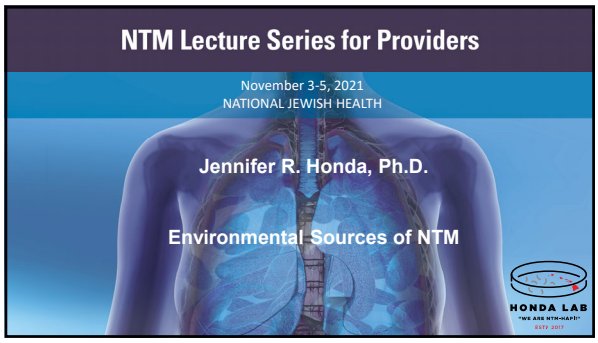
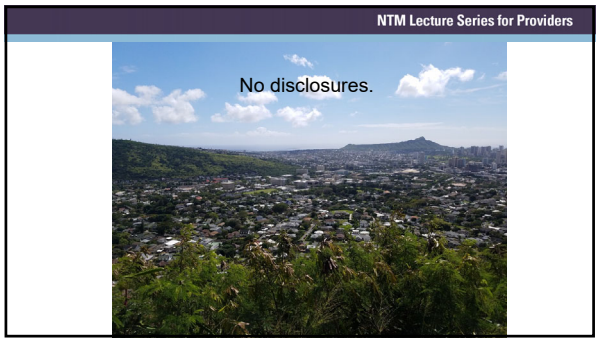
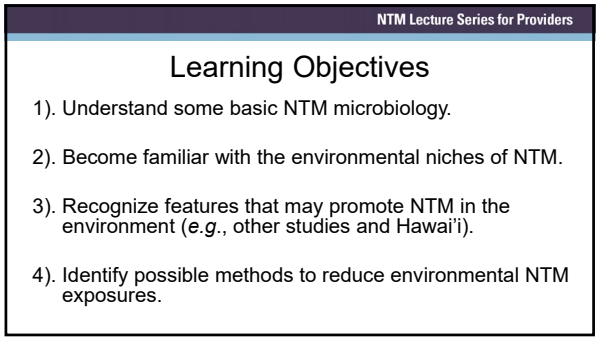
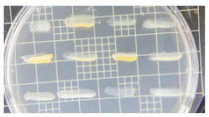






NTM Lecture Series for Providers

What Are Mycobacteria?

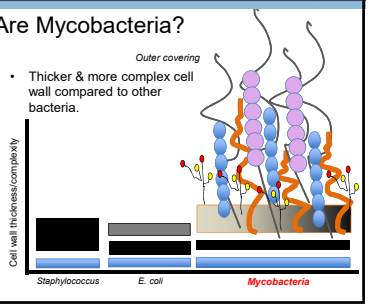


- > 190 different species
  http://www.bacteria.net/mycobacterium.html

Acid-fast bacteria
1) *Mycobacterium tuberculosis* (TB)
2) *Mycobacterium leprae* (leprosy)
3) **NTM.**

Outer covering

- Thicker & more complex cell wall compared to other bacteria.



NTM Lecture Series for Providers

Do All NTM Cause Lung Disease?

Mycobacterium gordonae
M. gilvum
M. smegmatis

Mycobacterium abscessus
***Mycobacterium avium* complex (MAC)**
- *M. avium*
- *M. intracellulare*
- *M. chimaera*

Mycobacterium tuberculosis (TB)

NTM Lecture Series for Providers

NTM Are One Of Two "Flavors"

"***Rapid***-growing mycobacteria"
(RGM)

Visible growth is typically observed between 3-10 days.

Mycobacterium abscessus (MABS)
- *M. abscessus* subsp. *abscessus*
- *M. abscessus* subsp. *bolletii*
- *M. abscessus* subsp. *massilense*

"***Slow***-growing mycobacteria"
(SGM)

Visible growth is typically observed between 10-60 days.

