Chapter 2

Introduction to Outbreak Investigations

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Learning Objectives

By the end of this chapter, the reader will be able to:

- Define the terms "epidemic," "outbreak," "case," and "cluster" from an epidemiological perspective.
- Describe factors that are used to determine the existence of an outbreak.
- List several ways that outbreaks are detected.
- Explain why it is important to investigate outbreaks.
- List and describe the basic components of an outbreak investigation.
- Describe how John Snow followed the processes of an outbreak investigation in his groundbreaking study of London's 1854 cholera outbreak.

Introduction

The terms "outbreak" and "epidemic" have become part of the world's general vocabulary, used broadly and frequently to describe health, financial, and social maladies—"an epidemic of obesity among our children," "an outbreak of corporate corruption," "an epidemic of failed marriages." The word "outbreak" gets our attention and indicates that something is awry. But what is an outbreak from an epidemiologic point of view, and how do we determine if an event or observation represents an outbreak? In this chapter, we define the key terms associated with outbreak investigations, discuss the importance of investigating outbreaks, outline the basic processes of an outbreak investigation, and describe how the pioneering epidemiologist John Snow followed these processes in his 1854 investigation of a cholera outbreak in London.

What Is an Outbreak?

To understand the concept of an outbreak, first we need to understand the epidemiological definitions of a few basic terms.

Outbreaks and Epidemics

An outbreak is an increase—often sudden—in the observed number of cases of a disease or health problem compared with the expected number for a given place or among a specific group of people over a particular period of time.[1] The definition of "epidemic" is essentially identical to that of "outbreak": "[t]he occurrence in a community or region of cases of an illness, specific health-related behavior, or other health-related events clearly in excess of normal expectancy."[2] The term "outbreak" may be used interchangeably with "epidemic," although public health officials often prefer "outbreak" to describe a localized epidemic, meaning one that is limited to a village, town, or specific institution. Investigators determine whether an epidemic (or outbreak) is taking place (or has taken place) by determining whether the number of cases of a certain disease—in a certain area, among a specific population, during a certain time of the year—is significantly greater than usual.[2]

If an outbreak or epidemic occurs over a very wide area, affecting a large proportion of the population in several countries or continents, the Director-General of the World Health Organization (WHO) has the responsibility to declare it a "pandemic" (*pan* = all and *demos* = people).[3] An example that predates the founding of WHO is the influenza pandemic of 1918, which killed an estimated 50 million people as it swept through North America, Europe, Asia, Africa, Brazil, and the South Pacific.[4] More recent examples of globe-spanning epidemics include the "Asian flu" pandemic of 1957–1958, the "Hong Kong flu" pandemic of 1968, and the emergence of influenza A (H1N1), which the WHO declared a pandemic in June 2009.[5] While infection with human immunodeficiency virus (HIV) is sometimes referred to as a "global epidemic" rather than a pandemic, an estimated 33 million people around the world were living with HIV in 2007.[6]

Declaring the existence of a pandemic can be controversial. When the global outbreak of H1N1 in 2009 turned out to be not as severe as expected, for example, some critics accused WHO of exaggerating the dangers of the virus under pressure from drug companies. In response, WHO announced early in 2010 that it would review the way it dealt with the outbreak once the pandemic had subsided.[7]

A health department may be called upon to investigate a wide variety of unusual health events, such as outbreaks due to food poisoning, geographic clusters of cancer, or a mysterious rash illness in a school. Although this book focuses mainly on infectious diseases, be aware that the terms "outbreak" and "epidemic" do not pertain only to communicable diseases. That is, these terms can be applied to noninfectious diseases such as cancers, nutritional deficiencies, smoking, or low-birth-weight babies. (We address investigating noncommunicable disease events in Chapter 13.) To suspect an epidemic or outbreak, public health officials need simply see an increase in the number of cases above what is expected for a given group for a given period of time.

Case

In epidemiology, the term "case" describes the particular disease, health disorder, or condition under investigation; it is also often used to describe a person in a population or study group who is identified as having the disease, disorder, or condition.[2] (In case-control studies, which are discussed in Chapter 7, cases may also be referred to as "patients in the case group" or "case patients."[8]) Investigators classify cases or case patients based on the case definition they develop as they explore a potential outbreak. A case definition takes into account the signs and symptoms of the disease or condition, as well as important epidemiologic characteristics of the patient—the "what, who, where, and when" of a disease outbreak. (Case definitions are described in detail in Chapter 4.) The epidemiological definition of a case is not the same as the normal clinical definition that physicians or other healthcare providers might use, although it may be similar.

