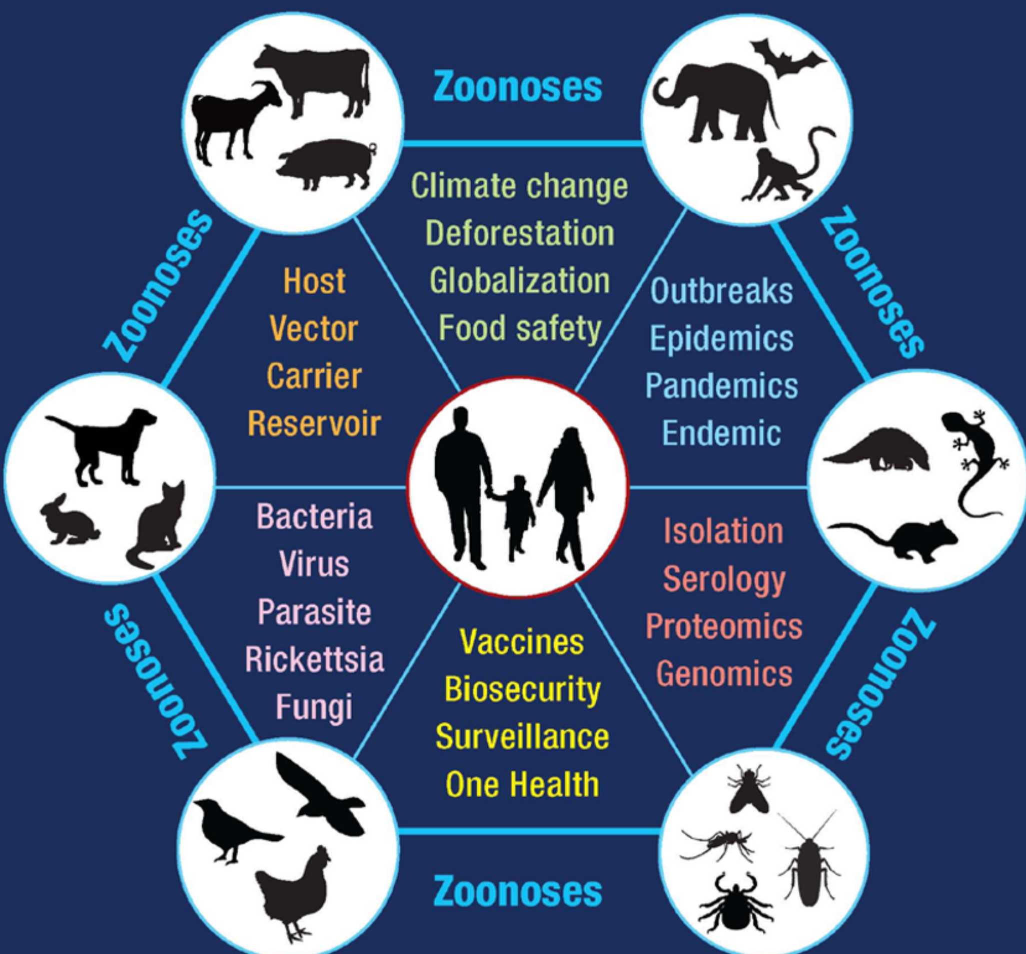
Textbook of Zoonoses



Jasbir Singh Bedi • Deepthi Vijay • Pankaj Dhaka

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Jasbir Singh Bedi
Guru Angad Dev Veterinary and Animal Sciences University
Punjab, India

Deepthi Vijay
Kerala Veterinary and Animal Sciences University
Kerala, India

Pankaj Dhaka
Guru Angad Dev Veterinary and Animal Sciences University
Punjab, India

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We dedicate this book to our colleagues and families who remain a constant source of inspiration and support throughout our life journey. We express our gratitude to GOD ALMIGHTY for blessing us with such wonderful companies.

Contents

Preface

Zoonoses are infections that are naturally transmissible between animals and humans. Zoonotic diseases need special attention, as most of the emerging infectious diseases of epidemic and pandemic potential belong to this category. Zoonoses have a substantial socioeconomic impact not only on the rural population of the world where the human–animal interface is quite porous, but also many of these infections are emerging due to the unsustainable expansion of our cities and other anthropogenic activities disturbing the biodiversity (e.g. deforestation, climate change, wars and conflicts, etc.).

How Did the Idea for Writing the Book Come Up?

