CHAPTER 1.2
Current Situation of Zoonotic Diseases

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Introduction

Zoonoses have their origin in the intimate interactions between human beings and domestic or wild animals and their ecosystems. Continuous, direct or indirect exposure of humans to animals and their products and subproducts increases the possibility that infectious and parasitic agents encounter an appropriate host among the numerous species of animals and arthropods. Inevitably under such conditions, humans contract the diseases that the host organisms harbor.

The experts agree that there are elements in common that influence and trigger the appearance, spread, and persistence of zoonoses. Among the most important are: (a) demographic and socioeconomic factors where poverty and overcrowding play an important role; (b) globalization that promotes the trade in animals and their products and subproducts between developed and underdeveloped countries; and (c) the extensive mobilization of people between different countries.

Zoonoses have a series of characteristics that account for their spread, severe impact, complicated control, and eventual eradication [1]. The following are among the most important factors:

a) Some of the agents responsible for zoonoses can infect a wide variety of animal species;

b) In the majority of cases they produce chronic diseases, with a tendency to remain in a latent or subclinical phase;

c) The clinical features and pathology of the human disease tend to be similar to those of the animal disease;

d) Such diseases not only affect health, but cause severe economic losses;

e) More than 1,415 agents are known to be pathogenic for humans; 868 are zoonotic agents (61%) and 80 affect different species of animals [2];

f) Wild animals represent a potential risk to public health; there is evidence that 70% of the zoonoses currently affecting humans have their origins in wild animals; moreover, these animals tend to be responsible for the persistence and even re-emergence of multiple zoonoses [3]; and

g) The control of zoonoses is a complex process because each case requires a different approach.
A large number of agents are capable of causing zoonotic diseases, and examples of important zoonoses are presented in this chapter. For academic purposes, the diseases included here were classified as: parasitic zoonoses, zoonoses transmitted by arthropods, bacterial zoonoses, and viral zoonoses.

**Parasitic zoonoses**

**Cysticercosis**

This parasitic disease is a serious public health problem in the poorest countries. It is a condition associated with a lack of hygiene in pig production systems, lack of quality control in foodstuffs of animal origin, deficiencies regarding epidemiological surveillance, and socio-cultural aspects ([4]. The most affected regions are Africa, Asia, and Latin America [5]. The World Health Organization (WHO) estimates that cysticercosis affects 50 million people globally, and in endemic areas, problems associated with neurocysticercosis are responsible for the death of at least 50,000 humans every year [6].

The European Union (EU) has proposed harmonized systems for the monitoring and notification of cysticercosis in animals and food. It is reviewing the current situation of the disease and carrying out monitoring in each of its member countries to identify public health needs and the policies required to address the problem. The proposal is oriented mainly to the monitoring of the species of greatest relevance to public health: *Taenia saginata* in cattle and *Taenia solium* in pigs. Monitoring is based on the inspection of meat according to the European legislation [7].

**Hydatid disease or cystic echinococcosis**

Echinococcosis is caused by *Echinococcus granulosus*, which has a lifecycle involving dogs and sheep. In dogs, the parasite occurs as flat worms, whereas in sheep the cycle phase presented is of a cystic nature. Human infection occurs through ingestion of water or food contaminated with the parasite’s eggs. Infection can also occur by direct contact with parasitized pets. It is a global disease, but predominates in underserved areas where there is close coexistence of humans with dogs and sheep [8]. The prevalence of echinococcosis in endemic areas varies between 0.22 and 24%. Control of the condition is based on: (a) periodic deworming of dogs; (b) preventing the dogs from swallowing meat and raw entrails of sheep origin; and (c) intensifying surveillance activities and preventive medicine.

As with cysticercosis, experts within the EU have proposed a program for monitoring and reporting cases of echinococcosis in animals and food [9]. This proposed program comprises the study of *E.*
*granulosus* through monitoring the intermediate hosts (sheep, goats, pigs, and cattle) with the participation of the health inspection services [7].

**Zoonoses transmitted by arthropods**

**Chagas disease**

Chagas disease is a zoonosis that involves many vertebrate reservoirs and triatomine bug transmitters. The disease is included in the WHO list of major neglected diseases [10]. It is also known as the American trypanosomiasis because it is widely present in this continent. The disease is caused by the flagellate protozoan *Trypanosoma cruzi*, which is transmitted through the blood-sucking arthropods of the Triatominae family. Chagas disease affects between 8 and 10 million people globally [11]. According to figures from the Pan American Health Organization [12], it is endemic in 21 Latin American countries, with 56,000 new cases and 12,000 deaths each year. About 30% of infected people develop cardiac damage, and up to 10% may present with severe damage to the digestive or nervous systems. In Argentina it is estimated that at least 1.5 million people are infected and more than 300,000 suffer from heart disease caused by Chagas disease. It is believed that Chagas disease causes 6,000 deaths per year in Brazil, 150,000 infected humans in Paraguay, and about one million in Bolivia. The number of people affected by Chagas disease in Europe is estimated to be between 68,000 and 122,000. Spain is the most affected European country with more than 50,000 registered human cases, and is the pioneer in the control of transmission.

