**Reducing Exposure to Nontuberculous Mycobacteria (NTM)**

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**Introduction to the Nontuberculous Mycobacteria (NTM)**

 NTM are bacteria with a lipid-rich, impermeable outer membrane that are found in almost every drinking water sample; including water in household plumbing. The lipid-rich outer membrane results in slow growth, antibiotic-resistance, disinfectant-resistance (e.g., chlorine), acid-tolerance, desiccation-resistance and propensity to stick to pipe surfaces (Brennan and Nikaido, 1995). The lipid-rich outer membrane is the major determinant of their ecology as: (1) NTM grow slowly because they use a great deal of energy to make the long chain fatty acids in the outer membrane, (2) NTM are impermeable to nutrients, but impermeability makes them resistant to disinfectants and antibiotics, (3) NTM are hydrophobic so they are very poor at taking up nutrients, but hydrophobicity drives surface attachment and growth (biofilm formation), where they will not be washed away in pipes, and (4) NTM hydrophobicity means they are more readily aerosolized than other bacteria (Parker et al., 1983).

**Sources of NTM**

 NTM are normal inhabitants of soils, natural waters, drinking water distribution systems, and household and building plumbing. Highest numbers of NTM in water are found in recirculating hot water systems in hospitals, apartments, and condominiums. NTM isolates in household plumbing and showerheads have been shown to be identical by DNA fingerprint to NTM from patients (Falkinham et al., 2008; Falkinham, 2011). A recent case-control study has shown that showers are the most significant sources of NTM in households (Tzou et al., 2018). NTM can survive and grow in phagocytic protozoa and amoebae that normally grow and digest other bacteria; this selection may be why they can grow in human white cells. High numbers of NTM are found in coastal estuaries (Chesapeake and Delaware Bays) and swamps (from Virginia to Texas coast), pine forest soils (Finland, New England), sphagnum vegetation (peat bogs, New England), and cranberry glades (West Virginia, New England). NTM grow in fresh and brackish (NaCl = 1-2 %) water, but absent in ocean water (3 % NaCl). Commercial potting soils have high NTM numbers (one million per gram) due to the inclusion of peat and samples of patient’s potting soils yielded NTM that were identical by DNA fingerprint to the NTM isolated from their lungs (DeGroot et al., 2006).

**Geographic Distribution of *Mycobacterium* Disease and Species in the United States.**

 The prevalence of NTM disease across the United States is not uniform, but exhibits “hot spots” and “low spots”. Florida, Louisiana, Santa Barbara, Philadelphia (Lande et al., 2019), and New York City are hot spots, while upstate New York and the southwest are low spots (Adjemian et al., 2012). High soil moisture content and humidity are strong predictors of NTM presence. High NTM numbers are also associated with recirculating hot water systems in hospitals and high-rise condominiums and apartments.

 Distinct NTM species also have unique distributions. On the eastern coast of the United States there exists a “Fall Line” that separates the geology of the rocky Appalachian Mountains (Piedmont) from the sandy coastal Tidewater region. Cities on the “Fall Line” include: Philadelphia (PA), Georgetown and Richmond (VA), Fayetteville (NC), Columbia (SC), and August (GA). Florida is entirely to the east of the “Fall Line”. To the east of the “Fall Line” patients are more likely to be infected with *Mycobacterium abscessus*, while to the west of the “Fall Line” patients are more often infected with members of the *Mycobacterium avium* complex (MAC). One of the current objectives of the Falkinham Lab is to find out why.

