CHAPTER THREE

Categories and Highlights of Significant Current Emerging Infectious Diseases

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Emerging infectious diseases (EIDs) may be thought of in various ways: by the category of the organism, the routes of transmission, the most prevalent methods of spread, or geographic distribution. Emerging infectious diseases will be discussed below in terms of the classification of the infectious agent (bacterial, viral, parasitic, fungal, and prion) and in terms of their chief mode of dissemination to humans—limited here to those agents that are food- and/or waterborne, zoonotic, or vectorborne and those that are transmissible by blood transfusion or transplant. Some of the latter categories overlap. For example, babesiosis is a parasitic, vectorborne disease that is also transmissible by blood transfusion. Another important aspect of infectious disease transmission and acquisition has to do with animal and human behavior and culture which are considered in detail in chapter 28. After this general discussion, chapters follow highlighting specific EIDs that are of special interest or importance. Numerous tables providing information about a large number of EIDs appear in Appendices A and B.

Some EIDs are transmitted to humans from their usual animal hosts and are known as zoonoses. About 75% of EIDs in humans are caused by zoonotic pathogens (Wolfe, Daszak, Kilpatrick, & Burke, 2005). In addition to microorganism, vector or vehicle, and host characteristics that may facilitate the transmission of emerging zoonotic diseases to humans, situations that bring humans and animals, especially wildlife, into increased close contact amplify the risk of zoonotic infectious disease emergence. This includes human behavior such as choice of travel or recreational pursuit, examples of which are the acquisition of leptospirosis by a vacationer from California exploring a cave in Malaysia (Mortimer, 2005) and *Escherichia coli* O157:H7 acquired by children at a petting zoo (Centers for Disease Control and Prevention [CDC], 2005). Other human factors include agricultural encroachment, for example, clearing the land in Venezuela for agricultural use, creating a more favorable environment for the cane mouse leading to an outbreak of Venezuelan hemorrhagic fever due to the Guanarito virus; and through weather and climate changes that may increase the population or range of vectors or wildlife reservoirs so that they are more apt to be in a higher density ratio with humans. An example of this is the 1993 hantavirus pulmonary syndrome outbreak in the southwestern United States due to the Sin Nombre virus. When increased rainfall resulted in increased vegetation, and increased food and shelter, for small rodents, their population grew and brought them closer to humans (Engelthaler et al., 1999; Lashley, 2004; Smolinsky, Hamburg, & Lederberg, 2003; Wolfe et al., 2005). In instances of drought and scarce food, rodents may be driven into human dwellings in search of food.

Recent literature has speculated on the potential infectious disease consequences of close contact between humans and nonhuman primates at temples throughout South and Southeast Asia where the temple monkeys have a role in Buddhist and Hindu culture (Jones-Engel et al., 2006). Molecular advances have resulted in increased recognition of certain diseases as zoonotic in origin as well as the discovery of new organisms that were not previously recognized. Emerging infectious diseases of zoonotic origin may appear as human infections in an episodic way, such as happens with Lassa fever (see chapter 8), or may more permanently jump the species barrier, often through a mutation in the organism as is believed to have occurred in the case of the human immunodeficiency virus (HIV) infection. It is believed that HIV-1 originated as the simian immunodeficiency virus from the *Pan troglodytes troglodytes* (Gao et al., 1999) and HIV-2 from the sooty mangabey (Hahn, Shaw, De Cock, & Sharp, 2000; see chapter 13). Some zoonoses are relatively benign, others cause limited disease, and still others result in more serious and extensive outbreaks.

As in other chapters, the definition of EIDs includes newly identified diseases caused by previously known organisms; newly identified diseases caused by previously unknown organisms; the recognition of a new organism; or a familiar organism whose geographic range has extended, whose host has changed, whose incidence has increased, or that has changed to become more virulent or antibiotic resistant. In many cases, identification of new microorganisms has occurred because of the recent availability of new molecular diagnostic techniques.

EMERGING INFECTIONS BY MICROORGANISM CLASSIFICATION

Emerging Bacterial Diseases

Bacteria were the first disease-causing microbes to yield to modern pharmacologic interventions. Morbidity from "old" bacterial illnesses such as tuberculosis (TB) and cholera, however, continues to be a problem. While fewer significant "new" bacteria and bacterial diseases have been identified in the last 35 years (e.g., legionellosis, discussed further in chapter 15; newer rickettsial diseases such as *Rickettsia honei* causing Flinders Island spotted fever, with further data available in Appendix A, Table A.4; and *Bartonella henselae,* the agent of cat scratch disease, discussed further below) when compared with newly identified viruses and viral diseases, other problems are seen. Bacteria have been identified as emerging or reemerging due to the spread to new geographic areas; infection of new hosts or populations, such as with cholera; and the emergence of antimicrobial-resistant forms or increasing virulence of certain strains. This may include multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB); vancomycin-resistant enterococci (VRE) infections caused by *Enterococcus faecalis* or *Enterococcus faecium*, resulting in significant problems from nosocomial infections; resistant forms of *Streptococcus pneumoniae*, the major bacterial cause of meningitis, pneumonia, and otitis media; or *Clostridium difficile*. Outbreaks of a new strain of *E. coli*, a familiar bacteria, known as O157:H7 fit this pattern causing diarrhea and hemolytic uremic syndrome (see chapter 9). Likewise, although cholera is an ancient disease, new virulent strains such as the El Tor strain of *Vibrio cholerae* have emerged, and there is an endemic focus of infection in the United States as well as increased cases due to imported foods or travelers (see chapter 4). *Staphylococcus aureus*, a frequent cause of infection in nosocomial settings and the immunosuppressed, has become resistant to various antibiotics, especially methicillin (methicillin-resistant *S. aureus*, or MRSA) and, more recently, to vancomycin, probably due to horizontal resistance transfer from VRE organisms (see chapter 2).

Other microorganisms are defined as resurgent due to changes in their geographic distribution or increased incidence of infection, often following the decline of the public health system. An example of the latter is the resurgence of diphtheria (caused by *Corynebacterium diphtheriae*) and pertussis (whooping cough; caused by *Bordetella pertussis*), both vaccine-preventable diseases, in former states of the Soviet Union. Pertussis is also being increasingly seen in adolescents and adults in the United States, and due to travel and migration unusual forms of diphtheria such as cutaneous lesions are being seen in developed countries (Crowcroft & Pebody, 2006; Halperin, 2007; Raguckas, Vandenbussche, Jacobs & Klepser, 2007; Sing & Heesemann, 2005). In another example, both *Clostridium novyi* and *Clostridium histolyticum* were considered emerging when they were responsible for illness outbreaks in injection-drug users via contaminated heroin in Great Britain, the former in 2000 and the latter in 2003 and 2004 (Brazier, Gal, Hall, & Morris, 2004). Also, mild cases of botulism from the toxin produced by *Clostridium botulinum* have resulted from inhalation of adulterated cocaine (Roblot et al., 2006). Another unusual way to develop botulism has been iatrogenic. Four persons developed botulism after injection of a concentrated unlicensed preparation of botulinum toxin A for cosmetic reasons (Chertow et al., 2006). New bacterial diseases such as Lyme disease, ehrlichiosis, anaplasmosis, and various rickettsial fevers have been identified (see chapter 16). Emerging bacterial diseases are summarized in Appendix A, Table A.1. Some of these diseases will be briefly discussed below or in individual chapters.

