

NTM

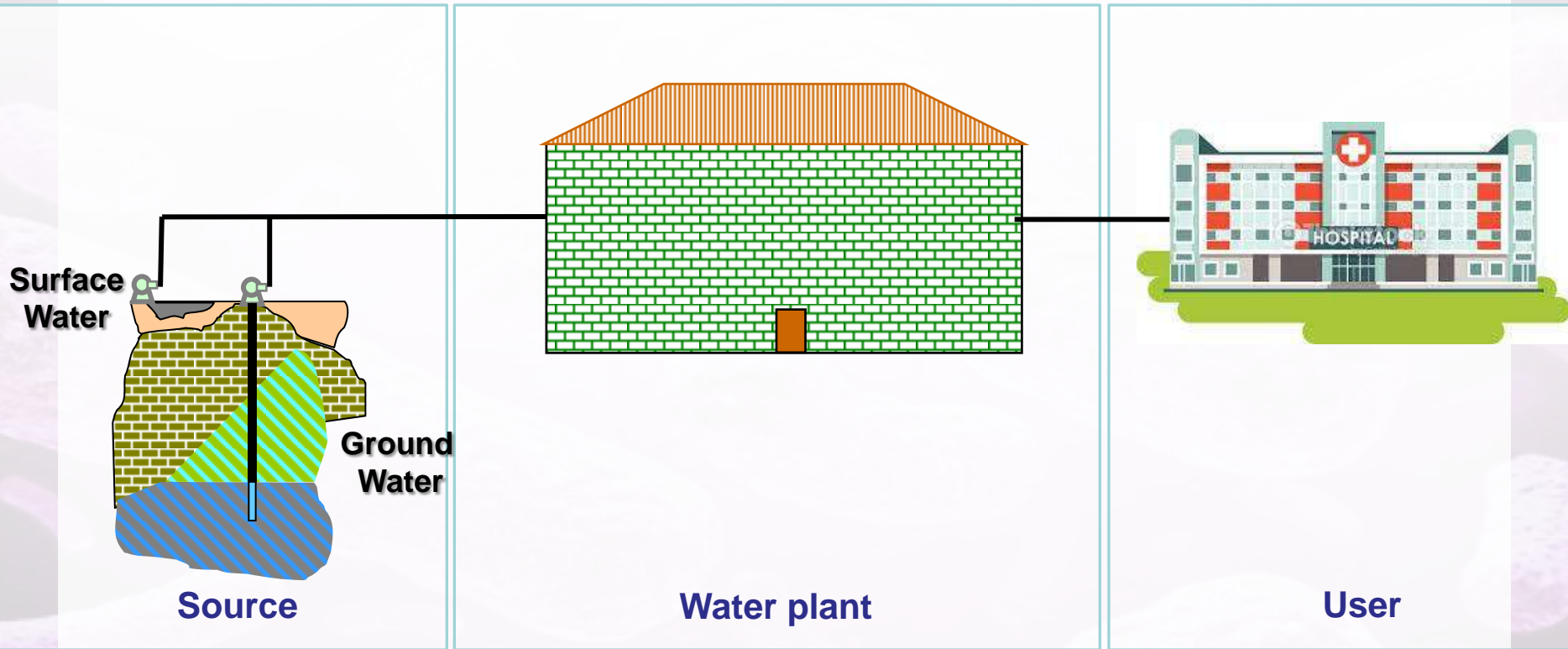
Nontuberculous Mycobacteria (NTM): Critical Updates and Strategies to Address this Emerging Hospital Waterborne Pathogen

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Virginia Tech

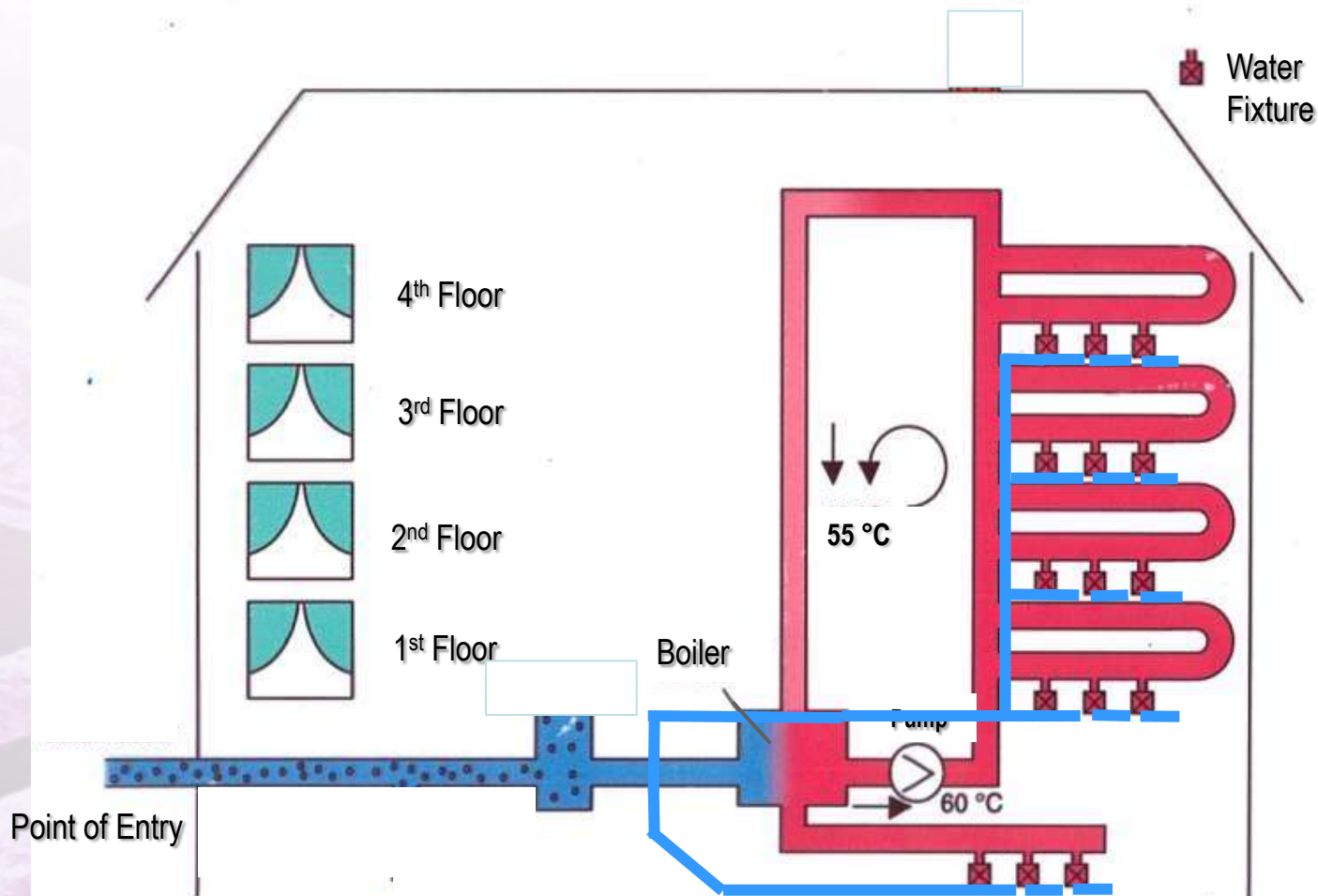
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Drinking Water Supply Chain