**How Do NTM End Up in Household Water?**

 NTM enter drinking water systems attached to soil particulates from surface waters. The source of NTM in household plumbing is piped water from a utility; well-water (groundwater) has very low numbers of NTM. Drinking water distribution systems are ideal habitats for NTM as chlorine kills off competitors for the limited nutrient allowing the slowing growing NTM to grow on low concentrations of nutrients (Falkinham et al., 2001). NTM also attach to pipe surfaces where they grow to form biofilms and can’t be washed away. Household plumbing is another ideal habitat for NTM: organic matter is present (especially in the water heater), lots of pipe surface area means the NTM can adhere and grow, the normal temperatures in in water heaters can’t kill the NTM, and even if there is no water flow (stagnant) the NTM can grow at low oxygen content. Recirculating hot water systems, such as found in high-rise apartments and condominiums and hospitals have very high numbers of NTM as the warmed water supports higher rates of growth. NTM in plumbing are readily aerosolized from taps, showerheads, and humidifiers where they can be inhaled. Humidifiers filled with household water generate high numbers of aerosolized (mist). Recently, we have identified another NTM-risk factor; second homes. Second homes are expected to have water in the pipes that has been there a long time; the plumbing term is high water age. That stagnant water is a place for growth of NTM (and other waterborne pathogens), so residents entering a second home after it has not been occupied for months or more will be exposed to higher numbers of NTM.

**NTM Infection Routes**

 All NTM-infected patients likely have a pre-disposing factor that makes them much more sensitive to NTM. NTM-infected patients are often infected with more than a single NTM strain. The predisposition to NTM infection will never disappear, thus an NTM patient can possibly be subject to repeated infection. An NTM patient can relapse and the identical strain isolated or can be infected with a second NTM species or type (Wallace et al., 2002). NTM infection can be a consequence of inhalation of an NTM aerosol (shower) or swallowing water with NTM and the NTM aspirated as a consequence of gastric reflux.

 Dusts, especially dusts from gardening activities and potting plants are sources of NTM infection. It appears that one NTM species, *Mycobacterium intracellulare* (a MAC member) prefers soil and is rarely found in water (Wallace et al., 2013). Further, DNA fingerprints of *M. intracellulare* isolates collected from dusts generated from their potting soils were identical with those of the patients (De Groote et al., 2006). Wear a pharmacy-purchased Type N95 dust mask when gardening.

Recently, the Falkinham Lab has discovered that the NTM are very desiccation-resistant. NTM cells can survive desiccation for up to 1 month. There are two reasons for NTM-desiccation-resistance: (1) the lipid-rich outer membrane holds water and (2) their residence water-retaining biofilms. Both extend survival in the absence of water. We recently discovered that one NTM, *Mycobacterium chimaera* (a MAC member) even grows in biofilms under conditions of desiccation. This is the reason one recommendation is to scrub surfaces of bottles for storage of sterile water or the water reservoirs of humidifiers.

**How Can We Reduce NTM Exposure?**

Studies of NTM sources and the factors that direct their presence in the human environment suggest some measures to reduce exposure. First, if you are worried about swallowing NTM, boil water for 10 min. That will kill NTM. **This list of recommendations has been updated May 3, 2021 because of a publication comparing the ability of killing fecal bacteria (*Escherichia coli*) by boiling water in a pan versus boiling water in an electric kettle. The electric kettle was far superior in its ability to kill the bacteria, so I recommend purchasing an electric kettle to boil water. They are available at the big box stores and online.**

If you travel, please consider purchasing “Spring Water”; in the Falkinham Lab’s experience, “Spring Water” has the fewest number of NTM.

What follows is a list of suggested measures that patients can introduce that may reduce NTM exposure. Few have been rigorously tested and are all based on observations of NTM. Therefore, all of these interventions are experiments, except the ones on raising water heater temperature and employing tap and shower filters. We have tested the latter two and shown they reduce or abolish NTM numbers.

