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Investigation of an Epidemic

Objectives Covered

1. Interpret the distribution of disease in a population according to time, place, and person.
2. Describe the composition of a rate in terms of the numerator and denominator, and explain the relationship between them and the importance of time.
3. Explain the use of rates for comparative purposes.
4. Define *attack rate,* and use it to identify a vehicle of transmission in a common-source outbreak of disease.

Study Notes

Epidemiology is the study of the distribution and determinants of disease in human populations. We try to find out who gets the disease and why. For example, is the disease more frequent among men or women, young or old, rich or poor, blacks or whites? Did they get the disease because of a genetic trait, an occupational exposure, or a lifestyle habit, such as cigarette smoking?

Epidemiology differs from clinical medicine in two important regards: First, epidemiologists study groups of people, not individuals. Second, epidemiologists study well people, in addition to sick people, and try to find out the crucial difference between those stricken and those spared. What is the trait common to the sick, yet rare in the well? Epidemiologists weigh and balance, contrast and compare. To determine if a study is an epidemiologic study, you should look for a control or comparison group. To make a comparison, you need to develop a rate. A rate is time based and is computed as

$$\frac{\text{events in the specified time period}}{\text{population at risk in the specified time period}}$$

It is usually expressed as events per 1,000 individuals, or some other convenient base.

The numerator is merely the number of people to whom something happened (i.e., they got sick or died) in the population at risk. The numerator must be derived from (i.e., be a subset of) the denominator. The denominator (the population at risk) has to be all the people at risk for the event. For mortality, the denominator is the entire population, because death is a universal risk, but in pregnancy rates, for example, the denominator would comprise only females of reproductive age.

Attack Rate

An attack rate measures the proportion of the population that develops disease among the total exposed to a specific risk over a specified time period:

$$\text{attack rate} = \frac{\text{number of people ill in the time period}}{\text{number of people at risk in the time period}}$$

In an outbreak of food poisoning, attack rates are computed for all items ingested. These attack rates are computed for those people who are exposed (i.e., ate the item studied) and, most importantly, those who are not exposed (i.e., did not eat the item studied), as shown in Table 1–1.

Table 1–1 Differential Attack Rates of Illness According to Food Histories in an Epidemic of Food Poisoning

Food	Persons Who Ate Specified Food			Persons Who Did Not Eat Specified Food			Difference in Attack Rates
	Number	Number ill	Attack Rate (%)	Number	Number ill	Attack Rate (%)	
Turkey	133	97	73	25	2	8	+65
Dressing	121	88	73	37	11	30	+43
Potatoes and gravy	127	92	72	31	7	22	+50
Peas	105	77	73	53	22	41	+32
Rolls	66	50	76	92	49	53	+23
Margarine	66	50	76	92	49	53	+23
Salads	4	1	25	154	98	64	−39
Desserts	36	22	61	122	77	63	−2
Sandwich	11	1	9	147	98	67	−58
Coffee	98	59	60	60	40	67	−7
Milk	18	12	67	140	87	62	+5

Source: Modified from Tong et al., 1962.

By inspecting attack rates for those who ate specific items, it is impossible to incriminate a single vehicle. Comparing the attack rates between those who ate and did not eat a specified food, however, is more informative. The last column on the right in Table 1–1 shows this difference. Simple differences in attack rates alone may not distinguish between causal and noncausal associations. For instance, both turkey and potatoes and gravy have large differences in their attack rates between those who ate and did not eat these foods.

To distinguish the separate effects of turkey and potatoes and gravy, it is necessary to cross-classify, as is shown in Table 1–2. An examination of this table clearly incriminates turkey as the suspected vehicle because the difference in attack rates among those who ate and did not eat turkey is quite large whether they ate potatoes and gravy, whereas the reverse is not true.

The association between potatoes and gravy and food poisoning disappears when account is taken of turkey consumption.

Attack Rates

| | | Turkey | |
		Yes	No
Potatoes and Gravy	Yes	High	Low
	No	High	Low

The food item potatoes and gravy was implicated only because of the strong tendency of people to consume that food item with turkey. An epidemiologist would say that turkey plays the role of a confounder. The concept of confounding, "guilt by association," is important and will be treated more fully in Chapters 2 and 4.