Water transport from source to communities

Recirculating Hot Water & Direct-Feed Cold Water Systems in Healthcare Facilities



NTM Sources - 1

- **NTM are normal inhabitants of:**
 - Drinking water distribution systems
 - premise plumbing (e.g., hospitals)
- **NTM disease linked by DNA fingerprints to:**
 - Showerheads
 - Drinking water
 - Bronchoscopes, arthroscopes
 - Disinfectant solutions

Spatial Clusters of NTM Lung Disease in US

- Seven high-risk areas of NTM lung disease encompassed 55 counties in 8 states, including parts of California, Florida, Hawaii, Louisiana, New York City, Oklahoma, Pennsylvania, and Wisconsin
- Five low-risk areas encompassed 746 counties in 23 states, Rhode Island, Minnesota, Michigan, West Virginia, and upstate New York

Am. J. Resp. Crit. Care Med. 186: 553-558 (2012)

Spatial Clusters of NTM Lung Disease in US

High Risk

Center	Counties (Radius km)	Risk
•Highlands, FL	24 (159.4)	1.9
•Santa Barbara, CA	18 (344.5)	2.0
•Montgomery, PA	5 (42.2)	2.2
•New York, NY	1 (0)	2.7
•Milwaukee, WI	1 (0)	3.6
•Kalawao, HI	3 (114.8)	3.7
•Plaquemines, LA	3 (70.2)	6.5

Am. J. Resp. Crit. Care Med. 186: 553-558 (2012)

Spatial Clusters of NTM Lung Disease in US

Low Risk

Center	Counties (Radius km)	Risk
•Washington, RI	16 (106.7)	0.5
•Iosco, MI	93 (351.4)	0.4
•Roane, WV	208 (268.5)	0.4
•Polk, MN	247 (689.7)	0.4
•Cayuga, NY	95 (289.0)	0.3

Am. J. Resp. Crit. Care Med. 186: 553-558 (2012)

NTM Sources - 2

- **NTM recovered from:**

Hot Water Heaters

Taps and Showerheads (70 % in US)

Bronchoscopes, Arthroscopes

Therapy Pools, Ice Machines

GAC Filters and Reverse Osmosis Filters

Refrigerator Taps and Ice

Humidifiers

Hospital Water Filters as *M. avium* Complex Source

- Isolation of *M. avium* or *M. intracellulare* from 75 bronchoscopy samples (Dec 2007-Feb 2009)
- Inconsistent with patient symptoms or conditions
- Water and biofilm samples collected from bronchoscopy preparation laboratory
- *M. avium*, *M. intracellulare*, *M. malmoense* isolated
- *M. avium* and *M. intracellulare* isolates from laboratory matched *rep*-PCR fingerprint patterns from bronchoscopes

J. Med. Microbiol. 59: 1198-1202 (2010)

NTM in Granular Activated Carbon (GAC) Filters

- Water with NTM poured through a silver-impregnated point-of-use GAC filter
- Input water 2.9×10^5 CFU/filter
- Sterile water (2 liters) poured through, effluent collected
- Week 3 6.6×10^7 CFU/mL effluent
- Week 5 9.4×10^7 CFU/mL effluent

J. Clin. Pathol. 52: 629 (1999)

NTM Characteristics

- Hydrophobic
- Grow in drinking water
- Disinfectant-resistant: 1,000-fold over *E. coli*
- Adhere to pipe surfaces and form biofilms
- Biofilm-grown 2 to 4-times more Cl-resistant
- Relatively heat-resistant
- Grow at low oxygen (stagnant water)
- Concentrated in aerosolized droplets

NTM are in Biofilms

Sample	Isolate	Number	Identification	rep-PCR Type
Water Samples		CFU/ml		
Cold bath	GF-W-1-1	60	<i>M. avium</i>	Type III
Hot bath	GF-W-2-1	77	<i>M. avium</i>	Type II
Cold sink	GF-W-3-1	30	<i>M. avium</i>	Type III
	GF-W-3-2	10	<i>M. Immunogenum</i>	Not Applicable
	GF-W-3-3	10	<i>M. avium</i>	Type III
Hot sink	GF-W-4-1	43	<i>M. avium</i>	Type II
Biofilm Samples		CFU/cm²		
Bath tap	GF-Sw-5-1	130,000	<i>M. avium</i>	Type I
Kitchen tap	GF-Sw-6-1	32,000	<i>M. avium</i>	Type IV

