

## Factors Involved in the Emergence and Persistence of Food-Borne Diseases†

### ABSTRACT

In recent years, a number of bacteria, viruses, and parasites have emerged as food-borne pathogens and resulted in numerous food-borne disease outbreaks. These outbreaks have had a major impact in terms of loss of human lives and economic costs. Genetic changes in microorganisms resulting in increased virulence, changes in social attitudes and eating habits, changes in food production and distribution systems, an increase in the number of immunocompromised individuals, and improved pathogen-detection methods are some of the factors that have contributed to the emergence/recognition and persistence of food-borne pathogens. The causes leading to the emergence of new food-borne pathogens or the reemergence of pathogens involve the interaction of several factors. This review discusses in detail factors involved in the emergence/recognition and persistence of several bacterial, parasitic, viral, and virus-like agents associated with food-borne diseases of public-health significance.

Key words: Emergence, food-borne pathogens, food-borne diseases

During the past 20 years, a number of microorganisms have emerged as food-borne pathogens. An emerging pathogen will be defined as one that is linked to a "new" disease, i.e., a disease that is perceived to be a novel, immediate, and serious threat to health (8). The reemergence of an "old" quiescent pathogen or disease can also occur. Factors involved in the emergence/recognition and maintenance of food-borne pathogens include changes in perception and recognition of what constitutes a food-borne pathogen or disease, changes in population (increase in the number of elderly, in the number of individuals with immunosuppressive conditions, and in the movement of individuals), changes in eating habits and in the ways foods are produced, processed, handled, and prepared, changes in microorganisms which lead to increased virulence, and changes in people's behavior (47, 51). The ability to isolate and identify "new" pathogens due to the development of improved, more sensitive detection methods has also played

an important role in recognizing the origin of food-borne disease outbreaks formerly classified as "cause unknown." In general, the emergence and persistence of food-borne diseases is complex and depends on the mutual interaction of a number of factors.

Some food-borne pathogens and the factors involved in their emergence/recognition and persistence as pathogens are listed in Table 1. These factors are discussed in more detail below.

### Bacterial infections

*Diseases related to the Aeromonas hydrophila group.* The *A. hydrophila* group, i.e., the motile aeromonads, include *A. hydrophila*, *A. caviae*, and *A. sobria*, which are characterized by growth at 37°C and motility (123). *Aeromonas* species were recognized as disease agents of cold-blooded animals long before they were suspected of being human pathogens (123). In recent years, there has been an increased awareness that the *A. hydrophila* group can cause human disease, particularly as opportunistic pathogens in immunocompromised individuals (4, 123, 139). The development of improved media for the isolation and detection of *Aeromonas* in foods (123, 124), in feces (3, 4), and in water (78) has aided in the recognition that certain members of the genus are human pathogens.

The members of the *A. hydrophila* group appear to be ubiquitous in food and water. They are present in foods of animal origin (red meats, poultry, fish, seafood, raw milk), and in produce and vegetables (1, 37, 99, 124) as well as in water from diverse sources, including activated sludge, estuaries, fresh or stagnant waters, and chlorinated or unchlorinated drinking waters (1, 4, 79). The motile aeromonads grow at refrigeration temperatures (17, 101); therefore, any food product containing a small number of *Aeromonas* may contain a large population after a few days of cold storage. Microorganisms that can grow and elaborate enterotoxins at refrigeration temperatures in foods could conceivably cause food-borne diarrhea and indeed, Buchanan and Palumbo (33) have suggested that members of the *A. hydrophila* group are potential food-poisoning agents.