Table 1–2 Attack Rates for Food Combinations

	Ate Turkey			Did Not Eat Turkey		
	Number	Number ill	Attack Rate (%)	Number	Number ill	Attack Rate (%)
Ate potatoes and gravy	127	92	72	0	0	—
Did not eat potatoes and gravy	6	5	83	25	2	8

Source: Modified from Tong et al., 1962.

Suppose now that both the food items were mildly contaminated such that neither by itself would cause illness but taken together they would. The subsequent attack rates are indicated below.

Attack Rates

| | | Turkey | |
		Yes	No
Potatoes and Gravy	Yes	High	Low
	No	Low	Low

Here we observe that the effect of potatoes and gravy depends on the presence or absence of turkey. Likewise, the effect of turkey is dependent on potatoes and gravy. Epidemiologists refer to this sort of phenomenon as effect modification (see Chapter 4 for further discussion).

Investigation of an Epidemic

An epidemic occurs when there are significantly more cases of the same disease than past experience would have predicted for that place, at that time, among that population. Disease in the individual may be considered the outcome of the interaction of three factors: agent, host, and environment. A triad—time, place, and person—is also used in the investigation of disease in the community.

Cases of the disease may be classified according to these three categories:

1. Time, which includes date of onset and duration of observation
2. Place, which includes dwelling and workplace
3. Personal characteristics, which include age, sex, and occupation

Scrutiny of the results of such classification may help one to recognize characteristics common among the sick and rare among the well.

Epidemic Curve

An epidemic curve gives a convenient picture of the epidemic, and certain limited deductions may be drawn. In a common-source outbreak, such as that just discussed, the time between the common exposure (e.g., the meal) and the peak of the cases approximates the incubation period of the disease. There are also few or no secondary cases, and the curve is unimodal, only one peak (Figure 1–1).

However, in a typical infectious disease, such as measles, which is spread from person to person, the picture of propagation, as shown by an epidemic curve, is not as clear. In a closed community, such as a school, barracks, or ship, it may be possible to trace successive waves of propagation, each resulting in a new crop of
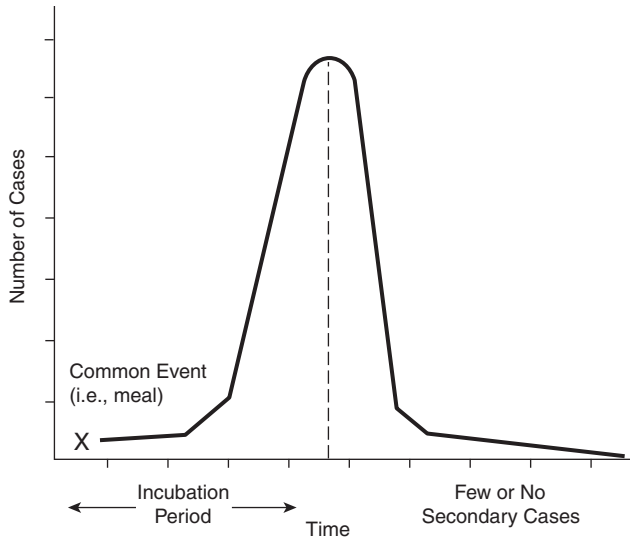
Figure 1–1 Common-Source Outbreak

cases, separated from the previous peak by an incubation period. The epidemic ceases when the supply of susceptibles is exhausted.

Analysis

When the data have been collected, they may be analyzed as follows:

1. Plot an epidemic curve. Incubation periods may be estimated if times of exposure are known.
2. Calculate attack rates for different age, sex, and occupation categories.
3. Plot the geographic distribution of cases by residence and/or workplace.

On the basis of the analysis under 1, 2, and 3 above, a suspected vehicle may be identified. Attack rates may then be computed for those exposed and not exposed to this vehicle. However, sometimes this is not possible. For instance, in the investigation of a busy restaurant, the total exposed to a particular food is often unknown. In such instances, we compare, between the sick and a sample of the well, the proportions exposed to the suspected vehicle, as illustrated below.

