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Zoonoses[☆]

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Glossary

Endemic A disease that is restricted to and constantly present in a particular country or locality.
Epidemic A disease that is prevalent and spreading rapidly among people.
Infection The state of being infected, especially by the presence in the body of bacteria, protozoans, viruses, or other parasites.
Lethality The percentage of people who die of a disease of all people sickened by that disease.

Pandemic An epidemic with a worldwide distribution.
Prodrome A warning symptom indicating the onset of a disease.
Reservoir host A species that serves as an immune host for a parasite that can cause disease in another species. Member of a population in which certain infectious agents can perpetuate.
Vector An animal, such as an insect, that transmits a disease-producing organism from one host to another.

Abbreviations

BSE	Bovine spongiform encephalopathy	PCR	Polymerase chain reaction
EEE	Eastern equine encephalomyelitis	SARS	Severe acute respiratory syndrome
EID	Emerging infectious diseases	VEE	Venezuelan equine encephalomyelitis
EMV	Equine morbillivirus	WEE	Western equine encephalomyelitis

Defining Statement

Zoonoses are the diseases and infections that are naturally transmitted between vertebrate animals and man. Emerging zoonoses are defined as zoonotic diseases caused either by apparently new agents or by previously known microorganisms appearing in places or in species in which the disease was previously unknown.

Introduction

Zoonoses are the 'diseases and infections that are naturally transmitted between vertebrate animals and man,' as defined in 1951 by the World Health Organization (WHO) Expert Committee on Zoonoses. The word zoonosis (zoonoses, plural) is the combination of two Greek words (*zoon*, animals; and *noson*, disease), and was coined at the end of the nineteenth century by Rudolph Virchow to

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designate human diseases caused by animals. Nevertheless, the term should also include vertebrate animal diseases caused by exposure to humans, such as measles in non-human primates, which is of major concern in any major primate center. The term 'zoonosis' is also considered to be shorter and more convenient than 'anthropozoonosis' (animals to humans) and 'zooanthroposis' (humans to animals), which are based on the prevailing direction of transmission between humans and other vertebrates. The word anthropozoonosis (anthropozoonoses, plural) is much more in use in the medical community than in the veterinary community. The well-accepted WHO definition of zoonoses requires some comments. The definition should include the word 'infestations' to cover more properly parasitic diseases. Zoonoses are usually limited to agents that can replicate in the animal host; therefore it does not include diseases caused by inoculation of venom or toxins of reptile or fish origin or by allergies to vertebrates. It also excludes diseases transmitted by animals or food of animal origin, which are vehicles of human pathogens, such as ice cream contaminated with the hepatitis A virus or a poliovirus. The concept of transmissibility in natural conditions is also important for zoonoses and excludes all experimental infections of non-human vertebrates with human pathogens (such as measles virus inoculated to ferrets). Transmissibility also distinguishes the true zoonoses, for which there must be epidemiological evidence of direct or indirect transmission from animal to humans, from the communicable diseases for which the contamination of humans and animals occurs from a common source without an epidemiological interrelation. However, animals may play a role in the amplification of the agent, such as when a horse sheds *Clostridium tetani* in the environment. For the most ubiquitous zoonoses, humans, and lower vertebrates are equally suitable reservoir hosts, and infection may be transmitted in either direction. The term amphixenoses applies to these infections which include some of the staphylococcoses and streptococcoses. Zoonoses exclude those diseases that are vector-borne only from humans to humans, such as malaria or dengue or Chikungunya viruses, even though some of these arboviral zoonoses can be considered as remote zoonoses or have remote wildlife cycles merely involved in human infections, as for dengue virus. Similarly, several human diseases have been proven to be of animal origin (zoonotic), but are no more transmitted to humans from their animal reservoirs, such as the human immunodeficiency virus (HIV). Such infections are described as remote zoonoses. Other infections are truly zoonotic, such as the severe acute respiratory syndrome (SARS) coronavirus or the recent MERS (Middle Eastern Respiratory Syndrome) coronavirus, but have the ability to then spread within human populations without any animal exposure. Finally, the reciprocity of the infection from animals to humans or from humans to animals illustrates the inter-transmissibility of zoonoses. However, humans represent, in most instances, an epiphenomenon in the natural cycle of infection between non-human vertebrates. Only in a few parasitic diseases, such as for *Taenia solium* or *Taenia saginata* infestations, are humans an obligatory host of the infection (euzoonoses). Usually, zoonoses are animal infections or diseases in which humans become occasional victims, sometimes able to re-infect animals or humans (extensive and reversible zoonoses), sometimes unable to spread the infection (restricted or limited zoonoses). In the latter case, humans can be considered an epidemiological dead end or *cul-de-sac*.

Classification and Importance

Classification

Zoonoses can be classified according to the etiologic agent – viral, bacterial, parasitic, mycotic, or unconventional (prions). However, it is the primary epidemiological classification based on the zoonosis maintenance cycle that is of major importance when considering alternatives for control measures. This classification divides the zoonoses into four categories.

