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| **B4.4 Case study** |



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**Investigating an outbreak of an unknown disease in Seewhat, April 2017**

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RRT Advanced Training Package

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# 1. Case study overview

## 1.1 Background

## 1.1 Introduction

Outbreaks and epidemics of infectious and non-infectious diseases are common events in all part of the world, it can be food poisoning in childcare centers or respiratory virus outbreak in home care centers. In most of the countries an outbreak will raise an alert and epidemiologists, public health officers, biologists, sociologists, communication experts and national authorities, when necessary, will take part of the investigation, support implement the appropriate measures to control the outbreak, and communicate to the public to control the outbreak.

In remote settings, the doctor or nurse is often alone managing the patients, the drugs supply, the surveillance reports and when it occurs the outbreak. In those places, a field epidemiologist will join the place together with the Rapid Response Teams. We shall consider remote settings as presenting some unique characteristics such as: frequent lack of capacity for radiological and laboratory investigation, difficulties to ascertain the dates (onset of the event, onset of disease) and obtain precise data, there are biases in patient number ascertainment due to the variability in accessing health care services due to distance or to cost of health care, reluctance vis a vis the authorities. All those factors that need to be taken into consideration before and during conducting the activities of the investigation.

In this case study, we tried to incorporate elements to retrieve the stress, the imprecisions, the difficulties to obtain correct data, so to simulate what are the challenges that the epidemiologist really face in the field and to highlight the most important challenge: drawing conclusion from poor and sparse data to guide the first control measures.

This case study was designed to help the field epidemiologist, the surveillance officer, or even the doctor or nurse alerting about the outbreak, to understand the steps of an investigation, the rational and objectives of each step and how essential those initial steps are to later identify the source of the outbreak and control the outbreak in the first days or weeks after the start, before it becomes bigger.

*Note: this case study is based on a real situation.*

## 1.2 Goal and target

This case study has been developed to illustrate the different steps of an outbreak investigation from the alert phase until the implementation of the public health measures for controlling the outbreak.

This case study is geared to all those who are likely to carry out outbreak investigations in the field, either having a coordination role or as a field epidemiologist, such as RRT member, surveillance officer in the field, healthcare center caregiver, field epidemiologist, Field Epidemiology Training Programme (FETP) fellow, etc.

## 1.3 Learning objectives

At the end of this case study, the trainee will be able to:

1. Identify the different steps of an epidemic investigation
2. Explain the rationality behind every step and how steps are articulated within each other
3. Conduct Time, Person, Place description
4. Draft and discuss hypothesis regarding transmission and origin of the agent causing the outbreak.



## 1.4 Groups composition and group work

* Trainees will work in groups of 4 persons
* Profiles mixed is preferred
* Each group will assign a rapporteur. Rapporteur changes for each of the two sessions, need to appoint 2 rapporteurs.

## 



## 1.5 Resources needed to facilitate the case study

**Resources for facilitators:**

* **B4.4 Case Study Instructor Guide** (this document): a detailed step-by-step guide to facilitate the case study.
* **B4.4b Case Study Presentation:** a PPT presentation to be used for introduction of the case study and questions and debriefing in plenary upon completion of each episode.

**Resources for participants:**

* **B4.4c Case Study Participant Guide:** a guide that includes the information and instructions to be given to participants, as well as questions and reference documents for each episode.

## 1.6 Duration and facilitation steps

The overall duration of this case study can be adapted to the context, and may range between 2.5 to 10 hours, depending on the learning needs of the audience.

As an example, this case study has been delivered over a 2.5-hour session for Master level students, over an eight-hour session in a workshop for WHO Surveillance Officers; over 2 hours at the Health Emergencies in Large Populations course (HELP).

The agenda below describes a 10-hour session for WHO Surveillance Officers.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Questions** | **Activities** | **Setting** | **Duration minutes** | **Action for facilitator** |
| Introduction | Check the classroom expertise in outbreak investigation - Introduce case study objectives, review participants expectations | In plenary | 5 |  |
| Q1. a-b | **Episode 1: The alert**  List questions, supportive activities and recommendations | In plenary | 5 | Distribute Q1 c-d-e |
| Q1 c-d | **Confirm**  Confirm outbreak and investigation needs  First actions | Group work | 25 | Distribute Q2 c |
| Q2 | **Episode 2: Bluetown Hospital**  List tasks of field epidemiologist | Group work | 10 | Distribute Q3 a-b and List of s & s |
| Q3 a-b  Q3 c  Quizz 1 | **Episode 3: The case definition**  What criteria to include?  Develop case definition | Group work | 40 | Distribute Q3 c |
|  | **Debriefing Q1 to Q3** | **In plenary** | **30** |  |
|  | Break |  | 15 | Distribute Q4 |
| Q4  Quizz 2 | **Episode 4: Case finding**  Method to find cases | Group work | 10 | Distribute Q5 + data basis |
| Quizz 3  Q5 a-b | **Episode 5: Describe the outbreak**  Prepare analysis plan and questionnaire  Analyse outbreak data | Group work | 30  40 |  |
|  | **Debriefing Q4 and Q5 a-b** | **In plenary** | **35** |  |
|  | Lunch break |  | 60 |  |
| Q5 c-d | Episode 5 continuing: Interpreting data | Plenary | 30 | Distribute Q6 a-b-c |
| Q6 a-b-c  Q6d | **Episode 6: Generating hypothesis**  What hypothesis do you make regarding the source of the outbreak?  What lab investigations?  What best study method to choose and why?  Interpret study results | Group work | 30  10  10  15  10 | Distribute Q6 d |
| Q7 | **Episode 7: Propose control measures** | Group work | 20 | Distribute Q7 |
| Q8 | **Episode 8: Reassess the situation** | Group work | 20 | Distribute Q8 |
|  | **Episode 9: Conduct further investigation**  What else to do to reach the objective of the investigation? | Group work | 15 | Distribute Q9 |
| Q9 | **Episode 10: Communication**  Prepare a Situation Report | Group work | 30 | Distribute Q10 |
|  | **Debriefing Q7 to Q10** | **In plenary** | **30** |  |
|  | Break |  | 15 |  |
|  | **Epilogue**  **10 steps of outbreak investigation** | In plenary | 10  10 |  |