Mexico has the most diverse triatomine bug population, with 39 documented species; at least 21 species are likely to be infected with *T. cruzi*, which makes them potential vectors of Chagas disease [13].

It is worth considering the abundance of wild, domestic, and peridomestic reservoirs.

Identified reservoirs include armadillos, opossums, mice, rats, squirrels, fruit bats, dogs, cats, martens, donkeys, and pigs. A significant number of domestic mammals are in direct contact with vectors and remain in human cohabitation [14].

Pharmacological treatment is strongly recommended in cases of acute, congenital, and reactivated Chagas disease, and for children with chronic infection (12–18 years old). It is also important to consider drug treatment in adults when the disease is in the chronic phase.

Benznidazole is used in the acute phase, in congenital cases, and in patients with chronic disease. Nifurtimox is used in both acute and chronic cases.
Leishmaniasis

Leishmaniasis is caused by *Leishmania donovani* and more than 20 other different *Leishmania* species; these protozoan parasites are transmitted by the bite of infected female phlebotomine sandflies. It affects the poorest people on the planet, and is associated with malnutrition, population displacement, poor housing, a weak immune system, and lack of resources [15]. It is estimated that globally it causes 1.3 million new cases and 20,000–30,000 deaths each year.

Humans may suffer from three main forms of the disease:

a) Visceral leishmaniasis (VL; also known as kala-azar) is fatal if left untreated. It is highly endemic in the Indian subcontinent and in East Africa. Approximately 200,000–400,000 new cases of VL occur globally each year.

b) Cutaneous leishmaniasis (CL) is the most common form and causes ulcers on exposed parts of the body; in Mexico the disease is also known as “the chicleros ulcer” because it frequently affects workers who tap rubber trees in the rainforests of the Yucatan peninsula. About 95% of CL cases occur in the Americas, the Mediterranean basin, the Middle East, and Central Asia.

c) Mucocutaneous leishmaniasis leads to partial or total destruction of the mucous membranes of the nose, mouth, and throat. Almost 90% of cases occur in Bolivia, Brazil, and Peru [15].

All the New World cutaneous leishmaniasis cycles are predominantly zoonotic, but the reservoir hosts vary by species and location, and in many cases are not fully known [16].

Domestic and sylvatic mammals infected with leishmaniasis may or may not show signs of infection, but they can be involved in the transmission of the disease. There is growing evidence that domestic dogs and cats may be involved in the maintenance of *L. infantum*, and that dogs may be important in cutaneous leishmaniasis in South America. Dogs play an important role because they are known urban reservoirs of visceral leishmaniasis in humans. The habit of keeping dogs and other domestic animals inside the house is thought to promote human infection, because dogs are the *L. infantum* reservoir hosts and attract sandflies; moreover, they are the main source of infection for the vectors, and can remain infective despite treatments that improve their clinical condition [17]. More than 50% of all infected dogs are asymptomatic carriers. Some transmission occurs directly from dog to dog, without sandflies; the significance of this finding remains to be determined. The prevalence of leishmaniasis in dogs is always higher than in humans, and infection in dogs usually precedes an outbreak in humans. Infected dogs, with or without clinical signs, can transmit the disease [18].
Because the transmission of leishmaniasis occurs through a complex biological system involving the human host, the parasite, a sandfly vector, and in some situations an animal reservoir, control of the disease is unlikely [16].

Bacterial zoonoses

Some examples of important zoonoses caused by bacteria are presented below:

**Leptospirosis**

Leptospirosis is caused by the bacterium *Leptospira interrogans*. More than 250 serovars of this species are known. They are registered as pathogenic in more than 160 species of domestic and wild animals, and some affect humans. The transmission of leptospirosis has no barriers and can occur both between species and between animals of the same species [19].

Infected animals that survive an acute infection become carriers of the agent and transmit it to their offspring. These animals often eliminate leptospires in their urine for several weeks or months, contaminating soil, facilities, water, and pasture. The role of infected rodents is very important. It is common for rats and mice to contaminate drinking water and stored food with their urine. *Leptospira* grow freely in stagnant water where there is organic matter [19].

