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REVIEW ARTICLE

Countering Zoonotic Diseases: Current Scenario and Advances in Diagnostics, Monitoring, Prophylaxis and Therapeutic Strategies

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Human life and health have interacted reciprocally with the surrounding environment and animal fauna for ages. This relationship is evident in developing nations, where human life depends more on the animal population for food, transportation, clothing, draft power, and fuel sources, among others. This inseparable link is a potent source of public health issues, especially in outbreaks of zoonotic diseases transmitted from animals to humans. Zoonotic diseases are referred to as diseases that are naturally transmitted between vertebrate animals and humans. Among the globally emerging diseases in the last decade, 75% are of animal origin, most of which are life-threatening. Since most of them are caused by potent new pathogens capable of long-distance transmission, the impact is widespread and has serious public health and economic consequences. Various other factors also contribute to the transmission, spread, and outbreak of zoonotic diseases, among which industrialization-led globalization followed by ecological disruption and climate change play a critical role. In this regard, all the possible strategies, including advances in rapid and confirmatory disease diagnosis and surveillance/monitoring, immunization/vaccination, therapeutic approaches, appropriate prevention and control measures to be adapted, and awareness programs, need to be adopted collaboratively among different health sectors in medical, veterinary, and concerned departments to implement the necessary interventions for the effective restriction, minimization, and timely control of zoonotic threats. The present review focuses on the current scenario of zoonotic diseases and their counteracting approaches to safeguard their health impact on humans.

Key Words: Zoonoses, Pathogens, Transmission, Public health, Diagnosis, Therapy, Prevention.

Introduction

Diseases that can be transmitted naturally between lower vertebrates and humans are referred to as zoonotic diseases, which account for approximately 60% of all human diseases (1). Zoonotic infections are prevalent worldwide, some of which may be endemic in certain areas, and most infections are caused by emerging, re-emerging, or neglected zoonoses (2). In addition, the possibility of disease transmission from humans to animals cannot be excluded (3). Zoonotic infections have different consequences that can directly or indirectly affect livestock health, produc-

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tion, and public life. The suffering and panic caused by clinical illness, the monetary loss, the negative impact on staff confidence, and the public perception contribute to the direct impact of zoonoses, while the restrictions and regulations imposed on livestock trade and transport, the costs associated with control programs, the negative impact on meat and animal feed and related sectors, among others, are the indirect impact of zoonoses (4). With the advent of diagnostic techniques and improved knowledge among medical and veterinary practitioners, ecologists, and biologists, more than 300 zoonoses of different etiologies, such as bacterial, viral, and parasitic origins, have been recognized. Emerging infectious diseases are diseases of infectious origin whose incidence in humans has recently increased or is likely to increase soon. These include new, previously undefined diseases and old diseases with new characteristics, most of which are zoonotic (5).

Zoonoses have affected humans since ancient times, when both domestic and wild animals were involved somehow. Rabies, plague, tuberculosis, anthrax, glanders, yellow fever, influenza, and some zoonotic parasitic diseases were known as zoonotic diseases before the 20^{th} century. Bubonic plague, which is transmitted by rats and fleas, has caused devastation and mass mortality worldwide since ancient times (6). An epidemic described as bubonic plague was mentioned in the Old Testament. The Black Death occurred in the 14th century and caused great losses in Africa, Asia, and Europe. This pandemic, which originated in the Far East, killed approximately a third of Europe's population. However, outbreaks of bubonic plague are still reported in Asia, Africa, and the Americas. Plague in humans has been associated with companion animals infested with fleas carrying Yersinia pestis in the western United States (7). Plague is a zoonotic disease that could reach alarming proportions as a public health disaster in developing countries where ecosystem erosion, human migration to new areas, and climate change will increase population contact with reservoir systems (8). Rabies was described in dogs in Mesopotamia in 2300 BC. Descriptions of rabies can also be traced back to early Egyptian, Chinese, Greek, and Roman civilizations (9). Rabies occurred in domestic and wild animals in Europe during the Middle Ages (10). Alexander the Great reportedly died of encephalitis caused by the West Nile virus (11).

The interdependence of different animal species on our planet requires the combined efforts of biologists, veterinarians, and medical practitioners to understand and subsequently control emerging zoonotic diseases. There has been a close collaboration between the veterinary and traditional medical professions to combat emerging and re-emerging zoonotic diseases, as their management is beyond the capacity of these two professions working alone. This has led to the concept of One Health, which always requires collaboration between different professions at local, national, and global levels (12–14). However, the shortage of data and the general uncertainties pose a significant challenge to the decision-making process regarding zoonoses. Thus, an integrated approach by both the medical and veterinary professions is essential for the treatment of such diseases (15).

Classification of Zoonotic Diseases

Zoonotic diseases are highly variable depending on the severity, mode of transmission, and spread of the causative pathogen, as well as the animal host involved. These can be transmitted to humans in several ways: a) through animal bites, licks, and scratches; b) foodborne and waterborne transmission can occur through consumption of improperly cooked food; c) soil or airborne transmission is possible; d) vector- or arthropod-borne transmission of zoonotic diseases (16,17). Many zoonotic diseases have their origins in wildlife, as this is an area where much research has not been done, and recent human activities such as wildlife encroachment have also contributed to the spread of disease from animals to humans (18). Several zoonotic diseases are transmitted by vectors, and the vector population depends on several factors. The viability of pathogens is directly affected by temperature, humidity, and other environmental factors. Climate change has played an important role in maintaining the vector population in the environment (19). Extreme shifts in weather patterns as a result of global warming and climate change affect biodiversity, which may create a space for the emergence of new diseases, the re-emergence of existing diseases, and outbreaks of infectious diseases, including the emergence of zoonotic agents (20). The emergence of the new cholera strain O: 139 and the outbreaks of West Nile virus, Rift Valley fever, and dengue fever in new geographic areas have been linked to the southern oscillation of El Niño (21,22). Consequently, zoonotic diseases are classified into four classes based on epidemiological categorization based on the zoonotic maintenance cycle: direct zoonoses (orthozoonoses), cyclozoonoses, pherozoonoses (metazoonoses), and saprozoonoses (21).

i. Through direct touch, contact with a fomite, or mechanical transmission, an infected vertebrate host can transmit direct zoonoses (orthozoonoses) to a susceptible vertebrate host. The pathogen undergoes minimal to no propagative modification and no major emergent changes during such a process. Examples include trichinosis, brucellosis, and rabies.
ii. To complete the evolutionary cycle of the pathogen, cyclozoonoses require some vertebrate host species, but not an invertebrate host. Human taeniasis, echinococcosis, and pentastomid infections are examples of common cyclozoonoses.
iii. Pherozoonoses, also known as metazoonoses, are spread by invertebrate vectors. The agent either mul-

tiplies, develops, or both in the invertebrate and, if possible, there is a prenatal phase (prepatent) before transfer to a different vertebrate host. Schistosomiasis, plague, and arbovirus infections are just a few of the many examples.

iv. Protozoanoses are characterized by a vertebrate host and a non-animal reservoir, such as food, soil, and plants. Examples include certain mycoses and several types of larval migrations.

Exotic animals in captivity are part of a major global emerging zoonosis. Exotic animals in pet shops, zoos, and circuses are also responsible for zoonoses (23). Ganter has reviewed the zoonoses of sheep and goats, including brucellosis, chlamydophilosis, Q fever, orf, Rift Valley fever, and bovine spongiform encephalopathy (24,25). Bird et al. have discussed the gaps in knowledge about Rift Valley fever that hinder its effective prevention and control. H7N9 avian influenza from poultry has become a significant public health concern (26,27). Interspecies transmission of zoonotic agents from their natural reservoir host is still uncommon, and human-to-human transmission is rare for most zoonoses. Such spillover increases the likelihood of the emergence of a highly transmissible, adapted virus (18,28).

Although there is a lack of authoritative and comprehensive data on the global prevalence of zoonoses in general, various reports from competent sources strongly suggest the ever-increasing trend of some diseases, along with the recognition of the possibility of a major pandemic threat to the human population. The unanticipated increase in human population growth ultimately results in increased wildlife interaction, which has apparently influenced the easy spread and adaptation of inherent wildlife pathogens to civilian populations. Han BA et al. have described that there is a disproportionate representation of mammal-borne zoonoses among emerging human diseases, and this has led to a research emphasis on mammalian reservoirs, as improved understanding of mammalian host distributions may lead to improved prediction of future zoonotic disease emergence hotspots and analysis of zoonotic disease risk factors. Various human interventions and their consequences, such as globalization, liberal trade, climate change, global warming, population explosion, changing lifestyles, food scarcity, public health deficiencies, biodiversity losses, and technological advances, have caused many life-threatening conditions (e.g., floods, shrinking water bodies, natural disasters), along with the flaring up of several infectious and non-infectious diseases and disorders affecting both humans and animals (29). Several emerging and re-emerging infectious diseases have posed a challenge to human health due to the increase in disease incidence and their devastating effects namely, bird flu, Ebola, Zika, severe acute respiratory syndrome (SARS), chikungunya, dengue, viral encephalitis (Japanese encephalitis, JE), and Kaysanur Forest Disease (KFD) to name a few, in addition to other already endemic diseases such as tuberculosis, malaria, plague and toxoplasmosis (30). Plourde et al. have highlighted the need for research to optimize monitoring, regular surveillance, patient management, and public health interventions to control the Zika virus epidemic worldwide. Therefore, this review focuses on zoonotic diseases, especially on their current global status, along with novel therapies and possible control measures (31).

