Outbreaks: Identification, Investigation, Management

Using SARS as a case study

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Learning objectives

1. Describe the epidemiology of SARS
2. Understand how to approach the investigation and control of a communicable disease outbreak
3. Discuss what public health control measures were used to control SARS
4. Understand the difference between isolation and quarantine
5. Appreciate the ecological and human behavioral factors that contributed to the emergence of SARS
6. Understand how practicing physicians fit in to outbreak recognition and control
Types of outbreaks

- Common vehicle or point source
- Person-to-person
- Vectorborne
- Zoonotic
Pneumonia of unknown etiology, Guangdong Province, China

On 10 February 2003 this message was posted on the Program for Monitoring Emerging Diseases web site:

“Have you heard of an epidemic in Guangzhou? An acquaintance of mine from a teacher's chat room lives there and reports that the hospitals there have been closed and people are dying.”

http://www.promedmail.org
Remarks of Dr Yeoh Eng-kiong, Hong Kong Secretary for Health, Welfare and Food.  
10 February 2003

- **Reporter:** Concerning the problem of pneumonia in the Mainland, is there any possibility that the disease can be transmitted to Hong Kong?

- **Dr. Yeoh:** We also have communication channels with the authorities in [Mainland] China and Macau so that if there are any infections that may spread to Hong Kong, we are alerted to this. The Department of Health has already contacted the authorities in Guangdong to understand what infection that is prevalent there and to see whether there is any particular risk of that infection coming to Hong Kong…The message to the citizens here should be that you should not be unduly concerned.

- Things poke along until the week of March 10, then…
It hits the fan

• ~300 cases of atypical pneumonia caused by an unidentified agent in Guangdong Province, China
  – Earliest onset 16 November 2002
• Known clusters in Hanoi, Vietnam, and Hong Kong among health care workers with death of WHO physician
• Cases also reported from Canada, Indonesia, Philippines, Singapore, Thailand
• WHO declares global health emergency on 12 March
The situation - 15 March 2003

- What was happening in Asia
  - Physician with SARS traveled from Guangdong to Hong Kong to Hotel M on 21 February
  - 10 guests on same floor of hotel spread SARS around the world
  - No link with H5N1 influenza

- What was happening in the US and Switzerland?
  - 150 cases reported to WHO through 26 February
  - 2 clusters with 7 cases in Canada
  - Health care worker from Singapore with contact to SARS patient flies from JFK to Germany
  - CDC activates Emergency Operations Center and issues health alert
Learning Objective 1: Describe the epidemiology of SARS

FIGURE 1. Chain of transmission among guests at Hotel M — Hong Kong, 2003

1. Health-care workers.
2. All guests except G and K stayed on the 9th floor of the hotel. Guest G stayed on the 14th floor, and Guest K stayed on the 11th floor.
3. Guests L and M (spouses) were not at Hotel M during the same time as index Guest A but were at the hotel during the same times as Guests G, H, and I, who were ill during this period.
Learning Objective 1: Describe the epidemiology of SARS
Approach to outbreak investigations
(or, OK, so what do you do next?)

- **Confirm diagnosis**
- Report outbreak to public health authorities
- Establish case definition
- Case finding
- Investigate cases for possible common factors
- Test hypothesis in case control studies
- Implement control measures
What’s the diagnosis?

- Atypical pneumonia
- Fever >38°C
- Non-productive cough
- Headache
- Chills, rigors, myalgias
- Progressive hypoxia and respiratory failure in 10-20% of hospitalized patients 8-12 days after onset of symptoms
- Case fatality rate up to 40%
- Usual suspects R/O’ed

This is a disease of unknown etiology, but you need to act in the absence of detailed microbiological knowledge.
Approach to outbreak investigations
(or, OK, so what do you do next?)

- Confirm diagnosis
- *Report the outbreak to public health authorities - not well done before March 2003*
- Establish case definition
- Case finding
- Investigate cases for possible common factors
- Test hypothesis in case control studies
- Implement control measures
Approach to outbreak investigations
(or, OK, so what do you do next?)

