

CHAPTER V:

THE EPIDEMIOLOGIC

INVESTIGATION

## IMPORTANT RESOURCES

## EPIDEMIOLOGY PROGRAM

## (Bureau of Infectious Disease and Laboratory Sciences)

## 617-983-6800 (Regular and Emergency Number)

## \_\_\_

June 2017

The epidemiologic investigation is an important part of the complete foodborne illness investigation that also includes the environmental and laboratory investigations. Each part of the investigation compliments the other and team work and open communication is of utmost importance. The purpose of the epidemiologic investigation is to identify a problem, collect data, formulate and test hypotheses. It involves the collection and analysis of more facts or data to determine the cause of illness and to implement control measures to prevent additional illness. The epidemiologic investigation should be a coordinated effort by the local board of health (LBOH) and the epidemiologists at the Massachusetts Department of Public Health (MDPH). Even if much of the investigation occurs at MDPH, it is imperative that the LBOHs understand the process and the importance of timely reporting of accurate information. The Working Group on Foodborne Illness Control (WGFIC) at MDPH is available for guidance and assistance through each step of your investigation.

# A. What is Epidemiology?

A text book definition of epidemiology is the study of the distribution and determinants of disease frequency in human populations. It is the collection and analysis of data to determine whether an association may exist between one or more exposures and the occurrence of disease. In practice, epidemiologists often employ statistics and probability to look at who gets sick or injured and why. In a sense, epidemiology is as old as medicine itself. Hippocrates suggested, in the fifth century B.C. that the development of human disease might be related to the external, as well as the personal environment, of an individual.

John Snow, a British physician is frequently considered the "father" of epidemiology. His investigations of cholera in London in the 1840's and 1850's drew together all three components of the definition of epidemiology: frequency, distribution and determinants of disease. When a cholera outbreak occurred in London, Snow determined that cases occurred most frequently in specific neighborhoods of the city that used water supplied by one company. Snow canvassed the involved neighborhood to determine the source of water for each household that had a case of cholera. Snow charted the frequency and distribution of cases and was able to discover possible causes and determinants of infections. At one point, cases were mapped to the supply of one particular water pump, so Snow had the handle of the implicated water pump removed. The approach used by Snow is still used today.

# B. Conducting an Epidemiologic Investigation

Epidemiologic investigations are usually conducted in outbreak situations. The primary reasons for conducting an epidemiologic investigation are to determine the cause of an outbreak and to implement control measures to prevent additional illness.

A questionnaire is often solicited to assist the investigator in developing better hypotheses about the etiologic agent's identity, source and transmission. The investigators interview ill and well persons, and calculate and compare rates of illness in both groups. They make time, place and person associations and calculate the probability that a food was the responsible vehicle.

The investigator incorporates results from epidemiological associations and the environmental and laboratory investigations, and uses these data in forming and testing hypotheses. Careful development of epidemiologic inferences, coupled with persuasive clinical and laboratory evidence, will almost always provide convincing evidence of the source and mode of spread of a disease. In situations where food and stool testing are negative, the cause of an outbreak is often implicated by epidemiological association.

Epidemiologic investigations also serve as a teaching tool. By carrying out the following steps you will gain an understanding of the systematic, logical approach an epidemiologist or "disease detective" follows in an investigation. It is important to note that the first and second steps are usually given immediate attention while other steps may often occur simultaneously.

It is often unclear when to conduct a full epidemiologic investigation. There is usually no question when you are notified about a large number of people getting ill at approximately the same time after eating at the same establishment or attending the same event. However, uncertainty arises when sporadic complaints are reported. You will need to consider whether the reports indicate that the affected cases are all suffering from the same illness and whether there is any evidence of an association among them. This underscores the need to follow-up a complaint to determine its validity and to initiate further action if necessary for every complaint you receive. Single complaints can very well be associated with an expanding outbreak!

When you are notified of an incident in which illness has resolved and no new cases have been identified, your decision to conduct an epidemiologic investigation should be based on an assessment of what you will gain from it. An investigation always serves as a learning tool, but if you do not have the time or personnel, a full investigation may not be warranted. You should ensure that appropriate control measures have been implemented to prevent future outbreaks.

This is especially true of home-based foodborne outbreaks. In many instances, the illness is confined to a finite number of people in a discrete time period. In addition, you are notified after the fact when there is little material left for testing and people have recovered. You should review food preparation techniques with the responsible parties and use the opportunity to educate them on proper food handling and preparation methods.

