Overview of Airborne Infections
&
Introduction to the Course

Edward A. Nardell, MD
Associate Professor
Harvard Medical School
Harvard School of Public Health
A word of thanks

Professor Emeritus, Melvin First
Part 1: Overview of Airborne Infections
TB and measles as model airborne infections

- Focus on TB (MDR, XDR-TB), but implications for other infections that are *partially, opportunistically, or conditionally airborne.*
  - Rhinovirus, influenza, adenovirus, SARS, BT agents (smallpox, anthrax), environmental agents (M. bovis, coccidiomycosis, Q-fever, Hanta - not necessarily person to person)
Airborne infections as a building-associated illnesses

- Hospitals, clinics, laboratories
- Other indoor environments
  - Prisons, jails, homeless shelters, residential facilities
  - refugee camps, crowded outdoor environments
  - transportation safety: Airliner, shipboard transmission
Pine Street Inn 1984 TB Outbreak

INH & SM res
Shelter
Transmission
Exogenous Reinfection

UVGI Air Disinfection
Air Filtration
Many other Interventions
TB Resurgence - NYC (1985-92)

TB Case → MDR TB → Shelters, Jails, Hospitals

- Treatment barriers
- Transmission

HIV + 5 - 10% / year
HIV - 5 - 10% / lifetime

Cure 50%
Tuberculosis in New York City—turning the tide

• “Epidemiologic patterns strongly suggest that the decrease in cases resulted from an interruption in the ongoing spread of M. tuberculosis infection, primarily because of better rates of completion of treatment and expanded use of directly observed therapy.

• Another contributing factor may have been efforts to reduce the spread of tuberculosis in institutional settings, such as hospitals, shelters, and jails.”
Importance of Transmission in Tomsk

- Retrospective study of the role of non-adherence and default and the acquisition of multidrug resistance

- Substance abuse was a strong predictor of non-adherence (OR 7.3 (2.89-18.46))
  - But non-adherence NOT associated with MDR-TB

- MDR-TB occurred among adherent patients who had been hospitalized in the course of therapy compared to those treated as out-patients
  - OR 6.34 (1.34 – 29.72) – began treatment in hospital
  - OR 6.26 (1.02 – 38.35) – hospitalized later during treatment
A little history

- Prior to 1935, contact, including direct droplet spread, was considered the only route of contagion (Chapin, Providence, RI).
  - 1910, *Sources and modes of infection*
    - "Bacteriology teaches that former ideas in regard to the manner in which diseases may be airborne are entirely erroneous; that *most* diseases are not likely to be dust-borne, and they are spray-borne for only 2 or 3 feet, a phenomenon which after all resembles contact infection more than it does aerial infection as ordinarily understood."
  
  *he thought TB might possibly be airborne*
TB transmission, c. 1930
Modes of transmission of infectious diseases

- **Environmental sources**
  - **water borne**: giardia, river blindness
  - **airborne**: coccidiomycosis*, histoplasmosis*
  - **soil**: clostridia, hookworm
  - **vector-borne**: malaria, Lyme disease
  - **zoonotic**: bird flu, bovine TB, Q-fever, Lyme disease (deer and tick required)

- **Fomites**
  - Laboratory infections
    - Bacteriology – aerosols, accidents
    - Pathology – autopsy aerosols, puncture wounds
  - Medical waste
Modes of transmission of infectious diseases - continued

- **Human to human transmission**
  - **Sexually transmitted** infections: gc, HIV
  - **Blood-borne**: HIV, hepatitis
  - **Food-borne**: salmonella, hepatitis, E. coli
  - **Close contact**: droplet spread: Staph, strep, pneumococcus, rhinovirus*, influenza*, smallpox*
  - **Airborne**: TB, measles, others*
Airborne infection requirements

- Pathogen must be dispersed as fine particles (1 – 5 um size)
  - Respiratory tract – cough aerosol
  - TB wound – water pik
- Remain suspended in air
- Reach the alveolar level (TB)
  - Resistant upper respiratory tract
- Minute infectious dose (droplet nucleus)
Strobe photo of cough/sneeze
Particle size* & suspension in air

- **Particle size & deposition site**
  - 100 μ
  - 20 μ
  - 10 μ – upper airway
  - 1 - 5 μ – alveolar deposition