- Confirm diagnosis
- Report the outbreak to public health authorities
- *Establish case definition - especially important for disease of unknown etiology*
- Case finding
- Investigate cases for possible common factors
- Test hypothesis in case control studies
- Implement control measures
Initial case definition

- No known pathogen associated with atypical pneumonia
- Case definition:
  - A person presenting after 1 February 2003 with history of fever $>38^\circ$ C AND
  - Cough, shortness of breath OR difficulty breathing AND
    - Close contact within 10 days of onset of symptoms with a person who has been diagnosed with SARS OR
    - History of travel, within 10 days of onset of symptoms, to an area in which there are suspected foci of transmission of SARS
Approach to outbreak investigations (still no diagnosis)

- Confirm diagnosis
- Report outbreak to public health authorities
- Establish case definition
- **Case finding**
- Investigate cases for possible common factors
- Test hypothesis in case control studies
- Implement control measures
How do you find cases?

- Intensive surveillance of hospitals where patients are most likely to go
  - Infection control nurses are often the best source
- Tracing of close contacts
- Absenteeism records (especially of health care workers)
- In many outbreaks surveillance of clinical laboratories for positive tests (not applicable for SARS -- yet)
- **Backbone is physician reporting of cases**
Case finding: finding all the cases that meet the case definition within the temporal and geographic boundaries of the investigation.

Cases can be found by asking physicians to report new cases they diagnose; by reviewing hospital or emergency department admissions records, laboratory results or deaths; or in some instances by examining absenteeism records from schools or workplaces. Additionally for some diseases, persons with whom the patient may have had contact can be traced and located; this practice is referred to as contact tracing or in sexually transmitted disease control as partner notification. When seeking reporting from hospitals, infection control nurses and physicians are often key informants because it is their business to know about every patient in the hospital with a potentially communicable disease in order to prevent nosocomial spread.
Approach to outbreak investigations

- Confirm diagnosis
- Report outbreak to public health authorities
- Establish case definition
- Case finding
  - Investigate cases for possible common factors
- Test hypothesis in case control studies
- Implement control measures
Total SARS cases and % health care workers by country

Learning Objective 2: Approach to investigation and control of an outbreak
Initial epidemiologic investigation

• “Agent” moderately infective
  – Attack rates 10%-60% (2.4-31.3 cases/1000 hours of exposure)
  – Some patients may be “super spreaders”
• Incubation period 2-10 days
• Health care workers at highest risk
  – Highest risk HCWs performed procedures that generated respiratory aerosols and droplets
• Risk factors for death: older age, smoking, underlying pulmonary disease
Notes on the Initial epidemiologic investigation

Investigating Cases for Possible Common Factors: Public health investigators will interview all cases (or occasionally a surrogate, like a parent) to find out what or to whom they may have been exposed before they became ill. The incubation period of the disease (the period between exposure and onset of clinical disease), if known, is particularly helpful in narrowing down the suspected time of exposure.

Typically these interviews are open ended, and cases relate everything they may remember about the time period in which they were exposed. If there is a firm diagnosis and the means of transmission are known, questions can focus on specific types of exposures, for instance, restaurants for food-borne outbreaks. In conducting these interviews pay particular attention to outliers, those who do not appear to fit the epidemiological picture. While they may represent sporadic (non-epidemic) cases, they may also be key to understanding the entire epidemic. For instance, a person with hepatitis A living outside the geographic area under investigation who came to a suspected restaurant and ate one food item once during the entire outbreak period will help narrow down the possibilities of time, place and type of exposure.
Learning Objective 2: Approach to investigation and control of an outbreak

Second wave of SARS, Toronto

FIGURE 2. Number* of reported cases of severe acute respiratory syndrome, by source of infection and date of illness onset — Toronto, Canada, April 15–June 9, 2003

* N = 74.
What does this suggest?

- Nosocomial* transmission
- Droplet or airborne spread
- Infection control is key to limiting transmission

*Nosocomial means acquired in a hospital or health-care facility
Other modes of transmission?

• Cluster of 321 cases at Amoy Gardens Apartments in Hong Kong
• Diarrhea in 66%
• Involved multiple floors and buildings
Other modes of transmission?

• Residents of Block E evacuated and placed in quarantine in remote location
• Possible aerosols of virus from malfunctioning J-traps* and sewer vents in Building E
• Respiratory spread to other buildings

*J-shaped pipes that in this case were in outflow pipes connecting floor drains to the main waste water outflow system. J-traps provide a water seal between the waste water main and the floor drain to keep odors and other gasses from ascending the pipes and entering the bathroom through the drain. Toilets have the same type of trap.
Modes of spread at Amoy Gardens

Cracked sewer vents and J-traps in floor drains could release fecal droplets of SARS-associated Co-V (coronavirus) under conditions of negative pressure when ceiling fan turned on. Spread from Building E most likely airborne.
Meanwhile, back at the laboratory...