People can become infected by contact with food, drink, and utensils that have been contaminated with the urine of various species, but humans are considered the final host of the dissemination chain. A case of human-to-human transmission via sexual contact has recently been registered. *Leptospira* enter humans or animals through oral, conjunctival, or nasal mucous membranes, and are inhaled in aerosols of the liquids that contain them. It has been speculated that the bacteria can even penetrate intact skin when it is softened by moisture.

Leptospirosis is regarded by the WHO, the “Oficina International de las Epizootias” (OIE), and the International Leptospirosis Society (ILS) as the widest disseminated zoonosis in the world. Between 300,000 and 500,000 new cases occur globally each year, with the range of mortality fluctuating between 5 and 20%. The highest prevalence occurs in developing countries, mainly in tropical and humid zones. Frequent outbreaks are associated with flooding because stagnant water contaminated with human or animal urine is favorable for the proliferation of the leptospires. This has been documented in several countries: Nicaragua in 1995 [20] and 1998, Puerto Rico in 1996, Argentina in 1998, and Tabasco, Mexico, in 2007. In these circumstances, people with the disease commonly present with respiratory and bleeding symptoms because it is frequently confused with Dengue fever (patients may be suffering from both diseases simultaneously). Leptospirosis outbreaks in the Philippines usually occur as a result of the flooding caused by typhoons, as was the
case following the typhoon that flooded Metro, Manila, at the end of September 2009; a few weeks later more than 2,000 patients presented with the signs and symptoms of leptospirosis, and 178 people died from the disease [21].

A sustained leptospirosis outbreak occurred in northeast Thailand between 1999 and 2003; the cause of the disease was not known until 2005, when the microorganism was isolated and identified as a clone of *L. interrogans* called ST34. A special technique for bacterial genotyping known as multilocus sequence typing was used to identify this clone [22].

The disease can be prevented in animals through intensive vaccination programs coupled with the application of biosecurity measures in the production units. Moreover, *in vitro* experiments and experiments on animals show that *Leptospira* are sensitive to numerous antibiotics. Severe human cases require intravenous doses of penicillin. Less serious cases can be treated with oral amoxicillin, ampicillin, doxycycline, or erythromycin. Third-generation antibiotics such as cephalosporins and quinolones are also effective.

**Tuberculosis**

The WHO estimates that more than 2 billion people globally are infected with bacteria of the *Mycobacterium tuberculosis* complex, and around 8 million new cases occur annually. The global proportion of human cases of tuberculosis (TB) of bovine origin in all its forms is estimated to be 3.1%. Developed countries report rates ranging from 0.5 to 7%.

Some countries have made significant progress in the control of human TB caused by *M. bovis* [23]. Such was the case of France, where the average number of cases of bovine TB accounted for 1–5 cases of human tuberculosis, with a prevalence of 0.35 in a population of 100,000. By 1995, the figure had been reduced to 0.07 per 100,000 people, and today cases are rare in France. It is important to note that whereas in some regions such as Southeast Asia, Latin America, the Caribbean, and various European countries, the prevalence of human TB has decreased, in Africa and the former Soviet Union the disease presents a serious recrudescence [24]. *M. bovis* and *M. africanum* were responsible for 13% of human TB cases in Nigeria. In rural areas of the United Republic of Tanzania, *M. bovis* was identified in 4% of culture-positive pulmonary cases [25] and in 10% of extrapulmonary human TB cases [26]. *M. bovis* was isolated from 6.9% of TB patients in a pastoral community in Uganda [27].

In Mexico, the Ministry of Health reported the occurrence of about 20,000 annual cases of TB in humans. Recent studies carried out in an area of endemic bovine TB revealed that up to 40% of cases of TB in humans were of bovine origin [28]. In 3rd-level hospitals, about 15% of human TB was caused by *M. bovis* [29].
Today TB in animals is a global problem. It is increasing rapidly in England and Wales. Spoligotyping has identified the same strains of *M. bovis* in cattle and badgers living in close proximity. For the last 5 years in England and Wales, there have been no more than 25 cases per year of TB in humans caused by *M. bovis*; however, cases in younger patients in the UK do occur, which suggests that cattle-to-human transmission could in fact be a problem in some developed countries. There have been a handful of documented cases where human infection was probably caused by airborne spread from cattle [30].

