CHAPTER 1

How an Outbreak is Investigated

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INTRODUCTION

It is worth summarizing and elaborating briefly on the steps (or activities) of outbreak investigation (Exhibit 1-1). Although the steps may not always occur in exactly this order, this is the general pattern of events. It is not unusual for more than one step to be occurring at the same time. Not all lists of outbreak investigation steps are identical, as some steps may be combined into one overarching step or may not be listed as a step but included in a discussion of outbreak methods. It is important to recognize that a list of outbreak investigation steps is less of a recipe to be followed precisely than it is guidance. Also, as the investigation progresses, knowing where one is at within the outbreak investigation steps can make it easier to stay organized and plan ahead for what may need to occur next. (The reader is also encouraged to examine other good reviews of outbreak investigation referenced at the end of this chapter.)[1–3]

VERIFY THAT AN OUTBREAK IS OCCURRING

Often a telephone call reports the suspicion of an outbreak. Someone has noticed something out of the ordinary, such as an unexpectedly high number of cases of a disease or syndrome. The call might come from someone who attended a group function, like a wedding, and now they and others

Exhibit 1-1 The Steps of an Outbreak Investigation

1. Verify that an outbreak is occurring.
2. Confirm the diagnosis.
3. Assemble an investigation team.
4. Create a tentative case definition.
5. Count cases.
6. Perform epidemiologic analysis.
7. Perform supplemental laboratory or environmental investigation (if indicated).
8. Develop hypotheses.
9. Introduce preliminary control measures.
10. Decide whether observation or additional studies are indicated.
11. Perform additional analyses or plan and perform additional study.
12. Perform new (investigation derived) control measures, and/or ensure the compliance of existing control measures.
13. Communicate prevention information and findings.
14. Monitor surveillance data.

they know are ill. It might come from a hospital infection-control nurse or hospital microbiologist who notices that they have more than typical numbers of a particular bacterial isolate in the laboratory or infectious disease among the patients. It could arise, however, from a thoughtful review of surveillance data (perhaps from a public health laboratory) demonstrating an unexpected rise. Whether the recognition arises from a community member, a health professional, or an astute public health employee, the first step of an outbreak investigation is to verify that there is indeed an outbreak occurring. This is the first, but not the only, time during an outbreak investigation that one must be careful not to assume anything and to have a healthy skepticism about the information that they are receiving.

A common method of verifying that an outbreak exists is to examine surveillance data (if that condition is a reportable disease). One of the important uses of surveillance data is outbreak detection. It can quickly be determined whether the suspicion of a high number of case reports of salmonellosis, shigellosis, or pertussis bears out as accurate by comparing the report to a median number of reported cases during a similar time period historically. In some cases, the disease is not known but the outbreak is initially recognized as a sudden rise in the onset of a sign or symptom such as rash or diarrhea. A report might be that someone attended a group event where food was served and that many persons are ill; however, until it has been confirmed that more than one person is truly ill with a similar illness and that they consumed food in common, it is premature to declare that a foodborne outbreak has occurred.

CONFIRM THE DIAGNOSIS

Another early step of the investigation is to confirm the diagnosis. A classic example of this would be when a hospital laboratory might report that they have several isolates of an uncommon bacteria or virus. Because the isolate is unusual, the laboratory might not have substantial expertise in identifying it; therefore, it is necessary to confirm the diagnosis by forwarding the isolates to a reference laboratory such as at the state health department or Centers for Disease Control and Prevention (CDC). In such reference laboratories, it can be determined, for example, whether the *Salmonella* outbreak is really five isolates of *Salmonella* (and which serotype is involved) or actually one or even no *Salmonella* at all.

ASSEMBLE AN INVESTIGATION TEAM

Depending on the outbreak and the public health jurisdiction(s) involved, an investigation team may need to be assembled. This is especially likely if it is of a remarkable size or complexity that it needs a more formal group to work on it. Sometimes the investigation is conducted by an individual for whom this is an occasional duty and there isn't a team per se, but individuals who react to the reports coming in and deal with them as needed (in other words, not every outbreak receives a full formal investigation). In some settings, a team already is assembled and on call for the next outbreak whenever it may occur. In that case, this step was actually the first step as that public health jurisdiction recognizes that outbreaks occur with a great enough frequency to have planned ahead; however, more commonly, outbreak teams are assembled based on the unique issues surrounding the outbreak.