- **Time to fall the height of a room**
  - 10 sec
  - 4 min
  - 17 min
  - Suspended indefinitely by room air currents

*NOT organism size*
Droplet vs. Airborne spread

- Transmission within a meter of the source
- Relatively large numbers of organisms in inoculum (small inoculum may be tolerated)
- Access to vulnerable site (mucosal membranes of eye, nose, mouth, trachea, etc.)
- Hand washing may be effective

- Transmission beyond a meter – shared breathing volume
- Relatively small numbers of organisms in inoculum – virulence required
- Access to vulnerable site – alveoli in the case of TB
- Hand washing not effective.
Example: TB Hospital outbreak - recovery room
Particle deposition: upper and lower respiratory tract

TB is an infection of the alveolar macrophage
Chapin doctrine challenged

- 1935, Wells challenged Chapin, arguing that measles was airborne and could be controlled with UVGI
- 1946, APHA: “Conclusive evidence is not available at present that the airborne mode of transmission is predominant for any particular disease”
- 1958-62, Riley’s experimental ward proved TB was airborne
Richard L. Riley & William F. Wells
Wells’ Air Centrifuge, 1931

- “On Airborne Infection, Study II. Droplets and Droplet Nuclei”
  *Instructor, Sanitary Service, HSPH

- In 1931 Wells developed his air centrifuge to sample bacteria from air
Droplet Nuclei Transmission

“An Investigation of the bacterial contamination of the air of textile mills with special reference to the influence of artificial humidification”

  - Harvard School of Public Health
  - In his 1955 text, Airborne Contagion and Air Hygiene, Wells shared credit with Richard Riley (HMS) for, “the basic distinction between infective droplet nuclei and germ laden dust”
Upper room UVGI effect on measles in day schools, (Wells, Am J Hygiene, 35:97-121, 1942)

Figure 1. Measles epidemic in Philadelphia, 1941. Weekly attack rate among susceptibles (home secondaries excluded).
Other, failed experiments:

- Perkins, Bahlke, Silverman, 1947
  - Mexico and Cato-Meridian Schools
    - 97% of children rode the bus to school
    - Wells: “Effective sanitary ventilation in the school does not guarantee adequate air hygiene among school children exposed outside of school”

- MRC, Southall, England, 1954
  - Many opportunities for infection outside of school in crowded urban tenements
Important air disinfection lesson

- Air disinfection can only be effective as a public health intervention if the areas treated are the *principal sites of transmission* in the community.
  - Probably true for TB in health care workers and shelter/prison staff, but less certain for shelter residents who leave the building.
    - *May be less true in high prevalence countries*
  - Unclear for common respiratory viruses
Subsequent NYAS meetings

- **1960: National Academy of Sciences (Miami)**
  - Airborne infections:
    - Psittacosis, Q fever, brucellosis, pneumonic tularemia and plague, mycoses, inhalation anthrax, tuberculosis
    - *Smallpox, measles, and rubella not mentioned*

- **1980: New York Academy of Sciences**
  - Measles predominantly airborne, role of contact unclear
  - Influenza, smallpox, legionella, common colds – probably mixed airborne and droplet spread
Wells/Riley Experimental TB Ward

- Riley RL. What nobody needs to know about airborne infection. (How It Really Happened) AJRCCM 2001; 163:7-8.

Quantitative air sampling for TB
Penthouse, Riley Experimental Ward – Wells GP Exposure Chamber

- Small exp. chamber for rabbits
- guinea pig exposure Chamber
- 35 cages
- 3-4 GP/cage
Interior corridor, Riley Ward

Fig. 2. Photograph of inner corridor of pilot ward.
Fig. 3. Photograph of one of the rooms in the pilot ward.
Infectivity of ward air

63 infectious particles
(120 GPs x 8 cf per day x 730 days)

= 1 infectious particle/11,000 cf

High enough to explain infection rate of nurses
Avg. 30 infectious particles added per day (1.25/hr)
but the laryngeal case generated 60/hr

Other, epidemiologic investigations have estimated 13 - 240/hr
Collaborators:

• MRC
  – Karin Weyer
  – Matsie Mphahlele
  – Kobus Venter
  – Martie van Walt
  – Bernard Fourie