The members of the *A. hydrophila* group produce a

Organism/Disease	Factors Involved in Emergence or Recognition	Factors Involved in Maintenance
<i>Aeromonas hydrophila</i> group/ various diseases	Increased awareness that <i>Aeromonas</i> spp. cause human illness Improvements in media and methods for isolation and detection of <i>Aeromonas</i> from food, water, and feces	Susceptibility of immunocompromised individuals to infection Ubiquitousness of <i>Aeromonas</i> in food and water Ability to grow and produce toxins and virulence factors at refrigeration temperatures
<i>Brucella suis</i> /brucellosis	Reemergence of brucellosis due to contact with feral pigs	Increased hunting of feral boars for export Contact with infected carcasses by hunters and abattoir workers Aerosol infection of workers in abattoirs Reluctance of abattoir workers and hunters to wear protective clothing when handling boar carcasses
<i>Campylobacter jejuni</i> / campylobacteriosis	Increased awareness of <i>C. jejuni</i> as a food-borne pathogen Development of selective media for stool and food samples	Drinking raw milk or untreated water Increased consumption of poultry products Contact with farm animals and pets Contamination of food by food handlers Concentration of large numbers of chickens in brooder houses and pigs and cattle in feedlots
<i>Clostridium botulinum</i> / infant botulism	Recognized as a separate disease	Feeding honey or corn syrup to children < 6 months of age Excessive iron due to iron-fortified infant formulas Other unknown factors
<i>Escherichia coli</i> O157:H7 /hemorrhagic colitis, hemolytic uremic	Increased awareness due to food-borne outbreaks Improved epidemiologic surveillance and reporting Emergence of a new <i>E. coli</i> strain with increased virulence	Drinking raw milk or unchlorinated water Eating raw or undercooked beef Increased eating in restaurants (including fast-food restaurants) Increase in nursing homes and child-care centers Susceptibility of elderly and young to infection Starvation of animals before slaughter Increase in industrialization of animal husbandry, slaughter, food-processing and food-distribution practices (concentration of activities to fewer and larger companies) Person-to-person transmission
<i>Listeria monocytogenes</i> / listeriosis	Increased awareness due to food-borne outbreaks Improved epidemiological surveillance and reporting	Use of refrigeration during food harvesting, transport or storage (allowing growth of <i>L. monocytogenes</i> ) Susceptibility of immunocompromised population to infection Eating raw or inadequately cooked foods Use of nonpasteurized milk in cheese preparation
<i>Salmonella enteritidis</i> / salmonellosis	Increased awareness Emergence of new strains with increased invasiveness for chickens	Failure to cook eggs thoroughly or use of raw eggs in food preparation Susceptibility of immunocompromised population to infection Induced molting of egg-laying flocks Increased industrialization of chicken breeding, raising, egg production and distribution (Concentration of activities to fewer and larger companies) Increased eating in restaurants Improper storage temperatures for shell eggs and raw egg products
<i>Vibrio cholerae</i> / epidemic cholera	Recognized as an outbreak in Lima, Peru Lack of chlorination in Lima's water supply	Eating raw fish and/or seafood ("ceviche") Poor maintenance of water supply and sewage

TABLE 1. *Cont.*

Organism/Disease	Factors Involved in Emergence or Recognition	Factors Involved in Maintenance
<i>Vibrio vulnificus</i> / gastroenteritis, wound infection, or septicemia	Increased awareness Increased ability to differentiate between very similar halophilic vibrios	disposal system; lack of chlorination and filtration of water supplies Lack of immunity in population Genetics of population (high level of O type blood) Easy travel to and from outbreak areas Contamination of food by food handlers
<i>Yersinia enterocolitica</i> / yersiniosis	First recognized as a food-borne pathogen in large milk-borne outbreak	Drinking raw milk or untreated water Contamination of food by food handlers Cross-contamination of foods by swine or swine products or by individuals handling swine products Increased use of refrigeration during food harvesting, preparation, transport or storage (allowing growth of <i>Y. enterocolitica</i> )
Norwalk and Norwalk-like virus/epidemic viral gastroenteritis	Virus particles demonstrated by immunoelectron microscopy in stool filtrates utilizing serum from symptomatic patient with nonbacterial gastroenteritis	Eating raw or undercooked seafood Drinking contaminated water or using ice prepared from contaminated water Contamination of food by food handlers Swimming in contaminated waters Person-to-person transmission
Rotavirus/sporadic viral gastroenteritis	Virus visualized by electron microscopy of duodenal biopsies and stool specimens from cases of nonbacterial gastroenteritis	Eating raw seafood Drinking contaminated water Increased use of child-care centers and nursing homes Person-to-person transmission (particularly among young children) Increase in foreign travel Contamination of food by food handlers
<i>Cryptosporidium</i> / cryptosporidiosis	Increased awareness of <i>Cryptosporidium</i> due to opportunistic infections in AIDS patients	Susceptibility of immunocompromised individuals to infection Increased use of child-care centers and nursing homes Contamination of surface water and water reservoirs by runoff waters from dairies and animal raising facilities or by runoff waters from grazing lands and farm lands fertilized with manure Contact with young animals and pets Drinking raw milk or untreated water Ability of organism to survive in chlorinated water systems Contamination of food by food handlers Person-to-person transmission
<i>Giardia lamblia</i> / giardiasis	Increased awareness of <i>Giardia</i> due to outbreaks of giardiasis in United States travelers returning from Soviet Union	Increase in international travel Susceptibility of immunocompromised individuals to infection Increased use of child-care centers and nursing homes

TABLE 1. *Cont.*

Organism/Disease	Factors Involved in Emergence or Recognition	Factors Involved in Maintenance
<i>Toxoplasma gondii</i> toxoplasmosis	Increased awareness of <i>T. gondii</i> due to opportunistic infections in AIDS patients	Ability of organism to survive in chlorinated water systems Contamination of water supplies by feces from wild animals Contamination of food by food handlers Person-to-person transmission  Presence of cats on farms and livestock-raising facilities Susceptibility of immunocompromised individuals to infection and recrudescence Increase in organ transplants Eating of cat feces contaminated feeds by animals raised for food Eating of raw or undercooked meats
BSE prion/bovine spongiform encephalopathy	Recognized as cause of outbreaks of neurological disease in cattle	Use of ruminant offal and slaughterhouse waste in cattle feeds

number of products that may be considered as candidates for virulence determinants such as hemolysins, hemagglutinins, cell-invasive and -attachment factors, and cytotoxic and cytotoxic enterotoxins, some of which cross-react with cholera toxin (4, 36, 92). *A. hydrophila* produced cytotoxin, hemolysin, and enterotoxin at 4, 10 and 22°C; however, *A. sobria* produced these factors at 10 and 22°C, but not at 4°C (101).

