8:30–9 A.M. MDT	**Registration and Breakfast**
9 –9:15 A.M. MDT	Welcome and Introduction to NTM *Charles Daley, MD*
9:15 –9:20 A.M. MDT	Bronchiectasis and NTM Care Center Network *John Torrence*
9:20–9:50 A.M. MDT	The Patient Perspective *Amy Leitman, JD (Director of NTMir)*
9:50–10:20 A.M. MDT	Overview of Bronchiectasis *Steven E. Lommatzsch, MD*
10:20–10:50 A.M. MDT	GERD and NTM Lung Disease *Jeffrey King, MD*
10:50–11:15 A.M. MDT	**Break/Exhibits**
11:15 A.M.–12 P.M. MDT	Treatment of NTM *Charles Daley, MD*
12– 12:30 P.M. MDT	Management of Side Effects/Toxicity *David Griffith, MD*
12:30–1:30 P.M. MDT	**Lunch**
1:30–2:00 P.M. MDT	Novel Therapeutics *Charles Daley, MD*
2–2:30 P.M. MDT	Nutrition Guidelines *Michelle MacDonald, MS, RD, CNE*
2:30–3 P.M. MDT	How We Should Think About Our Environment *Jennifer Honda, PhD*
3–3:15 P.M. MDT	**Break/Exhibits**

3:15–3:45 P.M. MDT	When Antibiotics Are Not Enough – A Surgical Approach *John Mitchell, MD*
3:45–4:15 P.M. MDT	Coping and Caring *Elizabeth "Devon" Smith, PhD*
4:15–4:45 *P.M. MDT*	What Can I Do To Feel Better? *Cheryl Torres, RRT*
4:45–5:15 P.M. MDT	Panel Discussion *All Faculty*
5:15 P.M. MDT	Closing Comments *Faculty*

Wi-Fi

Turn on your Wi-Fi and look for NJH-Guest. You'll see a pop-up window and will need to enter your email address.

Presentation Slides

During the conference and for 2 weeks after, the presentations will be available online. However, these slides are locked for editing.

https://www.nationaljewish.org/NTMPatientSlides

Evaluation link

Please complete the evaluation after today's program. Your feedback will help us develop high-quality educational programs in the future.

https://redcap.link/PatientEval

Conference Recordings

Recordings of the NTM Lecture Series will be available on YouTube approximately 4 weeks after the program. You will receive an email with a link to access the recordings when they are available.

Contact Us

If you have questions throughout the conference, please visit the Registration Desk or call the on-site contacts:

Meghan Brenner – 303.249.8096
Laniecia Demmer– 720.232.6174

Questions after the conference can be directed to proed@njhealth.org or 303.398.1000.

Disclaimer:
This material is for informational purposes only. It does not replace the advice or counsel of a doctor or health care professional. You should consult with, and rely only on the advice of, your physician or health care professional

NTM Lecture Series for Patients and Families

April 27, 2024 | Denver, CO

Educational Program Faculty Presenters

Charles Daley, MD (Program Co-Chair)
Chief and Professor of Medicine
Division of Mycobacterial and Respiratory Infections
National Jewish Health

David Griffith, MD
Professor of Medicine
Division of Mycobacterial and Respiratory Infections
National Jewish Health

Jennifer Honda, PhD, ATSF
Associate Professor
Director, NTM Center at Tyler
University of Texas Health Science Center at Tyler

Shannon Kasperbauer, MD (Program Co-Chair)
Associate Professor of Medicine
Division of Mycobacterial and Respiratory Infections
National Jewish Health

Jeffrey King, MD
Chief, Division of Gastroenterology
Medical Director, GI Procedures Unit
Associate Professor
Department of Medicine

Amy Leitman, JD
President
NTM Info & Research

Steven Lommatzsch, MD
Associate Professor of Medicine
Director, Non-CF Bronchiectasis Program
Division of Pulmonary, Critical Care and Sleep Medicine
National Jewish Health

Michelle MacDonald, MS, RDN, CDE
Clinical Dietitian Supervisor
Certified Diabetes Educator
Clinical Nutrition Services
Department of Medicine
Section of Nephrology & Diabetology
National Jewish Health

John Mitchell, MD
David Endowed Chair in Thoracic Surgery
Professor and Chief
General Thoracic Surgery
University of Colorado Hospital

Elizabeth "Devon" Smith, PhD
Assistant Professor, Psychologist
Department of Medicine
Division of Pulmonary, Sleep Medicine
National Jewish Health

John Torrence
Bronchiectasis and NTM Ambassador
COPD Foundation

Cheryl Torres, RRT
Pulmonary Physiology Tech II
Respiratory Care Department
Infectious Disease Unit
Lead Respiratory Therapist
National Jewish Health

NTM Lecture Series for Patient and Families

April 27, 2024 | Denver, CO

Faculty Biographies

Charles L. Daley, MD (Program Co-Director) is Chief of the Division of Mycobacterial and Respiratory Infections at National Jewish Health (NJH) and Professor of Medicine at NJH, the University of Colorado School of Medicine, and Icahn School of Medicine at Mount Sinai. Dr. Daley has served on and chaired expert panels for the World Health Organization (WHO), Centers for Disease Control and Prevention (CDC), Infectious Diseases Society of America and American Thoracic Society. He has participated on multiple guideline panels for these organizations including guidelines that address diagnosis, treatment (drug-susceptible and drug resistant) and prevention of TB. He recently Chaired the revision of the multi-society sponsored NTM Treatment Guideline. For his work with MDR-TB he was awarded the World Lung Health Award by the American Thoracic Society. He was previously Associate Editor for the American Journal of Respiratory and Critical Care Medicine and The European Respiratory Journal. His academic interests include TB global health policy and clinical and translational research related to TB, NTM infections and bronchiectasis.

David Griffith, MD is currently Professor of Medicine at National Jewish Health (NJH) in Denver, Colorado. Prior to joining NJH, he worked for 34 years at UT Health, Tyler, TX where he retired as Professor of Medicine in 2019. He held the William A. and Elizabeth B. Moncrief Distinguished Professorship for 17 years at UT Health. He is an Overseas Fellow of the Royal Society of Medicine and Fellow of the American Thoracic Society and American College of Chest Physicians.

Dr. Griffith was Chief of Tuberculosis Services at UT Health for 15 years. He was Medical Director for the Center for Pulmonary Infectious Disease (CPIDC) at UT Health, which provided thousands of free TB consultations for the State of Texas, for 17 years. He was the Assistant Medical Director for the Heartland National TB Center is San Antonio, Texas for 12 years. He was Medical Director for the Texas State Inpatient TB facility, the Texas Center for Infectious Disease (TCID) for 19 years.

Dr Griffith was a member of the writing committee for the American Thoracic Society (ATS) 1997 Guidelines for Diagnosis and Treatment of Nontuberculous Mycobacteria (NTM) and the chair of the writing committee for the ATS and Infectious Diseases Society of America (IDSA) 2007 Guidelines for Diagnosis, Treatment, and Prevention of NTM) Diseases. He is a current member of the international multi-society committee that has revised the NTM guidelines. He also serves as a member of the board of directors of the NTM Information and Research Foundation. Dr Griffith has authored or co-authored more than 200 peer reviewed manuscripts, reviews and book chapters related to NTM disease. He recently edited a book dedicated to the diagnosis and treatment of NTM infections.

Jennifer R. Honda, PhD was born and raised in Honolulu, Hawai'i. She received her B.S. from Colorado State University in Biology and Zoology, M.S. in Microbiology from the University of Hawai'i, and PhD in Microbiology from the University of Colorado Anschutz Medical Campus. Currently, Dr. Honda is basic science, translational mycobacteriologist and Associate Professor for the Department of Cellular and Molecular Biology and the School of Medicine at the University of Texas Health Science Center at Tyler where she is also the inaugural Director of a new NTM Center. Her research program actively studies the 1) environmental- 2) host– 3) microbial factors that contribute to NTM pulmonary disease emergence

globally. The Honda Lab consistently seeks to learn more about the environmental drivers of NTM, routinely cultures NTM from environmental and clinical samples, and utilizes these recovered isolates to explore the intra- and inter- NTM species differences that contribute to pathogenicity and host evasion. Active in the American Thoracic Society (ATS) Pulmonary Infections and Tuberculosis (PI-TB) Assembly since 2014, she is the recipient of an ATS Foundation award in Pulmonary Medicine, PI-TB's Rising Star in 2019, PI-TB Top Junior Faculty in 2021, and an ATS Fellow in 2022. The European Respiratory Society distinguished Dr. Honda in 2020 as an Innovator in NTM Science and Medicine.

Shannon Kasperbauer, MD (Program Co-Director) is an Associate Professor of Infectious Diseases at National Jewish Health and the University of Colorado Health Sciences Center. She is the director of education for the infectious disease division and manages the fellowship program. She has directed the Denver TB Course since 2007. Dr. Kasperbauer earned her medical degree at Wright State University School of Medicine in Dayton, OH. She completed her internship and residency in internal medicine at the University of Colorado, followed by her fellowship in infectious disease, also at the University of Colorado.

Dr. Kasperbauer has written many abstracts, has several publications, including book chapters and journal articles. She has given many presentations on infectious diseases, both nationally and internationally.

Dr. Kasperbauer's areas of interest include Chronic Respiratory Infections, General Infectious Diseases, Nontuberculous Mycobacterial Infections and Tuberculosis.

Jeffrey King, MD is Chief of Gastroenterology, Medical Director of the GI Procedures Unit, and Associate Professor of Medicine at National Jewish Health. He received his medical degree from the University of Massachusetts Medical School, and completed his residency and chief residency in Internal Medicine at Boston University Medical Center. He completed a combination research and clinical fellowship in Gastroenterology and Hepatology at the University of North Carolina, where his research included using novel cell surface markers to identify colon cancer stem cells.
Since coming to National Jewish Health in 2014, Dr. King's clinical interest has focused on the evaluation and management of reflux and esophageal motility disorders as they pertain to lung disease. He serves as the main GI consultant for the adult Cystic Fibrosis (CF) program – the largest of its kind in the United States. Through this role, he has received grant funding from the CF Foundation to improve the understanding and management of CF-related GI conditions, particularly the overlap between reflux and advanced lung disease in cystic fibrosis.

Amy Leitman, JD is the President of NTM Info & Research, a nonprofit advocacy group for patients with pulmonary nontuberculous mycobacterial disease. The daughter of a patient with NTM lung disease and bronchiectasis, she has spent the last 12 years championing the voice of the patient. In her role, Amy represents the interests and perspectives of patients, healthcare providers, researchers, industry, and other interested stakeholders, serves as a liaison to legislators, regulators, and independent organizations seeking patient input, and speaks at multi-stakeholder meetings. She has presented original patient preference research, co-authored several papers on NTM lung disease, and collaborated on patient-centered and epidemiologic research. Amy's career includes many years in communications and marketing, including for an NBA team and a major community nonprofit organization that mobilized

human and financial resources to strengthen local and international community social safety nets.A native of Montreal, Canada, Amy grew up in Toronto before moving to Miami, Florida where she earned her Bachelor of Arts and Juris Doctor from the University of Miami. She is a member of the American Thoracic Society, the Infectious Diseases Society of America, the American College of Chest Physicians (CHEST), the American Society for Microbiology, the European Respiratory Society, and the Drug Information Association. She also currently serves as the co-chair of the Regulatory Working Group for the EveryLife Foundation for Rare Diseases.

Steven Lommatzsch, MD is an Associate Professor in Pulmonary and Critical Care as well as the Director of Bronchiectasis at National Jewish Health in Denver, Colorado. His career has focused on airway disorders, and he has been a leader at the clinic for bronchiectasis and related diseases. With a wealth of experience in diagnosing and treating such conditions as Cystic Fibrosis, Primary Ciliary Dyskinesia, COPD and asthma, he is committed to staying in the forefront of medical advancements through research in these areas. His passion is fostering a collaborative approach with patients aimed at improving quality of life through personalized care.

Michelle MacDonald, MS, RD, CNE is a clinical dietitian and certified diabetes educator at National Jewish Health. She provides compassionate, comprehensive nutritional care to adult patients with various chronic conditions, including: cardiovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, gastrointestinal disease, interstitial lung disease, nontuberculous mycobacterial disease, overweight, rheumatoid arthritis, scleroderma, and type 2 diabetes.

Michelle works closely with multidisciplinary teams of specialty clinics, counseling both inpatients and outpatients. She is dedicated to helping patients use nutrition as a supportive therapy to manage disease and optimize health.

Michelle completed a Bachelor of Science in Human Nutrition at Cornell University, a Master of Science in Food Science and Human Nutrition at Colorado State University and a dietetic internship at the University of Northern Colorado.

John Mitchell, MD, a native of Colorado, received his undergraduate degree in molecular biology at the University of Colorado, and subsequently attended the University of Michigan Medical School on an Armed Forces Scholarship, graduating with honors. Over the next decade he completed residencies in both General and Cardiothoracic Surgery at the Massachusetts General Hospital in Boston, Massachusetts. During his residency, Dr. Mitchell also served as a Registrar in Cardiothoracic Surgery in Liverpool, England, and was the Linton research fellow at MGH. Following a four year period on active duty in the United States Navy, Dr. Mitchell joined the faculty at the Stanford University School of Medicine. He was subsequently recruited to the University of Colorado where he remains Professor and Chief of General Thoracic Surgery, and holds the Courtenay C. and Lucy Patten Davis Endowed Chair within the Department of Surgery.

Dr. Mitchell's primary clinical responsibilities are at the University of Colorado Hospital and National Jewish Health, both in Denver. His clinical and research interests focus on surgery for infectious lung disease, airway surgery, all thoracic oncology, and minimally invasive approaches to thoracic surgical procedures.

Dr. Mitchell currently serves as a Director of both the American Board of Surgery and the American Board of Thoracic Surgery, and also serves on the Board of Directors for the Society of Thoracic

Surgeons. He is a past President of the Western Thoracic Surgical Association, a past Governor of the American College of Surgeons, and is active in numerous national and international thoracic surgical societies. Finally, he is active in international outreach, improving thoracic health and education in Nepal.

Elizabeth "Devon" Smith, PhD is a licensed clinical psychologist. Her professional background has involved researching and treating psychological factors unique to chronic illness and health concerns. She has worked in a variety of medical settings, including oncology, primary care, cardiology, pulmonology, infectious disease, sleep medicine, and NTM related clinics. Currently, she is an Assistant Professor at National Jewish Health in Denver, CO.

Cheryl Torres, RRT started working at National Jewish Health after graduating from PIMA Medical Institute in 2006 as a Registered Respiratory Therapist. Working as a Tech 11 and Lead Respiratory Therapist in the Pulmonary Physiology unit, she is responsible to help maintain coordination within the department. Currently, she works primarily with the Infectious Disease Team educating patients on proper airway clearance devices and technique. Her department also helps with Neuromuscular patients (ALS) COPD patients in the Chronic Respiratory Failure Clinic. Other interests include Family Practice with ABI testing, Pulmonary testing and ECG's. Home Health visits for HFCWO vest setups and Cough Assist devices.

ACKNOWLEDGEMENTS

National Jewish Health would like to thank all of the sponsoring and exhibiting companies for their participation in the 2024 NTM Provider Lecture Series.

Please visit with the sponsor and exhibitors during the breaks.

Platinum Sponsor:

Insmed

Exhibiting Companies:

Baxter

National Jewish Health Advanced Diagnostic Laboratories

NTMir

RespirTech

Bronchiectasis and NTM Care Center Network

John Torrence

1

CCN Mission, Vision, and Strategic Goals

To establish a network of centers across the country, with the goal of reducing the time to diagnosis and supporting high-quality care for bronchiectasis and nontuberculous mycobacterial (NTM) lung disease patients.

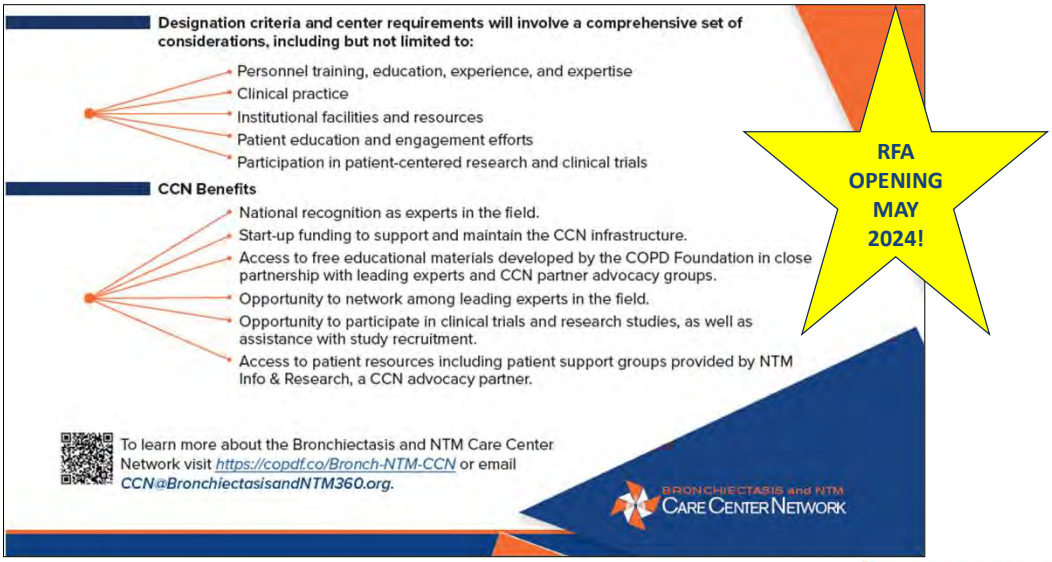
Every patient receives a prompt, accurate diagnosis; the highest quality, patient-centered care; and the resources, education and support necessary to properly manage their disease.

STRATEGIC GOALS

1. Accelerate time to diagnosis and deliver individualized, comprehensive, high-quality care.
2. Educate health care teams about bronchiectasis and nontuberculous mycobacterial (NTM) lung disease and the care required to achieve and maintain the best possible health outcomes.
3. Support research and clinical trials and the development of real-world evidence.
4. Deliver patient-centered education to improve long-term disease management.
5. Increase disease awareness as well as patient education and engagement.

2

Designation Criteria and Site Benefits



RFA OPENING MAY 2024!

BRONCHIECTASIS and NTM CARE CENTER NETWORK

3

3

Questions?

BRONCHIECTASIS and NTM CARE CENTER NETWORK

4

4

The Patient Perspective

Amy Leitman, JD
President, NTM Info & Research

NTM Info & Research

1

NTM Info & Research

By Patients, For Patients

Co-founders: Patient and caregiver

The website: ntminfo.org

The pamphlet: A resource for patients

2

NTM and Bronchiectasis: The Patient Experience

- Long delays to proper diagnosis
- Long, burdensome treatment regimens
- Side effects, some permanent
- Hemoptysis
- Severe cough
- Extreme fatigue
- Shortness of breath
- Unpredictability in day-to-day health and functioning
- Social isolation and stigma

3

DIAGNOSED: What now?

- What is it?
- Am I contagious?
- How will my life change?
- Will my family help me?
- Will my friends want to be around me?
- Am I getting the correct treatment?
- How long will I be on treatment?
- What are the side effects?
- Do other people have this?
- Where do I find more information?
- Am I going to die from this?

4

Patient-Focused Drug Development

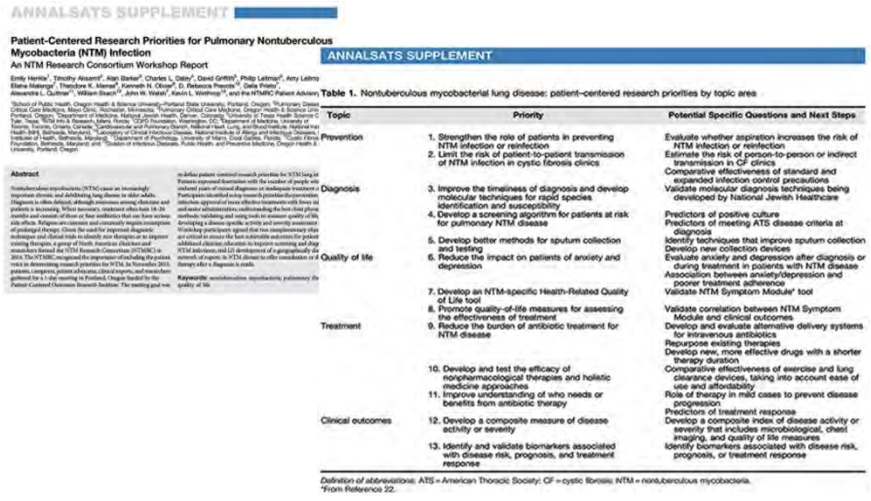
Patients reported these three symptoms as having the most significant clinical impact on their daily lives:

- Fatigue
- Cough
- Shortness of breath

Center for Drug Evaluation and Research (CDER), U.S. Food and Drug Administration (FDA). The voice of the patient: a series of reports from the U.S. Food and Drug Administration's (FDA's) Patient-Focused Drug Development Initiative: non-tuberculous mycobacterial (NTM) lung infection. Public Meeting: October 15, 2015. 2016 April [accessed 2016 April 30]. Available from: http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM496941.pdf

5

NTM Research Consortium



ANNALSATS SUPPLEMENT

Patient-Centered Research Priorities for Pulmonary Nontuberculous Mycobacteria (NTM) Infection
An NTM Research Consortium Workshop Report

ANNALSATS SUPPLEMENT

Table 1. Nontuberculous mycobacterial lung disease: patient–centered research priorities by topic area

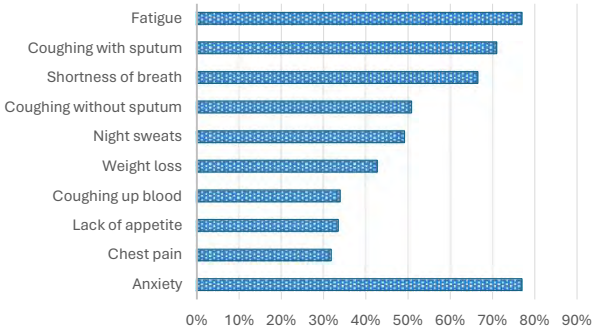
Topic	Priority	Potential Specific Questions and Next Steps
Prevention	1. Strengthen the role of patients in preventing NTM infection or reinfection	Evaluate whether aspiration increases the risk of NTM infection or reinfection
	2. Limit the risk of patient-to-patient transmission of NTM infection in cystic fibrosis clinics	Estimate the risk of person-to-person or indirect transmission in CF clinics
		Comparative effectiveness of standard and expanded infection control precautions
Diagnosis	3. Improve the timeliness of diagnosis and develop molecular techniques for rapid species identification and susceptibility	Validate molecular diagnosis techniques being developed by National Jewish Healthcare
	4. Develop a screening algorithm for patients at risk for pulmonary NTM disease	Predictors of positive culture Predictors of meeting ATS disease criteria at diagnosis
	5. Develop better methods for sputum collection and testing	Identify techniques that improve sputum collection
Quality of life	6. Reduce the impact on patients of anxiety and depression	Develop new collection devices Evaluate anxiety and depression after diagnosis or during treatment in patients with NTM disease Association between anxiety/depression and poorer treatment adherence
	7. Develop an NTM-specific Health-Related Quality of Life tool	Validate NTM Symptom Module* tool
	8. Promote quality-of-life measures for assessing the effectiveness of treatment	Validate correlation between NTM Symptom Module and clinical outcomes
Treatment	9. Reduce the burden of antibiotic treatment for NTM disease	Develop and evaluate alternative delivery systems for intravenous antibiotics Repurpose existing therapies Develop new, more effective drugs with a shorter therapy duration
	10. Develop and test the efficacy of nonpharmacological therapies and holistic medicine approaches	Comparative effectiveness of exercise and lung clearance devices, taking into account ease of use and affordability
	11. Improve understanding of who needs or benefits from antibiotic therapy	Role of therapy in mild cases to prevent disease progression Predictors of treatment response
Clinical outcomes	12. Develop a composite measure of disease activity or severity	Develop a composite index of disease activity or severity that includes microbiological, chest imaging, and quality of life measures
	13. Identify and validate biomarkers associated with disease risk, prognosis, and treatment response	Identify biomarkers associated with disease risk, prognosis, or treatment response

Definition of abbreviations: ATS = American Thoracic Society; CF = cystic fibrosis; NTM = nontuberculous mycobacteria.
*From Reference 22.

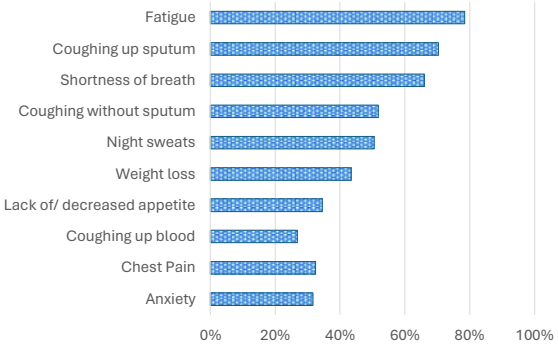
6

Patients: Telling Us How They Really Feel

Top Symptoms Patients Experienced



Most Bothersome Symptoms



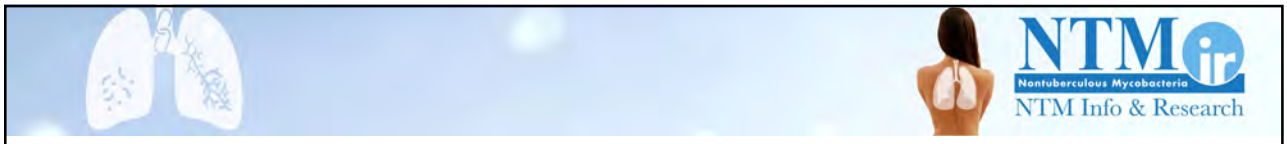
Development of Drugs for Nontuberculous Mycobacterial Disease: Clinicians' Interpretation of a US FDA Workshop (CHEST August 2020)

7

What Matters to Patients?

- Quality care
- Effective treatments
- Sound information
- Solid support

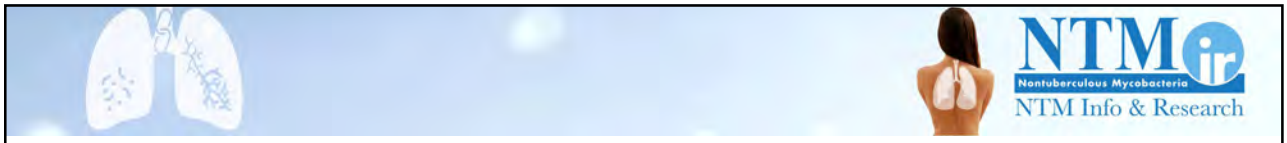
8



True Story…

"Oh no, I don't have NTM. I have MAC."

9



How You Can Help Your Patients

In addition to taking medicine, seek out the following:

- Regular follow-up testing
- Airway clearance and **referral to RT**
- Nutrition and referral to dietitian
- Exercise and fitness, referral to physiotherapy if needed
- Proper rest
- Psychological support mechanisms, referral to therapy
- Clinical trials

Contact us at NTM Info & Research for online support, support groups, and information on clinical trials

10

Manage Expectations: What to Expect When You're Expecting Side Effects

Peer support can be crucial in helping you learn from each other about side effects and how to reduce them. Support and knowledge can help reduce your anxiety and increase your likelihood of continuing treatment.

n = 98

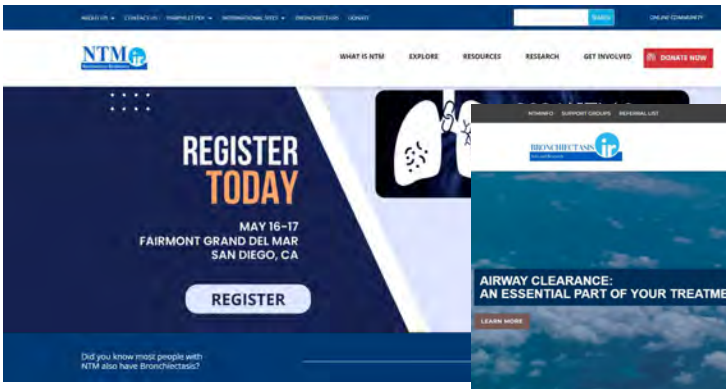
Hoarseness/Loss of Voice
Gargling with salt water: 12
Reduce frequency of dosing: 22
Discontinue temporarily: 8
Lozenges: 3

Coughing
Nebulize with bronchodilators: 10

GI side effects
Probiotics: 6

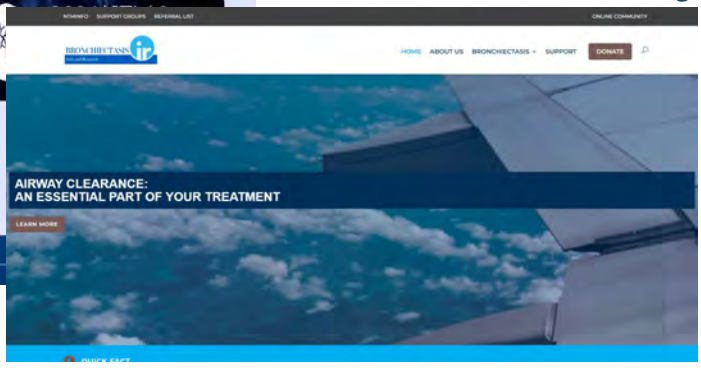
11

Resources for Patients

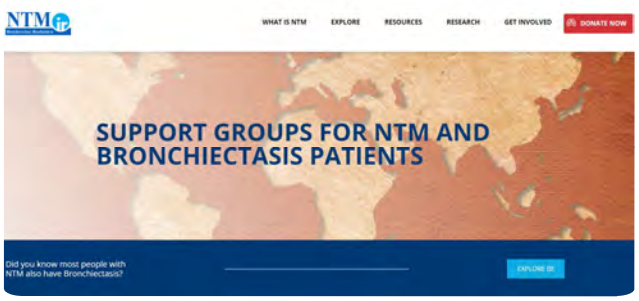


ntminfo.org

bronchiectasisinfo.org



12



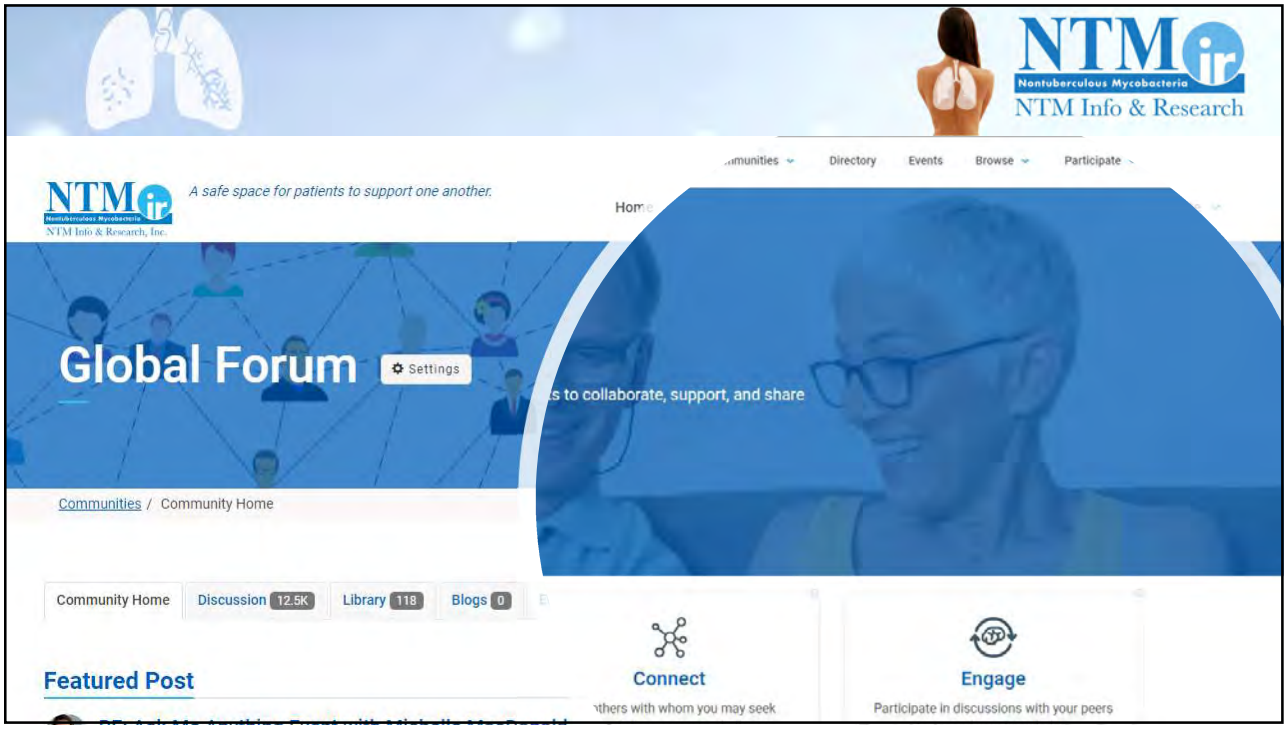
NTM ir
Nontuberculous Mycobacteria
NTM Info & Research

