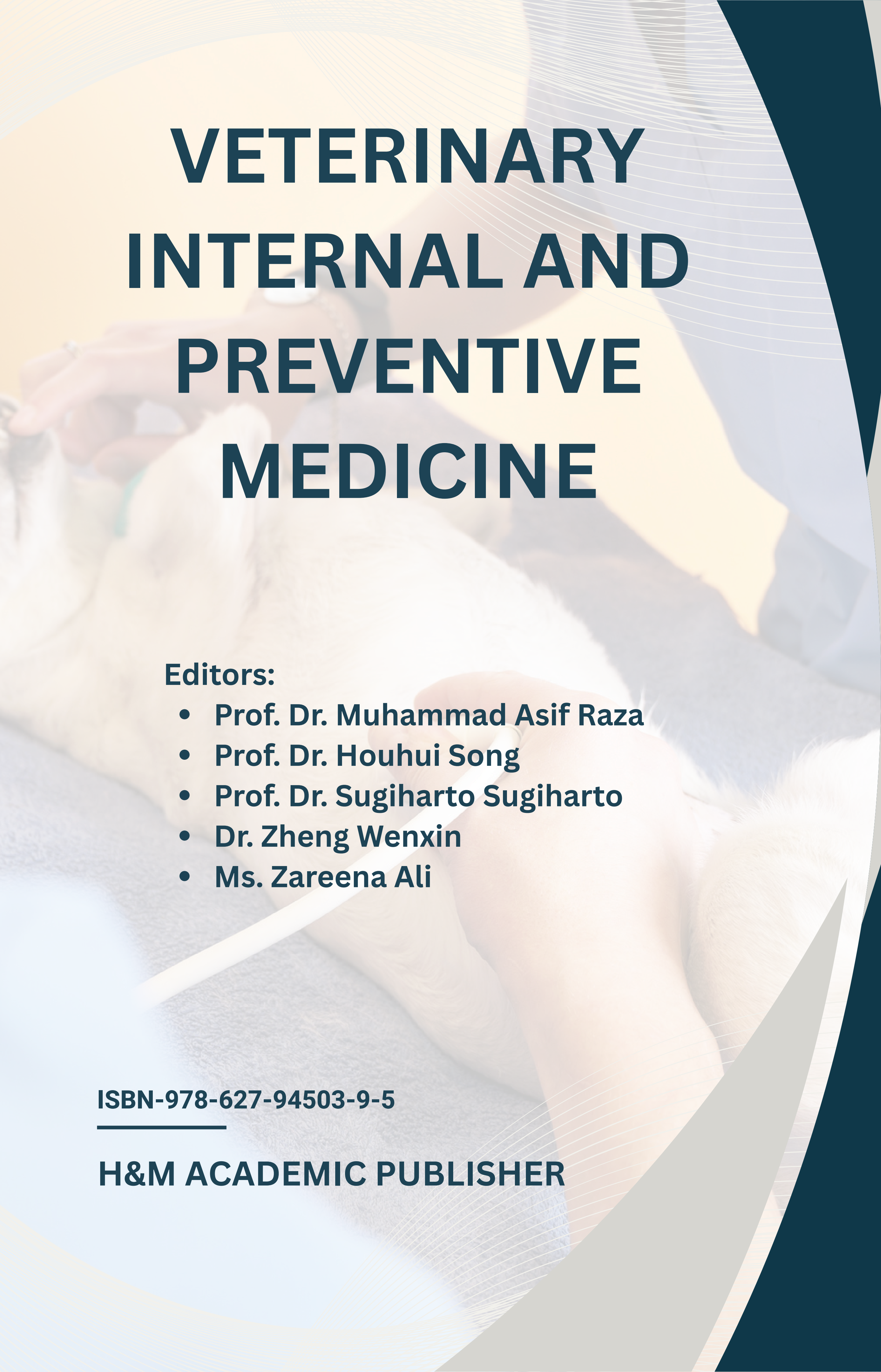

# VETERINARY INTERNAL AND PREVENTIVE MEDICINE

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# Enzyme Function and Regulation in Animal Disease Processes

01

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## ABSTRACT

Enzymes offer a complex role in biological systems because they are important in the diagnosis and treatment of animal illnesses by their Function and Regulation in Animal Disease Processes. In crystallization, the enzymology development across time is emphasizing important findings from Pasteur's and Berzelius' catalytic research to Sumner and Northrop's accomplishments. Moreover, enzymes also exist role in metabolic processes to highlight their use in industrial uses in food processing, feed additives and their necessity for life. In the context of modern era, potential and problems in animal management having significant developments in enzyme biotechnology including genetic alterations and the creation of thermostable enzymes. The connection between illness and enzyme dysregulation to concentrate on genetic metabolic diseases, cancer metabolism, and diagnostic enzymology. Particular focus is placed on the enzyme activity processes such as their catalytic efficiencies and structural classifications. The enzyme effects indicators on illness prediction and therapy monitors their variables performance outcomes like pH, temperature, and cofactors. This chapter outlines novel gene therapy techniques and also transforms the way of genetic illnesses treatment to highlight the connection between molecular medicine and enzymology. Furthermore, biochemical principles, historical perspectives, and state-of-the-art research integration also explored in this chapter which offers a thorough knowledge of the critical role enzymes play in animal health and disease processes.

**KEYWORDS**
Enzyme dysregulation, Animal disease diagnostics, Metabolic enzyme dysfunction, Feed enzymes, Enzymatic activity regulation, Veterinary biotechnology

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## INTRODUCTION

Since the 1940s, advances in biochemistry have significantly enhanced the use of enzymes in disease diagnosis to form the foundation of modern clinical chemistry. However, only in recent decades has interest in diagnostic enzymology grown significantly (Das et al., 2021). Despite numerous methods being documented in scientific literature, many remain underutilized, and vast areas of medical research remain unexplored regarding the diagnostic potential of enzyme reactions. Worthington Biochemical Corporation has compiled this section as an accessible guide to enzymology for laboratory personnel, drawing on its extensive theoretical and practical expertise in the field (Richter et al., 2021).

### Historical Evolution of Enzymes

The role of enzymes in biological catalysis has been recognized for over a century. Early studies in the 1800s revealed their role in digesting meat via stomach secretions and converting starch to sugar using saliva and plant extracts (Giuntini et al., 2022). In 1835, Swedish chemist Jon Jakob Berzelius described their action as catalytic. Louis Pasteur in 1860, observed that enzymes were essential for fermentation, assuming their activity was inseparable from living yeast cells aas Becking and Raat, 2022).

In 1897, German chemist Edward Buchner demonstrated that cell-free yeast extracts could ferment sugars into alcohol and carbon dioxide, coining the term "zymase" for his preparation. The word "enzyme," derived from the Greek "en" (in) and "zyme" (yeast), was introduced in 1876 by William Kühne to describe "unorganized ferments" that function independently of living cells (Fonódi et al., 2024). In 1926, American biochemist James B. Sumner achieved a breakthrough by isolating and crystallizing urease, earning the 1947 Nobel Prize. John H. Northrop and Wendell M. Stanley later devised methods to isolate and crystallize other enzymes, sharing the Nobel Prize with Sumner for their contributions (Creager et al., 2022).

## Enzymes and Life Processes

Metabolism is the sum of chemical and physical processes within living cells which drives life processes such as tissue renewal, energy production, waste elimination, and reproduction. Despite the complexity of these reactions, they occur efficiently due to catalysis. Catalysis accelerates chemical reactions without altering the catalyst itself, and in biological systems, enzymes serve this crucial role (Buller et al., 2023). Without enzymes, metabolic reactions would proceed far too slowly to sustain life. For instance, the breakdown of fatty acids to carbon dioxide and water occurs rapidly and smoothly in the body under mild physiological conditions, while similar reactions in vitro require extreme conditions of temperature and pH. Understanding enzymes their nature, functions, and mechanisms has spurred advancements in medicine and the life sciences (He et al., 2024). Feed enzymes gained prominence in the late 1980s and experienced significant growth post-1992 (Fig.01). Presently, they are primarily utilized in poultry diets to counteract the impact of viscous non-starch polysaccharides (NSPs) found in cereals like barley, wheat, rye, and triticale (Perera et al., 2022). Despite their availability for over 15 years, feed enzymes remain niche products and are predominantly used for poultry and, to a lesser degree. During the initial adoption phase (1990–1995), Europe emerged as the leading region for feed enzyme usage. At that time, the global market value was approximately $90 million. Today, the feed enzyme market has grown substantially and now valued at over $360 million (Fig. 01) (Nguyen et al., 2022).

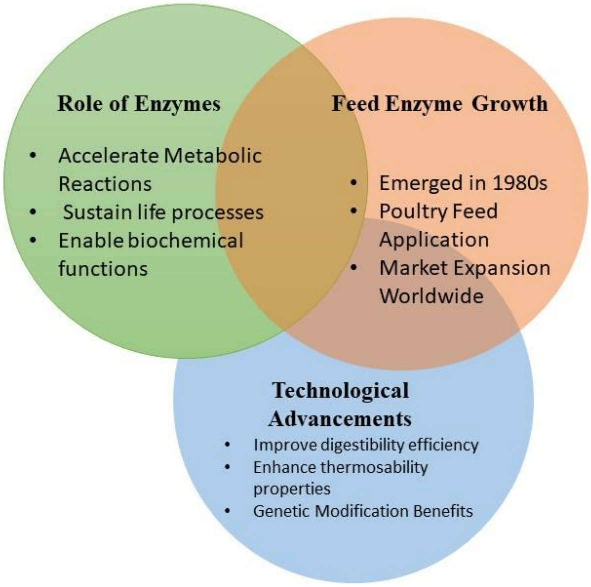

**Fig. 1.** Enzymes functions in Life process

Market growth aligns with increasing global demand for animal products and rising living standards. For instance, China has significantly expanded poultry production in recent years by relying on lower-quality feed ingredients. Advancements in feed enzymes and primary mode of action are reducing digest viscosity which has been well established, leading to the development of reliable formulations (Almassri et al., 2024). Improvements in enzyme thermos-ability is combined with advanced coating technologies that have enhanced product resilience against the heat, moisture, and friction encountered during feed processing. Moreover, the application of genetic modification (GM) technology has also revolutionized the feed enzyme industry. By expressing enzymes from non-traditional sources in GRAS (Generally Recognized as Safe) hosts, researchers have created recombinant proteins with superior enzymatic properties (Subbarayuduet al., 2024).

## Basic Principles of Enzyme Function

Enzymes may be analyzed using methods from molecular biology, molecular biophysics, and protein chemistry because they are proteins. Their structures can be examined by spectroscopic techniques, X-ray crystallography, and multidimensional NMR.

They are made up of 20 naturally occurring amino acids (Table.01). Enzymes also consist of folding units called domains, which contribute to their function (Table 01) (Zhou et al., 2022; Szpotkowski et al., 2023).

**Table 01.** Structure of Amino Acids on the Basis of its Enzymatic Activities

| **Amino Acid Structure** | **Functionality** |
|---|---|
| Primary Structure | The sequence of amino acids in the polypeptide chain, which defines the protein's structure and reactivity |
| Secondary Structure | Localized folding patterns within the chain, such as α-helices and β-sheets, formed through amino acid interactions |
| Tertiary Structure | The overall three-dimensional shape formed by secondary structures and side-chain interactions |
| Quaternary Structure | The arrangement of multiple polypeptide chains (subunits) that aggregate to form a functional enzyme. These subunits may be identical or distinct |

### Important Terminologies

- **Cofactor:** A non-protein chemical component necessary for enzymatic activity.
- **Apo-enzyme:** The inactive protein component of an enzyme.
- **Holoenzyme:** The active enzyme formed by the Apo-enzyme and its cofactor.
- **Coenzyme:** A non-protein compound required for enzymatic function.
- **Prosthetic Group:** A tightly or covalently bound coenzyme or metal ion (Makwana, 2022).

## 4.2. Sources of Enzymes

Enzymes are found in all living organisms and facilitate essential biochemical reactions. Microbial enzymes are particularly advantageous due to:

- Cost efficiency and production stability.
- Predictable enzyme content.
- Continuous supply due to minimal seasonal fluctuation.
- Reduced harmful components compared to plant and animal tissues (Nunes et al., 2024).

Historically, enzymes were derived from animal sources like cow pancreases. However, plant enzymes, such as peroxidase from horseradish, and microbial enzymes (e.g., catalase from Aspergillus niger), have gained prominence due to their superior stability and availability (Abdelhamid et al., 2024).

### Enzyme Naming and Classification

Most enzyme names end with "-ase" and reflect their substrate and catalytic action. The International Union of Biochemistry (I.U.B.) standardized enzyme nomenclature. Enzymes are classified based on their reactions (Fig.02). (Hassan et al., 2022):

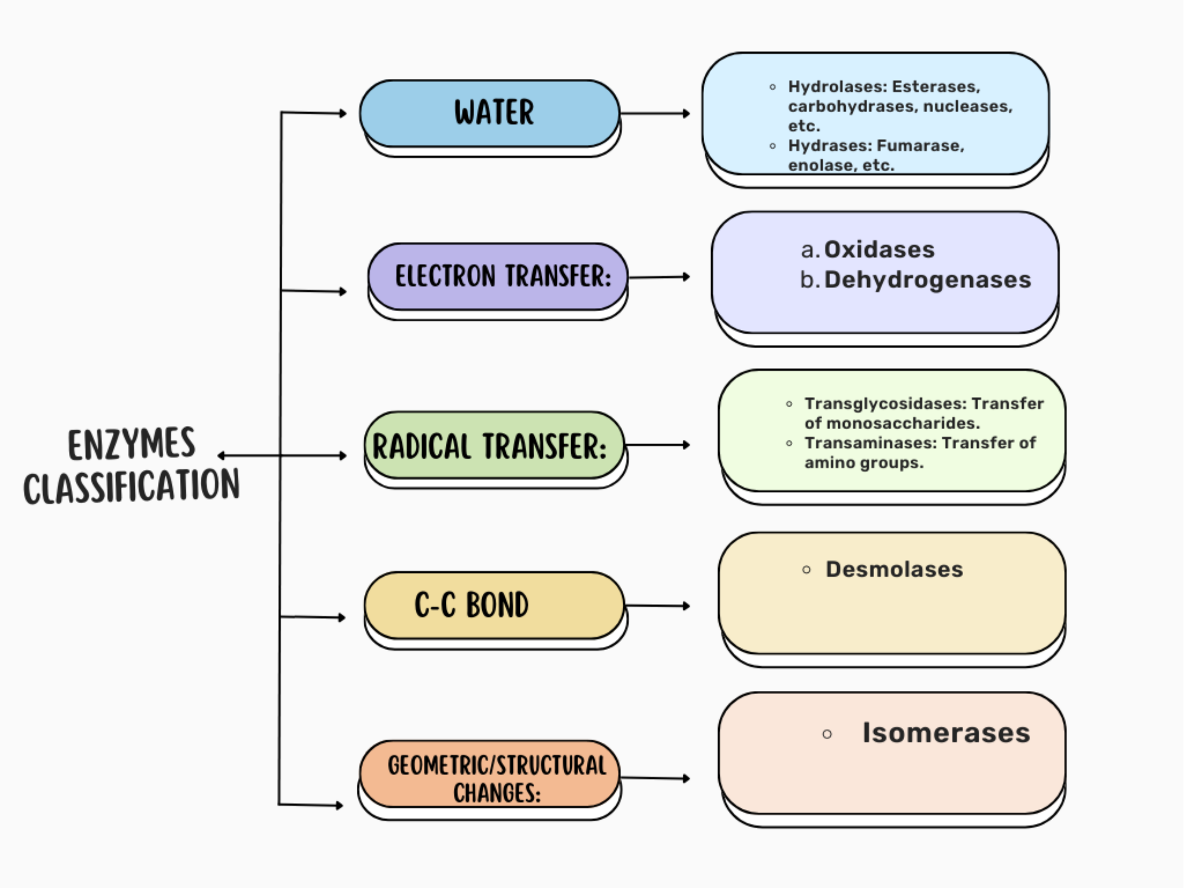

**Fig.02.** Classification of Enzymes based upon their Reactions

This classification provides a systematic understanding of enzyme functions and their catalytic mechanisms (Fig. 02) (Xu et al., 2023).

### Enzymes activity and factors which affects:

Enzymes are macromolecules that act as biological catalysts to accelerate reactions by lowering the activation energy required. This makes it possible for metabolic reactions to happen at notable speeds, which they otherwise might (Ghosh et al., 2021). The Lock and Key Model postulates that, like a key fitting into a lock, the active site is stiff and complementary to the substrate. The Induced Fit Model, which was put forth by Koshland in 1958, suggests that the enzyme changes its conformation when it binds to a substrate, resulting in an ideal fit for effective catalysis (Sanders et al., 2024).

Several factors are influencing activity of the enzymes:

- **Temperature:** Moderate temperature increases enhance reaction rates by increasing molecular motion, but excessive heat denatures enzymes can destroy their functionality (Knapp and Huang, 2022).
- **PH:** Each enzyme has an optimal pH range. Deviations from this range alter ionic charges to disrupt the enzyme's structure and active site (Albayati et al., 2024).
- **Substrate Concentration:** Reaction rates increase with substrate concentration until the enzyme becomes saturated. Beyond this point, the rate plateaus (Sreenivasulu et al., 2024).
- **Enzyme Concentration:** Higher enzyme levels result in more active sites, thus increasing reaction rates, provided the substrate is not limiting (Zandieh and Liu, 2021).

- **Cofactors and Coenzymes:** Many enzymes require additional molecules, such as cofactors or coenzymes to maintain the active site's proper shape or facilitate catalytic action (Kirschning, 2021).
- **Inhibitors:** Substances like competitive inhibitors compete with substrates for the active site, while non-competitive inhibitors alter enzyme structure by reducing activity.

Enzymes play a critical role in industrial applications due to their specificity, biodegradability, and efficiency under mild conditions (Sujitha and Shanthi, 2023). For instance:

- **Proteases** in biological washing powders degrade blood and food stains.
- **Meat tenderizers:** Proteases break down peptide bonds to make meat softer.
- **Food Industry:** α-Amylases increase the quality of baking and brewing, whereas glucose isomerase improves beverage sweeteners.
- **Dairy Industry:** Lipase aids in cheese flavor development.
- **Photographic and Paper Industries:** Proteases and amylases remove coatings and starch, respectively (Okpara, 2022).

## Enzyme Function in Infectious Diseases

Serum enzymes are useful for diagnosing animal illnesses, according to earlier reviews. With an emphasis on the kinetics of enzyme clearance is explored by the pathophysiological processes that underlie the rise in enzymes in plasma during illness (Noels et al., 2024). Increased plasma levels of enzymes can be caused by:

1. **Increased cell damage leakage:** For example, toxic hepatopathy may cause liver enzymes to leak.
2. **Increased synthesis of enzymes:** For instance, glucocorticoids might cause an increase in Alkaline Phosphatase (AP).
3. **Secretion blockage-induced regurgitation:** Amylase and lipase levels in the pancreas increase when ducts are blocked (Chen et al., 2023).

Enzyme-specific traits like size, subcellular location, synthesis rate and the degree, severity, and speed of tissue damage are all affect the rate of enzyme leakage (Gouveia et al., 2023). For instance, tiny cytosolic enzymes such as lactate dehydrogenase (LDH), aspartate transaminase (AST), and alanine transaminase (ALT) leak significantly in rat livers under anoxic conditions but the bigger mitochondrial-localized glutamate dehydrogenase (GDH) leaks very little. The molecular size and cellular location of important enzymes, including Alkaline Phosphatase (AP), GDH, AST, ALT, and LDH, are compiled in Table 1 (Petrichev, 2021).

Additionally, the pathway by which cellular proteins enter the bloodstream determines the extent of the enzyme rise in plasma. The liver and spleen which come into touch with blood to release enzymes straight into plasma but the enzymes from the heart and skeletal muscles enter more slowly through lymphatic drainage. In organs like the kidney and lungs, enzyme loss often occurs through renal tubules or alveolar spaces (Jandl et al., 2022).

## Tissue and Serum Enzyme Activates:

Enzyme activities vary across tissues and species are influenced by assay conditions. Most assays were conducted at 25°C with some at 37°C or 40°C where activity doubles compared to 25°C (Siddiqui et al., 2022). Despite variability, these data provide a reliable guide to enzyme distribution patterns across species. Enzymes like AST, LDH, and Isocitrate Dehydrogenase (ICDH) are ubiquitous by making their serum elevations non-specific to particular tissues. However, enzymes such as GDH, Sorbitol Dehydrogenase (SDH), Ornithine Carbamoyl Transferase (OCT), and Arginase (ARG) are predominantly hepatic, so their elevated serum levels indicate liver damage. ALT is liver-specific in species like dogs, cats, and rabbits but shows higher cardiac and skeletal muscle activity in cattle, and sheep, where its elevation may signal severe myopathy (Almodóvar-Payá et al., 2020). Creative Kinase (CK) is most abundant in skeletal and cardiac muscles with increased serum levels indicating conditions like active cardiomyopathy. Similarly, Gamma Glut-amyl Transferase (GGT) is highly active in the kidney with increased serum levels linked to hepatobiliary obstruction rather than hepatocellular necrosis (Oikonomidis and Milne, 023).

Alkaline Phosphatase (AP) is active in tissues like bone, kidney, and liver. Its elevation in hepatobiliary obstruction stems from overproduction in liver cells rather than reduced biliary excretion. Glucocorticoids in dogs induce a liver-specific AP iso-enzyme which is detectable through serum electrophoresis. Digestive enzyme regurgitation during pancreatic obstruction causes elevated serum amylase and lipase, commonly observed in acute pancreatitis (Szatmary et al., 2022). In humans, these enzymes also increase under conditions like intestinal obstruction, stress, and renal insufficiency. Amylase is secreted by human salivary glands which rises during parotid gland diseases but is not secreted by salivary glands in most other species (Proctor and Shaalan, 2021).

## Role of Enzymes in Body Functions and Disease Diagnosis

Enzymes are crucial biological molecules, some of which remain within the cells where they are synthesized, while others are secreted into body fluids like blood. These extracellular enzymes are further categorized into functional plasma enzymes and non-functional plasma enzymes (Strøm et al., 2020).

### a). Functional Plasma Enzymes

These enzymes are naturally present in the blood of healthy individuals and perform specific physiological roles. Examples include, Lipoprotein lipase, Pseudo cholinesterase, Pro-enzymes involved in blood coagulation and fibrinolysis (Dias and Nylandsted, 2021).

### b). Non-Functional Plasma Enzymes:

` These enzymes are produced by cells as a result of normal cellular deterioration, but they serve no functional use in the blood. Alkaline phosphatase (ALP), lactate dehydrogenase (LDH), and transaminases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) are a few examples (Shipman and Shipman, 2024).

## Enzyme Activity and Disease Diagnosis

Tissue damage can vary in degree based on the severity and commencement of the disease is associated with the release of non-functional plasma enzymes into the bloodstream. These enzymes are seen in trace levels in serum under typical settings (ti). Nonetheless, they are useful instruments for diagnosing diseases since their increased activity in bodily fluids can signal abnormal changes (Chu et al., 2022). More accurate disease diagnosis can be made by doctors by comparing the levels of enzyme activity in serum or plasma. Understanding iso-enzyme properties, including enzymatic kinetics, temperature and pH sensitivity, release rate from the origin cells, and clearance rate from circulation, is crucial for precise analysis. Enzyme markers not only aid in diagnosis but also offer valuable insights into the disease process, prognosis, and therapeutic response to enable more precise and effective medical care (Bodaghi et al., 2023).

Recent breakthroughs in recombinant DNA technology have sparked significant advancements in the development of gene therapy aimed at treating inherited genetic disorders. While individually rare, the combined prevalence of X-linked and autosomal recessive diseases affects more than 1 in 500 live births, imposing a substantial social and economic burden (Volberding et al., 2022).

Although prenatal diagnostics and carrier detection methods are available and they only cover a fraction of these disorders. Moreover, effective medical treatments remain limited for most of these conditions. Gene therapy is involved introducing genetic material to correct or replace defective genes holds promise as the ultimate therapeutic solution (Sayed et al., 2022).

## Gene Therapy in Research and Application

Genetic modifications in animal germ cells have been used to:

1. Create new animal models of human diseases.
2. Test the potential of gene transfer to correct disease phenotypes.

However, since these germline manipulations could permanently alter the genetic makeup of a species, such methods are not applied to humans. Instead, efforts in human gene therapy are focused on transferring genetic material to somatic cells to avoid heritable genetic changes (Kratzer et al., 2022).

## Methods of Gene Transfer

Gene transfer is typically conducted in one of two ways:

**a). In Vitro:** Genetic material is introduced to cultured somatic cells which are later transplanted back into the patient or animal model (Galli and Lazzari, 2021).

**b). In Vivo:** Genes are directly transferred into live animals. While this approach has potential, it poses higher risks and technical challenges compared to in vitro methods (Shakweer et al., 2023).

## Enzyme Dysregulation and Disease

Mutations in the genes that control the biosynthesis, assembly, or activity of metabolic enzymes frequently lead to inherited metabolic diseases. Severe and even fatal metabolic deficits can result from these mutations' enzyme abnormalities (Marchetti et al., 2022). The metabolism process which breaks down macromolecules such as proteins, lipids, carbohydrates, and nucleic acids facilitates both anabolism and catabolism to create and storage of energy. In healthy cells, metabolic enzymes help a sequence of biochemical activities that when oxygen is present result in the production of ATP through mitochondrial respiration (Skulachev et al., 2023). These procedures either eliminate or recycle their byproducts. This equilibrium can be upset by mutations in metabolic enzymes or by changes in their expression levels (upregulation or downregulation) which can result in metabolic abnormalities and aid in the development of cancer (You et al., 2023).

## The Warburg Effect and Cancer Metabolism

In 1927, Otto Warburg was the first to describe the Warburg effect which known as aerobic glycolysis. He noticed that even when oxygen is present in cancer cells' cytoplasmic glucose metabolism is changed and turning glucose into lactate (Kocianova et al., 2022). By consuming a lot of energy and incorporating nutrients into biomass, this adaptation helps cancer cells survive and proliferate. While aerobic glycolysis is a characteristic of cancer metabolism, oxidative phosphorylation has also been linked to the development of cancer (Zhang et al., 2023).

## Cancer and Metabolic Reprogramming

Metabolic reprogramming is a characteristic of carcinogenesis, tumour growth, and treatment resistance which occurs in cancer cells. The genetic context and tumour microenvironment (TME) have an impact on this rewiring (Yuan et al., 2024). Because on cometabolites function as signaling molecules that control gene expression and encourage tumor growth and they can accumulate as a result of enzymatic deficits (Lagunas-Rangel et al., 2024).

## Key Roles of Metabolic Enzymes in Cancer

Pathways essential to the growth and survival of cancer cells are activated by the overexpression or downregulation of metabolic enzymes. These enzymes support tumor growth and guard against nutritional deprivation. But whether disruption of metabolic enzymes causes or results from cancer (Kumar et al., 2022).

