1) polarized cell layers specialized for vectorial transport of ions and water towards and away from the lumen to regulate the superficial hydration of the vocal fold, and (2) non-polarized cell layers wherein ion/water fluxes are associated predominantly with volume regulation to serve as an adaptive baffle against mechanical stress of phonation. Given the juxtaposition of cell layers with different morphology and ion/water permeability, it is expected that together the layers may shape the curvature of the vocal fold edge to aid or hinder vocal fold oscillation. Inherent in this model are our suppositions that (1) transepithelial transport may involve cells in series, (2) the pericellular pathway is rendered impermeable to large solute by an occluding complex present between the cells at least at the lumen, and (3) water flux may occur by both the transcellular and pericellular pathways. In the model, the vectorial flux of water toward and away from the lumen is the sum of the ionically- and osmotically-driven water fluxes. The summation of oppositional fluxes permits tight regulation of superficial hydration. The model explains the recently observed failures of hydration treatments, but predicts greater success for treatments that selectively harness the distinct ionic and osmotic gradients to hydrate the vocal fold surface. Pilot data suggest that components of the epithelium may be fragile to a substantial inflammatory stimulus. We will further identify components of the model that are thought to be developmental (as during transition from a fluid-filled to an air-filled airway at birth). We will discuss the possibility that specific components may be the potential target of viral pathogens, sensitive to soluble agents like hormones, or play a role in disease states. Experiments to test this model may further our ability to prevent voice disorders and laryngeal disease.

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