There are few textbooks on zoonoses along with the information available on the websites of public health agencies. Our students and professional colleagues used to ask us 'Where can we get the required information on all the relevant zoonoses in one place?'. Our attempts to address this query inspired us to collect and present this *Textbook on Zoonoses* in a logical format, covering the required information for each zoonosis. The COVID-19 pandemic has made this the best possible time to write this book to further spread knowledge and awareness of zoonoses.

Who Should Use this Book?

Most zoonoses are multifaceted in origin, involving the interaction(s) of host(s) (both human and animal), agent and environment-related factors. Therefore, the effective tackling of zoonoses needs a 'One Health' approach, where collaborations between various professionals can produce synergistic effects for efficient prevention and control.

We hope this textbook will be of help to all public health professionals, mainly veterinary and medical professionals, to inspire learning and development of expertise in the field of zoonoses.

Book Content and Our Expectations

The book has six sections on bacterial, viral, parasitic, fungal, rickettsial and prion zoonoses. Each chapter describes the aetiology, epidemiology, clinical symptoms in humans and animals, diagnosis, treatment options, and prevention and control strategies of the mentioned disease. By using this book as reference material, we hope that public health students and professionals across relevant disciplines will develop a deep appreciation of the epidemiological and clinical characteristics of various zoonoses, which will enable them to play a valuable part in the 'One Health' taskforce of regional, national and global importance.

Jasbir Singh Bedi
Deepthi Vijay
Pankaj Dhaka

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This book stands on the shoulders of the knowledge imparted by the zoonoses and public health experts across the world, which we relied upon throughout the drafting of this textbook. We would also like to thank our families for patiently allowing us the time and wholeheartedly supporting us to finalise this text.

Jasbir Singh Bedi
Deepthi Vijay
Pankaj Dhaka

About the Authors

Dr Jasbir Singh Bedi is currently Director, Centre for One Health, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, India. Dr Bedi has served as an academician and researcher for the last 20 years in the areas of zoonoses and veterinary public health, and has been associated with research projects on zoonoses, food safety and antimicrobial resistance.

Dr Deepthi Vijay is an Assistant Professor at the Department of Veterinary Public Health, College of Veterinary and Animal Sciences, Kerala Veterinary and Animal Sciences University, Mannuthy, Kerala. Dr Deepthi has 7 years' in the academic areas of veterinary public health and epidemiology, with research expertise in various zoonoses and antimicrobial resistance in the animal health sector.

Dr Pankaj Dhaka is an Assistant Professor at the Centre for One Health, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, India. Dr Dhaka is involved in the academic and research activities of undergraduate and postgraduate students in the areas of epidemiology of zoonoses, farm biosecurity and antimicrobial resistance.

Introduction to Zoonoses

What are Zoonoses?

The word 'zoonoses' is derived from the Greek words *zōon* meaning 'animal' and *nosos* means 'disease' (the singular is 'zoonosis' and plural is 'zoonoses').

The term 'zoonoses' was coined by Rudolf Virchow during his study on *Trichinella* in 1855, to indicate the infectious disease link between animal and human health [1]. As described by the World Health Organization (WHO), 'A zoonosis is any disease or infection that is naturally transmissible from vertebrate animals to humans' [2].

Overview on Zoonoses

Since the Agricultural Revolution, humans have been afflicted by zoonoses. The classic zoonoses, such as rabies, plague, leptospirosis, brucellosis, bovine tuberculosis, cysticercosis, echinococcosis, toxoplasmosis and yellow fever, have been well known for centuries and are still causing major socio-economic effects in many parts of the globe. In recent years, new zoonotic entities (e.g. Lyme borreliosis, enterohaemorrhagic *Escherichia coli,* cryptosporidiosis, Ebola, Nipah, severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome (MERS), influenza viruses of animal origin (swine flu – H1N1), hantavirus, etc. are posing a serious threat to the globalised world. Among other issues, there is also concern regarding the potential 'bio-weaponisation' of many of the zoonotic pathogens, some of which have been used this way historically (e.g. anthrax and glanders).

A wide variety of animal species, domesticated, peridomesticated, and wild, can act as reservoirs for these pathogens. Therefore, considering the wide variety of animal species involved and the often complex natural history of the pathogens concerned, effective surveillance, prevention and control of zoonotic diseases pose challenges to public health.

The awareness of zoonoses is very important, more especially among occupationally at-risk groups like farmers, pet owners, veterinarians, etc. In this regard, 'World Zoonoses Day' is held every year on July 6. The day commemorates 6 July 1885, when the renowned microbiologist Louis Pasteur successfully administered the first vaccine against the rabies virus.