Mycobacterium avium complex (MAC)
- *M. avium*
- *M. intracellulare*
- *M. chimaera*
- others

NTM Lecture Series for Providers

Learning Objectives

1). Understand some basic NTM microbiology.

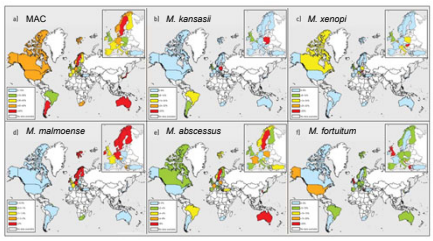
2). Become familiar with the environmental niches of NTM.

3). Recognize features that may promote NTM in the environment (*e.g.*, other studies and Hawai'i).

4). Identify possible methods to reduce environmental NTM exposures.

NTM Lecture Series for Providers

Where You Live May Matter



Hoefsloot, *et al.*, ERS, 2013

NTM Lecture Series for Providers

NTM Identified From Drinking Water Systems Globally

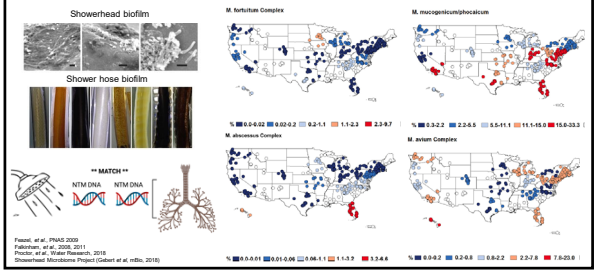
Location:	% NTM recovery:	Species:	Reference:
Mexico	**16% (19/120)**	*M. mucogenicum* most common; *M. avium*, no *M. abscessus*	Perez, *et al.*, BMC Res Notes, 2013
Greece	**22% (42/197)**	*M. chelonae* most common; no M. *abscessus*	Tsintzou, et al., Water, Air, Soil Poll, 2000
USA	**33% (46/139)**	9 species, *M. mucogenicum* most common; no M. *abscessus*	Covert, *et al.*, AEM 1999
Colombia	**50% (9/18)**	*M. mucogenicum* most common; no M. *abscessus*	Dávalos, *et al.*, Env Res & Public Health, 2021
Argentina	**52% (64/124)**	*M. gordonae* most common	Oriani, *et al.*, Int J. Mycobacter, 2019
Australia	**62% (236/384)**	*M. gordonae* most common; *M. abscessus* identified	Thomson, *et al.*, BMC Microb, 2013
Paris, France	**72% (104/144)**	*M. gordonae* and *M. nonchromogenicum* most common; Potentially pathogenic, 16%; no *M. abscessus.*	Le Dantec, *et al.*, AEM, 2002

In Pennsylvania, Genetically Similar *M. avium* Identified From Participant Lungs and Households

Matched Study	
	% NTM recovery:
Recovery from non-participant households	81% (30/37)
Recovery from *M. avium* participant households	91% (19/21)
Of the *M. avium* participant households	52% (11/21) matched to environment.

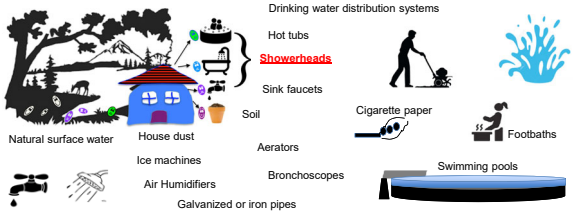
Lande, *et al.*, EID, 2019

NTM and Shower Biofilms



Feazel, *et al.*, PNAS 2009
Falkinham, *et al.*, 2008, 2011
Proctor, *et al.*, Water Research, 2018
Showerhead Microbiome Project (Gebert *et al*, mBio, 2018)

Other Environmental Niches of NTM



Chen, Breiteneby, NTMR, 2010
Honda, *et al.* PLOS Neg Trop, 2015
De Groote, *et al.*, AEM, 2006

Guimaraes, *et al.*, Am J Infect Con, 2016
Martin, *et al.* Am Rev Resp Dis 1987
Brancasco, *et al.* Microchem J, 2014

Falkinham, *et al.* J Clin Micro, 1995
Falkinham, *et al.* Sem Resp Crit Care Med, 2013
Falkinham, *et al.* J Water Health, 2007

NTM Lecture Series for Providers

Learning Objectives

1). Understand some basic NTM microbiology.