Considerations in assembling the team include determining a team leader. This is based on experience and expertise of the team leader, and therefore, it might be a communicable disease section chief if there was an outbreak of salmonellosis, whereas it might be an immunization section chief for an outbreak of measles. Alternatively, there could be a program staff level individual (ideally with epidemiologic training) who is well suited to this task, or an epidemiologist might be invited in from a higher level jurisdiction (such as state or federal government) when necessary skills are lacking locally or when an investigation was attempted but was unsuccessful and still needs resolution. A higher profile investigation or one involving multiple jurisdictions might be led by a state epidemiologist or other senior epidemiology personnel. The team leader may not always be an epidemiologist but may be a skilled administrator or environmental health worker. The most important thing is that it should make sense that someone in the lead belongs there as there is much to be gained with a well run outbreak investigation and much to be lost when it is poorly run.

Team members should be considered based on their experience, abilities, and availability. A team is best comprised of one or more members with experience, as the activities are likely to proceed much more smoothly with fewer misunderstandings or errors along the way; however, some team members may be inexperienced but need on-the-job training, or they may be needed to ensure that certain activities (such as interviewing) are adequately staffed to gather quickly the data needed for analysis. If they have the needed abilities (such as interviewing, data entry, or analysis skills), they can become useful contributing members once provided the appropriate guidance or training. However, providing guidance or training in the setting of an urgent outbreak investigation can pose quite a challenge with many priorities competing for one's time.

If medical record abstraction or other clinical-related work is needed as part of an investigation, a healthcare provider such as someone with nursing or medical training may be essential.

Given that outbreaks don't schedule themselves when it is convenient to staff them, however, an additional consideration is who can be available for the duration needed. Personnel are typically diverted off their routine duties (which may also be essential and can only be delayed briefly). They may need to travel, including staying overnight for several days or longer. It is best to staff an outbreak with personnel who can remain with their outbreak duties without interruption, although this may just not be possible at times.

CREATE A TENTATIVE CASE DEFINITION

Once convinced that an outbreak is really occurring and having confirmed the diagnosis (or syndrome) that is involved, a tentative case definition is needed to begin to determine the extent of the outbreak in a systematic way. Essentially, this is a surveillance system that one is creating within the outbreak investigation. If it is a reportable disease that is responsible for the outbreak, much of the outbreak definition may already be available. The case definition should involve elements of person, place, and time. Routine reporting of a reportable disease would not include the wedding, church supper, or other cohort information, nor would it necessarily include any geographic boundaries that might be needed to define the outbreak; therefore, a reportable disease case definition is often adapted but not just used without any modification at all in an outbreak setting.

This case definition is tentative because as additional information is learned then there may be a need to modify it so that it is most accurate and useful for analysis. It is important that when communicating with the media and others such as administrators who may not have epidemiologic training that the preliminary information is just that—preliminary. An outbreak investigation needs to remain flexible, including the possibility of revising the case definition to achieve its goals of disease control and prevention.

The creation of a case definition may involve a thoughtful discussion of sensitivity and specificity. In an attempt to identify every case of a disease that might lead to death or severe morbidity, a highly sensitive case definition might be needed; however, when performing data analysis of reported cases, a more specific case definition is desired to limit the influence that inclusion of those without the disease of interest that happen to meet the case definition may have on the analysis results. As an illustrative but extreme example, if an investigation wanted to identify nearly every case of influenza, the case definition might include anyone with fever; however, such a definition also captures cases of numerous other illnesses and thus lacks the specificity needed to trust any data analysis intended to be specific to the control of influenza. Alternatively, if the case definition required the isolation of the influenza virus, there would be a high degree of certainty about the cases reported, but because most persons with influenza do not have laboratory procedures performed that lead to isolation of the virus, relatively few cases would be reported. A case definition should avoid including any potential risk factors within it, as that would prevent the analysis of determining whether those risk factors are statistically associated with the exposure.

