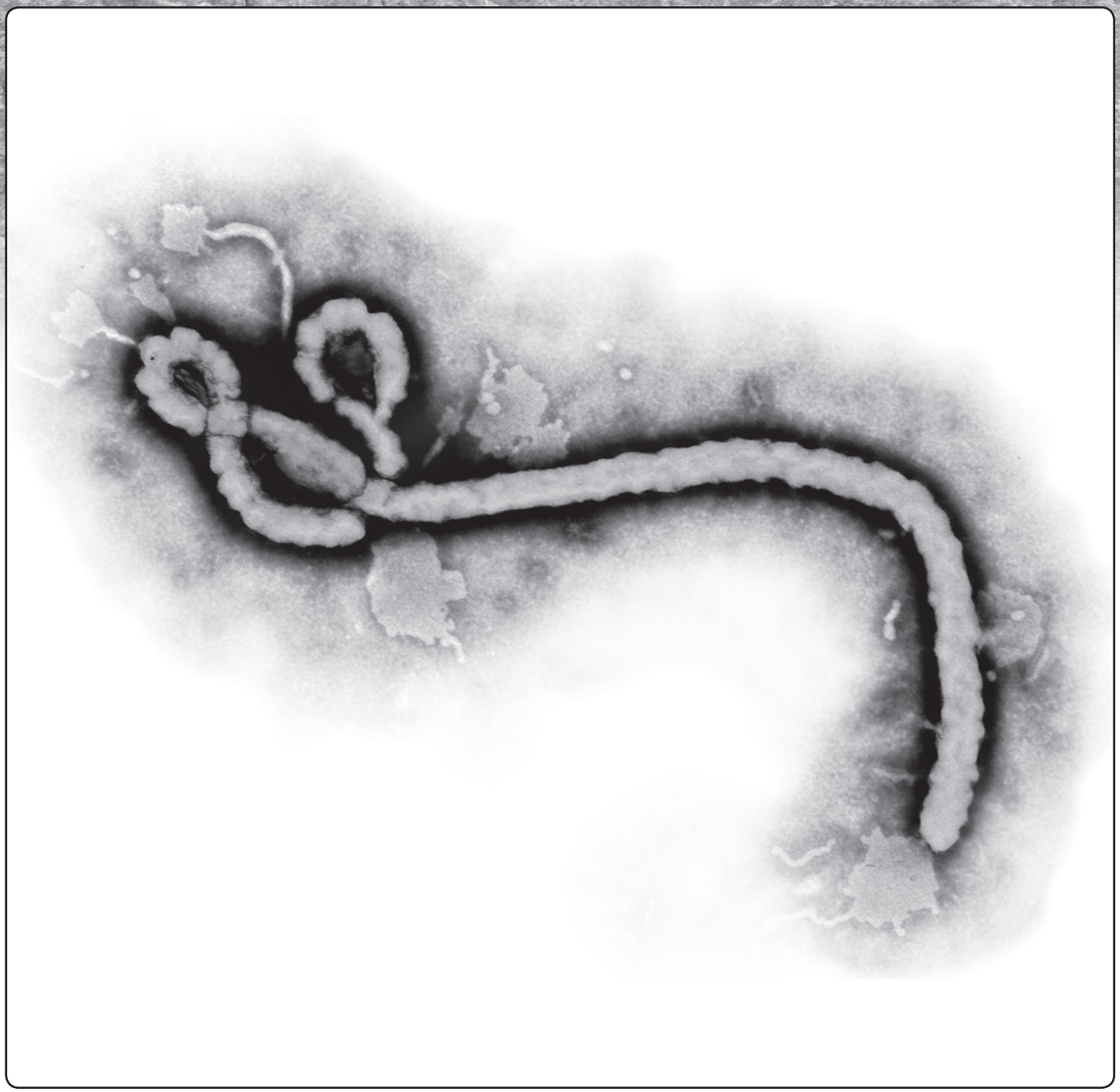
CHAPTER

28

Mammalian Disease and Zoonoses



CHAPTER OUTLINE

Humans and wildlife share a wide range of diseases (**Table 28-1**). Diseases are broadly defined as impairments to health. Genetic disorders, physiological or psychological imbalances, poor nutrition, stress, infections, or a combination of these may lead to disease. We are all too familiar with certain diseases such as diabetes, Parkinson's disease, and cancer. There are over 100 different types of cancer, and the American Cancer Society (2007) estimates that cancers cause over 7 million human deaths worldwide each year. Lesser known is that wildlife and domestic animals also contract many of these diseases, and **infectious diseases** transmitted between animals and humans (called **zoonoses**) are increasing globally. Over 70% of emerging diseases have animal origins, making zoonotic diseases one of the most important potential treats to public health (Chomel et al. 2007).

Zoonoses are not restricted to direct contact between humans and domestic animals. Many emerging zoonoses have wildlife origins, or wildlife species serve as **hosts** or **vectors** for spreading the disease (Friend 2006). Human–wildlife associations have increased greatly in recent years for a number of reasons. First, human population growth resulted in more people sharing space with wildlife. The 1994 **outbreak** of canine distemper virus (CDV) that decimated African lion prides in Serengeti National Park was due to increased contact between local domestic dogs carrying the virus and wild carnivores in nearby game reserves (Adler 1996; Roelke-Parker et al. 1996). Second, outdoor recreation and ecotourism are increasing, which also puts millions of people in potential contact with wildlife. In one case, expanding ecotourism in Africa is thought to be primarily responsible for the recent infection of African wildlife with human tuberculosis (*Mycobacterium tuberculosis*; Alexander et al. 2002). The ease of global travel and the globalization of food markets also serve to increase the emergence of zoonotic diseases. In some African and Amazonian countries, the rapidly expanding bushmeat trade (killing of wild animals for food or resale) increases the likelihood that wildlife-borne diseases will infect humans (e.g., Ebola, discussed later here). The bushmeat trade in the Congo Basin alone is estimated to yield 4 million tons of animal meat annually (Wolfe et al. 2005). Finally, wildlife often plays important, but less obvious roles in the ecology of diseases (Friend 2006, Perkins et al. 2005). The result is that environmental disruptions that effect wildlife can change the ecology of zoonses, leading to increased between-species transfer.

For any disease to occur, three factors must be present: (1) hosts must be susceptible to the virus, bacteria, or parasite causing the disease, (2) environmental conditions must promote the stability and viability of the **pathogen** (disease-causing organism), and (3) the host and pathogen must come into contact frequently enough for disease to occur (Friend 2006). When domestic pig farms in Malaysia expanded into areas inhabited by fruit bats carrying Nipah virus, the pig population became infected and subsequently transmitted the virus to farmers, causing over 100 human deaths (Johara et al. 2001). Thus, understanding the natural history of the pathogen and its animal hosts can minimize the potential for disease transmission to humans.

Infectious diseases have a variety of sources, including viruses, bacteria, and parasites (Table 28-1). The sections that follow provide examples of mammalian zoonoses by type of pathogen. Several examples of noninfectious diseases are covered here, but full treatment of this category is beyond the scope of this chapter. For more comprehensive

TABLE 28-1 Some of the Many Sources of Human Disease

Infectious Agents	Zoonotic Examples
Viruses	Rabies, West Nile fever
Bacteria	Tuberculosis, Lyme disease, Tularemia
Rickettsia	Rocky Mountain spotted fever, Q fever
Fungi	White-nose syndrome, histoplasmosis
Parasites	Echinococcosis, trichinosis, toxoplasmosis,
Prions	bovine spongiform encephalopathy, chronic wasting disease
Noninfectious Agents	**Disease Examples**
Microbial, algal, and plant toxins	Botulism, enterotoxemia, saxitoxin, aflatoxicosis
Synthetic chemicals	Pesticide poisoning, herbicides
Heavy metals	Lead and mercury poisoning
Neoplasia	Cancers
Genetic disorders	Down's syndrome, hemophilia
Diseases of immunity	Autoimmune disease
Systemic diseases	Diabetes
Deficiency diseases	Malnutrition, vitamin deficiencies
Psychoses	Depression, post-traumatic stress syndrome
Physiological disorders	Endocrine disruption, hypothermia

treatments of mammalian diseases, readers are referred to texts by Williams and Baker (2001), Samuel et al. (2001), Dierauf and Gullard (2001), and references therein.

Viral Diseases

Canine Distemper

Canine distemper is a viral disease that affects mammals in the order Carnivora. Although it is most common in domestic dogs, other members of the families Canidae, Mustelidae, Mephitidae, Hyaenidae, Ailuridae, Procyonidae, Pinnipedia, and some Viverridae and Felidae may be infected (feline distemper is a different virus exclusive to cats). Canine Distemper virus (CDV) is an RNA virus (paramyxovirus) related to measles and rinderpest (Kahn & Line 2005). CDV causes respiratory congestion, fever, suppression of the immune system, and neurological damage. Although a vaccine was developed for CDV, most of the world's dogs remain unvaccinated. Consequently, domestic dogs continue to spread CDV to previously unexposed wildlife (Pomeroy et al. 2008).

In East Africa, domestic or feral dogs spread CDV to African wild dogs (*Lycaon pictus*), lions (*Panthera leo*), and spotted hyaenas (*Crocuta crocuta*), leading to heavy mortality of these wild species (**Fig. 28-1**; Carpenter et al. 1998; Haas et al. 1996; Harder et al. 1996). Domestic dogs are also implicated in the spread of CDV to black-footed ferrets (*Mustela nigripes*), which nearly resulted in the extinction of the species in the American West (Williams et al. 1988). Similarly, dogs transmitted CDV to Caspian and Baikal seals (*Phoca caspica* and *P. sibirica*, respectively; Mamaev et al. 1995; Kennedy et al. 2000). CDV may even have contributed to the extinction of the Tasmanian wolf (*Thylacinus cynocephalus*) in Australia (Guiler 1961). The spread of CDV between species may result from mutations in the virus or changes in the host's immune response.

Munson et al. (2008) presented an intriguing new hypothesis for the spread of CDV in African lions. They provided evidence that extreme climate changes, coupled with co-infection by multiple pathogens, can cause massive mortality in host species. They analyzed blood samples from Serengeti and Ngorongoro Crater lions looking for evidence of CDV and other blood-borne pathogens. The results showed that at least five CDV **epidemics** occurred in these lion populations over several decades with little mortality; however, two CDV epidemics, one in 1994 and another in 2001, caused extensive lion mortality. What made these two outbreaks more **virulent** was the co-infection of lions with both CDV and a tick-borne **protozoan** parasite, *Babesia*. Interestingly, both high-mortality outbreaks were preceded by extreme droughts that resulted in the death of large numbers of herbivores. These dead and starving herbivores provided ample food for the resident lion prides. However, feeding on tick-infested Cape buffalo (*Syncerus caffer*) led to massive *Babesia* infections in the lions. The higher than normal parasite loads, coupled with

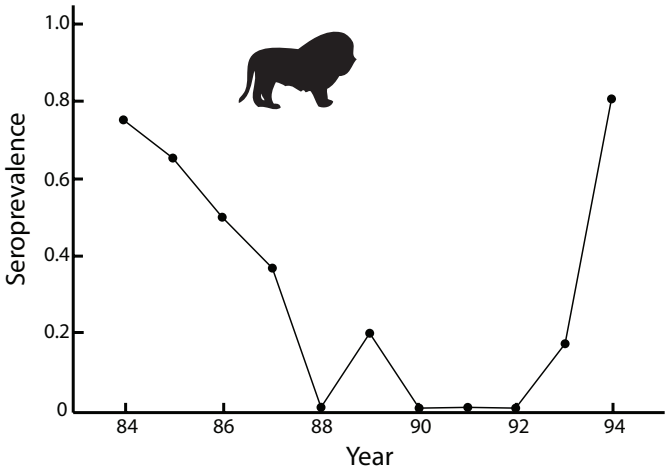


FIGURE 28-1 Rate of occurrence of lions seropositive for canine distemper virus (CDV) in the Serengeti from 1984 through 1994. Note the spike in CDV seroprevalence in 1992–1994. (Data from Packer, C., et al., *J. Anim. Ecology.* 68 (1999): 1161–1178.)

a simultaneous CDV epidemic, resulted in the suppression of immune system function and ultimately to mass mortality in the lion prides (Munson et al. 2008). Thus, climate change may contribute to pathogen virulence and host infection rates, a pattern that may become more common with future global climate change.

Monkeypox Virus

Monkeypox, an orthopoxvirus that results in skin lesions similar to those of smallpox, is another **emerging infectious disease**. Most human infections are clinically moderate, but severe infections can be deadly. Humans are infected through direct contact with animals carrying the virus. There are an increasing number of cases in Central and West Africa, where the disease is endemic.

