



FOCUS on Field Epidemiology

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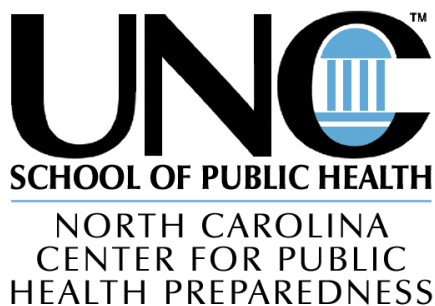
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An Overview of Outbreak Investigations

It's a quiet Friday afternoon at the local health department. You are hard at work when the phone rings and shatters the calm. On the other end of the line, a panicked voice explains to you that there have been two patients from a local nursing home admitted to the hospital with SARS-like symptoms, and you need to do something about it. You hang up the phone.

"Right," you say to yourself, "I need to do something about this problem!" But what should you do? Go to the hospital? The nursing home? What would you do when you arrive? Should you close down the nursing home? What would the other nursing home residents do? What if the press hears about this? What do you say?

The panic is mounting, but suddenly you remember your FOCUS periodicals! Every other month you have faithfully downloaded the periodical from the FOCUS website, building an entire field epidemiology reference book one topic at a time. You even have a handsome cover for the reference that you chose from the website. You turn to the first edition on outbreak investigation with a sigh of relief (although we suggest you read these before the outbreak occurs!).

FOCUS ON FIELD EPIDEMIOLOGY (FOCUS) is a periodical with a hands-on practical approach to various topics in field epidemiology. It can be used for self-study or as a teaching tool for trainers. It is an excellent instrument for lunch-and-learn seminars or in-service trainings. In addition, each periodical has a corresponding downloadable power point

presentation. Included in each periodical is a topic overview with examples, helpful illustrations, additional resources, and more! Discussion questions for individuals or groups and solutions for the questions are posted on the FOCUS website. Online self-evaluation questions complement each issue. FOCUS is available by downloading PDF files or by subscribing to the email mailing list. Participants who complete North Carolina Center for Public Health Preparedness (NCCPHP)-developed training products can earn a free personalized, printable certificate of completion. Good luck and enjoy!

Overview of Outbreak Investigation

Investigation of disease outbreaks is an important part of the health department's responsibility to protect the public's health. A health department may be called on to investigate a wide variety of unusual health events, including outbreaks due to food poisoning, geographic clusters of leukemia, or a mysterious rash illness in a school.

Outbreak investigations can identify the source of illness and guide public health intervention. Health departments may recognize outbreaks through routine surveillance activities, reports from astute clinicians or laboratorians, or reports from the persons affected by the outbreak.

This Focus on Field Epidemiology issue will provide a general overview of the basic steps of disease out-

break investigations. Future issues will provide more detail for each of these steps. Dr. John Snow's seminal work during an 1854 cholera outbreak in London will be presented as an example of how to conduct an outbreak investigation.

Why investigate?

Outbreak investigations afford a number of opportunities for health department personnel. First, outbreaks provide an opportunity to characterize a public health problem. For example, the investigation of 15 confirmed *Salmonella* cases in Minnesota uncovered a nationwide outbreak associated with consumption of Schwan's ice cream that may have gone undetected (1). This product was estimated to cause 224,000 cases of salmonellosis.

Second, investigation may identify risk factors that are associated with infection that are preventable. Epidemiologic investigations of *Escherichia coli* O157:H7 outbreaks have identified consumption of foods such as pink hamburgers (2), unpasteurized apple juice (3), or alfalfa sprouts (4) that consumers may avoid to reduce their risk of illness.

Third, outbreak investigations may provide new research insights into the disease even if no new cases are occurring. In 1986, identification of a small outbreak of chronic diarrheal illness of unknown etiology associated with consumption of unpasteurized milk has led to intense laboratory research into the presumed infectious agent of "Brainerd" diarrhea (5).

Finally, outbreak investigations provide opportunities for training of health department staff in methods of public health investigation and emergency response that are essential in the era of potential bioterrorism events (6).

The decision to investigate may be driven by several important factors. Limitations in financial resources, personnel, or staff expertise may often impede outbreak investigations. These barriers are not insurmountable, however. Training opportunities and assistance in disease outbreak investigations are available from state and federal agencies, such as the CDC. Although direct costs of an outbreak investigation are high, the benefits in reduced medical costs by preventing illness may offset these costs (7).