A case definition often has more than one category within it, such as confirmed versus probable or primary versus secondary. Confirmed cases typically represent cases that have been laboratory confirmed. It is important to make this distinction of "laboratory confirmed" versus just saying "confirmed" because some surveillance systems, such as the one used for pertussis in the United States, include cases without laboratory confirmation as confirmed cases if they are epidemiologically linked to a laboratory confirmed case. Probable cases usually refer to cases that have not met the relatively specific criteria of laboratory diagnostic testing but have other information that makes their likelihood of being true cases high.

The case definition is for the investigator's benefit. It is intended to assist the investigator with counting the cases and best determining the associated factors and source. This can madden the media, who are following some of these investigations and even public health officials who don't understand why the case count is changing, but keep in mind that its usefulness is in helping the investigator to provide a sound explanation for what has happened and why. The case definition in this setting is not designed to count most accurately exactly how many people got that disease. That number is likely to get underestimated in the race to solve and control the outbreak.

Primary cases are the cases that were exposed to the implicated source, whereas secondary cases usually arise from their contact with an infectious primary case. For example, a restaurant may be implicated in an outbreak. The cases that ate a *Salmonella*-contaminated food develop gastroenteritis and are called primary cases. They will shed the organism in their stool, and if they do not practice good hand hygiene after using the bathroom, they may transfer the organism to a family member or friend (such as if they prepared sandwiches for them). These new cases of salmonellosis may never have been to the implicated restaurant and are secondary cases. Unfortunately, sometimes you can have cases in the same household where the second case in the household could have been exposed to the implicated source but had a long enough delay after the first household case to be caused by secondary transmission as well. This needs to be kept in mind when designing the case definition.

When later performing analysis of the cases ascertained through outbreak investigation, it is important to exclude the secondary cases from the analysis of risk factors, especially when the goal is to identify the primary source of the outbreak. In addition, if there are sufficient numbers of laboratory-confirmed cases, probable cases may be excluded to increase the likelihood that an association is real and to avoid the possibility of bias against a true association if probable cases include some persons who met the case definition but do not (unknown to the investigation staff) have the outbreak disease. Thus, while chasing down laboratory specimens (sputum, vomit, feces, blood, or others) from many of the cases can involve a lot of work, it can pay off if it yields a big enough number of cases that you are confident really are cases.

CASE COUNTS

After a case definition has been created, the work of identifying as many cases as is feasible follows. In some situations, like a commercial product outbreak or one that has substantial morbidity or mortality and is not readily being solved, that means trying to get all of the cases reported often by announcing the outbreak through a variety of means, including electronic, fax, and press release, although there may be situations where the outbreak is so massive that efforts are eventually best directed toward prevention and control. In this uncommon situation where an outbreak is massive, an estimate of the case burden may be performed. It is a judgment call whether resources are to be expended on reporting tens of thousands of cases versus allowing passive reporting to decline naturally without active and persistent efforts. Broadcasting the existence of an outbreak may be indicated when there is a good prevention intervention (like an effective vaccine or immunoglobulin), and thus, raising awareness could help exposed persons prevent the onset of illness (such as in the case of hepatitis A exposure).

PERFORM EPIDEMIOLOGIC ANALYSIS

After there are cases to analyze and those data are entered into a computer database, it is time to perform descriptive epidemiology. This allows for many basic questions to be answered, especially when the number of cases on the initial "line list" where the first reports were summarized on paper or in spread sheet has become numerous. The initial analysis might include frequencies of all the variables, thus demonstrating basic patterns of the outbreak such as age, gender, racial, occupational, clinical manifestations, and exposure information. Cases may be examined for their geographical distribution, and the results may lead to a hypothesis regarding a suspected exposure site. If an onset of illness date and an exposure date are known, a mean or median incubation period might be calculated that can be compared with what is already known for certain suspected pathogens (most useful when the pathogen is unknown). Depending on the type of outbreak (such as respiratory or foodborne) and whether the number of persons who have been exposed is known, preliminary overall or food-specific attack rates can be determined. Several computer statistical software packages are available for analyzing outbreak data, but one of the more commonly used and freely accessible epidemiological software packages is Epi Info (available for free download from the CDC at http://www.cdc.gov/epiinfo/). Epi Info is particularly convenient for investigators with limited epidemiologic and analysis skills because it has many functions that do not involve writing any programming code.

