6

Outbreak Investigation

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As mentioned in the previous chapter, one of the uses of surveillance data is to help identify outbreaks of disease. In the fall of 1994, a Public Health Functions Steering Committee, comprising federal agencies and major national public health organizations, defined the 10 essential public health services and included, as Number 2, to "diagnose and investigate health problems and health hazards in the community" (Centers for Disease Control and Prevention [CDC], 2013). The committee mentioned outbreak investigation specifically as a way to diagnose and investigate health problems. **Outbreak investigation** involves recognizing a problem, collecting relevant information, analyzing likely risk factors, identifying and implementing appropriate control measures, evaluating the effectiveness of the control measures, and communicating the investigation results. This chapter describes the general steps that are undertaken in investigating an outbreak. These principles apply to the investigation of an acute infectious disease, but can also be applied to other kinds of outbreaks, including environmental, occupational, injury, or chronic disease problems.

OUTBREAK INVESTIGATION AS PUBLIC HEALTH RESEARCH AND PRACTICE

The most obvious reason for an outbreak investigation is to identify the source or mode of disease transmission so that control measures can be implemented to limit further spread of the disease. The information gathered in the investigation is important for evaluating the effectiveness of those control measures as well. Outbreak investigations offer other important opportunities for public health professionals in that they provide a natural experiment where investigators can evaluate the effect of an exposure or other risk factors that are impractical or unethical to conduct in a controlled experiment that uses humans or animals. For example, in 1991, endocrinologists in Massachusetts reported five cases of suspected hypervitaminosis D (an excess of vitamin D) to local health authorities. Investigation of this outbreak revealed that the affected persons had consumed milk from a specific local dairy that had been inadvertently overfortifying its milk with 30–35 times the recommended amounts of vitamin D. Investigators studied 243 exposed persons and were able to document the clinical effects of this type of exposure. Devising a clinical study to expose a similar group of persons to such excess levels of vitamin D would have been unreasonable (Scanlon, Blank, & Sinks, 1992).

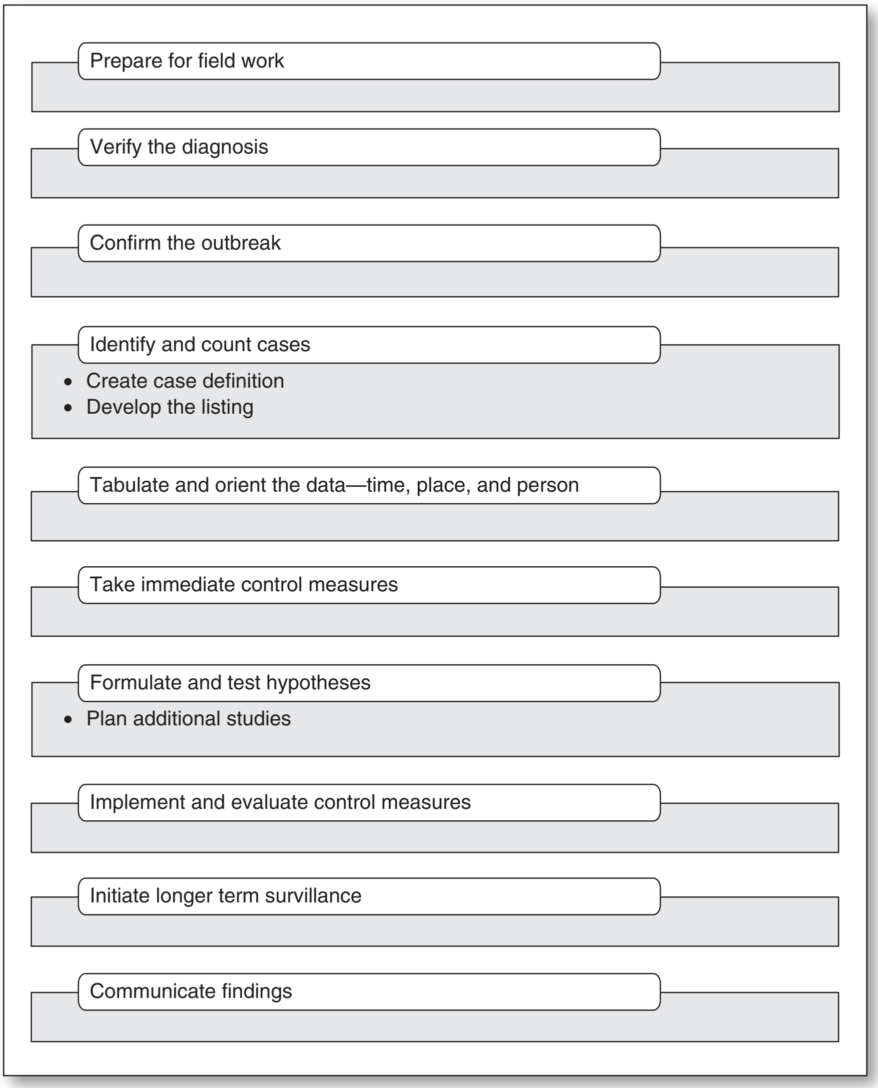
Outbreaks also allow investigators to study the natural history of a given disease and sometimes the opportunity to characterize a new problem. Before the introduction of West Nile virus (WNV) into North America, studies in Africa, the Middle East, and Eastern Europe had characterized the clinical syndromes associated with WNV infections, but did not measure the extent of asymptomatic infection or mild illness. Serosurveys conducted during the 1999 outbreak of WNV among an immunologically naïve population in New York City revealed that, for every case of WNV meningoencephalitis, 30 additional probable cases of mild WNV fever and 140 persons with symptomless or mildly symptomatic infections were identified (Mostashari et al., 2001).

Other important reasons to investigate outbreaks include

- responding to political or public pressures to identify an outbreak cause (e.g., a foodborne outbreak after a community gathering and public concern that an intentional or negligent contamination of the food item had occurred),
- fulfilling statutory requirements for the health office to investigate outbreaks (e.g., an outbreak that involves a commercial establishment or product), and
- training health workers in disease investigation and control.

Figure 6.1 lists the key steps in an outbreak investigation and forms the outline for the remainder of this chapter. Keep in mind two key points about this list. First, it is not a rigid, sequential task list. When conducting an actual investigation, epidemiologists usually perform multiple steps simultaneously. For example, investigators often try to identify patients while they are verifying the diagnosis and trying to confirm that an epidemic is occurring. Because the primary role of public health workers is to protect the public's health, one of the last steps in the sequence—implement and evaluate control measures—should be undertaken as soon as practicable control measures are identified. The second crucial point is that this is simply one way of approaching outbreak investigations. Undoubtedly, other protocols are equally effective.

Figure 6.1 Guidelines for Epidemiologic Field Investigations



CONDUCTING AN OUTBREAK INVESTIGATION

Prepare for Field Work

Depending on the setting in which investigators are working, they will have administrative and scientific tasks that must be completed before beginning the investigation.

Administrative

- **Jurisdiction.** Have you notified the persons with legal authority about the outbreak, and has the request for assistance come from the correct authorities? An astute clinician will often bring a potential problem to health authorities' attention but might not have the authority to initiate a public health investigation. For example, in the United States, "health" is under each state's jurisdiction. Federal authorities must not conduct an investigation unless they are invited by the state authorities, typically the state epidemiologist. Similar jurisdictional restrictions between local and state authorities also might apply within states.
- **Team composition.** Who will be on the investigation team, and who will be providing support from a distance (e.g., the central public health office)? Who is included in the chain of command for the team?
- **Resources.** What supplies (office or laboratory) will the team need? How will transportation be managed? How will the lines of communication between team members be managed? Will computer and Internet access be readily available? What lodging and meals for team members need to be prearranged? These items can be straightforward in a domestic investigation but considerably challenging in a resource-poor (rural or low-socioeconomic) environment.
- **Other.** What travel documents does each team member need? Does overtime for team members need to be preapproved?

Scientific

- **Background information on the suspected agent or mode of transmission**. To prepare for the investigation, team members gather information on likely agents and risk factors. Possible resources include the scientific literature, local or national subject-matter experts, records of similar past investigations, and reliable Internet sites (the CDC or research centers and universities).
- **Laboratory support and specimen handling**. What types of samples will the team most likely collect (environmental, clinical, other)? What types of collection equipment and specimen containers are needed? What are the conditions for sample shipping (room temperature, wet ice, dry ice)? How will the samples be shipped (commercial shipping firm, mail, courier)? Remember to involve the laboratory authorities early in an investigation, especially if you anticipate a substantial volume of samples.
- **Personal protection equipment.** What measures do you need to take for team members' safety? Consider such safety precautions as barrier protection (gloves, gown, and masks), respirators (have team members been fit-tested?), vaccinations, and prophylactic medications. These items might not be readily available in remote locations.
- **Current response.** What types of control measures have already been put into place? Medical treatments can change the clinical picture for individual patients just as community intervention measures can alter the disease profile in the community.

- **Local theories.** What do the local authorities think is causing the outbreak? This is a crucial question to ask the person requesting the investigation. Although investigators should maintain an open mind regarding all possible causes of the outbreak, the local authorities will have been working on the problem before calling for assistance. They likely will have considered and eliminated certain causes of the outbreak and can provide useful guidance to the team at the outset.

Verify the Diagnosis

As soon as possible, verify that the reports of disease or conditions causing the outbreak are accurate. The goal of this step is to rule out misdiagnosis, laboratory error, and pseudoepidemics. This can occur when either a real clustering of false infections or an artifactual clustering of real infections occurs. At the beginning of an investigation, if possible, the team should visit in person, interview, and even examine the patients. The team should review the medical records and, if indicated, obtain clinical specimens to confirm laboratory test results at a provincial or national reference laboratory to rule out laboratory error.

If clinical features are incompatible with laboratory results and the diagnosis cannot be verified, consider the possibility of a false infection. For example, false-positive diagnoses can result from contaminated antiseptic used to prepare skin for drawing blood cultures, use of nonsterile syringes to collect specimens for blood cultures, or environmental contamination of specimens during processing in the laboratory. For example, during an outbreak of neonatal sepsis among pediatric patients at two regional hospitals, investigators noted that the relatively mild illness reported among the patients was not typical of *Serratia* sepsis, which was also an unusual causative agent among this population. The investigation revealed that the blood collection tubes used by the two hospitals were contaminated with the outbreak strain of *Serratia* (Hoffman et al., 1976).

