CENTERS FOR DISEASE CONTROL, EPIDEMIC INTELLIGENCE SERVICE
New England Epidemiology Institute, 1992

AN OUTBREAK OF HEMORRHAGIC FEVER IN AFRICA

OBJECTIVES

After completing this case study, the student should be able to:

1. List the criteria for deciding whether a field investigation is warranted;
2. Describe the key tasks involved in investigating an epidemic of unknown cause, and, given a real outbreak, perform each step;
3. Describe the components of a case definition, and develop a case definition for a new disease; and
4. Given the appropriate data, perform descriptive epidemiology and explain the importance of this step.

PART I

On the 19th of September, 1976, the chief medical officer of the Bumba zone in northern Zaire radioed the Minister of Health in Kinshasa to report that an exceptionally lethal disease had become epidemic. Since the first of September, 17 patients at the Yambuku Mission Hospital in the Yandongi collectivity (county) and one Belgian missionary midwife employed by the hospital had developed an illness characterized by fever, vomiting, abdominal pain, and bloody diarrhea that rapidly progressed to death. The officer reported that the illness appeared to be spreading among the remaining 16 hospital staff members, as well as persons living along the roads leading from Yambuku.

The Bumba Zone is in the middle Zaire river basin, an area consisting predominantly of tropical rain forest. About 275,000 persons live there, mostly in small villages with fewer than 500 persons. The people are avid hunters and come in contact with a variety of wild animals. Dysentery, malaria, filariasis, measles, amoebiasis, pneumonia, tuberculosis and goiter are some of the common endemic diseases.

Question 1: Before considering a course of action, what other questions might you ask over the radio?

Question 2: What are some of the criteria you might use in deciding whether to launch a field investigation of an apparent outbreak?

Question 3: Assuming that you will launch an investigation, what operational decisions do you need to make before beginning the investigation?

Question 4: Before departing, review the steps of an outbreak investigation.

23 September - 3 October 1976

Epidemiologic teams, composed of Ministry epidemiologists and microbiologists and medical officers of two international medical missions to Zaire, were sent to the region. Thirty-two more persons with the disease had been hospitalized at the Yambuku mission hospital and these patients were examined. The illness was characterized by high temperature (> 39°C.), headache, bloody vomiting and diarrhea, chest and abdominal pain, arthritis, and prostration leading to death, usually in three days time. Jaundice was not present. Liver biopsy and blood specimens were collected from the patients and were sent to the World Health Organization (WHO) reference laboratories for further evaluation. On September 30th, the Yambuku hospital was closed because 11 of the 17 staff members had died of the illness. On October 3rd, Bumba Zone was quarantined.

Question 5: At this time, what broad categories of disease would you be considering?

PART II

13 October 1976

A previously unclassified virus, similar to the Marburg virus that causes a type of hemorrhagic fever, was isolated from liver specimens sent to WHO reference laboratories. A serologic test was quickly developed.

Question 6: What modes of transmission of illness should be considered in light of this information?

13-20 October 1976

Following contact with a Belgian missionary nurse who had been transported to the capital for medical care, a Zairian nurse in Kinshasa became ill and died. The Zaire Government asked for the formation of an international commission to assist in the investigation of the disease. On October 19th, 1976, following the first meeting of these consultants, a survey team was sent to Bumba Zone. In addition to cases from whom virus had been isolated or those with positive serology, the consultants identified other individuals with illnesses ranging from death following an illness of headache, fever, abdominal pain, vomiting, and bleeding, to only headache and fever following contact with another ill person.

Question 7: Given this spectrum of disease, how would you define a case?

PART III

The investigators chose to divide cases into three types:

- A proven case was a person from whom virus was isolated or demonstrated by electron microscopy or who had an indirect fluorescent antibody titre of at least 1:64 to virus within three weeks after onset of symptoms.
- A probable case was a person living in the epidemic area who died after one or more days with two or more of the following symptoms and signs: headache, fever, abdominal pain, nausea, vomiting, and bleeding.
- A possible case was a person with headache and/or fever for at least 24 hours, with or without other signs and symptoms, who had contact with a proven or probable case in the preceding three weeks.

Question 8: How would you proceed with the investigation at this point?

