Chapter 2
Animals and Mechanisms of Disease Transmission

2.1 Introduction

A diverse range of microbial pathogens can be transmitted from domestic and wild animals to human populations. These include viruses, bacteria, parasites, fungi, and prions. Strictly defined, not all infectious diseases common to animals and humans are zoonotic, and they can contract pathogens from the same sources, i.e., soil, water, plants, and invertebrates. For instance, acquisition of common human pathogens \[\text{Escherichia coli, Enterococci spp.}\] from animal food source with multiple antimicrobial resistance profile due to the liberal usage of antibiotics in animal feed may not be considered as zoonoses. Zoonotic diseases are due to transmissible infectious agents that affect more than one animal species, including humans, and cause clinical or subclinical infections. The resurgence of zoonotic infectious diseases in the past two decades globally is of major concern. These diseases have resulted in significant morbidity and mortality on a large segment of the global human population, with over a billion afflicted resulting in millions of annual deaths [1]. Moreover, outbreaks of zoonoses have had adverse impact on regional economies as a result of huge financial burden on the affected communities, but also indirectly affecting commerce or trade with more affluent consumer countries from the fear of spreading the affliction to their population. A systematic survey in 2007 estimated that in 1399 species of human pathogens, 87 of which were first reported in humans since 1980, most were viruses of animal reservoirs [1]. The World Organization for Animal Health estimates that 75% of emerging infectious diseases in humans originate from domestic or wild animals, appealing for collaboration between animal health and human public health organizations and authorities [www.oie.int/int/edito/en-avr09.htm]. A new strategy to incorporate animal health data to assist public health authorities was adopted by the European Union under the One Health concept [2]. The socioecology of zoonoses is complex and dynamic, and the epidemiology and resurgence of these diseases are influenced by various
conditions that can be classified as human related, pathogen related, animal/host related, and climate/environment related [3]. Significant interaction and combination of these factors are usually present.

2.2 Various Means of Transmission

2.2.1 Socioecology Factors

Human-related factors include the results of industrialization and expansion of communities to accommodate the global population explosion. Developmental progress with clearing of forests for new roads, residences, towns, and farmlands impinge on wildlife ecology. Moreover, human intrusion on animal ecosystem is influenced by globalization of trade, alteration of farming and food chain practices, increased hunting and pet ownership, ecotourism, and expansion of culinary practice [3]. Human exposures to animals and wildlife may be affected by changes in political regimes, conflict and wars, famine, mass migration and loosening of border controls, and breakdown of public health infrastructure. Furthermore, starvation and nutritional deficiencies usually result in a highly susceptible population to various diseases, including infections transmitted directly or indirectly from animals.

Pathogen-related factors are influenced by changes in the ecosystem and biodiversity that affect local fauna composition and quantity that may result in greater numbers of vectors and disease reservoirs/hosts, selection pressures for development of greater microbial resistance and virulence, and genetic variability [3]. Climate and environmental factors are of increased concern in recent years, as global climate change with abnormal north-south hemisphere alteration of climate pattern can influence host-vector life cycles and change in fauna and ecology of animals and vectors.

2.2.2 Mechanisms of Transmission

There are several ways by which animals can transmit infectious agents to humans, and these include: direct contact with live animals or carcasses, indirect contact through animal products such as milk or eggs, intermediary transmission through vectors [fleas, mites, ticks, mosquitoes, etc.], and remote contact from exposure to contaminated waters, soil, and air. Direct contact with animals or carcasses can result in transmission of disease by a few different ways, most commonly by oral ingestion as in foodborne zoonoses, or accidentally from handling pets without proper hand sanitization. Transmission of disease by animal bites, scratches, or mucosal exposure to infected secretions occurs relatively infrequently, such as in
rabies and animal-related wound infections. Exposure to animal pathogens can be through inhalation of droplets of infected secretions, as believed to have occurred in China with local outbreaks of avian influenza arising from exposures to infected fowls or ducks in open markets. On rare occasions inhalation of microbial spores or contamination of the abraded or broken skin from exposure to contaminated animal hide can result in infection such as anthrax.

Exposures to animal excretions are common causes of unsuspected animal infectious pathogens and in sporadic cases the origin is usually undetected. Only in local outbreaks of diseases can the source of infection be detected by epidemiological investigations, as sometimes found from ingestion of contaminated vegetables from infected manure used for fertilization, as in listeria infection after ingestion of contaminated cold-slaw. Inhalation of aerosolized excreta from infected animals is another means of transmission, i.e., in “cave disease” that occurs in spelunkers after exploration of bat-infested caverns contaminated with *Histoplasma capsulatum* spores or sporadic cases of hantavirus pulmonary disease from unwitting inhalation of rat excreta aerosolized with dust. Infected animal excretions may also transmit diseases through contamination of water used for drinking or bathing or from accidental skin exposure to puddles of water containing rat urine to produce leptospirosis.

Intermediary transmission by vectors represents a major mode of transmitting animal pathogens to humans. In most instances humans are incidental hosts and are not essential for maintaining the life cycle of the parasite or pathogen. Vector-transmitted zoonoses have been a scourge to humanity since antiquity and continue to plague human populations at present and for the foreseeable future. Chagas disease, transmitted by the “kissing bug” [triatomine], afflicted humans as early as 9000 years ago [4]. The causative parasite *Trypanosoma cruzi* [discovered in 1909] can be found in at least 150 species of domestic and wild animals; and paleoparastologists detected *T. cruzi* DNA from human mummies of ancient times [5]. Vector-borne zoonoses continue to emerge in the modern era, for example, Lyme disease, and expand with greater resurgence as exemplified by the global expansion of dengue fever and West Nile virus disease.

### 2.3 Animal Disease via the Food Chain

Accurate estimates of the global burden of foodborne infectious diseases are difficult to attain and are grossly underestimated in countries with active surveillance. Even in developed affluent countries such as the United States [US], most foodborne diseases are unreported, and only a fraction of these cases have a microbiological etiology confirmation. Estimates of foodborne infections are even more difficult to derive in developing countries, where there are inadequate facilities and healthcare infrastructure and the global burden of foodborne zoonoses is the greatest. It is estimated that each year at least one-third of world’s population is afflicted with foodborne infections and a large fraction from animal pathogens. International
collaboration spearheaded by the World Health Organization [WHO] launched surveillance programs since 2000 to determine the burden of foodborne diseases in resource-poor countries and globally [6]. Previous estimates from the Center for Disease Control and Prevention [CDC] in 2011 determined that 31 major pathogens acquired in the US caused at least 9.4 million episode of foodborne illness each year, but could be >48 million cases [7]. Common animal-derived pathogens such as nontyphoidal Salmonella spp., Campylobacter spp., and Toxoplasma gondii were the leading causes of hospitalization [58%]. It is surmised that about 30% of all emerging infectious diseases in the past 60 years were caused by pathogens commonly transmitted through food and were of animal origin [8].