Pathogens that cause anthrax, botulism, plague, tularemia, smallpox, brucellosis, glanders, melioidosis, Q-fever, and viral encephalitis are potent enough to be used as biological weapons or warfare agents and thus pose a global public health threat. Recently, Corona (Covid-19), Nipah, Zika, Ebola, dengue, Chicken Guinea, JE, Crimean Congo hemorrhagic fever (CCHF), and Swine Flu have also wreaked havoc and major threats to humanity, apart from the Hendra virus, Hantavirus, and others that pose challenges to global human existence (32,33). Several infectious pathogens affecting animals pose serious zoonotic and public health concerns not only by infecting existing populations or species but also by expanding their host range to new populations or species, increasing their geographic range, crossing continents, and even posing pandemic threats, in addition to challenging and threatening animal health and production systems (29,34). SARS-CoV (Severe Acute Respiratory Syndrome Coronavirus), MERS-CoV (Middle East Respiratory Syndrome Coronavirus), and SARS-CoV-2 (the virus responsible for COVID-19) are all coronaviruses that have caused significant human outbreaks in recent decades. This detailed discussion provides a comprehensive understanding of the differences and similarities in the pathogenesis, clinical features, and epidemiology of SARS-CoV, MERS-CoV, and SARS-CoV-2. While SARS-CoV and MERS-CoV had higher CFRs but were relatively contained, SARS-CoV-2 showed exceptional transmissibility, resulting in a global pandemic. The utilization of different receptors (ACE2 for SARS-CoV and SARS-CoV-2, DPP4 for MERS-CoV) and the resulting immune responses are critical factors in understanding their pathogenesis and clinical outcomes. Effective public health measures, vaccine development, and therapeutic interventions remain critical in the management of coronavirus outbreaks (Table 1).

Several studies have been published in India reporting *Mycobacterium avium subspecies paratuberculosis* (MAP) in different livestock species, animal-derived food and food products, natural resources, and humans (34,35). Different infectious agents, whether bacterial, viral, or parasitic, pose zoonotic threats through various entry routes. Several zoonotic pathogens can cause disease in humans, and the syndromes caused are also different. Thus, zoonotic diseases are classified according to the pathogen causing the disease (zoonotic diseases caused by bacteria,

Table 1. Key differences and similarities among the three novel coronaviruses, helping to illustrate the unique challenges each virus presents in pathogenesis, clinical features, and transmission dynamics

Feature	**SARS-CoV**	**MERS-CoV**	**SARS-CoV-2**
Pathogenesis			
Transmission	SARS-CoV is primarily transmitted via respiratory droplets and direct contact	MERS-CoV is a zoonotic virus with primary transmission from camels to humans; human-to-human transmission is also documented, mainly via respiratory droplets	SARS-CoV-2 is primarily spread via respiratory droplets, aerosols, and potentially contaminated surfaces
Cell entry	The virus uses the ACE2 (Angiotensin-Converting Enzyme 2) receptor for entry into host cells	It uses the DPP4 (Dipeptidyl peptidase 4) receptor to enter host cells	The virus uses the ACE2 receptor for entry, with TMPRSS2 (Transmembrane Serine Protease 2) facilitating the process
Replication	After binding to the ACE2 receptor, the virus enters the host cell and releases its RNA, using the host's machinery to replicate and produce new viral particles	Similar to SARS-CoV, it hijacks the host cell's machinery to replicate	Upon entry, the virus releases its RNA into the host cell cytoplasm, replicating similarly to the other coronaviruses.
Immune response	SARS-CoV triggers an immune response leading to inflammation and lung tissue damage. Immune dysregulation, including cytokine storms, contributes significantly to the pathogenesis	MERS-CoV elicits a significant inflammatory response and high viral loads in the lower respiratory tract, leading to severe respiratory complications	SARS-CoV-2 often leads to immune dysregulation with a robust inflammatory response, sometimes resulting in a "cytokine storm'' that contributes to severe lung damage and systemic organ failure
Clinical Features			
Incubation period	Typically, 2–7 d	2–14 d	Generally, 2–14 d
Symptoms	Initial symptoms include high fever, headache, general malaise, a dry cough, and respiratory distress	Presents with severe acute respiratory illness, including fever, cough, and shortness of breath; gastrointestinal symptoms like diarrhea are also common	Symptoms range from mild to severe, including fever, cough, fatigue, shortness of breath, loss of taste/smell, and gastrointestinal issues
Outcomes	Progresses to acute respiratory distress syndrome (ARDS) in severe cases, particularly in elderly individuals or those with comorbidities	High case fatality rate; severe complications include ARDS, kidney failure, and disseminated intravascular coagulation (DIC)	Severe disease can result in ARDS, thromboembolic events, and multi-organ dysfunction, primarily affecting older adults and those with underlying conditions
Epidemiological			
First reported	November 2002 in Guangdong Province, China	June 2012 in Saudi Arabia	December 2019 in Wuhan, China
Spread	Affected 29 countries, with approximately 8,000 cases and nearly 800 deaths	Primarily limited to the Middle East; cases reported in 27 countries, mainly due to travel	Rapid and global spread, leading to a pandemic with millions of cases and deaths worldwide
Control	Containment was achieved through quarantine, travel restrictions, and rigorous contact tracing by July 2003	Measures include controlling zoonotic transmission (camel-human) and implementing stringent infection control practices in healthcare settings	Ongoing efforts include vaccination programs, public health measures, travel restrictions, and community interventions.
Case fatality rate (CFR)	Approximately 10%.	Approximately 34%, the highest among the three viruses	Varies widely by region and age group, generally between 1–3%, with lower CFR compared to SARS-CoV and MERS-CoV but higher transmissibility

viruses, and parasites), the host affected (zoonotic diseases of cattle, horses, dogs, etc.), and the mode of transmission (vector-borne, airborne, waterborne) (Tables 2–5) (36–38).

Some of the major infectious diseases that are zoonotic and have the potential to pose significant public health concerns and threats to human populations include bacterial infections (anthrax, plague, glanders, Lyme disease, salmonellosis, campylobacteriosis, colibacillosis, brucellosis, leptospirosis, listeriosis, tuberculosis, tularemia, botulism, Johne's disease), viral infections (rabies, influenzas such as avian/bird flu and swine flu, West Nile virus [WNV], rotaviral enteritis), rickettsial diseases (chlamydiosis/psittacosis, Q fever, Rocky Mountain spotted fever), vector-borne diseases (JE, KFD, dengue fever, Nipah viral infection), fungal-borne infections (dermatophytosis, aspergillosis, histoplasmosis, sporotrichosis), parasitic infestations (cryptosporidiosis, toxoplasmosis, malaria) and prion diseases such as variant Creutzfeldt-Jakob disease/vCJD (9,39). The pandemics of Yersinia pestis

Table 2. Zoonotic diseases caused by bacteria and their symptoms

Disease	Animal host	Causal organism	Symptoms
Actinomycosis	Cattle, sheep, dogs, horses, pigs,	*Actinomyces bovis*	Swelling of lymph nodes
Anthrax	Bison, cattle, dogs, goats, horses, sheep	*Bacillus anthracis*	Respiratory organs, Skin, or gastrointestinal tract
Arcobacter infections	Cattle, pigs, sheep	*Arcobacter butzleri, Arcobacter skirrowii*	Abdominal pain and vomiting
Bordetellosis	Cats, dogs	*Bordetella bronchiseptica*	Respiratory problem
Brucellosis	Cattle, dogs, goats, sheep, pigs	*Brucella abortus, Brucella suis, Brucella melitensis*	Fever, back and joint pain, loss in weight
Bubonic plague	Rats, dogs, mice, rabbits, squirrels	*Yersinia pestis*	Fever, pain in abdomen, vomiting, diarrhea
Campylobacter enteritis	Cattle, cats, chickens, dogs, sheep, mink	*Campylobacter jejuni, Campylobacter coli*	Enteric disorder
Campylobacter fetus infection	Cattle, goats, sheep	*Campylobacter fetus*	Enteric disorder
Clostridioides difficile infection	Birds, cattle, horses	*Clostridioides difficile*	Colitis, diarrhea
Corynebacterium ulcerans	Cattle, cats, dogs	*Corynobacterium ulcerans*	Diphtheria
Ehrlichiosis	Sheep, cattle, cats, deer, dogs	*Anaplasma phagocytophilum, Ehrlichia sp., Neorickettsia sennetsu*	Fever, headache, fatigue, occasionally rash
Enterohemorrhagic Escherichia coli infections	Cattle, sheep, deer, dogs, pigs, poultry	*E coli*	Enteritis, hemolytic–uremic syndrome
Glanders	Horses, donkeys, mules	*Burkholderia mallei*	Fever, muscle tightness, sweating, muscle aches, pain in chest, headache
Helicobacter infection	Poultry, pigs	*Helicobacter pullorum, Helicobacter suis*	Peptic ulcer
Leprosy	Monkeys, mice, rats, cats	*Mycobacterium leprae*	Skin lesions
Leptospirosis	Wild and domestic animals	*Leptospira interrogans*	Fever, jaundice, pain in abdomen, red eye
Lyme disease	Horses, cats, dogs	*Borrelia burgdorferi*	Fever, headache, skin rash
Pasteurellosis	Poultry, pigs, cats, dogs, cattle, buffaloes, sheep, goats, deer	*Pasteurella multocida*	Fever, diarrhea, vomiting
Salmonellosis	Domestic animals, birds, dogs	*Salmonella enterica, Salmonella bongor*	Enteritis
Tuberculosis	Bison, cattle, deer, wild boars, camels, sheep,	*Mycobacterium bovis, Mycobacterium microti, Mycobacterium caprae*	Respiratory organs bone marrow
Tularemia	Rabbits, squirrels, wild rodents, deer, sheep, snakes, beavers, cats, dogs	*Francisella tularensis*	Diarrhea, dry cough, Joint pain
Vibriosis	Farm animals	*Vibrio parahaemolyticus*	Enteritis

(plague/Black Death), followed by various strains of influenza viruses (such as Spanish flu), the constant threat of HIV infection, cholera, and the recent pandemic threats of avian and swine flu, all have animal origins and a history of devastating effects on human life (40,41). Bovine spongiform encephalopathy (BSE), caused by prions, is a zoonotic disease that can cause variant vCJD in humans (42).