1. Direct zoonoses (orthozoonoses) are transmitted from an infected to a susceptible vertebrate host by direct contact, by contact with a fomite, or by a mechanical vector. Direct zoonoses may be perpetuated in nature by a single vertebrate species, such as dogs or foxes for rabies or cattle, small ruminants or swine for brucellosis (Figure 1).
2. Cyclozoonoses require more than one vertebrate species, but no invertebrate host, in order to complete the developmental cycle of the agent. Examples are human taeniasis or pentastomid infections (Figure 2). Most of the comparatively few cyclozoonoses are cestodiasis.
3. Pherozoonoses (also called metazoonoses) are zoonoses that require both vertebrates and invertebrates for the completion of their infectious cycle (Figure 3). In pherozoonoses, the infectious agent multiplies (propagative or cyclopropagative transmission) or merely develops (developmental transmission) in the invertebrate; there is always an extrinsic incubation period in the invertebrate host before transmission to a vertebrate host. Examples are arbovirus infections, plague, Lyme borreliosis, or rickettsial infections.
4. Saprozoonoses have both a vertebrate host and an inanimate developmental site or reservoir (Figure 4). The developmental reservoir is considered nonanimal, such as organic matter, including food, soil, and plants. In this group of zoonoses, direct infection is usually rare or absent. Examples are histoplasmosis, *Erysipelothrix* infection, or listeriosis.

Other classifications of zoonoses may include a classification based on the categories of people at risk or relating to the type of human activity, such as occupational zoonoses (which occur when people are infected during their professional activity; for example, brucellosis in farmers, veterinarians, or slaughterhouse employees, Lyme disease in foresters, rabies in wildlife trappers or taxidermists), zoonoses associated with recreational activities (e.g., plague, hantavirus infection, Lyme disease, tularemia, or parasitic larva migrans), domestic zoonoses (diseases acquired from pets), or accidental zoonoses (some very rare and peculiar circumstances of infection, as well as foodborne outbreaks).

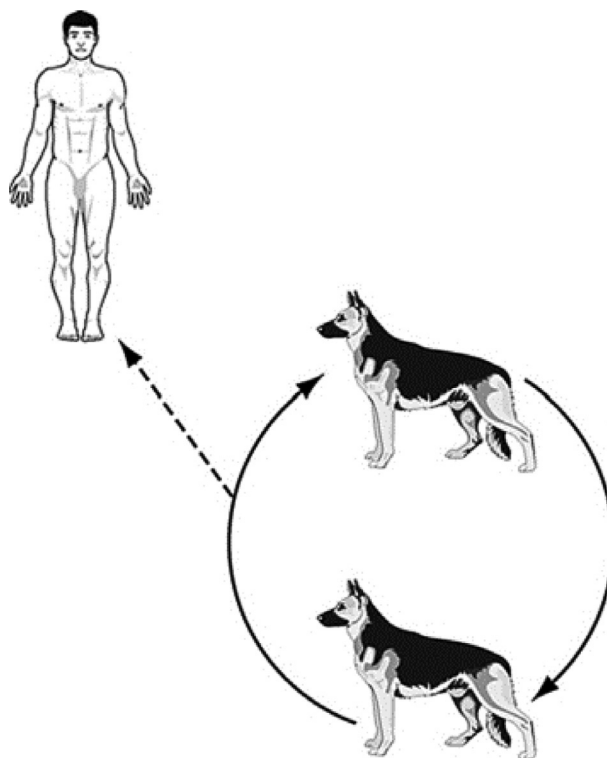


Figure 1 Epidemiological maintenance cycle of rabies, a direct zoonosis (orthozoonosis).

Another aspect of zoonoses classification concerns their clinical manifestations and their diagnosis. Clinical diagnosis of zoonoses is not always easy, especially if the symptoms are different in animals and humans, or if clinical signs are present only in humans. If clinical signs are observed in animals and humans, zoonoses are designated as phanerozoonoses. If symptoms are similar in both animals and humans, they are considered isosymptomatic (rabies and tuberculosis), whereas they are anisosymptomatic if the symptoms are different in humans and animals (anthrax, brucellosis, psittacosis, and Rift Valley fever). In some instances, subclinical infection is observed in animals and clinical illness in humans, or *vice versa*. In such cases, these zoonoses are designated as cryptozoonoses. Examples of animal infection, without overt clinical signs and human disease, are ornithosis pneumonia in humans and latent infection in pigeons and turkeys, leptospirosis meningitis in swine keepers, or *Escherichia coli* O157:H7 carriage in cattle and disease in humans. The opposite can also occur, such as the viral Ebola-like (Reston virus) infection, which is deadly in non-human primates, and leads only to seroconversion in infected humans. Finally, infection without any clinical symptoms may occur in both animals and humans, such as some arboviral infections, detected only serologically (Tahyna virus).

Medical and Economic Importance

Zoonoses are important to Public Health because of their number, their frequency, and their severity in relation to human health. There are more than 250 zoonoses according to the WHO Zoonoses Expert Committee. An analysis of human pathogens revealed that 58% of species were zoonotic, and 13% were emerging, of which 73% were zoonotic. A similar study found that 26% of human pathogens also infected both domestic and wild animals. Emerging pathogens are more likely to be viruses than other pathogen types and more likely to have a broad host range. There are very few vertebrates that are not involved with one or more zoonoses. Human infection most often occurs when infection persists in animals, such as rabies, brucellosis, or tuberculosis. Zoonoses frequency varies for each disease and depends on the geographical distribution of reservoirs, agents, and population density, as well as efficiency of controlled measures. Some zoonoses are ubiquitous, such as salmonellosis and leptospirosis. Others are geographically restricted, such as plague, or various arboviral diseases, including yellow fever. Some zoonoses are very rare or restricted to very limited areas, such as Ebola or Reston virus hemorrhagic fevers. The high lethality rate of some zoonotic diseases, despite their rarity, classify them as major zoonoses, such as hantavirus respiratory syndrome, rabies (in developed countries), herpes B virus infection, or infections with Marburg or Ebola viruses. Many zoonoses induce severe but usually nonlethal diseases in humans, such as brucellosis, and some are characterized by very mild symptoms in humans, such as Newcastle disease, pseudocowpox, or erysipeloid.

