CHAPTER

2

Fundamental Concepts of Public Health Surveillance and Foodborne Disease

> *At either end of any food chain you find a biological system—a patch of soil, a human body—and the health of one is connected—literally—to the health of the other.*
>
> *Michael Pollan*
> *The Omnivore's Dilemma, 2006*

During the past century, the American diet transformed significantly in what food we eat, how we grow or raise that food, and how that food arrives to our tables. Factors contributing to these changes included industry consolidation and globalization, health concerns and dietary recommendations, and culinary trends and dining habits. What and how we eat relate directly to the foodborne diseases we experience.

Preventing foodborne disease relies on our ability to translate knowledge of the principles of food safety to the practices of food production at each level of the food system. Foodborne disease outbreaks represent important sentinel events that signal a failure of this process.

2.0. Introduction

Determining whether this failure was due to the emergence of a new hazard or failure to control a known hazard is an important outcome of an outbreak investigation. This determination is critical to developing strategies to prevent future outbreaks and to evaluate the success of those strategies. A variety of surveillance programs are required to accomplish this complex task.

This chapter provides an overview of some factors responsible for recent trends and challenges in public health surveillance and foodborne disease in the United States.

2.1. Trends in Diet and the Food Industry

2.1.1. Dietary Changes

That we no longer are a nation of meat and potato eaters is evidenced by the most recent dietary recommendations of the U.S. Department of Health and Human Services and the U.S. Department of Agriculture (USDA), which emphasize the importance of eating a variety of fruit, vegetables, and protein.[2] From 1985 through 2005, the annual per capita consumption of fruit and vegetables rose from 89 to 101 pounds and from 123 to 174 pounds, respectively.[3] In 2006, the annual per capita consumption of seafood (fish and shellfish) was 16.5 pounds, compared with 12.5 pounds in 1980.[4]

The food industry has accommodated Americans' demand for a broader variety of food by moving from locally grown and raised products to routine importation of items once considered out-of-season or too exotic for Americans to buy. The burgeoning international agribusiness created by the demand for ready-to-eat and processed foods supports monoculture farming (i.e., the practice of growing one single crop), mega-feedlots (i.e., feedlots raising thousands of cattle), and mass importation and distribution of foods.[1, 5]

Concurrent with the changes in demand, technology has improved growing, harvesting, packaging, handling, and transportation practices, facilitating year-round importation of distantly grown, fragile foods, such as raspberries from the Southern Hemisphere. Less stringent trade agreements with major fruit-growing countries also have contributed to the growth of international imports: during 1990–2006, the annual cost of imports of fresh fruits and vegetables into the United States rose from $2.7 to $7.9 billion; simultaneously, the proportion of tropical fruits (primarily from Mexico and Costa Rica) constituting these imports increased from 7% to 15%.[3]

Increasingly more Americans eat their meals away from home. According to the National Restaurant Association's 2008 industry overview, 945,000 restaurant locations will have more than 70 billion meal and snack occasions. In 2005, 41% of all food spending was on food away from home, up from 26% in 1970.[86]

The increased number of meals eaten away from home most likely have influenced foodborne disease. A review of foodborne outbreaks in the seven states participating in CDC's Foodborne Disease Active Surveillance Network (FoodNet) revealed that 66% of outbreaks (222 of 336) occurring in 1998 and 1999 were associated with restaurants, and 9% (30 outbreaks) were associated with catered events.[6] In addition, a variety of studies of both sporadic and outbreak-associated foodborne illness, including infection with *Escherichia coli* O157:H7, *Salmonella* Enteritidis, *Salmonella* Typhimurium, and *Campylobacter jejuni*, suggest that commercial food-service establishments, such as restaurants, play an important role in foodborne disease in the United States.[7]

Culinary trends that use undercooked or raw

2.1. Trends in Diet and the Food Industry

foods—particularly dairy, fish, or shellfish—might be contributing to increased infections and outbreaks caused by the microorganisms associated with these foods.[19–25]

2.1.2. Changes in Food Production

Changes in what we eat and drink are not the only contributors to trends in foodborne disease. How our food is cultivated or raised, processed, and distributed and how and by whom our food is prepared also are factors. Food can be contaminated anywhere along the supply chain from farm to fork. The industrialization of food production, with concentrated animal feeding operations and increasingly intense agricultural practices, and the broadening distribution of food products have contributed to outbreaks of foodborne disease involving larger numbers of people, multiple states, and even multiple countries.[8–18] Changes in agricultural, processing, or packaging methods might facilitate bacterial contamination or growth,[8,9,16,23,26–34] and routine use of antibiotics to promote the growth of livestock and poultry has increased human infections caused by drug-resistant bacteria.[49, 50, 84, 85]

2.1.3. Trends in Food Product Recalls

Food recalls are one indicator of food-safety problems. Distributors or manufacturers voluntarily recall their food products for either of two reasons: (a) a problem discovered in the course of routine inspection of the food or its processing or distribution or (b) suspicion or identification of the product as the cause of human or animal disease. During February 2007 through February 2008, USDA and the federal Food and Drug Administration (FDA) reported more than 90 voluntary recalls of food associated with microbial contamination. These recalls demonstrate the breadth of products and pathogens responsible for foodborne diseases in the United States.[17,18]

During that period, many of the recalls were for contaminated meat, primarily ground beef and other beef products. However, distributors or manufacturers also recalled shellfish and smoked, dried, frozen, and uneviscerated fish; fresh fruit, herbs, and vegetables; canned vegetables; raw milk; cheese and other dairy products; chocolate; ready-to-eat foods; frozen pizza; peanut butter; sesame seeds; tahini; tofu; and bottled water. The products were distributed locally, nationally, or internationally and were sold not only by national chain retail stores and food services but also at farm stands and small health food stores carrying organic and "natural" products. In other words, no one is completely protected from the risk for contaminated food.[17,18]

Most of these recalls followed identification of bacterial contamination of a food or beverage. In at least 20 instances, the contamination was associated with reported human illnesses, including 628 residents of 47 states infected with *Salmonella* after eating contaminated peanut butter.[16] The contaminating pathogens most commonly identified in food recalls were bacteria: *Listeria monocytogenes*, Shiga toxin-producing *E. coli* (STEC), and *Salmonella* species; the latter two were associated most frequently with recalls resulting from foodborne outbreaks.

