

## Historical and Current Accounts of *Streptococcus pneumoniae* and *Haemophilus influenzae* as Residents of the Nasal/Pharynx

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### Abstract

*Streptococcus pneumoniae* and *Haemophilus influenzae* are the two major bacterial species responsible for upper respiratory infections historically and recently. The former is more common to adults, particularly the elderly, while the latter is more common to children. Vaccines are available against both pathogens, but they are rarely mixed together, and instead rely on treatment solely against one or the other pathogen.

**Keywords:** *Streptococcus pneumoniae*; *Haemophilus influenzae*; Nasal/Pharynx

### History

During the influenza pandemic of 1889 - 1892, Pfeiffer noted the constant presence of large numbers of small bacilli in the sputum of patients affected with the disease and suggested that the bacillus was the causative agent [1]. Yet, it went largely unnoticed until it was “rediscovered” during the greatest fatal pandemic in human history [2]. Although many of the victims died from the influenza virus within 12-36 hours from infection, the overwhelming number of people who died several days to weeks later were undoubtedly the victims of secondary bacterial infections, primarily from *Streptococcus pneumoniae* or *Haemophilus influenzae* [3]. Both are indigenous bacteria of the nasal/pharynx area and become pathogenic upon weakening of the host immune system. Thus, it is important that we review the current status of their existence as a result of an aging population that started to receive pneumococcal shots over the last ten years to avert fatalities caused by *S. pneumoniae*, but with no thought given to its neighbor, *H. influenzae*.

### Physiology and ecology

*Streptococcus pneumoniae* is a gram-positive micro-aero tolerant (lacks catalase) coccus. *Haemophilus influenzae* is a gram negative facultative short rod. Despite these morphological and physiological differences, these two organisms reside as neighbors, but become problematic upon weakening of the host immune response. An *in vitro* study of competition by Pericone, *et al.* showed that *S. pneumoniae* always overpowered *H. influenzae* by attacking it with hydrogen peroxide and stripping off the surface molecules that *H. influenzae* needed for survival [4].

When both bacteria were placed together into a mouse nasal cavity, only *H. influenzae* survived after 2 weeks. When either was placed separately into a nasal cavity, each one survived. Upon examining the upper respiratory tissue from mice exposed to both bacteria, a large number of immune cells was found. In mice exposed to only one of the species, neutrophils were not present.

Lab tests showed neutrophils exposed to dead *H. influenzae* were more aggressive in attacking *S. pneumoniae* than unexposed neutrophils. Exposure to dead *H. influenzae* had no effect on live *H. influenzae*.

The authors postulated two scenarios for this response:

- When *H. influenzae* is attacked by *S. pneumoniae*, it signals the immune system to attack the *S. pneumoniae*.
- The combination of the two species triggers an immune system response that is not set off by either species individually.

Although *S. pneumoniae* and *H. influenzae* have long been detected together in a multispecies biofilm in infected tissue, it remains questionable whether the relationship between the two is competitive or cooperative [5].

### Infection and immunity

Analogous to the gut microbiome, the respiratory microbiome at equilibrium could be beneficial to the host by priming the immune system and providing colonization resistance. In contrast, an imbalanced ecosystem might lead to bacterial overgrowth and development of respiratory infections. The authors postulate that specific ecological perturbations of the bacterial communities in the upper respiratory tract can occur in response to various lifestyle or environmental effectors, leading to loss of containment by resident pathogens, which would otherwise prevent bacterial overgrowth, and ultimately leads to local or systemic bacterial infections [6]. A generalization can be made that bronchial infections in children are brought about by *H. influenzae*, while those caused in adults by *S. pneumoniae*. It is unknown why this should be, as the latter is prevalent in the nasal/bronchial tract of children.

*H. influenzae* vaccines developed in the late 1980s-early 1990s had a dramatic effect among children. However, cases of vaccine failure and an increased susceptibility to invasive *H. influenzae* have been consistently reported among individuals with immunodeficiencies, such that diseases are becoming relatively more frequent than before [7].

Bronchitis caused by *H. influenzae* consists of a brownish-gray color, similar to that produced on agar plates with a fecal like odor as a result of indole production, identical to what is produced by *E. coli* in the gastro-intestinal tract. Indole is an intercellular signal molecule that regulates various aspects of bacterial physiology including biofilm formation and virulence [8].

Community-acquired pneumonia (CAP) is a serious lower respiratory tract infection associated with significant morbidity and mortality that is characterized by disputes over diagnostic evaluations and therapeutic decisions. Yet, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* remain the leading causes of CAP in immunocompetent patients [9].

The CDC recommends pneumococcal polysaccharide vaccine for all adults 65 years or older.

### Conclusion

Antisera for treatment of children infected with *Haemophilus influenzae* has been reasonably successful, as has pneumococcal vaccines for prevention of nasal/pharynx infections in the elderly population. Why the two vaccines for both organisms are not mixed together for the elderly remains a mystery and raises the question of whether or not susceptibility to *Haemophilus* infection may become problematic with them.

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