Environmental Sources and Transmission of Nontuberculous Mycobacteria

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KEYWORDS

• Nontuberculous mycobacteria • Environment • Genomics • Transmission • Climate change

KEY POINTS

- The fields of microbiology and comparative bacterial genomics have facilitated the identification of human built environments as hot spots for NTM colonization.
- The combination of microbiology and comparative bacterial genomics should be applied even more regularly to reveal new niches including animal reservoirs involved in NTM transmission.
- Hastened climate changes will likely increase the risk for environmentally transmissible respiratory NTM infections as formidable public health threats globally.

INTRODUCTION

Expanding the Field of Environmental Nontuberculous Mycobacteria Biology

Recognition of environmental nontuberculous mycobacteria (NTM) as human pathogens began in the 1960s and grew in notoriety in the HIV era.[1,2] NTM are now widely recognized as inhabitants of soil and dust but are also categorized as important drinking water-associated opportunistic pathogens that thrive in human-built water systems with the capacity to cause problematic disease in susceptible individuals.[3]

It has been suggested that NTM simply "surround people."[4–7] In 1979, Gruft and colleagues[8] demonstrated that aerosols from estuaries and ocean water in the southeast (SE) portions of the United States harbor NTM, demonstrating their innate survival in natural water sources.[9] By the mid-1980s, acidic soil from United States floodplains were reported as NTM niches.[10] High densities of NTM have been recovered from chicken farms in the SE United States, but low densities of NTM from chicken litter[11] hint to the potential of animals as possible reservoirs for NTM infection.[9] In 1995, *Mycobacterium avium* complex (MAC) was isolated from cigarettes, suggesting environmental smoke and pollutants that harm the lung may also carry infectious NTM.[12] It is clear, NTM are inhabitants of natural and human-engineered environments that survive, in part, due to selection by human actions[13] mixed with their intrinsic capacity for adherence and disinfectant tolerance that promote high numbers in homes and enrichment in plumbing systems.[6] Numerous reports reinforce potable water and drinking water distribution systems as important sources of NTM exposures.[14,15] In another study of people with MAC pulmonary disease and bronchiectasis controls in Japan, exposure to residential soil was a likely source of pulmonary MAC infection.[16] Thomson and colleagues[17,18] found pathogenic NTM including *Mycobacterium abscessus* in large urban water distribution systems in Australia. Falkinham and colleagues[6,19] reported low NTM counts from homes with wells and water heaters

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set to greater than 130°F and advocate that NTM are flexible adaptors that adeptly adjust to their changing environments.[7]

These earlier studies established fundamental information regarding the generalizable environmental niches of NTM using phenotypic and biochemical typing, DNA probe kits, and PCR–RFLP (polymerase chain reaction - restriction fragment length polymorphism) for NTM species identification.[20,21] As the field moves to investigate more specialized, novel NTM niches that go beyond freshwater and soil, such as outbreak investigations and large-scale environmental hazards to NTM transmission events, higher resolution techniques that apply both microbiological culture of environmental samples and bacterial genomics are now favored by the scientific community. Whole genome sequencing (WGS) has been used to study NTM transmission for nearly a decade. As a genotyping tool, comparative genomics now allows for a detailed examination of isolate relatedness and determination of whether isolates were derived from a common source or ancestor. Thus, there continues to be a pressing need to learn more about these organisms and applying NTM genomics at a broad scale will significantly accelerate the current understanding of environmental NTM biology, pathogenesis, and transmission.

Despite growing concerns of NTM as a significant public health problem and greater availability and accessibility to genomic tools, NTM niches and the role of the environment in the acquisition of infection and outbreaks remain understudied. Tracking these infections may help to understand how disease spreads within populations. These factors showcase the need for increased surveillance through mandatory pulmonary disease reporting on a global scale.[22]

The current review highlights and summarizes recent literature and new knowledge regarding the environmental sources of NTM, the newly described factors that likely influence the presence of NTM in the environment and demonstrate the application of NTM genomics to learn a great deal more about the breadth and diversity of NTM in their innate niches. It has been inherently difficult to pinpoint infection and outbreak drivers, and while the ubiquity of NTM is generalized, not all NTM are equally pathogenic. As more studies come to light, there will be a pressing need to know more about which NTM species colonize environments and how their genomes are studied to reveal a new understanding for the capacity of NTM to survive in the environment and infect the human lung and how to mitigate exposures with increased surveillance.