In order to prevent such risks to human health, most of the major zoonoses and those that are non-endemic (usually referred as foreign or exotic) but particularly life-threatening are required to be reported to official health agencies, such as the Ministry of

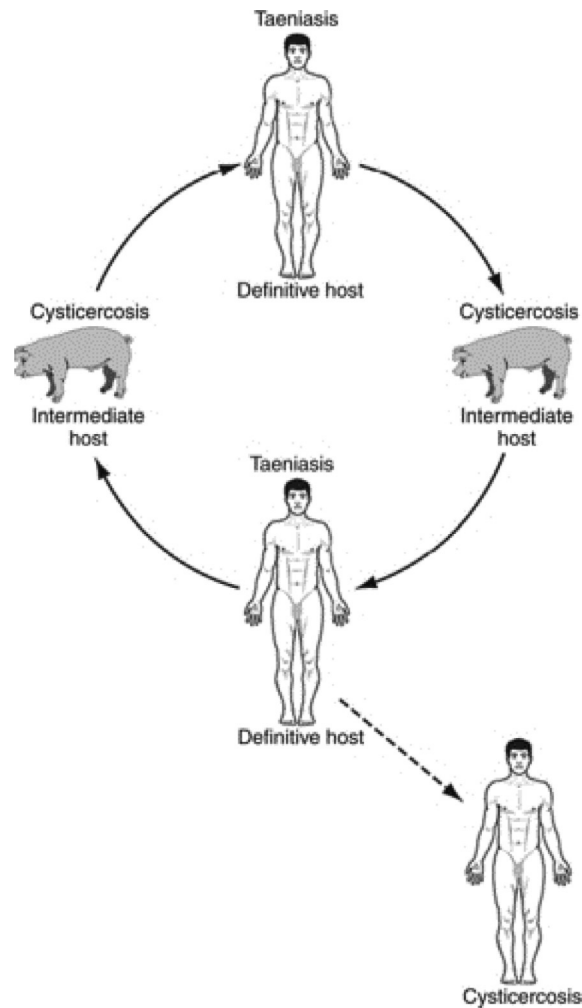


Figure 2 Epidemiological maintenance cycle of taeniasis and cysticercosis (*Taenia solium*), a cyclozoonosis.

Health in many countries or the Human Health Services in the United States, as well as international agencies such as the World Health Organization (WHO), the World Animal Health Organization (Office International des Epizooties, OIE), or the Food and Agricultural Organization (FAO). Many of them are also reported to the Ministry or Department of Agriculture, especially if these zoonoses are of economic importance to livestock production, such as bovine brucellosis or tuberculosis. However, it may happen that some diseases are declared only to one department, underlining the need of complete cooperation between Human Health Services and Agriculture Services. It has been estimated that 13 zoonoses are responsible for 2.4 billion cases of human illness and 2.2 million deaths per year. The vast majority occur in low- and middle-income countries, including toxoplasmosis, zoonotic tuberculosis and Q fever. In developing countries, zoonoses account for millions of cases of illness and deaths, underlining not only the loss of human life and suffering, but also their economic burden. The Global Burden of Disease captures the impact of zoonoses on human health in terms of disability-adjusted life years (DALYs). In low income countries, zoonoses and diseases which recently emerged from animals make up 26% of the DALYs lost to infectious disease and 10% of the total DALYs lost. In contrast, in high income countries, zoonoses and diseases recently which emerged from animals represent less than 1% of DALYs lost to infectious disease and only 0.02% of the total disease burden.

Zoonoses are also a tremendous economic burden to humans due to the loss of diseased animals and agricultural production, cost of prevention, and treatment, debilitation of and productivity losses to humans. It is quite difficult to evaluate such costs precisely, but some estimates have been published that illustrate the economic impact of zoonotic diseases. The direct cost of zoonotic disease outbreaks over the last decade has been estimated to be over US\$ 220 billion to affected economies as a whole. For instance, the global monetary burden of cystic echinococcosis has been estimated worldwide at US\$ 4.1 billion, including 46% of these costs for human treatment and 54% for animal health costs and at more than US\$ 4 billion of rabies. It is estimated that about one in eight livestock in poor countries are affected by brucellosis; this reduces milk and meat production in cattle by around 8%. In the USA, food borne diseases cause illness in 1 in 6 Americans (or about 48 million people) each year, resulting in about 128 000 hospitalizations and 3000 deaths and cause more than \$9 billion in health care-related costs each year.

