NTM* and Gram negative pathogens

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*Non-tuberculous mycobacteria

Outline

- Definitions
- Modes of Transmission
- Organisms of concern
- Pseudomonas
- Acinetobacter
- NTMs

Scenario 2..case continued

- Your IP director, reassures you that there have been no known cases of **Legionella** in your facility.
- However, she did notice that there's been a higher than usual number of cultures returning with **non-tuberculous mycobacteria**, specifically **M. avium intracellulare**.
- You both decide to look into this further..

Scenario: Increased number of cultures

- Since moving into the new hospital in 2014, patient volumes have increased and so has the size of the lung transplant program
- Pre and post transplant, bronchoscopy with BAL and/or wash
- Routine specimens sent to the lab:
  - In 2016, Mycobacterium avium-intracellulare complex noted at an increased rate compared to the old hospital
  - Cases are investigated and potential sources are identified
- Where are the NTMs coming from? Are they related?

Water-associated pathogens

- Water-based*:
  - naturally inhabit water and grow in water systems
  - i.e. *Legionella* spp causing Legionnaire's disease
- Waterborne*:
  - Can be transmitted via contamination of drinking water
  - Monitoring of fecal pathogens
  - Preventable via chemical treatment of drinking water
  - i.e. E.coli → gastroenteritis
- Water-related:
  - pathogens associated with a vector that requires water as part of its life cycle
  - i.e dengue via mosquitoes and schistosomiasis via snails

