DISEASE TRANSMISSION AND OUTBREAK INVESTIGATION

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GENERAL CONCEPTS

1. **What are the components of the epidemiologic triangle?**
Host, agent, and environment. A host is the living organism capable of becoming infected, an agent is a factor that must be present (or potentially missing) for the occurrence of a disease, and an environment is an extrinsic force or situation affecting the host's opportunity to be exposed to the agent. A vector may be present to bring the agent to the host (Fig. 5-1).

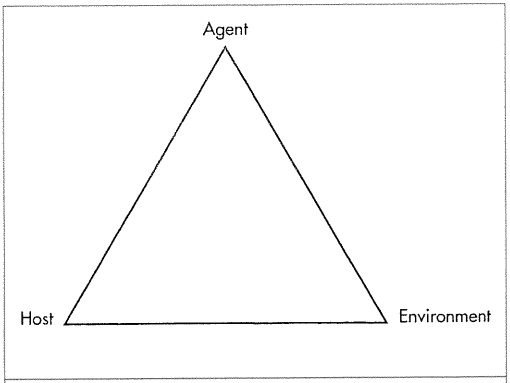

Figure 5-1. Epidemiologic triangle model of causation. (From Principles of Epidemiology, 2nd ed. Atlanta, U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, Epidemiology Program Office, Public Health Practice Program Office, 1992.)

2. **Explain the relationship among the legs of the epidemiologic triangle.**
Well-known as one of the elemental ecologic models in public health, the epidemiologic triangle is often used to explain the concept of disease causation. The host, agent, and environment are the necessary components of the triangle. When viewed as an equilateral triangle, any change in one leg will inevitably alter one or both of the remaining legs, causing either an increase or decrease in the frequency of the disease state.

3. **List some of the characteristics affecting disease frequency for the three components of the epidemiologic triangle.**
Host characteristics
- Age
- Genetics
- Sex
- Socioeconomic status
- Immunity

Agent characteristics

- Environment stability
- Virulence
- Resistance
- Infectivity
- Pathogenicity

Environment characteristics

- Biologic (e.g., vectors and reservoirs)
- Physical (e.g., heat and population density)
- Social (e.g., culture)

4. **What is the only known reservoir for the measles virus?**
The site where an infectious disease survives is considered a reservoir. While reservoirs can include both animate organisms and inanimate matter, humans are the only known reservoir for the measles virus.

5. **Explain how infectious agents are transmitted, and describe direct and indirect transmission.**
Disease transmission is classified as either direct or indirect. Direct transmission entails the transfer of the infectious agent by physical contact with lesions, blood, saliva, or other secretion. Infectious transfer from a direct aerosolization, such as a sneeze in another person's face, is also typically considered direct. Indirect transmission occurs when the infectious agent spends a variable intermediate period within or upon some substance or living organism prior to causing disease in the host.

6. **By which mechanisms can direct and indirect transmission take place?**
Direct transmission implies close contact, which is typically described as being within three feet of the infected individual in the case of droplet spread (e.g., coughing, sneezing, and talking). Activities that can cause immediate transfer of an infectious agent into a susceptible portal of entry, such as kissing, biting, or sexual intercourse, are methods of direct transmission. Indirect transmission, on the other hand, is either vehicle- or vector-borne. A vehicle may be any inanimate object or biologic material (e.g., blood and tissue) that acts as an intermediary in transferring the infective agent to the host.

7. **Is hepatitis A acquired through direct or indirect transmission?**
Hepatitis A is acquired via the fecal-oral route, which is considered indirect transmission. Pathogens must be capable of withstanding the environment outside their natural host for some period of time to be a viable source of indirect transmission.

An example of this type of transmission might occur when an employee (i.e., reservoir) with hepatitis A, working in a local fast-food restaurant, fails to wash his hands after using the bathroom. The employee then returns to the food preparation station and makes your deluxe jumbo burger. In the process, fecal material infected with hepatitis A is transferred to your lunch. Famished as usual, you consume every bite. In about a month you notice the onset of flu-like symptoms and yellow sclera. Your astute powers of self-diagnosis reveal that you have hepatitis A. Because you never actually came into direct contact with the person who prepared your burger, you acquired the hepatitis A via indirect transmission.