Toxic shock syndrome (TSS), a febrile illness associated with shock, multiorgan dysfunction, and high death rates, was first described in association with staphylococci in 1978 (Todd, Fishaut, Kapral, & Welch, 1978) but came to national attention in 1979–1980 when a new and initially puzzling entity was affecting young healthy women. The connection with menstruation, tampon use (especially the tampon absorbency), and TSS from *S. aureus* led to some misperceptions that TSS occurred only in association with these variables. Although TSS did initially appear to occur disproportionately in menstruating women, there has been an increasing proportion of nonmenstrual cases, with many reported subsequent to surgical procedures (Hajjeh et al., 1999; Reingold, 1998). *S. aureus* is a gram-positive, nonmotile, non-spore-forming cocci that can cause a wide spectrum of diseases such as skin conditions and abscesses, cellulitis, pneumonia, endocarditis, and osteomyelitis. It can produce toxins directly by the bacteria, for example, on the skin, and cause staphylococcal scalded skin syndrome or TSS, or it can produce toxin when present in food or drink and lead to gastroenteritis in the person who ingests it (M. Lorber, 2005; Moreillon, Que, & Glauser, 2005). Beginning in the 1960s, strains of *S. aureus* that were methicillin-resistant (as well as resistant to many other antibiotics) began to emerge (Fridkin et al., 2005). Infections due to MRSA have increased in prevalence worldwide, but until relatively recently they were considered nosocomial and were essentially endemic in hospitals, especially in intensive care units. It was noted that spread from patient to patient was largely via the hands of health care workers

(Henderson, 2006). The organism has also developed strains resistant to vancomycin, which were first reported in the United States in 2002 (CDC, 2002).

Beginning in 1993 with reports from Western Australia, community-associated (CA) MRSA strains began to emerge and have been isolated from both children and adults with skin and soft tissue infections, septicemia, TSS, necrotizing fasciitis, necrotizing pneumonia, and septic arthritis. CA-MRSA appears more prevalent among the homeless, men who have sex with men, prisoners, military recruits, children in day care centers, tattoo recipients, and others (CDC, 2006b; Grundmann, Aires-de-Sousa, Boyce, & Tiemersma, 2006). Community-associated strains are now finding their way into hospitals (Grundmann et al., 2006). Nosocomial MRSA is associated with persons having dialysis, organ transplantation, catheters, and surgical procedures; persons who have immune defects such as diabetes, HIV infection, alcoholism, older age, and so on; as well as those who are chronic nasal or skin carriers of *S. aureus* (Moreillon et al., 2005). Bahrain, Vasiliades, Wolff, and Younus (2006) consider bacterial endocarditis after CA-MRSA furunculosis an emerging infectious entity. Finding an effective antibiotic and implementing guidelines to reduce transmission are vital.

In the mid-1980s, a resurgence of severe, invasive group A streptococcal (GAS) infections was seen, leading to TSS and necrotizing fasciitis. Group A streptococcal infections had been known previously but had appeared to be declining prior to this resurgence, which was attributed to an increased virulence of the organism. It is also known that host susceptibility plays a vital role in predisposition of persons to GAS. Any illness caused by *Streptococcus pyogenes* can result in streptococcal TSS, which is an acute febrile illness often with tissue infection that can progress to shock, multiorgan failure, and death. The death rate is high—reported as 30% to 80% (Chuang, Huang, & Lin, 2005). GAS infection resulting in necrotizing fasciitis with or without TSS has emerged becoming known in the popular press as "flesh-eating" bacteria. Mortality is high with this condition, and survivors often need major debridement and/or amputation of limbs. About half of these cases are associated with TSS (Hasham, Matteucci, Stanley, & Hart, 2005). Necrotizing fasciitis due to CA-MRSA is also considered an emerging entity (Miller et al., 2005).

C. difficile infection increased 26% as a discharge diagnosis from hospitals between 2000 and 2001 in the United States. *C. difficile* is a gram-positive spore-forming bacteria capable of producing exotoxins (CDC, 2005). Its range of infection is from uncomplicated diarrhea to sepsis and death (Sunenshine & McDonald, 2006). It is a major component of antibiotic-associated diarrhea (Fordtran, 2006). Typically, it has affected older or severely ill patients in the hospital or long-term care settings but is now being found affecting previously healthy people in the community

(CDC, 2005). It is increasing in incidence and severity of disease due to increased virulence and multidrug resistance of some strains (Oldfield, 2006; Sebaihia et al., 2006). Transmission is by the fecal–oral route through hand and patient environment contamination (Fordtran, 2006; Sunenshine & McDonald, 2006).

Bartonella (formerly called *Rochalimaea*) *quintana* was recognized as the cause of trench fever during World War I, and another species, *B. bacilliformis*, was recognized as the cause of Oroya fever. Many new species have been identified, some of which resulted from renaming and some from phylogenetic studies resulting in reclassification of *Grahamella* species to *Bartonella* in 1995 (Slater & Welch, 2005). The number of species known to cause disease in humans is increasing and includes *B. bacilliformis*, *B. henselae*, *B. quintana*, *B. elizabethae*, *B. clarridgeiae*, *B. vinsonii*, *B. grahamii, B. washoensis*, and *B. koehlerae* (Boulouis, Chang, Henn, Kasten, & Chomel, 2005). The major diseases caused are trench fever, Oroya fever, cat scratch fever, bacillary angiomatosis (BA), bacillary peliosis (BP), endocarditis, and bacteremia, depending on the species. *Bartonella* are aerobic, fastidious, gram-negative bacteria, some of which have flagella such as *B. bacilliformis* and *B. clarridgeiae*. Some *Bartonella* may be transmitted by a vector such as the body louse, which transmit *B. quintana* and result in trench fever (Boulouis et al., 2005; Slater & Welch, 2005; Walker, Maguiña, & Minnick, 2006), and ticks and cat fleas are considered as possible vectors (Chomel, Boulouis, Maruyama, & Breitschwerdt, 2006).

B. henselae has been identified as the major cause of cat scratch disease. Cat scratch disease is the most commonly recognized *Bartonella* infection. In the United States, it is estimated that 25,000 cases occur each year. The cat flea is believed to be involved in transmission. Typically, in about 90% of cases there is a history of a cat bite, scratch, or lick, and one risk factor is having a cat in the home, especially with children under 1 year of age. Typically, children between 2 and 14 years of age are affected. The disease is usually self-limiting in the immunocompetent, in whom it usually occurs, with one or more papules, vesicles, or pustules occurring 3 to 10 days after the bite or scratch. Lymphadenopathy then develops, commonly axillary, cervical, or inguinal. These can take several months to resolve. Sometimes low-grade fever and malaise may be seen. Antibiotic therapy does not usually alter the course of infection. Complicated or atypical cat scratch disease can include neurologic, ophthalmologic, and systemic manifestations and is more likely in persons who are immunosuppressed (Boulouis et al., 2005; Slater & Welch, 2005; Walker et al., 2006).

In 1983, Stoler, Bonfiglio, Steigbigel, and Pereira described atypical skin lesions that became known as bacillary angiomatosis (BA) in persons with acquired immunodeficiency syndrome (AIDS). Bacillary angiomatosis is a vascular, proliferative lesion that occurs most frequently subcutaneously as nodules, or more superficially as papules, warts, or hyperkeratotic plaques that are typically reddish purple with a diameter of about 1 cm. Histologically, lobular proliferation of blood vessels is seen, and the lesions may bleed easily. Lesions may occur in other sites such as the gastrointestinal tract, the larynx, and bones and may also occur in the immunocompetent (Slater & Welch, 2005). Bacillary peliosis (BP) is a vasculoproliferative lesion resulting in the development of cystic blood-filled spaces that occurs most frequently in the liver parenchyma, spleen, and sometimes lymph nodes, nearly always in persons with AIDS (Slater & Welch, 2005). Bacillary angiomatosis and BP can result from both *B. quintana* and *B. henselae*. Bacteremia and endocarditis may occur in both the immunocompetent and the immunocompromised, often from *B. quintana*, *B. elizabethae*, and *B. henselae* (Walker et al., 2006).

