Case study: An outbreak of acute hepatitis in Baripada, Orissa

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Case study developed by a working group created by the Master of Applied Epidemiology (MAE) - Field Epidemiology Training Programme (FETP) from the National Institute of Epidemiology (NIE), Indian Council of Medical Research (ICMR), Chennai, Tamil Nadu, India. It is inspired by an investigation conducted by Dr Swain, 2003 scholar of the MAE assigned to the state of Orissa, India. Dr Gregory Armstrong and Jan Drobeniuc from the hepatitis division at the United States Centers for Disease Control and Prevention provided comments and suggestions.

Learning objectives

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

1. Identify the steps of the investigation of an outbreak;
2. Describe the characteristics of an outbreak in terms of time, place and person;
3. Use descriptive epidemiological data to generate hypotheses;
4. Use analytical epidemiological data to test hypotheses;
5. Formulate recommendations for the control of an outbreak.

Using this case study in a class

This case study is designed as a stand-alone and does not come with a facilitator's guide. The answers to all the questions for each section are provided as an introduction to the following section. To run this case study in a class, it is proposed to distribute it one page at a time. Scholars take turn to read it paragraph by paragraph aloud. Reading all paragraphs aloud and in turns has two advantages. First, everyone can quickly participate and go beyond the inhibition of having her/his voice heard in a large room. Second, time is given to the whole class to understand the issue and think about the answers. The scholar reading the question may try to answer it if s/he can propose an answer. Otherwise, the matter is discussed as a group. The next scholar reads the next question and so on until the end of the page. After the next part/ page is distributed, the next scholar continues with the first paragraph of the next part and so on until the case study is over. Once the epilogue has been read, it is proposed to go back to the first page to read the objectives again. This re-iterates the acquisitions and provides additional opportunity to clarify what may have been misunderstood or not fully acquired.

Part 1. A cluster of acute hepatitis in Baripada, Orissa

Baripada is a large municipality located in the district of Mayurbhanj, in the North of Orissa, close from the border with Jharkhand and West Bengal. The population of Baripada was 400 in year 1901. The city developed fast after the Indian independence and some of the urbanization has been difficult to keep under control. In the late 1990s, the population size exceeded 100,000.

On 8 February 2004, a number of private practitioners from Baripada municipality in Mayurbhanj district, Orissa, called the Assistant District Medical Officer (Public Health), Mayurbhanj to report large numbers of patients suffering from acute jaundice in the city. These practitioners reported that these cases of acute jaundice tended to cluster by households. At the same time, clinical laboratories established in the city of Baripada reported a large number of specimen submitted for analysis with a working diagnosis of acute hepatitis.

On 9 February 2004, a team of public health workers and supervisors led by Dr Susanta Swain, Field Epidemiology Training Programme (FETP) scholar from the 2003 cohort reached the city of Baripada to investigate the outbreak. On the day of the arrival of the team, 21 reports of acute jaundice had been received so far.

Question 1. A.

What are the key steps of the investigation of an outbreak?

Question 1. B.

Can the team determine whether or not they are dealing with an outbreak at this stage? What additional information would they need?

Part 2. Confirming the diagnosis

The steps of an outbreak investigation include (1) determining the existence of the outbreak, (2) confirming the diagnosis, (3) defining a case, (4) searching for cases, (5) using descriptive epidemiological data to generate hypotheses, (6) testing hypotheses using an analytical epidemiological study, (7) drawing conclusions, (8) comparing the findings with established facts, (9) communicating the findings and (10) executing prevention measures.

Reaching the field, the lead investigator and his team attempted to determine whether they were dealing with an outbreak or not. First, they checked that the population of the city had not changed recently because of massive population migration. The absence of such event reassured them about a change in the denominator. Second, they enquired about a potential recent change in the case definition or reporting mechanism. They could not find any artifact that would have lead to an increase in the numerator. Third, they enquired about the background rates of acute jaundice in the city and were told that under normal circumstances, about eight to 10 cases of such diseases were reported in the city each year. On the basis of these findings, they concluded that the outbreak was real.

When they arrived in Baripada, the team went to the hospital to see some of the affected case-patients and discuss with the clinicians who had been managing them. They learned that patients presented with fever, malaise and then with acute jaundice. Urines were dark. All patients experienced severe symptoms and 36 presented signs and symptoms of fulminant liver failure. Five deaths occurred in February 2004. None of the patients had any history or signs of pre-existing chronic liver disease. Laboratory investigations conducted among some of the hospitalized patients indicated high levels of aminotransferases, Serum bilirubin, and alkaline phosphatase. Two case-patients who had been tested were negative for IgM antibodies to hepatitis A virus (HAV) and to the hepatitis B virus surface antigen (HBsAg).