In contrast, direct transmission could occur when your best friend, who is nursing a cold, shows his less considerate side and sneezes in your face. So remember: to help prevent both direct and indirect transmission, always cover your mouth when you cough and wash your hands afterward!

8. **What is the chain of infection?**
The chain of infection is the mechanism by which transmission of an agent occurs from its reservoir to its host. Figure 5-2 is a useful schematic illustrating the chain of infection.

9. **How are infectivity, pathogenicity, and virulence different?**
According to the Centers for Disease Control and Prevention (CDC), infectivity is the proportion of persons exposed to a causative agent who develop an infectious disease. Infectivity can be measured by secondary attack rate. Pathogenicity is the ability of an organism to cause a disease state (morbidity), whereas virulence is the ability to actually cause death (mortality). The

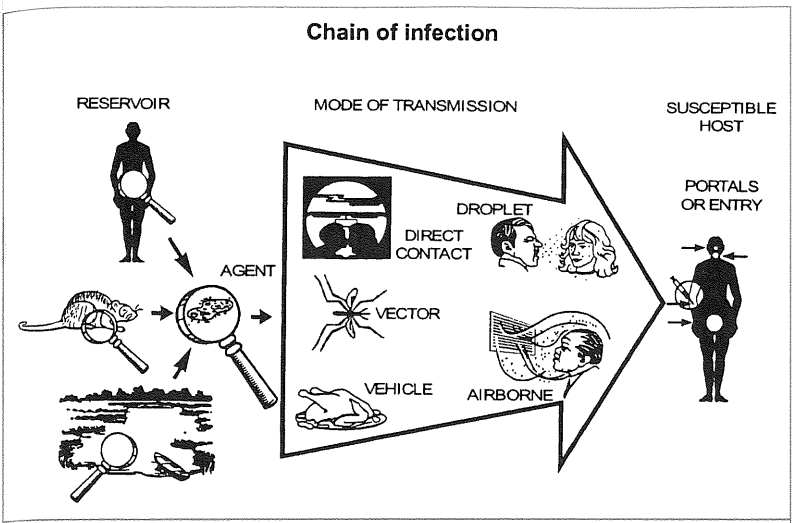

Figure 5-2. Chain of infection. (From Principles of Epidemiology, 2nd ed. Atlanta, U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, Epidemiology Program Office, Public Health Practice Program Office, 1992.)

virulence of a pathogen can be altered. For example, the discovery of penicillin in the late 1930s significantly reduced the mortality rate of pneumococcal bacteremia from about 90% to 10%.

10. **What percentage of hospital-acquired bacteria infections is resistant to at least one of the antibiotics most frequently prescribed for their treatment?**
The degree to which a disease-causing microorganism does not respond to drugs intended to eradicate it is known as its resistance. Overprescription of antibiotics has led to the mutation of many bacteria as a survival mechanism against our labors to eliminate them. This sophisticated strategy on the part of the bacteria has led to either the reduction or, in some cases, the complete ineffectiveness of current treatment regimens. More than 70% of hospital-acquired bacteria infections may demonstrate some level of resistance to at least one drug commonly used to treat them. At the level of the host, multiple factors determine resistance, including sex, age, socioeconomic status, baseline health, and nutrition status. In addition, genetic make-up determines individual resistance to various diseases (termed *innate resistance*).

11. **The concept of apparent and inapparent infection was conceived by which recipient of the 1928 Nobel Prize in Medicine?**
Dr. Charles Jules Henry Nicolle was the winner. While conducting research on guinea pigs he had infected with typhus, Nicolle made a rather astonishing discovery: some of the infected guinea pigs, despite displaying no apparent typhus symptoms, were capable of spreading the disease. Today we more commonly term *apparent* and *inapparent* infections as *symptomatic* or *asymptomatic* infections.