TIME

The teams conducted active case finding in over 250 villages in the region of Yambuku. As a result, they identified 463 cases meeting one of the case definitions. Of these cases, 38 met the definition for a proven case, 280 for a probable case and 155 for a possible case. A summary of the proven and probable cases by date of onset of disease is given below:

Table 1
Incidence and Outcome of Hemorrhagic Fever
By Date of Onset, Zaire, September and October, 1976

Onset Date	# proven and probable cases		
	Total	Deaths	Survivors
September			
1	1	1	0
2	2	2	0
3	2	2	0
4	1	1	0
5	4	4	0
6	3	3	0
7	6	6	0
8	5	5	0
9	6	6	0
10	8	8	0
11	7	6	1
12	10	10	0
13	9	9	0
14	13	13	0
15	11	11	0
16	10	10	0
17	9	9	0
18	9	9	0
19	14	14	0
20	12	11	1
21	12	12	0
22	15	15	0
23	18	18	0
24	22	22	0
25	14	13	1
26	10	10	0
27	8	7	1
28	5	4	1
29	6	4	2
30	4	3	1

Onset Date	# proven and probable cases		
	Total	Deaths	Survivors
October			
1	7	4	3
2	3	2	1
3	4	4	0
4	5	3	2
5	5	3	2
6	8	5	3
7	3	2	1
8	4	3	1
9	3	2	1
10	5	2	3
11	4	2	2
12	3	1	2
13	1	1	0
14	2	1	1
15	1	0	1
16	0	0	0
17	0	0	0
18	0	0	0
19	2	0	2
20	0	0	0
21	1	0	1
22	0	0	0
23	1	0	1
24	0	0	0
Total	318	283	35

Question 9a: Draw an epidemic curve. Indicate those cases which were fatal and those which survived.

Question 9b: Describe the epidemic curve. What does it suggest about the nature of the disease?

The Yambuku Mission Hospital was established by Belgian missionaries in 1935 in the Yandongi collectivity (county), one of seven in the Bumba zone. It serves as the principal source of medical care for 60,000 people in Yandongi and adjacent collectivities. Because it maintained a good supply of medicines, people passing through Bumba zone frequently travelled long distances to attend clinics there. At the time of the current epidemic, the hospital had a staff of 17, including a Zairian medical assistant and three Belgian nurse midwives. There was an active prenatal clinic that treated 6,000-12,000 patients each month.

Question 10: As mentioned earlier in the exercise, the Yambuku hospital had closed on September 30 following the death of 13 of the 17 staff members. Mark the date of hospital closing with an arrow on your epidemic curve and calculate the case-fatality rates through September 29, then for September 30 on. How would you interpret these data?

PERSON

The following table lists the number of proven and probable cases according to sex and age:

Table 2
Distribution of Hemorrhagic Fever by Age and Sex, Zaire, 1976

Age (years)	Male		Female		Total	
	Number	Percent	Number	Percent	Number	Percent
< 1	10	3%	14	5%	24	8%
1 - 14	18	6%	25	8%	43	14%
15 - 29	33	10%	60	19%	93	29%
30 - 49	57	18%	52	16%	109	34%
50+	23	7%	26	8%	49	15%
Total	141	44%	177	56%	318	100%

Question 11: What conclusions can you draw from this table?

Question 12: What additional information, if any, would help you to analyze these data?

PART IV

Table 3
Population in the Epidemic Zone By Age and Sex, Zaire, 1976

Age (years)	Male	Female	Total
< 1	800	850	1,650
1 - 14	8,200	8,150	16,350
15 - 29	5,500	6,000	11,500
30 - 49	6,250	6,750	13,000
50 +	3,000	4,500	7,500
Total	23,750	26,250	50,000

Question 13: Using the data in Tables 2 and 3, calculate age- and sex- specific attack rates (per 1000) for each group in Table 4. What conclusions can you draw from this information?

Table 4
Hemorrhagic Fever Attack Rates (Per 1,000) By Age and Sex, Zaire, 1976

Age (years)	Male	Female	Total
< 1			
1 - 14			
15 - 29			
30 - 49			
50 +			
Total			