Emerging Viral Diseases

The greatest number of significant emerging infectious agents and diseases are viral. Many of these are hemorrhagic fevers whose agents have been recognized relatively recently and tend to be seen in certain geographic distributions in North America (such as hantavirus pulmonary syndrome), Asia (such as hemorrhagic fever with renal syndrome), Africa (such as Ebola fever), and South America (such as Bolivian hemorrhagic fever), often with high mortality rates (see chapters 11 and 8). The arbovirus causing dengue has extended its range. In addition, metapneumovirus, monkeypox, severe acute respiratory syndrome (SARS), West Nile virus (see chapters 18, 19, 22, and 23), Nipah virus (see below), human bocavirus (see Appendix A, Table A.4), and others were recognized. The most notorious new viral EID was HIV infection/AIDS, which has had a considerable clinical, social, and political impact (see chapter 13). Less exotic, but nevertheless a very important viral disease, is influenza or the flu (see chapter 14), in which new strains have evolved. Also, further newly identified viruses cause hepatitis and other liver diseases such as hepatitis C (see chapter 12) and the TT virus. Chikungunya virus has been known since the 1950s in Africa but has extended its range not only to Asia but to islands in the Indian Ocean and affects more than 260,000 persons (Parola et al., 2006). As of fall 2006, this mosquito-borne virus has infected more than 25% of the inhabitants of the Reunion Islands and has characteristics and severity previously undescribed (Bessaud et al., 2006). Specific emerging viral infections are discussed in individual chapters and in Appendix A, Table A.4. Two are considered briefly below.

Influenza itself is not a true emerging infectious disease; however, the virus strains causing influenza mutate frequently, resulting in lack of resistance in human populations. Influenza has caused pandemics leading to the deaths of millions. Some flu strains have crossed species. For example, in 1997, in Hong Kong, a child died of viral pneumonia and multiorgan failure after an outbreak of H5N1 avian influenza occurred in fowl such as ducks and chickens. It was the first time that an avian influenza virus was isolated from a human with respiratory infection, and this led to fears of a new pandemic (Shortridge et al., 2000).

Currently, there is concern worldwide about the possibility of a new pandemic due to the avian influenza A strain H5N1. Despite the fact that human-to-human transmission has not been effective, by February 6, 2007, 272 confirmed human cases and 166 reported deaths had been identified by the World Health Organization (2007). As well as for human cases, surveillance is being maintained worldwide for cases in poultry, migratory birds, waterfowl, and the like, and depending on infection, various steps have been taken that include bans on imports, culling, restricting live markets and restrictions on movement of animals. Guidelines for pharmacological management of sporadic avian influenza A (H5N1) virus infection have been issued by WHO and would not apply to a pandemic situation (Schünemann et al., 2007). Other strains of influenza virus such as H9N2 have been isolated from poultry. This strain has also been isolated from pigs, other animals, and persons with influenza-like illness, and it is also a candidate for causing a pandemic (Shortridge et al., 2000). Because fowl are a reservoir for the influenza virus, the practice of raising pigs and ducks together as is done in China, where crowding is also a factor, allows viruses to recombine, with pigs as a vessel, and enables the virus to potentially cross the species barrier to humans. Altered viral genes can result not only in cross-species transfer but also in altered virulence (Hatta, Gao, Halfmann, & Kawaoka, 2001). This is also an example of how cultural practices and social conditions influence infectious disease spread. Avian influenza is discussed in depth in chapter 14. Another example of close contact of various food animals and their microorganisms with each other and with humans comes in the so-called "wet markets" featuring a wide variety of exotic animals including civet cats and bats that are sold as delicacies (Cheng, 2007; Chomel, Belotto, & Meslin, 2007; Woo et al., 2006). These markets are popular in Asia, and also in urban areas with large Asian populations such as San Francisco. Woo, Lau and Yuen (2006) discuss the role of the Chinese wet markets in the emergence, amplification, and dissemination of EIDs.

Both Nipah and Hendra viruses have been recently identified and are in the Henipavirus family (Eaton, Broder, Middleton, & Wang, 2006). Hendra virus was identified in Australia as follows. An outbreak of an acute, lethal respiratory disease in Hendra, a suburb of Brisbane, occurred in a group of thoroughbred horses in September 1994. A trainer and a stable hand became ill, and the trainer died of respiratory disease (Selvey et al., 1995). The next reported incident involved a sugarcane farmer in Mackay, near Hendra, who had assisted at autopsies of horses that had died of an acute illness in August 1994. He was subsequently diagnosed with a viral infection in 1995 that was then called equine morbillivirus (the earlier name for Hendra virus). The farmer died later of meningoencephalitis, which was believed to have been in a latent phase for a year before reactivating to result in his fatal illness. A search for a reservoir of the infection resulted in the isolation of the virus from fruit bats, known also as flying foxes, that was shown to be identical to the virus from the lung of one of the horses that had died. Presumably, in both cases the humans were infected by close contact with the horses that had been infected by the fruit bats (Mackenzie, 1999; Murray et al., 1998). Since that time, a few other human cases have been identified, most recently in 2004. Nipah virus, on the other hand, has caused larger, more serious outbreaks. It was first identified in humans in 1998 in Malaysia, where it caused mainly neurological illness including encephalitis, and was associated with infected pigs that acquired the disease from flying foxes (bats) carrying the organism. The most recent outbreaks have occurred in Bangladesh from 2001 to 2004, with a case fatality rate of approximately 75% and documented person-to-person transmission (Eaton et al., 2006; Eaton, Broder, & Wang, 2005). Both of these viruses have biosafety levels of 4, and Nipah virus is considered a potential agent for bioterrorism.

Emerging Fungal Diseases

In comparison with the other categories of microbes, fewer known emerging fungal diseases affect humans. Invasive fungi have increased in incidence. In many cases, they appear as opportunistic infections threatening patients who are immunosuppressed because of such conditions as HIV infection, malignancy, organ transplantation, prematurity, or even aging, and there is also a connection with medical interventions such as medical devices (Pfaller, Pappas, & Wingard, 2006). In immunocompromised persons, the opportunistic infection seen may depend on the infection endemic in the geographic area or on where the patient has traveled. *Penicillium marneffei*, for example, is most commonly seen in Southeast Asia, where it is a relatively frequent opportunistic infection in persons with HIV infection. It has also been seen in AIDS patients outside of this region (Vanittanakom, Cooper, Fisher, & Sirisanthana, 2006). Other endemic fungi such as *Coccidioides immitis* in the southwestern United States cause respiratory disease and are increasing in incidence in both the immunologically compromised and in those who have relocated to endemic areas, many of whom are elderly and have some degree of immunosuppression. Another problematic area is the recognition of some infections due to fungi originally thought to be nonpathogenic, and the finding that some species are becoming resistant to treatment with the standard antifungal agents (Kauffman, 2006; Pfaller, et al., 2006). Furthermore, there has been a change in etiology of these infections, with non-albicans *Candida* species and non-*fumigatus Aspergillus* species becoming more frequent as are other invasive moulds such as Zygomycetes (e.g., *Mucor* spp., *Rhizopus* spp.), *Fusarium* spp., and *Scedosporium* spp. and other yeasts such as *Trichosporon* spp. and *Cryptococcus gattii* (Kauffman, 2006; Nucci & Anaissie, 2005; Nucci & Marr, 2005).