Classification of Zoonoses

As per the joint WHO/Food and Agricultural Organization (FAO) Expert Group on zoonoses, the zoonoses can be grouped into three categories.

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A) **Classification of zoonoses based on aetiological agents:** Zoonoses can be caused by a range of pathogens such as viruses, bacteria, fungi and parasites. In a study, out of the listed 1415 pathogens known to infect humans, 61% were found to be zoonotic [3]. The classification of zoonoses based on the category of aetiological agents is given in Table I.1.

B) **Classification of zoonoses based on the reservoir host(s):** Zoonoses can be classified based on the reservoir host(s) and the life cycle of the infecting pathogen. The reservoir of an infectious agent is the habitat in which the agent normally lives, grows and multiplies. The reservoirs for zoonotic pathogens include humans, animals and the environment. Our incomplete understanding of the reservoirs can hamper the control of zoonoses (e.g. it is important to know the possible wildlife reservoirs of rabies in a given area). Based on reservoir hosts, zoonoses can be classified as follows.
   - *Anthropozoonoses*: The zoonotic diseases which can be transmitted to humans from lower vertebrates. Therefore, these infections primarily affect animals but can be naturally transmitted to humans (e.g. rabies, brucellosis, Q fever, leptospirosis, ringworm, etc.).
   - *Zooanthroponoses (also known as 'reverse zoonotic disease transmission')*: Those zoonotic diseases which can be transmitted to lower vertebrate animals from infected humans. Therefore, these infections are primarily of human origin (e.g. methicillin-resistant *Staphylococcus aureus*, *Cryptosporidium parvum*, *Ascaris lumbricoides*, etc.).
   - *Amphixenoses*: The zoonoses which are maintained in both humans and lower vertebrate animals, which may be transmitted in either direction (e.g. *Staphylococcus* infection, *E. coli* infection, salmonellosis, etc.).

C) **Classification based on the transmission cycle:** The transmission of zoonotic pathogens can occur through reservoir hosts (e.g. bats shedding Nipah virus into date palm collection vessels), and in other instances, can be facilitated by intermediate hosts (e.g. Nipah virus infection from bats to pigs in Malaysia resulting in pig-to-pig and pig-to-human transmission by aerosol route) or via insect vectors (e.g. West Nile virus as a mosquito-borne disease). Therefore, it is important to understand the transmission cycle of the pathogen for proper implementation of surveillance systems and control measures. Based on the requirement of intermediate host and inanimate objects, zoonoses can be categorised as follows.

Table I.1 Classification of zoonoses based on aetiological agents.

Sl. No.	Type	Examples
1	Bacterial zoonoses	Anthrax, brucellosis, coxiellosis, plague, leptospirosis, tuberculosis, Lyme disease, zoonotic tuberculosis, etc.
2	Viral zoonoses	Rabies, yellow fever, Ebola, Japanese encephalitis, zoonotic coronaviruses, Nipah, Rift valley fever, etc.
3	Parasitic zoonoses	Toxoplasmosis, taeniasis, cryptosporidiosis, echinococcosis, trichinellosis, leishmaniasis, etc.
4	Fungal zoonoses	Aspergillosis, blastomycosis, coccidioidomycosis, cryptococcosis, histoplasmosis, etc.
5	Rickettsial zoonoses	Epidemic typhus, endemic typhus, scrub typhus, tick typhus, Rocky Mountain spotted fever, etc.
6	Prions	New variant Creutzfeldt–Jakob disease (nvCJD)

- *Direct zoonoses:* Those zoonotic diseases which are perpetuated in nature by a single vertebrate species (e.g. anthrax, rabies, Q fever, etc.).
- *Cyclozoonoses:* Zoonotic diseases which require two or more vertebrate hosts to complete the transmission cycle. These can be further classified as follows.
  - Obligatory cyclozoonoses: The zoonotic diseases in which the involvement of humans as a host is compulsory to continue the transmission cycle (e.g. taeniasis).
  - Non-obligatory cyclozoonoses: The zoonotic diseases in which humans are accidentally involved in the transmission cycle of the pathogen (e.g. hydatidosis).
- *Metazoonoses:* The zoonotic diseases which require both vertebrate and invertebrate hosts to continue their transmission cycle. This can be further classified as shown in Table I.2.
- *Saprozoonoses:* The zoonotic diseases which require an inanimate object(s) for the completion of the transmission cycle are known as saprozoonoses. These can be further classified as follows.
  - Saproanthropozoonoses: The zoonoses which can transfer from animals to humans through inanimate substances (e.g. erysipeloid).
  - Saproamphixenoses: The zoonoses which can be shared between humans and animals through inanimate objects (e.g. histoplasmosis).
  - Saprometanthropozoonoses: These zoonoses require vertebrate hosts and invertebrate hosts as well as inanimate objects for the completion of their life cycle (e.g. fascioliasis).

