Outbreak investigation

• Methods
• Practical reference points

Marta Valenciano
Augusto Pinto
Investigate an outbreak
Why?

• Stop the epidemic
• Prevent new episodes
• Increase our knowledge
• Evaluate the surveillance system
• Put in place a surveillance system
• Learn to teach
Specific objectives of an investigation

Identify:
- Causal agent
- Transmission way
- source
- carrier
- Population at risk
- Exposition causing disease (risk factors)
Retrospective nature of investigation

• epidemic exists since several days, weeks, months.
• Based on the memory of the people
• Data already collected
  – To be or not to be used?

Never to late, but more difficult
Preparation

• Collect preliminary information
  – Available data
  – Consult experts (microbial, vet, entomo …)
  – Prepare a short memo
• Inform the concerned
• Get authorization, TA, trip
• Investigation committee
  – multidisciplinary
  – Define person in charge
  – Define tasks
Preparation « Check List »

• Documentation
  – Benenson
  – Publications
  – Addresses
  – Internet, Promed
  – Resource persons
  – Old questionnaires

• Material
  – Portable (batteries, softwares)
  – Calculator
  – Notebook
  – Camera
  – Maps
  – Lab equipment
Ex: Community epidemic due to S. Typhimurium, Jura, May-June 1997

Context

• Alert: PH medical officer
• 80 cases of salmonellosis in 5 weeks
• *Salmonella* Typhimurium
• Clustered in the South department of Jura
• No connection (a priori) among cases
• Pressure of media, of politicians
• Committee DDASS, Services Veterinaries, Centre National Reference, Inst Santé Publique
Investigation steps
the sequence is not important!

• Descriptive steps
  1) Is it an outbreak?

  2) Confirm the diagnosis:
      Of which diseases we talk?

  3) Define, find, count the cases

  4) Analyse data: When? Where? who?
Investigation steps

• Analyse
  5) Generate an hypothesis(s)
  6) Test the hypothesis(s)
  7) Compare the hypothesis with facts
  8) Conduct complementary studies

• Synthesis and action
  9) Write a report, communicate
  10) Control measure and prevention
1. Confirm the outbreak

• Outbreak
  – n° observed cases > n° expected cases

• Expected cases ??
  – Surveillance data
  – Clinicians, hospital registers
  – Hospital investigation, lab, doctors, schools..

• Be careful of artefacts !!!!
  – Seasonal variation: (diarrhoea)
  – Notification variation: (new surveillance system in place)
  – Diagnostic variation: (new technique)
  – Diagnostic mistake: (« false epidemic")
Nombre de cas de légionellose déclarés par semaine, France, janvier 1996 - août 1997

meeting
2. Confirm diagnosis

- Laboratory
  - serology
  - isolation, serotype, lysotype, etc.
  - toxic agent

- Meet the doctors
- See the patients
- Visit the laboratories

It is not necessary to confirm all the cases
Nombre hebdomadaire d'appendicectomies chez les habitants de l'île de la Désirade, août 1995 - juillet 1996.
(N=226)
3.1. Define a case

- Work instrument to count cases
- Criteria
  - Clinical and/or biological
  - Time, place person
- Sensible: find as much as possible cases
  - Beginning of outbreak, during the active case finding
  - Importance of the outbreak
  - No sick in the group of sick
- Specific
  - Prevent mistakes of classification
- Different levels of confirmation
  - Cases confirmed, probables, suspects
• Suspected cases
  – clinical case definition
  – enough for immediate action

• Confirmed cases
  – stool samples
  – laboratory
  – few cases (10-20)

Do not wait for laboratory results before starting treatment and control activities !!!
Ex: case definition
Outbreak of S. Typhimurium, Jura, May-June 1997

Confirmed case

- **Clinical:**
  - Diarrhoea (> 2 liquid stools/day)
  - or
  - Fever > 38°C (+ one day)
  and

- **Biological:**
  - identification of S. Typhimurium

- **Place, person:**
  - resident in Jura or neighbourhoods

- **Time:**
  - Since 12 May 1997

Probable case

- **Clinical:**
  - Diarrhoea (> 2 stools liq/day)
  - or
  - fever > 38°C (+ one day)
  - and

- **No biology but**
  - contact with a confirmed case

- **place, person:**
  - resident in Jura or neighbourhoods

- **Time:**
  - since 12 May 1997
• **Suspected cases**
  – clinical case definition
  – enough for immediate action

• **Confirmed cases**
  – stool samples
  – laboratory
  – few cases (10-20)

Do not wait for laboratory results before starting treatment and control activities !!!
3.2. Find and count the cases

- Information sources
  - All possible sources (NGOs, local leaders, etc)
  - Hospitals, health centres, laboratories, doctors, nurses
  - schools, camps, settlements
  - Radio, door to door
  - « snow ball »
  - Laboratory

