Accessible version can be found here:
https://www.cdc.gov/nceh/hsb/elearning/toi/Mod7/

Toxicological Outbreak Investigation Course

Module Seven (International):
Case Study
Module 6 Objectives

- Apply the steps of an outbreak investigation to a toxicological outbreak case study
- Interpret results of biologic and environmental samples
- Describe the purpose of relevant forms from the Toxicological Investigation Tool Kit
Introduction

- This case study is based on an investigation conducted in Bangladesh in 2009
- Some details have been modified
Step 1: Establish that an outbreak exists

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  - Step 2: Verify the diagnosis
  - Step 3: Prepare for field work
  - Step 4: Construct a working case definition
  - Step 5: Find cases systematically and record information
  - Step 6: Perform descriptive epidemiology
  - Step 7: Develop hypotheses
  - Step 8: Evaluate the hypotheses
  - Step 9: Refine hypotheses and perform additional studies
  - Step 10: Reconcile with lab data
  - Step 11: Implement control and prevention measures
  - Step 12: Initiate or maintain surveillance measures
  - Step 13: Communicate findings
The Call

- In April, a doctor at a rural hospital contacts the Ministry of Health
- That month, he had seen 11 children in the hospital with sudden illness; 3 had died
  - Symptoms included difficulty breathing, frothy oral discharge, and loss of consciousness
  - The children were aged 7 months to 10 years
  - The children all resided in a rural farming village
The Ministry of Health speaks with the local doctors and learns more information.

- Several calves and puppies in the region had become suddenly ill and died around the same time that the children had become ill.
- A similar group of illnesses occurred at this time last year.
- Last year, laboratory tests were negative for influenza, Japanese encephalitis, and Nipah virus.
The Ministry of Health decides that this is an outbreak
  - They decide to investigate to find the cause of the outbreak and address public concerns

Your team gets called into action
Step 2: Verify the diagnosis
Toxicological Outbreak

The Ministry of Health realizes this might be a toxicological outbreak, because it meets these criteria:

- Prior tests for an infectious disease were negative
- Fever has not been mentioned as a prevailing symptom
- Illness seemed to have a rapid onset
- So far, all reported cases had similar symptoms
- There were concurrent animal illnesses reported

What is the most important thing to do when learning an outbreak might have been caused by a toxic agent?
Toxicological Outbreak (cont.)

The Ministry of Health realizes this might be a toxicological outbreak, because it meets these criteria:

- Prior tests for an infectious disease were negative
- Fever has not been mentioned as a prevailing symptom
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- So far, all reported cases had similar symptoms
- There were concurrent animal illnesses reported

What is the most important thing to do when learning an outbreak might have been caused by a toxic agent?

- Consult with a toxicologist.
- Gather biological samples as early as possible.
Team Consults with Local Toxicology Experts

- The team knows it is important to collect biologic samples as soon as possible
- They contact the district hospital and learn that blood samples have been collected from 7 cases and are now being stored in a freezer
- They ask the district hospital to complete a specimen log to record descriptive information along with the specimens
What information do you want to collect on the specimen log?
What information do you want to collect on the sample log?

- Identifying information (e.g., person’s name)
- Collection date and time
- Sample type (e.g., blood, urine)
- Location where the sample was collected
- Descriptive data (e.g., age, sex)
Step 3: Prepare for field work

- Step 4: Construct a working case definition
- Step 5: Find cases systematically and record information
- Step 6: Perform descriptive epidemiology
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- Step 8: Evaluate the hypotheses
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Investigation Objectives

- The team begins to plan for the field investigation
- They develop four objectives:
  - Determine the extent of the outbreak
  - Describe the illness
  - Identify the etiology
  - Identify the route of exposure
Assemble the Team

They also assemble a team:

- Toxicologist
- Laboratorian
- Epidemiologist
- Anthropologist
Step 4: Construct a working case definition
The team speaks with the clinician who saw the patients and reported the most common symptoms:
- Difficulty breathing
- Excessive sweating
- Frothy oral discharge
- Loss of consciousness
- Convulsions/fits
- Urinary incontinence
- Vomiting
- Weakness in arms or legs
Case Definition

Develop a working case definition.