Products also were recalled that were contaminated with viruses (e.g., norovirus in shellfish), parasites (e.g., *Cryptosporidium* in bottled water), and toxins (e.g., *Clostridium botulinum* neurotoxin, *Staphylococcus aureus* enterotoxin, and tetrodotoxin produced by pufferfish).[17,18] The largest single food recall in the United States, a staggering 148 million pounds of beef, began after discovery that a California food processor used disabled (i.e., "downer") cows in beef production—a concern because of the theoretical risk for infection of the cattle with the agent associated with bovine spongiform encephalopathy (BSE) or "mad cow disease."[35–37]

2.2. Trends in Surveillance

Foodborne disease is an important cause of illness in the United States. In 1999, CDC estimated that foodborne diseases were responsible for 76 million illnesses each year, resulting in 325,000 hospitalizations and 5000 deaths.[38] During 1998–2002, 6427 foodborne disease outbreaks were reported to CDC, resulting in at least 128,370 individual illnesses and 88 deaths.[39]

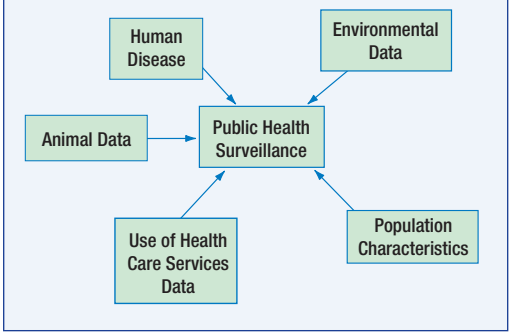
Our ability to use public health surveillance for tracking cases of foodborne disease and outbreaks, as well as behaviors and conditions that contribute to foodborne diseases, is critical to our understanding and control of these diseases.

2.2.1. Overview

Public health surveillance is the foundation of communicable disease epidemiology and an essential component of a food-safety program.[40] Surveillance data can reveal the burden of a particular disease in the community or the presence and scale of a possible outbreak. Surveillance data also can provide clues to the source of and contributing factors to disease outbreaks. Over time, surveillance data can identify disease and behavioral trends and enable investigators to learn more about the diseases being tracked and ways to prevent these diseases.

Surveillance programs conducted by public health and other health-related agencies are much broader than foodborne disease surveillance. Surveillance is conducted to identify waterborne diseases and diseases transmissible from person to person; breakdowns in infection control in health-care facilities; animal-based diseases that may affect people; patterns of behavior that increase risk for poor health, and many other reasons. Furthermore, surveillance programs typically use a variety of data sources to provide a complete understanding of a particular disease in the community and insight into its control (Figure 2.1).

Figure 2.1 Sources of information for public health surveillance



2.2.2. Selected Surveillance Systems of Relevance to Foodborne Diseases

Multiple types of surveillance systems are used in the United States related to foodborne disease. Some of them, including notifiable condition surveillance, complaints from consumers about potential illness, and reports of outbreaks, focus on the detection of specific enteric diseases likely to be transmitted by food and have been used extensively by health-related agencies for decades. More recently, new surveillance methods have emerged including hazard surveillance, sentinel surveillance systems, and national laboratory networks for comparing pathogen subtypes, which are particularly applicable to foodborne disease.[41]

Each surveillance system plays a critical role in detecting and preventing foodborne disease and outbreaks in the United States and each represents one part of the public health system needed to ensure food is safe as it moves from its original source through the food chain to the tables of U.S. citizens.

2.2.2.1. Notifiable disease surveillance

One of the oldest public health surveillance systems in the country is notifiable disease surveillance. Notifiable disease surveillance begins with an ill person who seeks medical attention. The health-care provider sends a

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specimen (for foodborne illness, this usually is a stool specimen) to the laboratory for the appropriate tests, and the laboratory identifies the agent responsible for the patient's illness so the patient can be treated. Next, the laboratory or health-care provider notifies local public health officials of the illness. Once the patient's information goes to a public health agency, the illness is no longer considered as an isolated incident but is compared with other similar reports. Combining the information in these separate reports allows investigators to identify trends and detect outbreaks.

All states and territories have legal requirements for the reporting of certain diseases and conditions, including enteric diseases likely to be foodborne, by health-care providers and laboratories to the local public health agency. In most states and territories, the law usually requires local public health agencies to report these diseases to the state or territorial public health agency. What to report and with what urgency vary by state. States and territories (or sometimes local public health agencies) then send the information to the National Notifiable Disease Surveillance System, which CDC oversees. In the past, disease reports usually arrived by mail or facsimile transmission, but many agencies now encourage telephone reporting and have developed electronic disease reporting locally. State public health laboratories also participate in national surveillance through programs such as the Public Health Laboratory Information System (PHLIS), a PC-based electronic reporting system for laboratory-confirmed isolates including *Salmonella* and *Shigella*,[42] and PulseNet (see below).[43]

Notifiable disease surveillance is "passive"—i.e., the investigator waits for a disease report from health-care providers, laboratories, and others who are requested or required to report these diseases to the public health agency—and is susceptible to diagnosis and reporting problems. As little as 5% of bacterial foodborne illness might be reported to CDC through notifiable disease surveillance.[44]

2.2.2.2. Foodborne disease complaints/notifications

Receiving and responding to complaints of disease from the public is a basic function of many public health agencies and other health-related agencies and can identify foodborne illnesses in the community and possibly clusters of persons with suspected foodborne disease.