Present Scenario of Zoonotic Diseases

Surveillance of zoonotic diseases is in high demand due to the involvement of both human and animal health concerns. Both active and passive surveillance approaches play an important role in achieving efficiency by employing a One Health system (43,44). It is reported that 60% of the infectious agents that affect humans and >75% of the emerging or re-emerging pathogens are zoonotic. Currently, the world is threatened by the emergence of several terrible diseases such as Ebola, Zika, and influenza of multiple origins (45). Much has been learned about these diseases in recent years, as they cause extensive damage to human populations and can be transmitted from animals to humans, with wildlife playing a key role in their spread (Figure 1) (46). As research in these areas is naive, there are several gaps in the diagnosis and control of the disease due to the lack of vaccines and in the treatment of patients due to the unavailability of drugs. Vectors also play an important role in the transmission of zoonotic diseases from one part of the country to another (47). Carrier status also contributes to the difficulty of controlling and eradicating zoonotic diseases. Effective control of zoonotic diseases is possible once the wild animals involved in transmission have been eliminated, so that the pathogen

Table 3. Zoonotic diseases caused by viruses and their symptoms

Disease	Animal host	Causal organism	Symptoms
AIDS	Monkeys, chimpanzees	*HIV Family—Retroviridae*	Immunosuppression, influenza-like symptoms
Avian influenza	Chickens, cats, ducks, turkeys, dogs, pigs, horses, seals, birds	*Influenza A virus Family—Orthomyxoviridae*	Flu like symptoms, pneumonia, diarrhea
Chikungunya fever	Monkeys, birds, rodents	*Chikungunya virus Family—Togaviridae*	High fever, muscle pain, severe joint pain, skin rash
Dengue fever	Monkeys, dogs	*Dengue virus Family—Flaviviridae*	High fever, skin rash
Ebola virus disease (Ebola hemorrhagic fever)	Monkeys, gorillas, chimpanzees, apes, antelopes	*Ebola virus Family—Flaviviridae*	Diarrhea, fever, muscle pain, headache, sore throat, vomiting, liver failure, weakness
Hantavirus infection (Hantavirus pulmonary syndrome)	Mice, rats, shrews, moles	*Hantavirus s Family—Hantaviridae*	Abdominal problems, respiratory problems, high fever
Marburg viral fever	Bats, monkeys	*Marburg virus Family—Flaviviridae*	Diarrhea, hemorrhage, fever, muscle pains, pain in abdomen
Monkey pox	Squirrels, Gambian rats, dormice, monkeys	*Monkeypox virus Family—Poxviridae*	Fever, pox lesions
Newcastle disease	Poultry, wild birds	*Paramyxovirus, Family—Paramyxoviridae*	Conjunctivitis
Rabies	Bats, cats, cattle, dogs, horses, monkeys, wolves, rabbits	*Rabies virus, Family—Rhabdoviridae*	Nervous system
Rift Valley fever	Buffaloes, sheep, camels, cattle, goats	*Rift Valley fever virus Family—Bunyaviridae*	Influenza- like symptoms
Severe acute respiratory syndrome (SARS)	Bats, dogs, cats, tigers, lions	*SARS coronavirus (SARS-CoV) Family—Coronaviridae*	Influenza-like symptoms
West Nile fever	Horses, birds, reptiles	*West Nile virus Family—Flaviviridae*	Headache, coma, tremors, convulsions, paralysis, skin rash, nodes, stiff neck, disorientation, swollen lymph
Zika fever	Apes, monkeys	*Flavivirus Family—Flaviviridae*	Fever, pain, conjunctivitis

Table 4. Zoonotic diseases caused by parasite and their symptoms

Disease	Animal host	Causal organism	Symptoms
Cryptococcosis	Cattle, dogs, horses, goats, birds, sheep, wild animals	*Cryptococcus neoformans*	Fever, respiratory problems, nausea, vomiting
Cryptosporidiosis	Cattle, deer, goats, horses, pigs, sheep	*Cryptosporidium parvum*	Diarrhea, abdominal pain, nausea, malaise
Cutaneous larval migrans	Dogs, cats	*Ancylostoma braziliense*	Subcutaneous tissue
Fascioliasis	Cattle, sheep, goats	*Fasciola hepatica, Fasciola gigantic*	Internal bleeding, fever, nausea, skin rashes, swollen liver, pain in abdomen
Hydatidosis	Buffaloes, sheep, goats, dogs	*Echinococcus granulosus*	Cysts in liver, lungs, bones, kidneys, spleen, pain in abdomen, respiratory problem
Trichinellosis	Pigs, dogs, cats, rats	*Trichinella spp.*	Gastrointestinal problems
Visceral larva migrans	Birds, cats, chinchillas, dogs, porcupines, rabbits, woodchucks	*Toxocara canis, Toxocara cati*	Gastrointestinal complications

cycle can be broken with an effective vaccine. In addition to the infectious nature of the zoonotic agents, they also have a negative impact on the economy of society by reducing a country's ability to import and export. With the recent increase in trade due to globalization and the alarming problem of global warming, the risk of emerging zoonotic diseases has increased. In this regard, it is proposed that the monitoring of the immunological status of horses and the systematic administration of vaccinations are necessary as a basic principle to prevent the existence and persistence of rhinopneumonitis, equine arteritis virus, West Nile fever, and influenza virus in the equine population of economic and zoonotic importance (48). Intensive breeding under the increased density of animals (including wildlife) and wildlife populations, living near humans may increase the risk of infections caused by *Mycobacterium bovis* (M. Bovis), Brucella spp., and *Francisella tularensis* (49). No one can deny that global warming has contributed immensely to the emergence of many zoonotic diseases. The interaction between changes in climate and

Table 5. Zoonotic diseases caused by protozoa and their symptoms

Disease	Animal host	Causal organism	Symptoms
African sleeping sickness	Antelopes, camels, cattle, horses	*Trypanosoma brucei*	Fever, headache, nausea, formation of erythematous plaque
Balantidiasis	Ruminants, pigs, rats	*Balantidium coli*	Gastrointestinal complications, weight loss, intestinal ulcerations
Chagas disease	Cats, wildlife reservoirs	*Trypanosoma cruzi*	Neural problems, swelling in lymph nodes, body aches, fatigue, nausea
Giardiasis	Cats, dogs, ruminants, pigs	*Giardia lamblia*	Anorexia, diarrhea, abdominal cramps, nausea
Leishmaniasis	Bats, cats, dogs, horses	*Leishmania infantum*	Lesions on skin, hepatosplenomegaly
Toxocariasis	Dogs, cats	*Toxocara canis, Toxocara cati*	Anorexia, asthma, fever, hepatosplenomegaly, rash, pneumonitis
Toxoplasmosis	Pigs, sheep, goats, poultry, rabbits	*Toxoplasma gondii*	Lymphadenopathy, fever, malaise, maculopapular rash, sore throat
Trypanosomiasis	Antelopes, camels, cattle, horses	*Trypanosoma brucei*	Fever, headache, pruritus, lymphadenopathy, hepatosplenomegaly

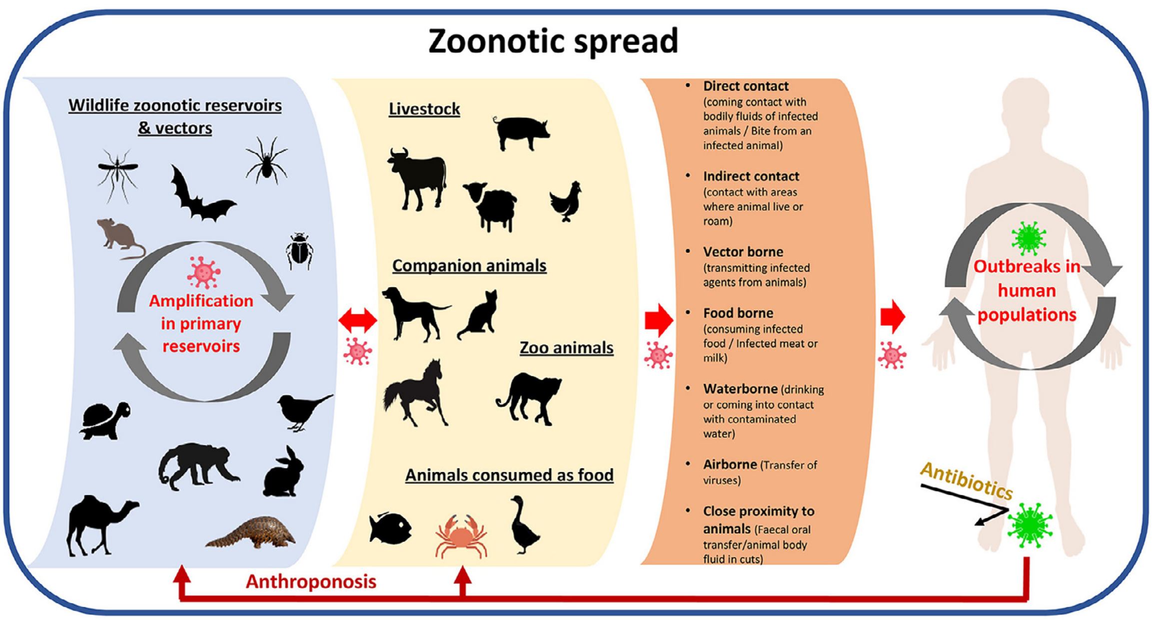

Figure 1. Illustration of the zoonotic spread of different types of diseases and their outbreak in human populations.

pathogens and vectors has been attributed to the increase in zoonoses. Changes in the activity of reservoirs such as bats have led to the spread of zoonotic diseases caused by Hendra, Mardburg, and Ebola viruses, and rabies variants (50,51). Similarly, the Nipah virus in Malaysia and West Nile virus infection in Israel have occurred via infected and healthy animals (and therefore also humans), nearby (52).