Cluster

Outbreak investigations often begin when investigators identify a suspected cluster of cases of a disease. A cluster is a geographical or temporal collection of cases that seem to be greater than the expected number for the given place and/or time. The many challenges of an outbreak investigation often begin with determining whether a suspected cluster is a true cluster.

When Does a Number of Cases Become an Outbreak?

Understanding these terms leads us to the first hurdle of an outbreak investigation—determining whether an outbreak is under way. This task is more complicated than simply counting cases. Potential outbreaks may be true outbreaks with a common cause, or they may be unrelated cases of the same disease. In general, the key determinant that an outbreak is under way is whether the number of cases is "unusually high" or falls within the expected range of cases for that population at that time of year. Before declaring an outbreak, investigators must take many factors into account:

- The etiologic agent
- The size and composition of the population
- The previous occurrence of the disease in the community
- The season

The *etiologic agent* is the pathogen that is causing the disease. Investigators need to know the agent's identity, and they need to determine whether it is rare or common. When a disease is relatively common, such as genital herpes or seasonal influenza, there may need to be a very large number of cases or the cases may need to be uniquely related before public health officials will consider them to represent an outbreak. In contrast, for rare diseases such as botulism, polio, smallpox, or anthrax, health officials may treat even a single case as an outbreak and embark on urgent health action. For example:

- Public health officials may act promptly when a single case of botulism is reported, by ordering the recall of contaminated commercial products or the destruction of contaminated home-canned goods, so as to prevent other people from becoming ill.[9]
- Although polio was eliminated in the United States in 1994, it continues to afflict children in Asia and Africa; U.S. public health officials remain vigilant for its return to this country, knowing that new cases of the disease are just a plane ride away.[10]
- A single case of smallpox would cause a worldwide alarm: The disease has not been diagnosed in the United States since 1949, and the last naturally occurring case in the world was in Somalia in 1977. Officials remain concerned that laboratory stocks of the virus that causes smallpox could be used as an agent of bioterrorism.[11]
- Four cases of inhalational anthrax detected in 2001 were the first confirmed cases of anthrax associated with intentional exposure in the United States. (Humans generally become infected when they come into direct contact with *Bacillus anthracis* spores from infected animals.) The discovery that anthrax had been used in a suspected case of bioterrorism led to a widespread criminal investigation and a rapid public health response to detect and treat additional cases.[12]

The *size and composition of the population* is another important factor in determining whether an outbreak is under way. Investigators need to learn quickly how many and which groups of people are becoming ill. Size matters: Obviously, 1,000 cases of influenza are likely to be of more concern in a community of 50,000 than in a city of 500,000. Likewise, an increase in the number of cases of a given disease must be considered in relation to changes in population size. For example, a college town is likely to have more reports of disease when school is in session than during the summer break or over the winter holidays. The make-up of a population is also important. Population characteristics such as age distribution and socioeconomic status can influence disease rates. For example, researchers who studied an increase in cases of tuberculosis in New York City from 1984 to 1992 found a strong association between poverty and tuberculosis.[13]

Previous occurrence of a disease in the community is a third factor in determining whether an outbreak is under way. Before investigators decide whether a certain number of cases constitutes an outbreak, they must know whether and how often the disease has been diagnosed in the community in the past. For example, if 51 cases of a disease are confirmed in one month in a county that averages 12 cases of the disease each month, and there are no errors in laboratory identification or reporting procedures, then it is likely the 51 cases represent an outbreak.

The *season* is the final determinant. Because the incidence of many types of infectious disease rises and falls seasonally, investigators must take the time of year into account when they explore a potential outbreak. The same number of cases of influenza, for example, might be "expected" for winter but "greater than expected" for summer.