The motile aeromonads have been associated with extraintestinal diseases such as wound infections (from contact with contaminated water or contaminated shellfish), septicemia, meningitis, and disseminated disease (4, 123). Most cases of extraintestinal infections involve immunosuppressed individuals and AIDS patients (4, 123, 139). Infections with *Aeromonas* species can lead to gastroenteritis, particularly in pediatric populations (4, 115, 117, 123). However, both immunocompetent and immunocompromised adults may also suffer from *Aeromonas*-induced gastroenteritis (4, 123, 139).

No confirmed food-borne disease outbreaks involving *Aeromonas* have been documented (156); however, Kirov (98) does list some incidents of food-borne disease in which *Aeromonas* species were suspected. Challenge studies in human volunteers and primates indicated that *A. hydrophila* does not act as a diarrheic pathogen (117). Nonetheless, Kirov (98) suggests that enterotoxigenic motile aeromonads present in refrigerated foods may pose a hazard to small children, the elderly, and other immunocompromised individuals.

**Brucellosis.** In Australia, brucellosis due to *Brucella abortus* has virtually disappeared (73, 137); however, there has been a reemergence of brucellosis due to infections with *B. suis*. Brucellosis due to *B. suis* is an occupational disease of hunters and abattoir workers who handle feral boar carcasses designated for export. The eradication of this disease in Australia is hindered by several factors. Exportation of feral boar meat is economically important. There is difficulty in eliminating *B. suis* infection in wild pigs, and in ensuring that hunters and workers in licensed game abattoirs protect themselves while handling wild pig carcasses (73, 137).

**Campylobacteriosis.** *Campylobacter jejuni* was shown to be a cause of diarrhea by identification of the organism in filtrates of fecal suspensions from diarrheic children (35). Further refinements in selective media and isolation techniques led to increased awareness that *Campylobacter* is a common cause of food-borne gastroenteritis (25, 150). In the United States, *C. jejuni* is the most frequent cause of bacterial gastroenteritis (164). Most of the outbreaks of *Campylobacter* enteritis have been associated with drinking raw milk or unchlorinated water (157). Poultry is linked to few outbreaks; however, the majority of *Campylobacter* cases are sporadic and are caused by eating or handling poultry (164). There has been an increase in poultry consumption by a more health-conscious population and this is a contributory factor to an increase in campylobacteriosis (81). *Campylobacter* is an intestinal-tract commensal in warm-blooded animals; thus, farm animals (and their products) and pets can be sources of infection (157). The environment can be contaminated by farm waste and the organisms can be spread from carcass to carcass during animal slaughter and processing (67). Concentrating and crowding of food animals in brooding houses and feedlots lead to the spread of *Campylobacter* among animals and to their caretakers. The increase in poultry consumption, the intimate association of *Campylobacter* with food animals and pets, and the drinking of raw milk ensure that *Campylobacter* gastroenteritis will continue to be a problem.

**Infant botulism.** Infant botulism is an example of a new and distinct clinical disease caused by an old pathogen, *Clostridium botulinum* (112, 127). In adult botulism, toxin is preformed in food, and the ingested toxin in food causes disease. However, in infant botulism, botulinum spores are ingested by the infant; the spores germinate, colonize the infant gut and form toxin. The toxin formed in vivo is absorbed from the intestinal tract and leads to the clinical syndrome of infant botulism (118). Ingestion of honey and corn syrup by infants has been associated with the disease, but only in a minority of cases (154). Other foods have not

been implicated; however, it is interesting that breast feeding has been associated with infant botulism (154). Nonetheless, Arnon (11) has pointed out that infants who died suddenly as a result of infant botulism were fed formula with added iron, whereas the more gradual onset, hospitalized cases occurred in infants that were primarily breast-fed. Most infant formulas are fortified with iron, whereas human milk is relatively iron-free (174); thus, little iron is available for the growth of iron-requiring *Clostridium* species. *C. botulinum* spores are ubiquitous, and environmental spores from dust and other sources are strongly associated with most cases of the disease (55,111). The factors involved in the maintenance of infant botulism appear to be largely unknown (55,111).

**Hemorrhagic colitis.** *Escherichia coli* O157:H7 is a newly evolved *E. coli* serotype that has become pathogenic through the acquisition of virulence factors (177). The organism has the ability to adhere intimately to intestinal cells by an attaching and effacing mechanism and produces one or more types of phage-encoded Shiga-like toxins. *Escherichia coli* O157:H7 has caused a number of fatalities in food-borne outbreaks. Increased epidemiological surveillance and reporting of these outbreaks have increased the public's awareness of the dangers associated with ingesting foods contaminated with *E. coli* O157:H7 (45,60,77). The majority of cases appear to be sporadic (77); however, outbreaks have attracted widespread attention and have been mainly associated with drinking raw milk or unchlorinated water and with eating raw or undercooked ground beef (77). Other implicated foods include apple cider, turkey, yogurt, and potatoes (16,77,116). Outbreaks have been associated with eating in restaurants and have occurred in institutional settings (nursing homes, child care centers, kindergartens). Association of the disease with institutional settings suggests that person-to-person transmission occurs and that the infectious dose is low (60,77). The elderly and very young are at risk because of their decreased immune capacity.