Hint: Consider what, who, where, when
Case Definition Developed by Team

- Any two of the following symptoms occurring on the same day:
  - Difficulty breathing
  - Excessive sweating
  - Frothy oral discharge
  - Loss of consciousness
  - Convulsions/fits
  - Urinary incontinence
  - Vomiting
  - Weakness in arms or legs

- Among persons aged 10 years or less
- Residing in Village A
- Occurring on or after March 1

The team decides to require the presence of at least two of the symptoms, to be more specific and reduce the risk of categorizing other sick people as cases.

They decide to go back to March 1st, in case it was occurring sooner but was just missed.
Step 5: Find cases systematically and record information
The team heads to the village to determine the extent of the outbreak.

How would you search for additional cases?
Find Cases Systematically and Record Information (cont.)

- The team searches for additional cases by:
  - Visiting nearby hospitals
  - Contacting public health officials in neighboring districts
  - Asking village leaders and family members for reports of similar illness
- No additional cases are found; it appears the outbreak is not ongoing.
The team constructs a line list to record information about the cases. An excerpt of this line list is shown below:

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Start Date</th>
<th>Cold Skin?</th>
<th>Excessive Sweating?</th>
<th>Outcome</th>
<th>Urine Collected?</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>M</td>
<td>April 2</td>
<td>Yes</td>
<td>Yes</td>
<td>Died</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>April 7</td>
<td>Yes</td>
<td>Yes</td>
<td>Survived</td>
<td>Yes</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>April 8</td>
<td>No</td>
<td>Yes</td>
<td>Survived</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>April 10</td>
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<td>Yes</td>
<td>Survived</td>
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</tr>
<tr>
<td>3</td>
<td>M</td>
<td>April 13</td>
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<td>April 13</td>
<td>Yes</td>
<td>Yes</td>
<td>Survived</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Hypothesis-Generating Interviews

- The team conducts hypothesis-generating interviews with the physician who saw the cases to learn more about the timeline of illness
- The physician recalls three cases in detail, as shown on the following slides
A female aged 2 years was brought to the Emergency Room

According to her parents:

- She was quite healthy
- After breakfast, she suddenly developed weakness in her right leg while she was playing with other children; this forced her to lie down on the ground
- Frothy discharge started coming through her mouth and nose, and she became unconscious; she also had convulsions and severe trouble breathing

Patient #1 died on her way to hospital.
A child aged 3 years was brought to the Emergency Room presenting with severe trouble breathing and frothy discharge through mouth and nose.

The child was semiconscious and gradually became unconscious.

- Pupils were pinpoint and not reacting to light
- Whole body was sweaty, cold, and clammy
- Heart rate and breathing were fast; pulse 179 beats/min, respiratory rate 62 breaths/min, and lungs full of fluid

The patient was provided oxygen and intravenous fluids, and received atropine, antibiotics, and steroids. Patient #2 recovered completely.
Patient #3

- A child about 8 years of age was brought to the Emergency Room at 8.30 am
- The patient presented with severe trouble breathing, frothy discharge through the mouth, and loss of control of bowels
  - Pupils were pinpoint (very small)
- The patient was provided oxygen and intravenous fluids, and received atropine, antibiotics, and steroids

Patient #3 recovered completely.
The team reviews a list of classic toxidromes to see if one of these matches with the clinical picture.

Do any of the toxidromes on the following slides match the clinical picture?
## Toxidrome Excerpt: Page 1 of 3

