Overview on Study Design for Outbreak Investigation

A workshop
NPW, Myanmar, Nov 27-Dec 1, 2017
Terms

- **Epidemic** = Outbreak
  (Outbreak -> a sense of emergency, Epidemic -> a sense of wide spreading)

- **Cluster** = an aggregation of cases in a given place & time

- **Pandemic** = The epidemic that spreads over many countries or regions of the world

- **Endemic** = A disease that normally occurs in an area
Terms

- **Index case:** the first disease case brought to the attention of the epidemiologist. The index case is not always the primary case.

- **Primary case:** the first disease case in the population (or family).

- **Secondary cases:** those persons who became infected from contact with the primary case or other previous secondary cases.

- **Outlier:** observation differing so widely from the rest of the data.
Example of Epidemic curve
General Purposes of Outbreak Investigation

- **Control** the current outbreak
- **Prevent** occurrence of future outbreak
- Respond to public or legal concern
- Research for more *knowledge* of the diseases
- *Evaluate* effectiveness of prevention programs
- *Evaluate* effectiveness of the existing surveillance

- Train health professionals
Specific objectives of investigation

1. Verify outbreak and diagnose the agent
2. Characterize magnitude, severity, & distribution
3. Identify population at risk
4. Identify source, mode of transmission, and risk factors
5. Provide appropriate prevention and control measures

An outbreak comes from a change in the way the host, the environment and the agent interact: This interaction needs to be understood to propose recommendations.
The design of Outbreak Investigation primary consideration

- No rule of Thumb
- Context of the outbreak, situation
- Settings
- Descriptive of the outbreak – patterns
- Natural history of diseases
- Ultimate goal for outbreak control and prevention
- Mix approach “One Health” are common
Type of Outbreak Source

• Common source
  • Point
  • Intermittent
  • Continuous

• Propagated source
  = person-to-person transmission

• Mixed source
Common source outbreak

- People are exposed just once, or continuously or intermittently to a harmful source
- Period of exposure may be brief or long
Epidemic curve of point common source outbreak

- **Point source**
  - All cases occur in 1 incubation period
  - Sharp upward
  - More gradual down slope
  - Able to predict exposure period
How to calculate exposure time

Example: typhoid fever -- median incubation period is 15 days
Minimum 3 days, maximum 60 days

(Date of onset

(No. of cases

Exposure time

Median Incubation Period (IP)

Min. IP

(Point source outbreak)
Example of an Epi-Curve for a Common Source Outbreak with Intermittent Exposure

Intermittent exposure often results in an epi-curve with irregular peaks that reflect the timing and the extent of exposure.
Example of an Epi-Curve for a Common Source Outbreak with Continuous Exposure

Continuous exposure will often cause cases to rise gradually (and possibly to plateau, rather than to peak).
Distribution of suspected Botulism cases by time and date of onset, 14-22 March (N=180)

Case detection and outbreak investigation was initiated at 11-12 am.
"Usual" sequence of events

1st case at PCU
Samples taken
Response begins

Days

Opportunity for control
"Ideal" sequence of events

Primary Case Response begins

Potential cases prevented
Exposure, time to infection and disease

Dynamics of infectiousness
- Latent period
- Infectious period
- Non-infectious period
  - Disease
  - Died/Cured

Dynamics of disease
- Incubation period
- Symptomatic period
- Non-diseased

susceptibility
symptoms

Incubation
period

Died/Cured
The study of the Outbreak

• **Case Investigation** (individual case, important for .... Diagnosis, detail of disease manifestation, emerging problem)

• **Cases Series**: collection of cases to describe the problem and descriptive characteristics

• **Survey** (active) - less common

• **Descriptive study** (Describe – pattern of occurrence in Place-Time-Person)

• **Analytic Study** (study the determinants, etiology, risk factor by analysis, testing hypothesis and evidences from laboratory / biological / environmental data)
Epidemiology Study

Very important to obtain and apply knowledge to prevent and control disease/outbreak

- Type: Observation vs. Experiment
- Retrospective or Prospective

<table>
<thead>
<tr>
<th>Retrospective</th>
<th>Cross-sectional</th>
<th>Prospective</th>
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</table>
Case Investigation