More recently, in a 2010–2011 outbreak of pertussis in New York, health officials identified 542 patients with laboratory-confirmed pertussis, but also noted that many of the patients did not have clinically compatible symptoms. They were able to demonstrate that certain pertussis vaccines contained considerable amounts of polymerase-chain reaction–detectable *Bordetella pertussis* DNA, and environmental sampling had identified the presence of this DNA in clinic environments. They postulated that inadvertent transfer of DNA from clinic environmental surfaces to clinical specimens resulted in contamination and led to false-positive results (Maxted et al., 2012).

Artifactual clustering of real infections can occur as a result of a change in the sensitivity of case finding, rather than an actual increase in disease incidence. To rule out artifactual clustering, consider the following questions:

- Has a new, more sensitive diagnostic test been introduced?
- Has the surveillance definition for the disease changed?

- Has a new practitioner entered the community who is either ordering more diagnostic tests or using different diagnostic criteria?
- Has public awareness about the disease led to more people seeking clinical evaluation?

Practical Point: Try to obtain clinical specimens or other samples already isolated for possible additional testing and analysis at the outset of the investigation. Obtaining samples as soon as possible—before they have been discarded by a laboratory—is crucial. Samples can always be thrown away, but they cannot be retrieved after they have been discarded.

Confirm the Outbreak

After the team has verified the diagnosis, the next crucial step is confirming that an outbreak is occurring. From the perspective of an epidemiologist, the terms *outbreak* and *epidemic* are synonymous: "The occurrence in a community or region of cases of illness, specific health-related behavior, or other health-related events clearly in excess of normal expectancy. The community or region and the period in which the cases occur are specified precisely" (Last, 1995, p. 54).

The key elements of this definition are *time*, *place*, and *person*. Of note, the public's perception of these terms is often considerably different from the epidemiologist's. *Outbreak* is often regarded by the public as a smaller, highly localized increase in disease occurrence, whereas *epidemic* is interpreted as a much more serious, widespread, and likely threatening increase in disease. Public health workers should be aware of the potential impact of how they describe a problem to the public. The public reaction to the statement "We have an outbreak of *Salmonella* in our city" will likely be quite different than the reaction to "We have an epidemic of *Salmonella* in our city." Sometimes, however, health authorities might want to elicit a more vigorous public response; hence, we hear such phrases as "the epidemic of teenage pregnancy" or "the obesity epidemic."

Other terms that are used when describing an increase in disease but are not synonymous with *outbreak* include the following (Last, 1995):

- **Cluster:** An aggregation of unusual events in place or time that is perceived to be greater than expected. The focus of the majority of cluster investigations is to try to determine what the actual expected rate is.
- **Endemic:** The constant presence of a disease or infectious agent within a given geographic area or among a population group.
- **Hyperendemic:** A disease that is constantly present at high incidence or prevalence rates and that affects all age groups equally.
- **Pandemic:** An epidemic occurring worldwide or throughout a geographic region, crossing international boundaries, and usually affecting a substantial number of persons.

How much in excess of normal expectancy is required before an increased number of cases constitutes an outbreak? It depends. Multiple factors can be considered when making this decision, including the following:

- How prevalent is the disease among the population?
- How severe is the disease (e.g., does it result in death or serious disability)?
- How transmissible is the disease?
- Does this disease usually occur seasonally?
- Are specific populations at high risk (e.g., older persons, young children, immunocompromised persons)?

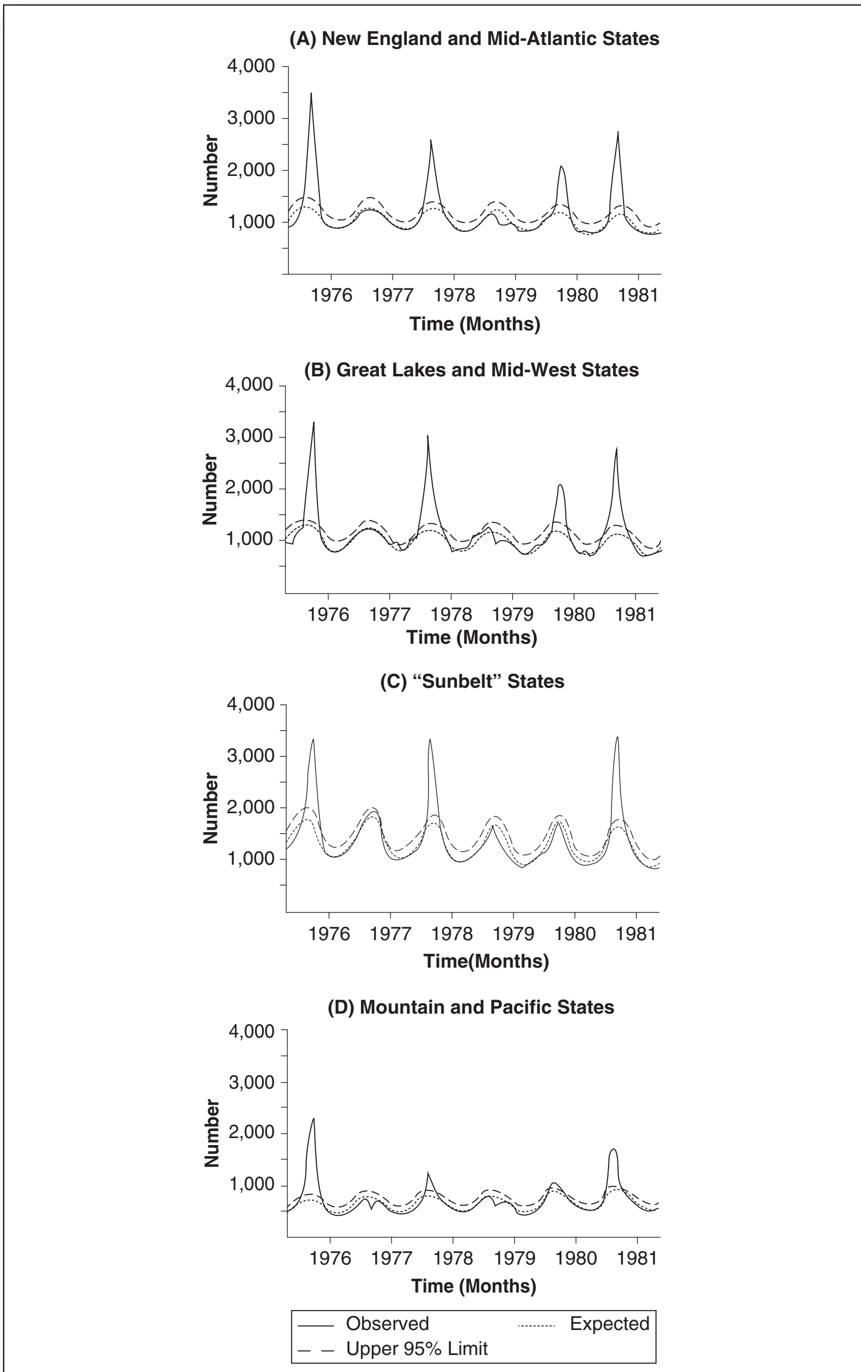
For certain conditions that rarely occur among a given population (e.g., rabies, plague, meningococcal meningitis), a single case might be considered more than expected. For conditions that are endemic in a community (e.g., salmonellosis, histoplasmosis), determining how many cases are more than expected might be much more difficult. For other conditions (e.g., seasonal influenza) that occur regularly in the community with relatively high numbers, health officials might calculate expected rates on the basis of a moving 5- to 10-year average to establish an epidemic threshold. For instance, by examining influenza rates in the United States for 1972–1985, researchers defined an epidemic as the number of observed cases increasing above the predetermined epidemic threshold that was set at 1.64 standard deviations higher than the predicted mean. During this period, 4 years occurred when the number of cases exceeded the epidemic threshold (Figure 6.2; Lui & Kendal, 1987).

During an outbreak response, investigators should count the number of cases and compare that with the predicted baseline number of cases for a defined time and place. So if you were asked to investigate an outbreak of surgical wound infections in a community hospital, your team would need to get an estimate of the number of such cases that normally occur. You could review the discharge records for the previous month or months. However, when using historical data to compare the magnitude of the current problem with the baseline, using rates is imperative. If the hospital had six surgical wound infections this month but the records reveal only two the month before and three each of the preceding months, is this an outbreak? Perhaps. What if the hospital had just opened up a new surgical suite and tripled the number of surgical cases performed? In that instance, the case rate this month might be the same as for previous months.

What if the team is asked to investigate an apparent increase in pediatric cases of severe respiratory syncytial virus (RSV) infections? Comparing the rates to the previous months might not be an accurate indication. RSV is a seasonal disease; therefore, the team should compare the rates in the facility for the same period the previous year or the year before that.

Calculating a baseline rate for a hospital outbreak is probably a best-case scenario. In community investigations, determining the baseline might be more difficult, and investigators might encounter problems that lack available data, have incomplete reporting or inefficient surveillance, or have absent or varying case definitions. For instance, in June 1981, investigators reported five cases of *Pneumocystis carinii* pneumonia (PCP) among young homosexual men in Los Angeles. This was an

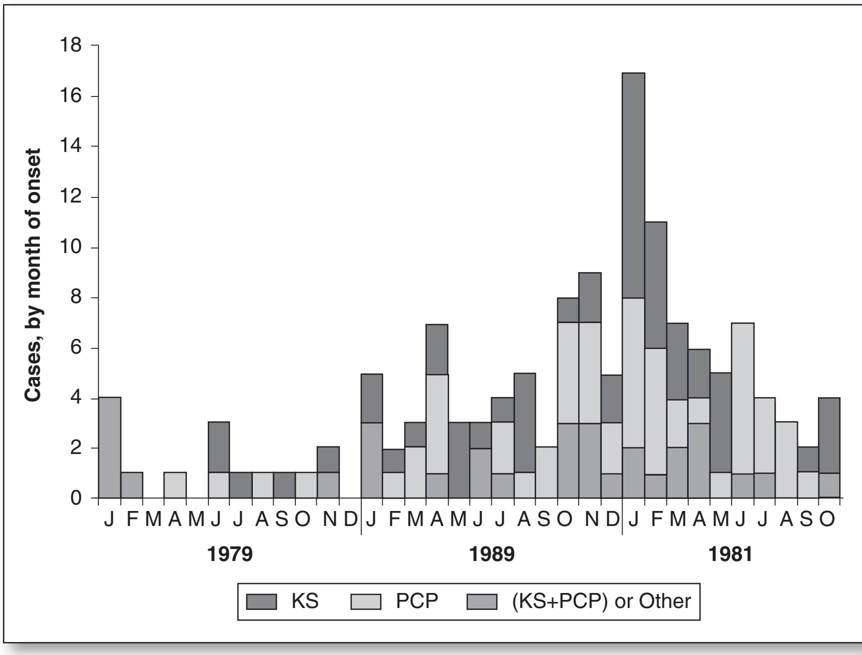
Figure 6.2 Regional Pneumonia and Influenza-Associated Deaths Reported to the National Center for Health Statistics, 1975–1981



Source: Lui and Kendal (1987).

unusual group of patients because they did not fit the profile of PCP patients: persons who typically have a known severe immunodeficiency (CDC, 1981). Was this an epidemic? To answer this question, a large team of public health workers conducted active surveillance and reviewed available tumor registries and other medical information systems. They were able to gather the information illustrated in Figure 6.3 (CDC, 1982).

