NON-TUBERCULOUS MYCOBACTERIAL INFECTION

WHERE IS IT & HOW DID I GET IT?

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GOALS OF TALK

• Identify sources of NTM in the environment

• Clarify the reasons that it is difficult to remove NTM from the household environment and thus why avoidance of NTM is “easier said than done”

• Gain perspective on whether the personal environment is the pivotal factor in acquiring the infection
GOALS OF THE TALK

• SEGUE TO LATER TALKS EMPHASIZING THAT INHALATION OF VAPOR IS NOT THE ONLY MECHANISM PROPOSED

• ESOPHAGEAL AND SWALLOWING DYSFUNCTION MAY PLAY A ROLE AS WELL

• THE NOTION OF THE “SUSCEPTIBLE PATIENT” MODEL
DIFFERENT LEVELS OF BACKGROUND KNOWLEDGE

• Commitment to the concept that “knowledge is power”

• Many know this material

• May be complex

• Apologies for discrepancy in level of information included
WATERBORNE ORGANISMS

Enteric organisms

• Grow within the gastrointestinal tract
• Well understood
• Cholera first recognized organism
• Spread by poor sanitation, diarrheal illnesses
• Managed by centralized water systems, sanitation
OPPP’S
“Opportunistic premise plumbing pathogens”

Saprozoic organisms

• Grow within *engineered* water systems
• Less well understood
• Not human-to-human spread
SAPROZOIC ORGANISMS

• Most recognized health-related organisms

• Non-tuberculous mycobacteria
  • Legionella
  • Pseudomonas

• Aspergillus
SAPROZOOIC ORGANISMS

• Grow within biofilms and sediments, *not freely*

• Cannot be controlled by water treatment alone prior to entry into the water distribution and other engineered water systems

• May be viruses, bacteria, fungi and protozoal diseases

• Legionella grows *within* free-living protozoa that reside in the biofilm

• Not all such organisms are pathogenic – “nature”

• **Need to understand biofilms to prevail**
BIOFILM

• The slimy film that coats all (non-copper) pipes
• All water mains, pipes leading to the home and in the home have them
• Amoebae live there as well and NTM live in them
• All but impossible to eliminate

BTW: Plastic rather than copper pipes proposed as a reason for uptick in NTM from showers, etc.
BIOFILM AND NTM

M. abscessus less adherent than M. avium and M. intracellulare on surfaces
THE LARGER ‘NON-PERSONAL” ENVIRONMENT

• May have *more* influence than the water at home!

• Harder *still* to control/ influence

• Likely explains differences in geographic distribution of M. avium vs. M. kansasii, etc.
# Relative Risk of Clusters of Pulmonary NTM Among Medicare Beneficiaries

## High Risk
- Highlands, FL 1.9
- Santa Barbara, CA 2.0
- New York, NY 2.7
- Kalawao, HI 3.7
- Plaquemines, LA 6.5

## Low Risk
- Washington, RI 0.5
- Iosco, MI 0.4
- Roane, WV 0.4
EVAPOTRANSPIRATION

“The process by which water is transferred from the land to the atmosphere by evaporation from the soil and other surfaces and by transpiration from plants”
NTM CLUSTER ANALYSIS

• Proportion of area as surface water
• Mean daily “evapotranspiration”

• However the overall risk is still very low

• Therefore both environmental AND host susceptibility factors must be considered in identifying risk factors for PNTM disease
NIH 2012 – Adjemian, continued

ASIAN-PACIFIC > WHITES

• 228 VS. 116/ 100,000

WESTERN STATES > EASTERN

• 149 VS 131

WOMEN > MEN

• 1.4 TO 1.0

Within the same environment, intrinsic factors are operative as well
SAPROZOIC ORGANISMS

INDOOR CONTROL MEASURES

• Central water reservoirs
• Regional water distribution systems
• Individual homes
• Public spaces
NTM HABITATS

• NATURAL WATERS
• DRINKING WATER
• HOUSEHOLDS
• AEROSOLS
  • Shower heads and water taps
• WATER FILTERS
• ROOM HUMIDIFIERS
• SOILS
• DUSTS
• BIOFILM FEATURE KEY IN HUMAN WATER
IMPEDIMENTS TO FREEING THE ENVIRONMENT OF NTM

NTM RESISTANT TO TEMPERATURES ACHIEVED IN HOT WATER HEATERS

MORE HEAT RESISTANT THAN LEGIONELLA PNEUMOPHILA

WATER HEATER @

- 50C (122F): 50 HOURS TO REDUCE 1000 NTM ORGANISMS/ml TO 1 ORGANISM
- 55C (131F) 2.7 HOURS
- 60C (144F) 12 MINUTES
IMPEDIMENTS TO FREEING THE ENVIRONMENT OF NTM

LIPID-RICH OUTER MEMBRANE

- Hydrophobic (water repelling) cell surface
- On bubble/ aerosol surfaces not freely in water
- Surface attachment/ biofilm formation
- Impermeable to hydrophilic (water attracting) nutrients
- Resistant to disinfectants
- Resistant to antibiotics
- Slow growth
NTM ERADICATION

The harder we try to eradicate NTM, the more we select for them as we succeed in eradicating competing organisms, allowing NTM to flourish.
NTM “AVOIDANCE”
INDIVIDUAL EXPOSURES TO POTENTIAL SOURCES OF NTM AND THEIR ASSOCIATION WITH INFECTION

• Very few individual behaviors associated with incident NTM infection

• Strong association of atmospheric water content within a geographic area

Only individual behaviors:
• Indoor swimming
• Living in a single family residence
• Reporting rusty pipes from household plumbing
NTM “AVOIDANCE”

- No soil-exposure associated infection
- Non-CF studies: Florida 2006 study found that 6 or more years of soil-related work is associated with PNTM
- 2012 Winthrop study-Pacific NW states- only individual activity association is using a spray bottle to spray plants
- NO association with indoor swimming pools
CONCLUSIONS FOR NOW

• Environmental AND host factors
• Water and water vapor involved
• Aerosol
• Biofilm

_Uncertain which individual exposure(s) and behaviors are involved_
ENVIRONMENT OR HOST?

CONCLUSIONS

• FAVOR A “SUSCEPTIBLE PERSONS” MODEL OF MAC DISEASE ACQUISITION

• HOST FACTORS OUTWEIGH “BEHAVIORAL FACTORS”

• BODY MORPHOTYPE CONFIRMED – BACK TO BASICS!
AEROSOL-GENERATING ACTIVITIES ARE NOT UNIVERSALLY ACCEPTED AS CAUSAL IN ACQUISITION OF MAC INFECTION IN HIV-NEGATIVE POPULATION
CONCLUSIONS FOR NOVEMBER 2016

TOO EARLY TO DRAW BROAD CONCLUSIONS REGARDING RISK OF SHOWERING OR OTHER WATER EXPOSURE IN PATIENTS WITH NTM LUNG DISEASE AND BRONCHIECTASIS

Aksamit, Philley and Griffith, 2013
CONCLUSIONS FOR NOVEMBER 2016

TWO HIT HYPOTHESIS

Environmental

- Organism virulence
- Organism exposure burden
  - Environment – Micro and Macro
  - Ingestion/ aspiration
  - Altering the microbiome

Genetic

- Single gene
- Polygenic
THANK YOU FOR LISTENING