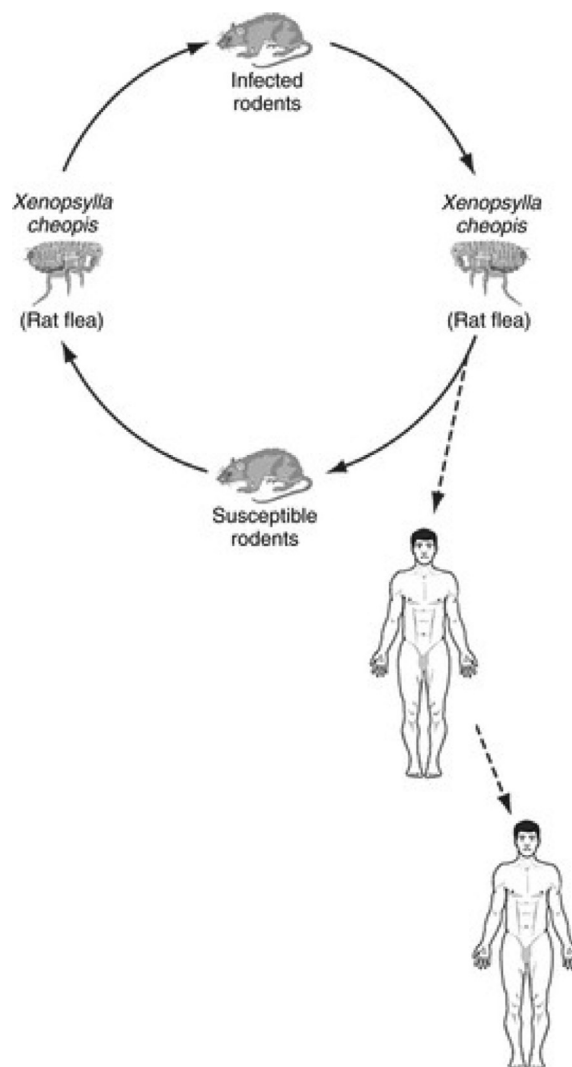


Figure 3 Epidemiological maintenance cycle of plague, a metazoosis.

Zoonoses also underline the important contribution of the veterinary profession and veterinary preventive medicine to human public health. The activities of veterinarians are to investigate zoonosis outbreaks, to establish surveillance systems in animal populations, to reduce disease prevalence in domestic animals by culling infected animals and restricting animal movements, and to monitor wildlife. Veterinarians are also a natural link between physicians, ecologists, and environment specialists.

Orthozoonoses (Direct Zoonoses)

Direct zoonoses are transmitted from an infected vertebrate to a susceptible vertebrate by direct contact, vehicle, or mechanical vector (Figure 1). The infectious cycle requires only one vertebrate species to perpetuate. Most of these zoonoses are transmitted to humans through direct physical contact with an infected animal. The disease that best illustrates the concept of direct zoonosis is rabies. Domestic dogs are the main animal species associated with rabies worldwide and with its transmission to humans. It is estimated that worldwide, between 40000 and 50000 people die every year from rabies, mainly from exposure to dog bites. Fortunately, rabies is a rare disease in humans in the United States, many countries in Western Europe, but numbers have increased recently in other parts of the world, including several Asian countries like China and several African countries. In Indonesia, a recent outbreak that started in 2008 and leading to more than 100 human deaths was associated to the introduction of a rabid dog and the dispersal of the virus in a highly susceptible and non-immunize dog population. One emerging concern with rabies in the New World is the transmission of rabies to human by bats, especially vampire bats in South and Central America. When introduced to the victim's wound *via* a bite, the rabies virus multiplies locally at the wound site and then invades the peripheral nerve(s) supplying that area. The virus migrates along the nerves to reach the central nervous system and radiates further through

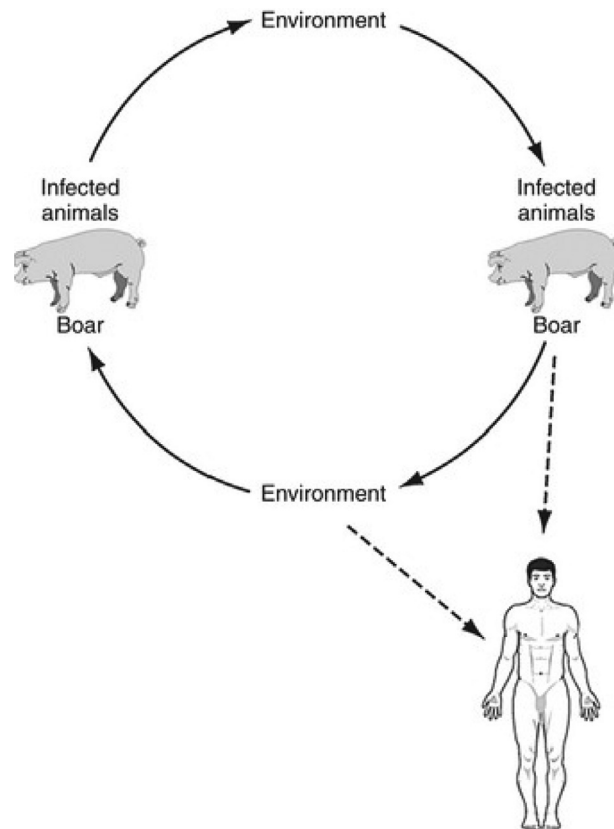


Figure 4 Epidemiological maintenance cycle of *Erysipelothrix* infection, a saprozoosis.