Figure 6.3 Incidence of Kaposi's Sarcoma (KS), *Pneumocystis carinii* Pneumonia (PCP), and Other Opportunistic Infections in the United States, 1979–1981



Source: CDC (1982).

Their data revealed a clear increase over the expected number of cases that began in 1980. This report documented the beginning of the HIV/AIDS epidemic in the United States. However, the effort to collect and analyze the data necessary to make this determination took 6 months. Establishing a baseline and verifying an epidemic can be a difficult and time-consuming process.

Identify and Count Cases

After confirming the existence of an outbreak, the next task is to identify as many cases as possible. The term that epidemiologists often use is *casting a broad net*. Investigators want to find as many cases as possible (sensitivity) without including noncases (specificity).

IMPORTANT TERMS

Sensitivity: the proportion of truly positive individuals that are identified as diseased by the test (true positive rate).

Specificity: the proportion of truly negative individuals who are identified as disease free by the test (true negative rate).

A critical element of case finding is establishing a clear, easily applied case definition. As with the case definitions for surveillance discussed in Chapter 5, case definitions for outbreaks should include the following elements:

- **Time:** specify when the disease occurred (often referred to as the *outbreak period*)
- **Place:** might be a geographic place (e.g., town, state, country), a specific setting (e.g., nursing home, school, workplace), or persons who participated in a function (e.g., wedding, meeting)
- **Person:** clinical characteristics (signs and symptoms) of those affected or the laboratory tests for persons possibly affected

One important point to remember is that for certain conditions, infected persons might present with an entire spectrum of symptoms. For example, patients infected with hepatitis might have no symptoms at all (subclinical disease), mild influenza-like illness, nondescript abdominal complaints, frank disease with classical jaundice, or death. The case definition might need to be designed to select different disease presentations.

A case definition is not necessarily static and can change during the course of an investigation. Initially, the working definition might be overly sensitive for identifying the maximum number of patients. The sensitivity of the case definition in these situations is inversely proportional to its specificity. As more information becomes available or laboratory testing is completed, the case definition can be narrowed to increase specificity. An example may help to clarify.

During an investigation of a Legionnaires' disease outbreak in Indiana, the team started their case finding with a highly sensitive case definition, as follows:

> **Case:** Illness in a person who was in Bloomington, Indiana [**place**], during the 2 weeks before illness onset [**time**] and who presented with a fever of ≥ 39.2ºC, radiologic evidence of pneumonia, and no bacterial isolates of clinical significance [**person**].

As the investigation proceeded and more laboratory data became available, they narrowed their case definition by requiring laboratory data to differentiate a *confirmed case* from a *presumptive case*, as follows (Dondero et al., 1980):

> **Confirmed case:** A case where paired sera demonstrate a fourfold or greater increase in indirect fluorescent antibody titer to ≥ 128.

> **Presumptive case:** A case with only a single serum sample available that demonstrates a convalescent-phase indirect fluorescent antibody titer of ≥ 256.

The initial case definition was highly sensitive and would likely have caught the majority of the patients with Legionnaires' disease who had sought clinical care. However, the specificity of the definition was lower and, therefore, might also have identified patients with viral pneumonia or other bacterial agents that were not isolated by laboratory testing. The confirmed case diagnosis has the advantage of not including these noncases, but at a cost of greater time and expense required to obtain the laboratory tests and a smaller sample size for the data analysis.

Practical Point: In most instances, the case definition will be applied by various members of the team in the process of case finding. Therefore, the definition needs to be unambiguous. If the case definition is "illness in a person with pneumonia, fever, and diarrhea," what are the potential problems?

- **Pneumonia:** Is this patient-reported pneumonia, clinician-diagnosed, or by radiologic evidence?
- **Fever:** How high does a patient's temperature have to be? (Many patients will report having a fever, but when asked how high, they will report, "I felt hot.")
- **Diarrhea:** One person's diarrhea might be another person's regular bowel pattern.

Be sure that your case definition has clear parameters (e.g., illness in a person with clinician-diagnosed pneumonia, oral temperature > 100ºF, and three or more loose bowel movements within 24 hours). Clearly defining how the definition should be applied is integral to obtaining accurate data.

After the case definition is developed, it should be used in a systematic search of the affected location to find cases. Identifying all of the affected patients in an outbreak is unnecessary; gathering a sample of the affected population where the sample size provides enough data to make statistically valid inferences about exposure and disease is all that is necessary. However, using a systematic approach to finding affected patients is important to avoid introducing an ascertainment bias into your sample.

Take case-control investigations, for example. Case-patients and control subjects often have been identified by conducting random-digit-dialing of telephone exchanges that match the numbers of known case-patients. This works because the three-digit exchange number tends to be restricted to a specific geographic area. Historically, the concern about this technique has been the potential for missing persons without telephones. If this group is different from the persons with telephones (socioeconomic status, education, race/ethnicity, renters versus homeowners), the sample will not reflect the general population. More recently, the dramatic increase in the use of cell phones has affected the utility of using telephone numbers to match for geographic area. Concerns now include the potential for age bias, since cell phones might be disproportionately used by younger persons (Kempf & Remington, 2007).

Using multiple sources to identify patients during an investigation is therefore crucial, and the team should consider several possible sources:

- **Medical offices:** The obvious first place to find affected persons is in hospitals, clinics, or physicians' offices in the area. The advantage of this approach is that it is relatively convenient, the data quality is usually good, and you often have diagnostic data that are helpful in the investigation. The disadvantage is that only persons with more severe illness will seek medical attention, and the persons you identify will be the sicker among all affected persons.
- **Laboratories:** During an infectious disease outbreak, laboratories are possibly the most important place to start. The data are usually reliable and can provide confirmation of specific diagnoses. In addition, laboratories often serve multiple providers and might provide results for a wider geographic area than just one clinical facility. The disadvantage is the same as with medical facilities—only patients who have sought care will be represented.
- **Surveillance data:** Public health surveillance data might be a valuable way to identify cases. The biggest challenge is the likely time lag between occurrence of disease and reporting to the surveillance system. During rapidly evolving outbreaks, this can be a serious limitation.
- **Institutions:** Large employers or schools often have clinics or systems for tracking absences.
- **Targeted surveys:** Sometimes conducting a community survey is necessary to identify affected persons. These might be random-sample surveys based on an established sampling frame, cluster surveys, or convenience surveys. A key consideration is whether the sampling technique used generates a sample that is representative of the community.
- **Friends/contacts:** Case finding might involve asking patients to identify others who are also sick. The main disadvantage with this approach is the potential for overmatching case-patients with control subjects (i.e., finding controls who are too similar to case-patients than a control from the general population would be).
- **Local/tribal/community leaders:** In smaller communities, the local leaders can be a resource for identifying ill persons. This is especially important in communities with limited resources.
- **Media/press:** Using the media for identifying cases can be a double-edged sword. In some instances, identification of a potential source of an outbreak by the press can seriously bias the reporting of affected persons—ill persons who were not exposed to the publicized risk factor might fail to report their illness, or persons who are not ill might report simply because they were exposed. In other cases, press attention helps by raising public awareness and encouraging ill persons to contact health care providers for evaluation.
- **Social media:** Public health investigators have used this resource as a way to contact widely dispersed groups of possible patients quickly. During a recent investigation of respiratory illness among attendees at a conference, all 715 attendees from 30 countries were contacted through social media (Twitter, Facebook, SurveyMonkey, and

relevant blogs). One major limitation of this resource is susceptibility to reporting bias (Reed et al., 2011).

- **Pharmacy records:** Local pharmacies can help identify persons who have purchased specific antibiotics or medications for symptoms (e.g., diarrhea, respiratory disease).
- **Novel data sources:** Investigators can use other resources as applicable, too (e.g., credit card receipts for patrons of a particular restaurant). Recently, a multistate outbreak of *Salmonella* was linked to contaminated pepper in a delicatessen meat product sold at a national warehouse club. The investigation team made extensive use of data collected from club membership cards linked to a database of every purchase made (CDC, 2010; see the case study at the end of this chapter).

When you are collecting case data, it is always helpful to construct a line list (Table 6.1). This is a simple way to record case information in a ledger, computer spreadsheet, or by another means. Each row in the line listing records the information for an individual patient; the columns include information on demographics (age, race, sex), contact information (address, telephone number), key times/dates (onset of symptoms, treatments, time of diagnoses, and so forth), and potential risk factors. Depending on the situation, other specific information might be included in the line listing (e.g., in a hospital-acquired infection: date of admission, wards, procedures, laboratory results, and staff caring for the patient).

With so much modern technology at our fingertips, we have a tendency to put all available information into a computer database or spreadsheet immediately. Although this is an important step for the eventual data analysis, early in the investigation a simple paper line listing is a quick and easy way to look for patterns.

Tabulate and Orient the Data—Time, Place, and Person

After the cases have been identified and the data collected, the next step is to tabulate and orient the data in terms of time, place, and person. Initial steps in this process typically include the following:

- **Time:** drawing an epidemic curve (i.e., graphing the number of cases across a time span)
- **Place:** drawing a spot map that indicates specific cases or case rates by location
- **Person:** thoroughly describing patients' characteristics

When investigators analyze the data to answer when, where, and who, they are describing the situation and the sample population. This process is often referred to as *descriptive epidemiology*.