Other Classifications

Classification According to the Ecosystem in which Pathogens Circulate [4]

- **Synanthropic zoonoses:** The zoonotic diseases which transmit through the urban (domestic) cycle where the sources of infection(s) are domestic and synanthropic animals (e.g. urban rabies, cat-scratch disease and zoonotic ringworm through pets).
- **Exoanthropic zoonoses:** The zoonotic diseases which transmit through the sylvatic cycle in natural foci through feral or wild animals (e.g. arboviruses, wildlife rabies, Lyme disease and tularaemia). **Note:** Some zoonoses can circulate in both urban and sylvatic cycles (e.g. yellow fever and Chagas disease).

Major Transmission Routes of Zoonoses

Generally, disease results from the interaction(s) of the host (person or animal), agent (e.g. bacteria, virus, parasite or fungi) and the environment (e.g. contaminated feed and/or water supply, dirty

Table I.2 Classification and examples of metazoonoses.

Type	Number of invertebrate hosts	Number of vertebrate hosts	Examples
I	1	1	Yellow fever, plague
II	2	1	Paragonimiasis
III	1	2	Clonorchiasis
IV	Transovarian transmission		Tick-borne encephalitis

farm conditions). The diseases can be transmitted directly or indirectly. A disease can be transmitted directly from animal to human (i.e. direct transmission) (e.g. rabies through dog bite). Indirect transmission can occur through common vehicles such as contaminated air or water supply, or by vectors such as mosquitoes, or inanimate objects. Some of the important modes of transmission for zoonotic diseases are listed below.

- Direct contact of a susceptible host with infected animals (e.g. scabies, brucellosis, leptospirosis, etc.).
- Direct transmission through animal bites (e.g. rabies) and scratches (e.g. cat-scratch fever).
- Transmission through contaminated animal food products, mainly due to improper food handling and inadequate cooking practices (e.g. *Salmonella* spp., *Clostridium perfringens*, *E. coli*, etc.).
- Faeco–oral transmission from animals to humans (e.g. salmonellosis, *E. coli*, *Toxoplasma gondii*, etc.).
- **Vector-borne transmission:** Vectors such as mosquitoes, ticks, fleas and lice can transmit zoonotic diseases to humans (e.g. yellow fever, Kyasanur forest disease, plague, etc.).
- **Air-borne transmission:** Air-borne transmission results from the inhalation of small particles (droplet nuclei) which are considered to have diameters $\leq 5\,\mu m$ (e.g. influenza viruses).
- Indirect transmission through contaminated soil (e.g. roundworm eggs can survive for years in contaminated soil). Allowing the faeces to dry out and disintegrate contaminates the soil which increases the risk of exposure to pathogens [5].
- Indirect transmission through contaminated water sources (e.g. *Cryptosporidium* spp., cholera, rotavirus infection, leptospirosis, etc.).

Note: Some occupational groups (e.g. farmers, butchers, veterinarians) are at high risk of exposure to zoonotic pathogens due to their frequent exposure to livestock which may result in increased occurrence of transmission. Further, these high-risk groups can also become carriers of zoonotic pathogens that may spread in the community.

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Understanding Concepts and Terms Related to Zoonoses

Globally, zoonoses are responsible for severe socio-economic losses, affecting global food security networks and thereby posing an increasing public health threat to our interconnected world. The endemic zoonoses are responsible for the majority of human cases of illness as well as for the reduction in livestock production in many parts of the world. In a study, 56 zoonoses were found to be responsible for around 2.5 billion cases of human illness and 2.7 million human deaths a year [1].

The emergence of novel zoonotic pathogens is one of the greatest challenges to global health security in the twenty-first century. The importance of zoonotic diseases can be observed from the fact that out of 1415 species known to be pathogenic to humans, 61% (868/1415) are considered to be zoonotic. And, out of 175 pathogenic species which are considered to be 'emerging' pathogens, 75% (132/175) are considered zoonotic [2]. In general, viruses account for a significant proportion of emerging infectious diseases (EIDs), and the majority have zoonotic origin, including ebolaviruses, human immunodeficiency virus (HIV), hantaviruses, Hendra and Nipah viruses, severe acute respiratory syndrome (SARS) coronavirus, influenza A viruses and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). These listed viruses are RNA viruses, which are considered as the primary aetiological agents of emerging infectious diseases (44% of total EIDs) due to their higher ability to infect new host species with exceptionally short generation times. The RNA viruses are also characterised by their rapid evolutionary rates due to the frequent error-prone replication cycles [3].

