

Endotracheal Tubes: The Conduit for Oral and Nasal Microbial Communities to the Lungs  
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This Editorial View accompanies the following article: Stéphan F, Mabrouk N, Decailliot F, Delclaux C, Legrand P: Ventilator-associated pneumonia leading to acute lung injury after trauma: Importance of *Haemophilus influenzae*. *Anesthesiology* 2006; 104:235–41.

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OUR French and other European colleagues have been instrumental in defining and investigating the pathogenesis of ventilator-associated pneumonia (VAP).<sup>1–3</sup> This infection occurs in patients who have endotracheal tubes for prolonged periods, and generally greater than 48 h. It has been shown that endotracheal tubes are covered with bacterial biofilms, inside and outside, within 11 h<sup>4,5</sup> and that the longer a patient remains intubated, the greater the chances are for the development of VAP.<sup>6,7</sup> It has also been documented that many of the microbes found in the lungs of hospitalized patients originate in the dental plaque and in the oral flora of these patients.<sup>8</sup> Therefore, it seems that aspiration of the oral flora, before or during tracheal intubation, is probably a major mechanism for VAP. This also suggests that we need a greater understanding of microbial communities in patients to fully understand the pathogenesis of this condition.

Many bacteria live in a stable relationship on our oral and nasal mucosa. The composition of the bacterial flora inhabiting these sites is highly specific to particular host species, suggesting host factors must be an important determinant in the selection of colonizing microbes.<sup>9</sup> *Haemophilus influenzae* is a gram-negative bacteria that colonizes the epithelium of the nasopharynx in many normal people as well as the upper and

lower respiratory tracks of patients with lung disease.<sup>10,11</sup> The mucosal surfaces are populated by diverse populations of bacteria that are altered by the use of selective antimicrobials and vaccines that target a limited array of colonizing species or strains. An example of this is with the advent of *Streptococcus pneumoniae* vaccination, children now have lower rates of vaccine-type *S. pneumoniae* carriage but higher rates of *Staphylococcus aureus* nasal colonization.<sup>11</sup>

Dr. Stéphan et al.<sup>12</sup> are to be congratulated for their careful investigation of trauma-associated ventilator associated pneumonia. Their results further document the importance of the oral-nasal flora in the pathogenesis of VAP. They also present data that suggest this same flora is involved in the pathogenesis of acute lung injury (ALI)/acute respiratory distress syndrome. *Haemophilus influenzae* was found to be the most frequent gram-negative bacteria associated with VAP and the most frequent bacteria associated with the development of ALI and the adult respiratory distress syndrome.<sup>12</sup> Although the mortality of the trauma patients did not seem to be affected by the development of VAP, trauma victims who had development of ALI or acute respiratory distress syndrome had a significant increase in mortality.<sup>12</sup> Therefore, prevention of VAP could possibly prevent ALI or acute respiratory distress syndrome.

Although the findings of Stéphan et al. are interesting and provocative, an air of caution is needed. The sample size of patients with VAP/ALI was small, and there was uneven distribution of patients with preexisting chronic lung disease in the VAP/ALI group. Colonization of the upper the airway with nontypeable *H. influenzae* is common, occurring in up to 80% of healthy adults. In addition, lower respiratory colonization is common in individuals with chronic lung disease, and acquisition of new strains is associated with an increased risk of exacerbation of chronic obstructive pulmonary disease.<sup>13</sup> Therefore, the association between VAP, ALI, and *H. influenzae* may have been artifactual and due to unequal randomization. In addition, amoxicillin-clavulanate, an antibiotic with superb activity against both  $\beta$ -lactamase-positive and -negative *H. influenzae*, was prescribed for 48 h for patients with open fractures. Although the number of patients with fractures was evenly distributed among groups, it is not clear whether those with open fractures who received amoxicillin-clavulanate were evenly distributed. Clearly, pretreatment could have skewed the results.

If the findings of Stéphan et al. are confirmed, administration to adults of a vaccine against nontypeable *H. influenzae* (under development) might provide protection against colonization and potentially prevent VAP due to this organism. Other preventative therapies for VAP might include a preoperative or pre-morbid assessment of the nasal-oral flora of patients who require prolonged tracheal intubation and might involve the addition of protective commensal bacteria or local, targeted therapies to decrease pathogenic flora in these locations. However, to develop these therapies, we need to understand which communities of bacteria exist in which patients, how these communities of bacteria interact with each other, and what happens to these communities when we administer prophylactic antibiotics.

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