

Nosocomial *Legionella micdadei* Infection in Transplant Patients: Fortune Favors the Prepared Mind

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In 1977, investigators from the University of Pittsburgh and the University of Virginia observed weakly acid-fast organisms in lung tissue of immunosuppressed patients with pneumonia of unknown causes (1,2). The patients from Pittsburgh were all renal transplant recipients. The organism, however, could not be grown on standard bacteriologic and *Mycobacterium tuberculosis* culture media, and was named the Pittsburgh Pneumonia Agent because it was unclear if it was a bacterium. After the discovery of *Legionella pneumophila*, lung tissue specimens containing the Pittsburgh Pneumonia Agent were inoculated into guinea pigs and embryonated eggs, and a bacterium was finally isolated (1). Pittsburgh investigators named this organism *Legionella pittsburghensis* or *Tatlockia micdadei*, and Centers for Disease Control (CDC) investigators named it *Legionella micdadei* (3). Forty-one other *Legionella* species have since been discovered, 18 of which have been implicated as causes of pneumonia (4). The relative rarity of infection from *L. micdadei* (and other species) derives from its lower virulence and less favorable growth kinetics in potable water, thus reducing the chance for exposure (4,5).

Patients with *L. micdadei* infection are more likely to be immunocompromised than patients with *L. pneumophila* infection, and mortality is lower (4,6). In some centers, *Legionella* is the most frequent cause of pneumonia in transplant recipients, accounting for 25% to 50% of cases (7). Heart, kidney, liver, and lung transplant recipients are at the greatest risk, while bone marrow transplants have the lowest risk. Nosocomial outbreaks in transplant hospitals have been reported, with attack rates as high as 50%. The hospital water system is the usual source. Aspiration of contaminated water, rather than aerosolization, is the dominant mode of transmission. This may explain the relatively lower incidence of *Legionella* infections in bone marrow recipients; since the organism is usually acquired in the early postoperative period following solid organ transplants, intubation may be the precipitating factor.

Nosocomial legionellosis is vastly underdiagnosed,

primarily because diagnostic methods are often not available in-house. Less than 19% of transplant hospitals performed routine laboratory testing for *Legionella* (8). Of greater concern, even among those hospitals that had experienced nosocomial Legionnaires' disease, only 21% applied routine *Legionella* testing for respiratory specimens.

In this issue of *The American Journal of Medicine*, Knirsch and colleagues performed a superb epidemiologic investigation of nosocomial *L. micdadei* infection in transplant patients (9). Isolation of *L. micdadei* from bronchoscopy specimens from two renal transplant patients who contracted pneumonia during a 1-week period prompted the authors to perform retrospective surveillance for *Legionella* infection. This surveillance was possible because of the fortuitous availability of stored sera used for white blood cell (HLA) crossmatching. In their initial survey, 11 transplant patients with pneumonia were found to have elevated antibody titers to *L. micdadei*, and in 3 of these patients *L. micdadei* was isolated from culture of bronchoscopy specimens, illustrating that fortune favors the prepared mind. The authors then isolated *L. micdadei* from several sites within the hospital's hot water supply. The environmental isolates had a DNA banding pattern that was identical to the clinical isolates, supporting the hypothesis that the hospital water supply was the source of the outbreak.

A hospital's ability to perform *Legionella* cultures in its microbiology laboratories is crucial for uncovering unsuspected nosocomial legionellosis. Knirsch et al were successful in isolating *L. micdadei* from patient specimens and the hospital water system, even though the medium used—nonselective buffered charcoal yeast extract (BCYE)—was suboptimal for the isolation of *L. micdadei* from bronchoscopy specimens. The isolation of *Legionella* usually requires the addition of antimicrobial agents to inhibit competing microflora. For optimal recovery, two selective media—BCYE-alpha supplemented with polymyxin B, anisomycin, vancomycin, and dyes, or BCYE-alpha supplemented with polymyxin B, anisomycin, and cefamandole—should have been used (10). The dyes (bromocresol purple and bromothymol blue) are important additives that allow for visual differentiation of *L. pneumophila* (light green colonies) and *L. micdadei* (blue colonies) (4) (Figure). Some *Legionella* species, including *L. micdadei*, are inhibited by antibiotics, particularly cefamandole (11); thus the vancomycin-containing