This information is then analyzed and used to develop hypotheses to explain the cause, source, mode of spread, or other aspects of the outbreak (i.e., the how and why). Investigators usually will analyze the existing data or conduct additional studies to

Table 6.1 Example Line Listing of Hepatitis A Cases

ID	*Date of Diagnosis*	*Town*	*Age (Years)*	*Sex*	*Hosp*	*Jaundice*	*Outbreak*	*IV Drugs*	*IgM Pos*	*Highest ALT**
01	01/05	B	74	M	Y	N	N	N	Y	232
02	01/06	J	29	M	N	Y	N	Y	Y	285
03	01/08	k	37	M	Y	Y	N	N	Y	3250
04	01/19	J	3	F	N	N	N	N	Y	1100
05	01/30	C	39	M	N	Y	N	N	Y	4146
06	02/02	D	23	M	Y	Y	N	Y	Y	1271
07	02/03	F	19	M	Y	Y	N	N	Y	300
08	02/05	I	44	M	N	Y	N	N	Y	766
09	02/19	G	28	M	Y	N	N	Y	Y	23
10	02/22	E	29	F	N	Y	Y	N	Y	543
11	02/23	A	21	F	Y	Y	Y	N	Y	1897
12	02/24	H	43	M	N	Y	Y	N	Y	1220
13	02/26	B	49	F	N	N	N	N	Y	644
14	02/26	H	42	F	N	N	Y	N	Y	2581
15	02/27	E	59	F	Y	Y	Y	N	Y	2892
16	02/27	E	18	M	Y	N	Y	N	Y	814
17	02/27	A	19	M	N	Y	Y	N	Y	2812
18	02/28	E	63	F	Y	Y	Y	N	Y	4218
19	02/28	E	61	F	Y	Y	Y	N	Y	3410
20	02/29	A	40	M	N	Y	Y	N	Y	4297

*ALT = Alanine aminotransferase

Source: CDC (2012, p. 2-2).

examine the association between disease status and exposure to potential risk factors. This process is referred to as *analytical epidemiology* (see the following descriptions).

Time

In an outbreak investigation, key events should be chronologically ordered to create a framework. The following aspects should be determined:

1. The time of onset of manifestations among patients and their contacts
2. The period of exposure to the causal agent or potential risk factors
3. Time when treatments were administered or control measures implemented; as noted previously, this can change the clinical picture for individual patients or the epidemic curve in a community when an effective control measure is implemented
4. Time of potentially related events or unusual circumstances that might relate to the outbreak: Did the persons who became ill recently attend a large gathering? Did a power outage occur that might have affected food storage? Did a storm lead to contamination of the water supply?

During an outbreak of coccidioidomycosis (a fungal lung infection, also known as San Joaquin fever) in 1994 in California, the majority of the patients and the highest attack rates were identified in Simi Valley. Investigators noted that the Northridge earthquake, magnitude 6.7, had occurred 7 days earlier. Because of the geography of Simi Valley, multiple landslides had occurred, generating large dust clouds. They postulated and eventually demonstrated that exposure to the dust clouds, which contained large amounts of fungal arthrospores, was a major risk factor for disease (Schneider et al., 1997).

An essential way to evaluate the time component of an outbreak is to use the data from the case finding to construct an epidemic curve, commonly called an *epicurve*. The epicurve is a simple histogram that plots the number of cases on the y-axis (the vertical axis) and the time of onset, or in certain instances the time of death, on the x-axis (the horizontal axis). Certain factors should be kept in mind when constructing an epicurve:

- Because time is continuous, each interval is contiguous; thus, no gaps exist between the different periods (this is a histogram, not a bar chart).
- Each patient is represented by a box of uniform size where the x-axis dimension is the time interval when the person became ill. Therefore, the area under the epicurve is proportional to the number of cases.
- The time interval on the x-axis is, by convention, one-quarter to one-third of the incubation period. If the interval is less than this value, it will stretch out the epicurve, and if it is considerably more, it will compress the epicurve. If the epicurve is distorted, making inferences about the transmission mode in the outbreak is difficult. For example, in an investigation of a *Salmonella* species outbreak where the incubation often is in a 12- to 16-hour range, the time interval on the epicurve should be 4 hours. However, with an investigation of an outbreak caused by an unknown agent where the incubation period has not been calculated, constructing an epicurve with the correct x-axis scale is difficult.

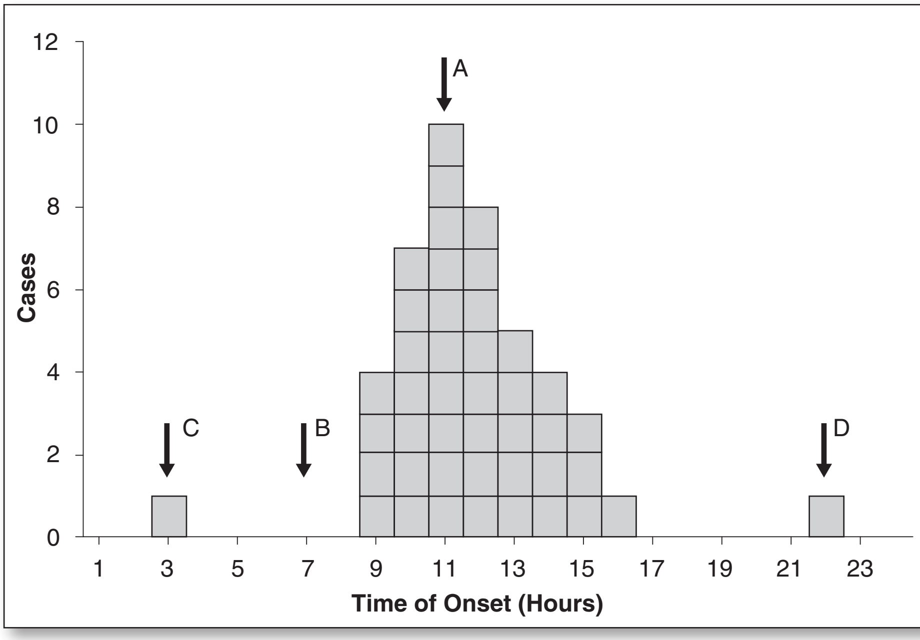
Epicurves

Examination of the shape of the epicurve is often helpful in determining the mode of transmission for a particular outbreak.

Point-source outbreaks

One of the most common presentations occurs with a single exposure of a susceptible population to the causative agent. This is referred to as a *point-source outbreak*. In point-source outbreaks, the epicurve typically indicates a single peak with a fairly steep leading edge and a more gradual downslope (Figure 6.4).

Figure 6.4 Cases of Gastrointestinal Illness by Time of Onset of Symptoms



This type of epicurve can be extremely helpful during the early investigative stages. In this example, the median point of the curve is demonstrated by arrow A, the common exposure is indicated by arrow B, and the incubation period for the disease is the time interval between A and B. Also in this example, two cases fall outside of the general population of cases and are marked by arrows C and D. These latter two cases are commonly referred to as *outliers*. In an investigation where a point-source exposure is apparent, the agent causing the outbreak is known, but the common exposure is unknown; investigators can use the known incubation period and median of the epicurve to calculate the likely period of exposure (arrow B). They then focus their investigation on the period around point B. Alternatively, if a common exposure is known but the specific agent is unknown, the team can use the epicurve to estimate the incubation period for the causative agent. This information is highly useful in narrowing down potential causes.

Practical Point: The outliers in investigations often provide extremely useful information and should be examined carefully. In Figure 6.4, two cases are clearly outside of the general group of cases, one of them occurring before the common exposure. If this were a foodborne outbreak, what possible explanations might exist for these cases?

- This might represent errors in the data collection or coding.
- They might be random cases completely unrelated to the outbreak investigation.
- Case C might represent the person who prepared the contaminated food item.
- The person associated with Case D might have been exposed to a small innoculum (simply tasted someone else's food).
- The person associated with Case D might have eaten the contaminated food item after the common exposure (leftovers).
- Case D might be a secondary case (i.e., the person was exposed to an ill person rather than directly to the food source).

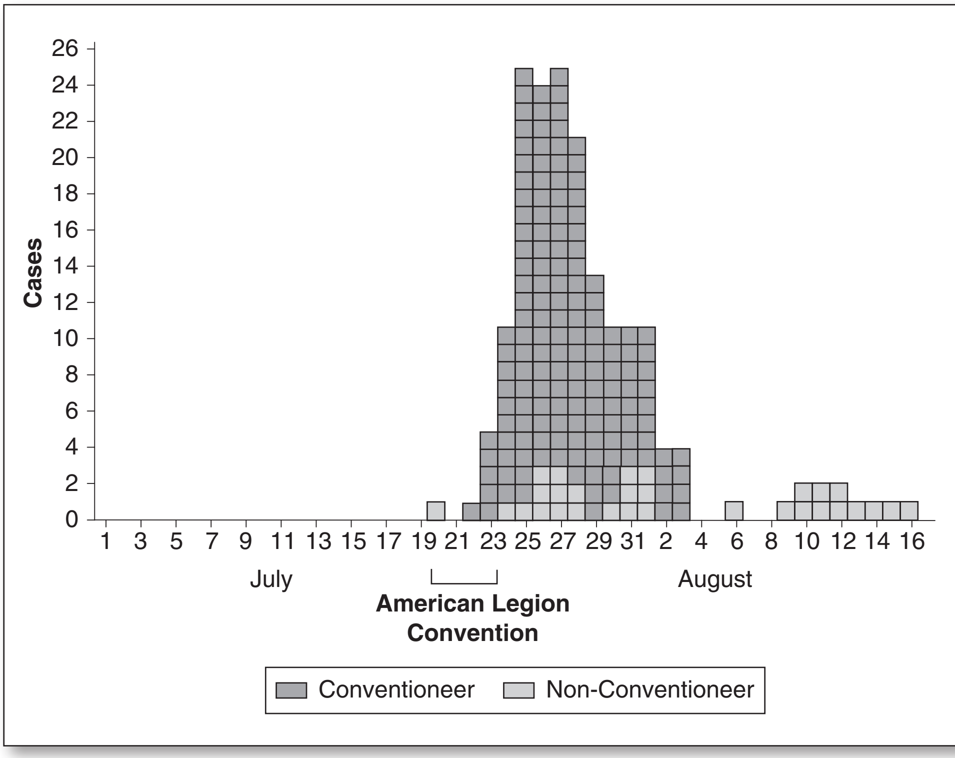
In July 1976, a severe respiratory disease broke out among persons who had attended the American Legion Convention held at a Philadelphia, Pennsylvania, hotel. The causative agent for this outbreak and the mode of transmission were unknown at the time. The epicurve for this outbreak (Figure 6.5; CDC, unpublished data, 1976) was highly indicative of a point-source outbreak. In this instance, the point source was the American Legion Convention. The team also recognized that the time spent in the lobby of the convention hotel was directly proportional to the risk for acquiring the disease (Fraser at al., 1977). The causative agent was subsequently identified as a novel gram-negative coccobacillus later named *Legionellae pneumophila* (Legionnaires' disease). This particular organism grows in stagnant water sources (e.g., cooling towers), and the investigation revealed that the main outflow for the hotel's cooling system was into the lobby.