Nontuberculous Mycobacteria and the Environmental Features that Drive Diversity

Nontuberculous mycobacteria distribution varies by geographic region

The worldwide geographic diversity of NTM infections has been well described.[23] In the United States, several geographic areas including California and Florida are NTM hot spots with Hawai'i a top area of NTM pulmonary disease and interest.[24–29] A team of microbiologists, geochemists, bioinformaticians, molecular biologists, epidemiologists, volcano research scientists, clinicians, and an extended community science network, performed the first large-scale NTM environmental sampling campaign across highly populated and natural areas within the State of Hawai'i to understand the unique island features that drive NTM prevalence and diversity.[30–34] Applying microbiological culture of environmental samples and comparative genomics, it was revealed that NTM are not as pan-ubiquitous as predicted, as microbiological recovery rates for environmental NTM were modest even in this geographic hot spot at 27% (764/2,831 environmental samples) (Honda, 2023, unpublished). More importantly, this island archipelago, while isolated in the middle of the Pacific Ocean, harbored a preponderance of clinically relevant NTM compared with species of NTM that do not cause human infections. In addition, clinically relevant NTM species frequently inhabited selected niches within broad environments, suggesting that the diversity of NTM species is critically important to understanding potential environmental risks for infection. In Hawai'i, the most frequently recovered NTM species from households were the opportunistic pathogens *Mycobacterium chimaera*, *Mycobacterium chelonae*, *Mycobacterium porcinum*, and *M. abscessus* compared with less frequently recovered and less pathogenic *Mycobacterium interjectum*, *Mycobacterium alvei*, and *Mycobacterium paraffinicum*.[34] These studies and others that apply microbiological culture of environmental samples for viable NTM isolates rely on gold-standard approaches but are limited by the inability of culture media and conditions to capture the total representation of all NTM isolates present in any sample. Yet, these data suggest that delineating which NTM species are in environment matters because each sampled niche did not necessarily harbor NTM or pathogenic NTM species by culture methods. By inference, NTM of human significance are not as pervasive in expansive environments initially described. Rather, NTM are more likely to be ubiquitous in selected niches within broad environments, an important distinction. Phylogenetic and sequence variant network analyses were used to

evaluate whether genetic diversity among environmental NTM species from Hawai'i differed from the continental United States revealing high or low genetic diversity varied among the species.[34]

New discoveries connecting nontuberculous mycobacteria, showers, and freshwater

Piping within built environments such as office buildings, schools, hotels, shopping malls, airports, and other similar structures may be colonization sites for NTM. Stagnant and unused water in these structures because of the recent COVID-19 pandemic may have created an enrichment of NTM in these systems. Hozalski and colleagues[35] applied a combination of culture-based assays, quantitative PCR, and quantitative microbial risk assessments to show flushing of stagnant shower water may reduce NTM concentration to below detection limits within 6 minutes. In homes, showers are a frequently sampled site to probe for environmental NTM.[4,34,36–40] Moving beyond NTM diversity reporting in showers, Shen and colleagues recently applied mass balance models to quantify the proportion of NTM transferred from building water to indoor air during showering. Then, estimations of live cells were performed using live cell sorting and flow cytometry, discovering NTM showed damaged membranes but retained their ability to grow in culture media, imitating respiratory secretions of people with cystic fibrosis (pwCF).[41]

Owing to multiple access challenges, documenting the presence of colonizing NTM upwards from the home to possible exogenous inoculation sites such as natural water or soil remains difficult to study and track. Conversely, it is presumed that water run-off from soil leads to inoculation of NTM into surface water or ground aquifers that enter water treatment plants, distribution systems, and innervate into homes and other human-built sites.[13] To address these gaps in knowledge, Nelson and colleagues[31] recently leveraged microbiology and geological partnerships, a combination of the microbiological culture of NTM in riparian environments, freshwater stream sediments and flow analyses, stream discharge calculations, and groundwater modeling to report evidence of NTM transport from Hawai'i streams into losing stream stretches and aquifers that enter public water supplies and home plumbing.