# C. Steps in an Epidemiologic Investigation:

**1. Confirm the existence of an epidemic or an outbreak.**

An epidemic or outbreak of foodborne illness is defined as two or more persons experiencing a similar illness after ingestion of a common food OR different food in a common place. An outbreak may also be defined as a situation when the observed number of cases unaccountably exceeds the expected number. However, with certain foodborne illness such as botulism or chemical poisoning, a single case would elicit an in-depth epidemiological and environmental investigation.

To determine if there is an outbreak, you can compare the current number of cases (incidence) with past levels of the same disease over a similar time period. If the number is unusually large or unexpected for the given place and time, you may have an outbreak. For example, in August of 2014, the infection control department of a community hospital noticed an increase in the number of stool specimens which tested positive for *salmonella sp.* in their laboratory over a two-day period. An investigation was begun by the hospital, the LBOH, and the MDPH epidemiologists, which resulted in the identification of 12 cases with matching PFGE patterns, who reported eating in the hospital cafeteria. Testing of the food employees in the cafeteria resulted in an additional

three cases of salmonellosis which matched the outbreak strain. These food employees were removed until cleared and the outbreak stopped. The hospital infection preventionists clearly identified this as an unusual occurrence which lead to the initiation of an investigation.

An outbreak may not always manifest itself in an obvious manner as above. Outbreaks dispersed over a broad geographic area, with few cases in any one jurisdiction are much more difficult to detect locally. This underscores the importance of establishing and maintaining a surveillance system and reporting to MDPH in a timely manner. An outbreak dispersed over a broad geographic area may then be more easily recognized.

When trying to confirm an outbreak, it is important to rule out other causes for increases in numbers of cases. For example, you might notice that several cases of *cryptosporidium* have been reported to you over the past month. When you compare the numbers with cases recorded for the same month the prior year, you notice an increase. On further investigation, you learn that the local hospital recently began testing all stool specimens for cryptosporidium. Another factor that has to be considered is the effect that electronic laboratory reporting (ELR) has had on reportable diseases since it has been widely implemented. ELR has led to more complete reporting but the higher numbers may be a "surveillance artifact" and not necessarily a cause for alarm. Media attention to other outbreaks of the same disease tend to heighten public awareness and can lead to an increased number of cases being reported.

**2. Confirm the diagnosis.**

Confirming the diagnosis is usually done by obtaining appropriate specimens for laboratory study and obtaining clinical histories. In some cases, it is best to actually look at the laboratory report. For example, in cases of hepatitis A, you must be certain that there is laboratory evidence of IgM anti-HAV (IgM hepatitis A antibody). Other evidence to support the diagnosis, such as a lab-confirmed case in a contact, can sometimes be used in lieu of laboratory results. In some instances, there will be outbreaks of unknown etiology, and there will be no laboratory results to confirm the diagnosis. Cases or outbreaks of diseases of unknown etiology are just as valid as those with known etiologies. Laboratory identification of a pathogen can validate the hypothesis and perhaps allow easier implementation of control and preventive measures. Therefore, time is of the essence when requesting and collecting clinical and food specimens.

Whether the etiology is known or not, the investigator must still characterize the illness by interviewing ill persons, family members or health care providers. This can be done through phone calls, informal interviews, or a more formal survey.

To initially assist in the organization of data, a good starting point can be the creation of a "line list." Case names and numbers are listed down the left-hand column, and the heading row at the top of the table should contain pertinent information such as the case's age, sex, onset time, and symptoms. This type of organization permits a simple means for comparison of many characteristics, for possible patterns, similarities, or associations, simultaneously.

Figure 5-1: Example of a Line List

**# Name Age Sex Onset Date Onset Time Symptoms**

1 Mary 32 F 5/4/15 1:00 PM Diarrhea, abd. cramps

2 Bob 25 M 5/4/15 1:30 PM Diarrhea

3 Carol 26 F 5/4/15 10:15 AM Diarrhea, nausea

4 Mark 18 M 5/3/15 11:30 PM Diarrhea, abd. cramps

**3. Determine the number of cases.**

The creation of a case definition helps determine the magnitude of the problem and the actual case numbers. A case definition is a set of criteria for deciding whether an individual should be classified as a case. The case definition places boundaries on who is considered a case, so the investigation does not include those with illnesses unrelated to the outbreak. The common elements of a case definition include information on symptoms, laboratory results, time, place and person.