Sometimes it is a relatively simple matter for investigators to determine whether a cluster of cases is an outbreak, but often it is not. For example, public health officials might suspect that a number of cases of severe respiratory illness signals an influenza outbreak. Upon closer examination, however, one case might be a severe cold, another might be bronchitis, a third might be pneumonia, and so on. Many people might be ill, but there would be no evidence of a specific outbreak. Apparent outbreaks of gastrointestinal illness can also be difficult to confirm. If everyone at the company picnic develops diarrhea, it may be relatively easy to determine that everyone who ate the potato salad got ill. If the cases are more widely scattered, however, or if the agent that caused people to become ill is not readily apparent, additional epidemiological detective work might be necessary. In a suspected outbreak of gastrointestinal illness, for example, investigators might need to order laboratory tests for diarrhea-causing pathogens and interview case patients to identify possible common exposures.

How Are Potential Outbreaks Detected?

Public health officials identify potential outbreaks in a variety of ways—through surveillance or health information systems, clinical laboratories, affected citizens, and astute healthcare providers, for example.

As discussed in Chapter 3, outbreaks are often detected through the routine and timely analysis of health information systems such as disease surveillance systems managed by state and local health departments. Health department staff may detect increases or unusual patterns of disease from weekly tabulations of case reports by time and place. Hospital administrators may discover an increased number of possible hospital-acquired infections through a weekly analysis of microbiologic isolates from patients by organism and ward or unit.

Members of affected groups are another important reporting source for apparent clusters of both infectious and noninfectious disease. A local citizen may call a health department to report that he and several co-workers came down with severe gastroenteritis after attending a banquet several nights earlier. Similarly, a community member may call to express concern that several cases of cancer diagnosed among her neighbors seem more than coincidental.

Nonetheless, many outbreaks come to the attention of public health officials because an alert clinician, infection control nurse, or clinical laboratory worker recognizes an unusual pattern of disease and notifies the health department.[14] Here is an example:

> In September 2002, a gastroenterologist contacted the Nebraska Health and Human Services System after seeing four patients who had recently been diagnosed with hepatitis C virus infection. Each patient had been treated at the same hematology/oncology clinic. A preliminary investigation revealed that 10 clinic patients had recently been diagnosed with hepatitis C virus infection, and that a

healthcare worker who administered medication infusions had repeatedly used the same syringe to draw blood from patients' catheters and catheter-flushing solution from saline bags that were used for several patients. This incident was one of several healthcare-related viral hepatitis outbreaks discovered in the United States between 2000 and 2002 because clinicians suspected that infections were healthcare related and contacted public health authorities.[15]

Physicians are not the only healthcare providers who might pinpoint potential outbreaks. Outbreaks have been detected thanks to reports from microbiologists, school nurses, and pharmacists, to name just a few of these sources. Early indications of a new disease, acquired immunodeficiency syndrome (AIDS), surfaced in 1981 when the Centers for Disease Control and Prevention (CDC) Drug Service received increased requests for pentamidine, a medication used to treat a rare form of pneumonia. (Due to the rarity of this illness at that time, the CDC Drug Service was one of the few sources for this drug in the United States.) Investigation of these requests led to a growing awareness of multiple emerging health problems among homosexual males in several major metropolitan areas. Investigation of the syndrome determined it was caused by infection with HIV.[16]

Sometimes reports from various members of the health community converge to bring an outbreak to light. In 1993, for example, the health department in Milwaukee, Wisconsin, identified a large community-wide outbreak of cryptosporidiosis—a parasitic disease characterized by severe diarrhea, cramps, and stomach upset—after receiving reports from multiple sources throughout the city. Pharmacists reported difficulty keeping over-the-counter and prescription antidiarrheal medications in stock. Clinical laboratories reported a significant increase in demand for the media used to perform routine stool cultures, resulting in requests to other labs and the Wisconsin State Laboratory of Hygiene for additional supplies. The local water authority was deluged by complaints from customers about increased water turbidity and water that tasted and smelled unpleasant. Many school nurses noted increased absences of students for diarrheal illnesses, and individual citizens jammed health department telephone lines with concerns about a diarrheal illness sweeping across their community. Before long, the health department had identified the largest waterborne outbreak of cryptosporidiosis reported in the United States—a public health emergency that affected more than 400,000 people.[17]

Most health departments have routine procedures for handling calls from healthcare providers and the public regarding potential disease outbreaks and clusters. These procedures focus on characterizing the problem—that is, determining the "what," "who," "when," "where," and "why" (or "how"):

- *What* is the problem? Is there a clinical description of the illness, including signs and symptoms, diagnosis, and duration? Was a physician consulted? Were any tests performed or any treatments provided?
- *Who* is ill and what are those individuals' characteristics (e.g., name, age, occupation)?
- *When* did the affected persons become ill?