Metals and minerals are features that modulate nontuberculous mycobacteria presence in the environment

Over 10 years ago, epidemiological studies applying logistic regression and univariate models using county-level environmental and sociodemographic data were performed to identify low and high-risk US areas for NTM pulmonary infections. Through this work, environmental features such as greater precipitation, high evapotranspiration levels, low elevation, percent of land covered by surface water, soil with greater levels of copper and sodium, and lower manganese levels were characteristics linked to increased risk for pulmonary NTM infections in the United States.[24] More recently, there is growing support showing high atmospheric moisture in certain geographic areas including Hawai'i, California, Florida, and Louisiana increase the risk for environmental NTM exposures.[42] Using the annualized registry data from the cystic fibrosis (CF) foundation, geospatial analyses revealed annual precipitation and soil mineral levels were associated with NTM sputum positivity in Florida.[43] In the context of soil, Glickman and colleagues[32] reported *in vitro* growth of environmentally derived *M. abscessus* isolates from Hawai'i was promoted in the presence of soil hematite, an iron oxide mineral. A multivariate, population-based study demonstrated that risk factors for pulmonary NTM isolation in North Carolina were more related to exposure to hydric and acidic soils rather than population density or road network density.[44]

In the past, high numbers of *Mycobacterium kansasii* lung infection cases were often observed in geographic areas with intense mining activity as in Australia.[45] Lipner and colleagues featured a variety of epidemiological models including geospatial, ecological models, population-based case–control studies, and population-based cohort studies using patient incidence data to evaluate the environmental minerals and trace metals role in NTM infections. This includes a Colorado-focused study reporting that for every 1 log unit increase in calcium and molybdenum concentrations in source water, NTM disease risk increased by 19% and 17%, respectively, compared with people who did not have NTM infections.[46] For those with CF in Colorado, the odds of *M. abscessus* infection was 79% for every 1 unit log increase of molybdenum in surface water compared with people who did not have NTM infections.[47] In Oregon, every unit increase in the log concentration of vanadium and molybdenum in surface water increased the risk for MAC and *M. abscessus* infection by 49% and 41%, respectively.[48] Although this new knowledge is important to the field, *in vitro* mineral and NTM studies to validate these findings alongside ecological studies to recover viable CF NTM pathogens from areas of high calcium and molybdenum concentrations remain missing areas of scientific research.

Revisiting animals as important nontuberculous mycobacteria reservoirs

Although not as widely studied as the built environment, animals may be important reservoirs for NTM. *Mycobacterium marinum* is associated with cold and warm freshwater and saltwater sources and can cause disease in fish, oysters, snakes, and eels.[49] The first human cases of *M. marinum* infection were reported in 1951 from Sweden as skin lesions on swimmers who frequented contaminated pools.[50] *Mycobacterium szulgai* is responsible for infections in fish and animals that live in or in close association with freshwater including crocodiles and clawed frogs, while *M,. avium* infections occur in dwarf cichlids, *Mycobacterium lentiflavum* in swordtails, and *M. abscessus* in zebrafish and milkfish.[51] The first report of *M. chelonae* was its isolation from sea turtles with pulmonary disease in 1903.[52] *Mycobacterium fortuitum* was originally isolated from neon tetra in 1953.[53] *M. avium* subspecies *hominissuis* was recovered from ornamental fish[54] and public aquarium long-tailed carpet sharks in the Netherlands.[55] Recently, Komine and colleagues[56] applied WGS to perform a phylogenetic analysis demonstrating the transmission of *M. marinum* among fish, invertebrates, seagrass, periphytons, biofilms, sand, and water.