There are more than 250 different foodborne diseases, the majority due to transmissible microbes [bacteria, viruses, parasites, and prions] and the remainder by chemicals and toxins [9]. Although foodborne zoonoses can be asymptomatic and the majority present with acute self-limited disease, occasionally severe disease and fatality occur and chronic disability can be present. Infection may result from eating raw or undercooked animal products, or contaminated vegetables and fruits, or drinking contaminated water or milk [9]. Moreover, infections and outbreaks can occur from prepared food contaminated by an ill person or asymptomatic carrier. It is often difficult to trace animal-mediated infectious diseases from non-meat products as shown by recent experiences. This is exemplified by the outbreak in Europe of a novel Shiga toxin-producing E. coli 0104:H4 from contaminated sprouts originating in Germany, resulting in 50 deaths, and the outbreak in the US with Listeria-contaminated cantaloupes which killed 29 people [10–12]. Foodborne zoonoses are usually classified according to the microbial etiology, and a list of various pathogens is summarized in Table 2.1 [this may not be totally inclusive].

### 2.3.1 Bacterial Foodborne Zoonoses

Campylobacter sp. and Salmonella sp. are the leading causes of bacterial foodborne zoonoses in the US and European Union from domestic acquisition [7, 13, 14]. Although the majority of outbreaks of these bacterial zoonoses are related to

| (a) Bacterial foodborne zoonoses and (b) Foodborne parasitic zoonoses |
|----------------------|-------------|-------------|-------------|
| **Microbes**         | **Animals**            | **Frequency**         | **Distribution**     |
| Campylobacter spp.   | Poultry, pigs, cattle, sheep, rabbits, and pets | >1 million/year in US | Worldwide |
| Salmonella spp.      | Same as above           | >1 million/year in US | Worldwide |
| Listeria monocytogenes | Cattle, ruminants     | >16,000/year in US   | Worldwide |
| E. coli—STEC         | Cattle, sheep, goat    | >265,600/year in US  | Worldwide |
| Yersinia enterocolitica | Pigs, other farm animals | N/A | Worldwide |

(continued)
Table 2.1 (continued)

| Microbes                    | Animals                          | Frequency | Distribution               |
|-----------------------------|----------------------------------|-----------|----------------------------|
| Vibrio species              |                                  |           |                            |
| *V. parahaemolyticus*       | Sea crabs, oysters                | N/A       | Southeast Asia, Eastern    |
|                             |                                  |           | Coast US                   |
| *Brucella abortus*          | Cattle                           | 500,000/year | Western Europe             |
| *B. mellitensis*            | Sheep and goats                  | N/A       | Mediterranean, worldwide   |
| *B. suis*                   | Pigs, cattle                      | N/A       | Asia, Africa, S. America   |
| *Coxiella burnetii*         | Sheep, goats                     | N/A       | Worldwide except New Zealand|
| *Mycobacteria bovis* (b)    | Cattle, buffaloes                 | N/A       | Worldwide                  |
| *Toxoplasma gondii*         | Pigs, sheep, cats, and rabbits    | ½ billion globally | Worldwide                |
| *Clonorchis sinensis*       | Freshwater fish, pigs, cats, rats| 35 million worldwide | Asia                     |
| *Fasciola hepatica*         | Wild and domestic ruminants      | N/A, variable | Worldwide, high rates in S. America, Nile Delta, Asia, Northern Europe |
| *Opisthorchis sp.*          | Canines, felines, freshwater fish| N/A, variable | SE. Europe, Siberia, SE. Asia, Northern Thailand |
| *Paragonimus westermani* [lung fluke] | Freshwater shellfish, crabs, pigs | 20 million global | Asia, Africa, Central and South America |
| *Diphyllobothrium latum* [fish tapeworm] | Freshwater fish | N/A | N. hemisphere, Baltic region, America, Northern Japan, China |
| *Taenia saginata* [beef tapeworm] | Cattle, deer, rare beef | 4 million global | Worldwide, cosmopolitan, high in E. Africa, SE. Asia, China |
| *Taenia solium* [pork tapeworm] | Pigs, undercooked pork | N/A | Central and S. America, Africa, SE. Asia, South and Eastern Europe |
| Visceral cysticercosis      | Fecal-oral                        | 10–20% in endemic areas population | Central and S. America, Africa, SE. Asia, South and Eastern Europe |
| *Angiostrongylus cantonensis* | Freshwater crabs, crayfish, rats—lung worm | N/A | SE. Asia, India, Australia, Caribbean, Southern US |
| *Anisakis simplex* [Herring worm] | Sea—fish, squids, marine mammals | N/A | Cosmopolitan, Spain, France, Japan, Netherlands, rarely in US |
| *Gnathostoma spinigerum* [Gnathostomiasis] | Freshwater fish, frogs, snails, chickens, cats, dogs | N/A | SE. Asia, Central America, Australia |

Data obtained from Kauss h, Weber A, Appel M et al. [eds]. Zoonoses: Infections transmissible from animals to humans, 3rd Edition, Appendix E, 2003, ASM Press, Washington, 423–37; Alturi VL, et al. Ann.Rev.Microbiol. 2011; 65: 523–41; Durr S, et al. PLOS Neglected Trop. Dis. 2013; 7: e2399, PMID: 24009789

HUS hemolytic uremic syndrome, TTP thrombotic thrombocytopenic purpura, STEC Shiga toxin E. coli, N/A not available
“high-risk” foods commonly associated with illness, for instance, pink hamburger, raw oysters, unpasteurized milk or milk products [cheese], runny eggs, and alfalfa sprouts [15], outbreaks have occurred with vegetables, fruits, peanut butter, and raw nuts [16]. The majority of resulting illnesses are usually self-limited gastroenteritis, but chronic complications may include irritable bowel syndrome, reactive arthritis/spondylitis, and rarely Guillain-Barre syndrome. These bacteria are widespread in nature and often colonize the intestines of many domestic and wild animals, i.e., poultry, pigs, cattle, sheep, etc. Hence, raw meat from these animals are frequently contaminated with pathogenic bacteria during the preparation of carcasses for wholesale or retail in broilers and supermarkets, with poultry more frequently colonized with disease-producing bacteria than pork or beef. The European Food Safety Authority reported that poultry meats from broilers were contaminated by Campylobacter in 75.8% and by Salmonella in 15.6% [17]. However, even higher rates were reported in China with the presence of Campylobacter in carcasses of chicken in 94%, duck in 96%, rabbit in 97%, pork in 31%, and beef in 35% [18]. Salmonella contamination of meats for retail in the marketplace of China was somewhat less, with rates in chicken of 54%, in pork of 31%, in lamb of 20%, and in beef of 17% [19].

Recent reports in the US ranked the disease burden of food source infections and listed ten pathogen-food combinations, which included five pathogens [Campylobacter, Salmonella, norovirus, Listeria monocytogenes, and T. gondii], detected mainly from eight food categories, poultry, pork, deli meats, dairy, beef, eggs, farm produce and complex foods. Poultry was ranked as the number one cause of significant disease burden [mainly Campylobacter and Salmonella], followed by complex foods [83% caused by norovirus], and thirdly by pork [largely from T. gondii]. The five pathogens listed account for more than 50% of the total food-related illnesses due to 14 pathogens, responsible for $8 billion overall cost and 36,000 quality-adjusted life years [20]. The global burden of nontyphoidal Salmonella infections [mainly from foodborne zoonosis] is estimated to be 80.3 million cases, with 155,000 deaths [21].