- Often used interchangeably in the literature

Gamage et al. ID Clin NA 2016

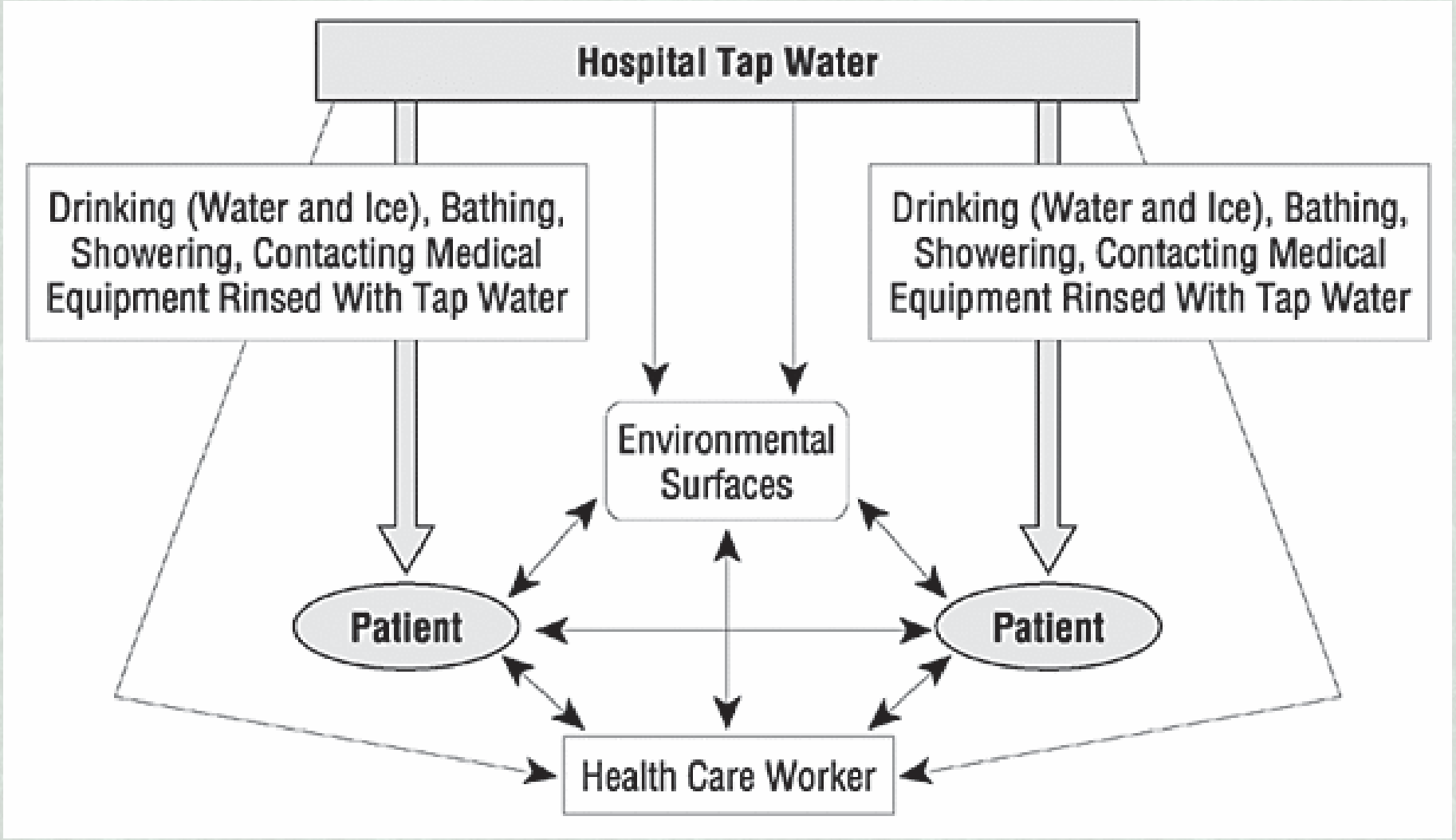
Water-based pathogens

- Also known as “opportunistic premise plumbing pathogens”
- Legionella spp, Pseudomonas aeruginosa & NTM
- Found in natural bodies of water & building water supply
- Not routinely monitored
- Key factors:
  - Disinfection resistant
  - Biofilm formation
  - Survival in free living amoeba
  - Growth at low O2 concentrations
  - Growth at low levels of organic carbon