Ghodbane and Drancourt (2013) reviewed the evidence for anthroponotic *M. tuberculosis* infection in non-human primates, other mammals, and psittacines [31]. They suggested that some infected animals may be sources for zoonotic tuberculosis caused by *M. tuberculosis*. Wildlife trade and zoos are important amplifying factors. Wildlife, farm animals, pets, food, and milk all represent a potential threat to human health.

**Anthrax**

Anthrax is a well-known disease that is caused by spore-forming bacteria, *Bacillus anthracis*. Herbivores are highly susceptible, and when they become sick, they suffer an acute and fatal course of the disease. Human infection occurs in three ways: by breathing spores, by eating meat from infected animals, and through skin lesions. During 2004, the disease was reported by 60 countries; all were developing countries, and the disease manifested itself in the cutaneous form in 95% of cases. The impact on livestock of this disease tends to be ignored [23].

Many studies have suggested the potential role of insects in the spread of *B. anthracis* to humans and domestic animals during anthrax outbreaks. This was confirmed by the research group headed by Fasanella [32]. They demonstrated the important role of the housefly *Musca domestica* in the dissemination of anthrax, and suggested that fly control should be included in anthrax control programs.

Anthrax remains an important issue in Turkey where cutaneous cases of the disease frequently occur [33; 34]. In Africa, the disease affects wild and domestic animals, and poses a serious risk to humans. In March 2014, three people died in Musoli, Kakamega County, Kenya, after they reportedly feasted on a cow that is believed to have been infected with deadly anthrax [35].

**Brucellosis**

Brucellosis (*Brucella melitensis*) is an unattended, sometimes unreported, disease that continues to affect humans and animals, predominantly in subsistence goat and sheep production in developing or underdeveloped countries. An example is provided by disease information from the Department of Lima, Peru: 20,000 new cases were diagnosed over a 10-year period (1993–2002) [36]. The
prevalence of this zoonosis in the United States of America is 0.03 per 100,000 people, whereas in France it is 0.15; in contrast, in countries such as Iran, Greece, and Portugal the prevalence is 30, 20, and 10 per 100,000 people, respectively. This zoonosis is a clear example of the lack of interaction between veterinary and public health sectors. The establishment of intensive vaccination programs for small ruminants, education about the importance of boiling milk before drinking it, and avoiding the consumption of cheese made from raw milk are strategies that favor a reduction of new human cases, particularly in countries where the elimination of reactor animals is not economically feasible [37].

Viral zoonoses

Rabies

More than 99% of all human rabies deaths occur in the developing world, and although effective and economical control measures are available, the disease has not been brought under control throughout most of the affected countries. Canine rabies is by far the most important form for public health, and accounts for 99% of human deaths caused by the rabies virus.

Dogs maintain and transmit the disease through bites, causing more than 50,000 human casualties annually. Mainly, developing countries in Asia and Africa are the ones that suffer from the burden of the disease. There is abundant evidence that in countries where intensive dog vaccination programs are performed, simultaneously with activities focused on the reduction of the stray dog population, the number of people who die annually from rabies decreases significantly [38]. These programs reflect the joint participation and synergy of veterinary and public health sectors. Unfortunately, these procedures are not applied in all countries. It is estimated that 55,000 people die each year in Africa and Asia because of the rabies virus [39]. The total global cost of rabies is estimated to be USD 583 million. Although in the majority of cases a dog is involved in spreading the disease, several countries in the Americas have documented cases of human rabies being caused by the bite of a vampire bat.

In Europe, the red fox (Vulpes vulpes) is the main rabies reservoir species. The disease is re-emerging in wild animals and dogs, which increases the likelihood of human exposure requiring post-exposure prophylaxis. During 2012 to 2013, rabies was diagnosed in 14 red foxes, two shepherd dogs, and one cat in northern Greece; 104 subsequent human exposures required post-exposure prophylaxis [40].

Between 1977 and 2000, a total of 630 cases of European Bat lyssavirus type 2 (EBLV) infection were identified in European bats [41]. Nathwani el al. (2003) reported the first recorded case of indigenous human rabies caused by a bat bite in the United Kingdom in 100 years [42]. It was a
fatal human rabies case caused by EBLV. The infection occurred in Scotland in a 55-year-old man. He worked voluntarily as a bat-handler and bat-rescuer for many years, and died of rabies caused by the bite of a bat. The patient had mixed symptoms of furious and paralytic rabies, which is strikingly similar to the only other reported case of human rabies due to EBLV. The authors showed that bat-transmitted rabies can be diagnosed ante-mortem using reverse transcription polymerase chain reaction (RT-PCR). Several hundred people in The Netherlands and two people in the United Kingdom have been vaccinated with a rabies vaccine after being bitten by an EBLV-infected bat, and to date, no EBLV infection has been confirmed in any of these people [40].

