Reduction in systemic epithelial ion transport in septicemia-related pulmonary edema due to changes in amiloride-insensitive sodium transport?

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TO THE EDITOR: In a recent review, O’Brodovich et al. (7) analyzed experimental evidence for the significance of amiloride-insensitive alveolar epithelial sodium transport in the mammalian lung. In a recent observational study of epithelial ion transport in children with meningococcal septicemia-induced pulmonary edema, indirect evidence of a systemic reduction in epithelial sodium transport as evident in sweat glands, salivary gland, and kidneys was found (1). Airway epithelial amiloride-sensitive sodium transport as measured in vivo by nasal potential difference (PD) in ventilated children with septicemia-induced pulmonary edema was, however, not reduced compared with controls. This can be explained by the conclusion of the authors of this review that infection alters amiloride-insensitive pulmonary sodium transport and fluid clearance. The importance of amiloride-insensitive sodium transport has been highlighted by the finding of large numbers of amiloride-insensitive cyclic nucleotide-gated channels in alveolar type I cells, which constitute 95% of the alveolar surface of the lung (4, 6). Likely candidates mediating this reduction in sodium transport are inflammatory mediators (2, 3). Pulmonary edema fluid from patients with lung injury reduced ENaC, α1-Na/K ATPase, and CFTR expression in alveolar type II cells and had increased levels of TNF and IL-1 (5). The more pronounced reduction of CFTR expression and protein levels on the cell surface compared with ENaC and Na/K ATPase may explain our finding of a closer correlation of reduced epithelial chloride transport with respiratory compromise in septicemia-induced pulmonary edema (1). The simultaneous reduction of ENaC expression may explain that sweat sodium levels unlike in cystic fibrosis were higher than sweat chloride levels (1).

The fact that there was no evidence of a reduction in systemic potassium transport in children with septicemia-related pulmonary edema may indicate that the ion channels involved are not nonselective cation channels. The strong correlation of parameters relating to sodium transport with those relating to chloride transport in septicemia-related pulmonary edema (1) may either point to a link between dysfunction of amiloride-insensitive sodium transport and CFTR dysfunction or an inhibition of basolateral Na/K ATPase leading to a reduction of both apical amiloride-insensitive sodium transport and CFTR function. Our findings on airway epithelial ion transport may not apply to alveolar epithelial ion transport, but our evidence for a generalized epithelial ion transport derangement suggests that it should reflect the changes. Future research could employ inhibitors of amiloride-insensitive sodium transport in nasal PD measurements in patients with pulmonary edema to gain insight into changes in respiratory epithelial sodium transport in critical illness in vivo.

REFERENCES