C. gattii is an emerging yeast infection that was known to cause illness in immunocompetent people and was largely restricted to Australia, where it was believed to have an ecologic niche related to eucalyptus. It is also known to affect persons with AIDS in the United States, Australia, Southeast Asia, Africa, and more rarely in Europe. Since 1999, it has been recognized as the cause of an outbreak on Vancouver Island in Canada that affected more than 100 persons (Chaturvedi, Dyavaiah, Larsen, & Chaturvedi, 2005; Kidd et al., 2004; Nucci & Marr, 2005). Infections have been also identified on the British Columbia mainland and in the states of Washington and Oregon in persons who have not traveled elsewhere. Infection is through inhalation, and both pulmonary and central nervous system disease can occur. *C. gattii* has been isolated in vehicle wheel wells and on footwear, and dispersal may also occur during forestry activities. Dispersal of the organism might also occur through bird and animal migration but the environmental conditions responsible for this emergence are not yet known (Kidd et al., 2007; MacDougall et al., 2007; Nucci & Marr, 2005). *Fusarium* spp. are ubiquitous in soil and plants but are increasingly associated with systemic and localized infections in humans (Zhang et al., 2006). As of May 18, 2006, the CDC (2006g) identified 130 confirmed cases from 26 states of *Fusarium* keratitis. Most of the people affected were contact lens wearers, and infection was severe enough that about one third required corneal transplantation. An association was made between use of Bausch & Lomb's ReNu with MoistureLoc contact lens solution and the infection. The product was voluntarily removed from the market on May 15, 2006. Emerging fungal infections are considered in depth in Chapter 10 and are summarized in Appendix A, Table A.2.

Emerging Parasitic Diseases

Many of the emerging parasitic diseases were thought of as affecting relatively few people in developed countries. This view began to change when an increased prevalence of what were thought of as rare or exotic infections began to be seen more commonly in connection with the immunosuppression of HIV disease. This view also had to be quickly reevaluated when the outbreak of cryptosporidiosis, resulting from contamination of the municipal water supply, affecting over 400,000 persons occurred in Milwaukee, Wisconsin, in 1993. Many of the parasitic diseases are already known, but parasites that have emerged relatively recently are *Cyclospora cayetanensis* (see chapter 6), *Cryptosporidium hominis* and *Cryptosporidium parvum* (see chapter 5), *Babesia microti* (see chapter 16), and microsporidia. Most are protozoal parasites, but increased helminth infections are also being seen. Many are food- or waterborne (see Appendix B, Table B.1) and are discussed later in this chapter. Malaria, an important parasitic disease worldwide, is increasingly changing its geographic range and becoming resistant to the usual agents used in treatment (see chapter 17).

A familiar parasite, *Trichinella*, usually acquired through ingestion of undercooked pork, is now emerging as a result of infected horsemeat in countries in Europe where eating horsemeat is popular. Acquiring the parasite may also result from eating bear meat and other exotic meats as the demand for variety and the unusual expands (Pozio, 2000; Slifko, Smith, & Rose, 2000). Likewise, *Taenia solium*, the pork tapeworm, was recognized in the 1980s as causing neurocysticercosis or infection of the central nervous system. Recognition of neurocysticercosis as a major cause of neurologic disease including epilepsy resulted from improved diagnostic examinations such as computed axial tomography and magnetic resonance imaging scanning; from large numbers of immigrants to the United States from developing countries who were diagnosed with neurocysticercosis (for example, in Los Angeles, the diagnosis increased fourfold between 1977 and 1981); and from improved serological assays for diagnosis that allowed accurate prevalence estimates. In the United States, most cases appear in immigrants or in persons born in this country who have traveled to rural areas in endemic countries such as parts of Africa, Asia, and Latin America (Garcia, Wittner, Coyle, Tanowitz, & White, 2006). In the United States, there are more prevalent foci of infection in the New York City area, Texas, and parts of California near the Mexican border. However, it may be an unrecognized problem in other areas, especially those with a high concentration of Hispanic immigrants ("Cyticercosis" 2007; Townes, Hoffmann, & Kohn, 2004). Seizures are the presenting symptom in the majority of cases, but some learning disabilities in children have been found to be indicators of neurocysticercosis (Garcia et al., 2006). Locally acquired cases are known in the United States. In one well-known instance, orthodox Jews in one New York community, who would not have themselves been in contact with pork, acquired neurocysticercosis through eating food prepared by immigrant domestic workers who carried *Taenia* (Schantz et al., 1992).

While malaria is no longer considered endemic in the United States, it once was, and its range and resistance patterns are extending. Conditions are met in the United States for the potential transmission of malaria, including people who have malarial parasites in their blood and the presence of the appropriate vector. While cases of malaria have been diagnosed in the United States subsequent to travel to endemic regions (see chapter 17), outbreaks of mosquito-borne transmission in New York, New Jersey, California, Texas, and other areas in the United States have been described. These are usually due to *Plasmodium vivax*, but some are also due to the more severe *Plasmodium falciparum*. In 2004, the last year data were available, the CDC (Skarbinski et al., 2006) reported 8 cases of malaria that were acquired in the United States.

Microsporidia are a group of obligate intracellular parasites that have been considered as protozoa but that may be reclassified to fungi because of the results of molecular phylogenetic analysis (Weiss & Schwartz, 2006). The first human case of microsporidiosis was reported in 1959 in a 9-year-old child with neurological symptoms (Matsubayashi, Koike, Mikata, Takei, & Hagiwara, 1959). Various genera and species infect humans, and the *Encephalitozoon* particularly affect immunosuppressed populations (Walker et al., 2006). In 1985, there were reports of diarrhea in patients with AIDS due to *Enterocytozoon bieneusi*, thus beginning the recognition of their importance in persons with AIDS (Desportes et al., 1985). At present, the following genera are known to cause human infection: *Vittaforma*, *Nosema*, *Pleistophora*, *Encephalitozoon*, *Enterocytozoon*, *Trachipleistophora*, *Anncaliia* (formerly *Brachiola*), and *Microsporidium* (Didier & Weiss, 2006; Franzen, Nassonova, Scholmerich, & Issi, 2006; Mathis, Weber, & Deplazes, 2005; Weiss & Schwartz, 2006). While immunocompromised persons are most susceptible to microsporidiosis, those who are immunocompetent may also develop infection. The microsporidia can cause a wide range of infection including the digestive, reproductive, muscle, respiratory, excretory, and nervous systems as well as eye infections, sinusitis, and disseminated infections (Weiss & Schwartz, 2006). Person-to-person transmission through the fecal–oral and oral–oral pathways, inhalation of air droplets, ingestion of contaminated water or food, and, in the *Encephalitozoon* species, sexual transmission are all possible (Mathis et al., 2005; Walker et al., 2006). Transplacental transmission occurs among some nonhuman species (Didier & Weiss, 2006).The microsporidia and other emerging parasitic diseases are summarized in Appendix A, Table A.3.

