Airborne Respiratory Infection in the Workplace: Influenza

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Introduction

- Human influenza: 500,000 deaths /y globally in a "good" year.
- Avian flu (H5N1) has killed ~65 people in several years.
- Three pandemics in 20th century
  - Deaths ranged from ~2 million to 20 million
  - Another pandemic expected eventually
  - H5N1 avian influenza has accumulated several of the mutations needed for a pandemic strain

Outline

- Technical aspects of understanding infection transmission and superspreading.
- What determines whether public health measures work?
- How this applies to influenza.
- Evidence that influenza is primarily airborne transmitted.
- Implications of airborne transmission for public health measures.
- What can be done.

The Measure of Contagiousness

- R_0: Basic reproductive number
  - the expected number of secondary infectious cases generated by an average infectious case in an entirely susceptible population.
  - $R_0 = kbD$
    - k = number of contacts by infectious person per unit time
    - b = probability of transmission per contact
    - D = duration of infectiousness

R: The Effective Reproductive Number

- R is less than R_0 in two circumstances:
  - When only a proportion (c) of the population is susceptible ($R = cR_0$)
    - Infected previously and now immune
    - Vaccinated
  - When quarantine and isolation reduce contact rates.
- When R < 1
  - Each case, on average, produces fewer than 1 additional case.
  - The outbreak ends.

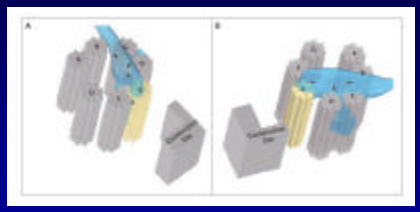
Contagiousness Depends on Agent, Environment, Behavior, and Medication

- $R_0 = kbD$
  - b, the probability of transmission per contact is a property of the agent and its mode of transmission.
  - k, the number of contacts by an infectious person per unit time is a property of the environment and behavior of infected persons.
  - D, the duration of infectious period is a property of the agent and access to medications.

Superspreading

Probable cases of SARS by reported source of infection, Singapore, Feb 25 – Apr 30 (*MMWR*)

Model of the Movement of the Virus-Laden Plume



Yu, I. T.S. et al. N Engl J Med 2004;350:1731-1739

The NEW ENGLAND JOURNAL of MEDICINE

SARS: Toronto Emergency Room

Airborne Transmission: Boeing 737-300 Flight 2 from Hong Kong to Beijing

Olsen, S. J. et. al. N Engl J Med 2003;349:2416-2422

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Superspreading in SARS

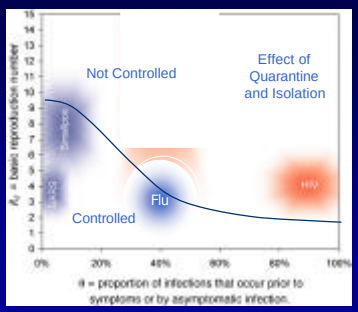
- Hotel M, Hong Kong:
  - Index case infected 10 guests.
- Amoy Gardens, Hong Kong:
  - Index case infected 187 people.
- Singapore:
  - 103 of first 201 probable cases were infected by just 5 source cases.
- March 16, Toronto ER:
  - Woman with early symptoms infected 9 to 13 people while registering husband.
- Airplanes: 6 SARS cases studied:
  - Only one case infected other passengers.
  - That one case infected 22 other passengers.

Key Factors Determine How Well Isolation and Quarantine Work

- R_0: basic reproductive number
- T_g: generation time
  - Mean time interval between infection of one person and infection of the people that person infects
  - R_0 and T_g determine the time scale of an epidemic
- θ: proportion of transmission occurring prior to onset of symptoms or asymptomatically
  - Determines the potential for successful symptom-based public health controls
- Mechanism of transmission not an issue for effectiveness – as long as proper type of isolation used.

Fraser C et al. PNAS 2004; 6146-51

What makes infections controllable?



Fraser, Christophe et al. (2004) Proc. Natl. Acad. Sci. USA 101, 6146-6151

Public Health Implications

- SARS and other infections transmitted only by symptomatic persons (small θ)
  - Can be controlled by isolation of cases.
  - Contact tracing and quarantine add to effectiveness of isolation
  - Feasible because of long generation time (T_g)

Public Health Implications (2)

- Influenza and HIV
  - Must be controlled by immunization or by reducing the contact rate among all persons.
  - HIV:
    - Social Isolation: Safe-sex programs for everyone
    - Large θ = isolation of symptomatic persons cannot work.
  - Influenza:
    - Social Isolation:
      - Cancel all public gatherings, close schools and workplaces
    - Rapid and broad based vaccine deployment
    - Large θ and small T_g = isolation of symptomatic will not work and there is very little time to respond!