One challenge that investigators faced during the 1976 outbreak was the unknown incubation for this newly discovered disease. Unsure of what interval to use for the x-axis, they drew multiple epicurves that resulted in differently shaped curves, based on how compressed or stretched the x-axis time intervals were drawn. The correct epicurve (Figure 6.5) indicated a point-source; however, other epicurves indicated other transmission modes, as described in the following section.

Propagated transmission outbreaks

In disease outbreaks where the infectious agent is transmitted *person to person*, the epicurve will typically demonstrate a biphasic pattern with two or more peaks (this is also referred to as *propagated transmission*). In the following hypothetical example

Figure 6.5 Legionnaires' Disease by Date of Onset, Philadelphia, Pennsylvania, July 1–August 18, 1976

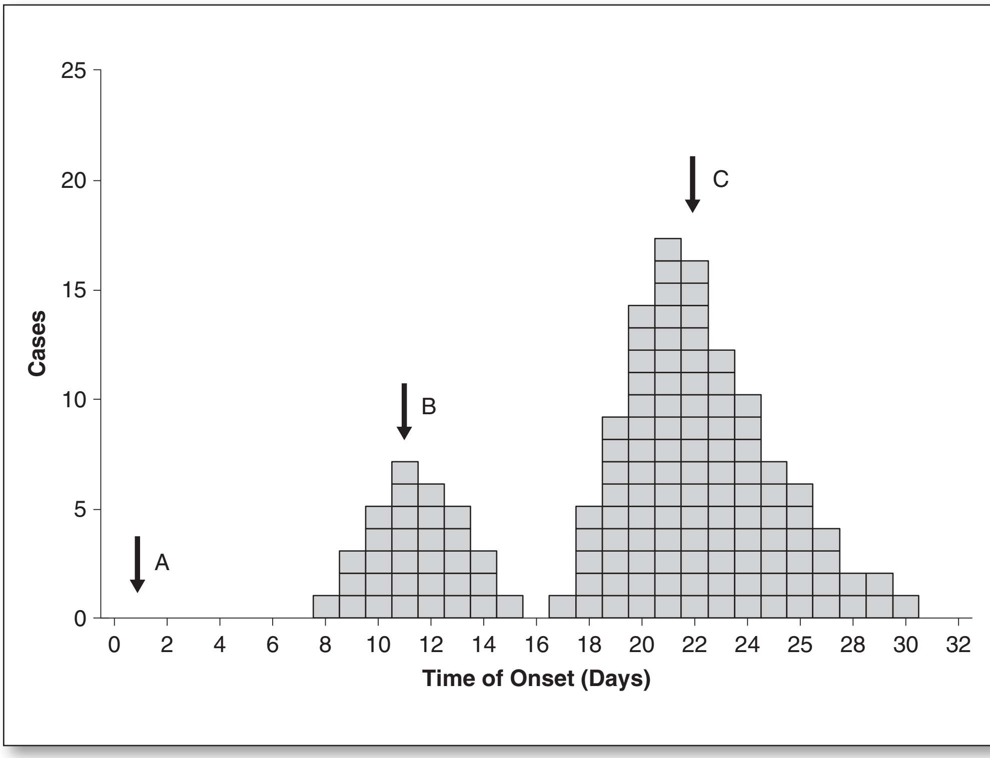


Source: CDC, unpublished data, 1976.

(Figure 6.6), a child infected with measles is introduced to a school where none of the children are immune (arrow A). The infected child acts as a point-source, and an initial group of cases (arrow B) with a curve similar to the point-source example described previously occurs (i.e., the time interval between the arrival of the infected child and the median of the first peak is equal to the disease incubation period). As these initial patients become ill, they infect other susceptible patients, and a wave of secondary cases occurs (arrow C). The time interval between the median of the primary and secondary case peaks is equal to the disease incubation period. Figure 6.6 depicts a textbook person-to-person transmission; in reality, the curve rarely looks this clean. Typically, the peaks indicate greater dispersion, and a clean and obvious delineation between the primary and secondary cases does not exist.

For example, from March 27 to May 5, 1995, seven suspected cases of viral hemorrhagic fever were identified in Kikwit, Zaire, a city of 400,000 people located approximately 200 kilometers east of the capital city, Kinshasa. All seven ill persons died (Figure 6.7). Additional suspect cases were identified. Serologic testing of specimens from Kikwit was consistent with Ebola-like virus infection. This was the beginning of a major Ebola outbreak. The epicurve prepared by the field teams (CDC, unpublished data,1995)

Figure 6.6 Cases of Measles by Time of Onset of Symptoms

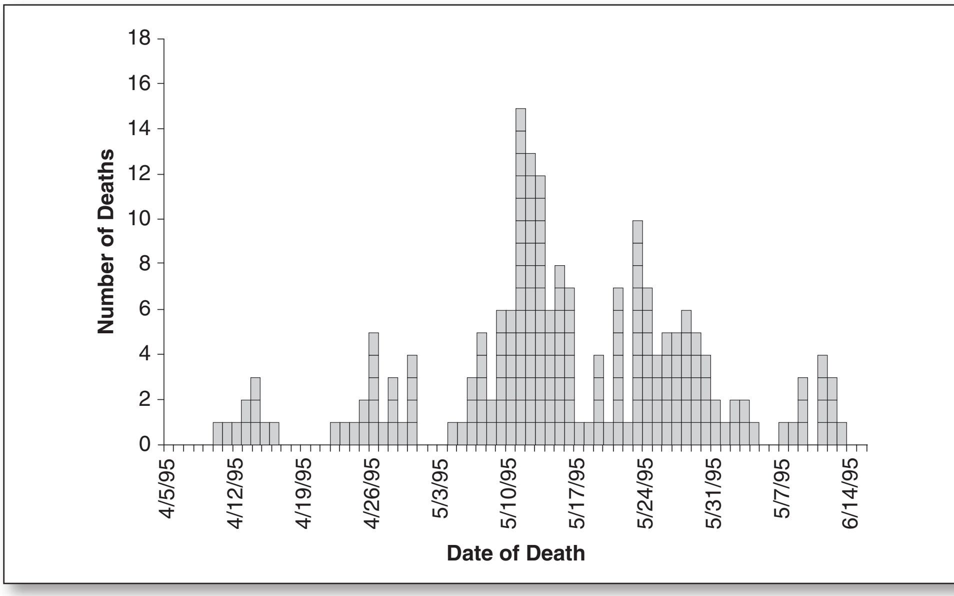


reveals a pattern typical for a person-to-person transmission mode, the mechanism usually observed in Ebola outbreaks where transmission is through direct contact with contaminated bodily fluids. This graph illustrates five fairly clear cycles of transmission where the incubation period appears to be 12–16 days. During this outbreak, a total of 315 cases with a 78% case-fatality rate occurred. Twenty-five percent of the cases occurred among health care workers (Breman, van der Groen, Peters, & Heymann, 1997). As the outbreak continued, the data curve tended to spread out, and the separation between the cycles was not as clean. This was likely caused by individual differences in susceptibility, size of inoculum, and time of infection.

Continuous source outbreak

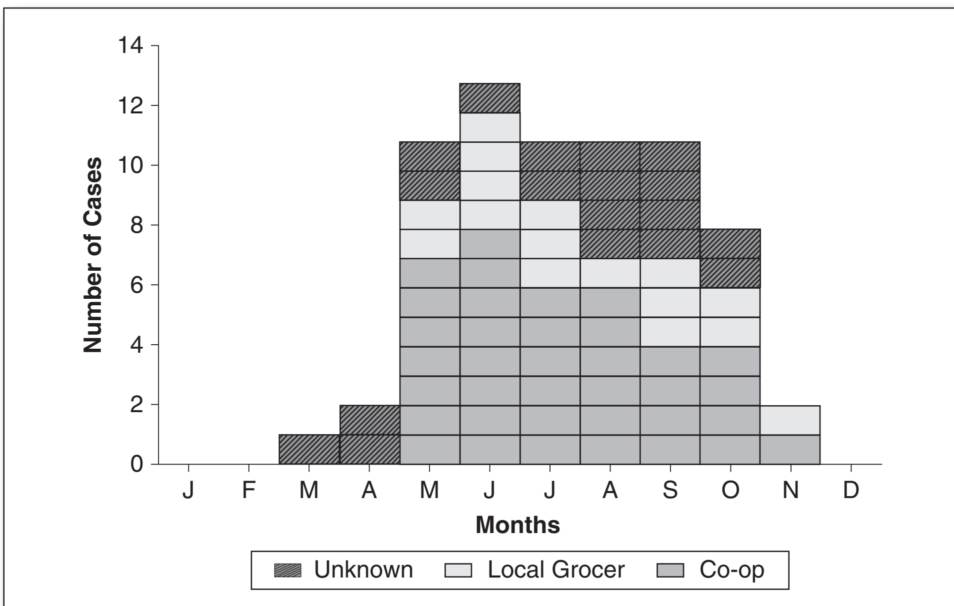
The third type of transmission that can be demonstrated by an epicurve is displayed in Figure 6.8. This type of pattern has a sharp upslope similar to the point-source outbreak. However, instead of a more gradual decline, a plateau phase continues for multiple incubation periods before the outbreak ends. For example, if a break occurs in a community's sewage system, leading to contamination of the water supply, a sharp increase probably will occur in the number of cases (sharp upslope). If the break is not repaired and the contamination continues, the number of infections will continue and eventually reach a steady state (plateau phase). When the break is repaired, the cases will decline.