NTM Concentration in Aerosols

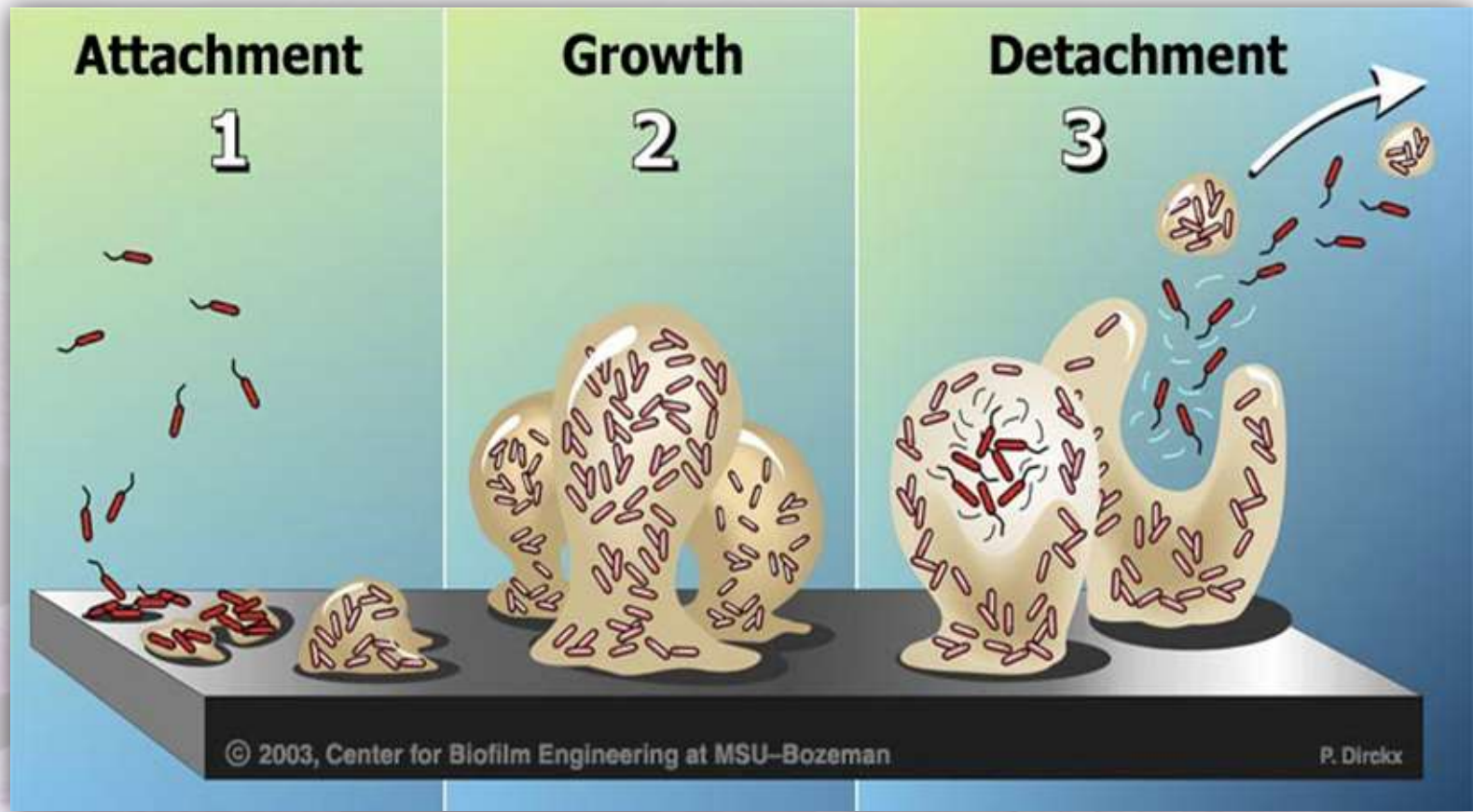
Bacterium	Aerosol Enrichment
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<i>E. coli</i>	< 10
<i>P. aeruginosa</i>	9,000 - 27,000
<i>L. pneumophila</i>	1,200 - 2,500
<i>M. avium</i>	1,400 - 9,800

Aerosol enrichment = concentration droplets/suspension

Am. Rev. Respir. Dis. 128: 652-656 (1983)

NTM are in Biofilms



Biofilm Phases

1. Particles are adsorbed to the inner surface of water pipes (conditioning)
2. Bacteria attach to the conditioned surface
3. Bacteria produce a sticky extracellular matrix & reproduce quickly
4. Biofilm increases in size and protects microorganisms within
 - » Some cells are **V**iable **B**ut **N**on **C**ulturable (**VBNC**)
5. Biofilm particles shear off under the force of water flow

Systemic Disinfection and Thermal Disinfection Effects on Biofilm

1. Disinfectant and heat attack biofilm
2. Biofilm becomes partly destroyed
 - » Cells in **VBNC** stage may survive
3. Bacterial cells return from **VBNC** to culturable stage
4. Culturable cells reproduce and form new biofilm

***M. avium* Adherence to Plumbing Surfaces**

Surface	CFU/cm²
Glass	1, 500
Stainless Steel	660
Galvanized	9,900
Copper	860
PVC	730

CFU/cm² after 3 hr exposure to 10⁵ CFU/mL

J. Appl. Microbiol 115: 908-914 (2013)

***M. abscessus* Adherence to Plumbing Surfaces**

Surface	CFU/cm²
Glass	590
Stainless Steel	570
Galvanized	70
Copper	160
PVC	150

CFU/cm² after 3 hr exposure to 10⁵ CFU/mL

J. Appl. Microbiol 115: 908-914 (2013)

Mycobacterial Biofilm Characteristics

- Lipid
- DNA
- Polysaccharide ?
- No mycobacterial genes for extracellular polysaccharide

Increased Chlorine Resistance of Suspension and Biofilm-Grown *M. avium*

	CT _{99.9} %	
Suspension	Biofilm-Grown Suspended	Biofilm-Grown in Biofilm
209	356	835

Note: *E. coli* CT_{99.9} % is 0.05

Appl. Environ. Microbiol. 72: 4007-4011 (2006)

Disruption of Biofilms

1. Disrupt biofilms to increase accessibility of disinfectants to biofilm cells
2. Biofilms composed of polysaccharide, DNA, lipids, and proteins
3. Disrupt ionic bonds with salt and hydrophobic bonds with detergent
4. Digestion/degradation of polysaccharides, DNA, lipids, and proteins with enzymes

Plumbing of hospital premises is a reservoir for opportunistically pathogenic microorganisms: a review

Williams, M.M., Armbruster, C.R., and Arduino, M.J.

Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention,
Atlanta, GA, USA; Department of Microbiology, University of Washington, Seattle, WA, USA, 2012

Conclusion:

- Several bacterial species are natural inhabitants of potable water distribution systems that are opportunistic pathogens to sensitive patients in healthcare facilities.
- Infection prevention is challenging since there is lack of understanding of the ecology, virulence and infectious does of these opportunistic infections
- Water distribution systems and equipment or services can serve as reservoirs for waterborne pathogens.

Plumbing of hospital premises is a reservoir for opportunistically pathogenic microorganisms: a review

Margaret M. Williams^{a*}, Catherine R. Armbruster^b and Matthew J. Arduino^a

^aDivision of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, GA, USA; ^bDepartment of Microbiology, University of Washington, Seattle, WA, USA

(Received 7 September 2012; final version received 6 December 2012)

Several bacterial species that are natural inhabitants of potable water distribution system biofilms are opportunistic pathogens important to sensitive patients in healthcare facilities. Waterborne healthcare-associated infections (HAI) may occur during the many uses of potable water in the healthcare environment. Prevention of infection is made more challenging by lack of data on infection rate and gaps in understanding of the ecology, virulence, and infectious dose of these opportunistic pathogens. Some healthcare facilities have been successful in reducing infections by following current water safety guidelines. This review describes several infections, and remediation steps that have been implemented to reduce waterborne HAIs.