# 2. Case study



## 2.1 Episode 1: The alert

Total 30 minutes

All together – ice breaking, short interactions: asking the following questions:

1. indicate who has already taken part in an outbreak investigation?

2. What he/she found more difficult? / What should we be insisting on?

### Episode 1- Step 1

Tuesday April 25th, 9.00 AM.

You are the epidemiologist in Treetown the capital of the country Seewhat, population 6 million. Seewhat is experiencing a humanitarian crisis in its territories located in the Northern part of the country where the population is estimated to be around 2 million, mainly nomadic and farmers. The ongoing conflict has lasted for three years with areas under rebels' controls not accessible, displaced population gathering around cities controlled by the government. There is a high malnutrition rate among children throughout the year, recent cholera outbreak and hepatitis E outbreak still going on in one of the main refugee camps hosting 300 000 persons. The climate is tropical, the rainy season has not started yet. Temperature averages are around 30 and 40° Celsius.

You receive the call from your colleague working in the district of Delamare in the north of the country.

He wants to alert you about an abnormal situation:

* The situation is worrisome: A total of 8 deaths have been reported at the district hospital of Bluetown since yesterday evening.
* More patients presenting with the same symptoms are under treatment in the hospital.
* At this time, the doctors do not know what it is.
* Some patients arrived and died on arrival, others arrived OK and died afterwards. They seem to be confused and are complaining about abdominal pain. Some are vomiting.
* The majority of them participated in a funeral ceremony of a religious leader last Friday night.
* Everybody here is afraid of Ebola and the panic is spreading in the community.

**Question 1:**

* Question 1a: In light of this information what are the next questions that you would ask? List them (objective: minimum information for action)
* Question 1b: How can you support the people in the field at that stage? (Confirmation of outbreak)

**Notes for debriefing question 1a and 1b:**

**Answer 1a:**

**Questions about the situation**

**The disease**:

* How many cases reported and among them how many deaths?

We need not only deaths but all cases that have been recognized at that stage

* Are they Children? Adults? Elderly? Male? Females?

Is there an age-group or sex of people more affected? This gives an idea of what disease we can suspect.

* What are the clinical signs and symptoms?

Some symptoms might not be important for the epidemiologist but very important for the clinician who will support the intervention team.

**Epidemiology related questions**

**The origin**:

* Of which disease the deceased person died of and when?

Several hemorrhagic fevers are associated with mourning in some communities; hence the cause of the death can orientate towards a disease. The date of the death is also indicating if there is a relationship with this event.

* Is there a suspected product (food, drink, drugs, other) that circulated during the ceremony that people ate or drank or smoke or manipulated?

Sometimes products produced locally (beer, tea, alcohol with fermentation or not), can be associated with mass intoxication. In that case people rapidly appoint to the product.

* Are there direct links between cases: are there family clusters? Patients without any epidemiological link with the suspected originating event?

In case of infectious disease, this gives indication of a transmission pattern: family cluster indicates transmission via direct contact; airborne if cases occur one after the other; food or waterborne if cases occur the same day.

No link between cases indicates that the disease might be spreading via asymptomatic carrier.

**Risk assessment related questions:**

* How many people attended the funeral?

In the hypothesis that there is a link between the event and the funeral ceremony, this information might give you an estimate of the population at risk of becoming sick in the next days and ultimately helps plan the medical support that is needed.

* From which area are the patients coming from: displaced camp, rural areas, town, remote area with difficult access?

If we are speaking of remote areas the hypothesis that other cases are occurring in the community without being able to reach health facility is high. We might have only the top of the iceberg.

* What is the hospital and laboratory capacity? How many doctors are available? Drugs available?

The first action is to save lives and stop the propagation of the disease. If the community can find supportive care at the hospital, they be more willing to come. Doctors need to be supported.

* Is material to implement infection control available on site? It is very important to make sure the health workers can safely treat the patients without exposing themselves. Capacity to apply basic standard precautions must be checked at that stage.
* What is the local team feeling about the situation? What do you need first?

The people at the field level are those who have the best information, and this should be considered as the most reliable source. Also keep in mind that fear and panic are not good advisors.

**Answer 1b**

**Actions to support people in the field at this stage:**

* Review the epidemiological situation in the area: frequent diseases and seasonality, exposure risks (industries, pesticides, environmental factors (e.g., pollution, etc.).
* Verify the existence of any abnormal trend in disease report and/or mortality during last weeks (in the county, district, country).
* Inform the MOH for them to call the hospitals in the surrounding districts for information and enhance surveillance of unexplained disease eventually related to funeral attendance.
* Prepare population data (see with colleagues in the vaccine department or the census office). Last census data and population growth rate.