Initially, researchers suspected nonhuman primates as the source of the monkeypox outbreaks (Marennikova 1972). Antibodies to the monkeypox virus were detected in several species of monkeys and apes from the Democratic Republic of Congo, but more wide-ranging studies, including other types of mammals, proved inconclusive. In the mid 1990s, another outbreak of monkeypox occurred in the Democratic Republic of Congo, and patient interviews revealed that all infected individuals had eaten bushmeat. The most commonly consumed meat was from squirrels (*Funisciurus* spp. and *Heliosciurus* spp.) and Gambian rat (or African giant pouched rat, *Cricetomys gambianus*; Hutin et al. 2001). These rodents are now believed to be the primary hosts for the monkeypox virus.

Attention shifted from Africa to North America in 2003, when monkeypox first appeared in the United States. Investigators discovered that the virus entered the United States in a shipment of exotic pets from Gambia (Centers for Disease Control 2003). The shipment contained about 800 small mammals, including infected squirrels and Gambian rats. These mammals arrived in Texas and were then distributed to several Midwestern pet stores. Within a few months, the Centers for Disease Control reported 80 human cases of monkeypox from six states. It appears that the virus was transferred from an infected Gambian rat to pet prairie dogs during interstate shipments and then on to humans who handled the prairie dogs. Fortunately, no deaths associated with monkeypox have been reported in the United States; however, the appearance of monkeypox in the United States illustrates the ease with which humans can move exotic pathogens around the globe.

Ebola Virus

Ebola hemorrhagic fever (EHF, or Ebola) is a rare, often fatal infectious disease that was discovered in 1976 in central Africa. The virus, a member of the family Filoviridae, is named after the Ebola River in the Democratic Republic of the Congo near the epicenter of the first outbreak (**Fig. 28-2**). Since then, Ebola outbreaks have been reported from a number of Central and West African nations, including Uganda, Sudan, Gabon, and the Ivory Coast. In 2003, 2005, and 2007, the Republic of Congo experienced additional Ebola epidemics that killed several hundred people (**Fig. 28-3**).

Symptoms of Ebola infection in humans include fever, vomiting, diarrhea, generalized pain, and often internal and external bleeding. Within a few days to 2 weeks, depending on the strain, the patient either begins to recover or dies from systemic organ failure (Pourrut et al. 2005). Human mortality rates are high; 80% of Ebola-infected patients worldwide have died. Transmission of the virus appears to be via exposure to infected body fluids. Epidemics occur in areas where hospitals and clinics do not have access to disposable needles and where basic hygiene and sanitation practices are not followed.

Researchers, attempting to locate a reservoir for the virus, analyzed over 30,000 animals from infected areas. Initially, the only evidence of Ebola virus was small fragments of RNA and DNA in the organs of rodents (*Mus setulous* and two species of *Praomys*) and one species of shrew (*Sylvisorex ollula*; Morvan et al. 1999). In 2001 and 2003, attention shifted to nonhuman primates and bushmeat species when the virus was found in gorilla, chimpanzee, and forest duiker carcasses that had been handled or consumed by infected individuals (Leroy et al. 2004). However, because these species also suffered high mortality from Ebola infection, the researchers concluded that they were probably not the natural host of the virus (Pourrut et al. 2005). Bats are now believed to be the natural host for Ebola virus (Leroy et al. 2005; Pourrut et al. 2007). Three

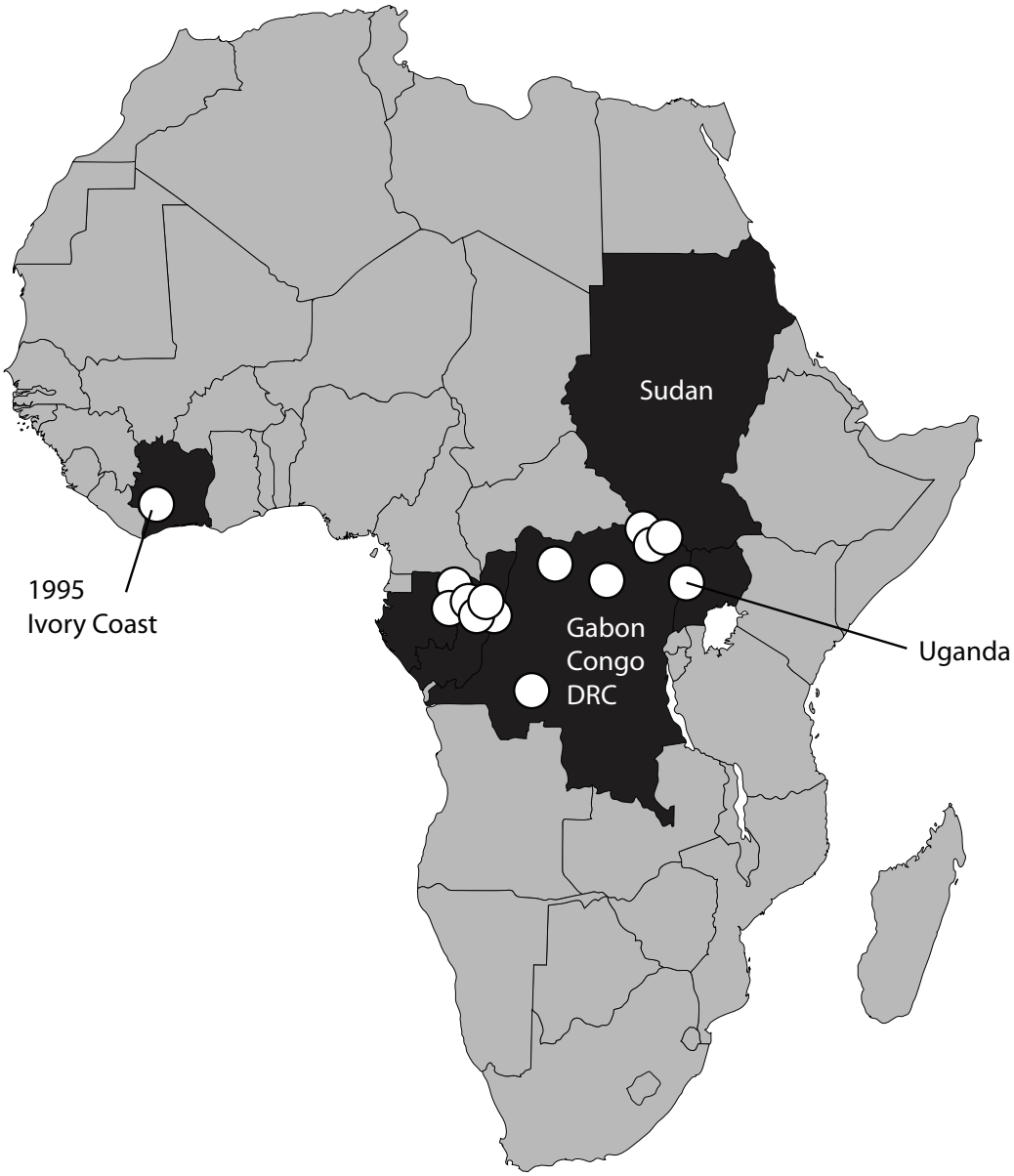


FIGURE 28-2 A map of African Ebola outbreaks in humans between 1976 and 2004.

species of fruit bat (*Epomops franqueti*, *Hypsignathus monstrosus*, and *Myonycteris torquata*) carry the Ebola virus but do not show any symptoms of the disease, suggesting that they are a reservoir species. These bats are long lived, roost in large colonies, and have a geographic range that overlaps the regions where Ebola epidemics are most common. Bats appear to harbor other related viruses, including Nipah virus, Marberg virus, and Lyssa viruses.

Lassa Fever

In 1969, in the Nigerian town of Lassa near Lake Chad, a viral hemorrhagic fever belonging to the Arenaviridae family emerged to infect humans (Frame et al. 1970). The Lassa virus is a zoonotic pathogen endemic to West Africa. Multimammate rats (*Mastomys natalensis*) are the probable reservoir of the disease. Multimammate rats are commonly found in association with humans in equatorial Africa. Their tender meat is also considered a delicacy in many regions. The rats carry the virus **asymptomatically** and shed the virus in their urine and feces. There are an estimated 300,000 to 500,000 cases of Lassa fever each year, resulting in approximately 5,000 deaths (Lecompte et al. 2006). Lassa fever is transmitted to humans via inhaling aerosolized feces or by consuming rodent meat. Humans then spread the disease via contact with body fluids or by sneezing or coughing.

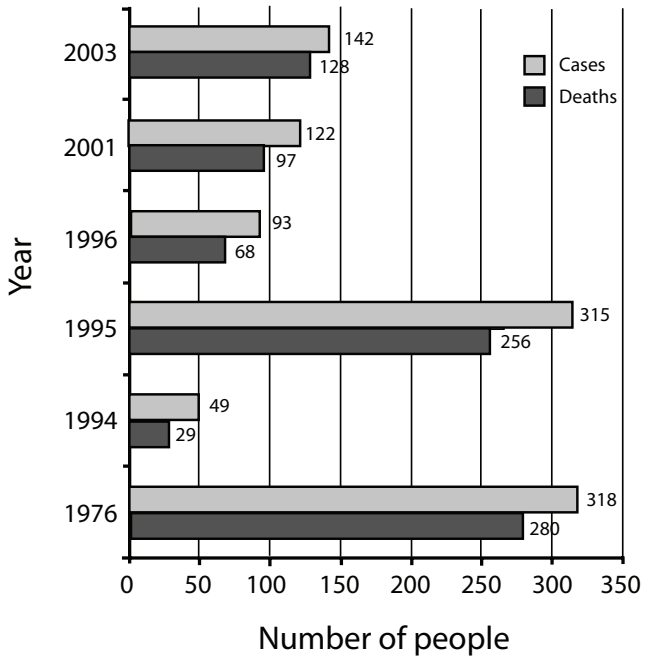


FIGURE 28-3 Number of Ebola cases and deaths reported in humans (1976–2003) by the Centers for Disease Control. (Adapted from *Known Cases and Outbreaks of Ebola Hemorrhagic Fever, in Chronological Order*, 2006, CDC.)

Nipah Virus

In 1999, pig farmers on the Malaysian peninsula began exhibiting unusual neurological symptoms, later diagnosed as severe febrile encephalitis. Later that year, the disease was identified in other regions of Malaysia. The common thread was exposure to large numbers of pigs (Chua et al. 2002a, 2002b). The epidemic subsided when over 1 million pigs were culled from affected regions, but not before 105 people had died from the disease. Nipah virus was later determined to be the causative agent in the epidemic.

The Nipah virus is a paramyxovirus whose natural reservoirs are pteropodid fruit bats, including the flying foxes *Pteropus vampyrus* and *P. hypomelanus*. The emergence of Nipah in 1999 is attributed to the expansion of pig farms into areas where large bat colonies were present. The farm at the epicenter of the epidemic was located at the edge of an orchard frequented by flying foxes, resulting in the exposure of pigs to bat feces and urine (Chua et al. 2002b). Infected pigs, showing signs of respiratory distress (coughing), quickly spread the virus as pigs were moved to other farms and to markets in Singapore. More recently, additional outbreaks of Nipah in humans have occurred in Bangladesh and India. Nipah virus has now been found in pteropodid bats in Cambodia (*P. lylei*; Reynes et al. 2005) and hipposiderid bats from Thailand (*Hipposideros larvatus*; Wacharapluesadee et al. 2005). In addition, antibodies to Nipah virus have been found in two species of pteropodid bats from Madagascar (*P. rufus* and *Eidolon dupreanum*) and in *Eidolon helvum* from Ghana in West Africa (Heyman et al. 2008; Lehle et al. 2007).

Hantavirus

The hantavirus family (Bunyaviridae) is another group of pathogens responsible for emerging infectious diseases, including hantavirus pulmonary syndrome and hemorrhagic fever with renal syndrome. Hantavirus was originally isolated in the Korean peninsula, but recent cases of another hantavirus species, the Sin Nombre virus, have caused public heath concerns in the western United States (Nichol et al. 1993). Muroid rodents are the primary reservoirs for hantaviruses. Typically, humans are infected when they are exposed to aerosolized rodent saliva or feces, or when bitten by an infected rodent. Several hantaviruses occur in the United States, and each virus has unique cricetid rodent species as its host. For example, deer mice (*Peromyscus maniculatus*) are the host for Sin Nombre virus (Childs et al. 1994).

Most species of rodents that host hantavirus in the United States do not frequent urban areas. Consequently, many of the early outbreaks of hantavirus pulmonary syndrome were from rural areas in New Mexico, Colorado, and Arizona. In these areas, scientists believe that increased precipitation from El Nino Southern Oscillations led to a sharp rise in *Peromyscus* populations, resulting in virus-infected mice entering houses and passing the virus to humans through their feces and urine (Hjelle & Glass 2000).