Question 2.A

What are the possible agents that could be causing this outbreak? For each, list the clinical and epidemiological elements that are compatible with the diagnosis and those that go against it.

Question 2.B

How would it be possible to confirm the diagnosis?

Part 3. Defining cases

After reviewing the clinical information, the investigators listed the agents that could have caused this outbreak. This included viruses and toxic substances. A number of severe infections can lead febrile jaundice (e.g., leptospirosis, malaria), but the clinical picture was different in this case. The sequence of fever followed by jaundice is suggestive of viral hepatitis. Among viral hepatitis viruses, HAV is a real possibility and hepatitis A can lead to fulminant liver failure. However, high levels of herd immunity tend to make community-wide outbreaks uncommon in India. HBV or hepatitis D virus (HDV) could cause that kind of clinical picture, but large outbreaks in the community are uncommon. Acute hepatitis C virus (HCV) infection usually does not cause marked clinical symptoms, is not associated with fulminant liver failure and outbreaks in the community are uncommon. Hepatitis E virus infection can cause disease of that kind and may occur as large community wide outbreaks. The initial negative serological tests for HAV and HBV infection need to be checked but could suggest HEV as the causal agent.

To verify the diagnosis, the investigators collected blood specimens from case-patients and sent the sera at the Regional Medical Research Centre (Indian Council of Medical Research), in Bhubaneswar, the state capital of Orissa. Of the 47 serum samples, all were negative for IgM anti-HAV, HBsAg and antibodies to HCV. However, all serum samples were positive for anti-HEV antibodies in ELISA, confirming that the investigators were dealing with a hepatitis E outbreak, the first one ever documented in Orissa.

The investigators are now about to look for cases so that they can describe the characteristics of the outbreak.

Question 3.A
What kind of elements should be contained in a case definition?

Question 3.B
What case definition could be suggested to look for cases?

Part 4. Searching for cases of acute hepatitis in Baripada

During an outbreak investigation, a case definition should contain time, place and person criteria. Sometimes, case definitions may be formulated at various levels of sensitivity and specificity so that they can be used for different purposes. For examples, possible cases are used to screen patients or members of the population, probable cases are used for case finding and confirmed cases are used for analytical studies.

During the Baripada investigation, the investigators decided to define a case as a combination of (1) loss of appetite with (2) yellow coloration of conjunctiva or colored urine that occurred suddenly since 19 January 2004 in a resident of Baripada.

The investigators are now about to search for cases systematically in the city of Baripada so that they can constitute their line listing and describe this outbreak in terms of time, place and person.

Question 4.A

What are the potential options available to search for cases during an outbreak investigation?

Question 4.B

What case finding strategy could be adapted to this specific situation?

Question 4.C

What minimum information will be required for each case? How should this information be organized?

Question 4.D

How would you analyze the data?

Part 5. Using descriptive epidemiological findings to raise hypotheses

A number of case finding strategies may be used during an outbreak as long as they are applied uniformly in the whole population being investigated. This ensures that the strategy leads to the identification of cases that are representative of all cases. The simplest way to identify cases is to take cases passively reported through the surveillance system. The next option is stimulated passive surveillance, which consists in investigators reminding reporting units to notify cases through the routine surveillance system. If a more extensive search is needed, active surveillance may be used. In this case, investigators actively collect information from reporting sites or laboratories (e.g., through phone calls or visits). Finally, door-to-door case search is the most exhaustive option if resources are available and other mechanisms are potentially insufficient. During this outbreak, investigators conducted an active door-to-door case search in seven days with the help of 44 field workers and collected information regarding age, sex, date of onset, signs and symptoms and potential exposures.

The investigators have now completed the search that led to the identification of 538 cases among which five deaths for a population of 105,422 persons (attack rate: 5,1 per 1,000 population, case fatality ratio: 0.9%). They constructed a line-listing. They also completed a report with the descriptive epidemiology findings, by time (Figure 1), place (Figure 2) and person (Table 1). Interviews of the case-patients did not allow identifying any common events among them, but the environmental health specialists of the district mentioned that the workers involved with all the sources of water supply in the city had been on strike from 2 to 10 January on the same year.