**a) Symptoms:** People with the same illness do not always have the same symptoms, but they will experience similar ones. It is important to remember that the symptoms of some foodborne diseases can mimic other foodborne diseases. The following list of symptoms can be used as a "general rule of thumb" for determining the incubation period and possible etiologic agent: chemical poisoning symptoms (vomiting) usually start within 1 hour; nausea and vomiting usually start within 6 hours of ingestion; cramps and diarrhea usually start between 6-20 hours of ingestion; diarrhea, chills and fever usually start between 12-72 hours of ingestion. An example of a case definition that is commonly used for foodborne illness outbreaks without a known cause is "an individual who attended a specific event and then experienced diarrhea or a combination of two to three other gastrointestinal symptoms within a specified time after the event."

**b) Laboratory Results:** If you are fortunate enough to have a laboratory confirmed diagnosis, this will make the task of defining a case much easier. During an outbreak of foodborne illness, efforts should be made to send all specimens and/or isolates to the Massachusetts State Public Health Laboratory (SPHL) for further identification, confirmation and to assure coordination of the investigation.

**c) Time:** If there appears to be a common meal involved, then the time between consumption of that meal and the onset of symptoms provides an indication of the incubation period. The incubation period and symptoms are helpful in determining which illnesses should be considered as possible causes of the outbreak and thus may facilitate decision-making regarding what types of laboratory tests should be run. As with symptoms, incubation periods can vary among individuals. Be sure to offer a range of time when considering an incubation period. For example, if you are investigating a *salmonella* outbreak, you may want to include as cases those persons who experienced symptoms consistent with the case definition anywhere from 6 to 72 hours after the meal in question.

**d) Place:** When there is a common meal involved, you already know the place. Sometimes, however, the only information available may be that cases are occurring in several different locations over the same time period. It is only after more information becomes available that the case definition will become more specific as to the location of the outbreak.

**e) Person:** The outbreak may, or may not, take place within a particular group of people. Therefore, characteristics such as age, sex, occupation, ethnic group, social affiliations or function attendance greatly assist in qualifying the case definition.

Your initial case definition should be general so that potential cases are not left out. Once you have more information about the outbreak, you can refine the case definition to "weed out" extraneous cases. Once you have the case definition in place, decide how to find additional cases. Do you feel comfortable relying on telephone reporting from healthcare providers? Do you feel the need to actively search for cases from area healthcare providers or area laboratories, use local media or enlist the help of the local hospital?

# The Questionnaire/Survey

A common method of finding cases, organizing and analyzing data is to conduct a questionnaire or survey among the population you believe to be at risk, such as the attendees of a suspect wedding. A questionnaire that targets specific questions about foods eaten and symptoms experienced is a valuable epidemiologic tool. Information is needed from both ill and well individuals, who are associated with the incident, and assists in developing better hypotheses about the etiologic agent's identity and source, including the means and time of transmission. Key questions to consider when developing a questionnaire:

* What are the demographic characteristics of the individual: name, age, sex, occupation, home and work address, and phone numbers?
* Was the individual exposed to the suspected source and when?
* What are the symptoms, date of onset, their order of occurrence and duration?
* What medical treatment has been sought and received?
* Is there a diagnosis or laboratory results?
* Who else has been exposed to a case during his or her infectious period? (secondary contacts)
* What foods were consumed in the last 72 hours or other appropriate time frame, before the time of onset? It is also important to interview and obtain food histories from those who ate the same suspect food and did NOT get sick.

These questions are intended as a guide. They will require modification to fit the particular circumstances surrounding the investigation. Questionnaires can be designed for personal or telephone interviews by the investigator. A self-administered form can also be distributed via e-mail or U.S. Postal Service. There are a number of online tools and software programs that can be used to develop questionnaires and analyze data. For more information about the development, distribution, and analysis of questionnaires, contact the Epidemiology Program at 617-983-6800. Examples of questionnaires can be found in Attachment 5-1 at the end of this chapter.

**4. Orient the data in terms of time, person and place.**

The purpose of data orientation or epidemiological characterizations is to arrange all incoming data so it means something. The investigator is searching for common associations based on TIME, PLACE and PERSON to strengthen or amend current hypotheses. A common method of data orientation is plotting, on a graph, the cases by time of symptom onset to get an **epidemic curve**. An epidemic curve is a graph that depicts the association of the time of illness onset of all cases that are associated with the outbreak. It helps to determine whether the outbreak originated from a common source or person to person. Time is plotted on the horizontal axis and the number of cases plotted on the vertical axis.