12. **Name the two types of immunity.**
- Passive immunity: antibodies formed in another person or animal are transferred to an individual. This type of immunity is short-lived.
- Active immunity: antigens are transferred to an individual via a portal of entry. Once the antigen enters the body, it stimulates the immune system to produce antibodies. Initial exposure of an antigen and the subsequent host antibody formation are termed the primary response. Immunoglobulin M (IgM) is the main antibody produced during the primary

immune response, whereas immunoglobulin G (IgG) dominates at the time of reexposure, when cellular memory kicks in. The formation of IgG explains why active immunity is more persistent than passive immunity.

13. **What types of immunity can be acquired artificially?**
Both passive and active immunity may be acquired by either natural or artificial means.

KEY POINTS: DISEASE TRANSMISSION

1. Host, agent, and environment make up the epidemiologic triangle.
2. Infectious agents can be transmitted directly or indirectly.
3. Pathogenicity is the ability to cause diseases, whereas virulence is the ability to cause death.
4. The primary attack rate is the number of people who become ill divided by all those at risk.
5. Both passive and active immunity can be acquired through natural or artificial means.
6. An epidemic is a greater than expected frequency of a disease or illness for a given population and time period.

14. **Acquired immunity may be conferred in one of two ways: either artificially or naturally. Name the method employed in providing an individual with artificially acquired immunity.**
Administration of a prophylactic vaccine such as measles-mumps-rubella (MMR), inactivated poliomyelitis, or pneumococcal pneumonia confers artificially acquired immunity by exposing an individual to the antigens of a particular viral or bacterial pathogen.

15. **An emergency department physician from a local hospital arrives at your practice, stating that he was just stuck with a needle from a known hepatitis B-positive patient. He is concerned because he never received the hepatitis B vaccine (he was "too busy" to get it). As part of the standard blood borne pathogens protocol in your practice, you immediately administer hepatitis B immune globulin, based on your understanding that it will confer what type of immunity?**
Passive artificially acquired immunity. Hepatitis B immunoglobulin is indicated for acute exposures to hepatitis B surface antigen (HBsAg) in an individual who has either never received the hepatitis B vaccine or is a known nonresponder to the vaccine. This temporary form of immunity promotes development of anti-hepatitis B surface antibodies in approximately 1–6 days, with a duration of protection from 2–6 months. Best when administered within 24 hours, it should be given no later than 7 days after the exposure to be effective. In the case of the previously unvaccinated doctor, or a patient whose titer has fallen below a protective level, the hepatitis B vaccine series should be given at the same time that hepatitis immunoglobulin is administered (at separate sites) to confer active, artificially acquired, long-term immunity.

16. **The initial fluid secreted by the mammary glands after childbirth is known as colostrum. You encourage new mothers to breast-feed because you are aware that colostrum provides which type of immunity to the infant?**
Colostrum provides naturally acquired passive immunity. This occurs when antibodies contained in the colostrum are ingested by the infant, cross the intestinal mucosa, and are transported to the blood.

17. **What is herd immunity?**
Herd immunity is the immunity of a group or community (Fig. 5-3). In other words, it is the resistance of a group to invasion and spread of an infectious agent based on the resistance of a high proportion of members of that group. This includes a vaccinated group.