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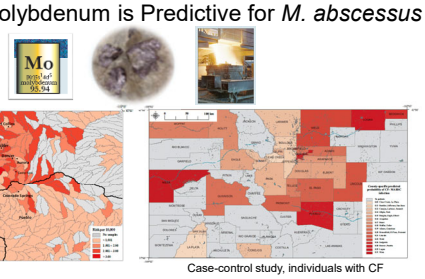
3). Recognize features that may promote NTM in the environment (*e.g.*, other studies and Hawai'i).

4). Identify possible methods to reduce environmental NTM exposures.

NTM Lecture Series for Providers

In Colorado, Molybdenum is Predictive for *M. abscessus*



Lipner, *et al.*, Int J Env Res Pub Health, 2020
Lipner, *et al.*, J Exp Science and Env Epi, 2021
https://pubs.usgs.gov/fs/2009/3105/pdf/fs2009-3105.pdf

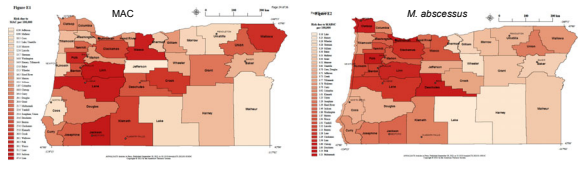
Case-control study, individuals with CF

NTM Lecture Series for Providers

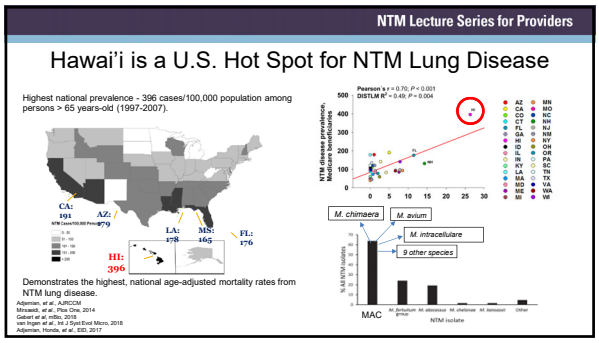
In Oregon, Molybdenum is Predictive for MAC

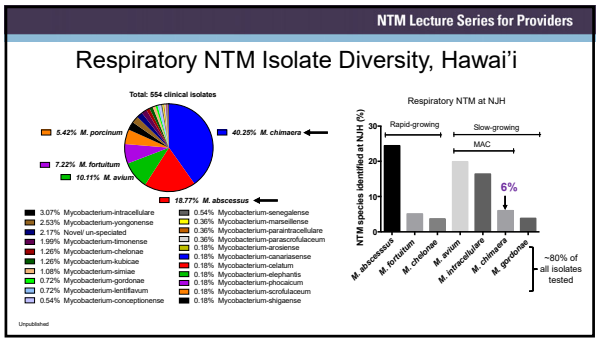
As molybdenum increases, MAC infections increase by 45%.

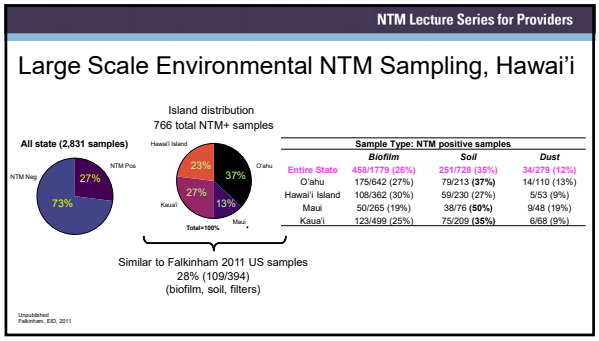
As vanadium increases, *M. abscessus* infections increase by 41%.