- *Where* are the affected persons located, including residential or work locations?
- *Why* (and *how*) do patients think they became ill? What are the relevant risk factors, suspected exposures, and suspected modes of transmission? Are there clues based on who did and did not become ill?

Accurate data collection during these initial reports is critical and can be the key to the timely recognition and investigation of an outbreak.

Why Investigate Outbreaks?

It is important to investigate disease outbreaks for many reasons. Perhaps the most immediate and important motivation is that people might still be getting sick from the same cause. To prevent additional cases, investigators need to identify and eliminate the source of the problem.[14]

Here are two examples of how a thorough investigation can characterize a health problem and allow public health officials to take appropriate actions to control the problem or keep it from happening again.

Example 1

From May 1 to October 15, 2010, a multistate outbreak of *Salmonella enteritidis* associated with shell eggs caused an estimated 1,813 cases of illness across the United States. Epidemiologic investigations in 11 states identified 29 restaurants or event clusters where more than one person had eaten before becoming ill with the outbreak strain. Additional investigation of several of these clusters traced the infections to contaminated shell eggs from one of two firms in Iowa: Wright County Egg and Hillandale Farms of Iowa. Eggs from both firms were shipped to distribution centers in several states and later distributed nationwide.

Wright County Egg conducted a nationwide voluntary recall of shell eggs in August, and later expanded the recall. Hillandale Farms of Iowa also conducted a nationwide voluntary recall. The U.S. Food and Drug Administration (FDA) posted lists of the brand names under which the eggs were packaged and pointed out identifying information on the packaging. Consumers were advised not to eat any potentially contaminated eggs they had purchased but to return them to the place of purchase for a full refund.[18]

Example 2

When the Minnesota Department of Health conducted a case-control study of an outbreak of *Salmonella* cases in the state in 1994, officials found that 11 of 15 confirmed cases had eaten Schwan's ice cream. They did not discover any other risk factors. Recognizing that the outbreak could be far reaching, the Department of Health announced its existence to the public and began a full-scale investigation. Investigators carried out national surveillance and interviewed customers who had eaten the implicated manufacturer's products. They compared the steps in the manufacture of tainted ice cream with those of products that were not known to be associated with the infections. They obtained and tested cultures from ice cream samples, the ice cream plant, and the tanker trucks that carried the ice cream "premix" to the plants.

Upon completing their studies, the investigators estimated that 224,000 people had been infected across the country, and concluded that the outbreak was most likely caused by the contamination of pasteurized ice cream premix when it was transported in trucks that had previously carried nonpasteurized liquid eggs containing *Salmonella enteritidis*. They recommended steps to prevent similar outbreaks in the future. Based on their fieldwork, the investigators characterized the disease as follows:

What: Infection with *Salmonella enteritidis*

Who: 224,000 people

When: September and October 2004, within a week of consuming Schwan's ice cream

Where: Nationwide (United States)

Why: Consumption of Schwan's ice cream made with contaminated premix[19]

There are several other good reasons why public health officials should investigate outbreaks. Notably, outbreak investigations may identify risk factors associated with infection that urgently need to be contained or that are preventable in the future. Epidemiologic investigations of *Escherichia coli* O157:H7 outbreaks, for example, have identified consumption of foods such as pink ("rare") hamburger meat,[20] unpasteurized apple juice,[21] or alfalfa sprouts[22] that consumers may avoid to reduce their risk of illness.