Falkinham III Waterbased pathogens 2015

The pathogenesis: a proposed model

Biofilm →Subsequent contamination or exposure via tap water

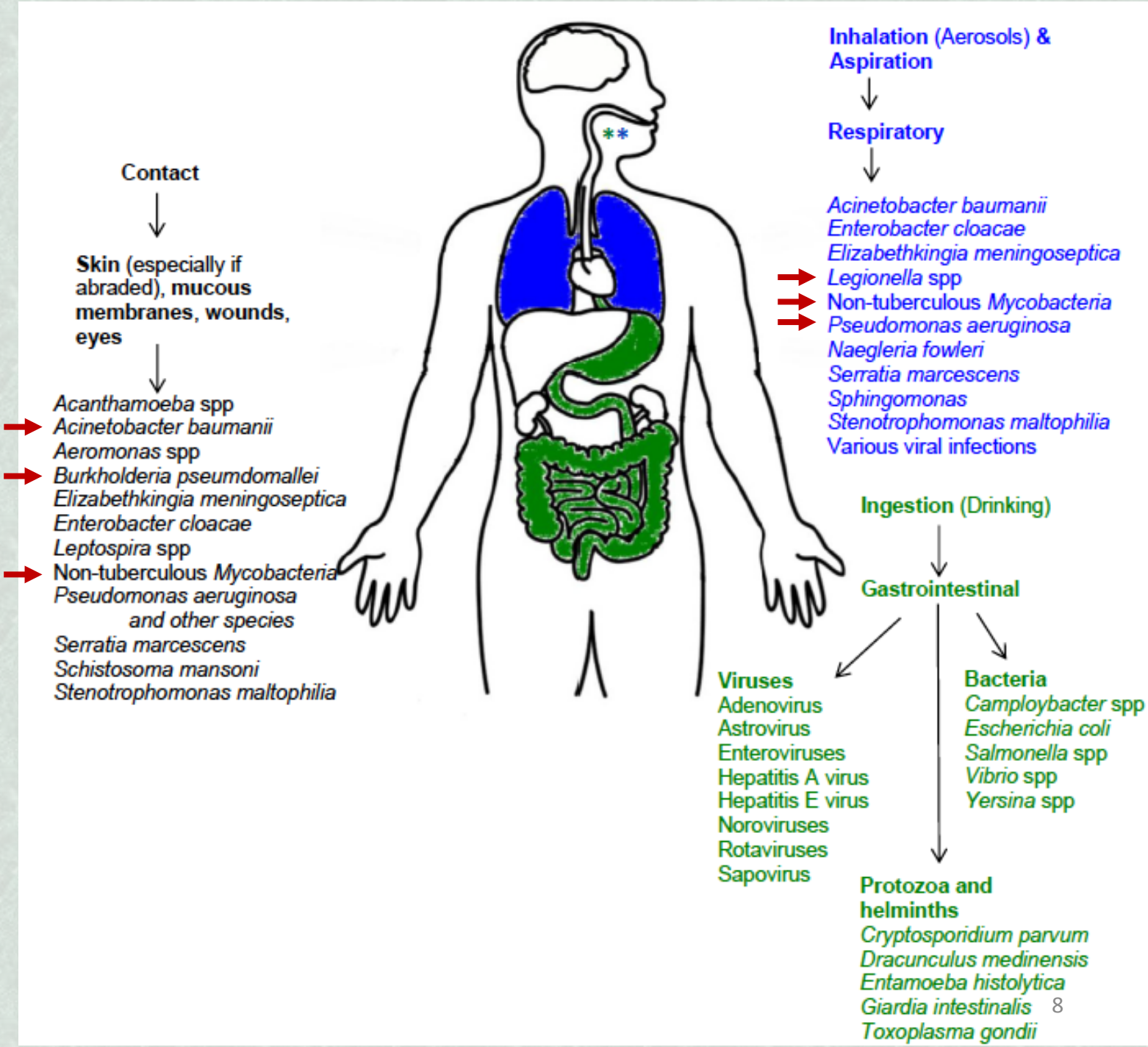


Anaissie, E. J. et al. Arch Intern Med 2002;162:1483-1492.
Slide courtesy of Dr. Trish Perl

Modes of Transmission

- Contact:
  - Direct: skin, wounds, mucous membranes
  - Indirect: medical device
- Inhalation of aerosols & aspiration
  - Respiratory infections
- Ingestion:
  - Gastrointestinal
  - Drinking or contaminated ice

Gamage et al. ID Clin NA 2016



Organisms of Concern (not all-inclusive)

Gram-negatives

- *Legionella* spp
- *Pseudomonas aeruginosa &* spp
- *Burkholderia cepacia*
- *Stenotrophomonas maltophila*
- *Sphingomonas spp*
- *Acinetobacter spp*
- *Serratia marcescens*

Non-tuberculous mycobacteria (NTM)

- Mycobacterium abscessus
- M.chimaera
- M. avium-intracellulare
- M.chelonae

Pseudomonas aeruginosa

- Gram negative aerobic bacteria
- Pseudomonas:
  - ~51,000 HAIs per year
  - 6000 Multi drug resistant
  - 400 deaths per year (2013)
- ~1400 deaths per year from waterborne nosocomial pneumonia (2014)

- Transmission:
  - contact with water,
  - Aspiration
  - transferred from HCW hands
- Clinical syndromes:
  - skin & soft tissue infections
  - Pulmonary (incl CF)
  - Bacteremia
  - Urinary tract infections

Gamage et al. ID Clin NA 2016

Pseudomonas aeruginosa & other spp

- Sources:
  - Potable tap water
  - Distilled water
  - Hydrotherapy pools & whirlpool spas
  - Dialysis water
  - Endoscopes
- Population at risk:
  - ICU patients
  - Burns
  - Cystic Fibrosis
  - Transplant (solid and liquid)
  - Malignancy—especially leukemia/lymphoma

Pseudomonas aeruginosa outbreak in a NICU

- June 2013-Sept 2014: 31 cases identified in a 28-bed NICU
- 42 environmental samples, 67% with Pseudomonas
- Case clusters temporally associated with LACK of point of use filters on faucets in patient rooms
- Cases:
  - room without POU filter (OR 37.55)
  - Exposure to PICC lines (OR 7.2)
  - Invasive ventilation (OR 5.79)
- PFGE from 2 cases indistinguishable
- Conclusion: Hospital water contaminated and lack of POU filter allowed for patient exposure

Bicking et al ICHE 2017 Jul; 38(7):801-808

P. aeruginosa SICU point of use filters

- 2 years: Infections due to *P.aeruginosa* in a SICU.
- Baseline testing of tap water: persistent colonization of all ICU water taps with a single *P. aeruginosa* clonotype.
- Intervention: Disposable point-of-use water filters in ICU faucets; changed in weekly and later, 2-week intervals.
- Findings:
  - Mean monthly rate (+/-SD) of *P. aeruginosa* infection/colonization episodes was 3.9 +/- 2.4 in the prefilter and 0.8 +/- 0.8 in the postfilter period.
  - *P. aeruginosa* colonizations were reduced by 85% (P < .0001) and invasive infections by 56% (P < .0003) in the postfilter period.
  - Microbiologic examinations of tap water revealed growth of *P. aeruginosa* in 113 of 117 (97%) samples collected during the prefilter period, compared with 0 of 52 samples taken from filter-equipped taps.

Trautmann et al AJIC 2002 (35) 86-9.