Zoonoses may occur as small outbreaks (anthrax, Nipah) or as neglected zoonoses such as bovine tuberculosis, Johne's disease, bovine and caprine brucellosis, rabies, and cysticercosis. Neglected zoonoses are constantly present in a locality and do not cause a huge outbreak; however, they affect the production status of animals and, through their persistence, humans, which in turn leads to the aggravation of poverty. A retrospective analysis of most of the threatening zoonotic pandemics reveals the origin of the pathogens concerned within animal species, followed by their emergence into the public health problem through ecological, genetic, behavioral, and socioeconomic changes. This fact can be seen in the history of HIV infection, severe acute respiratory syndrome (SARS), AIDS, pandemic influenza, and KFD. Despite the global advances in monitoring the emergence of novel pathogens, the possibility of zoonotic and pandemic outbreaks of these pathogens could not be predicted before human infection. Given the emergence of AIDS, avian influenza, Ebola, and SARS, it is crucial to understand what causes future pandemics and epidemics. The somewhat unexpected response is that we have no idea what causes animal viruses to spread quickly enough to cause pandemics or epidemics. Equally important is the question of why most animal viruses are unable to sustain human-to-human transmission. These are important but unanswered questions. It is important to include diseases like rabies when considering zoonoses. There is no evidence that an individual can get AIDS from a chimpanzee or a monkey. A link is still lacking. In this context, discussions about the origin of HIV have given rise to a disagreement about the basic nature of AIDS. According to the findings indicating that HIV originated in apes, AIDS was classified as a zoonosis (53). Zoonotic influenza A viruses are dangerous to humans because they can spread to other countries and cause pandemics when they adapt to immunologically naïve populations. Due to the relatively high number of human deaths and the potential for a pandemic outbreak, the H5N1 virus, which is still spreading among poultry in many countries in Europe, Asia, and Africa, and the newly discovered H7N9 virus in China is of particular concern. To cause zoonotic influenza, a pandemic A virus must be able to propagate effectively between humans by aerosol or respiratory droplet transmission, in addition to being able to attach to, invade, and replicate in the vital target cells in the respiratory tract of the new host (54).

For this reason, some areas have reported a high prevalence of zoonotic diseases, such as Brazilian stray dogs infected with Leishmania species responsible for visceral leishmaniasis in the studied area, observing the diversity of Leishmania species (55). This points out existing lacunae in predicting the emergence of new pathogens and the re-emergence of potential ones, along with all the possible data on their host of origin, and factors driving their emergence and virulence. Thus, critical control measures are warranted, with due emphasis on pandemic forecasting, targeted surveillance of ecological zones with crucial interfaces, and novel effective prevention strategies. (56). On the other hand, the social dynamics of disease exposure confirmed that risks are specific and associated with sex, class, occupation, and other dimensions of social difference. Moreover, Africa has been suggested as a 'hotspot' for zoonotic diseases due to disease spillover from animals to humans (57).

Modes of Transmission

Zoonotic pathogens can enter the human body through animal bites, insect or mosquito bites, oral ingestion, inhalation, or aerosol modes, skin lesions or scratches, and contact with mucous membranes and eyes (58). Important factors that may promote contact transmission of zoonotic diseases are those acting at the host, pathogen, or environmental levels (59). Common pathogen factors include immune evasion, low infectious dose, and elevated viral load. Also, common host factors include crowding, promiscuity, and the presence of co-infections. Recognition of these factors will lead to a better understanding of the spread of human-to-human pathogens and the development of risk evaluations for novel emerging pathogens. Moreover, non-native zoonotic diseases can pose a critical risk to ecosystems and human well-being. Environmental interactions and introduced species have created new challenges and risks to public health (60).

Because of the close relationship between wildlife, humans, and the environment, wildlife play a direct role in the spread and maintenance of several infectious diseases. The ecological relationships between the components of One Health are being disrupted by factors such as globalization, habitat degradation, climate change, species extinction, and biodiversity loss. This ultimately leads to the emergence of zoonotic infections and changes in their transmission patterns. Pathogens carried by wild animals can potentially harm livestock and humans, reduce agricultural yields, and disrupt wildlife (61). Mammals, reptiles, birds, fish, and amphibians are examples of wildlife species that serve as reservoirs for zoonotic infections that can be transmitted to humans or other animal hosts.

The role of wildlife in the epidemiology and transmission of zoonotic diseases is of concern. The type of disease involved and meteorological factors such as humidity, temperature, and precipitation have an impact on the transmission patterns of animal zoonoses. These patterns of transmission of these viruses among domestic animals, wild animals, and humans determine when they emerge and reemerge. Rapid population growth, ease of domestic and international travel, increased human exposure to animals and animal products, wildlife farming, careless hunting, handling, and transport of wild animals (including carcasses), consumption of wild meat (such as bushmeat), and variations in agricultural practices are some of the factors influencing these processes (61). There is a significant risk of pathogen transmission from wild animals to humans for both emerging and reemerging diseases. Most diseases affecting humans are acquired through direct contact with wild animals or vector-mediated sources (e.g., lyssaviruses, hantaviruses, Nipah virus, West Nile virus, leptospirosis, ehrlichiosis causative agents, and rabies). Infections such as coronavirus, Ebola virus, and HIV are most commonly transmitted by human-to-human contact (61).

Wild fauna/animals and migratory/wild birds act as important reservoirs of several important pathogens and thus contribute significantly to the spread of various infectious diseases/pathogens including avian/bird flu, Hendra and Nipah viruses, WNV, rabies, JE, brucellosis, leptospirosis, psittacosis, plague, and bovine tuberculosis (BTB) among others, which affect animal, poultry, and human health (62,63). Pathogens of zoonotic importance are transmitted by different animal species, including cattle, buffalo, equine (horses), ovine (sheep and goats), canine (dogs), and domestic/poultry birds (64,34). In addition to these species, wild animals, wild migratory and aquatic birds (such as wild waterfowl in the avian influenza outbreak), wild game pheasants, bats (e.g., fruit bats in the transmission of Nipah and Hendra viruses), raccoons, wolves, monkeys, and red foxes, among others, also play a critical role in various disease transmissions to humans and pose significant threats to human health (30,63,65–67).

Recently, *Mycobacterium avium subspecies paratuberculosis* (MAP) has emerged as a major health problem for domestic livestock and humans (68–70). The presence of live MAP bacilli in commercial supplies of raw and pasteurized milk and milk products indicates its public health significance (35). MAP is not inactivated during pasteurization and enters the human food chain daily. Recovery of MAP from patients with inflammatory bowel disease or Crohn's disease and from animal health workers suffering from chronic gastrointestinal problems suggests a close association of MAP with several chronic and other diseases affecting human health (71). *Mycobacterium avium subspecies paratuberculosis* (MAP) has been implicated in the etiology of Crohn's disease for many years. Its pathogenicity in humans remains unexplained despite numerous studies and research efforts. Critics claim that ileocecal TB and a granulomatous infection in ruminants known as Johne's disease are in many ways similar to Crohn's disease. Both are caused by species of the genus Mycobacterium. Skeptics claim that any correlation between MAP and CD is coincidental because it is present in both healthy control populations and people with Crohn's disease. The equivocal response of patients to antimicrobial treatment lends credence to this opinion. The true behavior of MAP in humans is not yet fully understood or explained, despite significant progress; however, the answer to this 120-year-old mystery may be close at hand (72).

However, other species, namely Macroglossus sp., Megaerops niphanae, and Myotis horsfieldii, have been introduced as new coronavirus hosts (73). Moreover, Fasciola hepatica, known as a zoonotic trematode, is mainly found in cattle and sheep, as well as snail intermediate hosts as natural reservoirs (74). In addition, European hedgehogs have been shown to play an important role in the transmission and spread of tick-borne pathogens in urban areas (75,76).

Allocati et al. have described bats as an important reservoir of several pathogens, as more than 200 viruses have been associated with bats, mostly RNA viruses, probably due to their great ability to adapt to changing environmental conditions through higher genetic variability (77).

The new characterization of lyssavirus has also demonstrated the importance of potential transmission pathways in different lyssavirus species. In addition to dogs, wildlife species also play an important role in the epidemiology of lyssaviruses (78). Klous G, et al. have extensively reviewed the intensity and type of contact patterns between livestock and humans that result in microbial transmission (79). Studies conducted in occupational settings provide some, but limited, evidence of exposure-response-like relationships between livestock-human contact and microorganism transmission. A better understanding of the contact pattern that drives microbial transmission from animals to humans is needed to provide options for prevention and thus deserves more attention. One study reported aerogenic transmission of *Coxiella burnetii* between flocks and herds after environmental contamination with ticks (80). The C. burnetii could be increasingly secreted during abortion and normal parturition and may be transported long distances by wind (81).

Animal trade, global travel, and migration have also been implicated in the emergence of zoonotic arboviruses (82–85). Food-borne pathogens can play a critical role in disease transmission through different sources such as milk, meat, eggs, water, and other processed or undercooked foods, thereby spreading infections such as salmonellosis, colibacillosis, hepatitis E virus (HEV) genotype 3, brucellosis, bovine TB, staphylococcosis, and botulism (86–92). A significant proportion of orally transmitted zoonotic diseases have been found to spread to diverse populations through bushmeat, which is obtained from the hunting of wildlife species. Bushmeat is an integral part of the traditional diet of many tribal cultures and has now become a growing food source in several civilized societies. This increasing trend of bushmeat and its associated trading activities in centralized markets increases the opportunity for wild animals to come into contact with diverse species, allowing dormant pathogens to resurface in suitable amplifying or susceptible hosts. Such trading and mingling culminated in the amplification of the coronavirus, causing SARS in civet cats from some wild species (93,94). Risk factors for *Toxoplasma gondii* infection include pet ownership, marital status, type of residence, eating habits, and source of drinking water (95). Moreover, the different climates of each island of the Canary Islands play an important role in the distribution and prevalence of *T. gondii* (96).

On the other hand, the evaluation of the genetic diversity of *T. saginata* in different geographical populations provides valuable knowledge about the origin, transmission, and spread of this pathogen, as well as the study of the selective pressures acting on *T. saginata* and how they are affected by them (97). It has also been reported that age, drug use, and educational status are risk factors for *T. gondii* infection in HIV-infected women of reproductive age (53).