Important Terms

Emerging Infectious Diseases

These are the diseases that have not occurred before (e.g. SARS in 2003, COVID-19) or have occurred previously but affected only small numbers of people in isolated places but now are rapidly increasing in incidence or geographical range (e.g. Zika was discovered in 1947 but the major epidemic was in 2015–2016) or have occurred throughout the human history but only recently been recognised as a distinct disease due to infectious agent (e.g. the causative agent of Lyme disease was discovered in 1982) [4].

Re-emerging Infectious Diseases

These are the diseases that once were major health problems globally or in a particular country, and then declined dramatically, but are again becoming health problems for a significant proportion of the population (e.g. malaria, rabies, cholera, tuberculosis) [4].

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Neglected Zoonotic Diseases

Neglected zoonotic diseases are a subset of neglected tropical diseases. The term 'neglected' highlights that 'these diseases affect mainly poor and marginalised populations in low-resource settings'. Examples include rabies, echinococcosis, taeniasis/cysticercosis, schistosomiasis, etc. Addressing this group of diseases requires collaborative, cross-sectoral efforts of human and animal health systems and a multidisciplinary approach that considers the complexities of the ecosystems where humans and animals coexist [5]. Ongoing efforts to establish the 'One Health' framework will be helpful in addressing these neglected zoonoses.

Transboundary Animal Diseases (TADs)

These may be defined as those epidemic diseases which are highly contagious or transmissible and have the potential for very rapid spread, irrespective of national borders, causing serious socio-economic and possibly public health consequences [6]. Globalisation, land encroachment and climate change contribute to outbreaks of such animal diseases, some of which are transmissible to humans, such as brucellosis, bovine tuberculosis, parasitic illnesses, anthrax, bovine spongiform encephalopathy and influenza viruses [6].

Endemic, Epidemic and Pandemic Diseases

- An *endemic* is defined as the habitual presence of a disease within a given geographic area. It may also refer to the usual occurrence of a given disease within an area (e.g. rabies and brucellosis in India).
- An *epidemic* is defined as the occurrence of disease above the normal expectancy in a region/country (e.g. Ebola outbreak in West African countries during 2014).
- A *pandemic* refers to a worldwide epidemic covering larger geographical regions (e.g. H1N1 outbreak in 2009; COVID-19 outbreak of 2019–2021).

Public Health Emergencies of International Concern (PHEIC)

A PHEIC is defined in the International Health Regulations (2005) as 'an extraordinary event which is determined to constitute a public health risk to other States through the international spread of disease and to potentially require a coordinated international response' [7]. This definition implies a situation that:

- is serious, sudden, unusual or unexpected
- carries implications for public health beyond the affected state's national border
- may require immediate international action.

Factors Responsible for the Emergence of Infectious Diseases [8]

Different determinants can contribute to the emergence of novel zoonotic agents. Among the factors that shape the emergence of zoonoses are human demographics and behaviour; technological developments, industrialisation and agricultural activities; unsustainable economic development and land use; international trade and travel; commerce-related activities; military expeditions and wars; microbial adaptation and change; and breakdown of public health measures due to natural or man-made calamities. Some examples of zoonoses emergence and responsible factors are described in Table 1 and Figure 1.

Table 1 Brief description of various factors associated with emerging infectious diseases.

Factors	Examples of specific factors	Examples of diseases
Ecological changes	Agricultural land use, depletion of human–wildlife interface, deforestation, changes in the ecosystem and associated biodiversity loss, and global climate change	Vector-borne diseases (e.g. Zika, dengue, etc.), schistosomiasis, Rift Valley fever, scrub typhus, leptospirosis, Lyme disease, hantavirus pulmonary syndrome, etc.
Human demographics and behaviour	Rapid population growth and migration (movement from rural regions to cities); war or civil conflicts	Leptospirosis, HIV, dengue, malaria, cholera, etc.
International travel and trade	Globalisation leading to the worldwide movement of goods and people	Dissemination of mosquito vectors (e.g. dengue, malaria), rodent-borne diseases, dissemination of O139 *Vibrio cholerae* in many parts of the globe
Technological advancement and industrial influences	Globalisation of food supplies; changes in food processing pattern and packaging; drugs causing immunosuppression; widespread misuse of antibiotics and dissemination of resistant bugs	Food-borne outbreaks of *E. coli* O157:H7 through contaminated beef, Creutzfeldt–Jakob disease from contaminated batches of human growth hormone
Microbial adaptation and changes	Microbial evolution, selection pressure on microbes and response to selection in the environment	The antibiotic-resistant phenomenon in bacteria, 'antigenic drift' and 'antigenic shift' in segmented RNA viruses
Breakdown in public health measures	Curtailment or reduction in prevention programmes including vaccinations; inadequate sanitation and vector control measures	Extensively drug-resistant tuberculosis; cholera in refugee camps during a natural disaster or war-related breakdown in public health infrastructure