the nerves in various organs, including the salivary glands. The virus is shed in the saliva and can be transmitted to a new victim through a bite. The incubation period for rabies varies from a few days to several months, and the virus can be shed in the saliva a few days prior to the appearance of any clinical neurological signs. This is the main reason why a dog that bites a human is quarantined for 10 days. If the dog is still healthy 10 days after the bite incident, one can assume that the dog was not shedding the virus at the time of the bite, and, consequently, that the bite victim does not need a rabies post-exposure treatment (a series of five doses of 1.0 ml of rabies vaccine injected intramuscularly on days 0, 3, 7, 14, and 28, according to the protocol used in the United States). Rabies is mainly characterized by neurological and behavioral disorders. During the initial prodromic phase, the dog is anxious, nervous, and suffers behavioral changes. After 2 or 3 days, the furious or paralytic form starts. In the furious form, lasting 1–7 days, the dog shows irritability, aggression, hypersensitivity, disorientation, and sometimes grand mal seizures. In the paralytic or dumb form, lasting 1–10 days, paralysis affects one or more limbs. Paralysis then progresses to affect the entire nervous system. Cranial nerve paralysis, especially laryngeal paralysis, is often the first recognized sign. Death occurs within 10 days. Prevention of rabies in dogs is based on vaccination of susceptible animals, confinement of animals, quarantine of biting dogs, and removal of stray animals. In the United States, the recommendations for state and local rabies vaccination and control measures are published yearly by the National Association of State Public Health Veterinarians. All states require rabies vaccinations for dogs. Interstate travel usually requires the possession of a health certificate and a proof of rabies vaccination. Several rabies vaccines are currently marketed for dogs in the United States and should be administered according to the manufacturer's instructions. Puppies should be vaccinated when they are 3 months old and revaccinated 1 year later at 15 months, after which they should receive annual or triennial boosters. If dogs with a current rabies immunization are exposed to a rabid animal, they should be revaccinated immediately, and kept under the owner's control and observed for 45 days. Unvaccinated animals are usually euthanized or may be placed in strict isolation for 6 months and vaccinated 1 month before release or upon entry into isolation.

Cyclozoonoses

Cyclozoonoses require more than one vertebrate species, but no invertebrate host for the completion of the agent's development cycle (Figure 2). Most of these zoonoses are cestodiasis. Infection with *Taenia solium* is an obligatory cyclozoonosis, as a human must be one of the vertebrate hosts. Cysticercosis, infection with the larval stage of the pork tapeworm *T. solium*, has been recognized as a cause of severe disease and occasional mortality in the United States, principally among immigrants from Latin

America. Gravid proglottids shed in feces of infected humans are ingested by pigs (in parts of the world where pigs are free-roaming and no sanitation system for eliminating human dejections is available). Humans acquire *T. solium* taeniasis by eating raw or undercooked pork containing cysticerci (*Cysticercus cellulosae*), which is very common in developing countries. Pigs usually do not suffer from the infestation. In humans, the scolex of the larva evaginates in the small intestine and attaches to the intestinal wall. In 2–3 months, the larva develops into an adult taenia and the first proglottids are expelled in the feces, thus renewing the cycle. The public health significance of *T. solium* lies in the fact that humans can also be infected by the eggs and can develop cysticerci in their tissues. Humans acquire cysticercosis by either ingestion of eggs with food (vegetables and fruits) and water contaminated by the fecal material of a taenia carrier or ingestion of eggs introduced to the mouth by the contaminated hands of an individual with poor hygienic habits or self contamination (anus–hand–mouth). Taeniasis is usually subclinical, but anal pruritus can cause autoinfestation. Cysticercosis is a more severe disease, neurocysticercosis being most dramatic with ocular and periocular forms. Months after the ingestion of eggs, the patient may develop seizures, epilepsy, dementia, hydrocephalus, or meningitis. Treatment is based on the use of albendazole or praziquantel. Steroids may be required to decrease the inflammatory sequelae after killing the parasite with antiparasitic agents. Hygienic measures and meat inspection at slaughterhouses are the basis for the prevention and control of human and swine infestation.

Pherozoonoses

The pherozoonoses (also known as metazoonoses) require invertebrate vectors for their transmission to vertebrate hosts. Many vectors can be involved, such as fleas, ticks, mosquitoes for many bacterial and viral diseases. Many parasitic infestations require crustaceans or mollusks for the completion of the parasite cycle. As examples, three zoonoses are described: one transmitted by fleas (plague), one transmitted by ticks (Lyme disease), and one transmitted by mosquitoes (equine meningo-encephalitides and West Nile virus infection) (Figure 3).

Plague

Plague is caused by the bacterium *Yersinia pestis*, a Gram-negative coccobacillus. Plague is a rodent disease endemic in many parts of the world with most human cases being reported from Africa and Asia, and to a lesser extent from the Americas. In the United States, human cases are uncommon, ranging from 2 to 17 cases per year, resulting from infected flea, rodent, or cat contact. Sciurid rodents (rock squirrels, California ground squirrels, chipmunks, and prairie dogs) are the primary plague reservoir in the western United States. The oriental flea (*Xenopsylla cheopis*), the common vector of plague, is well established in the United States, as well as many other flea species that are competent vectors, such as *Oropsylla montana*. This type of flea is found mostly in rural rodent species, particularly the rock squirrel in New Mexico and Arizona. Plague is a seasonal disease that occurs mainly in the late spring until early fall, when rodents and fleas are abundant. Bubonic plague in humans is usually characterized by fever after an incubation period of 2–7 days and the development of a large, tender, and swollen lymph node called buboe. The infection may result in severe pneumonic or systemic plague, especially in people exposed to infected cats suffering from pneumonic plague. Human infection is most often caused by an infected flea bite, but occasionally can result from exposure to infected materials *via* cuts or abrasions in the skin or *via* infected aerosols. Streptomycin and gentamicin are the antibiotics of choice for plague treatment. Tetracyclines or sulfonamides are usually given to case contacts to prevent disease spread. Mortality can be high (up to 60%) in the absence of treatment, especially in cases of pneumonic plague. Rodent and flea control, especially in endemic areas, is an essential part of controlling the infection, as well as the closing of infected campgrounds.