Modes of Respiratory Infection Transmission

- *Direct Contact*
  - Inoculation from hands or fomites
- *Large droplet*
  - Particles >10μm land on mucosa of a susceptible individual in close proximity
- *Airborne Transmission*
  - Droplet nuclei <5μm are inhaled & deposited in the respiratory tract, initiating infection.

Evidence for Airborne Transmission of Human Influenza (1)

- Case Reports
  - Airplane passengers: plane grounded 4 hr, 1 source case, 72% passengers became ill within 72 hours. Lower attack rate among persons who got off plan. (Moser MR et al. 1979)
- Human Experimental Infection
  - ID_{50} with aerosols 100x lower than with nose drops.
- Animal models
  - Ferrets: transmission of influenza A from sick to healthy ferrets through straight, S or U-shaped ducts (Andrewes and Glover 1941)
  - Mice: infected via influenza aerosol generator (Edward D et al., 1943)
  - Mice: inverse correlation between air exchange and infection rate regardless of mice proximity, infectious particles found in air (Schulman JL, 1967; Schulman JL, 1968)

Evidence for Airborne Transmission of Human Influenza (2)

- Livermore, CA Veterans Hospital July 1957 – March 1958
  - Upper Room Ultraviolet C
    - Used in 1 of 2 wings of hospital for TB prevention
    - Serology July, November, March
    - Long-term patients with restricted mobility
  - Seroconversion
    - 2% patients in UVC treated wing
    - 19% of patients in untreated wing
    - 18% of staff in both wings
- Suggests that ~80% of influenza is transmitted by fine particle aerosols

McLean, R. L. (1961). Am Rev Respir Dis **83**(2 Part 2): 36-38.

Evidence for Against Airborne Transmission of Human Influenza

- As cited in DHHS Pandemic Influenza Plan (Supplement 4: Infection Control)
  - "Data directly demonstrating large droplet transmission … is indirect and limited."
  - "Contaminated hands and fomites [have] been suggested as contributing factors in some studies."
  - "The epidemiologic pattern observed is generally consistent with spread through close contact."

What Does "Close Contact" Imply?

- Not much.
  - Possibility for direct contact
  - Possibility for direct hit with large droplet

  AND
  - Higher aerosol concentration
  - Less time for decay of infectiousness

Why is H5N1 Poorly Transmissible Between People?

H5N1 avian influenza

- Replicate in pneumocytes and GI tract of fatal human cases (but not airway epithelium)
- Direct contact and droplet transmission
- Not transmitted prior to symptoms (?)

Human strains

- Replicate in airway epithelial cells
- Airborne transmission by droplet nuclei
- Transmission before onset of symptoms in 30% to 50% of cases
- Generation time ≅ 2 days

What Can We Do to Limit a Pandemic If an Influenza Vaccine Is Not Ready When H5N1 Becomes Airborne?

- Depends on stage
  - Limited or rapid person-person spread
  - Cases anywhere or cases locally

What Can We Do to Limit a Pandemic If an Influenza Vaccine Is Not Ready When H5N1 Becomes Airborne?

- Purify the air for everyone
  - Schools, workplaces, hospitals, and other public spaces
  - Requires highly effective air purification (≥ 20 air changes per hour)
  - Upper room germicidal ultraviolet light
  - Requires action well before start of transmission
- Quarantine
  - Require everyone in public to wear surgical mask or N95 respirator
    - Cases anywhere
    - Need research on effectiveness of masks to prevent aerosol generation
  - Cancel all public gatherings and close all schools
    - Cases in region
  - Attempts to quarantine regions or nations from the rest of the world unlikely to be effective

Germicidal UV fixtures (louvered)

Classroom with UV Lights and Mixing Fan

How Can We Protect Healthcare Workers?

- Personal protection during outbreak:
  - Wear an effective N95 respirator
  - Wash Hands
  - Antivirals
    - Health care workers: early treatment (prophylaxis until vaccination in select groups if available – unlikely)
    - General population: early treatment
  - Get vaccinated as soon as available
- Engineering controls
  - Maximize dilution ventilation throughout hospital
  - Install upper room UVC lights in all occupied areas

How Can We Protect the Public?

- Require surgical masks or N95 respirator wear at all public gatherings and on public transport
- Promote respiratory hygiene and handwashing
- Air purification
  - Maximize dilution ventilation
  - Install upper room UVC lights in public gathering places
- Antivirals for early treatment
- Accelerated vaccine development and manufacturing