• Important in emerging disease (novel infection)
• SARs
• Avian Influenza
• MERS
• Severe community illness
• Hospital Infections, AMR
• Unusual cases
• New Threats : H7N6, SARI
• Animal Disease
Dr. Carlo Urbani (1956-2003)

Dr. Urbani was the first World Health Organization (WHO) officer to identify the outbreak of this new disease, in an American businessman who had been admitted to a hospital in Hanoi. Because of his early detection of SARS, global surveillance was heightened and many new cases have been identified and isolated before they infected hospital staff.
FIGURE 1. Chain of transmission among guests at Hotel M — Hong Kong, 2003

* Health-care workers.
† 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.
‡ 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.
First MERS in Korea and transmission

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<td>40</td>
<td>41</td>
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41명 확진자의 의료기관, 접촉기관, 발병일 현황

6월 5일 기준
Descriptive Study
John Snow investigation of Severe Diarrhea in London 1854

John Snow, M.D.
(1813 -1858)

Diarrhea deaths: 500 in only 10 days
Map: Place – Time – Patient and comparison study
# Descriptive comparison study

<table>
<thead>
<tr>
<th>Water company</th>
<th>Household</th>
<th>HH with cases</th>
<th>Death per 10000 HH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Southwark &amp; Vauxhall</td>
<td>40,046</td>
<td>1,263</td>
<td>315</td>
</tr>
<tr>
<td>Company</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamberth Company</td>
<td>26,107</td>
<td>98</td>
<td>37</td>
</tr>
<tr>
<td>Rest of London</td>
<td>256,423</td>
<td>1,422</td>
<td>59</td>
</tr>
</tbody>
</table>
Descriptive data collection and analysis

Obtain information

Identifying information
Demographic information
Clinical details
Risk factors

Time
Place
Person
Identify & count cases

Obtain information

Analysis of descriptive data

Present cases in
- time
- place
- person
Distribution by Time: Epidemic curve
Number of Hepatitis A cases by date of onset, total of 3 affected districts, 1 Jan 05-17 May 05

<table>
<thead>
<tr>
<th>DATE OF ONSET</th>
<th>NUMBER</th>
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<tbody>
<tr>
<td>2/1/2005-8/1/2005</td>
<td>0</td>
</tr>
<tr>
<td>9/1/2005-15/1/2005</td>
<td>0</td>
</tr>
<tr>
<td>16/1/2005-22/1/2005</td>
<td>0</td>
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<tr>
<td>23/1/2005-29/1/2005</td>
<td>0</td>
</tr>
<tr>
<td>30/1/2005-5/2/2005</td>
<td>0</td>
</tr>
<tr>
<td>6/2/2005-11/2/2005</td>
<td>0</td>
</tr>
<tr>
<td>13/2/2005-19/2/2005</td>
<td>0</td>
</tr>
<tr>
<td>20/2/2005-26/2/2005</td>
<td>0</td>
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<tr>
<td>27/2/2005-5/3/2005</td>
<td>0</td>
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<tr>
<td>13/3/2005-19/3/2005</td>
<td>0</td>
</tr>
<tr>
<td>20/3/2005-26/3/2005</td>
<td>0</td>
</tr>
<tr>
<td>1/5/2005-7/5/2005</td>
<td>0</td>
</tr>
<tr>
<td>8/5/2005-14/5/2005</td>
<td>N=634</td>
</tr>
<tr>
<td>15/5/2005-17/5/2005</td>
<td>0</td>
</tr>
</tbody>
</table>

Source: Panithee Thammawijaya
Distribution by Place: Map of Number of Case Distribution of Hepatitis A morbidity by district

Source: Panithee Thammawijaya
Thai New Year Songkran festival

No. of cases

Date of onset

First three cases

Cluster

3 cases without epidemiological linkage the cluster

Attack rate (per 100,000 pop.)