Other rodents are known to host other hantaviruses, including the white-footed mouse (*P. leucopus*), cotton rat (*Sigmodon hispidus*), rice rat (*Oryzomys palustris*), several species of voles (*Microtus* spp.), and Old World mice in the genus *Apodemus*, among others (Schmaljohn & Hjelle 1997). In addition, hantaviruses have also been found in masked shrews (*Sorex cinereus*), dusky shrews (*Sorex monticolus*), and northern short-tailed shrews (*Blarina brevicauda*) from the United States (Arai et al. 2007, 2008) and other shrews in Europe and Asia (Song et al. 2007a, 2007b).

Viral pathogens, such as hantaviruses, are assumed to have co-evolved with their primary hosts, resulting in little or no cost to the host in terms of survival or reproduction (Nemirov et al. 2004). However, Kallio et al. (2007) tested this hypothesis by studying the winter survival rates in bank voles (*Myodes glareolus*) infected with a European strain of hantavirus. Voles were monitored on 22 islands in Finland over a 3-year period. Overwinter survival of virus-infected bank voles was significantly reduced relative to uninfected control voles, suggesting that there are survival costs despite a long period of host–pathogen coevolution.

Rabies

Rabies is probably the best-known viral zoonotic disease. The virus itself belongs to the genus *Lyssavirus* (family

Rhabdoviridae), a group of RNA viruses that typically infects endotherms, including humans. Rabies infects bats, primates, cattle, and a wide range of carnivores (e.g., foxes, skunks, canids, mongoose, bears, and raccoons). Domestic dogs and cats may pick up the disease from contact with wild animals and thereby present a serious risk to humans.

The virus is present in the saliva of infected animals and is typically contracted from a bite. Aerosol transmission in humid bat caves was also thought to occur, but this has been questioned recently (Brass 2009). Once infected, the virus replicates and travels to the peripheral nervous system and eventually to the spinal cord and brain where it causes encephalitis. Later, the virus spreads to the salivary glands and other organs in the body. Late-stage symptoms include acute pain, uncontrolled movements, aggressive behavior, profuse salivation, and the inability to swallow water (Brass 2009). Eventually, the patient falls into a coma and nearly always dies. Infected animals show a similar disease progression, transmitting the disease to other animals (including humans) from viral pools in their saliva. In 2006, the World Health Organization estimated that there are 55,000 human fatalities from rabies infection worldwide. The vast majority of deaths occur in Asia (31,000 deaths) and Africa (24,000 deaths), where access to rabies vaccine is limited.

In much of Asia, Africa, and Latin America, dogs are the principal reservoir for the rabies virus. The pattern of terrestrial wildlife rabies cases in the United States is regional and species specific (**Fig. 28-4**; Brass 2009). In the mid-Atlantic and northeast United States, there is an epidemic of rabies in raccoons (**Fig. 28-5**). The virus began to spread from the southeast in the 1950s when infected raccoons were translocated to restock populations in the northeast (Nettles et al. 1979). Skunks are the primary wild host of rabies in the midwestern United States. In contrast, rabies in insectivorous bats is geographically widespread in the United States (Blanton et al. 2008).

In 2007, roughly 36% of the 7,258 animal rabies cases in the United States were from raccoons, with bats and skunks accounting for an additional 27% and 20% of cases, respectively (Blanton et al. 2008). Rabies in domestic pets has decreased in recent years from a high of over 2,000 cases in 1957 to less than 500 cases (6.6%) in 2007 (**Fig. 28-6**). Although raccoons are the largest reservoir for the rabies virus in the United States, they are not the primary source of human rabies infection. Bats continue to be the main source of human cases. Eighteen of the 25 cases (72%) of

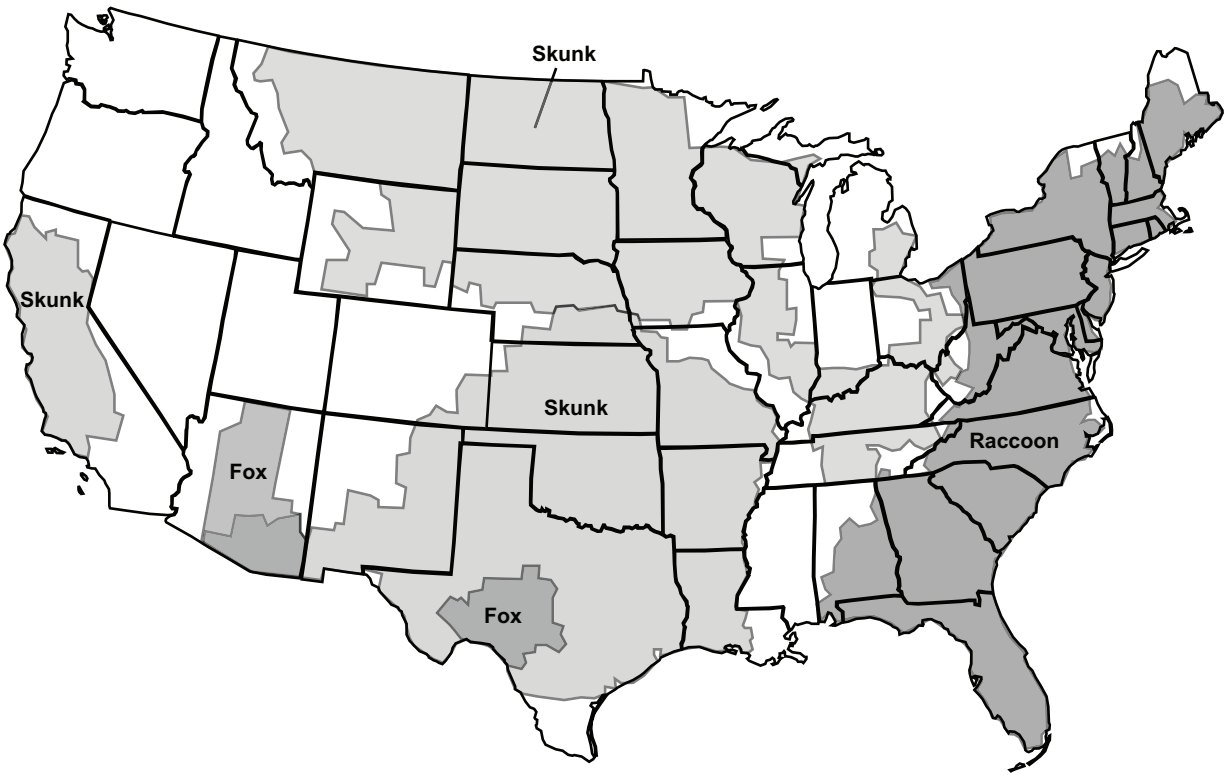


FIGURE 28-4 Map of the United States distribution of rabies in raccoons, skunks, and foxes. Note that the pattern of rabies in terrestrial carnivores is both host-specific and regional. Raccoon-borne rabies is common along the eastern coast, but skunk-borne rabies predominates in the middle of the country. (Adapted from Blanton, J. D., et al., *J. Am. Vet. Med. Assoc.* 233 (2008): 884.)

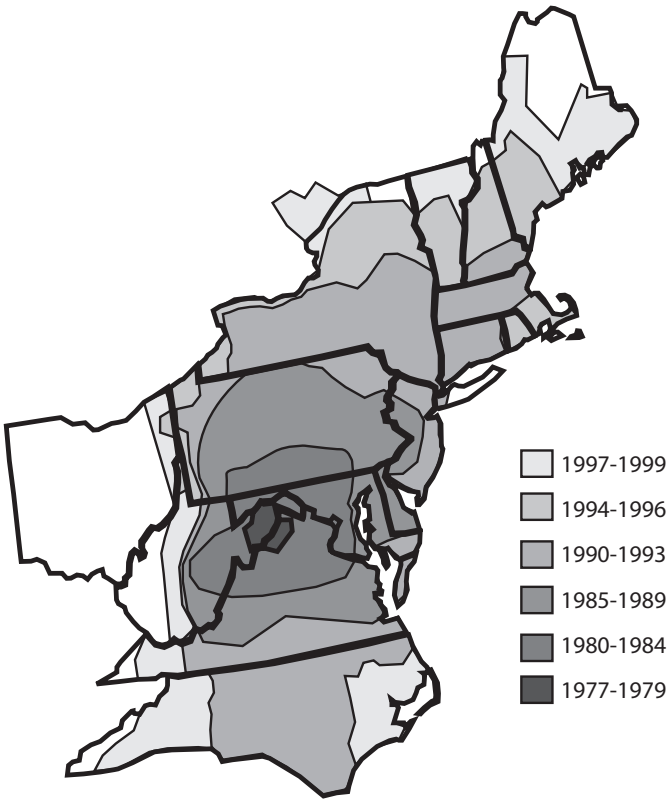


FIGURE 28-5 Map of rabies spread by raccoons in eastern states from 1977 to 1999. The epicenter of the disease was in northern Virginia, eastern West Virginia, and western Maryland. From those, it spread elsewhere rapidly. (Adapted from *MMWR* 49 (2000): 31–35.)

rabies in humans reported from 2000 to 2007 were from bats (Blanton et al. 2008). Bites from raccoons or dogs are painful, and people almost always seek treatment for their wounds. In contrast, inexperienced people who handle bats (without gloves) may be bitten without even realizing it, leading to infection, disease progression, and lack of proper treatment.

A pre-exposure vaccination series is an important safeguard for individuals working with mammals likely to harbor the rabies virus (veterinarians, animal-control officers, zoo personnel, and wildlife biologists). The pre-exposure series consists of three intramuscular injections given at day 0, day 7, and day 21 to 28. Even after the pre-exposure series, individuals at higher risk should have their **titers** checked periodically (titer refers to the concentration of antibodies in the blood).

Pre-exposure treatment is an important safeguard, as once clinical symptoms appear the disease is almost always fatal. Postexposure **prophylaxis** is also available for individuals lacking the pre-exposure series, but it should be administered as soon as possible after contact with the suspected rabid animal. Postexposure rabies prophylaxis includes injections of both human rabies immune globulin followed by a course of the rabies vaccine (Centers for Disease Control 2008). Human rabies immune globulin contains antibodies to the virus, which serves as passive protection until the body begins producing its own anti-rabies antibodies in response to the antigens present in the rabies vaccine (Brass 2009).

There are only six known cases of individuals surviving rabies infection without vaccination. In a recent case in November 2004, a teenage girl from Wisconsin became the first person to survive rabies using a new medical protocol. By the time medical assistance was sought, over a month after being bitten by a bat, her disease had progressed beyond the period when postexposure vaccination would have been helpful. In an attempt to save her life, doctors tried an experimental approach. They put her into a drug-induced coma and administered a suite of antiviral drugs. The goal was to slow the advance of the disease and give her body time to mount an immune response to the virus. Fortunately, she slowly regained much of her health and was released from the hospital 2 months later (Centers for Disease Control 2004), but 5 months after the initial hospitalization she still showed several serious disorders including involuntary body movements, a motor speech disorder, and an unsteady gait; Willoughby et al. 2005). This treatment (termed the Milwaukee-protocol) was also successfully used to treat a 15-year-old Brazilian boy bitten by a rabid vampire bat. Variations of the Milwaukee-protocol have now been used to treat over 20 additional rabies patients worldwide, but none of the others has survived (Brass 2009). Sadly, rabies remains a virtually incurable illness that causes great suffering for patients and their loved ones.

Prion Diseases

Bovine Spongiform Encephalopathy

In 1985, an unusual neurodegenerative disease first appeared in British cattle. It was later diagnosed as bovine spongiform encephalopathy (BSE), which in adult cattle leads to erratic movements, lost of postural control, body mass wasting, and loss of milk yields and is always lethal (Ducrot et al. 2008). Because infected cattle appeared crazed, it was termed "mad-cow disease" by the media, and it heralded the emergence of a new category of infectious diseases. The infectious agent in BSE is a rare mutant protein called a **prion**. For unknown reasons, the prion proteins are misfolded, resulting in damage to the central nervous system. Researchers concluded that BSE was acquired when healthy cows consumed animal feed containing meat and bone meal from animals contaminated with prions. In brain tissue, prions cause a cascade of protein deformation, leading to dense plaques and resulting in loss of mental and physical condition.