Outbreak investigations can also identify new pathogens that infect people. The strains of HIV-1 that caused the global epidemic of AIDS have been characterized as Group M viruses, for example, but a new strain was identified in the mid-1990s that was not detected consistently by standard HIV diagnostic tests. A case in the United States involving the new type, HIV-1 Group O, was reported in Los Angeles in 1996. The patient was a woman who had come to the United States from Africa, where most of the relatively small number of infections with this type have been detected.[23] Other examples include the Ebola virus, which was discovered in 1976 when investigators searched for the cause of a new type of viral hemorrhagic fever in Africa,[24] and the severe acute respiratory syndrome–associated coronavirus, which was discovered in 2003.[25]

Moreover, outbreak investigations can provide new research insights into a disease, even if no new cases are occurring. The investigation into the first cluster of human monkeypox cases in the United States in 2003, for example, revealed an unusual transmission route: Humans contracted the disease from pet prairie dogs that had been housed or transported with African rodents. Investigators associated 35 confirmed cases reported in five Midwestern states with prairie dogs obtained from an Illinois animal distributor, or from animal distributors who purchased prairie dogs from the Illinois distributor. All of the prairie dogs that transmitted monkeypox to humans appeared to have been infected through contact with Gambian giant rats and dormice that originated in Ghana.

These investigations led to public health strategies to control the outbreak, including banning importation and prohibiting movement of the implicated animal species, enhancing restrictions on intrastate animal shipment and trade, instituting premise quarantine, and euthanizing infected animals. Some potentially exposed persons also received pre- and post-exposure vaccination with smallpox vaccine.[26] (Because the monkeypox virus is related to the virus that causes smallpox, the smallpox vaccine can protect people from getting monkeypox as well as smallpox.)

Finally, outbreak investigations provide opportunities for public health practitioners to practice the process and methods of epidemiologic investigation that are essential to protect the public health. These same skills are likely to prove valuable when practitioners are called into action after a hurricane or flood, or asked to respond to an act of bioterrorism. Training and assistance in disease outbreak investigations are available from state and federal agencies, such as the CDC, but novice investigators will also benefit immensely from working alongside more experienced practitioners on outbreak investigations. Similar to physicians who "practice" medicine for the duration of their careers, implying that their skills continue to grow with experience, public health practitioners continue to hone their practice skills primarily with experience.

The Components of an Outbreak Investigation

Once they identify an outbreak, investigators should take a systematic approach, such as the process detailed in Table 2-1. Although we list the components of the process sequentially here, these steps often occur simultaneously or may be repeated as new information is received or uncovered. Some outbreak investigations may require only a phone call or two to complete; others, as we shall see, may involve assembling a multidisciplinary

TABLE 2-1 The Basic Components of an Outbreak Investigation

1. Verify the diagnosis and confirm the outbreak
2. Define a case and conduct case finding
3. Tabulate and orient data: time, place, and person
4. Take immediate control measures
5. Formulate and test hypothesis
6. Plan and execute additional studies
7. Implement and evaluate control measures
8. Communicate findings

outbreak investigation team and collaborating with state and federal health agencies, law enforcement agencies, and others. Likewise, some investigations may require few resources in terms of time and money; others may be lengthy and expensive.

1. Verify the Diagnosis and Confirm the Outbreak

As discussed earlier in this chapter, the first essential step is to confirm the existence of an outbreak. This effort may require investigators to learn as much as possible about a specific disease, and to review existing surveillance baseline data to determine whether a suspected cluster of cases exceeds the expected number of cases. Confirming any diagnosis with a laboratory is another important early step, especially if the pathogen that is making people ill is new or unusual. Confirming that an outbreak is under way may also require reviewing medical records, talking with healthcare providers, and even talking with patients themselves. Depending on the scope of the investigation, it may be necessary to assemble a multidisciplinary outbreak investigation team and gather necessary equipment and supplies to collect clinical or environmental samples.

2. Define a Case and Conduct Case Finding

The investigation team should create a case definition and begin to identify cases that may be associated with the outbreak. The case definition may evolve as the investigation continues—early on, it might be designed broadly to identify as many cases as possible; later, the definition might be narrowed to exclude false positives (people originally thought to be part of the outbreak but who are not included as investigators receive more information).

3. Tabulate and Orient Data: Time, Place, Person

Investigators should organize information collected from medical records or patient interviews in a line listing and summarize it according to person, place, and time—that is, who is getting sick, where, and when. "Who, where, and when" are the central questions investigators must answer before they can develop and test hypotheses about the cause of the outbreak.

4. Take Immediate Control Measures

If at any point the team identifies an obvious source of contamination, the health department (and other agencies involved in the investigation) should take immediate control measures. Making public announcements about steps people can take to minimize their risk of infection and instituting plant closings or product recalls are examples of public health actions in response to outbreaks. Acting on information that can safeguard the public's health is a core responsibility of public health practitioners.