PERFORM SUPPLEMENTAL LABORATORY OR ENVIRONMENTAL INVESTIGATION

Environmental or laboratory studies may be recognized as potentially useful early in some outbreak investigations. For example, in foodborne outbreak investigation where a food establishment such as a restaurant is implicated by several of the cases, a restaurant inspection by the local health authority is a routine response. This would typically occur even if that food establishment had received a routine inspection some time in the recent past. The inspection could reveal useful clues that may help with use or interpretation of the epidemiologic data (such as learning of ill food handlers or discovery that there was a recent plumbing problem). It may simply reveal sooner (rather than after data are entered and analyzed) that there are violations of required food sanitation practices that must be remedied for that business to stay in business. In other words, a control measure such as closing down a restaurant should not have to wait until epidemiologic analysis if an onsite inspection of an implicated site reveals the need for such actions. Alternatively, an implicated site may not be recognized as in need of inspection until epidemiologic analysis provides the hypothesis of such a site. This might be the case for an outbreak of sporadic cases of a disease (such as travel-associated Legionnaire's disease) where cases are not becoming recognized all at one time and the outbreak is picked up by a central repository of cases such as a national or international surveillance system.[4] Alternatively, the sporadic cases may become linked by a laboratory surveillance system that identifies identical bacterial strains referred from cases in disparate locations reported to different health jurisdictions.[5]

DEVELOP HYPOTHESES

The development of a hypothesis usually is a very early step in outbreak investigation. The first hypothesis may even come from a case, and it's possible that it could be correct ("My husband, daughter, and I are all sick and so is my sister's family. We both attended my cousin's wedding and I'm sure it was the chicken because it wasn't fully cooked.") Alternatively, a hypothesis may be difficult to develop as the information may not be revealing enough. This might occur when the questions that are needed to be asked simply have not been asked yet; however, enough is known of many diseases that cause outbreaks to lead experienced investigators to at least some hypothesis to explore with the descriptive data. For example, there have been many outbreaks of diarrheal disease attributed to *E. coli* O157:H7, and among the potential sources, undercooked ground meat is a well recognized source; therefore, it is common for cases of this disease to be asked whether ground meat was consumed. An examination of the frequency of having eaten ground meat among the cases is helpful because when many of the cases have this exposure it leads to a biologically plausible hypothesis that ground meat was the source of the outbreak. Although it is reasonable to consider ground meat in every *E. coli* O157:H7 outbreak (and therefore to inquire about it), the absence of a majority of the cases with such an exposure should raise the issue of alternative hypotheses; however, recall of an exposure can be poor, whether early or late in an investigation, leading to the response to a question about the true exposure that caused the outbreak not reaching 50% with a yes answer (William Keene, PhD, personal communication). Efficiency in solving outbreaks comes with increasing familiarity with the most common pathogens that cause them and the emerging information about these pathogens.

INTRODUCE PRELIMINARY CONTROL MEASURES

As early as possible, preliminary control measures should be introduced. Some of these control measures may be already established and incorporated into legislated rules and regulations for a reportable disease. In the case of botulism, removing any suspected product (such as a batch of a suspected home canned vegetable) might be performed immediately on the recognition of this source before any data analysis has occurred and possibly before any data have even been entered into a database. Similarly, there need not be an outbreak of meningococcal meningitis for the control measure of providing prophylactic antibiotics to close contacts of a case to occur. When more than one person with gastroenteritis implicates having eaten at the same restaurant and becoming ill within a biologically plausible time period, an inspection of that restaurant by the local health department is reasonable, although it is uncertain whether that restaurant is the source at this early time; therefore, a restaurant inspection is a reasonable preliminary control measure, but closing the restaurant might be premature.