42 GROUPS

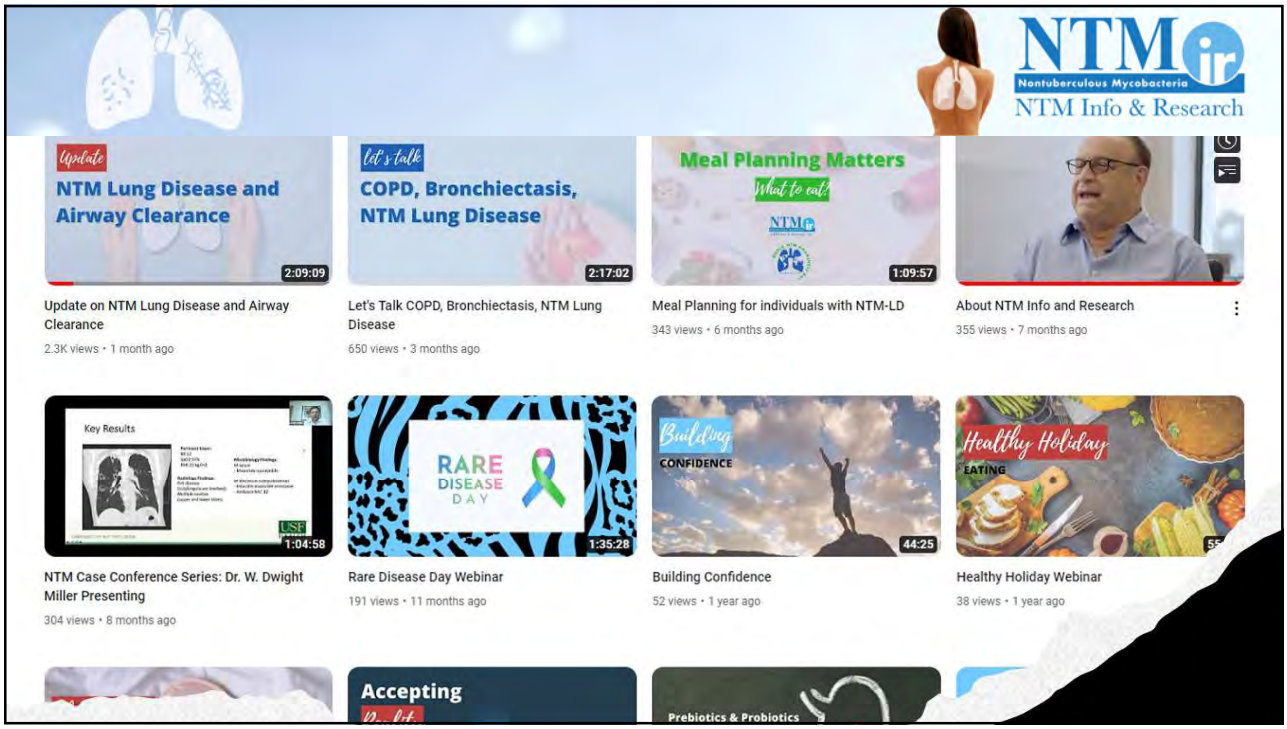
37 US

5 Ex-US

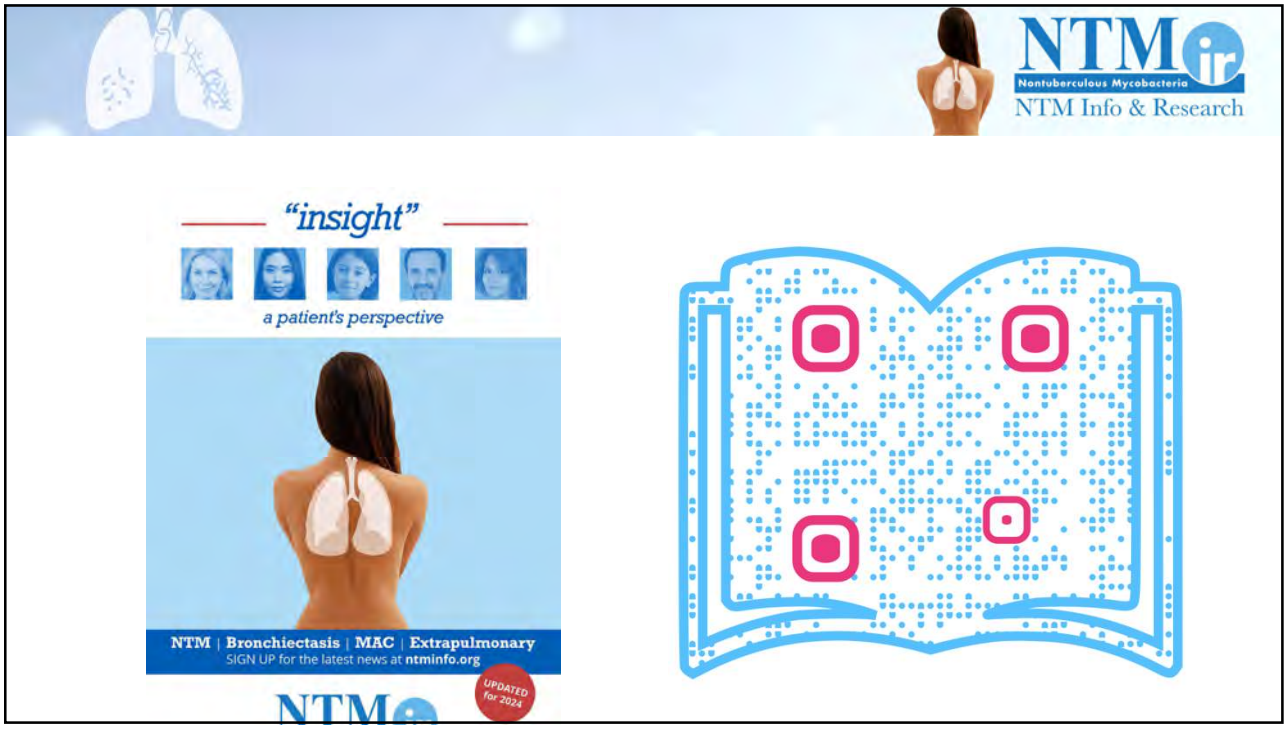
13



14


NTM ir
Nontuberculous Mycobacteria
NTM Info & Research
Update
NTM Lung Disease and Airway Clearance
2:09:09
Update on NTM Lung Disease and Airway Clearance
2.3K views • 1 month ago
let's talk
COPD, Bronchiectasis, NTM Lung Disease
2:17:02
Let's Talk COPD, Bronchiectasis, NTM Lung Disease
650 views • 3 months ago
Meal Planning Matters
What to eat?
1:09:57
Meal Planning for individuals with NTM-LD
343 views • 6 months ago
About NTM Info and Research
355 views • 7 months ago
Key Results
1:04:58
NTM Case Conference Series: Dr. W. Dwight Miller Presenting
304 views • 8 months ago
RARE DISEASE DAY
1:35:28
Rare Disease Day Webinar
191 views • 11 months ago
Building
CONFIDENCE
44:25
Building Confidence
52 views • 1 year ago
Healthy Holiday
EATING
Healthy Holiday Webinar
38 views • 1 year ago
Accepting
Prebiotics & Probiotics

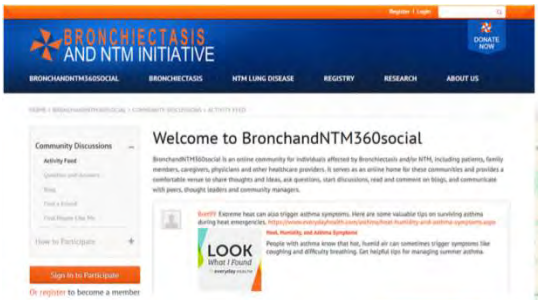
15


NTM ir
Nontuberculous Mycobacteria
NTM Info & Research
"insight"
a patient's perspective
NTM | Bronchiectasis | MAC | Extrapulmonary
SIGN UP for the latest news at ntminfo.org
UPDATED for 2024

16

NTM ir Nontuberculous Mycobacteria NTM Info & Research

360Social



Registry

17

NTM ir Nontuberculous Mycobacteria NTM Info & Research

May 16-17 | FAIRMONT GRAND DEL MAR | San Diego, CA

worldntmday.org

5/16-17: NTM/BE Patient Conference
7/1: World Bronchiectasis Day
8/4: World NTM Day

18

NTM Info & Research

14411 S. Dixie Hwy, Suite 205
Palmetto Bay, FL 33176

305-901-4NTM (4686)
ntmmail@nmtinfo.org
www.ntminfo.org

Facebook.com/NTMinfo @ntminfo @NTMinfo Youtube.com/ntmir NTMir

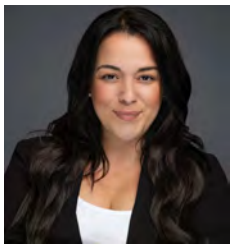
19

NTM Info & Research

Teamwork Makes the Dream Work

Helga Rosado,
Operations Director

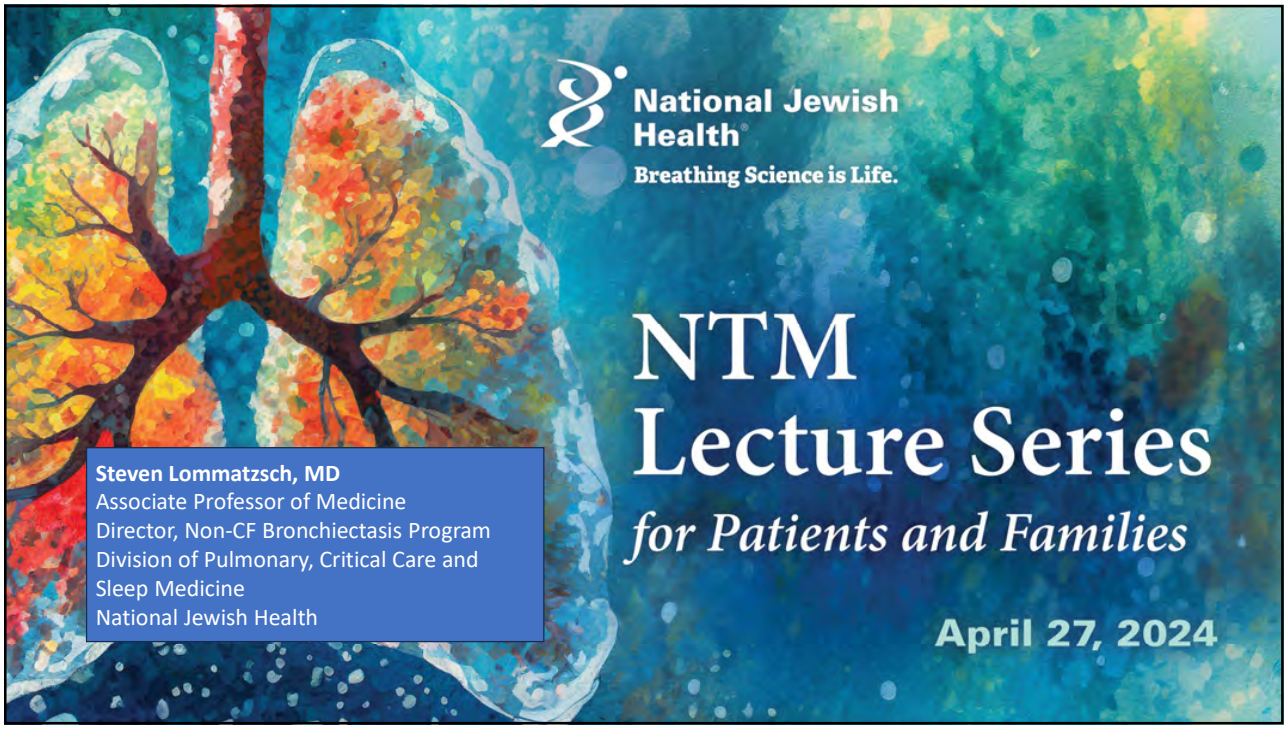
Trisha Kemp,
Community
Engagement Director



Vanessa Hevia,
Office Administrator

Laura Layton,
Community Manager

20



1

Overview of Bronchiectasis

- What is bronchiectasis
- How does one get bronchiectasis
- How is bronchiectasis treated
- Why is bronchiectasis relevant to Mycobacterial infection

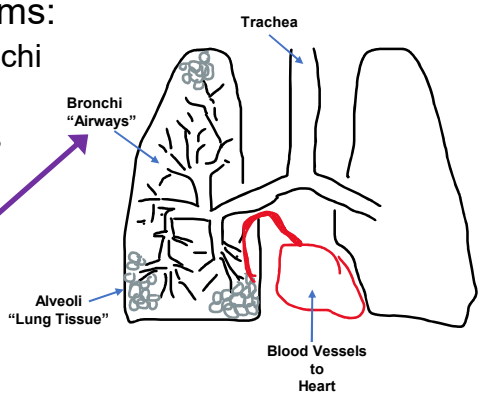
National Jewish Health

2

Normal Lung

- Composed of three main systems:
  - Airway System - Trachea & Bronchi
  - Tissue System - Alveoli
  - Vascular System - Blood vessels

Bronchiectasis is a problem with the BRONCHI = "Air tube problem"



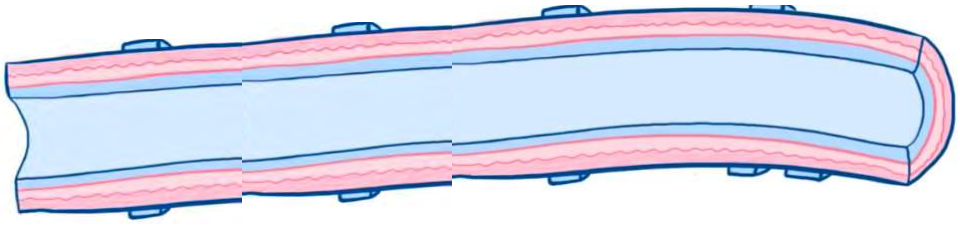
National Jewish Health

3

What is Bronchiectasis

From the Greek "bronkhos"
(windpipe or bronchial tubes) and "ektasis" (dilatation)[1]

Normal Bronchial Airway



1. Chalmers JD. *Chest.* 2017;151:1204-1206.

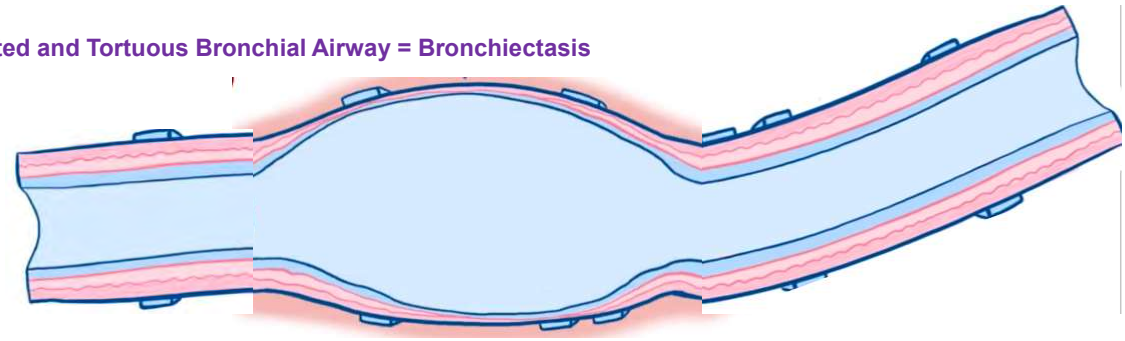
National Jewish Health

4

What is Bronchiectasis

From the Greek “bronkhos”
(windpipe or bronchial tubes) and “ektasis” (dilatation)[1]

Dilated and Tortuous Bronchial Airway = Bronchiectasis



1. Chalmers JD. *Chest.* 2017;151:1204-1206.

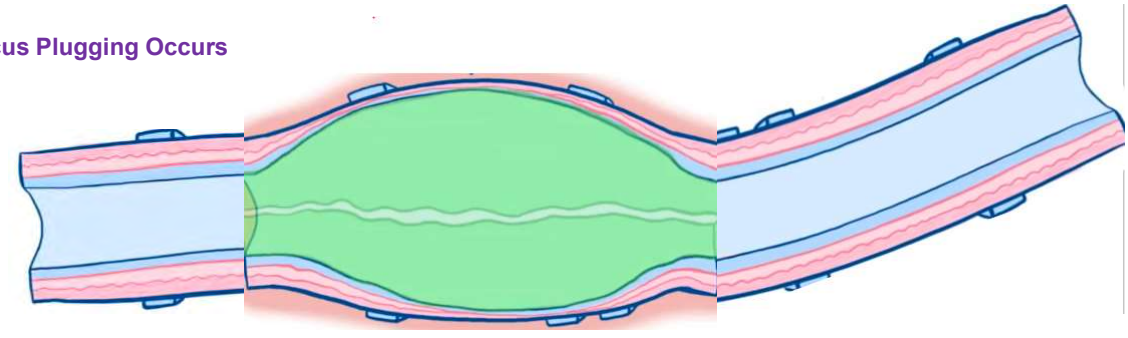
National Jewish Health

5

What is Bronchiectasis

From the Greek “bronkhos”
(windpipe or bronchial tubes) and “ektasis” (dilatation)[1]

Mucus Plugging Occurs



1. Chalmers JD. *Chest.* 2017;151:1204-1206.

National Jewish Health

6

Facts about Bronchiectasis

- Estimated that 350,000 to 500,000 adults in the US have the condition
- The condition is twice as common in women than men
- The disease increases in prevalence with increasing age
- The average number of times patients need to see their doctor in clinic to treat a respiratory illness is between 1 and 3 per year
- On average a patient with severe bronchiectasis is hospitalization once per year

National Jewish Health

7

Diagnosis

- Symptoms may be common to many respiratory diseases
  - Cough, sputum production, shortness of breath, etc
  - Often takes exacerbation or acute event to come to appropriate medical attention
- Many diseases can cause bronchiectasis
- True diagnosis requires radiographic imaging with computed tomography (“CT scan”)

National Jewish Health

8

Symptoms of Bronchiectasis

- Cough (98%)
- Chronic sputum production (78%)
- Dyspnea (62%)
- Fatigue (43%)
- Hemoptysis (27%)
- Wheezing (20%)

National Jewish Health

9

Causes of Bronchiectasis

CONGENITAL	• Tracheobronchomegaly • Cartilage deficiency • Pulmonary sequestration • Yellow nail syndrome • Young's syndrome • Alpha-1 antitrypsin deficiency • Primary ciliary dyskinesia • Cystic fibrosis
IMMUNODEFICIENCY	• Hypogammaglobulinemia • CLL • Chemotherapy • Immunosuppression
POSTINFECTIOUS	• Bacteria • Mycobacterium • Aspergillus • Viruses
RHEUMATOLOGIC	• RA • SLE • Sjögren's syndrome • Relapsing polychondritis • IBD
ASPIRATION/ INHALATION	• Chlorine • Overdoses • Foreign bodies
Other	• ABPA

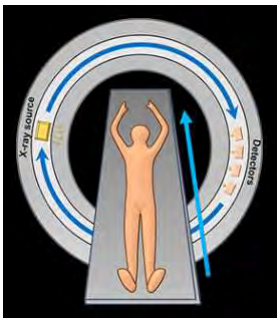
Abbreviations: ABPA, allergic bronchopulmonary aspergillosis; CLL, chronic lymphocytic lymphoma; IBD, inflammatory bowel disease; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

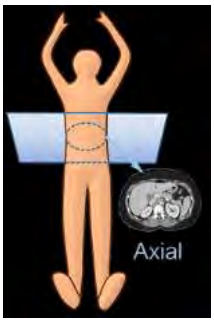
National Jewish Health

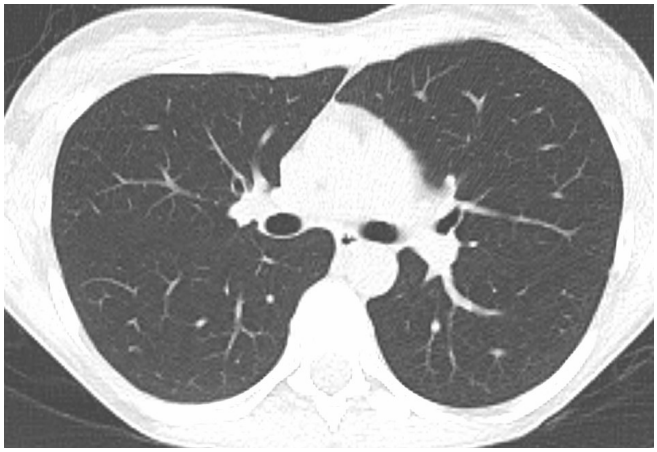
10

Imaging is Essential to Diagnosis

- Chest X-rays
- Chest CT scans





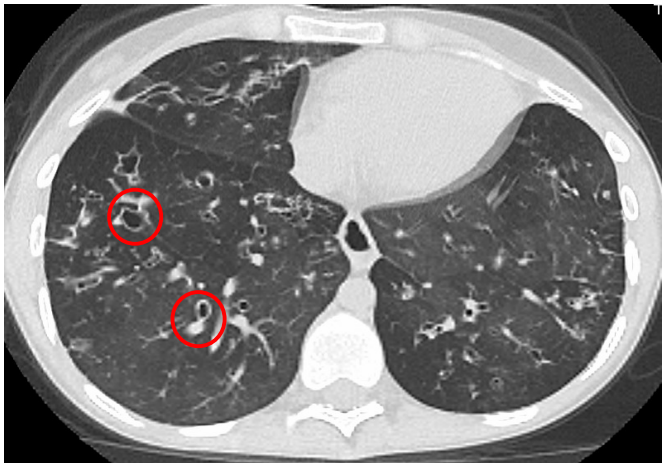


Example of normal chest CT scan

National Jewish Health

11

CT Scan Makes the Diagnosis



Hill AT, et al. *Thorax*. 2019;74:1-69.

CT Features (≥1 of the following)

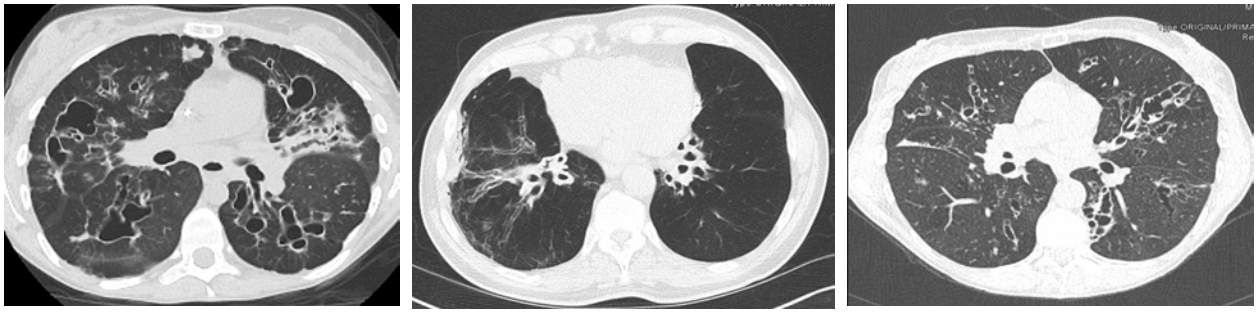
- Bronchoarterial ratio >1 (internal airway lumen/adjacent pulmonary artery) on CT scan
- Lack of airway tapering
- Airway visibility ≤1 cm of costal pleural surface or touching mediastinal pleura

National Jewish Health

12

Types of Bronchiectasis seen on CT scan

Saccular/cystic | Cylindrical/tubular | Varicose



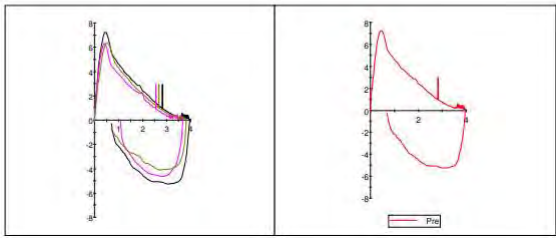
National Jewish Health

13

Other Testing

- "Breathing Test" – Spirometry
- Sputum cultures
  - Sometimes bronchoscopy
- Laboratory bloodwork
  - CBC and diff
  - RF/CCP, SSA, SSB, ANA, ANCA
  - IgE (initial per BTS)
  - Aspergillus precipitins (initial per BTS)
  - IgG, IgA, and IgM (initial per BTS)
  - Consider HIV testing
  - A1AT level/genotype
  - Antibody titers to pneumococcal vaccination (consider work-up per BTS)
  - Testing for PCD and CF (CF is first line per BTS if under 40yo)

---- SPIROMETRY ----	Pred	LLN	Actual	%Pred
FVC (L)	3.57	2.85	3.96	110
FEV1 (L)	3.08	2.47	2.84	92
FEV1/FVC (%)	86.46	74.73	71.75	82
FEF Max (L/sec)	6.68	5.06	7.24	108
FEF 25-75% (L/sec)	3.60	2.36	1.98	55
FIF Max (L/sec)	4.24		5.24	123
FEF50%/FIF50% (%)	90-100		50	
Expiratory Time (sec)			6.80	
Back Extrap Vol (L)			0.08	
FIVC (L)			3.25	



14

Treatment and Management Gaps

- There are currently no guidelines for the management of bronchiectasis in the United States
  - British Thoracic Society guideline, 2019 (updated from 2010)[1]
  - Thoracic Society of Australia and New Zealand position statement, 2023 (updated from 2015)[2]
  - European Respiratory Society guidelines, 2017[3]
- There are no therapies that are currently FDA-approved for the airway condition of bronchiectasis
- Much of the treatment of NCFBE has been influenced by cystic fibrosis research and management recommendations

National Jewish Health

15

Treatment Starts With Identifying Cause

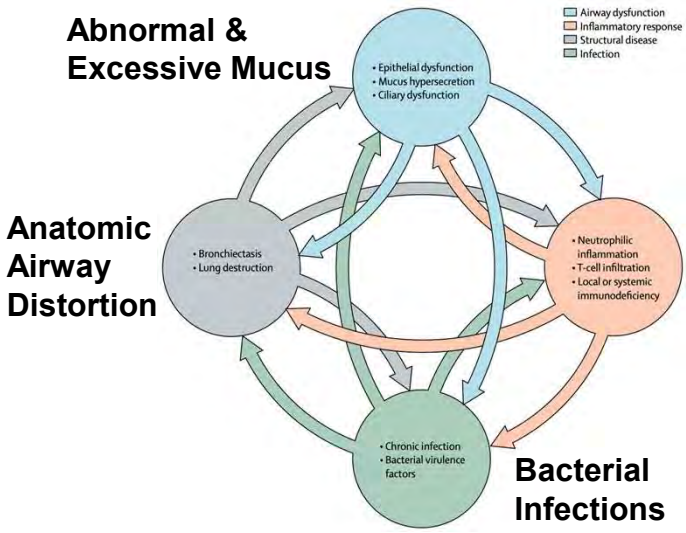
Condition / Disease	Treatment
ABPA	Oral steroids +/- oral antifungal
Alpha-1 antitrypsin deficiency	Alpha-1 protein replacement
Aspiration/GERD	Treat GERD and speech therapy
Cystic fibrosis	CFTR modulator therapy
Immunodeficiency (CVID)	IVIg replacement therapy
Infection (TB, NTM, etc)	Antibiotics
Rheumatologic/Autoimmune/ Inflammatory Diseases (RA, Sjogren's, IBD, etc)	Immunosuppression

Abbreviations: ABPA, allergic bronchopulmonary aspergillosis; CFTR, cystic fibrosis transmembrane conductance regulator; CVID, common variable immunodeficiency; GERD, gastroesophageal reflux disease; IBD, inflammatory bowel disease; IVIg, intravenous immunoglobulin; NTM, nontuberculous mycobacteria ; RA, rheumatoid arthritis; TB, tuberculosis.

National Jewish Health

16

Targeted Treatment—The Vicious Vortex



National Jewish Health

17

The 3 Cornerstones of Management

1. Airway clearance
2. Airway clearance
3. Airway clearance

Amazingly this cornerstone is often **forgotten** and **overlooked**!

National Jewish Health

18

Components of Treatment

1. Mucus Management
2. Inflammation Attenuation
3. Infection Control

- Decreases progression of airway distortion and scarring
- Maintains better lung function

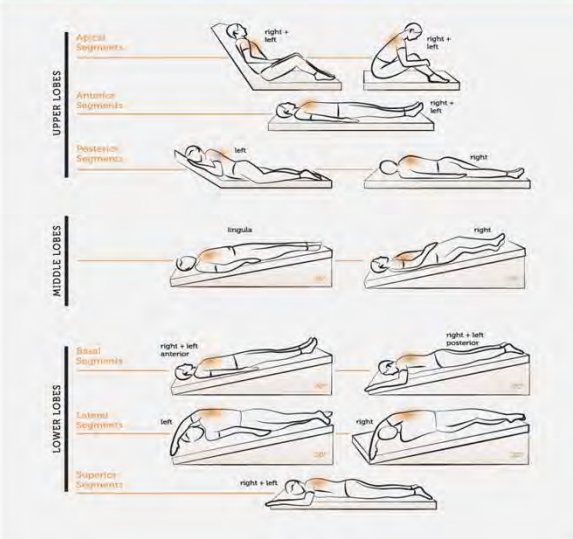
- Helps control patient symptoms
- Prevents illness / hospitalization
- Decreases likelihood of needing oxygen therapy

National Jewish Health

19

Airway Clearance - Mechanical

- Manual Chest Physiotherapy
- Active Cycle Breathing, Autogenic drainage, Huff Coughing
- Postural Drainage
- Positive expiratory pressure devices
- Oscillating devices, High-frequency chest wall oscillation, Flutter, Acapella devices
- Inspiratory muscle training
- Aerobic training/exercise



20

Airway Clearance - Pharmacologic

- Hypertonic saline (0.9%, 3%, 7%, 10%)
  - HR-QOL, 6MWT improvement, decrease healthcare utilization
- N-acetylcysteine (NAC) or “Mucomyst” nebulization
- Bronchodilator therapy – SABA before saline / airway clearance

National Jewish Health

21

I’ve heard it all….

- “I can cough it up, so I don’t need to do my airway clearance.”
- “I do not get anything up when I use it, so I stopped.”
- “I use it when I start to get sick.”

- If bronchiectasis is a disease of distorted airways getting plugged with mucus and trapping bacteria in that mucus, then the treatment starts with getting that mucus out to clear the lung of bacteria/infection.

National Jewish Health

22

Inflammation Attenuation

- Azithromycin daily therapy
  - Decrease exacerbations
  - Reduces Sputum Production
  - Improve lung function
  - Improve Quality of Life

"Macrolide" antibiotics are:
- Azithromycin
- Clarithromycin
- Erythromycin

It is important to **exclude** NTM infection with sputum cultures prior to starting therapy to avoid breeding resistance!

National Jewish Health

23

Control Infections

- Treat Exacerbations
- Chronic suppressive inhaled antibiotic treatment
- NTM – MYCOBACTERIAL THERAPY

National Jewish Health

24

Monitoring and Follow-up

- Regular visits with symptom assessments
- Spirometry – clinic based / home spirometry
- Sputum cultures
- Imaging / CT imaging (radiographic progression)
- Re-education and goals discussions

National Jewish Health

25

Future Treatments

- Treatments that decrease neutrophil activity
- Biologic agents target inflammation
- Nebulized immunoglobulin therapy
- Inhaled ascorbic acid and glutathione
- CFTR potentiator therapy
- Novel antimicrobial development

National Jewish Health

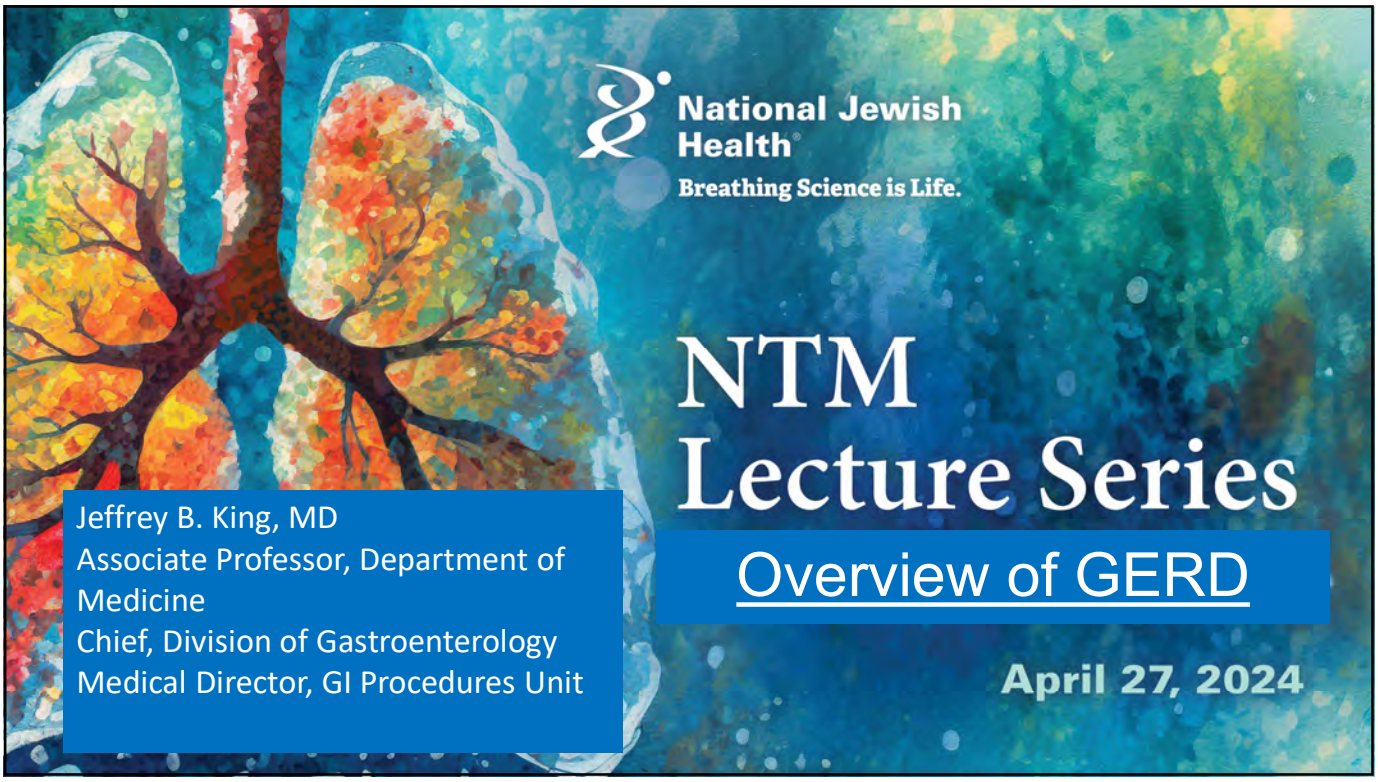
26

Thank you

- Any questions?

National Jewish Health

27



1

Disclosures

- I have no financial disclosures
- The off-label use of the medications baclofen and bethanechol will be discussed in this talk

2

Learning Objectives

I. Understand how GERD may effect NTM pulmonary disease
II. Understand options for reflux testing
III. Understand how reflux management may differ when trying to prevent aspiration

3

Outline

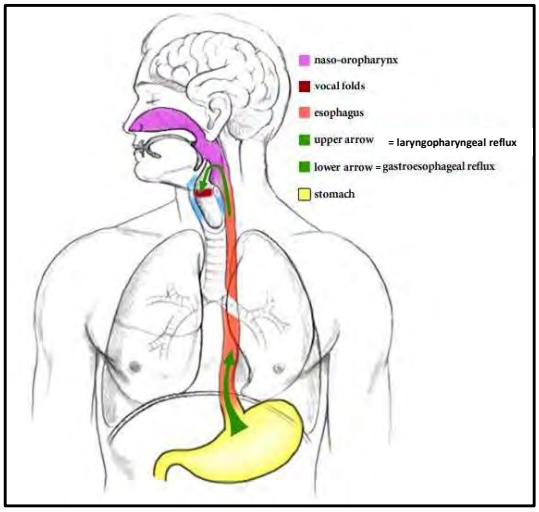
I. Relationship Between GI Tract and Lungs
II. GERD and NTM
III. Reflux Testing
IV. Treatment of Reflux

4

Relationship Between GI Tract and Lungs

5

Location, Location, Location



- **GERD (Gastroesophageal Reflux Disease):** symptoms or complications resulting from the reflux of gastric contents into the esophagus or beyond, including the oral cavity and/or lungs
- **Laryngopharyngeal Reflux (LPR):** retrograde movement of gastric contents into the larynx, pharynx, and upper aerodigestive tract
- **Aspiration:** entry of material from the oropharynx or GI tract into the larynx and lower respiratory tract (antegrade or retrograde)
- **GI-Related Aspiration (GRASP):** aspiration of material originating distal to the upper esophageal sphincter (retrograde only)

Am J Gastroenterol. 2013 Feb;108:308-28.

