Transmission of TB and Cough Aerosols

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Objectives

- To share data on cough aerosols and how it may inform TB infection control and global control
- To introduce emerging data on the dynamic nature of the immune response to early TB infection
- To introduce you to potential new technologies that may have an impact on TB infection control in the future
- To begin a discussion on how these new research data might inform infection control policies

Potential conflicts of interest - 1

- Patent pending on a device to facilitate use of the small membrane filter to improve the sensitivity of AFB microscopy
- Invention disclosure submitted on cough aerosol collection device
- Patent pending on ‘Easy Breathing Medical Mask’
Potential conflicts of interest - 2

- Co-investigator on NIH-NIAID SBIR grant on Single Particle Aerosol Mass Spectroscopy to detect airborne TB

- Site P.I. for study of Arykace, an inhaled liposomal amikacin for nontuberculous mycobacterial infections (Insmed, Inc.)
  - Served on a Medical Advisory Board for Insmed, Inc.

- Serving on a Data Safety Monitoring Board for a clinical trial of an inhaled ciprofloxacin product

Cough Aerosol Sampling System

Cough aerosol cultures positive in 28 of 101 culture confirmed TB cases. Aerosol cultures associated with more salivary sputum (OR 4.4) and lower days to positive (OR 1.17 per day decrease) in liquid culture.

Fennelly KP et al. AJRCCM 2012: 186:450

Variability of Infectious Aerosols in TB

Fennelly KP et al. AJRCCM 2012: 186:450
Cough aerosols predict new TB infection

Jones-Lopez EC et al. AJRCCM 2013: 187: 1007

Increased cellular activity in thoracic lymph nodes in early human LTBI

Figure 1 from Ghesani N et al. Am J Resp Crit Care Med 2014: 189: 748-750

Increased cellular activity in thoracic lymph nodes in early human LTBI

Figure 2. Correlation of PET intensity (SUV) and quantitative IGRA QuantiFERON™ data (TB ag – ntl).

Progression & regression of lesions using PET-CT


Size Distribution of Mtb Cough Aerosols

Fennelly KP et al. AJRCCM 2012; 186:450

Surgical Masks Reduce TB Transmission

Dharmadhikari AS et al. AJRCCM 2012; 185: 1104
Changes in cough aerosols with treatment

Fennelly KP et al. AJRCCM 2004; 169: 604

Possible methods of collecting cough aerosols in the future?

PneumoniaCheck™ invented by Dr. David Ku, Georgia Tech U

Cough samples as a replacement to sputum

Antonino Catanzaro (UCSD), Wael Elmaraachli (UCSD), Patrick Sislian (Deton), and Stephen Chapman (Deton)

- Sample quality affects Dx output
- Patients emit infectious droplets
- Deton’s device collects infectious cough droplets and delivers a ‘diagnostic-ready’ sample
- Proof of concept in CF patients

Device is under development and serves as a low-cost alternative to sputum.
Face Mask Sampling for Viruses


Project BREATHE: Better Respiratory Equipment using Advanced Technologies for Healthcare Employees

The next generation of respirators should:
- Perform their intended functions safely and effectively. (9 recommendations)
- Support, not interfere with, occupational activities. (5 recommendations)
- Be comfortable and tolerable for the duration of wear. (10 recommendations)
- Comply with current standards and guidelines. (4 recommendations)

Intention and Current Status
- Federal interagency effort, led by VA, to bring one or more new respirators to the U.S. healthcare marketplace, designed by and for healthcare workers
- Collaboration between VA, NIOSH and two major respirator manufacturers, 3M and Scott Safety Corporations
- Prototype development complete
- Clinical trial comparing comfort and tolerability begins this Summer, 2014.

Provided by Lew Radonovich, Director, VA National Center for Occupational Health and Infection Control (COHIC)

Preventing TB Transmission

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<tr>
<th>TB patient</th>
<th>Environment</th>
<th>Exposed Susceptibles</th>
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<tbody>
<tr>
<td>Rapid suspicion/diagnosis</td>
<td>Optimal dilution ventilation (&gt; 6 ACH)</td>
<td>Education: avoidance of exposure of HIV-infected or other immunosuppressed persons (DM, ESRD, etc) or genetically susceptible</td>
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<tr>
<td>Appropriate treatment (decrease bacillary load)</td>
<td>Do-crowding</td>
<td>Personal respiratory protection</td>
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<td>Mask on patient (e.g., for transport)</td>
<td>Airborne isolation (negative pressure)</td>
<td>Good nutrition: calories, protein, vitamin D (?)</td>
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<td>Cough suppression</td>
<td>UVGI</td>
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Mucomodulatory Agents?  
Inhaled antibiotics?
Summary

- Cough aerosol cultures are the best predictors of infectiousness.
  - Associated with more salivary sputum and low DTP in sputum culture (and lung function in CF).
  - Probably best surrogate of inhaled dose.
  - Inhaled dose predicts lung pathology in animal models.
- Cough aerosol cultures are associated with interferon gamma response among household contacts (HHCs).
- Interferon gamma responses among a small cohort of HHCs are associated with cellular activity in thoracic lymph nodes.
  - Latent TB is NOT so latent!
- Preventing TB transmission requires addressing TB case factors, environmental factors and exposed host factors.
  - Rapid diagnosis and treatment most important.

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