This brings up the important issue of when to pursue an extreme control measure such as closure of a business where the economic implications could be substantial for the business and are being weighed against the public health implications of delaying such an action. Each decision should be made on a case-by-case basis. If the decision is made to take the extreme action and it is wrong, there is risk for litigation and loss of credibility. If the decision is made not to take the extreme action and it is wrong, again there is risk for litigation and loss of credibility. Thus, with such a dilemma, what is one to do? Essentially, the basis for this decision should be made by weighing factors such as the severity of the illness, the vulnerability of the population exposed, and whether the suspected exposure is ongoing. An illness that is killing its victims is certainly worthy of a heavier hand than one that causes an inconvenient gastroenteritis with very rare mortality. If the exposure is threatening persons at higher risk for clinically severe manifestations such as infants, older individuals, or immunocompromised persons, it increases the weight of considering a more extreme measure (at least temporarily until more evidence comes in). If the exposure is a food and the product has been discarded or its preparation has been discontinued, then closure of a restaurant with the aim of controlling the outbreak would be of little benefit after this activity has already occurred. In the case of a business, it may be possible to reason with the owner or manager to lead to his or her enacting the control measure of closure on a voluntary basis. It may be decided that they have less to lose by closing voluntarily and appearing cooperative than by being closed involuntarily or announced in a press release from the health department.

Other preliminary control measures might involve public education about the mode of transmission and prevention methods that are recognized about the outbreak disease from previous experience. Alternatively, a more expensive or difficult outbreak control measure such as mass vaccination may need to wait for clear evidence from additional studies or supplemental laboratory testing that demonstrates whether the vaccination is appropriate. For example, in an outbreak of invasive meningococcal disease, the vaccine covers four of the five most common serotypes of the organism (types A, C, Y, and W135 of *Neisseria meningitidis*); therefore, if the laboratory investigation determines that the outbreak is due to serotype B, mass vaccination with the quadrivalent vaccine would not be expected to impact on the outbreak.

Finally, political considerations can trump everything as a decision may be made by a high-level administrator who has determined that there is a right side and a wrong side of this issue to be on and they have decided to get on what they consider to be the right side. At a minimum, the investigators can offer wise counsel to the administrator based on the evidence and any other information, but sometimes these decisions are out of the investigators hands.

DECIDE WHETHER OBSERVATION OR ADDITIONAL STUDIES ARE INDICATED

Before launching into additional studies such as case control or cohort studies to test hypotheses, a decision should be made whether further studies are warranted. Sometimes these additional studies may be done with the existing data depending on the question. In some situations, an outbreak has "burnt out." No further cases are being reported and it seems that whatever the exposure was, it may have all been consumed. The pursuit of additional study at this time may be of little public health use compared with the resources needed to carry it out. Sometimes a case control study may be possible as with an *E. coli* O157:H7 outbreak where one or two dozen cases have been reported over a few months in a geographic area where that is unexpected. Preexisting outbreak investigation questionnaires are available from the Internet (an example can be found at http://www.oregon.gov/DHS/ph/acd/keene.shtml). It may be tempting to pursue a case control study because there are well-recognized risk factors and asking these questions of controls is feasible; however, in the absence of a sound hypothesis, there is little chance for success with such an approach compared with the likelihood of wasting personnel resources.

One of the authors of a chapter in this book, Dr. Paul Blake, was formerly the head of the Foodborne and Diarrheal Diseases Branch at the CDC in Atlanta. Back in 1984, he authored a memorandum that provided guidance at the CDC on this issue. He emphasized the importance of interviewing the initial cases and that if such interviews did not lead to a hypothesis about the exposure that it would be best to have a more experienced interviewer reinterview them. If that still did not lead to a hypothesis, rather than pursue a study not based on a sound hypothesis, one could try to bring the cases together (with their consent either in person or perhaps by conference call) to discuss possible exposures that could weave a common thread among them. Their interaction with each other could lead to information that an interviewer might not think to have asked.

The in-depth and open-ended hypothesis-generating interview can be very useful to lead to the discovery of unexpected vehicles for disease. A single investigator would be best to perform each of these hypothesis-generating interviews. The interviews should be performed as soon as possible after the report of the case because recall may diminish with time. Recalling one Louisiana outbreak of cholera that Dr. Blake investigated, he said this:

> It was not until I interviewed the fourth case and he mentioned eating cooked crabs which the first three had also mentioned, that a chill went up my spine and I thought, "Cooked crabs could be the cause of this outbreak." We would never have otherwise included cooked crabs on a case control questionnaire because we did not consider cooked crabs to be a possible vehicle for cholera because they were cooked.[6]