Figure 6.7 Suspected Viral Hemorrhagic Fever Deaths, Bandundu Province, Zaire, April–June 1995



Source: CDC, unpublished data, 1995.

Figure 6.8 Distribution of Hepatitis A Cases by Month of Onset



Source: CDC, unpublished data, 1981.

The example in Figure 6.8 is taken from a field investigation of hepatitis A in California (CDC, unpublished data, 1981). Person-to-person transmission is a common mechanism identified in hepatitis A outbreaks; however, in this instance, the team was able to rule this out as a likely mechanism. The epicurve revealed a potential continuous source outbreak, and the team was able to identify a specific brand of orange juice, sold at multiple locations, as the implicated item. A single lot of contaminated product had been sold as a frozen concentrate. Because consumers had bought the contaminated juice and stored it in their freezers until use, this served as a continuous source of infectious agent.

Place

The second of the three primary descriptive categories (time, place, and person) must be considered next. When orienting patient data to place, consider the following:

- **Residence:** Where do the affected persons live? What hotel rooms did they stay in? For hospitalized patients, what rooms were they in?
- **Occupation:** Where do they work? Where do they go to school?
- **Activity sites:** Where do they go for recreational activities? Where do they shop? What other leisure activities do they have? At a convention or meeting, what sessions did they attend?
- **Exposure sites:** Map their proximity to known exposure sites (e.g., near a water tower in a legionellosis outbreak).

One of the key tools of the epidemiologist for assessing place-based factors is the spot map. This is a way to map the location of the patients by using one or more of the variables described. Spot maps can be useful when drawn at different observation levels. For example, maps can be used to describe the location of cases within a building or other structure, at the neighborhood or city block level, or at the county or state level. Maps can be oriented toward residence or specific exposure sites (e.g., areas visited during a convention, meeting, or rooms in which known patients are hospitalized), or they can be oriented to include certain activity sites.

Figure 6.9 is based on one of the most iconic spot maps of all time—John Snow's investigation of the Broad Street pump mentioned in Chapter 1 (Snow, Frost, & Richardson, 1936). In 1854, the prevailing theory of infectious disease transmission was the miasma theory that disease was caused by bad air; the modern germ theory of disease had not been widely disseminated. On the basis of earlier work with cholera, Snow, a London anesthesiologist, believed that contaminated water might be the cholera transmission route. During the 1854 outbreak, Snow decided to map out the locations of where all the persons with cholera either lived or worked. Because of his suspicion that water played a key role, he mapped out the public water pumps in the affected areas and questioned patients about where they got their water supply. It became clear from his initial map that patients were clustered around the Broad Street pump. The map clearly indicated a much higher density of cases clustered around the Broad Street pump

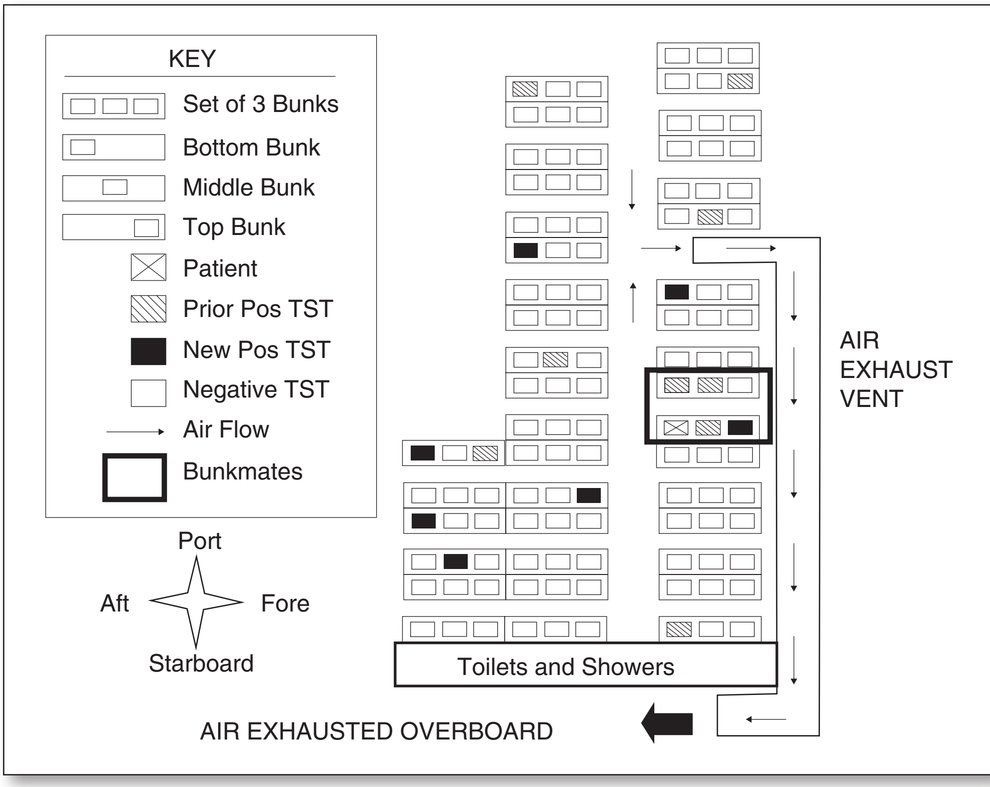
(Pump A) than the other four pumps in the area (Figure 6.9). Outliers also supported his conclusion that the pump was a risk factor for cholera. The first outlier consisted of ill persons from outside of the immediate area who had traveled to get their water from the Broad Street pump because it was reputed to be of higher quality than other water sources. Second, Snow noted a two-block area just east of the pump where no cases had occurred. When he investigated, he discovered that this was a brewery that had a separate deep-well water supply. In addition, workers were allowed a daily ration of malt liquor! The legend is that Snow, on recognizing the danger posed by the pump, removed the pump handle and stopped the outbreak. In reality, he presented his findings to the local borough council, and they ordered the pump closed.

Figure 6.10 is an example of a spot map drawn for an outbreak known to be associated with a facility (CDC, unpublished data, 2007). This map illustrates the berthing space on a Navy ship where one patient had cavitary tuberculosis that had been misdiagnosed as atypical pneumonia. With this map, the investigators displayed the sleeping spaces of the index patient (the box with the x), the general air

Figure 6.9 Distribution of Cholera Cases and Implicated Water Well, Golden Square Area of London, August–September 1854

Source: Snow, Frost, and Richardson (1936).

Figure 6.10 Spot Map Showing the Berths of Persons Infected With Tuberculosis



Source: CDC, unpublished data, 2007.

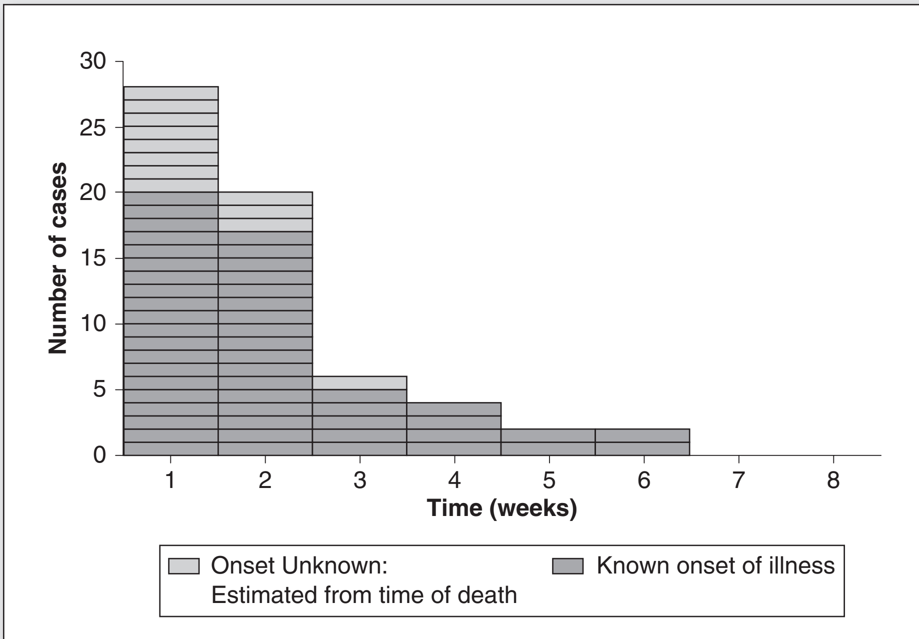
flow in the compartment, and persons with evidence of new tuberculosis infection (black boxes). This map helped prioritize the contact investigation and, because of the index patient's proximity to the main outflow vent, helped explain why so few cases occurred among the other sailors in the berthing compartment (CDC, 2007).

USING PLACE TO SOLVE AN ANTHRAX OUTBREAK

Perhaps one of the best examples of using place as a tool in solving an outbreak involved anthrax infections that occurred in the Russian town of Sverdlovsk in 1979 (Figure 6.11).

(Continued)

Figure 6.11 Onset of Illness by Week, Among Fatal Cases of Anthrax, Sverdlovsk, Russia, 1979



Source: Meselson et al. (1994).

Anthrax is a bacterial enzootic pathogen that has a stable spore stage, which is infectious for humans. As a result of these properties, this organism has been adapted for use as a biologic weapon. Anthrax infection among humans takes three forms. Cutaneous anthrax (95% of naturally occurring human cases) has a case-fatality rate of 5%–20%. Gastrointestinal anthrax caused by consumption of contaminated food products has a case-fatality rate of 25%–60%. Pulmonary anthrax, caused by inhalation of aerosolized spores, is estimated to have a case-fatality rate > 85% (Heymann, 2008; Mandell, Bennett, & Dolin, 2005).