The processing of foodborne illness complaints varies by agency on the basis of the suspected pathogen and agency resources. Some health departments are required by local or state statute to investigate all commercial food establishments named by sick persons. Most health departments record complaints in a log book or on a standardized form. Some health departments enter this information into an electronic database for easy review and analysis.

Some complaint systems are more publicized and involve community members more heavily. A Web-based system in Michigan (RUsick2) allows ill persons to share information about their illness and recent exposures and helps the health department identify clusters of persons with unsuspected foodborne disease. During a pilot test in 2002, this system resulted in an estimated fourfold increase in the reporting of foodborne illness complaints. Two foodborne outbreaks were identified that most likely would not have been identified through other means.[45]

2.2.2.3. Behavioral Risk Factor Surveillance System

The Behavioral Risk Factor Surveillance System (BRFSS) is a state-based system of health surveys that collects information about health risk behaviors, preventive health practices, and health-care access primarily related to chronic disease and injury. For many states, BRFSS is the only source of timely, accurate data on health-related behaviors.

CDC established BRFSS in 1984; currently, data are collected by random-digit–dialed telephone surveys in all 50 states, the District

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of Columbia, Puerto Rico, the U.S. Virgin Islands, and Guam. More than 350,000 adults are interviewed each year, making BRFSS the largest telephone health survey in the world. States use BRFSS data to identify emerging health problems, establish and track health objectives, and develop and evaluate public health policies and programs. Many states also use BRFSS data to support health-related legislative efforts.

BRFSS consists of core questions asked of all respondents across the country, and state-specific questions that are added by state and local health agencies each year. Although a minimum number of respondents is needed in each state to ensure statistical significance, states can choose to over-sample (place a higher number of phone calls) in certain regions or among certain populations to increase their ability to detect trends within those regions or populations.

Because of the length of time necessary to conduct the survey and lack of clinical information, BRFSS is not an appropriate tool for detecting foodborne illness. However, BRFSS can be used to identify behaviors, such as food handling methods, or trends, such as changes in the number of meals eaten outside the home, that can provide information about efforts to prevent foodborne illness.

2.2.2.4. Hazard surveillance

Food-control authorities have a regulatory and public health mandate to prevent diseases that can be unintentionally and intentionally transmitted through food. Approximately 75 state and territorial agencies and approximately 3000 local agencies assume the primary responsibility for licensing and inspecting retail food-service establishments.[46] Many of these same agencies oversee other aspects of the domestic food supply chain. The retail food-service industry segment alone consists of more than one million establishments and employs over 12 million people.[46]

Factors that contribute to foodborne outbreaks (e.g., factors that lead to contamination of food with microorganisms or toxins or allow survival and growth of microorganisms in food) are used to develop control and intervention measures at food-service establishments. Routine inspections then focus on implementation of these measures. Often referred to as Hazard Analysis Critical Control Point (HACCP) inspections, this is the basis for hazard surveillance. No national hazard surveillance system is available to food control authorities, although work being conducted through the Conference for Food Protection may evolve into a national system.

2.2.2.5. Contributing factor surveillance

Communicable disease control officials or foodborne outbreak surveillance officials from state and local health departments gather information about contributing factors in outbreaks from environmental assessments conducted by food control officials, from their own environmental assessments, or through some combination of the two and report it to CDC. Although the contributing factors may seem to require little explanation, they are a sophisticated listing of factors based on known microbiologic characteristics of and symptoms produced by specific pathogens, toxins, or chemicals and historical associations between known causative agents and specific food vehicles.

Whether based on etiology identification, vehicle identification, or both, factors contributing to an outbreak cannot be identified through a food-safety program inspection of a food-service or food-production establishment as conducted day to day by food control authorities. The process of identifying contributing factors associated with an outbreak must be driven first by describing what and how events probably unfolded, rather than by identifying regulation violations. Failures to implement regulatory requirements will come to light over the course of this process. Unfortunately, many food control

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authorities fail to adjust their day-to-day regulatory inspection process to adequately conduct an environmental assessment during investigation of an outbreak of foodborne; therefore, contributing factors often are not adequately assessed and reported.

CDC's Environmental Health Specialists Network (EHS-Net) was established in 2000 to better provide information about environmental causes of foodborne disease. Participants include environmental health specialists and epidemiologists from nine states and the FDA, USDA, and CDC. Improving environmental assessments in foodborne outbreak investigations and reporting contributing factor and antecedent data to CDC is one of EHS-Net's primary research activities. CDC is exploring development of a surveillance system for contributing factors and antecedents from foodborne outbreak investigations. This system would link to the existing surveillance system for foodborne outbreaks, CDC's electronic Foodborne Outbreak Reporting System (eFORS) (see below) and provide the level of detail from environmental assessments conducted during foodborne outbreak investigations that food control authorities need.

2.2.2.6. Foodborne Diseases Active Surveillance System (FoodNet)

FoodNet, a sentinel surveillance system, is an enhanced foodborne disease surveillance system led and largely funded by CDC, with 10 participating sites covering a population of about 45 million. FoodNet concentrates on a subset of enteric diseases that are documented by laboratory testing. In contrast to routine notifiable disease surveillance, it is an "active surveillance system" in that FoodNet site investigators regularly contact area laboratories to enhance reporting of foodborne disease.