At a restaurant, food poisoning occurred in 30 people, among whom 24, or 80%, ate raw oysters. This proportion alone is insufficient to incriminate oysters. It is necessary to investigate a sample of those diners not afflicted. Suppose we find that

in 30 well diners, only 3, or 10%, ate the oysters. This comparison provides evidence consistent with the notion that eating oysters was the cause of the outbreak. Further study such as that outlined below would be necessary to substantiate that notion.

Exercises: An Outbreak of Hepatitis in a Rural Community[1]

Introduction

On Friday, May 17, 1968, a request to assist in the investigation of an outbreak of infectious hepatitis was extended to the Hepatitis Unit of the Centers for Disease Control (CDC) in Atlanta, Georgia. It was learned that between April 30 and May 16, 1968, approximately 32 cases of infectious hepatitis had been reported to District #2 Health Department in North Trail, Michigan.

1. **Knowing that between April 30 and May 16, 1968, there were 32 cases of hepatitis reported to the County Health Department, could you conclude that this is a problem of epidemic proportions? Why?**

Background

Lake County (Figure 1–2) is located in the northern portion of the lower peninsula of Michigan. The county has an area of 576 square miles and a population of 9,680 (1960 census), 2,025 of whom live in North Trail, the county seat. The area is predominantly rural, divided between farmland and forest.

The epidemic investigation was centered on the city of North Trail, in the southwestern portion of the county. There are only two other communities of notable size in Lake County: Spruce City, population 435, and Basco, population 308.

The remaining area is divided into 14 subdivisions, with the population being mostly in the low middle socioeconomic class; in the summer there is also a large tourist population.

Seven cases of infectious hepatitis were reported to the Michigan District #2 Health Department in the year prior to April 1968. Four of these cases occurred in one family outbreak in August 1967. The remaining three cases were scattered in time, and no relationship could be established among them.

2. a. **Are 32 cases in excess of normal expectation?**
   b. **How do you establish whether this is greater than expected?**

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[1]The information in this section was drawn from Schoenbaum, S. C., Baker, O., and Jezek, Z. 1976. *Am. J. Epidemiol.* 104:74. The place names have been changed.

Figure 1–2 Location of Lake County, Michigan

Epidemic Investigation

By May 19, there were 39 reported cases of hepatitis. By May 25 the number had risen to 61, and by June 1 the last two cases were reported, bringing the total to 63.

The first step in the investigation consisted of personally interviewing all reported hepatitis victims. All interviews were conducted by the same two investigators at the patients' homes. Patients were questioned about the date of onset of illness, symptoms of illness, previous exposure to cases of hepatitis, visits out of the community, and history of receiving injections of blood products. In addition, information was obtained for all other members of the family concerning recent illnesses and the administration of gamma globulin. The patients and their families were

questioned about specific sources of water, milk, and food and about attendance at large gatherings or public places. At the time of the interview, a tap water sample was taken from each home for bacteriological analysis.

3. Ideally, what additional information should have been sought?

Epidemic Characteristics

Of Time

There were 63 cases of infectious hepatitis reported in Lake County between April 1 and May 8, 1968 (Figure 1–3). Of these, 61 had date of onset of illness between April 28 and May 26 (see Figure 1–3, which is an epidemic curve).

4. What inferences may be drawn regarding the probable time of initial exposure to the infection?

Of Person

The age- and sex-specific attack rates of Lake County cases with the date of onset of disease between April 28 and May 26 are illustrated in Table 1–3. Overall, the attack rate among males was almost twice as high as the attack rate among females, 8.1 per 1,000 versus 4.5 per 1,000 population, respectively.