During the 1979 Sverdlovsk outbreak, 96 human cases of anthrax infection were reported, with 64 deaths. At the time, Western authorities were suspicious that this was inhalational anthrax caused by a release from a military microbiologic facility that was believed to be a bioweapons production facility (Defense Intelligence Agency, 1986). Animal cases also occurred in the region, and the Soviet health authorities reported that the infected persons had contracted gastrointestinal anthrax when they obtained contaminated meat on the black market. In 1991, newly elected Russian Federation President Boris Yeltsin, who had been the head Communist Party official in Sverdlovsk in 1979, authorized a reinvestigation of the incident by a team of Western and Russian scientists. Despite attempts by the KGB (Committee for State Security) in 1979 to confiscate all of the data from the investigation, the team led by Harvard professor Matthew Meselson had access to patient records as well as clinical specimens (Meselson et al., 1994). The specimen analysis clearly indicated that the persons who died had suffered from inhalational, not gastrointestinal anthrax.

Anthrax has a usual incubation period of 1–7 days, but depending on the initial inoculum, this can extend to 60 days. The epicurve for this outbreak is highly indicative of a point-source transmission (sharp increase with more gradual decrease), which is consistent with an inadvertent release of an aerosol form of the bacteria. Investigators noted that the age distribution of the patients did not include children (the youngest patient was aged 24 years); therefore, they focused their investigation on where persons were during daylight hours (presumably, the adults were at work and the children at school). The team obtained a satellite photo of Sverdlovsk and mapped out the daytime locations for the patients (Figure 6.12).

Figure 6.12 Map of Sverdlovsk, Russia, Showing Location of Fatal Cases of Anthrax, 1979

Source: Meselson et al. (1994).

In this photo, each of the cases is indicated by a case number. The shape at the top left of the map outlines the Microbiology and Virology Institute, which the investigators labeled Compound 19. The adjacent shape outlines Compound 32, another part of the military complex, and the rectangle below that outlines an open-air tile factory where many of the infected persons worked.

The locations of the cases were tightly clustered around a line extending from Compound 19 and projecting 330° to the southwest. During the same period that the human cases were occurring, anthrax cases among domestic animals were being reported in the villages surrounding Sverdlovsk 50 kilometers away. When the investigators mapped the location of the villages, they found that they also lay along the line oriented at 330° from Compound 19. These observations were highly indicative of a windborne plume of anthrax originating at Compound 19.

The investigators had an apparent point-source transmission with a known agent, a probable source of the organism, but an unknown period of exposure. By using the epi-curve and the incubation period for anthrax, they were able to calculate the median onset of disease and focus their investigation on April 2. The meteorologic data from an airport located 10 miles from the ceramics factory revealed that the predominant wind pattern in April was east to west. Approximately 2% of the time, the winds blew from the north along a southeasterly vector (330°); April 2 was one of those days.

In 1992, the Russian government admitted that Compound 19 had been part of an offensive biologic weapons program. The release occurred when air filters on the factory exhaust were not properly activated (Christopher, Cieslak, Pavlin, & Eitzen, 1997). Meselson et al. (1994) performed complex mathematical modeling based on the infectivity of anthrax spores, rates of infection among the exposed persons, and the case locations. They calculated that the upper limit for the amount of weaponized anthrax released in this outbreak was one gram.

Person

After identifying and counting cases and orienting the data in terms of time and place, thoroughly characterize the patients by collecting the following information:

- **Identifying information:** Name, address, telephone number, respondent (e.g., self, parent of child, spouse)
- **Demographic information:** Birthdate or age, sex, occupation, education, socioeconomic status
- **Clinical information:** Signs/symptoms, severity or outcome (hospitalization, death), time of onset, duration, documented medical care (name and telephone number in case contacting the provider is needed), preexisting medical conditions
- **Epidemiology:** Risk factor information (exposures and contacts), activities in which respondents might have participated, contacts with ill persons (are others ill in the family?), other factors shared in common among the other patients

The ultimate goal is to calculate and compare rates between groups on the basis of potential risk factors. For this reason, gathering denominator data is critically important for deriving rates for risk estimates. This crucial step is often overlooked. Unless groups being compared are identical in terms of size and composition, simple case counts cannot be compared.

Formulate and Test Hypotheses

After completing the descriptive epidemiologic study when the data have been analyzed in terms of time, place, and person, the next step is to use the results of this analysis to formulate and test hypotheses.

As noted previously, the primary reason for the investigation is to identify effective actions to control the outbreak and to prevent additional cases or a recurrence of the problem. Developing hypotheses that explain the outbreak by characterizing the type of exposure, the agent, source or reservoir, mode of transmission, or risk factors is therefore important.

At times, a hypothesis will be apparent from the descriptive analysis of the time, place, and person data. However, using other methods to develop a testable hypothesis might be necessary. Possible approaches include

- looking at previous outbreaks with similar agents or exposures,
- reviewing information obtained from case interviews,
- conducting open-ended questioning among patients or their contacts (hypothesis-generating interviews),
- reviewing anecdotes and impressions or ideas from local community members and leaders, and
- examining outliers (i.e., cases that did not occur during the expected time sequence for disease; early or late cases).

Testing the hypothesis can sometimes be accomplished with the descriptive data that already have been collected during the case finding. In the majority of cases, using comparison groups to evaluate the contribution of different risk factors is necessary. This frequently requires **planning additional studies** to collect the data needed to evaluate risk factors, and the two most commonly used study designs are the case-control study and the cohort study. Chapter 7 contains a detailed explanation of these study designs; here I provide a summary of the advantages and disadvantages of each design for outbreak investigation (Table 6.2).

Outbreak investigation teams typically start with a case-control study because it is usually faster, cheaper, and permits evaluation of multiple risk factors. After a specific risk factor has been identified, the team might conduct a cohort study to determine the specific risk associated with that exposure.

Implement and Evaluate Control Measures

As noted at the beginning of this chapter, public health officials should act as soon as they have a rational basis for implementing control measures. Public health

Table 6.2 Advantages and Disadvantages of Case-Control and Cohort Studies for Outbreak Investigation

	Advantages	*Disadvantages*
Case-control studies (use odds ratio as the measure of association)	• are quick and relatively inexpensive • require fewer study participants • permit evaluation of multiple exposures • are well suited for rare diseases	• are backward in that they begin with the disease and look back to the exposure (determining if the exposure preceded the disease might be problematic) • are unsuitable for rare exposures • cannot directly calculate the risk associated with a specific exposure because the number of control subjects is variable • are prone to bias in selecting the control subjects and prone to recall bias
Cohort studies (use risk ratio as the measure of association)	• have a logical temporal sequence (i.e., investigators start with the exposure and observe for occurrence of disease) • permit calculation of the risk associated with the exposure • allow evaluation of multiple outcomes from a single exposure (e.g., a study looking at smokers and nonsmokers enables evaluation of lung disease, cardiovascular, or cancer as potential outcomes) • are well suited to studies of rare exposures	• might require substantial numbers of subjects if the disease is rare • tend to be more challenging logistically (longer term, more participants, more expensive) • can be subject to bias if subjects drop out for specific reasons • might result in participants' behavior being influenced and the results being biased because the participants are being observed • are dependent on records being available (retrospective cohort studies)

authorities do not wait until the end of an investigation to implement control measures; instead, they implement them as soon as practicable. The big challenge for investigators is to determine when sufficient information is available on which to base a decision. Act too soon and unnecessary negative economic or social consequences might result for the persons affected by the control measure (e.g., closing a restaurant, causing loss of income). Act too slowly and additional persons might become ill who would have been spared. Unfortunately, no hard and fast rules exist on exactly when to implement control measures; each situation is unique.

Common control measures available to public health authorities include the following examples:

- **Eliminating or treating the source**: Recalling an implicated product, removing an infected food handler from work and providing medical treatment, or eliminating insect breeding sites
- **Cohorting patients**: A common approach in hospitals, child care, and other institutional settings
- **Preventing further exposures**: Washing hands and covering coughs during an influenza outbreak, safe food preparation practices, educational efforts to change knowledge and behaviors to limit HIV transmission
- **Protecting populations at risk**: Vaccination or chemoprophylaxis for persons at risk

Finally, evaluating the effect of control measures and adjusting the public health response accordingly is crucial. This might involve initiating **longer term surveillance** to monitor the ongoing effectiveness of control measures and to provide early warning of disease recurrence.

Communicate Findings

The final, critical step in any investigation (and one that is often omitted) is to prepare a written record of the investigation and outcomes. Writing the report

- provides a way for the team to formally convey recommendations to the requesting authority,
- might be an institutional requirement (i.e., the institution supporting the investigation will probably require a formal report for the official record),
- records the activities and methods for future reference (if the same type of problem occurs again, future investigators will be aided by seeing how a previous investigation was conducted),
- ensures rapid dissemination or notification to others regarding a serious problem having immediate implications (e.g., communicable diseases, a contaminated commercial product),
- shares experience with others if especially interesting, and
- provides communication skill training.

Different formats might be used for the team's report, including a preliminary written report to the requesting authority, a final written report, publication in a public health bulletin (i.e., a state health department newsletter or a national-level epidemiology bulletin), an article for a peer-reviewed journal, or as an abstract and presentation at a professional meeting.

OUTBREAK INVESTIGATION: A CASE STUDY

The following investigation, conducted by local, state, and federal health authorities in 2009, demonstrates many of the steps in an outbreak investigation (CDC, 2010).

Background

In 1996, public health authorities established a laboratory-based surveillance system called PulseNet. Participating public health laboratories from across the country perform standardized molecular subtyping of enteric pathogens by using DNA fingerprinting with a technique called *pulsed-field gel electrophoresis*. The resulting fingerprints are sent electronically to a database maintained at CDC. Computer algorithms are used to determine if a statistically significant increase is occurring in any given bacterial subtype. By looking at data from across the entire country, the PulseNet system frequently is able to identify clusters that might not be apparent to a single state or local health department laboratory.