FoodNet sites also conduct surveys of the frequency of enteric illness and food consumption in the population[47] and practices in clinical laboratories.[48] FoodNet reports provide valuable insight into the national incidence of, and trends in, foodborne and diarrheal diseases[25,49–56] and has identified previously unrecognized sources of foodborne infection such as chicken as a risk factor for infection with *Salmonella* Enteritidis,[55,57] hummus and melon as risk factors for infection with *Listeria monocytogenes*,[58] and riding in a shopping cart next to raw meat or poultry as a risk factor for infection with *Salmonella* and *Campylobacter* in infants.[59,60] FoodNet also provides information to evaluate new strategies for conducting epidemiologic investigations, including investigations of outbreaks.

2.2.2.7. National Molecular Subtyping Network for Foodborne Disease Surveillance (PulseNet)

PulseNet is a national network of local, state or territorial, and federal laboratories coordinated by CDC that allows comparison of subtypes of pathogens isolated from humans, animals, and foods across local, state, and national jurisdictions. The name derives from pulsed-field gel electrophoresis (PFGE), a laboratory method used to determine the molecular fingerprints of bacteria. This test, developed and refined during the 1980s, revolutionized the investigation of foodborne disease outbreaks by identifying unique strains within a bacterial species. For example, each of the many strains of *Salmonella* has a unique PFGE pattern or fingerprint. Because foodborne outbreaks usually are caused by a single bacterial strain, investigators can identify illnesses in the subgroup of persons infected with the same strain of *Salmonella* as a cluster of possibly related cases, to be considered separately from persons infected with other strains of *Salmonella*, thus enabling investigators to focus on the correct group of individuals and more quickly identify the source of an outbreak. PFGE also can be used to characterize bacterial strains in food or the environment to determine whether those strains match the pattern responsible for an outbreak.[14,29,50,61–63]

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PulseNet has standardized the PFGE methods used by participating laboratories to distinguish strains of STEC, *Salmonella*, *Shigella*, *Listeria*, and *Campylobacter.* In addition, PulseNet maintains an electronic database of PFGE patterns that enables investigators from participating sites to upload their pattern and compare it with patterns of bacterial strains circulating nationally. This capability has vastly improved investigators' ability to rapidly detect even relatively small outbreaks in multiple sites across the country.[43]

2.2.2.8. National Antimicrobial Resistance Monitoring System–Enteric Bacteria (NARMS)

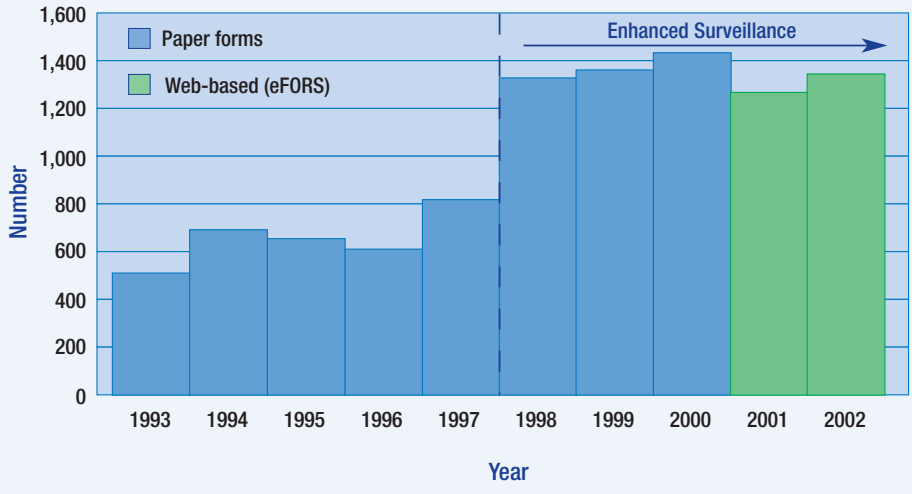
NARMS was developed to monitor antibiotic resistance patterns in selected enteric bacteria found in people, animals, and meat products. Bacterial isolates are forwarded to reference laboratories at CDC, USDA, or FDA and are tested against a panel of antimicrobial drugs important in human and animal medicine. Data collected by NARMS enables investigators to better understand the interaction between the use of antibiotics for livestock and the patterns of antibiotic resistance in animals and humans who ingest animal food products.[15,49,50,64–68]

2.2.2.9. Foodborne Outbreak Reporting System

The Foodborne Outbreak Reporting System was initiated by CDC in the 1960s to collect voluntary reports from public health agencies summarizing the results of foodborne outbreak investigations. In 1973, the database for the system was computerized. In 1998, CDC increased communication with state, local, and territorial health departments about foodborne outbreaks and formalized procedures to finalize reports from each state each year. These changes most likely led to a substantial increase in the proportion of outbreaks reported, resulting in a discontinuity in trends during 1997–1998[39] (Figure 2.2).

In 1999, the reporting form was expanded to collect information about a broader range of food items, places, and contributing factors and, in 2001, reporting became Web-based in a system called the electronic Foodborne Outbreak Reporting System (eFORS). Beginning in 2009, eFORS will include modules for reporting waterborne outbreaks and enteric disease outbreaks caused by person-to-person contact and by direct contact with animals. The expanded system will be called the National Outbreak Reporting System.

Figure 2.2 Number of reported foodborne disease outbreaks, United States, 1993-2002 *(from Lynch 2006)*



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2.2.3. Quality and Usefulness of Surveillance Data

Shortcomings of surveillance information hinder the use and usefulness of the data. These limitations must be considered when viewing these data.