Cattle may carry the organism in their intestinal tracts (49,77,176) and carcasses may become contaminated during slaughter and dressing operations. Rasmussen et al. (132) have shown that starvation of cattle (as may be done before shipping or slaughter) can lead to colonization of the intestinal tract by *E. coli* O157:H7. The organism grew in rumen fluid collected from fasted cattle but did not multiply in rumen fluid from well-fed animals. *Escherichia coli* O157:H7 growing in the rumen of fasted cattle will eventually colonize the intestinal tract. Other forms of stress due to crowding and transport may also contribute to colonization of cattle by *E. coli* O157:H7 (132). The increase in the industrialization of animal husbandry, slaughter, food-processing, and food-distribution systems, with its resultant concentration of activities into larger and fewer facilities, can also lead to the concentration of a problem (such as microbial contamination of meat products) and the distribution of that problem to a wide spectrum of the consuming public (14,81,140).

**Listeriosis.** Listeriosis was recognized as an important public-health problem when increased epidemiological surveillance and reporting of listeriosis outbreaks determined

that some major outbreaks were caused by food-borne *Listeria monocytogenes* (32). *Listeria monocytogenes* is an environmental bacterium and is present in the intestinal tracts of a variety of animals, including animals used as food (110). Thus, milk, dairy foods, meat, poultry, and also vegetables if grown on lands fertilized with animal manure may be contaminated with *L. monocytogenes* (18,28,39,108). Outbreaks have been associated with milk, soft cheeses, and coleslaw (19,145). The majority of listeriosis cases are sporadic and a substantial portion of sporadic cases are due to food-borne *L. monocytogenes* (31,128,144). Foods implicated in sporadic cases include soft cheeses, undercooked chicken, unheated frankfurters, and ready-to-eat foods from delicatessens. Since *L. monocytogenes* is capable of growth at refrigeration temperatures, use of low temperatures during the harvesting, preparation, transport, or storage of foods will not control the growth of the pathogen if it is present (58). Extended refrigerated shelf life also contributes to possible growth of *L. monocytogenes* in foods, particularly at the distribution and consumer levels. An additional factor in maintenance of disease caused by *L. monocytogenes* in the population is the susceptibility of immunocompromised individuals, including pregnant women, the very young, the elderly, individuals with immunosuppressive diseases, or those who are medically immunosuppressed (31,145).

**Salmonellosis.** *Salmonella enteritidis* was recognized as an important food-borne pathogen when epidemiological studies indicated that a significant number of outbreaks of gastroenteritis were due to eating *S. enteritidis*-contaminated intact Grade A shell eggs or products prepared with such eggs (44,138,158). Unlike previous outbreaks of salmonellosis caused by eggs in which the organisms had entered the eggs through cracks in the shell, *S. enteritidis* was present in intact sanitized Grade A eggs. Most cases of *S. enteritidis* infections are sporadic or are limited outbreaks in single families which, like large outbreaks, are associated with consumption of undercooked Grade A eggs (80). The strains of *S. enteritidis* implicated in intact shell egg outbreaks (phage type 4 in Europe and phage types 8 and 13a in the United States) are closely related, and the unusual invasiveness of these strains for chickens appears to have developed independently and simultaneously (155,159,169). These strains of *S. enteritidis* invade various tissues of the chicken, including the ovaries and oviduct (90,169). The presence of the organism in the reproductive tissue of the laying hen leads to contamination of the egg before the shell is laid down.

The eating habits of people are a major factor in the maintenance of *S. enteritidis* as a food-borne pathogen. Undercooked eggs (soft boiled, soft scrambled, soft poached, fried "sunny-side up") and the use of unpasteurized raw eggs in food products pose a risk to consumers. Persons who are immunocompromised are particularly vulnerable to *S. enteritidis* infections and should only consume eggs that are thoroughly cooked (113).

Improper storage of *Salmonella*-contaminated whole or pooled eggs during production, distribution, and preparation can permit the growth of *S. enteritidis* (27,29). *Salmonella enteritidis* inoculated into egg yolk grew 5 to 6 log units in 4 to 5 days at 15.5°C, but no growth occurred within 24 days at 7.2°C (29).

Poultry-raising practices contribute to the maintenance of *S. enteritidis* in chickens. As laying hens age, egg productivity declines. Subjection of hens to stresses such as water and feed deprivation or reduced light will induce molting and egg laying will resume. Such stresses can lead to a decrease in cell-mediated immunity with an ensuing increase in susceptibility to *Salmonella* infection and increased shedding of the organism by infected hens with resultant transmission to uninfected birds (9, 87, 88, 89, 130). Mishu et al. (113), investigating a restaurant outbreak involving eggs contaminated with *S. enteritidis*, were able to locate the farm where the eggs originated and also determined that the hens were infected with *S. enteritidis*. A few weeks before the restaurant outbreak, the farm had experienced labor problems and the hens did not receive food or water for 2 to 3 days. The food and water deprivation may have allowed the increased excretion of salmonellae into eggs laid by infected hens (113). Vaccination with an *S. enteritidis* preparation gave partial protection to hens against challenge by the pathogen (70). Vaccination coupled with proper cleaning and disinfection and rodent control should help control the incidence of *S. enteritidis* in laying hens.