**Formulate** r**ecommendations** that can be applied while facing an unknown and severe disease:

* Keep patients isolated from other patients in the hospital
* Organize an isolation sector in the area of the hospital if possible.
* Use Personal Protective Equipment when examining the patients or taking biological samples. If not available apply standard precautions (gloves, mask, disinfection of material used).
* Limit contact of patients with their family to a minimum while providing protection to the family member.
* Implement safe burial procedures (as during the Ebola epidemic).

### Episode 1 - Step 2

April 25h, later on, summary of the situation:

In April 25 a cluster of unexplained health event involving 14 cases with 8 deaths occurred in Bluetown Hospital in Bluetown capital of Delmare district. At that time, according to hospital data, the majority of cases reported having weakness, headache, abdominal pain, vomiting, diarrhea, and mental confusion and only one with a slightly increased body temperature (37,5 ⁰C). This event was preceded by the attendance to a funeral ceremony that started on April 21st and burial on April 22nd, 2017, of an eminent religious leader who died from complications associated with diabetes and hypertension one month ago. The number of people who attended the funeral is estimated to be around 100, they mainly originated from the local community of the district but not only.

The hospital's capacity is 50 beds. There is one doctor, one assistant doctor, four nurses and two midwives. There is an Ebola kit which can cover 50 patients with PPE, drugs, and material for biological sampling. There is no cold chain to store specimen. The laboratory capacity is limited to hemoglobin, white cells count and some biochemical tests.

In the fear of Ebola, the panic is spreading rapidly. Rumors are circulating that there had been poisoning during the wake ceremony, with voluntary target on the visitors because it is believed that the family of the deceased is not affected. Since the radio station is not broadcasting due to technical problems, the intervention of the police to disseminate message to the communities has been required to maintain the population calm.

The team is completely overwhelmed and is treating each case as if it was Ebola, taking oral swab and blood for immediate biochemical and hematological tests.

No information available on age and sex, suspected product, epidemiological link between cases at that stage.

**Question 1c:**

* Is it an outbreak? Justify your answer.

**Question 1d:**

* Is an investigation necessary?

**Quiz 1:**

What are you recommending as immediate actions? Set 3 key priorities among the following actions:

1. Alert the Ministry of Health
2. Leave the country
3. Alert the health partners in the country
4. Organize a crisis meeting in the capital inviting Delmare team to join
5. Organize a RRT mission to Delmare urgently
6. Provide a list of the laboratory to conduct laboratory investigations.

**Notes for debriefing question 1c, 1d, 1e:**

**Answer 1c**

At that stage it can be called a cluster: abnormal accumulation of cases in time and space. However, nobody expects such a sudden high number of deaths: it is an outbreak.

**Answer 1d**

Criteria for deciding to investigate are:

* Severity of illness
* Communicability
* Potential ongoing health threat
* Need to learn more about agent
* Public and politic concern
* Available resources

**Quiz 1:** correct answers are in bold

1. **Alert the Ministry of Health**
2. Leave the country
3. Alert the health partners in the country
4. Organize a crisis meeting in the capital inviting Delmare team to join
5. **Organize a RRT mission to Delmare urgently**
6. **Provide a list of the laboratory to conduct laboratory investigations.**



## 2.2 Episode 2: Bluetown Hospital

Wednesday 26th April. The hospital is located in Bluetown the capital of Delmare district, a 10-hour drive from Monrovia. According to census 2008, Bluetown has a population of 16,434 inhabitants, with an average household size of 5.1 people. Seafood, including different types of fish, are usually part of the diet of the population. The electricity is basically supplied by private and community generators.

The area of Bluetown is surrounded by mines activities. There is a history of water poisoning linked with water pollution from extractive chemicals a few years ago, however no documentation exists.

You and your team arrive on site on 25th of April very late at night.

The situation is electric: new patients reached the hospital and some of them died on arrival. The community is anxious about the disease Ebola with all the trauma still very much present from the last epidemic. Some patients escaped from the hospital, others refused to be treated and hide somewhere in the area. Rumors regarding the fact that the family of the deceased was not affected are widely circulating and intentional poisoning is suspected. Police had to intervene. There are rumors of cases in the houses hiding, of cousins who attended the funeral that are sick, and of neighbors that were seen vomiting.

From the interview of the national colleagues, you learn that theceremony consisted of the wake with meal, beverage, music and danse which starts in the evening and goes all night with people sleeping on site. The day after is the burial, church ceremony and “Repass” in the afternoon. Everybody who wants to attend the funeral is welcome. It took months for the families to gather enough money to offer a proper funeral to the deceased.

**In the morning of Wednesday 26th**, you receive your first briefing from the doctor who attended the patients:

|  |
| --- |
| *“When the alert of cluster of unexplained deaths was triggered yesterday, we started questioning all the patients or their family. The patient history revealed that all the cases attended the same funeral of religious leader, in Greentea county in Bluetown. Although the number is not specified, estimations are pointing that about 100 people attended the same funeral, some of them coming from other counties like, Little kuru, Marialand, Gedeh and Serrado. A group of people attended the wake, while others attended the burial and/or repass”.* |

**Quiz 2:**

* During the briefing with the doctor, as an epidemiologist, should you wear a PPE?

**Question 2:**

* Assuming that you are in charge of the investigation, list your tasks for the next few hours and indicate you will proceed to achieve them.