PLACE

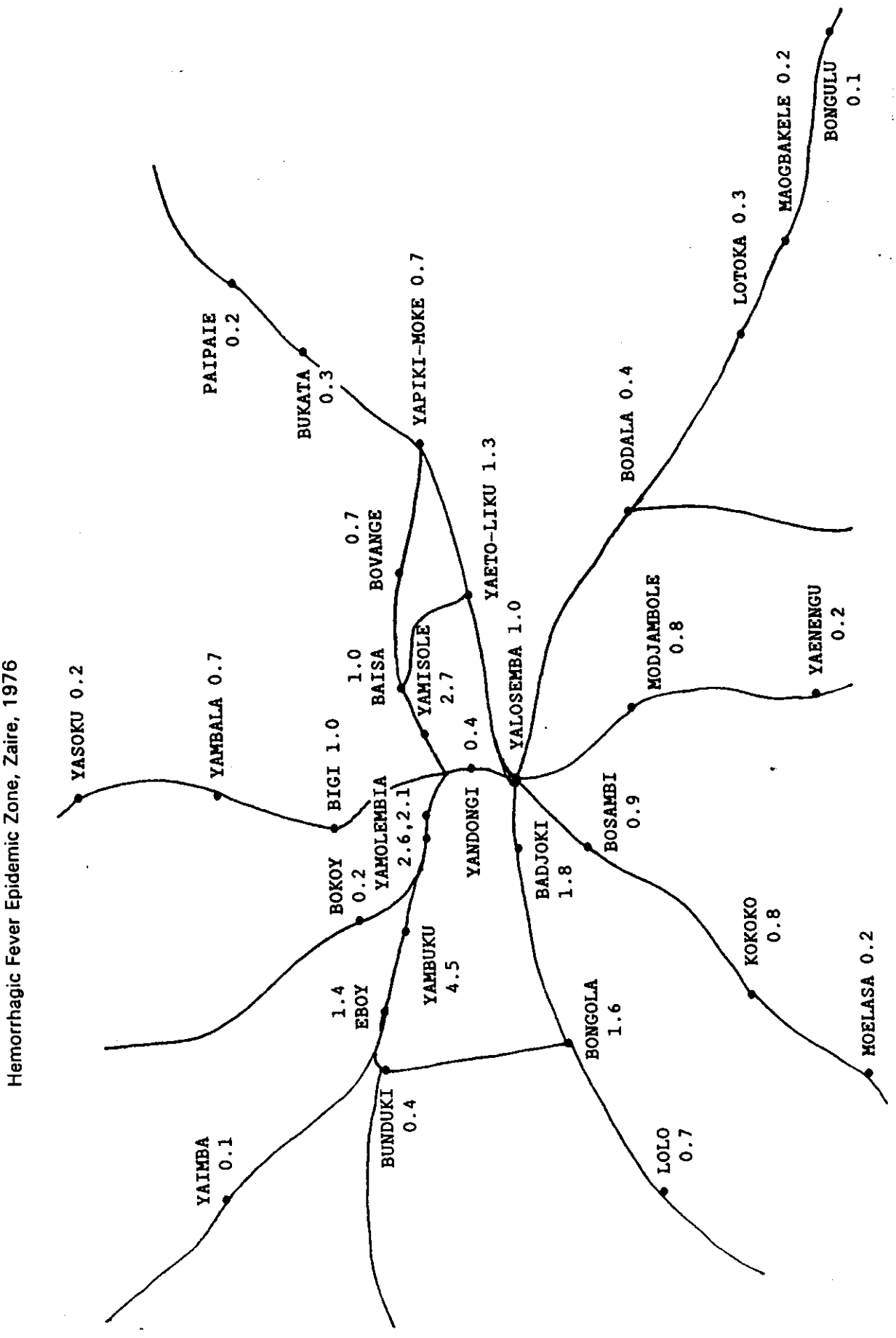
The attached figure shows the location of villages that had one or more cases during the epidemic, with the overall attack rate (in per cent) listed for each. These villages contained 42,264 (85%) of the estimated 50,000 persons living in the epidemic zone. The remaining 7,736 inhabitants live in eight non-infected villages. Other than Kinshasa, no towns outside the epidemic area were found to contain cases.

Question 14: What conclusions regarding place of onset and risk of disease seem warranted?

Question 15: Summarize the information regarding time, place and person and risk of disease.

Question 16: At this point in the investigation, what hypotheses would you consider regarding mode of transmission of this illness?

Question 17: How would you investigate these hypotheses?


Hemorrhagic Fever Epidemic Zone, Zaire, 1976
YASOKU 0.2
YAMBALA 0.7
BIGI 1.0
BOKOY 0.2
YAMOLEMBIA 2.6,2.1
1.4 EBOY
YAIMBA 0.1
BUNDUKI 0.4
YAMBUKU 4.5
YANDONGI 0.4
1.0 BAISA
0.7 BOVANGE
YAMISOLE 2.7
PAIPAIE 0.2
BUKATA 0.3
YAPIKI-MOKE 0.7
YAETO-LIKU 1.3
YALOSEMBA 1.0
BADJOKI 1.8
BONGOLA 1.6
LOLO 0.7
BODALA 0.4
BOSAMBI 0.9
MODJAMBOLE 0.8
KOKOKO 0.8
LOTOKA 0.3
YAENENGU 0.2
MAOGBAKELE 0.2
BONGULU 0.1
MOELASA 0.2

PART V

A case-control study was undertaken to determine whether exposure to a case and/or exposure to the Yambuku Mission Hospital were associated with development of disease. Data were obtained from each proven and probable case, and from a control matched to each case by age, sex, and village. The data were properly analyzed in matched fashion, but are presented unmatched to facilitate analysis in this case study. (The results are similar.)

