NON-TUBERCULOUS MYCOBACTERIAL INFECTION

EPIDEMIOLOGY & EVALUATION

Pulmonary disease
Non-HIV Population

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GOALS OF TALK

Epidemiology: The branch of medicine that deals with the incidence, distribution, and possible control of diseases

• Updates re epidemiology of the disease
  
  Many of you know much of this, but...

• Understand why epidemiology is important in understanding the disease

• Understand why epidemiology is important in evaluating the individual patient

• Gain perspective on how the host factors are the pivotal factors in acquiring the infection
EVALUATION

• Outline current evaluation *algorithm*
  – Often *multifactorial*
  – Emphasize importance of *systematic* evaluation

• Evaluate the *organism*

• Evaluate the *patient*

• Implications of findings

• Implications for management

As always, a lot to cover!
EPIDEMIOLOGY: PREVALENCE DATA

- Adjemian, Olivier, Seitz, Holland, Prevots, NIH. 2012
- Purpose: Assess prevalence of PNTM
- Medicare claims 1997-2007 – 5%
- Age 65+
- Annual prevalence rose from 20/100,000 to 47/100,000
- 8.2% per year increase
- Women 1.4 more likely than men to be PNTM case than men
PREVALENCE: POPULATION-BASED
Henkle, Winthrop, et al. 2015

- Contacted all labs in Oregon performing mycobacterial cultures on all-age Oregon residents
- 2007-2012
- Defined “cases” of PNTM “disease” as those meeting ATS criteria of 2 or more positive cultures or one BAL specimen (more precise)
- Median age was 69 years (0.9-97)
- Female to male 56:44
- Under age 60 more likely male
- Incidence increased with age
- Prevalence increased slightly over interval (not significant)
- MAC 86%. M.abscessus/ chelonae 6%
PREVALENCE: FIVE STATES 2008-2013
Donohue et al. 2-16

• Studied distribution of patients with at least **ONE** positive culture
• 2008-2013
• Maryland, Mississippi, Maryland, Wisconsin, Ohio
• Prevalence *rose* **8.7 to 13.9** per 100,000 over that five year period
• **Mississippi**: Cases greatest ages **80+**
• **Wisconsin**: Cases greatest ages **60-69**

Proportion of NTM isolates identified as MAC

- **60 - 70%**
- **>70 - 80%**
- **>80 - 92%**
Significant geographic variation exists in the distribution of NTM species in the US
• M. avium complex much more common in the South
• M. abscessus in the West
• ***Probable significant under-coding of disease based in ICD-9 coding
• Reviewed study above of Ford noting that most patients ran into clinical trouble based on co-morbidities rather than NTM

• Studied country of origin of patients:
  – M. fortuitum increased in Asian-born
  – M. lentiflavum increased in African-born

• Pathology specimens indicate that NTM reside in sub-epithelia of small airways of bronchiectatic airways and biofilms

THUS: Is it possible that individuals harbor organisms far longer than we think AND that they cause bronchiectasis?
Followed 369 patients with respiratory NTM isolates 2005-2006

84% MAC

35.1% died within 5 years

*Slight increase in those meeting ATS criteria (> 2 positive cultures): 28.7 vs. 23.4*

Conclusions:

- *Number of positive cultures does not correlate with outcome*, i.e. “cases” do not do worse than non-cases

- Most patients died from causes *other than NTM*
OUTCOMES: RISK FACTORS AND SPECIES
Ford, et al. 2017

- Washington State NTM cultures 1998-2011 examined
- Bronchiectasis most common co-morbidity for NTM isolation
- 72% of 168 followed had one major co-morbidity
- 56 patients met ATS criteria for treatment; 22 treated; 19% abscessus and kansasii

- ***Mortality rate most often from co-morbidities rather than from NTM
If you take care of your overall health, you are likely to do fine!
EPIDEMIOLOGY: LONG-TERM OUTCOMES
Henkle, Winthrop, et al. 2017

• Reviewed in 2014-2015 patients with one or more isolates 2005-2006
• 172 patients studied. M. avium 89% cases and 74% non cases
• 59% had multiple pos. isolates; 4% non-cases became cases
• 54% cases and 9% of baseline non-cases were treated
• Of those alive at 10 years,
  – 89% had persistence of positive CT findings
  – 49% had persistence of positive cultures