**Notes for debriefing question 2:**

**Answer quiz 2:**

Answer quiz 2: no, the epidemiologist does not need to wear a PPE: he/she keeps a distance from the doctor, he/she does not touch patients and keep safe distance (1 meter); there is no exposure to patient fluids nor direct contact with patients.

**Answer question 2:**

1. **Go to the hospital to obtain a good description of the cases.**

If possible, organize data using a questionnaire or a line list to fill directly.

Source of information: the doctor, the patients that are still admitted, the patients’ record (take pictures if the hospital director allows), the hospital registers, the families.

1. **Propose a case definition.**

It is important that everybody participating in the active search looks for the same thing.

1. **Ask for a** map of the district showing Bluetown and Greentea county.
2. **Establish the list of all funeral attendees.**
3. **Initiate the active search of other cases and implement contact tracing of all attendees.**

To complete the information and provide an exhaustive description of the situation. It is even more important here that you were told that patients are escaping the hospital.

Where to look for other cases: in the hospital, days before the alert, in the medical record, in the community.

House by house, following list of attendees, following advice of attendees, hospital personnel.

In that case contact tracing was used to inform the patient of the symptoms, recommend reaching the hospital rapidly and limiting their contacts and movements. No treatment was offered as prophylaxis as no diagnosis was made.



## 2.3 Episode 3: The case definition

The doctor shares with you his notes on patients admitted up to 26th April 2018, and you have to prepare a line list.

*Table: Signs and symptoms of patients admitted from April 23 to 26 in Bluetown hospital.*

|  |  |
| --- | --- |
| Signs and symptoms | Number of cases with signs and symptoms |
| General weakness | 19 |
| Abdominal pain | 15 |
| Headache | 17 |
| Vomiting | 14 |
| Confusion, agitation | 11 |
| Diarrhea | 9 |
| Respiratory signs | 5 |
| Purpura/Ecchymosis | 6 |
| Fever | 1 |
| Chest pain | 5 |

**Question 3a:**

* What are the usual criteria that must be included in an outbreak case definition?

**Question 3b:**

* Propose a case definition for this outbreak.

**Notes for debriefing question 3a and 3b:**

**Answer 3a:**

A case definition is based on clinical criteria and include place and time limits:

* **Clinical criteria:** The most frequently cited clinical signs and symptoms: Weakness, headaches, abdominal pain, vomiting, confusion and diarrhea, death.

Define the study population to include patients susceptible of being exposed. IN case of case-control study, Cases and controls are defined as belonging to that study population

* **Time:** We use two incubation periods to start the active search of cases. Here, assuming the contamination took place at the funeral, the majority of the patients got sick 4 days after the exposure. Two incubation period is 8 days. 23 minus 8 is 15.
* Lately we learned that the first case reported signs on April 21st at 10.00 AM. She participated in the funeral and prepared tea (designating any beverage). She was admitted on April 23rd and died on 25th. Initial diagnosis was high blood pressure. She was secondarily included among the cases and positive in lab test.
* **Place:** Several attendees lived in other counties. The place of living should not be used here. One patient who attended the funeral was recognized in Montserrat county where he lives with his family. Having visited the affected county limits the investigation to cases related to this event.

***Comment:*** *highlight the difficulty of having one case definition, the difference between criteria for case ascertainment and classification of case definition.*

**Answer 3b:**

Case definition adopted:

* **Suspected case**: Any person who presents with at least two symptoms: headache, vomiting, mental confusion, weakness **and/or** any other symptoms,
  + **and** with onset from 15th, April 2017
  + **and** who has been to Greentea County.
* **Probable case:** Any person who presents with at least two symptoms: headache, vomiting, mental confusion, weakness **and/or** any other symptoms **and** has attended a funeral **or** is epi-linked to anyone from the affected communities on April 22-23, 2017.

Other definitions:

* **Contact:** any person who has slept, eaten with, spent time in the same household or room of a case.
* Direct physical contact with a case (exposure to cough, sneeze, or saliva)
* Shared dishes/eating utensils of a case.
* **Attendee:** anyone who attended the funeral Event/s (Wake, Burial, Repast) in Greentea County on the 21-22nd April 2017**.**

Community case definition:

1. Any person who attended the funeral and got sick or any sick people identify sick in the community.
2. Any person who lives in or visited Greentea County who has had headache, hot skin, weakness, vomiting, watery pupu or mental confusion starting from April 10th, 2017.

**Question 3c:**

* Among the case definition of ‘suspected case’ proposed below, which one seems the most adapted to the objective of the active case finding? Can you rank them according to sensitivity?

|  |
| --- |
| **Suspected case:**   1. Any person who presents with two or more of the following symptoms (headache, vomiting, mental confusion, weakness and/or any other symptoms), with illness onset from 15th, April who has been to Greentea County. 2. Any person presenting with 2 or more of the following symptoms-headache, vomiting, abdominal pain, weakness, mental confusion since April 23, 2017. 3. Any person who presents with two or more of the following symptoms (headache, vomiting, mental confusion, weakness) and/or any other symptoms and has attended a wake, funeral, re-pass or is Epi-linked to any one from the affected communities on April 22-23, 2017. 4. A person who had visited or lived in Greentea County and presented with two or more symptoms including headache, vomiting, mental confusion, or weakness, with illness onset on or after April 15, 2017. 5. Any person who presents with three or more of the following symptoms: headache, weakness, vomiting, diarrhea, mental confusion, +/- fever (>35.8 °C rectal or >38.0 ° C axillary) and any other meningeal signs\*, with illness onset from 15th April 2017 who is a resident of or visited Greentea County or has an epidemiological link**\*** to a case from Greentea County.   \*Epidemiological link**:** Association to a case from Greentea. |

**Notes for debriefing question 3c**

**Answer 3c**

* The suspected case definition the most adapted at that stage of the investigation is number 2: there is no mention of place or exposure, and it allows to capture all patients with similar symptoms than the ones presented by the cases.
* Ranking from more to less sensitive: 2, 1, 4, 3, 5.