Recognition of the Outbreak

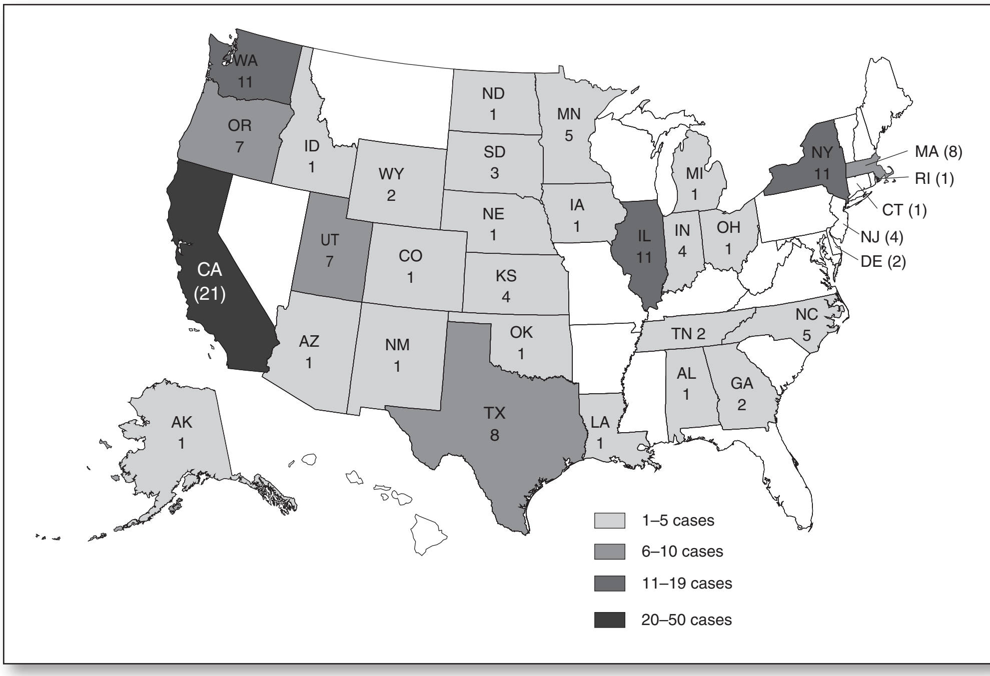
During August–September 2009, the PulseNet system detected a multistate cluster of *Salmonella enteritidis* serotype Montevideo cultures from 13 states that had identical DNA fingerprints, indicating a possible common source. The observed number of reports approximated the expected baseline of two to three reports per week, and the PulseNet system continued to monitor this common pattern. In November, the number of reported infections with the outbreak strain had increased to 15–20 samples per week, and CDC initiated a multistate investigation. By November 30, CDC had identified 127 cases in 30 states (Figure 6.13; CDC, unpublished data, 2010).

At this point in the investigation, the team had already completed certain basic steps. They had first verified the diagnosis; because PulseNet is a laboratory-based surveillance system, this step was fairly simple. Next, they confirmed the epidemic by comparing the number of cases of a single strain of *Salmonella* Montevideo reported to the national system to the historical rate of reports for this organism. Finally, the samples reported to the PulseNet system were instrumental in the first phase of identifying and counting cases.

The investigators then began a case-control study to try to identify the risk factors for infection. The team created the following case definition: a laboratory-confirmed infection with the outbreak strain of *Salmonella* Montevideo in a person with diarrhea onset, or if that date was not available, isolation date on or after July 1, 2009. (Note that this definition includes the elements of time, place, and person—although it does not define *diarrhea*.)

The investigators identified a total of 272 cases (Figure 6.14). The epicurve is not indicative of a point-source or person-to-person transmission mechanism but is more consistent with an ongoing source of infection.

Figure 6.13 Cases Infected With the Outbreak Strain of *Salmonella* Montevideo, United States, by State, November 30 (N = 127)



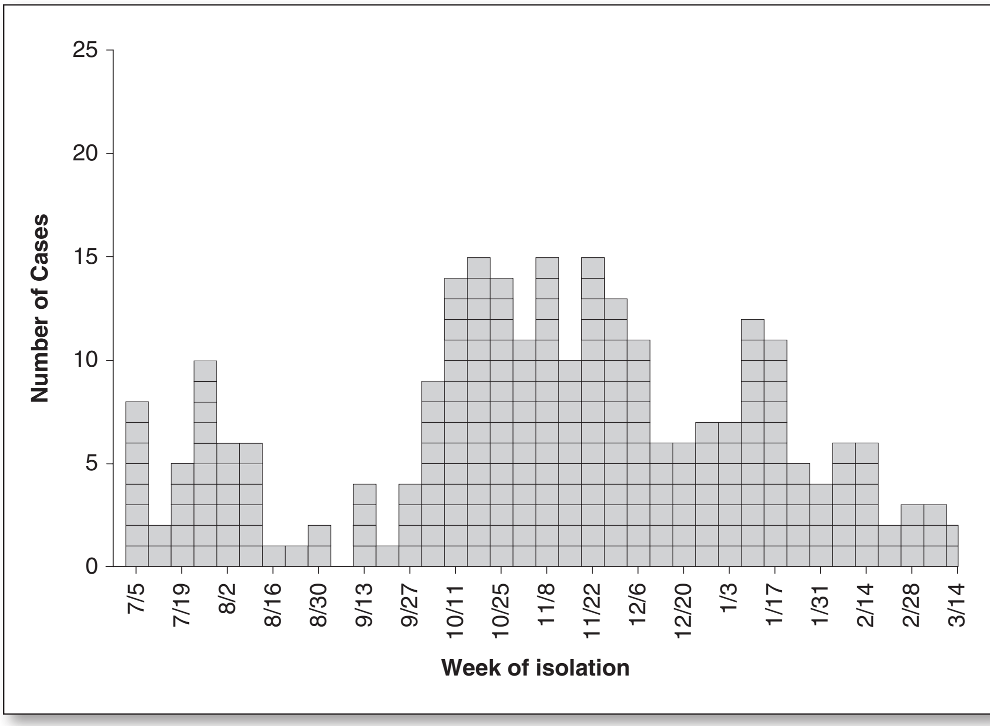
Source: CDC, unpublished data, 2010.

After gathering the basic descriptive data for this outbreak, the investigators began the process of hypothesis generating to try to identify potential risk factors for infection. They used different strategies.

- **"Shotgun questionnaire":** A long, standardized questionnaire that asked about > 300 possible exposures, including foods, beverages, and animal contact
- **Open-ended telephone interviews:** Less structured and focused on asking about travel, food consumption, and exposure to restaurants and grocery stores during the 7 days preceding illness
- **In-depth interviews:** Conducted in homes and included inventory of pantries and refrigerators

The open-ended questioning of one group of ill persons indicated that 58% reported having eaten salami, 75% reported having eaten delicatessen meats, and 55% reported having shopped at a national warehouse club store. Because the club store tracks purchases by all members, health officials in Washington were able to compile a complete record of all purchases made by seven ill persons. After

Figure 6.14 Number of Infections (N = 272) With the Outbreak Strain of *Salmonella* Montevideo, by Week of Isolation Date, United States, 2009–2010



Source: CDC (2010).

reviewing over 750 pages of shopping records, the team identified a brand of delicatessen meat (Company A) that had been purchased by five of the seven patients before they became ill. By comparing shopping records for patients in other states, they were able to identify 19 persons who had purchased the Company A product an average of 4 days before onset of illness.

After identifying a possible source of the infection, the investigators set up a case-control study where the control subjects were matched to the case-patients by neighborhood by using a reverse telephone directory system. Exposures evaluated in this study included the Company A delicatessen meats as well as other food items reported in the hypothesis-generating questionnaires. This study revealed that case-patients were four to eight times more likely to have eaten any Italian-style delicatessen meat.

The outbreak strain of *Salmonella* Montevideo was isolated from eight samples of Company A delicatessen meat collected from case-patient households and from retail stores. Two of these samples were taken from intact, sealed products obtained from retail stores. At this point, the team had formulated and tested a hypothesis, and on the basis of the initial results, they had conducted additional studies to further support their findings.

Working in collaboration with the Food and Drug Administration, the team implemented the following three control measures:

- Multiple consumer health advisories were issued by CDC, the Food and Drug Administration, the U.S. Department of Agriculture, and state and local health departments.
- Company A voluntarily recalled 1.3 million pounds of Italian sausage products.
- Additional recalls of 132,000 pounds of deli meat products were issued.

Further investigation at the Company A plant did not reveal any obvious lapses in food preparation protocols that might explain the massive contamination. The meat products were cooked at temperatures adequate to kill any *Salmonella*. However, after cooking, the meat was rolled in spices to apply a red and black pepper coating. Samples of pepper from Company A were also determined to contain the outbreak strain of *Salmonella* Montevideo. Contaminated lots of pepper were traced back to two separate spice companies, and these tracebacks resulted in an additional recall of >100,000 pounds of pepper. Ongoing surveillance for the outbreak strain of *Salmonella* Montevideo was maintained by PulseNet.

Conclusion

This investigation illustrates the key steps in an outbreak investigation, as outlined in Figure 6.1. Of note, after the team identified a likely vehicle (the delicatessen meat), they implemented well-designed control measures to protect the public's health. However, they also planned additional studies during the traceback to confirm the specific source of the contamination. Armed with the additional information that the pepper was implicated as the source of contamination for the meat products, they implemented additional control measures.

CURRENT ISSUES AND FUTURE DIRECTIONS

The way outbreaks are identified and investigated will continue to evolve in response to changes in technology and informatics. We have already seen a dramatic increase in the number of disease outbreaks that are first identified through clusters of case-reports picked up by increasingly sophisticated surveillance systems (e.g., PulseNet). However, with increasing sensitivity of those systems, the new challenge is to sort through the growing number of detected clusters to identify the significant public health events. As information technology improves, public health will likely have access to more timely data through the expanding use of electronic health records (EHRs). Large medical systems like the Veterans Administration are already developing the capability for real-time detection of outbreaks through monitoring of their EHR system.

Information technology also increases the tools that investigators can use to gather data. The case study described previously demonstrates the use of computerized shopping records to identify exposures reliably. Monitoring the frequency of specific inquiries to online search sites is being developed as a technique for monitoring infectious disease spread like the flu (www.google.org/flutrends/us/#US). The Internet is also being used with increasing frequency not just to get information out to consumers, but to gather information from them. Administering outbreak questionnaires electronically can dramatically improve the response time and efficiency of an investigation and lead to more rapid identification of control measures. This methodology has potential limitations, though, the most obvious being data security and privacy concerns.

Finally, changes in the technology available to teams in the field will affect the way investigations are conducted. Small handheld devices make data collection easier and faster, and they reduce errors when data from different field teams are consolidated. These devices can also aid in the interview process through the use of memory aids like photos or maps. Improvements in GPS technology have made mapping by field teams much easier and more accurate, thus improving the element of "place" in many investigations.

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