Ecological changes and cultures play a critical role in disease outbreaks, especially vector-borne diseases such as plague and malaria, among others (98). A vector-borne infection model of West Nile virus in a multi-host vector system also revealed the effect of host competition and changing vector feeding preferences on pathogen spread and invasion, as well as the seasonal epidemic pattern (99). Changes in the ecological interactions of host parasites during biological invasions may modulate the invasion process and the dynamics of endemic and/or exotic zoonotic diseases (100). Global environmental change as well as climate change often affect the epidemiological characteristics of emerging zoonotic diseases (101). Climate change, along with several other factors such as rapid deforestation and urbanization, has greatly altered the dynamics of host-arthropod vector interaction in the case of several parasitic zoonoses, namely, malaria, leishmaniasis, Chagas disease, babesiosis, and spirurid infection. (102,103).

Zoonotic diseases can spread in wildlife through hunting activities and the consumption of wild or bushmeat. Such diseases include trichinellosis, hepatitis E; leptospirosis, brucellosis; tuberculosis (from wild boars, wild canines, and felines); anthrax (from baboons and wild herbivores such as elephants, zebras, impalas, warthogs, and giraffes); hydatidosis (from giraffes, lions, warthogs, etc.). Other such diseases include Rift Valley fever (from llama and alpaca; eland); E. coli O157:H7 (from deer); and tularemia (from rodents) (63,104–106). Zoonotic diseases from wild animals can also spread through transportation, with both humans and animals acting as couriers. Complications are greater in the transport of wild animals, as their disease and vaccination status are not screened, as they are in humans (107).

The epidemiological transition in human population size and density from small nomadic groups to larger settled communities based on agriculture paved the way for the introduction and maintenance of so-called crowd diseases (108,109). These agricultural settlements were rooted in various factors such as waste dumping, unintentional release of rodents, and domestication of dogs and cats. All of these led to the emergence of pathogens through reservoirs and vectors that are associated with permanent human habitats (110,111). Statistical analysis has shown that seasonal and annual variations in human leptospirosis incidence are associated with favorable weather conditions (temperature 10–19, 9°C, and precipitation above 100 mm/m^2) (112).

Expansion of malaria outbreaks due to the rapid speciation of anthropophilic vector mosquitoes in Africa (113), expansion of toxoplasmosis through the fecal-oral route followed by the domestication of cats (114), the transformation of orally transmitted *Yersinia pseudotuberculosis* into a flea-transmitted, fatal form of bubonic plague by *Yersinia pestis* (115)—all these incidences point to the fact that the origin of many potent zoonotic outbreaks is mediated by ecological changes (116,61,5). The environment and its associated factors are critical in driving the spread of zoonotic pathogens as there are constant and drastic changes in the habitats associated with pathogens and their affected reservoir hosts. Driving changes such as habitat destruction, mechanization of farming practices, human encroachment into natural habitats, and climate effects have a critical impact on the interactions between pathogens and hosts and among host species. Since these interactions are at the core of disease emergence, such environmental changes ultimately result in the emergence of new pathogens and the expansion of the host range of existing pathogens (117,118). Changes in climate and habitat structure also have a significant impact on the distribution and dynamics of vectors, thus introducing the pathogens into naive host populations inhabiting those areas that in the past were geographically restricted from the entry of these pathogens. These scenarios of host range expansion, mixing of previously restricted vectors, and introduction of pathogens into novel vectors can be illustrated by the emergence of potential microbes such as West Nile virus (WNV), dengue virus, and Chikungunya virus (119,18). In 2011, Crimean Congo Hemorrhagic Fever (CCHF) was reported in the state of Gujarat, a recent example of the emergence of arthropod-borne viruses in the Indian subcontinent (120). Therefore, environmental issues could alter the distribution of zoonotic diseases and their transmission to humans, highlighting the critical environmental factors in zoonotic systems (121).

Reverse zoonoses are another concern where a pathogen can potentially spread from sick humans to animals through environmental contamination and contaminated food when animals are moved, either in zoos or for educational purposes. A fatal human metapneumovirus outbreak has been observed among wild chimpanzees in Tanzania, thought to be due to frequent visits to the animals by researchers and common people in the national park. Retail systems for animals and their products also pose a threat to the spread of reverse zoonoses (3,122).

Who is Most Affected?

Urbanization, globalization, income growth, increased hunting, pet ownership, and ecotourism are associated with global trends that may increase emerging zoonotic risks (123,124). Newborns, infants, young children, immunosuppressed individuals, the elderly, pregnant women, people undergoing antibiotic treatment, people under stress, veterinary professionals, butchers, animal owners and handlers, and livestock and poultry health workers are more likely to be affected by zoonotic pathogens (123,125,126). The immunocompromised group primarily affected by zoonotic disease also includes individuals with cancer, organ transplants, and infectious diseases such as AIDS and subsequent immunosuppressive treatments. These individuals are not only more susceptible to infection but are also more likely to suffer from the subsequent serious sequelae of diseases such as arthritis, myalgia, recurrent fever, physical inefficiency, and fetal malformations, to name a few (127). Professional or occupational exposure to zoonotic diseases among those involved in veterinary practice, animal rearing and handling, slaughterhouse management, animal food processing industries, and sewage workers is an ever-present threat (128). The possibility of spreading diseases such as psittacosis, bartonellosis, toxocariasis, and pasteurellosis is also a concern in nursing homes with pet-assisted therapies, so prevention policies are mandatory in these treatment settings (129). It has been reported that veterinary students from 24 different countries could have been exposed to different potential sources of zoonotic pathogens in the first years of their academic studies in the last 55 years (130).

Several zoonotic diseases can be found in these areas, especially in veterinary practice, and their outcomes can range from mild skin diseases, such as fecal-mouth disease (FMD), to fatal and dreadful cases, such as brucellosis, rabies, and toxoplasmosis. People living in forest-adjacent areas or villages, as well as those who depend on forest products for their livelihood, are highly susceptible to wildlife-transmitted zoonotic diseases such as KFD, monkeypox, and rabies, and can spread the disease to the public (109). Hospital staff and workers are also more susceptible to zoonotic cases, as our hospital systems are usually the first portals for infectious cases. If the medical and hospital systems are not adequately equipped for rapid and effective diagnosis and control of the spread of zoonotic diseases, all of these can incidentally facilitate the passive spread of zoonotic pathogens (131). The expansion in large-scale farming systems and food-processing facilities has led to the revelation of a larger proportion of the population to potentially contaminated food sources, and such an increase in the mobility of workers, animals, and food and commodities can be a quick mode of disease transmission into public life (18).

In the past, veterinarians and zoo workers were exposed to zoonotic diseases through their work. There has been a report of methicillin-resistant Staphylococcus aureus (MRSA) infection in elephant calves at the San Diego County Zoo, resulting in the development of pustules (cutaneous) along with cellulitis. Contact with the infected zoo animal can also lead to the development of cutaneous fungal infections, specifically ringworm infections (132,133). Getting bitten by wild or zoo animals is common for veterinarians, and most of the time, such incidences occur during restraint procedures and clinical inspections. As a result, wildlife professionals, veterinarians, and animal handlers working in zoos are at higher risk for diseases transmitted by animal bites, such as rabies, tetanus, tularemia, and simian B herpesvirus infection (134). In the recent past, some of the anti-poaching camp personnel in the Bandipur Tiger Reserve, Karnataka, India, fell ill due to the spread of KFD from macaques and langurs.

Practically speaking, these occupational groups cannot eliminate the risk of developing a zoonotic infection. However, they can very well limit the incidence by following specific critical steps and measures, such as rapid identification of zoonotic agents, use of protective clothing, recognition of potential vectors and fomites, and strict personal hygiene (135). Even in high-income countries like the US and Europe, homeless individuals in urban areas live in crowded conditions with limited sanitation and personal hygiene. There is increased exposure to ectoparasites and urban wildlife, which can transmit several infections to such people; however, no systematic evaluations are available to assess the risk of zoonotic disease to these populations.

The relationship between global patterns of zoonotic disease distribution and their local responses could be explained by an evaluation of animal health, public health, and world trade (136).

Diagnosis, Monitoring, and Networking Programs

Rapid diagnosis, effective surveillance, monitoring, and networking tools are essential to counter and contain the impact of zoonotic diseases, limit their spread, and implement appropriate prevention and control strategies (137). In addition to conventional diagnostic tools and techniques, advances in disease diagnosis and molecular methods are paving the way for quick, reliable, and confirmatory detection of infectious agents in animals of zoonotic significance that affect humans. These include polymerase chain reaction (PCR) and related versions of real-time PCR, quantitative PCR, multiplex PCR, loop-mediated isothermal amplification (LAMP), recombinant and natural secretory protein-based ELISA, biochips, biosensors, microarrays, gene sequencing and phylogenetic analysis, nanotechnology-based diagnostics, and others. (138–151). Diagnosis of a disease in its early stages is essential to control its spread to other susceptible populations. The current need is for field-based or pen-side assays that can be used at the place of sample collection to provide immediate diagnosis. Several field-based assays, such as lateral flow assays, latex agglutination tests, Dot ELISA, and loop-mediated isothermal amplification (LAMP) assays, are now gaining importance because they can be used at the field level (147–152,35). Several studies in India reported that microscopy, culture, PCR, and i_ELISA assays were used to diagnose Crohn's disease (CD) in humans, and the bioload of MAP was estimated in the human population from different regions of the country by mass screening. Of the 25,247 serum and 3,308 blood samples screened by indigenous ELISA and PCR, 33.4% and 8.8% of the population were positive for MAP infection, respectively (153,71). The i_ELISA was shown to be a reliable method for the diagnosis of CD. The prevalence of MAP was higher (27.6% by microscopy and 50% by culture) in people with gastrointestinal problems who worked with goat herds endemic for Johne's disease (154). Other workers used LAMP, PCR, and ELISA assays to diagnose leptospirosis in South Indian patients. They revealed that the LAMP assay could be a reliable method for leptospirosis diagnosis during the first week of illness, while the IgM ELISA was the mainstay of diagnosis from the second week onward (155). Another study demonstrated that the LAMP method is valuable for the rapid detection of *T. gondii* infection in human blood samples. It could be proposed as a simple assay for quick and reliable clinical diagnosis of acute toxoplasmosis in developing countries (156). On the other hand, administration of the FTA® card methodology for molecular characterization and sampling of Echinococcus granulosus sensu lato in Africa has been shown to be a valuable and simple field approach to evaluate the presence and genetic characterization of E. granulosus (157). It was also reported to be a reproducible and stable serum standard for the quantification of anti-hepatitis E virus (HEV) antibodies in HEV animal reservoirs. This study revealed a good range and reproducibility of anti-HEV antibody-positive rabbit serum (RS26), which effectively measured the dynamics of anti-HEV antibody concentrations in rabbits and pigs (158). ELISAs using recombinant antigens are also promising approaches for the diagnosis of some zoonotic diseases, such as feline toxoplasmosis (137).