Keywords: healthcare-associated infection; biofilm; potable water; premise plumbing; opportunistic pathogen

Introduction

Water distribution systems (WDS) and equipment or services using water can serve as reservoirs for waterborne

deficiencies, solid organ and hematopoietic transplants). The special circumstances that lead to waterborne HAI occur at the three-way intersection of non-sterile potable water, susceptible individuals, and a lapse in infection

<http://www.ncbi.nlm.nih.gov/pubmed/23327332>

NTM in Hospitals

- NTM ideally adapted to hospital plumbing
- Large surface to volume ratio in pipes
- Recirculating hot water systems
- NTM disinfectant-resistant
- Disinfection kills off competitors for nutrient
- Biofilm formation ensures persistence
- NTM-biofilms in instruments more resistant to cleaning and disinfection

Monochloramine and NTM

1. NTM resistant to monochloramine:

E. coli $CT_{99.9\%} = 73$

M. avium $CT_{99.9\%} = 581$

2. Switch from chlorine to chloramine resulted in disappearance of *Legionella pneumophila*, but increase in NTM numbers
3. Monochloramine breaks down to yield ammonia, stimulating growth in N-limited waters.
4. Nitrification produces nitrate and nitrite
5. *M. avium* grow on amino-N, ammonia, nitrate, nitrite

Risk Factors for NTM Disease

- Immunodeficiency: HIV-infection
- Immunosuppression: transplants, cancer, cancer therapy
- Genetic diseases: cystic fibrosis, α -1-antitrypsin deficiency
- Taller, slender, older women and men
- Reduced lung function: bronchiectasis, COPD

Sources of NTM Exposure

Aerosol Exposure



Ice machines



Waterborne microbes enter into the healthcare environment via:



Direct contact with water streams



Inadequately reprocessed medical devices

Hospital-Acquired NTM Infections

- Showerhead-associated
- Renal dialysis
- Kidney transplantation
- Bone marrow transplant patients
- Bacteremia following cardiovascular surgery
- Patients in ICU
- Breast infection following augmentation mammoplasty
- Pulmonary infections following bronchoscopy with contaminated bronchoscopes
- Joint infections due to NTM-contaminated arthroscopes
- Joint infection following steroid injections

Ice Machines





Ice Machine Statement from CDC

“Guidelines for Environmental Infection Control in Health-Care Facilities Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC)”

Ice Machines are a possible source of infection due to microorganism contamination

“Microorganisms may be present in ice, ice storage chests, and ice-making machines. The two main sources of microorganisms in ice are the potable water from which it is made and a transferral of organisms from hands. Ice from contaminated ice machines has been associated with patient colonization, blood stream infections, pulmonary and gastrointestinal illnesses, and pseudoinfections. Microorganisms in ice can secondarily contaminate clinical specimens and medical solutions that require cold temperatures for either transport or holding.”

Ice Machine Statement from CDC

“Guidelines for Environmental Infection Control in Health-Care Facilities Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC)”

Microorganisms associated with ice machine contamination from potable water:

- *Legionella* spp.
- **Nontuberculous mycobacteria (NTM)**
- *Pseudomonas aeruginosa*
- *Burkholderia cepacia*
- *Stenotrophomonas maltophilia*
- *Flavobacterium* spp.

Pseudo-Outbreak of “*Mycobacterium paraffinicum*” Infection and/or Colonization in a Tertiary Care Medical Center

Shu-Hua Wang, MD, MPH&TM; Preeti Pancholi, PhD; Kurt Stevenson, MD, MPH; Mitchell A. Yakrus, MS, MPH; W. Ray Butler, MS; Larry S. Schlesinger, MD; Julie E. Mangino, MD

ORIGINAL ARTICLE

Pseudo-Outbreak of “*Mycobacterium paraffinicum*” Infection and/or Colonization in a Tertiary Care Medical Center

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OBJECTIVE. To investigate a pseudo-outbreak of “*Mycobacterium paraffinicum*” (unofficial taxon) infection and/or colonization, using isolates recovered from clinical and environmental specimens.

DESIGN. Outbreak investigation.

SETTING. University-affiliated, tertiary-care hospital.

METHODS. *M. paraffinicum*, a slow-growing, nontuberculous species of mycobacteria, was recovered from 21 patients and an ice machine on a single patient care unit over a 2.5-year period. The clinical, epidemiological, and environmental investigation of this pseudo-outbreak is described.

RESULTS. Twenty-one patients with pulmonary symptoms and possible risk factors for tuberculosis were admitted to inpatient rooms that provided airborne isolation conditions in 2 adjacent hospital buildings. In addition, 1 outpatient had induced sputum cultured for mycobacteria in the pulmonary function laboratory. Of the samples obtained from these 21 patients, 26 isolates from respiratory samples and 1 isolate from a stool sample were identified as *M. paraffinicum*. Environmental isolates obtained from an ice machine in the patient care unit where the majority of the patients were admitted were also identified as *M. paraffinicum*.

CONCLUSIONS. An epidemiological investigation that used molecular tools confirmed the suspicion of a pseudo-outbreak of *M. paraffinicum* infection and/or colonization. The hospital water system was identified as the source of contamination.

Infect Control Hosp Epidemiol 2009; 30:848-853

- Ice taken from the ice machine on the same unit as the Pseudo-outbreak grew a *Mycobacterium* species on culture.
- The isolates recovered from the patients and the ice machines were conclusively identified as *M. paraffinicum* with 2 major PFGE types, which confirmed the pseudo-outbreak.
- Filters were installed on a number of ice machines on day 764. NTM species have not been isolated during any follow-up surveillance cultures from any ice machines with these filters in place.
- The water filters appear to provide an effective barrier against waterborne pathogens.

Outbreaks of NTM Infections Associated with Cardiac Surgery

- Outbreak of *Mycobacterium chimaera* infection associated with cardiac surgery (Switzerland).
- Linked to *M. chimaera* in water reservoir in heater-cooler-pump used during cardioplegia
- Outbreaks in Pennsylvania (*M. chimaera*) and North Carolina (*M. abscessus*)
- Outbreaks in United Kingdom, Australia
- FDA and ECDC Alerts
- Long lag between surgery and evidence of infection

Prolonged Outbreak of *Mycobacterium chimaera* Infection After Open-Chest Heart Surgery

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↙^a H. S., G. B., and B. H. contributed equally to this work.

↙^b E. C. B. and R. W. contributed equally to this work.



Non-tuberculous Mycobacterium (NTM) Infections and Heater-Cooler Devices Interim Practical Guidance: Updated October 27, 2015

Purpose:

CDC has identified a need for increased vigilance for NTM infections by health departments, healthcare facilities, and individual healthcare providers. [FDA recently issued a Safety Communication on Nontuberculous Mycobacterium Infections Associated with Heater-Cooler Devices](#) that addresses issues regarding the proper use and maintenance of these devices. CDC has been working with the FDA and local and state health departments to investigate heater-cooler units associated with NTM infections and/or found to be contaminated with NTM. This CDC communication is to (a) raise awareness among health departments, healthcare facilities, and healthcare providers of the possible



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Date Issued: October 15, 2015



RAPID RISK ASSESSMENT

Invasive cardiovascular infection by *Mycobacterium chimaera* potentially associated with heater-cooler units used during cardiac surgery

30 April 2015

Main conclusions and options for response

Since 2011, cases of infection caused by *Mycobacterium chimaera* have been detected in patients having previously undergone cardiac surgery in Europe (1-3).