Listeria monocytogenes, a nonsporulating, gram-positive bacillus, found mainly in ruminants but can affect all species of animals, is an infrequent and serious infection that can lead to meningitis with a mortality of 20–30% for at-risk persons [pregnant, neonates, elderly, and the immunocompromised] [12]. Listeria poses special risk in current trend of culinary habits, as 1–10% of ready-to-eat food may be contaminated with Listeria [22]; and the bacteria can survive and grow at low temperatures, high salt level, and low pH used in food processing [23]. Contaminated food products with Listeria more commonly include unpasteurized milk and dairy products [soft and feta cheese] and meat from ruminants and sometimes poultry [24]. Listeriosis has a variable incubation period of 2–70 days and the food source is often difficult to ascertain. The Active Surveillance Network in the US reported 762 listeriosis cases over a 6-year period [2004–2009], with an overall fatality rate of 18% [25]. However, most cases are unreported, and it is estimated that as many as 1600 cases of invasive listeriosis and 260 related deaths occur each year in the US [7]. In China L. monocytogenes had been recovered from about 4% of various types of prepared food samples and 6.28% of raw meat [26].
Enterohemorrhagic *E. coli* or Shiga toxin-producing *E. coli* [STEC] is a food-borne zoonosis transmitted to humans from contaminated food and water or contact with infected animals or persons. Infections are caused predominantly by *E. coli* serotype 0157:H7, but novel serotypes are emerging that produces the toxin, as exemplified by the outbreak in Europe with *E. coli* 0104:H4 [10, 11]. Infections can result in acute uncomplicated diarrhea or with severe hemorrhagic colitis and hemolytic uremic syndrome with acute renal failure and death [mainly children under 10 years of age], and thrombotic thrombocytopenic purpura [mostly in adults]. These severe complications occur in about 10% of infected subjects [27]. Infections with STEC are estimated to occur in about 265,630 persons with 31 deaths annually in the US [7]. Outbreaks of STEC infections occur worldwide but the global burden of disease is unknown. There are over 100 STEC serotypes, but most outbreaks and sporadic diseases are attributed to the 0157 serotype. The diagnosis is probably frequently missed as many laboratories only test for the 0157 STEC, without a test to detect Shiga toxin as recommended [28]. Shiga toxins [STXs] or verotoxins are potent cytotoxins, found mainly in zoonotic pathogenic *E. coli*, and are produced through lysogenic bacteriophages inserted into the chromosomes to encode the genes for six or more STXs [27]. Most STEC disease is the result of STX1 or STX2. Transmission of STEC readily occurs as the infectious dose is low [10–100 colony-forming units], and the bacteria are resistant to gastric acid [27]. The STECs are mainly found in cattle, sheep, and goats, but other animals can be carriers; and infection in humans mainly results from ingestion of undercooked beef or contaminated milk, yogurt, and cottage cheese and rarely from salads, vegetables, and apple juice [27]. The prevalence of STEC in cattle bowels ranges from 0.1 to 16%, and shedding of the pathogen in the excreta is intermittent [29].

The large outbreak of the hypervirulent STEC 0104:H4 that started in northern Germany and spread to 15 European countries in 2011 is unique. The epidemic affected over 4000 people and caused 54 deaths, and 22% of those afflicted developed the hemolytic uremic syndrome [10]. Several unusual features of this outbreak included median incubation period of 8 days which usually is 3–4 days with STEC 0157; 88% of the cases with hemolytic uremic syndrome occurred in adults [men age 42 years], which generally occurs in children. The pathobiologic mechanisms differed from the STEC 0157 infections in the absence of the usual virulence enterocyte effacement locus, characteristic for enteropathogenic *E. coli* used for epithelial adherence. However, this strain possessed several genes and virulence plasmids typical for enteroaggregative *E. coli*, carried primarily by humans [10]. This suggest that the STEC 0104 strain resulted from mixing of human and animal [cattle] STEC to produce a recombination of genes in a novel bacteria probably of a zoonotic source.

Some foodborne bacterial zoonoses including *Yersinia enterocolitica* infection have declined significantly in the US since 1996 [30]. Outbreaks are rarely reported and sporadic cases that occur are mainly associated with consumption of undercooked pork. In China two outbreaks of *Y. enterocolitica* occurred in the early 1980s which affected more than 500 people [31]. The main animal reservoir is the pig, as a pharyngeal commensal [32], but the organism has been isolated in more than ten different types of animals in China, and 32% of the strains were considered pathogenic [33]. Foodborne vibriosis due to non-cholera species is mainly from con-
sumption of raw or undercooked seafood, especially oysters, appears to be increasing in the US, and is estimated to cause about 800,000 illnesses, 500 hospitalizations, and 100 deaths each year [7, 34]. Vibrios are natural commensals in marine and estuarine seawater, and *Vibrio parahaemolyticus* is the most common cause of foodborne infection, presenting mainly as a self-limited gastroenteritis. *Vibrio vulnificus*, which is associated with soft tissue infection and septicemia, is rarely foodborne [34]. Other bacterial foodborne zoonoses which are rare in North America but more common in the Mediterranean basin and developing countries include Q-fever and brucellosis. Persistence of these pathogens in these regions may largely be related to unregulated animal husbandry. *Streptococcus suis* infection is an emerging foodborne zoonosis in Asia and is reviewed in a separate chapter.

### 2.3.2 Foodborne Parasitic Zoonoses

Foodborne animal-related parasitic infections are globally distributed, and the burden of disease is underestimated in developed countries. In the US it is estimated that only 2% of foodborne illnesses are caused by parasites annually [7]. However, *T. gondii* which is the most common foodborne parasite is frequently subclinical, and only 15% of recently infected subjects are clinically ill [35]. *T. gondii* is the most widespread parasitic infection in the world and infects half a billion people or one-third of the global population [27, 29]. The parasite infects a wide variety of domestic and wild animals, and nearly all warm-blooded animals can be infected. The seroprevalence of toxoplasmosis varies greatly in different countries, which may be related to culinary habits and hygienic standards. Although toxoplasmosis can be transmitted from contamination of the hands while changing cat [kitten] liter from sporulated oocysts, most infection results from ingestion of raw or undercooked meat with tissue cysts. The prevalence of infection in cat ranges between 10 and 80%, and oocysts are shed only in the first 14 days of primary infection [36]. Consumption of raw or undercooked pork and lamb is most commonly implicated in the transmission of toxoplasmosis, less commonly from beef due to a short developmental stage in cattle, but infection can occur from eating raw/undercooked liver, caribou, and seal meat and rarely from drinking contaminated water [36]. The seroprevalence of toxoplasmosis in Central Europe ranges between 37 and 58%, in the US 3 and 35%, in Latin America 51 and 72%, and in West Africa 54 and 77% [36]. Infection in healthy persons is usually subclinical or sometimes present with the mononuclear syndrome, but infection in pregnancy and immunosuppressed hosts can produce serious consequences. Congenital toxoplasmosis in the first trimester occurs in about 15% from primary infection and may cause severe complications [abortion, microcephaly, hydrocephalus, and mental retardation]; and infection in the third trimester can result in less severe abnormalities [chorioretinitis, epilepsy, deafness, jaundice at birth, learning difficulties later in life] but more frequently about 65% [36].