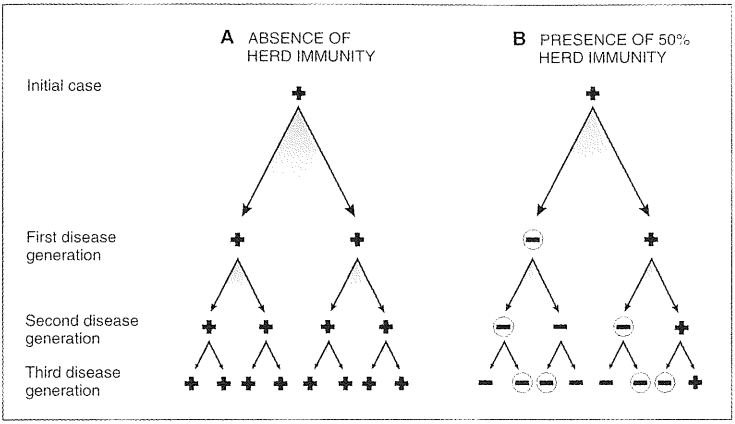

Figure 5-3. The effect of herd immunity on the spread of infection. The diagrams illustrate how an infectious disease such as measles can spread in a susceptible population if each infected person were exposed to two other persons. In the absence of herd immunity *(A)*, the number of cases doubles in each disease generation. In the presence of 50% herd immunity *(B)*, the number of cases remains constant. The plus sign represents an infected person, the minus sign represents an uninfected person, and the circled minus sign represents an immune person who will not pass the infection to others. (From Jekel JF, Katz DL, Elmore JG: Epidemiology, Biostatistics, and Preventive Medicine, 2nd ed. Philadelphia, W.B. Saunders, 2001.)

18. **Why is the loss of herd immunity against smallpox in the United States an increasing public health concern in relationship to biologic warfare?**
Since the World Health Organization officially declared smallpox to be eradicated worldwide in 1980, with the last naturally occurring case in 1977, immunization programs for this disease have ceased. Without the benefit of naturally occurring disease or active artificial immunity in the form of vaccination, herd immunity cannot develop. Therefore, should smallpox be released as a weapon of bioterrorism, the lack of group immunity may make it a deadly threat.

19. **What change at the molecular level effects a change in antigenicity of the human immunodeficiency virus (HIV), making it difficult to develop an effective HIV vaccine?**
A process known as antigenic drift is the culprit. Antigenic drift is the development of point mutations over time. In certain viruses, like HIV, this can happen quite easily because of a high replication rate. Antigenic drift causes small changes in the virus, which decrease the host immune response by lowering the efficacy of the cellular memory of T and B cells.

20. **Is antigenic drift the same thing as antigenic shift?**
No. Antigenic shift is a major and more immediate change than antigenic drift in the surface proteins of a virus, leading to extensive alteration in genetic information. The influenza virus is notorious for its tendency toward antigenic drift and antigenic shift, resulting in many historically significant epidemics.

21. **As the newly appointed physician for a local public health department, your first charge is to investigate a repeating pattern of cases of aseptic meningitis in the community. Because you aced your epidemiology class in medical school, you recall that the proper epidemiologic terminology for this excess pattern would also be what?**

Periodicity. Figure 5-4 shows the pattern of aseptic meningitis in the United States from 1986–1994.

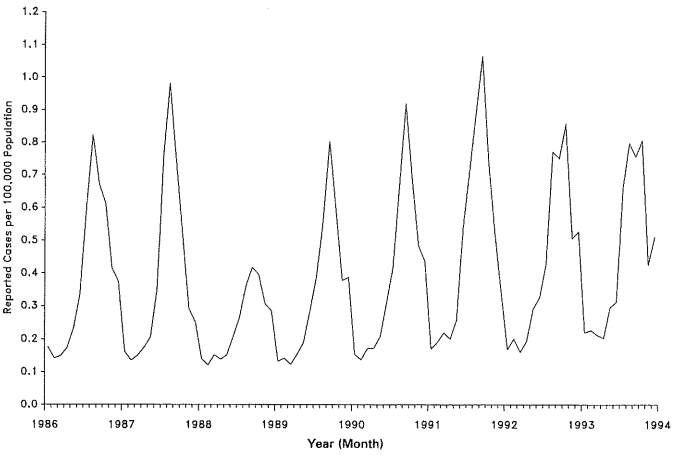

Figure 5-4. Aseptic meningitis, reported cases per 100,000 population by month, United States, 1986–1993. (From CDC: Summary of notifiable diseases, United States, 1993. MMWR 49:49, 1994.)

22. **You are paged in the middle of the night and notified that one of your patients, a 65-year-old woman with a history of congestive heart failure and chronic obstructive pulmonary disease, was just admitted to the hospital with a *Streptococcus pneumoniae* infection. The attending physician in the emergency department assures you that the patient has been started on penicillin and will be just fine. Comforted by his reassuring tone, you return to bed. The next afternoon you are paged by the nurse on the floor, who tells you that your patient had become septic and was transferred to the medical intensive care unit. What went wrong?**

Antibiotic resistance. Penicillin-resistant *Streptococcus pneumoniae* was first documented in New Guinea in 1967, and later appeared in the United States in the 1980s.