The increase in the industrialization of poultry breeding, poultry rearing, egg production, and egg distribution also contribute to the persistence of *S. enteritidis*. Parent meat or laying chickens are derived from chicken stocks bred by a few primary breeding companies. Some companies have control over all stages of production of raising chickens for meat and eggs (7). The concentration of chicken meat and egg production activities into a few companies can, if *S. enteritidis* is present, lead to widespread distribution of infected chickens and eggs (7, 14, 140, 163).

**Epidemic cholera.** In early 1991, cases of cholera were recognized in Lima, Peru, marking the reappearance of epidemic cholera for the first time in the Americas in almost a century (42, 74). The major factor leading to the reemergence of cholera was due to a decision by Peruvian officials to terminate chlorination of water supplies in order to reduce possible cancer risks (6, 160).

Poor maintenance of much of Latin American water systems is an important contributory factor to the continuation of epidemic cholera in the Americas. Large municipal water systems have frequent cutoffs, intermittent flow, low water pressure, and illegal connections (to avoid paying for water use), thus making sewage cross-contamination possible (160, 167). Municipal sewers discharge directly into rivers and harbors with resultant contamination of shellfish and fish stocks. Immigrants from rural areas are concentrated adjacent to large cities into small towns lacking adequate potable water and sewage-disposal systems. All of these factors plus the lack of adequate chlorination make it unlikely that *Vibrio cholerae* will be easily eliminated (74, 160, 165, 167).

Eating habits also contribute to continuation of the epidemic. Consuming raw seafood or raw fish prepared in lemon juice ("ceviche"), cooked crab (probably contaminated after cooking), raw vegetables (from vegetable crops grown on lands fertilized with sewage), unboiled water or food and beverages prepared by street vendors, and food

purchased at fiestas and consumed without reheating have resulted in cases of cholera (74, 121, 160, 165, 173).

Genetics plays a role in cholera epidemics, also. The most severe form of cholera is seen in individuals with type O blood; at least 75% of Peruvians are type O and the prevalence of the type O blood group may be high in many other Latin American countries (74, 135, 165, 166, 167). Because cholera has been rare in the Americas, there is little immunity to the disease and most of the population are susceptible. In addition, vaccination gives only limited protection to individuals with blood group O (135, 166).

No outbreaks have been reported in the United States; however, cases of cholera have occurred in individuals who consumed contaminated seafood transported by friends and relatives from epidemic areas (129). Seventy-six passengers on a plane from Buenos Aires to Los Angeles developed cholera from eating a cold seafood salad that was placed on the flight at Lima (129). Secondary spread of cholera from these ill individuals has not occurred because of adequate chlorination of water and excellent sewage-disposal systems in the United States.

**Vibrio vulnificus infections.** *Vibrio vulnificus* is a nonfecal, free-living bacterium that is ubiquitous in marine environments. *Vibrio vulnificus* was recognized as a pathogen when halophilic lactose-fermenting vibrios were isolated from the blood of patients who had recently eaten oysters and from wounds of patients exposed to seawater or from wounds incurred during handling shellfish. The ability of clinicians to identify and distinguish between very similar vibrios led to the association of *V. vulnificus* with gastroenteritis, wound infection, or septicemia (24, 93).

A recent report concerning *V. vulnificus* infections in Florida described 124 individuals who had been infected during 1981/1992 (46). Primary septicemia was present in 58%, wound infections in 28%, and gastroenteritis in 14%. Forty-four deaths were recorded, of which 40 were attributed to septicemia (46). Eating raw oysters prior to the onset of illness was reported in 81% of the patients with primary septicemia and in 88% of the patients who eventually succumbed due to septicemia. Risk factors leading to septicemia from *V. vulnificus* infections include eating raw oysters and having medical conditions such as liver dysfunction and syndromes that lead to increased iron in serum, including chronic cirrhosis, hepatitis, thalassemia major, hemochromatosis, hematopoietic disorders, and other diseases involving chronic iron overload (34, 93). Other immunosuppressed individuals who consume raw or undercooked seafood are more susceptible to infection, also. Reportedly, healthy people who have come in contact with seawater (swimming, boating, or crabbing) may acquire *V. vulnificus* wound infections (93).

**Yersiniosis.** *Yersinia enterocolitica* was recognized as a food-borne pathogen when a large number of school children became ill from drinking chocolate milk that had probably become contaminated after pasteurization. Thirty-six children were hospitalized and appendectomies were performed on 16 of the children (22). In food-borne yersiniosis, there is often clinical presentation of lower right quadrant abdominal pains which may be confused with appendicitis. Upon surgery, the appendix is usually normal or only slightly inflamed (65, 122).