Giardiasis caused by *Giardia lamblia* [*G. intestinalis*] is not usually a foodborne parasitic infection but is carried by dogs, cats, cattle, sheep, pigs, and rodents and...
indirectly causes human infection from contamination of drinking water and food. It is worldwide in distribution and causes millions of infection each year. Other foodborne parasitic zoonoses are rare in well-developed countries, but cryptosporidiosis was fairly common in AIDS patients before the advent of highly active antiretroviral agents. Cryptosporidium parvum is an intracellular protozoa that affect over 150 mammalian species and is worldwide in distribution; it causes disease in calves and less commonly in lambs, cats, and dogs [36]. Transmission is by contaminated food or water, and outbreaks can occur from contaminated municipal drinking water as the organism is chlorine resistant. It is estimated that >56,000 domestically acquired infection occurs annually in the US [7]. In healthy subjects C. parvum causes a self-limited gastroenteritis, but the immunosuppressed hosts are prone to severe, protracted diarrhea with dehydration, weight loss, or wasting, and it is an AIDS-defining disease.

Several parasitic foodborne diseases are common in developing countries but are rare in North America and Europe, largely due to differences in standards of hygiene and governments regulations, and culinary practices. Consumption of undercooked infected meat and fish poses a major health risk to people of Asia and other tropical and subtropical regions of the world. Foodborne parasitic zoonoses are estimated to affect about 150 million people in China alone [31]. National surveys in China between 2001 and 2004 indicated that the number of people affected with clonorchiasis, trichinelllosis, paragonimiasis, and angiostrongyloidiasis had increased compared to previous surveys in 1988–1992 and are of public health concern [31, 37]. Clonorchis sinensis is a trematode that can be asymptomatic or cause liver/biliary tract disease in all Asian countries from consumption of raw freshwater fish or shrimps; and it is estimated to that 35 million people who are infected globally, with 15 million residing in China [31]. The cycle of the liver fluke is perpetuated by fecal contamination of freshwater by animal hosts [humans, pigs, cats, and rats], with ingestion of larvae by snails and release of cercariae to infect fish. Eradication and control has been difficult as rice paddies, swamps, ponds, and streams commonly have infected fish [mainly carps], which is a main source of food supply. In some provinces of China, about 17% of freshwater fish are infected with C. sinensis, and rates of infection in the population vary from 4.75% to 31.6% [31, 38]. Despite the common practice of eating raw fish [sushi] in Japan, clonorchiasis is very rare, as the fish is mainly from the sea. The bulk of the infected people with clonorchiasis are asymptomatic, but heavy burden of infection for many years can result in gall-bladder and liver disease, cholangitis, and cholangiocarcinoma.

Viral zoonoses transmitted by food are few in number and include mainly hepatitis E and severe acute respiratory syndrome [SARS] which are reviewed in separate chapters. Prion, a transmissible altered protein, was first recognized to cause disease in sheep [scrapie] for more than 50 years, but more recent transmission to humans from consumption of beef from cattle with bovine encephalopathy [“mad cow disease”] had arisen in Britain and spread to Europe almost two decades ago. A summary of some foodborne zoonoses is shown in Table 2.1.
2.4 Pets as a Source of Zoonoses

The domestication of animals for companionship in human societies probably exists for over 10,000 years. Ancient Egyptian writings in the Kahun Papyri [1900 BC] acknowledged the recognition of animal diseases; and ancient Mesopotamians passed laws [Eshuna Code of 2300] for containment of rabid dogs [39]. The number of households or the proportion of families in the world with pets is unknown but this is quite substantial. In affluent countries pet ownership is increasing, not only for cats and dogs but also for more exotic animals. In the US it was estimated in 2006 that 37% of households owned 72 million pet dogs and 32% owned 81 million cats [2007 US Pet Ownership and Demographics Sourcebook]. Similar figures were available for the United Kingdom [UK] with 8 million pet dogs in 23% of households and 8 million cats in 19% of households [http://www.pfma.org.uk].

Companion animals can cause infectious diseases by several means of transmission such as by direct contact, bites scratches, incidentally by fecal-oral route, and indirectly by vectors, i.e., fleas, ticks, sandflies, and mosquitoes. Pet ownership rarely results in disease transmission overall, and most infections that result are usually asymptomatic or subclinical [e.g., toxoplasmosis from handling infected cat litter]. The majority of zoonoses reported from pets are related to dogs and cats, but there is a wide variety of animals and pathogens that can be involved such as reptiles/amphibians, birds, rodents, monkeys, and even pet-household pigs. The risk of infection of potential zoonoses depends on the animal, local zoonoses endemic in the region, hygienic practice, laws governing animal vaccinations and license, and restrictions of exotic animals in households. The major pet-associated zoonoses are shown in Tables 2.2, 2.3, 2.4, and 2.5.

### Table 2.2 Pet animal-associated zoonoses: diseases by bites and scratches

| Microbes            | Animals          | Disease                       | Distribution                        |
|---------------------|------------------|-------------------------------|-------------------------------------|
| Rabies virus        | Dogs and cats    | Rabies encephalitis           | Worldwide, esp. Africa and Asia     |
| Pasteurella multocida | Cats and dogs   | Wound infection               | Worldwide                           |
| Pasteurella canis   | Dogs             | Soft tissue infection         | Worldwide                           |
| Capnocytophaga canimorsus | Dogs    | Cellulitis, sepsis in splenic dysfunction | Worldwide                           |

### Table 2.3 Pet animal-associated zoonoses: vector-borne disease

| Microbes            | Animals | Disease                                      | Vector          | Distribution                                      |
|---------------------|---------|----------------------------------------------|-----------------|---------------------------------------------------|
| Leishmania infantum | Dogs    | Visceral leishmaniasis                      | Sandflies       | Southern Europe, Central and S. America, Asia, North Africa |
| Bartonella henselae | Cats    | Cat scratch disease, bacillary angiomatosis | Cat fleas       | Worldwide                                         |
| Rickettsia rickettsiae | Dogs | RMSF                                         | Dog tick        | US, Central and northern South America           |
| Rickettsia conorii  | Dogs    | MSF                                          | Dog tick        | Southern Europe, Middle East, North Africa, India, Pakistan |
| Ehrlichia canis     | Dogs    | Ehrlichiosis                                 | Dog tick        | Venezuela [rare]                                 |
In most developed countries, pet-associated clinically recognized infections are usually secondary to accidental bites, scratches, or contact of open wounds with saliva of cats or dogs. Dog bites most commonly affect children, and in the US 4.7 million people a year suffer from dog bites, with 368,345 persons requiring emergency room treatment for dog-bite injuries [40]. Rabies, a fatal zoonosis transmitted by dog or cat bite, is rare in North America and most well-developed countries, and most cases occur in Africa and Asia with 55,000 deaths globally each year [41]. The majority of cases result from dog bites [99%] and most frequently from free-roaming animals. In North America rabies is mainly associated with bats in human cases. Animal rabies has declined in all domestic vertebrates in the US since 2010, with only 69 affected dogs but 303 infected cats, 63% of all domestic animals [42]. Free-roaming cats account for most of the human exposure incidents and need for postexposure rabies prophylaxis in the US [43].