Bacterial resistance is a natural consequence of the evolutionary process and is achieved via the process of adaptation. While the antibiotic itself is not the actual cause of the resistance, the drug's efforts to eliminate the infection trigger the bacterium's survival instincts, which ultimately leads to genetic changes. Essentially, resistance occurs because the bacterium makes an end-run around our efforts to stop it by either natural resistance (i.e., vertical evolution via spontaneous mutation) or acquired resistance (i.e., horizontal evolution via the acquisition of genes for resistance from another organism through transduction, conjugation, or transformation).

In the case of penicillin resistance, the bacteria reinvent themselves in an effort to survive and elicit enzymes that destroy the drug or alter its ability to bind to and damage the cell walls. While it is crucial that we employ every effort to slow this process down, the reality is that, because of rapid bacterial cell growth and the sophistication of genetic processes such as mutation and selection, it is unlikely we will ever be capable of stopping it.

23. **The increase in pneumococcal infections during winter months is best described by which epidemiologic term?**
Seasonal variation is the cyclic pattern for attack rates related to common pathogens. Particular pathogens are more likely to occur at certain times of the year. *Streptococcus pneumoniae, Staphylococcus aureus,* and influenza A and B are more likely to appear in the winter, legionellosis usually comes in the summer, and *Mycoplasma* species show up in summer and fall in the Northern Hemisphere. Figure 5-4 shows both the periodicity of aseptic meningitis and the seasonal variation of the illness.

24. **As the head of infectious disease in a small, rural hospital, staff often turn to you with exposure questions. You receive a call from the nurse manager of the emergency department, notifying you that a patient was just admitted with chickenpox pneumonia. She is concerned because one of her newly hired nurses, who had cared for this patient, was just notified by employee health that her varicella titer had come back negative. Based on our knowledge of the incubation period of varicella, what advice would you give the nurse manager?**
Health care workers are vigilant of chickenpox patients because of the long incubation period and the need to furlough the nonimmune workers (i.e., those with no natural immunity and those nonimmune workers who did not receive alive attenuated varicella virus vaccine) for 10–21 days after exposure. The incubation period is the time interval between initial contact with the infectious agent and the first appearance of symptoms associated with the varicella infection. The varicella virus has a long incubation period of 14–21 days. According to the Massachusetts Department of Public Health, susceptible health care workers shall be excluded from work from the 10th through 21st days after their last exposure. However, if the nurse in question receives varicella zoster immunoglobulin (VZIG), her exclusion should be extended to 28 days after exposure. Exclusion of workers is often emphasized 4 days before the beginning of the incubation period, because the varicella virus is communicable 2 days before onset of rash. Should the nurse contract the disease, she must remain out of work until she is no longer contagious, typically 6–8 days or until all the blisters are crusted over.

25. **What is an attack rate?**
An attack rate is somewhat akin to an incidence rate. Typically, attack rates are used for a specific group of people during a certain time period. It is often used to quantify epidemics.

$$\text{Primary attack rate} = \frac{\text{No. of people at risk in whom illness develops}}{\text{Total number of people at risk}}$$

An example of primary attack rate is the outbreak of *Salmonella* infection that occurred in October 2004 at a restaurant in East Oshkosh. Of the 200 patrons who ate there, 100 fell ill. Therefore the attack rate would be 100/200 = 50/100 = 0.5 = 50%

26. **One hundred school-aged children were exposed to varicella and 10 contracted chickenpox. The 10 children were forced to stay home with their younger, non-school-aged siblings, who had never been exposed to chickenpox. Unfortunately for the parents, of the 20 younger siblings, none of them had received the chickenpox vaccine; subsequently, 5 of them contracted chickenpox. Based on this information, what would the secondary attack rate be for this chickenpox outbreak?**
The secondary attack rate is a ratio: the number of new cases among contacts occurring within the accepted incubation period following exposure to a primary case divided by the total number of exposed contacts (i.e., person-to-person spread of the disease from primary cases to other persons). The formula for secondary attack rate is as follows:

$$\frac{\text{No. of cases who develop the disease within the incubation period}}{\text{No. of susceptible individuals who were exposed to the primary cases}}$$

The secondary attack rate of chickenpox among unvaccinated close contacts in this group of siblings would be 5/20, or 25%.