1. **Raise Water Heater Temperature.** Turn up your water heater to 130° F (55° C). NTM patient household plumbing that did not have NTM had higher hot water temperatures (130° F or 55° C or higher), compared to households whose hot water heater temperature was 125° F (50° C) or lower (Falkinham, 2011). Recent studies (09/01/15) have shown that raising hot water heater temperatures in 10 homes that had *M. avium*, resulted in disappearance of *M. avium* from 10 of the 10 homes by 12 weeks. That work is being written up for publication. We are continuing to look for *M. avium* in those households to be sure we are not selecting for heat-resistant NTM.
2. **Water Heater Type.** Water heaters are thermos-like glass or stainless steel tanks where the water is heated by electricity or gas. In addition, there are “tank-less” or “instant” water heaters; they heat water on-demand and lack large tank for storage. NTM adhere to both glass and stainless steel surfaces. I prefer glass as it does not corrode; even stainless steel rusts. I also prefer gas heating as investigators looking for *Legionella pneumophila* sources discovered it grew in the tanks because the water in the tank was stratified by temperature, so the *L. pneumophila* cells could find their optimal temperature for growth. The convective currents generated by a gas flame at the bottom of the tank mixed the water to prevent stratification. Tank-type water heaters do support growth of NTM, whether gas or electric, glass or steel. The key is that there is a large volume of warm water with sediment that supports NTM or pathogen growth. That’s why I recommend regularly draining water heaters. The alternative to having a tank is to use a “tank-less” or “instant” water heater. They lack a large tank and heat water on demand. Thus, in theory, there is no opportunity for NTM to grow in a tank; the heated water has a short residence insufficient for growth. One disadvantage of the “tank-less” water heaters is that they lack capacity to provide hot water to different locations. However, I cannot make a recommendation for or against “tank-less” water heaters as we simply have not tested any.
3. **Flush and Run Water in Unused Lines to Reduce Water Age.** Water age refers to the time water stays in pipes in houses. The average water age in household plumbing is 1-3 days. Residence of water for over 3 days leads to a loss of disinfectant and the resulting growth of NTM and other waterborne pathogens. Increased water age can occur in plumbing in areas of a house that are unused; for example, in an unused bathroom or unoccupied wing of a house. The solution is simple, have someone not at risk for NTM disease to flush commodes and run water (5 min) in taps in unused bathrooms and in seldom used laundry tubs, half baths, and outside faucets.
4. **Install Filters to Prevent Passage of NTM.**  Water filters whose pore sizes are less than 0.2 micrometers will prevent the passage of NTM. A number of manufacturers produce and sell such filters; primarily for the hospital market (e.g., Pall Medical and Aqua-Tool). They have been tested and shown to prevent passage of NTM and other waterborne pathogens like *Legionella pneumophila*. There are even showerheads with those same 0.2 micrometer pore size. One drawback is that the filters clog up readily, prevent passage for only 30 days, and are expensive. To prevent clogging of the 0.2 micrometer pore size filter, the manufacturers suggest installation of a 1-5 micrometer pore size filter upstream; it is cheaper and will reduce clogging and thereby increase the life of the 02 micrometer pore size filter.

Rather than install a 0.2 micrometer showerhead or tap filter on every household tap, please consider limiting an NTM patient’s use to a single bathroom (tap and showerhead) and kitchen tap. Such an installation would limit exposure to the most likely sources waterborne pathogens.

