Nosocomial Aspergillosis Is Waterborne

Elias J. Anaissie and Silvia F. Costa

1Myeloma and Transplantation Research Center, University of Arkansas for Medical Sciences, Little Rock, Arkansas; and 2Hospital das Clinicas, Sao Paulo, Brazil

(See the counterpoint by Hajjeh and Warnock on pages 1549–53)

Invasive aspergillosis (IA) is a serious infection in patients who have cancer or who have undergone transplantation, and it is thought to be primarily airborne; however, the incidence of IA continues to increase despite the use of expensive hospital air filtration systems, which suggests that hospital sources other than air may also be a source of aspergilli. In this report, we present data in support of our hypothesis, which is that water may be one such source of airborne aspergilli in hospitals that implement adequate air filtration systems and precautions. For the sake of this debate, we will define “primarily airborne aspergillosis” as infections that are acquired from unfiltered outside air that has been introduced into the hospital (the current consensus about the mode of transmission of nosocomial aspergillosis), while “secondarily airborne aspergillosis” will refer to infections that are acquired from spores aerosolized from a water source (our hypothesis). Community-acquired IA will not be discussed.

Our hypothesis assumes that appropriate air precautions are implemented to prevent the entry of outside air into hospital wards and to protect patients during their transfer to various hospital units. The data that we present were obtained by sampling a hospital ward at the University of Arkansas for Medical Sciences (Little Rock, Arkansas), where air precautions include double high-energy particulate air filtration in all patient rooms, in addition to laminar airflow (LAF) units in select rooms. These precautions are effective in this unit, as evidenced by the significantly lower concentration of airborne Aspergillus species in the unit when compared with the outdoors and by the additional reduction of airborne aspergilli when the LAF system is operating [1].

**DATA SUPPORTING WATER AS A SOURCE OF NOSOCOMIAL ASPERGILLOSIS**

Aspergillus can be waterborne: proof of principle. Several reports of near-drowning accidents that have involved otherwise healthy individuals have clearly demonstrated that the opportunistic molds, including Aspergillus species, can cause fungal pneumonia and that only a small amount of water (≈150 mL) is needed to cause devastating infections. These reports represent proof of the principle that pulmonary aspergillosis can be waterborne [2, 3].

**Aspergillus species inhabit hospital water systems worldwide.** As early as 1985, Aspergillus species and other opportunistic molds were shown to inhabit water distribution systems that deliver water to hospitals in 14 cities in Europe and the United States [4]. These molds have also been recovered from samples of hospital water [1, 5]. At our institution, sampling of water acquired at patient taps recovered Aspergillus species in 75 (21%) of 358 samples [1].

Waterborne Aspergillus species can aerosolize, and their concentration is highest near water activity. At our institution, the concentration of Aspergillus species bioaerosols is significantly higher in areas of high water activity (mean concentration in bathrooms, 2.95 cfu/m³) than it is in areas with little or no water activity.
activity (mean concentration in hallways, 0.61 cfu/m³; P = .03) [1]. These findings of a concentration gradient of airborne aspergilli (highest next to water activity and lowest away from it) strongly suggest that aerosolization of aspergilli may be primarily waterborne in the hospital setting. These findings do not support the accepted belief that these fungi are transmitted from the hallways into patients’ rooms (e.g., brought in by visitors, staff activity, or leakage of outside air from doors or elevator shafts). In the latter scenario, the concentration gradient of airborne aspergilli would be expected to be in the opposite direction (i.e., highest in hallways and lowest in bathrooms).

**The distribution of Aspergillus species in hospital water is identical to that of hospital bioaerosols.** The rank-order distribution of aspergilli concentration gradient by species (in descending order, *Aspergillus niger*, *Aspergillus fumigatus*, *Aspergillus flavus*, and other species) is identical in hospital water and bioaerosols [1]. This further suggests that the aspergilli recovered in hospital bioaerosols originate from hospital water.

**Aspergillosis can be acquired from hospital water.** An outbreak of nosocomial *A. niger* infection was traced by molecular studies to a hospital water source (an ice-making machine) [6]. We recently linked *A. fumigatus* that had been recovered from a patient who had nosocomial aspergillosis to the patient’s hospital shower [7]. This patient, who had refractory lymphoma, died of 1A due to *A. fumigatus*. Isolates recovered from the shower wall in the patient’s room were revealed to have the same genotype as the isolate obtained by bronchoscopy, whereas repeated testing of room air failed to yield *A. fumigatus*.