## 2.4 Episode 4: Case finding

**Question 4:**

* How do you find more cases? List activities and sources.

**Quiz 3:**

* When going to review the records of the patients at the hospital, as an epidemiologist, should you wear PPE?

**Notes for debriefing question 4**

**Answer 4:**

**Sources of data:**

* Review register of hospitals, of health facilities in the county
* Implement enhanced surveillance (awareness of all health care workers and community officers)
* Active surveillance: calling each health facility every day
* Active case finding among participants and follow up of contacts of cases
* Raising awareness via radio, TV, community leaders for patients to care
* Get the list of the funeral attendees and do active case search, contact tracing of cases.

**Answer quiz 3**:

No there is no need to wear PPE as there is no direct contact to contaminated fluid. The epidemiologist does not need to wear a PPE: he/she keeps a distance from the doctor, he/she does not touch patients and keeps safe distance (1 meter); there is no exposure to patient fluids nor direct contact with patients.

|  |
| --- |
| **New findings**   * The active case search revealed more patients in the community and allowed to identify retrospectively cases who presented to hospital and were not yet identified as cases. * The burial team members reported that some dead bodies were presenting with purpura. * Active follow up of the first survivors allows us to observe that a few convalescent patients presented with purpura and ecchymosis on the extremities. * Two cases occurred in Marialand, a district close to Treetown region: a man who attended the funeral, the disk jockey (DJ) of the party died in another district than the affected one. His wife, who did not attend the funeral, has taken care of him: she died 24 hours after him with the same clinical symptoms. |

**Quiz 4:**

Select the correct response. This last information is key because it indicates that:

1. It is a sexually transmissible disease
2. It is an infectious disease responsible for secondary case
3. It is a highly transmissible disease
4. It is a virulent disease

**Answer quiz 4:**

* The correct answer is 2. This latest information indicates that the disease can be transmitted from person to person. That is new as until now it was suspected that the disease was due to a unique source during the funeral ceremony. It helps refining the selection of disease which can be suspected.



## 2.5 Episode 5: Describe the outbreak

### 

**Question 5a: Data collection**

* What information do you need? How are you going to analyse it?
* Optional question: Do you collect information on “sex “or on “gender”? what is the difference?

**Using the line listing (provided in Annex 1, a separate Excel spreadsheet):**

**Question 5b:**

* What is the attack rate among the participants at the funeral?

**Question 5c:**

* Draw the epidemic curve. What transmission pattern do you suspect?

**Question 5d:**

* Draw a map of the geographical distribution of the cases. How do you interpret these results?

**Question 5e:**

* Provide a description of patients.

**Notes for debriefing question 5**

**Answer 5a:**

Answer 5a: Prepare the analysis plan: description by Time, Place, Person. The information to be collected includes:

* Time:
  + When did the cases occurred?
  + How are they distributed in time?
  + Is there date of onset for all? If not, what date can we use?
* Place:
  + How are the case distributed geographically?
  + Are there geographical clusters?
  + How extended is the outbreak?
* Person:
  + Age distribution of cases, of deaths?
  + Gender distribution?
  + Signs and symptoms distribution?
  + Occupation?
  + Link between cases?

Preparing questionnaire:

* Standards
  1. Demographics: age, gender
  2. Medical data: signs and symptoms, outcome of disease
  3. Exposure: link between cases, activities
  4. Laboratory (confirmed, probable, suspect cases)
  5. Eventually vaccination status
* Sex or gender?
  1. Sex = biological characteristic
  2. Gender= define a social role and social interactions

You can refer to the Outbreak toolkit to find questionnaire for several disease and for unknown disease as well reaching the website here: [Standardized data collection tools (who.int)](https://www.who.int/emergencies/outbreak-toolkit/standardized-data-collection-tools)

**Answer 5b: Attack rate**

Attack rate at the date of May 1st (AR) is 31 / 110 28%. Note that the denominator is uncertain because it was difficult to list all the attendees as it was an open invitation to all villagers. Some did not want to be registered in the list.

**Answer 5c: Describe the distribution of cases by time: The epidemic curve**



*Figure 2: The epidemic curve, cases of unknown disease, April 2017. Data, May 8th, 2017.*

*Interpretation of epi curve:* ***Point source then inter- human transmission***

**Answer 5d: Describe the geographical distribution of the cases**

If possible, draw a map (if using R or another GIS software) but because time is limited a table showing the geographical distribution can also be done.

The title of the map must indicate the number of cases described, the date, and if possible, the main attractions: marketplace, churches, schools, roads, that can help understanding what has happened.