Conclusion: It is usually a long-term infection
EPIDEMIOLOGY II

SOURCE OF THE ORGANISM
OPPP’S
Opportunistic premise plumbing pathogens

• NTM are saprozoic organisms
  – Grow within *engineered* water systems
  – Less well understood
  – Not human-to-human spread
BIOFILM

• The slimy film that coats all (non-copper) pipes
• All water mains, pipes leading to the home and in the home have 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
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”
Retrospective chart review 65 children in Florida
21(32.3%) had 2+ positive sputum cultures NTM
3 year follow-up

CF patients who lived within 500 meters of water were 9.4 times more likely to have NTM

Perhaps a new in-between level of water exposure:
Not the ambient climate and not the pipes in your house
M. chimaera isolated from multiple patients who had undergone bypass procedures

Is it possible that non-sterile water used in hospital heating and cooling devices can cause contamination and clinical infection
EPIDEMIOLOGY CONCLUSIONS

• Mycobacteria are from water – biofilm
• Ambient water and home water are both factors
  – Hawaii and Louisiana – “atmospheric”
  – Plumbing – “in your four walls”
  – ****Living near a stream – new level of concern

• There is no true “safe haven from NTM; you just change the relative risk of which organism

• The host factors seem to prevail

• Play your cards right re overall health and you’ll do OK re NTM!
EVALUATION
EVALUATION: THE ORGANISM

- Source of the isolate
  - Sputum
  - Induced sputum
  - Bronchoscopy

- How many isolates?
- How many organisms?
- What are our expected findings? Per geography
  - M.simiae
- What other organisms are isolated? Pseudomonas? Aspergillus?
EVALUATION: THE ORGANISM

• M. avium
  – Count on macrolide sensitivity (clarithromycin/ azithromycin)
  – Test clarithro as same class as azithromycin
  – Other antibiotic (e.g. ethambutol, rifamycins) tests far less reliable
  – Commercial labs less reliable
  – Amikacin can be tested
  – Ethambutol used “anyway”

• When to request sensitivity?
  – Repeat treatment
  – Treatment “failure”
    • Too slow to convert sputum
    • Patient worse
Rapid growers (RGM):

- Separate M. abscessus from chelonei and fortuitum
- Further identify abscessus
- **Inducible** resistance
  - Erythromycin ribosomal methylase gene, *erm*(41) modifies the binding site for macrolides resulting in resistance in presence of macrolide
  - Functional gene present in most *M. abscessus* subspecies *abscessus* and *bolletii*
  - *M. abscessus massiliense* does not possess this gene
EVALUATION: THE ENVIRONMENT

• Water and soil organism
• Agriculture workers
• Hot tubs
• (Steam rooms, room humidifiers, others??

• Problem: It is in everyone’s home
  – Husband and wife
  – Apartment and pool health club
  – Different M. avium subtypes and home sources!!

• Geography
  – Regional – Hawaii, Louisiana vs. desert states
  – Proximity to water
EVALUATION: THE PATIENT

HOST FACTORS LIKELY OUTWEIGHT ALL OTHERS
EVALUATION: THE PATIENT

• Anatomic predisposition
  – Bronchiectasis
    • Location and extent
  – COPD
  – Interstitial lung disease
  – Other lung damage
    • Sarcoidosis
• Immune deficiency
  – Immunoglobulin deficiency
  – Alpha-1-antitrypsin def
  – Cystic fibrosis (younger patients) – subclinical types – sweat test/blood
  – Ciliary dysfunction

  – *Most other genetic abnormalities not clinically relevant*
EVALUATION: THE PATIENT

• Recent additions:

• Swallow dysfunction (Dr. Balou) - *routine*

• Esophageal dysfunction (Dr. Khan) - *routine*

• Vocal cord dysfunction (Dr. Amin) – *per above*

*We are particularly fortunate to have these specialists involved*
EVALUATION: THE PATIENT

• Immune compromise: External factors
• Medications:
  • Immune modifying
  • Need to be specific
    – Prednisone/ systemic steroids-
      • Relative
      • How much?
      • For how long?
    – Biologics/ TNF alpha inhibitors
    – Inhaled/ topical steroids
      • New to the list
      • Relative as well
CONCLUSIONS FOR NOVEMBER 2017

TWO HIT/ MULTI HIT HYPOTHESIS

• Environmental
  – Organism virulence
  – Organism exposure burden

• Genetic
  – Single gene
  – Polygenic
  – Other intrinsic factors
THANK YOU FOR YOUR ATTENTION