1. **Carrying Water to Drink While Travelling.** My colleague, Jennifer Honda at National Jewish Medical and I are measuring the ability of several commercial bottle types to provide NTM-free water. One type has a 0.2 micrometer filter and can provide NTM-free water for at least 3 weeks. The other type has a UV-lamp and it too can provide NTM-free water for up to 3 weeks. We challenged the efficacy of either the filtration or UV system by adding a “cocktail” of *Mycobacterium* species strains to the bottles reservoir. Both type of bottles reduce numbers of NTM in the water (greater than 99.9 %). We purchased the bottles on-line and are in the process of writing up the results.
2. **Drain and Refill the Water Heater Every Six (6) Months.** Hot water heaters have a resident population of NTM; they are even capable, like *Legionella*, of supporting their growth; making the water heater an NTM or *Legionella* source.  Highest NTM numbers are in the sediment that collects in the bottom.  Attach a hose to the drain and let the water, sediment, and bacteria nourish the garden every 6 months. If you do it every month and find that you always see sediment (NTM cells), then increase the frequency of draining.
3. **Disinfect Showerheads.** Showerheads support a rich and diverse microbial population. In one survey 70 % of showerheads in the United States had NTM (Feazel et al., 2009). Unscrew the showerhead and submerge it in undiluted bleach for 30 min. Remove it from the bleach and rinse before screwing it back on the shower tap.
4. **Replace Showerhead with One that Produces Fat Streams and Not a Mist.** NTM cells are concentrated in aerosol droplets (Parker et al., 1983). Many “low-flow” showerheads produce a fine mist that contains droplets with high numbers of NTM; small enough to enter the alveoli. Replace such a “low flow” or misting showerhead with one that has large holes (greater than 1 mm diameter).
5. **Beware of Granular Activated Carbon/Charcoal (GAC) Water Filters.** GAC filters are widely marketed and sold directly to consumers to reduce the bad taste of drinking water. They work by binding chlorine. other disinfectants, metals, and organics that impart a bad taste to water. However, they promote the growth of NTM without preventing their passage, as shown in an EPA study (Rodgers et al., 1999). The pores of GAC filters are not small enough to prevent bacterial passage; the tortuous path of movement merely delays passage for a while. NTM are quite happy in GAC filters; they attach and grow on the carbon-bound organics and metals as they are resistant to the disinfectant. The manufacturer’s recommendation for replacement of the filters is based on the capacity to remove disinfectants, metals, and organics; not on preventing passage of bacteria. In our hands, the recommended time to replace a GAC filter is longer than the time when high NTM numbers pass the filter. If you want to remove disinfectants, metals and organics from drinking water, install a GAC filter upstream of a 0.2 micrometer filter.
6. **Don’t Drink Water or Use Ice from a Refrigerator.** Many refrigerators come with outside taps for chilled water and ice. Don’t use them as high numbers of NTM are in refrigerator tap water and ice. In one instance, the DNA fingerprint of the isolates from the refrigerator tap water were identical to those of a patient who drank the water (Falkinham, 2011). The tap water coming into the refrigerator collects in a large reservoir and the warmth of the machinery warms the water (before cooling), so the reservoir has lots of NTM. Use ice-trays and bottles that are filled with boiled (10 min) or 0.2 micrometer-filtered water if you want cold water.
7. **Humidifiers: A Big Problem.** Humidifiers, whether small room-size or whole house HVAC systems, transfer water to air. They can also transfer microorganisms, especially NTM, *Legionella pneumophila*, and *Pseudomonas aeruginosa*. Transferring NTM from water to air is the problem. Humidity helps breathing, but it exposes one to NTM-laden aerosols. As humidifiers come in two sizes, room and house-size with different considerations, they will be dealt with separately.

**Room-Size Humidifiers**. Small, room-size humidifiers can generate aerosols with high numbers of NTM; even from reservoir water containing relatively low numbers of NTM (500 CFU/mL). In particular, the new ultrasonic humidifiers generate a high density aerosol mist that are rich in NTM (Hamilton and Falkinham, 2018). If you need to humidify your air (especially during winter), only use a room evaporative humidifier. Evaporative humidifiers boil water and the mist is blown by a fan or simply rises. Boiling will kill any NTM or bacterial cells and thereby be relatively free of NTM. The ultrasonic humidifiers do not heat the water, but use ultrasonic vibration to produce aerosol droplets. If a room-size humidifier blows water through a wetted filter (called an evaporative humidifier), don’t use it as the water wetting the filter will have NTM that can be aerosolized.