*Figure 3: Geographical distribution of cases of unknown disease, April 2017. Data, May 8th, 2017.*

*Interpretation of the map:*

*Most cases are concentrated in one place. We can see that there are two schools. This is important information because most of the cases were students and were going to school. Also, the index case is a teacher in one of the two schools.*

**Answer 5e: Describe the person**

1. The severity of the disease/episode:

* Calculate the case fatality rate (CFR): 42%
* Majority of deaths occurred within 24-48 hours after onset of disease
* Distribution of age and sex of the patients who died:



1. Distribution of the age of the cases:
   * Age range: 10-62 years old
   * Median age: 23 years old
   * 68% of cases were aged between 10 and 29 years old
   * Sex ratio M/F = 0.82



1. Occupation

For 18 cases with information provided: 13 are students, 2 businesspersons, 1 housewife, 1 mason, 1 teacher*.*

1. Description of the signs and symptoms presented by the cases:

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| **Signs and symptoms** | **Cases** | **Proportion** |
| **General weakness** | **28** | **90%** |
| **Abdominal pain** | **24** | **77%** |
| **Headache** | **22** | **71%** |
| **Vomiting** | 18 | 58% |
| **Confusion, agitation** | 16 | 52% |
| **Diarrhea** | 15 | 48% |
| **Respiratory signs** | 6 | 19% |
| **Purpura/Ecchymosis** | 6 | 19% |
| **Fever** | 6 | 19% |
| **Chest pain** | 5 | 16% |

*Table 1: signs and symptoms, unknown disease outbreak, April 26th*



*Note: This is to stress that the simple description of the cases distribution and characteristics is not enough. The epidemiologist must interpret the data in a meaningful way to advance in the investigation.*

*A good analysis is sometimes sufficient to conclude, and more analytical studies (case-control, cohort studies) are not always needed****.***

**More analysis that could be conducted to help the investigation:**

**The incubation periods**

Considering that the likely exposure of the patients to etiological agent happened during the funeral conducted on April 22, 2017, the incubation period was from 0-9 days with pick on day 1 and day 2 (67% of the cases).

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*Figure 4: Distribution of cases from exposure to the funeral to onset of illness, unknown disease outbreak, May 8th.*

**The treatment provided**

The cases were treated systematically with analgesics, intravenous fluids, antimalarial, antibiotics, oxygen and others depending on the signs and symptoms. The antibiotics were ampicillin combined with gentamicin (provided to two patients who survived), ceftriaxone (provided to two patients who survived) and cotrimoxazole (provided to three patients who survived).

**Highlighting results that are of importance for the investigation:**

To ascertain the disease:

* About 80% of the deaths occurred within 24 hours after the onset of the symptoms. One death occurred between 24 to 48 hours after the onset of the symptoms and one after 48 hours. This is a severe disease.
* Incubation periods vary and evocate two sources of disease: one common exposure and secondary person to person transmission.

Laboratory results: Ebola investigation negative.

To understand the event: Summary of patients’ description

* Majority of patients are young adults and teenagers.
* Women are most affected than men.
* They are mainly students.
* The index case is a teacher at one of the two schools.
* The majority of cases are primary cases and attended the party.
* There is one (or two, this is not clear for a little girl who died) secondary cases who did not attend the party

Illustration of the information revealed by the investigation:



**It is important to stress that a good description of the outbreak provides a lot of useful information.**



## 2.6 Episode 6: Generating hypothesis

### Episode 6 - Step 1

**Question 6a:**

* Following the description of the outbreak you made, what are your hypothesis regarding the source of the agent and the transmission mode?

**Question 6b:**

* What laboratory investigations do you request and which samples to take?

**Question 6c:**

* What epidemiological analytical study do you recommend testing your hypothesis?

**Notes for debriefing question 6, step 1**

**Answer 6a:**

Note that conducting analytical studies is time and resource consuming and one must be very clear of the objectives and limitations of such studies conducted ad hoc in the field before engaging in it. Many case-control studies cannot lead to results because of too many limitations when conducted (choice of controls, lack of clear objective of the study because initial hypothesis is not clear, etc.)

First hypothesis: Food or beverage poisoning: The event started just after the mass gathering of the funeral. The majority of patients attended the funeral. The incubation period is compatible with food born disease (staph, strepto).

Q/R: Those who brough food back home did not get the disease.

Probable risk factors: exposure includes attendance at the funeral; consuming contaminated food served at the wake. Exposure to smoke cannot be excluded and as such environmental exposure can also be suspected. Consumption of an ileal product must also be suspected and is very difficult to identify because of the fear of being accused of the participants.

**Answer 6b: laboratory investigations:**

**Patients**:

* Samples have been collected including orals swabs and cardiac punctions and cerebrospinal fluid (CSF) from deceased and blood samples, urines, and CSF from hospitalized cases.
* Laboratory testing including EVD was rapidly reported as negative.
* Autopsies were performed for two patients who died in Gedeh, near Bluetown the capital.

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| **New findings:**   * All other tests send to Atlanta and no results available so far. However, the analysis conducted on site indicate an **infectious disease in the blood cells investigations.** * **Environmental investigation:** Food samples collected from homes of cases, including deceased in Greentea and Marialand and are sent to the National Reference Laboratory. These samples included sugar, cake, pepper, seasoning, garlic, salt, cooking soda, soft drink. * **Water samples were tested** in and found to be negative for coliforms and E. Coli. Water was also tested for chemical and heavy metals (lead, arsenic and cupper) |

**Answer 6c**

If the list of participants could be complete and accurate, and if human resources to follow each participant could be available, we could discuss a follow up of all participants and hence conduct a **cohort study**.

