Suspected Legionnaires' Disease in Bogalusa
A *Disease Detectives* Exercise from the
Centers for Disease Control and Prevention

PART 1
(Time to completion: 10 minutes)

On October 31, 1989, two physicians in Bogalusa, Louisiana, reported more than 50 cases of acute pneumonia (severe infection of the lungs) to the state health department. Most cases had occurred within a 3-week interval in mid- to late-October. All of the patients were adults; six had died. Information from several patients suggested that the cause of the illness may have been legionellosis, a disease caused by infection with the bacterium Legionella pneumophila.

You are the EIS Officer (CDC disease detective) assigned to the Louisiana health department who received the telephone calls from the concerned physicians.

1. What additional information do you need to decide whether or not this is a real public health problem? Base your answer on the scientific method used by disease detectives when they investigate an outbreak.

*This exercise is adapted for high school use from an investigation conducted in Bogalusa, Louisiana, in 1989. The original case study is used each year in CDC's Epidemic Intelligence Service (EIS) Summer Course, which trains incoming EIS Officers.

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PART 2
Distribute this part only after completion of Part 1
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Serologic testing is the analysis of samples of blood serum for the presence of antibodies to specific disease agents, including bacteria and viruses. Antibodies that indicate recent infection are called IgM class; antibodies indicating infection in the more distant past are called IgG. In Bogalusa, blood samples from several patients during the earliest (acute) phase of illness were negative for antibody to the Legionella bacterium (note, however, that for most infectious diseases, antibodies cannot be detected during the first few weeks of illness). No sputum (substances produced by the lining of the lungs and other parts of the respiratory tract) specimens had been collected for Legionnaires' testing because the hospital's laboratory was not equipped to perform the tests.

2. What else, other than a true outbreak, could account for a sudden increase in the number of cases of a disease being reported to a health department?

3. Before leaving your office to begin the investigation in Bogalusa, what preparation do you need to make?

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PART 3
Distribute this part only after completion of Part 2
(Time to completion: 15 minutes)

Background on Legionnaires' Disease
The following information about Legionnaires' disease is abstracted from Control of Communicable Diseases in Man, 16th edition. In an actual epidemiologic investigation, you might consult a reference publication such as this to refresh your memory on pertinent details about a specific disease:

> Legionnaires' disease is characterized by pneumonia caused by the bacterium Legionella pneumophila. The name "Legionnaires' disease" was given to this illness following a large outbreak among people attending a convention of American Legion military veterans in Philadelphia, Pennsylvania, in July 1976.
>
> The incubation period (time between exposure to an infectious agent and becoming ill) for Legionnaires' disease ranges from 2 to 10 days. The disease often begins with loss of appetite, malaise (fatigue and generally feeling unwell), muscle aches and soreness, and headache. These symptoms are followed by rapidly rising fever and chills. Chest X-rays usually show patchy areas of inflammation and fluid accumulation in the lungs. The diagnosis is confirmed by
>
> - isolating the bacterium on special culture media; or
> - showing that the bacterium is present by using an immunofluorescent stain on involved tissue or respiratory secretions; or
> - finding a four-fold or greater increase in titers (antibody levels) in serum samples taken between the acute (early illness) and convalescent (usually 3-4 weeks after the acute period) phases of the disease; or
> - finding a single high titer in a patient with symptoms or signs of Legionnaires' disease
>
> Cases of Legionnaires' disease occur individually and in outbreaks. L. pneumophila is airborne and grows easily in systems that use water. The bacterium gets into the air through aerosole-producing devices, such as hot water systems, air conditioning cooling towers, or evaporator condensers. Consequently, it can be transmitted rapidly to a number of people. When outbreaks are detected, the source must be found quickly and then decontaminated to prevent widespread infection.

Some people are at particularly high risk of becoming seriously ill if they become infected. These include 1) older people, especially older smokers; 2) people with diabetes, chronic lung disease, kidney disease, or cancer; and 3) people with weak immune systems. Men are usually about two-and-a-half times more likely than women to be affected by L. pneumophila.

Background on Bogalusa

Bogalusa is located in Washington Parish and has a population of about 16,000. The largest employer, a paper mill, is located in the center of town adjacent to the main street and includes five prominent industrial cooling towers. These towers and the mill's three paper machines emitted large volumes of aerosol along the main street. Many people suspected these aerosal sources had caused the outbreak. A few public buildings with cooling towers were also considered potential sources.

Bogalusa had a 98-bed private hospital (Hospital A) and a 60-bed public hospital (Hospital B). Three additional hospitals were in the surrounding parish. All of the patients with Legionnaires' disease were at Hospital A. Table 1 shows the number of patients discharged with a diagnosis of pneumonia at Hospital A since January 1986. Between January 1986 and September 1989, only one pneumonia patient was diagnosed as having Legionnaires' disease.