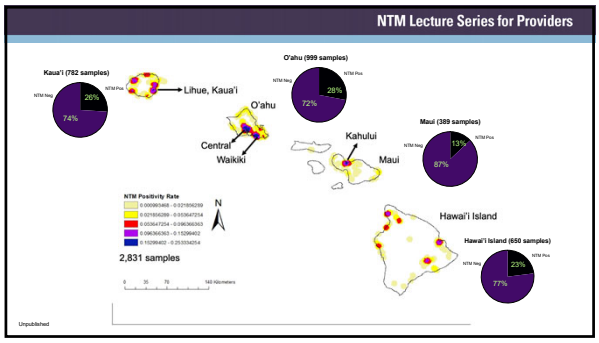


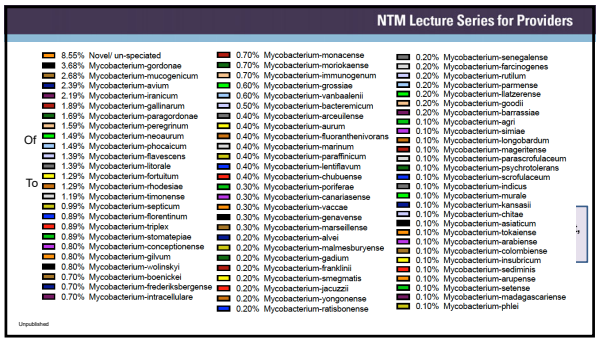
Lipner, *et al.*, Annals ATS, 2021

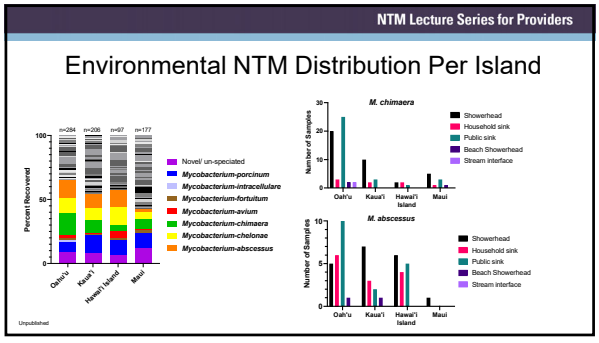












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NTM in Indoor vs Outdoor Hawai'i Environments

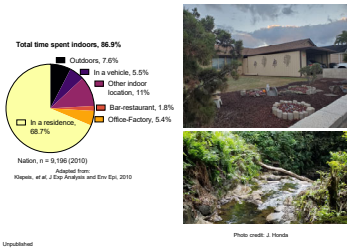
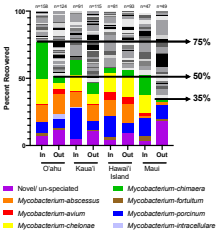


Photo credit: J. Honda



Unpublished

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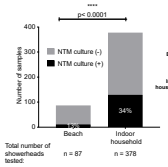
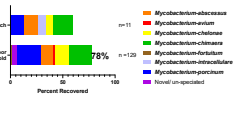
Are All Showerhead Biofilms Created Equal?

Photo credit: J. Honda





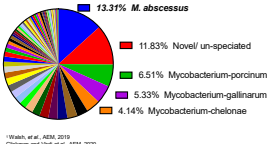
Are there unique environmental factors influencing NTM in the Hawai'i environment?