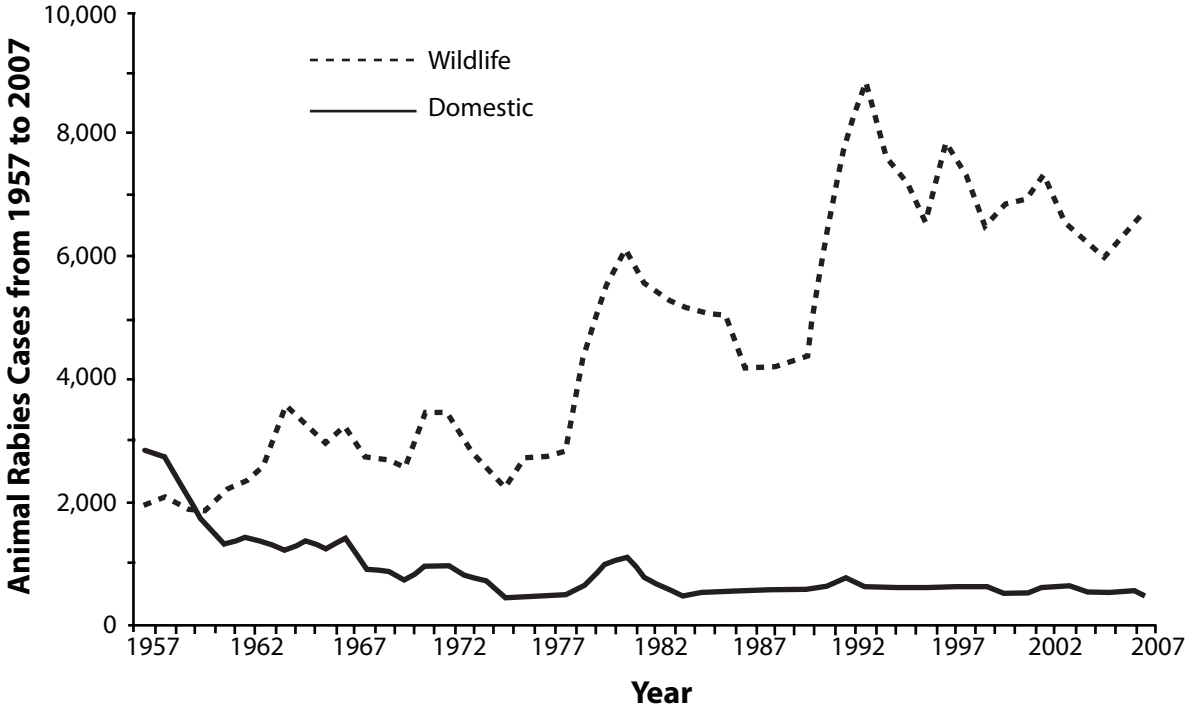


FIGURE 28-6 Graph of animal rabies cases reported in all wildlife combined and in domestic animals from 1957 to 2007. Rabies in domestic animals has fallen, whereas rabies in wildlife has increased. (Data from Blanton, J.D., et al., *J Am Vet Med Assoc.* 233 (2008): 884.)

The epidemic of BSE in Great Britain continued into the early 1990s; it peaked in 1993, with over 1,000 new cases reported each week. Although troubling for farmers, real concern over BSE began when epidemiological and laboratory tests revealed a link between BSE outbreaks in cattle and a new prion disease that affected humans (variant Creutzfeldt-Jakob disease, vCJD). The humans and cows had similar symptoms, and many of the human patients had consumed tainted beef. Before measures were taken to curtail the use of meat byproducts and bone-meal in cattle feed in 1989, an estimated 400,000 BSE infected cattle had been processed for human consumption in Europe (Valleron et al. 2001). As of 2009, over 200 people (mostly in Europe) had died from vCJD; the number of deaths will likely continue to rise because the **incubation period** can be several years to decades.

The link between BSE and vCJD caused a crisis in the beef industry. Consumers lost confidence in meat safety. Many BSE-free nations refused to import beef from Europe, and millions of cattle were slaughtered to prevent further spread of the disease. In 2003, BSE was reported in a cow from Washington State in the United States. Meat of the BSE-positive cow went to market, but most of it was successfully recalled before sale (Animal and Plant Health Inspection Service 2004). As of 2009, two additional U.S. cases have been reported from Texas and Alabama, along with 16 cases from Canada and 35 cases from Japan (for current numbers of BSE worldwide see the Office International des Epizooties at www.oie.int/eng/info/en_esb.htm).

Chronic Wasting Disease

Another type of transmissible spongiform encephalopathy called chronic wasting disease (CWD) affects wildlife. Like BSE, this disease attacks the brain, leading to neurodegeneration and death in infected animals. CWD has been identified in free-ranging and captive mule deer, white-tailed deer, elk, and moose populations in North America and in moose in Korea (Sigurdson 2008). This disease poses serious problems for wildlife managers because CWD is spreading over an increasingly wide geographic area, and because of its close relationship to other prion diseases that may be transferred to humans.

CWD was originally described in 1967 in captive mule deer in Colorado. Since then, it has spread to wild populations of deer, elk, and moose in surrounding states. By 2006, the CDW-infected area had expanded outward to include parts of Utah, South Dakota, and Kansas. Isolated centers of CWD infection in wild deer also appeared in Wisconsin and Illinois, in southern New Mexico, and in wild white-tailed deer in New York and West Virginia (Williams et al. 2002). In 2008, CWD was also found in the Canadian provinces of Alberta and Saskatchewan. Wildlife biologists believe CWD spreads in wild populations via direct nose-to-nose contact or by contact with infected excreta (Williams 2005). Movement of CWD to isolated sites far from the initial

outbreak likely occurred via interstate shipment of infected animals. A variety of state, provincial, and federal agencies have developed or are developing programs to control the spread of CWD. However, control of CWD in wild deer and elk populations is extremely difficult, and the disease will probably continue to spread in the future.

Bacterial Diseases

Plague

Plague is an infectious disease caused by the bacterium *Yersinia pestis,* which caused several human epidemics or **pandemics** during historical times. People infected with plague develop fever, body aches, and nausea. Left untreated, plague is nearly always fatal. Plague exists in three clinical forms: bubonic, septicemic, and pneumatic plague (Stenseth et al. 2008). Bubonic plague, the most common form, occurs when a person is bitten by a *Yersina*-infected flea and bacteria are passed into the person's body tissues, where the bacteria reproduce and enter the lymphatic system where it causes bulbous swellings of the lymph nodes (bubos). Septicemic plague occurs when toxins produced by the bacteria cause numerous tiny clots throughout the body, reducing clotting ability and leading to uncontrolled bleeding. Individuals with septicemic plague have black hematoma patches under the skin and may cough up blood. The third and least common type, pneumatic plague, results from secondary spread of bubonic plague to the lungs, where it can be spread directly from human to human via coughs and sneezing.

Bubonic plague can be treated with antibiotics if they are administered soon after infection. Without treatment, bubonic plague kills approximately 50% of infected individuals within 1 week (Stenseth et al. 2008). Untreated septicemic and pneumonic plagues are typically fatal.

The spread of plague to humans depends on rodent hosts and their fleas (**Fig. 28-7**). Fleas harboring the plague bacterium begin to starve as the bacteria reproduce and form a plug that blocks entry to the flea's stomach. The hungry fleas bite aggressively and regurgitate the bacteria into the wound of a new host (e.g., commensal rodents or humans). Humans can be infected via flea bites or by handling infected meat or animals. Plague-infected cats, for example, are known to pass the bacteria on to humans. In addition, it now appears that birds of prey and mammalian predators may spread the plague over wide regions (Stenseth et al. 2008). Epidemics occur when the typical rodent hosts begin to die and the fleas seek other species for blood meals.

There have been three major pandemics (an epidemic occurring on a large or global scale) of plague in historic times. The earliest occurred in northeastern Africa in the 5th century and spread to the eastern Mediterranean. Historians estimate that the Plague of Justinian, as it is known, killed approximately 25% of the humans in the region (Rosen 2007). A second massive pandemic, the Black Death, swept through Eurasia in the 14th century, killing over 200 million people. The largest epidemic death toll in human history, this plague significantly altered the course of human history (Herlihy & Cohn 1997). The most recent of the three pandemics began in 1855 in China. It spread rapidly to five continents as ships carried trade goods along with infected rats across the globe. In 1900, the pandemic reached the United States at the port of San Francisco. The United States was largely spared from the plague, however, with only 500 reported cases. Asian countries were less fortunate; over 15 million people died from this global plague over 20 years (Echenberg 2007).

Plague still exists in rodent populations across the world (**Fig. 28-8**), including the United States. In the United States, plague is rare but widespread in western states. Here, human outbreaks occur when ground squirrels, prairie dogs, chipmunks, or woodrats die in large numbers, forcing infected fleas to find new hosts (Eisen et al. 2007). On

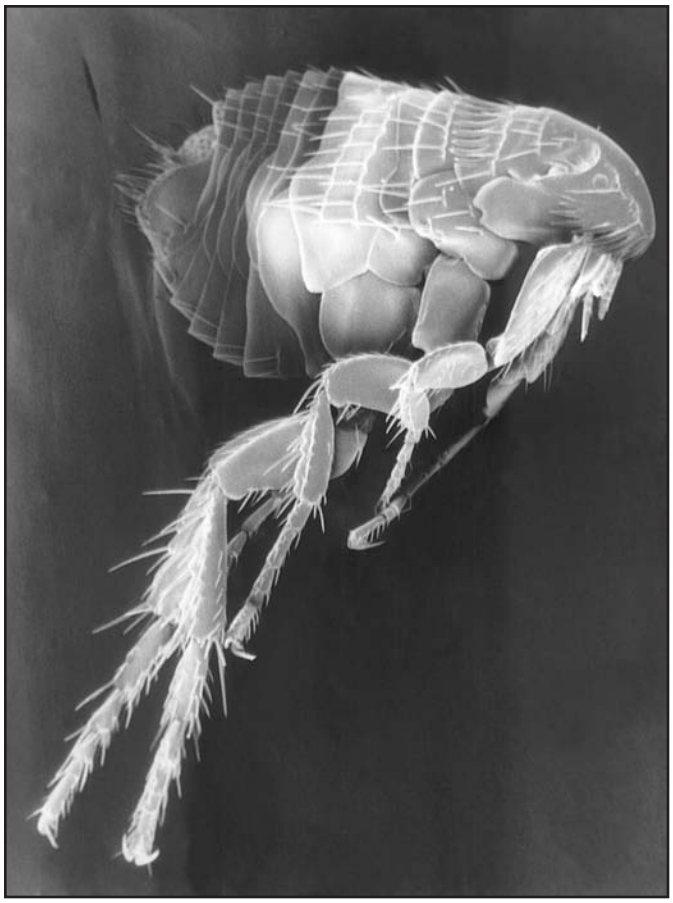
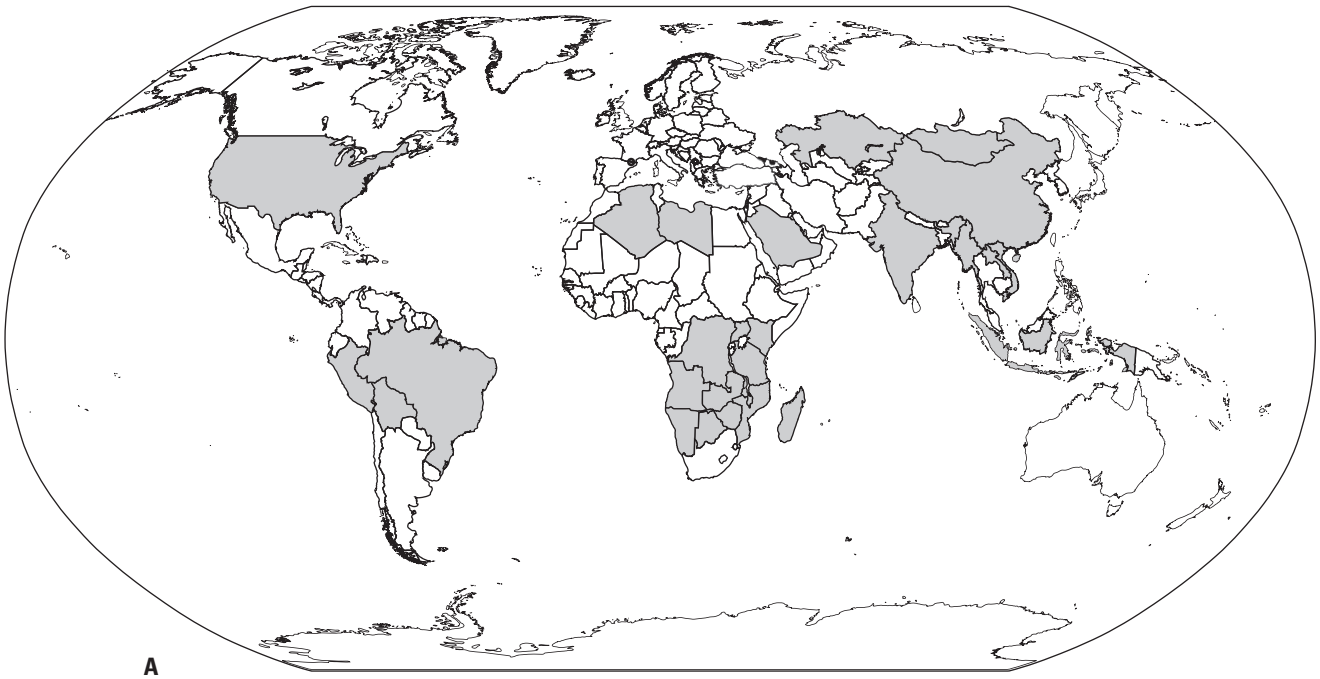


FIGURE 28-7 Scanning electron micrograph of a flea.