Table 1. Number of Patients Diagnosed with Pneumonia Discharged from Hospital A, by Month, January 1986 – October 1989

	1986	**1987**	**1988**	**1989**
January	12	20	21	16
February	14	19	26	19
March	7	21	8	27
April	12	10	11	13
June	4	11	11	6
July	5	5	9	8
August	5	9	12	7
September	6	7	13	8
October	15	8	10	70
November	?	8	11	
December	?	11	20	
Total	**75**	**129**	**153**	**174**

Review of charts for pneumonia patients at Hospital A during October revealed that many patients were admitted with a febrile illness (i.e., an illness especially including fever) characterized by weakness, lethargy, and mental confusion. Some patients had a dry cough, and several reported having watery diarrhea. Chest X-rays were consistent with pneumonia. Most patients were residents of Bogalusa or the surrounding areas of Washington Parish.

4a. What are possible interpretations for the data in Table 1?

4b. If you wanted to intensify the investigation, what steps would you take next?

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PART 4
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5. Would you want a relatively sensitive or a relatively specific case definition in this setting? With your decision in mind, develop a case definition for this outbreak.

Tip: A "sensitive" case definition is broad enough to identify nearly all true cases ("true positives") of the disease being investigated. However, because it is so broad, a sensitive definition may also draw in similar illnesses with different causes (known as "false positives"). In contrast, a "specific" case definition is narrow enough to exclude false positives, but may exclude some true positives that have slightly unusual symptoms.

6a. How would you go about case-finding?

6b. Do you need to find every case?

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PART 5
Distribute this part only after completion of Part 4
(Time to completion: 10 minutes)

The Louisiana health department chose to lead the epidemiologic investigation, but they asked for laboratory support from CDC. CDC also sent a second EIS Officer from Atlanta to help with the investigation. The field investigation team arrived in Bogalusa on November 8.

The EIS Officers were given the opportunity to address the hospital staff about the outbreak. In addition to being certain that hospital staff could recognize (diagnose) and appropriately treat patients with Legionnaires' disease, the investigators needed to enlist their support, cooperation, and assistance. Some of the points they covered during the meeting were

- what to look for when diagnosing Legionnaires' disease and what specimens are needed for lab tests;
- the risks and sources for infection and the fact that Legionnaires' disease is not spread directly from person to person;
- how to report cases to public health authorities and why it is important to do so promptly;
- how to treat the infection (the antibiotic erythromycin is recommended);
- what they knew to date about the outbreak; and
- plans for the continuing epidemiologic investigation.

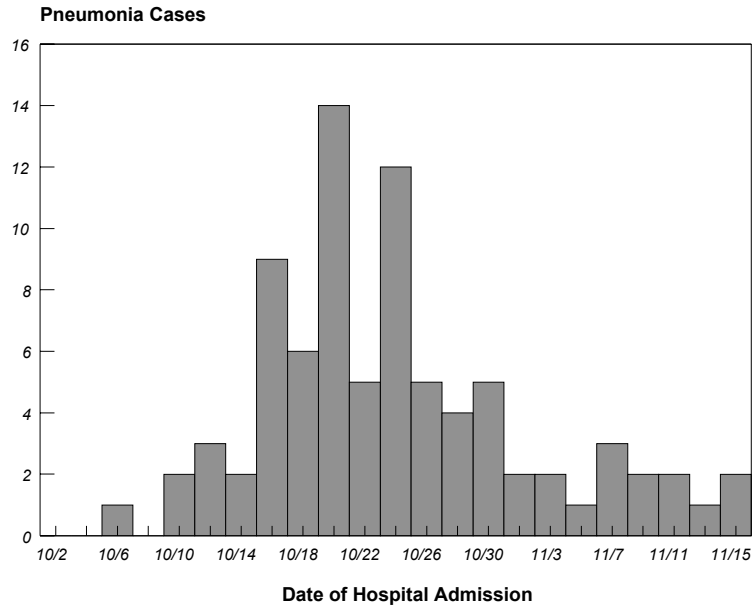
The investigators set up active surveillance (ongoing collection, analysis, and dissemination of data on illness) for finding cases at all five local hospitals. They also used a questionnaire to abstract information from medical records on everyone admitted or discharged with a diagnosis of pneumonia, respiratory distress, or possible Legionnaires' disease since October 1, 1989.

A **possible case** of Legionnaires' disease was defined as illness in a resident or visitor of Washington Parish who (1) was 20 years of age or older, (2) was admitted to one of the five local hospitals after October 1, 1989, and (3) had an X-ray or a chest radiograph that indicated pneumonia. **A confirmed case** had to meet the criteria for a possible case, plus there had to be lab evidence of Legionnaires' disease.