Political pressure may play a role in the decision to investigate. Politicians may demand public health action based on the demands of concerned citizens or news media coverage. In one example, an outbreak of mass psychogenic illness in a school may have been prolonged, in part, due to the concerns of the local parents (8).

Most importantly, public health and scientific factors influence the decision to investigate. How serious is the disease? How likely is the outbreak to continue? Is enough known about the disease to act immediately without epidemiologic investigation? Unfortunately, the decision to investigate an outbreak usually must be made quickly and in the face of limited information.

What are the steps of an outbreak investigation?

Once an outbreak is identified, there are several key steps that provide a systematic approach to investigation (Table 1). Although these are listed sequentially, the steps often occur simultaneously or may be repeated as new information is received. The outbreak investigation can be divided broadly into the preliminary phase, analytic study phase, and control and follow-up phase. Dr. Arthur Reingold's paper, *Outbreak investigations—a perspective* (9) and future issues of *Focus on Field Epidemiology* explore these steps in greater detail.

During the preliminary phase, the health department staff should quickly become "instant experts" in the disease, learning as much as possible about the disease, its symptoms, and its possible causes and routes of transmission. The first essential step in an outbreak investigation is to confirm the existence of an outbreak. Review of existing surveillance baseline data may be used for this purpose. Confirmation of the diagnosis with a laboratory is important, especially if the pathogen is new or unusual. Without confirmation, the situation may become a "pseudo-outbreak," like one that occurred in Florida when the emerging pathogen *Cyclospora cayetenensis* was misidentified by the laboratory (10).

Field preparation should begin once the decision to investigate has been made. This includes assembling a multidisciplinary outbreak investigation team and gathering necessary equipment and supplies to collect clinical or environmental samples. Expertise may be required in clinical medicine, epidemiology, environmental health, and microbiology.

The team should create a case definition and begin to identify cases that may be associated with the outbreak. Information collected during this phase from medical records or patient interviews should be organized into a line listing and summarized according to time, person, and place. If an obvious source of contamination is identified, immediate control measures should be taken.

In the analytic study phase, the investigative team should develop hypotheses regarding the cause of the outbreak from literature reviews. Knowledge of previous

outbreaks and an understanding of the microbiology of the pathogen may provide useful clues, and open-ended interviews with several of the case-patients may provide additional insight into the cause of the outbreak. Testing the list of hypotheses involves conducting analytic studies such as retrospective cohort studies or case-control studies.

In parallel to the epidemiologic investigation, environmental sampling should be considered. In a food-borne outbreak, for example, food and beverage samples should be collected as soon as possible. Ideally, microbiological testing of these samples should be focused by the results of the analytic study.

During the final stage of the outbreak investigation, control measures should be taken to prevent further illness and prevent future outbreaks. This stage involves working with government regulators, industry, and health educators. A mechanism to evaluate the short- and long-term success of the intervention should be instituted. A detailed summary of the investigation and specific recommendations should be prepared and disseminated to all participants.

Additionally, health promotion messages should be prepared for the general public. Communication—among the team members and with the public—is crucial to the success of an outbreak investigation, and the news media can be very helpful in presenting information to the public (11). The team should agree on the information to be released and identify a single member to interact with the media.

Snow on Cholera

Modern infectious disease epidemiology often traces its origin to Dr. John Snow's investigation of the 1854 cholera outbreak in London. Snow, using the general principles of outbreak investigation outlined above, was able to determine that the outbreak of the deadly disease was occurring through fecal contamination of

the water supply. More specifically, he was able to determine which of the local water supply companies was responsible for the outbreak using an analytic study design.

The following case study walks through each step in the outbreak investigation, using Snow's experiences as examples. The quotations below are taken from the book, *On the Mode of Communication of Cholera*, published online by the University of California at Los Angeles School of Public Health website (see: <http://www.ph.ucla.edu/epi/snow.html>).

1. Verify the diagnosis and confirm the outbreak

Cholera is an acute, diarrheal illness that is often mild or without symptoms, but in 5% of patients it can be severe, characterized by profuse watery diarrhea, vomiting, and leg cramps. Rapid loss of body fluids leads to dehydration and shock, and without treatment, death can occur within hours. The microbiological etiology of the disease, *Vibrio cholerae*, was unknown to Snow at the time. Coincidentally, Filippo Pacini identified *Vibrio cholerae* during an outbreak in Florence one year before in 1853. Pacini's discovery was confirmed and made widely known by Robert Koch in 1884.

