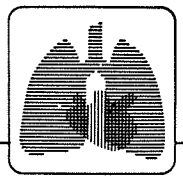

review

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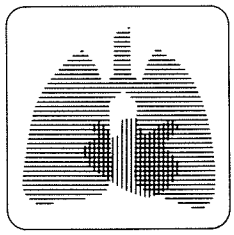

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review

Transmission of Legionella by Respiratory Equipment and Aerosol Generating Devices*

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Nosocomial Legionnaires' disease has become increasingly common, contributing up to 30 percent of hospital-acquired pneumonias in some institutions.[1-3] Although it has been clearly established that hospital water distribution systems serve as the primary reservoir for hospital-acquired legionellosis, the precise mode of transmission remains unclear.[4] Given that *Legionella pneumophila* colonizes potable water, respiratory equipment filled or rinsed with tap water may serve as a secondary reservoir for infection. Contaminated aerosols generated by respiratory equipment could then transmit airborne *L pneumophila* into the respiratory tract of patients. The purpose of this report is to review the role of respiratory equipment in causation of Legionnaires' disease, with special attention to humidifiers and nebulizers.

Respiratory Devices

Humidifiers

Humidifiers are water-filled devices that mechanically add water vapor to air, oxygen, or other gases without the production of particulate water.[5]

Simple humidifiers do not use heat. The most elementary design is the "pass-over" or "blow-by" humidifier in which the gas passes over the water surface and then flows to the patient. A second type of simple humidifier is the bubble diffuser humidifier in which the gas is conducted below the surface of the water and broken into bubbles allowing intimate gas to liquid surface contact which enhances evaporation. The bubble diffuser is the most commonly used humidifier in respiratory therapy.

Room humidifiers increase the ambient humidity in a patient's room. The most common room humidifier is the centrifugal humidifier in which water is raised by atmospheric pressure to the surface of a spinning disc on which the blades of the blower are mounted. Through centrifugal force, water is flung from the edge of the spinning disc against a screen or breaker combs thereby generating an aerosol.[5,6] (Since these devices actually produce aerosols which evaporate in the air of the room, they actually should be classified as "nebulizers."[5]) Because these devices use a large reservoir for water, the potential for microbial proliferation is substantial.

Demonstration experiments have shown that guinea pigs exposed to a room humidifier contaminated with Legionella experienced subclinical infection as demonstrated by seroconversion.[7] In a hospital setting, a portable room humidifier filled with Legionella-contaminated tap water disseminated the organism up to distances of 300 cm (Fig 1).[8] Furthermore, recovery of aerosolized Legionella increased with proximity to the humidifier and seroconversion of exposed animals was directly proportional to concentration of Legionella in humidifier water.[7,8]

Humidifiers have been implicated in transmission of Legionnaires' disease in humans. Five of eight patients with nosocomial Legionnaires' disease in an Italian hospital had been exposed to bubble diffuser humidifiers filled with water containing *L pneumophila*, serogroup 1.[9] An immunosuppressed patient at the University of Chicago Hospital exposed to a room humidifier filled with contaminated tap water for 15 days subsequently acquired Legionnaires' disease.[10] The statistical association between disease and humidifier exposure was highly significant. Use of a room humidifier was also associated with 18 cases of nosocomial Legionnaires' disease in a two-year period in a limited retrospective study.[11] In all three of the above studies, the humidifiers had been filled with tap water.[9-11]

Room humidifiers filled with distilled water have also been linked to hospital outbreaks of Legionella infection; one patient with *L dumoffii* was exposed to a room humidifier presumably filled with contaminated distilled water.[12]