- Several groups using DNA primers identified a previously unknown coronavirus as the cause of SARS
- Virus isolated from lung biopsy and nasopharyngeal aspirates of SARS patients
- Serologic and PCR assays rapidly developed
- Organism’s DNA sequenced
SARS Diagnostics
Electron Microscopy

C Humphrey, Pathology Activity Program
Nasopharyngeal and stool shedding of SARS co-V by duration of clinical illness

Peiris: personal communication
Approach to outbreak investigations

- Confirm diagnosis
- Report outbreak to public health authorities
- Establish case definition
- Case finding
- Investigate cases for possible common factors
- Test hypothesis in case control studies
- Implement control measures

Learning Objective 2: Approach to investigation and control of an outbreak
End of learning objective 2
Control measures

• *Case management*
• Contact management
• Hospital/facility infection control
• Community response and quarantine
• Border responses
SARS Containment Strategy: Case Management

Basic Activities

– Home isolation
  • Suitable for providing adequate care
  • Adequate infection control measures possible
– Hospital isolation if medically necessary

Enhanced Activities

– Community-based facility isolation
– Facility must meet patient care and infection control requirements

Case management is isolation. Patients with disease (who are presumably infectious) can be isolated in a suitable location to prevent them from exposing others. Most persons who do not require hospital-level medical care and whose family can provide some degree of infection control precautions can be isolated at home.
Control measures

• Case management
• *Contact management*
• Hospital/facility infection control
• Community response and quarantine
• Border responses
Contact management
(AKA contact tracing)

- Promptly identify, evaluate and monitor close contacts of SARS cases
- Prevent spread from contacts by monitoring for evidence of infection and the need for isolation
- Rapid identification and evaluation of all close contacts of SARS cases is critical to stopping disease transmission
Notes on Contact management.

This refers to *contact tracing*, which is the identification, evaluation and monitoring of those who have been exposed to persons who are infectious. Monitoring could, for instance, be daily checks for febrile illness by a public health worker; those who develop clinical disease or what may be early clinical disease are rapidly isolated. This was done for SARS at Toronto General Hospital, where all medical and hospital staff had to have daily fever checks before being allowed into the facility. While contact tracing is common public health practice (and used extensively in sexually transmitted disease control where exposures are less ephemeral than riding on a bus with someone who is coughing), it had never been attempted on such as vast scale as during the SARS epidemic. Contact management can also include *quarantine*, the sequestration of persons exposed to a disease who have not yet developed clinical illness and are presumably not yet shedding microorganisms. Quarantine can take on multiple forms; persons can be quarantined at home, at their worksites (as was done after an accidental laboratory release of SARS coronavirus at the National Institute for Virology in Beijing in April 2004) or in special quarantine facilities. Persons are usually quarantined for the maximum reported incubation period of the disease and are released if they are clinically well at the end of that period. The risk with large quarantine facilities is that someone will develop disease, and everyone who had not previously been exposed will be exposed. Quarantine was used extensively in Beijing and Hong Kong for SARS, and by the end of the SARS epidemic more than 30,000 people had been quarantined in a tent complex in Beijing for 14 days each, but there were no secondary cases of SARS reported. Most isolation and quarantine are voluntary, but public health officials can mandate them.
Contact Tracing:
Public Health Activities

• Identify all persons exposed to SARS cases
  – Infectious period: onset date - 10 days following symptom resolution

• Prioritize contacts to be monitored if needed, based on:
  – Likelihood of SARS diagnosis in index patient
  – Duration and nature of exposure
  – Contact host factors
Contact management: What do you do when you’ve found them?

Enhanced Activities
– Monitoring with activity restrictions
  • Home quarantine
  • Working quarantine
  • Facility-based quarantine
– Active monitoring for all in quarantine
– May be voluntary or mandatory
– Range of options for optimizing compliance
Definitions

• **Isolation**
  – Separation and restricted movement of *sick* persons with contagious disease
  – Often in a hospital setting
  – Primarily at individual level, may be populations

• **Quarantine**
  – Separation and restricted movement of *well* persons presumed exposed to contagion
  – Often at home, may be designated residential facility
  – Applied at individual or community level

• May be voluntary or mandatory
How well did quarantine work for SARS?