## Future Directions in Enzyme Research

The field of food science has advanced from traditional methods of food enhancement lie mechanically manipulating food components, to sophisticated, high-tech food design and manufacturing due to a result of the rapid advancements in biological sciences and food technology. The future of food production will rely heavily on advancements in synthetic biology, artificial intelligence, and additive manufacturing, with the goal of making food healthier, more nutritious, and tastier (McClements et al., 2021).

Future food production using cell culture has the potential to significantly reduce greenhouse gas emissions by 87%, slash water use by over 90%, and boost land efficiency by up to 1000 times compared to traditional food sectors. Compared to traditional meat production, and foods like culture meat whether plant-based or cell-cultured which offer a number of advantages, including advantages for the environment, nutrition, safety, and health (Hadi and Brightwell, 2021). Prominent biotech firms are Memphis Meats, Beyond Meat, and Impossible Foods are making significant investments to create and market artificial meat and other cutting-edge culinary items (Kim et al., 2025).

For food processing, creating effective methods is essential to maximizing the texture, flavour, and nutritional profile of culture meat (Hossain et al., 2024). Enzyme-based technologies have become a vital tool in this field since they are non-toxic and environmentally benign while also cutting down on processing time, material prices, and energy use. In order to improve food texture, glutamine transaminase (TGase) and proteases have been optimized to change cross-linking and lower allergies. In addition to improving the nutritional content and processing efficiency of raw materials, enzymes are now utilized to provide individualized solutions for food flavor profiles (Pang et al., 2021).

## Conclusion

Enzymes catalyze crucial metabolic events to provide a deep disease causes understanding by the intersection of animal health and the biological sciences. Their accuracy possesses a variety of functions in catalysis to highlight how essential they are to preserving metabolic balance and for focused therapeutic and diagnostic uses. Enzyme technology has been becoming more and more significant to animal nutrition and global food security which is seen by developments in feed formulations and recombinant protein manufacturing. However, scientists are finding out the underlying causes of enzyme dysregulation causes in order to improve animal health and mitigate illness.

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# Zoonotic Diseases and Their Impact on Public Health: Prevention and Control Strategies

02

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## ABSTRACT

Zoonotic diseases that spread from vertebrate animals to humans produce a significant threat to global public health. These diseases which originate from numerous microorganisms such as bacteria, viruses, fungi and parasites account for 60% of all recognized infectious diseases. They can be transmitted through direct interaction with infected animals, insect carriers, spoiled food or water, and through the air. Factors like environmental alteration, disforestation, globalization, and increased contact between humans and animals increased the risk of zoonotic spillover and leading to the emergence of new illnesses. Substantial outbreaks, including coronavirus disease, Ebola virus disease, and avian influenza, demonstrates the impact of zoonoses on health organizations and global economies. The one health approach which integrates human, animal, and environmental health, is crucial in stopping and managing these diseases. Important policies include vaccination plans for both humans and animals, enhance biosecurity, food safety measures, and early detection systems via surveillance networks. Furthermore, vector control, public health education, and international collaboration further enhance prevention efforts. New tools such as genomic investigation, risk mapping, and machine learning algorithms known as predictive models offer methods for early warning and adapted response strategies. Additionally, evaluations of the economy highlight the cost-effectiveness of preventive actions compared to reactive methods. By integrating scientific information, promoting cross-sector collaboration, and implementing proactive policies, threats posed by zoonotic diseases can be effectively mitigated. Continuing these coordinated efforts is vital for global health maintenance and for reducing the likelihood of future pandemics.

**KEYWORDS**
Zoonotic diseases, One health, Emerging infectious diseases, Disease surveillance, Vector-borne transmission, Public health strategies.

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## 1. INTRODUCTION

Humans always contact with animals in some way. A zoonotic disease is illness or inflammation that can be transferred from vertebrate animals to humans and from humans to vertebrate animals in a natural way. The percentage of zoonotic human pathogens are more than 60%. This comprises of broad diversity of viruses, bacteria, parasites, fungi, protozoa and other pathogens. Factors that are considerably impact the arrival, revival, dispersal and pattern of zoonoses are climate alteration, development, animal relocation and trade, travel and exploration, and natural factors. Over time, there are many arrival and revival zoonotic diseases (Rahman et al., 2020).

One Health is a multidisciplinary approach for studying public health issues affecting humans, animals, and their environments. This is achieved through implementing specially designed programs and research activities that contain multiple sectors. One Health recognizes that the health of humans is closely tied to the health of animals and the environment, and vice versa. The One Health action framework contain five distinct pillars: food safety, the bond between humans and animals, antimicrobial resistance, water contamination, and zoonoses. A key requirement for establishing and running a One Health platform is the progress of an interdisciplinary team of public health specialists, including medical doctors, biologists, veterinarians, ecologists and public health administrate (Horefti, 2023).

### i. Historical Significance and Major Outbreaks

Animal hosts connected to zoonotic diseases have a remarkably varied scope. These hosts include both wild and domestic animals, which can lead to foodborne zoonoses. Monitoring animal pathogens is a key focus of public health strategies to confirm their presence. Natural reservoirs or viral zoonoses include bats, which have recently been shown to be a major host in the case of COVID-19, a pandemic that has had a profound global impact. Research has revealed that bats are the primary host in this instance. In Iran, a total of nineteen zoonoses cases involving camels have been reported, with camels having close contact with farmers and being susceptible to TB, rabies, plague, Middle East respiratory syndrome, and Q fever. Birds are the main reservoir for the Influenza A virus (Recht et al., 2020).

### ii. Role of Zoonoses in Global Public Health

One health important part is supervision and monitoring systems that start early identification and fast response to zoonotic diseases. These systems gave necessary data for controlling outbreaks and safety of both human and animal populations. In animal early detections of germs can prevent spillover events that cause significant infections like yellow fever, Ebola. The framework of one health demonstrated that interlinked health of humans, plants, animals, ecosystems identified the risk occurred by alteration of climate, destruction of habitat, and agricultural practices that lead to reverse zoonosis from that disease transferred from humans to animals. For the disease transmission reduction vaccination and WASH type prevention strategies employed. For community practices improvement educational efforts done that consisting of training, awareness campaign that are necessary to close knowledge gaps mainly in rural areas (Ahmed et al., 2025).

Over time many collaborative efforts have been made to decrease zoonotic diseases and to address global threats by global organizations such as the FAO, WHO and OIE. These actions are a part of One health approach which involves and connects animals, humans and environmental health (Anderson et al., 2010). One of the most remarkable collaborations is the Tripartite Zoonoses Guide (TZG) which was published in year 2019. The guide gave instructions and methods about maintaining a multi sectoral coordination for management of zoonotic diseases in many countries. Another significant initiative is the Global Early Warning System (GLEWS), which was established to share and detect zoonotic threats before time. This collaboration involves data and warnings from WHO, OIE and FAO to help create a fast global response. For monitoring of avian influenza in animals and timely updates related vaccine strains a joint platform of FAO and OIE collaborates with WHO named as the OFFLU Network. This collaboration became more significant during the H5N1 and H7N9 outbreaks (Dauphin, 2015).

### iii. Prevention and Control Strategies

For the precaution and control of zoonotic diseases describe an essential risk for public health systems, because of dual effect on both human and public health. The requirement of productive control is strong relation between medical and veterinary parts. It may be ineffective and costly if the source of infection in animals is not addressed. For instance, in places where rabies is regular, just giving people medicine after they're exposed to post-exposure prophylaxis isn't as productive as collaborating it with large scale dog vaccination. A complete strategy of prevention consisting of vaccination, laboratory experiments, control of population, and combined surveillance systems. For instance, some zoonoses may affect animals mostly rather than humans. Increasing surveillance of disease, outbreak response and laboratory diagnostics can advantage multiple infections (Shiferaw et al., 2017).

For the prevention and control of zoonotic diseases, which pose a significant threat to public health systems, a strong relationship between medical and veterinary aspects is crucial. Failing to address the source of infection in animals can be ineffective and costly. Like in areas where rabies is prevalent, simply treating individuals with post-exposure prophylaxis is less effective than combining it with large-scale dog vaccination. Enhancing surveillance, outbreak response, and laboratory diagnostics can help in the control of multiple infections. Travelers visiting endemic areas should take adequate precautions against prevalent diseases (Sadhukhan, 2022).

## 2. Classification of Zoonotic Diseases

### i. Bacterial Zoonoses

The zoonotic bacterial diseases can transmit from animals to humans in many methods. The transmission may form through scratches and bites of animal. Zoonotic bacteria came from food animals that attain humans through fecal oral route, food products that contaminated by animals improper handling of food, and improper cooking (Cantas & Suer, 2014). Bacterial zoonotic disease such as Leptospirosis is a worldwide issue, but it occurs most frequently in tropical and subtropical environments. It is estimated that over 10 million cases occur each year globally, resulting in significant morbidity and mortality. The burden of disease is highest in the Caribbean, Central and South America, South-East Asia, Oceania, India, South Asia, and Eastern Europe. Although well-validated global data on leptospirosis are lacking, the estimated global annual incidence in temperate regions is 0.1–1 case per 100,000 population, while the incidence in tropical climates exceeds 10 cases per 100,000 population. (Chikeka & Dumler, 2015).

### ii. Viral Zoonoses

After bacterial zoonotic diseases, viral zoonotic disease also represents necessary problems of public health across the globe. Most of the viral zoonoses are classified as emerging infectious diseases because they are newly detected or shown alterations in epidemiological characteristics. Most of viral zoonoses have limited host ranges, while others may attack a broad range of vertebrates. Viral zoonoses transmission occur through many routes. They consisted of direct contact like rabies virus, indirect contact like hantavirus, nosocomial contact like Ebola virus, aerosol transmission like severe acute respiratory syndrome coronavirus 2 and vertical transmission like Zika virus (Reed, 2018).

For instance, the virus appears to have been circulating in Australian flying foxes for a long time, the first detection of HeV emergence was in 1994. In two independent spillover events, this previously unknown paramyxovirus claimed the lives of 15 horses and two humans who had close contact with infected horses. Over the last few years, the incidence of HeV spillover events in Australia has drastically increased, peaking in 2011 with 18 independent outbreaks in horses in Queensland and New South Wales. In total, 89 horses have died of HeV infection from 49 independent spillovers. Out of seven human infections, four were fatal (Wang & Crameri, 2014).

### iii. Parasitic Zoonoses

Zoonotic parasitic diseases are also transmitted throughout the world, and simultaneously linked with foodborne infections and bites of insects. Newly identified zoonotic disease in humans is sarcocystic species. In human myositis caused by sarcocystosis. The major recognized zoonotic parasite is *Trypanosoma* that cause disease burden like sleeping sickness in sub-Saharan Africa and Chagas disease in America. *Trypanosoma evanis* was first case of human disease in India. Another emerging parasitic zoonotic disease in Europe is dirofilariasis. For monitoring of emerging parasitic zoonoses global surveillance should be employed (Fong & Fong, 2017).

## 3. Mechanisms of Transmission

The essential pathways for transmission of emerging zoonoses are vector borne and aerosol droplet transmission pathway. Pathogens emerged from wildlife is essential to understand the ways of transmission (Fig. 1). Because pathogens with distinct pathways of transmission may have distinct treatment and control technique, understanding the essentiality of each pathway (Loh et al., 2015).

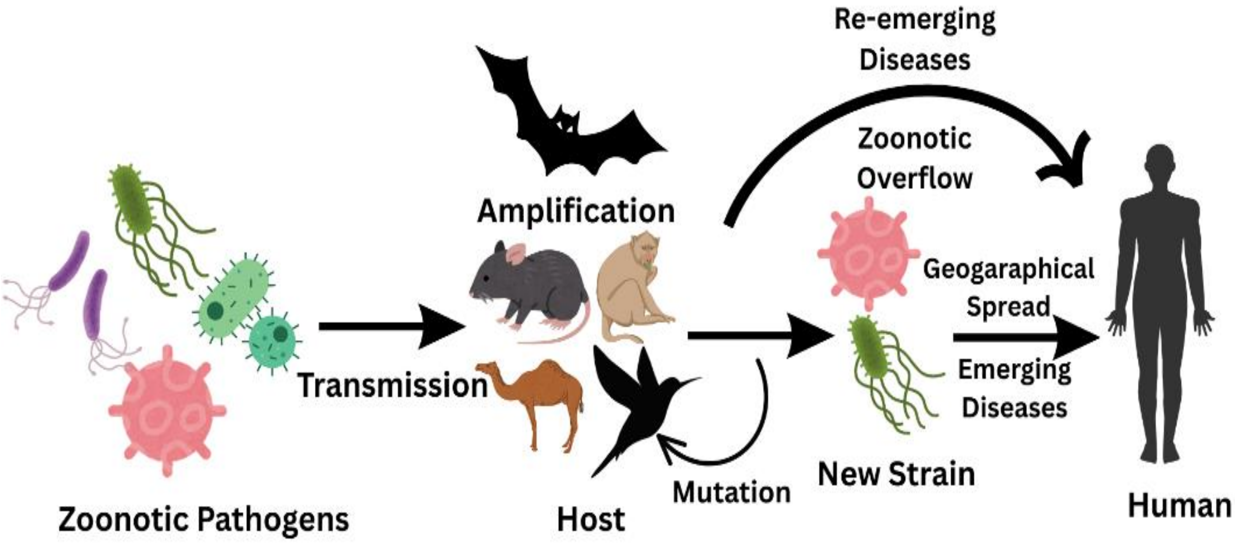

**Fig. 1:** Role of Wildlife in the Transmission of Emerging and Re-Emerging Zoonotic Diseases (Retrieved from Canva Pro).

### i. Direct Contact Transmission

Sixty percent of all human diseases are zoonotic diseases that transferred from vertebrate animals to humans. Livestock linked with infectious diseases are major harm to human health. In agriculture sector large economic loss is due to zoonotic disease occurrence. Contact with livestock animals result in the transfer of pathogens by ingestion, inhalation also during incidents like animals biting and other injuries. From respiratory and fluid sources aerosols contamination with pathogens play essential role in the spreading of microorganisms between humans, although from animals to humans (Klous et al., 2016).

### ii. Vector-Borne Transmission

Vector borne zoonoses is infection that occurred by microorganisms that affect humans and animals. An abundance of vectors like ticks, mosquitoes, flies, fleas, bugs and lice may transfer several bacteria, viruses, helminths and protozoa to animals and humans. The load of vector borne transmission still substantial in poor rural areas (Dantas-Torres & Otranto, 2022). Zoonotic essentiality vector borne diseases are the global risk in life of human and on animal welfare also. Local emergence of vector borne pathogens is commonly introduced by alteration in ecology, changing in behavior of human, increase enzootic cycles, pathogens employed from trade and travel of anthropogenic, and genomic alteration of pathogens. One pathogen confirmed, environmental factors related to host and vector features can shape development selective burden and results in increased use of people as hosts transmission. The best vector borne zoonotic pathogens are West Nile virus and Nipah virus (Khan, 2015).

### iii. Foodborne and Waterborne Transmission

Diarrheal diseases are caused by foodborne and waterborne pathogens that are major cause of illness and death in least developed countries. Although in the developed countries it is identified that population are affected by foodborne pathogens each year. It is identified that it occurred due to alteration in animal production systems and in chain of food production (Schlundt et al., 2004).

Zoonotic diseases have a significant impact on human health and the economy, particularly in the agricultural sector, where direct contact with livestock can lead to the transmission of pathogens through ingestion, inhalation, or injuries such as bites. Additionally, vector-borne transmission involves insects like ticks, mosquitoes, and fleas that spread a wide range of pathogens increasing the risk of their emergence and transmission. Foodborne and waterborne transmission is also a major concern, especially in developing regions, causing widespread diarrheal diseases due to changes in animal production and food supply chains. Together, these transmission routes highlight the complex and multifaceted ways zoonotic diseases spread, underscoring the need for integrated control strategies across environmental, animal, and human health sectors.

## 4. Epidemiological Impact on Public Health

### i. Disease Burden and Global Health Statistics

Zoonotic diseases establish large number of emerging infections, many of which are mistreated in global health significances. These diseases effect both public and animal health areas, complicating their organization. Neglected zoonotic disease global burden remains scattered. They should be united into global infection burden assessments for a more precise understanding of their effect (Di Bari et al., 2023).

### ii. Zoonotic Spillover and Emerging Infectious Diseases

Zoonotic spillover is defined as that the transmission of microorganisms from wild animals to humans. Most of the human contagious diseases are obtained from pathogens that originally spread in non human animal species. This revealed that spillover has a essential role in the emergence of human contagious diseases. By knowing those factors that facilitate the spread of microorganisms from wild animals to humans is necessary to form strategies that focused on the spillover events frequency reduction (Ellwanger & Chies, 2018). COVID-19 is an infectious disease posing a massive challenge to global health, which will likely persist until an effective vaccine is found or herd immunity is achieved. Until effective vaccines are available for a significant proportion of the global population, public health measures such as social distancing, isolation, and quarantine are necessary to prevent the spread of the virus. The WHO recommends protective measures such as frequent hand washing, avoiding contact with eyes, nose, or mouth, maintaining a distance of at least 1 m between people, and practicing respiratory hygiene to help prevent the spread of the disease (Chowdhury & Oommen, 2020).

### iii. Economic Consequences of Zoonotic Outbreaks

These diseases are classified into 3 categories of economic impact that are high, moderate and low. This can happen when a microorganism has potential of zoonotic crosses over into humans when that normally does not happen even if they have potential to occur. Ther is data about methods aspects used in elimination or disease rejection. The gathered data of information is introduced when it is beneficial in order to better understand the implications of economy of disease. Once there iss better understanding of economic impact potential of a zoonoses incursion it becomes necessary to check the prevention and control stategies costs and benefits (Miller & Parent, 2012).

## 5. Prevention Strategies

Emerging contagious diseases have their animal source, and at human animal interface emergence happens, when infections in animals rupture the species hurdle to infect humans, they are initially identified in the population. The reaction is often emergency occupation series to hold and control the infection in human populations and confirm the infection source in nature at a same time. Medicine sectors of animal and human are currently working toward contacting more closely at interface of human-animal through risk assessment and joint surveillance. It should be much cost effective simultaneously to learn from emergence events of past and to transfer pattern from surveillance of disease, identification, and human response to prevention of disease by understanding and reduce the factors or determinants that influence infection of animal. Determinants are understood clearly from old emergence events study and consisting of human induced alteration in natural environment, agriculture systems, urban areas and animal-based foods processing and roles of global trade, movement and climate alteration (Fig. 2). Better consideration of these features increased from investigation of past epidemiology and present emergence actions, modeling and study of interventions cost effectiveness that could consequences in their mitigation, could gave evidence essential to better report the economic and political hurdles to prevention of animals infection (Heymann & Dixon, 2013).

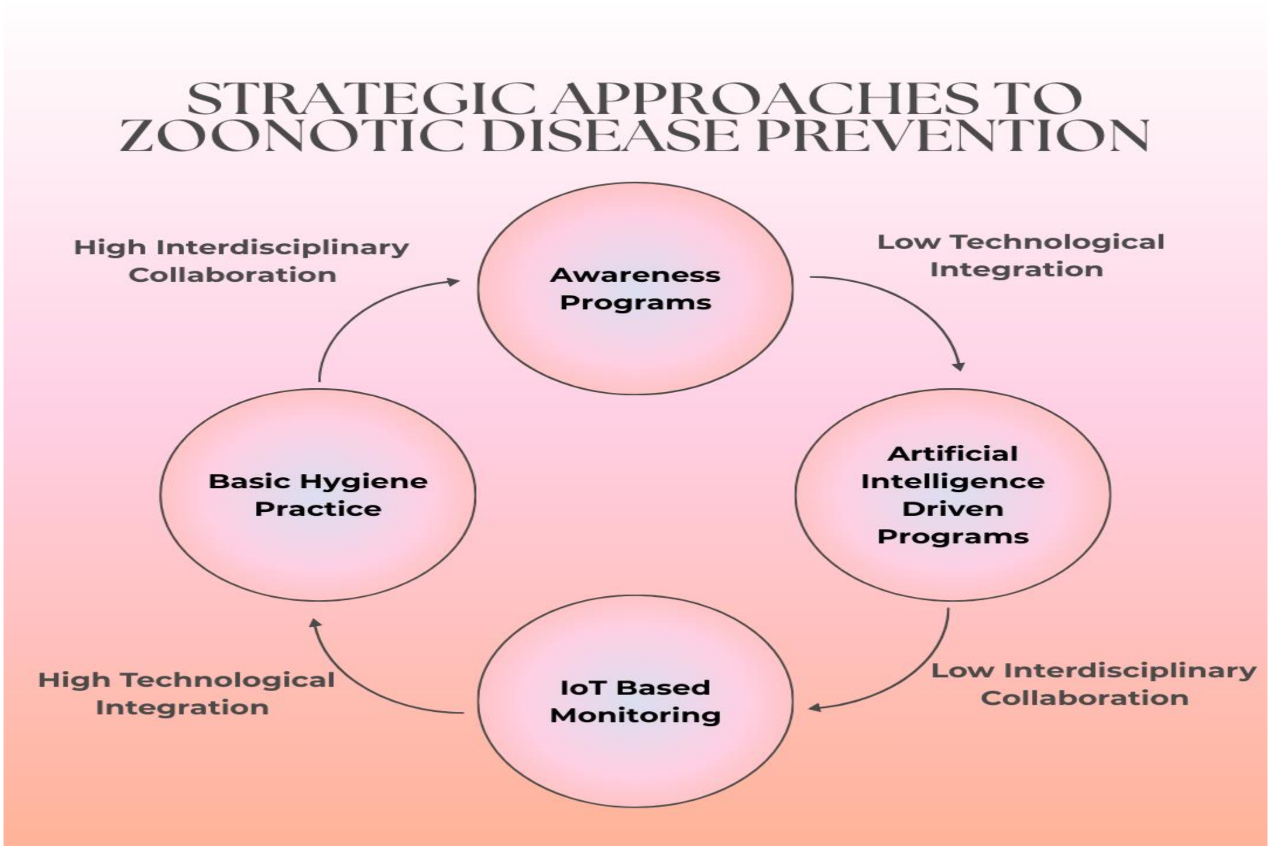

**Fig. 2:** Integrated Strategies for Zoonotic Disease Prevention Through Collaboration and Technological Advancements (Retrieved from Canva Pro).

### i. Vaccination Programs for Animals and Humans

Vaccines are essential for the control and prevention of zoonotic contagious diseases in humans and domesticated animals. The purpose of vaccination in almost all cases is to prevent human diseases indirectly by immunizing companion and domesticated animal disease sources. The technique of immunizing reservoirs of wild animal for diseases prevention in humans or animals is more stimulating and received limited number of attentions. Although biopharmaceutical industry health divisions of human and animal are generally separate and isolated, and there is no planned method for new vaccines development showing for the prevention of disease spread from wild or domestic animals to humans. Many animal diseases are transferred to humans for which animal vaccination is not possible using currently available techniques, due to complex disease ecology, a method of numerous wild animal species in cycles of transmission and access difficulty to the host. The successful and practical method for those diseases is immunization of human. For instance, yellow fever that attained from mosquitoes that are infected by wild monkeys, hantavirus infection that developed through direct and indirect contact with rodents, and Ebola Marburg, and unembellished respiratory coronavirus infections that attained from contact with bats or hosts of animal that infected through bats (Monath, 2013).

### ii. Biosecurity Measures in Livestock and Wildlife Management

Globalization showed higher trade in livestock and products of livestock, which accounts for almost partial of global agricultural economy. The improved trade has also resulted in increased in infection risk to human and livestock. The essentiality of zoonotic and other conagious diseases greater incidence are crack in livestock management biosecurity, closer contact between humans and wildlife and nurture of close association of poultry and livestock with people. The plan of farm biosecurity contains assessment of risk and careful planning to lead the targeted risks. Infectious diseases with highest risk should be arranged and practices should be done to check the disease transmission. A biosecurity plan revealed esssential issues consisting of location and farm layout, animal health observes, and farm management system. An active biosecurity plan should be elastic and exposed to new techniques and methods. A broad variety of biosecurity observes has been suggested for distinct species of livestock and production management either for general prevention of disease, or specific contamination risks (Manuja et al., 2014).

### iii. Surveillance and Early Detection Systems

Zoonoses surveillance is essential multi-disciplinary attempt, passage not only health of human and animal, environmental strength and public health training and strategy. The organized roles of farming animals, pets, population of human and atmosphere for transmission and pathogenesis of zoonotic diseases formed a number of different surveillance challenges. Data is desired on how good to assembly these interdiscilinary investigation efforts (Vrbova et al., 2010).

### iv. One Health Perspective on Zoonotic Disease Control

Most of the zoonoses can cause frequent outbreaks, however others may cause latent pandemics worldwide and have been stated public health crisis of worldwide concern by WHO. Due to world interrelation, the risk of certain infection somewhere is a risk everywhere. The high hazard of spillover and burden of emerging and re-emerging infectious diseases has been enlarged by the general contact among animals, humans and environments because of livestock and human population exponential growth fast increasing urbanization and farming management alteration, close contact between domestic animals and wildlife associated by forest invasion, destruction of habitat and alterations in ecosystem, globalization in the trade of animal and products of animals, AMR, and climate altering. Land practice alteration because of inappropriate use and misuse of natural resources, although with the climate deviations effects like flood, deficiency, fire in forests and effect of heat island have linked to serious ruin and devastation of whole ecosystems. In comparison, habitat of wildlife disintegration due to organization development, urbanization and unregulated misuse associated through widespread hunting, consumption and trade that take part in reduction of biodiversity, increasing vector of disease and interaction with host and worsening infection spillover diagonally both wild and domestic animals and humans. Environmental pollution has also enabled the transmission of disease via water, soil and air. Additionally foodborne microorganisms like viruses, bacteria and parasites have enlarged the disease worldwide weight. Contaminated food consumption causes food borne disease and death of six-hundred and 400,000 people each year respectively. Animal origin, vegetables, fruits and contaminated water is the cause of foodborne disease. However, safety of food should be guaranteed through an cohesive multi-disciplinary method (Shrestha et al., 2018).

## 6. Control and Containment Measures

The most extensive method for the control for zoonotic diseases has been the large-scale scrapping of individuals of wildlife reservoir or pathogen intermediate host. For instance, to control the vectors of arthropod and annoyance parasites population culling is use. Host populations wildlife reservoir culling has been accepted and planned to restrain transmission of numerous bacterial and viral pathogens to humans and trained livestock, along with decrease population record as better strategy of prevention to bound human spillover. The second main approach to zoonotic micro-organisms control is vaccination of wildlife population and intermediate hosts. In future, immune preventive could be worn as an ethically approved alternative to wildlife species culling critical to maintenance of zoonotic pathogens. There are also applied restrictions to culling for example culling by hunting can be hard when certain species lives in closed environment of human population. For instance, a complex situation that bounds control of population options is the situation of white-tailed deer, which voluntarily populate suburban areas (Childs & Gordon, 2009).