Emerging Prion Diseases

In the past, there have been debates over the nature of prions, a type of protein particle that is devoid of nucleic acids. Prion proteins that are altered usually through conformational changes such as misfolding are considered to be the etiologic agents of a group of fatal neurodegenerative diseases known as the transmissible spongiform encephalopathies (TSEs), also called the prion diseases (Collinge, 2005). Animal diseases include bovine spongiform encephalopathy (BSE), scrapie, and others. In humans, TSEs include inherited (also called genetic or familial), sporadic, and acquired forms. The human TSEs that have attracted the most attention are Creutzfeldt–Jakob disease, especially that acquired through iatrogenic means such as growth hormone injections and corneal transplants; variant Creutzfeldt–Jakob disease (vCJD), a human form of BSE, commonly referred to as "mad cow" disease; and kuru, acquired through formerly practiced ritualistic cannibalism in the Fore tribe in Papua New Guinea. The current BSE epidemic in the United Kingdom emerged in the 1980s and has been reported in other countries as well. Linkage to vCJD was first noted in a 1996 report (Will et al., 1996). It was not until March 2006 that the European Union lifted the ban on British beef imports. North America has not been immune to BSE. In Canada, a BSE-infected cow was discovered in Alberta in May 2003, and two more were confirmed in 2005. The United States confirmed BSE in a dairy cow in Washington that had been imported from Canada, and in June 2005, BSE was confirmed in a cow in Texas born in the United States. In March 2006, another case was confirmed in a native-born cow in Alabama. All were born before the 1997 feed regulations were put in place. The trade repercussions varied in severity and time (Mathews, Vandeveer, & Gustafson, 2006). Prion diseases can be transmitted via stainless steel surgical instruments; because infective prions have shown resistance to the usual sterilization procedures, there are recommendations for sterilization (Belay & Schonberger, 2005). Continued concern about transmission from infected meats, meat products such as gelatin, or even products such as bone meal has led to various bans of imported products. Effects and reactions are political, social, and economic. Prion diseases are considered in depth in chapter 21.

SELECTED TRANSMISSION MODES OF EIDS

Vectorborne Diseases

Vectors usually are arthropods, especially insects, that are capable of transmitting microorganisms to vertebrate hosts. Arthropods are vectors for viral, bacterial, and parasitic agents. Arthropod-borne viral diseases called arboviruses are more common than bacterial or parasitic diseases spread in this way. More than 40% of viruses that infect mammals move from host to host by arthropod vectors (van den Heuvel, Hogenhout, & van der Wilk, 1999). Vectors such as mosquitoes can also be dispersed by air travel and by container ships, allowing the possible establishment of new foci, depending on whether other conditions such as climate are favorable (Tatem, Hay, & Rogers, 2006). There are about 100 known arboviruses that are pathogenic for humans—some of which are emerging or reemerging and others that do not fit this classification. Among bacteria, the group known as rickettsiae is often arthropod associated. Rickettsial diseases include many of the "spotted" and tick-bite fevers (Parola, Paddock, & Raoult, 2005). Examples of emerging vectorborne diseases are listed in Appendix B, Table B.3. Selected important vectorborne EIDs are further discussed in relation to recreational activities and travel in chapter 25 as well as in relation to specific diseases such as Lyme disease, ehrlichiosis, anaplasmosis, babesiosis, and malaria in chapters 16 and 17.

Primary vectors are the major species involved in transmission of a specific disease, while secondary vectors include species involved in transmission of a specific disease only under certain conditions (Goddard, 1999). Thus, not every mosquito can transmit *Plasmodium vivax*, one of the parasites causing malaria. Rather, *P. vivax* is mainly transmitted by the *Anopheles* mosquito, species of which are distributed throughout the United States. Arthropods may transmit microorganisms mechanically (e.g., when flies feed on excrement and then walk on food) or biologically (e.g., when the organism multiplies or develops in the arthropod, as in the multiplication of *Plasmodium* in mosquitoes transmitting malaria) (Ribeiro & Valenzuela, 2006). Mosquitoes are the major vector of infectious diseases in humans, followed by ticks (Parola & Raoult, 2001). Arthropods known to transmit microorganisms leading to disease are listed with a disease example:

- mosquitoes (*Culex pipiens*, West Nile virus, and West Nile fever),
- lice (the body louse, *Rickettsia prowazekii*, and epidemic typhus),
- ticks (the deer tick, *Borrelia burgdorferi*, and Lyme disease),
- mites (mouse mite, *Rickettsia akari*, and rickettsialpox),
- midges (biting midges, Oropouche virus, and Oropouche fever),
- fleas (the oriental rat flea, *Yersinia pestis*, and plague), and
- flies (tsetse fly, *Trypanosoma brucei gambiense*, and sleeping sickness or human African trypanosomiasis, Gambian type) (Guerrant, Walker, & Weller, 2006; Mandell, Bennett, & Dolin, 2005).

Of interest in understanding, managing, and ultimately preventing and controlling the vectorborne EIDs is knowledge about (a) the contributions of ecologic, meteorologic, and climactic conditions in influencing environmental, vector, and reservoir variables; (b) the biology of the vector and the host reservoir; and (c) the human characteristics that contribute to emergence including behavior and culture (see chapter 28). Vectorborne diseases are particularly affected by environmental factors, including climate and weather conditions such as temperature increase, rainfall amounts, and other factors such as carbon dioxide concentrations, urbanization, deforestation, irrigation, agricultural techniques, increased global trade, and travel (Sutherst, 2004). For example, the emergence of the Sin Nombre virus resulting in hantavirus pulmonary syndrome initially in the southwestern United States was said to occur following specific weather conditions that led to an increase in prevalence of the piñon nuts that fed deer mice carrying the hantavirus as well as promoting the growth of the vegetation providing shelter for them (Engelthaler et al., 1999). A concern with vectorborne diseases is the potential for an organism to adapt to a new vector and thus expand its geographic range. An example is the outbreak in eastern Arizona from 2002 to 2004 of Rocky Mountain spotted fever outside its usual range via the common dog tick, *Rhipicephalus sanguineus*, as a vector for the causative rickettsia, *Rickettsia rickettsii* (Demma et al., 2005). In another instance, the Lone Star ticks usually found in the Southeast have been increasing in number in New England. They are more aggressive and are known to be able to transmit such diseases as ehrlichiosis, Rocky Mountain spotted fever, and tularemia but are not yet known to transmit Lyme disease, which is endemic in the area ("Lone Star tick," 2006).

Foodborne and Waterborne Diseases

Overlap exists to some extent between foodborne and waterborne infectious diseases. Those organisms that are ingested and then cause illness (usually gastrointestinal) are usually transmissible through food, water, or both. In addition, food may be contaminated by water sources during activities such as planting, growing, harvesting, processing, preparation, and handling. The fecal–oral and person–person modes are the major routes of transmission of foodborne and waterborne EIDs. Causes of emerging foodborne illness include viruses, bacteria, parasites, altered prions, toxins that may or may not be of microbial origin, and other nonmicrobial substances. Each year approximately 76 million cases of foodborne illness and about 5,000 deaths occur in the United States (CDC, 2006d). In many countries, particularly developing ones, true global estimates are lacking for many reasons including the inability to link most outbreaks with a given food, lack of organization and funds to conduct surveillance, and other reasons (Flint et al., 2005). In the United States, the Foodborne Diseases Active Surveillance Network (FoodNet) of the CDC's Emerging

Infections Program collects data from 10 states across the country to compare infections due to specific bacterial and parasitic infections as does the Division of Foodborne Disease Outbreak Surveillance System of CDC. Not all are included in surveillance. In the most recent report of FoodNet for 2005, the highest number of cases in descending order of frequency were from *Salmonella*, *Campylobacter*, *Shigella*, *Cryptosporidium*, *Listeria*, *Vibrio*, and *Cyclospora* species as well as *E. coli* O157:H7.