<table>
<thead>
<tr>
<th>Toxidrome</th>
<th>Signs and Symptoms</th>
<th>Potential Toxic Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioid</strong></td>
<td>Lethargy, miosis, respiratory depression. Can progress to coma, pulmonary edema,</td>
<td>• Opium/snuff</td>
</tr>
<tr>
<td></td>
<td>hypotension, bradycardia</td>
<td>• heroin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Prescription medications:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Codeine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hydro/oxycodone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hydro/oxymorphine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fentanyl</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Desomorphine aka krokodil</td>
</tr>
<tr>
<td><strong>Anticholinergic</strong></td>
<td>Cutaneous flushing, hyperthermia, dry skin, mydriasis, dry mucous membranes,</td>
<td>• Belladona alkaloids</td>
</tr>
<tr>
<td></td>
<td>disorientation, hallucination, seizures, tachycardia, hypertension, urinary</td>
<td>• Jimson Weed/Datura</td>
</tr>
<tr>
<td></td>
<td>retention</td>
<td>• Brugmansia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Diphenhydramine</td>
</tr>
<tr>
<td>Toxidrome</td>
<td>Usual Signs and Symptoms</td>
<td>Potential Toxic Agents</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------------------------------------------</td>
<td>----------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Hallucinogen</td>
<td>Disorientation, hallucination, panic</td>
<td>Peyote, Psilocybin mushrooms, LSD, PCP, Lysergic acid containing plants: morning glory, Hawaiian woodrose</td>
</tr>
<tr>
<td>Sympathomimetic</td>
<td>Tachycardia, hypertension, hyperthermia, diaphoresis, mydriasis, hyperreflexia, anxiety, seizures</td>
<td>Ma Huang (ephedrine), Amphetamines, Cocaine, Khat and other cathinones, Bath salts</td>
</tr>
<tr>
<td>Toxidrome</td>
<td>Signs and Symptoms</td>
<td>Potential Toxic Agent</td>
</tr>
<tr>
<td>-------------------</td>
<td>------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Cholinergic crisis</td>
<td>Salivation, diarrhea, lacrimation, bronchorrhea, diaphoresis, urination Miosis, fasciculations, weakness, bradycardia or tachycardia, hypotension or hypertension, altered mental status, seizures</td>
<td>• Nicotine • Organophosphate insecticides • Carbamate insecticides • Medicinal car bamates (e.g., physostigmine)</td>
</tr>
</tbody>
</table>
Toxidrome

- The team decides that the illness most closely resembles a **cholinergic crisis**
- Based on this, and because the outbreak occurred in a farming region, they narrow their focus to organophosphate and carbamate insecticides
The team interviews local farmers and family members to figure out what insecticides are in the area.

What are two questions you might ask farmers?
The team interviews local farmers and family members to figure out what insecticides are in the area.

**What are questions you might ask farmers?**

- What types of insecticides are used in farming?
- When is the last time those insecticides were applied?
- Where were the insecticides purchased?
- Where are the insecticides stored?
Several farmers report spraying chemicals on their fields to help keep the pests away.

Two insecticides that are reported by multiple farmers include carbofuran and diazinon.
### Hypothesis-Generating Interviews (cont.)

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Purpose</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbofuran</td>
<td>• Rice paddy&lt;br&gt;• Home vegetable gardens</td>
<td>• Purchased in pellet form&lt;br&gt;• Mixed in a large bowl with urea and thrown by hand into wet paddy fields</td>
</tr>
<tr>
<td>Diazinon</td>
<td>• Rice paddy&lt;br&gt;• Home vegetable gardens</td>
<td>• Mixed with urea and spread on paddy field and by hand&lt;br&gt;• Mixed with top soil in vegetable gardens&lt;br&gt;• Also mixed with water and sprayed on rice paddy fields</td>
</tr>
</tbody>
</table>
Step 6: Perform descriptive epidemiology
Descriptive Epidemiology

- Summarize the data you collected during the case finding and hypothesis-generating interviews by...
  - Person
  - Place
  - Time
### Scenario: Attack Rates

<table>
<thead>
<tr>
<th></th>
<th>Cases (n=50)</th>
<th>Total number of children (n=500)</th>
<th>Attack rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1 year</td>
<td>5</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>3 year</td>
<td>22</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>4 years</td>
<td>18</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>8 years</td>
<td>3</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>10 years</td>
<td>2</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>45</td>
<td>250</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>250</td>
<td></td>
</tr>
<tr>
<td><strong>Village</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>2</td>
<td>125</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>38</td>
<td>125</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>8</td>
<td>125</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>2</td>
<td>125</td>
<td></td>
</tr>
</tbody>
</table>

Summarizing by person...

Investigators refer to the line list they created and calculate attack rates...

How do you calculate an attack rate?
### Scenario: Attack Rates (cont.)