The most common clinical infection reported in humans associated with pets is wound infection after puncture wounds, crush injuries, or soft tissue tears. Mixed infection with oral flora of the animal, including Pasteurella species, streptococcus, Staphylococcus aureus, and anaerobes, is mainly found. In cat-bite wounds, Pasteurella sp. [mainly P. multocida] is found in 75% to 90% and in dog-bite wounds in 20–50%, but mainly Pasteurella canis [44]. Anaerobes, Fusobacterium species, and Bacteroides sp. are present in 30–40% of animal-bite wounds; and a fastidious gram-negative bacteria, Capnocytophaga canimorsus or C. cymodemgi,
most commonly from dog bites, can cause serious infection in the elderly, asplenic subjects, alcoholics, and the immunosuppressed who are prone to severe sepsis and metastatic infection with mortality >30% [45].

### 2.4.1 Vector-Borne Zoonoses from Pets

Vectors are important transmitters of companion animal zoonoses worldwide; see Table 2.3. The most important disease globally in this category is visceral leishmaniasis which is caused by *Leishmania infantum* [L. chagasi], transmitted by sandflies from the major reservoir of domestic dogs [39]. The disease is endemic in many countries of southern Europe, South and Central America, northern Africa, and Asia; and a high proportion of dogs in these areas are infected. It was estimated by the WHO in 2007 that about 12 million people were infected worldwide and 2 million new cases occurred annually; also there was increased risk of severe disease in the HIV-infected population [46]. Control of leishmaniasis in the endemic areas is a great challenge and extension to non-endemic regions is of great concern, due to increasing travel access of pets across borders. Control measures instituted in Brazil consisted of serologically testing dogs and culling positive animals [47], and vaccination of dogs with a commercial vaccine [Leishmune] has resulted in decreased prevalence in canine and human leishmaniasis from reduced transmission [48].

Cat scratch disease is the most common zoonotic infection caused by *Bartonella* bacteria. It is of worldwide distribution but more common in temperate zones where pets are kept indoors. The cat although asymptomatic is a large reservoir for human infections with *Bartonella henselae, Bartonella clarridgeiae, and Bartonella koehlerae*. Cat scratch disease occurs mainly in children and is transmitted by the infected flea feces via the claws of kittens from scratching. Thus it is a vector-borne infection transmitted from cats with bacteremia to other cats and humans by fleas. Dogs can be infected with various *Bartonella* species, but their role in human disease is unclear [49]. The infection is usually manifested by fever and regional lymphadenopathy, but rare severe complications can occur such as encephalitis, granulomatous hepatitis, retinitis, choroiditis, arthritis, and osteomyelitis [27]. In patients with AIDS, *Bartonella henselae* can rarely cause a rash of bacillary angiomatosis with secondary lesions in the liver [bacillary peliosis], spleen, and lymph nodes. In developing countries the prevalence of *Bartonella* seropositivity in cats is about 27% and bacteremia approximately 10% [39].

There are several tickborne diseases common to both humans and companion animals that are of concern with respect to increased transmission and diseases in human communities. These include borreliosis [Lyme disease], ehrlichiosis, babesiosis, rickettsiosis, anaplasmosis, Q-fever, tularemia, and tickborne encephalitis, found in Europe and Northwestern Asia [39]. However, only a few of these conditions have been documented to be transmitted via contact with pets. In some of these diseases, the pets [dogs and cats] are not natural hosts for the vectors [i.e., black-legged deer ticks], but the animals may facilitate human exposure from outdoor activities, such as Lyme disease, ehrlichiosis, babesiosis, and anaplasmosis.
Hence, the pets pose a minimal risk to humans to predispose to acquiring these conditions. Infections in the pets as diagnosed by a veterinarian may be used as a sentinel for monitoring the risk of disease in the community of an endemic area [50]. Dog ticks can transmit rickettsia infection to humans, and dog ownership is a risk factor for acquiring rickettsiosis in endemic regions. Rocky Mountain spotted fever [RMSF] is endemic in many states of the US, greatest in the mid-south Atlantic states and west south-central region than the Rocky Mountain States, but also present in Central America [Mexico, Costa Rica, and Panama] and northern South America [Columbia and Brazil] [27, 51]. The main vector for RMSF is the American dog tick, *Dermacentor variabilis*, in the Eastern US, but in the Western US, it is the Rocky Mountain wood tick, *Dermacentor andersoni*. Only the adult ticks accidentally feed on humans, but all stages of the tick are infected and the organism is transmitted to the offspring transovarially [51]. The brown dog tick, *Rhipicephalus sanguineus*, is the vector for RMSF in Mexico, Arizona, California, Texas, and Brazil [52, 53]. Field mice, other rodents in the wild, rabbits, and their ticks are the natural reservoir for *R. Rickettsiae*, and the dog is an incidental host. Mediterranean spotted fever [MSF], caused by *Rickettsia conorii*, is also transmitted by the brown dog tick from bites or from mucus membrane contact with crushed tick [53]. The endemic areas are found across southern Europe, northern Africa, the Middle East, the Indian subcontinent, and parts of Asia. Dogs are subclinically infected and are important biological hosts. The prevalence of MSF in dogs in endemic areas can be high, 26–60%, and the cycle of the rickettsia is maintained between rodents, ticks, and dogs, with humans as accidental hosts. The disease often starts with an eschar at the site of bite; then progresses to maculopapular, erythematous rash with fever; and usually lasts for about 10 days [27]. *Ehrlichia canis* [a rickettsia-like organism] causes severe disease in dogs and rarely can be transmitted to humans. The vector is the brown dog tick, and human disease with *E. canis* has been reported primarily from Venezuela [54].