27. What is an example of case-fatality ratio (CFR)?

CFR is typically expressed as the percentage of individuals who are diagnosed with a certain disease and subsequently die because of that particular illness within a specified time period. For example, say that 1000 college students in Boston were infected with meningococcal meningitis. In 2003, 10 of the students died of complications directly related to the disease. Therefore, the case-fatality rate would be 10 deaths/1000 diagnosed cases, or a CFR of 1%, in 2003.

28. How can I remember the difference between epidemic, endemic, and pandemic?

You could try harkening back to your high school language classes and look at the base words:

- *Epi*demic: in Latin, *epi-* means "in addition." When defining an epidemic, one refers to the fact that each infected person is infecting multiple other individuals, so the number of infected persons is growing exponentially. In other words, each infected person is rapidly "adding" to the problem.
- *En*demic: the Latin meaning of this base is "in." Remember that endemic refers to a disease that is always present, to a greater or lesser extent, in folks who live "in/en" a particular geographic location.
- *Pan*demic: in Greek, *pan* means "all." A pandemic is an epidemic that is widespread over a large area or "all" of a geographic area. Recall that a *pan*oramic view is a view of the "big" picture or "all" of the geographic area.

And, of course, remember that "-demic" is the root for "people" in Greek!

29. So what is an epidemic in plain English?

An epidemic is simply a higher frequency of disease or injury than is expected for a typical population and time period.

30. What is an outbreak?

Another term for epidemic.

KEY POINTS: DETECTION OF INFECTIOUS DISEASE

1. Always consider multisystem disease and review all confounders in diagnosing an infectious illness.
2. Put emergent treatable infectious diseases on the top of differential lists.
3. Physical, biologic, and occupational illnesses and chemical agents need to be considered in this potential bioterrorism-induced disease environment and era.
4. Unusual presentations of commonly known pathologic infectious diseases are common.

31. Recalling that histograms are useful tools, you choose to plot the recent outbreak of influenza using this method. What would such a diagram be called in epidemiologic terms?

The use of a histogram to illustrate the course of an epidemic (by plotting the number of cases by time of onset) is referred to as an epidemic curve. An epidemic caused by a

single common exposure (i.e., point-source epidemic) is often caused by contaminated food or water. The point-source epidemic curve has a sudden rise and fall, with a common incubation period for those affected (Fig. 5-5). Propagated epidemics, often spread by person-to-person contact, have a plateau, representing the overlap of exposures and incubation periods (Fig. 5-6). Uncontrolled propagated epidemics will have progressively taller peaks.

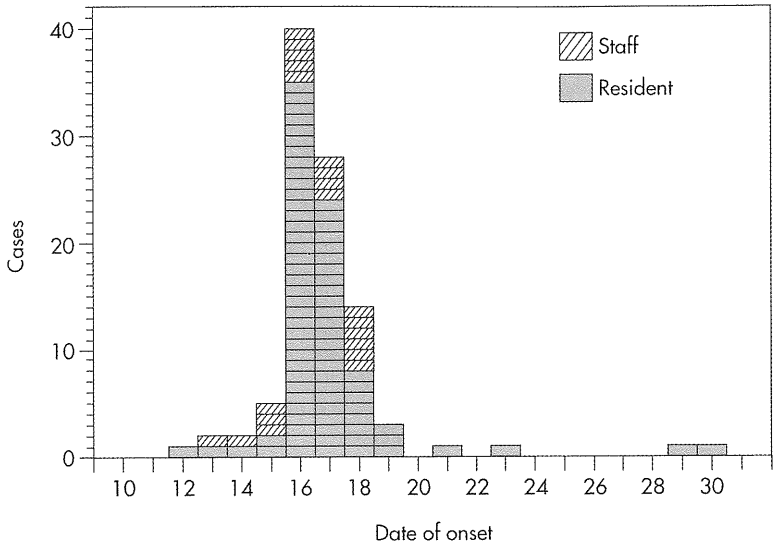

Figure 5-5. A point-source epidemic curve of an outbreak of influenza in a nursing home—Louisiana, August, 1993. (From CDC: Influenza A outbreaks—Louisiana, August, 1993. MMWR 42[36]:689–692, 1993.)