In that situation, there is a need to go fast to identify the disease that is killing many young persons and the most appropriate decision is to conduct a case control study, which is less resource and time consuming.

The objective of the case study is to identify the product that could cause this disease and make sure it is not circulating anymore.

The sample size is small and to avoid empty cells it is better to match several controls to one case.

It is recommended to have an epidemiologist with experience to conduct the case control study.

### Episode 6 - Step 2

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| **A case control study was conducted:**   * We conducted a 1:2 unmatched case control study with 25 cases and 50 controls. Both cases and controls attended one of the three events of the funeral (wake, burial or repass). * We used a questionnaire elaborated to capture demographic and clinical information about the patients as well as exposure to different food and drinks during the most important events they attended in the past weeks and exposure to chemicals, including heavy metals. |

**Question 6d:**

* What is your interpretation of the results of the case study?

And what is your final hypothesis?

Please see the table presenting the results of the case-control study.



**Notes for debriefing question 6, step 2**

The case control study revealed that there were four products and event which can be associated with significant results to the fact of being a patient during the funeral:

1. Event: attending the wake (the wake happens on the first night of the funeral ceremony, people join to share meal, beverages and dances throughout the night.
2. Drinking tea: tea was mentioned to be any beverage made by the people and that does not contain alcohol
3. Eating sandwich: sandwiches were provided by the family of the deceased. They have been prepared by one person in the village.
4. Drinking Egg nog: a beverage with alcohol and eggs made locally.

Interpretation: the confidence interval for attending the wake is extremely large which lowers the power of the association between the wake and being a patient. This should not be retained as a risk factor.

Drinking tea and drinking Egg nog has a large, odd ratio but the confidence interval is large. Both products are very different in terms of composition.

Eating sandwiches was reported for most of the participants to the funeral.

The multiplication of products here is eluding what could have been the product at the origin of the outbreak. More information is needed to look at how the method for analysis of the data has been applied: number of patients and control in each box? Respect of the hypothesis for normal distribution of the cases? Etc.

Real interpretation (after knowing what was the exact agent that caused the disease): Initial common exposure (co primary cases) to unique source during the funeral: either one already sick person (the teacher who served the tea) and/or smoked environment with high risk of exposure due to confined place, close relationships. Then person to person transmission.

Impossible to go further because the investigation did not collect information on what happen during the funeral beside what people have eaten and drink.



## 2.7 Episode 7: Propose control measures

**Question 7:** Which measures can you propose at that stage to limit the extension of the outbreak? Please list the proposed measures.

**Notes for debriefing question 7**

**The Public Health Response and communication**

At county level

1. Active and early recognition of case: Disseminating case definition to all health facilities, organising active surveillance of participants to funeral, implement contact tracing around cases
2. Update the patient line list with required variables in order to construct the infection chain (family ramification contact, friend contact, school and church attendances)
3. Work with community leaders, school authority, spiritual leaders and the public: sensitization to minimize fear and panic
4. Involve traditional and spiritual healers in the response to 1) coordinate with the county health team in responding to this outbreak and 2) provide valuable information on uses and habits that can help identifying the source of the outbreak
5. Engage community in active case identification (without stigma), in distributing correct information on the stage of the investigation, and implement the reinforcement of hand washing as a standard precaution even without knowing the cause
6. Provide quality care for patients in the hospital to attract new cases to seek for treatment and limit extension in the community.
7. Provide proper protection of the health workers

At National level: WHO support

* National team to disseminate laboratory results in timely manner
* Provide motivational package for contact tracers and active case finders
* Conduct press briefing to update media houses and ensure consistent messages to minimize fear and panic.
* Continue to provide technical, operational, and logistical support for the on-going response in the affected Counties.
* Conduct autopsy on the remaining corpses in Monrovia.
* Work with counties to review and validate contact and attendees
* Follow up on aliquots results.

## 2.8 Episode 8: Reassess the outbreak

**Question 8**: Why reassess the outbreak and adapt control measures?

**Notes for debriefing question 8**

**Answer 8:**

1. Collect the results of all laboratory investigations performs
2. Document the acceptability of the control measures taken
3. Verify if new cases are still occurring or being reported
4. Evaluate impact of control measures
5. Evaluate impact of communication to the public

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| In Greentea, the cases have dropped suddenly one week after the funeral and the start of the outbreak. Teams were tired and started to be demotivated because they could not find the cause of the outbreak. Since no more cases were occurring, the interest in the search for the cause decreased drastically. |

General comment: At a certain stage of the investigation the epidemiologist needs to step back and take some distance from the ongoing investigation to:

1. Synthetize all information gathered via the data collection and analysis, the interviews with key informants and community leaders, informal talk with the drivers, vendors, doctors, health workers, colleagues from the country and any person in the community.
2. Verify if each hypothesis that was raised has been tested and has reached a conclusion, either to accept or to reject it. This must have been done using tangible proofs and argumentation.
3. Evaluate if the control measures that have been proposed so far are accepted, implemented, and have an impact.

That activity must lead to decide if further investigations are necessary and if yes which one and with which methodology.



## 2.9 Episode 9: Conduct other investigations

**Question 9:** What other investigations can be implemented to identify the source of the outbreak?

**Notes for debriefing question 9**

**1. Laboratory investigation:**

Clinical lab serving hospitals and health care facilities: Perform diagnostic testing of patient samples

In many outbreaks many samples are taken and send to laboratory in or out of the country. In many cases only few positive results are sent back. When this occurs the investigation usually stop.