Forty-three (70%) of the total Lake County cases occurred in schoolchildren, the remainder in the post-school population. Thirty-six of the 43 schoolchildren had attended the North Trail Public School. New cases occurred at St. Luke's School,
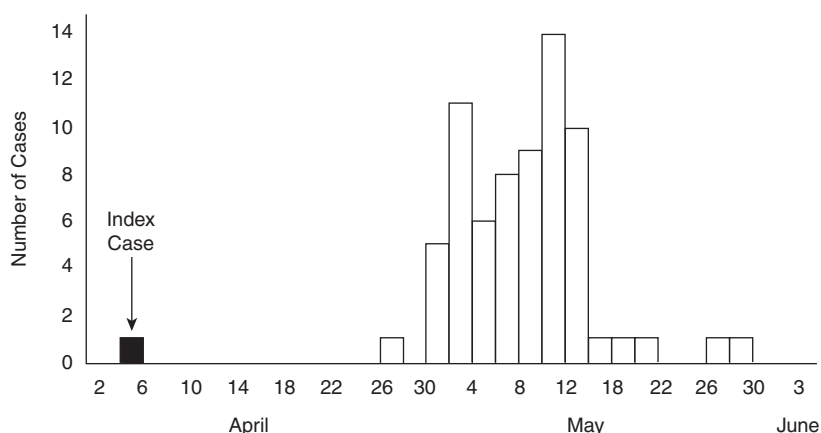
Figure 1–3 Cases of Infectious Hepatitis, April–May 1968, Lake County

Table 1–3 Attack Rates of Infectious Hepatitis by Age and Sex—Lake County, April 28–May 26

Age Group	Total Population by Age	Number of Cases			Attack Rate Per 1,000 Population		
		Male	Female	Total	Male	Female	Total
0–4	1740	0	0	0	0.0	0.0	0.0
5–9	1000	2	2	4	3.7	4.5	4.0
10–14	989	12	6	18	22.2	13.4	18.2
15–19	868	16	7	23	35.9	16.6	26.5
20–24	494	1	3	4	4.2	11.8	8.1
25–29	455	0	1	1	0.0	4.6	2.2
30–34	435	3	0	3	14.1	0.0	6.9
35–39	545	1	2	3	4.0	6.7	5.5
40–44	540	2	0	2	7.4	0.0	3.7
45–49	588	1	0	1	3.4	0.0	1.7
50–54	526	2	0	2	7.6	0.0	3.8
55+	1500	0	0	0	0.0	0.0	0.0
Totals	9680	40	21	61	8.1	4.5	6.3

the Spruce City School, and the Basco School. There was one Lake County case at Brecken School in neighboring Penton County.

5. a. **How many cases were younger than 5 years old?**
   b. **Which decade of life had the highest attack rate?**
   c. **What hypothesis relative to time and person can you make at this point in this investigation?**

Of Place

Lake County has four school districts, two of which are extensions from adjacent Penton County. The largest district is the one served by the North Trail Public School (a single building complex located near downtown North Trail, serving 1,525 pupils in kindergarten through 12th grade). Seventy percent of the pupils of this school use the school buses. North Trail also has a Roman Catholic parochial school with 240 pupils, grades 1 through 8. This school uses the same buses as the North Trail Public School. Table 1–4 shows attack rates by grade for North Trail Public School and St. Luke's School. The attack rates are uniformly low through grade 6, but beginning in grade 7 there is an increase in the attack rates in the public school. The peak attack rate, 8.6%, occurred in grade 10, followed by substantially lower attack rates in grades 11 and 12. There is a marked difference in the attack rates between the 7th and 8th grade classes of the public and parochial school.

Table 1–4 Attack Rates by Grade and School in Cases of Infectious Hepatitis—Lake County, April 28–May 26

	North Trail Public School				Saint Luke's School		
Grade	Number in Class	Number ill	Attack Rate (%)	Grade	Number in Class	Number ill	Attack Rate (%)
K.	126	2	1.6				
1	128	0	0.0	1	37	1	2.7
2	121	0	0.0	2	41	1	2.4
3	107	0	0.0	3	37	0	0.0
4	106	2	1.9	4	26	0	0.0
5	120	1	0.8	5	30	0	0.0
6	111	1	0.9	6	32	0	0.0
7	110	3	2.7	7	26	0	0.0
8	120	6	5.0	8	21	0	0.0
9	143	7	4.9				
10	128	11	8.6				
11	112	1	0.9				
12	93	2	2.2				

6. **What can you conclude from this information about the distribution of disease in terms of place?**

Analysis Related to Age

Note that Table 1–3 gives the frequency distribution of hepatitis cases by age and that Table 1–4 gives it by school and grade.