Remember that NTM will grow in biofilms in the humidifier’s water reservoir. Therefore, scrub the surface of the reservoir before refilling to reduce the number of NTM and other waterborne pathogens in the biofilm. I suggest you use a bathroom scrubbing agent. You can even disinfect the reservoir by adding Clorox® (1 cup to 10 cups water) for 30 min. Then be sure to rinse repeatedly until you can’t smell the chlorine before use.

**Household-Size Humidifiers (HVAC).** In an on-going study of NTM-patients in Philadelphia (the same hospital and area where the elderly, slender women were first identified at risk for NTM pulmonary disease), our colleagues at the Lankenau Medical Research Institute (led by Dr. Leah Lande) discovered that all the NTM-infected women have whole house humidifiers that are simple fabric or plastic woven filters with a channel above with holes for tap water to drip down through the filter. Those systems are like the “swamp coolers” used in the desert southwest to cool homes. The wet filter cools the air during passage. However, NTM adhere to the filter material where they grow and are transferred the household air that is drawn through the filter. Such house-size humidifiers are difficult, if not impossible to disinfect. Theoretically, if the incoming water to the filter was sterilized by 0.2 micrometer filtration or ultraviolet (UV) irradiation, the filter was disinfected regularly like a showerhead, the duct work leading in and out of the humidifier throughout the whole house was free of NTN, and the incoming air was free from outside dust, the humidified air would be relatively free from NTM.

**Room- Versus House-Size Humidifiers.** I prefer the room-size as they are portable and easier to clean (biofilm-removal) and disinfect (Clorox®). Successful employment of a whole house humidification system requires disinfection of the existing ductwork, a daunting task.

1. **Avoid Dusts from Potting Soils.** Commercial potting soil is rich in peat and peat harbors very high numbers of NTM (1 million per gram). As peat or potting soil dries, the dust generated has high numbers of NTM.  In a study of pulmonary NTM patients, we found that a proportion (who were gardeners) had been infected from their potting soil (DeGroote et al., 2006). When gardening use a pharmacy-purchasable mask (Type N95) to avoid dust inhalation.
2. **Ultraviolet (UV) Light Disinfection.** There are a number of companies manufacturing and selling whole house or single tap devices to kill microorganisms in drinking water with UV light. Although the results are mixed, it appears NTM may be more resistant to UV compared to *Escherichia coli*, the standard; perhaps a 5-fold higher dosage is needed to kill 99.9 % of NTM cells than to kill *E. coli*. If a UV system can provide at least a 5-fold higher dosage (the combination of UV light strength and duration of exposure), it will kill NTM. However, UV will only kill cells that pass by the UV-lamp. UV-will not kill cells in biofilms. Further, UV only kills cells that are exposed in the dark. In the presence of light NTM cells, like other bacteria, can repair the damage (called photoreactivation), thus reversing the killing.
3. **Pink Slime and NTM.** Recently, by reading the article of Feazel et al. (2009) on NTM in showerheads, we discovered that whenever a biofilm sample had salmon pink-pigmented bacteria (*Methylobacterium*), there were no NTM. Based on that information, we looked closely at the water in our Philadelphia M. avium patient household data and confirmed that if Methylobacterium were present, Mycobacterium were absent (Falkinham et al., 2016). Further work documented that a biofilm of *Methylobacterium* spp. cells prevented the adherence of *M. avium* cells and a M. avium biofilm prevented *Methylobacterium* spp. adherence (Munoz-Egea et al., 2017). Evidently, the two cannot coexist in biofilms. Taps or showerheads in a home with NTM don’t have *Methylobacterium*. As not all taps or showerheads in a home will have NTM, use those that show evidence of a pink scum or film; the pink scum will be seen on shower curtains, shower walls, or in crevasses in a shower or sink. As killed *Methylobacterium* spp. cells can inhibit *M. avium* or *M. abscessus* adherence, I need to initiate a project to identify the cellular *Methylobacterium* spp. component is sufficient to inhibit *M. avium* adherence and produce that for premise plumbing and medical equipment.

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