5. Formulate and Test Hypotheses

As team members gather and organize information, they should develop hypotheses about the cause of the outbreak. For example, investigators may find useful clues by researching previous outbreaks and studying the epidemiology and microbiology of the pathogen. They can gain additional insight by interviewing case patients. Conducting analytic studies such as retrospective cohort studies or case-control studies will allow the team to test one or more hypotheses.

6. Plan and Execute Additional Studies

In parallel to the epidemiologic investigation, an environmental investigation may be undertaken that includes environmental sampling. In a foodborne outbreak investigation, for example, the team should collect and test food and beverage samples as soon as possible.

7. Implement and Evaluate Control Measures

During the later stages of an outbreak investigation, the investigation team may work with government regulators, industry, and health educators to undertake control measures to prevent further illness and future outbreaks. The team should design mechanisms to evaluate the short- and long-term success of the investigation, summarize the investigation, and prepare and disseminate specific recommendations.

8. Communicate Findings

At the conclusion of the study, or earlier if necessary and appropriate, the team should prepare health promotion messages for the general public. Communication—both among team members and with the public—is essential for the success of an outbreak investigation, and the news media can be helpful in presenting information to the public.[27] The team should agree on the information to be released, and should appoint one member of the team to act as the point of contact for media inquiries.

In the coming chapters, we discuss each component of the outbreak investigation process in detail. First, however, we walk through the process, using one of the earliest and most famous historical outbreak investigations as an example. (Other well-known investigations can be found in Berton Roueche's collection, *The Medical Detectives.*[28])

Snow on Cholera

> The most terrible outbreak of cholera which ever occurred in this kingdom, is probably that which took place in Broad Street, Golden Square, and the adjoining streets, a few weeks ago. Within two hundred and fifty yards of the spot where Cambridge Street joins Broad Street, there were upwards of five hundred fatal attacks of cholera in ten days. The mortality in this limited area probably equals any that was ever caused in this country, even by the plague: and it was much more sudden, as the greater number of cases terminated in a few hours.[29]

Thus begins *On the Mode of Communication of Cholera*, Dr. John Snow's description of his investigation of the 1854 cholera outbreak in London, which is often cited as the first instance of modern infectious disease epidemiology. Using the principles of outbreak investigation outlined in the preceding section, Snow determined that the outbreak of the deadly disease was caused by fecal contamination of the water supply. More specifically, he used an analytic study design to determine which of the local water supply companies was responsible for the contamination, and convinced authorities to take action to control the outbreak.

The following case study outlines the outbreak investigation process, using Snow's experiences as examples.

1. Verify the Diagnosis and Confirm the Outbreak

Cholera is an acute, diarrheal illness that is often mild or without symptoms, but in 5% of patients it can be severe, characterized by profuse watery diarrhea, vomiting, and leg cramps. Rapid loss of body fluids leads to dehydration and shock; without treatment, death can occur within hours. The microbiological etiology of the disease, *Vibrio cholerae*, was unknown to Snow at the time. (Coincidentally, Filippo Pacini had identified *V. cholerae* during an outbreak in Florence one year earlier, in 1853. Pacini's discovery was confirmed and made widely known by Robert Koch in 1884.) Having studied several cholera outbreaks, Snow hurried to Broad Street when he learned of the new outbreak.

> There were a few cases of cholera in the neighborhood of Broad Street, Golden Square, in the latter part of August; and the so-called outbreak, which commenced in the night between the 31st August and the 1st September, was, as in all similar instances, only a violent increase of the malady. As soon as I became acquainted with the situation and extent of this irruption of cholera, I suspected some contamination of the water of the much-frequented street-pump in Broad Street, near the end of Cambridge Street.[29]

2. Define a Case and Conduct Case Finding

Snow defined a case as a death from cholera. Although he did not use microbiological confirmation in his case definition, death from watery diarrhea during the London outbreak was a reasonable case definition. His case definition was highly sensitive (meaning it would include most cholera cases), but it was also highly nonspecific (meaning it would not exclude noncholera diarrheal deaths). This definition enabled Snow to verify that a severe outbreak of cholera was taking place. He conducted case finding through mortality records by contacting medical practitioners in the neighborhoods around Golden Square.