### 2.4.2 Parasitic Zoonoses from Pets

Besides toxoplasmosis pets can transmit other parasites to humans. Transmission of giardiasis and cryptosporidiosis by pets has been proposed but not documented to be related to pet contact [55]. Helminthic zoonoses can be indirectly transmitted to humans from cats and dogs, mainly in children. There is concern that dog tapeworm disease [echinococciosis] is reemerging in some countries of Europe and that toxocariasis, from cat and dog roundworms, is still persisting in large endemic areas [56]. Echinococciosis is a cystic [hydatid] disease produced by tapeworms of canids and humans become accidentally infected by ingestion of fertile eggs or proglottids. *Echinococcus granulosus* causes cystic hydatid disease which is a global zoonosis transmitted within a dog-sheep cycle in sheep-rearing pastoral regions. *Echinococcus multilocularis* is a less common infection but produces a more invasive and aggressive disease, alveolar echinococcosis, and the red or arctic fox is the natural final host [36]. *E. granulosus* infection is fairly common in the Mediterranean basin and
is reemerging in southern Europe endemic areas [57]. The sheep strain of *E. granulosus* prevalence in farm or shepherd dogs in Italy and Spain varies from 0% to 31%, in Lithuania 14.2%, and in Wales it increased from 0% in 1993 to 10.6% in 2008 [56]. The pig strain of *E. granulosus*, subspecies intermedius, is present in the Baltic countries, Poland, Austria, and Romania. Home slaughter of farm animals such as sheep and pigs in several of these countries may be responsible for maintaining the cycle of the parasite between farm animals and the dogs by feeding slaughtered animal parts such as offal to the pets. *E. multilocularis* prevalence is lower in pets and dogs and cats are incidental hosts. However, there is evidence that pet and human infections are present in many areas of Eastern, Central-Eastern, and Southeastern Europe [58]. In Switzerland alveolar echinococcosis has been slowly increasing from 0.10–0.16 cases per 100,000 to 0.24 per 100,000 people, and increased prevalence in the fox population of 30–60% [59]. It has been estimated that 490,000 dogs in Switzerland are infected with *Echinococcus multilocularis* and up to 13,000 dogs in Germany; and in the cat population, the prevalence ranges from 0% to 5.5% in various endemic areas [56].

Toxocariasis [visceral larva migrans] from roundworms of cats (*Toxocara cati*) and dogs (*Toxocara canis*) are present worldwide in carnivorous animals and humans, predominantly affecting children. The prevalence of *T. canis* in dogs of Western Europe varies from 3.5% to 34%, lowest for household pets and highest for rural animals; and in cats *T. cati* is present in 8–76%, depending on the environment [56, 60]. The prevalence of *Toxocara* infection and worm burden is highest in puppies and kittens less than six months of age. Children become infected from ingestion of embryonated eggs from contaminated soil while playing and without adequate hand sanitization. Playing with pets is usually not a source of the infection as the eggs need several weeks to become infectious [56]. High rates of soil contamination [10–30%] with *Toxocara* eggs have been found all over the world in areas where children commonly play, backyards, sandpits, parks, and lake beaches, and patent eggs can survive for up to a year; and dog roundworm eggs are most commonly found in public parks, while cat roundworm eggs most commonly contaminate sandboxes [56]. *Toxocara* infection in the global population is common with 80% in children and 50% under 3 years of age, but most infections are subclinical or misdiagnosed. In human communities the seroprevalence of toxocariasis varies from 2.5% in Germany, 4.6–7.3% in the US, 19% in the Netherlands, and up to 83% in children of the Caribbean [56]. Clinical syndromes such as visceral larva migrans with liver, small intestine, lung, and heart involvement are very rare, and ocular and brain involvement with seizures may be seen [61].

### 2.5 Birds and Bats in Zoonoses

The most important avian-related zoonosis is the avian influenza which is reviewed in Chap. 3. Birds and bats can play a role in dissemination of some pathogens via environmental contamination with colonized excreta which may not be considered as zoonoses, such as histoplasmosis and cryptococcosis. Birds are involved in the
transmission of infectious diseases by several mechanisms, as a food source [poultry], as pets, and as wild birds. Birds in the wild play a major role in the amplification and life cycle of several zoonotic viruses, which are transmitted by vectors such as mosquitoes. These include West Nile virus, western equine and eastern equine encephalitis viruses which are endemic in North America, and Venezuelan equine encephalitis virus which is endemic in Central and South America; in the latter disease, horses and not birds are the amplification hosts. Bats are being recognized as important hosts for several emerging novel viral zoonoses, but their role in transmission of infections is rarely through direct contact, and in most cases the association with bats is obscure.

**2.5 Birds and Bats in Zoonoses**

**2.5.1 Pet Birds**

Infectious diseases from pet birds are uncommonly recognized or reported but may be from direct contact, droplet, fomites, and from vector transmission. Areas of transmission of infectious disease can be in the homes, pet shops, bird fairs, and markets and through international trade. Pet birds are primarily songbirds [Passeriformes] such as canaries, finches, and sparrows and Psittaciformes parrots, parakeets, budgeries, and lovebirds. A previous study in 2007 estimated that there were 11–16 million pet or exotic birds in the US [62]. One of the most important bird zoonosis is psittacosis, also known as chlamydophilosis, ornithosis, or parrot fever, caused by *Chlamydia psittaci*. Although psittacines are highly susceptible to infection and are the primary hosts, other birds can be infected including canaries, finches, etc. Most recognized human infections occur in veterinarians and bird breeders, and owners represent only about 40% of the cases [63]. Clinical diseases vary from mild respiratory infection to severe interstitial pneumonia, and infection occurs from inhalation of contaminated dust or excretion of infected birds. Asymptomatic psittacines and pigeons are the most important source of infection [27]. In a study from Belgium, involving 39 breeding facilities, infection with *C. psittaci* was detected in 19.2% of birds [mainly psittacines] and 13% of owners and workers. Of the persons with viable organisms isolated, 66% had mild respiratory symptoms and 25.6% of bird owners reported a history of pneumonia shortly after ownership. Despite antibiotic therapy of the birds in 18 breeding facilities, 66.6% were still positive for viable *C. psittaci* [64]. It is unclear from this report whether this was due to the development of antibiotic resistance or due to reinfection.

Pet birds, especially psittacines, are sources and excretors of mycobacteria species, most commonly *Mycobacterium avium* and *Mycobacterium genavense*, but they are rarely ill from the infection [64]. These bacteria are ubiquitously present in the environment and probably disseminated widely by birds via their feces [pigeons and birds in the wild], and there is no evidence that pet birds play a significant role in human infections. On rare occasion *Mycobacteria tuberculosis* have been transmitted from an infected owner to the pet bird [green-winged macaws], and this may have resulted in acute infection [Mantoux skin test conversion] in veterinarians handling the sick birds [65, 66]. *M. tuberculosis* infection has also been reported in a canary and Amazon parrot [67]. Incidental infections that could arise from pet birds
include *Salmonella* and *Campylobacter* gastroenteritis [63]. Vector-borne infections such as West Nile virus could affect captured birds in an open-air aviary and zoos and thus act as reservoir for infections to humans via urban mosquitoes. Ixodes ticks that transmit Lyme disease can also infect birds, and although migrating birds in the wild may play a role in spreading the vectors to new regions [68], captured or pet birds are not likely to facilitate the transmission of Lyme disease to humans.