PERFORM ADDITIONAL ANALYSES OR PLAN AND PERFORM ADDITIONAL STUDY

If a sound hypothesis exists, additional analysis may be performed such as a cohort or case control study. Entire books can be written on these study methods. The cohort study gets its name from the convenience of having the entire population exposed clearly defined as with a church supper, catered banquet, or persons who share the same well for their drinking water. In the latter example, it can be difficult to demonstrate an association because everyone may have had the exposure, and thus, you do not know whether the well water drinkers are ill because they drank the well water or because they have some other common exposure. In this type of situation, it can be helpful if a dose-response relationship can be demonstrated. The more well water those exposed drank, the more likely they became ill. In the case of a heavily contaminated vehicle, this may be more difficult to show.[7]

Multiple studies may be needed to get to final conclusions. In the case of an Illinois outbreak caused by the parasite Cryptosporidium, the first study performed was a community case control study to determine whether a popular water park was the exposure site. Other possibilities considered included other recreational water exposure such as a lake, contact with animals, and drinking a possibly contaminated beverage. After exposure to the water park was strongly associated with having cryptosporidiosis, a cohort study was performed among water park attendees to determine the exposure within the water park. This study demonstrated the importance of ingesting the pool water. Finally, supplemental laboratory investigation involving testing of the water filter system for the presence of the parasite was also performed.[8] These studies taken together made a strong case for the source being the water at the water park.

Selecting controls for a case control study can be a challenge. Controls should not have had the outbreak disease but should have had a similar likelihood of having been exposed as the cases (as best one can establish this). This may be handled by picking controls that live in the same neighborhood as the cases or are referred by controls (friends and family). They may be matched to cases by age group or gender to control for behavioral differences that are influenced by these factors, some of which may be unknown to the investigator. After a control is identified and the interviewing has begun, it should be established right away whether the control could meet the case definition completely or even partially (perhaps qualifying as a probable or suspect case). Exclusion criteria should be established to ensure that any controls could not actually be cases. Although this might ideally be done with laboratory testing, this is often not realistic, and thus, screening them with questions that determine whether they satisfy the case definition is more feasible. Controls that may meet the case definition should be investigated further and reclassified as cases as needed.

A variety of biases could be introduced when selecting cases and controls for further study.[7] These include sampling bias if there is a need to select among the cases as when there are a very large number but a large number of interviews are not feasible or statistically necessary to evaluate a hypotheses (an uncommon fortuitous situation to be in). Diagnostic suspicion bias may occur if the cases are well aware of the suspected vehicle, perhaps from widespread media attention. Diagnostic access bias may interfere with selection of controls because cases may have (by definition) had access to diagnostic tests and thus been recognized as cases while controls may include persons who, for reasons that could be relevant to the analysis, were less likely to access such diagnostic testing. Misclassification bias can be dealt with by the screening of controls for any similar illness to cases as stated previously here. Other biases such as recall bias or interviewer bias must also be considered. A good outbreak investigation will consider these biases and interpret the results with them in mind.

Several factors may support a decision to perform additional analytic studies even when the outbreak appears to be over when it is first recognized. These include a high morbidity or mortality of the disease, high visibility of the outbreak as with substantial media attention, enthusiasm by those affected by the outbreak (where their cooperation and/or their desire for an answer to what happened is high), and the novelty of the pathogen, its mode of transmission, or its clinical manifestations such that it provides an opportunity to learn something new about the organism or disease. Another important factor is the availability of personnel and financial resources to continue with the investigation.

Sometimes outbreak investigation studies are referred to as "quick and dirty" because biases are not substantially dealt with in the study design and the number of cases and controls is not derived from any power calculations based on the hypothesis and assumptions. This is a reality of outbreak investigation because, as they are essentially experiments of nature, there is no control over how many cases will have occurred. The best one can do is pursue case ascertainment aggressively to attempt to populate the database with as many cases as may be needed to lead to statistically significant findings. It should also be recognized that even statistically significant findings are not the same thing as cause and effect, or simply stated, if it is 95% likely that an association did not occur by chance, it is still 5% likely that it could have; therefore, for any results from these studies, there should be biologic plausibility. Also, the finding (or association) should account for most of the cases if the source of the outbreak will be attributed to that finding and be of a sufficiently high magnitude to be relevant.