Land animals may also be zoonotic reservoirs associated with the emergence and spread of NTM. In areas of the Iberian Peninsula, *M. avium* subsp *avium* and *hominissuis* were documented in wildlife including badgers and wild pigs.[57–59] In a recent study from Spain, a collaboration between researchers and veterinarians showed both wild and livestock pigs harbored potentially pathogenic NTM, suggesting ungulates as a primary animal reservoir for NTM.[60] Additionally, population genomics studies have revealed the dominant strains and transmission of *M avium* subsp *paratuberculosis* within dairy herds, even reporting the frequency of mixed-strain infections.[61–63]

Classical molecular and biochemical tests were applied to identify *Mycobacterium gastri* from abdominal organs and lymph nodes of a 9 year old captive and immune-suppressed red panda from a Japan zoo, but was unable to identify point sources of exposure, prevalence, and gene analyses.[64] *M. avium* subsp *hominissuis* was identified using 16S rRNA and IS1245 and IS901 sequencing of bronchoalveolar lavage samples collected from zoo tapirs with the protracted disease in Germany, which was also detected in tapir swimming pool water, pool walls, and sleeping beds.[65] To clarify the taxonomy and host ranges of the various subspecies of *M. avium*[66] and *Mycobacterium intracellulare*[67,68] known to infect humans, animals, and birds, comparative genomic studies have been performed. For example, a recent study applied WGS to investigate NTM isolates from birds diagnosed with avian mycobacteriosis at the San Diego Zoo over a 12 year period, and uncovered transmission patterns of *M. avium* subsp *avium*.[69]

Overall, applying comparative genomics to understand the role of animals in the zoonotic transmission of environmental NTM is a burgeoning field that would benefit from increased numbers of studies focused on NTM genetic diversity in animals and studies to determine the molecular and drug resistance correlates associated with disease using NTM isolates recovered from the environment, animals, and humans. Such studies would improve our understanding of the interconnectedness of these important NTM infections.

Applying Genomics to Demonstrate Matched Environmental and Clinical Nontuberculous Mycobacteria Isolates

To understand where in the environment people acquire their infections, most prior studies have applied molecular tools including DNA probe kits, PCR–RFLP, and culture multilocus enzyme electrophoresis to differentiate and match environmental to clinical isolates. These studies were tabulated and summarized in 2015 in a literature review by Halstrom and colleagues.[70] In **Table 1**, studies since the Halstrom review are summarized that transition to using combinations of molecular and genomic genotyping methods to determine genetically matched environmental and clinical NTM isolates. These include studies from the United States and Korea applying dual variable-number tandem repeat genotyping and WGS or WGS alone to show genetic similarities between household and clinical isolates of NTM (eg, *M. avium*, *M. fortuitum*, *M. chimaera*, *M. abscessus*, and *M. intracellulare*).[71–78]

Utility of Genomic Sequencing to Understand the Dominant Circulating Clones of M. abscessus, Global Disease Transmission Patterns and Outbreak Investigations

WGS and comparative genomics have advanced our understanding the genetic diversity of global clinical *M. abscessus* isolates, and to a lesser extent, MAC isolates. Dominant circulating clones (DCCs) of *M abscessus* have been observed in geographically diverse locations[79] first described among widely separated outbreaks of *M. abscessus* subsp *massiliense*,[80–82] among CF pulmonary

Table 1
Summary of PubMed studies since 2016 that have matched environmental to clinical isolates using genomics

Country	Clinical Samples	Environment Investigated	NTM + Environmental Samples: No. of Environmental Samples Collected	Matched Occurred Between Environment and Clinical Sample	Species Matched	Species Characterization Method	References
United States	Patient (n = 120) respiratory isolates	Water biofilm from 5 US states (n = 80)	19:80	13:57 (environment: environment + clinical)	*M. avium*	Culture Variable-number tandem repeat genotyping; whole genome sequencing	Iakhiaeva et al[71]
United States	Patients (n = 38), skin biopsy (n = 9/13 with test results), isolates (n = 13)	Tattoo studio tap water (n = 10), bottles of gray wash ink (n = 5), faucet swabs (n = 2)	11:13	1:1 (tattoo ink:skin biopsy) 8:4:3 (tattoo ink:skin biopsy:tap water)	*M. fortuitum*, *M. abscessus*	Culture Whole genome sequencing	Griffin[70]
United States	Patient (n = 26) control (n = 11) sputum or BAL	Variety of household plumbing, humidifiers	95:334	11:21 (respiratory: environment)	*M. avium*	Culture Variable-number tandem repeat genotyping; whole genome sequencing	Lande et al[71]
United States	Hospital outbreak patients (n = 11); clinical controls (n = 11)	Hospital water outlets (n = 4)	N/A	4:7:1 (environmental isolates: outbreak hospital clinical isolates: control clinical isolates)	*M. abscessus*	Culture Whole genome sequencing	Davidson et al[72]