Although Snow did not use a microbiologically confirmed case definition, death from watery diarrhea during the London outbreak was a reasonable case definition for cholera. Although this case definition is highly sensitive (meaning it will include most cholera cases), it is also highly nonspecific (meaning it will not exclude non-cholera diarrheal deaths). The outbreak description by Snow verifies the existence of the outbreak.

"The most terrible outbreak of cholera which ever occurred in this kingdom, is probably that which took place in Broad Street, Golden Square, and the adjoining streets, a few weeks ago. Within two hundred and fifty yards of the spot where Cambridge Street joins Broad Street, there were upwards of five hundred fatal attacks of cholera in ten days. The mortality in this limited area probably equals any that was ever caused in this country, even by the plague: and it was much more sudden, as the greater number of cases terminated in a few hours."

2. Define a case and conduct case finding

A case was defined as a death from cholera and Snow conducted case finding through records, medical practitioners, and in the neighborhoods around Golden Square.

"I requested permission, therefore, to take a list, at the

Table 1. The basic steps of an outbreak investigation

1. Verify the diagnosis and confirm the outbreak
2. Define a case and conduct case finding
3. Tabulate and orient data: time, place, person
4. Take immediate control measures
5. Formulate and test hypothesis
6. Plan and execute additional studies
7. Implement and evaluate control measures
8. Communicate findings

General Register Office, of the deaths from cholera, registered during the week ending 2nd September, in the subdistricts of Golden Square, Berwick Street, and St. Ann's, Soho, which was kindly granted. Eighty-nine deaths from cholera were registered, during the week, in the three subdistricts. Of these, only six occurred in the four first days of the week; four occurred on Thursday, the 31st August; and the remaining seventy-nine on Friday and Saturday."

3. Tabulate and orient the data; time, person, place

Snow first created a line listing of case-patients, including age, gender, and address. These cases were plotted on a map and it was observed that they occurred in proximity to the pump on Broad Street. The epidemic curve showed that a point source outbreak is likely (Figure 1).

"On proceeding to the spot, I found that nearly all the deaths had taken place within a short distance of the pump. There were only ten deaths in houses situated decidedly nearer to another street pump. In five of these cases the families of the deceased persons informed me that they always sent to the pump in Broad Street, as they preferred the water to that of the pump which was nearer. In three other cases, the deceased were children who went to school near the pump in Broad Street. Two of them were known to drink the water; and the parents of the third think it probable that it did so. The other two deaths, beyond the district which this pump supplies, represent only the amount of mortality from cholera that was occurring before the irruption took place."

An epidemic curve can orient the data by time and provide evidence of the outbreak. The shape of the curve can be used to determine the type of outbreak

(e.g. point source or person-to-person transmission) and if the outbreak is ongoing.

4. Take immediate control measures

Snow suspected the Broad Street pump and, in the now famous symbol of public health action, removed the pump handle from the well.

"I had an interview with the Board of Guardians of St. James's parish, on the evening of Thursday, 7th September, and represented the above circumstances to them. In consequence of what I said, the handle of the pump was removed on the following day"

5. Formulate and test hypothesis

Although Snow knew that the cases were due to drinking from the Broad Street well, additional evidence of the association was found among a group of persons who were not exposed to the well water.

"There is a Brewery in Broad Street, near to the pump, and on perceiving that no brewer's men were registered as having died of cholera, I called on Mr. Huggins, the proprietor. He informed me that there were above seventy workmen employed in the brewery, and that none of them had suffered from cholera, -- at least in a severe form, -- only two having been indisposed, and that not seriously, at the time the disease prevailed. The men are allowed a certain quantity of malt liquor, and Mr. Huggins believes they do not drink water at all; and he is quite certain that the workmen never obtained water from the pump in the street. There is a deep well in the brewery, in addition to the New River water."