### i. Vector Control and Habitat Management

Vector control is the principal technique accessible for controlling numerous vector borne diseases. Furthermore, for some diseases like dengue, west nile vector control is only technique that used for the protection of population. The goal of vector control is to bound the spread of pathogens by decline or eradicating contact of human with vector. Extensive range of vector control tools present, which can be widely categaroized into chemical and non chemical based apparatus. Tools attack undeveloped vectors can perform by killing the undeveloped stages or by eradicating appropriate aquatic habitats like habitat alteration and management. Tools attacked the function of adult vectors by killing them and falling contact of vector with reservior hosts of human and animal. There are also numerous novel vector control tools under process like mosquitoes genetic management, vectors bacterial illness and eave tubes of treated insecticide (Wilson et al., 2020).

### ii. Zoonoses Education and Public Health Resilience

Zoonotic diseases execute a massive burden on the global healthcare systems. The expenses related with control, analysis, treatment and defensive measures might be great. The regulatory magnitude of this burden consisting of expenditure on monitoring, investigation, public health inventiveness, the organization of healthcare systems and treatment and vaccinations development. Direct medical expenditures are only aspect of impact on economy. Zoonotic illness waves can cause disturbance in economy by decline output of agriculture, forming lost workdays, and reducing productivity. For example, zoonotic disease waves in livestock can cause many losses for farmers financially, adjust their security of food and livelihoods. Expenses associated with measures of public health response, like isolation, monitoring management and communication campaigns to endorse measures of prevention, also include burden of economy. A complete plan that consists of preventive measures, primary identification, active treatment and supportive efforts between health departments of human and animal must be employes to show the zoonotic disease financial burden. For quick identification and response to outbreaks of zoonotic disease, it is necessary to participate in research, surveillance and organization of public health. This will eventually moderate the financial weight on healthcare structures and societies throughout the world. Administrations, public health systems and organizations of healthcare may assign possession and formed policies to avoid, identify and successfully respond to those illness by recognizing the most important public health significances and financial weight of zoonotic diseases (Saleem et al.).

### iii. Legal and Regulatory Frameworks

Administration and international organizations need to better be identified the wide and interlinked factors associated with arrival and repetition of zoonotic diseases consisting of all natural habitat invasions, especially deforestation and fast urbanization, farmed and wild animals commercial trade and activities of human that increase and spread risk of disease like pollution of environment, inadequate vaccine usage and antimicrobials and movement of global population. Methods to date have intensive on secondary prevention that prevention of outbreaks from rising into an epidemic or pandemic, instead of primary prevention that measures the outbreak arrival prevention through active actions before the process of disease start. That consisting of human activities regulation contribution to risk of disease and reduced exposures of risk (Lee, 2022).

The global community has long recognized the need for international collaboration and governance to contain the spread of infectious diseases. In 1951, the WHO adopted the existing conventions and related agreements as the International Sanitary Regulations, which became binding on WHO member states. In 1969, the regulations were revised and renamed the International Health Regulations. The International Health Regulations of 1969, with only minor changes over several decades, aimed to strengthen the use of epidemiological principles as applied internationally, to detect, to improve sanitation in and around ports and airports, to prevent the dissemination of vectors, and, in general, to encourage epidemiological activities on the national level so that there is little risk of outside infection establishing itself. The regulations themselves, however, focused tightly on the control of a short list of diseases. While the agreement encouraged epidemiologic activities, the only obligations lay in the capacity to report specific diseases such as cholera to the WHO and maintain minimal public health capabilities at ports and borders (Katz & Fischer, 2010).

## 7. Challenges and Future Directions

A foremost hurdle is the partial collaboration of multisectoral among human, wildlife, animals, and food safety departments, which delays surveillance integration and sharing of data and response coordination at animal-human boundary, mainly for emerging diseases like influenza and Middle East respiratory syndrome coronavirus. Moreover, eradication hard works are deliberated by inappropriate coverage of vaccine for diseases like rabies and brucellosis, which are avoidable through strategic measures of public health and control of animal. Gaps in surveillance, low awareness in public, and incomplete research moreover complex the disease management like Crimean-Congo hemorrhagic fever, foodborne diseases and toxoplasmosis. Furthermore, national programs organization lack, poor waste administration, and imperfect diagnostic abilities worsen the risk (Fig. 3). To report these difficulties, it is essential to adopt an approach of One Health, increased coordination between intersectoral, enhanced systems of surveillance, strengthen education of public, employed evidence depend measures of control, create a natural mission force for elimination of zoonotic disease with effectively monitoring at both governorate and national levels (Awaidy & Al Hashami, 2020).

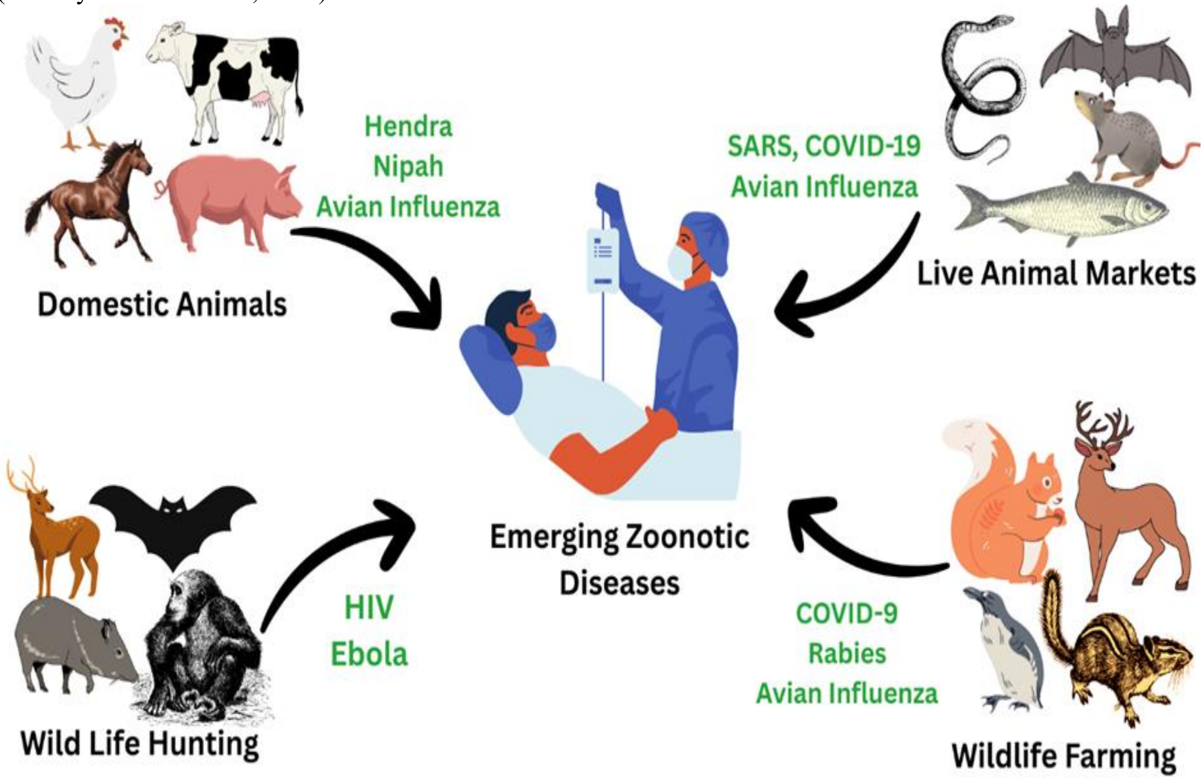

**Fig. 3:** Examples of Zoonotic Diseases Transmitted Through Direct Contact with Animals, During handling, Farming, or Bites. Highlighted Diseases Include Rabies, Nipah, Avian Influenza, and Ebola. (Retrieved from Canva Pro).

### i. Emerging and Re-emerging Threats

Increased of illness in incidence during past two periods or expected to greater in the adjacent future is commonly known as emerging diseases. Emerging and re-emerging diseases are on increasing movement and have been risk to human till date. Mainly of the zoonotic nature emerging and re-emerging diseases reported since past three era chiefly on viral basis. The main reason of these emerging and re-emerging diseases is not clear; there are most of the features are involved in their formation. These features are complicated in nature and classified into infectious origin factors like bacteria, virus, prion, human and ecological features (Saba & Balwan, 2021).

Monkeypox (Mpox) is a contagious illness caused by the monkeypox virus, which is part of the same family of viruses as variola, vaccinia, and cowpox. It was first detected in the Democratic Republic of the Congo in 1970 and has since caused sporadic cases and outbreaks in a few countries in West and Central Africa. In July 2022, the WHO declared a public-health emergency of international concern due to the unprecedented global spread of the disease. Treatments are available once the illness has taken hold. During the 2022 outbreak, most cases occurred among men who had sex with men, and there was a range of 7–10 days between exposure and the onset of symptoms (Srivastava et al., 2023).

The recent reemergence of Nipah virus, belonging to the family Paramyxoviridae, caused 17 case fatalities among the 19 infected patients (89% mortality) in South India. The outbreak has drawn immense global attention and underlines the need for adequate preparedness in the event of such episodes resurging in the future. The possibility of a new viral syndrome was actively considered in view of the unusual unique clinical features, the unexpected rapid deterioration, and clustering of the cases. After the initial Nipah virus outbreak in Malaysia in 1998–1999, the spread had occurred to Singapore, and further epidemics have occurred later in Bangladesh (Kumar & Kumar, 2018).

## Conclusion

A zoonotic disease is a major and substantial and rising threat to global health. Zoonotic diseases are illness or inflammation that can be transferred in a natural way from animals to humans and from humans to animals. They account for concluded 60% of all identified human diseases. Numerous features affect the spread of these infections such as climate alternation, animal trade, movement and close interconnection between human and animals. To efficiently handle these diseases, organized plan is required. These plans are organized by One Health which unites professionals in human health, animal health and environmental science. To avoid and handle zoonotic diseases numerous steps are involved like vaccination of both human and animals, increasing hygiene measures and guaranteeing animal health. Moreover, controlling the population of insect such as ticks and mosquitoes, and ensuring food and water safety can also be beneficial in treating and controlling zoonotic diseases. Public awareness concerning these illness and health employers training also plays essential role in reducing their transmission. Outbreaks of zoonotic diseases can poorly affect public health as well as economy. These outbreaks also associate with infection, mortality and economic setbacks, mainly in cultivation and production of food. It is necessary for administration, researchers and healthcare experts to team up in controlling future outbreaks. To control these infections various steps can be helpful such as sharing important information, increasing health departments and taking active measures as issues rise. Planning of active measures to stop this illness from transmitting will be taken seriously. Outstanding the necessity for more responses after outbreaks is a crucial step for public safety.

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# One Health Strategies for Preventing Antimicrobial-Resistant Infections: Linking Livestock, Environment, and Human Health

03

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## ABSTRACT

Antimicrobial resistance (AMR) is gaining importance globally as a critical health issue. It has a significant impact on humans, animals, and the environment. Due to its complex and interconnected nature, tackling it required more than individual efforts from different sectors. This chapter explores the One Health approach as a comprehensive framework that brings together human health, veterinary medicine, agriculture, and environmental management to control the AMR issue through collaborative efforts. It highlights the main drivers and transmission routes of resistance, emphasizing the role of poor stewardship, environmental contamination, and unregulated antibiotic use. The chapter also presents various practical, cross-sector strategies, including antimicrobial stewardship, infection prevention, environmental interventions, public awareness, and improved policy and regulation to combat this challenge. Special attention is given to the role of community involvement and the behavioural and social determinants responsible for antibiotics misuse, particularly in low and middle-income countries. It also underscores the pressing need for more research and robust surveillance systems to gain a deeper understanding of the problem's full scope. However, the One Health approach offers a practical and equitable solution to protect the effectiveness of antibiotics and reduce the burden of growing threat of antibiotic-resistant infections across people, animals and the environment.

**KEYWORDS**
Antimicrobial resistance (AMR), Antibiotic stewardship, One Health, AMR surveillance, Environmental interventions, Veterinary medicine, Public health, Community engagement, AMR surveillance

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## INTRODUCTION

Antimicrobial resistance (AMR) poses a serious threat to public health, animals, and the environment. Infections are becoming difficult to treat, or even impossible to treat in some conditions (Msemakweli et al., 2024). Clinics and hospitals are not the only places affected; food security, agricultural production, ecosystems, and the global economy are all equally impacted. If ignored and unchecked, AMR is expected to kill 10 million people annually by 2050, surpassing the death toll from cancer and leading to a global economic burden worth trillions of dollars (Msemakweli et al., 2024; Littmann et al., 2020).

The ability of microorganisms to develop resistance against different antimicrobials is a natural evolutionary change. However, the process has been accelerated by unregulated and irrational use of antibiotics not only in human medicine, but also in animal farming, agriculture and environmental practices (Samanta & Bandyopadhyay, 2019). The routine use of antibiotics in livestock for growth promotion and disease prevention has contributed significantly to the emergence of antibiotic-resistant strains. These resistant strains can spread between animals, humans and the environment, crossing both species barriers and geographical borders. These superbugs with resistant genes spread through soil, water systems, food chains, and direct human-animal contact (Hossein & Ripanda, 2025). There are several factors which play an important role in the dissemination of resistant bacteria, including poor infection control practices in healthcare and agricultural settings, improper wastewater treatment, and the regular cross-border travel of people and goods (Puvača et al., 2022).

Addressing this issue is not possible for any single sector because of its complexity. The One Health approach is practical solution to address this issue. Under One Health umbrella, specialists from different fields collaborate together, such as medicine, veterinary science, and environmental science, to overcome the gaps that often exist between these disciplines (Heim & Stärk, 2021).

This chapter discusses how One Health strategies can help prevent antimicrobial-resistant infections by connecting different sectors. It highlights the major strategies such as antimicrobial stewardship, infection control measures, environmental sanitation, surveillance systems, and alternative treatment options. It also emphasizes the importance of strong policy frameworks and the active involvement of the community.

## The One Health Approach: Bridging Human, Animal, and Environmental Health

The concept that human, animal and environmental health is closely interlinked is not new, but One Health has gained formal acknowledgement recently. The collaborative and integrated approaches are direly needed to control the spread of diseases and health risks (Promoting the Science of One Health, 2023).

Global organizations like World Health Organization (WHO), Food and Agriculture Organization (FAO), World Organization for Animal Health (WOAH), and United Nations Environment Programme (UNEP) describe One Health as “an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems.” These three areas are intricately linked; anything that has an effect on one will undoubtedly have an effect on the others. Reducing the use of antibiotics in animals, for instance, helps prevent antibiotic residue contamination in the environment and will benefit humans as well (Pitt & Gunn, 2024; Rai et al., 2024).

Outbreaks of zoonotic diseases such as SARS, avian influenza, and, more recently, COVID-19, have demonstrated over time how environmental and animal factors can have a direct impact on human health. These incidents serve as a reminder of how crucial the one health idea (Sharan et al., 2023). This relationship is further highlighted in the case of AMR since resistant bacteria are unable to distinguish between species or geographical boundaries. Antibiotic-resistant bacteria can move easily through food, water, close contact, and shared areas, among people, domestic animals, wildlife, and the environment (Martak et al., 2024).

The One Health policy is currently being adopted by health professionals globally to prevent and control antibiotic resistance. Coordinated measures based on the One Health approach have become increasingly important since the WHO's Global Action Plan on Antimicrobial Resistance (AMR) was introduced in 2015. More than 140 nations have created national action plans thus far, most of which are founded on the ideas of One Health. One Health promotes lasting solutions, like better waste management and diagnostics, over quick fixes (Pal et al., 2024).

## Key Factors Contributing to Antimicrobial Resistance Across Human, Animal, and Environment

Irrational antibiotic use in humans, animals, and the environment is a major contributor to the emergence and dissemination of resistance (Salam et al., 2023). Understanding the root cause of this issue across different sectors is essential to resolve this problem effectively.

### 1. Human Health Sector: Overuse and Misuse of Antibiotics

The availability of antibiotics without prescription is a common practice globally. Patients even take antibiotics for viral infections without proper diagnosis of causative agents, skip antibiotic doses, and do not complete their prescribed courses. These are the practices that facilitate the emergence of antibiotic resistance. In hospital, poor infection prevention and control (IPC) practices, including poor hand washing and improper sterilization of medical equipment, accelerate the emergence and dissemination of antibiotic-resistant organisms. In low-resource setups, limited availability of diagnostic tools often leads to prescription of empirical and broad-spectrum antibiotics, which is the major reason for increasing selective pressure on microbes promoting antimicrobial-resistance (Aslam et al., 2020).

### 2. Animal Health and Agriculture: Routine Antibiotic Use

Livestock and poultry sectors are major contributors to the AMR crisis. In intensive farming systems, antibiotics are commonly used not only for the purpose of treatment but also for enhancing growth and for prophylactic purposes (Nazeer et al.,2024). Such practices play important role to help bacteria to develop resistance against routinely used antibiotics, which can then spread to humans through various ways, including the usage of contaminated meat or dairy products, direct contact with animals or farm environment, and runoff from farms that pollute water sources. Aquaculture is also a major contributor due to direct use of antibiotics in water that can adversely affect aquatic species and water based-ecosystems (Naheed et al., 2025; Matheou et al., 2025).

### 3. Environmental Sector: The Silent Reservoir

The environment is playing a dual role in the AMR threat, acting as the reservoir and a pathway for the dissemination of AMR. There are multiple routes through which resistant bacteria enter the environment, including the release of untreated hospital and pharmaceutical waste, agricultural runoff that contains antibiotics and animal faeces, and careless disposal of leftover medications by households (Samreen et al., 2021).

These substances once entered the environment can stay in soil and water for a longer period and transfer resistant genes through horizontal gene transfer between different microbes. Additionally, wildlife and migratory birds can carry and spread the resistant bacteria across different areas and borders. Although wastewater treatment facilities play an important role in managing the waste but often unable to completely remove the antimicrobial residues and resistant genes (Sharma & Sharma, 2020).

A report published in 2024 by the European Environment Agency reported that antimicrobials that were mostly used in veterinary hospitals were found in samples of surface water from 12 countries. This highlighted the leakage of antibiotics from livestock to the environment (*Eighth Annual Report on Antimicrobial Agents Intended for Use in Animals*, 2024).

### 4. Globalization, Climate Change, and Mobility

International travel, food and animal trade, and climate change have a direct impact on AMR dynamics. When people frequently travel from one country to another, resistant pathogens get opportunity to spread rapidly across different countries. Climate change, such as an increase in temperatures, floods, and droughts, can change microbial communities and increase the use of antibiotics because of infections and lack of hygiene (Frost et al., 2019; Mohsin et al., 2020).

## Evidence of AMR Transmission Between Domains

Antimicrobial resistance (AMR) is not limited to a single setting. It circulates among humans, animals, and the environmental settings through various closely linked routes. Advances in molecular epidemiology, whole-genome sequencing, and environmental surveillance have made these transmission paths easier to explore (Ikhimiukor et al., 2022). The adoption of One Health perspective will help to trace and understand the mechanisms involved in resistance spread across species and systems.

### 1. Foodborne Transmission from Livestock to Humans

The food chain is one of the most common transmission pathways. Antibiotic-resistant Salmonella, Campylobacter, and *Escherichia coli* present in livestock can contaminate animal products, including meat, milk, or eggs, without preventive measures during slaughter or processing. These resistant pathogens spread to humans if food is not cooked or handled properly, and can make people sick (Rafiq et al., 2022). Unfortunately, multidrug-resistant *E. coli* strains that were isolated from poultry have been genetically similar to the strain found in human urinary tract infections. This is evidence that resistant bacteria can transfer from livestock to humans (Kazemnia et al., 2014).

### 2. Direct Contact and Occupational Exposure

Farmers, veterinarians, and pet owners are at high risk of acquiring resistant bacteria because these people remain in close contact with animals. For example, there are cases of livestock-associated MRSA (LA-MRSA) detection in pig farms worker and their family members. These bacteria can survive in the nose of humans without making them sick instantly, but later on they can cause serious infections due to immunosuppression and can spread to hospitals and clinics (Crespo-Piazuelo & Lawlor, 2021).

### 3. Environmental Spread via Water, Soil, and Air

Environment has a significant role in the dissemination of resistant bacteria and resistant genes. Antimicrobial residues and resistant organisms are present in the wastewater discharged from hospitals, pharmaceutical industries, and agricultural operations. If not treated properly, these contaminants can enter rivers, lakes, and be absorbed by soil in agricultural fields. Crops irrigated with such contaminated water can carry resistant bacteria and can spread them to consumers. Additionally, it has been identified that even the movement of air in and around animal farms and wastewater treatment plants can play an important role in the spread of resistant bacteria, highlighting another overlooked pathway in the transmission of resistance (Samreen et al., 2021).

### 4. Horizontal Gene Transfer Across Species

In bacteria, reproduction is not the only way to transfer resistant genes to other bacteria; however, bacteria can share resistant genes with different species through the mechanism of horizontal gene transfer (HGT). This process can take place in the gut of both animals and humans, in soil, and in water. Studies have detected plasmids with extended-spectrum beta-lactamase

(ESBL) genes in various sources, including livestock, wildlife, sewage, hospital and community samples, highlighting how prevalent and interconnected this problem has become (Vinayamohan et al., 2022).

### 5. Wildlife and Long-Distance Spread

Wildlife such as migratory birds, rodents, and insects also have a significant role in the transmission of AMR from one place to another. For example, Birds can pick up resistant bacteria from contaminated sites including, hospitals, industries and agriculture, as they travel long distances, they disseminate the resistant bacteria to different areas and regions becoming mobile reservoirs in the spread of resistance. The spread of resistance is not a straight path; instead it circulates continuously among different sectors. A resistant bacterial strain identified from agriculture may find its way into hospital, mutate and acquire new traits, and through untreated waste can re-enter the environment. These pathways make AMR a global threat which needs immediate attention (Li et al., 2024).

## One Health-Based Preventative Strategies

In order to effectively control the spread of antimicrobial resistance (AMR), the individual efforts are insufficient. There is an urgent need for systemic, interconnected strategies involving human health, animal health, agriculture, and environmental systems (Salam et al., 2023). Based on One Health strategies, the following preventative measures are not only needed to control the spread of resistance but will also help to identify the root cause of this serious issue to reduce its emergence and transmission.

### 1. Antimicrobial Stewardship in different Sectors

Antimicrobial stewardship (AMS) refers to the careful and responsible use of antibiotics so they can remain effective for a longer period. It is emphasized that antibiotics should be only used when prescribed, correct dose should be given and antibiotic course should be completed. In human health, stewardship programs promote strengthened diagnosis, reduce antibiotic usage in hospitals, and train doctors and medical staff to prescribe antibiotics more wisely. In veterinary medicine, stewardship includes banning antibiotics for growth promotion, improving disease diagnosis in animals to prescribe specific antibiotics, and encouraging vaccination to reduce the use of antibiotics and prevent infections (Arunkumar et al., 2025). Denmark introduced a "Yellow Card" system that monitors antibiotic use in farms. Farmers who exceed the permitted limit face penalties. This resulted in a noticeable reduction in antibiotic consumption in livestock. Implementation of this system reported significant reduction in antibiotic usage (Arunkumar et al., 2025).

### 2. Infection Prevention and Control (IPC)

The need for antibiotics can be reduced by making strategies to prevent infections for which antibiotics are needed. Infection prevention can be achieved by applying biosecurity protocols, including quarantining the new animals before introducing them to the herd, providing clean drinking water, ensuring a ventilation system, and preventing overcrowding of animals as mandatory protocols (Arunkumar et al., 2025). In hospital settings, infections can be prevented by doing proper sterilization of equipment and by washing hands regularly to maintain hand hygiene. Infected patients should always be kept separate, and continuous training of hospital staff should be conducted. Additionally, promoting hygiene, sanitation, and vaccination in communities can help to prevent both zoonotic and resistant infections (Zheng et al., 2023).

### 3. Surveillance and Monitoring Systems

The presence of effective surveillance system is very helpful for tracking antibiotic resistance patterns, informing policies decisions and enabling prompt action. Integrated surveillance systems WHO's GLASS and FAO's InFARM collects AMR and antibiotic use data from different sectors (Kumar et al., 2020). Techniques like Whole-genome sequencing (WGS) has been increasingly used to find out the major parameters responsible for resistance and pathways through which antibiotic resistance spreads (Waddington et al., 2022). National Action Plans (NAPs) are very important for controlling antibiotic resistance, but they work best when different ministries, including health, agriculture, environment collaborate and share progress (Munkholm et al., 2021). The TrACSS system is helping many countries to assess and improve their antimicrobial resistance-related work by promoting co-operation between different sectors and ensuring the alignment with international AMR strategies (Sabbatucci et al., 2024).

### 4. Promotion of Antibiotics Alternatives

The use of antibiotic alternatives, which could be helpful in health and productivity should be promoted to reduce the use of antibiotics. The vaccines could be used as alternative to reduce the risk of infection in humans and animals. To improve gut health and strengthened immune system, probiotics and prebiotics can be utilized (Nazeer et al., 2024). Some alternatives such as phage therapy, antimicrobial peptides (AMPs), and herbal products are still being researched. Improved genetics in livestock by doing selective breeding to produce disease-resistant organisms can also be helpful to reduce the use of antibiotics (Gupta & Sharma, 2022). In China*,* national plan made for the year 2022, it was decided to invest in vaccines for livestock and phage therapy research to limit the use of antibiotics and promote the use of alternatives to prevent the emergence of resistance (Yang et al., 2019).

### 5. Multisectoral Education and Training

Multisectoral education and training play a very crucial role in fighting against antimicrobial resistance in different fields of life. For example, proper training of farmers should be conducted so that they can learn about animal health, how to maintain hygiene to prevent infections, and what are the alternative ways are to prevent and control infections rather than giving animals antibiotics for prophylaxis and treatment purposes (McEwen & Collignon, 2018). Medical professionals should be trained about rational antibiotic prescription in order to avoid overuse and misuse, infection prevention and control measures, and advance diagnostic techniques so that antibiotics can be preserved for future use by following antibiotic stewardship principles. Public awareness can also play a significant role in preserving the effectiveness of antibiotics through campaigns regarding how the antibiotic misuse can be prevented, what is proper way of disposal of unused medicines, and how to maintain hygiene to prevent infections (Mendonca, 2023). These strategies are only effective when they are carried out together. Stewardship without infection prevention and control (IPC) strategies can reduce antibiotics misuse, but transmission of infections cannot be controlled. Responses are delayed when surveillance is carried out without action. One Health integrates these components into a cohesive, mutually supportive framework (Septimus, 2018).

## Environmental Interventions

Inside the AMR triangle, the environment is a mostly ignored component, although it functions both as a storage and as a transport system for resistant bacteria and genes. Untreated pharmaceutical effluents and animal waste runoff are some routes through which the environment is contaminated, creating a cycle of resistance that can affect both humans and animals. It follows that managing the environment is not optional; it is a basic requirement for the One Health approach to AMR prevention (Martak et al., 2024).