### 2.5.2 Bats

Bats [Chiroptera] are found on all continents except Antarctica, and they represent about 20% of mammalian species and are important in maintaining a balanced ecology and a striving agriculture industry [69]. However, bats are reservoirs for several zoonotic pathogens and may represent amplification hosts for emerging viruses [70]. In the past two decades, it has become evident that bats are important in the life cycle of novel viral pathogens, arising from tropical and subtropical countries and with the potential for global expansion. There are several features of these creatures that facilitate the spread of infectious diseases and novel pathogens: the large diversity of species with different feeding habits, the ease of migration by flying, their nocturnal activity that allows contact and spread of diseases to other animals [domestic or in the wild], and the ecology and social activity in forming large communities that facilitate the potential to harbor and spread multiple viral pathogens [71]. Bats form the largest aggregate of mammals worldwide with over 900 species, and their diversity of diet is unparalleled among mammals [72]. Various species feed on insects, fruits, leaves, flowers, nectar, pollen, fish, blood, and other vertebrates. The ability to fly may in part explain their feeding, roosting, and social behavior. Insectivorous bats are found at all latitudes and bats living above 38°N and below 40°S are all insectivorous. Few species of bats are carnivorous or sanguinivorous [blood sucking], and they are confined to tropical and subtropical regions [72]. The nocturnal feeding habit, highly specialized sense of hearing, and ability to capture their prey by echolocation [sonar] facilitate transmission of infection among various mammals.

It has been recognized for many decades that bats can be reservoirs for rabies and transmit the disease to humans by bites [vampire bats], scratches, or direct contact and by aerosol of the virus in bat caves [73]. Bat rabies occurs worldwide and can be found in islands free of canine rabies. In North America there are 40 species of insectivorous bats that can be infected with rabies. Transmissions of bat rabies have been reported in North America, Central and South America, and Europe [73]. In most cases of bat rabies, there is no definite history of a bite, and in North America indigenously acquired rabies in humans are primarily bat rabies variant associated with the silver-haired bat [73].

There are several features of the bat life cycle and ecology that are favorable for maintaining and transmission of zoonoses. Bats have a long life-span of 24–35 years, and their crowded roosting behavior predisposes to intra- and interspecies transmission of viruses and persistence of infection, which allows for cross infection of other vertebrates [74]. There are a large number of viruses that have been isolated from bats, but
most of them have not been shown to cause human disease [74]. The viral zoonoses associated with bats besides rabies include Nipah and Hendra viruses, and SARS-coronavirus (SARS-CoV)-like virus of bats have all arisen in Southeast Asia or Asia; and the newly recognized MERS-coronavirus (MERS-CoV) from the Middle East may also have a reservoir in bats; see Table 2.6. There are other viruses found in bats that are arthropod-borne diseases of the families alphavirus, flavivirus, and bunyavirus, but their role in maintaining the life cycle and as reservoir of these agents is unclear [74].

| Disease Type of bats | Means of transmission | Distribution |
|---------------------|-----------------------|--------------|
| **Lyssavirus-1-rabies virus** | Vampire & insectivorous | Bite, aerosol, direct contact | South and Central America, North America |
| **Lyssavirus-2-7 [rabies like]** | | | |
| Lagos bat virus | Fructivorous | Aerosol, contact? | Africa |
| Mokola virus | Fructivorous | Aerosol, contact? | Africa |
| Duvenhage virus | Fructivorous | Aerosol, contact? | South Africa |
| European bat virus | Insectivorous | Aerosol, contact? | Europe |
| Australian bat virus | “Flying foxes“ | Contact | Australia |

**Henipaviruses**

| Disease Type of bats | Means of transmission | Distribution |
|---------------------|-----------------------|--------------|
| Hendra virus | “Flying foxes“ | Contact with horses | Australia |
| Nipah virus | “Flying foxes“ | Contact with pigs | Malaysia, Bangladesh, India, Singapore |

**Coronaviruses**

| Disease Type of bats | Means of transmission | Distribution |
|---------------------|-----------------------|--------------|
| SARS-CoV | Fructivorous | Contact with palm civets, raccoon dogs | China |
| MERS-CoV | Fructivorous | Contact with camels? | Middle East |

**Rubulavirus**

| Disease Type of bats | Means of transmission | Distribution |
|---------------------|-----------------------|--------------|
| Menangle | “Flying foxes“ [fructivorous] | Contact with pigs | Australia |

Data obtained from references [71, 74], Krauss H et al., Zoonoses. Infectious Diseases transmissible from animals to humans. 3rd Edition, 2003, ASM Press, Washington, Appendix E, p 423–37

2.6 Animals in the Wild

Wildlife poses increasing challenges with respect to emerging and existent zoonoses. Available evidence suggests that ecological changes in the environment ecosystems, such as nutrient enrichment, often exacerbate infectious diseases caused by parasites with simple life cycles [75]. The mechanisms include changes in host and vector density, host distribution, resistance, and virulence/toxicity of pathogens. Many emerging zoonoses occur as a result of increasing exposures of domestic animals and humans to wildlife. Predicting the emergence of novel zoonoses will require tracking the general trends of emerging infectious diseases, analyzing the risk factors for their emergence, and examining the environmental changes that are
influential [76]. Wolfe et al. [77] estimated that the three main factors that govern the emergence of new wildlife zoonoses are the diversity of wildlife pathogens in a region, the zoonotic pool; environmental changes that affect the presence of pathogens in the wildlife population; and the frequency of contacts of domestic animals and humans with wildlife harboring potential zoonoses. Emergence of a new infectious disease usually results from a change in ecology of the hosts or pathogens or both [76]. The frequency and density of wildlife infectious agents with the potential to cross over to humans appears to be greatest in tropical and subtropical regions of the world, where humans are encroaching on large areas of previously virgin forests, i.e., in Africa, Asia, and the Amazon basin. Environmental factors such as global climate change are predicted to result in expansion of wildlife zoonoses, especially vector-borne diseases. The recent emergence of chikungunya fever in the western hemisphere with rapid spread throughout the Caribbean, Southern US, and Central and northern South America may be related to recent climate change.