- In Beijing 30,000 persons quarantined in homes or quarantine sites for 14 days (2,521 probable cases of SARS)
- Included persons with direct exposure to SARS patients and febrile travelers from cities with SARS outbreaks
- No secondary transmission in quarantine
- Effective in halting transmission
- Quarantine too broad (no lab confirmation of SARS); contacts of contacts were quarantined
Control measures

- Case management
- Contact management
- Hospital/facility infection control
- Community response and quarantine
- Border responses
Infection control measures

• Nosocomial transmission was a huge multiplier in SARS epidemic
• Controlling respiratory secretions reduces transmission
• Basic infection control measures
  – Encourage patients to alert staff if they are suffering febrile respiratory illness
  – Give patients a surgical mask to wear or tissues to cover their noses and mouths
  – Encourage patients to practice hand hygiene after touching their faces.
Patient isolation

• Separate patients with febrile respiratory illness from other patients in waiting areas
• Use droplet precautions until SARS is ruled out
• Most transmission appears to occur from infectious droplets but airborne transmission can occur
• CDC recommends that SARS patients be managed with airborne PLUS contact precautions
Airborne isolation

- Potential SARS patients should be placed in airborne infection isolation or negative pressure rooms (AIIRs).
- Healthcare workers should wear a fit-tested N95 (or higher) respirator or personal air purifying respirator (PAPR) in addition to gowns, gloves and eye protection.
Patient cohorting

- Some facilities have few (or no) negative pressure rooms.
- Facilities will need to decide at what point they will choose to ‘cohort patients’ by grouping them together into a single ward that lacks negative pressure
  - Focuses SARS-related resources in one area
  - Physically separates SARS patients from others
  - Was an effective strategy in parts of Toronto and Taiwan
Demand for infection control supplies outstripped supply in this hospital in Guangzhou
Control measures

- Case management
- Contact management
- Hospital/facility infection control
- Community response and quarantine
- Border responses
SARS Containment Strategy: Community Response

Basic Activities
– Public information and education
– Promote “respiratory hygiene” and hand washing

Enhanced Activities
– Focused measures to increase ‘social distance,’ ie, greater separation between persons to reduce airborne transmission
– Community-wide measures to increase social distance
– Widespread community quarantine
Ways to increase “effective social distance”

- Implement “snow day” restrictions
  - Close schools, daycare centers, etc.
  - Cancel large gatherings (concerts, theaters)
  - Minimize other exposures (markets, churches, public transit)
- Ask non-essential workers to stay home
- Consider additional measures
  - Distribution of surgical masks?
  - Temperature screening in public venues
  - Scaling back transportation services
Hierarchy of community responses to SARS

- Number of cases/exposed
- Exposure category
  - Known
  - Unknown (unlinked)
- Generations of transmission
- Morbidity and mortality
- Ease/ rapidity of spread
- Movement in / out of community
- Resources for response
- Risk of public panic

No restrictions

Targeted population - specific restrictions

Community-wide measures to increase social distance

Compulsory activity restrictions
  - Curfews on activities
  - Closing of mass transit
  - Closing access routes
  - Closing borders
Control measures

• Case management
• Contact management
• Hospital/facility infection control
• Community response and quarantine
  • *Border responses*
SARS Containment Strategy: Border and travel responses

• Basic Activities
  – Travel advisories and alerts
  – Distribution of health alert notices
  – Responding to ill passengers

• Enhanced Activities
  – Pre-departure and arrival screening
  – Quarantine of travelers from areas with SARS
  – Restriction of non-essential travel
  – Eventually can escalate to border closures
HEALTH ALERT NOTICE
FOR INTERNATIONAL TRAVELERS ARRIVING IN OR RETURNING TO THE USA FROM HONG KONG AND GUANGDONG PROVINCE, PEOPLE’S REPUBLIC OF CHINA, AND HANOI, VIETNAM

TO THE TRAVELER: During your recent travel, you may have been exposed to cases of severe acute respiratory disease syndrome. You should monitor your health for at least 7 days. If you become ill with fever accompanied by cough or difficulty in breathing, you should consult a physician. To help your physician make a diagnosis, tell him or her about your recent travel to these regions and whether you were in contact with someone who had these symptoms. Please save this card and give it to your physician if you become ill.

TO THE PHYSICIAN: The patient presenting this card may have recently traveled to Hong Kong or Guangdong Province in the People’s Republic of China or Hanoi, Vietnam, where cases of atypical pneumonia have been identified. If you suspect atypical pneumonia (also being called severe acute respiratory disease syndrome [SARS]), please contact your city, county, or state health officer (see http://www.cdc.gov or call the CDC Emergency Operations Center 770-488-7100).