Figure 1: Cases of acute hepatitis by week of onset, Baripada, Orissa, India. January-March 2004

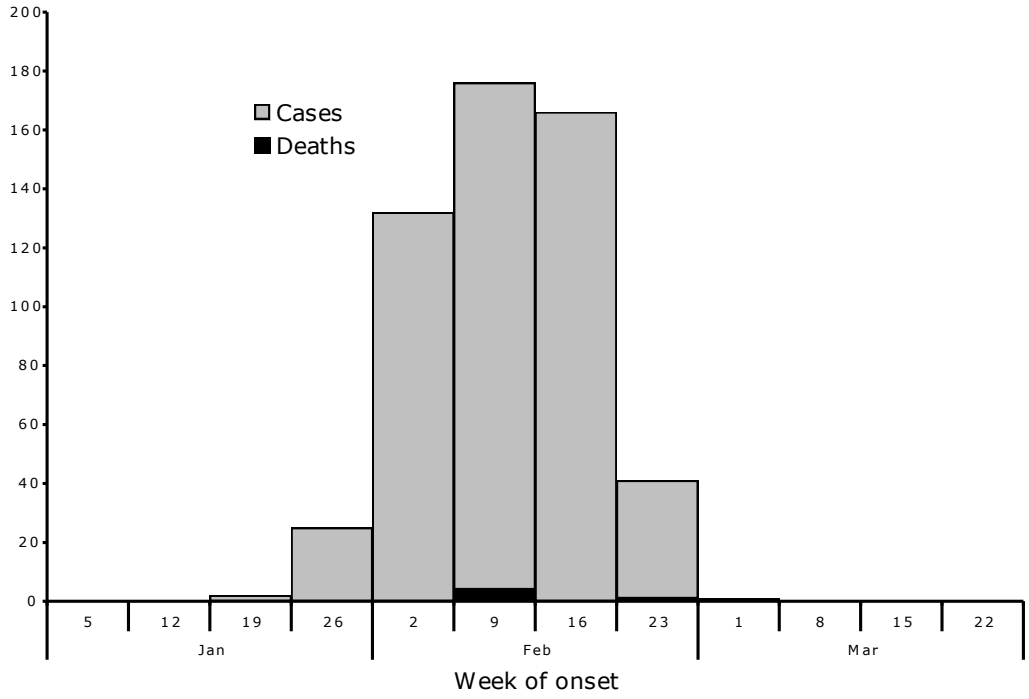

Figure 2: Attack rate of acute hepatitis in the various areas of Baripada municipality, Orissa, India, February March 2004 [1]

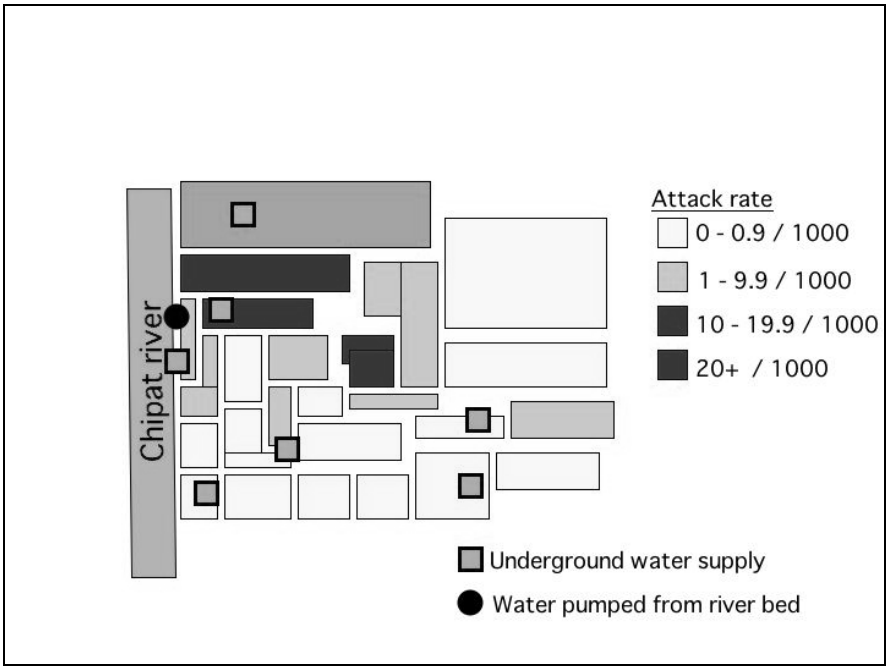

Table 1: Incidence of acute hepatitis by age and sex, Baripada municipality, Orissa, India, 2004.