Human factors that contribute to the emerging wildlife zoonoses include population expansion, with urbanization of previous forested areas that encroach on wildlife habitat. Deforestation of tropical forests for commercial log industry and agriculture expansion and hunting of wildlife are major sources of increased human contact with wildlife zoonoses. Deforestation and road construction in virgin forests also displace small wildlife reservoir of infectious pathogens, result in dispersal to new habitat, and expose livestock and domestic animals to these microbes and indirectly to humans. This may have occurred in the US where new road construction caused dispersal of the white-footed mouse [Peromyscus leucopus] which is a reservoir for Borrelia burgdorferi and resulted in expansion of Lyme disease to new areas [78]. Hunting of wildlife is an ancient tradition that increases the risk of exposure to multiple zoonotic pathogens. Hunting for bushmeat involves contact with potential infectious pathogens at several stages: tracking, capturing and handling the animals, then butchering and transporting the carcass, and trading and consumption of the meat. Moreover, there is increased exposure to potential infected vectors while hunting. Africa poses the greatest risk for emergence of novel wildlife zoonoses which may threaten the health of the global population, by adaptation and transmission from humans to humans. Bushmeat trade and consumption and demand in West and Central Africa appear to be highest in the world, four times greater than in the Amazon basin, with about 4.5 million tons of bushmeat marketed for consumption annually or >287 g per person per day [79, 80]. Furthermore, the practice of hunting primates for bushmeat is still a common practice in Africa, which is associated with a particular high risk for crossover infection to humans, especially chimpanzees which are phylogenetically the closest to humans [77]. This is commonly believed to be a major factor in the emergence of HIV and Ebola virus from Africa. Other factors driving the emergence of novel zoonoses from Africa may include the ecologically diverse wildlife in large areas of tropical rainforests, new and changing patterns of land utilization, and the increased demand for bushmeat in urban communities [77]. The reverse pattern of transmission of domestic animal pathogens to wildlife to maintain a large natural reservoir of zoonoses is also possible, but transmission to humans would still be more likely to occur from contact with domestic livestock. Table 2.7 shows some of the major zoonoses associated with wildlife.
| Microbes         | Diseases                  | Transmission                      | Animals                  | Location                       |
|------------------|---------------------------|-----------------------------------|--------------------------|--------------------------------|
| **Arenaviruses** |                           |                                   |                          |                                |
|                  |                           |                                   |                          |                                |
| Hemorrhagic fevers | Argentinian HF     | Aerosol of excreta                | Field mice               | Argentina, Paraguay            |
| [HF Junin virus] |                           |                                   |                          |                                |
| Machupo virus    | Bolivian HF             | Aerosol of excreta                | Field mice               | Bolivia                        |
| Guanarito virus | Venezuelan HF          | Aerosol of excreta                | Field mice               | Venezuela                      |
| Lassa virus      | Lassa fever             | Aerosol of excreta, food contamination | Mice                     | West Africa                    |
| **Bunyaviruses** |                           |                                   |                          |                                |
|                  |                           |                                   |                          |                                |
| California E. viruses | Encephalitis | Mosquitoes                         | Rabbits, squirrels       | N. America                     |
| Crimean-Congo viruses | Crimean-Congo HF | Ixodes ticks                        | Rodents, cattle hedgehogs | Congo, Asia, E. Europe         |
| **Hantaviruses** |                           |                                   |                          |                                |
|                  |                           |                                   |                          |                                |
| Hantaan virus    | Korean HF               | Excreta in water and aerosol      | Field mice, bats         | East Asia                      |
| Seoul virus      | HFRS                     | Via excreta                        | Norwegian rats           | Worldwide, seaports            |
| Puumala virus    | Nephropathia epidemica  | Via excreta                        | Bank voles               | Europe                         |
| Dobrava virus    | Balkan hemorrhagic fever| Via excreta                        | Field mice               | S. Europe                      |
| Sin Nombre virus | HPS                      | Via excreta                        | Deer mice                | US, North Mexico               |
| Laguna Negra virus | HPS                   | Via excreta                        | Field mice               | Argentina                      |
| Andes virus      | HPS                      | Via excreta                        | Rice rats                | S. America                     |
| **Filoviruses**  |                           |                                   |                          |                                |
|                  |                           |                                   |                          |                                |
| Marburg virus    | Hemorrhagic fever       | Blood contact                      | Monkeys                  | East Africa                    |
| Ebola virus      | Hemorrhagic fever       | Blood, meat contact                | Chimpanzees, gorillas    | West Africa, Congo             |
| **Flaviviruses** |                           |                                   |                          |                                |
|                  |                           |                                   |                          |                                |
| Japanese E. virus | Encephalitis            | Culex mosquitoes                   | Boars, birds, snakes, farm animals, bats | Asia, SE. Asia |
| St. Louis E. virus | Encephalitis           | Culex mosquitoes                   | Wild and domestic birds, bats | N. America, Mexico |

(continued)
| Microbes                  | Diseases       | Transmission          | Animals                        | Location                           |
|--------------------------|----------------|-----------------------|--------------------------------|------------------------------------|
| West Nile virus          | Encephalitis   | Aedes and culex mosquitos | Wild birds                   | Africa, Asia, Americas, Australia  |
| Dengue virus             | Dengue fever   | Aedes mosquitos       | Monkeys                       | Asia, Africa Americas, Caribbean   |
| Yellow fever virus       | Hepatitis      | Several mosquitos     | Monkeys                       | Africa, South and Central America  |
| Powassan virus           | Encephalitis   | Ixodes ticks          | Rabbits, squirrels, skunks    | North America, Mexico, Russia      |
| Tickborne E. virus       | Encephalitis   | Ixodes ticks          | Feral and domestic animals    | Europe, Asia                       |
| **Bacteria**             |                |                       |                                |                                    |
| *Leptospira interrogans* | Leptospirosis  | Rat urine via water   | Rodents, foxes, hares         | Worldwide, mainly tropics          |
| *Yersinia pestis*        | Plague         | Rodent fleas          | Rodents, squirrels, marmosets  | Asia, S. America, SW. US           |
| *Francisella tularensis* | Tularemia       | Ticks, fleas, lice,  | Hares, rodents, squirrels     | US, Russia, Europe                 |
| *Rickettsia typhi*       | Murine typhus  | Fleas                 | Rats                           | Tropics, subtropics, Europe, US    |
| *Orientia tsutsugamushi* | Scrub typhus   | Mites                 | Rodents, rabbits               | Eastern Asia, Australia, Pacific islands |
| *Spirillum minus*        | Rat-bite fever | Bite of rodents       | Rats and mice                  | Mainly Asia                        |
| *S. moniliformis*        | Rat-bite fever | Rat bites             | Rats, mice, squirrels, ferrets | Worldwide                          |
| *Borrelia species*       |                |                       |                                |                                    |
| *B. burgdorferi*         | Lyme disease   | Ixodes ticks          | White footed-mice deer, roe, hedgehog | Worldwide, esp. US, Cen. Europe, Asia |
| *B. duttoni*             | Relapsing fever| Soft ticks            | Wild rodent, domestic animals | Africa                             |
| *Ehrlichia species*      |                | Ehrlichiosis          | Ixodes ticks                   | US, Europe, Mali                   |
| **Protozoa**             |                |                       |                                |                                    |
| *Plasmodium knowlesi*    | Malaria        | Anopheles mosquitoes  | Wild macaques                  | Southeast Asia                     |
| *Babesia microti*, *B. divergens* | Babesiosis   | Ixodes ticks          | Rodents, rabbits, cattle       | Worldwide, all continents          |
| *Trypanosoma Cruzi*      | Chagas disease | Triatomin bugs        | Wild and domestic animals      | Central and South America          |
| *Trypanosoma brucei*     | Sleeping sickness | Tsetse flies   | Antelopes, monkeys, lions, hyenas, domestic animals | Africa |

Data obtained from Refs. [27, 36, 71], Krauss H et al. [eds.], Zoonoses: Infectious Disease Transmissible from animals to humans. 3rd Edition, 2003, ASM Press, Washington, Appendix E, p 423–37

*HPS* hantavirus pulmonary syndrome, *HFRS* hemorrhagic fever with renal syndrome, *E* encephalitis
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