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Table 1
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Country	Clinical Samples	Environment Investigated	NTM + Environmental Samples: No. of Environmental Samples Collected	Matched Occurred Between Environment and Clinical Sample	Species Matched	Species Characterization Method	References
United States	Isolates from patients with left ventricular assist devices (n = 4)	Water specimens (sink, shower) (n = 14); Ice machines (n = 2)	2:14 2:2	8:0 (*M. abscessus* isolates from water and ice machines:clinical isolates) by culture 16:16 (Samples from water and ice machines:clinical) by culture independent	*M. abscessus*	Culture Whole genome sequencing and subsequent Culture independent	Klompas et al[73]
United States	Patients with CF (n = 80 isolates)	Health care setting (biofilm, dust) (n = 161)	11:161	0:11 (environment: patient isolates)	*M. abscessus* , *M. avium* (no match)	Culture Whole genomic sequencing	Gross et al[74]
United States	Patients with CF (n = 11 isolates)	Health care setting (biofilm, dust) (n = 132)	8:132	1:8 (environment: patient isolates)	*M. chimaera*, *M. avium* (no match)	Culture Whole genomic sequencing	Gross et al[75]
Korea	NTM patients cohabitating for > 15 yrs (n = 3 pairs); sputum (n = 4); bronchial washings (n = 2)		(Home 1) 7:12 (Home 2): 0:15 (Home 3): 1:15	1:1 (environment: patient isolates) 1:1 (environment: patient isolates) 1:1 (environment: patient isolates)	(Pair 1) *M. avium* (Pair 2) *M. intracellulare* (Pair 3) *M. intracellulare*, and *M. abscessus*	Culture Whole genomic sequencing	Yoon et al[76]

isolates across Europe and Australia,[83] and in the United States CF Centers.[84,85]

Owing to the increased awareness of *M. abscessus* DCCs and access to WGS, a plethora of retrospective studies have been published using WGS to evaluate the potential for person-to-person or health care-associated transmission of NTM. Recent *M. abscessus* studies were performed as single or multi-site investigations in Europe,[86–89] Australia,[90] Canada,[91] and Asia[92–94] with findings of genetically similar isolate clusters in a subset of patients. For most clusters, there was limited evidence for health care overlaps or social connections between patients that pointed to widespread person-to-person transmission, although it could not be ruled out in some cases. In the most extensive study of clinical *M. abscessus* isolates to date, the authors analyzed ~2300 isolates from 906 patients sequenced as part of the routine Public Health England diagnostic service.[95] This unbiased sample set included CF and non-CF isolates, and genomic analyses revealed high-density clusters distributed over a wide geographic area. Epidemiologic studies showed that CF and non-CF patients were equally likely to have clustered isolates, and there were few identifiable links between patients in clusters. One intriguing finding was that patients were 1.14 times more likely to have clustered isolates for each 10 years in age, regardless of underlying condition. The authors suggested that this could be due to repeated exposures to an unknown environmental vector, which is an important and key hypothesis yet to be explored on any large scale.