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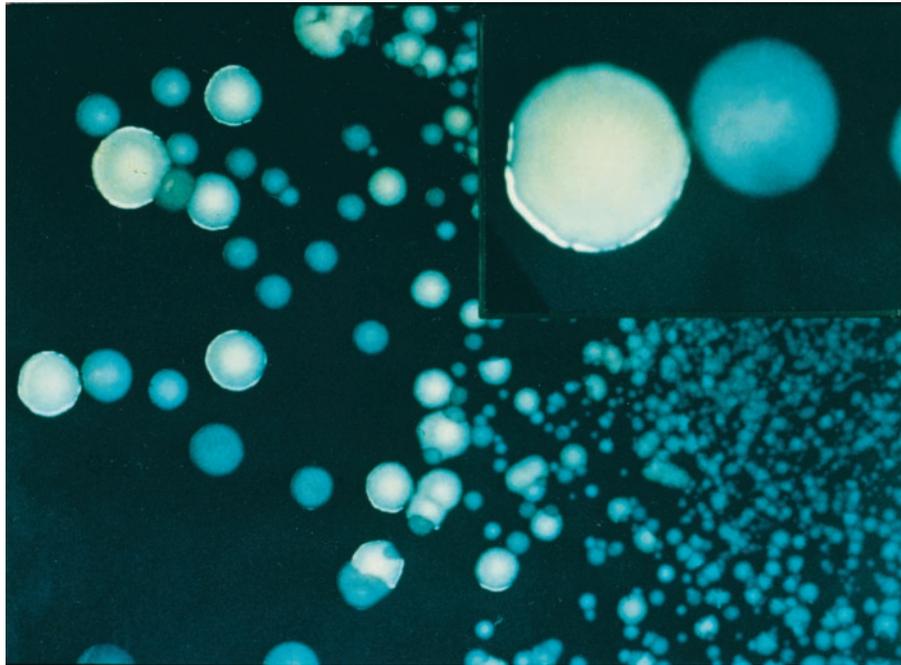


Figure. *Legionella* colonies on buffered charcoal yeast extract (BCYE) medium containing bromocresol purple and bromothymol blue dyes. These dyes allow visual differentiation of *Legionella micdadei* (and *L. maceachernii*) from the other *Legionella* species. The inset shows a small blue colony of *L. micdadei* and a large green colony of *L. pneumophila*.

medium is superior for the isolation of *Legionella* species other than *L. pneumophila* (12). Acid buffer pretreatment also reduces the overgrowth of other bacteria. If acid buffer pretreatment and selective media had been used, this outbreak may have been detected sooner. With the routine use of multiple selective, dye-containing media for sputum specimens, we have found a similar yield from expectorated sputum as compared with bronchoscopy specimens. That bronchoscopy specimens often give the first clue to legionellosis probably occurs because, in most hospitals, specialized tests for *Legionella* are more likely to be performed in bronchoscopy specimens than in sputum specimens.

In general, culturing *Legionella* species other than *L. pneumophila* from a water supply source requires the use of a selective medium that does not contain cefamandole (eg, polymyxin β , anisomycin, vancomycin, and dyes); acid buffer pretreatment increases the recovery. Alternatively, BCYE agar with glycine, vancomycin, polymyxin β , and dyes can be used to isolate *L. pneumophila* and *L. micdadei*, with the added benefit of distinguishing these two species by coloration. However, supplementation with glycine may inhibit the growth of some other *Legionella* species.

The ability to identify *Legionella* microbiologically may lead to the discovery of occult legionellosis in other groups of patients. It is no coincidence that previous cases of community-acquired and pediatric legionellosis were reported from hospitals that had enhanced capability to

identify *Legionella* in their microbiology laboratories as a result of nosocomial outbreaks, such as at Columbia-Presbyterian Medical Center when cases of legionellosis were subsequently discovered in nontransplant patients.

In the current investigation, although the hospital performed thermal disinfection of the hot water system ("superheat and flush") with subsequent negative cultures, two culture-confirmed cases occurred 5 weeks later, coincident with the isolation of *L. micdadei* from the hot water system. Following this, supplemental continuous chlorination of the water system was instituted successfully for several months. However, when the chlorinator malfunctioned, *L. micdadei* reappeared in the water system, and 5 additional culture-confirmed cases occurred. We and others have experienced similar problems with hyperchlorination. Apparently chlorine penetrates poorly into the biofilm harboring the *Legionella*, such that reappearance is rapid when the chlorinator malfunctions. In contrast, in a controlled experiment involving a contaminated hospital water supply, 6 to 12 weeks passed before *Legionella* returned after a copper-silver ionization disinfection system was deliberately inactivated (13).

Some state health departments in the United States and national communicable disease centers in Europe have instituted guidelines that encourage routine environmental culturing for *Legionella* in hospital potable water. Such guidelines have been highly effective in Pittsburgh hospitals (14). Had such an approach been mandated earlier, the morbidity and mortality from nosocomial le-

gionellosis at Columbia-Presbyterian Medical Center and other New York hospitals may have been prevented. The institution of routine environmental cultures has several benefits. First, the isolation of a particular *Legionella* organism from the water supply would have mandated the implementation of laboratory testing that would have been targeted for that organism, including the use of the appropriate culture medium. Second, physicians and infection control practitioners can apply these tests to all patients with nosocomial pneumonia, not just transplant recipients, and can uncover outbreaks prospectively, rather than retrospectively. The results of Knirsch et al's study confirm the observation from the CDC that "even a single nosocomial Legionnaires' disease case may be an important sentinel indicating the likelihood of additional (undiscovered) transmission" (15).

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