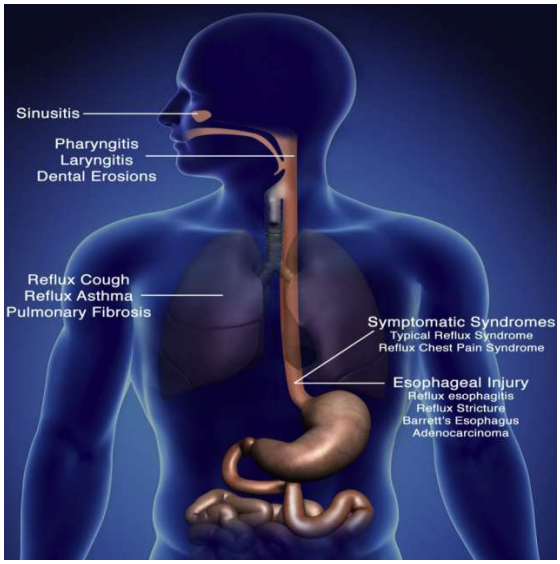
6

How Common is GERD?

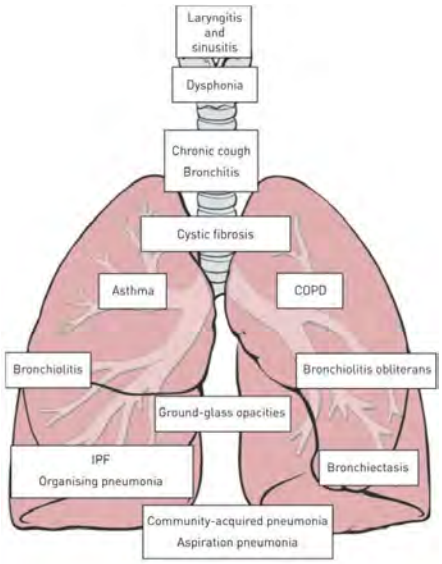
- 60% of adults experience reflux symptoms over a 12 month period
- 30-40% had reflux symptoms in the last month
- 20-30% have weekly symptoms
- 10% have symptoms ≥ twice weekly

7

Manifestations of GERD



Best Pract Res Clin Gastroenterol. 2013 Jun;57(3):415-31.



ERJ Open Res. 2020; 6: 00190-2019.

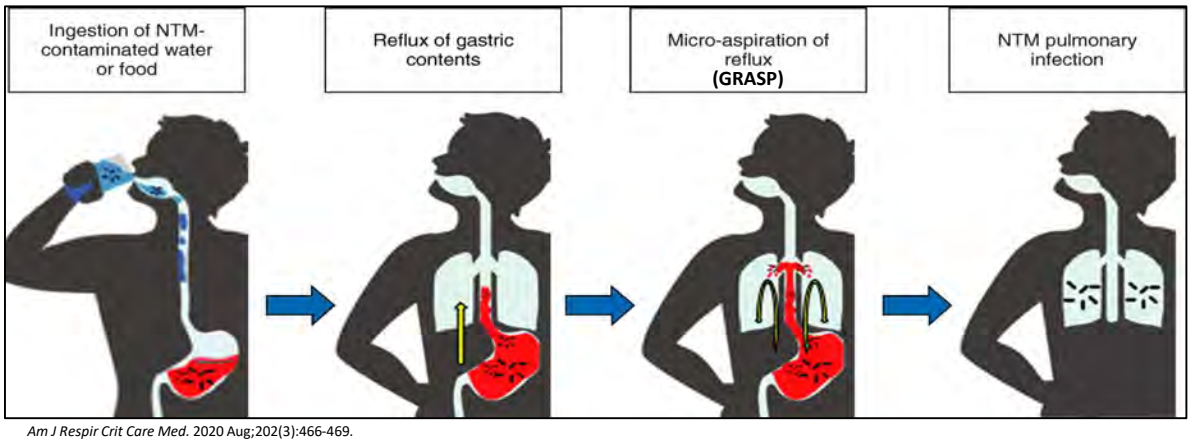
8

GERD and NTM

9

How Does GERD Relate to NTM?

- NTM are ubiquitous environmental organisms



Am J Respir Crit Care Med. 2020 Aug;202(3):466-469.

- In the proper host setting, this may cause chronic infection

10

GERD and NTM

Table 4—*Prevalence of GERD and Consumption of Acid-Suppressive Medication in Cases (MAC+) and Controls (MAC−)**

Variables	MAC+	MAC−	p Value (Fisher Exact Test)
GERD	25 (43.1)	16 (27.6)	< 0.0001
Antacids	4 (6.9)	14 (24.1)	0.038
H2RAs	15 (25.9)	6 (10.3)	0.013
Proton-pump inhibitor	12 (20.7)	7 (12.1)	0.127
Prokinetic agents	4 (6.9)	0	0.039
Any acid suppression	27 (56.3)	26 (44.8)	0.165

*Data are presented as No. (%).

Chest. 2007 Apr;131(4):1166-72.

11

GERD and NTM

Table 3—*Demographic Characteristics of GERD-Positive and GERD-Negative Patients With the Nodular Bronchiectatic Form of NTM Lung Disease**

Characteristics	GERD Positive (n = 15)	GERD Negative (n = 43)	p Value
Age, yr	56 (43–63.5)	57 (53–66.5)	0.320
Female gender	13 (87)	37 (86)	1.000
Body mass index, kg/m^2	20.0 (18.6–21.7)	20.6 (19.5–22.2)	0.316
Smoking status			
Non-smoker	14 (93)	40 (93)	1.000
Ex-smoker	1 (7)	3 (7)	
Etiology			
M avium complex	5 (33)	22 (51)	0.368
M abscessus	10 (67)	21 (49)	
AFB smear positive	12 (80)	19 (44)	0.033
Involved lobes on HRCT, No.			
Bronchiectasis	4 (3–4)	2 (2–3)	0.008
Bronchiolitis	4 (3–5)	2 (2–4)	0.005
Pulmonary function tests			
FVC, % of predicted	93.0 (83.0–102.0)	87.0 (77.5–93.5)	0.170
FEV_1, % of predicted	92.5 (76.5–107.0)	88.0 (72.5–102.0)	0.508
FEV_1/FVC, ratio	76.0 (67.0–84.0)	74.0 (71.0–80.0)	0.880
Peak expiratory flow, % of predicted	92.0 (80.0–111.5)	96.0 (74.5–99.0)	0.748

*Data are presented as the median (interquartile range) or No. (%). Bronchiolitis was defined as the presence of small centrilobular nodules (< 10 mm in diameter) or branching nodular structures (tree-in-bud pattern) on HRCT.

Chest. 2007 Jun;131(6):1825-30.

12

GERD and NTM

- U.S. Bronchiectasis Research Registry
- 1,826 patients with bronchiectasis
- 63% had history of NTM
- GERD: 51% NTM patients, 40% no NTM

Chest. 2017 May;151(5):982-992.

13

GERD and NTM

- Korean National Health Insurance Service National Sample Cohort
- Matched GERD patients with non-GERD patients (1:4) from 2003-2014.
  - ICD-10 codes and PPI use > 3 months.
- Looked at who developed NTM.

Chest. 2023;163(2):270-280.

14

GERD and NTM

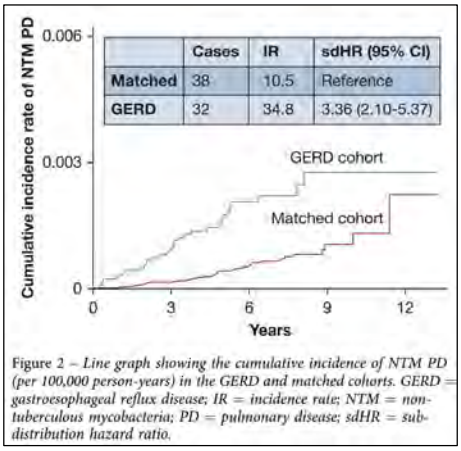


Figure 2 – *Line graph showing the cumulative incidence of NTM PD (per 100,000 person-years) in the GERD and matched cohorts. GERD = gastroesophageal reflux disease; IR = incidence rate; NTM = nontuberculous mycobacteria; PD = pulmonary disease; sdHR = subdistribution hazard ratio.*

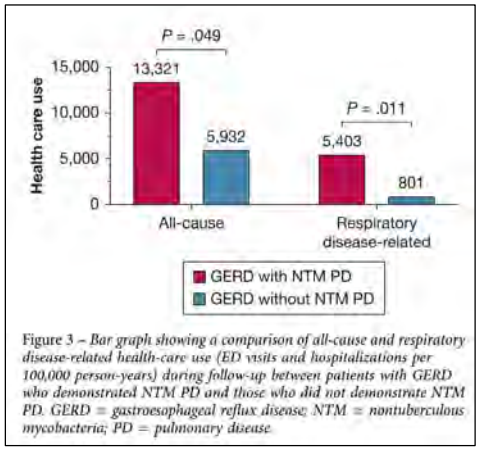


Figure 3 – *Bar graph showing a comparison of all-cause and respiratory disease-related health-care use (ED visits and hospitalizations per 100,000 person-years) during follow-up between patients with GERD who demonstrated NTM PD and those who did not demonstrate NTM PD. GERD = gastroesophageal reflux disease; NTM = nontuberculous mycobacteria; PD = pulmonary disease.*

Chest. 2023;163(2):270-280.

15

How Do We Detect/Measure GRASP?

- **WE CAN'T!!!**
- What can we measure?
  - Gastroesophageal reflux
  - Esophageal motility
  - Stomach motility
  - Sputum cultures
  - Lung inflammation/damage
  - Lung function
- There are no agreed-upon criteria for diagnosing GRASP
- Current testing may tell us how at-risk or not at-risk a patient is for GRASP

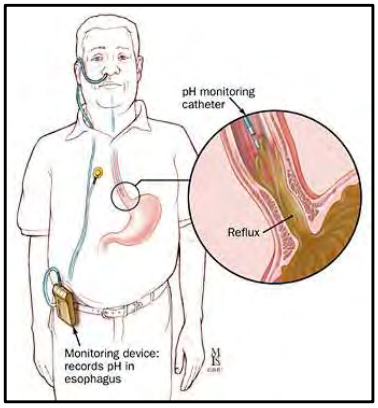
16

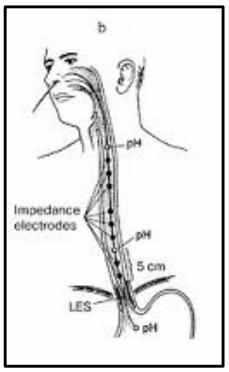
Reflux Testing

17

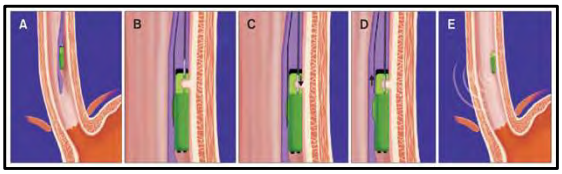
Reflux Testing

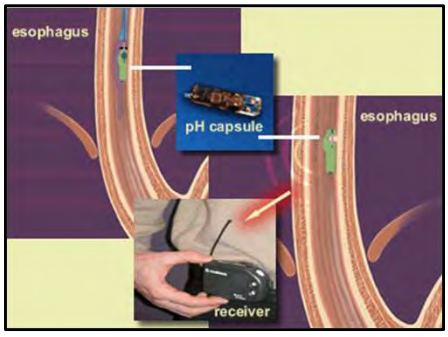
pH-Impedance Testing





Bravo pH Testing





18

pH-Impedance vs. Bravo

	pH-Impedance	Bravo
Time	22-24 hrs	48-96 hrs ✓
Where in Esophagus	Top and bottom ✓	Bottom
Discomfort	Yes	Minimal ✓
Detects Acid	Yes ✓	Yes ✓
Detects Non-acid	Yes ✓	No

19

Treatment of Reflux

20

How Can We Reduce Reflux?

1. Lifestyle modifications
2. Medications
3. Antireflux procedures

21

Lifestyle Modifications for GERD

Table 3. Efficacy of lifestyle interventions for GERD

Lifestyle intervention	Effect of intervention on GERD parameters	Sources of data	Recommendation
Weight loss (46,47,48)	Improvement of GERD symptoms and esophageal pH	Case–Control	Strong recommendation for patients with BMI>25 or patients with recent weight gain
Head of bed elevation (50–52)	Improved esophageal pH and symptoms	Randomized Controlled Trial	Head of bed elevation with foam wedge or blocks in patients with nocturnal GERD
Avoidance of late evening meals (180, 181)	Improved nocturnal gastric acidity but not symptoms	Case–Control	Avoid eating meals with high fat content within 2–3 h of reclining
Tobacco and alcohol cessation (182–184)	No change in symptoms or esophageal pH	Case–Control	Not recommended to improve GERD symptoms
Cessation of chocolate, caffeine, spicy foods, citrus, carbonated beverages	No studies performed	No evidence	Not routinely recommended for GERD patients. Selective elimination could be considered if patients note correlation with GERD symptoms and improvement with elimination

BMI, body mass index; GERD, gastroesophageal reflux disease.

Am J Gastroenterol. 2013 Feb;108:308-28.

22

Management of Suspected Extraesophageal Reflux – AGA Recs

Grade B: recommended with fair evidence that it improves important outcomes

I. Acute or maintenance therapy with once- or twice-daily PPIs (or H_2RAs) for patients with a suspected extra-esophageal GERD syndrome (laryngitis, asthma) with a concomitant esophageal GERD syndrome.

Grade D: recommend against, fair evidence that it is ineffective or harms outweigh benefits

I. Once- or twice-daily PPIs (or H_2RAs) for acute treatment of patients with potential extraesophageal GERD syndromes (laryngitis, asthma) in the absence of a concomitant esophageal GERD syndrome.

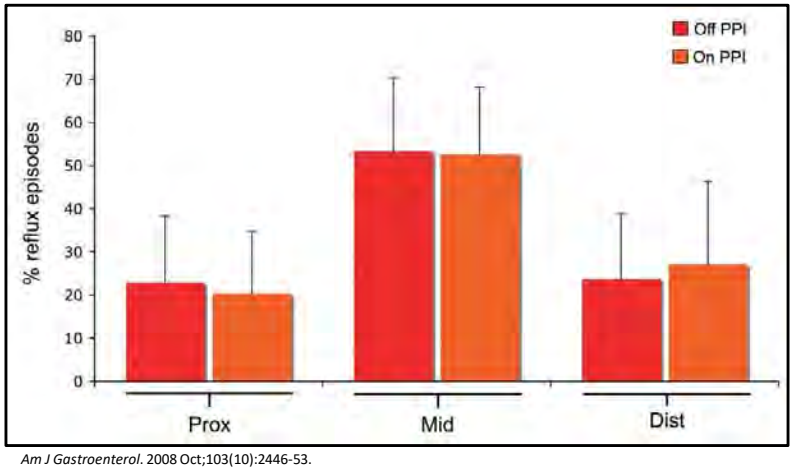
Grade Insuff: no recommendation, insufficient evidence to recommend for or against

I. Once- or twice-daily PPIs for patients with suspected reflux cough syndrome.

Gastroenterology. 2008;135:1383-91.

23

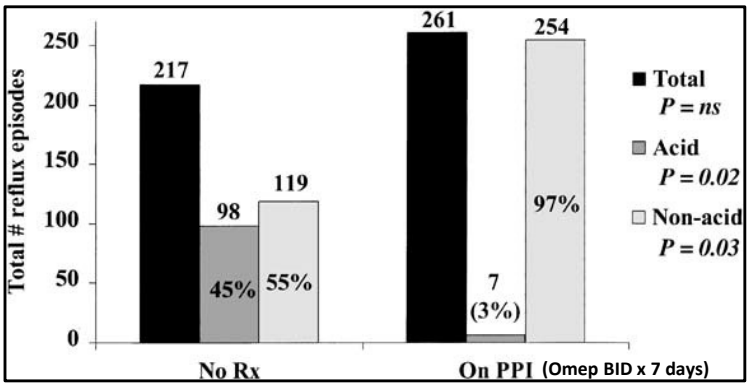
Why Aren't Acid Reducers the Right Choice?



Am J Gastroenterol. 2008 Oct;103(10):2446-53.

24

Why Aren't Acid Reducers the Right Choice?

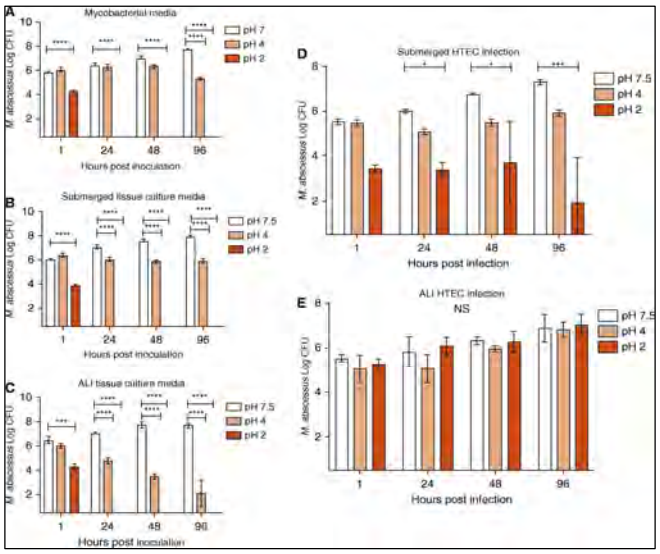


** PPIs REDUCE ACID, NOT REFLUX **

Gastroenterology. 2001 Jun;120(7):1599-1606.

25

Can Acid Reducers Worsen NTM?

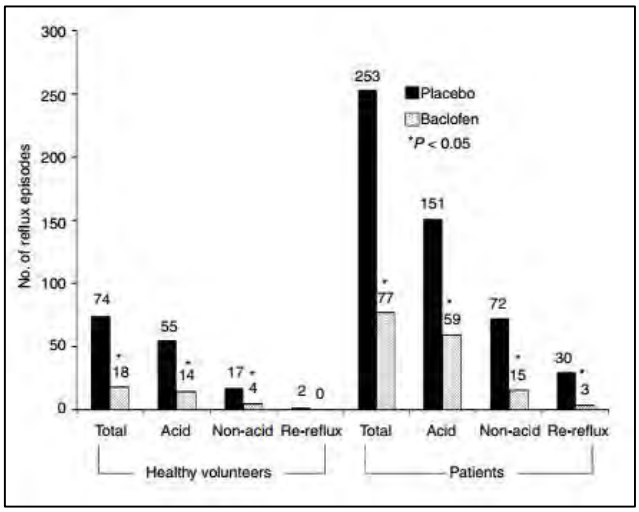


Am J Respir Crit Care Med. 2020 Aug;202(3):466-469.

26

Are There Medications That Reduce Reflux?

Baclofen



Aliment Pharmacol Ther. 2003 Jan;17(2):243-51.

Bethanechol

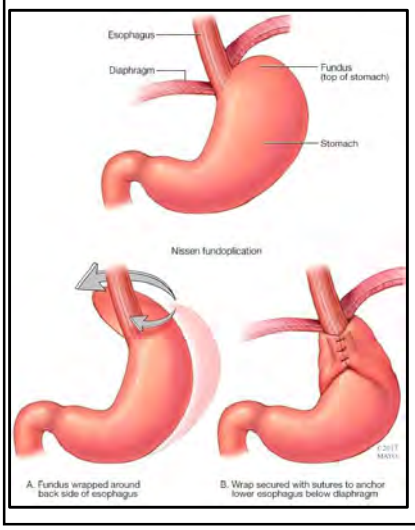
- Improves esophageal motility/clearance
- Increases LES pressures
- Anecdotal evidence of reducing reflux
- ** No reflux studies **

Yale J Biol Med. 1999 Mar-Jun;72(2-3)173-80.
J Clin Gastroenterol. 2007 Apr;41(4):366-70.
Gut. 1999 Sep;45:346-54.

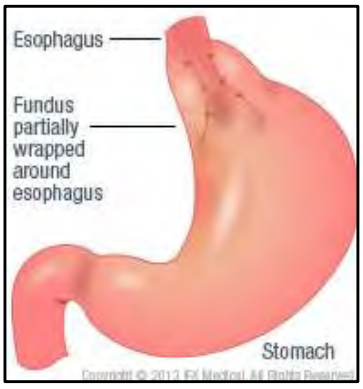
27

Antireflux Surgeries

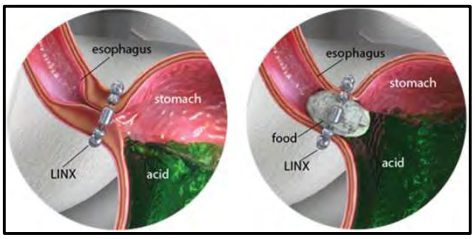
Nissen Fundoplication



Partial Fundoplication



LINX Procedure



28

Take Home Points

- The GI tract and airway are close together
- GRASP likely plays a role in NTM infection
- We cannot definitively diagnose GRASP
- Choose the proper reflux test and interpret properly
- Not all reflux is acid; acid reducers don't reduce reflux
- Lifestyle mods, meds, and surgery can reduce reflux

29

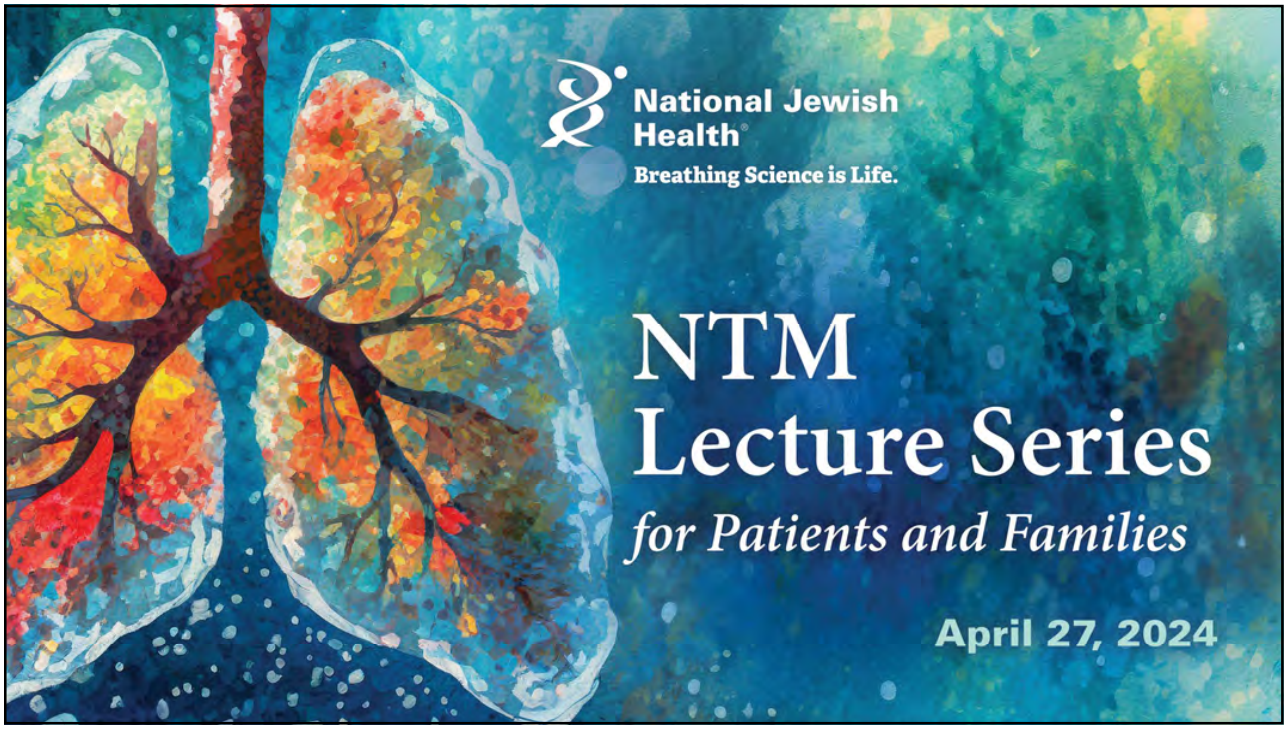
Thank You

30

References

1) *Am J Gastroenterol*. 2013 Feb;108:308-28
2) *Best Pract Res Clin Gastroenterol*. 2013 Jun;57(3):415-31
3) *ERJ Open Res.* 2020; 6: 00190-2019
4) *Am J Respir Crit Care Med.* 2020 Aug;202(3):466-469
5) *Chest*. 2007 Jun;131(6):1825-30
6) *Chest*. 2007 Apr;131(4):1166-72
7) *Chest.* 2017 May;151(5):982-992
8) *Chest*. 2023;163(2):270-280
9) *Am J Gastroenterol*. 2008 Oct;103(10):2446-53
10) *Gastroenterology*. 2008;135:1383-91
11) *Gastroenterology*. 2001 Jun;120(7):1599-1606
12) *Aliment Pharmacol Ther*. 2003 Jan;17(2):243-51
13) *Yale J Biol Med*. 1999 Mar-Jun;72(2-3)173-80
14) *J Clin Gastroenterol*. 2007 Apr;41(4):366-70
15) *Gut*. 1999 Sep;45:346-54

31



1

Treatment of Nontuberculous Mycobacterial (NTM) Infections

Charles L. Daley, MD
Professor of Medicine
National Jewish Health,
University of Colorado,
Icahn School of Medicine, Mt. Sinai

Chief, Division of Mycobacterial and Respiratory Infections
National Jewish Health

National Jewish Health

2

Disclosures

Consultant: Genentech, Pfizer

Advisory Board Member: AN2, Hyfe, Insmed, MannKind, Matinas BioPharma Holdings, Inc., Nob Hill, Paratek Pharmaceuticals, Spero Therapeutics, Zambon

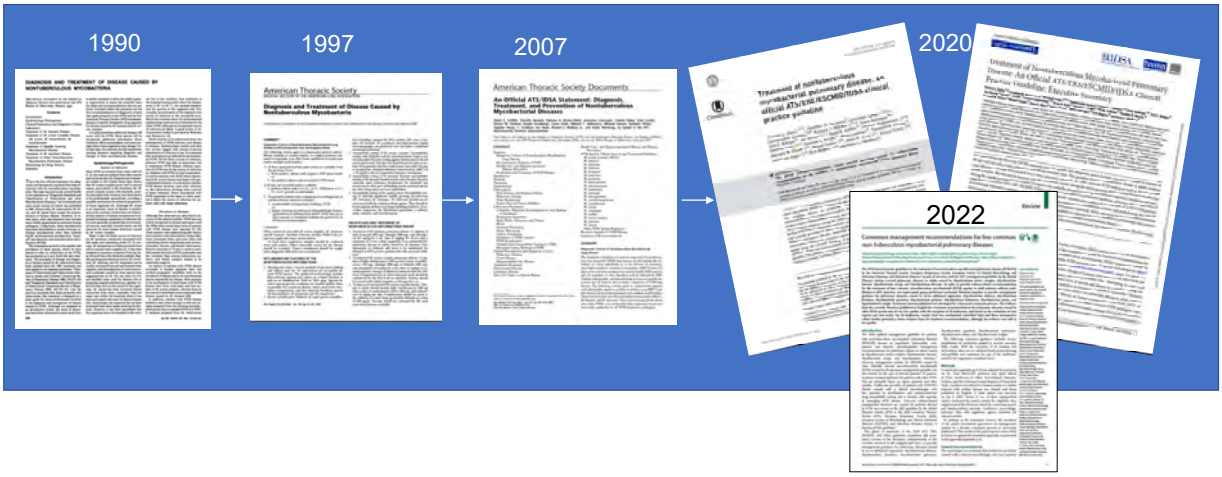
Data Monitoring Committee: Ostuka Pharmaceutical, Bill and Melinda Gates Foundation

Contracted Research: AN2 Therapeutics, Bugworks, Insmed, Juvabis, Paratek Pharmaceuticals

National Jewish Health

3

NTM Treatment Guidelines



Daley CL, et al. CID 2020;71:5-913 and Euro Respir J 2020;56:2000535
Lange C, et al. Lancet Infect Dis 2022;22:e178-190

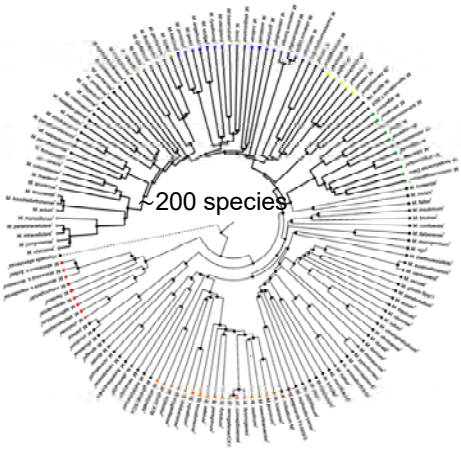
National Jewish Health

4

NTM Treatment Guidelines

<u>*Slow Growers*</u>
***M. avium* complex**
M. kansasii
M. Xenopi

<u>Rapid Growers</u>
M. abscessus



<u>*Slow Growers*</u>
M. malmoense
M. simiae
M. szulgai
M. genevense
M. gordonae

<u>*Rapid Growers*</u>
M. chelonae
M. fortuitum

National Jewish Health

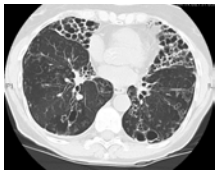
5

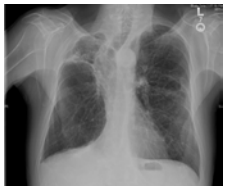
ATS Diagnostic Criteria For NTM Lung Disease

Clinical

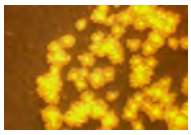
Cough
Fatigue
Weight Loss

Radiographs





Bacteriology



≥ 2 positive
sputum cultures

National Jewish Health

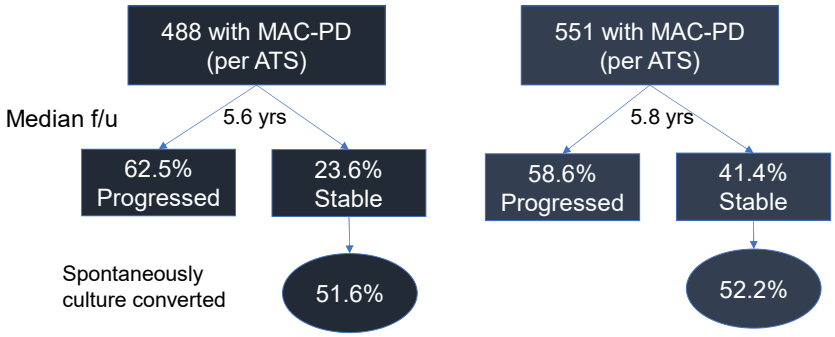
Daley CL, et al. CID 2020;71:5-913 and Euro Respir J 2020;56:2000535

6

Watchful waiting or initiation of treatment?

Guideline recommendation

In patients who meet the diagnostic criteria for NTM pulmonary disease, we suggest initiation of treatment rather than watchful waiting, especially in the context of positive acid-fast bacilli sputum smears and/or cavitary lung disease (conditional recommendation, very low certainty in estimates of effect).



Hwang JA, et al. Eur Respir J 2017;49:1600537

Kwon BS, et al. Resp Med 2019;150:45-50

Daley CL, et al. *CID* 2020;71:5-913; *Euro Respir J* 2020;56:2000535

National Jewish Health

7

Whom to Treat?

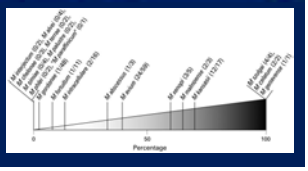
Risk Factors Associated with Progression

Host/Demographic Factors
- Male gender
- Older age
- Presence of comorbidities
- Low body mass index

Laboratory Factors
- Elevated inflammatory indices (ESR, CRP)
- Anemia
- Hypoalbuminemia

Radiographic Factors
- Fibrocavitary
- Extent of disease

Microbial Factors
- Bacterial load
- Species



Kwon BS et al. *Resp Med*. 2019;150:45-50.
Moon SM et al. *Resp Med*. 2019;151:1-7.

National Jewish Health

8

NTM Pulmonary Disease: Whom to Treat

Consider the:

Patient

Organism

Goals of Treatment

National Jewish Health

9

NTM Pulmonary Disease: Whom to Treat

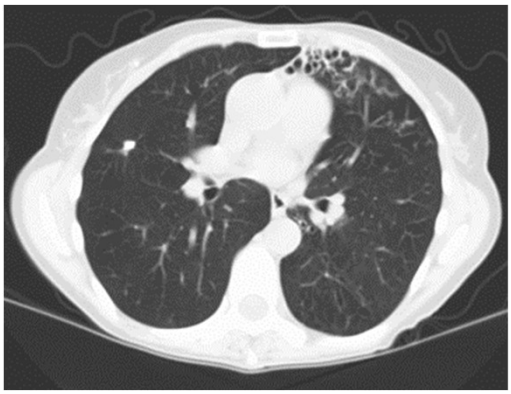
Patient

- Increased risk of progression?
  - Cavitation, positive AFB smear, other risk factors?
- Clinical symptoms and overall condition?
  - Asymptomatic vs very symptomatic
- Extent of radiograph abnormalities and whether there is evidence of progression?

National Jewish Health

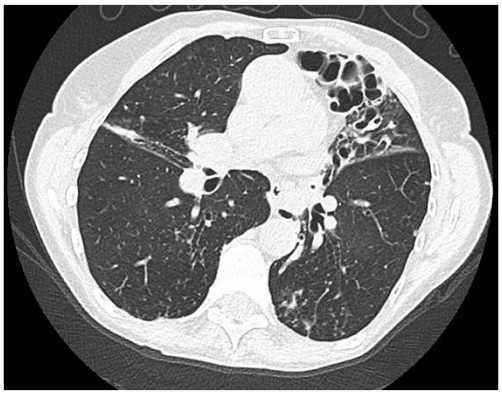
10

NTM Pulmonary Disease: Whom to Treat



65 yr old woman
Chronic cough

8 yrs



Diagnosed with MAC

"Bronchitis" 2-3 times/yr

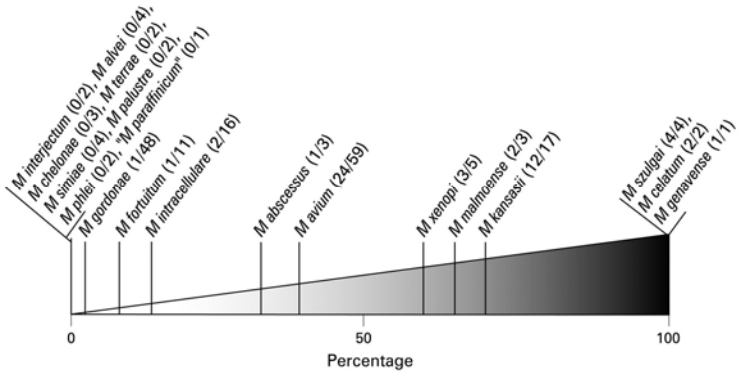
National Jewish Health

11

NTM Pulmonary Disease: Whom to Treat

The degree of pathogenicity (ability to cause disease) varies greatly among NTM

Organism



National Jewish Health

12

NTM Pulmonary Disease: Whom to Treat

Goals of Treatment

What are we trying to achieve?