**Aspergillosis is similar to other waterborne infections.** *Aspergillus* species share several similarities with the agents of legionellosis and other nosocomial waterborne infections. These similarities are as follows:

1. Amplification in water reservoirs. *Legionella* species, *Aspergillus* species, and other organisms can multiply in water reservoirs [4, 8].
2. Established association with water biofilms. This association between *Aspergillus* species, *Legionella* species, other organisms, and water biofilms is well established [4, 8].
3. Growth requirements. *Legionella* species, *Aspergillus* species, and other agents grow best at intermediate temperatures (25°C–45°C), and their growth is inhibited in colder (<10°C) and warmer (≥60°C) environments [4, 8].
4. The association between infection with these agents and construction activity. Before being linked with water, legionellosis was thought to be transmitted through aerosolization of bacteria during construction [8]. We now know that the risk of infection with this waterborne pathogen is increased during construction, probably as a result of the dislodging of bacteria from the water biofilm during periods of high water demand, such as during construction [9]. Similarly, aspergillosis has long been linked to construction activity [2].
5. Mode of transmission (aerosolization, ingestion, contact). Although aerosolization is thought to represent the most likely mode of transmission of infection caused by *Legionella* species or *Aspergillus* species, data exist indicating that ingestion of or direct contact with these pathogens leads to serious infection [2, 8]. Waterborne pathogens that share these similarities with *Aspergillus* species include *Stenotrophomonas maltophilia*, vancomycin-resistant enterococci and other bacteria, *Pseudomonas aeruginosa* and other *Pseudomonas* species, atypical mycobacteria, and *Legionella*, *Acinetobacter*, *Enterobacter*, *Burkholderia*, *Flavobacterium*, *Alcaligenes*, *Chromobacterium*, *Rahnella*, *Ewingella*, *Serratia*, and *Cryptosporidium* species [4].

**Similarities exist between aspergillosis and other waterborne fungal infections.** Opportunistic molds cause serious waterborne nosocomial infections. They include disseminated *Fusarium solani* infections [10], endophthalmitis caused by *Acremonium* species [11], and fungemia, pneumonia, and disseminated infections caused by *Exophiala jeanselmei* [12].

**LIMITATIONS OF THE DATA SUPPORTING AIR AS A SOURCE OF NOSOCOMIAL ASPERGILLOSIS**

The incidence of aspergillosis is increasing despite the use of air precautions. Despite the widespread implementation of expensive air filtration systems to prevent the entry of contaminated outside air into hospitals, the incidence of aspergillosis continues to increase [2].

**The epidemiological data in support of primarily airborne nosocomial aspergillosis are incomplete.** Reports supporting primarily airborne nosocomial aspergillosis are retrospective in nature and contain limited or no information on key factors, such as patient-days at risk and degree of risk; in addition, the studies did not sample water as a potential source of infection [2]. Studies that have identified LAF as a protective factor against aspergillosis also suffered from questionable allocation of patients to LAF or non-LAF rooms and the provision of additional preventive measures, including sterile water, to LAF patients [2]. Furthermore, recent prospective studies failed to show a correlation between concentration of airborne *Aspergillus* species (usually sampled in hallways and not in patients’ bathrooms) and cases of nosocomial aspergillosis or patient colonization by aspergilli [13, 14].

Although some studies have shown molecular relatedness between hospital airborne and clinical strains of *Aspergillus* species [15], none of these studies sampled water to determine whether the environmental strains were primarily airborne (from unfiltered outside air) or secondarily airborne from a water source.
CONCLUSIONS

In hospitals that implement appropriate air precautions to prevent nosocomial aspergillosis, a primary source of airborne aspergilli is hospital water. This hypothesis is based on several findings: (1) waterborne aspergillosis has been reported after near-drowning accidents, (2) aspergilli inhabit hospital water systems, (3) the concentration gradient of airborne Aspergillus species in the hospital setting is highest near water activity, (4) the rank-order distribution by species of airborne aspergilli mirrors that observed in hospital water, (5) waterborne aspergillosis has been reported in the hospital setting, and (6) aspergillosis resembles other waterborne nosocomial infections including those caused by fungi.

References