By November 19, the team had identified 83 patients who met the "possible case" definition, fourteen of whom had died without being tested for Legionella. Of the 83 patients, 65% were female. About 75% of the patients lived in Bogalusa, and about half (41) lived on the east side of town. Most patients had been admitted to the hospital in mid-October, and by mid-November, there were few if any new cases (see Figure 1). To date, no sputum culture had shown growth for Legionnaires' disease or other pathogens.

Before designing the method they would use to analyze the investigation, the team considered their leading hypotheses.

Figure 1. Epidemic curve of pneumonia outbreak, Bogalusa, Louisiana, 1989



7a. How would you generate plausible hypotheses to test in this type of investigation?

7b. What, if any, are your ideas at this point?

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PART 6
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(Time to completion: 10 minutes)

At this point in the investigation, the leading hypothesis was outdoor exposure to cooling towers—primarily because previous studies had demonstrated the role of cooling towers as a source of Legionella pneumophila in other outbreaks, and there were several such towers in the town. Rather than jumping to conclusions, however, investigators began to compile a list of retail stores and other commercial establishments that were frequently mentioned by some of the case-patients who had been interviewed. Investigators also noted the unusual preponderance of women who had become ill.

8. Would you use a case-control study, a cohort study, or some other method to test the hypotheses in this outbreak? Why?

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PART 7
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(Time to completion: 10 minutes)

The investigators conducted a case-control study. They found that 66 of the patients who were still living met the "possible case" definition. Laboratory results confirmed that 15 of these patients had Legionnaires' disease and ruled out the disease for 10. The results for the remaining 41 were pending.

9. What case definition would you use for your case-control study?

10. What are some possible sources of controls?

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PART 8
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(Time to completion: 15 minutes)

Investigators decided to select controls from office records of physicians who had admitted the patients with Legionnaires disease to the hospital. They enrolled two controls per case, for a total of 28 case-patients and 56 controls. Case-patients and controls were asked about exposures to cooling towers and nearby buildings. Among their findings, they learned that

- 3 of the 28 case-patients and 7 of the 56 controls reported visiting Hospital B, and
- 7 of the case-patients (1 was unsure) and 12 of the controls (6 were unsure) reported visiting the Post Office.

11a. Calculate the odds ratios for illness with Legionnaires' disease among people who visited Hospital B and those who visited the Post Office.

11b. Why might the numbers of cases and controls in these two odds ratio calculations differ? How would you interpret the results?

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PART 9
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(Time to completion: 15 minutes)

After investigators interviewed all case-patients and controls, they calculated odds ratios for each exposure for both groups. Their results follow:

Table 2. Exposures to buildings, Legionnaires' disease outbreak, Louisiana, 1989

	Cases Exposed/Total (%)	Controls Exposed/Total (%)	Odds Ratio	P-value
Indoor exposure to buildings with cooling towers				
Retail Store A	3/28 (11%)	10/54 (19%)	0.5	0.5
Post Office	7/27 (26%)	12/50 (24%)	1.1	0.9
Hospital A	5/28 (18%)	12/54 (22%)	0.8	0.9
Hospital B	3/28 (11%)	7/56 (13%)	0.8	1.0
Paper Mill	2/28 (7%)	4/56 (7%)	1.0	1.0
Outdoor exposure to stores near paper mill cooling towers				
Retail Store A	3/28 (11%)	10/54 (19%)	0.5	0.5
Retail Store B	10/28 (36%)	15/52 (29%)	1.4	0.7
Retail Store D	5/28 (18%)	7/54 (13%)	1.5	0.5
Retail Store E	6/28 (21%)	9/54 (17%)	1.4	0.8
Restaurant A	2/26 (8%)	5/52 (10%)	0.8	1.0
Bank A	11/28 (39%)	19/53 (36%)	1.2	0.9
Butcher Store A	12/27 (44%)	10/54 (19%)	3.5	0.03
Any of the above	19/28 (68%)	33/56 (59%)	1.5	0.6
Outdoor exposure to stores near other large cooling towers				
Drug Store A	7/28 (25%)	15/55 (27%)	0.9	1.0
Drug Store B	13/28 (46%)	20/54 (37%)	1.5	0.6
Doctors Plaza A	2/27 (7%)	8/56 (14%)	0.5	0.5
Retail Store F	4/28 (14%)	6/54 (11%)	1.3	0.7
Exposure to stores frequently reported by case-patients				
Grocery Store A	25/27 (93%)	28/54 (52%)	11.6	<0.01
Grocery Store B	19/28 (68%)	23/54 (43%)	2.9	0.05
Retail Store C	22/28 (79%)	30/54 (56%)	2.9	0.07

12. How would you interpret these data? In other words, which exposures suggest an association with illness, which one accounts for the greatest number of cases, and what are the implications?