- Cure?
- Bacteriologic conversion?
- Relief of symptoms?
- Prevention of progression?
- All of the above!

National Jewish Health

13

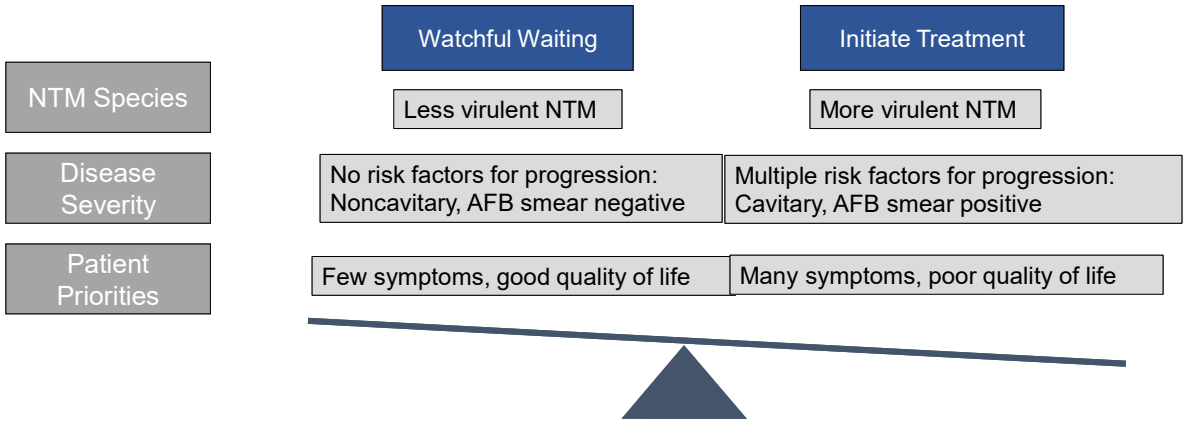
NTM: Treatment Outcomes by Species

NTM	Expected Cure
M. kansasii	≥ 95%
MAC	56% to 85% Depends on extent of disease
M. abscessus	25-80% Depends on subspecies

National Jewish Health

14

Decision to Treat



Daley CL, et al. *CID* 2020;71:5-913 and *Euro Respir J* 2020;56:2000535

National Jewish Health

15

Why Early Diagnosis and Treatment Are Important

- Disease progression occurs within 3-5 years in ~60% of persons who meet ATS/IDSA diagnostic criteria[1-3]
- Lung function declines[4,5]
- 5-year all-cause mortality can be as high as 10%-33%[6-8]
  - Mortality is not usually due to NTM itself
  - Mortality higher in untreated than treated MAC (33% vs. 22%)[6]

1. Hwang JA, et al. *Eur Respir J*, 2017;49:1600537; 2. Kwon BS, et al. *Respir Med* 2019;150:45-50; 3. Moon SM, et al. *Respir Med* 2019;151:1-7; 4. Park HY, et al. *Chest* 2016;150:1222-1232; 5. Kimuzuka Y, et al. *PLoS ONE* 2019;14:e0216034; 6. Ito Y, et al. *Int J Tuberc Lung Dis* 2012;16:408-14; 7. Diel R, et al. *BMC Infect Dis* 2018;18:206; 8. Jhun BW, et al. *Eur Respir J* 2020;55:1900798.

National Jewish Health

16

Treatment of NTM: Background

- Treatment requires multidrug regimens
  - Varies by species
  - Frequently associated with side-effects
- Treatment duration is long
  - 12 mos after culture becomes negative (conversion)
- Treatment outcomes are suboptimal
  - Vary by species
  - High rates of recurrence and reinfection.

Griffith DE, et al. *Curr Opin Infect Dis*. 2012;25(2):218-227.

National Jewish Health

17

Mycobacterium avium Complex

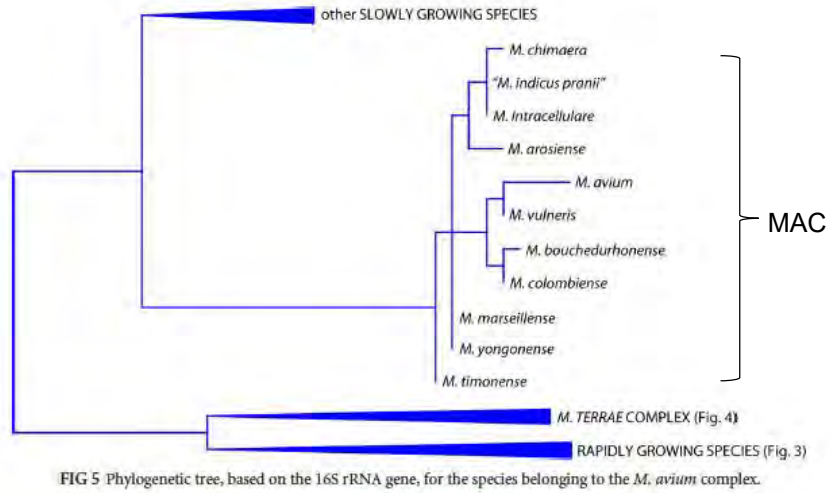


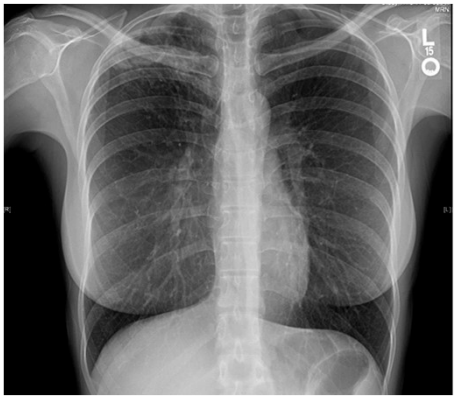
FIG 5 Phylogenetic tree, based on the 16S rRNA gene, for the species belonging to the *M. avium* complex.

Tortoli E. Clin Micro Rev 2014;27:727-752

National Jewish Health

18

35 year old Caucasian woman with cough for several weeks



National Jewish Health

19

Drugs Used for the Treatment of MAC

First-Line Oral	Alternative Oral	Parenteral (IV, IM)	Inhaled
Macrolides azithromycin clarithromycin	**Fluoroquinolones** moxifloxacin ciprofloxacin	**Aminoglycosides** amikacin streptomycin	**Aminoglycosides** amikacin
Rifamycins rifampin riifabutin	**Oxazolidinones** linezolid tedizolid		
Ethambutol	Bedaquiline		
	Clofazimine		

National Jewish Health

20

Mycobacteriology Laboratory Results

Common Report

Identification:
M. avium complex

Drug susceptibility:
Amikacin R
Clarithromycin S
Rifampin S
Ethambutol R
Linezolid R
Moxifloxacin I

Preferred Report

Identification:
100 colonies of *M. intracellulare ssp chimaera*

Drug susceptibility:	**MIC**
Amikacin	8
Clarithromycin	2
Linezolid	32
Moxifloxacin	2
Clofazimine	0.25

National Jewish Health

21

Recommended Initial Treatment Regimens for MAC Pulmonary Disease

Phenotype	No. of Drugs	Preferred Regimen[a]	Dosing Frequency	Duration
Nodular-bronchiectatic	3	Azithromycin (clarithromycin) Rifampin (rifabutin) Ethambutol	3 times weekly	12 months beyond culture conversion
Cavitary	≥ 3	Azithromycin (clarithromycin) Rifampin (rifabutin) Ethambutol Amikacin IV (streptomycin)[b]	Daily (IV aminoglycoside may be used 3 times weekly)	

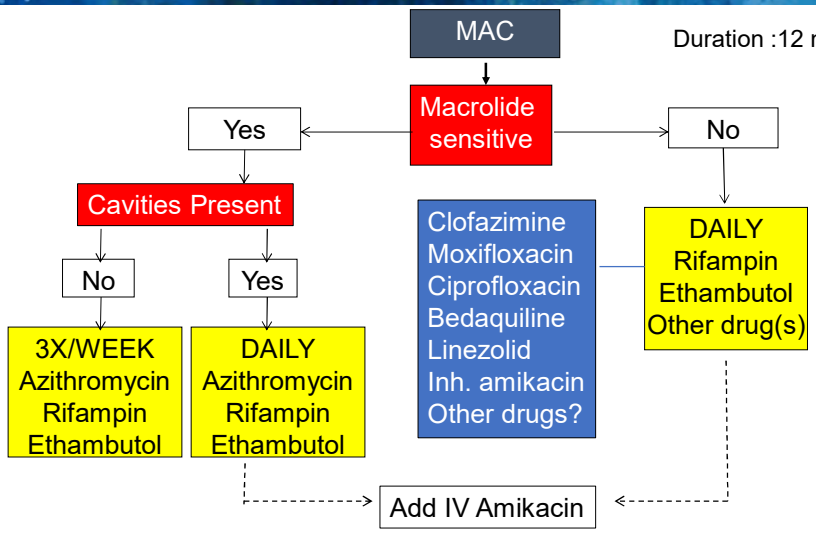
a. Alternative drugs could include clofazimine, moxifloxacin, linezolid (tedizolid), bedaquiline
b. Consider for cavitary, extensive nodular bronchiectatic or macrolide resistant disease

National Jewish Health

Daley CL, et al. CID 2020;71:905-913 and Euro Respir J 2020;56:2000535

22

Treatment of Pulmonary *M. avium* complex



National Jewish Health

23

Treatment Outcomes for MAC

	Culture Conversion	Microbiologic Recurrence	Reinfection
Macrolide susceptible			
Non cavitary Cavitary	70% - 80% 50% - 80%	25-48%	46-75%

Griffith DE et al. *Am J Respir Crit Care Med.* 2006;174:928-934.
Jeong BH et al. *Am J Respir Crit Care Med.* 2015;191:96-103.
Moon SM et al. *Eur Respir J.* 2016;50:1602503.

Wallace R et al. *Chest.* 2014;146:276-282.
Koh WJ et al. *Eur Respir J.* 2017;50.
Morimoto K et al. *Ann Am Thorac Soc.* 2016;11:1904.

Boyle DP et al. *Ann Am Thorac Soc.* 2016;13:1956-1961

National Jewish Health

24

Treatment Outcomes for MAC

	Culture Conversion	Microbiologic Recurrence	Reinfection
Macrolide susceptible			
Non cavitary Cavitary	70% - 80% 50% - 80%	25-48%	46-75%
Macrolide resistant			
No surgery/aminoglycoside* Some surgery/aminoglycoside Surgery + prolonged aminoglycoside*	5% 15% 80%	–	–

* ≥ 6 months parenteral aminoglycoside

Griffith DE et al. *Am J Respir Crit Care Med.* 2006;174:928-934.
Jeong BH et al. *Am J Respir Crit Care Med.* 2015;191:96-103.
Moon SM et al. *Eur Respir J.* 2016;50:1602503.
Wallace R et al. *Chest.* 2014;146:276-282.
Koh WJ et al. *Eur Respir J.* 2017;50.
Morimoto K et al. *Ann Am Thorac Soc.* 2016;11:1904.
Boyle DP et al. *Ann Am Thorac Soc.* 2016;13:1956-1961

National Jewish Health

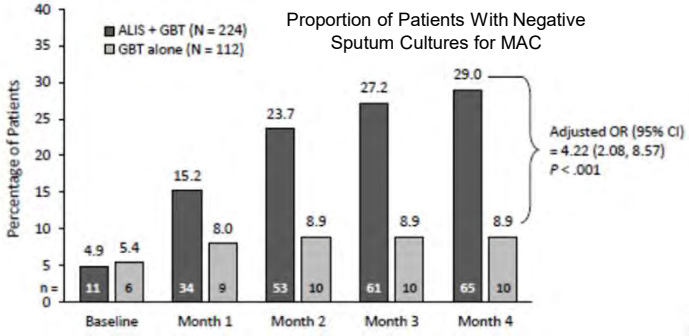
25

Treatment Refractory MAC Pulmonary Disease

Guideline recommendation

In patients with MAC pulmonary disease who have failed therapy after at least six months of guideline-based therapy, we recommend addition of amikacin liposome inhalation suspension (ALIS) to the treatment regimen rather than a standard oral regimen, only. (strong recommendation, moderate certainty in estimates of effect).

CONVERT Study – Randomized, controlled study of ALIS in treatment refractory MAC pulmonary disease



Griffith D, et al. AJRCCM 2018;198:1559-1569

National Jewish Health

26

Recommended Treatment Regimens for MAC Pulmonary Disease

	No. of Drugs	Preferred Regimen[a]	Dosing Frequency
Nodular-bronchiectatic	3	Azithromycin (clarithromycin) Rifampicin (rifabutin) Ethambutol	3 times weekly
Cavitary	≥ 3	Azithromycin (clarithromycin) Rifampicin (rifabutin) Ethambutol Amikacin IV (streptomycin)[b]	Daily (IV aminoglycoside may be used 3 times weekly)
Refractory[c]	≥ 4	Azithromycin (clarithromycin) Rifampicin (rifabutin) Ethambutol Amikacin liposome inhalation suspension or IV (streptomycin)[b]	Daily (IV aminoglycoside may be used 3 times weekly)

a. Alternative drugs could include clofazimine, moxifloxacin, linezolid (tedizolid), bedaquiline
b. Consider for cavitary, extensive nodular bronchiectatic or macrolide resistant disease
c. Sputum culture positive after 6 months of guideline-based therapy

National Jewish Health

Daley CL, et al. CID 2020;71:905-913 and Euro Respir J 2020;56:2000535

27

M. avium complexa: Summary

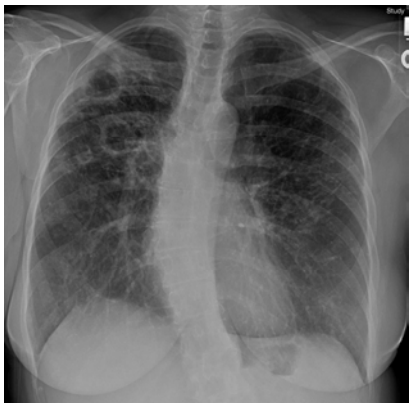
- MAC pulmonary disease should be treated with a macrolide-based regimen
- An aminoglycoside should be considered in cavitary disease and when macrolide resistance is present
- The optimal duration of therapy is not know but should be *at least* 12 months beyond the point of culture conversion
- Macrolide susceptible MAC is usually cured
- In treatment refractory MAC, amikacin liposome inhalation suspension should be added to guideline-based therapy
- Recurrences are common and usually due to reinfection with another strain (or species)

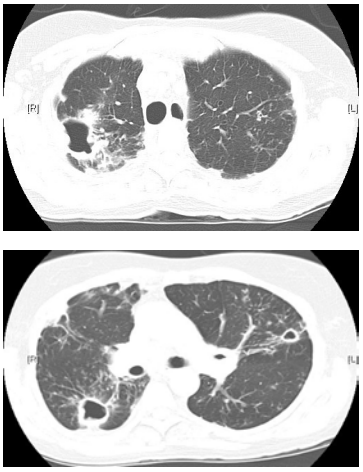
National Jewish Health

28

NTM Lecture Series for Patients

68 year old woman with chronic cough and fatigue



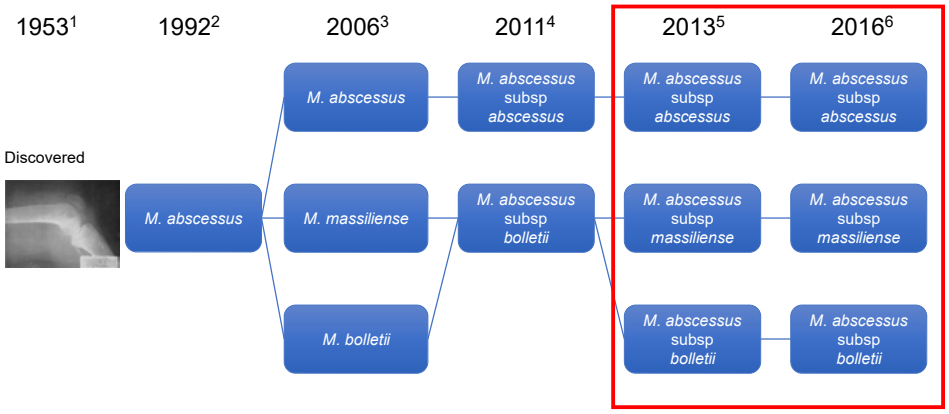


National Jewish Health

29

NTM Lecture Series for Patients

Mycobacterium abscessus: An Evolving Taxonomy



[1]Moore M J Invest Derm 1953;20:133
[2]Kusunoki S. Int J Syst Bacteriol 1992;42:240
[3]Adekambi T. Int J Syst Bacteriol 2006;56:133
[3]Adekambi T. Int J Syst Bacteriol 2006;56:2025
[4]Leao SC. Int J Syst Evol Microbiol 2011;61:2311
[5]Cho YJ. PLoS ONE 2013 8(11):e81560
[6]Tortoli E. Int J Syst Evol Microbiol 2016;66:4471

National Jewish Health

30

Drugs Used for the Treatment of *M. abscessus*

First-Line Oral	Alternative Oral	Parenteral (IV, IM)	Inhaled
Macrolides azithromycin clarithromycin	**Fluoroquinolones** moxifloxacin ciprofloxacin	**Aminoglycosides** amikacin streptomycin	**Aminoglycosides** amikacin (off-label use)
Oxazolidinones linezolid tedizolid		**Carbapenems** imipenem meropenem	
Cycline omadacycline		**Cephalosporins** cefoxitin	
clofazimine bedaquiline		**Cyclines** tigecycline omadacycline eravacycline	

National Jewish Health

31

Mycobacterium abscessus: Macrolide Resistance

***M. abscessus* is resistant to most antimicrobials**

Resistance to macrolides impacts treatment outcomes

Two types of resistance:

Mutational Resistance

Mutation in *rrl* gene

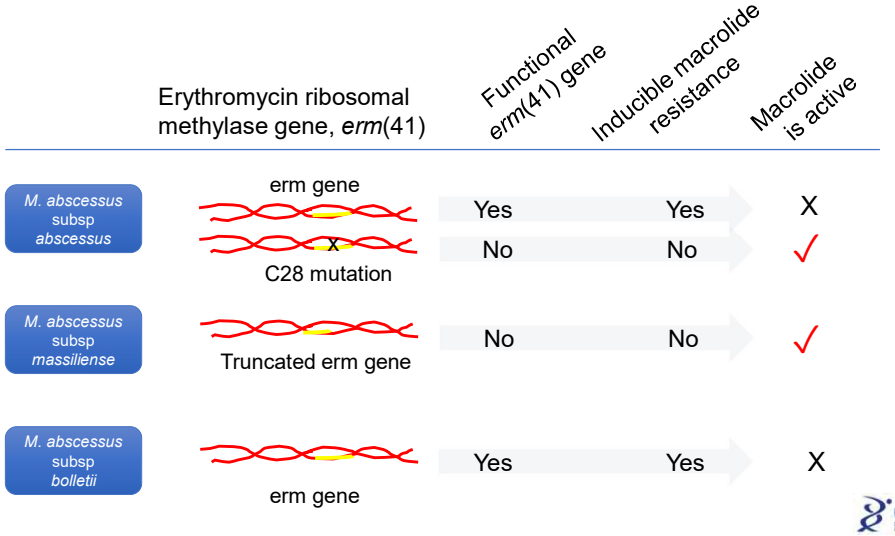
Inducible Resistance

Erythromycin ribosomal methylase gene, *erm*(41)

National Jewish Health

32

Mycobacterium abscessus: Inducible Macrolide Resistance



National Jewish Health

33

Mycobacteriology Laboratory Results

Common Report

Identification:
M. chelonae-abscessus group

Drug susceptibility:
Amikacin R
Cefoxitin I
Clarithromycin S
Tigecycline S

Preferred Report

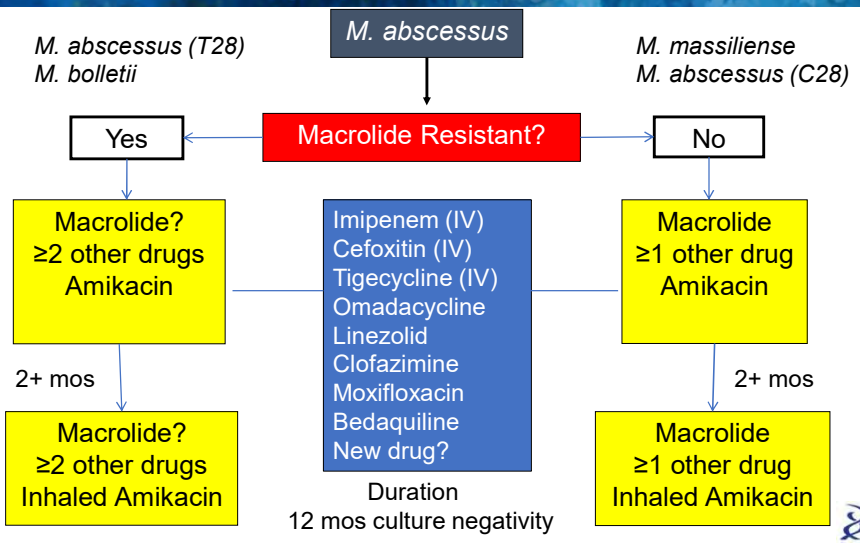
Identification:
200 colonies of *M. abscessus,* subspecies *abscessus*
erm(41) – present, T28C mutation

Drug susceptibility:	**MIC**
Amikacin	8
Cefoxitin	16
Clarithromycin	1
Imipenem	16
Tigecycline	0.125
Clofazimine	<0.5

National Jewish Health

34

Treatment of *M. abscessus* complex



National Jewish Health

35

Treatment Outcomes for *M. abscessus vs. M. massiliense*

Study	Population	Treatment	N	Sputum conversion	Failure to convert	Recurrence*
Koh, 2011	Non Cystic Fibrosis	*M. abscessus* *M. massiliense*	24 33	25% **88%**	58% **3%**	17% **9%**
Lyu, 2014	Non Cystic Fibrosis	*M. abscessus* *M. massiliense*	26 22	42% **96%**	27% **0%**	31% **5%**
Roux, 2015	Cystic Fibrosis	*M. abscessus* *M. massiliense*	12 7	25% **86%**	- -	- -
Park, 2017	Non Cystic Fibrosis	*M. abscessus* *M. massiliense*	19 17	26% **82%**	74% **18%**	55% **0%**

*Most recurrences are due to reinfection

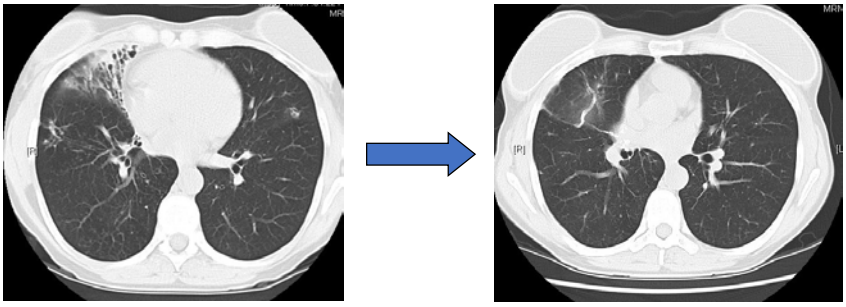
Koh WJ, et al. Am J Respir Crit Care Med 2011;183:405-10
Choi H, et al. Antimicrob Agents Chemother 2016 epub
Park J, et al. CID 2017;64:301-8

National Jewish Health

36

Surgery

56 year old Caucasian woman cleared her MAC but not the *M. abscessus*



	Treatment Success
Jeon, 2009	58% (med) vs 88% (med+surg)
Jarand, 2011	39% (med) vs 65% (med+surg)

National Jewish Health

37

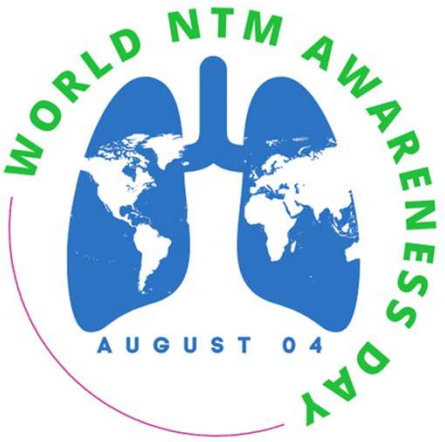
M. abscessus: Summary

- *M. abscessus* has high levels of *in vitro* resistance to many antibiotics
- Treatment requires a combination of intravenous, oral, and inhaled antibiotics
- Treatment outcomes are usually good when the *erm*(41) gene is not functional
- Most recurrences appear to be due to reinfection or another species
- Surgical resection may increase bacteriologic conversion

National Jewish Health

38

World NTM Awareness Day!



National Jewish Health

39

Management of Side Effects/Toxicity

David Griffith, MD

Slides are available at www.njhealth.org/NTMPatientSlides

Novel Therapeutics

Charles Daley, MD

Slides are available at www.njhealth.org/NTMPatientSlides

NUTRITION + NTM

Michelle MacDonald, MS, RDN, CDCES

April 27, 2024

1

NUTRITION + NTM - OVERVIEW

- Importance Of Nutrition – Why It Deserves Respect
- Diet Trends – Are They Right For You?
- Nutrition Guidelines – Calories, Carbohydrate, Fat, Protein
- A Little Extra Help – Appetite Stimulants, Tube-Feeding
- Dietary Supplements – A Little Is Good, A Lot Is *Not* Better

2

☞ IMPORTANCE OF NUTRITION
WHY IT DESERVES R-E-S-P-E-C-T

3

№ 1. GOOD NUTRITION = STRONG IMMUNITY

Reference: Oregon State University, Linus Pauling Institute, Micronutrient Information Center. (2023).

4

№ 1. GOOD NUTRITION = STRONG IMMUNITY

- The immune system constantly works to protect the body from:
  - infection
  - disease

5

№ 1. GOOD NUTRITION = STRONG IMMUNITY

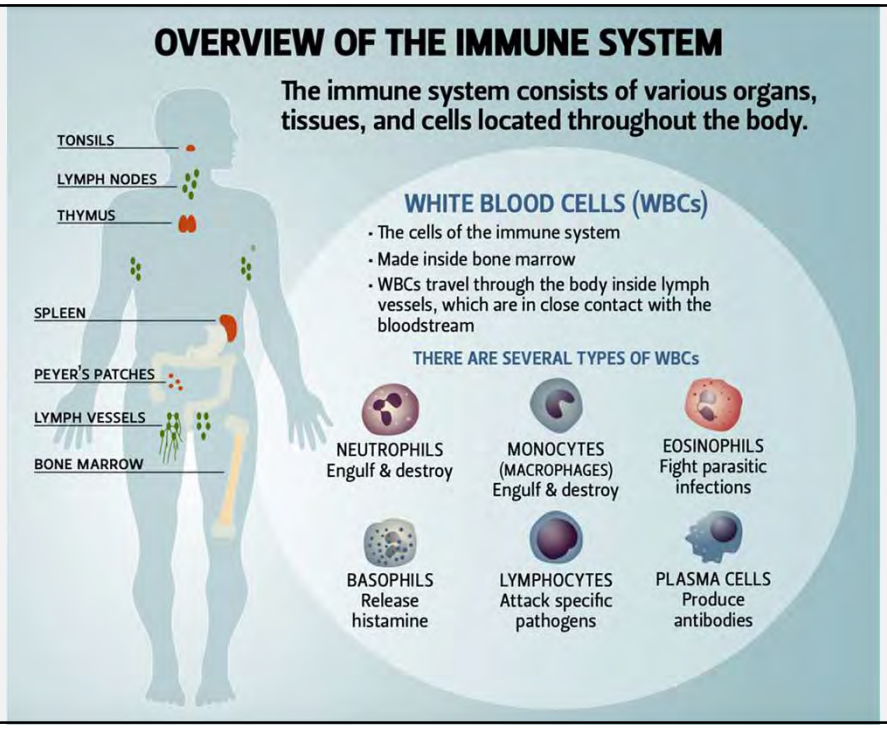
- The immune system relies on an adequate supply of nutrients for its baseline functions + ramping up activity when necessary.

6

№ 1. GOOD NUTRITION = STRONG IMMUNITY

- It is well established that malnutrition (inadequate calories and/or protein) and deficiencies in one or more essential minerals or vitamins diminish immune function.

7



8

OVERVIEW OF THE IMMUNE SYSTEM

The immune system provides three levels of defense against disease-causing organisms:

1 BARRIERS
Prevent entry
- Skin and mucus membranes
- Stomach acid and digestive enzymes
- Beneficial bacteria that live in the colon (the gut microbiota)

2 INNATE IMMUNITY
General defense
WBCs called neutrophils and macrophages engulf and destroy foreign invaders and damaged cells

3 ACQUIRED IMMUNITY
Specific defense
- WBCs called T lymphocytes (T cells) target and destroy infected or cancerous cells
- WBCs called B lymphocytes (B cells) and plasma cells produce antibodies that target and destroy infected or cancerous cells

9

IMMUNE SYSTEM – 3 KEY FEATURES

INFLAMMATION

- Isolates the injured or infected area
- Helps deliver immune cells, chemical messengers, and antibodies to sites of injury or infection

Important nutrients
- EPA
- DHA

Connection
- Inappropriate activation or the inability to turn off inflammation can lead to tissue damage and chronic disease
- EPA and DHA have anti-inflammatory activity that can help keep inflammation in check

10

IMMUNE SYSTEM – 3 KEY FEATURES

OXIDATIVE BURST

- Certain immune cells produce a concentrated burst of reactive oxygen species (ROS), damaging substances that help kill invading organisms

Important nutrients

- Vitamin C
- Vitamin E
- Iron
- Zinc
- Copper
- Selenium

Connection

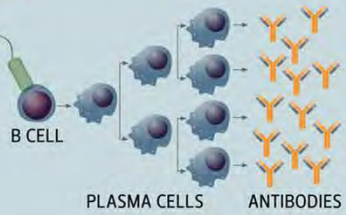
- Prolonged and continuous exposure to ROS can lead to damage and disease
- The listed antioxidant nutrients protect immune cells and keep the oxidative burst in check

11

IMMUNE SYSTEM – 3 KEY FEATURES

PROLIFERATION

- Refers to an increase in the number or amount of something
- The immune system is constantly producing cells, chemicals, and proteins to carry out its functions
- When it encounters a foreign invader, it ramps up production to respond as needed



Important nutrients

- Vitamin A
- Vitamin D
- Folate
- Vitamin B_{12}
- Vitamin B_6
- Iron
- Zinc

Connection

- Proliferation requires energy, building blocks, and cofactors to produce the many cells and substances needed to mount an effective immune response
- The listed micronutrients have essential roles in the production and development of all new cells in the body, including immune cells

12

№ 2. GOOD NUTRITION COMBATS WASTING

Reference: Jensen et al. (2010).

13

№ 2. GOOD NUTRITION COMBATS WASTING

- NTM is a consumptive condition. Inflammation causes wasting:
  - ↑ resting energy expenditure (↑ calories burned)
  - ↑ breakdown of *lean body mass*; loss of muscle mass + function may occur rapidly or slowly (cytokine-mediated)
  - ↑ protein excretion
  - ↓ appetite (cytokine-mediated)

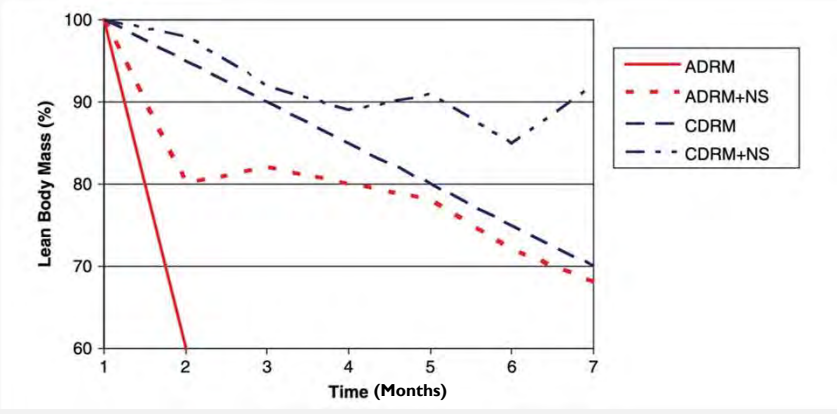
14

№ 2. GOOD NUTRITION COMBATS WASTING

- The point at which the severity or persistence of inflammation results in a decrease in lean body mass associated with functional impairment is "disease-related malnutrition."

15

DISEASE-RELATED MALNUTRITION



ADRM - acute disease-related malnutrition
CDRM - chronic disease-related malnutrition
ADRM**+NS** - ADRM **with nutrition support**
CDRM**+NS** - CDRM **with nutrition support**

16

№ 3. LOW BMI = POOR OUTCOMES

Reference: Youssefnia et al. (2022).

17

BMI (BODY MASS INDEX) DEFINITION

- BMI = [(weight in lb) / (height in inches)^2] x 703
  - Female: 5' 4", 100 lb
  - BMI = [(100 lb) / (64)^2] x 703 = 17.2 kg/m^2

18

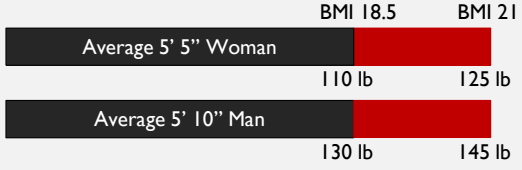
№ 3. LOW BMI = POOR OUTCOMES

- Low BMI < 18.5 adversely effects outcomes:
  - ↑ disease progression
  - ↑ number of diseased lung segments
  - ↑ NTM-Lung Disease (NTM-LD) specific mortality
  - ↓ response to antibiotic therapy (anecdotal evidence)

19

GOAL WEIGHT FOR BMI ≥ 18.5

- Goal weight for 5' 4" or 5' 5" woman ≥ 110 lb
- Goal weight for 5' 9" or 5' 10" man ≥ 130 lb



20

BEWARE OF BODY IMAGE

- Preference for being thin
- Fear of getting fat
- Concern for gaining belly fat

21

☞ DIET TRENDS
ARE THEY RIGHT FOR YOU?

22

DIET TRENDS
ARE THEY RIGHT FOR YOU?

