Overview: Airborne Infections and Control Strategies

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Part 1: TB and measles as model airborne infections

- Implications for other airborne infections:
  - influenza, smallpox, anthrax
- Implications for transportation safety
  - Airliner, shipboard transmission
- Reducing vulnerability
  - Vaccination
  - Isolation/quarantine
  - Air disinfection and personal respiratory protection
    - Ventilation
    - Air filtration
    - UV air disinfection
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)

Treatment barriers
MDR TB
Transmission

TB Case → Cure 50%

Shelters, Jails, Hospitals
HIV +
HIV -

5 - 10% / year
5 - 10% / lifetime
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

- Poster: "Do not spit. Spitting is dangerous."
- Poster: "Spray or sneeze with a handkerchief."
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Airborne infection requirements

- Pathogen must be aerosolized (1 – 5 um size)
  - Respiratory tract – cough
  - TB wound – water pik
- Remain suspended in air
- Reach the alveolar level (TB)
  - Resistance of 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

Hospital outbreak - recovery room

Prevalence of Tuberculin Reactivity for Patients Present on January 14, 15, or 16

SOURCE: Norton, Stress, Cushion, Weisman, Srigley, J Infect Dis, 1961; 25:216-26
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)*

[Graph showing the effect of UVGI in schools]
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 meetings

- **1960: National Academy of Sciences (Miami)**
  - Airborne infections:
    - Psittacosis, Q fever, brucellosis, pneumatic 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.
Penthouse, Riley Experimental Ward - Wells GP Exposure Chamber

guinea pig exposure Chamber
35 cages
3-4 GP/cage

Small exp. chamber for rabbits

Interior corridor, Riley Ward

Fig. 2. Photograph of inner corridor of 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
  - 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
  - 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

Comparment 3: 40.5%
Comparment 4: 30.8%
Comparment 5: 28.3%
Comparments 6 & 7: 21.4%
Avg navy rate 8%
46/81 infected 56.8%

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

Measles transmission in a school – role of ventilation

- E. C. Riley modified the Soper or Reed-Frost model to airborne infection
- Soper: \( C = rI \)
- Reed-Frost: \( C = S(1 - e^{-t}) \)
  - 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.

Wells-Riley model

- Adapted to multiple generations and multiple 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....

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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

### 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*

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

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

**Organism**
- Number of viable organisms
- Virulence

**Host resistance**

**Pathogenesis**
- Disease
- Infection

**Part 2: Interventions**
- Reducing vulnerability
  - Vaccination
  - Isolation/quarantine
- Air disinfection
  - Ventilation
  - Air filtration
  - UV air disinfection
- Respiratory protection
**Airborne Infection - Interventions**

**Pathogenesis**
- Host resistance
- Isolation
- Treatment
- Disease

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

**Organism**
- Number
- Viability
- Virulence

**Source strength**
- Take off
- Landing

**Treatment**
- Drug resistance
- Administration
- Controls

**Immunization**
- Can be extraordinarily effective
  - Smallpox
- Not always effective
  - TB and influenza
  - Predominant flu strain in a guess
    - Major epidemic like 1918 predicted

**Immunocontrol**
- Dilution
- Filtration
- UVGI

**Masks on patients**
### XDR-TB

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Among 53 XDR TB patients</th>
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<tbody>
<tr>
<td></td>
<td>n (%)</td>
</tr>
<tr>
<td>Prior TB Treatment History (n=47):</td>
<td></td>
</tr>
<tr>
<td>No prior TB treatment</td>
<td>26 (55%)</td>
</tr>
<tr>
<td>Cure or Completed treatment</td>
<td>14 (30%)</td>
</tr>
<tr>
<td>Default or Treatment Failure</td>
<td>7 (15%)</td>
</tr>
<tr>
<td>Prior Hospitalization (n=42):</td>
<td>28 (67%)</td>
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Modeling XDR Transmission  

- Estimate that with no interventions, 1300 XDR cases in Tulega Ferry by the end of 2012.
  - More than 50% nosocomially transmitted
  - 72-96% among HIV infected persons.

- Situation in much of rural Sub-Saharan Africa:
  - Crowded single room 30-40 patient wards
  - 40% beds occupied by HIV-infected patients
  - Restricted budgets for technological interventions

- Also modeled community transmission

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<table>
<thead>
<tr>
<th>Intervention</th>
<th>Est. % XDR averted</th>
</tr>
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<tbody>
<tr>
<td>Community-based treatment and deferred hospitalization</td>
<td>&lt; 10%</td>
</tr>
<tr>
<td>Rapid drug susceptibility assays</td>
<td>2 – 4%</td>
</tr>
<tr>
<td>Involuntary detention (without isolation rooms)</td>
<td>3%</td>
</tr>
<tr>
<td>Improved natural ventilation, Air filtration, UV air disinfection</td>
<td>33%</td>
</tr>
<tr>
<td>Personal protective measures - Respirators and masks – enforced</td>
<td>2% total cases, 1/3 cases in staff</td>
</tr>
<tr>
<td>Voluntary counseling and testing with ARV therapy</td>
<td>1% of admitted patients, 24% in the community.</td>
</tr>
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Modeling XDR Transmission

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<th>Intervention combinations</th>
<th>Est. % XDR averted</th>
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<tr>
<td>Reducing length of stay + enforced use of respirators and masks</td>
<td>28% (21-33%)</td>
</tr>
<tr>
<td>Add natural ventilation</td>
<td>37% (26-40%)</td>
</tr>
<tr>
<td>Add drug susceptibility assay, hospital based VCT with ARV, and separation of patients in 5 bed units</td>
<td>48% (34-50%)</td>
</tr>
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Importance of the Unsuspected TB Case
Arzobispo Loayza Hospital
(Emerg Inf Dis 2001; 7:123-7)