- How many? No strictly all

- Collected information
  - demographics
  - clinical and biological
  - eventual expositions
4. Data description

- Time
- Place
- Persons
4. Data description

Time: epidemic curve

- Cases distribution according the date (hour, week) of onset of signs
- Onset, pick, importance, time, end of epidemic
- Abnormal cases
- Allow to make hypothesis:
  - incubation period, pathogen responsible
  - kind of source, kind of transmission
  - exposition time
- Epidemic evolution
Ex: epidemic curve hepatitis A
Incubation: 2-6 weeks
Ex epidemic curve: cases due to S. Typhimurium
According to week onset symptoms or isolated bacteria,
Jura, May-June 1997.
4. Data description

- Place of living
- Place of exposition (work, foods, journeys, tour)
- Maps (points clouds, attack rate)

Identify areas at risk, population at risk
4. Data description

Persons

• Distribution of cases by age, sex, profession, etc (Numerator)
  – ex: 50 women, 100 men

• Distribution of variables in the population from where cases are coming (Denominator)
  – ex: 1500 women, 1000 men

• Compute attack rate
  – ex: women 50/1500 , men 100/1000

=> Identification of sub-group(s) at risk
**Ex: description “person”**

*Infection S. Typhimurium, attack rate by age group, Jura, May-June 1997*

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>nbr of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>2</td>
</tr>
<tr>
<td>1 - 5</td>
<td>36</td>
</tr>
<tr>
<td>6 - 14</td>
<td>22</td>
</tr>
<tr>
<td>15 - 64</td>
<td>29</td>
</tr>
<tr>
<td>&gt; 65</td>
<td>9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>98</strong></td>
</tr>
</tbody>
</table>
Ex: description “person”

Infection S.Typhimurium, attack rate by age group, Jura, may-June 1997

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>nbr of cases</th>
<th>population</th>
<th>Attack rate / 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>2</td>
<td>522</td>
<td>383</td>
</tr>
<tr>
<td>1 - 5</td>
<td>36</td>
<td>16014</td>
<td>225</td>
</tr>
<tr>
<td>6 - 14</td>
<td>22</td>
<td>30385</td>
<td>72</td>
</tr>
<tr>
<td>15 - 64</td>
<td>29</td>
<td>157989</td>
<td>18</td>
</tr>
<tr>
<td>&gt; 65</td>
<td>9</td>
<td>41948</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>98</td>
<td>246858</td>
<td>40</td>
</tr>
</tbody>
</table>
5. Make hypotheses

Starting from:
- Descriptive information (T,L,P)
- Knowledge of the disease
- Exploratory study on some cases

Explaining:
- The causal agent
- The source
- The way of transmission
- The carrier

DIFFICULT !!!!
**Ex: making hypothesis**

**Infection of *S. Typhimurium***

- Descriptive data:
  - Agent: *S. Typhimurium* lysotype 12 atypical
  - Time, epidemic curve: persistent common source
  - Place: cases clustered in the south of Jura
  - Persons:
    - Attack rate higher among children
    - All ages affected
    - Muslim among the cases
**Ex: making hypothesis**  
**Infection S.Typhimurium may-June 1997**

<table>
<thead>
<tr>
<th>Informations descriptives</th>
<th>Hypothesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.Typhimurium</td>
<td>meat (cow), salami, poultry, milk products, etc</td>
</tr>
<tr>
<td>South of Jura</td>
<td>Regional products, local distribution</td>
</tr>
<tr>
<td>Children more affected</td>
<td>Consumed products (also) by some children</td>
</tr>
<tr>
<td>Muslims among cases</td>
<td>Porck less probable</td>
</tr>
<tr>
<td>Good wheater season</td>
<td>Barbecue, poultry</td>
</tr>
<tr>
<td>Documentation</td>
<td>Epidemic of roasted poultry described</td>
</tr>
</tbody>
</table>
5. Making hypothesis exploratory survey

• Find or formulate an hypothesis
• Interview some cases:
  – Open questionnaire and complete
• Common exposition?

Example Jura:

• Big questionnaire, inclusion of regional products (cheese)
• 17 cases interviewed
**Ex results exploratory survey: Exposition of cases to specific foods, Jura, May - June 1997**

<table>
<thead>
<tr>
<th>Aliments</th>
<th>Ont consommé</th>
<th>Total renseignés</th>
<th>% de cas exposés</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chipolatas</td>
<td>6</td>
<td>15</td>
<td>40</td>
</tr>
<tr>
<td>Poulet cuit</td>
<td>5</td>
<td>17</td>
<td>29</td>
</tr>
<tr>
<td>Poulet cru</td>
<td>7</td>
<td>16</td>
<td>44</td>
</tr>
<tr>
<td>Steack haché</td>
<td>7</td>
<td>17</td>
<td>41</td>
</tr>
<tr>
<td>Porc</td>
<td>9</td>
<td>17</td>
<td>53</td>
</tr>
<tr>
<td>Veau</td>
<td>8</td>
<td>17</td>
<td>47</td>
</tr>
<tr>
<td>Comté</td>
<td>13</td>
<td>17</td>
<td>77</td>
</tr>
<tr>
<td>Fromage A</td>
<td>14</td>
<td>16</td>
<td>88</td>
</tr>
<tr>
<td>Bleu de Gex</td>
<td>6</td>
<td>10</td>
<td>60</td>
</tr>
</tbody>
</table>
6. Testing hypothesis