Healthcare providers involved in caring for patients who have undergone open-heart surgery should be vigilant for cases of endocarditis or other cardiovascular infection of unidentified origin and consider testing specifically for slow-growing non-tuberculous mycobacteria such as *M. chimaera*. Regulatory bodies in charge of licensing and agencies monitoring the safety of such devices should be aware of the potential association of invasive cardiovascular infections caused by *M. chimaera* with heater-cooler units and relevant information should be disseminated to all centres performing cardiac surgery.

ECDC is maintaining vigilance for additional information that can be used to further evaluate the public health risk of invasive cardiovascular infection by *M. chimaera* associated with heater-cooler units and will update its risk assessment as new evidence is obtained.

Reducing NTM Exposure

- **Reduce Introduction of NTM:**

 - High hot water heater temperature

 - Sterilize water by heat or filtration

 - Disinfectant introduction

- **Instruments:**

 - Exposed surface scrub

 - Non-exposed surfaces have limited access

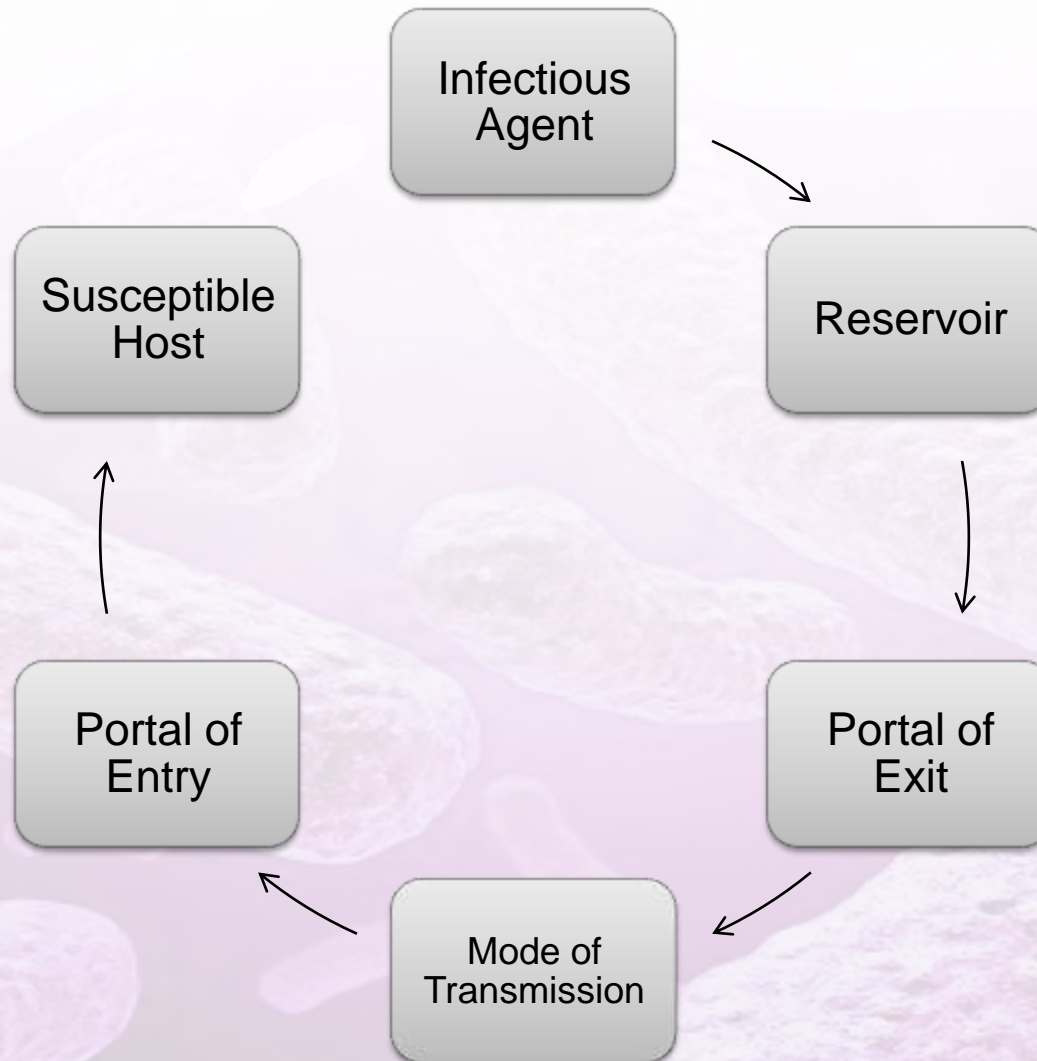
 - Biofilm disruption required for inaccessible sections

 - Disinfection efficacy limited by biofilm resistance

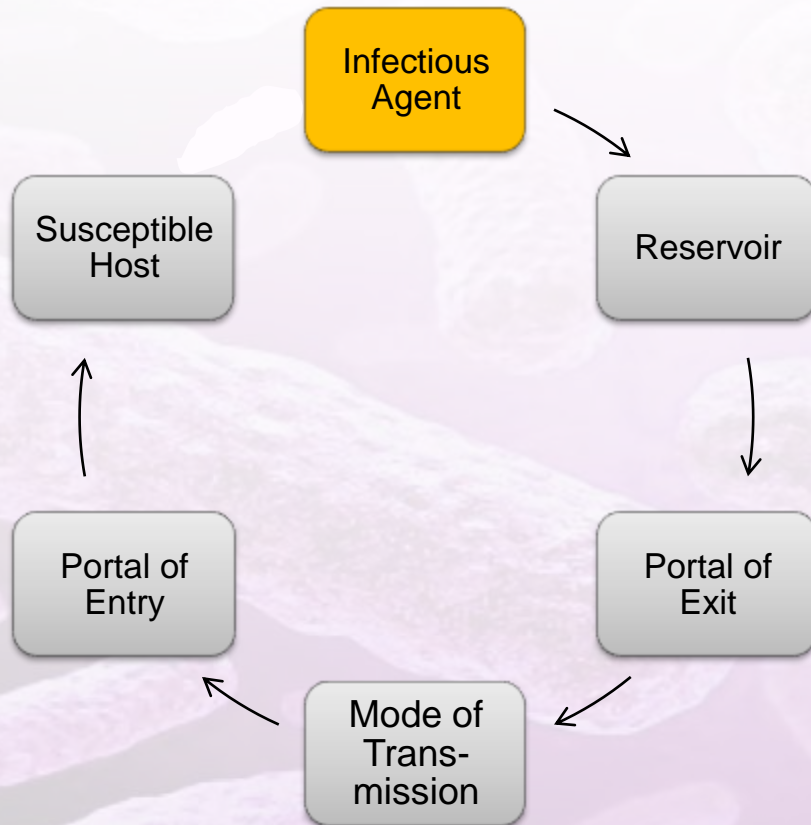
Proving Efficacy of Measures

- **Difficulty of Measuring Disinfectant Efficacy:**
 - Aggregation
 - Water-Acclimation
 - Biofilm-formation
 - Viable, but nonculturable (VBNC) ?
- **End-Point:**
 - 99.9 % killed (?)
- **Regrowth:**
 - Reappearance within 4 weeks