• 250 of 349 pts admitted to on female ward in 1997 were screened for TB
  – sputum
  – CXR
  – history
  – physical exam
Importance of the Unsuspected TB Case - 2
Arzobispo Loayza Hospital
(Emerg Inf Dis 2001; 7:123-7)

• 40 pts (16%) had positive cultures
  – 26/40 (65%) smear positive
  – 13/40 (33%) unsuspected
  – 8/40 (20%) had MDR
    • Incl. 6/8 MDR unsuspected
      – 3/6 were smear positive

Conclusion -
• 13% est. TB prevalence on admission to gen. med. ward in Lima
  • Should be repeated in other hospitals
• 3 in 250 (> 1%) new admissions had UNSUSPECTED smear + MDR TB!

Importance of:
1. improved triage
2. air disinfection in general care areas
Hospital Ventilation and risk of TB in HCWs
Menzies’ Canadian Hospitals Study (Ann Intern Med 2000; 133:779-789)

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<th>Factor</th>
<th>Adj. Odds Ratio (95% CI)</th>
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<tr>
<td>Resp. therapy</td>
<td>6.1 (3.1 – 12.0)</td>
</tr>
<tr>
<td>Nursing</td>
<td>4.3 (2.7 – 6.9)</td>
</tr>
<tr>
<td>Housekeeping*</td>
<td>4.2 (2.3 – 7.6)</td>
</tr>
<tr>
<td>&lt; 2 ACH (non IR)**</td>
<td>3.4 (2.1 – 5.8)</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>3.3 (1.5 – 7.2)</td>
</tr>
<tr>
<td>Mod-high risk Hosps.</td>
<td>2.2 (1.3 – 3.5)</td>
</tr>
<tr>
<td>Low Isolation rm. Vent.</td>
<td>1.0 (0.8 – 1.3)</td>
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Building Usage
Population density and distribution as a TB risk factor

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

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<th>10 Small facilities</th>
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Same 2% risk = 18 exposed, Now 80 protected = 82% risk reduction!!

2% risk = 98 exposed
TB Triage – PIH (Haiti)

Community based TB treatment

Hospitalized patients

General ward
Sm -, HIV +/-

TB Pavilion
Sm+, HIV-

6 isolation rms
SM+ and HIV+

TB Pavilion
• Fenestrated walls
• Louvered windows
• UV lamp
• High ceilings
• Overcrowded
General Medical Ward
• Very crowded
• Sliding window
• Paddle fan – off
• UV lamp in the far corner

Isolation rooms
• 6 rooms off a common corridor
• 1 room with window closed – exhaust fan, UV lamp in the corner,
  • door hard to close due to negative pressure
• 1 room with window open –
  • no negative pressure
• Air from 2nd room sucked into other 5 rooms
New PIH LaColline Hospital
• Open, wide outside corridors
• Decorative grates rather than doors

Isolation rooms now open to outside corridor:
• Similar exhaust fan
  • UV fixture not well placed

Pediatric ward
• Too few windows
• Sliding windows instead of louvered ones
  • Block half the opening
  • Closed in rain
Outdoor waiting areas
• Too few UV fixtures if used at all.

Annual Risk of Infection Among Medical Students of Universidad Peruana Cayetano Heredia in Lima, Peru

• 488 students
• Pos. PPD increased from 3.5% to 45.9% over 7 years
• 6%/yr. avg.
Comparing Medical Student Infection Rates:
Hospital Cayetano and Hospital Loayza

Room Volume Per Bed:
Hospital Cayetano and Hospital Loayza
Natural Ventilation

- Geography specific
- Can provide large ventilation rates
- Low cost
- Optimal for outdoor waiting areas, sputum induction, separating isolation rooms

- Not a panacea
  - Cannot control direction of airflow
- What happens at night, in cooler seasons, etc?
  - Unreliable except in certain geographies
Respiratory protection

Respirators

For health care workers

Surgical masks

For patients – special circumstances

Respirator considerations

• May be the only protection for health care workers in many settings.
  – Mostly for known or suspected cases
  – Cannot wear all day
• Should be fit tested – not difficult
  – Various size respirators needed.
• Expensive – only disposable N-95 or EU equivalent should be used.
  – Can be used as long as structurally intact, but become fomites for other contact spread organisms
  – Better, “clinical” non-disposable respirator needed
  – Problem of what is the standard in the hospital
Respirator collage, ca. 1990’s

Air filtration

- HEPA should retain all respirable particles
- Limitations:
  - Number of ACH possible (noise, drafts, short-circuiting of air) – maybe 10 max
  - Cost of HEPA filters
Upper Room UV Air Disinfection

- Principles:
  - kills airborne organisms in the upper room
    - UV confined to space above people’s heads
  - lower room air disinfection by air mixing
    - with good mixing, 20 or more added equivalent air changes possible
  - Viruses and TB UV susceptible
    - Measles halted in day schools in 1930s
Advantages of Upper Room UV

- Cost relatively low compared to ventilation
- Ideal throughout high-risk areas
  - not just isolation rooms
  - ERs, waiting areas, corridors, shelters, jails
  - may be suitable for developing countries
- No noise or drafts
- Low maintenance

Limitations of Upper Room UV

- Engineering specifications not firmly established - few “experts”
  - ASHRAE and EPRI efforts to develop interim and final guidelines, pending ongoing research
- Dependent on room air mixing
- >70% humidity may decrease efficacy*
- Safe, but precautions necessary
- Efficacy field trials underway
  - no field trials of ventilation, filtration, or respirators
Germicidal UV fixtures (louvered)