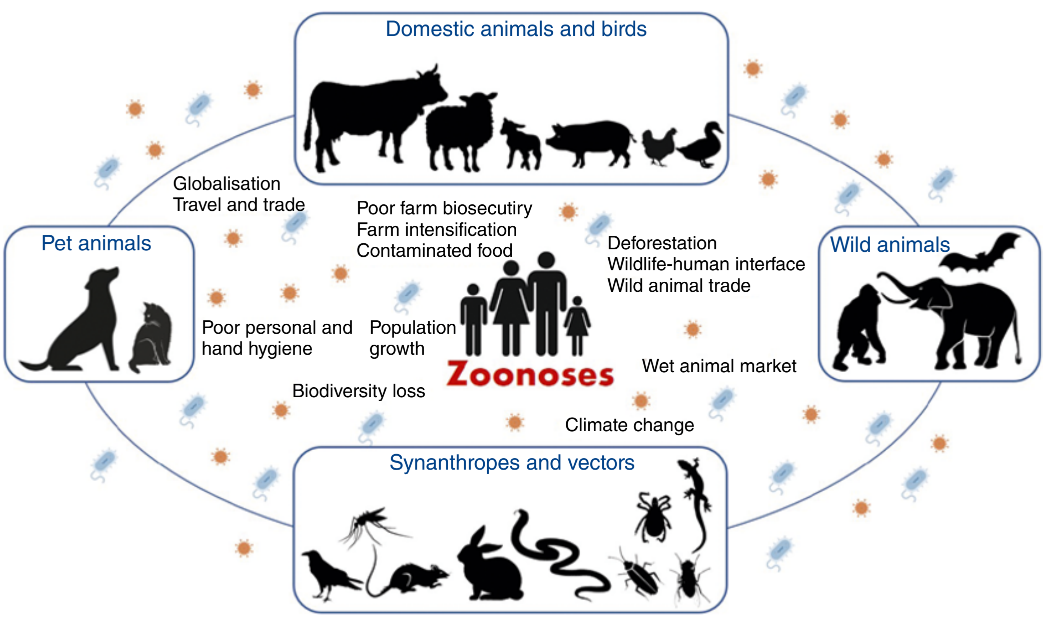

Figure 1 The important factors for emergence of zoonoses in humans.

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Section 1

Bacterial Zoonoses

1

Anthrax

Etymology

The word 'anthrax' is derived from the Greek word *anthrakis* which means 'coal'. This is linked with the characteristic dark necrotic skin-eschar in the cutaneous form of anthrax in humans.

Synonyms

Siberian plague, black bane, charbon, splenic fever, ragpicker's disease, hide porter's disease, wool sorters' disease, Cumberland disease, malignant pustule, malignant carbuncle and Milzbrand.

Aetiology and Pathogen Characteristics

Anthrax is an anthropozoonotic infection caused by *Bacillus anthracis*. The organism is a Gram-positive, aerobic or facultative anaerobic, non-motile, non-haemolytic, spore-forming, rod-shaped bacteria. The organism develops a capsule in the body of the host.

Sporulation

Spores are the dormant form of bacteria that are highly resilient, with resistance to temperature extremes, drought and UV light, possibly due to the protection of DNA in a crystalline core. In the case of *B. anthracis*, sporulation may initiate due to poor nutrient availability and in the presence of oxygen. Some of the characteristics of *B. anthracis* include the following.

- Spores can survive in dry soil for 60 years [1]; the longest reported survival of spores, i.e. 200 ± 50 years, is from bones retrieved during archaeological excavations at Kruger National Park in South Africa [2].
- The pathogen is categorised as a Centers for Disease Control and Prevention (CDC) 'category A' biological agent. The spores can be used as bioweapons due to their size of 2–6 microns diameter, which is an ideal size for impinging on the human lower respiratory tract. Moreover, anthrax spores lend themselves well to aerosolization.