Chain of Infection

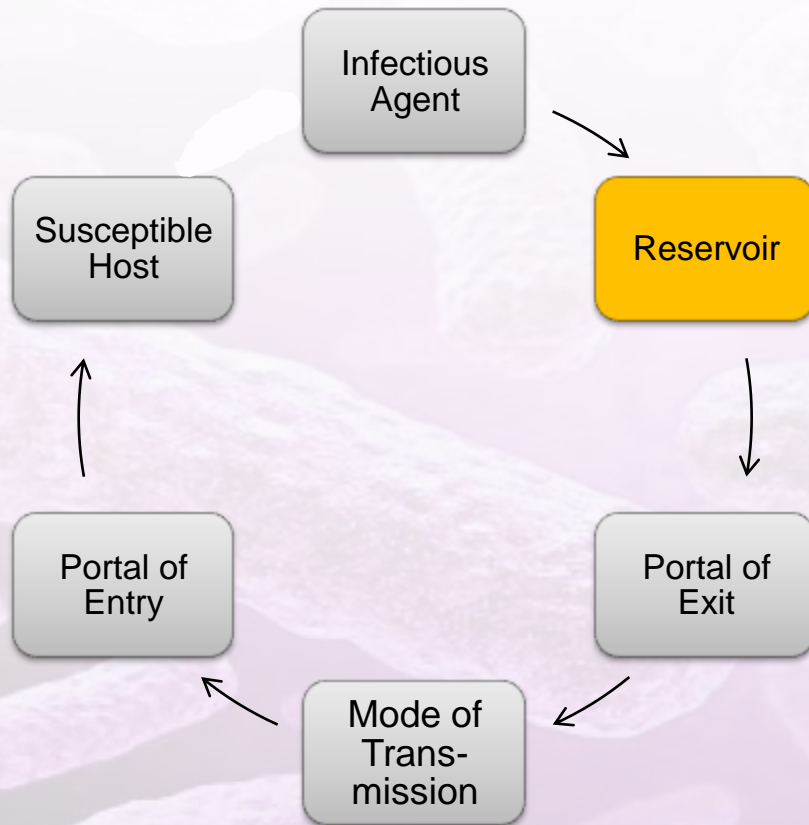


Chain of Infection - Infectious Agent

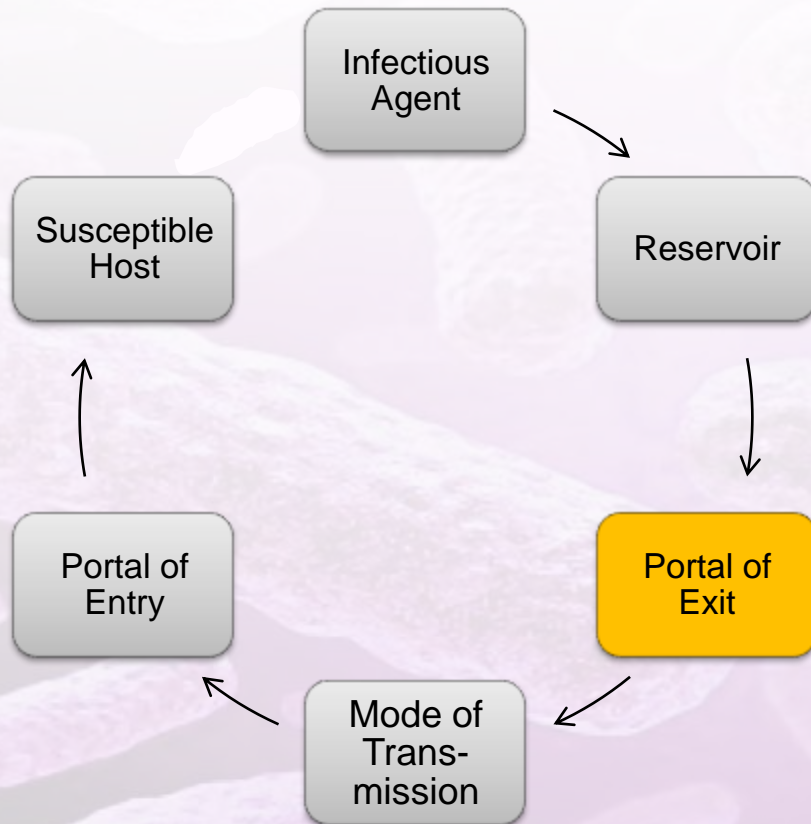


- *Pseudomonas* spp.
- *Legionella* spp.
- **Nontuberculous Mycobacteria**
- *Acinetobacter* spp.
- *Stenotrophomonas maltophilia*
- *Sphingomonas paucimobilis*
- *Aeromonas hydrophila*
- *Cryptosporidium* spp.
- *Klebsiella* spp.
- *Escherichia coli*
- *Aspergillus* spp.