Outbreak investigators should also be familiar with the binomial probability method. When enough information is available, this method can allow for estimation of the probability that a particular exposure was present among cases by chance alone. Without performing a case control study, the results of such a study can be estimated. For example, in an outbreak caused by *Salmonella enterica* serotype enteritidis, routine food exposure interviews had not indicated a common exposure. A much expanded questionnaire was then used, and it led to a hypothesis concerning consumption of raw almonds. Using the binomial probability method, the rate of consumption of almonds (and other foods) was compared with the background rates of consumption of these foods based on available Oregon survey results. It was helpful that background information on the expected rate of consumption of almonds was available for the Oregon population. In that survey, 9% of 921 Oregon residents had consumed raw almonds in the preceding week; however, all five of the sporadic cases had consumed raw almonds in the week before illness. These and other data from this investigation contributed to a recall of 13 million pounds of almonds![9] Additional information on this method can be found on the Internet (http://www.oregon.gov/DHS/ph/acd/outbreak/binomial.xls and http://faculty.vassar.edu/lowry/binomialX.html), and "A Population Survey Atlas of Exposures" is available from the CDC (http://www.cdc.gov/foodnet/reports.htm).

PERFORM NEW CONTROL MEASURES AND/OR ENSURE THE COMPLIANCE OF EXISTING CONTROL MEASURES

Depending on the outbreak, new control measures may derive from the investigation results. If identification of an exposure such as a food item or activity like swimming is revealed as the source of the outbreak only after additional studies were performed, a food may need to be recalled and product embargoed, or perhaps a swimming pool or lake may need to be closed to the public. New environmental and laboratory investigations may follow as an attempt is made to explain more fully the origin of the outbreak. In the case of a foodborne outbreak, a trace back might help to explain where an imported product became contaminated. Alternatively, when monkeypox was imported to the United States, a trace back determined that the outbreak likely began from giant Gambian rats imported from Ghana that later mixed with highly susceptible United States prairie dogs sold (unknowingly infected) to lovers of "pocket pets."[10]

It is an important practical matter to ensure that control measures put into place are being carried out. This is usually not an issue unless the persons who are directly responsible for carrying out the control measure (such as closing a restaurant or catering business) fail to accept that the control measure is sound or perhaps if they do not trust the source of the prevention information. If a publicly accessible area is restricted, such as when a beach is closed because it is a risk, it should be a routine matter that someone is assessing that there are no swimmers and that the sign(s) posted is readily visible and posted in the appropriate languages to make sure that the message is readily understood.

COMMUNICATION OF PREVENTION INFORMATION AND FINDINGS

Communication is a key issue from the beginning to the end of the outbreak. Within the outbreak investigation team, information such as telephone and fax numbers and e-mail addresses are all basic information to be exchanged. Regularly, the team should be meeting either in person or by conference call to update each other, and it is beneficial to summarize the update in a written format such as an e-mail circulated internally among those with responsibility directly or indirectly for the investigation such as high-level administrators. It is especially important for no assumptions to be made related to communication. In other words, it can be an unwise gamble to assume that someone else is sharing important information with the team leader or an administrative person in a central office if that is not known with certainty. Redundancy of communication may be inefficient, but it is far less of a sin than lack of communication.

The public and other stakeholders of the outbreak are important communication targets as well. These may include hospital staff such as emergency room physicians or infection control workers, day care workers, school principals or teachers, parents, and the media. Depending on what information is being released, those responsible at the site of the outbreak (such as a restaurant or hotel manager or hospital administrator) should be made aware of basic developments, as their level of anxiety can be very high and their cooperation may be linked to the trust that can come from good communication. Partnering organizations, such as the U.S. Department of Agriculture or the Food and Drug Administration as well as state or local equivalents, should also be updated. Those who need to be informed and what they need to be told may vary based on the specifics of the outbreak investigation.