Acinetobacter spp

- Gram negative aerobic bacteria
- 2009-2010: ~1500 HAIs in >2000 hospitals
- ~7300 cases with drug-resistant Acinetobacter of which 500 deaths/year
- 151 outbreaks 2000-2015; 47% mortality

- Transmission:
  - Inhalation & aspiration
  - Contact
  - Contaminated surfaces
    - ICU, ventilators
  - Health Care Workers
    - Found 4-33% of HCW hands
    - Transfer of epidemic strain reported
- Dry surfaces: survival ~26-27 days

CDC HICPAC Envt Inf Control Health care facilities 2003
Gamage et al. ID Clin NA 2016
Wieland et al. AJIC. 2018(46):6, 643-648

Acinetobacter spp

Clinical Syndromes:

- Pneumonia
- Intracranial infections (trauma or neurosurg procedures)
- Mediastinitis
- Device associated infections
- Skin & soft tissue infections
- Bacteremia

Sources:

- Medical equipment with moisture
  - Humidifiers, ventilators
- Water bath
- Tub immersion
- Faucet aerators
- Dental unit water lines
- High touch surfaces

CDC Guidelines for Environmental Infection Control in Health-care Facilities, 2003

Table 13. Other gram-negative bacteria associated with water and moist environments

Bacteria	Implicated contaminated environmental vehicle
Burkholderia cepacia	• Distilled water [527] • Contaminated solutions and disinfectants [528, 529] • Dialysis machines [527] • Nebulizers [530–532] • Water baths [533] • Intrinsically-contaminated mouthwash [534] (This report describes contamination occurring during manufacture prior to use by the health-care facility staff. All other entries reflect extrinsic sources of contamination.) • Ventilator temperature probes [535]
***Stenotrophomonas maltophlia, Sphingomonas* spp.**	• Distilled water [536, 537] • Contaminated solutions and disinfectants [529] • Dialysis machines [527] • Nebulizers [530–532] • Water [538] • Ventilator temperature probes [539]
Ralstonia pickettii	• Fentanyl solutions [540] • Chlorhexidine [541] • Distilled water [541] • Contaminated respiratory therapy solution [541, 542]
Serratia marcescens	• Potable water [543] • Contaminated antiseptics (i.e., benzalkonium chloride and chlorhexidine) [544–546] • Contaminated disinfectants (i.e., quaternary ammonium compounds and glutaraldehyde) [547, 548]

Clinical Infectious Diseases

INVITED ARTICLE

HEALTHCARE EPIDEMIOLOGY: Robert A. Weinstein, Section Editor

Healthcare Outbreaks Associated With a Water Reservoir and Infection Prevention Strategies

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Hospital water may serve as a reservoir of healthcare-associated pathogens, and contaminated water can lead to outbreaks and severe infections. The clinical features of waterborne outbreaks and infections as well as prevention strategies and control measures are reviewed. The common waterborne pathogens were bacteria, including *Legionella* and other gram-negative bacteria, and nontuberculous mycobacteria, although fungi and viruses were occasionally described. These pathogens caused a variety of infections, including bacteremia and invasive and disseminated diseases, particularly among immunocompromised hosts and critically ill adults as well as neonates. Waterborne outbreaks occurred in healthcare settings with emergence of new reported reservoirs, including electronic faucets (*Pseudomonas aeruginosa* and *Legionella*), decorative water wall fountains (*Legionella*), and heater-cooler devices used in cardiac surgery (*Mycobacterium chimaera*). Advanced molecular techniques are useful for achieving a better understanding of reservoirs and transmission pathways of waterborne pathogens. Developing prevention strategies based on water reservoirs provides a practical approach for healthcare personnel.

Keywords. waterborne outbreaks; healthcare-associated infections; water; outbreaks.

CID 2016;62(11):1423-35

Water & point of use fixture outbreaks

Table 15. Water and point-of-use fixtures as sources and reservoirs of waterborne pathogens*

Reservoir	Associated pathogens	Transmission	Strength of evidence+	Prevention and control	References
Potable water	*Pseudomonas*, gram-negative bacteria, NTM	Contact	**Moderate:** occasional well-described outbreaks.	Follow public health guidelines.	(See Tables 12–14)
Potable water	Legionella	Aerosol inhalation	**Moderate:** occasional well-described outbreaks.	Provide supplemental treatment for water.	(See Table 11)
Holy water	Gram-negative bacteria	Contact	**Low:** few well-described outbreaks	Avoid contact with severe burn injuries. Minimize use among immunocompromised patients.	665