7. **Why is it important to calculate attack rates by age? Note once again that the majority of cases in Table 1–3 fall within the age group between 10 and 19 years, which is confirmed by the attack rates.**
8. **Using the information calculated about place and person, what conclusions can you draw now?**

Source of Epidemic

Using the information concerning time, place, and person, the investigators gathered relevant information concerning the school population. Children who attend kindergarten through grade 6 are not allowed to leave the campus for lunch. They may eat food prepared at the school cafeteria or may bring a lunch from home. Children in grades 7 through 12 at the North Trail High School, however, may leave the school during lunch hour. Because the school is only one block from

the main street of North Trail, many students go downtown for lunch each day. St. Luke's School, however, does not allow any of its students, grades 1 through 8, to leave the campus for lunch. All parochial students must eat in the school cafeteria or bring lunch from home.

Convinced that there was a common source of exposure, the investigators began to look for a vehicle of transmission. The first major sources investigated were those of food and water. An exposure history is given in Table 1–5 of 41 hepatitis cases, aged 10 to 19, in Lake County in May 1968.

> 9. a. **From the information given in Table 1–5, what hypothesis can be formed about the source of the infection?**
>   b. **Is this type of data alone sufficient to identify a single source?**

Food History of Well Individuals

To this point, the investigators concentrated on the sick individuals in the population. The attack rates were computed for specific food sources. To build a case, it is now necessary to examine food sources in the well population. By comparing the differential rates of exposure to sources between the well and the ill populations, an investigator should be able to further elucidate the true source of the infection.

> 10. a. **Examine Table 1–6. When the six listed exposures are compared, which source shows the largest differential between well and ill?**
>   b. **Explain the high exposure rates to water in both the sick and well groups.**

Milk Source

All commercial milk sold in Lake County comes from dairies located outside the county. None of the commercially produced milk in Michigan is limited to Lake County alone.

Table 1–5 Exposure History of 41 Hepatitis Cases, Ages 10–19, Lake County, May 1968

Food or Water	Yes	No	Unknown	Percent Known Exposed
Restaurant A	15	25	1	36.6
Restaurant B	17	23	1	41.5
North Trail Dairy Queen	28	12	1	68.3
Spruce City Dairy Queen	8	32	1	19.5
North Trail Bakery	37	3	1	90.2
North Trail municipal water supply	36	5	0	87.8

Table 1–6 Comparison of the Exposure History of 41 Cases of Hepatitis A in the 10- to 19-Year-Old Age Group with the Exposure History of a Group of 56 Well Household Members in the 10- to 19-Year-Old Age Group, Lake County, May 1968

	Number Yes	Number No	Number Unknown	Percent Known Exposure
	Hepatitis Cases			
Restaurant A	15	25	1	36.6
Restaurant B	17	23	1	41.5
North Trail Dairy Queen	28	12	1	68.3
Spruce City Dairy Queen	8	32	1	19.5
North Trail Bakery	37	3	1	90.2
North Trail water	30	5	0	87.8
	Well Household Members			
Restaurant A	22	31	3	39.3
Restaurant B	15	39	2	26.8
North Trail Dairy Queen	39	17	0	69.6
Spruce City Dairy Queen	6	50	0	10.7
North Trail Bakery	26	29	1	46.4
North Trail water	51	4	1	91.1

11. **What conclusions can you draw about milk possibly being the source of the contamination?**

Food Sources

Common exposure to a food item could explain the characteristics of this common-source outbreak. The only food items prepared and consumed locally are the foods served in the restaurants, salads sold in the delicatessens, Dairy Queen ice cream, and baked goods. Most of these products have been eaten at some time by the majority of the local residents. Almost all the cases who lived in Lake County gave a history of eating baked goods from the North Trail Bakery. However, it was impossible, from this information alone, to determine whether the bakery was the source of the epidemic or simply a very popular establishment in town.