Healthy trends	Consider facts + needs with NTM
Drink 8-8oz glasses water	Limit plain water + hydrate with calorie beverages
A lot of fruits + vegetables	Adequate calories help maintain + restore healthy weight
Low-fat	A heart-healthy diet may be up to 40% good fats
Low-carb	Healthy grains/starches provide nutrients, energy + help build muscle
No red meat	Extra protein helps to meet increased needs + prevent loss
No dairy	Dairy does not cause mucus, is not inflammatory + benefits > costs
No gluten	Gluten is not inflammatory + benefits > costs
No sugar	Some added sugar is okay + can be enjoyed sensibly

23

☞ NUTRITION GUIDELINES
CALORIES, CARBOHYDRATE, FAT, PROTEIN

24

NUTRITION GUIDELINES
CALORIES

- ADD vs. SUBTRACT
- Estimated calorie needs = 30% higher with NTM
- Goals = 2000+ calories/day (women); 2400+ calories/day (men)

25

NUTRITION GUIDELINES
PROTEIN

- ADD vs. SUBTRACT
- Estimated protein needs = 30% higher with NTM
- Goals = 60-90+ grams/day distributed evenly between meals

26

NUTRITION GUIDELINES
CARBOHYDRATES

- ADD vs. SUBTRACT
- Balance meals with bread, oatmeal, rice, pasta, potatoes
- Enjoy dessert

- *To manage blood sugars:*
Pick healthy carbs, limit portions, enjoy with mixed meals at middle or end of meals

27

NUTRITION GUIDELINES
FAT

- ADD vs. SUBTRACT
- A heart healthy Mediterranean-style diet may be up to 40% fat

- *To manage cholesterol:* *Pick unsaturated fats: avocado, canola oil, extra-virgin olive oil, fish/seafood, nuts/seeds*

28

☞ A LITTLE EXTRA HELP
APPETITE STIMULANTS, TUBE-FEEDING

29

A LITTLE EXTRA HELP
APPETITE STIMULANTS

- Indications for appetite stimulant:
  - Poor appetite is a major barrier
  - Profound fatigue and decline
  - Weight restoration is essential

30

A LITTLE EXTRA HELP
APPETITE STIMULANTS

- Mirtazapine +/- Methylphenidate
- Megestrol
- Dronabinol

Reference: Lexicomp. (2023).

31

A LITTLE EXTRA HELP
APPETITE STIMULANTS

Mirtazapine (Remeron®) *Antidepressant*	
Side effects	↑ appetite, ↑ weight, ↑ mood, ↑ sleep ↑ sedation, tired, weak
Dosing	7.5 mg at bedtime to start, ↑ to 15-30 mg
Administration	Without regard to meals
Mechanism of Action	Interacts with central mechanisms regulating appetite + intake; ↑ mood

32

A LITTLE EXTRA HELP
APPETITE STIMULANTS

Mirtazapine (Remeron®) +/- Methylphenidate (Ritalin®) *Antidepressant +/- Central Nervous System Stimulant*	
Side effects	↑ appetite/weight, ↑ mood, ↑ sleep, ↑ energy
Dosing	7.5 mg at bedtime to start, ↑ to 15-30 mg 2.5 mg twice daily (8am, 12pm), ↑ 5 mg
Administration	Without regard to meals 30-45 minutes before meals
Mechanism of Action	Interacts with central mechanisms regulating appetite + intake Mildly stimulates central nervous system

33

A LITTLE EXTRA HELP
APPETITE STIMULANTS

Megestrol (Megace®) *Appetite Stimulant*	
Side effects	↑ appetite, ↑ weight ↑ dizziness, passing out ↓ energy + strength
Dosing - Avoid use in older patients	↑ risk of clots
Mechanism of Action	May antagonize metabolic effects of inflammatory cytokines

34

A LITTLE EXTRA HELP
APPETITE STIMULANTS

	Dronabinol (Marinol®) *Appetite Stimulant*
Side effects	↑ appetite, ↑ weight, mind-altering
Dosing - Avoid use	Cost prohibitive, Poor insurance coverage, Less effective than other options
Mechanism of Action	Activates cannabinoid receptors CB1, CB2

35

A LITTLE EXTRA HELP
TUBE-FEEDING

- IF efforts to restore weight with oral intake, high-calorie shakes, and appetite stimulant(s) are not successful,
- THEN tube-feeding may be considered.

36

☞ DIETARY SUPPLEMENTS
A LITTLE IS GOOD, A LOT IS *NOT* BETTER

37

DIETARY SUPPLEMENTS
A LITTLE IS GOOD, A LOT IS *NOT* BETTER

- Daily multimineral/multivitamin, iron-free
- Calcium + vitamin D
- Vitamin C
- Zinc

38

REFERENCES

1. Oregon State University, Linus Pauling Institute, Micronutrient Information Center, https://lpi.oregonstate.edu/mic/health-disease/immunity-in-brief#protein-energy-malnutrition. Accessed 4/14/23.
2. Oregon State University, Linus Pauling Institute, Micronutrient Information Center, https://lpi.oregonstate.edu/sites/lpi.oregonstate.edu/files/lpi-immunity-infographic_0.pdf. Accessed 4/14/23.
3. Jensen, G., Mirtallo, J., Compher, C., Dhaliwal, R., Forbes, A., Grijalba, R., Hardy, G., Kondrup, J. Labadarios, D., Nyulasi, I., Pineda, J., Waitzberg, D. (2010). Adult Starvation and Disease-Related Malnutrition: A Proposal for Etiology-Based Diagnosis in the Clinical Practice Setting From the International Consensus Guideline Committee. *Journal of Parenteral and Enteral Nutrition,* 34(2), 156-159.

39

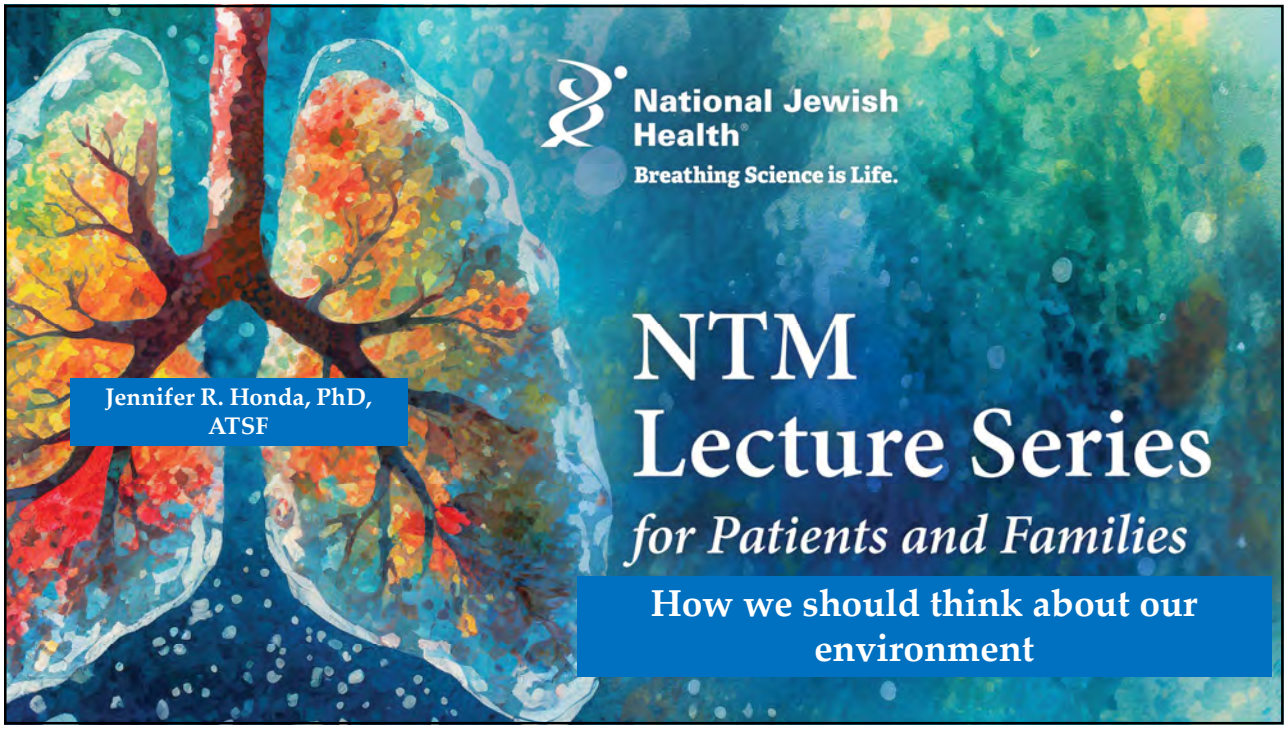
REFERENCES

4. Youssefnia, A., Pierre, A., Hoder, J., MacDonald, M., Shaffer, M., Friedman, J., Mehler, P., Bontempo, A. da Silva, F., Chan, E. (2022). Ancillary treatment of patients with lung disease due to non-tuberculous mycobacteria: a narrative review. *Journal of Thoracic Disease*, 14(9), 3575-3597.
5. Lexicomp. Accessed 4/22/23.

40

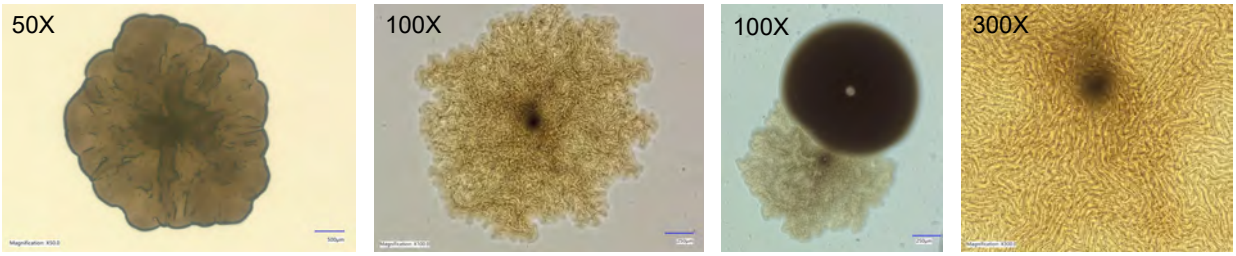
THANK YOU!

41



1

NTM Microbiology 101



- NTM are bacteria with a thick and heavy protective outer covering [1]
  - Adherence to plumbing pipe surfaces [2]
  - Broad resistance to disinfectants, chemicals, and antibiotics [3]
  - Can be biofilm pioneers [4]
- Resistant to low pH of stomach [5]
- Withstand exposure to high temperatures (50-60 ºC); *M. avium* tolerates 45ºC [4]
- Metal resistance [6].

Adaptable

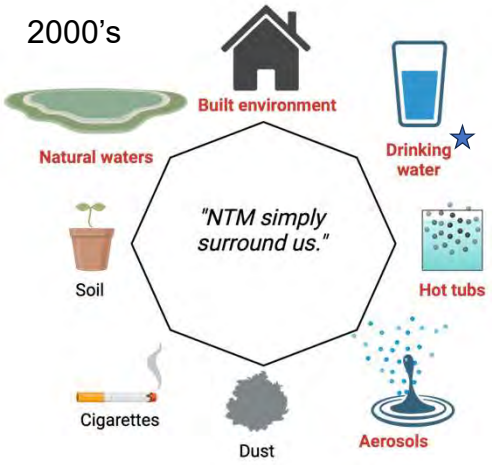
[1] Brennan, *et al.*, Annu Rev Biochem, 1995; [2] Mullis, *et al.*, J Appl Micro, 2013; [3] Rastogi *et al.*, Antimicr Agents Chemo 1981; [4 5] Falkinham *et al.*, Clin Chest Med, 2002; [5] Portaels *et al.*, Ann Microb, 1992; [6] Falkinham *et al.*, Antim Agents Chemo 1984.

National Jewish Health

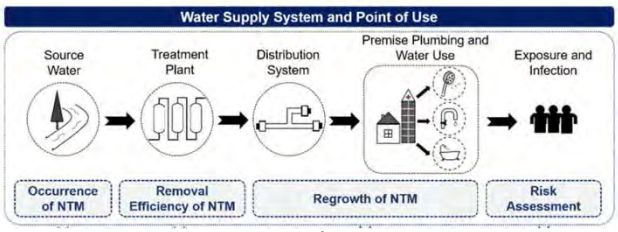
2

NTM environments, 2000's

2000's



One of the most serious waterborne infections. [1,2]



"We predict an increasing incidence of interactions between humans and mycobacteria in the coming years. [3]

[6] Faklinham et al., J Appl Micro, 2009; [1] Gan et al.. H2O Open Journal, 2022; [2] Collier, *et al.*, Estim Burden HealthCare, 2021; [3] Falkinham *et al.*, Clin Chest Med, 2002; Primm *et al.*, 2004
Image created in BioRender

National Jewish Health

3

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

Which species of NTM is found, matters.

National Jewish Health

4

"Anonymous" no longer

- Inhalation from the environment – shower water and soil aerosols; spa exposures [1,2 3,4]
- Oral ingestion – drinking water [5]
  - Survival in stomach acid and reflux into the lung
- Aerosols from ultrasonic humidifier use [6]
- Dermal contact [7]
- Hospital ice and ice machines [8]
- Heater-cooler devices [9] and bronchoscopes [10]
- Biofilms in water lines in dental drilling and cleaning devices [11,12]
- Glass, copper, galvanized steel, PVC [13, 14, 15]

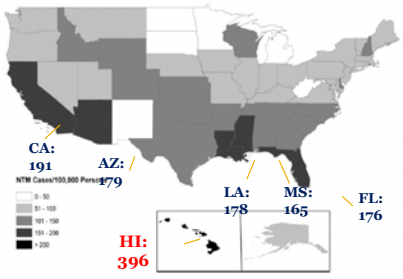
[1] Thomason *et al.*, Appl Env Microi, 2013; [2] Gebert *et al.*, mBio, 2018; [3]Uwamino, *et al.*, J Infect Chemoth; 2020; [4] Nakanaga, *et al.*, J Clin Micro, 201; [5] Hamilton, *et al.*, Water Research, 2017; [6] Hamilton *et al.*, J Med Microbio, 2018;[7] Patel *et al.*, Case Rep Dermatol Med, 2013; [8] Millar *et al.*, Int J Mycobacteria, 2020; [9] Sax *et al.*, Clin Infect Dis, 2015; [10] Gubler et al., Chest, 1992; [11] Schulze-Robbecke, *et. al.*, Tubercle Lung Dis, 1995; [12] Wang *et al.*, Eur Resp J, 1995; [13] Steed, *et al.*, Appl Env Micro, 2006; [14] du Moulin, *et al.*, *JAMA*, 1988; [15] George, *et al.*, Am Rev Respir Dis 1980.

National Jewish Health

5

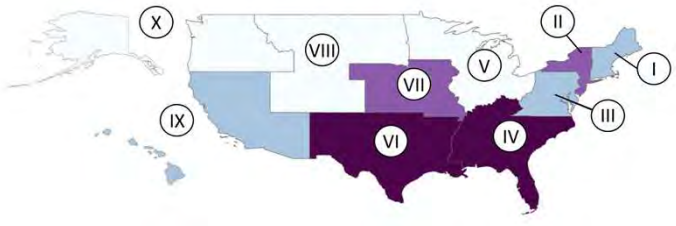
Where you live may matter

NTM national prevalence – 1997-2007 [1]



396 cases/100,000 population among persons > 65 years-old

NTM culture positivity (%); 2019-2022 National Commercial Lab [2]



[1] Adjemian, *et al.*, AJRCCM, 2012; [2] Marshall *et al.*, BMC infectious Disease, 2002

National Jewish Health

6

What's new regarding NTM in the environment

- Greater **water age** (combined time in distribution system and home plumbing stagnation time) promotes *M. avium* [1]
- *M. abscessus* **hot water persistence** is higher at residences than office buildings; *M. intracellulare* hot water occurrence is influenced by water age and square footage; *M. avium's* hot water occurrence is affected by **distances between tank and tap** [2]
- Presence of certain **metals** - as molybdenum increases, MAC infections increase by 45% (OR); molybdenum associated with disease risk in CO; as vanadium increases, *M. abscessus* infections increase by 41% (OR). [3]
- **Low risk for hospital** transmission of *M. abscessus* at an Adult Cystic Fibrosis Program [4]

[1] Haig *et al.*, mBio, 2018, [2] Donohue, *et al.*, Science Total Environment, 2022; Lipner, *et al.*, Annals ATS, 2021; Gross et al., ERJ, 2024

National Jewish Health

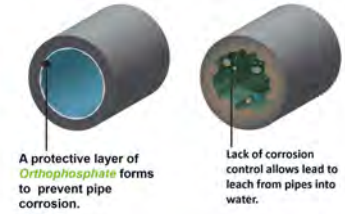
7

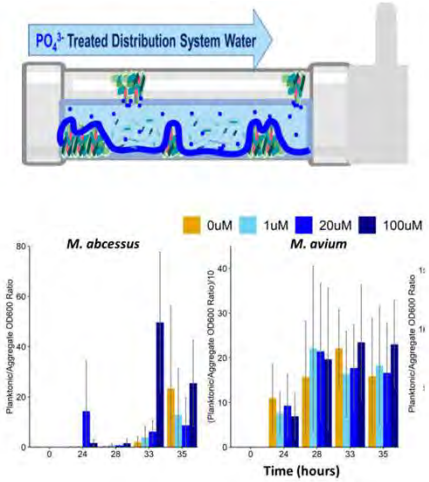
Freshwater features that may contribute to NTM

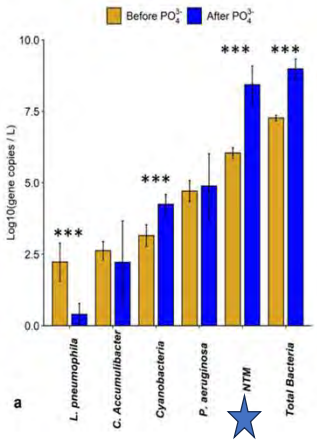
***Mycobacterium avium* in Community and Household Water, Suburban Philadelphia, Pennsylvania, USA, 2010–2012**

Leah Lande, David C. Alexander, Richard J. Wallace, Jr., Rebecca Kwait, Elena Iakhiaeva, Myra Williams, Andrew D.S. Cameron, Stephen Olshefsky, Ronit Devon, Ravikiran Vasireddy, Donald D. Peterson, Joseph O. Falkinham, III

Many drinking water systems commonly add orthophosphates to reduce the release of metals and control for lead and copper in pipes. [1]







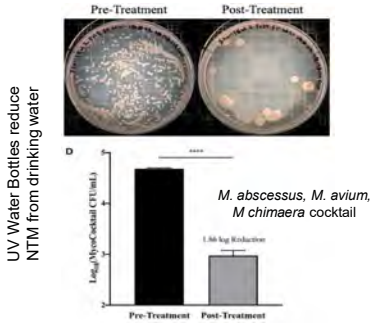
Lande *et al.*, EID, 2019; [1] Pittsburgh Water and Sewer Authority, 2019; [2] Spencer-Williams, et al., Env Science and Tech., 2023

National Jewish Health

8

Longstanding suggestions on how to reduce exposures

- Clean showerheads and faucet taps regularly.
- Avoid misting showerheads
- Ventilate bathrooms, showers, other steam areas.
- Use a water filter.
- Raise the temperature of household water heater and drain.
- Avoid humidifiers.
- Wear dust mask.
- Reduce acid reflux.
- Self-supplied water (*e.g.*, wells, collected rainwater) is a protective factor, Virginia [5]
- Avoid dusts from soil * [1, 2]
- Boil water for 10min before use [3].
- Use of UV water bottles [4]



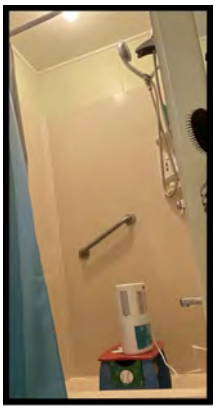
Falkinham, Clin Chest Med, 2015; Honda, Clin Chest Med, 2023; [1] Hamada *et al.*, Int J Myco 2016; [2], Reed *et al*, Am J Epidem, 2006; [3] Falkinham, WhiteJ, 2013; [5] Norton, *et al.*, Frontiers in Public Health, 2020; [5] Mullen, *et al*, EID, 2024.

National Jewish Health

9

Reducing shower humidity reduces aerosolized NTM

Saturated vapor pressure is a climate variable that affects NTM prevalence [1,2,3]



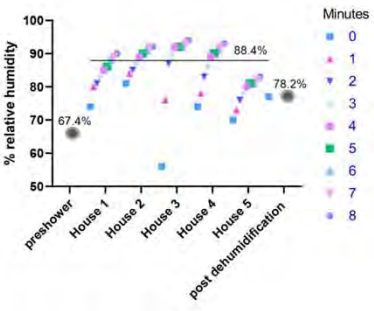


Table 1 Dehumidification reduced *Mycobacterium chelonae* aerosolization, sampling round 1 (37 °C)

	Biofilm		Air		
House:	Showerhead biofilm (swab):	Showerhead biofilm (swab), post- disinfection	Pre shower air (SAS):	Post shower air (SAS):	Post de-humidi-fication (SAS):
1	*M. chelonae*	No NTM	No NTM	*M. chelonae*	No NTM
2	No NTM	No NTM	No NTM*	No NTM*	No NTM*
3	No NTM	No NTM	No NTM	No NTM	No NTM
4	No NTM	No NTM	No NTM*	No NTM*	No NTM
5	No NTM	No NTM	No NTM*	No NTM*	No NTM

(*) Limitation - indicates instances where mold overgrowth likely reduced NTM detection

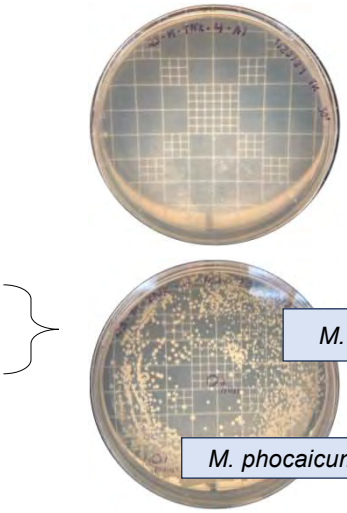
Kostecki, *et al.*, BMC Research Notes, 2024

National Jewish Health

10

Showerhead filters do not reduce NTM, a pilot

	Biofilm		Water
House:	Pre-intervention Showerhead biofilm (swab):	Post-intervention Showerhead biofilm (filter):	Post-intervention Showerhead water:
1	No NTM	Pending	*M. gordonae*
4	No NTM		*M. phocaicum, M. chelonae*
5	No NTM		*M. porcinum*
6	No NTM		No NTM

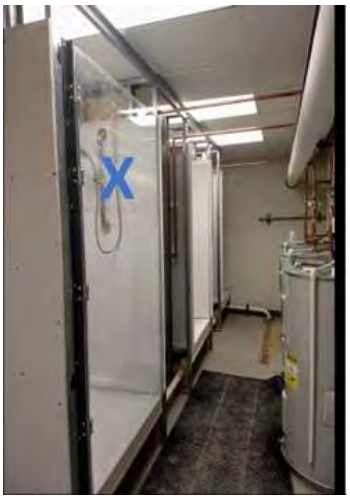


Unpublished

National Jewish Health

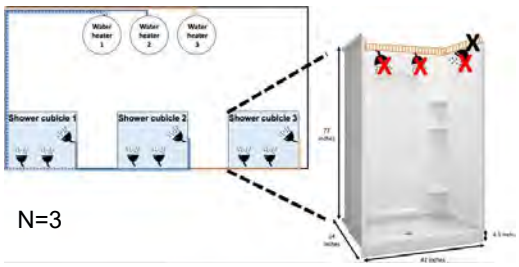
11

Antimicrobial showerheads do not impact aerosolization



Pitell and Haig, Fronters in Microbiome, 2024;

1. Proprietary multistage antimicrobial filter
2. Antimicrobial silver-embedded
3. Conventional plastic



N=3

Drinking water associated pathogens did not differ between showerhead type.

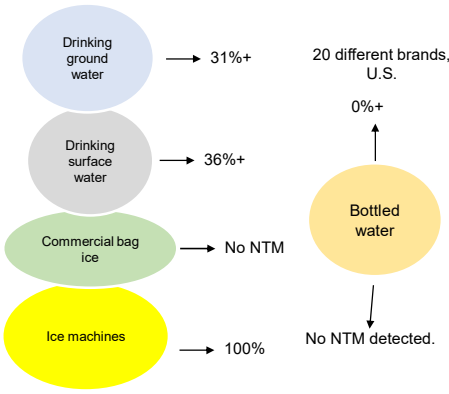
Each peaked as showerhead aged.

# of days of showerhead operation important.

National Jewish Health

12

Expand Drinking Water Awareness



Bottled Water (Honda Lab)

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
Covert, *et al,* AEM, 1999
Totaro, *et al,* J Water Health, 2018
https://www.bottledwater.org/public/CCL4%20Microbes%20of%20Interest%20in%20Drinking%20Water_0.pdf0
Honda Lab, unpublished.

National Jewish Health

13

Aloha Hawai'i – Teaching us about NTM



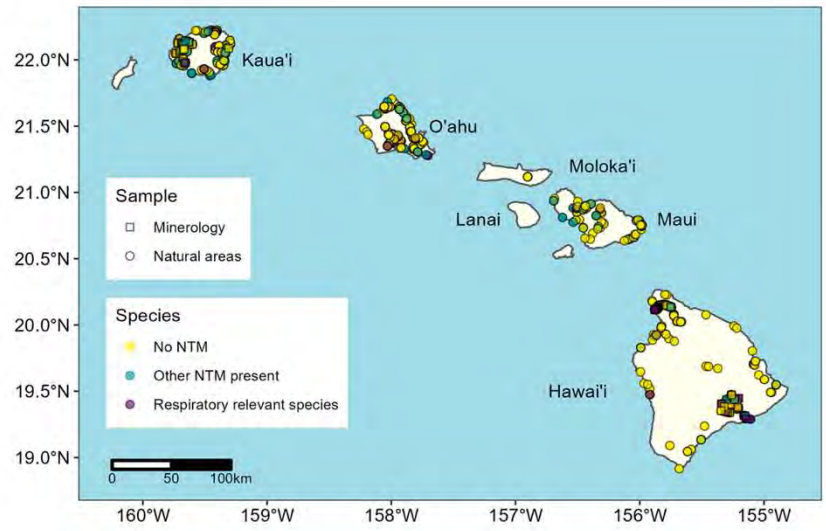




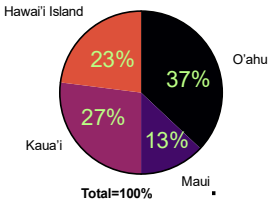
1. Enrichment in the built environment (Honda *et al*., Plos Neg Trop 2016; Virdi, *et al*, Microorganisms, 2020)
2. Preference for iron minerals, hematite in soil and aversion to gibbsite (Glickman *et al*., App Env Micro, 2020)
3. Like highly expansive, moist soils containing high iron oxides and hydroxides (Parsons *et al*., Appl Env Micro, 2022)
4. Vanadium in groundwater increases MAC lung disease risk (Lipner *et al*., Env Epi, 2022)
5. Water transport from riparian zones into losing stream stretches, aquifers, and into homes (Nelson *et al*., Geohealth, 2021).
6. Local feral pigs harbor pathogenic NTM species. (Hendrick, et al, in preparation.)

14

Larger cities are NTM hot spots



Island distribution
766 total NTM+ samples



National Jewish Health

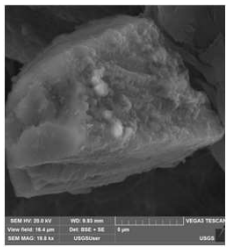
15

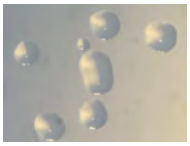
Active volcanism contributes to NTM

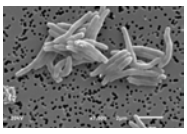
Kīlauea volcano, Hawai'i Island, 2018

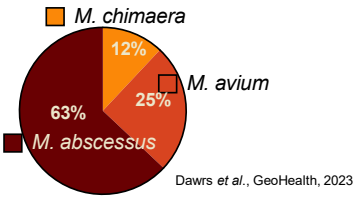
Photo credit: USGS

Kīlauea ash, SEM





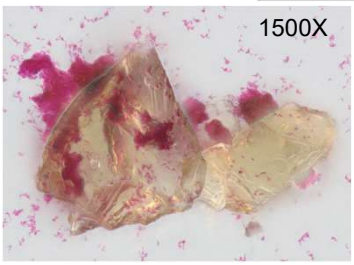


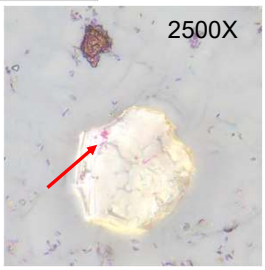


Dawrs *et al.*, GeoHealth, 2023

Total = 8 NTM recovered from Kilauea ash

AFB

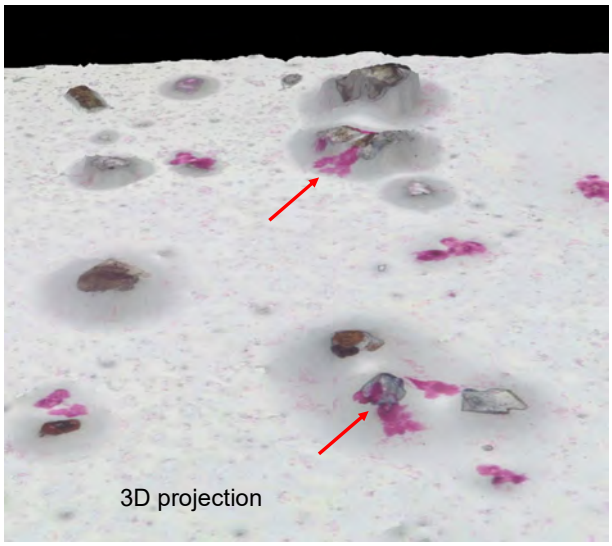




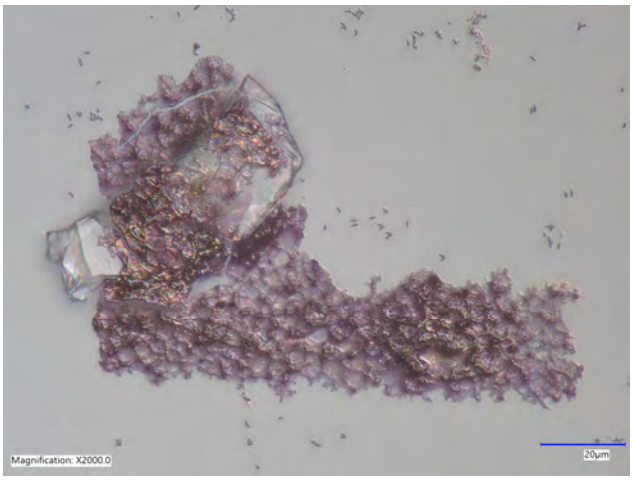
National Jewish Health

16

Active volcanism contributes to NTM



3D projection



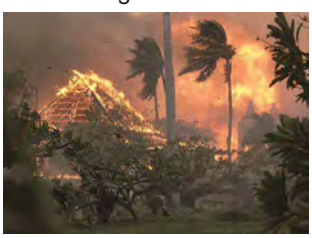
National Jewish Health

17

NTM and the Lāhainā wildfire

The Lāhainā Maui wildfire is earmarked both as the *worst natural disaster in Hawai'i history* and the *deadliest U.S. wildfire in over 100 years.*

August 2023



https://www.sfchronicle.com/climate/article/maui-fire-before-after-photos-18290051.php.

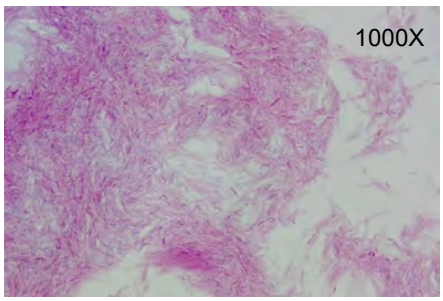
February, 2024, Lāhainā

National Jewish Health

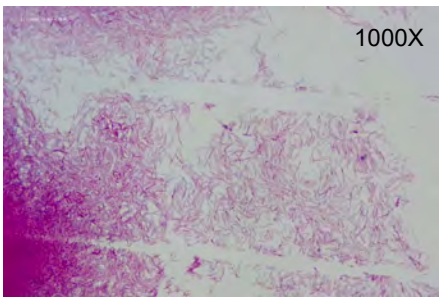
18

NTM and the Lāhainā wildfire

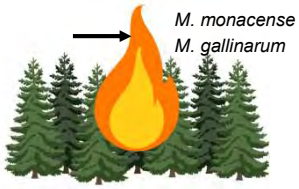
Soil and ash (burnt ground)
Non-household



Soil and ash (burnt ground)
Household



Wildfire ash, Kansas

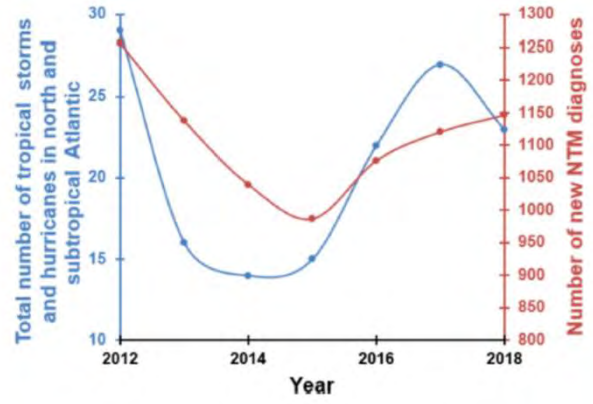


National Jewish Health

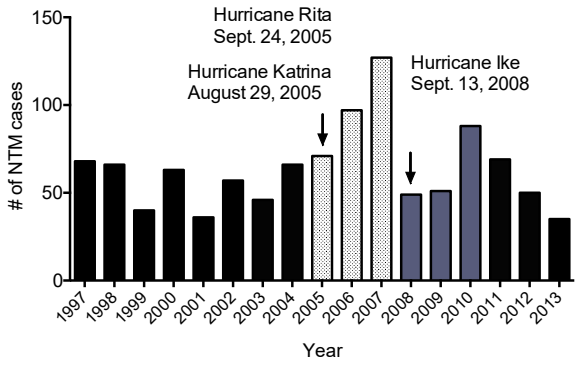
19

In addition to volcanic eruptions and wildfires…..