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Historical Overview on Anthrax

- **1834:** The first case of human anthrax was detected in 1834 in the USA, and in 1938, Delafond demonstrated the causal organism microscopically in the blood of animals.
- **1877:** Robert Koch discovered the anthrax bacillus and also hypothesised Koch postulates.
- **1881:** Louis Pasteur developed the first whole-cell anthrax vaccine.
- **1930s:** Discovery of Sterne-type vaccines. The vaccine is based on an avirulent non-encapsulated strain 34F2 (pXO1^{+ve} and pXO2^{-ve}), which can stimulate a protective immune response. The Sterne strain is currently the predominant strain used for immunisation of domesticated animals against anthrax. It is administered to livestock in a dose containing up to 10 million viable spores.
- **1979:** Anthrax outbreak in Sverdlovsk (USSR) caused 61 deaths and 11 non-fatal cases in 6 weeks. Some researchers concluded the outbreak could have resulted from the accidental spread of anthrax spores by the wind from a microbiology facility at the local military compound [3].
- **2001:** Use of anthrax spores in a bioweapon attack in the USA by mailing of spores to seven locations, which resulted in 22 cases of anthrax (including five deaths) [4].
- **2009:** The first outbreak of injectional anthrax was reported in heroin users in Scotland. The source of contamination was proposed to be goat skins that were used to transport the heroin [5].

Pathogenesis and Virulence Factors

The bacterium *B. anthracis* is likely to be evolved from *Bacillus cereus* that acquired two extrachromosomal plasmids, pXO1 and pXO2, from the environment through lateral genetic transfer.

The plasmid **pXO1** encodes tripartite toxin complex as follows.

1) **Protective antigen** (PA, 83 kDa): This permits the entry of toxins into the host cell.
2) **Oedema factor** (EF, 90 kDa): This is responsible for oedema toxin (PA + EF). Due to this toxin, the calmodulin-dependent adenylate cyclase increases intracytoplasmic levels of cAMP that lead to alteration of water homeostasis which results in oedema. The oedema toxin can induce lethality in the host mainly by targeting hepatocytes.
3) **Lethal factor** (LF, 89 kDa): This is responsible for lethal toxin (PA + LF). It is a zinc metalloprotease toxin that can cause the hyperinflammatory condition in macrophages by activating the oxidative burst pathway and release of reactive O_2 intermediates. It cleaves and inactivates mitogen-activated protein kinase kinases (MAPKKs) 1–4, 6 and 7, which play a crucial role in responses to diverse stimuli, such as mitogens, heat shock, proinflammatory cytokines and cellular stresses. It is responsible for the production of proinflammatory cytokines (TNF-α and IL-1β). The lethal toxin causes lethality by targeting the cardiovascular system, in particular cardiomyocytes and vascular smooth muscle cells.

The plasmid **pXO2** encodes proteins that synthesise a poly-γ-D-glutamic acid capsule which confers resistance to phagocytosis.

Transmission Cycle

Most mammals are susceptible to anthrax. The disease is most commonly seen in herbivores (e.g. cattle, sheep, goats) whereas pigs, equines, dogs and camels are reported to be moderately susceptible. The disease has also been commonly reported in wild animals (e.g. lion, hyena, elephant, jackal, giraffe, zebra, etc.).

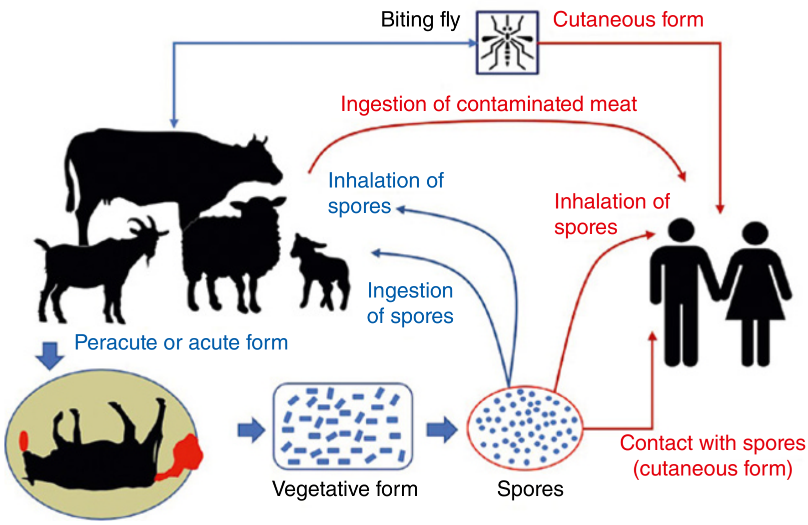

Figure 1.1 The transmission cycle of anthrax between animals and humans.