In reality the epidemiologist must trace back all laboratory samples sent, obtain results and inform the doctor so that he/she can inform the patient, including negative results.

Reconciliation of sample with patient is one of the biggest problems in outbreak: a good identification of sample must be organised as soon as a sample is taken from a patient. Unique identifiers are usually used for that: linking patient and biological samples.

**2. Conduct environmental investigations:**

Examine and sample food, water sources, buildings materials, or environmental surfaces

This will provide information about the exposure to agent, the contamination during food preparation, or manufacturing, exposure during recreational activities, document contaminated environment.

In local, state, and federal public health labs: you can try to test water, soil, dust, food, and clinical specimens and eventually conduct forensic testing, and molecular fingerprinting.

Molecular fingerprint will help identify agent and subtype and to link cases with sources by strain identification

Hospital clinical lab and Public Health labs can report cases. However, in many countries, samples collected during investigation go to PH labs.

**3. Perform integrated outbreak analysis (IOA)**

This approach allows to integrate more aspects to consider during the response to an outbreak: sociological and economic impact, perception and believes of the population affected and how the outbreak and the information that is released are captured and integrated into the public discourse.

This is extremely useful during prolonged and complex response type Ebola. This approach implies a strong collaboration between epidemiologists, sociologists, anthropologists, economists, and other disciplines involved in the response to an outbreak.

Example of studies:

* Anthropological: studying perception, behaviors, interpretation that can affect prevention and reaction
* Gender issues: inequity in accessing health services, increased risk factors, targeting control and preventive measures

**4. Conduct sequential case-control studies: Narrow down exposures to identify risk factor**



## 2.10 Episode 10 Communicate findings

**Question 10**: Prepare a situation report for the authorities of the district of Delmarre

**Notes for debriefing question 10**

**Answer 10**: Press release: see Situation report attached in Annex 2

Communication throughout the investigation is key to supporting the response.

Communication must be transparent and clear, adapted to each public.

It has to be in place as soon as the investigation starts.

Different public must be addressed:

* Staff within your team and agency
* Other health agencies
* Local and state health departments, national health department, other health services for specific population (e.g., Indian)
* Health care providers and facilities
* The public: media, schools, business.

How to communicate:

* Assign a credible spokesperson
* Organise reliable communication
* Be available to the media
* Issue frequent updates
* Acknowledge what you don’t know
* Be prepared and anticipate questions
* Who is at risk? How can the disease be prevented?
* Provide sufficient detail to meet PH needs and address public concern
* Control rumors: ensure correct information is publicized
* Don’t over reassure.

****

**Epilogue**

On May 8 the laboratory of CDC Atlanta informs that *Neisseria meningitidis* serogroup C has been isolated from cardiac fluid and oral swab of three of the patients.

This was an outbreak of septicemia due to Neisseria Meningitidis C, a rare form of the disease causing outbreak, that started with the funeral. The index case is probably the teacher who was serving the tea during the wake as she was sick before the ceremony. She might have contaminated the participants during the wake via some activities that increase the risk for droplets transmission such as yelling, coughing or talking very closely with others. The fact that the strain was secondarily identified as very virulent explains the high case fatality rate.

The lack of information collected during the epidemiological investigation regarding what did the patients do and with who, where they were sit in the room and where were the ventilators placed impaired the possibility to understand the mechanisms of propagation of the disease in this environment.



MOH responses included:

* Chemoprophylaxis of all contacts was conducted.
* Vaccination was not indicated due to the long delay between the event and the disclosure of the results.
* Vaccination against meningococcal C is not indicated in Seewhat.
* The strain was first isolated in Niger in 2016, it is a highly virulent strain.
* The investigation did not allow to understand the exact transmission routes because it was immediately oriented towards food poisoning. We ignore how so many co primary cases happen in such a short time (discotheques, smokes, other?).

## List of annexes

* Annex 1: Line list Delmare investigation (Excel spreadsheet)
* Annex 2: SITREP MOH 7 May 2017 (PDF document)

***Thank you for successfully conducting outbreak investigation in Seewhat!***

For further readings on this episode please see the following:

Bozio CH, Vuong J, Dokubo EK, Fallah MP, McNamara LA, Potts CC, Doedeh J,Gbanya M, Retchless AC, Patel JC, Clark TA, Kohar H, Nagbe T, Clement P,Katawera V, Mahmoud N, Djingarey HM, Perrocheau A, Naidoo D, Stone M, George RN, Williams D, Gasasira A, Nyenswah T, Wang X, Fox LM; Liberian Meningococcal Disease Outbreak Response Team. Outbreak of Neisseria meningitidis serogroup C outside the meningitis belt-Liberia, 2017: an epidemiological and laboratory investigation. Lancet Infect Dis. 2018 Dec;18(12):1360-1367. doi: 10.1016/S1473-3099(18)30476-6. Epub 2018 Oct 15. PMID: 30337259; PMCID: PMC6545567.

Perrocheau A, Jephcott F, Asgari-Jirhanden N, Greig J, Peyraud N, Tempowski J. Investigating outbreaks of initially unknown aetiology in complex settings: findings and recommendations from 10 case studies. Int Health. 2023 Jan 11:ihac088. doi: 10.1093/inthealth/ihac088. Epub ahead of print. PMID: 36630891.



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