### 1. Wastewater Treatment and Sanitation Infrastructure

The discharge from hospitals, pharmaceutical industries and livestock farms pollutes the wastewater system due to high quantities of drug residues and resistant micro-organisms. Without proper treatment, contaminated wastewater is discharged into rivers, lakes, and agricultural canals, leading to spread of contamination and antibiotic resistance. To resolve these issues, there is a need to upgrade wastewater treatment plants (WWTPs) with advanced technologies such as UV radiation, membrane filtration or oxidation. These methods can remove the antibiotic residues and resistance genes. Moreover, pretreatment systems can be installed in pharmaceutical industries and hospitals to lessen the burden on municipal treatment systems. In rural and peri-rural areas, decentralized treatment systems can help to reduce the dissemination of antibiotic-resistant organisms in limited resource areas (Pei et al., 2019).

### 2. Regulation of Pharmaceutical and Chemical Waste

The waste from pharmaceutical industries is not monitored properly in many countries. In wastewater, even a very small amount of antibiotics can put selective pressure on microbes present in the environment. To tackle this problem, there is a need to set discharge limits for antibiotics and pharmaceutical ingredients in pharmaceutical waste. In case of new drugs, it should be mandatory to check impact on environment. If no harmful impact on the environment, then it should be approved and licensed. Moreover, adoption of the green chemistry method in pharmaceutical production can help to reduce the harmful impact of toxic chemicals on environment and minimize the ecological damage (Rayan, 2023).

### 3. Manure and Sludge Management

Animal waste is a rich source of resistant bacterial strains and unmetabolized antibiotics. It becomes a major source of AMR dissemination in the environment due to improper handling and its usage as fertilizer without proper treatment. Effective management skills are needed to reduce the impact on environment. Techniques, including composting and anaerobic digestion, can help to reduce the load of microorganisms and can also break down antibiotic residues. The timing and method of manure application are also very important (Lima et al., 2020). If injected deep, it can have less impact on resistance transmission than manure spread on the surface. The best strategy is to control the use of antibiotics in animals, which will ultimately control the amount of antibiotics and their residues in manure (Hilaire et al., 2022). Different studies proved that if manure is well composted, it will have less antibiotics and will be safe to use as compare to raw or liquid manure (Youngquist et al., 2016; Tien et al., 2017).

### 4. Environmental Surveillance and AMR Hotspots Mapping

The areas near wastewater treatment plants, animal production units and pharmaceutical industries act as hotspots for AMR. The regular tracking and mapping of these areas is something that is needed. Sampling should be done regularly from different sites, such as water, soil and sediment of hotspot areas to detect resistant bacteria (Nadeem et al., 2020). The use of modern techniques, including metagenomics, can help to get detailed information about the environmental resistome. Risk mapping tools are helpful to identify and prioritize the areas which are at high risk and also guide policymakers (Wang et al., 2020). A toolkit was introduced by WHO for environmental aspects of AMR, for countries developing National Action Plans under One Health (Glover & Naylor, 2023).

### 5. Sustainable Agriculture and Land Use Practices

Reducing environmental AMR is not only dependent on less use of antibiotics; it needs a shift towards sustainable land management. The integrated crop-livestock systems can decrease the dependency on chemical-based fertilizers. In addition to this, agroecological practices that are closer to natural farming promote diversity of microbial life that is helpful to limit the resistant organisms (Howe & Soupir, 2021). The establishment of buffer zones and vegetation strips near farms and water bodies can prevent surface water erosion and surface water overflow (Uusi-Kämppä & Yläranta, 2017). The environment is a leading contributor to the AMR crisis. The safety of the ecosystem from antimicrobial contamination will protect all species that rely on it for their survival.

## Policy and Governance Frameworks

Strong and legally bound regulations that coordinate actions in different sectors are needed to effectively prevent the spread of antimicrobial resistance. For the implementation of One Health strategies, governance structures are required at global, national, and local levels to provide the legal, financial, and institutional foundations. However, the practical implementation of policies is the biggest challenge in low and middle-income countries. Lack of resources and regulatory practice are the major reasons behind this failure.

### 1. Global Governance and Coordination

AMR is now strongly considered a threat at the global level for health security, food systems, and development. Many initiatives have been taken to fight against this growing threat, including, WHO Global Action Plan on AMR (2015)**,** which outlines five strategic objectives, including raising awareness, reducing infection rate, optimization of antimicrobial use, development of integrated surveillance systems, and promoting investment in new tools and interventions, all based in the One Health approach (Lim, 2020).

A Quadripartite collaboration was established in 2022 by the WHO, FAO, WOAH, and UNEP to coordinate One Health actions on AMR, including strategic recommendations and epidemiological tracking. In 2024, the Quadripartite launched a Joint Action Plan with cross-cutting priorities such as environmental regulation, AMR innovation funding, and equitable access to antibiotics (De La Rocque et al., 2023).

AMR is closely linked to many Sustainable Development Goals (SDGs), which is why it's not only a health priority, but fighting against this threat is important to achieve the SDGs. A One Health-based approach, combining human, animal, and environmental health, is mandatory to make progress across multiple SDGs (Gurung et al., 2024).

### 2. National Action Plans (NAPs)

National Action Plans have been developed by more than 140 countries for AMR. They are based on the WHO framework and tailored to local needs. These plans have the following objectives:

- Regulation of antimicrobial use in human and veterinary sectors
- Improvement of laboratory and surveillance capacity
- Promotion of infection prevention and biosecurity
- Raising awareness through education and communication

However, many NAPs face funding issues, lack coordination among different sectors, and are poorly implemented. In many countries, there are no checks on sales of veterinary drugs, and a system for monitoring environmental AMR is unavailable (Willemsen et al., 2022).

### 3. Legal and Regulatory Mechanisms

Robust legislation is essential to enforce responsible antimicrobial use and manage environmental risks. There should be a law that only licensed practitioners can prescribe antibiotics to mitigate the misuse. A ban is needed on the use of antibiotics as growth promoters. The European Union has banned the use of antibiotics as growth promoters since 2006 (Castanon, 2007). Laws are also needed for environmental discharge limits of pharmaceutical residues, especially in wastewater from industries. However, practical implementation is a major shortcoming in many regions, as antibiotics are being sold freely in markets (Cameron et al., 2025).

### 4. Governance Challenges

Although the issue of AMR has grabbed political attention at international levels, different ministries, including health, agriculture, and environment, often work separately rather than adopting the One Health approach for better results. In the majority of rural and private sectors, rules for antibiotic usage are not being implemented. Important stakeholders such as, farmers, private veterinarians, pharmaceutical companies, and communities are not included in planning and implementation. The major issue that most of the NAPs face is the insufficient funding, which contributes to implementation failure (Waswa et al., 2024).

### 5. The Way Forward: Strengthening Policy for Prevention

To overcome these gaps and shortcomings, governments and global bodies must invest in cross-sector infrastructure and human resources**,** multisectoral coordination units with legal authority, support AMR-sensitive policies in agriculture, trade, and environmental protection**,** foster public-private partnerships for innovation and access to alternatives, Monitor and evaluate policies using accountability frameworks (Esiovwa et al., 2022).

The African Union introduced a continental AMR scorecard for tracking the progress due to the implementation of One Health strategies among member states. Good governance can play a strong role in prevention. If laws, political cooperation and practical implementation are not followed, then these strategies will remain limited to the papers. A One Health approach to policy, demands coherence, collaboration, and accountability across systems (Zhou et al., 2024).

## Community Engagement and Education

Although global frameworks and national policies are the main support for controlling antimicrobial resistance (AMR), Involvement and support from local communities can make it more successful (Mitchell et al., 2021). Farmers, pet owners, healthcare workers, pharmacists, patients, and even schoolchildren all can play a significant role in either promoting or preventing resistance. Effective community engagement and education are essential tools in shifting behaviour, promoting accountability, and building resilience against AMR at the grassroots level (Tang et al., 2023).

### 1. Raising Awareness Among the General Public

Misunderstanding and misinformation about antibiotics are widespread. Many people still use antibiotics for viral infections and are unaware of completing the antibiotic course despite resolving the symptoms (Yewale & Shenoy, 2022). Mass media campaigns in schools, posters in clinics, and community theatre are effective strategies for increasing AMR awareness. World Antimicrobial Awareness Week (WAAW) is observed from 18 to 24 November globally to promote responsible antibiotic use (Yewale & Shenoy, 2022).Culturally tailored messages using local language and practical examples from daily life are more effective because people pay attention, understand better and follow the advice (Benski et al., 2020).

### 2. Education and Training for Health and Veterinary Professionals

Healthcare workers and veterinarians are skilled and trained persons; however, due to limited access to updated guidelines or advanced diagnostic techniques. They are unable to transfer updated information to others. To improve prescribing practices, continuous professional education is essential. Health and veterinary professionals should be trained in antibiotic stewardship, diagnosis and effective communication skills. They should be trained to say "no" to unnecessary antibiotic requests. Para-veterinarians and private drug sellers should also be included in the training because in lower- and middle-income countries, people first turn to them for help (Rocha-Pereira et al., 2017; Khan et al., 2020).

A study from Kenya that was conducted in 2023 showed that targeted stewardship training of livestock officers resulted in a significant drop in the sale of over-the-counter antibiotics within period of just six months (Sohaili et al., 2024).

### 3. Engaging Farmers and Food Producers

Farmers mostly do misuse of antibiotics due to a lack of information, financial pressure, and the absence of proper veterinary guidelines**.** Farmer field schools and agriculture extension programs play a valuable role in training the farmers about animal health, vaccination, hygiene, and biosecurity practices. In addition, sharing success stories and peer-to-peer learning among farmers can help normalize less antibiotic use, also they will get an idea that reduced use will not affect their profit (Mitchell et al., 2021). In Vietnam, participatory training for pig farmers reduced prophylactic antibiotic use by 55% without affecting productivity (Postma et al., 2016).

### 4. Mobilizing Civil Society and Youth

Civil society organizations (CSOs), local NGOs, and youth networks can help in spreading AMR awareness among communities. Women's associations and school teachers can act as influential messengers, while youth media groups can promote AMR education in creative formats such as films, debates, TikTok videos, or local campaigns (Ranganathan & Ranjalkar, 2023).

### 5. Behavior Change Communication (BCC) Strategies

Behaviour change has more impact than just providing information; it requires motivation, social support, and an enabling environment. Telling people about what others are doing can influence them positively, e.g., telling farmers that the majority of people now vaccinate their animals rather than giving antibiotics, can change their behaviour as well**.** Feedback tools like prescription audits or mobile alerts help providers to self-monitor and improve their habits. Involving the community in providing solutions also leads to long-lasting change. Behavioural change is important in AMR prevention. Community involvement is also a core strategy. Empowered Individuals and communities with proper knowledge and awareness are the most powerful agents in breaking the cycle of resistance (Lundborg & Tamhankar, 2014).

## Research Gaps and Future Directions

Despite significant progress in recognizing and responding to antimicrobial resistance (AMR) through a One Health lens, major scientific and implementation gaps persist. Addressing them is essential to strengthen evidence-based policy, optimize interventions, and develop sustainable, cross-species solutions (Chen et al., 2024).

### 1. Surveillance and Data Integration Gaps

Although AMR surveillance systems are present in the human health sector, in low- and middle-income countries (LMICs), surveillance systems are less developed for the animals and environment sectors. This could be due to multiple reasons, including, lack of standardized data collection tools in these sectors, making it difficult to do comparisons. Moreover, data from very few countries is recorded and shared from clinical, veterinary, and environmental sources into a unified AMR monitoring framework. This is the responsibility of all countries to share their data to see the complete picture. There is also limited data available on how the resistance genes spread among different sectors and ecosystems. In future, it is mandatory to build real-time, cross-sectoral AMR dashboards and databases using genomics and geospatial tools (Iskandar et al., 2021).

### 2. Limited Evidence on AMR Interventions in LMICs

The majority of AMR-related literature comes from high-income countries. Although the high use is reported in animals from low- and middle-income countries. There is limited evaluation of the involvement of informal drug sellers and implementation of local feed bans. Additionally, economic and behavioural drivers behind antibiotic use in smallholder systems are under-researched (Sulis et al., 2021). Looking ahead, we will need funds for operational research and pilot projects that evaluate scalable, community-adapted One Health interventions.

### 3. Underexplored Environmental Pathways and Silent Hotspot

Pharmaceutical effluent, wildlife, and aquaculture are important environmental drivers of AMR, and it is urgently needed to explore them in detail. There is limited research available on microbial ecology and resistome evolution in contaminated environments. Additionally, wildlife surveillance is also needed, especially in migratory birds. It is critical to know the global epidemiology and transmission of AMR. In future, to tackle this issue, the development of sensitive, low-cost tools for environmental AMR detection and resistome tracking are needed urgently (Samreen et al., 2021; Li et al., 2024).

### 4. Innovation Gaps: Alternatives to Antibiotics

There is a pressing need to develop and promote alternatives to antibiotics in both human and veterinary sectors. However, research on these most demanding fields, such as vaccines, phage therapy, probiotics, plant-based antimicrobials, and host-directed therapies, has funding issues. In addition, advanced laboratory tools that provide help in appropriate antibiotic use at the hospitals or farms are required for the implementation of the stewardship strategies (Alsaadi et al., 2022).

### 5. Policy Research and Governance Models

More research is needed to know what works in governance**,** especially in the context of One Health. Key questions remain about how to balance stakeholder interests**,** enforce policies in informal sectors, and incentivize compliance. Decentralized approaches to multisectoral governance (e.g., at district or municipal level) remain underexplored, despite their potential to provide solutions (Zhou et al., 2024).

### 6. Social Science and Behavior Change Research

Many AMR interventions assume that knowledge will change behavior, but the social drivers of AMR are complex and context-dependent. For this, we need a deeper understanding of community norms**,** beliefs, and trust in authority that shape antibiotic decisions. Co-designing solutions with local populations is still rare but increasingly recognized as essential (Lorencatto et al., 2018). Therefore, investment is required in interdisciplinary social science research that complements biomedical solutions. Solving AMR is not just a technical challenge; it's also a systems and societal challenge. Investing in One Health research that cuts across disciplines, borders, and species is critical to creating a resilient, evidence-driven response to AMR (Mitchell, Hawkings, et al., 2023).

## Conclusion and Call to Action

Antimicrobial resistance (AMR) is the fastest-growing global threat with very serious impacts. It is dangerous not only for humans but also for animals, food production, and the environment. We cannot put all the responsibility on one sector, because all sectors are interlinked in spreading this issue; similarly, solutions can also be found by combining all the sectors. The best solution to tackle AMR is a One Health approach, where human, animal, and environmental health are all interlinked and lead to a practical and holistic direction forward.

In this chapter, we discussed the factors responsible for the spread of AMR and how resistance is spreading between people, animals, and the environment. We also explored different strategies that have been proven effective, including prudent antibiotic use, enhanced surveillance, cleaner environments, public awareness and engagement, new areas of research, especially antibiotic alternatives. Collective efforts can make a difference; no single action is enough on its own.

What we need now is a genuine and long-lasting change in how we respond to tackle antimicrobial resistance. It is the right time to break down walls between different sectors, moving from short-term fixes to long-term thinking, and shifting from raising awareness to taking ownership. Everyone has a part to play. Governments must create stronger rules and systems. Researchers should help connect evidence with action. Health professionals and farmers must adopt safer practices. Communities should be informed and actively involved. And international organizations need to support low-resource countries in implementing One Health strategies into action. Time is limited, but it's not too late. If we work together with commitment and resources, we can still protect the power of antibiotics for the future. AMR affects all of us, across borders and generations, so our response must be just as united.

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# Climate Change and the Shifting Landscape of Zoonotic Disease Patterns

04

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## ABSTRACT

Zoonotic diseases spread between humans and animals and pose a substantial threat to worldwide health security, accounting for over 60% of all recognized infectious illnesses. Determined by bacterial, fungal, viral and parasitic organisms, these diseases are exacerbated by features such as climate change, worldwide travel, urbanization and deforestation, which increased cross-species spillover opportunities. Climate brought environmental shifts such as an increase in temperature, transformed rainfall forms and environmental disruption, making favorable conditions for hosts and vectors, thus enabling the spread of zoonotic diseases. Emerging communicable illness threats such as COVID-19, avian influenza, Ebola and Rift Valley Fever emphasized the need for integrated surveillance systems, cross-sector collaboration and early warning systems. Susceptible populations in low-income and agricultural surroundings are unreasonably tolerant of the burden, disrupted livelihoods, food insecurity experience, and limited access to healthcare. The One Health approach that combines the health disciplines of human, environmental and animal serves as a foundation for handling this problem through preventive measures such as control of vectors, vaccination, sanitation and education of health. Integrating inventions such as GIS mapping, real-time diagnostics, remote sensing, and predictive modelling further enhanced disease forecasting and response. Future research much concentrate on investment in health infrastructure, interdisciplinary collaboration, and global cooperation to lessen risks posed by zoonotic pathogens.

**KEYWORDS**
Zoonotic diseases, One health, Climate change, Disease surveillance, Vector-borne pathogens, Health strategies, Risk prediction.

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## 1. INTRODUCTION

An expert committee in 1951 described zoonoses as infections and diseases that naturally spread between vertebrate animals and humans. However, at the end of the 19th century, Rudolf Virchow, a German physician and pathologist, introduced the term zoonoses to describe human infections commonly shared with animals. Zoonoses are considered the most suitable in contrast to anthropozoonoses and zooanthropozoonoses. Anthropozoonosis are diseases that originate in animals and can be passed on to humans. For instance, rabies (transmitted by animals like bats, dogs, or foxes) and some forms of influenza. Zooanthroponosis are diseases that start in humans and can be transmitted to animals. Examples such as tuberculosis (which can be transmitted to cats and monkeys) and some types of influenza. Several variations of pathogens have been spread from wildlife to humans. The relation between a human and an animal needs to form first before an organism can become a hazard or threat to a population (Leal Filho et al., 2022).

### i. Zoonotic Diseases in the Context of Climate Change

Climate alteration has a multifaceted effect that also influences the well-being of humans and animals. For instance, climate change modifies habitats, interrupts the environment, and disturbs the performance and division of wildlife species. Because of this, the risk of zoonotic diseases worsens. Knowing these mixed relations is dominant for expecting and handling the strong hazards linked with zoonotic illness in a climate change situation. Human activities primarily driven by climate change, such as deforestation, fossil fuel burning, and industrial development, are associated with major changes in the global atmosphere and weather patterns. These alterations include increasing temperature, changes in precipitation patterns, rising incidence and concentration of complex atmospheric events. Like weather, revolutions have reflective consequences for biodiversity, environmental consistency, and human well-being (Ojeyinka & Omaghomi, 2024).

### ii. Historical and Emerging Trends in Zoonotic Outbreaks

The effect of COVID-19 and recent epidemics on livelihoods and human well-being has emphasized the need to better understand the trends in communicable disease spillover. Climate alteration and other parts of ecosystem change are predicted to enhance the frequency of zoonotic disease spillover, whereas an increase in the density of human population helps the in the transmission of disease. Until now, data on the occurrence of zoonotic disease spillover and its changeability over time are incomplete, which makes it difficult to identify its consequences for global well-being. While old movements in zoonoses spillover gave understanding of the predictable occurrence and harshness of future epidemics (Meadows et al., 2023)

The period in which the influenza virus started to infect humans or produce a pandemic cannot be determined with certainty, but many chroniclers agree that the first influenza pandemic could have happened possibly in 1510. The Russian flu that happened between 1889 and 1893 was the first identified pandemic. This pandemic was probably caused by an A/H3N8 virus, depending on serological and epidemiological data. The virus spread quickly as it took four months to evade the planet. The pandemic virus reemerged every year for three years and produced an estimated one million deaths worldwide (Piret & Boivin, 2021).

## 2. Climate Change and Environmental Transformations

The human and animal connection are continuously influenced by the effects of climate alteration and natural factors. Travel, trade and tourism are the main human aspects affecting the epidemiology of zoonotic illness. All these features combined to make zoonotic diseases like Lyme disease and West Nil fever of public health concern in the developed world. However, effects of climate change are projected to be inferior for the world, where political and socioeconomic situations are challenging and worsened by a deficiency of epidemiological zoonotic diseases studies (Naicker, 2011).

Zoonotic pathogens are affected by environmental changes that can take various shapes. Initially, the changes in climate affect pathogen burden directly in the host individual, like by changing immunocompetence. Secondly, the composition of species or community densities of host or vector can be affected by alterations in climate and landscape characteristics. Thirdly rate of contact between zoonoses hosts, humans and vectors can respond to climate and landscape alteration. For example, Dizney and Dearing presented that environmental alteration that decreases diversity of mammals, raises infection of hantavirus and deer mice prevalence by increasing intraspecific and decreasing interspecific relation rates (Estrada-Peña et al., 2014).

### i. Rising Temperatures and Global Warming

Global warming occurs due to an increase in fossil fuel burning and alterations in land use, which cause the emission of greenhouse gases, including methane, CO2, and nitrogen dioxide. Fossil fuel burning and human activities that have connected to a rise in greenhouse gases in the atmosphere. These alterations in climate are likely to have an incredible effect on zoonotic diseases. The climate changes may give a favorable environment for insect vectors propagation, transmission period maintenance, a decrease in the generation period and introduction of animals or vector reservoirs. Changeability in climate affects the wild animal population dynamics, and these dynamics affect disease transmission within the animal populations, and other populations or humans. For instance, Ixodes scapularis Lyme disease tick vectors have increased in Canada northward, whereas, cases of Lyme rise from 144 in 2009 to over 4,600 in 2023 (Pal et al., 2013).

Changing temperature effects on the spread of organisms in wildlife and livestock likely cause serious illness in humans, as contrast to the effects on illnesses that have a burden in humans. Increasing temperature may cause seasonal and expansion alteration in zoonotic diseases, which shows that infection contributes to a shift in environmental division (Fig. 1). For instance, in African trypanosomiasis shift division near East African uplands was predicted, whereas invasion would have effect on food security and economic work, although worsen spillover into humans. However, they focused initially on illnesses that have a serious burden in humans, like vector-borne zoonotic diseases (Becvarik et al., 2023).

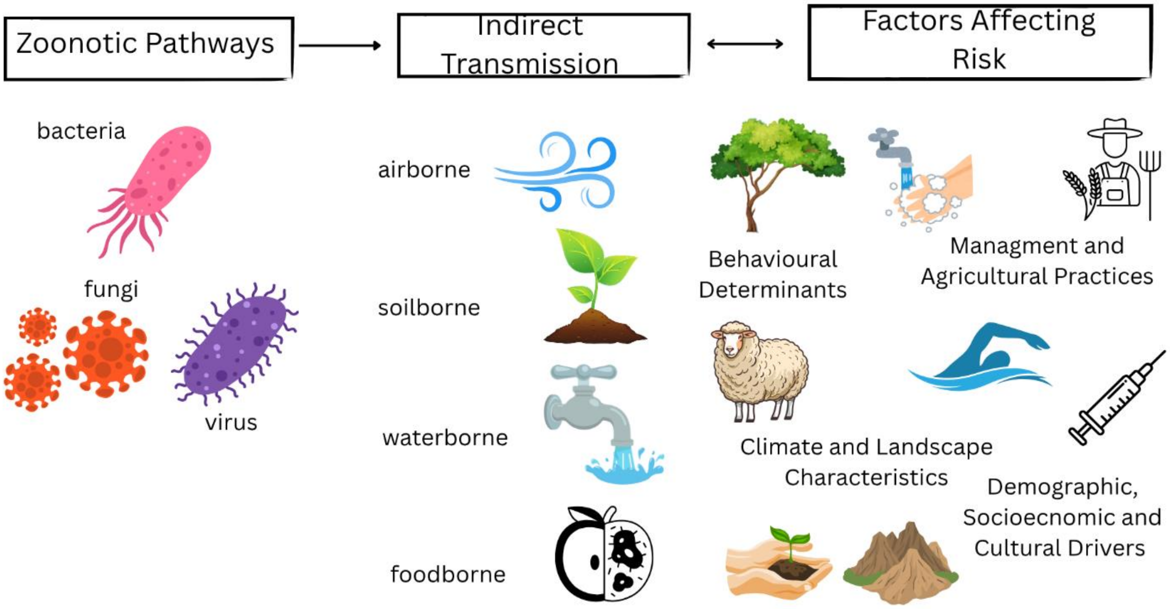

**Fig. 1:** Illustration of alternative indirect pathways for zoonotic pathogen transmission, excluding vector-borne routes, with emphasis on environmental risk dynamics. (Designed using Canva Pro).

### ii. Altered Rainfall Patterns and Humidity Extremes

The zoonotic diseases that spread are influenced by a variety of environmental features, including climatic factors like humidity, temperature, precipitation and ecological variables like biodiversity as well as vegetation and land use alteration. These fundamentals can affect pathogen possibility, vector lifecycles and host vulnerability. Between these environmental features, humidity and temperature play essential roles in regulating disease spread through their effect on pathogen vulnerability outside hosts, behavior, vector life cycle and host defensive responses. Understanding the impacts of humidity and temperature can enhance predictive models and update resource distribution for targeted public health interventions. If associations can be severely measured, environmental monitoring information on these factors could provide initial warning systems for latent epidemics, allowing for active prevention efforts. Increased temperature within suitable varieties was generally linked with increased spread risk, whereas extremely high or low temperatures had an adverse impact. Heavy rainfall and high humidity were connected to the outbreak of vector-borne illnesses like malaria by allowing vector breeding. A study in Uganda revealed that above 20 mm weekly rainfall was followed by a 30% increase in cases of malaria within a month. Moreover, reduced incidence of various diseases, such a dengue fever, was observed with high rainfall (Zhang et al., 2024).

## 3. Climate-Responsive Zoonotic Pathogens

### i. Bacterial Zoonoses Influenced by Climate

Alterations in climate may influence the geographic division and prevalence of seasonal factors, but frequently not in the expected way. Furthermore, these atmospheric features similarly have a substantial effect on the infection environmental reservoirs. Precipitation, particularly substantial rainfall, may affect the frequency and quality of drinking level (Darbandi et al., 2023). Bacterial diseases have also been connected to rising climate variations and global warming. Leptospira is a zoonotic bacterium associated with climate variation. A leptospirosis outbreak occurred due to flooding in Brazil, especially in those areas that don't have appropriate drainage. In 1998, flooding and rainfall increase after a storm in Honduras, Nicaragua and Guatemala produced leptospirosis outbreak. Also increased in cholera, malaria and dengue fever numbers of cases was reported. Vibrio cholerae is a zoonotic pathogen whose incidence is connected to climate variability. As the temperature of the ocean increases with global warming, outbreaks of cholera rise as various plankton blooms that provide energy for Vibrio cholerae (Rodríguez-Morales & Delgado-López, 2012).

### ii. Viral Zoonoses and Vector Expansion

Bats are expected to produce zoonotic spillovers into human populations due to the genetic connection between human and bat viruses. Fruit bats, which are the Ebola virus disease animal reservoir, will increase its range by 15–25% in West and Central Africa by 2050 due to change in climate. Although climate alterations brought migratory patterns for genetic mixing among populations of bats. These epidemiological shifts confuse current efforts to block. However, unexpected phylogenetic and host shifts familiarize new pathways of illness in human populations. Due to some avian flu strains' high lethality and virulence, their endemic presence in Asia, are expanding host reservoirs (Chitre et al., 2024).