> I requested permission, therefore, to take a list, at the General Register Office, of the deaths from cholera, registered during the week ending 2nd September, in the subdistricts of Golden Square, Berwick Street, and St. Ann's, Soho, which was kindly granted. Eighty-nine deaths from cholera were registered, during the

> week, in the three subdistricts. Of these, only six occurred in the four first days of the week; four occurred on Thursday, the 31st August; and the remaining seventy-nine on Friday and Saturday.[29]

Figure 2-1 shows cholera deaths in Golden Square during the outbreak.

3. Tabulate and Orient the Information: Person, Place, Time

To pinpoint the "who, when, and where" of the outbreak, Snow created a line listing of cases, including the age, gender, and address of each patient. He plotted his cases on a map and observed that they occurred in proximity to the pump on Broad Street. This information suggested that the case patients could have been infected from water at the pump, and that it was a point-source outbreak.

> On proceeding to the spot, I found that nearly all the deaths had taken place within a short distance of the pump. There were only ten deaths in houses situated decidedly nearer to another street pump. In five of these cases the families of the deceased persons informed me that they always sent to the pump in Broad Street, as they preferred the water to that of the pump which was nearer. In three other cases, the deceased were children who went to school near the pump in Broad Street. Two of them were known to drink the water; and the parents of the third think it probable that it did so. The other two deaths, beyond the district which this pump supplies, represent only the amount of mortality from cholera that was occurring before the irruption took place.[29]

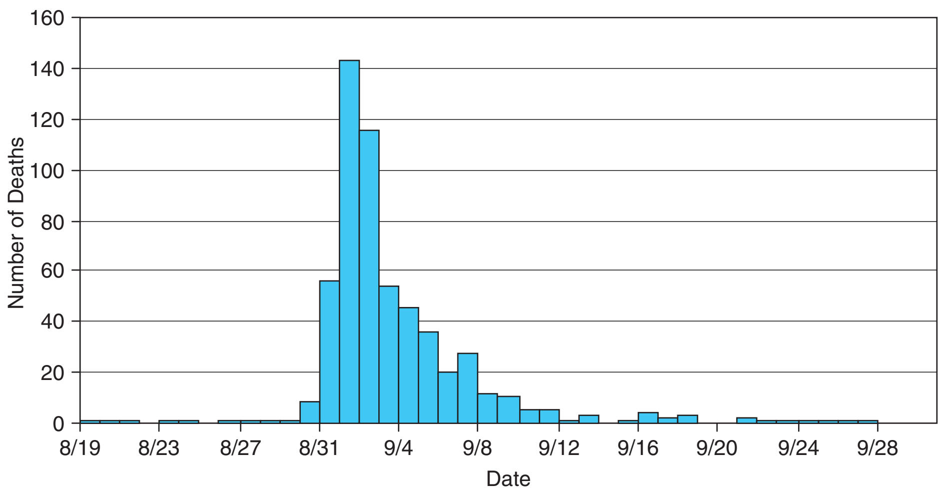

Figure 2-1 Cholera deaths in the Golden Square Section of London, 1854

Data from: Snow J. *On the Mode of Communication of Cholera*. 2nd ed. London, England: John Churchill, New Burlington Street; 1855.

4. Take Immediate Control Measures

Snow suspected the Broad Street pump was the source of the cholera. In a now famous symbol of public health action, he called for the removal of the pump handle from the well so that people could not access the contaminated water.

> I had an interview with the Board of Guardians of St. James's parish, on the evening of Thursday, 7th September, and represented the above circumstances to them. In consequence of what I said, the handle of the pump was removed on the following day.[29]

5. Formulate and Test Hypotheses

Although Snow was convinced that drinking from the Broad Street well was making people ill, he found additional evidence of the association among a group of persons who were not exposed to the well water.