Herbivores are considered the primary host for anthrax. Upon the death of the host, bacteria in the carcass are exposed to air through haemorrhages, opening of the carcass by scavengers, etc. On exposure, the bacteria sporulate and persist in the soil for prolonged periods which can be the source of infection to other animals or humans. The soil can act as a long-term reservoir for spores of anthrax bacilli. In addition, regions with high humidity, alkaline soils and a high amount of organic matter are categorised as 'incubator areas' for the survival or persistence of anthrax spores. An overview of the transmission cycle of anthrax in animals and humans is provided in Figure 1.1.

Factors Affecting the Transmission of Anthrax

Transmission in Animals

- Ingestion of contaminated fodder, water and processed feed (meat/bone meal, meat scraps).
- Inhalation of spores during wallowing in contaminated water sources.
- Climatic conditions may influence the animal's contact with spores.
  - Grazing closer to contaminated soil in dry periods when grass is sparse increases the chances of animal contact with spores.
  - Enforced grazing at restricted sites (contaminated areas/burial sites) when water sources become scarce is also considered an important risk factor.
- Spiky grass and grits can cause orogastrointestinal lesions in animals which can be infected by germination of spores.
- Calcium-rich soils with neutral-to-alkaline pH can act as favourable sites for spore development. Such regions are also known as 'anthrax belts'.
  Note: *Role of calcium in spore formation*: calcium is integral to the dehydration of vegetative cell genome precursors, which is necessary for its effective long-term storage in spore form.
- Mechanical transmission of the pathogen can occur by biting flies (e.g. *Hippobosca* spp., *Tabanus* spp.).
- The use of contaminated surgical instruments for dehorning and docking may cause disease transmission.

Transmission in Humans

Animal products including meat, hide, hair or bone from infected animals can be heavily contaminated with anthrax spores, which can act as important sources for human infection. Anthrax is considered an occupational hazard among butchers, textile workers, wool industry workers, farmers, knackers, veterinarians, workers concerned with the processing of animal products (e.g. tannery) and laboratory workers.

Anthrax in Animals

The susceptibility and clinical signs of anthrax in different species of animals are described below.

- **Herbivores** (bovines, sheep, and goats): Herbivores generally exhibit per-acute infection which may lead to sudden death. At death, blood exudes from the rectum and other natural openings of the animal. The blood of the infected dead animal does not clot and there is absence of rigor mortis in the carcass. It has been found that the blood of the infected animal may contain $>10^8$ bacilli/mL [6].
- **Horses**: Equines mainly exhibit acute symptoms and die within 2–3 days of infection. In some animals, biting flies may transmit the pathogen and cause large oedematous lesions on breast, abdomen, neck and shoulders.
- **Pigs**: Pigs are more resistant to anthrax than bovines and mainly exhibit localised signs which include oedema of the throat, pharyngeal and cervical lymph nodes.
- **Dogs and cats:** Dogs and cats are considered to be resistant to anthrax. Dogs that have scavenged anthrax carcasses may suffer from severe inflammation and oedematous swelling of the throat, stomach, intestine, lips, jowl, tongue and gums.
- **Birds**: In birds, apoplectic type of death is observed due to anthrax whereas less acute cases may exhibit carbuncular lesions on comb or extremities.

Anthrax in Humans

The clinical forms of anthrax in humans are described below.

1) **Cutaneous anthrax:** The cutaneous form of anthrax is responsible for 95% of global human cases and is mainly reported in developing countries following contact with infected animals and their products. Cutaneous anthrax usually develops 1–7 days after exposure, but incubation periods as long as 17 days have been reported [7]. The characteristic clinical signs are anthrax eschars on exposed regions of the body, i.e. face, neck, hands and wrists. Malignant oedema is a rare complication of the cutaneous form which is characterised by severe oedema, induration, multiple bullae and symptoms of shock (Note: The common description of this form as 'malignant pustule' is a misnomer because the lesion is not purulent and painless.)
2) **Inhalation anthrax:** This occurs mainly due to inhalation of spores (size $<5\,\mu m$) which reach the lower respiratory tract. The incubation period ranges from 1 to 60 days.