Cytokine effects on epithelial ion transport protein expression in leptospirosis

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To the Editor: A recent study investigated epithelial sodium transporter expression in an animal model of leptospirosis with the objective of determining the mechanisms involved in the pathogenesis of pulmonary edema in this condition (1).

The authors found a reduced expression of the epithelial sodium channel (ENaC), no change in sodium-potassium-ATPase (Na-K-ATPase), and an increase in Na-K-2Cl cotransporter (NKCC) channel expression in pulmonary cells. The most likely mechanism explaining these changes in epithelial ion transporter expression is the effect of the cytokines tumor necrosis factor (TNF) and interleukin-1 (IL-1). Plasma levels of TNF are associated with severity of disease and mortality in patients with leptospirosis (5). TNF downregulated ENaC but not Na-K-ATPase expression in alveolar epithelial cells in vitro, and IL-1, which is also likely to be elevated as part of the response with proinflammatory cytokines in this condition, has been found to upregulate NKCC channels (3). Another example of a condition with high TNF and IL-1 levels and impairment of systemic epithelial ion transport described previouly is meningococcal septicemia, where there was also evidence of a reduction of epithelial sodium transport with increased renal fractional sodium excretion and increased sweat and saliva sodium levels in patients with pulmonary edema (4). Future research needs to investigate how TNF and IL-1 exert their effects on alveolar epithelial cells and whether, for example, soluble TNF receptors can divert TNF from the classic receptor and activate ENaC in this condition as described in another experimental model previously (2).

REFERENCES