> There is a Brewery in Broad Street, near to the pump, and on perceiving that no brewer's men were registered as having died of cholera, I called on Mr. Huggins, the proprietor. He informed me that there were above seventy workmen employed in the brewery, and that none of them had suffered from cholera,—at least in a severe form,—only two having been indisposed, and that not seriously, at the time the disease prevailed. The men are allowed a certain quantity of malt liquor, and Mr. Huggins believes they do not drink water at all; and he is quite certain that the workmen never obtained water from the pump in the street. There is a deep well in the brewery, in addition to the New River water.[29]

Present-day epidemiologists would have conducted an analytic study at this phase—for example, a case-control study using case patients and persons without disease at the brewery as a comparison group. However, based in part on the evidence provided by the brewers, Snow concluded "that there had been no particular outbreak or increase of cholera, in this part of London, except among the persons who were in the habit of drinking the water of the above-mentioned pump-well."[29]

6. Plan and Execute Additional Studies

Snow suspected that a previous cholera outbreak in 1848 was associated with the London water supply. He further suspected a single supplier of water, the Southwark and Vauxhall Company, was associated with the contamination. To test his hypothesis, Snow compared the mortality rate due to cholera (number of cholera deaths per 10,000 households) between two companies that supplied water in a single geographic area south of the River Thames.

> The experiment, too, was on the grandest scale. No fewer than three hundred thousand people of both sexes, of every age and occupation, and of every rank and station, from gentlefolks down to the very poor, were divided into two groups without their choice, and, in most cases, without their knowledge; one group

> being supplied with water containing the sewage of London, and, amongst it, whatever might have come from the cholera patients, the other group having water quite free from such impurity.[29]

The resulting study implicated the Southwark and Vauxhall Company, which had drawn its water from the downstream section of the River Thames, which was more heavily contaminated with sewage. Compared to the water supply companies in the rest of London, customers of Southwark and Vauxhall were nearly six times more likely to die from cholera than the general population; customers of Lambeth were less likely to die from cholera than the general population (Table 2-2).

7. Implement and Evaluate Control Measures

Snow concluded *On the Mode of Communication of Cholera* with 12 specific recommendations to prevent illness. These included prevention of transmission by medical practitioners, isolation of patients, treatment of the water supply, suggested water sources for London, disposal of human waste, and quarantine of persons suspected to have been exposed in foreign countries.

8. Communicate Findings

Snow shared his findings with members of the medical profession and government officials in Parliament.

> After the Registrar-General alluded, in the "Weekly Return" of 14th October last, to the very conclusive investigation of the effects of polluted water in the south districts of London, there was a leading article, in nearly all the medical periodicals, [*Medical Times and Gazette, Lancet,* and *Association Journal*] fully admitting the influence of the water on the mortality from cholera. It may therefore be safely concluded that this influence is pretty generally admitted by the profession.[29]

TABLE 2-2 Comparison of the Cholera Mortality Rate per 10,000 Households by Water Source in London, 1848

Water Supply	Households	Deaths	Deaths/10,000 Households	Rate Ratio (95% CI*)
Southwark and Vauxhall	40,046	1,263	315	5.7 (5.3–6.1)
Lambeth	26,107	98	37	0.7 (0.6–0.8)
Rest of London	256,423	1,422	55	1.0 (referent)

*CI = confidence interval

Source: Snow J. *On the Mode of Communication of Cholera*. 2nd ed. London: John Churchill, New Burlington Street; 1855.

Summary

In epidemiology, the terms "epidemic" and "outbreak" describe an increase in the observed number of cases of a disease or health problem compared with the expected number for a given place or among a specific group of people over a particular period of time. ("Outbreak" is often used to describe a localized epidemic.) Public health practitioners may be called upon to investigate outbreaks due to food poisoning, geographic clusters of cancer, or a mysterious illness in a school. Outbreak investigations often begin with information from surveillance or health information systems, clinical laboratories, affected citizens, or astute healthcare providers about a suspicious number of cases of a disease or health problem. To determine whether a potential outbreak is a true outbreak, investigators gather such information as what pathogen is causing the infection, who is becoming ill, and where and when the cases are occurring.

When an outbreak is detected, a thorough investigation can allow public health practitioners to take actions to control the outbreak and prevent additional people from becoming ill. Outbreak investigations can also identify risk factors associated with outbreaks, discover emerging pathogens, and provide new research insights. Taking part in investigations also gives practitioners important experience. Outbreak investigators typically follow an eight-step process. Investigators may carry out these activities simultaneously, or they may repeat some of them as more information comes to light. John Snow's *On the Mode of Communication of Cholera*, published in 1855, is a classic example of the process of an outbreak investigation.

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