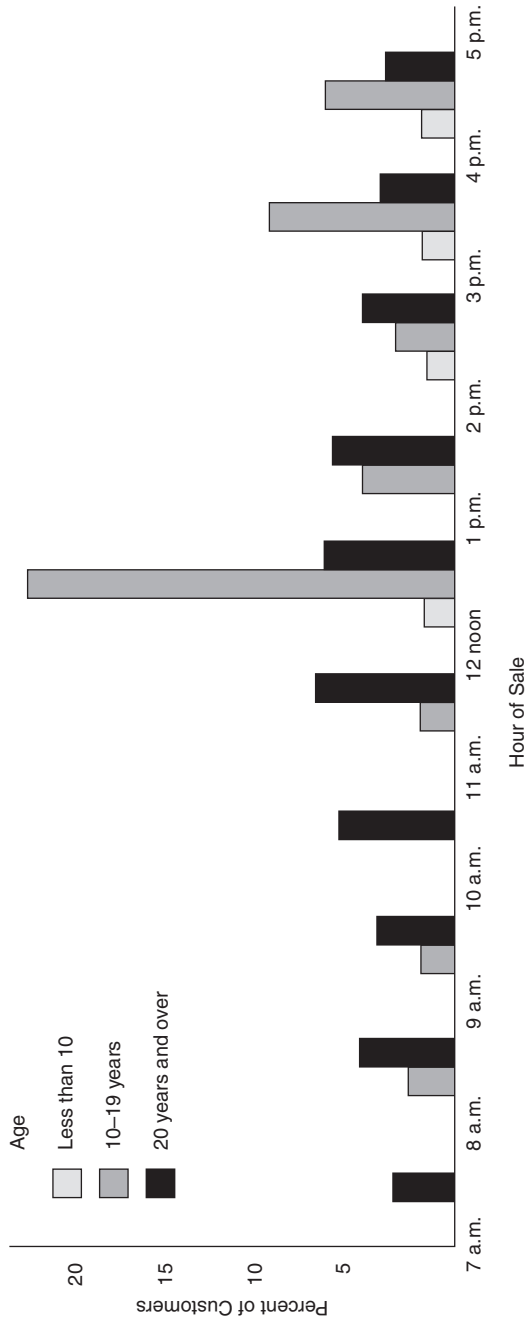12. **Study Figure 1–4. How do these data aid in the investigation?**

Figure 1–4 Percent of Total Persons Patronizing North Trail Bakery by Hour of Sale and by Age, June 3, 1968

Review of Case Histories

To further study the problem, the investigators sought cases who lived outside Lake County. In any such investigation, detailed case histories often revealed supporting evidence.

Case 1 The subject was a 45-year-old female schoolteacher who lives in Purley, a town on Lake Huron, 60 miles from North Trail. Her only contacts with Lake County were when she passed through North Trail on March 20, April 5, and April 14 on the way to visit her father who lived on Lake Michigan's shore of the state. She stopped only on the first two occasions. On March 20, she had only a cup of coffee in a North Trail restaurant. On April 5, she bought some cupcakes and a coffee cake. On May 5 she became ill with hepatitis.

Case 2 A 35-year-old housewife who lives in Detroit, Michigan.

Case 3 The 8-year-old daughter of Case 2.

Case 4 A 49-year-old housewife who lives in Potomac is the sister-in-law of Case 2 and the aunt of Case 3. Both Case 2's family and Case 4's family own summer cottages in Lake County (10 to 15 miles from North Trail). They went to their cottages on April 8, 9, and 10 to open them for the season. At no time did Case 4 or Case 3 go in or near the city of North Trail. On April 9, Case 4 took care of Case 2's children while Case 2 went into the city to conduct some business. At that time Case 2 bought some pastries at the North Trail Bakery to bring to the cottage for lunch. All three cases ate the same kind of glazed donut. Case 2 and Case 3 became ill on May 7th, and Case 4 became ill on May 11th. No other member of either family had the same kind of pastry, and no other member of either family is known to have been ill since being in Lake County.

Case 5 A 35-year-old mother of six purchased assorted glazed and iced products at the North Trail Bakery on April 6. She took the baked products home, where they were consumed by her and her family.

Cases 6 and 7 Case 5's two older daughters ate some of them.

Cases 8 and 9 Case 5's two youngest sons returned home later in the day and consumed all but one glazed item.