CDC HICPAC Envt Inf Control Health care facilities 2003

Reservoir	Associated pathogens	Transmission	Strength of evidence+	Prevention and control	References
Dialysis water	Gram-negative bacteria	Contact	**Moderate:** occasional well-described outbreaks.	Dialysate should be ≤2,000 cfu/mL; water should be ≤200 cfu/mL.	2, 527, 666– 668
Automated endoscope reprocessors and rinse water	Gram-negative bacteria	Contact	**Moderate:** occasional well-described outbreaks.	Use and maintain equipment according to instructions; eliminate residual moisture by drying the channels (e.g., through alcohol rinse and forced air drying).	669–675
Water baths	Pseudomonas, Burkholderia, Acinetobacter	Contact	**Moderate:** occasional well-described outbreaks.	Add germicide to the water; wrap transfusion products in protective plastic wrap if using the bath to modulate the temperature of these products.	29, 533, 676, 677
Tub immersion	Pseudomonas, Enterobacter, Acinetobacter	Contact	**Moderate:** occasional well-described outbreaks.	Drain and disinfect tub after each use; consider adding germicide to the water; water in large hydrotherapy pools should be properly disinfected and filtered.	678–683
Ice and ice machines	NTM, Enterobacter, Pseudomonas, Cryptosporidium Legionella	Ingestion, contact	**Moderate:** occasional well-described outbreaks. **Low:** few well-described outbreaks	Clean periodically; use automatic dispenser (avoid open chest storage compartments in patient areas).	601, 684–687

Faucet aerators	Legionella	Aerosol inhalation	**Moderate:** occasional well-described outbreaks.	Clean and disinfect monthly in high-risk patient areas; consider removing if additional infections occur.	415, 661
Faucet aerators	Pseudomonas, Acinetobacter, Stenotrophomonas, Chryseobacterium	Contact, droplet	**Low:** few well-described outbreaks	No precautions are necessary at present in immunocompetent patient-care areas.	658, 659, 688, 689
Sinks	Pseudomonas	Contact, droplet	**Moderate:** occasional well-described outbreaks.	Use separate sinks for handwashing and disposal of contaminated fluids.	509, 653, 685–693
Showers	Legionella	Aerosol inhalation	**Low:** few well-described outbreaks	Provide sponge baths for hematopoietic stem cell transplant patients; avoid shower use for immunocompromised patients when Legionella is detected in facility water.	656
Dental unit water lines	Pseudomonas, Legionella, Sphingomonas, Acinetobacter	Contact	**Low:** few well-described outbreaks	Clean water systems according to system manufacturer's instructions.	636, 694–696
Ice baths for thermodilution catheters	Ewingella, Staphylococcus	Contact	**Low:** few well-described outbreaks	Use sterile water.	697, 698

Reservoir	Associated pathogens	Transmission	Strength of evidence+	Prevention and control	References
Decorative fountains	Legionella	Aerosol inhalation	**Low:** few well-described outbreaks	Perform regular maintenance, including water disinfection; avoid use in or near high-risk patient-care areas.	664
Eyewash stations	Pseudomonas, amoebae, Legionella	Contact	**Low:** few well-described outbreaks **Minimal:** actual infections not demonstrated.	Flush eyewash stations weekly; have sterile water available for eye flushes.	518, 699, 700
Toilets	Gram-negative bacteria	n/a	**Minimal:** actual infections not demonstrated.	Clean regularly; use good hand hygiene.	662

CDC HICPAC Envt Inf Control Health care facilities 2003

Non-tuberculous mycobacteria (NTM)

- Acid-fast bacilli, >150 species
- Opportunistic water- and soil-borne pathogens
- Known to flourish in drinking water, plumbing despite disinfectants & heat
  - Contaminated Ice, rinsing equipment with tap water
- Wide range of infections depending on the organism
  - Pulmonary disease
  - Skin, soft tissue & bone infections (including surgical site infections)
  - Cervical Lymph node involvement
  - Disseminated in immunocompromised host
- >180,000 cases pulmonary NTM in 2014

NTM characteristics

- Lipid-rich outer membrane with long-chain fatty acids
- Resistant to disinfectants
  - 20-100x more R to Chlorine
  - Slow growers >fast growers
- Thrive at air-water surface of biofilm, ready for aerosolization
- Hardiness:
  - Wide pH range 4-9
  - Growth at low O2 concentrations (as low as 6%, albeit slower)

Table 1. The double-edged sword of the lipid-rich outer membrane of the NTM

Advantage	Attribute	Disadvantage
Surface adherence	Hydrophobic surface	Few cells in suspension
Air:water concentration		
Disinfectant resistance		Impermeable to nutrients
Antibiotic resistance		
Readily aerosolized		Slow growth
Hydrophobic surface	Mycolic lipid synthesis	Diversion of resources
Impermeable	Thick lipid membrane	Reduced transport/export

Falkinham III. Clin micro newsletter 38:1, 2016

Temperature & NTMs

- Thermophilic, temp >45C
  - M.xenopi
  - M.smegmatis
  - M.avium*
- Time required to kill 90% of M.avium
  - 4 min at 60C (140F)
  - 54 min at 55C (131F)
  - >16 hours at 50C (122F)