32. **What is the incubation period of a disease?**
It is the elapsed time of inapparent changes between exposure of the host to the infectious agent and the onset of the host's clinical illness. The incubation period is often a useful tool in determining the source of a point-source epidemic by back-calculating to determine the probable period of exposure of those affected to develop a list of likely causes.

33. **At 4:00 AM you are paged by the student health nurse at a local college, who states that 52 students in the waiting room are complaining of nausea, vomiting, and diarrhea of sudden onset. She fears an outbreak of *Salmonella* poisoning from the "chicken surprise" at the student dining hall last evening. What should you do?**
Initiate the 10 steps of an outbreak investigation listed below, as outlined by the Center for Disease Control and Prevention:
(1) Prepare for field work, (2) establish the existence of an outbreak, (3) verify the diagnosis, (4) define and identify cases, (5) describe and orient the data in terms of time, place, and person, (6) develop hypotheses, (7) evaluate hypotheses, (8) refine hypotheses and carry out additional studies, (9) implement control and prevention measures, and (10) communicate findings.

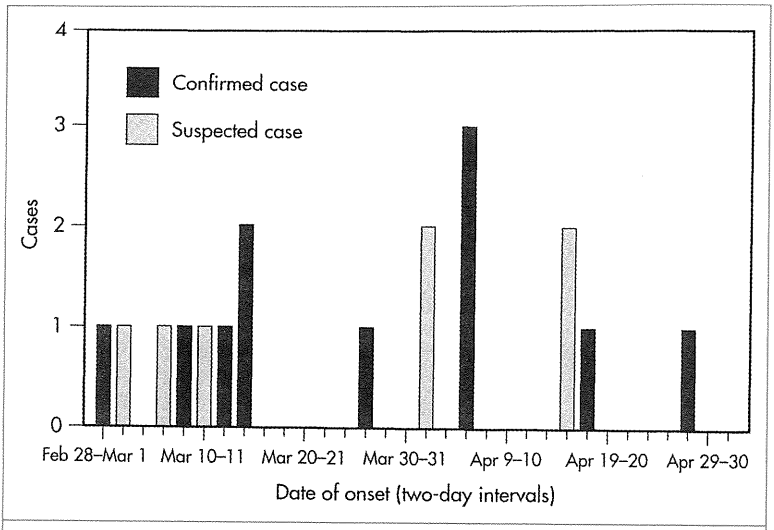

Figure 5-6. A propagated epidemic of *Escherichia coli (E. coli)* 0104:H21 infection resulting from continued exposure to contaminated milk—Helena, Montana, 1994. (From CDC: Outbreak of acute gastroenteritis attributable to *Escherichia coli* Serotype 0104:H21—Helena, Montana, 1994. MMWR 44[27]:501–504,

34. **A 62-year-old registered nurse in an acute care facility called the employee department, claiming she was diagnosed by her primary care physician with methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia. She was certain that she had acquired it from a patient who was just diagnosed as MRSA-positive. How can you tell if she contracted MRSA from that particular patient?**

Isolates of MRSA may be recovered from both the registered nurse and the patient. Genotyping, using pulsed-field gel electrophoresis (PFGE) testing, may then be performed on isolates from both individuals. If the PFGE patterns match, she has made her case.

35. **A health care worker presents in your office after a blood borne pathogen exposure to a source patient who is known to be hepatitis C-positive. You evaluate the worker, initiate treatment, and follow up as recommended by the CDC. You are interested in keeping a vigilant eye on this patient because of the source patient's history. What can you do, in addition to CDC recommendations, in terms of surveillance?**

An enhanced medical surveillance program may be useful in this setting for the following reasons:

- Up to 20% of hepatitis C conversions revert to no viral load.
- Early diagnosis is critical if reversion occurs; early counseling is critical if postexposure conversion happens because treatment within 6 months to a year improves outcome and prevents sustained viral response in 98% of health care workers.
- The enzyme-linked immunosorbent assay (ELISA) hepatitis C antibody test has a low specificity with a false-positive rate of up to 40%.