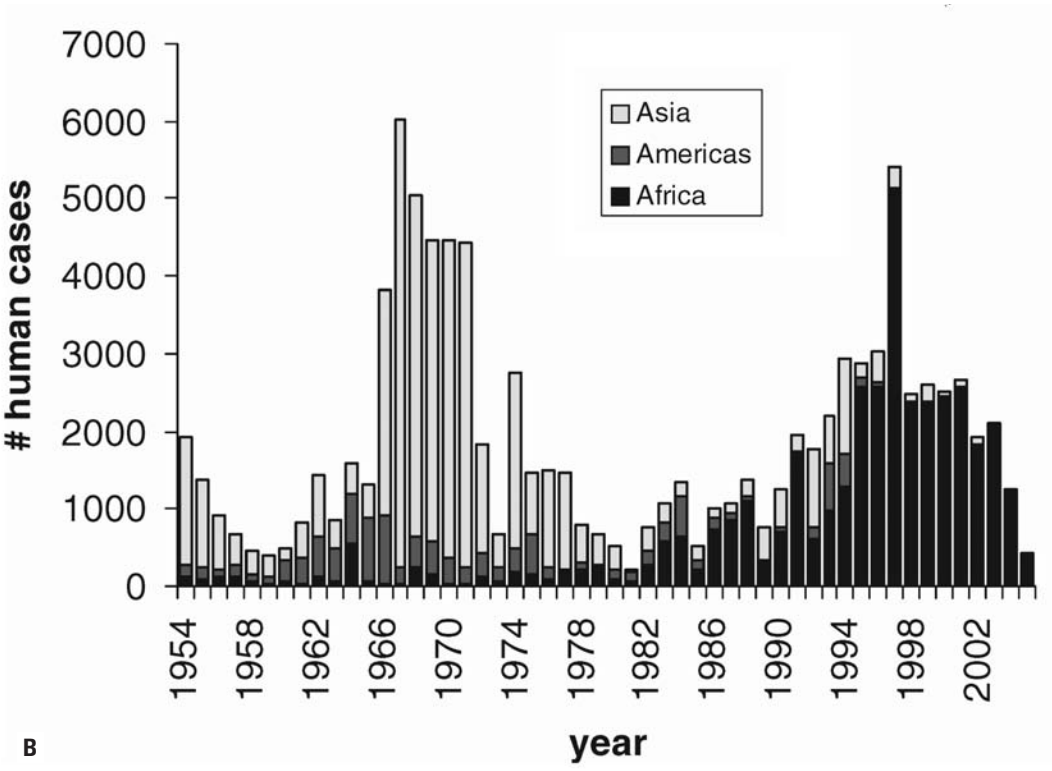


FIGURE 28-8 (A) World map showing countries with known cases of plague in wildlife species (gray). (B) Annual number of human plague cases over different continents reported to the World Health Organization in the period 1954–2005. (Reproduced from Stenseth, N.C., Atshabar, B.B., Begon, M., Belmain, S.R., Bertherate, E., et al. (2008) Plague: Past, present, and future. *PLoS Med* 5 (1): e3. doi:10.1371/journal.pmed.0050003.)

a global scale, the World Health Organization reported 1,000 to 5,000 human cases of plague annually since 1990, and officials remain concerned about a re-emergence of plague. The pattern on the African continent is particularly troubling; 1,822 cases of human plague (95% of the world totals) were reported in six countries (Democratic Republic of the Congo, Madagascar, Malawi, Mozambique, Uganda, and Tanzania) in 2002 (World Health Organization 2004).

Furthermore, recent climate modeling predicts that warmer springs and wetter summers may favor the reemergence of plague in some rodent populations (Stenseth et al. 2006). Thus, predicted future climate change, increasing human populations, and human mobility and transport greatly increase the threat of human infections.

Lyme Disease

Lyme disease is an infectious disease that is caused by the bacterial pathogen B*orrelia* carried by *Ixodes* ticks. Humans contract Lyme disease when bitten by an infected tick. In North America, the black-legged tick or deer tick (*Ixodes scapularis*; **Fig. 28-9**) is the vector for the disease, but in Europe, the sheep tick (*Ixodes ricinus*) is primarily responsible for transmission to humans (Ostfeld et al. 2006).

A number of factors make diagnosis difficult. Symptoms may take over a month to appear. People exhibit a wide range of symptoms, including a bulls-eye shaped rash on the skin surrounding the tick bite, fever, fatigue, and arthritis-like joint pain. Later-stage symptoms, which often appear many months after infection, include joint aches, immunosuppression, fatigue, memory loss, neuropathy, meningitis, and various other neurological symptoms. Lyme disease is treated with antibiotics, but left untreated, it can result in chronic disability and in rare cases death from meningitis. Lyme disease cases are on the rise in the United States, especially in the northeast, mid-Atlantic states, Wisconsin, Minnesota, and northern California. In 2007, the Centers for Disease Control reported over 27,000 cases of Lyme disease, an 8.5% increase from 2005.

FIGURE 28-9 An *Ixodes* tick. Ticks in this genus are responsible for transmitting the bacteria that causes Lyme disease to vertebrate hosts, including humans.

Lyme disease derives its name from the village of Lyme, Connecticut, the epicenter of a 1975 outbreak. Since then, researchers have clarified the ecology of the disease cycle (Allen et al. 2003; Ostfeld et al. 2006). Lyme disease is most prevalent in northeastern United States, where suburban expansion into deciduous forest ecosystems brings the pathogen, ticks, and their vertebrate hosts into close proximity. *Ixodes* ticks require separate blood meals from three hosts during their lifetime (**Fig. 28-10**). Uninfected larval ticks hatch in summer and begin to seek suitable vertebrate hosts for their first blood meal. Satiated with blood, the larval tick falls to the forest floor and molts into a nymph. The *Ixodes* nymphs remain inactive throughout the winter; in late spring, the nymphs begin to search for new host (lizards, birds, or small mammals may serve as hosts). After a blood meal from the second host, the nymphs again drop off the host and molt into adult ticks. Adult *Ixodes* ticks tend to seek larger mammalian hosts for their last blood meal. The bacterial pathogen is acquired by the tick during either the larval or nymphal blood meal from an already infected host. Only nymphs and adults pass the pathogen to humans.

Nymph-stage ticks are most likely to pass the *Borrellia* pathogen to humans because they are abundant and seek hosts during the summer months and because they are much smaller and more easily overlooked than adult ticks. Thus, the risk of human infection is positively correlated with the density of infected nymph-stage ticks. High nymph densities are correlated with wetter summers, which in turn increase the risk of exposure to Lyme disease (Brownstein et al. 2005; Subak 2003). Similarly, the abundance of white-tailed deer, a primary host for adult ticks, strongly affects Lyme disease risk in humans (Daniels et al. 1993; Rand et al. 2003).

Understanding how tick density influences the risk of exposure to Lyme disease is complicated. Nevertheless, Ostfeld et al. (1996, 2001) have begun unraveling these complexities, summarized here (see Ch23 and Fig. 23-25): Oak trees (*Quercus* spp.) produce highly variable acorn crops. When acorn crops are large (mast years), they provide excess food for small mammals and white-tailed deer. Following mast crops, white-footed mice, eastern chipmunks, and white-tailed deer populations increase (McShea & Schwede 1993), providing larval ticks with more potential hosts. Jones et al. (1998) reported large increases in larval tick abundance following artificial addition of

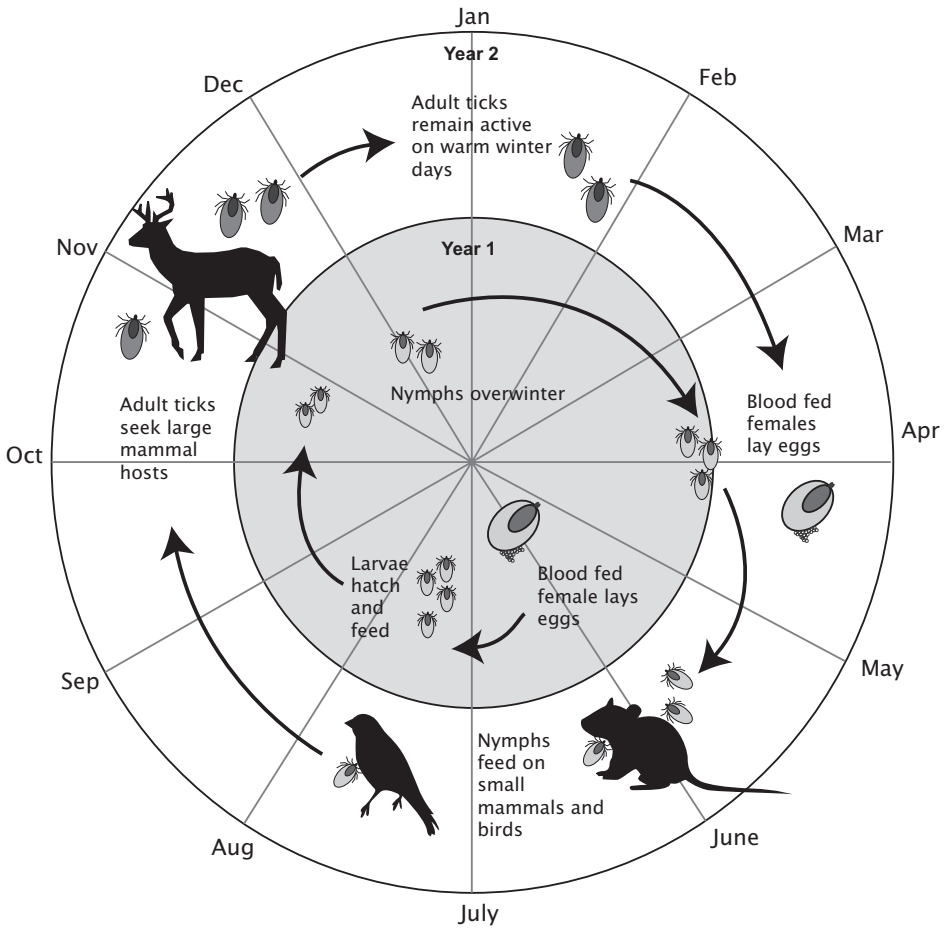


FIGURE 28-10 Two-year life cycle of *Ixodes* ticks. After feeding on a host, female ticks lay their eggs in May to July of the first year (inner circle). The eggs hatch into larvae that overwinter in year 1. In the spring, the resulting nymphs seek out small mammal and bird hosts (outer circle). The blood-fed nymphs mature into adult ticks in October to December, when they seek out large mammal hosts including white-tailed deer. The cycle repeats when blood-fed females lay their eggs in the spring. Both nymphs and adult ticks may feed on and infect humans. The nymphs are believed to be most likely to infect people because nymphs are smaller and less conspicuous, and thus, their bites often go unnoticed.

acorns that mimicked a mast event. The risk of contracting Lyme disease in a given year was elevated when mouse abundance increased in the pervious year and when mast acorn crops occurred 2 years prior (Ostfeld et al. 2001). However, Brisson et al. (2008) showed that acorn crops and white-footed mice are only part of the story. Their data suggest that masked and short-tailed shrews are the primary hosts for infected *Ixodes* ticks. At their study sites in New York, blood meals from white-footed mice were responsible for only 8.5% of infected tick larvae and 25% of infected nymphs. By comparison, shrews provide approximately 35% of the blood meals for larval ticks. Four species of small mammals (white-footed mice, chipmunks, short-tailed shrews, and masked shrews) account for over 80% of infected nymphs. These results suggest that Lyme disease control strategies that focus solely on white-footed mice may prove ineffective at controlling the rate of Lyme disease in humans.

Parasitic (Nonzoonotic) Diseases

Toxoplasmosis

Toxoplasmosis is disease caused by the protozoan parasite *Toxoplasma gondii*. It infects most mammals, including humans, but cats (Felidae) are the primary host of the sexual stage of the parasite (Fayer 1981). Infected cats shed large numbers of **oocysts** (a thick-walled structure containing developing parasites) with their feces for several weeks after infection. These enduring oocysts can survive in the environment for months before being accidentally ingested by another mammalian host. The parasites survive in the new host as cysts in muscle and brain tissues; they can be passed on when an infected animal dies and is consumed.