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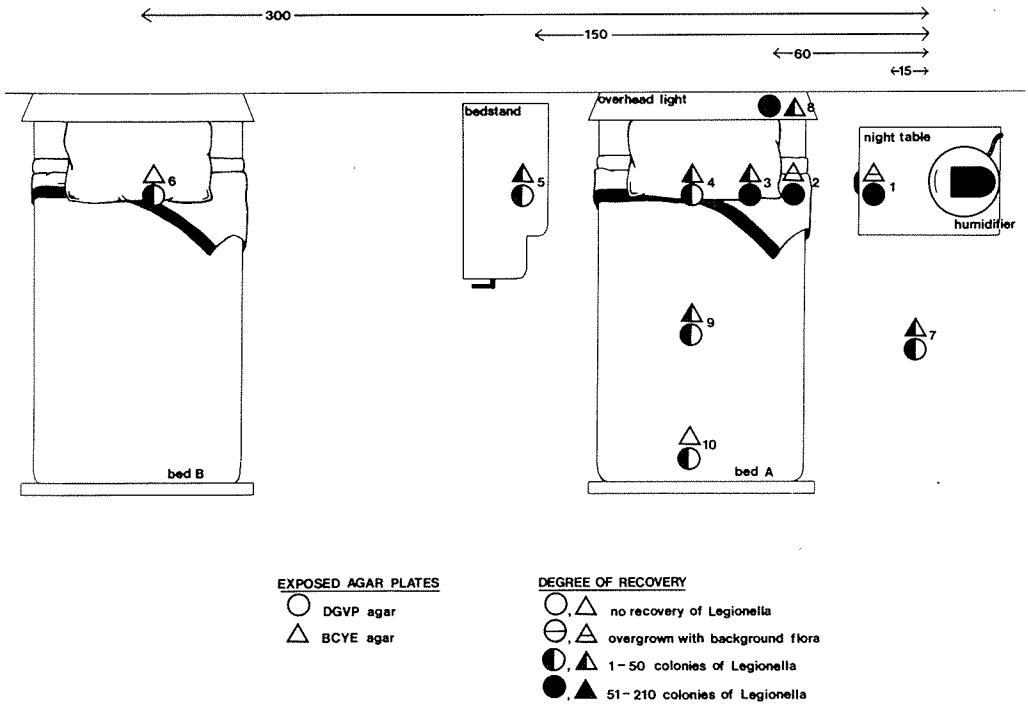

FIGURE 1. Overhead schematic of patient room. A portable cool-vapor humidifier containing *L pneumophila* disseminated the organism throughout the room. BCYE = buffered charcoal yeast extract agar; DGVP = BCYE media supplemented with dyes, glycine, vancomycin, and polymyxin. Reprinted with permission.[8]

Surgical patients, perhaps due to greater likelihood of respiratory tract manipulation for anesthesia and endotracheal intubation, have been especially susceptible targets for nosocomial Legionnaires' disease. In fact, up to 50 percent of nosocomial Legionellosis in some hospitals occurred in surgical patients.[2,13-15] Kaan et al[16] described a postlaryngectomy patient who died from pneumonia following exposure to a room humidifier. *Legionella pneumophila,* serogroups 4 and 5, were isolated from the patient's lung and from the tap water and jerry can used to fill the humidifier reservoir.

Nebulizers

Nebulizers are devices that generate aerosols of uniform particulate size.[5,6] These water particles, if less than 1 μm, can bypass upper airway protective mechanisms and directly enter the alveoli. The three types of nebulizers are named according to their respective mechanism of aerosolization: Venturi jet, ultrasonic, and spinning disk.

Medication jet nebulizers have been shown to aerosolize respirable size (<5 μm) droplets containing *L pneumophila* when 1 ml of nebulizer water was seeded with 500 colony-forming-units of the organism.[17]

A strong epidemiologic link between jet nebulizers and nosocomial Legionnaires' disease was reported by Arnow et al.[10] They found that inhalation of contaminated tap water aerosols from jet nebulizers was a highly significant risk factor for four patients who acquired nosocomial Legionnaires' disease.

Ultrasonic nebulizers have been examined as a potential secondary reservoir for transmission of nosocomial Legionnaires' disease. *Legionella micdadei* (Pittsburgh pneumonia agent) was isolated from the couplant reservoirs of ultrasonic nebulizers in a hospital with endemic Pittsburgh pneumonia, although a causal relationship to nosocomial disease was not documented.[18] A significant association between nebulizer use and nosocomial Legionnaires' disease was also seen in the previously-cited study which implicated humidifiers; the authors noted that the nebulizers were rinsed with tap water.[11]

It is worth noting that in addition to filling nebulizers with tap water, rinsing the chambers of hand-held medication nebulizers has been suggested as a source of contamination. In one study of 13 patients with nosocomial Legionnaires' disease due to *L pneumophila,* serogroup 3, there was a trend toward more frequent use of nebulizer medications in patients with Legionnaires' disease. It was subsequently established that jet nebulizers were often rinsed with tap water.[17] Medication nebulizers have also been implicated in one of the few reports of pediatric nosocomial Legionella infection. Two children with Legionnaires' disease received nebulizer treatments using equipment likely to have been rinsed under tap water.[19]

It should be noted Community-acquired Legionnaires' disease has also been associated with such devices. One patient developed Legionnaires' disease three days after cardiac transplantation.[20] Although all hospital water sites cultured for Legionella were negative, the water in the ultrasonic nebulizer in the patient's home showed heavy colonization by *L pneumophila* and had been in use almost continuously for the two weeks prior to admission for Legionnaires' disease. Monoclonal antibody subtyping of the patient's isolate of *L pneumophila* matched that of the nebulizer isolate (Yu VL, Gervich D, unpublished data).