- Objectives
  - Specific exposition: the carrier and the source
  - Factors facilitating or protective: host, agent, environment

- Survey to identify aetiology:
  - Retrospective cohort
  - Case-control
6. Testing the hypothesis Cohort

- Closed group, banquet, defined group
- For each exposition:
  - Attack rate among the exposed
  - Attack rate among the non exposed
  - Relative risk and CI at 95%
- Specific risk for each exposition
### Ex: Cohort
attack rate of gastroenteritis according to the consumed food, Ile de France, March 98

<table>
<thead>
<tr>
<th>Aliments</th>
<th>Ont consommé</th>
<th>N’ont pas consommé</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>TA%</td>
</tr>
<tr>
<td>Punch</td>
<td>51</td>
<td>92</td>
</tr>
<tr>
<td>Eau bouteille</td>
<td>35</td>
<td>77</td>
</tr>
<tr>
<td>Poulet</td>
<td>135</td>
<td>95</td>
</tr>
<tr>
<td>Riz</td>
<td>130</td>
<td>98</td>
</tr>
<tr>
<td>Sauce</td>
<td>94</td>
<td>96</td>
</tr>
<tr>
<td>Salade de fruits</td>
<td>28</td>
<td>96</td>
</tr>
<tr>
<td>Glaçons</td>
<td>8</td>
<td>88</td>
</tr>
</tbody>
</table>

*TA = Taux d’attaque*
*RR = Risque Relatif*
*IC = Intervalle de Confiance*
6. Testing the hypothesis case-control

• Compare
  – Proportion of exposed among cases
  – Proportion of exposed among the non cases (controls)

• Compute Odds Ratio and IC at 95%

• Select controls
  – “No sick”
  – Susceptible (ex: no immunised)
  – Coming from the same population of cases
  – The same opportunity to be exposed
Exposition of cases and controls to specific foods,
Jura, may-June 1997
7. Compare the hypothesis done with the results

- Compare the results
  - clinical observation
  - biological examinations
  - epidemiological studies
  - statistical tests

- The hypothesis should be:
  - plausible
  - biologically acceptable
  - explain causal agent, source, mode transmission, time of exposition

PERFECT!!!!!
Ex Comparison of hypotheses done with observed facts, Jura, May-June 1997

Cheese A

• Raw milk (plausible)
• Consumed by children (data persons)
• Regional product (data place)
• Collect cheese among the cases (data microbiological)
  – S. Typhimurium identified in 3 cheeses A
  – Other cheeses negatives
8. Complementary studies

- At the same time, and oriented by the epidemiological survey
  - Environmental survey
  - Microbiological survey

- Plan more systematic studies
  - More cases, more controls
  - Dose-effect, facilitating factors..
Ex complementary studies,
epidemic of S. Typhimurium, Jura, May-June, 1997

- Microbiological survey:
  - Food collection among cases
  - Sample collection among cases suppliers
  - Comparison of human specimens and food products

- Survey on the distribution network of cheese A

- Survey among the producers:
  - Veterinary
  - Labour medicine
  - Environmental
Ex Complementary studies,
Epidemic of S. Typhimurium, Jura, may-June,
Survey distribution network

Wholesaler

Cheese dairy
9. Making a report

- Forced to make a synthesis
- Document the event (evaluation, legal)
- Allow to communicate
- Allow to propose recommendations
- Pedagogical tool
10. Take some measure of controls and prevention

• Don’t wait the end of the investigation:
  – General measures at beginning
  – Specific measures according to the results

• Kinds of measures to control:
  – the source (e.g.: chlorination of water)
  – the transmission (e.g.: hygiene measures)
  – the carrier (e.g.: recall a lot of suspected cheese)
  – reduce the susceptibility of host (e.g.: vaccination))

• Example Jura:
  – Personal Hygiene
  – Cook well the meat
  – Recall of the incriminated lot
"The art of epidemiological reasoning is to make some reasonable conclusions starting from imperfect data"

George W. Comstock
« But try to have some data almost perfects... it is easier »

* an epidemiologist *

- For that
  - Multidisciplinary group well coordinated
  - A good description T, P, P
  - Good collection and conservation of samples

- Don’t forget ! (last but not least)
  - Ethical aspects, (animals????)
  - Respect the participants (obtain their agreement)
  - Local debriefing
Outbreak Detection and Response
Outbreak Detection and Response

Opportunity for control