On the other hand, sensitive serologic tests could aid in the diagnosis of some zoonotic diseases, including acute Borrelia miyamotoi disease (159). In addition, immunochromatography-based rapid cartridge assays (RCAs) support community laboratories with a fast diagnostic method for cryptosporidiosis (160). Moreover, the diagnostic performance of the lateral flow assay (LFA) for the detection of Leptospira-specific IgM in canine sera demonstrated that LFA is a quick and reliable method for the early and fast detection of Leptospira-specific IgM during the acute phase of canine leptospirosis (161). A combination of cytochrome c oxidase subunit I gene fragment amplification with DNA sequencing, an AluI digestion test, and a high-resolution melting analysis (HRM) assay was used to determine Echinococcus species and genotypes and revealed specific and rapid methods for the accurate determination of Echinococcus species (162). A study reported that multiple analyses, including a virus neutralization test, a commercially available competition ELISA, real-time reverse transcriptase PCR, and an in-house immunofluorescence assay, could detect anti-Rift Valley fever virus (RVFV) antibody status in both non-immunized and immunized dairy cattle from the Nile Delta in Egypt (163). The development and validation of a sensitive quantitative real-time RT-PCR test for the reliable and broad-spectrum detection of rabies virus demonstrated a valid diagnostic procedure and epizootic surveillance in Africa using a double-checking strategy (164).

High sensitivity and specificity, lower cost, ease of standardization in different laboratories worldwide, and safer production are the main advantages of the ELISA test.

Field-based diagnostic assays have already been developed for most zoonotic diseases, which can be used to diagnose the diseases promptly. For certain neglected zoonotic diseases such as anthrax, tuberculosis (bovine), brucellosis, echinococcosis, leishmaniasis, neurocysticercosis, and rabies, several diagnostic techniques have been developed. Such techniques include microscopy, culture examination, matrix-assisted laser desorption ionization, and time-of-flight mass spectrometry. Priority has been given to parallel maintenance of Biosafety Level 3 infrastructures and gradual use of various test platforms to improve specimen handling and improve diagnostic sensitivity and specificity, respectively (165).

Zoonotic disease surveillance requires an understanding of the ecology, pattern, and nature of such diseases and trends in their occurrence. In the current era, geographical information systems (GIS) have gained popularity as useful tools for tracking and monitoring vector-borne diseases and other water-borne diseases by mapping the location of herds and flocks. Based on ecological data analysis of the site, soil type, water sources, and geology, they can help predict diseases or epidemics (166). Another tool, the Global Positioning System (GPS), is used to locate regions of high disease prevalence and to monitor control programs. A combination of GIS and GPS could help develop effective disease control strategies (144). In the current milieu of emerging zoonoses, especially from wildlife carriers and vectors, collaborative steps are warranted from all the many disciplines involved in the One Health initiative to curtail this threat, and thereby ensure optimum health not only for humans but also for their fellow creatures, including animals, plants, and ultimately our Mother Earth.

Although rabies is a fatal zoonotic disease, underreporting in developing nations remains a concern due to surveillance challenges. However, proxy measures (such as reports of the incidence of rabid animal bite injuries collected from hospitals and clinics) have proven valuable. Data on dog bite injuries can now be collected in real-time from clinics via mobile telephone service, which ultimately minimizes the communication gap (167,168). The risk of interspecies transmission of influenza from companion animals (such as dogs) to humans is low, but dogs can certainly transmit influenza, so surveillance for novel influenza viruses should be a priority (169,170).

Advances in Immunomodulatory, Prophylactic, Therapeutic, and Vaccine Development Approaches

Vaccines

Prevention of most infectious pathogens is achieved through effective vaccines and immunization programs. Various types of killed, live, and attenuated vaccines are available to combat infectious agents, including those of zoonotic concern. Framework I, II, and III vaccines have been formulated for the immunization of humans, livestock, domestic animals, and wildlife, respectively (171).

Advances in science have paved the way for the development of effective, safe, and novel vaccines that induce protective immune responses, including DNA vaccines, edible (plant-based) vaccines, vector vaccines, protein/peptide vaccines, reverse genetics-based vaccines, virus-like particles (VLPs), gene-deleted mutant vaccines, reassortant vaccines, and chimeric vaccines (172–175). Besides these advances, different types of immunoadjuvants, such as toll-like receptor (TLR) agonists, adjuvant combination formulations (Syntex adjuvant formulations), and vaccine delivery systems (oral, spray, liposome, and nanoparticle-based delivery), are now gaining importance to enhance vaccine immunity and the desired level of protection against various pathogens. Current strategies such as the differentiation of infected and vaccinated animals (DIVA) test, prime-boost vaccination, and administration of booster vaccinations need to be appropriately adapted with regular and judicious follow-up of vaccination programs, which would help formulate timely and valuable prevention and control strategies (176,149).

The design and development of mucosal vaccines need to be emphasized due to their cost-effectiveness, ease of administration (no needles), less hazardous (no medical waste), and potential or usefulness for mass population immunization such as during epidemics and pandemics. These can induce protective immunity against pathogens of interest both locally and systemically. Vaccine development is a time-consuming process; however, some flexibility in regulation may be modulated based on the impact of the disease. Recently, the two-pronged one-health approach implemented in Australia to control Hendra virus infection in horses resulted in the development of a subunit equine vaccine to prevent the natural route of virus transmission and post-exposure therapeutic management in humans with monoclonal antibodies. This recombinant vaccine, which was found to provide protective immunity not only to equines but also to cats and ferrets, has been authorized for field use, making it the first vaccine licensed against a Biosafety Level 4 pathogen (177,178). Moreover, a DNA vaccine encoding the S1 protein of the Middle East respiratory syndrome coronavirus promotes strong protective humoral and cellular immune responses in mice (179).

Live attenuated and killed vaccines against neglected zoonotic diseases such as bovine tuberculosis, paratuberculosis (Johne's disease), and brucellosis revealed future research to improve effective and reliable vaccines using live attenuated and killed vaccine platforms (180,181). In addition, the killed vaccine encoding the highly pathogenic 5' strain of *M. paratuberculosis* 'Indian Bison type' genotype promotes a strong protective humoral immune response and therapeutic effects in domestic animals (182,183). Also, plant-based vaccines against zoonotic diseases are reported as ideal booster vaccines that could eliminate multiple boosters of attenuated bacteria or viruses. Chloroplasts have been used to express several viral and bacterial antigens for protection against diseases such as plague, tuberculosis, anthrax, and classical swine flu (184,185). Vaccination of zoonotic reservoirs of human pathogens has been successfully used to control rabies in raccoons and foxes.

Encapsulation of a live-vaccine virus with a pH-sensitive polymer increased the safety of a reservoir-targeted Lyme disease vaccine and demonstrated protection against B. burgdorferi infection (186). Similarly, the most effective control of the cestode Taenia solium is known to be a combined application of vaccination and chemotherapy in young animals (187).

These types of novel approaches to vaccine development are mandatory to limit the emergence of new zoonotic threats.

Therapy or Treatment

Antimicrobials and antibiotics are available for the treatment and cure of bacterial and zoonotic diseases; however, emerging resistance in several microbial pathogens has limited their use (188,189). Many previously unrecognized pathogens are being identified as potent opportunistic agents, primarily due to the increasing proportion of immunocompromised individuals who are susceptible to infection. Several factors, such as the epidemic trend of AIDS, continuous use of immunosuppressive therapies after organ transplantation or other surgeries, and overuse of modern medicines, play a critical role in this situation, and ultimately, a large proportion of people become unresponsive to conventional selective therapies and remain chronically infected. In such circumstances, treatment of infected and affected individuals with effective therapeutics and individualized drugs will control the further spread of infectious agents and prevent new cases. In addition, most medically relevant bacterial pathogens have been shown to possess efficient quorum signaling (QS) systems for cell-to-cell communication and to form well-protected sessile communities or biofilms. These microbial structures confer inherent antibiotic and immune resistance to the bacteria, paving the way for persistent chronic infections (190). The lack of strategic control and management of hospital-acquired contagious diseases increases the risk of their unfortunate and terrible spread. Furthermore, the availability of a high-quality genome of Echinococcus canadensis could play a significant role in better understanding the biology of pathogenic organisms, the development of species-specific control tools, mechanisms of parasite development, and novel methods for drug discovery (191).

Critical preventive measures, including pre- and post-exposure prophylaxis, should be implemented and strictly followed to limit the possible human-to-human transmission dynamics of serious infectious or zoonotic pathogens. Following the detection of high-risk zoonotic diseases, medical and hospital administrators need to be vigilant in implementing post-exposure regimens, such as post-exposure vaccination of all hospital personnel, isolation of patients, and safe disposal of body wastes and associated treatment materials (192,56). On the other hand, treatment outcomes vary from recovery in some patients to relapse and chronic symptoms despite therapy in others. Therefore, it is necessary to participate in gene expression profiling and RNA sequencing to reveal better knowledge of outcomes and investigate disease processes (193). One study revealed the effect of mass chemotherapy in domestic animals on the decrease of T. b. human rhodesiense African trypanosomiasis (rHAT) in eastern Uganda (194). Elimination of the reservoir of rHAT infection suggests important and cost-effective methods for controlling rHAT. In addition, controlled serological approaches or additional incisions off the slaughter line for bovine cysticercosis have a significant economic impact on the beef carcass sector with costly treatment (195). The use of insecticides (in a restricted manner) can reduce the population of vectors such as ticks and thereby reduce the burden of neglected parasitic zoonotic diseases such as trypanosomiasis, babesiosis, anaplasmosis, and East Coast fever (196–198).