Lyme Disease

Lyme disease, also called Lyme borreliosis, is caused by a spirochete, *Borrelia burgdorferi*. This disease accounts for most of all tick-borne human infections reported in the United States, with more than 25 000–5 000 reported human cases per year. In the northeastern United States, where more than 90% of the human cases have occurred, the reservoir is constituted by the white-footed mouse (*Peromyscus leucopus*) and the black-legged tick (also known as deer tick) (*Ixodes scapularis*). In the western United States, the western black-legged tick (*Ixodes pacificus*) is the main vector of infection. Small mammals (particularly rodents) are an important host of these ticks' larvae and nymphs and are critical for maintenance of *B. burgdorferi* in nature; deer are an important host for the adult tick stages. The considerable increase in deer population in the United States since the middle of the twentieth century has led to an unprecedented proliferation and extension in the distribution of the deer ticks, which could explain the increase of this human health problem in peri-urban habitats. Most human infections with *B. burgdorferi* in the United States occur during the months of May through August, when both *I. scapularis* nymphal-stage activity and human outdoor activity are at their peak. Acute Lyme disease is a flu-like illness that develops after a 7–10 days incubation period and is generally accompanied by a characteristic annular rash (erythema migrans) that appears where the infecting tick has attached. Neurologic lesions usually follow, including cranial neuritis, peripheral neuropathy, encephalopathy, arthralgia, carditis, or ocular lesions. Weeks or months later, chronic arthritic lesions may appear. When detected early, antibiotics such as doxycycline or amoxicillin are very effective in preventing chronic forms of the disease. Prevention is largely based on wearing protective clothes and tick repellents when going outdoors in tick-infested areas.

Equine Encephalitides

Arboviral diseases have a worldwide impact, especially in tropical and subtropical countries. The first record of eastern equine encephalomyelitis (EEE) in the United States was in 1831 by a physician who described an episode of neurologic disease in horses in Massachusetts. Venezuelan equine encephalomyelitis (VEE) was first described in northern South America in the 1920s and western equine encephalomyelitis (WEE) in the western United States in 1847. Equine encephalomyelitis viruses have been isolated only in the Western Hemisphere. Since 1999, when West Nile virus reached the New World, it has been a major public health burden across North America, causing almost 40 000 human cases, including more than 1500 human deaths and tens of thousands of deaths in horses. About 1 in 5 people who are infected will develop a fever with other symptoms. Less than 1% of infected people develop a serious, sometimes fatal, neurologic illness.

In horses, clinical signs range from subclinical or unapparent infections to a mild or severe, and frequently fatal, clinical course of disease. For the first few days, nonspecific fever is observed followed by neurological signs, such as profound depression and stupor or hyperexcitability. Human beings can be infected by EEE virus, sylvatic and epizootic VEE virus subtypes and variants, and WEE virus. The clinical syndrome can vary from a mild influenza-like illness to a severe encephalitic disease. Deaths have been reported primarily in children and the elderly. Direct transmission from horses to humans usually does not occur; the vectors are various mosquito species. The human disease has been reported frequently during equine epizootics, but human infections generally follow equine infections by ~2–3 weeks.

Equids are the most important amplifiers and indicators of epizootic VEE virus activity. Usually, reservoirs are birds (EEE) or rodents (VEE) or both (WEE), and various species of mosquitoes (*Culex tarsalis* for WEE, *Culiseta melanura* and *Aedes sollicitans* for EEE, and several species for VEE). EEE epidemics occurred in recent years in Florida, Georgia, and South Carolina in horses, with a few human cases, because of heavy spring rains leading to an exceptionally large population of *C. melanura*. In 2013, health departments reported almost 100 presumptive or confirmed human cases of arboviral disease to the Centers for Disease Control and Prevention (California serogroup virus: 81 cases, Eastern Equine Encephalitis: six cases and Powassan virus: 11 cases). A major outbreak of VEE occurred in 1995 in Venezuela and Colombia with an estimated 13 000 and 45 000 human cases, respectively. Hundreds of horses died. Cases were also reported in humans and horses in El Salvador and Panama in the fall of 1995.

Effective prevention measures are based on destroying mosquito-breeding places; destroying adult mosquitoes; avoiding nighttime outdoor activity in affected areas, especially at dusk and dawn; applying mosquito repellents; and wearing long-sleeved shirts and long pants. Safe and effective monovalent or bivalent formalin-inactivated EEE and WEE virus vaccines are commercially available for horses and should be administered regularly in endemic areas. Similarly, equine vaccines are available to immunize horses against West Nile virus.

Saprozoonoses

Saprozoonoses are zoonoses that require a non animal site to serve either as a true reservoir of infection or as a site for an essential phase of development. Human erysipeloid and animal erysipelas are examples of this type of zoonotic infection (Figure 4). Swine erysipelas is a common infection in many parts of the world. Many species are susceptible to *Erysipelothrix insidiosa* (*rhusiopathiae*), but it is an important economic problem in the pig industry in absence of vaccination. After an incubation of 1–7 days, pigs develop a very high fever, with anorexia, prostration, and usually the apparition of characteristic cutaneous lesions, presenting as red urticarial plaques (Diamond disease). The animals either die or recover rapidly. The chronic form is more insidious and characterized by arthritis and endocarditis. In humans, infection results from an accidental inoculation during a necropsy or during slaughtering of infected pigs, and is mainly a professional disease. In most of the cases, the infection is localized at the inoculation site (fingers, hands, or arms). After an incubation of 1–2 days, an erythematous and edematous skin lesion, usually very itchy, is observed. Arthritis can occur in some instances. Recovery occurs in 2–4 weeks. Septicemia is rare, but often fatal, death being caused by the endocarditis. The treatment of choice in both humans and animals is penicillin. Wearing protective clothes, especially gloves, is an important measure to prevent human infection.