- Non-thermophilic (cold water systems)
  - M.kansasii
  - M.gordonae
  - M.fortuitum
  - M.chelonae
  - M.abscessus
  - M.mucogenicum

*M.avium can grow in hot-water and cold-water systems

Squier C et al. Current ID reports 2000, 2: 490-496

Reservoirs of NTM

- Ubiquitous in soil & bodies of water
- Thrive when other microorganisms killed after disinfection
- Devices:
  - Showerheads: most heavily colonized with NTM
  - Faucets (especially with aerators)
  - Ice dispensers
  - Humidifiers
  - Hot tubs
- Municipal water supply in 83% of dialysis centers in US colonized

Table 2. Sources of NTM

• Soils and dust from soils
• Natural water in lakes, rivers, streams, swamps
• Drinking water distribution systems
• Plumbing in houses, hospitals, condominiums, and apartments
• Aerosols from humidifiers in households, hospitals, condominiums, and apartments
• Water and ice from refrigerators

1. Squier C et al. Current ID reports 2000, 2: 490-496
2. Carson LA et al. Prev of NTM in water supplies of HD centers. Appl Environ Microbiol, 1998, 54:3122-3125

NTM Pseudo-outbreaks

- High rates of colonization → no clinical symptoms
- Bronch/Endoscopy: tap water irrigating site or rinsing off tip; improper reprocessing of instruments (with tap water)
- Ingestion of contaminated ice or water and subsequent sputum specimen + for NTM

Table 14b. Pseudo-outbreaks

Pathogen	Vehicles associated with pseudo-outbreaks
Mycobacterium chelonae	• Potable water used during bronchoscopy and instrument reprocessing [610]
Mycobacterium fortuitum	• Ice [607]
Mycobacterium gordonae	• Deionized water [611] • Ice [603] • Laboratory solution (intrinsically contaminated [625] • Potable water ingestion prior to sputum specimen collection [626]
Mycobacterium kansasii	• Potable water [627]
Mycobacterium terrae	• Potable water [608]
Mycobacterium xenopi	• Potable water [609, 612, 627]

CDC HICPAC Envt Inf Control Health care facilities 2003

NTM infections or colonization

Table 14a. Infections or colonizations

Pathogen	Vehicles associated with infections or colonizations
Mycobacterium abscessus	• Inadequately sterilized medical instruments [613]
Mycobacterium avium complex (MAC)	• Potable water [614–616]
Mycobacterium chelonae	• Dialysis, reprocessed dialyzers [31, 32] • Inadequately-sterilized medical instruments, jet injectors [617, 618] • Contaminated solutions [619, 620] • Hydrotherapy tanks [621]
Mycobacterium fortuitum	• Aerosols from showers or other water sources [605, 606] • Ice [602] • Inadequately sterilized medical instruments [603] • Hydrotherapy tanks [622]
Mycobacterium marinum	• Hydrotherapy tanks [623]
Mycobacterium ulcerans	• Potable water [624]

CDC HICPAC Envt Inf Control Health care facilities 2003

NTM prevalence in hospital water supply

- Southern Alberta, surveillance x 3 years (2009-2012)
- 15 different sampling sites with 52 samples at entry and 183 endpoint
  - 106/183 (58%) positive for NTM
  - All 15/15 surveillance sites were positive at some point
- Two main species:
  - M.gordonae and/or M.avium found
- Positive cultures due to distal end contamination since water on entry to facility was culture negative.

Crago B et al. J Hospital Infection 87(2014): 59-62.

M.abscessus Hospital outbreak

- Jan 2013-July 2013: baseline, 0.7/10,000 patient days
- Aug 13-May 14: phase 1 of outbreak, 3/10,000 pt days
  - 36/71 (51%) lung transplant patients, + respiratory culture
  - → Tap water eliminated and rates→ down to baseline
- Dec 2014-June 2015: phase 2
  - 12/24 (50%) of cardiac surgery patients with invasive infections
  - →Intensified disinfection protocol; Sterile water protocol for Heater-cooler devices and patient care.
- Molecular analysis indicated 2 clonal strains of M. abscessus

Baker et al. Two-phase Hospital associated outbreak of M.abscessus: Investigation & Mitigation. CID 2017;64 (1 April)