Various factors, such as the emergence of drug-resistant microbial pathogens due to the inappropriate use of antibiotics and antimicrobials, the residual toxicity of antibiotics and drugs in the food chain, and the increase in incidences and epidemics of emerging and re-emerging pathogenic microbes and their newer strains, have led to the discovery and search for various other alternative therapeutic regimens and options, including novel and complementary treatment modalities as described below.

Novel, Emerging, and Alternative/complementary Theorems

High research progress and advances in science have provided effective, novel, emerging, and alternative/complementary treatment options, including phages (bacteriophages, virophages, mycophages), enzybiotics, apoptins, cytokines, avian egg yolk antibodies (IgY), stem cells, RNA interference, si-RNA, monoclonal antibodies, probiotics, nanomedicines, toll-like receptors, panchgavya, nutritional immunomodulation, phytonutrients, herbs, and plant metabolites, and others (199–206). Due focus needs to be given to explore and validate the wide potential of these valuable options by expanding and intensifying further research and clinical trials for the design and development of effective drugs, medicines, therapeutics, and immunomodulatory pharmaceuticals for the prevention and treatment of infectious and zoonotic diseases and their adverse health effects. Such advances could mitigate the adverse effects of emerging and evolving pathogens that pose zoonotic threats by enhancing host immunity and combating infectious microbes.

Prevention and Control

The prevention and control of zoonotic diseases is difficult because of several obstacles, the most important of which are.

Lack of Information

Information technologies play a critical role as an important supporting issue in disease surveillance (207). There is a lack of an approach to sharing information on zoonoses across various platforms. Social and economic losses due to infected and at-risk populations are not well defined. Most veterinarians are aware of major animal diseases; however, their approach is less focused on zoonotic diseases and zoonotic aspects of diseases. Medical clinicians generally fail to recognize zoonoses in human patients or focus on treating individuals rather than taking an epidemiological approach for effective prevention and control. The public is not aware of the prevalent diseases and how to protect themselves. A classic example of this is the widespread lack of awareness among farmers of the use of prophylactic vaccines to prevent brucellosis (208,209). Lack of education about the cause and control options of cystic echinococcosis among sheep rearing in distant communities in Peru has resulted in the persistence of the disease (210,211). The knowledge, awareness, perceptions, and attitudes of a community in Ghana living near a colony of straw-colored fruit bats (Eidolon helvum) following the Ebola virus disease outbreak in West Africa showed that the community members had little awareness of and interest in preventive and protective measures against this deadly virus (212). In Nepal, there is a lack of knowledge among people about the potential zoonoses from free-roaming dogs, and there is an urgent need for awareness and education programs (213). This situation is exacerbated by inadequate communication between veterinarians, medical professionals, public health organizations, and administrators.

Problems with Monitoring and Surveillance Programs

Most zoonotic diseases remain undiagnosed, so there are no proper treatment or reporting strategies, making monitoring and surveillance an arduous task. National survey data on zoonotic schistosomiasis in the Philippines grossly underestimate the true burden (214). For most diseases, there are few regular surveillance systems in undeveloped and underdeveloped countries. General association and cross-sectorial surveillance between the public health and animal sectors were identified as the most important requirements for better control of zoonotic diseases. In this regard, the first five years of the One Health approach to Campylobacter alleviation surveillance provided important risk analysis data and control trends for

Campylobacter (215,216). Moreover, surveillance of veterinary activities such as improved slaughter hygiene, proper meat inspection, proper disposal of condemned offal, and animal owner awareness are important for hydatid cyst prevalence (217). On the other hand, effective surveillance and control programs for bovine brucellosis as a re-emerging disease are still under discussion and need to be improved (218).

No Ownership

Zoonotic diseases fall in 'no man's land'. There is an unwillingness or inability to take responsibility for zoonotic infections in both the medical and veterinary sectors. Ways to prepare for cross-transmission during an outbreak are also not well known (219).

No Combined Intersectoral Effort

Compared to other infectious diseases, there are few national-level programs for zoonotic diseases in several countries. There is an urgent need for a combined effort by medical, veterinary, and environmental professionals to prevent the transmission of these zoonotic diseases (220). Sustained efforts from all three mentioned sectors are needed to control zoonotic diseases. On the contrary, the government only suggests outbreak warnings and dos and don'ts during an emergency due to these zoonotic diseases. A multisectoral approach to control zoonotic leptospirosis in Fiji has been formulated to reduce the case fatality rate by half (221). A survey revealed a lack of knowledge among farmers about hydatidosis and other potential zoonotic parasites in dogs in Portugal, pointing to the need for health education and closer collaboration between veterinarians and public health professionals (222). Adopting a multisectoral One-Health approach is a critical policy requirement for India and other developing countries, and the goal should be to promote a policy environment that incorporates assessment and mitigation of the downstream impacts of different agendas. Chatterjee et al. emphasized the need to transcend institutional boundaries with a multi-sectoral and multi-actor approach, along with mapping the policy process for improved control of endemic and neglected zoonoses in sub-Saharan Africa (223,224).

Improper and Inadequate Funding

There is a lack of funding for awareness programs, prevention, and control strategies, and compensation for livestock owners whose animals must be destroyed when a notifiable disease is diagnosed, and the animal must be destroyed according to law and veterinary practice. In some cases, the procedures for providing compensation could be more precise or more complicated, thereby hampering control measures. The control of neglected zoonotic diseases, which are endemic and require long-term monetary support, is becoming increasingly difficult due to the lack of funding (225). Funding for the prevention and control of zoonotic diseases is not a priority for government agencies worldwide, especially in developing countries. Goutard FL et al. suggested that under the umbrella of the One Health approach within a risk-based surveillance approach, the framework of a combination of participatory methods and modern technologies could help to overcome the constraints in low-income countries (226). Such unconventional approaches could be combined to optimize surveillance of emerging and endemic diseases in the challenging environments of poor countries.

Lack of Effort to Commercialize Vaccines and Biological Products

A recombinant Taenia solium antigen vaccine has been developed to prevent transmission of the disease, but unfortunately, such a vaccine has not been commercialized. As a result, the poor farmers cannot vaccinate their pigs, which are kept in a free-range system. As a result, the socioeconomic burden increases (225–227).

Strategies for the prevention and control of zoonoses vary considerably depending on the type of zoonosis (228). Most cyclozoonoses, direct zoonoses, and a few saprozoonoses can be prevented and controlled by effective strategies implemented by the veterinarian, as animals play a crucial role in these zoonotic diseases. For example, the elimination of stray dogs can prevent zoonotic diseases such as rabies, visceral larva migrans, and hydatid cysts. Similarly, metazoonoses can be controlled by targeting vertebrate hosts, invertebrate vector hosts, or both. A simple and effective means of controlling metazoonoses is to use insecticides against the vectors. Tuberculosis, on the other hand, requires early and effective diagnosis, a strict vaccination policy, isolation, and the separation or culling of affected animals; disinfection of premises can prevent and control its transmission to humans. Since direct zoonoses involve droplet infection or transmission through dust or secretions, air disinfection is essential to prevent further spread. Methods such as irradiation can effectively eliminate the immature forms of Trichinella spiralis, which causes trichinosis when contaminated meat is consumed.

In several cases, foodborne and waterborne zoonotic diseases go hand in hand (229). Waterborne zoonotic diseases do not cause overt clinical disease in animals, although they can cause significant problems in humans. The primary goal of any water treatment should be to treat the water at its source so that disease transmission can be blocked at the initial stage. Strategies such as cleaning and disposing of animal waste away from water bodies and preventing infected animals from accessing water sources can minimize the problem of waterborne zoonotic diseases (230). Persons at risk of waterborne diseases, such as the young, the elderly, and immune-compromised persons, as well as those in constant contact with water, such as fishermen, should be alerted about zoonotic diseases that can be transmitted through water.

Key factors for effective prevention and control strategies for zoonotic diseases include good management practices, monitoring of appropriate biosecurity checkpoints, maintaining the desired level of hygiene and sanitation program, isolation and quarantine, trade restrictions, early diagnosis, and prevention of further transmission and spread of zoonoses, which together would reduce the incidence and outbreaks of these diseases, and the associated public health problems (231). Effective animal intervention strategies must be adapted to control zoonoses (232,233).

However, in the current scenario of advanced globalization of trade and international progressive and collaborative strategies, it is difficult to control, limit, and monitor the movement of human, animal, and animal products across countries. In addition to these factors, other issues such as changes in agricultural and animal husbandry practices, global warming events, an increasing population of vectors and reservoirs/carriers of various disease-causing microbes, and the emergence and re-emergence of changing and newer pathogens have made the overall prevention and control of zoonoses more challenging.

Vector populations and reservoirs, which play a leading role in the spread of many zoonotic infectious agents, must be controlled, as must wildlife diseases of zoonotic significance, to limit the transmission of such diseases and their potential risks and threats to public health (63,82,83,233). Breaking the cycle of transmission, such as arboviral infections, is an effective measure to be adopted, as these are responsible for the spread of several critical zoonotic diseases.

The transmission of zoonotic pathogens requires the intervention and adaptation of appropriate hygiene and sanitation measures along with the necessary biosafety practices by persons and professionals working, handling, or living with animals, especially during their handling or care, post-mortem, collection and handling of tissues and other specimens, and reducing the likelihood of the spread of infectious agents through the routes of different contaminated fomites and other substances.

Emergency preparedness plans must be implemented at the local, regional, state, and national levels depending on the severity of the zoonotic disease spread, along with public awareness and the necessary follow-up of disease investigations and prevention plans to counter such threats and safeguard human health. Suspected incidents and cases must be promptly detected, isolated, and contained to control further spread of the zoonotic pathogen. Livestock and poultry owners and producers must be advised on effective disease management practices to prevent and control the transmission of zoonotic pathogens to humans.

