

Could Aspiration Be the Major Mode of Transmission for *Legionella*?

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"Epidemic fever is caused by the air. Because all men inhale the same wind, when the air is infected with such pollutions that are hostile to the human race, the men fall sick."

Hippocrates
Breaths XI

Hippocrates was one of the first to recognize that pneumonias that are acquired by aerosolization are highly contagious or characterized by a high attack rate for exposed individuals. For example, airborne pneumonias caused by varicella-zoster, *Mycobacterium tuberculosis*, *Francisella tularensis*, *Yersinia pestis*, and *Coccidioides immitis* are either highly contagious or have a high attack rate. Also, previously well individuals can readily contract pneumonias for those organisms that are aerosolized.

On the other hand, pneumonias occurring in the context of aspiration have a low attack rate because acquisition depends primarily on the susceptibility of the individual patient. Individuals with compromised host defense systems, especially those with underlying pulmonary disease or immunosuppression, are the principal victims.

The most widely accepted mode of transmission of *Legionella pneumophila* is aerosolization. Airborne transmission of *L. pneumophila* with inhalation of contaminated aerosols is the prevailing thesis. Even today, most physicians including infectious disease and pulmonary specialists believe that the original 1976 American Legion outbreak was somehow linked to air conditioners, despite the fact that no such link was ever made.

This aerosolization theory was accepted uncritically largely for two reasons. (1) Cooling towers were implicated as the source in the first well-defined outbreak of nosocomial legionellosis in 1978 [1], although this original study had numerous flaws that have been detailed elsewhere [2]. Furthermore, the potable water distribution was not assessed as a potential source in this study because in 1978 such a

link had not yet been established. (2) Pontiac fever, the nonpneumonic form of legionellosis with attack rates of about 95%, had been convincingly linked to airborne transmission. The organism was isolated from the lungs of guinea pigs exposed to air at the site of the outbreak [3].

However, Legionnaires' disease is not an infection with a high attack rate. Instead, it has a strikingly low attack rate. In that regard, it is interesting in retrospect to review previous outbreaks. In the original 1976 Philadelphia hotel outbreak, the attack rate of the American Legion delegates was only 6.8% and for hotel employees it was even lower [4]. Affected individuals had a high incidence of conditions that could predispose to subclinical aspiration, including alcohol ingestion, or conditions that could impede pulmonary clearance of aspirated microorganisms, such as cigarette smoking. Even though well-publicized outbreaks at the Wadsworth Veterans Administration Medical Center and Pittsburgh Veterans Administration Medical Center ultimately totaled several hundred patients, the overall attack rate was less than 1%.

Given the new information that water distribution systems of large buildings may be contaminated, it now appears plausible that acquisition of the organism in the 1976 American Legion outbreak occurred not via an air conditioning system, but via the water distribution system. Many authorities on Legionnaires' disease have not been aware that ingestion of water at the hotel was significantly associated with acquisition of disease [4]! Also, it is notable that with the recognition of the importance of the hospital water distribution system as a reservoir for Legionnaires' disease in 1982 [5], virtually all nosocomial outbreaks occurring since have consistently implicated the water distribution system as the culprit.

Thus, I suspect that the *primary* mode of transmission is by aspiration rather than aerosolization. The accumulated evidence for aspiration as a mode of transmission is impressive. In a prospective pneumonia study at our institution, risk factors for acquisition of Legionnaires' disease were similar to risk factors for acquisition of other bacterial pneumonias. Of note was the observation that preceding surgical procedures were more common in the patients with Legionnaires' disease than for patients

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with pneumonias of other etiology ($p < 0.08$) [6]. General anesthesia with endotracheal intubation may have been the predisposing factor for aspiration. Similarly, an outbreak of nosocomial legionellosis at Stanford University Hospital occurred mainly in patients undergoing cardiothoracic surgery; pneumonia usually occurred in the early postoperative period [7,8]. Patients with Legionnaires' disease have also been shown to be significantly more likely to have undergone endotracheal intubation [9] and to have longer duration of intubation [8].