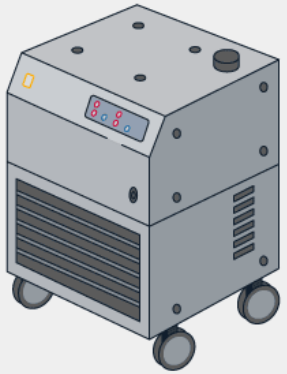
M.chimaera & heater-cooler devices (HCDs)

- >250K cardiac bypass procedures done annually
- In 2016, FDA/CDC issued safety communication: heater-cooler devices associated with infection
- 339 medical device reports (2010-2016)
  - 99 Facilities, 5 different manufacturers
  - US: 154; Outside of US: 185
  - 107 reports of infection (86 patients); 232 reports of HCD contamination (no infection)
  - Latency of up to 60 months
- Possible sources: Contaminated water/ice

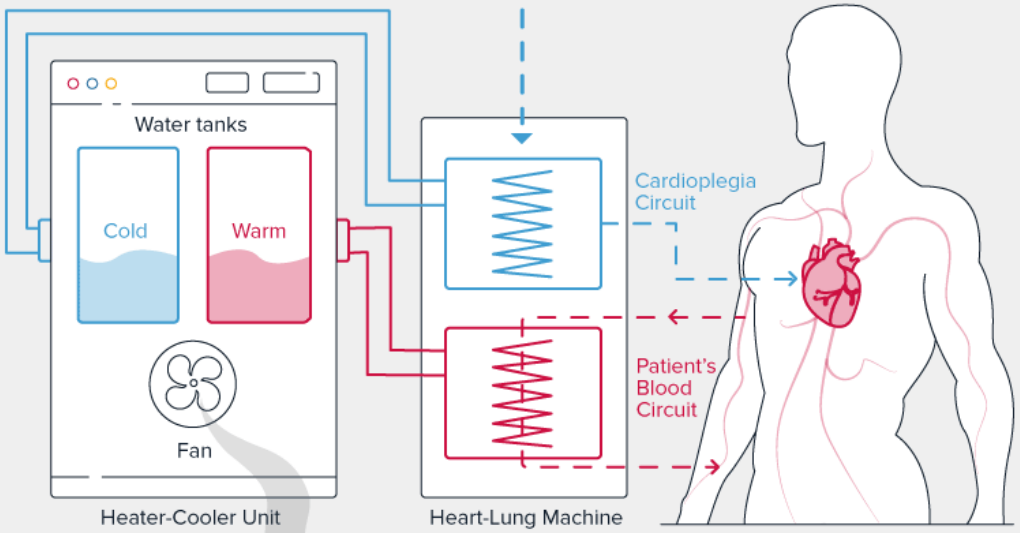
Allen et al. Ann Thorac Surg 2017;104:1237–42

3T HEATER-COOLER UNITS

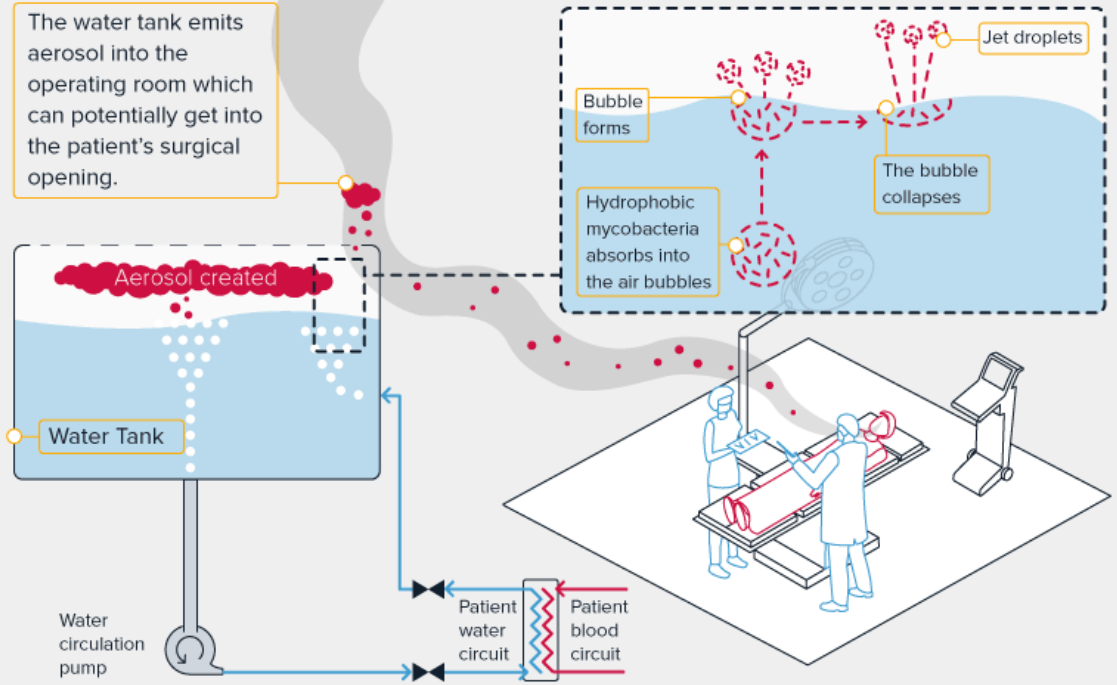
and the Potential Risk of NTM Infections