Alonso et al. have analyzed the content and information in several reviews on zoonoses and found that the focus of veterinary research has been on livestock problems rather than public health issues, although there seems to have been a shift in the last decade (234). They also found that studies on impact and control were limited. In recent years, a partnership between medical and veterinary professionals has been required to control emerging zoonotic diseases (235). This has given birth to a newer concept called the One Health approach, which has received increasing attention from researchers in recent years (236). The environment and climate also have a significant influence on the maintenance of pathogens transmitted between humans and animals (237). Ogden et al. have described how climate change may affect divergent arthropod disease vectors, multivoltine insects, and ixodid ticks. Weather, climate, and climate change can have very different effects on the spatial and temporal occurrence of vectors and the pathogens they transmit, thereby changing the disease patterns and prevalence or incidence (238). Shanko et al. have provided an overview of zoonoses, discussing the role of veterinarians and medical personnel in combating zoonoses and the importance of multi-sectoral alliances in zoonoses control (239).

There is a strong bond between humans and animals, especially pets, where people are emotionally attached to their pets. This increases the potential for the spread of infectious diseases from animals to humans (239). Several key considerations, such as improved communication across disciplines and agencies, assessment and development of surveillance programs, examination of the links between animal health determinants and human health outcomes, and finally, cross-disciplinary training and research, are needed to develop effective control measures for zoonotic diseases. Collaboration between medical, veterinary, and public health professionals at the national and international levels is required during an outbreak situation to control its spread among different communities and to other parts of the world as 'one medicine' (201,206,236,240,241).

The spread of emerging and re-emerging zoonotic diseases is hampered by the need for better knowledge of disease dynamics and the transmission cycle of the pathogen (242). It is reported that about 60% of emerging infectious diseases are zoonotic, of which about 72% are wildlife-borne, e.g., the Ebola virus, SARS, and KFD. Emerging diseases pose a significant threat since they require identification, prevention, and control; therefore, there is a need for collaboration between medical and veterinary researchers. Several training courses, symposia, and conferences should be organized regularly under a broad theme involving interdisciplinary research that can help to understand the dynamics of the diseases so that effective control measures can be established (237). Thus, the current focus should be on a public health approach that includes veterinary, medical, and biological research to develop effective prevention and control measures. A multidisciplinary approach is essential, involving the health, agricultural, environmental, and other social sectors, both nationally and internationally (243,9).

The One Health approach has already had a good impact, and some examples support the establishment of this approach in different parts of the world where there is less knowledge about this concept (244). At the core of One Health is the recognition of the interdependence of human, animal, and environmental health. Zoonoses are one of the foundations of One Health. Millions of people have died from zoonotic diseases over the years; the COVID-19 pandemic is the most recent example of an outbreak and pandemic that has occurred. Zoonoses have an impact not only on public health but also on society and the economy. Since its inception, One Health has made significant contributions to the protection of people, animals, and the environment by preparing for, monitoring, and mitigating such public threats. Examples include the control of rabies in Bali, Indonesia; the management of Q fever in the Netherlands; the Human Animal Infections and Risk Surveillance (HAIRS) group in the United Kingdom; the control of foodborne Salmonella in the European Union; and also the collaboration between FAO, OIE, and WHO in 2010, taking into account the control of rabies, zoonotic influenza, and antimicrobial resistance (245). The Center for Disease Control and Prevention (CDC) of the United States uses this approach by bringing together people from different fields, such as physicians, ecologists, medical doctors, and veterinarians, to keep an eye on infectious diseases and to control the threats that these diseases pose to the public. This partnership has also allowed us to learn about the spread of diseases between human and animal populations (37). The One Health approach has also been used to develop some methods for controlling emerging zoonotic infectious diseases. However, the standardized evaluations and ethical cases of One Health as an alternative approach to more traditional public health methods are largely called for in the essays (246,247). Furthermore, it is revealed that the One Health Systems Mapping and Analysis Resource Toolkit (OH-SMART) has been successfully applied in West Sumatra, Indonesia, and is proposed as a promising tool for health systems development and related functions for developing multi-sectoral collaborations (248).

The One Health concept is an interdisciplinary approach that recognizes the interconnectedness of human health, animal health, and environmental health. It recognizes that human health is intricately linked to the health of animals and the environment in which we all live. Zoonotic diseases exemplify the importance of this interconnectedness. While the One Health system has been introduced and adopted to some extent, there is a consensus among experts that further elaboration is needed to fully realize its potential to effectively address the challenges posed by zoonotic diseases. By strengthening the interconnectedness of human, animal, and environmental health, the One Health approach can offer a more comprehensive and holistic perspective when addressing these complex health issues. When we consider zoonotic diseases such as Ebola, rabies, or avian influenza, it is evident that these diseases do not respect species boundaries. The conditions that facilitate the transmission of these diseases often involve interactions between humans, animals, and the environment. For example, deforestation or encroachment into wildlife habitats can lead to increased contact between humans and wildlife, creating opportunities for the pathogens to jump from animals to humans. The One Health approach can help identify and address the root causes of zoonotic diseases by emphasizing the interconnected nature of human, animal, and environmental health. The approach can involve collaborative efforts between human health professionals, veterinarians, ecologists, and other experts to develop strategies for disease surveillance, prevention, and control that encompass all aspects of the ecosystem. Furthermore, an expanded focus on the interconnectedness of human, animal, and environmental health can lead to a more sustainable and resilient approach to managing zoonotic disease outbreaks. By understanding how changes in one sector can affect others, we can proactively implement measures to mitigate risks and promote the health and well-being of all living beings. In brief, while the One Health system provides a valuable framework for addressing zoonotic disease challenges, further elaboration on the interconnectedness of human, animal, and environmental health is essential to fully realize its potential. By adopting a holistic perspective and integrating the expertise of various disciplines, we can work towards a healthier and more harmonious coexistence between humans, animals, and the environment (249).

Some of the personal and individual preventive strategies that are to be adopted to protect against zoonotic diseases are: keeping hands clean and maintaining proper hygiene measures; proper and safe handling of food materials; preventing ourselves from being bitten by mosquitoes and ticks both during the day and at night; paying sufficient attention to the pets that stay near their owners; and, more importantly, always being aware of the possibility of contracting a zoonotic disease from any source that one encounters and taking the necessary precautions and care.

Last but not least, educational materials on zoonotic diseases should be made available to the farming community as well as to pet owners. This can be achieved by creating an online website or database (with free public access) and disseminating accurate information (249,250).

Conclusion and Prospects

Zoonoses, a vicious consequence of human-animal association, have been recognized for centuries and currently account for more than 300 contagious diseases. The infectious agents involved in zoonoses comprise pathogenic microbes, including bacteria, parasites, fungi, and viruses. Tropical populations are particularly susceptible to zoonotic diseases due to the lack of infrastructure, financial insecurity, and lack of sophisticated epidemiological interventions. Thousands of people, especially those from developing countries, are exposed to zoonotic threats every year that affect social health systems. The consequences of such outbreaks affect social health status and disrupt social structure, animal food production, and trade, causing a negative drift in socio-economic development. Emerging and re-emerging zoonoses pose a constant pandemic threat with unimaginable and devastating public health consequences. Various factors contribute to the emergence of diseases, including changes in human demographics and behavior, advances in technology and industry, global economic growth, indiscriminate land utilization, unprecedented developments in international travel and trade, reducing the resistance of the microbial population against antimicrobial and chemotherapeutic agents, and the breakdown of public health measures. These multiple impacts are critical in influencing the eco-biological balance and the dynamic interactions within it, namely the interactions of various pathogens, their hosts, and other related hosts with wild and domestic habitats, and ultimately, their impact on human life and health. As these interactions are highly relevant to the emergence and spread of zoonotic diseases, special attention should be paid to such environmental factors, and appropriate measures can be adopted as mitigation strategies for effective and timely responses to outbreaks. It is essential to provide broader government support to encourage the discovery of new vaccines. Clear ideas on the use of antigens in the vaccine and the resulting immune response are essential to minimize the existing warning generated by the emergence and re-emergence of zoonotic diseases. Top priority must be given to the production and commercialization of vaccines. From the perspective of the Indian subcontinent, there is a need to assess the management aspects of dairy farming, along with culture and dietary habits and farmers' perceptions of zoonoses. Raising awareness in the farming sector is essential for the development of improved control measures.

Among the various pitfalls in the control of zoonoses, negligence on the part of the national and international health sectors plays a significant role, and these threats should be prioritized. Human encroachment on wildlife and associated habitats through deforestation and the adoption of forest areas for livestock farming widely contributes to the spread of wild reservoirs of some potent viral pathogens into human areas, thereby causing emerging diseases such as Nipah and Hendra viral infections. Protective measures to counter these risks and threats must be implemented with multipronged strategies, especially at the human-animal ecosystem interface. Strategies for predicting disease outbreaks should be strengthened by integrating newer mathematical modeling systems with advances in diagnostics, communications, and bioinformatics to identify unknown pathogens in other species, and novel approaches must be adopted to detect those microbes that are likely to infect humans. In implementing these management measures, due consideration should be given to the complexity of human-animal interactions and their environmental factors. In addition to these measures, adequate and effective communication and collaboration among different health sectors concerned with human health and that of domestic and wild animals in their ecosystems must be followed and implemented. Certainly, veterinary medicine and its allied sectors, with their extensive and eminent history of contributions and promotions towards the globally admired concept of health, can play a pivotal role in safeguarding public health and upholding the principles of healthcare for all living beings. Success in the prevention, control, and eradication of major zoonoses is directly related to the ability to mobilize resources in different sectors, coordination and intersectoral approaches, and financial aspects between regional, national, and international veterinary and public health services. Improvement of the surveillance systems together with advanced diagnostics, especially for emerging zoonoses, should be the priorities of the public health sector at both regional and national levels.

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Conflict of Interest

The authors report that they have no known financial conflicts of interest.

Availability of Data

No data were used for the research described in the article.

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