2.2.3.1. Completeness of detection and reporting of foodborne diseases

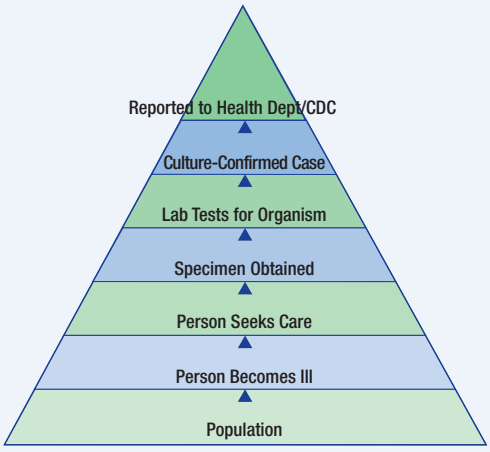
Although the national capacity for detection and surveillance of potentially foodborne disease has improved considerably in the past 20 years,[51] for a number of reasons, surveillance statistics reflect only a fraction of cases: (a) some people do not seek medical attention for vomiting or diarrhea of limited duration or do not seek care because they lack health-care coverage, (b) health-care providers do not always obtain diagnostic tests for illnesses likely to be self-limited, (c) not all types of infections can be diagnosed with routine laboratory testing, and (d) laboratories and health-care providers may fail to report the illness to their local public health agency.[6,52,69,70]

For example, according to a population-based survey undertaken in 1996–97 in selected states, only 12% of persons with a diarrheal illness (14.6% of those with bloody diarrhea and 11.6% of those with non-bloody diarrhea) sought medical care. Among those who sought medical care, 21% were asked by their physician to provide a stool specimen for culture, and 89% of these complied with this request. [71]

As a result, cases of foodborne illness are lost at each step in the diagnosis and reporting process and thus are not included in national statistics. Some investigators portray this disparity between the occurrence of foodborne illness and the reporting of cases to the health department by using a burden of illness pyramid[44] (Figure 2.3).

Key to the success of surveillance is confirmation of the agent causing a foodborne disease. However, because most diarrheal illnesses are self-limited and laboratory test results often are not used to guide the initial course of treatment for a patient, health-care providers often do not request stool cultures. Physicians are more likely to request a culture for persons with acquired immunodeficiency syndrome, history of travel to a developing country, bloody stools, diarrhea of >3 days' duration, or fever or who require intravenous rehydration.[70]

Figure 2.3 Burden of illness pyramid reflecting the proportion of foodborne illnesses that make it through each step of the diagnosis and reporting process. (*from Angulo, et al., 1998*)



Lack of laboratory confirmation can hinder appropriate management and treatment of the individual patient with acute diarrhea and inhibit surveillance and other public health actions.[70,72] For the individual patient, identification of the specific agent can

- Help in the appropriate selection of antimicrobial therapy, shortening the patient's illness and reducing morbidity.
- Support the decision not to treat, if the patient would not benefit from antimicrobial therapy or would even be harmed by the use of antibiotics (e.g., prolongation of the carrier state with salmonellosis).

2.2. Trends in Surveillance

- Guide the use of invasive diagnostic techniques (e.g., avoid colonoscopy if an infectious etiology is identified).

From a public health perspective, an pathogen-specific diagnosis and prompt notification of public health authorities can[70,72]

- Enhance actions to prevent the spread of infection to others through patient education and exclusion of ill persons from food preparation or care of individuals at increased risk for poor outcomes from foodborne diseases.
- Allow tracking of trends in foodborne diseases through surveillance.
- Enhance the detection and control of outbreaks, particularly outbreaks caused by low-level contamination of food or exposures over a wide geographic area.
- Provide antimicrobial sensitivity data for the community.
- Prevent the emergence of drug resistance through the more judicious use of antibiotics and avoidance of broad-spectrum antibiotics.

Although the costs associated with laboratory testing are an important consideration, diagnostic stool testing provides information for both individual patient care and public health purposes. Health-care providers need improved parameters for stool testing.

2.2.3.2. Quality and usefulness of information collected

Unfortunately, public health surveillance and outbreak investigation programs have evolved independently from food-safety programs, and current human health statistics address the questions of communicable disease control authorities better than the questions of food control authorities.[73]

Many factors influence decisions about which surveillance data to collect and how to collect them, both of which affect the quality and usefulness of the data. The contributing factor category of data reported to CDC through the Foodborne Outbreak Reporting System is a good example of how these decisions are made and how surveillance systems evolve over time to balance user needs, identification of data to include, willingness of officials to report, and accuracy of officials' reports.

Before October 1999, contributing factor data were reported and summarized into five broad categories: Improper storage or holding temperature; Inadequate cooking; contaminated equipment or working surfaces; food acquisition from unsafe source; poor personal hygiene of food handler; and other. Food control authorities used the information, but the broad categories were not detailed enough and did not fully meet their needs. Articles by Bryan et al., Guzewich et al., and Todd et al.[41,40,74,75] framed information gleaned from foodborne disease surveillance systems in terms of the key end user—those charged with foodborne disease prevention. One article was devoted to data on vehicles and contributory factors and described the value and limitations of these data, as well as how they can be summarized and presented.[75] The article included a recommended list of specific contributing factors to be reported. To meet the needs of data users, CDC incorporated the contributing factors suggested by Bryan into the new foodborne outbreak reporting form in October 1999. Another factor, glove-handed contact by handler/worker/preparer, was added.