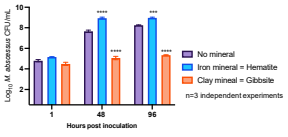
Unpublished

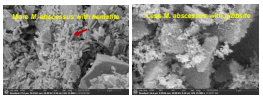
NTM Lecture Series for Providers

Soil Minerals That Contribute to Soil NTM in Hawai'i

U.S. soil is an unlikely source for pathogenic NTM. MAC more likely in wet, acidic soil.[1]







[1]Walsh, et al., AEM, 2019
Glickman and Vinci et al., AEM, 2020

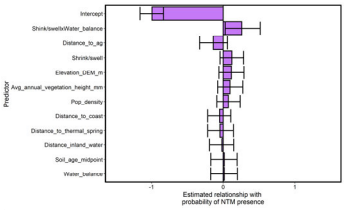
NTM Lecture Series for Providers

Hawai'i soil features and NTM

Estimates are based on 733 samples collected from 461 geographic sites.

Arielle Parsons, PhD

Krishna Pacifici, PhD



NTM probability highest in:

- Expansive soils with a high water balance
- Rich in ferric oxide.

Parsons, *et al.*, In preparation, 2021

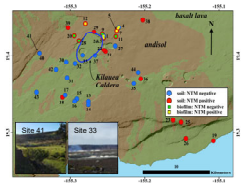
NTM Lecture Series for Providers

Kilauea Volcano, Hawai'i Island

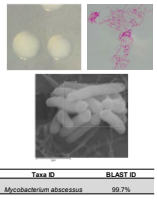
https://www.usgs.gov/media/before-after/recent-changes-k-lauea-volcano-october-4-2021
Photo credit: https://www.usgs.gov/center-news/photo-and-video-chronology-k-lauea-may-29-2018

NTM Lecture Series for Providers

Do NTM inhabit volcanic environments?

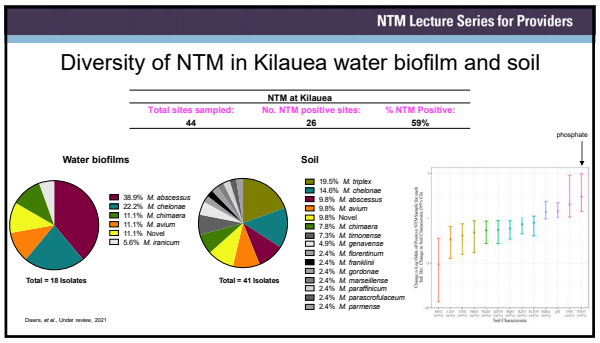


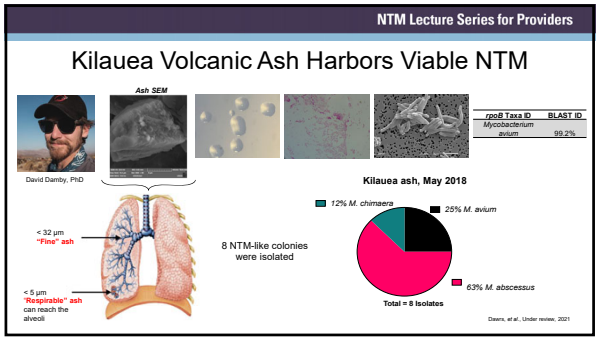
Kilauea steam vent

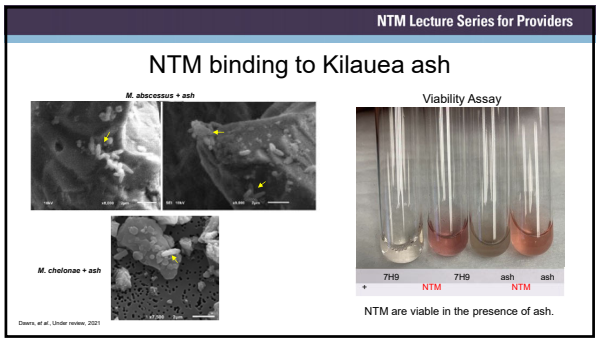


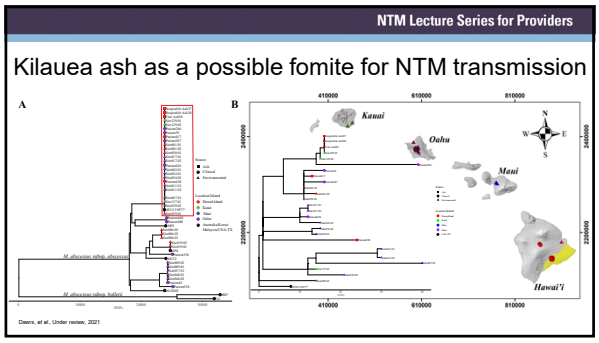
Taxa ID	BLAST ID
Mycobacterium abscessus	99.7%