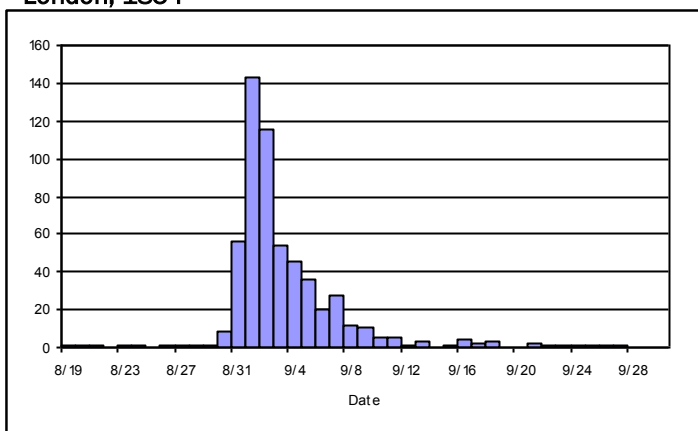
In modern times, epidemiologists would have conducted an analytic study at this phase. For example, a case-control study using case-patients and persons without disease at the Brewery as a comparison group. However, based in part on the evidence provided by the brewers, Snow concluded,

"...that there had been no particular outbreak or increase of cholera, in this part of London, except among the persons who were in the habit of drinking the water of the above-mentioned pump-well."

6. Plan and execute additional studies

Snow suspected that a previous cholera outbreak in 1848 was associated with the London water supply. He suspected a single supplier of water, the Southwark and Vauxhall Company. He compared the mortality rate due to cholera (number of cholera deaths per 10,000

Figure 1. Cholera deaths in the Golden Square Section of London, 1854



households) between two companies who supplied water in a single geographic south of the River Thames.

“The experiment, too, was on the grandest scale. No fewer than three hundred thousand people of both sexes, of every age and occupation, and of every rank and station, from gentlefolks down to the very poor, were divided into two groups without their choice, and, in most cases, without their knowledge; one group being supplied with water containing the sewage of London, and, amongst it, whatever might have come from the cholera patients, the other group having water quite free from such impurity.”

The resulting study implicated the Southwark and Vauxhall Company, which had drawn its water from the downstream (and more heavily sewage contaminated) section of the River Thames.

The rate ratio indicates that, compared to the water supply companies in the rest of London, customers of Southwark and Vauxhall were nearly 6 times more likely to die from cholera than the general population, and that customers of Lambeth were less likely to die from cholera than the general population (Table 2).

7. Implement and evaluate control measures

At the end of his treatise On the Mode of Communication of Cholera, Snow made 12 specific recommendations to prevent illness. These recommendations included prevention of transmission by medical

practitioners, isolation of patients, treatment of the water supply, suggested water sources for London, disposal of human waste, and quarantine of persons suspected to have been exposed in foreign countries.

8. Communicate findings

Snow shared his findings with members of the medical profession and government officials in Parliament.

“After the Registrar-General alluded, in the “Weekly Return” of 14th October last, to the very conclusive investigation of the effects of polluted water in the south districts of London, there was a leading article, in nearly all the medical periodicals, [Medical Times and Gazette, Lancet, and Association Journal] fully admitting the influence of the water on the mortality from cholera. It may therefore be safely concluded that this influence is pretty generally admitted by the profession.”

Conclusion

Snow conducted a systematic investigation to determine the mode of transmission of cholera before the germ theory was firmly established. The historical example of his investigation serves as a model of “shoe leather epidemiology,” critical thinking, and public health action to the present day.

Useful resources to become an “instant expert” on a health topic during an outbreak

- Michael Gregg. Field Epidemiology. 2nd edition. Oxford University Press, 2002. [Also see the book review in the American Journal of Epidemiology (2002;156:783-784].
- CDC. Information for Public Health Professionals- Investigating Foodborne Disease Outbreaks. Available online at: http://www.cdc.gov/foodborneoutbreaks/info_helathprofessional.htm
- Control of Communicable Disease in Man, 17th edition. Chin, J (ed). APHA, 2000.
- Principles & Practice of Infectious Diseases, 5th edition. Mandell GL, Bennett JE, Dolin R (eds). Churchill Livingstone; 2000.
- National Library of Medicine. PUBMED. Available online at: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?>

Table 2. Comparison of the cholera mortality rate per 10,000 households by water source in London, 1848

Water supply	Households	Deaths	Deaths/10,000 households	Rate ratio (95% CI)
Southwark and Vauxhall	40,046	1263	315	5.7 (5.3-6.1)
Lambeth	26,107	98	37	0.7 (0.6-0.8)
Rest of London	256,423	1422	55	1.0 (referent)

In this issue of FOCUS, the steps listed for an outbreak investigation comprise a brief introduction and a rough guide. Future Focus on Field Epidemiology issues will explore each step in more detail. However, only through the process of conducting investigations repeatedly over an entire career will public health professionals truly learn the methods of outbreak investigations.

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