

#### Review

# Review: Environmental mycobacteria as a cause of human infection



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#### ABSTRACT

Pulmonary infections with nontuberculous mycobacteria (NTM) are recognized as a problem in immunodeficient individuals and are increasingly common in older people with no known immune defects. NTM are found in soil and water, but factors influencing transmission from the environment to humans are mostly unknown. Studies of the epidemiology of NTM disease have matched some clinical isolates of NTM with isolates from the patient's local environment. Definitive matching requires strain level differentiation based on molecular analyses, including partial sequencing, PCR-restriction fragment length polymorphism (RFLP) analysis, random amplified polymorphic DNA (RAPD) PCR, repetitive element (rep-) PCR and pulsed field gel electrophoresis (PFGE) of large restriction fragments. These approaches have identified hospital and residential showers and faucets, hot-tubs and garden soil as sources of transmissible pathogenic NTM. However, gaps exist in the literature, with many clinical isolates remaining unidentified within environments that have been tested, and few studies investigating NTM transmission in developing countries. To understand the environmental reservoirs and transmission routes of pathogenic NTM, different environments, countries and climates must be investigated.

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Abbreviations: RFLP, restriction fragment length polymorphism; RAPD, random amplified polymorphic DNA; PFGE, pulsed field gel electrophoresis; RT-PCR, real time polymerase chain reaction; HPLC, high performance liquid chromatography; HP, hypersensitivity pneumonitis; Rep-PCR, repetitive polymerase chain reaction; AFLP, amplified fragment length polymorphism.

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### Factors affecting the acquisition of pulmonary NTM

Pulmonary infections with nontuberculous mycobacteria (NTM) are an increasing problem in many countries. Symptoms include chronic cough, hemoptysis, weight loss, fever and progressive fatigue - similar to Mycobacterium tuberculosis (MTB) pulmonary infection. Diagnoses are made with chest radiography, detection of acid fast bacilli (AFB) in sputum and cultures from sputum and bronchoalveolar lavage (BAL) fluids [1]. The increasing prevalence may reflect an aging population, as symptomatic infections are most common in post-menopausal women and older men. NTM infections can also manifest as lymphadenitis, disseminated disease, or skin, tissue or bone disease. Disseminated NTM disease is associated with genetic defects in the Th1 pathway, and lymphadenitis is often seen in patients with advanced HIV disease, whilst skin, tissue and bone infections usually follow trauma at the site of infection. Pulmonary NTM infections in older individuals with no recognized immune defects carry a high morbidity and economic cost, as current treatments have multiple side effects and an intention-to-treat cure rate of <50%. Even in apparent cures, the relapse rate is 50% at 3 years [2]. It is important to determine the source and mode of transmission of pathogenic strains in the environment for the advancement of prophylactic measures, as subtle immune deficiencies are rarely evident prior to the diagnosis of NTM disease.

Pathogenic NTM comprise many species and strains found in water and soil. To elucidate NTM disease risk, clinical and environmental NTM isolates need to be matched. This will identify critical environmental reservoirs and routes of transmission. The following is a review of studies where clinical and environmental strains of mycobacteria were matched and a discussion of the limitations to the methodologies employed.

#### NTM are common in many environments

NTM have been isolated from drinking water pipelines [3,4], water tanks [5], hot tubs [6], residential faucets [7,8], hospital

faucets and ice machines [9,10], diagnostic laboratories [11], bottled and municipal water, commercial and hospital ice [12], potting soil [13], house dust [14,15], water damaged building materials [16], showerheads [17], shower aerosols [8], hottub aerosols [6], coniferous forest soils [18], brook waters [19], cigarettes [20], livestock [21], coastal mosses [22] and seawater [23]. Reports span multiple countries (including the USA, Australia, the UK, France, the Netherlands, Denmark, Czechoslovakia, Italy, Finland, Germany, Madagascar, Tanzania, Taiwan, Japan and Korea) and various climates. While many isolates were not directly associated with human disease, these reports show that NTM reside in a variety of natural and artificial environments.

#### Environments of interest are defined

Inhalation of aerosols appears to be the primary transmission route of NTM causing pulmonary disease. This usually occurs in artificial water environments such as hot-tubs and showers, but may involve garden soil and house dust. Mycobacteria may aerosolise more readily than other bacteria as they have highly hydrophobic cell walls. NTM have been isolated from natural water environments in which aerosolisation increase the concentration of NTM in the air [24,25]. However, these studies will not be discussed here as the aerosols were not linked to NTM disease.

Species-level identification of NTM isolates is sufficient to determine the presence or absence in an environment, but strain level identification is required when matching clinical and environmental isolates. For species level NTM identification, cheap lower resolution techniques include phenotypic and biochemical typing, RT-PCR, species specific DNA probe kits, HPLC of mycolic acids and sequencing of select genes (namely 16S, *rpoB* and/or *hsp*65). Serotyping [5] and phage typing [26] have been utilized, but are now less popular as more species of mycobacteria have been recognized.

With low resolution techniques, environments of interest can be selected based on assessments of NTM presence. Demonstrations of transmission causing disease require higher resolution typing techniques such as RFLP, PFGE, or Download English Version:

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