### iii. Parasitic Zoonoses and Environmental Suitability

Ecological conflicts have an impact on the proliferation and emergence of malaria and parasitic zoonotic pathogens such as trypanosomiasis, leishmaniasis, filariasis, and giardiasis. Each alteration in the environment, whether happening as a natural phenomenon or through human interference, affects the framework and ecological balance within which illness is breed of vectors, hosts, and parasites, forms and spreads disease. Each organism inhabits a specific ecological niche, and vector subpopulations are behaviorally and genetically different as they adjust to a synthetic environment (Patz et al., 2000).

Rift Valley fever is the most serious zoonotic disease of sub-Saharan Africa, which produces disturbing health and economic effects on national ruminants and humans. They produce serious epizootics outside Africa. Rift Valley Fever is a latent risk for the USA and Europe. Various Rift Valley Fever epidemics are supposed to be activated by high numbers of adult mosquitoes' emergence that spread the Rift Valley Fever Virus, particularly of the Culex and Aedes genera. Mosquito emergence and division are strongly connected to climatic and ecological conditions such as high flooding and rainfall. Although human performance creates upright water, such as building and irrigation of a dam. High level of Rift Valley Fever seropositivity has been recorded in populations of buffalo, it is recommended that the Rift Valley Fever virus could persist for a long period in wild animals, giving a determined source of reinfection of populations of cattle (Redding et al., 2017).

### iv. Fungal and Novel Pathogens in Changing Climates

Scientists expect that dangerous weather events will become more common and serious as global temperatures increase. Severe weather has both instant and long-lasting impacts on the fungal environment, increasing the exposure risk and subsequent illness. Environmental disturbance produced by severe climate events, including wildfires, dust storms, and cyclones, can release fungal spores into the air, increasing airborne exposure risk. Between 1988 and 2011, dust storms gathered in the south-western US, coinciding with a rise in coccidioidomycosis cases. While the connection between coccidioidomycosis and dust storms is not identified, many scientists said that dust storms can imposed a danger of infection with Coccidioides and can transmit arthroconidia infection to new areas. Inhalation and dermal contact with fungal spores are common ways of transmission of fungal related diseases (Williams et al., 2024). Moreover, Candida auris is a multidrug-resistant nosocomial fungus that has emerged globally and has become a substantial challenge for microbiologists and clinicians worldwide. Candida auris is a resilient pathogen that survives harsh disinfectants, dry conditions, and high-saline atmosphere. It eagerly takes over non-living environments and vulnerable patients, producing invasive illnesses that exact a high toll (Chakrabarti & Sood, 2021).

## 4. Evolving Transmission Pathways

### i. Climate-Driven Vector Ecology Changes

The climate alteration impact on vector-borne spread is mixed, with both direct and indirect influences on insect vectors. Vectors, especially ticks and mosquitoes, show notable phenotypic flexibility, allowing them to adapt to atmospheric variations through changes in behavior, including feeding time, and latent selection of site and physiological factors, including immune responses, thermal tolerance and dryness resistance (Abbasi, 2025). In Canada, the emerging infectious illness is Lyme disease, mainly because of the environmental range expansion of the Ixodes scapularis. Global warming is predicted to quicken the spread of Ixodes scapularis in Canada, given the occurrence of suitable hosts and habitat, and influence the tick-borne zoonoses. In north side, cases of Lyme illness rise over thirty fold in Canada from 2009 to 2023. In Canada, the emerging Lyme illness impact on human well-being requires proper health messages to the public and diagnostic guidance provided to public consultants. Lyme disease's early diagnosis and treatment are typically successful. But treatment of systemically distributed Lyme disease in later stages is much difficult and expensive for the patient and well-being facilities. While changes in atmosphere and biological identification of the transmission of zoonotic diseases, their effect is extremely handled in vulnerable human populations (Ogden et al., 2008).

## 5 Vulnerable Populations and Societal Consequences

Foodborne and zoonotic illnesses of animal origin are increasing, and the health and socioeconomic effects are rising, as practiced by various countries, but most especially by developing nations. The population of the poor and marginalized tolerates an unreasonably increase share of the load that those diseases produce. The development and establishment of accurate measures, particularly against zoonotic illnesses and foodborne illnesses, has been revealed hard. The population's health has been recognized to have a deep impact on the social and economic circumstances of a nation. There is a strong connection between poverty and disease. Efforts to reduce in poverty rate without addressing the control of disease often contribute to the transmission of disease (Seimenis, 2012).

### i. Food Insecurity and Livelihood Disruption

Climate alterations can disturb the production of food through the consequences of increased temperature, alterations in rainfall, extreme weather, an increase in sea level, degradation and loss of agricultural land. The susceptibility of climate alteration effects will vary in distinct regions, among distinct populations and by gender. Nutrition and human health are affected by climate change through the utilization and absorption effects. Climate change affects foodborne diseases, which increases the need for nutrition while simultaneously decreasing absorption such as food spoiled with pathogens, animal disease organisms, harmful algae, toxic products, fungal toxins, pesticides, chemicals and veterinary drugs (El Samra, 2017).

From 1997 to 1998 and from 2006 to 2007, there was an outbreak in Kenya. These outbreaks occurred in the pastoral communities that are Garissa and Ijara regions. These areas are considered by seasonal vector movement because of high rainfall and successive flooding. Therefore, the spread of Rift Valley Fever in these areas are because of vectors. Human activities are also involved in the spread and transmission of Rift Valley Fever. This is linked to numerous activities associated with human-animal behavior, including blood, tissue, secretions, food processing and veterinary procedures (Ng'ang'a et al., 2015). In human illness, the part of the zoonoses could increase by 60%, with 70% of these from only wildlife species. These animals are birds, pets and companion animals. Fish and marine species also take part in the infectious illnesses of zoonotic origin. Insects are vectors of zoonotic illness and play as a transitional reservoir for numerous pathogens (Fig. 2). Globally, two billion people see insects, beetles, caterpillars and many other bugs as a food source. It is revealed how potential zoonotic diseases could be spread to these populations. Edible insects pose a danger of zoonotic diseases carrying numerous bacterial, foodborne and parasitic pathogens (Borham et al., 2025).

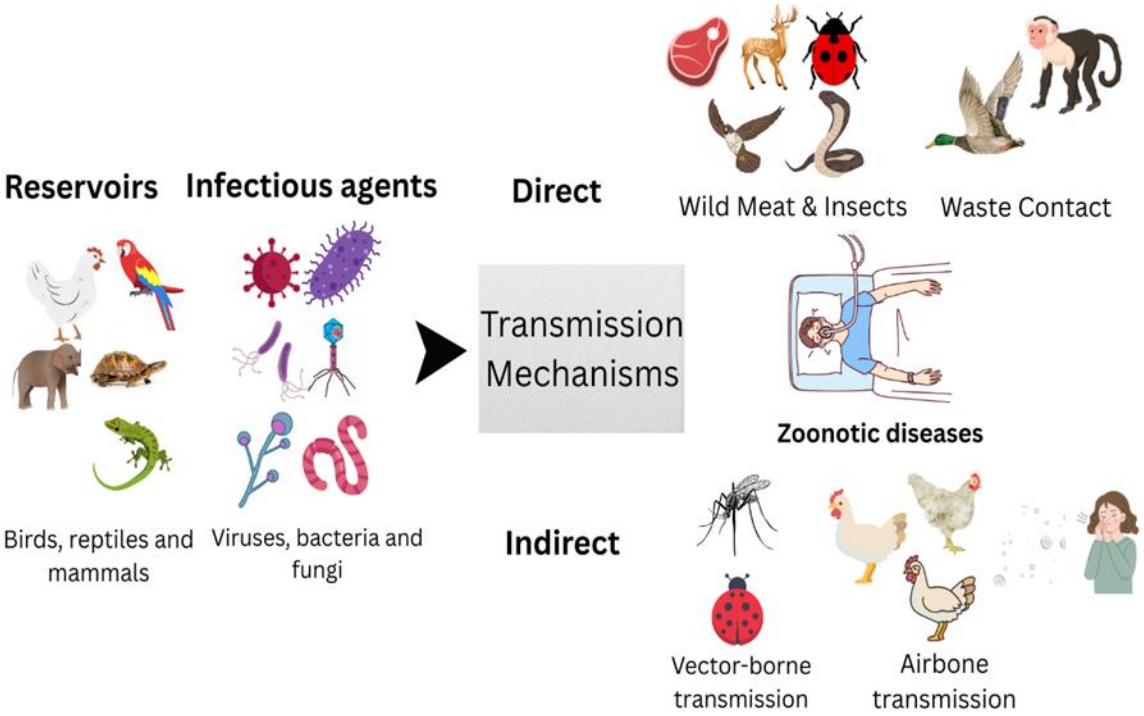

**Fig. 2:** Wildlife role in the transmission of emerging and re-emerging zoonotic diseases. Wildlife reservoirs harbor diverse pathogens that are spread to humans through direct contact or indirect mechanisms, facilitating the spread of zoonotic infections. (Designed by me using Canva Pro).

### ii. Climate Inequity in Zoonotic Disease Burden

Poor individuals have higher exposure to zoonotic diseases through farming, living in communities of agriculture, greater contact with wild and pre-domestic animals, and lower access to sanitation and hygienic water. Additionally, zoonotic diseases decrease the productivity of livestock and pose essential barriers to trade in livestock components, although they pose more hurdles to know the harms. These effects are caused by poverty in developed states. To lessen these inequalities, timely outbreaks identification and prediction of is important. Technologies of emerging surveillance are essential tools in this effort (Grace & Cook, 2023).

## 6 Surveillance, Monitoring, and Predictive Modelling

### i. Integrating Climate Data into Health Surveillance

Incorporation of real-time data in the investigation showed a transformative method in the infectious illness management field, leveraging streams of continuous data to increase analytical modelling and response strategies. This procedure consists of continuous collection, dispensation, and consumption of data from numerous sources to provide the latest information important for early identification, monitoring and administration of infectious illness outbreaks. The perception of real-time data incorporation states the constant and immediate gathering of data from various sources, which is then incorporated and examined to update decision-making procedures. This approach differs gradually from traditional diagnostic procedures, which depend on constant or delayed data (Udegbe et al., 2023).

A study done by researchers in Uganda showed that climate data incorporation, particularly temperature and rainfall, into a system of health surveillance increased malaria outbreak prediction. Over several years, by determining weekly data, they found that rising rainfall was followed by an increase in malaria cases. Increased temperature also contributes in the spread of malaria by enhancing parasite and mosquito development. Using an autoregressive time series model, the study determined that climate factors could serve as an appropriate warning system, allowing public health organizations to take active steps, including community awareness campaigns and resource distribution, before outbreaks peak. This example illustrates the real-time climate data potential in spreading disease surveillance from reactive to predictive systems (Fig. 3) (Merkord et al., 2017).

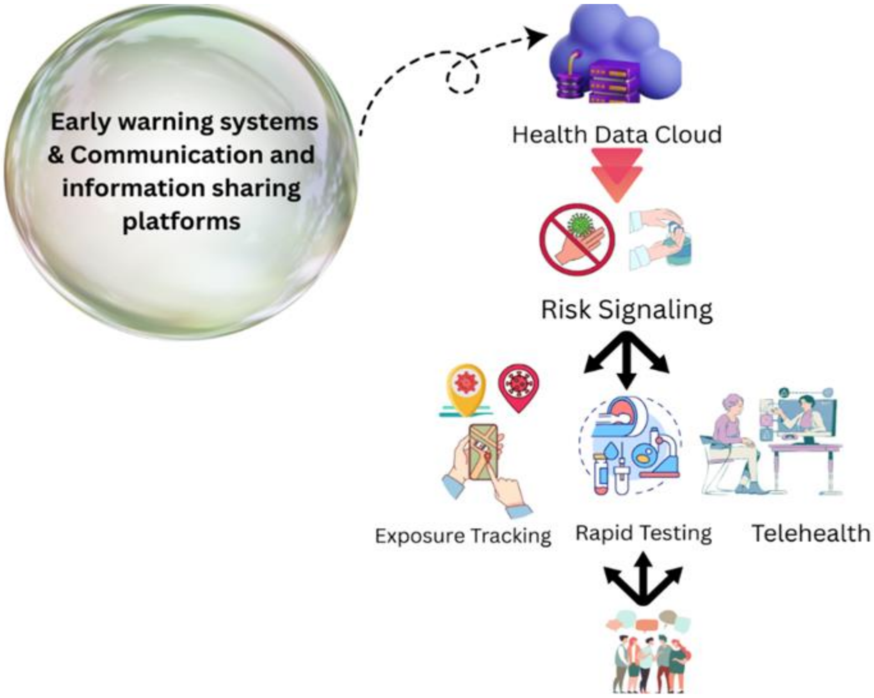

**Fig. 3:** Strategies to strengthen the response to zoonotic disease outbreaks. Zoonotic diseases effective control requires early identification, rapid response, intersectoral coordination, and improved surveillance systems. (Designed using Canva Pro).

### ii. Geographic Information Systems (GIS) and Remote Sensing

Remote sensing is the gathering of information of an area, object, or event depending on measurements. Data is taken through radiation of electromagnetic interactions with the surface of Earth, showed by spaceborne sensors and airborne sensors. A sensor is an instrument that identifies and measures radiation as a physical aspect and converts into a shape that is transmitted to the getting system. When electromagnetic radiation attacks a surface, energy is captured. Some energy is transmitted through the surface, various are reflected. It's the released radiation that's noted on either a digital sensor or photographic film. Since the radiation wavelength and intensity are based on the surface, each surface has a characteristic spectral signature (Mironga, 2004).

The increasing occurrence of dengue in India, especially in urban slums, makes advanced tools incorporation important including GIS mapping, for effective surveillance of the disease and involvement. Between 2011 and 2013, a study was conducted in Andhra Pradesh, used spatial cluster analysis to determine the division of dengue cases and showed substantial geographic differences across districts. The study revealed a higher prevalence among males and younger age groups, especially children who are aged from 1 to 10 years, possibly because of behavioral features and distinctions in immunity. The study determined clear spatial groups of dengue. The study highlights the spatial tools and GIS potential in determining dengue hot spots, supporting targeted interventions, and public health policies information in resource-limited settings (Mutheneni et al., 2018).

## 7 Challenges, Gaps, and Research Priorities

### i. Interdisciplinary and Institutional Barriers

Most of the world's greatest issues, such as zoonotic disease emergence, can be determined through interdisciplinary research. Though interdisciplinary research findings are vulnerable because of distinctions in languages, training, and understanding. That miscommunication led to a misunderstanding that delays the research agendas and public policy development. These misunderstandings can also increase public fear and wildlife conservation harmful effect. For instance, inappropriate communication and misunderstanding of the connection between various bats and zoonoses have showed the pursuit of bats globally (Shapiro et al., 2021).

### iii. Future Research Directions and Capacity Building

The diseases are increasing in prevalence that posing a serious risk to the global economy and health, and important advancements in diagnostics and, development of vaccines. Outdated laboratory procedures have been advanced by rapid diagnostics methods such as polymerase chain reaction, next-generation sequencing, Loop-mediated isothermal amplification, and nanoparticle-based biosensors, which suggest a high understanding, applicability and specificity, although in limited resource settings. These inventions, such as testing and diagnostics platforms, have enabled real-time surveillance and early detection, as confirmed during the Ebola epidemic in 2014 and the ongoing use of coronavirus-specific real-time polymerase chain reaction assay. To successfully lessen zoonotic threats, research in the future should focus on universal and rapid diagnostics development, stages of novel vaccines for a wide range of pathogens and increasing global collaboration which integrates human, environmental and animal health perspectives. Capacity building through nonstop health professionals training, investment in surveillance systems and public awareness campaigns is important to prepare for and respond to future outbreaks efficiently (Pal et al., 2024).

## 8 Conclusion

Zoonotic diseases continue to increase as a worldwide public health disaster, particularly in the framework of climate change and ecological disturbance. These diseases are not only a risk to human well-being but also affect the population of animals, socioeconomic stability and food systems, particularly in limited resource settings. The connection of the rise in human-animal interaction, environment, and climate change simultaneously contributes to the frequency and transmission of zoonotic diseases. Preventive methods, rather than sensitive responses, offer the cost-effective path forward. The One Health approach plays a crucial role in collaborative response across animal, human and environmental health organizations. Scientific tools such as GIS, real-time surveillance, remote sensing and predictive modelling should be incorporated into the planning of public health to anticipate outbreaks. Researchers and policy makers must arrange interdisciplinary research, the sharing of data, and capacity building to respond effectively to emerging threats. A proactive worldwide coordination approach is a key to reducing outbreaks in future and protecting both planetary and population health.

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# Probiotics and Postbiotics in Veterinary Internal Medicine: Enhancing Gut and Immune Health

05

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## ABSTRACT

This chapter explores the roles of probiotics and postbiotics in enhancing gut and immune health in veterinary internal medicine and aims to provide a comprehensive understanding of how these biotic compounds support animal health, productivity, and offer alternatives to conventional antibiotics. Gut microbiota plays an important role in animals health and serve as an important component for immune modulation, digestion and protects against pathogens. Gut brain immune axis further enhances the influence of gut microbiome on neurological function and stress response. In veterinary internal medicine use of probiotics and postbiotics turn out as an alternative to antibiotics and provide many benefits such as increased gut health, decreased disease occurrence and enhancing productivity in animals. Probiotics are live microbes that provide health benefit to host when administrated in right amount. Probiotics employ various mechanisms such as modulation of immune system, exclusion of pathogens and production of antimicrobials. In contrast postbiotics are non living products or byproducts that provide enhanced benefits including improved safety, standardization and stability in harsh conditions. The diversity of microbes in gut is influenced by various factors such as diet, age, genetics, and antibiotic use. Imbalance in these microbial communities result in dysbiosis which leads to diarrhea, inflammation, and decline in performance. In many animals' species supplementation with probiotics and postbiotics has shown tremendous results including poultry, swine, cattle, dogs, and cats, improving gut health, nutrient absorption, and resistance to infections. Additionally, advanced delivery systems such as encapsulation increases viability and release of biotic compounds. Recent research and regulations are advancing the application of this biotics in veterinary medicine. Together, probiotics and postbiotics offer a safe, and effective approach to improving animal health and productivity while addressing global concerns about antimicrobial resistance. Their use in animal diets has demonstrated benefits such as enhanced gut integrity, immune regulation, and productivity. Continued research and innovation in formulation and delivery will further strengthen their role as sustainable and safe alternatives to antibiotics in animal health management.

**KEYWORDS**
Probiotics, Postbiotics, Veterinary Medicine, Immune Modulation, Microbiome Dysbiosis, Functional Feed Additives.

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## 1. INTRODUCTION

Immune system and gut forms a compound united system that provides enhanced and productive digestion and immunity against ingested pathogens and bacterial toxins (Cummings et al., 2004). The gut microbiota can be defined as a complex collection of microbes such as viruses, bacteria, fungi and archaea living in the digestive tracts of organisms. Gut microbiota serves as a defence again pathogens by acting as a barrier which reduces the attachment and growth of pathogens (Yue et al., 2024).

### i. Gut Brain Immune Axis

Second brain is a term which usually refers to enteric nervous system. Gut brain axis is a bidirectional system that refers to continuous communication between gastrointestinal tract and brain. It affects animals stress response and behaviours and consists of hormonal, immune and neurological pathways. Research has revealed that gut microbes effect neurotransmitter levels and HPA axis in dogs (Kiełbik & Witkowska-Piłaszewicz, 2024).

### ii. Role of Microbiota in Animal Health

In animals the gut microbiota can be defined as a microbiota organ that gives strength to digest plant material that are not naturally present in host animal. These are also a source of pathogens related to humans and veterinary. Research showed that manipulation in these microbes can lead to increased host performance and health along with decreased pollution (Alexander & Plaizier, 2016). Microbiota in animals also showed relationship with different physiological conditions such as nutrition in host. In animal husbandry the most important factors are feed and growth. For instance, a study showed increased feed efficiency in cattle and chickens in relation to Clostridiales (Ikeda-Ohtsubo et al., 2018).

### iii. Importance of Postbiotics and Probiotics

Diverse changes in diet and treatment method have showed enhance animal health and decreases the threat of enteric diseases. The relationship between gut microbiota, diet and microbes showed effects on both nutrition and growth. These involves probiotics and postbiotics which displayed enhanced gut health in animals. These feed additives optimize the environment of health and lead to better health and nutrition (Yue et al., 2024).

## 1. The Gastrointestinal Microbiome in Animals

### i. Composition and Diversity of the Microbiome

A healthy gut consists of mainly Firmicutes, Bacteroidetes, Actinobacteria and Proteobacteria. Animal microbiota is very diverse and have up to 20 different bacterial phyla of which most common three phyla are Bacteroidetes, Proteobacteria and Firmicutes. The less present phyla which is common but very less seen in lower taxonomic level is Actinobacteria. The more specific phylum in animal is Acidobacteria and Fusobacteria respectively (Ikeda-Ohtsubo et al., 2018). In capriane animals the most abundant fungal microbiota is reported to be Ascomycota and Basidiomycota (Lv et al., 2023). The most represent archaea in gut of animals are methanogens belonging to genus Methanobrevibacter (St-Pierre & Wright, 2013).

### ii. Factors Influencing Microbial Populations

Many factors can change the gut microbiota such as diet, age, antibiotics and genetics. The first impact on gut health after birth of an organism is diet such as breast milk or formula milk which shape the gut microbiota. Research showed that vegetarian diet reveals more healthy gut characterized by species such as *Eubacterium, Roseburia and Ruminococcus* (Hasan & Yang, 2019). Different heredity factors such as antibiotics, poor nutrition, chemo and radiotherapy and drugs have effect on gut health (Bajinka et al., 2020). For example, in dogs the extruded diet showed high carbohydrate and protein levels then the dogs fed with raw diet typically showing low percentage of carbohydrates (Fig. 1) (Schmidt et al., 2018).

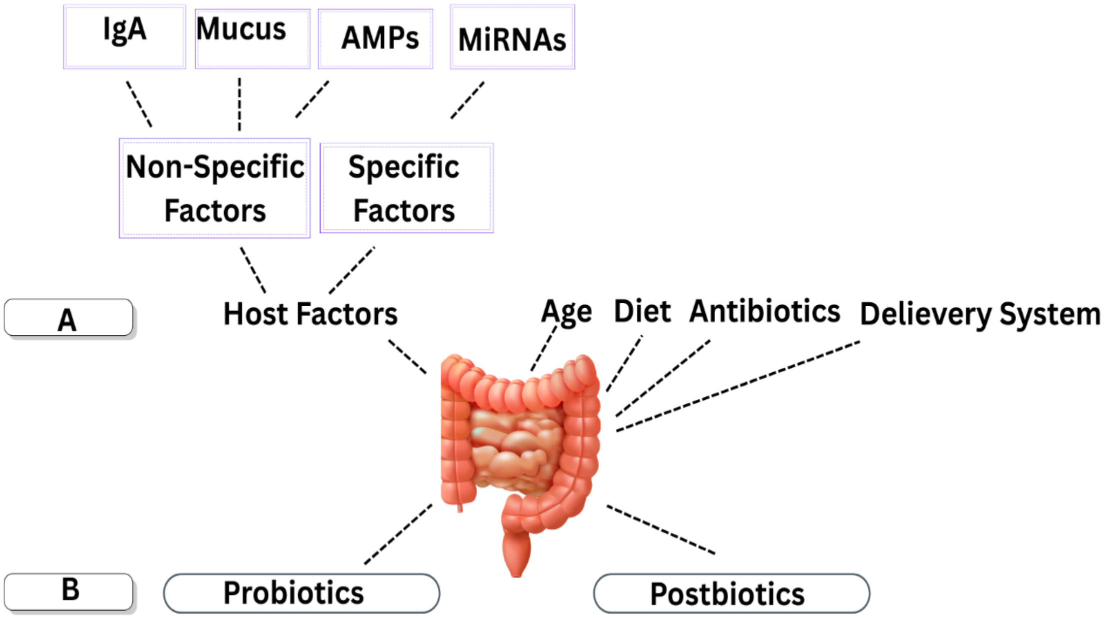

**Fig. 1:** (A) Factors that Affect Gut Microbiota (B) Various Ways to Modulate them (Designed using Canva Pro)

### iii. Microbiome Dysbiosis and Its Clinical Implications

Microbes present in the intestinal tract effects different process such as vitamin supply, immunity maturation, effect on brain and transformation of nutrients. A healthy gut is referred as a balance of diverse microbiota. Any changes in gut can lead to dysbiosis or imbalance. One of the recent health issues is microbial dysbiosis defined as the decreased diversity of gut microbiota. It is also known as less diverse microbial community in the gut linked with onset of infection or driving cause and force of disease mechanisms. This can lead to autoimmune diseases such as colorectal cancer, inflammatory bowl disease and diabetes (Bajinka et al., 2020). In newborn animals a not fully developed immune system can lead to infections such as diarrhea. For instance calf diarrhea is an example of antibiotic associated diarrhea in calves a growth disease which leads to economic losses in farms (Du et al., 2023).

## 2. Probiotics: Mechanisms and Functions

According to FAO and WHO probiotics can be defined as live microorganisms which when administered in adequate amounts confer a health benefit on the host (Reid, 2016). These are nonpathogenic microbes that improve the balance of microbiota especially in intestine such as *Lactic acid bacteria, Saccharomyces boulardii yeast* and *Bifidobacterium species* added in food and supplements. Probiotics exerts many health benefits such as lower pH, modulate host immune and reduces pathogenesis by pathogens (Williams, 2010).

### i. Sources of Probiotic Strains

Probiotics uses are increasing day by day in both animals and humans. In humans mostly probiotics came from dairy products whereas in animals the sources are other animals. In animals' species the source of probiotics is other animals mostly gastrointestinal tract from pigs, ruminants and poultry. Faeces of various animals such as pigs and chickens are source of probiotics. It can also be extracted from animals and plants fermentation material. In pigs' enteritis is reduced and health is improved by *Propionibacterium freudenreichii* which is isolated from dairy products. Similarly, from small intestine of piglets most of the *Lactobacillus* strains are isolated (Sornplang & Piyadeatsoontorn, 2016)**.**

### ii. Mechanism of Action

Probiotic strains fight for the limited nutrients and substrates needed by pathogens for fermentation. They also protect attachment of pathogens and microbes to host by improving the barrier of intestine. They secret substances like bacteriocins and organic acids and act as antimicrobials. *Lactobacillus acidophilus* produces two substances acidolin and bacteriocin lactacin B. Both these compounds inhibit pathogenic organisms. They also adjust the mucosal immune function. Research showed that for three weeks, 16 volunteers has been provided with milk containing *Streptococcus thermophilus, L. acidophilus, and Bifidobacterium bifidum Bb12* and then inoculated with *Salmonella typhi* Ty21a vaccine. The results showed increase immune response and enhance serum titre (Hemaiswarya et al., 2013). Probiotics not only increase the production of mucous but also protect the transfer of microbes from stomach to blood by enhancing the function of junction proteins. They also modulate the working and maturation of immune cells such as T cells and dendritic cells. Probiotics regulate the function and production of several neurotransmitters such as dopamine and serotonin (Fig. 2) (Latif et al., 2023).