Characteristics		Cases	Population	Attack rate per 1,000
Age	0-4	1	9,488	0.1
	5-9	11	13,705	0.8
	10-14	37	12,213	3.0
	15-44	416	49,689	8.4
	45+	73	20,706	3.5
Sex	Male	341	53,449	6.4
	Female	197	51,973	3.8

Question 5.A

How can the epidemiological information contained in these figures and this table be described?

Question 5.B

How can this information be interpreted?

Question 5.C

What are the potential hypotheses that could be generated on the basis of these data?

Question 5.D

How could these hypotheses be tested?

[1] The initial map drawn in the field was a rough spot map, with one spot representing a case. This was later transformed into a map for which population-based incidences were calculated to adjust for the population sizes of the various parts of the city.

Part 6. An analytical study to test the main hypothesis

Cases were reported from 19 January to 1 March 2004 with a peak around the 14 February 2004. With respect to the geographical distribution, the incidence was higher in one part of the city that is close to a specific source of water supply for which water was pumped from the nearby river. In the rest of the city where the attack rate was lower, there were a number of sources of water all supplied with underground water. With respect to the attack rate by age and sex, there was a higher attack rate among persons from 15 to 44 years of age and a slightly higher attack rate among male.

The shape of the epidemic curve suggested a persisting common source outbreak. Given the incubation period for HEV infection (about one month), the exposure probably occurred early in January. The geographical distribution of the cases suggested a clustering around the source of water supply pumped from the riverbed. The attack rate by age and sex suggested that the exposure affected the whole population although young adults were at higher risk to develop symptoms. The timing of the strike among the employees of the municipal water system coincided with the probable time period during which the exposure took place. This led the team to investigate how the strike affected the source of water supply pumped from the riverbed. It turned out that (1) while the water pumped from the river was usually treated, the treatment was interrupted during the strike in January and (2) the distribution of this source of water supply corresponded to the distribution of the areas with higher attack rates in the city. None of the other hypothesis-generating interviews led to suspect any other event nor factor that could explain the outbreak.

At this stage of the investigation, the leading hypothesis was that the discontinuation of the water treatment during the strike of the employees of the municipal water supply system led to the supply of un-treated river water to the population between 2 to 10 January 2004, which led to the outbreak. The investigators have now decided to test this hypothesis in an analytical epidemiological study.

Question 6.A

What are the options available to the investigators in terms of study design? Which one may be preferable? Why?

Question 6.B

What kind of study participants should be recruited for this study? What criteria should be used to select them?

Question 6.C

What kind of data should be collected among study participants?

Part 7. Identifying the source of the outbreak

The investigators had the choice between a case-control study and a cohort study to test the main hypothesis of this outbreak. Because the incidence in the population was low, even in the parts of the city where the attack rate was at its highest, a case-control study was preferable. Thus, they decided to conduct a case control study in the city to compare cases and control in terms of their use of the suspected source of water supply.

The investigators used the case definition they had formulated at the case search stage for the case control study (See: Part 4. Searching for cases of acute hepatitis in Baripada, Page 5). For the controls, they selected healthy persons from the general population at random in the various areas affected. Within each area, they selected as many controls as they were cases. Then, they used standardized questionnaires to collect information from case-patients and control-subjects about demographic characteristics and about the source of water they were using in the house.

The investigator have now completed their fieldwork and finished tabulating the data (Table 2).

Table 2: Consumption of the suspected water source among case-patients and control-subjects, Baripada, Orissa, 2004.

	Acute hepatitis	Controls	Total
Drunk river water	493	134	627
Did not drink river water	45	404	449
Total	538	538	1,076

Question 7.A

How should the data be analyzed? What measure of association need to be calculated? How?

Question 7. B

Calculate the appropriate measure of association. How do you interpret the results?

Question 7. C

Would you conduct additional investigations?

Part 8. Examining this outbreak in the context of what is known of hepatitis E

Because the investigators made the choice to use a case control design, the appropriate measure of association to calculate for the analysis is the odds ratio. Applying the formula of the odds ratio to the 2x2 table generates an odds ratio of (493 x 404) / (45 x 134) which comes to 33. The 95% confidence interval of this odds ratio is spread from 23 to 47. Because it does not include one, it is reasonable to say that the association observed was not caused by chance. This result suggests that the null hypothesis – that there was no association between the pipeline water and hepatitis E - can be rejected.