Humans typically acquire the parasite when they eat undercooked meat containing cysts, accidentally ingest a cyst from cat feces (e.g., when cleaning a litter box), or drink contaminated water (Jones et al. 2003). The Centers

for Disease Control estimate that between one-third and two-thirds of the world population are infected by this parasite. Healthy people show no adverse effects of the parasite burden; however, in people with compromised immune systems, such as those suffering from HIV/AIDS, the *Toxoplasma* infection may lead to encephalitis or other neurological diseases.

Humans are not the only hosts to be negatively affected by this parasite. Wildlife biologists recognized a 10% decline in sea otter populations in California since 1995. Miller et al., (2002) found *Toxoplasma* infections in 42% of **serological** samples from living sea otters and 62% from samples taken from dead otters. The evidence pointed to freshwater runoff from the coast as the source of the otter infection. Evidently, increased coastline development resulted in increased transport of feline feces infected with *T. gondii* into the coastal marine ecosystems.

Parasites and Climate Change

Research on emerging infectious diseases in mammals has focused on tropical and temperate species; however, the region with the fastest rate of emerging diseases infecting wildlife may be northern temperate and Arctic environments (Dobson et al. 2003). Recent studies in Arctic and sub-Arctic regions are beginning to reveal unexpected patterns of parasite infections in northern ungulate species (reviewed in Kutz et al. 2004).

One revealing example is the recent discovery of a nematode parasite of muskoxen (*Ovibos moschatus*). The lung nematode *Umingmakstrongylus pallikuukensis* was found in dead muskoxen in Arctic regions of Canada in 1988 and was later described as a new parasite species. This large nematode (up to 65 cm long) forms cysts in the lungs of infected ungulates (Kutz et al. 2001). Adult nematodes encysted in the lungs of a mammalian host lay eggs within the cyst. The newly hatched larvae crawl up the bronchial tubes to the mouth, where they are swallowed and are carried into the gut and out with the feces of the host animal. Once on the ground, the larvae enter the foot of terrestrial slugs (gastropods), which serve as an intermediate host for the nematode. Muskoxen presumably ingest the nematode larvae when they eat gastropods hidden in vegetation or when they eat vegetation contaminated with nematode larvae. Ingested larvae make their way to the lungs and develop into adult parasites.

Little is known about the survival and fecundity of muskoxen infected with *U. pallikuukensis*, but Kutz et al. (2004) suggest that parasitic infection may be responsible for a 50% decline in muskoxen populations in parts of the Northwest Territories and Nunavut, Canada. They further hypothesize that high *U. pallikuukensis* infection rates in muskoxen result from an unprecedented warming trend in the region over the past 2 decades (mean annual temperatures have increased nearly 2°C from 1948 to 2003). Indeed, climate changes are known to affect the host–pathogen–environment triad and have been implicated in the emergence of many mammalian diseases (Dobson et al. 2003; Root et al. 2003). How host–parasite systems will respond to future climate changes in unknown, but it is possible that infectious diseases, including parasites, will continue to emerge, causing significant mammalian population declines or even mammalian extinctions.

Parasites and Species Extinction

As this example illustrates, parasitic diseases can cause significant population declines in wildlife; however, the degree to which parasitic infections can cause host extinctions has not been fully investigated. The International Union for Conservation of Nature and Natural Resources (IUCN) estimated that 24% of mammal species are threatened with extinction (IUCN 2006); however, parasites are rarely considered to be important contributors to extinction risk because threatened host species exist in small, isolated populations (Lyles & Dobson 1993). Pederson et al. (2007) suggested that parasites (especially multihost parasite) can contribute to parasite-caused extinction in mammal species for several reasons. First, parasites that infect multiple species can maintain high population densities in alternative hosts, leading to parasite-induced declines in mammalian hosts less suitable for the parasite (Fenton & Pedersen 2005). In addition, some parasites and vector-borne diseases continue to spread in the face of declining host populations. Thus, it is possible that emerging infectious diseases represent an important extinction risk for some threatened mammal species (Pedersen et al. 2007; Smith et al. 2006).

Two orders, Artiodactyla and Carnivora, account for a large majority (88%) of mammals threatened by parasites (Kutz et al. 2004). Not surprisingly, the families in these orders with the highest number of species threatened by parasites also include domesticated mammals (both livestock and companion animals). The parasites most likely to occur in threatened mammal species are viruses and bacteria capable of infecting a broad range of hosts including domesticated mammals. One unexpected finding was that parasites transmitted by close contact were far more likely to increase the risk of extinction than those transmitted by arthropod vectors or other routes (Pedersen et al 2007). Furthermore, many of the parasite-induced outbreaks resulted from "direct contact with domesticated animals, in some cases from infections that would not have spread or persisted in wildlife in the absence of domesticated animals." Their results suggest that measures should be taken to reduce contact between threatened wild mammals and any related domesticated species (Pederson et al. 2007).

Other Emerging Pathogens (Nonzoonotic)

White-Nose Syndrome

A mysterious new epizootic disease appears to be decimating bat colonies throughout the northeastern United States. Wildlife scientists first discovered the disease in two caves near Albany, New York in 2006 (Blehert et al. 2009). By March 2009, the disease had spread to caves and mines in eight additional states (Massachusetts, New Jersey, Vermont, West Virginia, New Hampshire, Connecticut, Virginia, and Pennsylvania) and killed an estimated one-half million insectivorous bats (Blehert et al. 2009; Gargas et al. 2009).

The disease, called white-nose syndrome (WNS), is characterized by patches of white fungal **hyphae** on the face and wings of infected bats (**Fig. 28-11**). Blehert et al. (2009) were able to identify the fungus as a new species, *Geomyces destructans*. This new fungus grows optimally at temperatures below 10°C, like those found in bat hibernacula. Infected bats often arouse from hibernation in the middle of winter, rapidly deplete their energy stores, and may leave the hibernacula altogether. So far, the disease has infected colonies of little brown bats (*Myotis lucifugus*), northern long-eared bats (*Myotis septentrionalis*), big brown bats (*Eptesicus fuscus*), and tricolored bats (*Perimyotis subflavus*). The U.S. Fish and Wildlife Service estimates that 90% of bats have perished at some hibernacula in the northeastern United States. They also fear that declines in the endangered Indiana bat (*M. sodalis*) populations in 2008–2009 may be due to WNS.

Scientists are still trying to understand whether the fungus is the pathogenic agent or just a postinfection symptom of some as yet unknown disease. Several hypotheses have been suggested to explain the massive die-off of bats infected with WNS. One hypothesis is that the fungus simply takes advantage of bats weakened by reduced fat reserves and disrupted hibernation cycles brought on by changes in winter climate in recent years. Another possibility is that the bats are weakened by loss of insect prey because of the extensive use of pesticides to combat West Nile Virus and agricultural pests. Scientists also do not know how the syndrome spreads from cave to cave so rapidly. One possibility is that the migratory habits of these bats contribute to the spread of WNS, but federal and state agencies have also closed several caves and mines to prevent spread of the fungus by cavers. The United States Forest Service provides current information on WNS and cave closings at its website (www.fws.gov/northeast/white_nose.html).

Devil Facial Tumor Disease

Most people are aware of the death toll from human cancers; approximately 13% of human deaths worldwide are attributable to cancer (World Health Organization 2009). Nevertheless, few people are aware that cancer is also a major threat to certain wild animal populations. A case in point is the Tasmanian devil (*Sarcophilus harrisii*). These large carnivorous marsupials are threatened with extinction from an emerging form of cancer called "devil facial tumor disease" (Bostanci 2005).

This unusual cancer is a highly aggressive form of parasitic (nonviral) cancer that spreads when devils bite one another (McCallum & Jones 2006, and references therein). Initially, small tumors or lesions that become cancerous appear around the mouth and face and spread to other regions of the body (**Fig. 28-12**). The disease was first reported in 1996 and has spread widely, resulting in a 20% to 50% decline in devil populations across most of Tasmanina (Hawkins et al. 2006).

What makes this cancer unique is that it can be directly transmitted when cancer cells from an infected animal are passed directly to another individual by biting or feeding on the same prey carcass. Research suggests that the Tasmanina

FIGURE 28-11 Little brown bats (*Myotis lucifugus*) with white-nose syndrome in a New York hibernaculum.

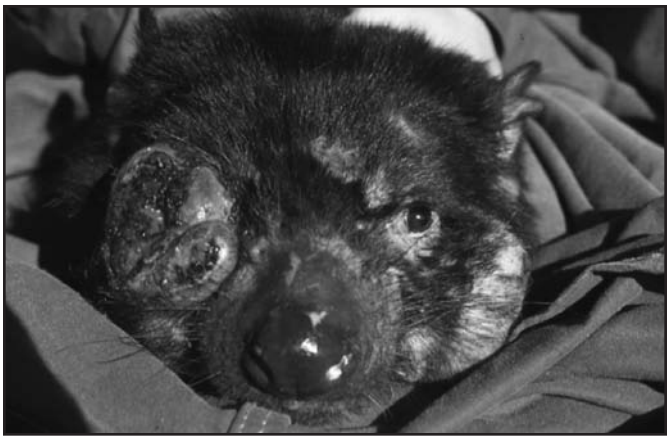


FIGURE 28-12 A Tasmanian devil (*Sarcophilus harrisii*) with devil facial tumor disease.

devil's immune system does not recognize the tumor cells as foreign because the devil's cells and the cancer cells share the same immune genes (Woods et al. 2007). If acquired, the cancer is fatal within a few months. In addition, the cancer has mutated into at least nine strains, further complicating control efforts. At the current rate, it is possible that Tasmanian devils could be extinct in the wild in less than 25 years (McCallum et al. 2007). As a result, in 2008, the Tasmanian devil was listed as "endangered" on the Red List of the IUCN.

A number of management practices are currently in effect to help rescue the species. Tasmanian wildlife biologists culled infected devils in several regions to help stem the spread of the disease. They have also created barriers to prevent infected devils from entering "clean zones" in parts of Tasmania that remain disease free. Finally, cancer-free devils have been relocated to mainland Australia in an attempt to isolate genetic breeding stock for future reintroductions to Tasmania (Jones et al. 2007).

Marine Mammal Diseases

Marine mammals are charismatic sentinels of our ocean environments. Nevertheless, marine mammals are not immune to emerging diseases. In recent years, over 30 disease agents have (re)emerged to infect cetaceans and pinnipeds (Miller et al. 2001). Some of these have resulted in mass mortality of marine mammals. For example, an epizootic morbillivirus killed an estimated 50% of coastal Atlantic bottlenose dolphins (*Tursiops truncatus*) along the eastern United States in the late 1980s (Lispcomb et al. 1994). This event was closely followed by a mass mortality event half a world away in Russia, where 10% of Baikal seals (*Pusa siberica*) died from another morbillivirus related to canine distemper (Mamaev et al. 1996). Another wave of morbillivirus infection spread across the Mediterranean Sea, resulting in thousands of dolphin deaths in 1990 (Domingo et al. 1990; Friend 2006, and references therein). These events were followed by other large- and small-scale outbreaks in a variety of cetacean and pinniped species. In addition to viral pathogens, marine mammals are also susceptible to bacterial, fungal, and parasitic diseases (Friend, 2006). Brucellosis and leptospirosis, for example, are the most important emerging bacterial disease of pinnipeds (Miller et al. 2001).

The California sea otter (*Enhydra lutris*) populations have experienced a substantial decline in recent years. Detailed examination of dead sea otters revealed that emergent diseases are important sources of mortality for sea otters. In almost 40% of sea otters examined, death was caused by parasitic, fungal, or bacterial infections (Thomas 2001). The main causes of adult sea otter mortality (64% of deaths) between 1998 and 2001 were from acanthocephalan parasites, *Toxoplasma gondii* encephalitis, cardiac disease, and shark attack (Kreuder et al. 2003). Ordinarily, parasitic infections in animals with healthy immune systems would remain subclinical (no detectable clinical symptoms). In this study, parasites caused 38% of sea otter deaths. The findings of protozoan parasites and other pathogens that are typically associated with terrestrial hosts suggest that land-to-sea transmission of infectious agents is increasing along the California coastline.

Cardiac disease was a primary factor in the deaths of 13% of adult sea otters examined by Kreuder et al. (2003). Sea otters wounded by sharks or suffering from cardiac disease were more likely to suffer infections from the protozoan parasite *T. gondii*. These mortality patterns suggest that parasitic infections weaken the sea otters, making them more susceptible to shark attacks. Most sea otters eaten by sharks are not available for study, and therefore, the percentage of disease-infected sea otters is likely higher than reported based on **beachcast** samples alone (Jessup et al. 2004).