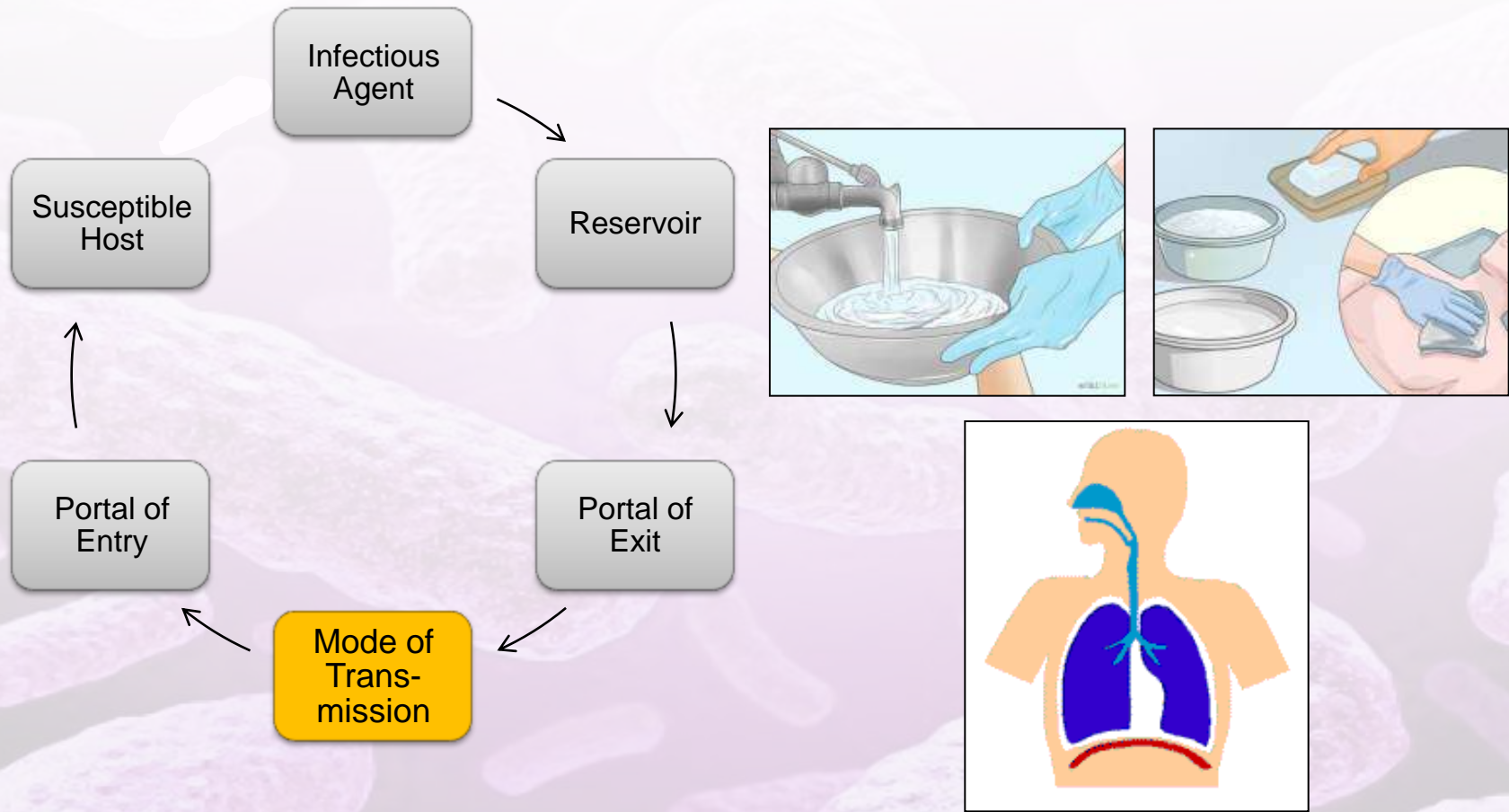
Chain of Infection - Reservoir



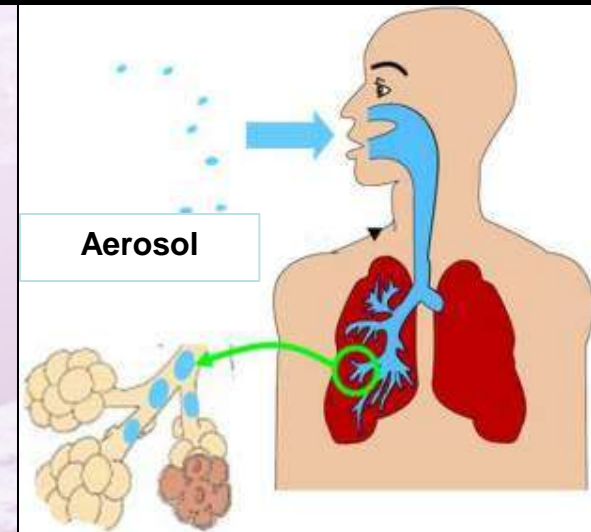
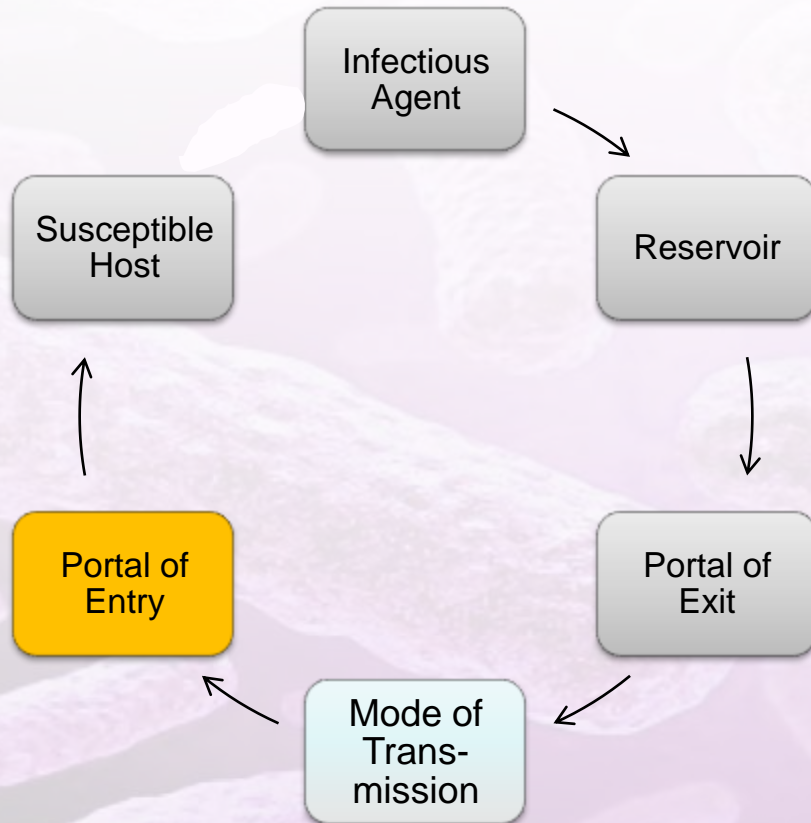
Chain of Infection - Portal of Exit