Case 10 Case 5's 5-year-old daughter and her twin came home and, after a dispute, Case 10 won possession of the glazed delicacy. She became ill, but her twin did not.

The father, who was away at work throughout the day, did not eat any of the bakery goods and remained well.

13. Are the above data compatible with the bakery being the source of infection?

The occurrence of infectious hepatitis 1 month after direct exposure to the North Trail Bakery was illustrated by Case 1. Cases 3 and 4 showed that only contact with baked products could be associated with infectious hepatitis, because they had no contact with the North Trail municipal water supply, with any of the restaurants in North Trail, or with any other local food-handling establishment. None of these four cases had any history of contact with anyone known to have infectious hepatitis or jaundice. None had a history of infections or administration of blood products within 6 months prior to the onset of illness, and none had a history of recent ingestion of shellfish.

14. What would your next step in the investigation be?

One of the cases in Lake County was a baker's assistant. This 34-year-old white male is reported physically and mentally handicapped. He visited his physician on April 6, 1968, complaining of "vomiting and a cold." His wife visited the same physician 2 days later complaining of nausea and generalized headaches. The patient continued to work until April 11, when the diagnosis of infectious hepatitis was made. Co-workers at the bakery reported that the patient had dark urine for at least 4 days before he stopped working. He did not return to work until April 23. Figure 1–3 shows the complete epidemic. Note that the baker's assistant is the initial case (in black).

15. a. Does the epidemic curve reveal the incubation period for hepatitis?
b. Does this curve still support a common source of infection?
16. Knowing that infectious hepatitis virus is killed by heat, what further investigation would you undertake to confirm the source of the virus?

Investigation of the Bakery

The North Trail Bakery has served the region for 34 years. It makes a variety of breads, pastries, donuts, cookies, pies, and cakes. Besides over-the-counter sales in downtown North Trail, the bakery supplies all sweet rolls and donuts and some of the bread to each of the restaurants in the North Trail area and to grocery stores in Lake County.

The baker's assistant helps in practically every process of the baked goods. In particular, he is responsible for making and glazing donuts and for icing much of the pastry. Observation by investigators revealed that icing was spread on the pastries by hand and items to be glazed were dipped into the glaze by hand. Since the pastry is not cooked further after glazing or icing, these processes are likely points of contamination.

Both glaze and icing may be kept for several days and old batches may be used to start new ones. Bakery products not sold in 1 day may be sold in the next business day as "day-old pastries" or may be frozen for sale in the next 1–2 weeks.

Therefore, contaminated foods could be available for consumption over a period of several days or weeks. In the midst of the epidemic investigation, as it became clear that the bakery was an increasingly likely source, a blood sample was taken from each person who worked in the bakery to ascertain whether there were any cases of hepatitis present at the time in the bakery employees.

An SGPT (an enzyme test for liver function) was performed on each blood sample, and in all instances the SGPT was within normal limits. Because the epidemic curve showed that the outbreak was ending at this time (June 3) and because there was no elevated SGPT level found, the bakery was permitted to remain open.

17. **Do you agree with this decision? Support your view.**
18. **If none of the bakery employees appeared ill, why were SGPT tests performed?**

Control Measures

Serum gamma globulin was immediately offered to all residents, and 7,000 to 8,000 doses were distributed after June 3, 1968.

19. a. **Since the epidemic had ended, why was it necessary to administer the gamma globulin?**
    b. **How would you evaluate the effectiveness of this control measure?**

Reference

Tong, J. L., Engle, M., Cullingford, J. S., Shimp, D. T., & Love, C. E. (1962). *American Journal of Public Health, 52,* 976.

Recommended Reading

Gordis, L. (2008). *Epidemiology* (4th ed.). Philadelphia: W. B. Saunders. Chapter 2 discusses disease transmission providing a unified approach to acute and chronic disease.
Mausner, J. S., & Kramer, S. (1985). *Mausner and Bahn: Epidemiology—An introductory text* (2nd ed.). Philadelphia: W. B. Saunders. Chapter 11 provides a clear discussion of epidemic investigation within the broader context of infectious disease epidemiology.