Foods involved in outbreaks in the United States have included raw chitterlings, where adults who had handled raw chitterlings infected their infants and children by contact (104), pasteurized milk, which was probably contaminated with *Yersinia* after pasteurization (22, 75, 76, 162), tofu that had been packed in untreated water (12, 161), and reconstituted powdered milk that had been contaminated by a food handler (119, 149).

*Yersinia enterocolitica* is found in the gastrointestinal tracts of domestic and wild animals and humans (142, 148) and in water, raw meats, raw milk, and raw vegetables (65). Most isolates, particularly those from foods, appear to be nonpathogenic except for those from swine and pork (57, 59). The main reservoir for pathogenic *Y. enterocolitica* is swine, and the organism is found in ground pork and porcine tongues (5, 142, 168). Foods may contain pathogenic *Yersinia* if cross-contamination with raw pork occurs or if foods are handled by swine caretakers.

Environmental and food-processing conditions that lead to the inactivation of salmonellae will inactivate *Y. enterocolitica* (59). However, *Y. enterocolitica* is psychrotrophic: the organism must be eliminated from foods that are normally kept refrigerated and that may have come in contact directly or indirectly with swine or pork products (57, 59).

#### *Viral infections*

*Epidemic viral gastroenteritis.* The Norwalk virus was recognized as a pathogen when it was visualized by immunoelectron microscopy in stool filtrates obtained during an outbreak of gastroenteritis in Norwalk, Ohio (95). Its pathogenicity and infectivity were demonstrated by serial passage of the virus in adult volunteers (56, 180). Norwalk virus infections are common in the United States. Approximately 5% of children under 12 years of age are seropositive for Norwalk virus; by 35 years of age, 45% of the population are positive, and by age 65, 60% are seropositive (146). The incidence of outbreaks and cases of Norwalk virus and other Norwalk-like organisms appears to be increasing; however, this is probably due to an awareness and recognition of these agents as human pathogens and the development of improved diagnostic techniques (103).

Norwalk virus is a major cause of nonbacterial gastroenteritis in older children and adults. The sites where the outbreaks have occurred are quite diverse and include banquets, cruise ships, nursing homes, day-care centers, hospitals, cafeterias, recreational lakes, swimming pools, camps, hotels, schools, dormitories, and fast-food restaurants (38, 41, 83, 97, 100, 102, 114). Infections have occurred from recreational swimming in or drinking of contaminated water, using ice made from water in which the virus was present, eating raw or undercooked oysters and other shellfish harvested from contaminated waters, eating fresh-cut fruit served at banquets and eating salads or other uncooked items (38, 43, 48, 72, 83, 94, 97, 102, 114). In the period 1973 to 1987, Norwalk virus was implicated in 15 food-borne disease outbreaks involving 6474 cases; food items incriminated were bakery products, fruits and vegetables, and shellfish (13). Other means of transmission include person-to-person contact and contamination of food by infected

food handlers (50, 81, 84, 100, 134). Contaminated equipment, food from an unsafe source and/or poor personal hygiene accounted for > 50% (11/15) of the food-borne outbreaks associated with Norwalk virus (13). Poor personal hygiene was the largest contributing factor and was involved in 78% of the outbreaks of Norwalk virus gastroenteritis.

*Sporadic viral gastroenteritis.* Rotaviruses are the most common cause of severe diarrhea in infants and young children; death may occur in cases of severe dehydration (death is rare in developed countries). Most children are seropositive by four years of age (41). Approximately one-third of the parents of infected children become ill; the virus may infect travelers to developing nations and may cause illness in the elderly and in individuals with immunocompromising conditions (10, 41, 91). Rotavirus infection has also been shown to be a cause of diarrhea in HIV-positive individuals (2). Human rotavirus was first detected by thin-section electron microscopic examination of duodenal biopsies from children with acute diarrhea (20) and was observed by electron microscopy of diarrheic stool specimens (21, 66). The infectivity, pathogenicity, and serological response to infection by rotavirus was studied by serial passage of the virus in adult volunteers (96, 172).

Rotavirus is generally transmitted by person-to-person contact and infections have occurred in hospital pediatric wards, child-care centers, and geriatric care centers (23, 41, 50, 133). Rotavirus is shed in large numbers in feces of both asymptomatic and symptomatic individuals (23, 50, 146) and, therefore, the virus has been found in both sewage and water (10, 91). Levels of chlorine normally used in water treatment are not effective against rotavirus and the virus survives for long periods in both sewage and water (10). Thus, it is not surprising that water has been shown to be a source for outbreaks of rotavirus infections (10, 91).

Foods are a probable vehicle of rotavirus infection, particularly for adults, although there is little documentation. The use of sewage or human manure to fertilize vegetable crops, contamination of shellfish grown in sewage-polluted waters, or preparation of foods by infected food handlers are routes by which rotavirus can enter foods (10). A large rotavirus outbreak that occurred at a banquet, discussed in an unpublished report cited by Bean and Griffin (13), was apparently caused by an infected food handler preparing cold food items.