More recent studies showed that DCCs represent a substantial proportion of non-CF isolates derived from both pulmonary and extrapulmonary infections in the United States, Europe, Australia, and Asia.[95–99] The widespread presence of DCCs has led to intense speculation about the extent of person-to-person transmission of *M. abscessus* as well as the evolutionary origins and trajectory of DCCs.[100] A study analyzed mutational signatures in *M. abscessus* genomes and proposed that non-CF carriers, particularly smokers, helped disseminate DCCs globally in the mid-to-late 20th century, which led to subsequent clonal expansions in the CF population.[98]

Hospitals are increasingly recognized as *bone fide* sites of NTM colonization and possible outbreaks.[101] Hospital water and surgical sources have been associated with severe NTM infections including *M. chelonae* infections associated with LASIK eye and plastic surgeries.[102] At least 17 published reports show NTM isolation from hospital ice or ice-making machines.[103] WGS was recently applied to confirm the genetic similarity between *M. abscessus* isolates recovered from ice machines of a US hospital and cardiac surgery patient specimens associated with commercial water purification systems.[75] A 2 phase hospital-associated outbreak of *M. abscessus* occurred among lung transplant and cardiac surgery patients and was linked to contaminated water sources from the addition of a new hospital wing,[74,104] resolving with the successful implementation of water engineering interventions and tap water avoidance protocols.[104,105] A separate outbreak of *M. abscessus* was reported among pwCF in a hospital in Hawai'i, and improved adherence to infection control practices reduced future cases.[106]

Within the hospital environment, equipment pieces are point sources for pathogenic NTM exposure. *M. fortuitum* outbreaks have been associated with hospital bronchoscopy units.[102,107] But the highest profile scenarios in recent time are the well-documented global outbreaks of *M. chimaera* infections associated with open-chest heart surgeries and medical devices, that is, heater–cooler units (HCUs), with more than 140 cases of severe infections identified worldwide.[108–112] A recent review summarized WGS applications related to *M. chimaera* and HCU infections; thus, these studies are not discussed at length here.[113] Dental procedure rooms are also not immune to NTM colonization, as contaminated tap water used for pediatric pulpectomies during dental procedures was identified as a point source for *M abscessus* outbreaks.[114] Promising research in statistical process control methods are currently being evaluated to improve NTM surveillance and early outbreak detection in health care environments.[115]

Recently, a standardized approach for NTM outbreak investigations at US CF Centers was developed by Gross and colleagues,[116] focusing on all clinically relevant NTM species through a multi-site study called healthcare-associated links in transmission of NTM. Using combined environmental sampling, the microbiological culture of NTM isolates, watershed analyses, and integrated pan-genome analyses, the health care-associated transmission of *M. abscessus* was found to be rare in a Colorado Adult CF Center.[76] *M. avium* transmission events may be possible among pwCF and a cluster of *M. intracellulare* subsp *chimaera* pulmonary infection was linked to a health care water source.[77] These studies reinforce the notion that genomic comparisons alone are insufficient to conclude transmission and underscore MAC species as important yet understudied NTM that may be acquired in CF health care environments.

Overall, there have been fewer genomic studies focused exclusively on the global transmission of MAC compared with *M. abscessus*. Two large

studies evaluating clinical MAC isolates were recently performed in the United States[117] and England.[118] The US study focused on clinical isolates from CF Centers in 23 states and reported that *M. avium* and *M. intracellulare* populations were genetically diverse. Only a few isolated clusters among pwCF were identified. The English study included CF and non-CF isolates from a London hospital and identified both *M. avium* subsp *hominissuis* and *avium* in the clinical isolate population. This study also observed a small proportion of isolated clusters among patients. In both studies, clinical *M. avium* and *M. intracellulare* populations did not have DCCs like *M. abscessus*, but most *M. chimaera* isolates belonged to few high-density clades suggesting narrow genetic diversity in this subspecies. A common theme among clinical MAC WGS studies was the observation of mixed strain or mixed species infections in up to 30% of cases that was also observed when sequencing colony sweeps derived from sputum samples.[119] This contrasts with *M. abscessus* infections that are primarily clonal.[83,85,120] The ability to determine infection status (ie, single vs. mixed infections, relapse vs. reinfection) is a clear benefit of WGS and critically important for understanding potential inoculum sources of different NTM species and designing prevention and treatment strategies moving forward.