For public inquiries, call Centers for Disease Control and Prevention (CDC) hotline: English 888-246-2675, Español 888-246-2857, TTY 866-874-2646.

Distributed to >2 million airline passengers
Learning Objective 3: Public health control measures used to control SARS

Distributed at 13 US-Canada land crossings and the Toronto airport
What finally happened?

- 8,096 cases and 774 deaths (9.6% CFR*) in 29 countries on four continents
- Countries most affected:
  - China 5,327
  - Hong Kong 1,725
  - Taiwan 346
  - Canada 251

*Case fatality rate, or % of sick persons who die
Learning Objective 3: Public health control measures used to control SARS

SARS cases by province
China, 2003
Learning Objective 3: Public health control measures used to control SARS

FIGURE. Number of suspected cases* of severe acute respiratory syndrome, by exposure category and date of illness onset — United States, 2003

- Traveler to high-risk area
- Close contact
- Health-care worker

* N = 166.
† Mainland China, Hong Kong, Singapore, or Hanoi.
Learning Objective 3: Public health control measures used to control SARS

Probable cases of SARS by week of onset
Worldwide* (n=5,910), 1 November 2002 - 10 July 2003

* This graph does not include 2,527 probable cases of SARS (2,521 from Beijing, China), for whom no dates of onset are currently available.
Where did it come from?

- Likely zoonotic transmission
- Epidemiology suggests restaurant workers at increased risk in Guangdong
- Virus detected in Himalayan palm civets (*Paguma larvata*) markets in Guangzhou
- US bans importation of all civet spp. (Family: *Viverridae*) in January 2004
What has happened since the initial outbreak?

- 2 subsequent laboratory outbreaks
  - Singapore, 1 case in September 2003
  - Beijing, 8 cases in April 2004
    - Two researchers at National Institute for Virology developed SARS
    - Secondary transmission to 7 others
    - Institute closed and staff quarantined
- Biosafety level 3 required for handling SARS-associated CoV
- Bats recently found to be natural reservoir of SARS-like CoV
Current WHO case definition

**Suspect case**
- A person presenting after 1 November 2002 with history of high fever (>38 °C) AND cough or breathing difficulty AND ≥1 of the following exposures during the 10 days prior to onset of symptoms:
  - Close contact with a person who is a suspect or probable case of SARS OR
  - History of travel to an area with recent local transmission of SARS OR
  - Residing in an area with recent local transmission of SARS

**Probable case**
- Suspect case with
  - Radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome (RDS) on chest X-ray OR
  - Positive for laboratory test for SARS coronavirus OR
  - Autopsy findings consistent with the pathology of RDS without an identifiable cause

Case definitions become more specific as more is known about the clinical disease and the pathogen
Lessons learned

• SARS can spread rapidly around the world
• Healthcare facilities played central role
• Most cases were spread person-to-person
• Missed cases can lead to many additional cases
  – *Early case diagnosis and detection* can prevent further transmission
How do clinicians fit in?
Preparing for SARS
Key clinical concepts

• Non-specific clinical presentation
  – Difficult to distinguish from other respiratory diseases
• No rapid diagnostic test exists that can reliably detect infection *early* in the illness
• Nearly all laboratory-confirmed cases have x-ray evidence of pneumonia by day 7 of illness
First line of response: The astute clinician

Screen all persons being hospitalized for CXR-confirmed pneumonia:

• In the last 10 days, have you traveled to mainland China, Hong Kong or Taiwan or been in close contact with other ill persons who have?
• “Are you employed as a healthcare worker with direct patient contact?”
• “Do you have close contacts who have been told they have pneumonia?”
If patient hospitalized with pneumonia answers “yes” to at least one of three screening questions:

Providers:

• Notify state or local health department
• Consider SARS testing if no alternative diagnosis found in 72 hours

*Testing for SARS-CoV should only be done in consultation with public health agencies*
The $64,000 question: Will SARS re-emerge?

• Potential sources of re-emergence
  – Animal reservoir
  – Humans with persistent infection
  – Unrecognized transmission in humans
  – Laboratory exposure
• SARS most likely to recur outside U.S.
• Potential for confusion with newly emerging influenza A strains
  – Well-established global surveillance is important to recognition of first case
The late Dr. Carlo Urbani (right), WHO-Hanoi
Credits

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