• CSIR
  – Sidney Parsons

• CDC
  – Paul Jensen
  – Charles Wells
  – Paul Arguin

• Mpumalanga Province

• Harvard
  – Edward Nardell
  – Melvin First
  – Ashwin Dharmadhikari

• Other
  – Dave McMurray
  – Randall Basaraba
  – Ian Orme
  – Paul Van Helden

• Funding
  – USAID/CDC
  – MRC
  – Harvard CFAR
  – Brigham & Women’s Hospital
  – NIOSH/NIH RO1
The AIR Facility
Whitbank, Mpumalanga Province
Fate of aerosolized TB

- 10% survive aerosolization
  - of those, 50% (5%) survive 6 hrs. (Loudon)
  - if inhaled, only 0.25 to 50% (2.5%) lodge in the lung
Airborne Infection on a Ship

  - One seaman with a positive TB skin test - not treated
  - 10 months later he became sick, Dx “Virus”
    - 6 mos. later, Dx TB, 5 cm cavity, +++ smear
    - Used to study airborne transmission in a closed environment (ventilation system examined)
  - All crew and officers admitted to hospital for complete exam, all TB tested 6 mos earlier
46/81 infected 56.8%

Compartment 3: 40.5%
Compartment 4: 30.8%
Compartment 5: 28.3%
Compartment 6 & 7: 21.4%

Avg navy rate 8%

Only significant contact between 1 & 2 was common air
Conclusions: Houk study

- No evidence of transmission from fomites
  - dust, sweeping, etc. not a concern
- Transmission in various ship compartments was proportional to fraction of air coming from compartment occupied by source case
  - Occupants did not otherwise have contact
Influenza transmission on an airplane

3/14/77 – Boeing 737

- 53 on board
- Anchorage – Homer – Kodiak, Alaska
- 4.5 hr delay at Homer airport
- 37/53 (72%) developed flu symptoms
- Influenza A by titer or culture
- Source: 21 yo woman with chills, fever and severe cough – sera showed Influenza A
OVERHEAD VIEW

Figure 3. Schematic of a Boeing 737 aircraft.
COUGH!
Cough: Do you think the Centers for Disease Control would let me fly if I were contagious?
RELAX...
I'M JUST A TAMPA BAY DEVIL RAYS FAN.
STAHLER.

SPELL 'TUBERCULOSIS'

P-A-N-I-C

SPELLING BEE

86
Measles transmission in a school – role of ventilation

- E. C. Riley modified the Soper or Reed-Frost model to airborne infection
- Soper: \( C = rI \cdot S \)
- Reed-Frost: \( C = S(1 - e^{-Ir}) \)
  - Where \( r = \frac{pqt}{Q} \)
    - \( p \) = pulm ventilation
    - \( q \) = source strength
    - \( t \) = exposure time
    - \( Q \) = room ventilation rate
Riley tested his model on a measles outbreak that had occurred in 1947 in upstate New York.
Figure 2. Floor plan of the upstate New York elementary school which experienced a measles epidemic in spring, 1974. The main building, constructed in 1961, is shown in bold outline. The main ventilating system (36,000 cfm) was located at F-1. The 1971 addition, lower right, was supplied by a smaller 15,000 cfm ventilating system located at F-2. On the plan, room number appears above and grade below.

Wells-Riley model

- Adapted to multiple generations and various environments
- Results predicted actual infection rates as a function of ventilation
- Used for several TB outbreaks
  - ICU
  - Office building
  - Respiratory protection
  - Airplane exposure
Mechanical Ventilation – theoretical limits of protection

- 27/67 (40%) office workers infected over 30 days
  - 1 secondary case
  - Poor ventilation
- 1st air change removes 63%, 2nd removes 63% of what is left, etc.
- Double ventilation = reduce risk by half, and so on...