**Avian influenza**

Influenza type A viruses are responsible for causing disease in humans and various animal species including poultry, horses, pigs, and even marine animals. Influenza virus type A contains two main types of surface proteins: hemagglutinin (H or HA) and neuraminidase (N or NA); 15 different types of hemagglutinin (H) and 9 types of neuraminidases (N) are currently known. Genetic and antigenic differences in surface H and N proteins are responsible for the existence of a multitude of subtypes of the influenza virus.

Avian influenza is an infectious disease of birds caused by influenza type A virus. The majority of avian influenza viruses do not infect humans, but some of them, such as H5N1, cause serious human infections. A fatal case of influenza occurred in 1997 in a child in Hong Kong. The virus was identified as influenza type A H5N1 avian virus [43]. From 2003 to 2014, 658 laboratory-confirmed human cases of avian influenza A H5N1 virus infection were officially reported to WHO from 15 countries, and 388 people subsequently died. Apparently, this influenza A H5N1 virus is not easily transmitted among people, so the risk of community-level spread of the virus remains low [44].

Other avian influenza type A viruses that affect people have been identified in China, such as H7N9 and H10N8 viruses. To date, a total of 375 laboratory-confirmed cases of avian influenza A H7N9 virus in humans have been registered, which have resulted in 115 deaths; most of these cases were reported in China [44]. The source of human infection by this virus is not known. However, it appears to be associated with exposure to infected live poultry or contaminated environments, including markets where live poultry are sold. Evidence suggests that transmission of this virus from birds to humans is not an easy process, although it seems to be more transmissible than the H5N1 virus. WHO advises countries to continue strengthening influenza epidemiological and virological surveillance.
Hantavirus

After the hantavirus was discovered in 1993, evidence of infections caused by similar strains was published all over the world. In people, this infectious agent causes a disease characterized by severe pulmonary inflammation associated with respiratory failure and cardiovascular collapse [45].

Some strains of the virus may produce acute renal failure rather than lung disease. Each year between 150,000 and 200,000 new cases of severe human infection occur, with hemorrhagic fever and renal syndrome. The mortality rate among these cases is considered to be between 3 and 15%.

The animal hosts responsible for spreading hantavirus in different regions are various species of rats and mice. They are usually asymptomatic carriers. These rodents eliminate the virus through feces and urine. People become infected when they inhale aerosols containing viral particles. The presence of the virus has been demonstrated in Russia (Dobrava strain), China and Southeast Asia (Seoul and Hantaan strains, the latter gave its name to the virus), and the southern part of the United States and northern Mexico (Black Creek Canal and nameless strains). It has also been detected in the South American Andes (Andes strain), Brazil (Juquitiba strain), and Paraguay (Black Lagoon strain), and is presumed to be present in all Central and South America countries. In Scandinavia, the virus (Pumala strain) is responsible for causing acute renal failure and occasionally lung disease.

Hendra virus

Hendra virus is a paramyxovirus that was first identified at the Australian Animal Health Laboratory (CSIRO) in samples collected from a horse trainer in Queensland, Australia; the virus killed the trainer as well as his horses. Hendra is the name of the suburb in Brisbane where the outbreak occurred. Once the virus was isolated, the disease was reproduced and the genetic sequencing of the virus was carried out [46].

The Hendra virus can infect more than one animal species. Some fruit bats are natural virus hosts, but they do not suffer from any clinical pathological process. It has been shown that horses, cats, and guinea pigs may excrete the virus in their urine. During the past 15 years, the disease has been confirmed in seven people, four of whom died from the infection.

Studies published in 2005 identified the cell membrane receptors through which Hendra and Nipah viruses enter the cell to infect it. Potential vaccines are currently being investigated to protect against virus infection. Researchers are also focusing on the identification of potential sites of action of antiviral drugs [47].
Nipah virus

Like the Hendra virus, Nipah is a paramyxovirus whose natural host is a fruit bat of the genus *Pteropus*. This virus was detected for the first time during an outbreak of the disease identified in Kampung Sungai Nipah, Malaysia, in 1998; the intermediate host in this epidemic was found to be the pig. However, in an outbreak caused by the Nipah virus in Bangladesh in 2004, there was no intermediary host; human infection occurred when people consumed date palm sap contaminated by infected bats. Person-to-person transmission has also been documented. The disease has a wide range of clinical manifestations varying from asymptomatic to acute respiratory syndrome and even deadly encephalitis [48-51]. Subunit vaccines have been investigated to provide protection against this virus [47].

References.


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