Based on these facts, you may wish to obtain an antibody hepatitis C test at baseline and then order a polymerase chain reaction (PCR) viral RNA hepatitis C test and an antibody-hepatitis C test at 1, 3, and 6 months.

INFECTIOUS DISEASE USE IN BIOLOGIC WARFARE AND TERRORISM

36. What characteristics of infectious diseases make them attractive for use in biologic warfare and terrorism?

Any or all of the below characteristics may make a particular infectious disease attractive:

- Contagiousness
- Incubation period
- Viable methods of distribution (e.g., aerosolization)
- Inadequate or complete lack of herd immunity
- Mobile society, allowing rapid spread of disease beyond original area of distribution

37. Which disease(s) listed below might be used in a bioterrorist attack?

- Smallpox
- Anthrax
- Bubonic plague
- Q fever
- Botulism
- Tularemia
- Viral hemorrhagic fever
- Brucellosis

According to the CDC, all of the agents listed have potential for use in biologic warfare.

38. What organisms are considered by the CDC to be of the greatest threat with respect to bioterrorism?

The CDC designates organisms of this sort as category A. These agents include anthrax, plague, smallpox, tularemia, and viral hemorrhagic fevers, as well as botulinum toxin.

39. What is syndromic surveillance?

According to the CDC Division of Public Health Surveillance and Informatics, syndromic surveillance is the process of collecting and interpreting health data that precede an actual diagnosis and may signal a case or outbreak that would trigger additional public health response.

40. Why might schools be a good first source for epidemiologic evidence of a bioterrorist attack?

Using the premise of syndromic surveillance, a specified population, such as school children, may be monitored for symptoms related to exposure to infectious agents. Five-day-a-week required attendance, absence notification and recording, and, in many instances, the availability of school nurses to perform data collection make school children an excellent population for epidemiologic surveillance. In addition, school children may serve as efficient vectors for transmission of bioterrorism pathogens, with one child potentially infecting an entire family. Early detection of disease trends may lead to preemptive intervention strategies to avert a major disaster.

41. How can I get real-time information about preparation and response to the use of infectious agents in terrorist events?

The CDC clinician registry for terrorism and emergency response provides updates on bioterrorism preparedness and training opportunities free to registered users at http://www.bt.cdc.gov/clinregistry/index.asp.

42. Why are intermediate particles smaller than 5 μm important in aerosolization of infectious agents?

Particles smaller than 5 μm but greater than 1 μm will have the highest probability of transmitting infection. These intermediate-size particles can be respired more easily and deposited in the deep gas exchange regions of the lungs. Although particles greater than 5 μm are capable of transmitting infection via the pharynx or nasal cavity, they usually remain suspended and are removed upon exhalation. Suggested methods of aerosolization have included the use of crop dusters and entrainment into ambient air space through ventilation systems at offices and schools.

43. **Why might infectious agents be more damaging than chemical agents?**
Infectious agents have the ability to replicate, and some are contagious. Once chemical weapons have been released and decontamination is achieved, they no longer continue to expose a larger population. However, as in the case of smallpox, infectious agent transmission can continue until the last case is contained. Containment can be difficult because of varying incubation periods and individual immunogenicity.

44. **How long can the smallpox (i.e., variola) virus remain viable outside the human host?**
The variola virus can remain in a viable state on inanimate objects such as clothing and pillows for months. During the French and Indian War, the British distributed blankets infected with smallpox, which killed off almost 50% of the Indian tribes.

45. **Since vaccinia is a live vaccine, can my patients develop smallpox from it?**
No. Although vaccinia and smallpox are both orthopoxviruses, they are different organisms. While vaccinia can cause serious reactions such as generalized vaccinia, which may look similar to smallpox, it does not cause the actual disease.

WEBSITES

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EPIDEMIOLOGY AND BIOSTATISTICS

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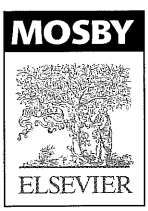

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