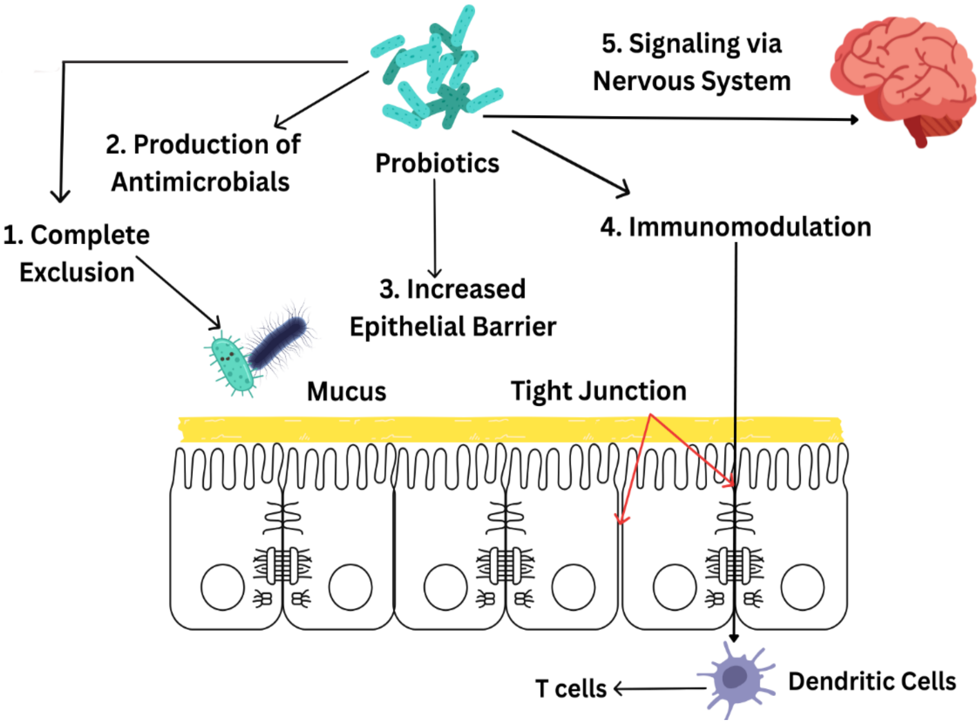

**Fig. 2:** Mechanism of Action of Probiotics (Designed using Canva Pro)

### iii. Clinical Applications

Probiotics are necessary for treating intestinal infections and increasing immune function in animals. Probiotics are used as supplements for an alternative to antibiotics. In cattle use of a live yeast as daily supplement showed increase in ADG, feed intake and weight. Similarly, cattle metabolism and immune response is increased by yeast and *Bacillus subtilis*. In female piglets *Lactobacillus bulgaricus* enhance growth by balancing the gut microbiota. Moreover, spore forming bacterial strains enhance ADG and decrease diarrhea by 6%. Additionally, in swine probiotics balance the immune function (Liu et al., 2023).

## 3. Postbiotics: The Next Frontier

Postbiotics is a Greek word where post stands for after and bios means life. The term postbiotics refer to microbes which are not viable. These microorganisms can be dead, cells or some parts of cells such as cell walls. Postbiotics are defined as non-living metabolic products or byproducts derived from probiotic microbes that exert a positive effect on host (Vinderola et al., 2022).

### i. Types of Postbiotic Compounds

Postbiotics are metabolic products extracted from probiotics and are less affected by environment like temperature and pH. There are different components of postbiotics such as enzymes, SCFA, CFSs etc. Short chain fatty acids (SCTA) are produced by fermentation of polysaccharides of plants in gut. It includes propionate, acetate and butyrate. They form salts of fatty acids like butyrate salt, acetate salt and propionate salt. Function of these short chain fatty acids depend on type and amount. For instance, acetate salt enhances productivity of poultry and livestock and increase appetite. In gut microbial enzymes also play important role in nutrients digestion. These enzymes play role in animal biochemical and physiological levels such as antioxidants. For example, antioxidant function of serum can be enhanced by *L. planturum* postbiotics. Microbes present in gut produce many antimicrobial substances like organic acids which are present in cell-free supernatants which help in maintaining microbes balance in gut. CFS from *Lactobacillus* exert anti-biofilm and antioxidant function. Cell fragments are also a type of postbiotics which enhance activity of immune system by triggering immune response as well as by production and activation of inflammatory mediators such as *Bacillus coagulans* which showed immune modulation in vitro (Liu et al., 2023).

### ii. Immunomodulatory and Anti-inflammatory Actions

Probiotics are live and viable but postbiotics are dead and not viable. Efficacy of postbiotics is related to metabolites like lipids, carbohydrates and other organic compounds produced during fermentation (Fig. 3). The composition of postbiotic compounds can also be manipulated by heat response. Any interaction between host and product can cause effect such as anti-inflammatory effects. There are examples where an immunomodulation mechanism by postbiotics is derived into a in vitro process of macrophage and dead viable *Lactobacillus casei* cells that resulted in increased pro inflammatory cytokines and Toll like receptors. It is also suggested that *Lactobacilli* spp. show immunomodulation by enhancing Th1-associated cytokines and decreasing Th2-associated cytokine. Two more fermentation byproducts giving health benefits are extracellular vesicles (EVs) and exopolysaccharides (EPS). Many bacterial taxa can produce these polymers such as *Bifidobacterium* species. They give benefits such as antioxidant and lower cholesterol. For instance, antitumor activities are shown by EPS from *Lactobacillus plantarum* 70810 (Wegh et al., 2019).

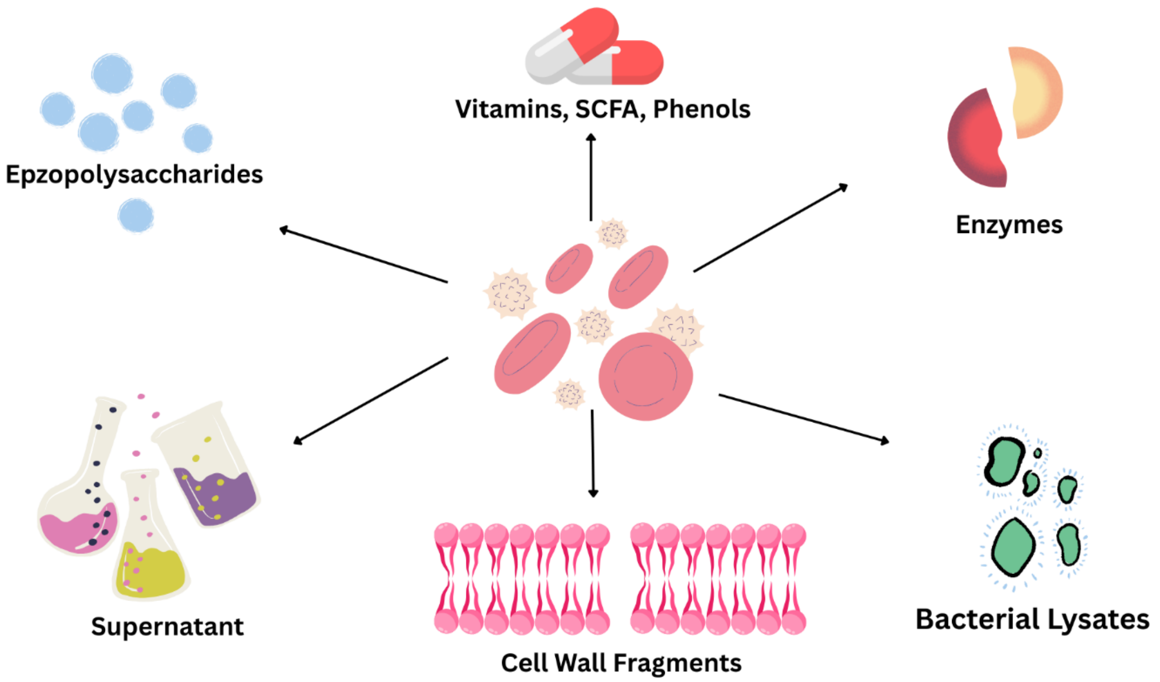

**Fig. 3:** Approaches to Postbiotics Production (Designed using Canva Pro)

### iii. Advantages Over Probiotics

Production of bacterial culture and prediction of probiotics nature is not easy. In probiotics a major issue is standardization of does which is not a case in postbiotics. Postbiotics have many benefits such as they are easy to store, shelf life is longer, easy to transport and doesn't need maintenance of low temperature as compared to probiotics. As compared to probiotics, postbiotics have additional benefits such as high quantitative control. Other then therapeutic benefits postbiotics have safety advantages too. Postbiotics safe host from the exposure of viable pathogens especially children with a poor immune system (Fig. 4). Functional food are dietary products which give many health advantages with other nutritional benefits. To enhance immune function of food postbiotics are added as supplements in functional food. For example, postbiotics such as *B. breve* and *S. thermophilus* reduce food allergy in one month of child (Żółkiewicz et al., 2020).

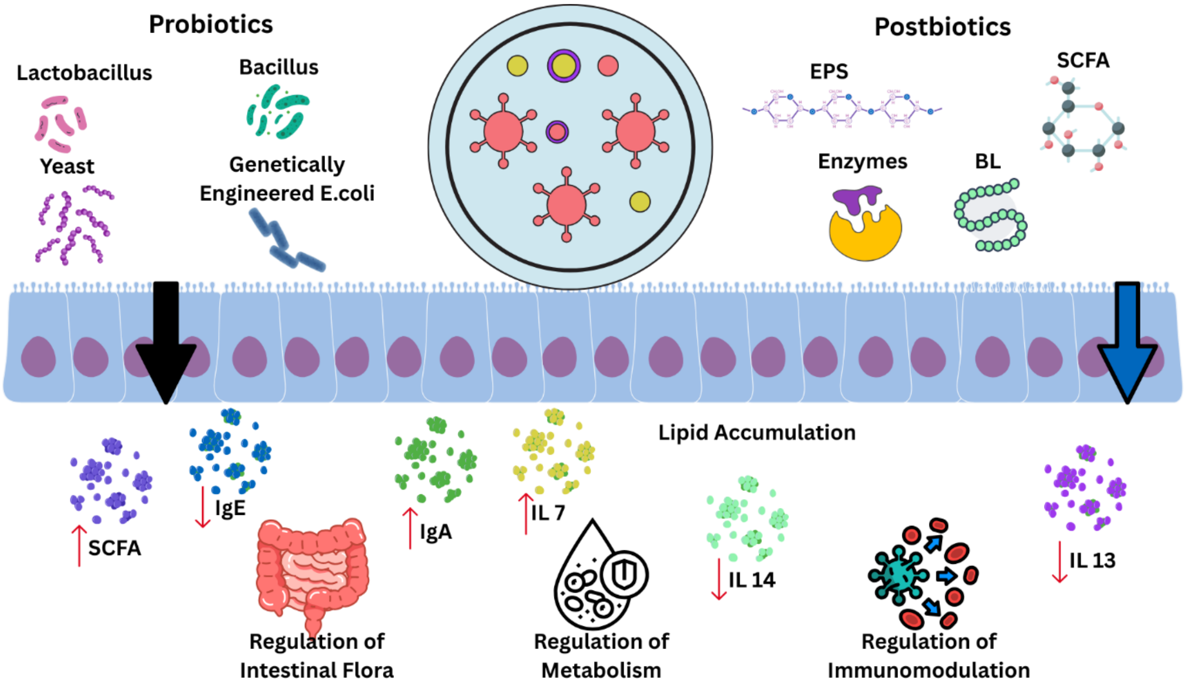

**Fig. 4:** Components of Postbiotics and Probiotics

## 4. Probiotics and Postbiotics in Companion Animals

### i. Dogs

Probiotics gave many health benefits in animals such as protection against pathogens and decreasing inflammation. Probiotics are added in many pets' food and treats. Research showed that there are some proof that diseases like chronic and acute GI can be prevented by probiotics. More studies showed that biotics helps in treating canine acute diarrhoea. Postbiotics not only adjust gut microbiota but also give benefits such as modulation of immune system and barrier function enhancement. Postbiotics showed modulation of gut and enhanced immune response in dogs having supplements of *Saccharomyces cerevisiae*. They also showed markers modulation of stress and inflammation. Additionally, these dogs showed less proinflammatory cytokines (Wilson & Swanson, 2024).

### ii. Cats

For dogs and cats many literatures reported use of lactic acid-producing bacteria, such as *Lactobacillus* species, *Enterococcus* species which modulate GI and immune system. Cats with antibiotic associated diarrhoea showed improved health by addition of supplement of *E. faecium* after 14 days of use. In 7 to 27 weeks old cats, it also showed increased lymphocytes. In cats, postbiotics such as *S cerevisiae* showed enhanced digestion and crude fibre as well as reduced faecal lactic acid levels. Cats fed with higher dose of postbiotics show decreased gross energy digestibility (Wilson & Swanson, 2024).

## 5. Probiotics and Postbiotics in Livestock and Poultry

Many probiotics and postbiotics are used to maintain modulation of gut microbiota and prevent from pathogen growth present in pigs, cattle and chicken farms.

### i. Poultry

Protection of poultry is essential component of good breeding. The pathogen which is most common in broiler breeding is *Salmonella sp*. Research reported that chickens treated *Lactiplantibacillus plantarum* LTC-113 showed reduced pathogens growth in gut and balanced junction gene against *Salmonella Typhimurium*. In another case study orally given *Lactobacillus johnsonii* showed decreased gut attachment by *Salmonella* and *Clostridium perfringens*. Another study showed that damage to mucosa of intestine and weight loss can be prevented by two strains *Enterococcus faecium* and *Ligilactobacillus salivarius* when given with probiotics. In another study use of *E. faecium* in feed showed enhanced weight of eggs as well as reduced *Bacteroidetes* (Zamojska et al., 2021).

### ii. Swine

Pigs are reported to be very delicate regarding modifications in their breeding environment. Disturbance and disbalance in gut microbiota are stressful for pigs. During this time pigs suffered from gut disorders, diarrhea, growth problems and increased death rate. Some studies suggest that strains such as *L. salivarius* and *Lactobacillus delbrueckii subsp. lactis* extracted from gut of pigs' can stop growth of microbes by producing organic acid with bacteriocin-like proteins. In another case study piglets are given soy milk with biotic feed with *L. delbrueckii subsp. delbrueckii* TUA4408L. They not only improved gut microbiota but also enhanced *Lactobacillus and Lactococcus*. It also helped in increased immunity, growth and better meat quality (Zamojska et al., 2021).

### iii. Cattle

In cows' inflammation of udder is known as mastitis that cause pain, reduced appetite, reduced milk, high temperature, inflammation and redness. It caused negative effect on production of milk and decreased productivity. Disease is difficult to manage due to microbes such as *S. aureus* and *Streptococcus uberis*. The disease is tried to be manage by biotics such as *Lactococcus lactis* DPC3147 which showed a cure rate of 45 percent. One study showed that bacteria can be reduced in cow teats by stopping the growth of *E. coli* by lactic acid (Zamojska et al., 2021).

### iv. Antibiotic-Free Production

The greatest invention of 20th century is control of human and animal diseases by antibiotics. But overuse of antibiotics unfortunately caused high antibiotic-resistant pathogens. Livestock breeder's main role is to increase production and decrease death rate. Use of probiotics and postbiotics in livestock and poultry not only balanced the gut microbiota but also decreased production of microbes and pathogens in pig, cattle, piglets and chickens. Studies showed increased in effects of *B. Subtilis*. The case studies also suggest that it can be an alternative for antibiotics and growth promoter in chickens. Not only it increases immunity and weight but also reduces mortality (Zamojska et al., 2021).

## 6. Veterinary Formulations and Delivery Systems

In veterinary market postbiotics and probiotics are employed as an alternative to antibiotics and considered as safe option to promote growth and production in poultry. They not only enhance immune function but also act as immunomodulation factors in animals' health. They are present at moderate prices in land and online markets providing customers health benefits. Postbiotics not only manage intestine problems but also show many clinical as well as non-clinical functions (Heniedy et al., 2024).

### i. Forms

There are various routes of administration of pharmabiotics such as oral, rectal, ocular, nasal, topical and vaginal. Oral use formulations contain tablets, powder and capsules. For topical administration creams and lotions are employed. For vaginal application tablets and capsules are used and sprays are employed for rectal application. A study showed that a biofilm containing probiotics is administrated in eye. Oral tablets are preferable because of its low cost and is easy to use. A study showed that *Saccharomyces cerevisiae* was added as probiotic in an oral tablet. Chewable tablets are form of drug and supplements of food used as pharmaceutical dosage. A study showed benefit of chewable probiotic tablets to children with dental problems (Kandur et al., 2024). Another study showed that the strain of *Lactobacillus reuteri* can be given in the form of powder and improves all clinical factors (Butera et al., 2022).

### ii. Encapsulation and Stability

A process of capsulating or trapping a material such as food products in very small size which prevent the product from natural threats and only releasing material when all conditions are feasible is known as microencapsulation. Microencapsulation of biotics lead to many benefits such as enhanced product bacterial cell count, enhanced function of probiotics in gastrointestinal tract, used in fermenters and insertion in functional food. Studies showed that when probiotics are encapsulated, they exert enhanced survival rate. Microencapsulation gives a coating to bacteria that protects them and make them resistant to many harsh conditions, as well as to stomach juice and acids. Encapsulated probiotics are prevented from conditions such as harsh condition of GT tract and are released in required amount at desirable place. This culture also expressed high survival rate in dairy. On alginate beads strains showed better performance especially strains of *Bifi-dobacterium spp.* and *L. acidophilus* in dessert such as yogurt. The additive employed for encapsulation is Tween 80 (Riaz & Masud, 2013).

## 7. Safety, Efficacy, and Regulatory Aspects

### i. Quality control

Microbes employed as probiotics should meet all safety measures such as should not be toxic, no resistance to antibiotics as well as meet required functional measures such as survival in gastric conditions, stable, and viability of cells. They are tested and the quality is controlled continuously. Essential controls are needed such as all viable number of microbes should be documented, purity should be met, and there should be limited contaminants such as molds and yeasts (Zavišić et al., 2023). Similarly, postbiotics quality control ensures that the organism must be nonviable. An inactivation step is also required. Also, after preparation there's a limit on viable microbes so that nonviable provides health benefits (Vinderola et al., 2025). For instance, the infant formula contains many probiotics microbes and culture powder which were contaminated with *Salmonella.* The problem was managed by addition of antibiotics to reduce the growth of probiotic microbe (Joosten et al., 2006).

### ii. Regulatory Landscape

Various biotics have their related regulation based on their functions and need whether for health benefit or to cure an infection. European Food Safety Authority (EFSA) has provided regulations on how to observe and claim about benefits of probiotics to population. There are also products termed as medical food. FDA established medical evaluation of these medical food which can only be directly administrated under a physician and are used to manage a disease based on FDA principles. FDA also provide guidelines such as Current Good Manufacturing practices for the making and quality control of drugs. They ensure that the product fulfil all standards such as safety and efficacy (Spacova et al., 2023).

## 8. Future Directions and Emerging Trends

### i. Synbiotics and Microbiome Modulation

Probiotics efficacy has showed many varieties. Response to this biotics is different depending on diversity of gut microbiota and variety of microbes. Personalized probiotics concept has emerged to address these conditions where probiotics are made according to host gut microbiota conditions. Various gut microbiota is linked with age, diet, lifestyle and consistency of stool (Min et al., 2024). One approach is faecal microbiota transplantation (FMT) where transfer of faecal content from donor to a host with a dysbiosis microbiome takes place. FMT has shown success in treating infection of *Clostridium difficile* and exerts a notable example of microbiome manipulation (Shukla et al., 2024).

### ii. One Health and Antimicrobial Stewardship

Probiotics and postbiotics have shown tremendous role in modulation of gut microbiome so that these microbes should be beneficial in curing diseased hospital patients as well as faecal carriers having alteration of microbiota. One of the most notable functions is fighting resistance by eliminating pathogenic isolates such as *Bifidobacterium bifidum* ATCC 29521 which reduces the amount of *Shigella* and *Escherichia*. Also, *Lactobacillus plantarum* showed decrease of pathogens such as *Proteobacteria* and *Actinobacteria.* Some ex vivo studies showed that probiotics such as *Lactobacillus plantarum* and *Clostridium* inhibits antimicrobial resistant pathogens. Oral supplements are used for patients with resistant strains (Aghamohammad & Rohani, 2023).

## 9. Conclusion:

In veterinary health addressing problems like microbial dysbiosis, infectious diseases, and antibiotic resistance needs innovative solutions. Both probiotics and postbiotics have shown potential in this regard by increasing digestion, enhanced immune response and increasing overall animal productivity. Probiotics exerts benefits by viable microbes' action whereas postbiotics provide an additional advantage with stable, non-viable nature. They provide antimicrobial, anti-inflammatory, and antioxidant effects which makes them beneficial in managing gut infections, increasing feed efficiency, and regulating immune response in both companion animals and livestock. Gut microbiota play an important role in maintaining animal health, with imbalances leading to dysbiosis, inflammation, and reduced performance. Factors such as diet, age, and antibiotic use highly effects microbial diversity. Supplementation with probiotics and postbiotics has shown positive outcomes in various species such as poultry, swine, cattle, dogs, and cats by enhancing nutrient absorption, triggering immune function, and reducing disease incidence. Clinical applications in conditions like diarrhea, mastitis, and gut infections demonstrate their therapeutic potential. Innovations in delivery systems, such as encapsulation, improve bioavailability and functionality. Regulatory developments further support their integration into veterinary practice. Overall, the consistent evidence across species and systems reinforces the value of probiotics and postbiotics in improving animal health and productivity while aligning with broader goals of antimicrobial stewardship and sustainable animal care.

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# Advanced Diagnostic Techniques and Early Detection of Animal Diseases

06

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## ABSTRACT

Infectious microbial diseases are a major cause of morbidity and mortality worldwide, necessitating accurate and timely diagnosis for effective control, prevention, and treatment. Several traditional and cutting-edge diagnostic techniques are employed in veterinary medicine. Both conventional techniques such as cell culture, serological assays, and microscopy, as well as advanced molecular approaches like polymerase chain reaction (PCR), loop-mediated isothermal amplification (LAMP), real-time reverse transcription PCR (rRT-PCR), and next-generation sequencing (NGS) are described comprehensively. Biosensors, along with nanotechnology-based innovations, offer sensitive, rapid, and convenient diagnostic solutions. Moreover, incorporation of artificial intelligence (AI) along with deep learning models, especially convolutional neural networks (CNNs), has validated significant capability in image-based monitoring as well as the detection of diseases and decision support. Current chapter explores advanced techniques employed in veterinary medicine and highlights existing limitations in deep learning and how tackling these might unlock the peak potential of deep learning to solve multifaceted, real-world problems and enhance AI innovation. Overall, the chapter emphasizes significance of adopting AI-driven approaches for improvement of veterinary diagnostics and reinforces animal health systems globally.

**KEYWORDS**
Diagnosis, LAMP, microbial, PCR, techniques, veterinary

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## 1. INTRODUCTION

Infectious microbial diseases are a significant cause of mortality and morbidity worldwide. Accurate and timely diagnosis is a primary step on the path to control, prevention, and treatment of disease. Effective diagnostic methods are essential for identification as well as proper treatment of disease and controlling outbreaks within population. Mainstream diagnostics are categorized into three broad groups: 1) classical methods as cell culture and microscopy; 2) biochemical methods as colorimetric tests and immunoassays; 3) advanced biotechnology approaches as molecular genotyping, nanotechnology, and DNA microarray. Classical procedures are regarded as cost-effective and gold standards, while advanced techniques are swifter and more sensitive in several cases. Despite these benefits, classical diagnostic approaches have limitations such as slow results, laborious preparation of samples, lower sensitivity, and occasionally ineffective detection. Currently, more accurate and faster methods are region-specific requirements in which new diseases as well as pathogens are emerging daily. Rapid molecular techniques improved the capabilities of the laboratories for identification and characterization of microbial pathogens thoroughly. However, given the limited resources available, especially in developing countries, new methods must be prioritized for accurate policy decisions (Srivastava et al., 2018).

A veterinarian's core competency is to identify the cause of observed clinical signs in distinct animals as well as populations via providing diagnosis of disease. Clinicians should identify risk factors that are ultimate cause and contribute to expression of disease, for preventing disease recurrence. Hence, true causality is a combination of ultimate and proximate causes; therefore, both must be addressed in mitigation efforts. Evaluating causality is improved when diagnosis is based on a comprehensive assessment of entirely available evidence and with mindfulness of potential laboratory along with the individual's cognitive biases and errors. Diagnostic investigation ought to follow a systematic and repeatable procedure that ensures appropriate sample collection, laboratory test results generation, and estimation of generated data reliability. Final diagnosis of disease produced from this method should align with whole pertinent clinical observations with generated test data (Burrough et al., 2025).

## 2. Classification of diagnostic techniques

### 2.1 Conventional approaches

Traditional testing procedures are still employed in veterinary medicine. Conventional serology, methods based on electron microscopy, cell culture, virus neutralization, immunoassay, and immunodiffusion techniques to diagnose animal diseases are labor-intensive and time-consuming (Suminda et al., 2022).

### 2.2 Advanced diagnostic techniques

Presently, techniques based on immunological assay as Enzyme-Linked Immunosorbent Assay (ELISA) and Immunofluorescence (IF) assay as well as different molecular detection-based methods as polymerase chain reaction (PCR), reverse transcription polymerase chain reaction (RT-PCR), multiplex PCR, real time PCR, DNA microarrays, nucleic acid sequencing techniques (first generation and next generation sequencing) allow for improved diagnosis. Additionally, the generation of pathogen-specific proteins permitted assays development which might differentiate non-vaccinated from vaccinated animals. Various companies are creating relatively reasonable, fast and smaller devices based on advanced technologies to rapidly detect infections in domestic animals by addressing varied diagnostic issues such as genetic relationships between viruses or bacteria related to companion and livestock animals, and mutation detection in bacterial or viral genomes that result in resistance against antibiotics or antivirals. Second and third-generation sequencing platforms offer many benefits over conventional microbiological diagnostic procedures, including the capability for the detection of non-culturable or fastidious pathogens as well as co-infections. High-throughput sequencing (HTS) or next-generation sequencing (NGS) methods enable researchers to concurrently identify wide-ranging DNA sequences by either deploying a particular genetic region as amplicon/metabarcoding-based methods or entire genetic material. Furthermore, sequencing technologies are employed for characterizing viral diversity in animals and humans. From epidemiology to viral quasispecies evolution as well as metagenomic characterization of microbial communities along with unidentified pathogens, molecular identification has noteworthy implications (Minakshi et al., 2014).