In a prospective study performed in a population of patients with head and neck cancer, 30% of the postoperative pneumonias were attributed to *Legionella*, one of the highest incidences ever recorded for nosocomial legionellosis [10]. These patients have almost a universal propensity for aspiration since the site of tumor and surgical resection is the oropharynx. In addition, most of these patients have a history of heavy cigarette smoking—a risk factor not only for head and neck cancer, but also for Legionnaires' disease.

Dournon *et al* [11] described a case of aspiration pneumonia following gastric lavage with tap water for a drug overdose. The patient was shown to have Legionnaires' disease due to two unusual serogroups of *L. pneumophila*, serogroups 3 and 6, which were subsequently found in the tap water [11]. Marrie *et al* [12] described an endemic situation of nosocomial legionellosis in which patients with Legionnaires' disease were significantly more likely to have received mechanical ventilation and nasogastric tubes. Virtually all patients with Legionnaires' disease had nasogastric tubes in place that were flushed with tap water; the tube feedings were also diluted with tap water. Marrie *et al* [12] hypothesized that microaspiration of contaminated potable water was the mode of transmission. When tap water was replaced by sterile water, both for drinking and for tube feedings, the cases essentially disappeared.

One of our first cases of nosocomial Pittsburgh pneumonia (caused by *Legionella micdadei*) occurred in a hospitalized patient following an episode of a generalized seizure with documented aspiration. We have also observed numerous cases of Legionnaires' disease following documented aspiration [13] and this has been confirmed by others [14–17].

Aspiration of contaminated water is an obvious possibility especially since ice machines, which are a primary source of drinking water in the hospital, can be colonized with *L. pneumophila* [18]. Colonization of oropharyngeal flora by *L. pneumophila* is a theoretical possibility [13,19–23], but has never

been consistently documented. After I gargled and then swallowed a suspension of *L. pneumophila* in tap water, very low numbers of the organism could be isolated 30 minutes after gargling, but not at 60 minutes [13].

Now, in this issue of the *Journal*, Blatt and colleagues [24] report a detailed and careful epidemiologic study at Wilford Hall USAF Medical Center. They observed 14 cases of nosocomial Legionnaires' disease in 1 year. *L. pneumophila* of the same serogroup and monoclonal antibody type was isolated from both patients and the water distribution system. The organism was not isolated from the hospital cooling towers. Like the study by Marrie *et al* [12], the case-control study by Blatt and colleagues showed that nasogastric tube use was a significant risk factor for acquisition of nosocomial Legionnaires' disease.

Interestingly, shower use was a negative risk factor. Numerous prospective studies [25,26] and now Blatt's have failed to link showering to acquisition of disease. The association with showers has been suggested by a number of investigators [27] including us [28]. What was not revealed in our report of isolation of *L. pneumophila* from showerheads at Northwestern, Wadsworth Veterans Administration Medical Center, and Pittsburgh Veterans Administration Medical Center was that subsequent epidemiologic investigation at all of the hospitals failed to link showering to acquisition of the disease. Thus, although the organism was isolated from showers, causation should not have been assumed. Although a few studies have suggested that showering may be a mode of transmission [29,30], these studies were all retrospective and detection bias would always be a problem.

The Blatt study provides a continuing impetus for focusing on potable water distribution systems when cases of Legionnaires' disease are discovered. In outbreak situations, showering is temporarily prohibited until disinfection measures directed at the hospital water supply are enacted, but it is clear that proscription of tap water and ice for drinking may be more important [12].

It is ironic that the issue of mode of transmission has now come to the forefront 15 years after Legionnaires' disease was discovered. In order to clarify the issue, future epidemiologic studies of *Legionella* infection should focus on aspiration as well as aerosolization as a major mode of transmission. The implications for prevention of this pneumonia are obvious. The original aerosolization theory triggered an intensive search for cooling towers as a reservoir. Given the fact that the role of cooling towers is now being questioned, it is appropriate to also question the validity of the aerosolization the-

ory. It would be ironic if recently issued detailed guidelines on disinfection and maintenance of cooling towers, evaporative condensers, and air conditioners ultimately proved to be misguided and unnecessary.

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