Although CDC adjusted the foodborne outbreak reporting form to address the needs of system users with regard to contributing factor data, the change is not without controversy among those who report and use this information. Some question whether food control authorities have the expertise to accurately identify the most likely contributing factors from among the now complicated list of factors. Some believe the contributing

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factor list is too complex for a surveillance system and should be removed entirely or returned to the pre-1999 abbreviated list. Still others believe without a context for the factors reported—even the pre-1999 abbreviated list of factors has limited, if any, value. As new information becomes available about the value of specific data elements, the contributing factor surveillance system, like all surveillance systems, will continue to evolve.

2.3. Etiologic Agents Associated with Foodborne Diseases

2.3.1. Overview

Foodborne illnesses have myriad causes including microorganisms (e.g., bacteria, viruses, parasites, and marine algae) and their toxins, mushroom toxins, fish toxins, heavy metals, pesticides, and other chemical contaminants (Table 2.1). These agents cause human disease through a number of mechanisms and are often categorized into those caused by toxins present in food before it is ingested (preformed toxins) and those caused by multiplication of the pathogen in the host and damage resulting from toxins produced within the host (enterotoxins) or adherence to or invasion of host cells (infection).

Details about the most common foodborne disease causing agents, including signs and symptoms, incubation periods, modes of transmission, common food vehicles, and control measures, can be found in:

- American Public Health Association. *Control of Communicable Diseases Manual*. Washington, DC: APHA;2008.
- CDC. CDC A–Z Index. Available at http://www.cdc.gov/az/a.html
- U.S. Food and Drug Administration. The Bad Bug Book. Available at http://www.foodsafety.gov/~mow/intro.html
- International Association of Milk, Food and Environmental Sanitarians. *Procedures to Investigate Foodborne Illness*. 5th edition. Des Moines, Iowa: IAMFES (reprinted 2004).
- CDC. Diagnosis and management of foodborne illnesses: A primer for physicians and other health-care professionals. Morb Mortal Wkly Rep 2004:53(RR-4). Available at http://www.ama-assn.org/ama/pub/category/3629.html

Table 2.1. Examples of agents that commonly cause foodborne illness, by agent type and mechanism of action

TYPE OF AGENT	GENERAL MECHANISM OF ACTION	EXAMPLE
Bacteria	Preformed toxin	*Bacillus cereus* *Clostridium botulinum* *Staphylococcus aureus*
	Infection and production of enterotoxins	*Bacillus cereus* *Clostridium botulinum* *Clostridium perfringens* *Enterohemorrhagic Escherichia coli* Enterotoxigenic *E. coli (STEC)* *Vibrio cholerae*

2.3. Etiologic Agents Associated with Foodborne Diseases

Table 2.1. Examples of agents that commonly cause foodborne illness, by agent type and mechanism of action *Continued*

TYPE OF AGENT	GENERAL MECHANISM OF ACTION	EXAMPLE
	Infection	*Bacillus anthracis* *Brucella spp. (B. melitensis, B. abortus, B. suis)* *Campylobacter jejuni* Enteroinvasive *E. coli* *Listeria monocytogenes* *Plesiomonas shigelloides* *Salmonella spp.* *Shigella spp.* *Streptococcus pyogenes* *Vibrio parahaemolyticus* *Vibrio vulnificus* *Yersinia enterocolytica and Y. pseudotuberculosis*
Virus	Infection	Hepatitis A Norovirus (and other caliciviruses) Rotavirus Astroviruses, adenoviruses, parvoviruses
Parasite	Infection	*Cryptosporidium* *Cyclospora cayetanensis* *Diphyllobothrium latum* *Entamoeba histolytica* *Giardia lamblia* *Taenia saginata* *Taenia solium* *Toxoplasma gondii* *Trichinella spiralis*
Marine algae toxins	Preformed toxin	Brevetoxin (neurotoxic shellfish poisoning) Ciguatoxin (ciguatera) Domoic acid (amnestic shellfish poisoning) Saxitoxin (paralytic shellfish poisoning)
Fungal toxins	Preformed toxin	Aflatoxin Mushroom toxins (amanitin, ibotenic acid, museinol, muscarine, and psilocybin)
Fish toxins	Preformed toxin	Gempylotoxin (escolar) Scombrotoxin (histamine fish poisoning) Tetrodotoxin (puffer fish)
Chemicals		Antimony Arsenic Cadmium Copper Fluoride Lead Mercury Nitrites Pesticides (e.g., organophosphates, carbamate) Thallium Tin Zinc

2.3. Etiologic Agents Associated with Foodborne Diseases

2.3.2. Patterns in Etiologic Agents Associated with Foodborne Disease Outbreaks

Patterns in the agents causing foodborne disease outbreaks have been identified through the voluntary reporting of outbreaks to CDC through eFORS. In the most recent CDC surveillance summary of U.S. foodborne disease outbreaks (covering 1998–2002), bacteria (including their toxins) accounted for 55% of reported outbreaks that had an identified cause (Figure 2.4). The most common bacteria were Salmonella, E. *coli*, *Clostridium perfringens, Staphylococcus aureus, Shigella, Campylobacter, Bacillus cereus*, and *Vibrio* species (Figure 2.5). *Listeria monocytogenes* and *Clostridium botulinum* also were reported but were less common, bacterial causes of foodborne disease.[39]

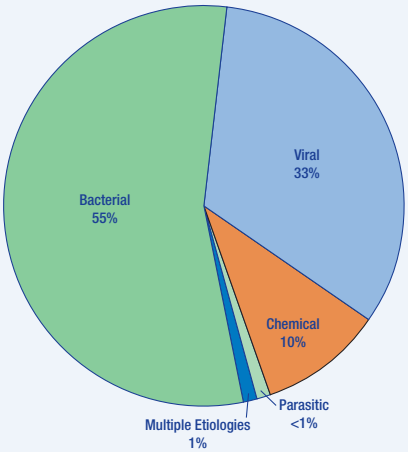
During the same surveillance period, viruses constituted 33% of identified causes of foodborne disease outbreaks, increasing from 16% in 1998 to 42% in 2002. (In 2006, 54% of outbreaks with a known etiology resulted from viruses.[76]) The increase in proportion of outbreaks from viral pathogens probably reflects the increased availability of methods to diagnose viral agents in recent years.[39,77] During 1998–2002, noroviruses were the most common viral cause of foodborne outbreaks (93%), followed by hepatitis A (7%). Astroviruses and rotaviruses played a minor role in foodborne disease outbreaks.