Ecologists assume that the increasing rates of infectious disease in southern sea otter populations results from recent anthropogenic sources. Petroleum spills, sewage discharge, and fisheries depletion are all known to have negatively affected sea otter populations. However, these anthropogenic events can be reduced or eliminated by appropriate management strategies. Few management tools are currently available to reduce the effects of chronic runoff of pollutants or to stem the emergence of novel pathogens in coastal marine ecosystems. Not surprisingly, many ecologists hypothesize that California sea otter populations will continue to decline or grow at much slower rates than sea otter populations in the more pristine coastal waters of Washington, British Columbia, or Alaska.

Conservation Medicine

There is no doubt that zoonotic diseases are increasing worldwide and that they pose a significant threat to human

health and the health of livestock. Equally important, nonzoonotic diseases in wildlife threaten the biodiversity and viability of several important ecosystems. In response, a new interdisciplinary field of study has emerged in the past decades: **conservation medicine** (Aguirre et al. 2002).

Conservation medicine addresses comparative human, animal, and ecosystem health. This new field bridges the traditional disciplines of biomedical and veterinary science with conservation biology. The goals are to understand (1) the emergence and resurgence of infectious diseases, (2) the impacts of environmental pollutants on wildlife, and (3) how habitat fragmentation and the loss of biodiversity alter the health of ecological communities (reviewed in Aguirre et al. 2002).

The effects of human-induced environmental decline ripple through landscapes, communities, and ecosystems, yet their consequences remain poorly understood. The conservation medicine approach is to bring together teams of physicians, veterinarians, ecologists, microbiologists, pathologists, landscape ecologists, marine biologists, toxicologists, epidemiologists, climate biologists, economists, and political scientists to attack environmental and health problems simultaneously from multiple angles. As many of the previous examples illustrate, seemingly minor changes to the environment can result in significant increases in disease (Patz et al. 2004). Removal of top predators can result in unanticipated changes to the trophic structure of a community (e.g., increasing deer populations and the spread of Lyme disease in New England). Habitat loss can put wild and domestic species in closer proximity leading to cross-species disease transmission (e.g., CDV in Serengeti lions). Global trade and travel increasingly places people in contact with other people, organisms, and goods from around the world, leading to the emergence of infectious diseases such as HIV, severe acute respiratory syndrome, avian influenza, West Nile virus, H1N1 "swine" flu, and a host of other infectious diseases (Binder et al. 1999).

Conservation medicine is already making important contributions to our understanding of animal, human, and environmental health. Equally important, the insights generated are being used to help shape conservation priorities worldwide. Mammalogists and wildlife biologists have much to gain from, and much to contribute to, this emerging discipline.

SUMMARY

Humans and wildlife share a wide range of diseases. Infectious diseases transmitted between animals and humans are called zoonoses. Over 70% of emerging diseases have animal origins, making zoonotic diseases some of the most important potential threats to public and wildlife health.

Human–wildlife associations have increased greatly in recent years for a number of reasons. First, human population growth means more people sharing space with wildlife. Increasing outdoor recreation, ecotourism, and development encroaching on remnant wildlife habitat also puts millions of people in potential contact with wildlife. The relative ease and mass daily movements of global travel and the globalization of food markets also serve to increase the emergence of zoonotic diseases, moving them worldwide very quickly to immunologically naïve populations where they can cause catastrophic population declines. The rapidly expanding bushmeat trade increases the likelihood that wildlife-borne diseases will infect humans. Finally, wildlife often plays important but less obvious roles in the ecology of infectious diseases. The result is that environmental disruptions that affect wildlife can change the ecology of zoonoses, leading to increased between-species transfer.

Infectious diseases have a variety of sources, including viruses, bacteria, and parasites. Viral diseases are common in wild and domesticated mammals. For example, domestic or feral dogs spread canine distemper virus to wild dogs, lions, and spotted hyenas in Africa and to black-footed ferrets in the western United States. Other viral diseases include rinderpest, monkeypox, Ebola virus, Nipah virus, hantavirus, and rabies.

In much of Asia, Africa, and Latin America, rabies is spread by dogs, but the pattern of terrestrial wildlife rabies in the United States is regional and species specific. In the mid-Atlantic and northeast United States, rabies is epidemic in raccoons, whereas skunks are the main terrestrial vectors in the Midwest. In contrast, rabies in insectivorous bats is geographically widespread in the United States.

Other important diseases in mammals include those caused by mis-folded proteins called prions (e.g., chronic wasting disease), bacteria (e.g., plague, anthrax, and Lyme disease), parasites (e.g., toxoplasmosis), and fungi (e.g., white-nose disease in bats). Very recent outbreaks of new diseases such as white-nose syndrome in bats in the United States and devil facial tumor disease (an aggressive cancer) in Tasmanian devils reveal that mammalian diseases continue to endanger mammal populations and will likely lead to extinction of some species.

In response, a new interdisciplinary field, conservation medicine, has emerged. Conservation medicine addresses comparative human, animal, and ecosystem health. This new field attempts to understand (1) the emergence and resurgence of infectious diseases, (2) the impacts of environmental pollutants on wildlife, and (3) how habitat fragmentation and loss of biodiversity alter the health of ecological communities.

KEY TERMS

Asymptomatic
Beachcast
Conservation medicine
Emerging infectious disease
Epidemic
Host
Hyphae
Incubation period
Infectious disease
Oocyst
Outbreak
Pandemic
Pathogen
Prions
Prophylaxis
Protozoan
Serological
Titer
Vectors
Virulent
Zoonoses

RECOMMENDED READING

Aguirre, AA, et al. 2002. *Conservation Medicine, Ecological Health in Practice*. Oxford University Press, NY.

Binder, S, et al. 1999. Emerging infectious diseases: public health issues for the 21st century. *Science, 284,* 1311.

Blanton, JD, et al. 2008. Rabies surveillance in the United States during 2007. *Journal of the American Veterinary Medical Association, 233*(6):884.

Blehert, DS, et al. 2009. Bat white-nose syndrome: an emerging fungal pathogen? *Science, 323*:227.

Bostanci, A. 2005. A devil of a disease. *Science, 307*:1035.

Daszak, P, AA Cunningham, & AD Hyatt. 2000. Emerging infectious diseases of wildlife—threats to biodiversity and human health. *Science, 287*, 443–449.

Dierauf, LA & FMD Gullard. 2001. *CRC Handbook of Marine Mammal Medicine*. CRC Press, Boca Raton, FL.

Friend, M. 2006. *Disease Emergence and Resurgence: The Wildlife-Human Connection.* U.S. Geological Survey, Reston, VA.

McCallum, H & M Jones. 2006. To lose both would look like carelessness: Tasmanian devil facial tumor disease. *PLoS Biology, 4*(e342):1671–1674.

Pederson, AB, et al. 2007. Infectious diseases and extinction risk in wild mammals. *Conservation Biology, 21*:1269–1279.

Smith, KF, DF Sax, & KD Lafferty. 2006. Evidence for the role of infectious disease in species extinction and endangerment. *Conservation Biology, 20*:1349–1357.

Stenseth, NC, et al. 2008. Plague: past, present, and future. *PLoS Medicine, 5*(e3):9–13.

REFERENCES

Adler, T, 1996, A common dog virus diminishes lion pride. *Science News*, 49:70.

Aguirre, AA, et al. 2002. *Conservation Medicine, Ecological Health in Practice*. Oxford University Press, NY.

Alexander, KA, et al. 2002. *Mycobacterium tuberculosis*: an emerging disease of free-ranging wildlife: *Emerging Infectious Disease*, 8:598–601.

Allen, BF, F Keesing, and RS Ostfeld. 2003. Effect of forest fragmentation on Lyme disease risk. *Conservation Biology*, 17:267–272.

APHIS. 2004. Bovine spongiform encephalopathy in a dairy cow—Washington State, 2003. *Morbidity and Mortality Weekly Report*, 52:1280–1285.

Arai, S, et al. 2007. Hantavirus in northern short-tailed shrew, United States. *Emerging Infectious Diseases*, 13:1420–1423.

Arai, S, et al. 2008. Phylogenetically distinct hantaviruses in the masked shrew (*Sorex cinereus*) and dusky shrew (*Sorex monticolus*) in the United States. *The American Journal of Tropical Medicine and Hygiene*, 78:348–351.

Binder, S, et al. 1999. Emerging infectious diseases: public health issues for the 21st century. *Science*, 284:1311.

Blanton, JD, et al. 2008. Rabies surveillance in the United States during 2007. *Journal of the American Veterinary Medical Association*. 233(6):884.

Blehert, DS, et al. 2009. Bat white-nose syndrome: an emerging fungal pathogen? *Science*, 323:227.

Bostanci, A. 2005. A devil of a disease. *Science*, 307:1035.

Brass, D, 2009. Rabies vaccine strategies, concepts of rabies prophylaxis for the caving community. *PRS* 109:6–16.

Brisson, D, DE Dykhuizen, & RS Ostfeld. 2008. Conspicuous impacts of inconspicuous hosts on the Lyme disease epidemic. *Proceedings of the Royal Society*, B, 275:227–235.

Brownstein JS, TR Holford, D Fish. 2005. Effect of climate change on Lyme disease risk in North America. *EcoHealth*, 2:38–46.

Carpenter, M, et al. 1998 Genetic characterization of canine distemper virus in Serengeti carnivores.

Veterinary Immunology and Immunopathology, 65:259–266.

Centers for Disease Control and Prevention. 2003. Update: Multistate outbreak of monkeypox—Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003: Morbidity and Mortality Weekly Report, 52:589–590 and 616–618.

Centers for Disease Control and Prevention. 2004. Recovery of a patient from clinical rabies—Wisconsin, 2004. *Morbidity and Mortality Weekly Report*, 53:1171.

Centers for Disease Control and Prevention. 2008. Human rabies prevention—United States: recommendations of the advisory committee on immunization practices (ACIP). *Morbidity and Mortality Weekly Report*, 57, no. RR-3.

Childs, JE, et al. 1994. Serologic and genetic identification of *Peromyscus maniculatus* as the primary rodent reservoir for a new hantavirus in the southwestern United States. *Journal of Infectious Diseases*, 169:1271–80.

Chomel, BB, A Belotto, F-X. Meslin. 2007. Wildlife, exotic pets, and emerging zoonoses. *Emerging Infectious Diseases*, 13:6–11.

Chua, KB, BH Chua, and CW Wang. 2002a. Anthropogenic deforestation, El Nino and the emergence of Nipah virus in Malaysia. *Malaysian Journal of Pathology*, 24:15–21.

Chua, KB, et al. 2002b. Isolation of Nipah virus from Malaysian Island flying-foxes. *Microbes and Infection*, 4:145–151.

Cohn, JP. 2008. White-nose syndrome threatens bats. *Bioscience*, 58:1098.

Daniels, TJ, D Fish, I Schwartz. 1993. Reduced abundance of *Ixodes scapularis* (Acari: Ixodidae) and Lyme disease risk by deer exclusion. *Journal of Medical Entomology*, 30:1043–1049.

Dierauf, LA and FMD Gullard. 2001. *CRC Handbook of Marine Mammal Medicine*. CRC Press, Boca Raton, Fl.

Dobson, A, et al. 2003. Pathogens and parasites in a changing climate. 33–38 in *Climate Change and Biodiversity: Synergistic Impacts. Advances in Applied Biodiversity Science 4*, (L Hannah and T Lovejoy, eds.), Center for Applied Biodiversity Science, Conservation International Washington, DC.

Domingo, M, et al. 1990. Morbillivirus in dolphins. *Nature*, 348:21.

Ducrot, C, et al. 2008. Review on the epidemiology and dynamics of BSE epidemics. *Veterinary Research*, 39:15 (electronic).

Echenberg, M. 2007. *Plague Ports: The Global Urban Impact of Bubonic Plague, 1894–1901*. NY University Press, NY.

Eisen, RJ, et al. 2007. Human plague in the Southwestern United States, 1957–2004: spatial models of elevated risk of human exposure to *Yersina pestis*. *Journal of Medical Entomology*, 44:530–537.

Fayer, R. 1981. Toxoplasmosis update and public health implications. *Canadian Veterinary Journal*, 22:344–352.

Fenton, A, and AB Pedersen. 2005. Community epidemiology framework for classifying disease threats. *Emerging Infectious Diseases*, 11:1815–1821.

Frame, JD, et al. 1970. Lassa fever, a new virus disease of man from West Africa. *American Journal of Tropical Medicine and Hygiene*. 19:670–676.

Friend, M. 2006. Disease emergence and resurgence: the wildlife-human connection. U.S. Geological Survey, Reston, VA.