Tropical storms



Hurricanes

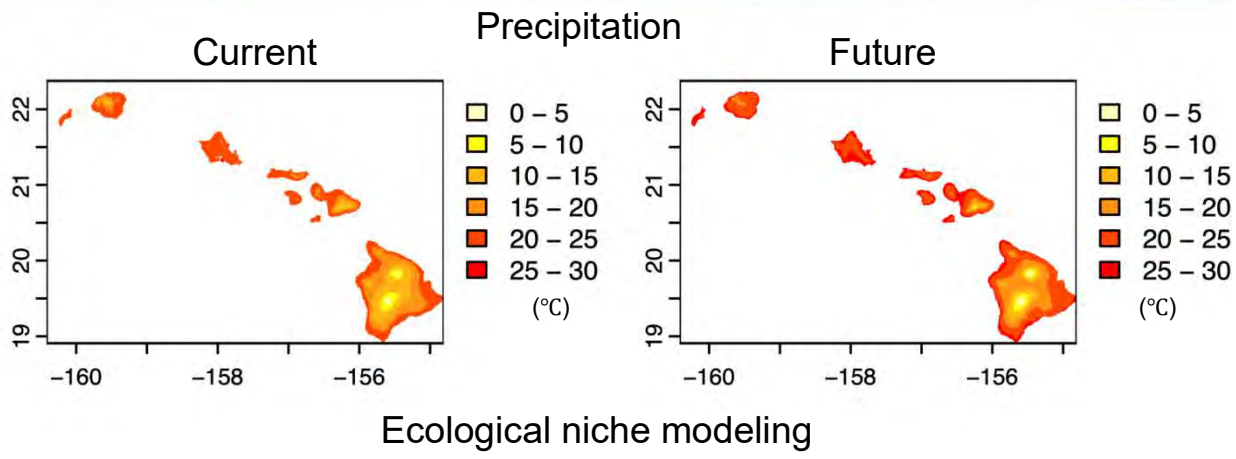


Honda *et al*, 2015; Kambali, *et al.*, 2021

National Jewish Health

20

Our environments will likely get warmer



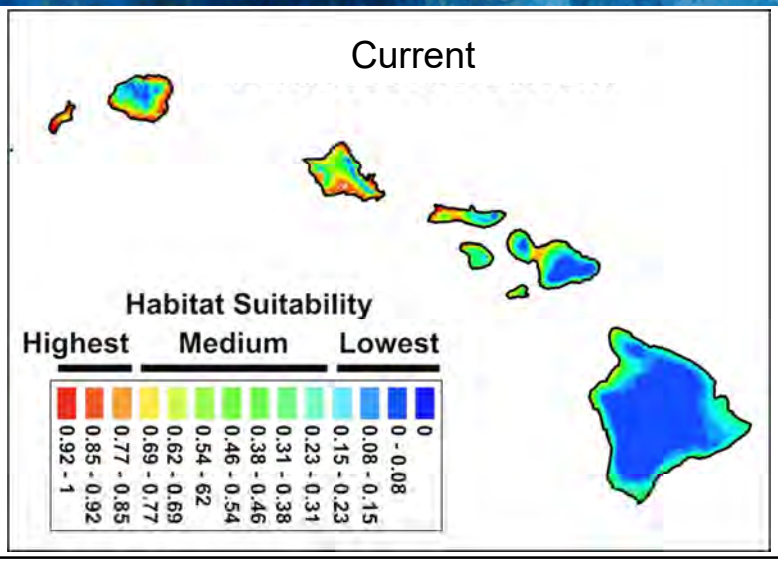
Ecological niche modeling

Unpublished
** Joshua Banta, PhD, University of Texas Health Science Center at Tyler
Jim Crooks, PhD, National Jewish Health

National Jewish Health

21

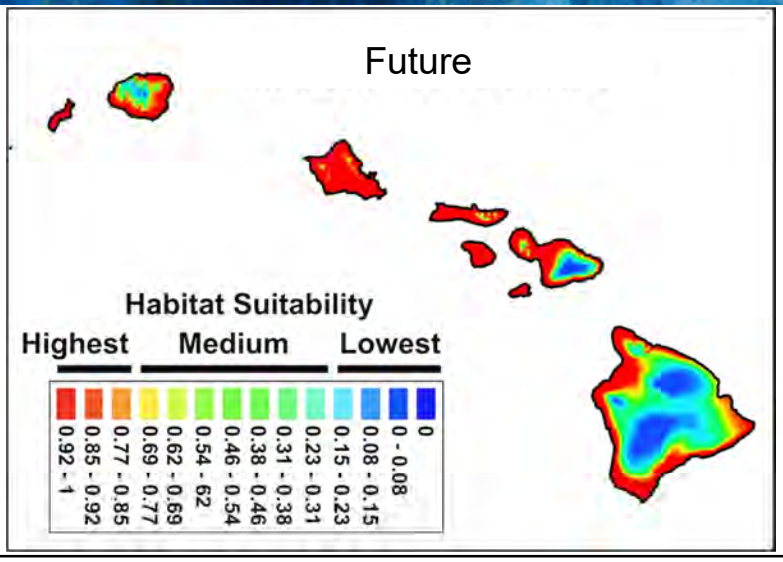
M. abscessus in Hawai'i



National Jewish Health

22

M. abscessus in Hawai'i

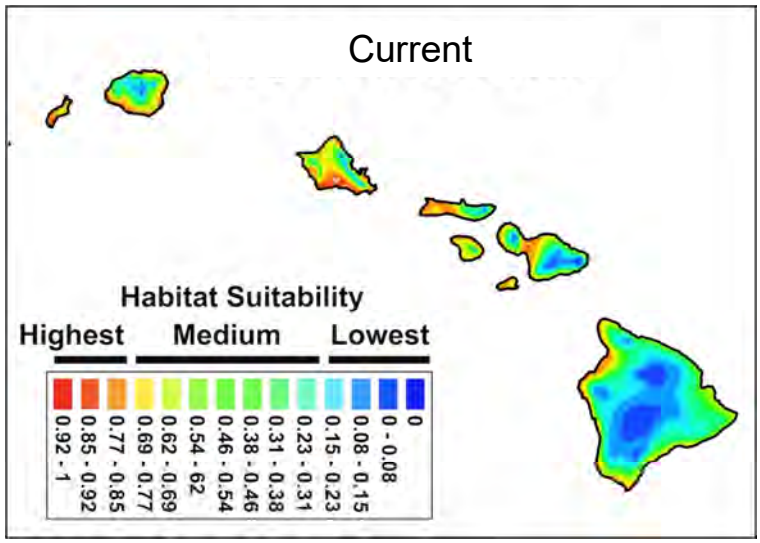


Future climate data from the years 2041 - 2070 based on the IPSL-CM6A-LR climate model and a shared socioeconomic pathway

National Jewish Health

23

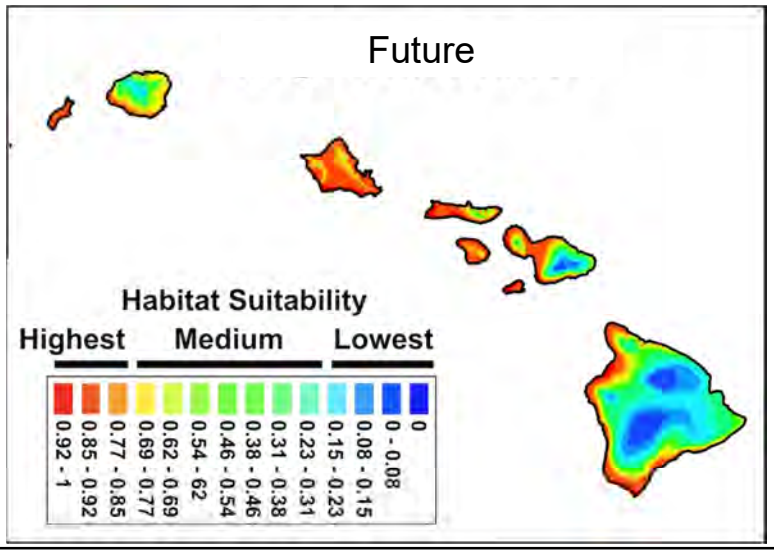
M. gordonae in Hawai'i



National Jewish Health

24

M. gordonae in Hawai'i

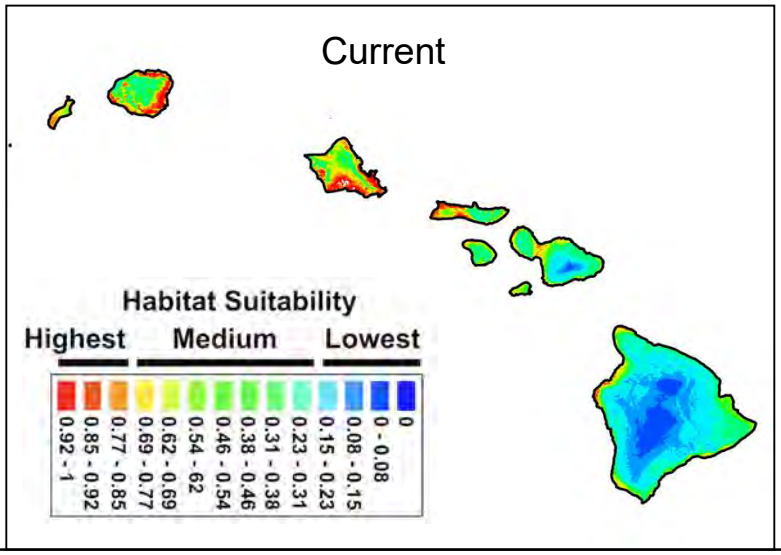


Future climate data from the years 2041 - 2070 based on the IPSL-CM6A-LR climate model and a shared socioeconomic pathway

National Jewish Health

25

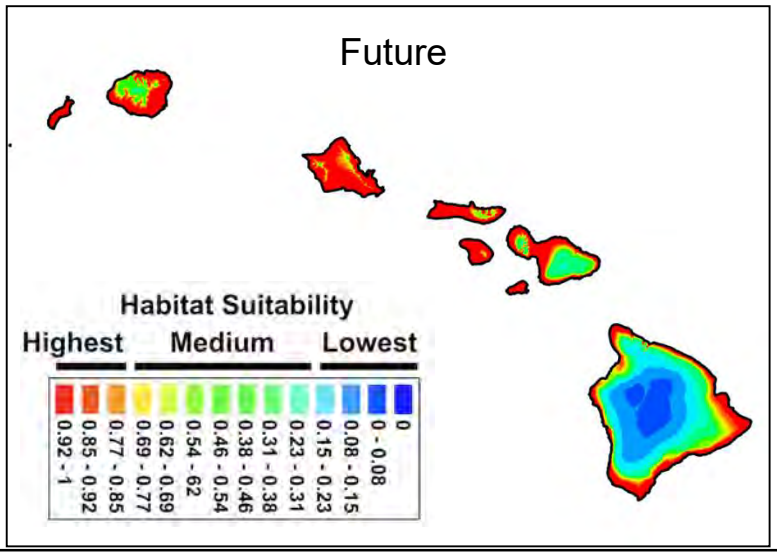
M. chelonae in Hawai'i



National Jewish Health

26

M. chelonae in Hawai'i

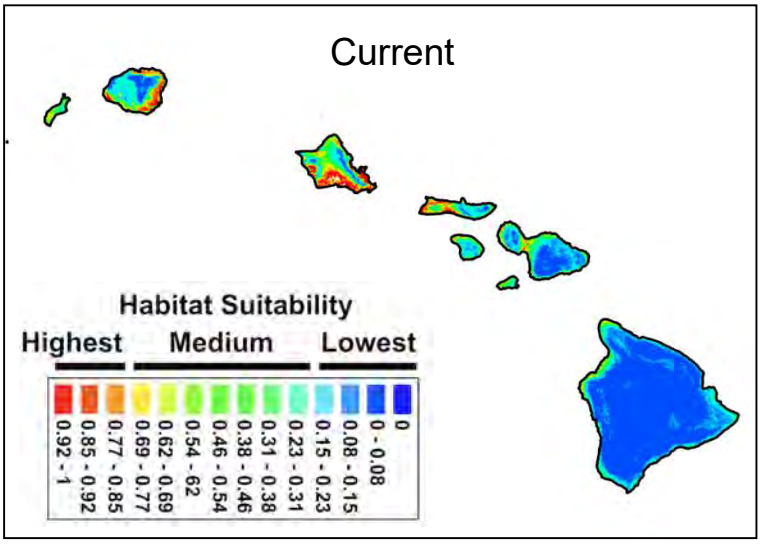


Future climate data from the years 2041 - 2070 based on the IPSL-CM6A-LR climate model and a shared socioeconomic pathway

National Jewish Health

27

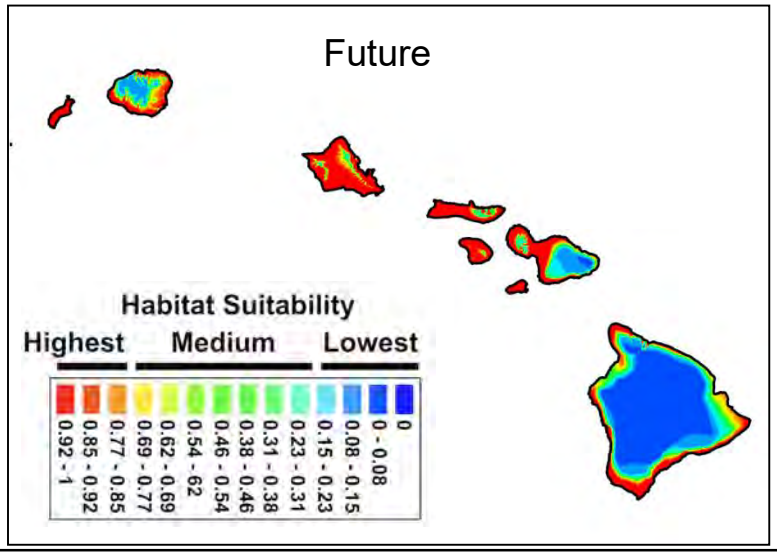
M. chimaera in Hawai'i



National Jewish Health

28

M. chimaera in Hawai'i

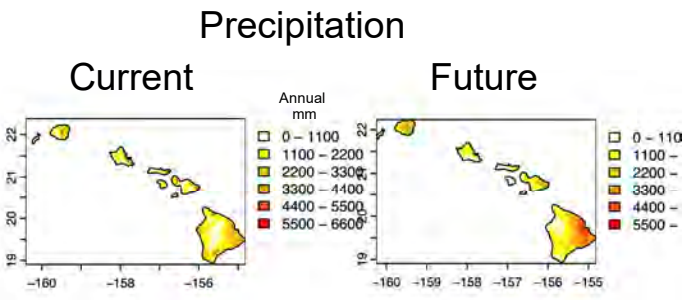


Future climate data from the years 2041 - 2070 based on the IPSL-CM6A-LR climate model and a shared socioeconomic pathway

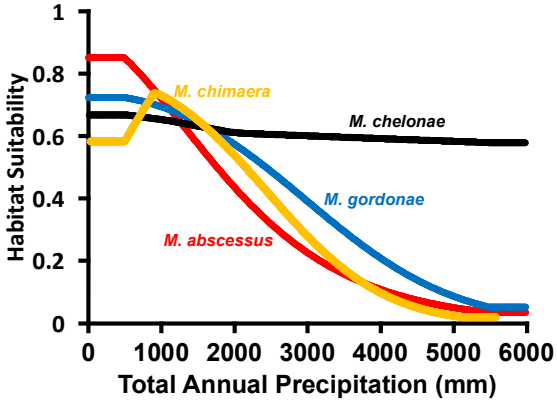
National Jewish Health

29

Colonization of *M. chelonae* across areas with wide ranges of precipitation



Among people with CF in FL: Precipitation and NTM
(Foote, *et al.*, PloS One, 2021)

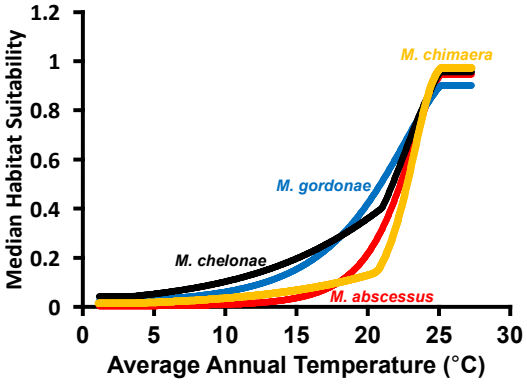


National Jewish Health

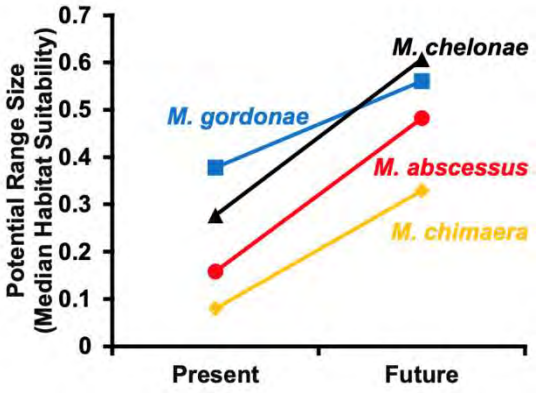
30

Emergence of NTM under future climates

M. chimaera will thrive in hotter climates.



Greater NTM emergence under future climates.

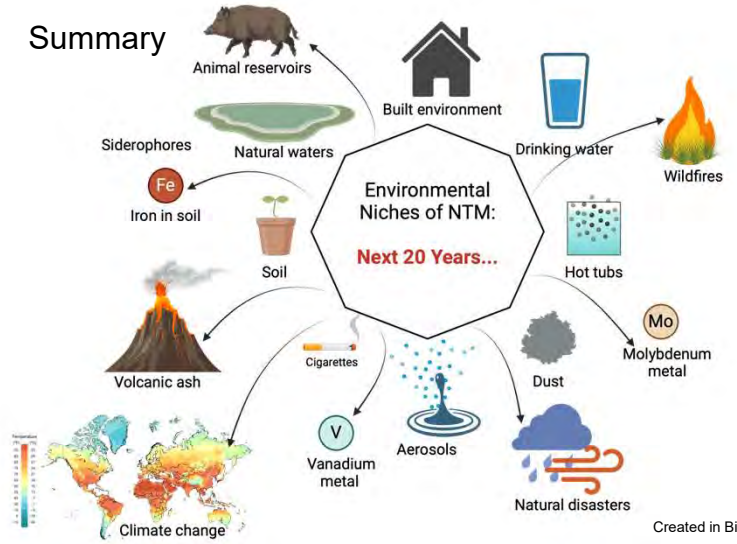


National Jewish Health

31

Conclusions

Summary



Future directions

"We predict an increasing incidence of interactions between humans and mycobacteria in the coming years.

↓

Climate changes may be increasingly recognized pressures for the emergence of environmentally acquired NTM.

National Jewish Health

32

Acknowledgements

Honda Lab
Rachel N. Wilsey
Tiana N.M. Koch
Kristin T. Dean
Madelyn M. Terrell
Lianghao Ding, PhD
Adrian Hornby, PhD

Prior Lab Members
Stephanie Dawrs
Ravleen Virdi
Grant Norton
Charmie Vang
Jobel Matriz

U of Texas, Tyler
Julie Philley, MD
PJ McShane, MD
Richard Wallace, MD
Barbara Brown-Elliott
Joshua Banta, PhD

National Jewish Health

** Edward D. Chan, MD
** Michael Strong, PhD
** Nabeeh A. Hasan, PhD
** L. Elaine Epperson, PhD
** James Crooks, PhD
Cody M. Glickman
Melissa Lowe
Jo Hendrick
Brady Holst
Scott Alper, PhD
Rebecca Davidson, PhD
Fan Jia, PhD
Human Cell Core

UT Tyler
**Josh Banta, PhD

University of Idaho
Leda Kobziar, PhD

NTM Hawai'i Consortium: '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, University of Hawai'i Maui College, Brigham Young University Laie, Mike Burnett, Homeschoolers, Department of Tropical Medicine University of Hawai'i, Hawai'i Division of Wildlife

Brigham Young University
Dept. of Geological Sciences
Provo, UT
** Steve Nelson, PhD
Schuyler Robinson
Leeza Brown

Hawai'i Volcano Observatory
** Tamar Elias

Hawai'i Volcano Observatory
** Tamar Elias

North Carolina State University
Krishna Pacifici, PhD
Arielle Parsons, PhD

Volcano Science Center,
US Geological Survey
David E. Damby, PhD

Kaiser Permanente, Hawai'i
Stacey Honda, MD
Vanessa Simiola

Lahaina Wildfire Team
Chris Shuler, PhD, Julynn Li, Kellie Cole, Pacific Whale Foundation, U of Hawai'i Maui College, Renee Takeuchi, PhD (USGS, CA), Community scientists, All Hands Hawai'i Network

Funding: Padosi Foundation, NSF Ecology, Evolution and Infectious Disease (#1743587), NIH R21AI171587, NSF RAPID for Lahaina, Maui #2345008, UT Stars Award, UT Recruitment Funds.

UTTyler HEALTH SCIENCE CENTER

National Jewish Health

33

"Flat Stanley" Travels with our "Flat Stanley"

Ho'okipa Beach Park , Maui

Haleakalā , Maui

Waipuilani Park, Maui

National Jewish Health

34

Surgery for Pulmonary NTM Disease

John D. Mitchell, M.D.
Davis Endowed Chair in Thoracic Surgery
Professor and Chief
Section of General Thoracic Surgery
University of Colorado School of Medicine
Consultant, National Jewish Health

University of Colorado Anschutz Medical Campus

1

Disclosures:

Intuitive – Teaching, Consultation

Director, American Board of Thoracic Surgery

Councilor, American Board of Surgery

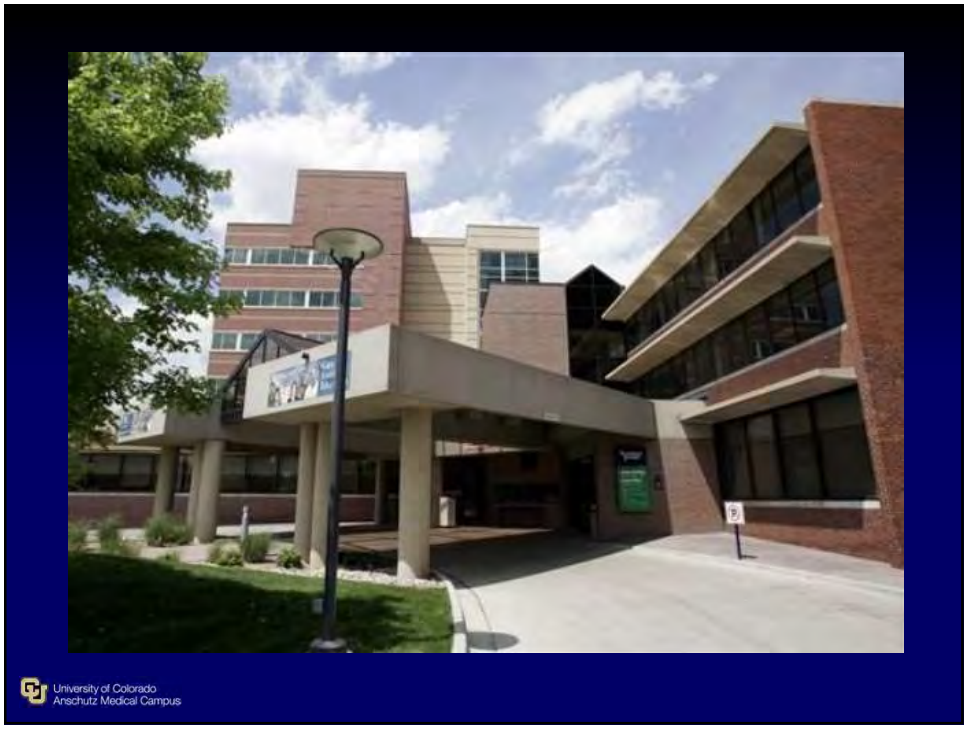
Director, Complex General Surgical Oncology Board

Treasurer-Elect, Society of Thoracic Surgeons

Board of Governors, American College of Surgeons

University of Colorado Anschutz Medical Campus

2


University of Colorado
Anschutz Medical Campus

3


University of Colorado
Anschutz Medical Campus

4

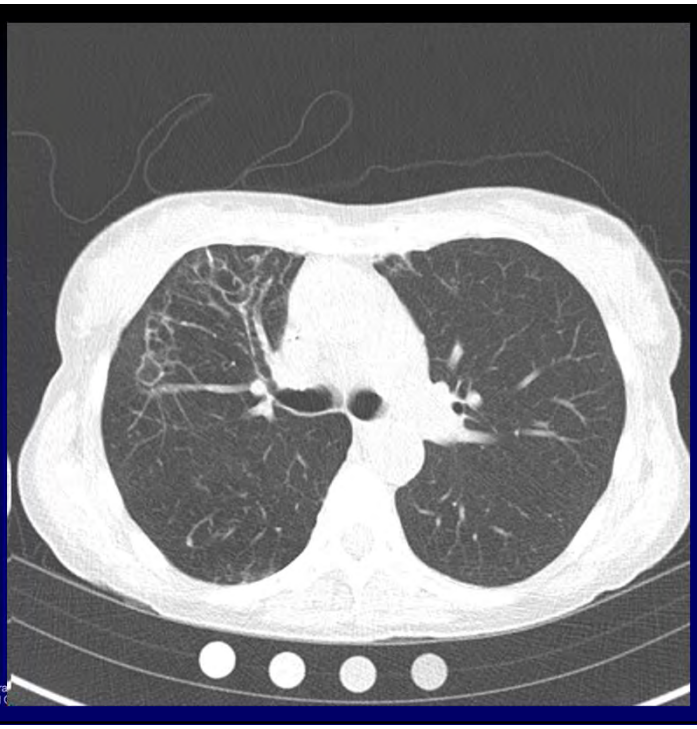
Surgery for Pulmonary NTM Disease

Case Presentation

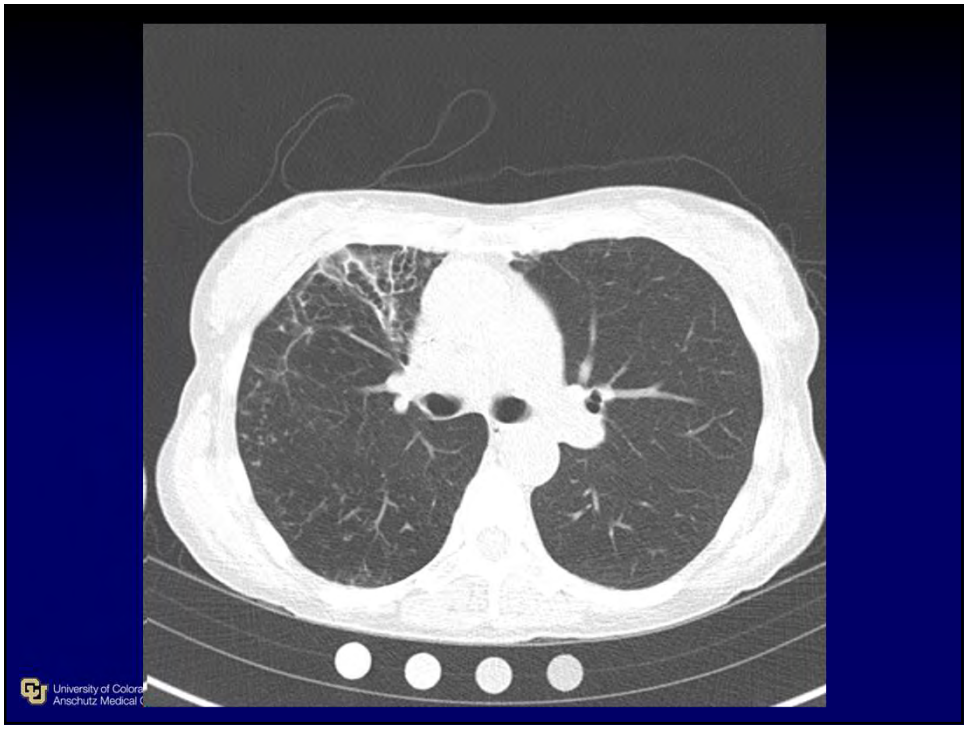
- 65 year old female
- Chronic productive cough, recurrent infection
- Documented MAC infection by ATS criteria
- Repeated treatment failures, now macrolide resistant
- Referral and evaluation at NJH
- Imaging suggests areas of focal bronchiectasis involving right lung