## 3. Molecular diagnostic techniques

### 3.1 Polymerase Chain Reaction (PCR)

PCR is the most promising technique currently employed in forensic science, diagnostics, and bioscience. Initially, PCR was created to detect mutations in the HBB gene, which causes sickle-cell anemia. Knowledge acquired during this research on HBB gene was deployed in analysis of HLA-DQ alleles, which resulted in developing a genotyping method for a multiallelic locus via employing amplicon hybridization with allele-specific oligonucleotides. Technique applied in forensic science and transplantology. Various clinical applications of PCR are deployed, especially in microbiology and clinical genetics, to detect bacterial and viral infections. The efficacy of PCR as a diagnostic tool to identify infectious diseases was first confirmed in 1987 and further expanded in later years (Zhu et al., 2020).

To diagnose bovine tuberculosis, PCR is employed to detect Mycobacterium tuberculosis in tissue collected during necropsy from animals that are suspected of having bovine tuberculosis infection. PCR is only performed on tissues that have microscopic or histological evidence consistent with bovine tuberculosis. Results can usually be achieved within 7 days and categorized as either negative or positive. Positive tests on PCR are highly indicative that the animal is diseased with bovine tuberculosis. PCR has been extensively evaluated to detect Mycobacterium tuberculosis complex (MTC) in clinical samples, mostly sputum from human patients, and has lately been deployed for tuberculosis diagnosis in animals (Wagari, 2016).

### 3.2 Real-Time Reverse Transcription Polymerase Chain Reaction (rRT-PCR)

PCR is an extremely sensitive laboratory method that has demonstrated applicability in medical and biological sciences and possesses the capability for providing quantitative and qualitative results. PCR modification with diagnostic employment is rRT-PCR, applied for detection of target RNAs in clinical specimens, particularly to diagnose microorganisms in molecular diagnostic laboratories (Rahbari et al., 2021). Molecular tests to detect viral RNA as RT-PCR, are suitable to identify viruses in lower biocontainment. Virus is inactivated in the primary step of the assay via adding guanidium isothiocyanate as well as phenol, comprising standard RNA extraction kit reagents such as TRIzol (Invitrogen) or Tri-Pure (Roche Diagnostics), and in addition, control reagents are prepared synthetically (Drolet et al., 2012). Real-time RT-PCR has displayed superior specificity and sensitivity in contrast with currently utilized antigen detection approaches to isolate viruses and traditional reverse transcription PCR (RT-PCR) for numerous livestock diseases and has proved reliable for generating quick results in a portable format (Carrillo et al., 2010).

Foot-and-mouth disease (FMD) is a very devastating viral disease of cloven-hoofed animals and is regarded as serious risk to livestock industry globally (Kumar et al., 2011). RNA virus of FMD belongs to Aphthovirus genus, within family Picornaviridae, and has a positive-sense genome with about 8300 nucleotides. FMD virus is categorized into seven antigenically different serotypes (O, A, C, Asia 1, SAT 1, SAT 2, and SAT 3) along with various and incessantly evolving subtypes (Hoffmann et al., 2009). Affected species are domesticated ruminants (goats, sheep, cattle, camels, buffalo) and pigs, together with over 70 wildlife species. Morbidity may exceed 100% in the susceptible population (Kumar et al., 2011). RT-PCR techniques play a significant role in sensitive and rapid FMD virus detection in variety of clinical samples. Over the past 10 years, advancements were made to RT-PCR protocols to detect FMD virus, which paralleled the development of molecular diagnostics. Originally, assays employing agarose-gel electrophoresis to detect amplified products as well as targeting conserved regions of genome along with 5' untranslated region were developed. Nevertheless, these labor-intensive methods have an elevated risk of producing false positives owing to PCR amplicons carry-over and therefore are not promising for routine testing of numerous samples.

Latest development in rRT-PCR methodology, deploying fluorescently labelled probes for detection of PCR amplicons, enhances the diagnostic capability of molecular assays. These assays are very sensitive and avoid opening the tube after amplification, thus lowering risk for test sample cross-contamination via post-PCR products. Besides the widely employed 5-nuclease (TaqMan®) method utilizing dual-labelled as well as modified minor groove binding probes, assays have also been developed employing other rRT-PCR formats as PriProET and hybridization probes. To reduce operator errors and enhance assay throughput, rRT-PCR methodology for FMDV might be automated via employing robots for the extraction of nucleic acid and a liquid handling instrument for setting up reaction mixes. These enhancements increased rRT-PCR assays acceptance for diagnostic purposes, together with the application of quality control systems (Hoffmann et al., 2009).

African swine fever (ASF) is a viral disease with an increased mortality rate in wild boars and domestic pigs. ASF is a serious infection in pigs, instigated by African swine fever virus (ASFV) infection, and demonstrates mortality nearly 100% (Li et al., 2022). Another febrile disease of swine is classical swine fever (CSF) that remains a major concern for swine industry worldwide owing to significant economic impact as well as potential for damaging outbreaks. CSF virus (CSFV) is the causative agent and has a positive-sense single-stranded RNA genome. CSF and ASF exhibit comparable clinical signs in pigs that are affected; thus, tentative diagnosis based on clinical symptoms and postmortem inspection of suspicious cases should be confirmed through laboratory investigation. The rRT-PCR technique offers simplified yet accurate detection of CSFV and ASFV in a single reaction without requiring nucleic acid purification. The efficiency of assay in identifying ASFV as well as CSFV was thoroughly validated employing entire blood samples, serum samples, and tissue samples, which were collected from pigs, wild boars, and boar–pig hybrids within experimental conditions, and confirmed that three ASFV genotypes (I, II, and X) might be detected (Shirafuji et al., 2024).

Influenza A viruses are significant pathogens that constantly challenge both animal and human health (Shi et al., 2023). Influenza viruses are negative-stranded enveloped RNA viruses that belong to Orthomyxoviridae family. Influenza virus A genus instigates avian influenza (AI) via infecting birds (Monne et al., 2008). Influenza A virus genome consists of eight gene segments such as hemagglutinin (HA), nonstructural (NS) and matrix (M) protein, neuraminidase (NA), basic polymerase 1 (PB1), nucleoprotein (NP), acidic polymerase (PA), and basic polymerase 2 (PB2). Each segment encodes 1-3 proteins. Influenza viruses are categorized into various subtypes based on NA and HA proteins antigenicity. At present, 9 NA and 16 HA subtypes have been identified in avian species. H1N1, H3N2, and H2N2 viruses triggered 4 influenza pandemics from 1918 onward, and H1N1 along with H3N2 viruses continuously co-circulating in humans worldwide. AI viruses are sustained and spread in wild birds. Although various subtypes of viruses have been identified in domestic poultry, especially waterfowl that live near wild birds, just 3 HA subtypes as H7, H5, and H9 spread and found in domestic poultry over wide-ranging geographic areas. Certain strains possessing the HA gene of H7 or H5 subtypes are extremely virulent for poultry and have instigated serious problems for poultry industry as well as public health globally (Shi et al., 2023). Traditional AI diagnostic tools such as virus isolation and hemagglutinin inhibition are chronophagic and require facilities that are not easily available in several affected areas. Owing to sensitivity and rapidity, molecular tests like rRT-PCR are increasingly employed by veterinary and medical diagnosticians to diagnose AI. The rRT-PCR assay to simultaneously detect subtypes H7, H5, and H9 is a useful tool for fast surveillance and screening in domestic and wild birds. The rRT-PCR technique deployed to monitor AI virus in wild birds and poultry demonstrated capability for the detection of various genetic lineages of the subtypes as H7, H5, and H9 viruses involving H5N1 subline ages prevalent in Africa and Eurasia (Monne et al., 2008).

The rRT-PCR assay is also regarded gold standard for identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Despite high specificity along with moderate sensitivity and being approved as the gold standard method for COVID-19 confirmation, this technique indicated a vast amount of false-negative outcomes that must be greatly considered. Hence, troubleshooting as well as following the guidelines can efficiently increase the precision and accuracy of obtained results (Rahbari et al., 2021).

### 3.3 Loop-Mediated Isothermal Amplification (LAMP)

Molecular methods have been created for increasing specificity and sensitivity of traditional diagnosis as well as immunological techniques. Though PCR is only accessible to specific facilities owing to the need for exceptional detection devices. LAMP, another molecular method, is a substitute for PCR. LAMP assay is highly efficient, specific, and swift gene amplification technique in which the reaction is run at constant temperature (Martínez-Valladares and Rojo-Vázquez, 2016). LAMP detect and distinguish pathogen species rapidly and exhibit higher sensitivity along with specificity rather than conventional PCRs to detect the presence of DNA in fecal samples (Ni et al., 2014). The qualitative LAMP technique took just 1 hour and 10 min for detection of Fasciola hepatica (F. hepatica) in affected sheep feces (Martínez-Valladares and Rojo-Vázquez, 2016). LAMP method also exhibited excellent specificity for employment in Echinococcus multilocularis (E. multilocularis) infection diagnosis in canine hosts (Ni et al., 2014).

Sheep pox and goat pox are commercially significant diseases in sheep and goat producing regions of world. These occur from infection via goat pox virus (GTPV) or sheep pox virus (SPPV), respectively, and are close members of genus Capripoxvirus in family Poxviridae. Clinically, goat pox and sheep pox show identical symptoms and thus cannot be differentiated easily. Combining three sets of LAMP primers provides a robust analytical technique that is fully capable of differentiating between SPPV and GTPV (Zhao et al., 2014). Moreover, a single-step reverse transcription LAMP (RT-LAMP) method detected FMD virus without thermal cycling in a single tube in an hour. RT-LAMP was reliably faster as compared to rRT-PCR, and ten FMDV transcript copies were identified in twenty-two minutes (Dukes et al., 2006). Additionally, the H7N9 virus RT-LAMP technique was developed and confirmed detection of H7N9 influenza virus with high specificity and sensitivity. The RT-LAMP technique demanded minimal laboratory instruments and could identify different H7N9 influenza virus sources. Although the recommended diagnostic process for the H7N9 virus was rRT-PCR technique, however, rRT-PCR requires a costly machine system and skilled laboratory workers (Bao et al., 2014).

### 3.4 Next-Generation Sequencing (NGS)

The continuous technological advances in high-throughput sequencing (HTS), also known as next-generation sequencing (NGS), have caused a dramatic decline in DNA sequencing costs, enabling technology to be easier to access for average. NGS technologies have transformed the genomics field completely (Suminda et al., 2022). NGS technologies introduced between 2004 and 2006 revolutionized biomedical investigation. A significant rise in data output owing to nanotechnology principles along with innovations, permitted enormously parallel sequencing of individual DNA molecules. NGS has two main types: second-generation sequencing (short-read NGS) and third-generation sequencing (long-read NGS).

#### 3.4.1 Second Generation Sequencing

Second-generation technologies like Ion Torrent or Illumina platforms normally start with fragmentation of DNA, end-repair of DNA, adapter ligation, surface binding, and in-situ amplification. These “short read” sequencing techniques involve extensively parallel sequencing of short reads, through which millions of distinct sequencing reactions occur simultaneously. However, being short-read techniques by nature, sequencing data above long DNA stretches should be reassembled, which presents challenges with low-complexity regions or structural variations.

#### 3.4.2 Third Generation Sequencing

Third-generation sequencing as Oxford Nanopore or Pacific Biosciences technology platforms, can generate read lengths above 10 kb, far exceeding short-read or Sanger sequencing techniques. These “long-read” techniques can overcome problems detected with short-reads as structural variants and genome-wide repeats. Compared to short-read approaches where high molecular weight DNA production is a limiting factor, this technology requires minimum steps for library preparation as well as direct targeting of intact DNA molecules in real-time. Primary limitation of third-generation techniques as compared to second-generation procedures was the accuracy of reads, which is consistently advancing, especially with developments in software analysis (Hu et al., 2021).

The MinION portable sequencer from Oxford Nanopore Technologies (ONT) has capability of sequencing in distant, decentralized laboratories near to outbreak location. Suitability of MinION sequencing system as tool for characterization of FMD was evaluated. MinION could generate consensus sequence that was 100% identical to reference sequence for all except two tested samples. Consensus sequences that were 100% identical to reference sequence, were achieved after 2 minutes of sequencing for almost half (4/9) of tested samples. Consensus sequences generated after 2 minutes did not achieve 100% accuracy. A BLASTn search conducted for these sequences consistently revealed the same phylogenetic position, albeit with a lower identity percentage. Thus, it was revealed that accurate data sequencing might be generated within short time (Brown et al., 2021). Additionally, MinION appears favorable for on-site as well as real-time sequencing of entire swine Influenza A virus (IAV) genomes. The employment of MinION can increase swine IAV testing scalability in the field and improve outbreak response of swine IAV illness owing to superior raw read accuracy (Chauhan and Gordon, 2022).

The recommended four primer sets for ASFV might be multiplexed in distinct PCR reactions and consequently deployed for distinguishing among ASFV genotypes via utilizing nanopore sequencing technique. ONT sequencing was combined with multiplex PCR. This allowed four amplicons sequencing within a single barcode and multiplexing of numerous samples in one sequencing run, leading to shorter turnaround times, roughly 5 h for preparation of library and sequencing on the ONT platform, whereas Sanger sequencing normally requires one working day. Furthermore, ability to sequence larger genomic regions permits the complete p72 coding region (about 2 kb long) to be sequenced, that recently employed to propose novel ASFV classification in six genotypes (Licheri et al., 2024).

## 4. Biosensor and Nanotechnology Based Approaches

Biosensors are analytical devices for swift and effective diagnosis of infectious diseases owing to simplicity, potential for miniaturization, and real-time analysis. Numerous biotechnological innovations have offered biosensors for viral and bacterial identification and monitoring over the past thirty years. Biosensors have been designed for detection of targets such as nucleic acid or protein sequences associated with pathogens via employing sensitive and specific recognition properties of the bioreceptors, such as DNA probes, aptamers, antibodies, and glycans. These sensing elements relate to a transducing element (optical, electrochemical or colorimetric) which emits a direct signal upon target recognition. Although majority of presented analytical instruments are only employed in research laboratories, it is anticipated that further biosensors will emerge in the future due to fast spread of infectious livestock diseases. Novel biosensors reported based on biochemical recognition approaches to rapidly and precisely detect E. coli just like PCR-based methods (Vidic et al., 2017).

In recent years, enormous research efforts have focused on employing different nanoparticle (NP)-based enhancers, which resulted in development of nanomaterials-assisted PCR (nano-PCR). NP-based enhancers as gold nanoparticles (Au NPs), carbon nanotubes, semiconductor quantum dots, and carbon nano-powders have been demonstrated to enhance PCR efficiency and specificity. Au NPs are the most renowned and efficient enhancers, which are proficient in improving two PCR rounds regarding both yield as well as specificity. Au NPs exhibit unique physical and chemical properties as a high surface-to-volume ratio, design flexibility, easy surface modification with multiple ligands, improved electron transfer, catalytic effect regarding electrochemical reactions, and biomolecule labelling, which make such an enhancer specifically appropriate to design novel, along with improved biosensors. Au NPs based RT-PCR and rRT-PCR techniques were employed to diagnose Japanese encephalitis virus (JEV) rapidly and accurately. Additionally, a portable Au NPs based biosensor employing surface-enhanced Raman scattering (SERS) attained influenza virus identification with a detection limit of 1 pg/μL. Viral pathogens detection via deploying Au NPs-based biosensors provided notable improvement in viral disease diagnostics. Implementation of Au NPs-FMDV biosensor in RT-PCR as well as rRT-PCR was conducted to evaluate the enhancement effect of Au NPs-FMDV biosensor in analytical sensitivity, specificity, dynamic range, efficacy, and detection limit of rRT-PCR and RT-PCR. Au NPs-FMDV biosensor revealed excellent analytical as well as clinical performance to diagnose FMDV. Analytical sensitivity along with dynamic range (detection limit) of Au NPs-FMDV biosensor was 10 RNA standard copy numbers in RT-PCR and 1 RNA standard copy number in rRT-PCR with 94.5% efficiency, value of 0.989 R2, slope of −3.544, and 100% specificity without showing cross reactivity with SVDV (Hamdy et al., 2018).

## 5. Artificial Intelligence and Digital Technologies

Artificial intelligence (AI) has transformed various industries, including veterinary medicine field. AI has confirmed enormous potential in clinical examining, diagnosing, and treating animals owing to evolving capabilities and usages. AI applications are far-reaching and diverse in veterinary medicine, and one remarkable application is the creation of AI-powered diagnostic methods. These systems employ machine learning algorithms for evaluation of enormous data volumes such as lab results, medical records, and imaging studies, which assist in diagnostic processes. AI algorithms aid veterinarians in making more accurate diagnosis via detection of patterns and identification of subtle anomalies. Clinical examination is another important AI application. AI-powered devices and sensors in real-time can monitor significant signs and behavior of animals, allowing fast detection of health problems. AI algorithms equipped with wearable devices can track heart rate, temperature, respiratory rate, and additional parameters, offering clinicians important data for assessment and diagnosis. Besides, AI has confirmed effectiveness in planning treatment and outcome prediction via analysis of historical data and deploying AI algorithms as well as machine learning. AI can detect patterns as well as make predictions, which support veterinarians to diagnose complex diseases. For example, AI algorithms have validated efficacy for identification of respiratory conditions, enlargement of left atrium on canine thoracic radiology, skin disorders, equine colic, and behavioral problems in animals. This accuracy enables veterinarians to provide targeted treatments, lessening misdiagnosis and ensuring efficient care for animals (Albadrani et al., 2024).

### 5.1 Machine learning (ML)

Machine learning (ML) is a fundamental approach in AI that permits computers to analyze data and forecast outcomes without requiring explicit programming. ML comprises two main categories as traditional ML and deep learning (DL). Traditional ML procedures such as support vector machines, random forests, and k-nearest neighbours (k-NN) are widely used in livestock health, including calving and oestrus prediction, detection of lameness, and disease monitoring. While traditional ML methods have proved effective in veterinary diagnostics and precision livestock farming, these frequently demand manual feature engineering that limits their effectiveness for complex data. Conversely, DL is an AI subset that can process large volumes of complex data relative to ML along with additional expenses of demanding greater computation power. Neural network-based DL models automatically acquire relevant features during the training process from data, decreasing requirement for broad manual intervention. At present, machines can attain more nuanced methods through DL for detection of trends in data, resulting in accurate predictions as well as insights across various applications. DL technology is the driving force behind numerous recent developments in AI, including image recognition, speech recognition, and processing natural language. There are two main DL methods such as convolutional neural networks (CNNs) and recurrent neural networks (RNNs). RNN is a DL technique, devised for formulation of sequential patterns in videos and texts. RNN was adopted to detect chronic kidney diseases in cats from patient historic electronic hospital records and attained high classification accuracy of 0.989 and 0.907 for specificity and sensitivity, respectively. CNNs are commonly employed by DL architectures to analyze images in veterinary medicine. CNNs can process visual data via learning features spatial hierarchies, making them notably capable for disease identification, classification along with segmentation in medical imaging. Furthermore, variational autoencoders (VAEs) and generative adversarial networks (GANs) showed potential in mitigating the requirement of broad labelled datasets in analysis of medical imaging (Xiao et al., 2025).

### 5.2 Deep Learning in Disease Diagnostics

CNNs are one of the most well-known and widely employed innovative deep learning algorithms for analyzing and processing visual data as videos and images automatically without requiring manual feature engineering. Lumpy skin disease (LSD) demonstrated clinical symptoms such as fever, nodules development on skin, internal organs, and mucous membranes. Recent studies deployed CNNs to detect and classify lumpy skin illness from images. In an investigation, 10 pretrained models, including MobileNetV2, VGG16, InceptionV3, and DenseNet201 were assessed in comparative analysis. VGG16 achieved 96.07% accuracy on one dataset and MobileNetV2 attained 96.39% accuracy on another dataset, highlighting their efficiency in LSD detection. Deep learning models have been established for detection of diseases (poultry farming encounters difficulties from diseases such as Salmonella, coccidiosis, and Newcastle disease) from fecal images. A system combining ResNet50 to classify and YOLO-V3 to detect objects trained on fecal images of 10,500 chickens. YOLO-V3 attained a mean average accuracy of 87.48% for detection of interesting regions, while ResNet50 achieved 98.7% classification accuracy. Diseases of skin in livestock like sheep, goats, and cattle can be recognized via deploying deep learning models. EfficientNetB7, DenseNet201, and MobileNetV2 models were applied for the classification of skin diseases, attaining 99.01%, 97.08% and 95.31% accuracy, respectively. EfficientNetB7 revealed superior performance for the detection of disease. Beyond image-based diagnosis, deep learning has also been implemented on genomic data for the identification of diseases (Bello et al., 2025).

### 5.3 AI Tools in Veterinary Radiology

RapidRead is an AI-powered radiology tool created by Antech and a reporting tool that was designed to assist diagnostic decision-making. Other commercially accessible AI-radiology systems are Radimal, which employs machine learning to recognize patterns across numerous imaging modalities, and another one is SignalPET, which provides real-time automated interpretation of radiographic results. These solutions indicate an emerging shift toward incorporating AI into diagnostic workflows in veterinary medicine to improve speed, consistency, and scalability. The Vertebral Heart Scale (VHS) is a tool employed for the prediction of congestive heart failure as well as quantification of cardiac dilatation on radiography. AI performance to measure VHS to two board-certified specialists was evaluated in a study. Each operator assessed 30 cats and dogs' thoracic lateral radiographs by utilizing two different techniques for identification of cardiac short axis on cats and dogs' radiographs. The individual assessments made by AI, radiologist, and cardiologist were comparable in determining VHS in cats and dog patients (Arshad et al., 2025).

### 5.4 Limitations and Future Directions

All DL models demonstrate robustness to a certain extent; current techniques are still defective, which makes them prone to criticism. Owing to big data availability across several domains, data quality can become problematic during DL model training. DL models training might also be very expensive, time-consuming, and requires numerous correct instances for improving accuracy, which limits their employment for daily purposes and in critical security systems. The generated models are also domain-specific and hence, exhibit restricted applications. Additionally, DL is vulnerable to misclassification and deception, which might threaten the financial and social securities of corporations and/or individuals. The probability of models becoming ensnared in local minima renders several models unsuitable for online applications. Future networks should attempt to produce possible outcomes set, rather than providing a single final prediction for input, which can facilitate tackling the issue of unclear or distorted inputs. Developing novel strategies for optimizing parameters, mainly hyperparameters, is an additional possibility that necessitates further investigation. Capsule architectures may control future DL models owing to their ability to provide an improved method of information routing between layers. DL models can possibly contribute to ongoing innovations in the AI field and resolving far more complicated problems, if existing challenges are addressed (Ahmed et al., 2023).

## Conclusion

Infectious diseases remain a substantial threat to animal health and livestock production worldwide. Timely and accurate diagnosis is essential for effective control, prevention, and treatment of diseases. Traditional methods like culture and microscopy are labor-intensive and time-consuming. Advanced molecular methods like PCR, LAMP, rRT-PCR, and next-generation sequencing allow accurate and rapid disease detection. AI and DL models, mainly CNNs, further enhanced disease identification through image analysis along with data analysis. AI tools integration with wearable devices provides real-time monitoring of diseases and advances veterinary decision-making. Addressing existing limitations in deep learning can unlock the peak potential of deep learning to solve multifaceted, real-world problems and enhance AI innovation. With sustained technological advancements, these techniques will play a significant role in the future of veterinary diagnostics. Therefore, prioritizing swift, accurate, and available diagnostic tools is crucial for effective disease prevention globally.

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# Advances in Diagnosis and Therapeutics of Bovine Tuberculosis

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## ABSTRACT

Zoonotic disorders pose significant challenges regarding their economic and health implications. Bovine tuberculosis is a major problem with a complicated epidemiology that affects people, domestic animals, and wildlife. Granuloma formation in tissues, particularly in lymph nodes, lungs, liver, kidneys, and intestines, is a defining characteristic. *Mycobacterium bovis* is the primary etiological agent of Bovine Tuberculosis. Pathogens may disseminate through enterogenous and aerogenous pathways. The objective of this study was to identify knowledge gaps to inform control policy, highlighting where novel research could contribute to addressing these gaps, specifically regarding Bovine tuberculosis and other zoonoses. Therefore, the advancement of novel, cost-effective, and efficient theragnostic tools is essential to address these challenges. Nanotechnology has significantly advanced medicine by enabling multifunctional approaches to diagnose and treat zoonosis. This is achieved through the targeted and regulated delivery of antimicrobial agents that bind to overexpressed infectious macrophages.

**KEYWORDS**
Antimicrobial, Bovine, Nanotechnology, Tuberculosis, Zoonosis

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## 1. INTRODUCTION

Zoonotic diseases are characterized by the ability to transmit infection between humans and animals. Scientists widely suggest that about 3/5 of all human diseases have their origins in animal species; however, about 75% of recently emerging infectious diseases are all potentially of zoonotic origin (Nga et al., 2019). Domesticated animals contribute to the transmission of various diseases into human body (Klous *et al.,* 2016; Morand et al., 2014). Approximately 60% of emerging infectious diseases are zoonotic, out of which 72% have been estimated to have their origins in wildlife. Zoonotic infection spreads through contact between humans, livestock, captured animals, and wild species (Conteddu et al., 2024). Companion animals might harbor a wide variety of infections, which can be parasitic, bacterial, fungal, and viral. Among the ones that are introduced by scratches and bites, cat-scratch disease, and diverse aerobic and anaerobic infections, Pasteurellosis prevails. Seven endemic zoonotic infections of interest are listed as brucellosis, echinococcosis, rabies, anthrax, human African trypanosomiasis, cysticercosis, and bovine tuberculosis (Halsby et al., 2014; Hundal et al., 2016).

## 2. Bovine Tuberculosis

Tuberculosis (TB) afflicts an extensive diversity of mammalian hosts and is known to have existed for millennia. TB has been a major killer for 200 years when compared to other major diseases (Elsayed and Amer, 2019). Koch identified *Mycobacterium tuberculosis* (Mtb), the etiology of TB, in 1882, and Smith recognized *M. bovis* as a distinct species from Mtb in 1898. Incidence of bovine TB is economically significant, attributed to loss of productivity, morbidity, and mortality as well as potential zoonotic risk. However, even in developed countries, including the USA, Australia, and some European nations, regional disease foci are still present (Borham et al., 2022).

TB as a significant sickness of animals and humans affects 2 billion individuals or 1/3 of global inhabitants, and 1.5-2 million individuals succumb to TB annually. It is a multi-species and complicated disease that can exist in one of three forms: bovine, avian, and human TB (Jemal, 2016). Bovine tuberculosis (BTB) is an infectious bovine illness instigated by *Mycobacterium caprae* and *Mycobacterium bovis,* which infects wild mammals, humans, and domestic small ruminants (Domingo et al., 2014). TB consists of lesions that include mesenteric lymph nodes with potential presence of mycobacteria, which has been one of the biggest health hazards to humans (Admassu et al., 2015). Disease lesions in TB cattle mainly affected respiratory lymph nodes in about 90% of cases (Menzies and Neill, 2000).