HOW THE DEVICE WORKS



OPERATING ROOM CONTAMINATION



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Biofilm noted

Fig 2. Inside a heater-cooler device (LivaNova/Sorin Stöckert 3T, Munich, Germany) demonstrating biofilm formation in the plastic tubing (ie, discoloration) despite cleaning per manufacturer recommendations.

Table 4. Number of MDR Reports by Type of Organism

Type of Organism	Number of MDR Reports
NTM total	253
Mycobacterium chimaera	59
Mycobacterium abscessus	25
Mycobacterium avium complex (includes *M. avium*, *M. intracellulare*, *M. avium-intracellulare*)	32
Mycobacterium fortuitum	6
Mycobacterium mucogenicum	5
Mycobacterium kansasii	1
Mycobacterium llatzerense	2
Mycobacterium (unspecified)	75
NTM/atypical mycobacterium	48
Acid fast bacilli + unspecified	3
Pseudomonas aeruginosa	8
Unidentified organism	41[a]
Bacteria (unidentified coliform-HPC)	35
Cupriavidus pauculus	3
Legionella species	2

[a] Three MDR reports described concerns about device contamination without microbiological testing.

Note that the counts do not equal the number of Medical Device Reporting (MDR) reports, as there are cases in which multiple organisms may be identified in 1 MDR report.

HPC = heterotrophic plate count; NTM = nontuberculous mycobacteria.

Recommendations

- Devices taken out of service
- Patients notified

General Guidelines for HCDs
➢ Adhere to cleaning, disinfection, and maintenance schedules per manufacturer's device labeling.
➢ Use only sterile or filtered (0.22 µm or less) water including when making ice needed for patient cooling.
➢ Direct the HCD exhaust vent away from the surgical field.
➢ Remove from service HCDs that demonstrate biofilm formation (discoloration/cloudiness in the fluid lines/circuits), have tested positive for NTM, or have been associated with patient infection.
➢ Testing of HCDs to identify units contaminated with NTM is not recommended at this time.
➢ Hospitals should alert their local or state health departments if they have identified HCD related patient infections.
➢ Hospitals should educate healthcare providers who may care for patients exposed to HCDs regarding the signs and symptoms of NTM infections, understanding that there may be a long latency period, sometimes months to years, between exposure and infection.

Measures to halt outbreaks of waterborne HAI

- Repair of water systems
- Disinfection of water distribution systems including tanks
- Water system maintenance programs
  - Entire water systems
  - Monitoring of faucets, other end points (ice machines)
- Avoidance of tap water (especially advocated for immunosuppressed patients)
- Restriction of equipment to water system until immediately before use
- Cleaning of equipment in contact with tap water

Scenario: Increased number of cultures

- Since moving into the new hospital in 2014, patient volumes have increased and so has the size of the lung transplant program
- Pre and post transplant, bronchoscopy with BAL and/or wash
- Routine specimens sent to the lab:
  - In 2016, Mycobacterium avium-intracellulare complex noted at an increased rate compared to the old hospital
  - Cases are investigated and potential sources are identified
- Where are the NTMs coming from? Are they related?

Scenario

- Even accounting for patient volumes, increased number of positive cultures is significant
- Predominantly seen in Lung transplant population
- Decision to culture Operating room ice machine, bronchoscopes, medivators (filters) and faucets in CV ICU
- Faucets have biofilm visible
- Multiple NTMs identified: MAI, M.abscessus, M.immunogenum

Investigation: outbreak vs pseudo-outbreak

- Most patients not symptomatic or on treatment.
- Ice machine: cleaned, filters changed
- Sterile water recommendations to patients s/p lung transplant
- Medivator: filter contaminated with tap water
- Water management team

Conclusions

- Infections due to NTMs, Legionella and other Gram-negatives associated with significant morbidity & mortality
- Temperature & Disinfectant—may not inhibit growth
- Biofilm is key to all these pathogens longevity in water systems
- Stagnation facilitates biofilm production

Thank you

Questions?

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