To begin to identify factors that facilitate the survival of *M. avium* in diverse niches, Keen and colleagues[121] compared and annotated the genomes of 65 human clinical isolates, 31 animal, and 13 soil *M. avium* isolates to generate a core genome alignment to construct a maximum phylogenetic tree. From these analyses, specific *M. avium* genotypes associated with human infections, animals, and free-standing environments and isolates could be distinguished by their core and accessory genomes, patterns of horizontal gene transfer, and virulence factors. To identify genomic processes that facilitate *M. abscessus* survival in diverse niches, this same group sequenced 175 isolates longitudinally collected from 30 people with *M. abscessus* infection and found highly related isolate pairs across hospital centers with a low likelihood for transmission.[122] A mercury resistance plasmid, likely needed for environmental survival, was detected in early isolates but lost from later isolates suggesting a fitness compromise for survival in the lung.

Environmental Threat Events that Influence Nontuberculous Mycobacteria Colonization

As colonizing bacteria of water, soil, and dust, NTM distribution, abundance, diversity, and transmission may be significantly impacted in a variety of ways, elevating the consideration of NTM as climate-sensitive respiratory pathogens. Already, increased moisture in the air has been linked to higher NTM disease prevalence rates.[24] Tsunamis, typhoons, and other natural disasters such as flooding and earthquakes cause large-scale movement of water, soil, and dust and can increase exposures and exacerbate disease risk.[123] As such, increased NTM incidence and prevalence rates have been reported in Florida during times of hurricanes.[124] Dried soil caused by severe droughts may more easily aerosolize NTM into long-distance traveling plumes. *Mycobacterium* 16S gene sequences have been detected in dust caused by natural desert dust events.[125] Warmer climates melt snow and glaciers which may become a new source of NTM dissemination into freshwater conduits. In Asia, a high abundance of *Mycobacterium* sequences has been detected from snow collected from high altitude sites of Mt. Tateyama in Japan contaminated with pollutants from neighboring industrial areas of Beijing.[125] Thawing glaciers due to climate changes have been linked to increased frequency of volcanic eruptions[126] and viable *M. abscessus*, *M. avium*, and *M. chimaera* have been recovered from freshly erupted ash from the Kilauea volcano, Hawai'i after its largest eruption in 250 years.[127]

DISCUSSION

The role of the environment in human NTM acquisition remains a hot topic among those in the NTM community and those who endure these infections. There will likely be no single, globally applicable checklist of equally important defining environmental determinants associated with NTM pulmonary disease emergence. However, regional and worldwide climatic and environmental factors will determine NTM diversity and personalize risk for infection to each location. As such, pulmonary disease surveillance in locations globally is increasingly needed. A significant barrier is the inability to accurately pinpoint exposure sources due to the lengthy lag time between environmental exposure and clinical presentation. International health security in the context of NTM requires dramatic improvement, but the game-changing recent advances in NTM genomics and transmission as discussed are creating positive leaps forward. Finding ways to intervene, reduce, and/or control environmentally acquired NTM infections will be the next field for which solutions are needed.

SUMMARY

NTM resilience in diverse environments ideally positions these opportunistic pathogens as formidable public health challenges and warrants innovative and equitable management solutions to reduce infections.[128] Future studies should focus on moving beyond retrospective studies or single snapshots in time studies to favor prospective, longitudinal studies and increased disease surveillance to exponentially improve our ability to forecast environmental features that promote or reduce environmental NTM prevalence.

CLINICS CARE POINTS

- Successful management of NTM pulmonary disease requires a multifaceted approach including a keen awareness of possible environmental niches, knowledge of reported features that promote NTM in the environment, and cognizance of the geographic hot spots for infection.
- The combination of microbiology and comparative bacterial genomics has begun to uncover the contribution of zoonotic transmission to the interconnectedness of NTM diseases.
- Studies of *M. abscessus* outbreaks using genomic sequencing have revealed the global circulation of dominant clones.
- Microbiological, molecular, and genomic tools have been used in combination to identify possible environmental sources of exposure by genetically matching environmental isolates to respiratory isolates.
- Evidence based results concerning the usefulness of interventions to reduce and/or control environmentally acquired NTM infections will certainly empower clinical care and improve patient outcomes.

DISCLOSURE

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