Twenty-eight individuals exposed to an ultrasonic mist machine in a grocery store contracted Legionnaires' disease.[21] This machine continuously generated a mist over the produce section. A higher incidence of Legionnaires' disease was associated with longer duration of shopping at the store and proximity to the mist machine. *Legionella pneumophila*, serogroup 1, isolated from the lung specimens of two patients matched *L pneumophila* from the reservoir of the mist machine. The investigators also showed that the machine was capable of aerosolizing Legionella-containing 1 to 5 μm water droplets. Interestingly, 92 percent of patients were exposed to the mist for only 2 h or less, compared to up to 15 days in other reports of nosocomial infection. This may have reflected the heavy colonization of Legionella in the misting machine, a machine that is undoubtedly cleaned and disinfected less frequently than hospital respiratory equipment.

This outbreak is unusual in that only 7 percent of patients had used corticosteroids, and only 29 percent had an underlying chronic disease (*ie*, congestive heart failure or diabetes mellitus).[21] The case population was also atypical for Legionnaires' disease with regard to sex in that more women developed the disease. Furthermore, the attack rate was high, and the sparsity of underlying lung disease was conspicuous. We have argued that the mode of transmission for most outbreaks of Legionnaires' disease may be due to aspiration, given the low attack rate and predilection for patients with chronic lung disease.[4] In this outbreak, however, the thesis of aerosolization as a mode of transmission seems better supported.

Other Respiratory Care Devices

Other mechanical devices have been implicated in the transmission of aerosolized Legionella. These include hand-powered resuscitation bags and intermittent positive pressure breathing ventilators. It should be emphasized that although these respiratory devices are not filled with water, simple rinsing of tubing components with contaminated tap water may seed a secondary reservoir with Legionella-containing residual water droplets.

Hand-powered resuscitation bags are frequently dismantled and rinsed with tap water to remove secretory debris. After rinsing a resuscitation bag or its tubing with contaminated tap water, *L pneumophila* could be recovered on culture plates 20 cm away by squeezing the bag.[8] In such a scenario, aerosols

Table 1—*Legionellosis Associated with Respiratory Equipment*

Reference	Device	Setting	No. of Patients	Immuno-suppressed, %	Lung Disease, %	Surgery/ Transplant, %	No. Days Prior to*	Infecting Organism†	Epid Link‡
Arnow et al[10]	Nebulizer, humidifier	University hospital	4 1	100	0	20	>7	Lp 1,6 Lp 6	No
Bouvet et al[22]	Tracheostomy	Home	1	100	0	0	5	Lp 6	Yes
Brady[19]	Nebulizer, face masks	Pediatric hospital	7	70	70	0	>12	Lp	No
Joly et al[12]	Nebulizer, humidifier	University hospital	5	80	>20	>20	<10	L dumoffii	Yes
Jones et al[11]	Nebulizer, humidifier, IPPB	Community hospital	18	44	NA	NA	>10	Lp 1,4,5	No
Kaan et al[16]	Humidifier	Hospital	1	0	0	100	<9	Lp 6 Lp 4,5	Yes
Mahoney et al[21]	Mist machine	Grocery store	28	7	0	NA	<2 h	Lp 1	Yes
Mastro et al[17]	Nebulizer	Community hospital	13	77	92	NA (0?)	<15	Lp 3	Yes
Moiraghi et al[9]	Humidifier, chest drain	Hospital	5 3	0	0	60	>10	Lp 1	No
Phillips et al[20]	Humidifier	Home	1	NA	NA	100	14	Lp 1	Yes

*Days prior to Legionnaires' disease = number of days of exposure to the device before clinical symptoms of Legionnaires' disease.
†Lp = *L pneumophila*.
‡Epid link = Epidemiologic links; infecting organism type matched environment organism type (see text).
NA = not available.