University of Colorado Anschutz Medical Campus

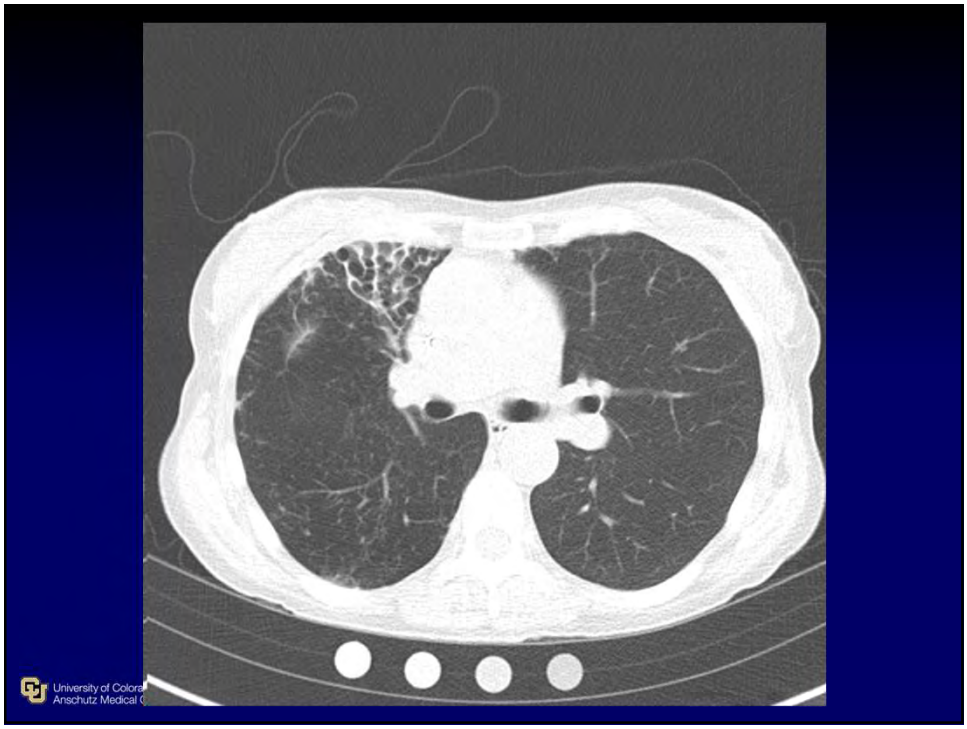
5



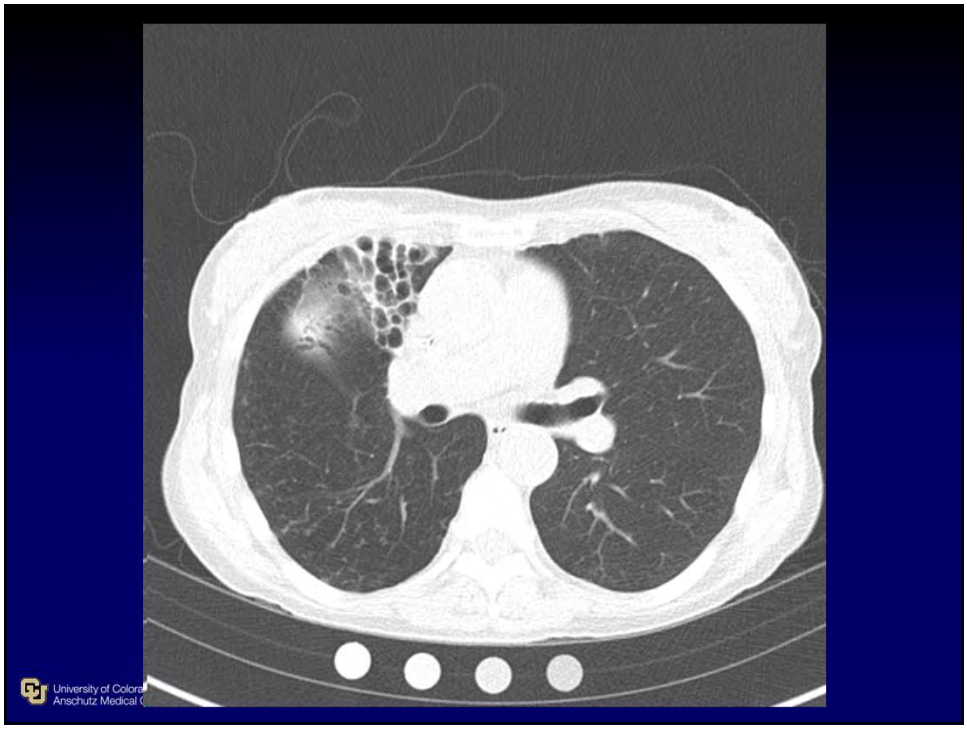
6



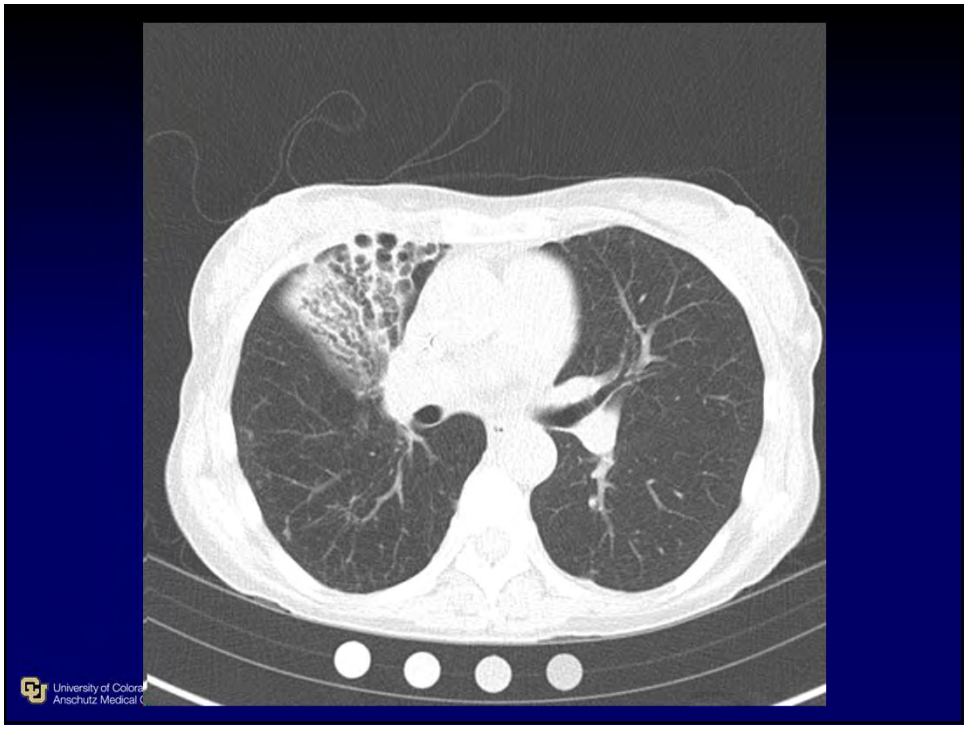
7



8

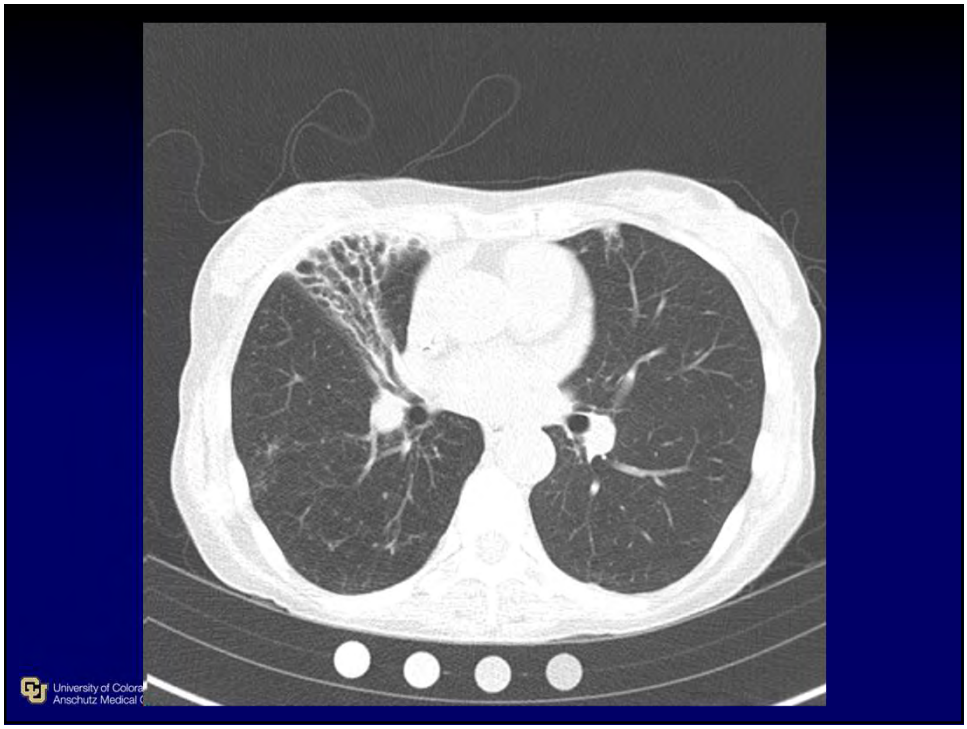


9

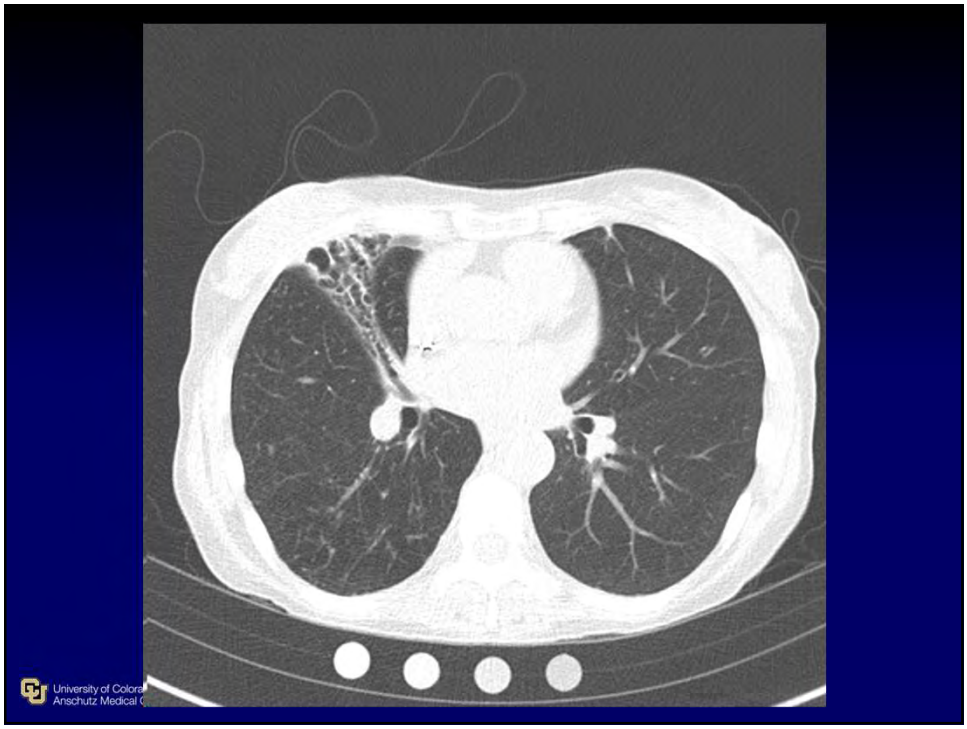


10

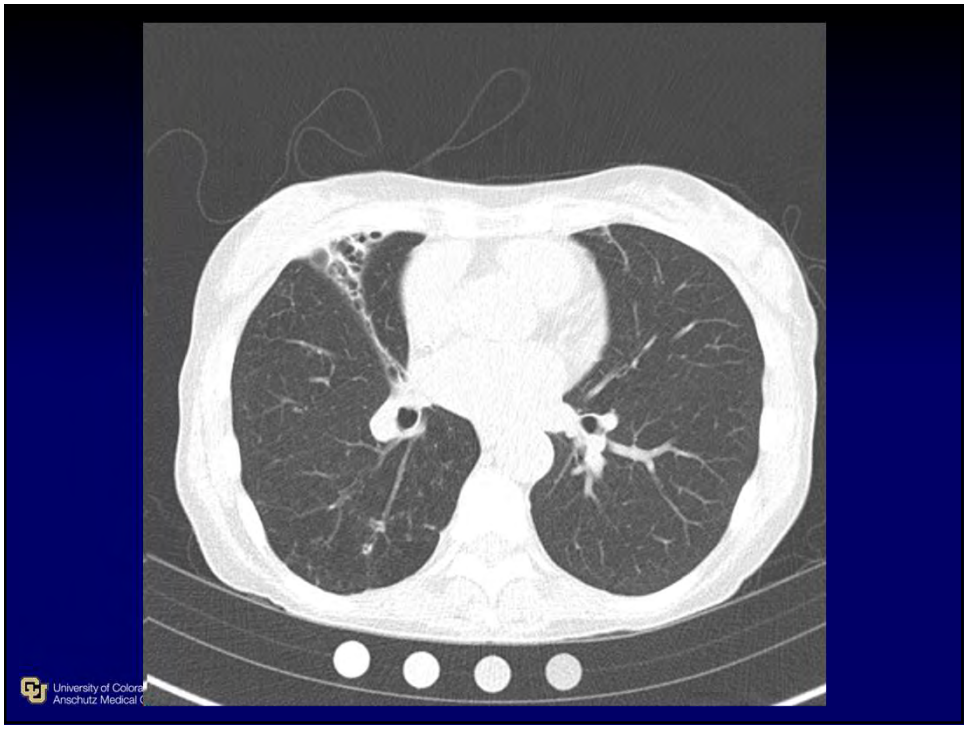
11



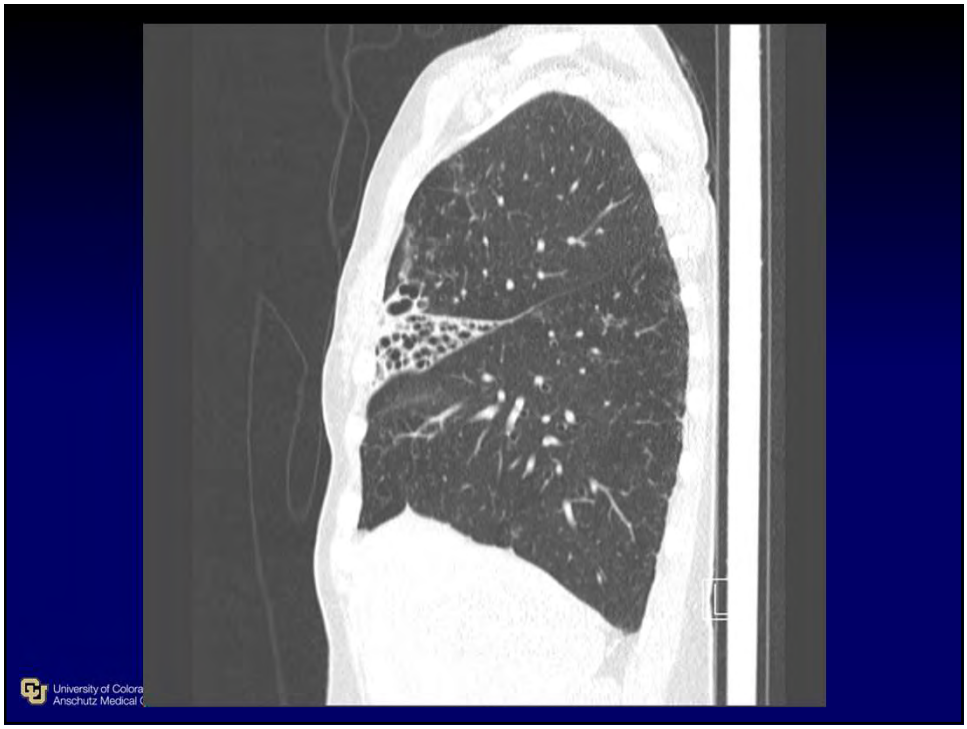
12



13



14



15

16

Surgery for Pulmonary NTM Disease
Pre-Surgery Treatment

- Initiate multidrug regimen, including IV Amikacin
- Planned Robotic RML, RUL anterior segment resection in 8 weeks after initiation of therapy
- 2 – 4 day hospital stay with surgical procedure
- 7 - 10 day stay in Colorado at time of surgery

University of Colorado Anschutz Medical Campus

17

Surgery for Pulmonary NTM Disease
Indications for Surgery

Persistent, focal (cavitary or bronchiectatic) lung disease after antimicrobial treatment, usually in the setting of recurrent symptoms, documented treatment failure, or antimicrobial resistance.

Surgical resection should be seen as an adjunct to antimicrobial therapy, which remains the mainstay of treatment.

University of Colorado Anschutz Medical Campus

18

Surgery for Pulmonary NTM Disease
Basics of Surgical Therapy

What is the Goal?

University of Colorado Anschutz Medical Campus

19

Surgery for Pulmonary NTM Disease
Basics of Surgical Therapy - Goals

- Eradicate infection
  - Culture negative
  - Off antibiotics
  - Symptom free
- Symptom control
  - Intractable cough
  - Hemoptysis
- Limit damage to uninvolved lung

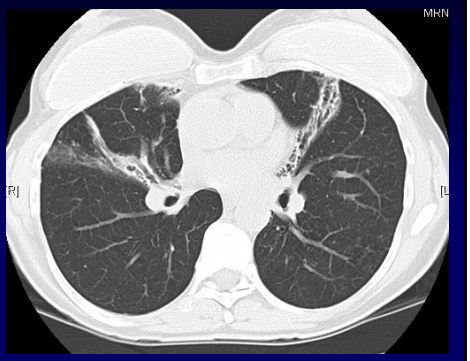
University of Colorado Anschutz Medical Campus

20

Surgery for Pulmonary NTM Disease

Presentation

- Middle-aged females, thin, Caucasian, nonsmokers, right middle lobe / lingular disease
- Isolated large, thick-walled cavitary disease.
- Elderly men, smokers, ETOH abuse, underlying COPD. Resembles TB, may progress to complete lung destruction.



University of Colorado Anschutz Medical Campus

21

Surgery for Pulmonary NTM Disease

Presentation

- Middle-aged females, thin, Caucasian, nonsmokers, right middle lobe / lingular disease
- Isolated large, thick-walled cavitary disease.
- Elderly men, smokers, ETOH abuse, underlying COPD. Resembles TB, may progress to complete lung destruction.

University of Colorado Anschutz Medical Campus

22

Surgery for Pulmonary NTM Disease

Presentation

- Middle-aged females, thin, Caucasian, nonsmokers, right middle lobe / lingular disease
- Isolated large, thick-walled cavitary disease.
- Elderly men, smokers, ETOH abuse, underlying COPD. Resembles TB, may progress to complete lung destruction.

University of Colorado Anschutz Medical Campus

23

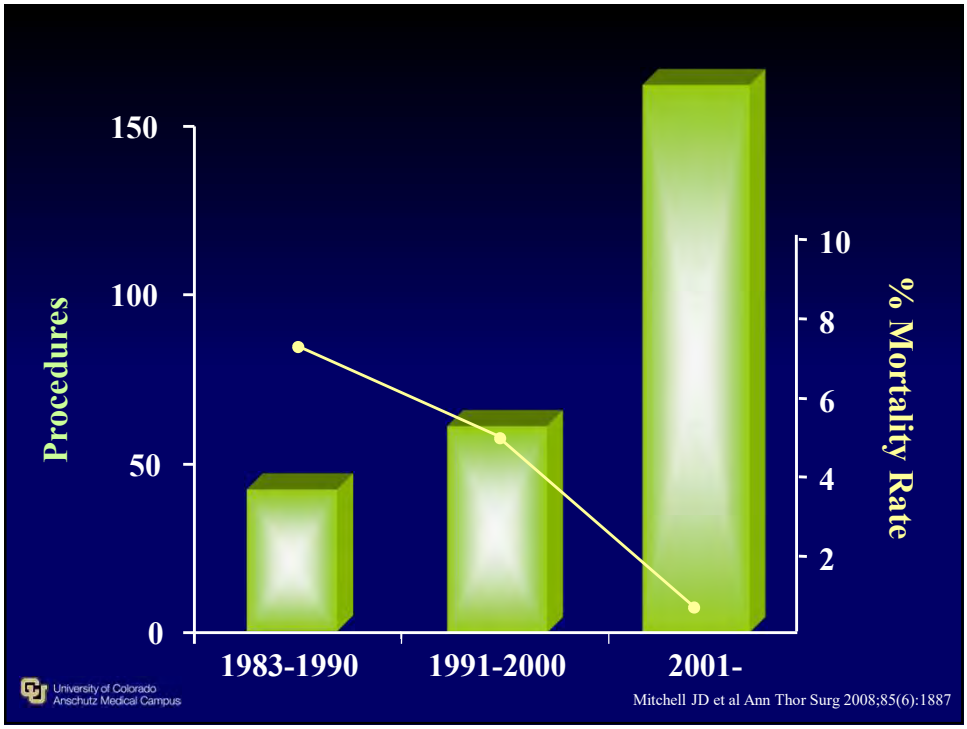
Surgery for Pulmonary NTM Disease

Results of Surgical Therapy

- Corpe, 1981: 131 cases, mortality 6.9%, BPF 5.3%, 93% sputum conversion rate
- Nelson, 1998: 28 cases, mortality 7.1%, BPF 3.6%, complication rate 32%, 88% sputum conversion rate
- Mitchell, 2008: 265 cases, mortality 2.6%, complication rate 18%, BPF 4.2%, 87% sputum conversion rate
- Shiraishi, 2013: 60 cases, mortality 0%, complication rate 12%, BPF 8.3%, sputum conversion 100% → 90% at 2 years
- Kang, 2015: 70 cases, mortality NR, complication rate 21%, BPF 7.1%, sputum conversion rate 81%
- Asakura, 2017: 125 cases, mortality 3%, complication rate 22%, BPF 6.4%, sputum conversion rate 94%

University of Colorado Anschutz Medical Campus

24



25

Surgery for Pulmonary NTM Disease

2023 Meta Analysis

- Examined overall outcomes for adjunctive surgery in patients with NTM disease

15 Studies
1071 Patients →

Sputum Conversion: 93%
Recurrence: 9%
mean F/U 34 months
Complication Rate: 17%
In-Hospital Mortality: 0%

University of Colorado
Anschutz Medical Campus

Kim J-Y et al CHEST 2023; 163(4):763-777

26

Surgery for Pulmonary NTM Disease
Minimally Invasive (VATS) Approach

- Study period: July, 2004 to June, 2010
- 171 patients → 212 cases
  - 41 patients had bilateral resections
- Mean age: 59 years (26 – 82 years)
- Predominately Caucasian (93%) and Female (93%)

University of Colorado Anschutz Medical Campus

Mitchell JD et al Ann Thor Surg 2012 Apr;93(4):1033-40

27

Surgery for Pulmonary NTM Disease
Minimally Invasive (VATS) Approach

- Prior thoracic surgery in 10%
- Mean duration of medical therapy prior to referral for surgery: 61 months (4-354 months)
- Indications for surgery: Focal parenchymal disease with recurrent hemoptysis or pulmonary infections, or failure or intolerance of medical therapy

University of Colorado Anschutz Medical Campus

Mitchell JD et al Ann Thor Surg 2012 Apr;93(4):1033-40

28

Surgery for Pulmonary NTM Disease

Minimally Invasive (VATS) Approach

Lobectomy	126
Segmentectomy	73
Mixed	13

Conversion to thoracotomy in 10 cases (4.7%)

No operative mortality; Complications in 19 patients (8.9%)

Mean hospital length of stay 3.7 days (1 – 23 days)

University of Colorado Anschutz Medical Campus

Mitchell JD et al Ann Thor Surg 2012 Apr;93(4):1033-40

29

Surgery for Pulmonary NTM Disease

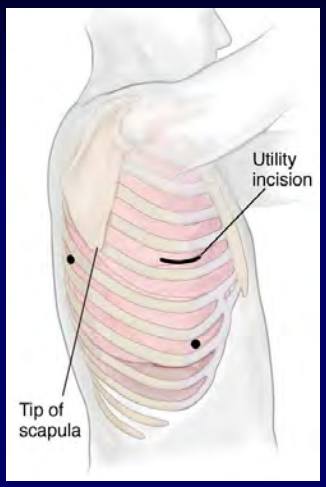
How do patients really do?

University of Colorado Anschutz Medical Campus

30

Surgery for Pulmonary NTM Disease
"VATS" Approach

- VATS Lobe/Segmentectomy
  - Two 1 cm incisions
  - One 3 cm "utility" incision
  - No rib spreading
- Operation otherwise identical to open approach
- Double lumen tube
- No epidural catheter
- Prior surgery not absolute contraindication



University of Colorado Anschutz Medical Campus

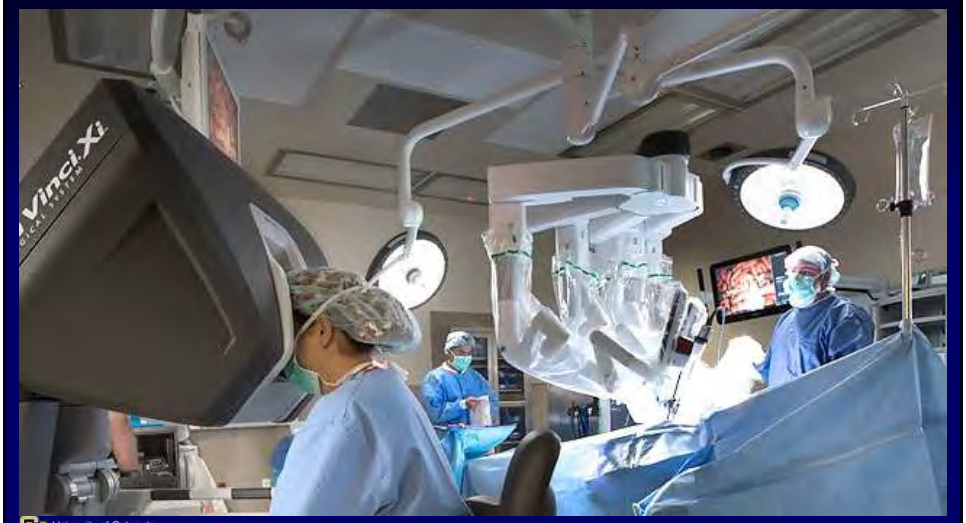
31

Thoracoscopic Surgery
Instruments

University of Colorado Anschutz Medical Campus

32

Surgery for Pulmonary NTM Disease
Robotic Approach



University of Colorado
Anschutz Medical Campus

33

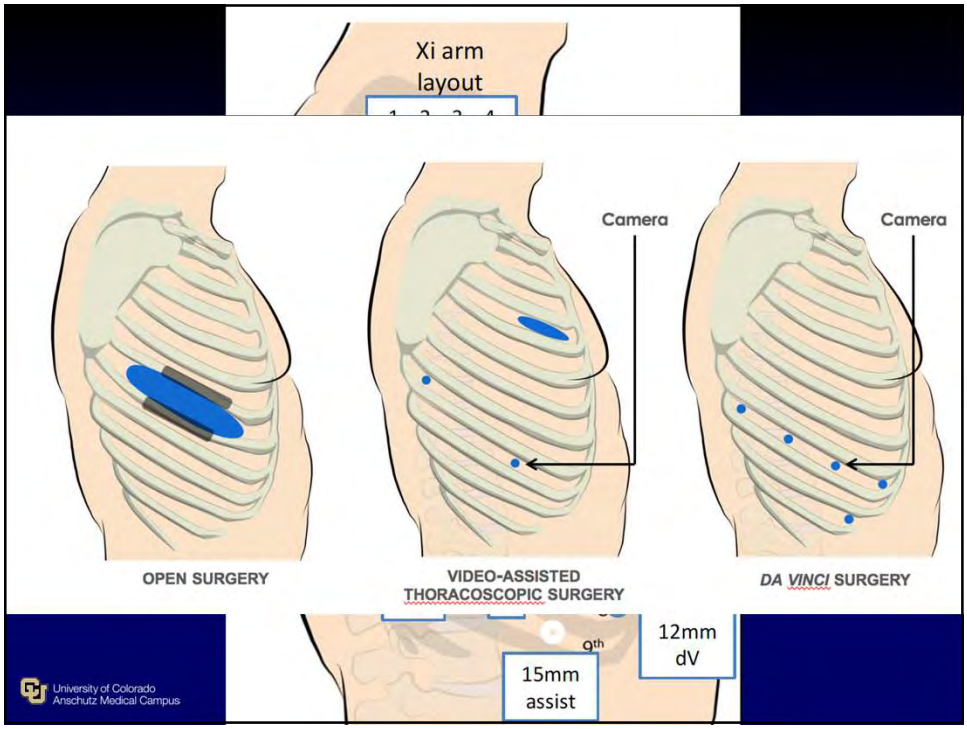
University of Colorado
Anschutz Medical Campus

34

Robotic Assisted Surgery
Instrumentation

University of Colorado
Anschutz Medical Campus

35



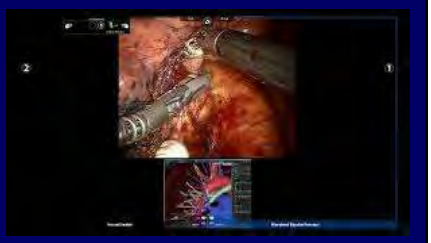
36

Robotic Assisted Thoracic Surgery

What are the Advantages?

- Optics
  - Magnified 3D HD
  - Immunoflourescence (FireFly)
  - TilePro

- Surgeon Autonomy
  - Integrated energy, stapling
  - 4th Arm = Reliable assistant



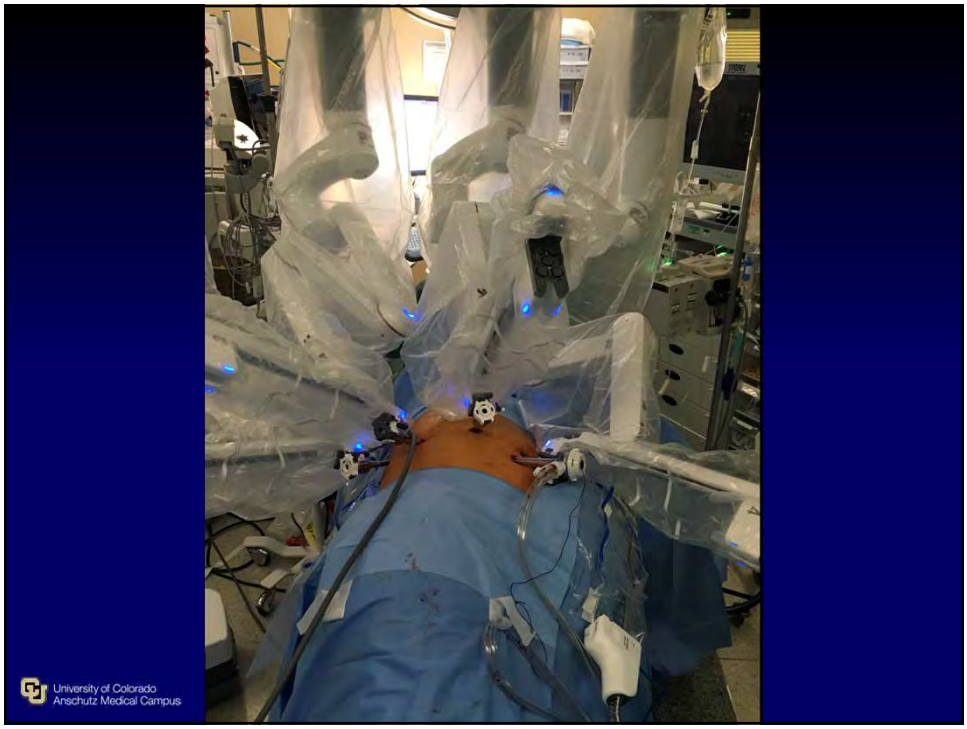
- Simulation
- Ergonomics

University of Colorado Anschutz Medical Campus

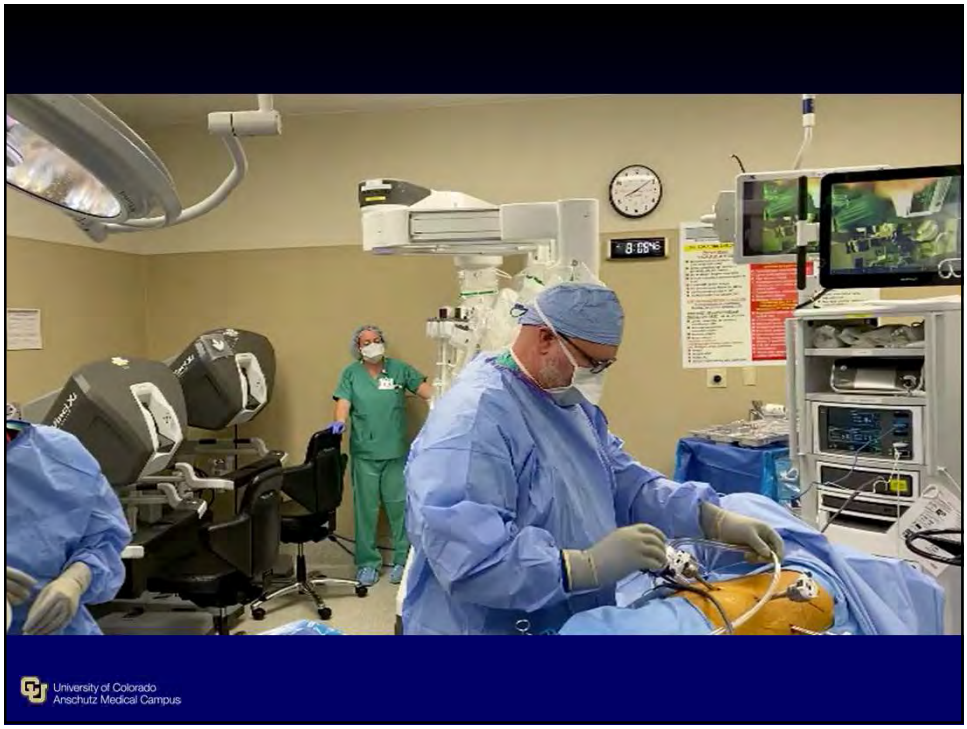
37

University of Colorado Anschutz Medical Campus

38


University of Colorado
Anschutz Medical Campus

39


University of Colorado
Anschutz Medical Campus

40


University of Colorado
Anschutz Medical Campus

41


LOGIN
CONSOLE 2
A-D
E-K
L-Q
R-Z
DR. ALBRIGHT, DREW
DR. ALFARO, LEO
DR. BAILEY, DAVID
DR. BAUER, AUDREY
DR. BIG, BIGGY
DR. BOYD, REECE
DR. C WHITTIER, SARAH
DR. CALDERWOOD, CAMILLE
NEW USER
CONSOLE 2

42


University of Colorado
Anschutz Medical Campus

43


BRAKE
BRAKE
LOGIN

44

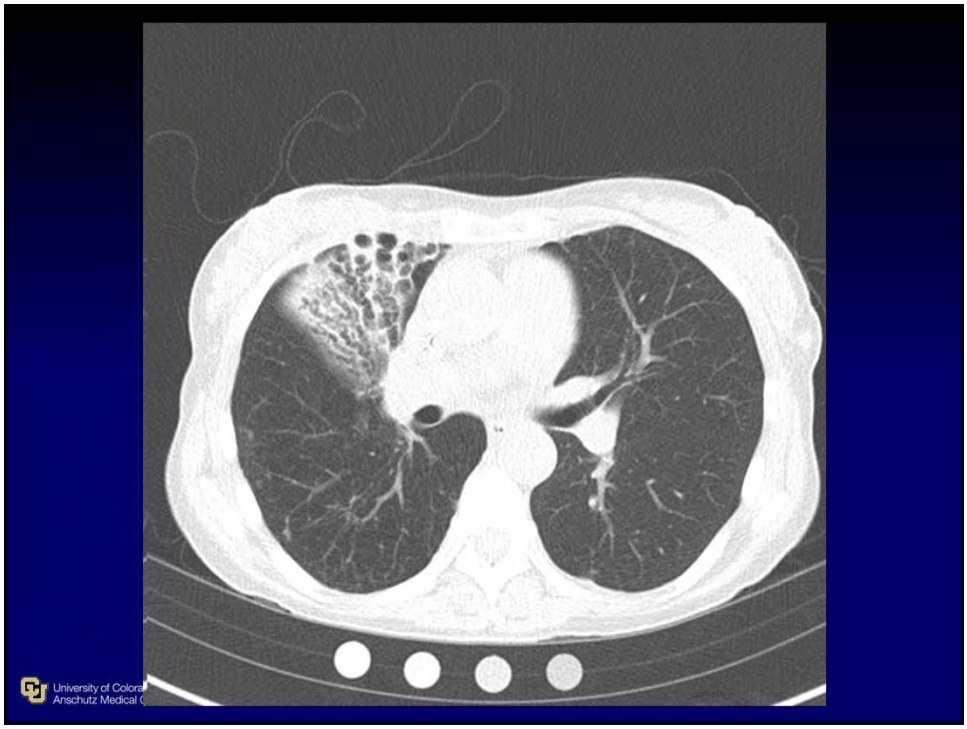
45


1
LONG BIPOLAR GRASPER
SOFT COAG
AUTO STOP OFF
80W MAX
8
GIVE
2
1X
30DEG ENDOSCOPE PLUS
30° △
30° ▽
3
CADIERE FORCEPS
GIVE
4
TIP-UP FENESTRATED GRASPER
GIVE
MESSAGES VISIBLE
AUDIO CONTROLS
ENERGY CONTROLS
GIVE ALL
NO USB DETECTED
DR. BIGGIE BIG

46


MONOPOLAR
BIPOLAR
CUT
POWER LIMIT
180
MAX WATTS
ADJUST LIMIT
EFFECT
4
AUTO
DRY
COAG
SWIFT
FORCED
CLASSIC
POWER LIMIT
150
MAX WATTS
ADJUST LIMIT
EFFECT
5
DR. BIGGIE BIG'S ENERGY PRESETS
'PRESET A' (NOT SET)
'PRESET B' (NOT SET)
'PRESET C' (NOT SET)
EDIT PRESETS
CLOSE
DR. BIGGIE BIG

47


University of Colora
Anschutz Medical

48

University of Colorado Anschutz Medical Campus

49

Surgery for Pulmonary NTM Disease

BPF after Pneumonectomy

Shiraishi, 2010: MDR-TB vs. NTM pneumonectomy

- No operative mortality
- MDR-TB: 22 patients (7 right, 15 left)
  - Male 72%, Sputum negative 63%
  - BPF rate 4.5% (1 right)
- NTM: 11 patients (7 right, 4 left)
  - Female 72%, Sputum negative 9%
  - BPF rate 45% (4 right, 1 left)

University of Colorado Anschutz Medical Campus

Shiraishi Y et al. ICVTS 2010;11:429

50

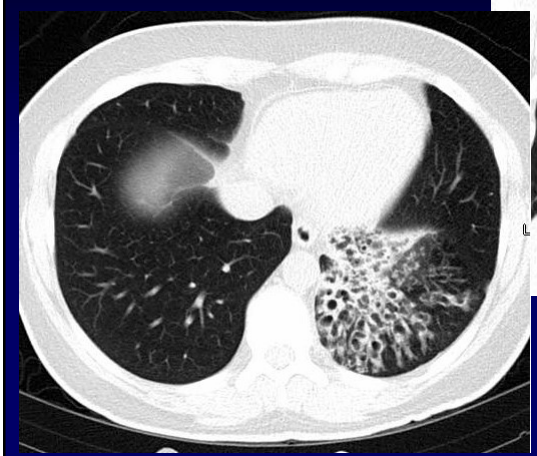
Surgery for Pulmonary NTM Disease

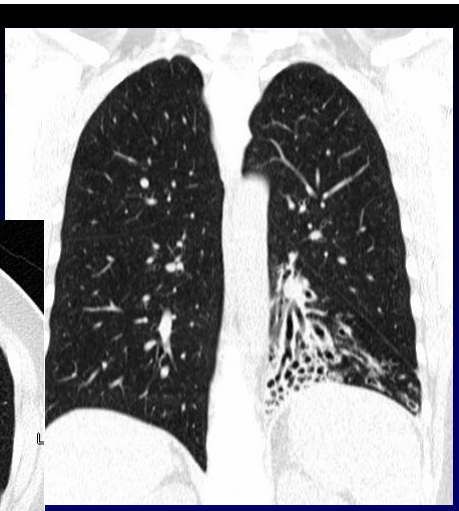
Common Questions

- Should I have surgery to treat my NTM infection?
- Can I have my surgery using a minimally invasive (VATS or Robotic) approach?