<table>
<thead>
<tr>
<th>Age</th>
<th>Cases (n=50)</th>
<th>Total number of children (n=500)</th>
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</tr>
<tr>
<td>10 years</td>
<td>2</td>
<td>100</td>
<td>2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>Cases (n=50)</th>
<th>Total number of children (n=500)</th>
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</tr>
</thead>
<tbody>
<tr>
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<td>45</td>
<td>250</td>
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<td>5</td>
<td>250</td>
<td>2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Village</th>
<th>Cases (n=50)</th>
<th>Total number of children (n=125)</th>
<th>Attack rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2</td>
<td>125</td>
<td>2%</td>
</tr>
<tr>
<td>B</td>
<td>38</td>
<td>125</td>
<td>30%</td>
</tr>
<tr>
<td>C</td>
<td>8</td>
<td>125</td>
<td>6%</td>
</tr>
<tr>
<td>D</td>
<td>2</td>
<td>125</td>
<td>2%</td>
</tr>
</tbody>
</table>

How do you calculate an attack rate?

**Attack rate:**

\[
\frac{\text{# cases with exposure}}{\text{# children with exposure}}\]
The attack rate was highest among...
- 3 and 4 year old children
- Males
- Children who lived in village B

Based on these findings, you might do further informal data collection to determine what these groups had in common.

### Scenario: Attack Rates (cont.)

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<tr>
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<td>2%</td>
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</tbody>
</table>
The team describes symptom frequency:

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold skin</td>
<td>10</td>
<td>91</td>
</tr>
<tr>
<td>Excessive sweating</td>
<td>9</td>
<td>82</td>
</tr>
<tr>
<td>Frothy discharge</td>
<td>9</td>
<td>82</td>
</tr>
<tr>
<td>Weakness in arms or legs</td>
<td>8</td>
<td>73</td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>7</td>
<td>64</td>
</tr>
<tr>
<td>Difficulty breathing</td>
<td>5</td>
<td>45</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5</td>
<td>45</td>
</tr>
<tr>
<td>Convulsions</td>
<td>5</td>
<td>45</td>
</tr>
<tr>
<td>Fever</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>Confusion</td>
<td>3</td>
<td>27</td>
</tr>
</tbody>
</table>
Observations

- The team performs observations in the village to determine possible ways that children could have been exposed to pesticides.
- They note that the village consists of a cluster of houses surrounded by rice paddy and vegetable fields.
Observations (cont.)

- The team follows a small number of children around for the morning and observe what types of activities they perform
- They choose the morning hours because that is when most cases became ill
They draw a map of the village so they can better visualize where cases resided.
Observational Summaries

- Children spend most of their time playing outside, in and around a mud pile.
- Children play unobserved; family members do not pay much attention to what they do.
- Children sometimes eat unripe mangoes that fall on the ground overnight; the mangoes are not washed before eating.
Descriptive Epidemiology

The team constructs an epi curve:

Summarizing by time...
Step 7: Develop hypotheses
The team previously developed a hypothesis that the etiologic agent is carbofuran or diazinon insecticide.

They would like to develop a hypothesis for what exposure caused the outbreak.
What is one hypothesis you might draw from the epi curve?
Develop Hypothesis (cont.)

What is one hypothesis you might draw from the epi curve?

• Based on the epi curve, it does not appear that all children were exposed during a single event
• If that had been the case, we would have expected the cases to have occurred within a shorter range of time
What is one hypothesis you might draw from the epi curve? (cont.)

- Thus, they hypothesize the risk must have been present in the environment over a period of time.
The team hypothesizes that there was not a single exposure that caused the illness, but rather an exposure that occurred multiple times.

Based on their observational summaries, they decide to target their investigation:

- To exposure to mud, or
- To exposure to eating food that has dropped to the ground.
Once you have developed hypotheses, the next step is to conduct a study to evaluate the hypotheses.

**Step 8: Evaluate the hypotheses**
Types of Data Collected

A typical investigation involves collecting:

- Epidemiologic data
- Clinical data
- Laboratory data
The team conducts a case-control study

What would you consider when selecting controls?
The team conducts a case-control study

What would you consider when selecting controls?

- Controls should be as similar as possible to cases
- Because all the cases are children, it might be better to select controls who are children
The team aims to try and enroll 3 controls for every 1 case

- They decide to match based on age

- They need to develop an epidemiologic questionnaire to collect data on potential exposures
Questionnaire Modification

Design a question to ask study participants about exposure to mud
Design a question to ask study participants about exposure to mud

Things to consider:

- In addition to asking about what the cases had been exposed to, they should attempt to quantify how much exposure occurred.
- They should focus these questions on the time period right before the illness occurred.
The team decides to ask these questions about mud:

Did your child play in mud on [date]?