From the line listing and/or questionnaire, you will have collected information on the characteristics of the ill persons. Very often, simply by knowing these descriptive aspects, the diagnosis, and then plotting an epidemic curve, the source, mode of transmission and who is at risk can be determined. **Once the population at risk has been determined, appropriate control measures can be instituted.**

The shape of the epidemic curve may suggest what kind of outbreak is occurring. A *point-source* *outbreak* looks different than a *propagated* or *person-to-person* *outbreak* and a *continuous-common-source* *outbreak*. Epidemic curves are also useful when communicating to lay persons, such as consumers, food service owners and employees and the public, the nature and magnitude of the outbreak.

The **Point-Source Outbreak** is an outbreak of disease or illness in which susceptible individuals are exposed simultaneously to one source of infection such as a wedding reception. The epidemic curve for this type of outbreak is characterized by a sharp rise to a peak followed by a decline, usually less abrupt than the rise and all of the cases tend to fall within one incubation period.

Figure 5-2: Point-Source Outbreak Epidemic Curve

A **Propagated or Person-to-Person Outbreak** is an outbreak of disease or illness that is spread from one person to another rather than from a single source. The graph will assume the classic epi curve shape of progressively taller peaks, each being one incubation period apart. The curve will continue for the duration of several incubation periods of the disease.

Figure 5-3: Propagated or Person-to-Person Outbreak Epidemic Curve

In a **Continuous Common-Source Outbreak** persons are exposed to the same source but exposure is prolonged over a period of days, weeks, or longer. The epi curve rises gradually.

Figure 5-4: Continuous Common-Source Epidemic Curve

**5. Develop a hypothesis that explains the specific exposures(s) that may have caused the disease and test this by appropriate statistical methods.**

Using the information gathered from the previous steps, consider the possible source(s) from which the disease may have been contracted. To test or prove your hypothesis, you would want to apply more analytical techniques such as statistical testing. The Epidemiology Program can assist with this aspect of the investigation. Food-specific attack rates (AR), odds ratio, relative risk, and p-value are some of the statistical tests that can be used to test a hypothesis.

**6. Compare the hypothesis with the established facts and draw conclusions.**

Based on evidence gathered, you have a hypothesis that a particular food was the vehicle of transmission in a *salmonella* outbreak. You then need to ask yourself how the particular food became contaminated with *salmonella* and could this be verified with the results of the environmental investigation. In other words, are your epidemiologic results plausible and consistent with other investigational findings? For instance, the food might not be a typical food that harbors *salmonella*. However, it could become contaminated when ill or infected food employees prepare the food without adequate handwashing or use of gloves. Food can also become cross-contaminated with food that might have *salmonella*, such as raw chicken, if food is not prepared properly. Compare your hypothesis to the results of the environmental investigation. Did the inspector note how the implicated food was made and served? Was it possible for this scenario to have happened? Some of the questions that need to be addressed to make sure that your hypothesis is not only statistically sound, but makes sense in the real world, are:

* Could your hypothesized events have happened?
* Is your hypothesis consistent with the environmental aspects of the investigation?
* Is it likely the vehicle of transmission identified became contaminated with the organism that has been isolated?

Not all outbreaks have a resolution. In fact, it is rare when everything comes together and a cause can be definitively determined. Careful development of epidemiologic inferences coupled with persuasive clinical and environmental evidence will almost always provide convincing evidence of the source and mode of spread of a disease. In most cases, there will be enough evidence to present a plausible hypothesis.

**7. Execute control and preventive measures.**

Before initiating any control measures, think about the effectiveness, timeliness, costs, available resources, personnel requirements and possible ramifications of proposed actions. Are the recommendations realistic for the establishment involved? For example, will they be able to install the new dishwasher or the 3-bay sink that was recommended? If not, what are the alternatives? Be advised that some control measures should be implemented very early in an outbreak investigation, such as the removal of ill food employees, or the embargo, recall or destruction of contaminated food items. All corrective actions must be verified by the LBOH to ensure that steps to reduce or eliminate the hazards have actually occurred.

**8. Prepare a written report.**

After analysis of epidemiologic and environmental data, conclusions should be summarized in a report. This is one of the most important steps in the outbreak investigation. Not only does the report detail your agency's efforts, but identifies a potential source(s) of the outbreak and suggests control measures to prevent future illness. Information on writing a report is detailed in Chapter X, Summarizing the Investigation.

# References:

Council to Improve Foodborne Outbreak Response (CIFOR). Guidelines for Foodborne Disease Outbreak Response. 2nd edition. Atlanta: Council of State and Territorial Epidemiologists; 2014.

# Attachment:

**Attachment: 5-1:** Sample Questionnaires

Attachment 5-1: Sample Questionnaires