Viruses are a frequent cause of gastroenteritis from food but are not easily monitored due to laboratory requirements. For example, norovirus is not routinely monitored in this surveillance, yet it is considered that noroviruses cause a large proportion of foodborne gastroenteritis in the United States, causing more than 23 million infections each year (Estes, Prasad, & Atmar, 2006). Noroviruses (formerly Norwalk viruses) were recognized in 1972 in connection with a gastroenteritis outbreak in Norwalk, Ohio, that occurred in 1968. In a recent outbreak due to norovirus infection at a fast-food restaurant in Michigan in 2005, gastroenteritis affecting over 100 people resulted from a food handler who returned to work within a few hours of his own gastrointestinal illness, which he had acquired from his child (CDC, 2006c). Rotavirus diarrhea, occurring primarily in children, was first identified in 1973 in Australia. In another instance, several hepatitis A virus outbreaks, including one in 2003 in Pennsylvania, were due to green onions imported from Mexico and served in a salsa (Wheeler et al., 2005). Raw fruits and vegetables are increasingly a source for foodborne disease. *Cryptosporidium*, usually thought of as a waterborne infection, can also be transmitted directly from food and was transmitted to 88 people in Washington, DC, through raw produce prepared by an infected food handler (Quiroz et al., 2000).

Several factors are thought to be responsible for the increase in the number and type of foodborne diseases. These include:

- demographic changes resulting in growing numbers of the population with immune compromise such as in chronic illness, HIV infection, aging, or posttransplant;
- breakdown in surveillance;
- demand for organic foods;
- demand for exotic food, in some cases resulting in smuggled trade of delicacies such as bushmeat that may be infected and in travel to eat exotic meats such as civet cats which are considered a delicacy but which have been implicated as a source of the 2003 SARS outbreak in southern China (Cheng, 2007);
- demand for more and out-of-season produce leading to importation from some developing countries where agricultural practices result in compromised food safety;

- increased consumption of internationally distributed foods, such as when a cholera outbreak in Maryland resulted from ingestion of coconut milk imported from Southeast Asia and an incident of staphylococcal food poisoning in the United States was associated with eating mushrooms canned in China;
- cultural food practices and habits such as eating undercooked pork leading to trichinosis in Laotians in the United States and eating raw or lightly cooked foods of animal origin such as shellfish, fish (as sushi or sashimi), or ground beef (as in steak tartare or served very rare);
- decrease in knowledge of food safety practices in the home such as washing hands thoroughly after handling raw poultry;
- reliance on convenience foods with a higher consumption of food not prepared in the home (this includes food from both eat-in restaurants and take-out facilities such as fast-food restaurants and supermarkets; it also includes partial preparation of foods such as melons sliced in the produce section of supermarkets, allowing contamination of the inner surface by microbes on the outer surface);
- greater prevalence of food served in a salad bar or buffet setting, allowing contamination or varying temperature controls; and
- economic development changes (e.g., shifting from a cold season oyster harvest to year round harvests in the Gulf of Mexico has been associated with the emergence of *Vibrio vulnificans* in oysters [Slutsker, Altekruse, & Swerdlow, 1998], which could be prevented if raw and undercooked oysters were not eaten).

Another contributing factor is rising temperatures of ocean water. In one instance, gastroenteritis occurred among passengers on a cruise ship. The source was raw oysters contaminated with *Vibrio parahaemolyticus*, a gram-negative bacterium that inhabits warm waters. In this instance, they were harvested from Alaskan waters, formerly thought to be too cold to support high enough levels of the organism to cause disease (McLaughlin et al., 2005). In 2006, a large outbreak occurred connected to eating raw or undercooked oysters from Washington ("*Vibrio parahaemolyticus*, Shellfish," 2006).

Contamination of foods can occur at multiple points from planting, growing, harvesting, and initial processing through transporting, distributing, later processing, preparing, and serving. Contamination can arise from contaminated irrigation water; use of manure or human fertilizer; poor sanitary practices in the fields, in handling areas, and during preparation, and serving; contaminated wash water; use of unclean vehicles for transportation and/or distribution; and cross contamination. In a graphic illustration, observers have described Guatemalan raspberries in open containers waiting for shipment being contaminated by bird droppings until they were coated in white. The first identified outbreaks of *C. cayetanensis* in the United States resulted from eating contaminated Guatemalan raspberries (see chapter 6). Outbreaks arise from newly recognized pathogens and also from known pathogens contaminating foods not previously known to support their growth such as lettuce, green onions, spinach, and apple cider (*E. coli* O157:H7).

Because of changes in food distribution, outbreaks may now be widespread and harder to recognize. For example, an outbreak of *Salmonella* serotype Enteritidis infection was noticed because of an increase of gastroenteritis in southern Minnesota. An ice cream premix that was pasteurized at a plant on-site had to be transported to another plant to be made into a nationally distributed brand of ice cream. The tanker trucks had previously been used to haul raw eggs. Postpasteurization contamination of the premix resulted in about 250,000 illnesses from eating the ice cream prepared from the premix that became contaminated during transport (Hennessy et al., 1996). *Salmonella* serotype Enteritidis is decreasing after being the most commonly implicated *Salmonella* serotype contaminating eggs, many of which were contaminated by the transovarian route. The decrease is attributed to programs to prevent the organism from infecting flocks, early refrigeration of eggs, and education about the risk of eating raw or undercooked eggs (Braden, 2006). In 2006, two outbreaks involving 29 persons of *Salmonella enterica* serotype Enteritidis were traced to certain frozen stuffed chicken entrees that were prepared in the microwave. It is believed that the microwave cooking may have resulted in not evenly heating the entrees to the required temperature for full cooking ("Salmonellosis, frozen chicken," 2006).

The consumption of fish, often raw or undercooked, has increased due to several factors: improvements in transport of fish, greater accessibility, awareness of health benefits, cultural influences, and increased per capita income. Sushi bars serving raw fish have multiplied. A new disease, metorchiasis, is caused by the North American liver fluke, *Metorchis conjunctus*, a helminth that is considered to have emerged in 1993. In Montreal, Canada, 27 persons became ill after eating sashimi (raw fish) infected with this organism at a picnic. The long-term oncogenic potential of this infection is unknown (MacLean, 1998). Another popular way of eating fish raw, as ceviche, prepared with lemon or lime juice to "cook" it, has resulted in foodborne infection. Gnathostomosis (gnathostomiasis), caused by a nematode, is another parasitic disease contracted from undercooked fish (Rojas-Molina, Pedraza-Sanchez, Torres-Bibiano, Meza-Martinez, & Escobar-Gutierrez, 1999). Other foodborne trematodes such as liver, intestinal, and lung flukes are considered emerging, in part because of the expansion of aquaculture and greater ease in bringing freshwater fish and crustaceans to both local and international markets (Keiser & Utzinger, 2005). For example, in California, a small number of cases of *Paragonimus* (a lung fluke) infection occurred in California after eating raw or undercooked freshwater imported crab ("Paragonimus," 2006). In China, an outbreak beginning in August 2006 involved imported partly cooked Amazonian black snails, which are considered a delicacy. This resulted in more than 130 cases of *Angiostrongylus* meningitis ("*Angiostrongylus* meningitis," 2006).