#### *Parasitic infections*

*Cryptosporidiosis.* While a few cases of cryptosporidiosis were known before the AIDS epidemic, clinicians actually became aware of the disease with the recognition that the protozoan, *Cryptosporidium*, caused an opportunistic life-threatening unrelenting diarrhea in HIV-infected individuals (71, 126); other immunocompromised individuals are at risk also (152). The parasite causes an acute self-limiting diarrhea in immunocompetent individuals. In developed countries, 25 to 35% of the population are seropositive for *Cryptosporidium*, indicating that infection is quite common (152). The incidence of infection is higher in less developed areas.

The organism can be transmitted via animal contact (particularly by young farm animals or pets), by person-to-

person contact, and by the ingestion of fecally contaminated food and water (40, 52, 62). Waterborne outbreaks are common and wastewater in the form of runoff waters from dairies and feedlots or from manured lands can contaminate surface and recreational waters (40, 52). Chlorination levels employed at the present time are ineffective against the parasite (52, 152) and filtration does not always remove *Cryptosporidium* from drinking water, as has been demonstrated in a recent massive waterborne outbreak in Milwaukee (64, 107). Food-borne transmission of *Cryptosporidium* has been documented; some of the suspect foods included salad, raw goat and cow's milk, sausage, and frozen tripe (152). Person-to-person transmission is common and is found within families, and among children in day-care centers, the elderly in nursing homes, and patients in hospitals (40). The failure of individuals to practice good personal hygiene and the use of untreated water are major contributing factors to *Cryptosporidium* infections in the population.

*Giardiasis*. In the early 1970s, physicians and public-health officials were made aware of the importance of *Giardia lamblia* as an agent of gastrointestinal disease when a number of travelers to the Soviet Union became ill with giardiasis (30, 171). The increased awareness led to the subsequent demonstration that *G. lamblia* was widespread in the United States, particularly in untreated water supplies. At the present time, giardiasis is the most commonly reported pathogenic protozoan disease in the United States (179). Giardiasis frequently develops in travelers to underdeveloped countries, in children in child-care centers, in the elderly in nursing homes, and in individuals who drink contaminated water or ingest contaminated foods (152, 179).

Humans are the major reservoir of *G. lamblia* but the parasite is present in farm animals, pets, and various wild animals; their excreta may contaminate the environment and water supplies (152, 179). Animal caretakers may be infected by contact with animals harboring the parasite. *Giardia lamblia* cysts are resistant to sanitizers and to the various agents used in water treatment; coagulation-sedimentation-filtration methods are necessary to eliminate the parasite from drinking water (152, 179).

*Giardia lamblia* has been the cause of a number of waterborne disease outbreaks involving chlorinated but unfiltered water (105). The parasite is transmitted person-to-person via the fecal-oral route, by drinking contaminated water, and by ingesting food prepared by individuals with poor personal hygiene (152). Food-borne outbreaks have implicated salads, sandwiches, home-canned salmon, and ice (152). In all of the food-borne outbreaks, items were either uncooked or not reheated after preparation, and the source of the parasite was an infected food handler. Lack of proper hand-washing and of proper treatment of water supplies are important factors in the maintenance of *Giardia* infections.

*Toxoplasmosis*. Before the AIDS era, toxoplasmosis was seen mainly as a rare disease of pregnant women. Infection by the *Toxoplasma gondii* protozoan during pregnancy may result in abortion, stillbirth, or congenital toxoplasmosis with severe sequelae to the child although

the mother is usually not ill (61, 68). Toxoplasmosis is a common infection but a rare disease in immunocompetent individuals; most infected individuals show no clinical signs (68, 151). Approximately half of the United States population is seropositive and it has been estimated that at least 500 million of the world population demonstrate a positive serological reaction to *T. gondii* but show no signs of illness (68, 151). In AIDS patients, toxoplasmosis is an opportunistic disease that may develop into toxoplasmic encephalitis (71, 86). Other immunocompromised individuals may also develop clinical toxoplasmosis (68, 109, 151). Disease in immunocompromised individuals is generally not due to a new infection by *T. gondii* but represents reactivation (or recrudescence) of an old infection. When an individual is infected with the parasite, the actively multiplying organisms eventually form quiescent cysts in various tissues and the cysts persist for the life of the individual. In immunocompetent individuals, the immune system can keep the tissue parasites in the inactive cyst form; however, with the breakdown of the immune system by disease or immunosuppressive drugs, the cyst wall is dissolved and the parasites escape, multiply, and produce active toxoplasmosis (151).

Toxoplasmosis is a cat-driven disease, i.e., feline species are the primary hosts, whereas virtually all warm-blooded animals can act as the secondary hosts. The oocysts of *T. gondii*, excreted in the feces of felines (and only in felines), are deposited in soil, water, or animal feeds (61, 68, 151). While animals other than felines do not excrete the parasite, infections to humans can occur from eating raw or undercooked meat from animals containing *T. gondii* tissue cysts (153). Livestock that eat feeds or hay contaminated by the feces of *T. gondii*-infected cats (cats are used as biological rodenticides on many farms) develop infection that eventually results in tissue cysts in edible parts of the animals (151). Therefore, eating raw or undercooked meats and having cats as pets are major factors involved in the maintenance of *T. gondii* as a food-borne pathogen.