New and Emerging Zoonoses

The concept of emerging infectious diseases (EID) appeared in the late 1980s, when major outbreaks occurred around the globe and surprised many scientists who considered infectious diseases to be maladies of the past or limited to the underdeveloped world. The spectrum of infectious diseases is changing rapidly in conjunction with dramatic societal and environmental changes. Exponential human population growth with expanding poverty and urban migration is occurring worldwide, international travel and trade is increasing, and technology is rapidly changing – all of which affect the risk of exposure to infectious agents. Disease emergence often follows ecological changes caused by human activities such as agriculture or agricultural change, migration, urbanization, deforestation, or dam building. Of these new diseases, surprisingly, most of the emergent viruses and many of the emergent bacteria are zoonotic. As indicated by Jones and colleagues, EID events are dominated by zoonoses (60.3% of EIDs): the majority of these (71.8%) originate in wildlife (e.g., severe acute respiratory virus, Ebola virus), and are increasing significantly over time. ‘Emerging zoonoses’ are defined as zoonotic diseases caused either by apparently new agents or by previously known

microorganisms, appearing in places or in species in which the disease was previously unknown. Natural animal reservoirs represent a more frequent source of new agents of human disease than the sudden appearance of a completely new agent. Most emerging infections appear to be caused by pathogens already present in the environment, brought out of obscurity or given a selective advantage by changing conditions and afforded an opportunity to infect new host populations. More than 50 new pathogens have been identified during the last 40 years, such as Hendra virus, Nipah virus, South American hantaviruses, new lyssaviruses, SARS and MERS coronaviruses and new *Ehrlichia* and *Babesia* species causing human diseases or deaths.

Factors explaining the emergence of a zoonotic or potentially zoonotic disease are usually complex and related to the infectious agent itself, involving mechanisms at the molecular level such as genetic drift and shift enhancing the virulence (many viral infections) or the acquisition of multidrug resistance (bacteria); modifications of the immunological status of individuals or populations; environmental and social changes, including ecological changes caused by human activities (such as agriculture or agricultural change, migration, urbanization, deforestation, or dam building), and human demographic and behavioral changes; travel and trade; technology and industry; and the breakdown of public health measures. Water irrigation is certainly one of the most important agricultural techniques used to expand agricultural land. It may also be associated with the emergence of mosquito-borne diseases. In Asia, the incidence of Japanese encephalitis, which causes almost 30000 human cases and 7000 deaths annually, is closely associated with rice field irrigation, creating large areas of stagnant water. In Africa, the dramatic expansion of Rift Valley fever in Egypt in 1977 and in Mauritania in 1987 appears to be associated with dam construction and irrigation in areas either densely populated with humans and domestic animals (Egypt) or with large naive ruminant populations (both Egypt and Mauritania).

Human population movements or upheavals, caused by migration or war, are often important factors in disease emergence. Urbanization has led to mass movement of workers from rural areas to cities. Outbreaks of brucellosis in urban communities such as in Lima, Peru, or in some of the conflict areas of the Gaza Strip and West Bank in Israel and Palestine are illustrations of the effects of uncontrolled urbanization. The continuous spread of human populations to new living areas is also a factor to consider in the emergence of new zoonoses. In South America, major outbreaks of vampire-bat rabies occurred in Peru and Brazil following the settlement of new agricultural communities in the remote jungle.

Farming of new animal species, such as ostriches, may lead to new disease outbreaks. An outbreak of Congo–Crimean hemorrhagic fever occurred in South Africa in a slaughterhouse specialized in slaughtering ostriches. In that outbreak, 16 human cases were suspected, with at least one death. Infected ticks may have been the source of human infection or exposure to the viremic birds. Similarly, major concern has been raised about deer farming and outbreaks of bovine tuberculosis occurring in these herds. Translocation of exotic animal species for farming can also lead to new diseases or new reservoirs of infection. Outbreaks of western equine encephalitis occurred in emus in Texas in 1992 and in California in 1994.

The new trend of keeping exotic pets can also lead to the emergence of new zoonotic diseases, such as the epidemic of lymphocytic choriomeningitis in pet hamster owners in the United States and Germany in the early 1970s and more recently in pet store employees exposed to infected mice, the modern epidemic of iguana-related salmonellosis in the United States and other countries around the world, and the first ever reported outbreak of monkeypox in the New World associated with pet prairie dogs infected from contact with exotic rodents imported from Africa.

The spread of diseases has been associated with human migrations for centuries. From the plague epidemics of the sixth, fourteenth, and nineteenth centuries to the dispersion of yellow fever from Africa to the Americas or dog rabies from Europe to the Americas, zoonotic diseases have found new reservoirs to adapt to, while human populations were expanding over the continents. Increased human population flux through air transportation, associated with the dramatic reduction in travel time over long distances, has increased the possibility of the global transport and dispersal of infectious agents in a short period of time. Transoceanic travel by steamers was considered responsible for the spread of the third plague pandemic at the end of the nineteenth century. Now, any location on the globe can be reached within 24 h. The latest outbreaks of Ebola fever clearly exemplifies the risk, as the first case of Ebola fever reported in South Africa was caused by a sick patient seeking care far from the initial outbreak in Equatorial Africa.