Foodborne illnesses have a public health impact beyond the discomfort of acute gastroenteritis. Many can cause disability and chronic sequelae, particularly in those who are immunologically compromised to some degree such as the elderly, children, transplant recipients, and persons with HIV infection. An example is Guillain–Barré syndrome and reactive arthritis secondary to *Campylobacter* infection (Leirisalo-Repo, 2005; Tam et al., 2006). Foodborne illness is often underreported, particularly when milder or nonspecific in nature. Some foodborne pathogens are also spread through water or from person to person, and some of these pathogens are probably not yet identified.

Among well-publicized outbreaks of food-related emerging infections have been those of *E. coli* O157:H7 through contaminated ground beef, unpasteurized apple cider, spinach, lettuce, and alfalfa sprouts (see chapter 9); *Cyclospora* contamination of Guatemalan raspberries, mesclun lettuce, fresh snow peas, and fresh basil leaves (see chapter 6); vCJD and contaminated beef (see chapter 21); *Listeria monocytogenes* and hot dogs, soft cheeses, and deli meats (Gottlieb et al., 2006); and strains of *Salmonella enterica* serotype Newport contaminating alfalfa sprouts (CDC, 2001a). Increasingly, fresh produce such as lettuce has been a vehicle for more foodborne illnesses than previously known, such as outbreaks of *Yersinia pseudotuberculosis* linked to fresh lettuce. Research is revealing more about methods of contamination. For example, in the case of *E. coli* O157:H7, lettuce plants irrigated with contaminated water can take up the organism, ultimately resulting in distribution throughout the leaves of the plant. Warm tomatoes that are put into cold water can take up *Salmonella*. Thus, protection must be tailored to these sources of infection because consumer washing of the produce in these cases would not be protective (Tauxe, 2004).

L. monocytogenes is an anaerobic nonsporulating gram-positive bacterium capable of causing various illness in both humans and animals. In the past, it has been mostly associated with disease in those who are immunocompromised, including the elderly and pregnant women, their fetuses, and newborns (Gottlieb et al., 2006; B. Lorber, 2005). Transmission is foodborne or occurs vertically from the infected mother to child transplacentally or at birth, although less commonly there can be cross-infection in nurseries (B. Lorber, 2005). Epidemic illnesses have been largely linked to refrigerated ready-to-eat foods such as coleslaw, hot dogs, deli meats, milk, soft low-acid cheeses such as Brie and feta, pâté, and, in one instance, to contaminated corn in a salad (Aureli et al., 2000; CDC, 2001a). In a recent outbreak, in 2002, turkey deli meat was the source of infection, and the investigation led to new regulations for control (Gottlieb et al., 2006). The usual clinical picture includes diarrhea, nausea, vomiting, and fever, which commonly progresses or presents as bacteremia or meningitis. The case fatality rate is high, being about 25%. Pregnant women are particularly vulnerable, with manifestations of an acute febrile illness often with headache, backache, and myalgias along with bacteremia. There is a high risk of spontaneous abortion, stillbirth, or neonatal death, and among women with listeriosis in pregnancy, about two thirds of surviving newborns develop neonatal listeriosis (B. Lorber, 2005).

Waterborne emerging infections may result from ingestion of contaminated drinking water or from contact with contaminated recreational water. Such infections may originate in the community in which the person resides or may occur in the course of recreational pursuits in developed areas, during travel to foreign locales, or in wilderness areas (see chapter 25 for a discussion of EIDs in relation to travel and recreation). Conditions such as flooding may provide temporary favorable conditions for outbreaks of emerging infectious diseases through a variety of mechanisms including runoff from contaminated fields. Contaminated water may contaminate food such as in grocery store spray systems, or contamination may result from direct exposure to organisms in these sprays such as *Legionella pneumophila*. Waterborne infections can also occur from showering. In an outbreak of legionellosis in a children's hospital, showering was implicated as the means of exposure to contaminated potable water (Campins et al., 2000). Hospital water supplies and water used for therapeutic purposes can unwittingly become the source for emerging infections such as *Legionella* and atypical mycobacteria (Emmerson, 2001). *L. pneumophila* infections can be acquired through exposure to sprays from whirlpools, hot tubs, spas, and the like and have even been associated with visiting an aquarium (Greig et al., 2004). *Legionella* is discussed in depth in chapter 15. Noroviruses have increasingly been associated with drinking water outbreaks, often causing gastroenteritis. They are often difficult to recognize because of the difficulty in growing them prior to newer technology that uses genome-based methods, because an outbreak may not be recognized, and because the number of organisms may be low. Noroviruses have been implicated in both waterborne and foodborne outbreaks on cruise ships, hospitals, nursing homes, and other closed environments. Infection is widespread and common. In developed countries, more than 50% show antibodies to norovirus. Incubation periods are typically 24 to 48 hours and result in gastroenteritis. There is a high secondary attack rate. Typically, resolution occurs spontaneously, but sometimes there are recurrent outbreaks; for example, in one instance 12 recurrent outbreaks were reported despite attempts to determine the source and to disinfect the ship between sailings (Maunula, Miettinen, & von Bonsdorff, 2005; Treanor & Dolin, 2005).

The CDC defines recreational water settings as swimming pools, wading pools, whirlpools, hot tubs, spas, water parks, interactive fountains, and fresh and marine surface waters such as lakes, beaches, and springs (CDC, 2006f). The most frequent illnesses resulting from recreational waterborne infections are gastrointestinal illness, dermatitis, respiratory, and meningoencephalitis, the latter resulting from infection by free-living amoeba such as *Naegleria fowleri* when warm fresh water or heated swimming pool water is forced up the nose of a person engaging in water activities including swimming or diving, usually during the summer when conditions are favorable for such infection (CDC, 2004, 2006f; Visvesvara & Maguire, 2006). In an outbreak in 2003, multiple members of a college football team developed MRSA after using a spa treated with an unapproved disinfectant (CDC, 2006f). In one outbreak in Maine, involving a toddler wading pool in July 2002, 9 persons were affected. The cause was *E. coli* O157:H7. Tap water was used to fill the pool, and it is believed that high density and a fecal accident were contributing factors (CDC, 2004).

Drinking water systems may be community or noncommunity systems. The latter may be transient or nontransient. Millions of people per year use noncommunity water systems while traveling or working, usually without being aware of this. For example, transient noncommunity systems include highway rest stations, restaurants, and parks with their own water systems. Treatment, standards, and regulations vary according to the type of system (CDC, 2006e). Contamination of drinking water may occur through surface or groundwater source contamination, breaks in the integrity of well and/or distribution systems, and breaks in disinfection or water treatment. Waterborne disease outbreaks associated with both drinking water and recreational water are discussed below.

During 2003 and 2004, the most recent data available, 19 states reported 36 outbreaks of waterborne infection associated with drinking water, 30 of which were associated with water intended for drinking, causing illness in about 2,760 persons. Of the outbreaks where a cause was identified, 17 or 68.0% were of known infectious etiology: 76.5% were bacterial including 61.5% that were caused by *Legionella* spp., and others such as *Campylobacter* spp. and *E. coli* O157:H7; 11.8% were mixed etiology, 5.9% were caused by a parasite, and 5.9% were caused by norovirus. Included in mixed etiology were *Helicobacter* spp., *Campylobacter* spp., *Cryptosporidium* spp., *Entamoeba* spp., and *Giardia* spp. (CDC, 2006e). In 1997, in one of the cryptosporidiosis outbreaks in Texas, about 1,400 persons became ill after a lightening storm caused a spill of raw sewage that resulted in contamination of municipal utility district wells, illustrating how weather conditions can play a role, even indirectly, in the emergence of infectious diseases (CDC, 2000). Earlier, *Cryptosporidium* was responsible for the largest known outbreak of emerging infectious disease, an occurrence of contamination of drinking water in the United States, when about 403,000 persons became ill in Milwaukee, Wisconsin, in 1993 (MacKenzie et al., 1994; see chapter 5).