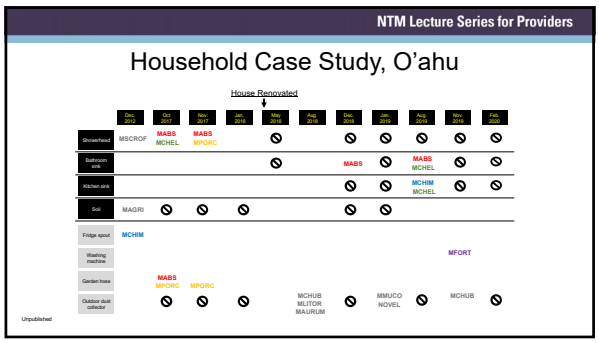
Dawrs, *et al.*, Under review, 2021







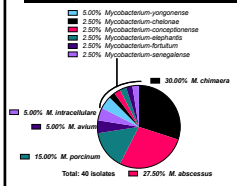




NTM Lecture Series for Providers

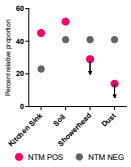
NTM in Hawai'i – A Matched Study

Respiratory NTM in 40 NTM Pos. Participants



Matched Study	
	No. of ENV kits:
NTM POS	35
NTM NEG	34

Donor:	Species IDed:	Match to:
7	*M. chimaera*	Kitchen sink & Soil
54	*M. abscessus*	Kitchen sink
66	*M. porcinum*	Kitchen sink
14	*M. yongonense*	Kitchen sink



Unpublished

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Summary - Hawai'i Top Ten NTM

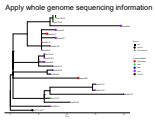
	Ranking	Top Respiratory NTM:	Top Environmental NTM:
Higher virulence	1	*M. chimaera*	*M. abscessus*
	2	*M. abscessus*	*M. chelonae*
	3	*M. avium*	*M. chimaera*
	4	*M. fortuitum*	*M. porcinum*
	5	*M. porcinum*	*Novel/un-speciated*
	6	*M. intracellulare*	*M. gordonae*
	7	*M. yongonense*	*M. mucogenicum*
	8	*Novel/un-speciated*	*M. avium*
	9	*M. timonense*	*M. iranicum*
Lower virulence	10	*M. chelonae*	*M. gallinarum*

NTM Lecture Series for Providers

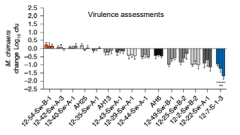
Testing new hypothesis – ongoing work

Biorepository:	
	No. of ENV Isolates:
M. chimaera	154
M. abscessus	182
M. chelonae	153
M. porcinum	183
M. avium	27
M. intracellulare	11
M. fortuitum	20
Other NTM isolates	733
Total:	**1,463**

Apply whole genome sequencing information



Virulence assessments



Macrophages | ALI, lung organoids | Mice | Amoebae

Honda, et al., AJRCMB, 2019
Unpublished

NTM Lecture Series for Providers

Learning Objectives

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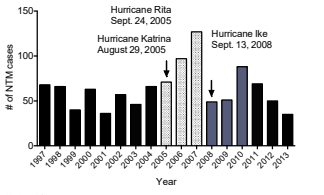
NTM Lecture Series for Providers