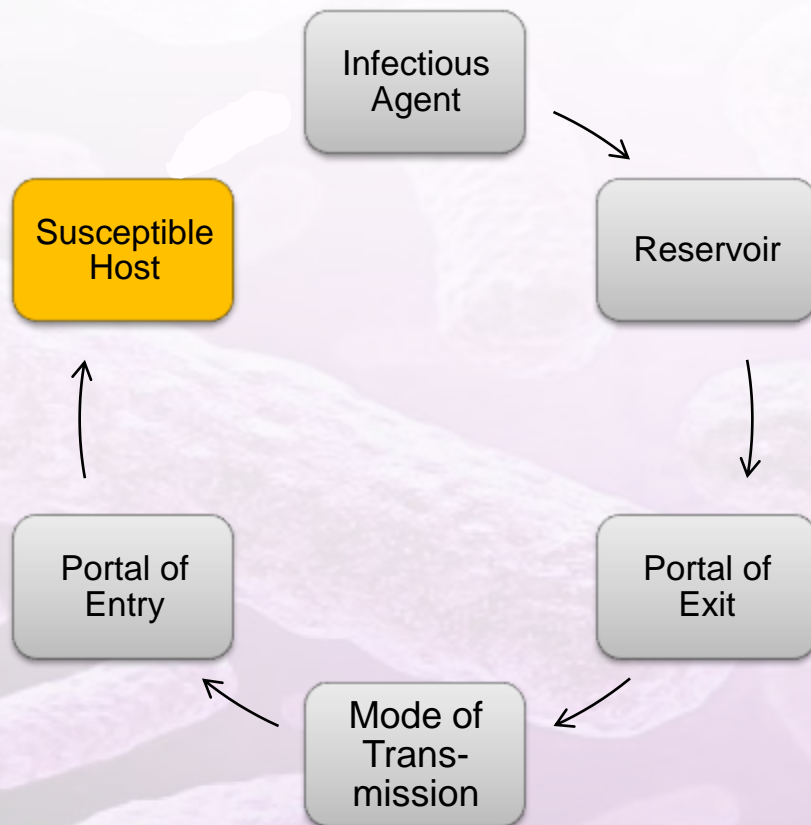
Chain of Infection - Mode of Transmission



Chain of Infection - Mode of Transmission



Chain of Infection - Susceptible Host



- Bone Marrow Transplant
- Solid Organ Transplant
- Neonatal Intensive Care
- Pediatric Intensive Care
- Hematology/Oncology
- Surgical Intensive Care
- Medical Intensive Care
- Cardiac Intensive Care
- Respiratory Intensive Care

Other pathogenic bacteria, protozoa, and fungi that can be detected within water systems:

Opportunistic Premise Plumbing Pathogens (OPPPs)

- *Pseudomonas* spp.
- *Legionella* spp.
- Nontuberculous Mycobacteria
- *Acinetobacter* spp.
- *Stenotrophomonas maltophilia*
- *Sphingomonas paucimobilis*
- *Cryptosporidium* spp.
- *Acanthamoeba*, *Hartmanella*,
Vermamoeba



Remediation Strategies - 1

- Raise hot water heater temperature ($> 55^{\circ} \text{C}$)
- Hyper thermal disinfection (70°C)
- Hyper chlorination: 5 ppm for 1-12 hr
- Hyper-oxygenation: greater than 21 % oxygen
- Filtration; pore size less than $0.22 \mu\text{m}$
- Biofilm-resistant pipe composition or coating
- OPPP-resistant biofilm formation by modulation of normal biofilm composition (e.g., *Methylobacterium*)

Remediation Strategies - 2

- Remediation strategies based on observations, not thoroughly tested
- Remediation strategies based on characteristics of NTM and other OPPPs, for example:
 - » NTM and some other OPPPs are microaerobes
 - » NTM absent in homes with high hot water heater temperature
- Consider that remediation approach will select for alternative OPPPs to NTM and/or NTM-treatment-resistant mutants

Removal of waterborne pathogens from liver transplant unit water taps in prevention of healthcare-associated infections: a proposal for a cost-effective, proactive infection control strategy

Zoy ZY, Hu BJ, Qin L, Lin YE, Watanabe H, Zou Q, Gao XD
Clinical Microbiol Infect. 2014 Apr; 20(4):310-4

Clin Microbiol Infect. 2014 Apr;20(4):310-4. doi: 10.1111/1469-0691.12299. Epub 2013 Jul 23.

Removal of waterborne pathogens from liver transplant unit water taps in prevention of healthcare-associated infections: a proposal for a cost-effective, proactive infection control strategy.

Zhou ZY¹, Hu BJ, Qin L, Lin YE, Watanabe H, Zhou Q, Gao XD.

⊕ Author information

Abstract

Hospital water supplies often contain waterborne pathogens, which can become a reservoir for healthcare-associated infections (HAIs). We surveyed the extent of waterborne pathogen contamination in the water supply of a Liver Transplant Unit. The efficacy of point-of-use (POU) water filters was evaluated by comparative analysis in routine clinical use. Our baseline environmental surveillance showed that Legionella spp. (28%, 38/136), Pseudomonas aeruginosa (8%, 11/136), Mycobacterium spp. (87%, 118/136) and filamentous fungi (50%, 68/136) were isolated from the tap water of the Liver Transplant Unit. 28.9% of Legionella spp.-positive water samples (n = 38) showed high-level Legionella contamination ($\geq 10(3)$ CFU/L). After installation of the POU water filter, none of these pathogens were found in the POU filtered water samples. Furthermore, colonizations/infections with Gram-negative bacteria determined from patient specimens were reduced by 47% during this period, even if only 27% (3/11) of the distal sites were installed with POU water filters. In conclusion, the presence of waterborne pathogens was common in the water supply of our Liver Transplant Unit. POU water filters effectively eradicated these pathogens from the water supply. Concomitantly, healthcare-associated colonization/infections declined after the POU filters were installed, indicating their potential benefit in reducing waterborne HAIs

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Prevention of Patient Exposure to Rapidly Growing *Mycobacteria* (RGM) in the Water Supply (US/CDC)

Effect of point-of-use filter on RGM during a 24-week assessment of sink water in a long-term care facility

RGM counts \log_{10} CFU/L	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24
NS sinks, unfiltered	3.28	3.78	3.77	3.16	3.88	3.45
NS sinks, 2-week-old filter	ND	ND	ND	ND	ND	ND
NS sinks, new filter	ND	ND	ND	ND	ND	ND

Modified after Table 1 by Williams MM *et al.*

- *Mycobacterium chelonae* was consistently isolated from the water supply.
- Hyper-chlorination reduced RGM by 1.5 \log_{10} initially, but the population returned to original levels within 90 days. RGM were reduced below detection level in filtered water, a 3- \log_{10} reduction.

Williams MW *et al.*, *Infect Control Hosp Epidemiol* 32:2011

0.2 micron Sterilizing Grade POU Filtration

Critical Validation

- ASTM F838-05 and Health Industry Manufacturers Association (HIMA) guidance for validating 0.2 μm sterilizing grade filters.
- POU filters retain *Brevundimonas diminuta*, the validating bacterium specified in healthcare industry standard laboratory liquid microbial challenge tests used for validating 0.2 μm sterilizing grade filters, to $> 10^7$ CFU/cm².
- A summary of the methods used for microbial challenges for retention of bacteria and bacteriostatic properties
- Microbial challenge rig diagram, microbial challenge test result data for retention, intermittent use, and evaluation of bacteriostatic properties

Question & Answer