Regarding recreational waterborne outbreaks during the same period, 26 states reported 62 outbreaks associated with recreational water (about 30% were fresh water and about 70% were treated water), causing illness in about 2,698 persons. About two-thirds were infectious in origin. The etiology was 32.3% bacterial, 29.0% unidentified, 24.2% parasitic, 9.7% viral, and 4.8% due to a chemical or toxin. Clinically, the most frequent outcomes seen were gastroenteritis, followed by dermatitis, meningoencephalitis, and acute respiratory illness. The most frequent bacterial pathogens were *Pseudomonas aeruginosa* (usually causing dermatitis), *Legionella* spp., *Plesiomonas shigelloides,* MRSA, *Shigella sonnei*, *Leptospira* spp., and others. The most frequent parasite was *Cryptosporidium*, followed by *Giardia intestinalis*, and *Naegleria fowleri*. Norovirus was identified in most of the outbreaks due to viral etiology, and there was one outbreak in which echovirus 9 was responsible for causing meningitis (CDC, 2006f). Prevention of food and waterborne infections is discussed in Appendix C, Tables C.1, C.2, and C.3.

Transfusion- and Transplant-Transmitted Emerging and Reemerging Infections

With the knowledge that HIV infection could be acquired via transfusion of blood or blood products came extensive political pressure to ensure the absolute safety of the transfusion of blood and blood products, especially in the United States. The ability to transmit infection by transfusion depends on a variety of elements including the pathogenicity of the agent, its prevalence in the blood donor population, the ability to persist in a host and if so in which cell type, recipient immunity, whether an asymptomatic phase is present, and if the infectious agent can persist in stored blood.

Changes in approaches to blood donation and screening have resulted in minimal risk for transfusion-transmitted diseases in the United States but not in zero risk. Elsewhere, the picture is different. The majority of countries do not have policies in place that would ensure safe blood donations, and many of these countries have a heavy burden of emerging infectious agents (Dodd & Leiby, 2004; Klein, 2000).

At times, pockets of specific risk occur that need to be immediately addressed such as the 1997 deferral of blood donations of members of the National Guard who had been exposed to ticks during a training exercise. Several later developed ehrlichiosis or Rocky Mountain spotted fever (Klein, 2000; McQuiston, Childs, Chamberland, & Tabor, for the Working Group on Transfusion Transmission of Tick-borne Diseases, 2000). Other examples of specific deferrals in response to potential emerging or reemerging infectious-disease risk include the decision in the United States to restrict donations as described in chapter 21 for those at risk for acquisition of the agent (altered prions) responsible for bovine spongiform encephalopathy and vCJD, including deferral for relatives of persons with Creutzfeldt–Jakob disease, and deferral of Desert Storm veterans because of exposure to *Leishmania donovani*, the parasitic agent of leishmaniasis (Klein, 2000). In light of the wider than realized spread of vCJD, most notably in Britain and western Europe, more stringent blood donation restrictions have been put in place to exclude persons who may have become infected with vCJD but who are not symptomatic. Donors of other tissues might also be considered for exclusion (Roos, 2001).

The HIV epidemic focused attention on transfusion and transplant safety issues in regard to emerging infections. Even in the last 20 years, a variety of viral agents with the potential to be transmitted via blood transfusion have emerged. In addition to HIV-1 and -2, they include human T-cell lymphotropic virus 1 (HTLV-1); HTLV-2; hepatitis C; Kaposi's sarcoma-associated virus, or human herpesvirus 8; the hepatitis G virus, or GB virus C; human herpesvirus 6; the putative hepatitis-linked TT virus, and West Nile virus (Alter, 2005; Dodd & Leiby, 2004). The potential for other nonemerging agents to be transmitted in this way also occurs. These agents include cytomegalovirus, dengue virus, *Trypanosoma cruzi*, *Plasmodium* spp., Epstein–Barr virus, and others, some of which pose particular risk to subsets of recipients such as those who are immunosuppressed. It is also believed that the SARS coronavirus may be transmissible in this way (Dodd & Leiby, 2004). Other microorganisms such as *B. microti*, and the prions responsible for variant Creutzfeldt-Jakob disease are transfusion transmissible (Alter, Stramer, & Dodd, 2007; Dietz et al., 2007; Leiby, 2006). Some agents pose a greater risk in areas with a high density of persons who have emigrated from countries where these agents are prevalent. They may also pose a risk to travelers needing a blood transfusion in countries where screening of the blood supply does not occur and where there are high concentrations of persons who have been infected (some chronically) with infectious agents such as those that cause malaria, HIV infection, hepatitis, dengue, trypanosomiasis, and others. For example, in Latin America, Chagas disease, caused by *T. cruzi*, is endemic. In the United States, persons who acquired the disease in childhood and who have immigrated to this country may be chronically infected, even if they are currently asymptomatic. Thus, the frequency of the organism in human blood varies across the population, being higher in areas of high concentration of immigrants from endemic countries. It has been suggested that prospective Latin American donors in the United States should be screened for *T. cruzi*, but this is a very sensitive area (Kirchhoff et al., 2006). Chagas disease has also been transmitted by transplantation (CDC, 2006a). In the United States in 2003 and 2004, one case and no cases, respectively, of transfusion-transmitted malaria in the United States were reported (Eliades et al., 2005; Skarbinski et al., 2006). Appendix B, Table B.3, provides information on transfusion-transmitted emerging/reemerging infectious diseases.

The current system used in the United States to ensure blood safety includes sensitive screening tests; education and stringent screening, questionnaires, selection, and deferral procedures for donors; postdonation product quarantine; a safety surveillance system; and donor tracing and notification when needed. Newer methods of testing donated blood such as nucleic acid testing increase blood safety (Chamberland, Alter, Busch, Nemo, & Ricketts, 2001). Xenotransplantation, the use of tissues and organs for animal to human transplantation, poses a potential risk of the transfer of zoonoses from the animal donor not only to the human recipient but also to persons who come into professional or personal contact with him or her. Of particular concern are viruses, especially those that can cross species barriers. The porcine endogenous retroviruses have been noted as particularly worrisome since pigs are thought to be a major potential future source of tissues and organs for transplant for infants and children (Cox & Zhong, 2005). These issues are discussed in the U.S. Public Health Service guideline on infectious disease issues in xenotransplantation (CDC, 2001b). Human-to-human transplantation has been a method of spread for CJD (see chapter 21), and rabies has also been transmitted by transplantation (Srinivasan et al., 2005). Parvovirus B19 has been transmitted by transplantation of both solid organs and stem cells. Since it is not screened for, the incidence is probably underestimated. It can manifest as refractory anemia posttransplant (Eid, Brown, Patel, & Razonable, 2006). There has been a reported case of lymphocytic choriomeningitis virus, causing meningitis, being transmitted by organ transplantation (Foster et al., 2006).

CONCLUSION

Emerging infectious diseases may belong to any of the classifications of infectious agents and are transmitted to humans by a variety of mechanisms. The reasons for their emergence may be complex and are delineated in chapter 1. Often, several factors converge so that conditions become favorable for an organism to emerge. The best ways to protect against the major consequences of such outbreaks is by having a good public health infrastructure with appropriate surveillance mechanisms and response plans and by educating health care practitioners to be alert when encountering a patient with unusual symptoms. The chapters in part II highlight specific emerging infectious diseases that have affected or have the potential to impact health care significantly.

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