Parasites accounted for 0.3% of outbreaks with identified etiologies. *Cryptosporidium*, *Cyclospora*, and *Trichinella* each constituted 0.1% of reports.[39, 78]

Marine algae and fish toxins, mushroom toxins, and other chemicals accounted for 10% of outbreaks with an identified cause. The most commonly reported chemical causes were scombrotoxin (54%) and ciguatoxin (38%). Only 0.02% of outbreaks with a known etiology were caused by heavy metals and other chemicals.[39]

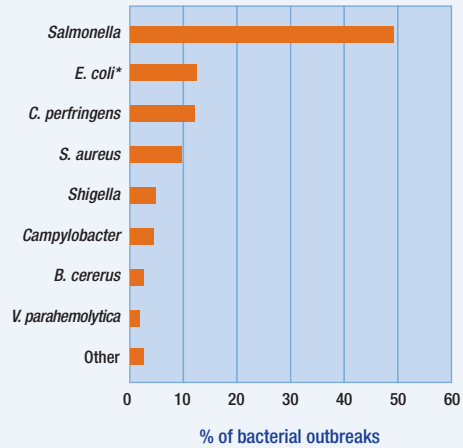
For a large proportion (67%) of outbreaks reported during 1998–2002, no etiologic agent was identified. Reasons include inadequate collection of stool specimens, delay in the

Figure 2.4 Foodborne disease outbreaks by confirmed etiology, United States, 1998–-2002* *(from Lynch, 2006)*



*Includes only outbreaks for which an etiology was determined. For 67% of outbreaks, no etiologic agent was identified.

Figure 2.5 Distribution of bacterial foodborne disease outbreaks by etiologic agent, United States, 1998–2002 *(from Lynch, 2006)*



*Most foodborne outbreaks caused by E. coli were STEC.

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collection of specimens, and inappropriate testing of specimens. [79, 80] Because laboratory methods for confirming viral disease are less available than tests for bacteria, many outbreaks of foodborne illness from viruses probably fall into the "unknown etiologic agent" category. [79]

In addition, not all outbreaks are detected, investigated, and reported through eFORS. Outbreaks that are most likely to be brought to the attention of public health authorities include those that can cause serious illness, hospitalization, or death.[39] Furthermore, outbreaks of diseases characterized by a short incubation period, such as those caused by a chemical agent or staphylococcal enterotoxin, are more likely to be recognized than diseases with longer incubation periods, such as hepatitis A.[79] Therefore, the relative frequency of various causes of foodborne disease outbreaks based on eFORS or similar data should be interpreted with caution.

2.3.3. Determining the Etiologic Agent in an Outbreak

2.3.3.1. Laboratory confirmation of etiologic agent

Laboratory testing of clinical specimens from cases is critical in determining the etiology of a suspected foodborne disease outbreak and implementation of appropriate control measures. For most foodborne diseases, stool is the specimen of choice; however, blood, vomitus, or other tissue or body fluid occasionally are indicated. Specimens are collected as soon as possible after onset of illness from at least 10 individuals who manifest illness typical of the outbreak and who have not undergone antibiotic treatment. Methods for collection, storage, and transport vary depending on the suspected agent (e.g., bacteria, virus, parasite).[39,81,82]

Isolation of the causative agent from a suspected food item can provide some of the most convincing evidence of the source of a foodborne outbreak. Food testing, however, has inherent limitations. Specific contaminants or foods might require special collection and testing techniques, and demonstration of an agent in food is not always possible. Furthermore, results of testing are often difficult to interpret. Because contaminants in food change with time, samples collected during an investigation might not be representative of those ingested when the outbreak occurred. Subsequent handling or processing of food might result in the death of microorganisms, multiplication of microorganisms originally present at low levels, or introduction of new contaminants. If contamination of the food is not uniform, the sample collected might miss the contaminated portion. Finally, because food is usually not sterile, microorganisms can be isolated from samples but not be responsible for the illness under investigation. As a result, food testing should not be undertaken routinely but should be based on meaningful associations.

2.3.3.2. Other clues to the etiologic agent

While awaiting laboratory confirmation, the following information can help shorten the list of likely agents causing an outbreak:

- Predominant signs and symptoms among ill individuals,
- Incubation period, if known,
- Duration of illness, and
- Suspected food, if known.

An example of how predominant signs and symptoms and incubation period can be used to help determine the etiologic agent in an outbreak is provided in Appendix 2.

Note: Determining the incubation period for an illness (i.e., the time from exposure to the etiologic agent to development of symptoms) is influenced by whether the calculation is based on the onset of prodromal symptoms that occur early in the course of an illness (e.g., general feeling of being unwell) or

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specific signs of enteric disease (e.g., vomiting or diarrhea) that may occur a bit later during the illness. Because the onset of the latter typically is more clearly recalled by cases, some investigators consistently use the onset of these "harder" symptoms to calculate the incubation period.

2.3.3.2.1. Signs, symptoms, incubation period, and duration of illness

In identifying the likely etiologic agent in an outbreak on the basis of signs, symptoms, incubation period, and duration of illness, it is often helpful to first categorize a suspected foodborne illness as resulting from a preformed toxin or infection.