Graph:
- 15 cfm/person
- 30 cfm/person
Modeling airplane TB transmission


- Based on an actual outbreak on a Boeing 747, 1 infectious TB case, 3 passengers infected in the immediate vicinity
- Employs the Wells-Riley model
- Assumes a source case as infectious as one who infected 40% of her co-workers in an office outbreak
Four hypothetical scenarios:

#2: occupants even and ventilation also even
Ventilation varies by compartment, source front or back; occupants not evenly distributed

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Q (cfm)</th>
<th>C</th>
<th>t (min)</th>
<th>C (tot)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Class</td>
<td>4400</td>
<td>0.32</td>
<td>420</td>
<td>0.426</td>
</tr>
<tr>
<td>Business</td>
<td>3300</td>
<td>0.085</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Economy</td>
<td>2200</td>
<td>0.017</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Economy</td>
<td>1100</td>
<td>0.003</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For the INDEX CASE:

- Q = 11000 cfm
- q = 0.212 q/m
- S = 400

- p = .353 cfm
- t = 420 min
- C (tot) = 3.35
Conclusions: airplane model

- Risk is least for all if ventilation is proportional to occupants
- Airliners are just one of many congregate settings where TB transmission can occur
- HEPA filtration should be highly effective
Propagation of *Mycobacterium tuberculosis*

**Aerobiology**
- Environmental stresses:
  - Temperature and humidity
  - Oxygen
  - Radiation

**Organism**
- Number
- Viability
- Drug resistance

**Host**
- Resistance

**Pathogenesis**
- Disease
- Infection

**Source**
- Strength

**Environmental Factors**
- Room volume
- Room ventilation

**Take off**

**Landing**

**Treatment**
Airborne Infection - Interventions

Aerobiology
Environmental stresses:
- Temperature and humidity
- Oxygen
- Radiation

Pathogenesis
- Infection
- Disease

Host resistance
- Number
- Viability

Organism
- Drug resistance
- Virulence

Source strength
- Take off
- Landing

Treatment
- Admin. Controls
- Isolation
- Immunization
- Resp Protection
- UVGI
- Dilution

Dilution
- Filtration

Masks on patients
- Patients

Take off Landing
- Isolation
- Treatment of latent infection
Part 2: Introduction to the Course

- **Rationale for the course:**
  - Unprecedented funding for global TB and HIV control (GFATM, PEPFAR, World Bank, Gates Foundation, etc)
  - Few consultants with knowledge and experience with all of the necessary tools to make buildings safer re. airborne infections.
    - Many examples of poorly designed buildings or renovations – contributing to transmission rather than preventing it.
  - **Goal:** to build global capacity in the design and engineering of buildings to prevent airborne infections
Target audience:

- Engineers and architects who can serve as consultants for health departments, NGOs, or in the private sector.
- Other health care professionals with technical expertise (industrial hygienists, infection control practitioners)
- Administrators, physicians, and nurses who utilize design professionals.
What this course is not:

- A general course in the control of TB, other respiratory infections, or BT agents
  - it intentionally focuses disproportionately on **design and engineering** at the expense of administrative controls, respirators, public health, etc
- A substitute for a professional degree in engineering or architecture
Continuing Communication

- Global Health Delivery On Line
  - GHDonline/infection control
    - An on-line community of best practice
    - Free, interactive
    - Resource for documents, including these talks
    - On line discussion
  - Future uses:
    - List consultants
    - Track consultations
    - Share case studies
Interventions

- **Airborne Transmission Control**
  - Administrative controls (includes building and laboratory design)
  - Environmental or engineering controls (includes building design)

- **Conventional air disinfection**
  - Ventilation
    - Natural*, mechanical, and mixed mode ventilation
  - Air filtration – HEPA, ULPA, etc.
  - Biological safety cabinets
  - UV air disinfection (upper room, in duct)

- (Unconventional air disinfection: electrostatic filters, electrostatic ion precipitation, chemical fogs, TEG, etc.)

- Respiratory protection, including fit testing
Building Usage
Population density and distribution as a TB risk factor

Large facility: 1. higher probability of infectious cases
               2. more people exposed

2% risk = 98 exposed

10 Small facilities

Same 2% risk = 18 exposed,
Now 80 protected = 82% risk reduction!!
Other strategies not discussed:

Immunization

- Can be extraordinarily effective
  - smallpox
- But, not always effective
  - TB and influenza
  - Predominant flu strain in a guess
    - Major epidemic like 1918 predicted
    - H1N1 continues to kill and may get worse
    - But, SARS did not come back........
The Daily Agenda

Please take out your copy