University of Colorado Anschutz Medical Campus

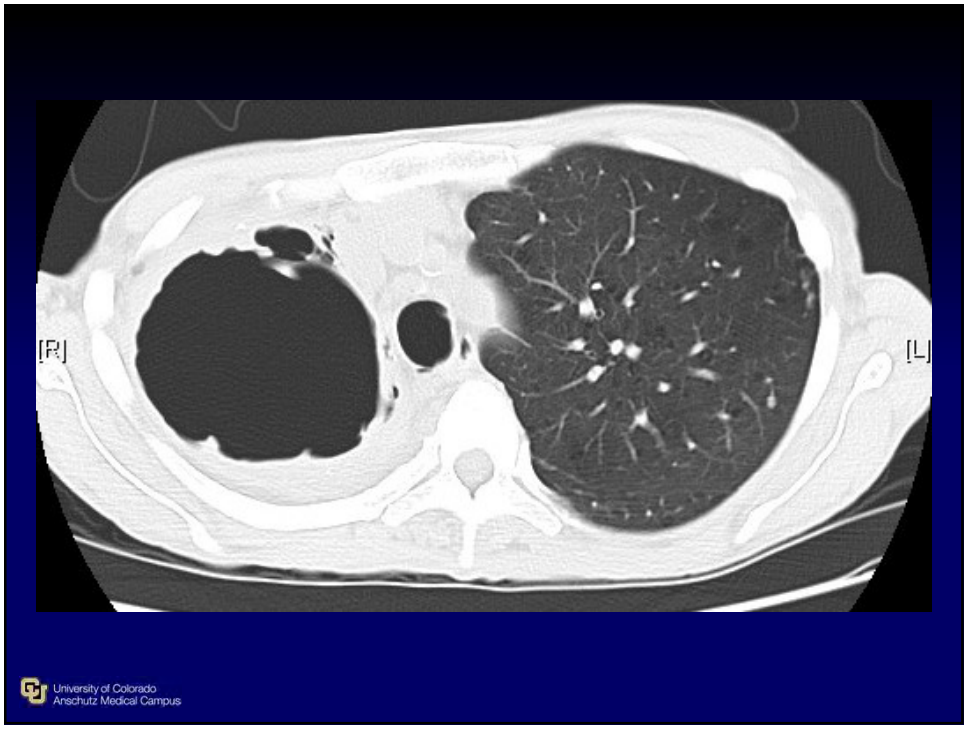
51



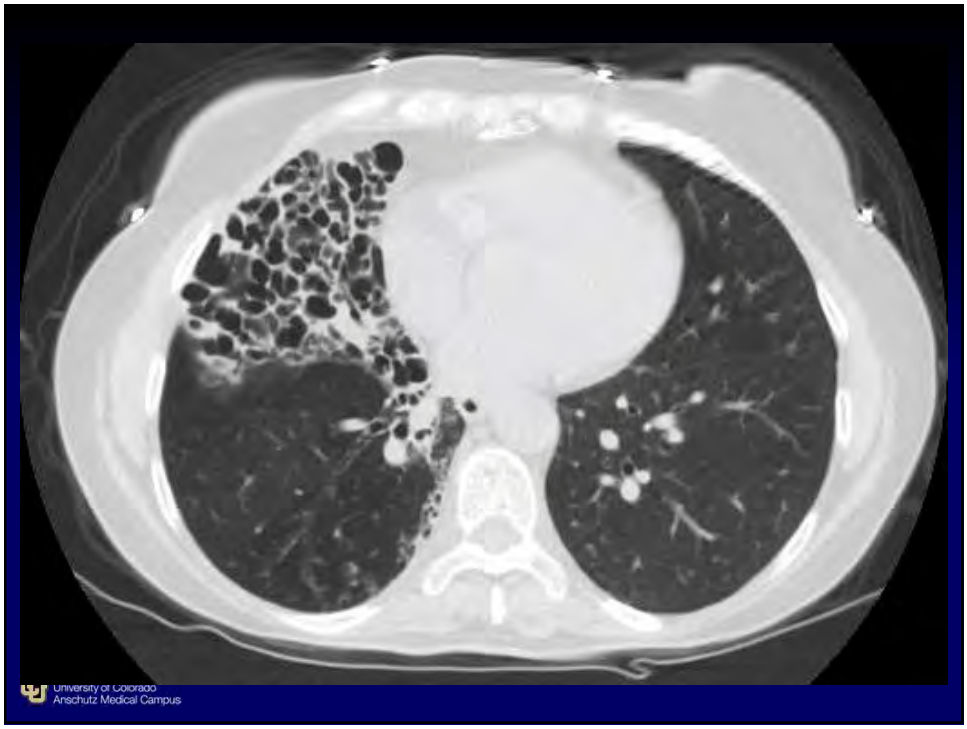


University of Colorado Anschutz Medical Campus

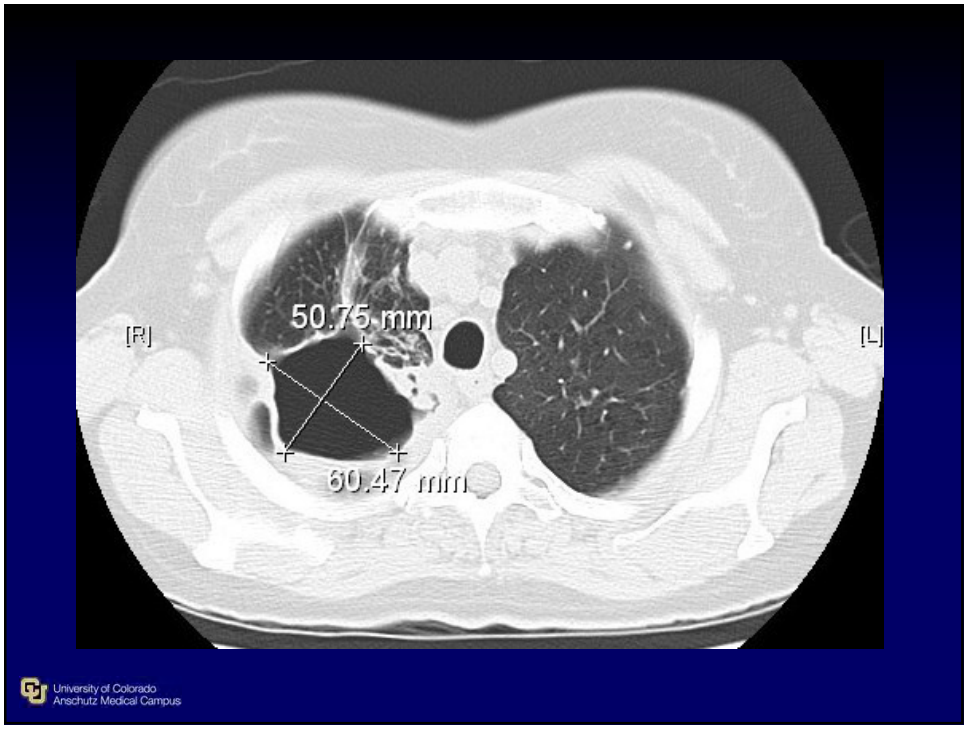
52


[R]
[L]
University of Colorado
Anschutz Medical Campus

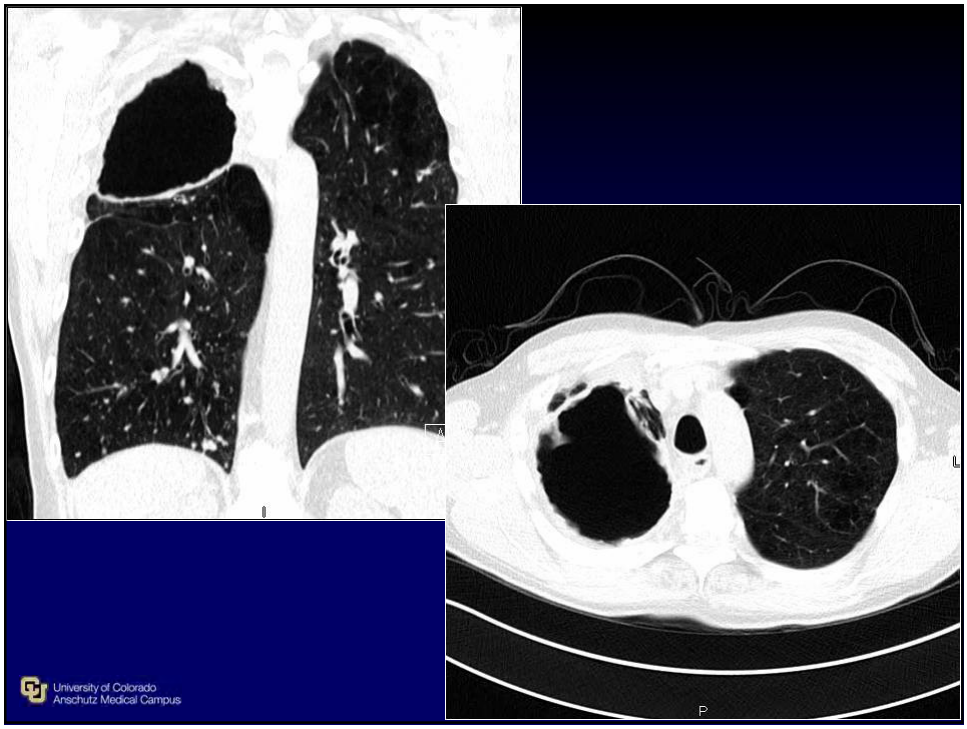
53


University of Colorado
Anschutz Medical Campus

54


[R]
50.75 mm
[L]
60.47 mm
University of Colorado
Anschutz Medical Campus

55


University of Colorado
Anschutz Medical Campus

56

Surgery for Pulmonary NTM Disease

Common Questions

- Should I have surgery to treat my NTM infection?
- Can I have my surgery using a minimally invasive (VATS) approach?
- Can I have the surgery and skip the medicine?
- When should the surgery occur?
- What will my breathing be like after the surgery?

University of Colorado Anschutz Medical Campus

57

Surgery for Pulmonary NTM Disease

Summary

- Surgical resection in pulmonary NTM disease may lead to improved outcomes in selected cases
- Complex lung resection and muscle flap use often possible using modern minimally invasive techniques
- Coordination of care best approached in multidisciplinary environment
- Resection for infectious lung disease differs from resection for cancer: experience counts

University of Colorado Anschutz Medical Campus

58

COPING AND CARING

Elizabeth Devon Smith, PhD
Assistant Professor & Clinical Psychologist
National Jewish Health

1

OVERVIEW

- Stress and NTM
- Coping: Building a skill set
- Caring: Social support
- Caring: Professional support

2

STRESS AND NTM

3

STRESS AND NTM

- Stress is common among patients with various health conditions, including NTM
  - Adjustment to new lifestyle
  - Fears about future health
  - Balancing family worries
  - Depression, anxiety, anger/frustration
- Managing your stress can…
  - Improve your quality of life
  - Help you manage your condition long-term
  - Improve your mental and physical health
  - Help you make lasting changes

4

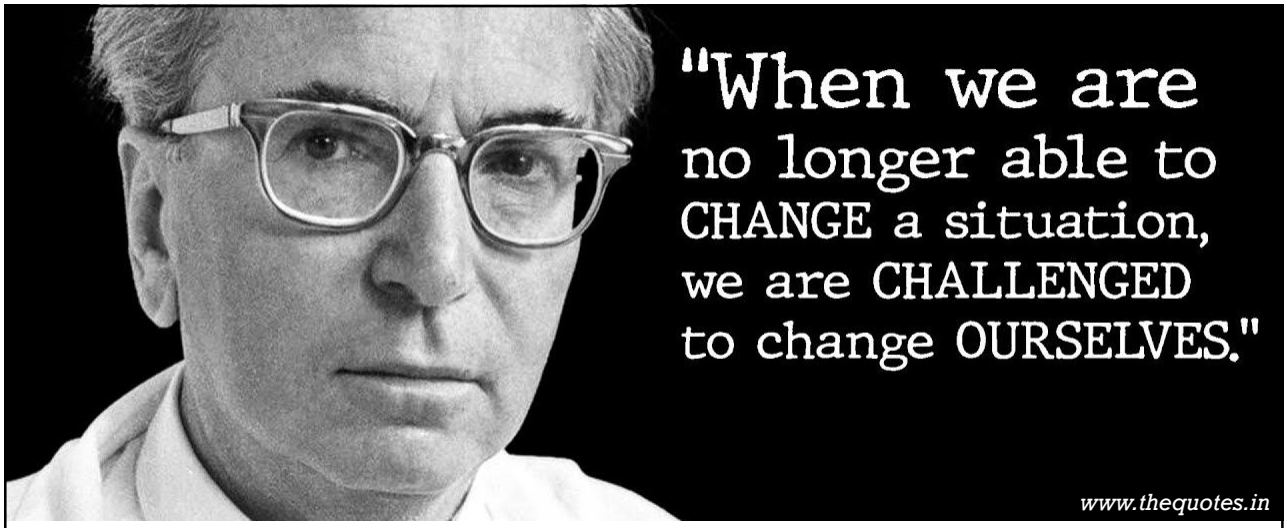
LONG-TERM STRESS

- Long-term stress: repeated on a regular basis or does not improve with time
  - If perceived threat doesn't subside within a few days, body starts to cope by releasing hormones (like cortisol) to sustain preparedness for about 1 month
  - Eventually wears on you both physically and emotionally
  - Exhaustion state is triggered (after 1-3 months) when body can no longer cope with stressor

5

IS YOUR STRESS CUP OVERFLOWING?

6



STRESSORS MAY BE UNAVOIDABLE,
BUT STRESS REACTIONS CAN BE MODIFIED

7

BUILDING A SKILL SET

8

YOUR EXISTING SKILL SET

- Everyone has coping skills, or things that help us relax or de-stress
- What coping skills work well for you?
- Choosing active rather than passive strategies are more helpful in the long run
  - Active: adaptive strategies that benefit you by being proactive and addressing problems and discomfort appropriately
  - Passive: maladaptive strategies, such as avoidance, denial, ignoring, that often take the form of unhealthy behaviors (skipping medical treatments, substance use)

9

COPING SKILLS: THOUGHTS

10

THE POWER OF THOUGHTS

- When a situation occurs, automatic thoughts pop into our mind, which can influence how we feel and behave
- We tend to latch on to thoughts that come to mind first or most often, regardless of accuracy
- However, latching on to thoughts that are negative, inaccurate, or unhelpful creates patterns of negative self-talk

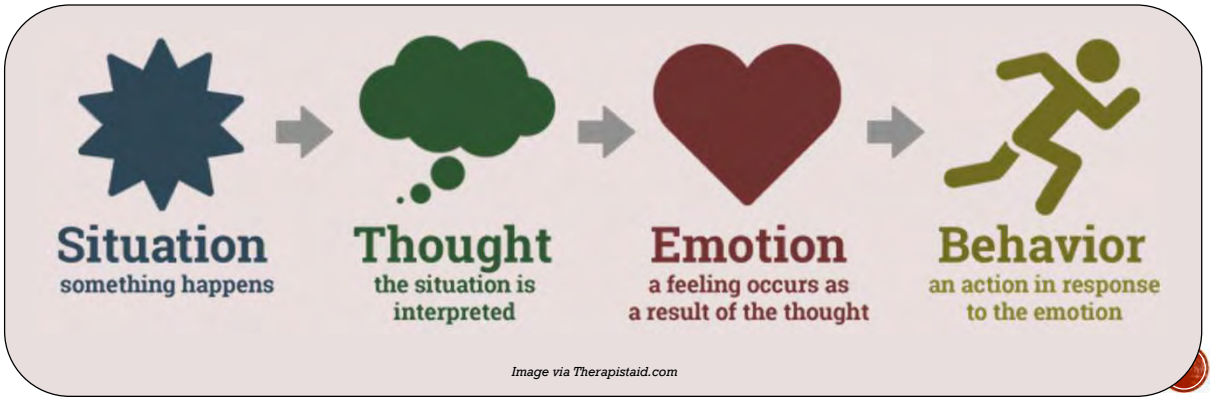
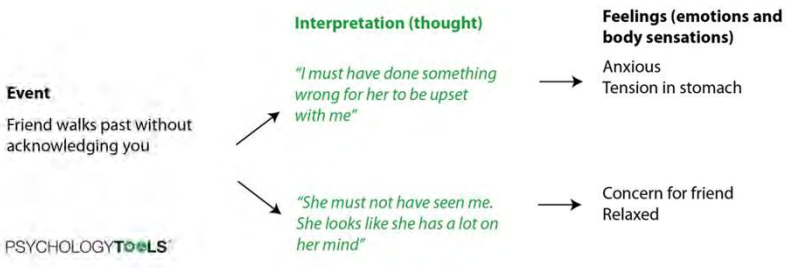


Image via Therapistaid.com

11

INTERPRETATIONS

- Often, it's not events or situations that bother us
- Instead, it is the way that we interpret events – the meaning that we give to them – that gives rise to our feelings



12

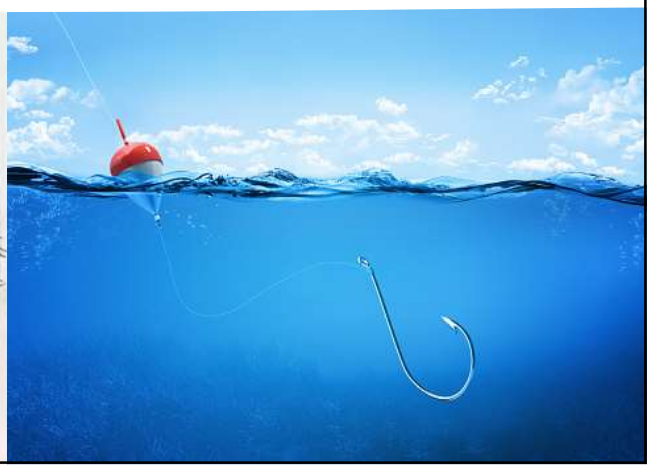
GLASS HALF EMPTY OR HALF FULL?

- Usually, there is another way of looking at a situation, even if it is not immediately apparent to us
- No right or wrong
  - AND not OR
- Developing flexibility in our thinking reduces our distress

13

COPING SKILL: UNHOOK FROM THOUGHTS

- Defuse from the thought
  - "This is just a thought and not all thoughts are true"
- Notice a thought without believing it or struggling with it
- Stepping back and observing without getting tangled up
  - "I'm useless" vs. "I'm noticing I'm having thought that 'I'm useless"
- Seeing thoughts for what they are…just words or pictures
- Letting thoughts come and go



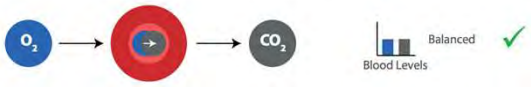
14

COPING SKILLS: BEHAVIORS & ACTIONS

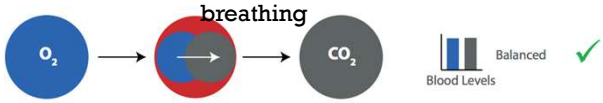
15

THE POWER OF BREATH

Normal breathing



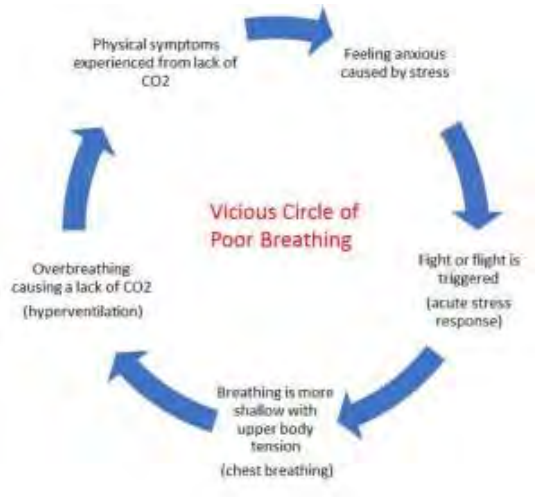
Exertion breathing



Panic breathing

Psychology Tools

16



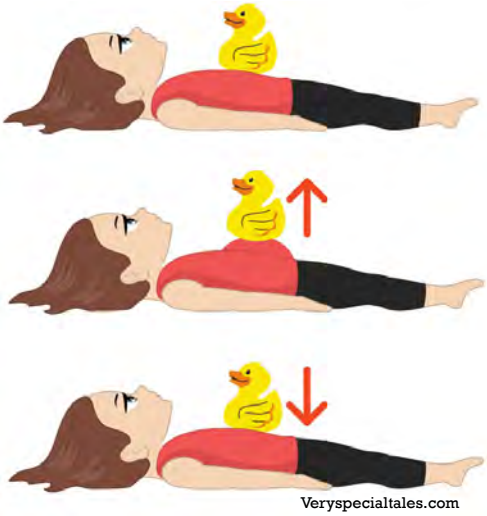
theinnerimpact.com

CHEST VS. BELLY BREATHING

- Living with NTM, you know the importance of breathing and how difficult things can be when breathing doesn't feel quite right
- Chest breathing: shallow and irregular
- Diaphragmatic "belly" breathing: deeper and steady, allowing for normal oxygen/carbon dioxide exchange

17

COPING SKILL: DIAPHRAGMATIC BREATHING



Veryspecialtales.com

18

COPING SKILL: 5-4-3-2-1

19

COPING WITH ACTIONS: PRIORITIZING SELF-CARE

- Self-care is about making yourself a priority and engaging in activities you ***could*** enjoy
- We often let our mood dictate what we do, so when we're stressed or unwell, we end up doing very little that we could enjoy, which makes us feel worse
- Self-care can be small activities
- The most important part is to be intentional

20

COPING WITH ACTIONS: IMPROVING SLEEP

- Good sleep health can be characterized by a few different aspects:

1. Satisfaction with quality of sleep (feeling rested)
2. Sleep regularity (getting in and out of bed around the same time every day)
3. Timing of sleep (majority of sleep occurring during nighttime and early AM)
4. Sleep continuity (not spending more than 30 minutes awake during sleep time)
5. Sleep duration (sleeping about 6-9 hours per night)
6. Daytime alertness (able to stay awake throughout the day without dozing)

- Having frequent and persistent issues with multiple aspects of sleep health may indicate a need to improve sleep habits

21

SLEEP PROMOTING BEHAVIORS

1. Set an earliest bedtime and latest wake time and follow it every day of the week
   - Keep your initial schedule close to your baseline averages
   - Let sleepiness guide actual bedtime to limit time in bed to time sleeping
   - Don't compensate for missed sleep (increase your sleep drive for the next night!)
   - Get a dose of sunlight first thing in the AM

https://mobile.va.gov/app/insomnia-coach

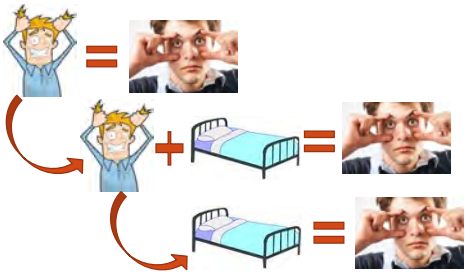
22

SLEEP PROMOTING BEHAVIORS

Spending too much time awake in bed can make it harder to sleep…

2) Eliminate sleep incompatible behaviors and get out of bed when you can't sleep
   - When in bed, don't read, watch TV, eat, use phone in bed, think, worry, or try to sleep
   - If 15-20 minutes pass and you are not sleeping (for any reason)… GET OUT OF BED
     - If you can't leave the bed (safety), sit up in bed in a distinctly different position
   - Do something relaxing until you feel you can sleep then try again
     - Have this planned before bed
   - Repeat as needed
   - Stay consistent! This promotes unlearning the association between the bed and arousal

https://courses.lumenlearning.com/atd-bhcc-intropsych/chapter/classical-conditioning/



23

SLEEP PROMOTING BEHAVIORS

- Nap smart
  - Build in a 30 minute nap/rest period
  - Should be 7-9 hours after final wake time
  - When you're acutely ill, you may need more sleep and that's ok!
  - If you tend to sleep more during the day and find yourself experiencing nighttime sleep disruption, another option is to recalibrate expectations

24

CARING: SOCIAL SUPPORT

25

SOCIAL SUPPORT

- Role Changes in the Family
  - Have roles within the family changed due to NTM? (or do you anticipate future changes?)
  - Communication: discuss the best way for you to manage role changes
  - Allow yourself to grieve AND focus on the roles that you still fill
  - Recognize that it is not necessarily negative for other family members to take on new roles
  - Roles tie into identity and self-worth
    - I keep our house clean; therefore I am a valuable person
  - Has your identity changed?
    - Make sure you still can identify positive aspects of yourself
    - Remember that there are many important ways to contribute to your family and to society

26

SOCIAL SUPPORT

- Social support= the comfort we receive from people in our life that help us through the good, the bad, and the ugly
- Research supports quality over quantity
  - Even a single source of social support can buffer stress and increase well-being
- Social support comes in different forms
  - Important to know what type of social support you need in a given situation and pair it with the most appropriate support person

CALM-CF, Bathgate

27

SOCIAL SUPPORT

- How to enhance the quality of your support network:
  - Ask for what you need (instead of assuming others will know)
  - Ask yourself the following:
    - Am I willing to ask for help?
    - Am I willing to receive help?
    - Am I asking the right people?
    - Am I withdrawing from others?
  - Unhelpful thoughts might be preventing you from getting the support you need:
    - I need to be strong and manage on my own
    - I'm the only one who can do everything right
    - I don't want to burden people with my problems
  - Challenge these thoughts by asking yourself:
    - Is this 100% true 100% of the time?
    - What are the potential consequences?
    - Is this a fact or an opinion?

28

COPING: PROFESSIONAL SUPPORT

29

PROFESSIONAL SUPPORT

- Sometimes, stress can lead to depression or anxiety
- Or sometimes, the stress can just feel overwhelming
- Either way, professional support is always an option
- Chronic illness (and much of life, in general) involves some suffering
  - BUT there is no need to excessively suffer

30

DEPRESSION

- **Depression** affects up to one-third of people with a chronic illness
- Feeling sad or down is completely normal
- Sometimes, depression is mild and short term
- However, depression can become more severe and might start getting in the way of day-to-day life
- Signs that you should seek treatment are: (1) your depression lasts most of the day, almost every day, for over 2 weeks or (2) gets in the way of your relationships, activities, or work.

31

ANXIETY

- Chronic illness can also lead to **anxiety**, which is completely normal
- Mild anxiety can be managed with the coping skills
- However, like depression, anxiety can become more severe and start to interfere with your life
- If anxiety becomes overwhelming or influences your behavior, talk therapy and/or medication can help

32

TREATING DEPRESSION AND ANXIETY

- For mild to moderate depression and anxiety
  - Medications very effective
  - Psychotherapy very effective
  - Medications and psychotherapy equally effective
- For severe depression and anxiety, medication is often crucial
- Most effective approach is medication and psychotherapy together
- Medication usually has quicker results but psychotherapy is more effective than medication at preventing relapse

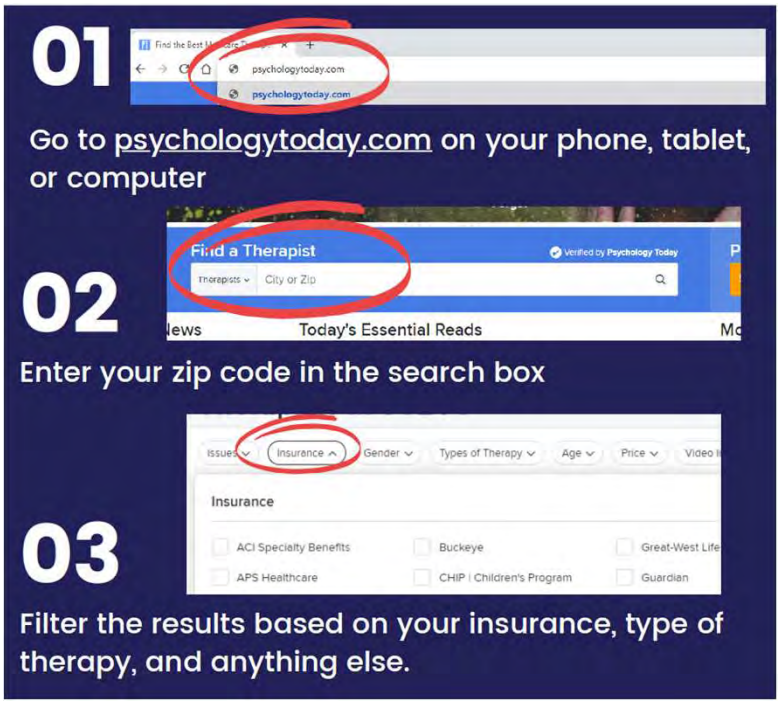
33

TREATMENT RESOURCES

- Association for Behavioral and Cognitive Therapies
  - www.abct.org
  - 212-647-1890
- American Psychological Association
  - www.apa.org
  - 800-374-2721
- American Association for Marriage and Family Therapy
  - www.aamft.org
  - 703-838-9808
- American Psychiatric Association
  - www.psychiatry.org/
  - 202-559-3900

34

FINDING A THERAPIST



35

TYPES OF THERAPY

- Cognitive Behavioral Therapy (CBT)
  - Very effective for depression and anxiety
  - Structured and time-limited
  - Involves changing behaviors and unhelpful thoughts/beliefs
- Acceptance and Commitment Therapy (ACT)
  - Great option for persistent mental health symptoms and coping with chronic health conditions
  - Instead of changing thoughts and behaviors, focus on acceptance and finding meaning in life despite challenges
- Family Systems Therapy
  - Helpful for handling changes in relationship dynamics due to illness

36

SUPPORT GROUPS

- NTM Info & Research (NTM-IR): dedicated to helping people with NTM (and their families) live their best lives through education, information, and support
- The NTM-IR website has a directory of local support groups for those with NTM and bronchiectasis (many are currently virtual!)
- Support groups can be a great way to not feel so alone
- https://ntminfo.org

37

SOME FINAL THOUGHTS

- Stress
  - Chronic illnesses can impact stress levels
- Coping: Building a skill set
  - Make the most of your existing coping skills
  - When developing additional coping skills, experiment and keep an open mind
- Caring: Social support
  - Roles in your family may change and that's ok
  - Re-evaluate your identity and find ways to maintain self-worth
  - Match the social support to your needs
- Caring: Professional support
  - Medications are useful and talk therapy is useful
  - Psychotherapy is beneficial for treatment of depression and anxiety, as well as for general adjustment to life and family changes
  - Support groups can connect you to others who have similar experiences

38

QUESTIONS?

39

National Jewish Health

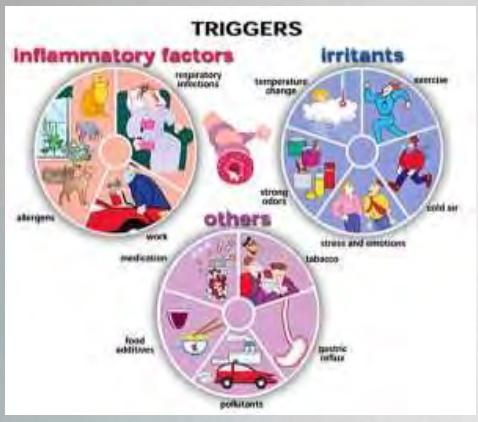
Airway Clearance: Improving Quality of Life

CHERYL TORRES RRT

1

Inflammation and Phlegm

2



- Respiratory infection
- Cigarettes smoke
- Allergens
- Emotional stress
- Odors/perfumes/aerosols
- Pet dander
- Exercise
- Cold air
- Air pollution

3

Pulmonary Hygiene

Foundation for therapy:

- Non-tuberculous Mycobacteria (NTM) Bronchiectasis
- Cystic Fibrosis
- Asthma

4

Most commonly asked questions

1. Which device is available for the patient
2. Where do I start
3. Is their insurance going to cover the device
4. What can we do to help expedite insurance coverage
5. Which company do we fax Rx too
6. Is this a DME product

5

What Is Airway Clearance ?

Non-invasive forms of therapy to help mobilize and clear mucus from the airways

Methods used:

- Positive Expiratory Pressure (PEP)
- Oscillating Positive Expiratory Pressure (OPEP)
- High Frequency Chest Wall Oscillation (HFCWO)
- Volara – Oscillation, Lung Expansion Therapy with Nebulizer
- Chest Physical Therapy (CPT)

6

Why We Need Airway Clearance

Normal function of the airways

- helps with movement and removal of secretions from the lungs. Cilia move back and forth mobilizing mucus to the larger, central airways where it can be expectorated easier

Compromised function of the airways can result from

- Impaired or ineffective function of the cilia
- Chronic Respiratory Infections
- Overproduction of thick, sticky mucus
- Ineffective cough

7

AerobiKA with Manometer

Oscillating Positive Expiratory Pressure

- Powered by the patients exhaled breath
- Adjustable resistance for different medical diagnoses
- Can be used in line with a nebulizer

8

Acapella DH, DM Valve

- Powered by patients exhaled breath
- Green Acapella used for most adult patients
- Blue Acapella used for pediatric or low lung volumes
- Not designed to be used with in line nebulizer

9

Secretion Management
Inhaled Saline Nebs

- Hypertonic Saline
  (3%, 7%, 10%)
- Normal Saline
  (0.9%)
- Bronchodilators

Nebulizer can be used in line with AerobiKA

10

OPEP Airway Clearance Device

Aerobika – Cleaning and Sterilization

Single patient use

- Designed for daily clean in warm soapy water
- Dishwasher safe, top shelf dishwasher
- High disinfection: boiling, microwave steam bag, 70% Alcohol, 3% Hydrogen Peroxide

Acapella – Cleaning and Sterilization

Single patient use

- Designed for daily clean in warm soapy water
- 70% Alcohol, 3% Hydrogen Peroxide

11

Reusable Breath Actuated Nebulizer (R BAN)

Single Patient Use

Breath actuated technology nebulizer

- Aerosolized medication is only delivered when patient inhales through the device)
- Breath actuation and Continuous mode options
- Minimal aerosol dispersed into environment
- Average treatment time is 10 - 15 minutes
- 6-month reusable nebulizer. Single patient use

Cleaning:

- Daily: Warm, soapy water after each use
- Weekly Sterilization: Boiling 5 – 10 minutes

12

OMBRA Compressor

- Table Top Compressor
- Compressor PSI : 42
- Operating Pressure : 19.5

- Standard compressor can be used if using Saline or Bronchodilator only
- Stronger PSI recommended for Inhaled Antibiotics

(OMBRA)

13

Vest Therapy

(HFCWO)

High Frequency Chest Wall Oscillation

14

There are 2 types of High Frequency Units

- **Machine Powered:**
  - Hill Rom - The Vest
  - Respirtech - InCourage
  - Electromed - Smart Vest

Battery Powered:

- Hill Rom - Monarch
- BioPhysics - AFFLO

15

Who supplies the equipment ?

The Vest - Hill Rom
set up in patient home
InCourage - Respirtech
set up in patient home
Smart Vest - ElectroMed
set up in patient home

Monarch - Hill Rom
set up in patient home

AFFLO - DME
Measured by DME, Delivered, and Schedule for Demonstration

16

The Vest

- Machine powered
- Dual Hose
- Buckle closure
- Comes in full vest, chest vest and wrap

17

InCourage

- Machine powered
- Dual Hose
- Buckle closure
- Full vest and wrap

18

Smart Vest

- Machine powered
- Single Hose
- Velcro closure
- Full vest and wrap

19

Portable

Vest Units

20

Monarch
Portable Vest

21

AFFLO
Portable Vest

Battery Pack allows for **freedom of movement during treatments**

Average weight is 8 lbs

3 treatment settings
x 3 intensity levels
9 setting variations

Quiet during operation

7 sizes available

22

Volara

- **Three therapies in one unit**
- **CPEP –**
- Continuous Positive Expiratory Pressure
- **CHFO –**
- Continuous High Flow Oscillation
- **NEBULIZER –**
- Can be used with Bronchodilator and Hypertonic Saline

23

Benefits of Proper Pulmonary Hygiene

- Enhances mucus mobilization and removal
- Decrease recurrent lung infections
- Decrease Antibiotic use
- Decrease Hospitalization
- Noticeable decrease in cough
- Improve gas exchange
- **Improves Quality of Life**

24

Disclaimer

- *Currently employed by* ***National Jewish Health***

- ***Electromed*** *Inc and Respirtech Inc to provide setup and instruct patients on their new airway clearance device.*
- ***Hill Rom***
- ***Respirtech***

Provide setup and instruct patients on their new airway clearance device.

25

References

- Braverman, JM. Airway clearance indications: an overview. Advanced Respiratory (1998-2001) 800-426-4224

- Irwin RS, Boulet LP, Cloutier MM, Gold PM, Ing AJ, O'Byrne P, Prakash UBS, Pratter MR, Rubin BK, Managing Cough as a Defense Mechanism and as a Symptom: A Consensus Panel Report of the American College of Chest Physicians. Chest 1998;114(2):133S-181S

26

NOTES

NOTES

NOTES

NOTES

NOTES

NOTES

NOTES

NOTES