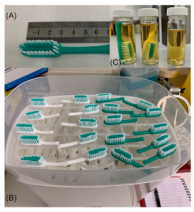
Reduce Aerosol Generating Events



Honda, et al. Chest, 2015
Image: https://www.cdc.gov/special-topic/flint
Image: https://volcanoes.usgs.gov/volcanic_ash/ash_gas.html

NTM Lecture Series for Providers

Steam Disinfection of Toothbrushes Reduces NTM



M. abscessus subsp. *abscessus* (n=2)
M. abscessus subsp. *bolletii* (n=2)
M. abscessus subsp. *massiliense* (n=2)

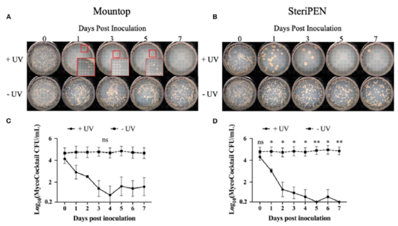
None of the 80 isolates examined survived at 91℃ for 4 min. [1]

** Boiling water for 10-15min reduces NTM. [2]

[1] Miller, et al., Pediatric Pulmonology, 2020
[2] Falkinham, Whitau, 2013

NTM Lecture Series for Providers

UV Disinfection Systems Reduce NTM in Drinking Water



Norton, *et al*, Frontiers In Public Health, 2020

NTM Lecture Series for Providers

Expand Drinking Water Awareness

Drinking ground water → 31%+
Drinking surface water → 36%+
Commercial bag ice → No NTM
Ice machines → 100%

Bottled water: 20 different brands, U.S. 0%+; No NTM detected.

Bottled Water (Honda Lab, 2021):

Water Tested:	Type of water (Source = U.S.A.) unless noted:	Characteristic:	Results:
1	Bottled Water, Brand 1	Natural spring water	None
2	Bottled Water, Brand 2	Purified water	None
3	Bottled Water, Brand 3	Natural spring water	None
4	Bottled Water, Brand 4	Water from snow	None
5	Bottled Water, Brand 5	Volcanic rock filtered water	*Mycobacterium neoaurum* *Mycobacterium phocaicum*
6	Bottled Water, Brand 6	Volcanic rock filtered water	None
7	Bottled Water, Brand (non-U.S.A)	Volcanic rock filtered water	None
8	Distilled water	Commercially available	None
9	Sink faucet 1	Municipal water, Colorado	*Mycobacterium abscessus*
10	Sink faucet 2	Municipal water, Colorado	None
11	Sink faucet 3	Municipal water, Colorado	None
12	Water fountain	Municipal water, Colorado	None
13	Wall mounted water bottle filling station	Municipal water, Colorado	None

Holtzman, *et al*, J Food Protect 1997
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https://www.bottledwater.org/public/CCL4%20Microbes%20of%20Interest%20in%20Drinking%20Water_0.pdf0
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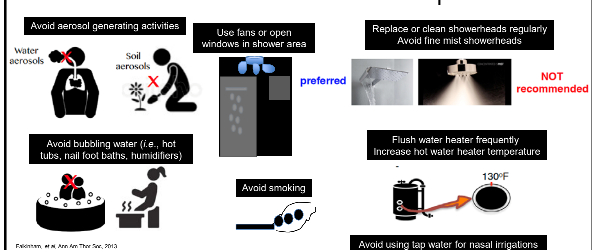
NTM Lecture Series for Providers

Established Methods to Reduce Exposures



Falkinham, *et al*, Ann Am Thor Soc, 2013
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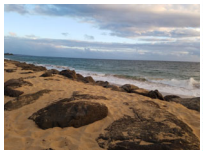

'Iolani School, The Kamehameha Schools, Seabury Hall, Kailua High School, Waianae High School, Kapa'a High School, Island School, University of Hawai'i at Hilo, Diagnostic Labs Hawai'i, University of Hawai'i Maui, Brigham Young University Laie, Mike Burnett, Homeschoolers, Citizen Scientists of Hawai'i, Department of Tropical Medicine University of Hawai'i, Hawai'i Division of Wildlife

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