containing Legionella could potentially be propelled directly into the respiratory tract. In fact, an immunosuppressed patient developed Legionnaires' disease after cleaning his tracheostomy cannula with contaminated tap water at home.[22] In two separate investigations, patients contracting nosocomial Legionnaires' disease were significantly more likely to have undergone endotracheal tube placement and to have longer duration of intubation when compared to patients with pneumonias of other etiology.[23,24]

Intermittent positive pressure breathing ventilators have been associated with nosocomial legionellosis, or more likely, their tubing attachment components. The use of IPPB was epidemiologically linked to Legionnaires' disease in 18 hospital patients over a two-year period; again, it was noted that the IPPB equipment was rinsed with tap water between treatments.[11]

Table 1 summarizes Legionnaires' disease outbreaks and case reports associated with aerosol-generating devices. In all studies, filling or rinsing of the device with Legionella-contaminated water and subsequent dissemination through aerosols was the suspected mode of transmission. Three major underlying conditions predisposed hospitalized patients to the acquisition of Legionnaires' disease: immunosuppression associated with corticosteroids or chemotherapeutic agents, chronic lung disease, and surgery involving the head and neck or organ transplantation. While most reported cases occurred in hospitals, cases from the community involving home use of respiratory devices and the misting machine in the grocery store contributed to approximately one third of the total number of cases.

Conclusions

Although the dissemination of Legionella from respiratory equipment to the susceptible patient seems plausible (Table 1), nevertheless, we caution that the evidence is not definitive given some obvious shortcomings in the anecdotal reports and outbreak investigations. As a guide to future investigations in which respiratory equipment is a putative source, we suggest that the following points be kept in mind:

Subtyping both the patient isolate and environmental isolate by monoclonal antibody and other molecular techniques would strengthen an epidemiologic association.

Case-control analysis for endemic or outbreak situations should evaluate other modes of transmission, especially aspiration. Presumably, odds ratios for respiratory equipment use would be higher than for other potential modes of transmission in those reports in which respiratory equipment is the legitimate culprit.

Air sampling studies should be performed for the implicated equipment; demonstration of aerosolization of Legionella would provide impressive circumstantial evidence.

If respiratory equipment is implicated as a possible source of infection, current hospital practices need to be modified, often with some disruption, and alternatives need to be applied; thus, rigorous investigation is necessary or incorrect conclusions may lead to expensive and unnecessary practices.

On the other hand, the overall body of evidence is such that we now recommend the use of sterile water for filling and rinsing humidifiers, nebulizers, and all other respiratory equipment. We have banned portable room humidifiers from our hospital. As discussed, even rinsing respiratory device tubing with tap water may create a secondary reservoir for Legionella. Subsequent reattachment of the device to the patient could directly instill Legionella-containing respirable droplets into the respiratory tract. A key point elucidated by Mastro et al[17] was that devices such as medication nebulizers may retain water 12 h after rinsing.

The effectiveness of such recommendations relies on the compliance of respiratory therapists and nursing personnel. As noted in one outbreak, hospital personnel violated hospital policy by rinsing equipment under tap water.[19] Faucets provide the forceful stream of water necessary to dislodge patient secretory debris from respiratory apparatus tubing or to rinse residual medications from medication nebulizers. However, this common practice may be associated with increased risk of nosocomial infection. Furthermore, even improper handling or replacement of ultrasonic nebulizer components may allow tap water to be aerosolized instead of sterile water from an adjacent compartment.[18] In summary, hospital personnel should be educated on the potential for aerosolizing pulmonary pathogens with these devices and the proper maintenance of respiratory equipment. The use of sterile water in these devices should be mandatory.

Interestingly, guidelines from the American Association for Respiratory Therapy recommended the use of sterile water but accepted the use of tap water providing that a surveillance program was in place for monitoring tap water contamination.[25] These recommendations were published in 1977 prior to the knowledge that *L pneumophila* could be widespread in hospital water distribution systems.[26] Guidelines from the Centers for Disease Control in 1982 recommended that sterile water only be used in nebulizers or humidifiers but did not address the issue of rinsing respiratory equipment with tap water.[27]

If the hospital has a policy to culture water routinely for Legionella as has been recommended by Pittsburgh investigators,[28,29] knowledge of colonization in the water would provide a strong incentive for complying with the above recommendations.

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