Illnesses from preformed toxins are caused by ingestion of food already contaminated by toxins. Sources of preformed toxin include certain bacteria, poisonous chemicals; heavy metals; and toxins found naturally in animals, plants, or fungi. Preformed toxins most often result from bacteria that release toxins into food during growth in the food, such as *Staphylococcus aureus*, *Bacillus cereus*, and *Clostridium botulinum*. The preformed toxin is ingested; thus live bacteria do not need to be consumed to cause illness.

Illness from a preformed toxin manifests more rapidly than does illness from an infection because time for growth and invasion of the intestinal lining is not required. The incubation period for illnesses from a preformed toxin is often minutes or hours.

Signs and symptoms depend on the toxin ingested but commonly include vomiting. Other symptoms can range from nausea and diarrhea to interference with sensory and motor functions, such as double vision, weakness, respiratory failure, numbness, tingling of the face, and disorientation. Fever is rarely present.

Infections result from growth of a microorganism in the body. Illness results from two mechanisms:

- Viruses, bacteria, or parasites invade the intestinal mucosa and/or other tissues, multiply, and directly damage surrounding tissues.
- Bacteria and certain viruses invade and multiply in the intestinal tract and then release toxins that damage surrounding tissues or interfere with normal organ or tissue function (enterotoxins).

The necessary growth of the microorganism, damage of tissues, and production and release of toxins takes time. Thus, the incubation periods for infections are relatively long, often days, compared with minutes or hours as with preformed toxins. The incubation periods for viruses (excluding hepatitis A) tend to be shorter than for bacteria which tend to be shorter than the incubation periods for most parasites.

Symptoms of infection usually include diarrhea, nausea, vomiting, and abdominal cramps. Fever and an elevated white blood cell count can also occur. If an infectious agent spreads from the gut to the bloodstream, other organs (e.g., liver, spleen, gallbladder, bones, and meninges) can be affected, resulting in an illness of longer duration, increased severity, and signs and symptoms associated with the particular organ affected.

2.3.3.2.2. Suspected food

Certain microorganisms are associated with certain food items because the food derives from an animal reservoir of the microorganism or the food provides conditions necessary for the survival and growth of the organism. As a result, the food item suspected in an outbreak, if known, occasionally can provide insight into the etiologic agent (Table 2.2). However, most foods can be associated with a variety of etiologic agents, and new vehicles for transmission emerge each year. Therefore, care must be taken in inferring the etiologic agent based on the suspected food item.

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Table 2.2. Examples of food items and commonly associated microorganisms *(from Chamberlain 2008)*[83]

ITEM	COMMONLY ASSOCIATED MICROORGANISM
Raw seafood	*Vibrio* spp., Hepatitis A, Noroviruses
Raw eggs	*Salmonella* (particurlarly serotype Enteritidis)
Undercooked meat or poultry	*Salmonella* and Campylobacter spp., Shiga toxin-producing *Escherichia coli* (STEC), *Clostridium perfringens*
Unpasteurized milk or juice	*Salmonella*, *Campylobacter*, and *Yersinia* spp., STEC
Unpasteurized soft cheeses	*Salmonella*, *Campylobacter*, *Yersinia*, and *Listeria* spp., STEC
Home-made canned goods	*Clostridium botulinum*
Raw hot dogs, deli meat	*Listeria* spp.

2.3.4. Mode of Transmission

Many agents responsible for foodborne illness also can be transmitted by other routes, such as water, person to person, and animal to person transmission. For example, it is estimated that only 20% of shigellosis cases, 10% of cryptosporidiosis cases, and 40% of norovirus infections result from foodborne transmission.[38] Consequently, early in the investigation of a potential foodborne disease outbreak, investigators should consider all potential sources of transmission and collect information from ill persons about sources of water, exposure to other ill persons and child care settings, contact with animals, and food and other exposures.

Although in depth case interviews and epidemiologic, environmental health, and laboratory studies are necessary to confirm suspicions about the mode of transmission in an outbreak, characteristics among cases or timing of illness onset might provide clues that suggest one mode of transmission over others and allow investigators to focus on investigating that source.

2.3.4.1. Transmission by a food

Illness among individuals with the following characteristics might suggest transmission of an agent by food:

- Individuals who have shared a common meal or food, and onset of illness is consistent with when the shared meal or food was consumed;
- Individuals with distinctive demographic characteristics (i.e., age group, sex, and ethnicity) and possibly unique food preferences; and
- Individuals with a geographic distribution similar to the geographic distribution of food products.

2.3.4.2. Transmission by water

The following clues might be suggestive of transmission of an agent by public drinking water:

- Widespread illness affecting both sexes and all age groups;
- Geographic distribution of cases consistent with public water distribution but not food distribution patterns (e.g., limited to individuals residing within city limits);

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- Absence of cases among breast-fed babies or individuals who drink only bottled water or beverages from boiled water;
- Dose-response with increasing attack rates among persons drinking more water;
- Concurrent complaints about water quality in the affected community; and
- Involvement of multiple pathogens.

A clustering of cases adjacent to cattle ranches or farms that are served by well water might suggest transmission by contaminated well water. A clustering of cases among children, particularly those who have shared a common recreational water exposure such as a water park, community pool, or lake might suggest transmission by recreational water.

2.3.4.3. Transmission from person to person

Person-to-person transmission should be suspected when:

- Cases cluster in social units, such as families, schools (and classes within schools), dorms or dorm rooms, and sororities/fraternities and
- Cases occur in waves separated by approximately one incubation period of the etiologic agent.

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