Gargas, A, et al. 2009. *Geomyces destructans* sp. nov. associated with bat white-nose syndrome. *Mycotaxon*, 108:147–154.

Guiler, ER. 1961. The former distribution and decline of the thylacine. *Australian Journal of Science*, 23:207–210.

Haas, L, et al. 1996. Canine distemper virus infection in Serengeti spotted hyaenas. *Veterinary Microbiology*, 49:147–152.

Harder, TC, et al. 1996. Canine distemper virus from diseased large felids: biological properties and phylogenetic relationships. *Journal of Genetics and Virology*, 77:397–405.

Hawkins, CE, et al. 2006. Emerging disease and population decline of an island endemic, the Tasmanian devil *Sarcophilus harrisii*. *Biological Conservation*, 131:307–324.

Hayman, DTS, et al. 2008. Evidence of henipavirus infection in West African fruit bats. *PLoS One*, 3:2739electronic.

Herlihy, D and SK Cohn, Jr. 1997. *The Black Death and the Transformation of the West*. Harvard University Press, Cambridge, MA.

Hjelle, B and GE Glass. 2000. Outbreak of hantavirus infection in the Four Corners region of the United States in the wake of the 1997–1998 El Niño–Southern Oscillation. *Journal of Infectious Diseases*, 181:1569–1571.

Hutin, YJF, et al. 2001. Outbreak of human monkeypox, Democratic Republic of Congo, 1996–1997: *Emerging Infectious Diseases*, 7:434–438.

Iehlé, C, et al. 2007. Henipavirus and Tioman virus antibodies in pteropodid bats, Madagascar. *Emerging Infectious Diseases*, 13:159–161.

IUCN 2006. IUCN Red List of threatened species. IUCN, Gland, Switzerland. Available from www.redlist.org.

Jessup, DA, et al. 2004. Southern sea otter as a sentinel of marine ecosystem health. *EcoHealth*, 1:239–245.

Johara, MY, et al. 2001. Nipah virus infection in bats (Order Chiroptera) in Peninsular Malaysia. *Emerging Infectious Diseases*, 7:439–441.

Jones, CG, et al. 1998. Chain reactions linking acorns to gypsy moth outbreaks and Lyme disease risk. *Science*, 279:1023–1026.

Jones, JL, D Kruszon-Moran, M Wilson. 2003. *Toxoplasma gondii* infection in the United States, 1999–2000. *Emerging Infectious Diseases*, 9:1371–1374.

Jones, ME, et al. 2007. Conservation management of Tasmanian Devils in the context of an emerging, extinction-threatening disease: Devil facial tumor disease. *EcoHealth*, 4:326–337.

Kahn, CM, and S Line. 2005. *The Merck Veterinary Manual*, 9th edition, Merck & Co., Inc. NJ.

Kallio, ER, et al. 2007. Endemic hantavirus infection impairs the winter survival of its rodent host. *Ecology*, 88:1911–1916.

Kennedy, S. et al. 2000 Mass die-off of Caspian seals caused by canine distemper virus. *Emerging Infectious Diseases*, 6:637–639.

Krebs JW, et al. 1996. Rabies surveillance in the United States during 1995. *Journal of American Veterinary Medicine Association*, 204:2031–44.

Kreuder, C, et al. 2003. Patterns of mortality in southern sea otters (*Enhydra lutris nereis*) from 1998–2001. *Journal of Wildlife Diseases*, 39:495–509.

Kutz, SJ, EP Hoberg, and L Polley. 2001. A new lungworm in muskoxen: an exploration in Arctic parasitology. *Trends in Parasitology*, 17:276–280.

Kutz, S, et al. 2004. "Emerging" parasitic infections in Arctic ungulates. *Integrative and Comparative Biology*, 44:109–118.

Lecompte E, et al. 2006. *Mastomys natalensis* and Lassa fever, West Africa. *Emerging Infectious Diseases*. 12:1971–1974.

Lehle, C., et al. 2007. Henipavirus and Tioman virus antibodies in pteropodid bats, Madagascar. *Emerging Infectious Diseases*. 13:159–161.

Leroy, EM, et al. 2004. Multipe Ebola virus transmission events and rapid decline of Central African wildlife. *Science*, 303:387–390.

Leroy, EM, et al. 2005. Fruit bats as reservoirs of Ebola virus. *Nature*, 438:575–576.

Lipscomb, TP, et al. 1994, Morbilliviral disease in Atlantic bottlenose dolphins (*Tursiops truncatus*) from 1987–1988 epizootic: *Journal of Wildlife Diseases*, 30:567–571.

Lyles, AM and AP Dobson. 1993. Infectious disease and intensive management: population dynamics, threatened hosts and their parasites. *Journal of Zoo and Wildlife Medicine*, 24:315–326.

Mamaev, L. et al. 1995. Characterisation of morbilliviruses isolated from Lake Baikal seals (*Phoca sibirica*). *Veterinary Microbiology*, 44:251–259.

Mamaev, LV, et al. 1996. Canine distemper virus in Lake Baikal seals (*Phoca sibirica*). *Veterinary Record*, 138:437–439.

Marennikova, SS, et al. 1972. Isolation and properties of the causal agent of a new variola-like disease (monkeypox) in man: *Bulletin of the World Health Organization*, 46:599–611.

McCallum, H and M Jones. 2006. To lose both would look like carelessness: Tasmanian devil facial tumor disease. *PLoS Biology*, 4(e342);1671–1674.

McCallum H, et al. 2007. Distribution and impacts of Tasmanian devil facial tumour disease. *EcoHealth*, 4:318–325.

McShea WJ and G Schwede. 1993. Variable acorn crops: responses of white-tailed deer and other mast consumers. *Journal of Mammalogy*, 74:999–1006.

Miller, D, RY Ewing, and GD Bossart. 2001. Emerging and resurging diseases. Pp.15–25 in *Marine Mammal Medicine*, (L Dierauf and F Gulland, eds.) CRC Press, Boca Raton, FL.

Miller, MA, et al. 2002. Coastal freshwater runoff is a risk factor for *Toxoplasma gondii* infection of southern sea otters (*Enhydra lutris nereis*). *International Journal of Parasitology*, 32:997–1006.

Morvan, JM, et al. 1999. Identification of Ebola virus sequences present as RNA or DNA in organs of terrestrial small mammals of the Central African Republic. *Microbes and Infection*, 1:1193–1201.

Muson, L, et al. 2008. Climate extremes promote fatal co-infections during canine distemper epidemics in African lions. *PLoS ONE*, 3:e2545.

Nemirov, K, A Vaheri, and A Plyusnin. 2004. Hantaviruses: co-evolution with natural hosts. *Recent Research in Developing Virology*, 6:201–228.

Nettles, VF, JH Shaddock RK, Sikes, and CR, Reyes. 1979. Rabies in translocated raccoons. *American Journal of Public Health*, 1979;69:601–2.

Nichol, ST, et al. 1993. Genetic identification of a novel hantavirus associated with an outbreak of acute respiratory illness in the southwestern United States. *Science*, 262:914–917.

Ostfeld, RS, Jones CG, and JO Wolff. 1996. Of mice and mast: ecological connections in eastern deciduous forests. *Bioscience*, 46:323–330.

Ostfeld, RS, et al. 2001. Effects of acorn production and mouse abundance on abundance and *Borrelia burgdorferi* infection prevalence of nymphal *Ixodes scapularis* ticks. *Vector Borne Zoonotic Diseases*, 1:55–63.

Ostfeld, RS, et al. 2006. Climate, deer, rodents, and acorns as determinants of variation in Lyme-disease risk. *PLoS Biology*, 4:1058–1068.

Packer, C, et al. 1999. Viruses of the Serengeti: patterns of infection and mortality in African lions. *Journal of Animal Ecology*, 68:1161–1178.

Patz, JA, et al. 2004. Unhealthy landscapes: policy recommendations on land use change and infectious disease emergence. *Environmental Health Perspectives*, 112:1092–1098.

Pederson, AB, et al. 2007. Infectious diseases and extinction risk in wild mammals. *Conservation Biology*, 21:1269–1279.

Perkins, SE, I Cattadori, and PJ Hudson. 2005. The role of mammals in emerging zoonoses. *Mammal Study*, 30:S67-S71.

Pomeroy, LW, ON Bjornstad, and EC Holmes. 2008. The evolutionary and epidemiological dynamics of the paramyxoviridae. *Journal of Molecular Evolution*, 66:98–106.

Pourrut, X, et al. 2005. The natural history of Ebola virus in Africa. *Microbes and Infection*, 7:1005–1014.

Pourrut, X, et al. 2007. Spatial and temporal patterns of Zaire ebola virus antibody prevalence in the possible reservoir bat species. *Journal of Infectious Disease*, 196:S176-S183.

Rand PW, et al. 2003. Deer density and the abundance of *Ixodes scapularis* (Acari: Ixodidae). *Journal of Medical Entomology*, 40:179–184.

Reynes, JM, et al. 2005. Nipah virus in Lyle's flying foxes, Cambodia. *Emerging Infectious Diseases*, 11:1042–7.

Roelke-Parker, ME, et al. 1996. A canine distemper virus epidemic in Serengeti lions (*Panthera leo*): *Nature*, 379:441–445.

Root, TL, et al. 2003. Fingerprints of global warming on wild animals and plants. *Nature*, 421:57–60.

Rosen, W. 2007. *Justinian's Flea: Plague, Empire, and the Birth of Europe*, Viking Adult, NY

Samuel, WM, et al. 2001. *Parasitic Diseases of Wild Mammals*, 2nd edition, Iowa State University Press, Ames, Iowa.

Schmaljohn, C and B Hjelle. 1997. Hantaviruses: A global disease problem. *Emerging Infectious Diseases*, 3:95–104.

Sigurdson, C, 2008. A prion disease of cervids: Chronic wasting disease. *Veterinary Research*, 39:41(electronic).

Smith, KF, DF Sax, and KD Lafferty. 2006. Evidence for the role of infectious disease in species extinction and endangerment. *Conservation Biology*, 20:1349–1357.

Song, J-W, et al. 2007a. Newfound hantavirus in Chinese mole shrew, Vietnam. *Emerging Infectious Diseases*, 13:1784–1787.

Song, J-W, et al. 2007b. Seewis virus, a genetically distinct hantavirus in the Eurasian common shrew (*Sorex araneus*). *Virology Journal*, 4:114–119.

Stenseth, NC. et al. 2006. Plague dynamics are driven by climate variation. *Proceedings of the National Academy of Sciences*, 103:13110–13115.

Stenseth, NC, et al. 2008. Plague: past, present, and future. *PLoS Medicine*, 5(e3):9–13.

Subak, S. 2003. Effects of climate on variability in Lyme disease incidence in the Northeastern United States. *American Journal of Epidemiology*, 157:531–538.

Thomas, NJ, 2001. Sea otter mortality. U.S. Geological Survey, National Wildlife Health Center Information Sheet, Madison, Wis., June 2001.

Valleron, AJ, et al. 2001. Estimation of epidemic size and incubation time based on age characteristics of vCJD in the United Kingdom. *Science*, 294:1726–8.

Wacharapluesadee, S, et al. 2005. Bat Nipah virus, Thailand. *Emerging Infectious Diseases*, 11:1949–51.

Williams, ES, et al. 1988. Canine distemper in black-footed ferrets (*Mustela nigripes*) from Wyoming. *Journal of Wildlife Diseases*, 24:385–398.

Williams, ES and IK Barker. 2001. *Infectious diseases of wild mammals*. Iowa State University Press, 3rd edition, Ames, Iowa.

Williams, ES, et al. 2002. Chronic wasting disease of deer and elk: a review with recommendations for management. *The Journal of Wildlife Management*, 66:551–563.

Williams, ES. 2005. Chronic wasting disease. *Veterinary Pathology*, 42:530–549.

Willoughby, RE, et al. 2005. Survival after treatment of rabies with induction of coma. *The New England Journal of Medicine*, 352:2508–2514.

Wolfe, ND, et al. 2005. Bushmeat hunting, deforestation, and prediction of zoonoses emergence. *Emerging Infectious Diseases*, 11:1822–1827.

Woods, GM, et al. 2007. The immune response of the Tasmanian devil (*Sarcophilus harrisii*) and devil facial tumour disease. *EcoHealth*, 4:338–345.

World Health Organization 2004. Weekly Epidemiological Record, 33(79):301–308.

PHOTO CREDITS

Opener Courtesy of Frederick Murphy/CDC; **28-7** Courtesy of Janice Haney Carr/CDC; **28-9** Courtesy of Scott Bauer/USDA ARS; **28-11** Courtesy of Nancy Heaslip, New York Department of Environmental Conservation/U.S. Fish and Wildlife Service; **28-12** Courtesy of Dr. Menna Jones, University of Tasmania