If yes, how many times did your child play in mud on [date]?
Biologic Sample Collection

- Most organophosphate and carbamate insecticides have short half-lives, ranging from hours to days
- The team decides to collect blood samples from controls, in order to serve as a comparison group
Environmental Sample Collection

- The investigators decide to collect mud samples.
- They decide not to collect any samples of food on the ground, because ...

How should they choose where to collect mud samples from? What are some factors they should consider?
Environmental Sample Collection (cont.)

How should they choose where to collect mud samples from? What are some factors they should consider?

- Collect two types of samples:
  1) Samples that seem to be associated with illness (for example, the mangoes that cases ate prior to becoming ill, or the mud that children were playing with before they became ill)
  2) Samples that do not seem to be associated with illness (for example, samples from a different part of the village)
Collect samples based on what cases would have been exposed to

- For example, if children were playing on a mud pile, then it would make more sense to collect samples from the surface of the pile as opposed to digging in and collecting mud from the inside.
Step 9: Refine hypotheses and perform additional studies
Refine Hypotheses and Perform Additional Studies as Needed

- The team collected epidemiologic data from 11 cases and 29 controls
- Because they performed a case-control study, they calculate odds ratios for the exposures
Analytic Epidemiology (2x2 Table)

<table>
<thead>
<tr>
<th>Play in mud?</th>
<th>Case</th>
<th>Control</th>
<th>Total</th>
<th>% Ill</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>9</td>
<td>9</td>
<td>18</td>
<td>50%</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
<td>20</td>
<td>22</td>
<td>9%</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>29</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>% Exposed</td>
<td>82%</td>
<td>31%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

How would you compare the strength of association between exposure and case status?
If there is no association between exposure and disease, then odds ratio will equal 1.0.

The higher the risk ratio or odds ratio, the stronger the association between exposure and disease.
## Analytic Epidemiology (2x2 Table)

<table>
<thead>
<tr>
<th>Play in mud?</th>
<th>Case</th>
<th>Control</th>
<th>Total</th>
<th>% Ill</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>9</td>
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<td>18</td>
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<tr>
<td>No</td>
<td>2</td>
<td>20</td>
<td>22</td>
<td>9%</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>29</td>
<td>40</td>
<td></td>
</tr>
</tbody>
</table>

- % Exposed: 82% | 31%

### Calculate Odds Ratio (OR)

\[
OR = \frac{9 \times 20}{2 \times 9} = 10
\]

Can we conclude that playing in mud caused the outbreak?
Can we conclude that playing in mud caused the outbreak?

- The odds ratio of 10 suggests a strong association between playing in mud and becoming a case.
- However, it is possible there could be a confounding factor.
- It would be strongest if we can detect high levels of insecticide in the mud where children were playing.
Step 10: Reconcile with laboratory data
Reconcile with Laboratory and Environmental Data

The team examines the results of the biologic samples

<table>
<thead>
<tr>
<th></th>
<th>Cases (n=7)</th>
<th>Controls (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carbofuran</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Detected</td>
<td>29%</td>
<td>0%</td>
</tr>
<tr>
<td>Range</td>
<td>9.5 to 1061</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td><strong>Diazinon</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Detected</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Range</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
</tr>
</tbody>
</table>
Serum Results

- Carbofuran has a very short half-life in the body
- The team decides to stratify based on how soon the blood sample was collected after presentation to the hospital
The 2 cases who had samples collected within two hours of presentation to the hospital had detectable levels of carbofuran.

The 7 cases who had samples collected more than 10 hours after presentation to the hospital did not have detectable levels of carbofuran.

<table>
<thead>
<tr>
<th></th>
<th>&lt;2 hours (n=2)</th>
<th>&gt;10 hours (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbofuran</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Detected</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Range</td>
<td>9.5 to 1061</td>
<td>&lt;LOD</td>
</tr>
</tbody>
</table>
Serum Results (cont.)