Figure 3: Site where the river water was pumped for the supply to the city, Baripada, 2004

At this stage, it is necessary to better document the circumstances that may have led to the contamination of the water. The investigators enquired about the normal treatment that is applied to the river water after pumping (Figure 3) before distribution. They learned therefore from the water supply department of the city that under normal conditions, the water from the river goes through a process that includes flocculation, sedimentation, rapid graded filtration and chlorination.

Question 8. A

Are the results of this investigation compatible with what was already known about hepatitis E outbreaks?

Question 8. B

Did we learn new features of hepatitis E through this outbreak investigation?

Part 9. Communicating the findings

The conclusion of the investigation is that a large hepatitis E outbreak occurred in Baripada, Orissa, from February to March 2004. This outbreak was caused by the delivery of contaminated water to the population through the municipal water supply. The discontinuation of the water treatment during a strike of the employees of the municipal water supply system between 2 and 10 January 2004 lead to the supply of untreated surface water to the population. This conclusion is compatible with what is known of HEV, including its usual mode of transmission and incubation period.

The investigation of this outbreak adds to the knowledge about HEV. First, infections with this virus had never been reported in the State of Orissa. Hence, this episode suggests that careful laboratory testing should be done during hepatitis outbreak to spot unusual pathogens. Second, the occurrence of the outbreak one incubation period after the window during which treatment was interrupted is compatible with the fact that the water treatment usually applied to the water was effective to some extend. To date, this evidence was not available. HAV is somewhat close, phylogenetically, to HEV, and is sensitive to concentrations of chlorine used in municipal water systems. Caliciviruses are also close to HEV. There are several reports of calicivirus outbreaks occurring after chlorination systems have failed. Some evidence also suggests that caliciviruses are resistant to chlorine. However, this is based on studies in which large numbers of infectious doses were used for which it cannot be ruled out that the chlorine used in the experiments had substantially reduced the number of viable virus particles. Overall, the Baripada investigation brings new elements to the knowledge about epidemiology of HEV infection, as the type of water treatment procedures that are effective in inactivating HEV in the water supply were not known.

At this stage, the investigation team needs to report back the results of the investigation.

Question 9. A

To what audiences should the results of this investigation be reported?

Question 9. B

What do you expect of the various audiences to whom the results of this outbreak investigation will be reported?

Question 9. C

What media will you be using to reach each of these audiences?

Question 9. D

What are should be the short term, medium term and long-term recommendations following this outbreak?

Question 9. E

What this outbreak investigated too late?

Part 10. Epilogue: Executing prevention measures

Reporting the results of this investigation is important. Different audiences might need to be targeted according to the circumstances. First, the investigators should report to public health managers, preferably in the form of an oral briefing, so that the recommendations can be proposed to ensure that action is taken. Second, they should report to epidemiologist colleagues and laboratory specialist in the form of a report containing the epidemiological evidence that documents the conclusion of the investigation. Third, may need to report back to political or administrative leaders, either directly or through the local public health manager, in the form of talking points and / or a summary. This will be important for the authorities to understand that the situation is being handled, as it should. Fourth, they could have needed to report to the community through press releases and / or interviews health education message to help the public in taking active steps towards prevention. However, in the case of this investigation, the evidence was generated at a time when it was too late to usefully inform the public. Finally, the scientific community needs to know about this investigation through presentations and / or manuscripts containing new scientific information that may advance public health.

In terms of recommendation, the investigators did not make particular recommendations for the short term other than reassuring the population as the exposure has been discontinued. However, they took good care to avoid the spread of unnecessary measures that would not be supported by the evidence and that could direct the attention away from the real issues. For the medium term and long term, the investigators worked with the district health authorities to initiate a dialogue with the municipal water supply about (1) quality assurance measures that could ensure the continuous quality of the water supply and (2) the type of minimum service that could be put in place in the case of strikes.

This outbreak was not investigated too late: It was investigated as soon as the report was made available. While a better surveillance system might have captured the outbreak earlier, none could have identified the problem in time to do anything about the event that led to the exposure. Despite the impossibility to intervene in time on the source of infection, this investigation was useful in documenting a process by which prevention opportunities were missed. It also allowed knowing more about HEV and its epidemiology. It is never too late to investigate an outbreak, delays just make the problem slightly more difficult to solve.