Table 5a
Exposure to Yambuku Hospital Among Cases and Controls,
Hemorrhagic Fever Investigation, Zaire, 1976

		CASES	CONTROLS
EXPOSURE TO YAMBUKU HOSPITAL	YES	128	26
	NO	190	292
		318	318

Table 5b
Exposure to Persons with Hemorrhagic Fever (HF) Among Cases and Controls,
Hemorrhagic Fever Investigation, Zaire, 1976

		CASES	CONTROLS
EXPOSURE TO PERSON WITH HF	YES	192	30
	NO	126	288
		318	318

Question 18: Analyze these data by calculating a measure of association and test of statistical significance. Is contact with the hospital a risk factor? Is contact with a person with hemorrhagic fever a risk factor?

Forty-three cases and 4 controls were exposed both to the hospital and to a person with hemorrhagic fever.

Question 19: How might you disentangle the effects of the two exposures? Set up the proper analysis.

The following table presents the distribution of incubation periods among the 318 cases.

Table 6
Distribution of Incubation Periods*,
Hemorrhagic Fever, Zaire, 1976

Incubation Period (Days)	# Cases
3	5
4	12
5	18
6	58
7	22
8	24
9	85
10	80
11	9
12-15	5

* Interval from first contact at hospital and/or person with disease to date of onset

Question 20: Using the data in Table 6, graph, describe, and interpret the data on incubation period of the disease.

PART VI - CONCLUSION

The investigators conducted a case-control study within the hospital to identify factors associated with spread of infection. All 85 cases who had contact with the Yambuku mission hospital but not with another case had received one or more injections at the outpatient service or the general medical wards. Fewer than 1% of controls had received injections at the hospital during the epidemic.

The index case occurred in a 44-year-old male instructor at the mission school who presented to the outpatient clinic at Yambuku Mission Hospital on August 26th with a febrile illness thought to be malaria. This man had recently returned from a tour of the Mobaye-Bongo zone in the northern equator region. He was given chloroquine by parenteral injection on 26 August. His symptoms worsened on September 1st, and he died on September 8th.

The next 9 cases which occurred during the first week of September were all among individuals who received injections at the outpatient clinic of the hospital. In total, 22 of the females in the 15 - 29 year old group acquired their disease by injection, most of which were administered at pre-natal visits. Only two of the male cases age 15 - 29 years acquired disease through this mode of transmission.

Investigation revealed that parenteral injection was the principal mode of administration of nearly all medicines at the mission hospital. Each morning five syringes and needles were issued to the nursing staff for use at the outpatient department, the prenatal clinic, and the inpatient wards. These syringes and needles were apparently not sterilized between use on different patients but rinsed in a pan of warm water instead. At the end of the day they were sometimes boiled. The surgical theater had its own supply of instruments, syringes, and needles, which were stored separately and autoclaved after use.

Virus transmission was interrupted by stopping injections and by isolation of patients in their villages. Use of protective clothing and respirators, strict isolation of hospitalized patients, and careful disposal of potentially contaminated fomites may also have helped in controlling the epidemic.

The virus responsible for this illness was named Ebola virus, after the name of a small river a few kilometers from Yambuku. Ongoing studies in Zaire, Sudan, Central African Republic and Cameroon are investigating the nature of this disease, which since 1976 has been shown to be endemic in the Congo river basin. An epidemic of Ebola disease occurred in southern Sudan in 1979 and consisted of 33 confirmed cases with a case fatality rate of 67%. The low frequency of person-to-person transmission of Ebola virus, along with the high mortality rate, indicates that the agent probably has an animal or some other reservoir in nature, although animals and insects appeared to have no role in transmission during the epidemic.

The International Commission was disbanded on January 1977 following an investigation involving hundreds of persons and costing more than one million dollars. The following recommendations were made to the Government of the Republic of Zaire:

1. Maintain active national surveillance for acute hemorrhagic disease. Require regular positive and negative reporting. Investigate all suspected cases and take appropriate action including collection of diagnostic specimens, institution of clinical isolation procedures, and the use of protective clothing for medical personnel.

2. Distribute pertinent information to medical and other personnel participating in surveillance and update this material by appropriate documents.

3. Organize a national campaign to inform health personnel of the proper methods for sterilizing syringes and needles in order to ensure that patients are not infected with diseases from other patients as a result of poor technique.

4. Maintain a list of experienced Zairian personnel so that the appropriate action can be taken without delay in the event of a new epidemic.

5. Maintain a stock of basic medical supplies and protective clothing for use of suspected outbreaks.

6. Keep plasma from immune donors in readiness and obtain further information concerning the effectiveness of this treatment.

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