Source: Panithee Thammawijaya
Distribution by Person: Specific Attack Rate

Hepatitis A Attack Rate by Age Group, total of 3 affected districts, 1 Jan 05-17 May

<table>
<thead>
<tr>
<th>Age group</th>
<th>Attack rate (per 100,000 pop)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
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<tr>
<td>11-20</td>
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<td>21-30</td>
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<td>31-40</td>
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<tr>
<td>41-50</td>
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<tr>
<td>51-60</td>
<td></td>
</tr>
<tr>
<td>over 60</td>
<td></td>
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</tbody>
</table>

Source: Panithee Thammawijaya
Distribution by Person: Occupation and Gender Distribution

Percentage of the Hepatitis A cases by occupation, total of 3 affected districts, 1 Jan 05-17 May 05

Male : Female ratio = 1.6 : 1

Source: Panithee Thammawijaya
Map of Wangnua district:
Distribution of HAV cases and Ice,
1 Jan 05-17 May 05

**Attack rate of**
Subdistrict that have 
Wiangpapao Ice  
= 528

Subdistrict that not have 
Wiangpapao Ice  
= 82  
(Or 6.4 times!!)

Source: Panithee Thammawijaya

- = 5 HAV cases
- = Wiangpapao Ice
- = Wangnua Ice
Case Control
In a botulism outbreak, home-canned bamboo shoots was suspected to be the implicated food.

Odds of eating bamboo shoots was 201 times greater among cases than controls.
Result:
Case-control study in Hepatitis A Outbreak

- Case 70: Control 98

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Adjusted OR*</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ice (Any)</td>
<td>1.51</td>
<td>0.57 - 4.35</td>
</tr>
<tr>
<td>Ice from Wiangpapao</td>
<td>3.55</td>
<td>1.76 - 7.17</td>
</tr>
<tr>
<td>Ka Nom Jeen</td>
<td>0.93</td>
<td>0.44 – 1.95</td>
</tr>
<tr>
<td>Party</td>
<td>1.10</td>
<td>0.54 – 2.30</td>
</tr>
<tr>
<td>Restaurant</td>
<td>1.20</td>
<td>0.62 – 2.32</td>
</tr>
<tr>
<td>Bottle water</td>
<td>1.37</td>
<td>0.70 – 2.65</td>
</tr>
<tr>
<td>Tap water</td>
<td>0.89</td>
<td>0.32 – 2.36</td>
</tr>
</tbody>
</table>

*Multiple logistic regression controlling for age and village of subjects

Source: Panithee Thammawijaya
Special studies, e.g., environmental and laboratory studies

scenario: Contaminated ice from Wiang Pa pao was the most suspected source of the outbreak.
Field testing:
Was the well water fecal contaminated?
Was chlorination adequate?
## Result: Laboratory result of environment

<table>
<thead>
<tr>
<th>Source</th>
<th>Specimen</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wiangpapao Ice factory (10 June 2005)</td>
<td>Water from well</td>
<td>Positive for HAV-RNA (RT-PCR)</td>
</tr>
<tr>
<td>Wiangpapao Ice factory (10 June 2005)</td>
<td>Water from reservoir</td>
<td>Positive for HAV-RNA (RT-PCR)</td>
</tr>
<tr>
<td>A patient’s house (10 June 2005)</td>
<td>Water from well</td>
<td>Positive for HAV-RNA (RT-PCR)</td>
</tr>
<tr>
<td>Wiangkalong drinking water factory (10 June 2005)</td>
<td>Drinking water</td>
<td>Negative for HAV-RNA (RT-PCR)</td>
</tr>
<tr>
<td>Wangnua drinking water factory (10 June 2005)</td>
<td>Drinking water</td>
<td>Negative for HAV-RNA (RT-PCR)</td>
</tr>
<tr>
<td>Juice (10 June 2005)</td>
<td>Juice</td>
<td>Negative for HAV-RNA (RT-PCR)</td>
</tr>
</tbody>
</table>

Source: Panithee T, BOE
Cohort Study
In a shigellosis outbreak, fermented vegetable was suspected to be the implicated food.

A person who ate the fermented vegetable was 6.2 times more likely to be ill than a person who did not eat...
Outbreak Investigation
....in Reality....

Outbreak suspected

Verification

Form Outbreak Investigation and Control Team

Confirm Diagnosis

Site visit

Case definition

Organize Data

Line list

Descriptive Epidemiology

Hypothesis & Testing

Recommendations

Report Publication

Control measures
Thank you

Q/A