The importation of monkeys for research was the source of the first Ebola-like outbreak investigated in the United States. In September 1989, numerous cynomolgus monkeys shipped from the Philippines died during their quarantine of suspected simian hemorrhagic fever, but in fact also of Reston virus. The raccoon rabies epidemic in the United States was caused by the importation of infected animals for hunting purpose, incubating the disease to disease-free areas with a large susceptible population. Expanding human habitats to suburban areas cause us to be in contact with the wildlife reservoir of these expanding zoonoses. The dramatic increase of Lyme disease cases in the United States and the considerable number of post-exposure rabies treatments required in the northeastern part of the United States are direct consequences of this expansion. The increasing international trade in live animals and foodstuff has favored the spread of enteric zoonotic infections, especially salmonellosis and campylobacteriosis. Foodborne zoonoses are increasing in both developed and developing countries. According to the Pan American Health Organization many of these diseases have increased as much as 100% during the 1990s. In some countries, the incidence is estimated to be as high as 10% of the population. Salmonella outbreaks caused by new serotypes or multidrug-resistant serotypes are being reported more and more frequently. It is suspected that modifications in the processing of rendering products led to the bovine spongiform encephalopathy (BSE) epidemic in Great Britain.

The recognition of new zoonotic diseases may also be related to improved technology for investigating and identifying these pathogens. The identification of infection caused by *E. coli* O157:H7 is an example of how better tools for the diagnosis of infectious diseases can allow a better assessment of a pathogen increasingly found in our food chain. Many new infectious agents

have been identified following carefully conducted epidemiological investigations, leading, for instance, to the suspicion of animal contacts (e.g., for bacillary angiomatosis and cat scratch disease, or hantavirus pulmonary syndrome) and the use of modern molecular techniques. Molecular epidemiology is one of the promising outcomes of the interaction between epidemiology and the laboratory. The agent of the hantavirus pulmonary syndrome was first identified by detecting genetic material in specimens collected from dead and sick patients by means of polymerase chain reaction (PCR). It was one of the first cases in which a disease of unknown origin was identified through molecular epidemiology. In other instances, molecular epidemiology was essential for the detection and identification of bacteria resistant to cultivation, such as the agent of bacillary angiomatosis and cat scratch disease, *Bartonella henselae*. Among the various factors associated with the emergence of new zoonoses, microbial adaptation must be considered. Such an event appears more likely to occur with viruses than with bacteria. Influenza viruses are examples of genetic shift and drift, which may lead to new variants and recombinant strains, causing worldwide pandemics. The few cases of EMV in Australia clearly exemplify the risk of new zoonoses from an unknown reservoir. It is thought that WEE virus arose from a recombination event that seems to have involved a Sindbis-like virus and EEE virus ~100–200 years ago. Strains of *Salmonella* resistant to various antibiotics are emerging in the industrial farming environment of the poultry, pig, and calf industries. The risk that these strains may be entering the food chain is of major concern.

The breakdown of public health measures and deficiencies in public health infrastructure must not be neglected among the various risk factors associated with disease emergence or reemergence. The economic crises of the late 1980s, early 1990s and late 2000 (2008) have had a major impact on the financial and human resources available to prevent and control infectious diseases. Disease prevention is funded by only a few percent (3%) of all the billions of dollars devoted to human health in the United States, and even less is devoted to public health surveillance and information systems. The increase in urban population, increase in poverty, increase in susceptibility to infectious agents because of lack of immunization, reduction of public health support and privatization, and reduction of vaccination programs have led to an explosive situation in which infectious diseases can claim more ground.

Prevention and Control

The prevention and control of zoonotic diseases has a three-tier action – the direct protection of humans, reduction or elimination of the infection in the animal reservoir, and anti-vector measures. The direct protection of humans applies mainly to occupational diseases in the laboratory, the workplace, or the rural environment. Preventive measures include the wearing of protective clothing, including gloves and glasses or goggles, appropriate air filtration systems, regular disinfection, vector (e.g., insect or rodent) control, and water treatment. Health education, including safe dietary habits and proper food hygiene, is also a major component of zoonosis prevention. Specific vaccination against zoonotic pathogens may be appropriate, such as leptospirosis vaccination in sewage workers or rabies vaccination in high-risk workers (veterinarians, taxidermists, etc.).

Zoonoses control in animals is an imperative goal of veterinary public health activity. Priority should always be given to disease eradication by the culling of sick and infected animals. The treatment of sick animals should be reserved to very specific instances in which it does not compromise the screening of infected animals, such as cases of anthrax in cattle. Disease control is based on the quarantine of sick and infected animals, testing and segregation of infected flocks or herds, restriction of animal movements, and immunization of exposed animals whenever vaccines are safe and available. Hygienic management on the farm or at the slaughterhouse must also be emphasized. The control of vectors and vehicles is essential to prevent the spread of infectious agents to non-infected animals or humans and to disease-free areas. The destruction of infected material or products is essential to control the spread of infection, especially from the food chain. The thorough disinfection of contaminated areas will reduce or stop the spread of zoonoses. Feed hygiene and the elimination of pests and vermin must be performed continuously to control all types of zoonoses, especially pherozoonoses and saprozoonoses. The harmonization of national and international rules and regulations and interagency cooperation under the sponsorship of international organizations such as the FAO, OIE and the WHO are necessary to prevent and control the spread of zoonoses.

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