What is said in oral versus written communication is also worth considering because written word typically becomes part of a permanent record. It may be read or reread, sometimes with unintended negative intonation. E-mails may be sent to one party and forwarded to another. Written communication may be released to attorneys if legal action follows. It is a practical matter for any investigator to be open and honest in all of their communication but to be concise and clear without unneeded unbalanced accusation or risk of breeching confidentiality by recording names unnecessarily. An example of this could be when the investigation staff might name a person or restaurant they are investigating in an e-mail that is forwarded to someone outside of the investigation team who then reveals this name prematurely perhaps to the media. The person to whom this e-mail was forwarded may have had too little information about the details of the outbreak or too little experience with these situations. The use of terms "Hotel X," "Product A," "Nurse B," or Restaurant Y" arose to help protect the unnecessary release of identities where that information could be damaging and would not benefit public health. Alternatively, if protection of public health warrants it, communication broadly of the name of a person, institution, or other exposure source is warranted. Investigators should be aware of legal requirements in their jurisdictions concerning matters that involve confidentiality.

Communicating the prevention message of the outbreak and the findings through internal report or scientific publication is also important. In the case of the latter, agreement early on concerning who will be assigned the lead authorship is very important to avoid conflict or resentment later on. This is especially important when more than one person on the team might be qualified to lead the investigation or to undertake the writing of a scientific article describing it. It is also especially important when multiple public health jurisdictions are involved, including when federal assistance is performed at the state or local level.

MONITOR SURVEILLANCE DATA

Finally, it is important to continue to monitor surveillance data as the outbreak ends. This may reveal that the control measures were inadequate and that new hypotheses and new investigation may be needed. Also, secondary outbreaks may arise. For example, after the massive cryptosporidiosis outbreak in Wisconsin (described in this book), additional smaller outbreaks were recognized as the parasite was shed by persons with cryptosporidiosis in a variety of settings such as a swimming pool.[11]

CONCLUSION

The steps of outbreak investigation are extremely useful to keep in mind during an outbreak to help provide some order to what can be a stressful and fast moving or complicated process. Outbreak work is reactive. Although some outbreaks are actually over when they are recognized, many are in progress and have an urgency to them. The hours can be long but some of an epidemiologist's best work actually is performed in this intense setting. The examples in this book will hopefully provide the reader with an illustration of how some of these steps have played out in real outbreaks of infectious diseases. Keep in mind, however, that sometimes not all of the steps need to get done before a press release comes out to announce the concern. There is an art to making the decision of how far to go with an investigation, and that comes with much experience. Nonetheless, it is a gamble every time.

REFERENCES

1. Reingold AL. Outbreak investigations: a perspective. *Emerg Infect Dis* 1998;4:21–27.
2. Gregg MB. Conducting a field investigation. In Gregg MB, ed. *Field Epidemiology*, 2nd ed. New York: Oxford University Press, 2002:62–77.
3. Magnus M. Outbreak investigations. In *Essentials of Infectious Disease Epidemiology*. Sudbury: Jones and Bartlett, 2008:43–61.
4. Ricketts KD, Yadav R, Joseph CA. European Working Group for Legionella Infections. Travel-associated Legionnaires disease in Europe: 2006. *Euro Surveill* 2008;13:18930.
5. Jones TF, Scallan E, Angulo FJ. FoodNet: overview of a decade of achievement. *Foodborne Pathog Dis* 2007;4:60–66.
6. Yoder J, Ritger K, Dworkin MS. Foodborne outbreak investigation: how do I find the implicated food when I have few cases and no good hypothesis? Illinois Infectious Disease Report (Volume 3, Spring 2006). Retrieved June 25, 2008, from www.idph.state.il.us/health/infect/ID_Report_Spring06.pdf.
7. Palmer SR. Epidemiology in search of infectious diseases: methods in outbreak investigation. *J Epidemiol Com Health* 1989;43:311–314.
8. Causer LM, Handzel T, Welch P, et al. An outbreak of Cryptosporidium hominis infection at an Illinois recreational waterpark. *Epidemiol Infect* 2006;134:147–156.
9. Keady S, Briggs G, Farrar J, et al. Outbreak of *Salmonella* serotype enteritidis infections associated with raw almonds: United States and Canada, 2003–2004. *MMWR* 2004;53:484–487.
10. Reed KD, Melski JW, Graham MB, et al. The detection of monkeypox in humans in the Western Hemisphere. *N Engl J Med* 2004;350:342–350.
11. Mac Kenzie WR, Kazmierczak JJ, Davis JP. An outbreak of cryptosporidiosis associated with a resort swimming pool. *Epidemiol Infect* 1995;115:545–553.