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PART 10
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(Time to completion: 15 minutes)

Additional epidemiologic analysis showed a dose-response relationship between time spent in Grocery Store A and risk of disease—that is, there was a direct relation between the amount of time people spent in the store and their risk for disease. The investigators visited Grocery Store A and looked for sources of water in aerosol form. An ultrasonic mist machine was operating over one section of the produce display. No one at Grocery Store A was familiar with the maintenance or operation of this machine. With permission from the store manager, investigators cultured a specimen of water from the mister's reservoir. The culture contained Legionella pneumophila serotype 1 (LP-1). Cultures from various cooling towers around town also contained LP-1, but of different subtypes. The investigators suspected that the misting device may have been related to the outbreak.

13a. At this point, do you have enough information to make recommendations—in other words, have the basic criteria of causation been satisfied?

13b. How would you proceed with this investigation?

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PART 11
Distribute this part only after completion of Part 10
(Time to completion: 10 minutes)

Before making any recommendations, the disease detectives took four additional steps:

- They conducted a serosurvey on all of the grocery store employees in Bogalusa. (In a serosurvey, blood samples from a specific group of people are analyzed for antibodies to a particular bacteria. In this study, technicians looked for antibodies against LP-1.)
- They conducted a second case-control study to determine whether exposure to Grocery Store A's misting device was associated with developing Legionnaires' disease.
- They cultured ten similar misting devices from other parts of the country.
- They asked for permission to perform autopsies on two patients who had died of pneumonia early in the outbreak.

Here is what the investigators found:

- The serosurvey showed that employees at Grocery Store A were three times more likely than employees at the other grocery stores to have elevated antibody titers to Legionella. This finding (3 to 1) is the prevalence ratio, or the ratio of the prevalence of antibody, in each group. The p value, or probability that these findings are significant, is 0.02.

Here is how the prevalence ratio was calculated: Analysis of the blood samples showed that 13 of the 48 (27%) employees from Grocery Store A had elevated antibody titers to Legionella. In contrast, 7 of the 75 (9%) employees from the other grocery stores had elevated antibody titers to Legionella. The ratio of these two percentages (27/9, or 3) is the prevalence ratio.

More about P values: The p value is the probability that the results are no different than they would have been as a result of chance alone. When a p value is below 0.05, the finding is considered "statistically significant," meaning that calculations show enough mathematical difference between the two groups to rule out chance and justify the hypothesis—in this case, the assumption that Legionella was the cause of the outbreak.

- Analysis of the second case-control study revealed a significant association between being sick and buying produce that was nearest the mister. Of the 10 mist machines from other parts of the country, 6 grew Legionella.

- The subtype of Legionella found in the grocery store misting device was also isolated from a small cooling tower that was far from public access and not near Grocery Store A.

- Lung tissue taken from the two autopsied patients contained the same subtype of Legionella found in Grocery Store A.

Until now, the news media had not been aware of the outbreak, the investigation, or the results.

14. Who needs to know about these findings? How would you go about reporting the findings?

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PART 12
Distribute this part only after completion of Part 11
(Time to completion: 5 minutes)

The disease detectives concluded that aerosols from the misting device had caused the outbreak, but they were reluctant to publish their finding until viable Legionella was isolated from aerosols produced by the machine. In mid-December, the machine was removed from Grocery Store A and sent to CDC for further study, but proof that it was contaminated with Legionella would take several weeks. Given the likelihood that other mist machines were contaminated, the Food and Drug Administration was notified. They, in turn, developed guidelines for maintaining these machines.

In early January, the Bogalusa newspaper printed the first article about the outbreak, without knowing its cause. This story was quickly picked up by the New Orleans paper and national news services. Soon, Bogalusa was overrun by reporters wanting to find out the cause of the outbreak. They focused their attention on the paper mill in the center of town and demanded to know the culture results from the cooling towers.

The Louisiana state health department issued a press release and notified other health officials through electronic mail about the mist machine findings. Grocery industry officials were notified about the potential problem in trade newspapers and at meetings. The electronic mail message became public and was widely quoted in newspaper articles.

The type of misting device implicated in the outbreak was new to the grocery industry and served no purpose except to attract shoppers. It did not help to preserve produce. The health department received reports of similar types of machines used in other settings, such as amusement parks and indoor aquariums. The findings were published in CDC's weekly bulletin, the Morbidity and Mortality Weekly Report (MMWR), after laboratory staff were able to isolate Legionella organisms from aerosols produced by the machine. The Journal of Infectious Diseases also published the findings in order to reach an even wider audience of health care professionals and to ensure that physicians specializing in the treatment of Legionnaires' disease and other infectious diseases were aware of this previously unrecognized vehicle for transmitting Legionella.