- These data suggest that carbofuran may be the etiologic agent that caused the illness, because levels are higher in cases than controls.
These data suggest that carbofuran may be the etiologic agent that caused the illness, because levels are higher in cases than non-cases.

There is not much known about how much carbofuran is required to be ingested before it will cause illness.
Serum Results (cont.)

- These data suggest that carbofuran may be the etiologic agent that caused the illness, because levels are higher in cases than non-cases.
- There is not much known about how much carbofuran is required to be ingested before it will cause illness.
- However, from the little data that does exist, it appears that the levels in the biologic samples from the two cases were high enough to cause the toxic syndrome that was seen.
Environmental Sample Results

- The investigators also receive data on the environmental samples that had been collected.
- The table on the next slide shows carbofuran and diazinon levels in various environmental samples.
Levels of Carbofuran and Diazinon in Environmental Samples

<table>
<thead>
<tr>
<th>Type of Sample</th>
<th>Carbofuran (µg/kg)</th>
<th>Diazinon (µg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mango #1</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Mango #2</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Mango #3</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Mango #4</td>
<td>&lt;LOD</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Soil #1</td>
<td>68</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Soil #2</td>
<td>0.8</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Soil #3</td>
<td>417</td>
<td>&lt;LOD</td>
</tr>
<tr>
<td>Soil #4</td>
<td>0.3</td>
<td>&lt;LOD</td>
</tr>
</tbody>
</table>
Team Consults with Toxicologists for Interpretation of Environmental Data

- None of the environmental sample tests results seem to be high enough to have made the children sick
- The highest level detected was 417 $\mu$g/kg
  - This would be safe even if a child had consumed a couple of teaspoons of this amount every day
Levels of Carbofuran in Environmental Samples

What are some of the reasons why the levels were not that high in the environmental samples?
Levels of Carbofuran in Environmental Samples (cont.)

What are some of the reasons why the levels were not that high in the environmental samples?

- Toxic agents are not always distributed evenly throughout media; we do not know if these values are representative of what children were exposed to.
- The carbofuran could have broken down or washed away before these samples were collected.
Conclusions

Given this information, the investigators conclude:

- The etiologic agent was carbofuran, due to...
  - Higher levels in cases compared to controls
  - Levels were higher when collected immediately after illness
- The source of exposure is unknown
- It is possible that there was not a single exposure source, but rather children may have been exposed in different ways, even in the same village
Step 11: Implement control and prevention measures
Implement Control and Prevention Measures

- Cases had stopped occurring prior to the team’s arrival, and no further cases occurred during their investigation.
- It appeared that whatever the source of carbofuran was in the environment, it had likely gone away.
  - Perhaps a recent rainstorm had washed away pesticide residue from the fields.
- Thus, there was not an urgent need to implement control and prevention measures.
Farmers are not likely to stop spraying potentially toxic chemicals on their fields, because not using these chemicals could mean that pests could destroy crops and families would not have enough food to eat.

What are possible control and prevention measures that could be considered?
Control and Prevention Measures (cont.)

What are possible control and prevention measures that could be considered?

- Wash fruits and vegetables before eating them
- Follow instructions for proper use of pesticides; do not apply too much, and wear proper protective equipment
- When a pesticide is applied, keep children away from the area for at least a couple of days
Step 12: Initiate or maintain surveillance measures
The team meets with local public health leaders to discuss whether they should initiate surveillance.

What would be the pros and cons of initiating surveillance?
Step 13: Communicate findings
Communicate Findings

- The team communicates their findings to the local community
- They know the community will want to know why carbofuran was not detected in all cases

Develop some talking points to explain why carbofuran was not detected in all cases
Communicate Findings (cont.)

Develop some talking points to explain why carbofuran was not detected in all cases

- Like all toxic agents, pesticides are metabolized and eventually leave the body
- Not all cases had biologic samples collected immediately upon presentation to the hospital
Communicate Findings (cont.)

Develop some talking points to explain why carbofuran was not detected in all cases (cont.)

- Maybe the particular pesticide that caused illness was extremely toxic, and only a very small amount was needed to make a person sick
- Maybe this level is below the threshold at which the laboratory can detect the pesticide in a sample (below the limit of detection, <LOD)
What questions do you have about the information presented in this module?
Thank you for your participation!