#### *Prion-mediated infection*

*Bovine spongiform encephalopathy (BSE)*. BSE, a transmissible spongiform encephalopathy, was first seen in cattle in the United Kingdom in the mid-1980s (54). The disease affects the brain, resulting in degeneration of neurons, hypertrophy of the supporting astrocytes, and a diffuse sponge-like appearance of brain tissue with eventual death of the animal (54). More than 100,000 cattle in the United Kingdom have been affected since 1985 (125). BSE appears to be a new disease (54); however, Eddy (63) disputes this and claims that BSE had occurred occasionally in the past. The infective agent is a "prion" (54, 143), a small proteinaceous infectious particle that resists inactivation by procedures that modify nucleic acids. It is an abnormal isoform of a normal cellular protein, the prion protein—PrP (15, 131, 143). Prions are not inactivated by most food-processing conditions and in fact, complete destruction is not achieved with autoclaving at 134°C for one hour (54).

The presence of BSE has been linked to feeding cattle with tankage (protein supplement) produced by rendering and drying offal and waste products from ruminants (103).

Thus, BSE may be related to the use of scrapie-infected sheep in tankage preparation since scrapie is a transmissible spongiform disease of sheep and is endemic in the United Kingdom (54). The appearance of BSE followed a change, in 1981/1982, in the way tankage was prepared. A combination of increasing fuel prices, since heat is used for the rendering process, and the elimination of solvents for lipid extraction led to changes that apparently did not inactivate the BSE agent present in the raw materials used to prepare tankage (103, 178). The unextracted fat may protect the BSE agent against heat inactivation; this did not occur when fat was extracted with solvents under the older system (178). The use of ruminant tissue in tankage for cattle was banned in the United Kingdom in July 1988 (54), but since BSE has an incubation period of 3 to 6 years, the disease will continue to be seen in cattle for some time to come. Hoinville (85) reported that the incidence of BSE in animals born after the "feed ban" (July 1988) is much lower than in animals born before the ban.

BSE does not seem to have been transferred to humans; however, Dealler and Lacey (54) believe that cattle are the likely major source of the infectious agent for nonfamilial Creutzfeldt-Jakob disease (CJD), a transmissible spongiform encephalopathy of man. The Centers for Disease Control (47) have indicated that animal diseases with zoonotic potential (including BSE) should be monitored, thereby suggesting that a potential for transmission of BSE to humans exists. There is no proof that association with cattle or eating bovine products leads to CJD. However, in recent reports from the United Kingdom, two dairy farmers, whose herds were infected with the BSE agent, were diagnosed with nonfamilial CJD (53, 141). Neither individual had a medical history indicative of quiescent CJD. While these cases do not statistically associate CJD and BSE, they are suggestive.

BSE has not been seen in the United States. Recently, Bleem et al. (26) indicated that the risk of transmission of the sheep scrapie agent to cattle in feeds is probably infrequent, but United States rendering and feed industries do follow practices that allow possible incorporation of sheep scrapie agent into ruminant feeds. Apparently, surveillance for BSE in cattle has been implemented in the United States (26).

## CONCLUSIONS

Since change is the way of life, it is certain that new pathogens will emerge and that old pathogens will re-emerge in response to change. Major factors that contribute to emergence of new food-borne pathogens include microbial genetic changes and evolution (toxin and other virulence genes are readily exchanged among microorganisms), technological changes in the food industry, improvement in the methodology of isolation, detection, and identification of microorganisms, changes in people's behavior (particularly in eating habits), increasing numbers of people with conditions that result in immunosuppression, increased migration and movement of individuals, and increased foreign commerce.

An effective surveillance program will facilitate early

detection and investigation of newly emerging or reemerging diseases and allow the use of effective strategies for control and prevention. Early detection of emerging diseases will help to alleviate economic losses in terms of lost productivity and medical costs. Roberts and Smallwood (136) estimated the costs to the United States from all food-borne illness to be \$4 to \$8 billion annually; Todd (170) estimated \$8 billion annually, whereas Garthright et al. (69) estimated the annual cost of food-borne illness to the United States to be somewhat higher, at \$23 billion. Five pathogens account for a large part of the estimated costs of food-borne disease in the United States: *T. gondii*, \$2,628 million; *Salmonella*, \$1,188 to \$1,588 million; *Campylobacter*, \$907 to \$1,016 million; *E. coli* O157:H7, \$229 to \$610 million; and *L. monocytogenes*, \$209 to \$230 million (175). The total estimated costs due to infections by these five organisms is \$5,161 to \$6,075 million annually. With the exception of *Salmonella*, these pathogens have emerged fairly recently.

Various factors involved in the emergence and persistence of infectious diseases, vector-borne diseases, virus diseases, and antibiotic resistance are discussed in the following monographs: *The Antibiotic Paradox: How Miracle Drugs are Destroying the Miracle* (106); *Demography and Vector-Borne Diseases* (147); *Emerging Infections: Microbial Threats to Health in the United States* (103); *Emerging Viruses* (120); and *A Dancing Matrix: How Science Confronts Emerging Viruses* (82). It is important that food microbiologists be familiar with the factors, changes, and conditions that are involved in the emergence and maintenance of disease agents.

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