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Modern Healthcare Versus Nontuberculous Mycobacteria: Who Will Have the Upper Hand?

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Nontuberculous mycobacteria (NTM) are opportunistic pathogens that have a strong affinity for healthcare. As illustrated in a report by Baker et al in this issue of *Clinical Infectious Diseases*, NTM are capable of exploiting myriad pathways to expose and infect patients [1]. NTM occur naturally in the environment and can be found in soil and water, including the potable water systems that supply many US healthcare facilities. There, in hospitals and clinics alike, they find opportunities to take advantage of immunocompromised hosts, breaches in host defenses, and novel technologies including medical devices.

Baker et al describe a bimodal or "2-phase" outbreak of *Mycobacterium abscessus.* Phase 1 primarily involved pulmonary infections among lung transplant patients. Phase 2 primarily involved patients exposed to heater-cooler devices (HCDs) during open-chest cardiac surgery. The phases were not completely distinct, which added to the challenge of investigating what unfolded as a large outbreak involving multiple modes of transmission. The investigation and comprehensive mitigation measures described in this report offer important lessons regarding transmission and prevention of healthcare-associated NTM.

NTM—*Mycobacterium avium* and *M. abscessus* in particular—are well-recognized causes of pulmonary infections among patients with underlying lung disease or immunocompromising conditions [2]. While pulmonary NTM infections are often community-acquired, healthcare exposures also have a role and must be considered in the differential diagnosis. The investigation by Baker et al began with the team noting an increase in respiratory cultures for *M. abscessus*, with many occurring among lung transplant patients cared for in a new hospital addition. Through their investigation, Baker et al recognized the necessity of protecting their at-risk patients from tap water exposures. Patients subsequently received only sterile water for speech therapy and respiratory care, as

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well as for oral care, bathing, enteral tube flushes, and consumption. The success of these avoidance measures illustrates that seemingly innocuous tap water exposure might not be appropriate in transplant or intensive care units. While the authors advise adoption of this "sterile water protocol" as a strategy to contain outbreaks, this strategy should be considered in the routine care of vulnerable patients.

Careful attention to water use at the point of care is not the whole story. Source control is an important risk mitigation strategy when managing environmental threats such as NTM and other waterborne pathogens. Recognizing this, Baker et al moved "upstream" to evaluate their new hospital addition's water distribution system. The findings were concerning. They discovered low flow rates, recirculating hot water that bypassed heat exchangers, and, consequently, low residual disinfectant levels and temperatures. In effect, the recent construction created favorable conditions within the potable water system for NTM amplification. How was this possible in a new state-of-the-art facility? The answer relates to good intentions, unintended consequences, and, perhaps, a lack of forethought. Increasingly, new healthcare facility construction aspires to incorporate energy-efficient design principles, including Leadership in Energy and Environmental Design (LEED) certification. While this is a laudable goal, healthcare facility water systems serve different purposes and needs than commercial or residential projects.

Procedure and operating room settings seem especially well suited to NTM transmission, for reasons we do not fully understand. We do recognize in this context that normal host defenses, including skin and mucosal barriers, are routinely breached. Large surgical incisions are an obvious example, but injections and other less invasive procedures can result in a viable exposure pathway for NTM. Some recent examples include the use of residential-style humidifiers in a laser-assisted in situ keratomileusis procedure room, pediatric dental pulpotomy procedures, medical tourism for cosmetic procedures, and dermal filler injections [3–6]. All proved capable of facilitating NTM transmission. Some clearly involved direct or indirect exposures to water.

This brings us to the second major mode of *M. abscessus* transmission identified in the report by Baker et al. In the spring of 2014, when the potential outbreak was first noted, retrospective case finding identified several cardiac surgery patients with positive cultures. Additional cases appeared sporadically over the following year. With the decline in cases among lung transplant patients, a distinct cardiac cluster became evident. The infected cardiac patients were also distinct in terms of their clinical presentation, which was marked by extrapulmonary invasive disease.

With the benefit of hindsight, it is clear that the cardiac surgery component of this larger *M. abscessus* outbreak must have been related to contamination of HCDs. Recall that in mid-2015, Sax et al [7] reported in this journal an outbreak of *Mycobacterium chimaera* infections in Switzerland. This was a smoldering outbreak that involved a half-dozen cardiac surgery patients with invasive NTM infection presenting with long latencies over a period of several years. That report provided evidence for a new NTM pathway, with airborne transmission originating from contaminated water in Sorin 3T HCDs that were used to support cardiopulmonary bypass. Subsequently, numerous cases of invasive *M. chimaera* (or

related *M. avium* complex) infections have been reported among patients who had open-chest surgery involving this specific heater-cooler model [8]. The accumulated evidence now indicates that point-source contamination occurred at the production site, apparently when units were tested using local water prior to being shipped worldwide, and that these HCDs provided a favorable environment for the formation of biofilms harboring this strain of *M. chimaera*, with potential for aerosolization and dispersal of NTM in operating rooms [8, 9].

This report of *M. abscessus* infections provides the clearest evidence to date that invasive NTM infections associated with HCDs are not limited to *M. chimaera.* Local water sources can also seed these devices with locally circulating NTM. Sterile or filtered water is required for use in HCDs according to updated and revised manufacturer instructions and regulatory guidance. In addition, guidance from the Centers for Disease Control and Prevention and others advises clinicians to be alert for any NTM infection in patients with a history of open-chest cardiac surgery [10]. This vigilance needs to continue as infections can take months or years to manifest and HCDs, once seeded with biofilm and NTM, are nearly impossible to decontaminate; mitigation strategies to contain the risks posed by these devices represent a work in progress.

Recent experience now dictates that when evaluating a patient with NTM infection, the source of their infection warrants careful consideration as well as their clinical management. If a healthcare exposure was part of the infection's pathway, this needs to be communicated and investigated. In these instances, NTM's upstream pathway may be one that reflects a device issue or deficient care practice involving other healthcare providers and institutions. Prompt engagement with public health partners is essential in these instances.

So, can modern healthcare get the upper hand on NTM? It can if we embrace that patient safety calls for a more balanced and thoughtful approach to water system design, water use, and even medical device design. Institution-specific, comprehensive plans for protecting patients need to extend from the central water system hardware to every clinical application and potential exposure. Infection risks, which extend to other waterborne pathogens such as *Legionella*, should be anticipated and explicitly accounted for in these plans. Infectious disease specialists and their allies should play a central role in this undertaking and are in a prime position to identify prevention strategies and sound the alarm when safeguards fail or new risks emerge.

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