### 2.1. Etiology

Major etiology of Btb is *Mycobacterium bovis* (*M. bovis*), owned by the *Mycobacterium tuberculosis* complex, together with significant human pathogens, *Mycobacterium tuberculosis, Mycobacterium africanum, Mycobacterium canettii, Mycobacterium pinnipedii, Mycobacterium caprae,* and *Mycobacterium microti*. These infectious pathogens are closely associated with mycobacteria, having 99.9% chromosomal uniqueness and are all phylogenetically adjacent species that instigate TB with relatively analogous pathology in diverse mammal species (Romha et al., 2018). Attributed to obligatory metabolism, possible pathogenicity or saprophytic nature, the Mycobacteria genus causes mycobacteriosis of warm and cold-blooded animals and includes 163 species and 13 subspecies (Kuria et al., 2018). *M. bovis* is believed to have the broadest host range and can infect ungulates, carnivores, marsupials, rodents, lagomorphs, and primates, including humans (Reis et al., 2021).

### 2.2. Epidemiology

Generally, molecular epidemiological studies aim to characterize infectious agents comprehensively to find the physical source, route of transmission, virulence genes, antigens relevant to vaccine development, and drug resistance. Practically, in specialized TB laboratories, molecular epidemiology is used to identify outbreaks and infection source, the connection between different outbreaks and animal reservoirs of *M. bovis* existence (El-Sayed et al., 2016). BTB is a zoonotic pathology that is endemic in the UK and Ireland and has a global distribution including the continents of Africa, Middle East, Europe, Asia, and America (Fig. 1). It is a slow, incurable, and disabling disease that poses a major challenge to the UK cattle industry and with serious societal health impacts in countries that do not have mandatory eradication schemes (Denholm et al., 2020).

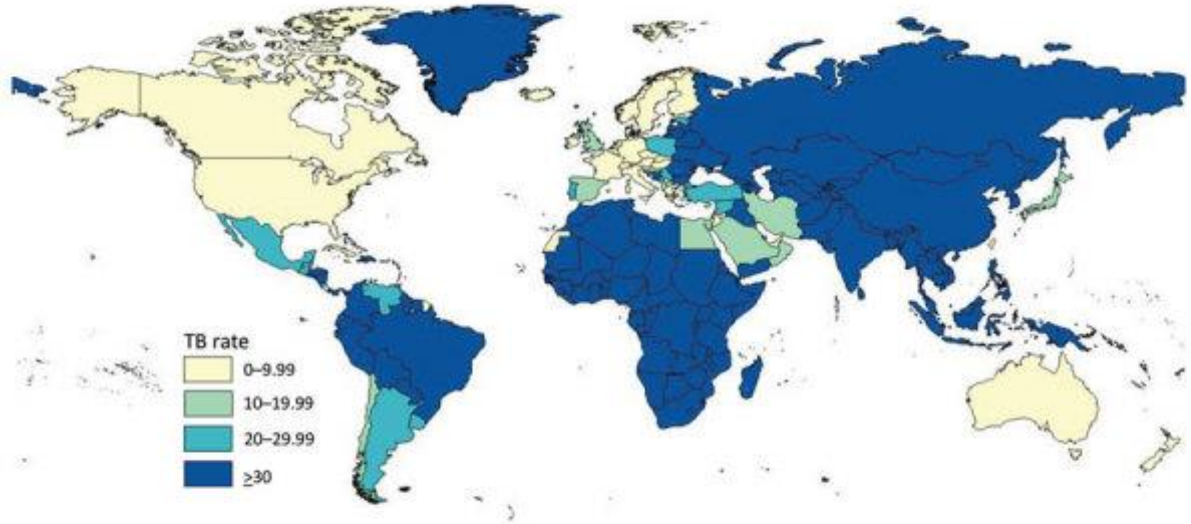

**Fig. 1.** TB rates (per 100,000 population) worldwide, according to World Health Organization reports, 2014. TB, tuberculosis reproduced with the permission of Copyright © 2020 (Tsang *et al.,* 2020).

### 2.3. Risk Factors

Various BTB risk factors have been identified in cattle globally. These risk factors comprise numerous parameters regarding wildlife, cattle contact, movement, and animal density (Humblet et al., 2010). The main risk associated with the transmission of BTB is the introduction of infected cattle to herds during the movement of cattle (VanderWaal et al., 2017). Additionally, risk factors at the animal level include genetics, sex, breed, age, behavioral factors, milk yield, nutritional status, and reproductive condition. The risk factors at herd level entail herd kind, farm node, herd size, contact with nearby herds, farm region, and BTB history. Risk factors at environmental level involve weather, soil type, transmission through invertebrates, birds, and protozoa (Broughan et al., 2016).

### 2.4. Transmission and Pathogenesis

*M. bovis* disease is usually acquired by direct interaction with animals of tuberculous origin, since bacteria can be discharged in saliva, semen, exhaled droplets, open peripheral lymph nodes (LNs), urine, milk, feces, uterine and vaginal discharges (Aboukhassib et al., 2016; Ameni et al., 2013; Waters et al., 2015).

The infection route interrelates with the distribution and the localization of the TB lesions. Infection is chiefly by inhaling but occasionally by swallowing infected food, water, and pastures, rarely by transplacental, coital or intramammary infection, and more rarely by entry of the agent into the body through broken skin. Therefore, the utmost commonly affected organs are the nasopharynx, the LN and lung oropharyngeal mucosa, and the retropharyngeal LN, as the most frequent pathway of infections is through the aerogenous and oropharyngeal route (Domingo et al., 2014). Based on human-to-cattle transmission, humans infected with *M. bovis* cannot spread the infection to cattle (Romha et al., 2018). The potential risk of this transmission might be expressed through the aerosol infection of a person, particularly in rural settings when animals move in close association with tuberculotic humans (Kassa et al., 2012). The infection can also be caused by tobacco juice pouring into the mouth of cows, as outdated antiparasitic in Ethiopia few regions (Ameni et al., 2011).

After *mycobacteria* enter by alveolar spaces or mucous membranes are taken up by macrophages and are transported into the bloodstream through the bronchioles lining, and conveyed to LNs, lungs parenchyma. Tubercle bacilli have capability of evading macrophage killing with the help of mycobacterial lipids like lipoarabinomannan of its antigen 85 complex. Mycobacteria ultimately persist and proliferate in phagosomes and destroy phagocytes (Thoen et al., 2008). Viable bacteria diseased after first infection enter draining LNs, lymphatic capillary vessels, and begin a focus on new infection (Domingo *et* al., 2014).

The caseonecrotic granuloma, a tubercle that is the result of the host's attempt to localize the disease process and allow inflammatory and immunological processes to eliminate bacilli, is one of the characteristics of tuberculosis (Fig. 2). Furthermore, *Mycobacterium* directly contributes to the growth of the granuloma by producing virulence factors such as ESAT-6 (Osman et al., 2022). Cell-mediated immunity (CMI) responses are developed within 10-14 days, and there is enhanced ability of the macrophages to intracellularly assassinate bacilli (Thoen et al., 2008). Granuloma development goes through four phases: Initial, where the initial lesions involve piles up together with an aggregate of lymphocytes, Langhans-type multinucleated giant cells, epithelioid macrophages, and neutrophils. Solid, comparable to the Initial stage, however, with central infiltrates of lymphocytes, slack fibrous and capsule neutrophils. Necrotic, vast central necrosis and complete fibrous encapsulation are present. Necrotic and mineralized: with multicentric necrosis mineralization, multiple coalescent caseonecrotic granulomas and thick fibrous encapsulation (Waters et al., 2015).

**Fig 2.** Samples of lungs and lymph nodes contain central zones of caseous necrosis surrounded by pale thin fibrous capsules, reproduced with the permission of Copyright © 2022 (Palmer et al., 2022).

Tuberculosis has two stages of spreading in body; one is the primary complex and second is the post-primary dissemination. In cattle, tubercle of primary complex commonly occurs in cervical and thoracic LNs, with parenchyma of lung being affected in only 10 to 30% of the cases (Domingo et al., 2014). Main complex is the primary lesion at point of entrance and in local LNs, which can be unnoticed during a necropsy, deprived of specific attention. This tiny granuloma blocks the forward transfer of infectious agent in adjacent tissues and could be detained over an extended period. Bacilli in the center of lesion fail to multiply but can become dormant, and a latent infection might take years (Alvarez et al., 2009).

Recrudescence of silenced pathogens occurs in some animals, tissue devastation progresses, initially minor granulomatous lesions are enhanced, and become necrotic, caseated, mineralized, and fibrosed, leading to chronic dissemination. In additional settings, in which an immune reaction is flaring, a generalized form is assigned by mycobacteria in vascular or lymphatic circulation. Acute miliary tuberculosis is the most widespread form of generalization. This generalization can be initial in primary infection or can be late in the post-primary stage or after reinfection. Widespread generalization causes diffuse lesion caseation in some forms of generalization. Such forms are common in pulmonary appearance and are commonly referred to as rupture forms and presumed that the CMI of the host has diminished (Domingo et al., 2014). Infection is localized for months or years, followed by generalization. The level of disease progression depends on the dose of challenge, cow breed, and their immune and general health condition (Vordermeier et al., 2016).

The pathogenesis of BTB is complex and depends on the host's immune response to mycobacterial infection; animals can recover from disease progression or persistent infection without further worsening (Liebana et al., 2008). The primary host defense against *Mycobacterium* spp. is cell-mediated immunity (CMI), which is mediated by T-lymphocytes that release lymphokines. These lymphokines recruit, immobilize, and activate additional blood-borne mononuclear cells at sites where virulent mycobacteria are present. Granulomas at all stages are mainly composed of CD3+ and CD4+ T cells, representing T lymphocyte subtypes. Additionally, reduced levels of CD8+ T cells and γδ T cells may be observed during Stages I-III (Waters et al., 2015). Furthermore, CMI induces a delayed hypersensitive response, in which monocytes and lymphocytes become indirectly or directly allergenic toward antigens (Berrada, 1993).

## 2.5. Diagnosis

### 2.5.1. Clinical Signs in Animals and Humans

In bovines, symptoms occur as follows: low-grade fluctuating fever, progressive weight loss, diarrhea, intermittent cough, weakness, swollen LNs, and loss of appetite (Une and Mori, 2007). Less obvious consequences of infection include milk production reductions of 10 to 20%, loss of fertility, lower carcass and carcass condemnation when slaughtered, and marketability constraints (Collins, 2006). LNs swell in the body of certain animals, including retropharyngeal and other LNs, and they rupture and drain. The swelling of LNs can even block the airways, intestinal tract, and blood vessels. Involvement of the digestive tract might result in bloating, occasional diarrhea, and constipation. Weakness and severe emaciation with acute respiratory distress might ensue in terminal phases (Good et al., 2018).

### 2.5.2. Postmortem Diagnosis

The post-mortem inspection revealed that nearly 47% of probable BTB lesions in the slaughtered cattle carcasses have been identified (Fig. 3a,b). Nonetheless, the anatomic pathology analyses have played a significant role in diagnosis of BTB in preventive programs (Biet et al., 2005).

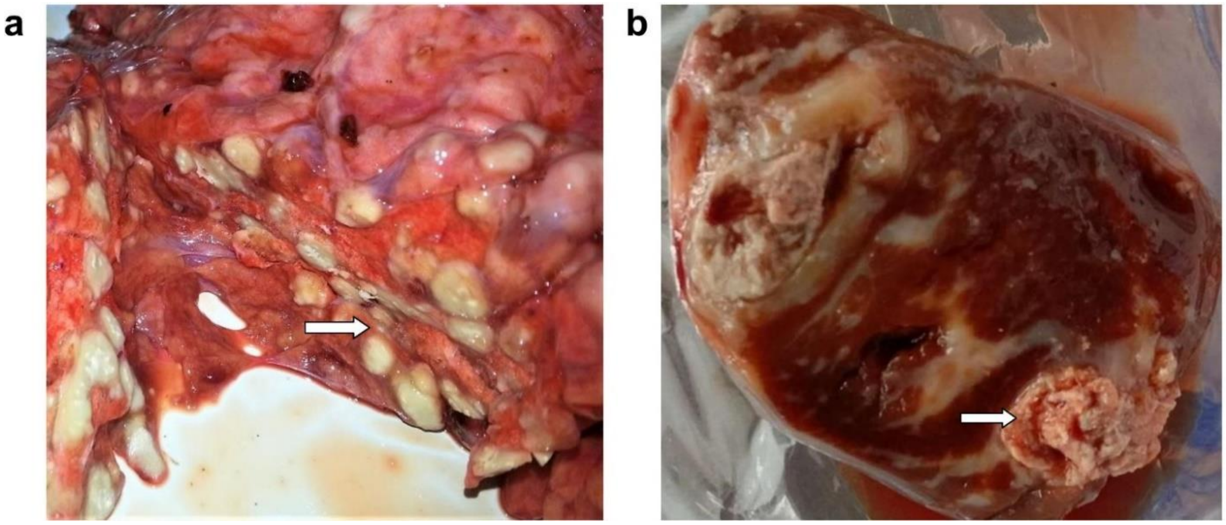

**Fig. 3.** Typical tuberculous-like lesions observed macroscopically in (**a**) lung and (**b**) liver. Calcified area marked with arrows. Reproduced with the permission of Copyright © 2024 (Haque et al., 2024).

### 2.5.3. Histopathological diagnosis

Histopathological evidence of acid-fast bacilli may also be utilized. Additional direct TB tests rely on identification of the bacteria in a sputum sample or a biopsy (both human and animal cases), or at postmortem, in tuberculous lesions of the organ (usually animal). Mycobacteria can be detected in a specific sample using Ziehl-Neelsen stain and light microscopy or auramine O stain and fluorescence microscopy. These methodologies are founded on the tinctorial characteristics that are prevalent in some mycobacteria and microorganisms of the genus Nocardia, Rhodococcus, and Corynebacterium, termed acid-resistant bacilli. This process is referred to as the preservation of the fuchsine-heated substance after it has been treated with alcohol-acid. Microorganisms that are resistant to alcohol and acid can be observed under a microscope when utilizing this specific form of coloring (Marais et al., 2008).

### 2.5.4. Immunological diagnosis

Immunological testing involves *in-vivo* delayed-type hypersensitivity (DTH), which is the presence of the tuberculin skin test (TST) in BTB diagnosis. This evidence is an indirect way to make a diagnosis of TB and it can detect them at early stages of infection and it takes three to eight weeks since it is done using standard instruments and reagents. A widespread test was suggested by Robert Koch in 1890 (Ramos et al., 2015).

### 2.5.5. Bacterial isolation

In the isolation of mycobacteria by culture, optimum media must be capable of supporting rapid and luxuriant growth as well as determining the characteristic features of mycobacteria, particularly colony morphology, growth rate, and pigment production. The prolific growth of *M. tuberculosis* in media containing glycerol producing the typical rough, tough and buff colonies is called a eugenic whereas, *M. avium* grows well in glycerol containing media and this growth is also known as eugenic while, *M. bovis* display scanty, slender growth on glycerol containing medium which is called dysgenic but it can grow abundantly in pyruvate containing medium without glycerol (Birhanu et al., 2015).

### 2.5.6. Molecular diagnosis

Prolonged time in microbial isolation (it starts after six weeks) and biochemical analysis to identify mycobacteria phenotypically have induced developmental efforts in molecular methods to diagnose *Mycobacterium* species in either human or animal origins. Epidemiological data can be examined, outbreaks diagnosed, virulence factors, clonal constitution of the pathogen population, and species distribution in geographically discrete locations are all possible with the appearance of new molecular techniques. It has also facilitated exploration of evolution, taxonomies reclassification, and new species. This information can contribute to control, preventive, and/or curative aspects of human and animal disease (Bolaños et al., 2017).

### 2.5.7. Gamma interferon assays

Since 2006, an assay-IFNy (Bovigam R, Prionics, Switzerland) developed with the help of which one can confirm the presence of CMI response that the body of an animal develops against mycobacterial disease. T-lymphocytes of diseased animals are identified using Monoclonal anti-IFN. Healthy animals give a negative result against infection *M. bovis*, characterized by the absence of IFN. This in vitro test offers the advantage of not impacting the immune status of animals and can be replicated within the same animal; therefore, it is essential to observe the desensitization period. This test demonstrated improvements in sensitivity, increased likelihood of rapid repetition, elimination of the need for a second farm visit, and enhanced objectivity in test performance and interpretation (Faye et al., 2011).

### 2.5.8. Enzyme-linked immunosorbent assays (ELISA)

Indirect ELISA uses a method to determine the binding of a specific antibody to an antigen. To diagnose the infected cattle with *M. bovis*, antigens typically used include the purified protein derivative and individual or related purified antigens of *M. bovis* that include antigens of the Ag85 complex, which constitutes a large portion of proteins secreted, and MPB70 and its equivalent homologous protein, MPB83, proteins secreted by mycobacteria with limited species distribution. A recent lateral flow test, designed to detect multiple antigens, has shown promising advancements in the diagnosis of tuberculosis in certain animal species. A newly developed type of animal serological test is founded on antibody detection via fluorescence polarization (Ramos et al., 2015).

### 2.6. Global impact of *M. bovis*

World Health Organization (WHO) acknowledges the development of the roadmap of zoonotic TB due to the important connection of *M. bovis* transmission between animal and human health. Bovine TB is more widespread globally than in the United States, due to relative lack of standardized public health policy regarding eradication of *M. bovis* in the animal population (Cosivi et al., 1998). This Paradigm Shift has raised awareness about the group of people affected by the risk of zoonotic diseases as an underserved population that needs more coverage (Cosivi et al., 1998). Bovine TB has a direct impact on the health of this population as well as health of their livestock, which indirectly affects their livelihood. Livestock products provide protein through meat and milk, serve as sources of material goods like wool and leather that contribute to economic income, and offer labor in agricultural practices, supporting employment for 70% of the 1.4 billion individuals living in poverty worldwide. The mortality of infected livestock would significantly impact their lives, similar to the effects observed among the herds of affected farmers in the United States (Ramos et al., 2015; Cosivi et al., 1998; Quadr et al., 2021).

The WHO reported that in 2019, *M. bovis* was responsible for 143,000 new tuberculosis cases and 12,300 deaths worldwide. African and Asian nations exhibited the highest prevalence of bTB, representing over 91.0% of the recorded fatalities (Tulu et al., 2021). The bTB leads to decreased milk production, weight loss, sterility, mortality, and the condemnation of carcasses. The annual estimated loss to the global livestock industry due to bTB is around US$3 billion. Test-and-slaughter programs have resulted in bTB-free status in certain countries while others have not, influenced by various epidemiological factors, including the presence of other *M. bovis* maintenance hosts. (Gong et al., 2021).

## 2.7. Advances in Bovine Tuberculosis Treatment

### 2.7.1. Nanotechnology-Based Therapies

The recent exploration of nanotechnology-based therapies has focused on their potential to replace antibiotics and other medications in the free stage, utilizing drug delivery through nanoparticles (Griffiths et al., 2010). Nanoparticle (NP) delivery demonstrates a remarkable ability for the slow, sustained, and controlled release of biodegradable particles (Sosnik et al., 2010). Nanoparticles (NPs) employed as drug delivery vehicles are submicron colloidal particles, measuring < 1 μm. In therapeutic applications, drugs may be covalently attached to the surface of particles or integrated within the particle matrix. NP materials utilized are biocompatible and biodegradable, encompassing polymers that may be either natural (e.g., gelatin and albumin) or synthetic (e.g., polylactides and polyalkylcyanoacrylates), as well as solid lipids (SLNR and NLCR) (Nasiruddin et al., 2017). Various nanomaterials that can be utilized in quick diagnosis and therapy, useful in treatment of TB due to high rates of interest, include noble metals (e.g., Au, Ag, Zn), semiconducting materials like metal oxides and carbon nanotubes. These nanomaterials had a large propensity to display the signal on the recognition of the targeted DNA biomarker (Zahran et al., 2023).

Gold (Au) NPs have diverse applications in contemporary biology and medicine, serving as antigen carriers and therapeutic agents, as well as for immunological and therapeutic purposes (Staroverov and Dykman, 2013). The unique optical properties of AuNPs, including resonant light scattering and surface plasmon resonance (SPR) absorption, combined with their superior biocompatibility, indicate their potential in tuberculosis diagnostics and treatment. AuNPs have been effectively modified in laboratory settings to enhance the speed and efficiency of BTB protein detection (Xu et al., 2018). The ability of AuNPs to bind to a wide variety of molecules can be exploited to make *Mycobacterium* detection techniques faster and more sensitive (Jomehpour *et al.,* 2025). Selenium (Se) NPs possess the ability to inhibit the growth of two types of mycobacteria: *Mycobacterium tuberculosis* (Mtb), and *mycobacterium smegmatis* (Msm). Se NPs have both *in vitro* anti-growth effects on *mycobacteria* by weakening their cell envelopes (Estevez et al., 2020). In addition, gallium (Ga) NPs possess a significant potential to regulate rise of cytokines. The inhibition of *Mycobacterium tuberculosis* coinfection in macrophages by GaNPs alters the iron-related enzymatic process. It also alters the release of cytokines which might be implicated in TB (Choi et al., 2019). Silver (Ag) NPs also have a potential solution to counter *mycobacterium* because they have proved to be effective as an inhibitor in growth of *Mycobacterium tuberculosis* and hence can apply to many medical devices to prevent infection and drug application (Praba et al., 2013).

Overall, NPs of specific diameters are applicable in medical fields, as larger NPs are typically avoided due to their association with embolisms. They are rapidly removed from circulation due to efficient phagocytosis. In contrast, as the size of NPs decreases to ultra-small dimensions, their clearance rate in the kidney increases. Moreover, due to their extremely small dimensions, these entities may exhibit heightened toxicity and reactivity (Fig. 4), attributable to the significantly increased surface area-to-volume ratio, which correlates with enhanced biological and chemical activity. This leads to an increase in free radicals and reactive oxygen species (ROS) production (Yi et al., 2016). Attributed to the liberation of ROS, oxidative stress, inflammation, and severe cell damage appear. These NPs tend to accumulate in mitochondria and disrupt the antioxidant cellular defense system (El-Sayed and Kamel, 2020).

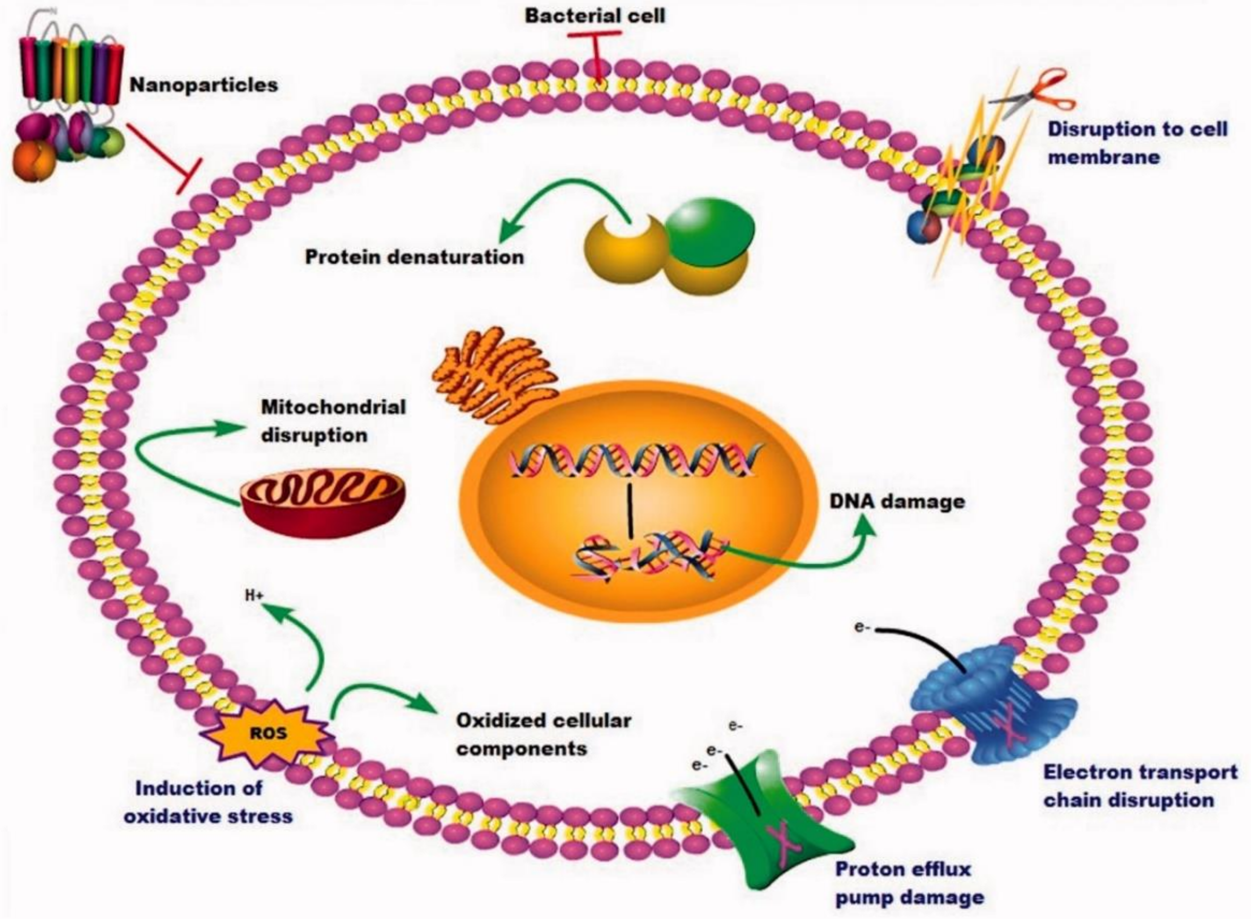

**Fig. 4.** The cytotoxic effect of the nanoparticles on bacterial cells reproduced with the permission of Copyright © 2020 (Algharib et al., 2020).

### 2.8. Future Prospective

The increase in tuberculosis and drug-resistant diseases in developing countries underscores the urgent need for more effective diagnostic tools and vaccines. Currently, there is an absence of a highly efficient method for the detection of tuberculosis. Future considerations may involve the establishment of targeted delivery technologies to enhance therapeutic outcomes while reducing side effects and toxicity, alongside ensuring compatibility with existing TB agents to maximize efficacy in combination therapies.

## Conclusion

BTB is a significant zoonotic disease impacting both animals and humans globally. *M. bovis* is a spillover microbial agent capable of transmission from livestock to humans. Further molecular epidemiology research is necessary to determine the dynamic spread of BTB, identify prevalent genotypes in both animals and humans, and understand the evolutionary relationships among strains. This study presents an overview of NP-based delivery systems, which serve as a viable, cost-effective, and promising alternative for potential tuberculosis chemotherapy. Improved disease treatment may rely on enhanced medication bioavailability, reduced dosing frequency, and prolonged stability. NPs can enhance the efficacy and practicality of various solid dosage forms, such as tablets, capsules, microparticles, and granules. The potential application of medication carriers made from a combination of natural and synthetic polymers is noteworthy.

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# Microbial Infections in Animals: Pathogenesis, Diagnosis and Treatment

## 08

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## ABSTRACT

The dynamic relationship between pathogens, hosts, and environmental factors in animals takes place due to microbial infections, which can significantly impact both veterinary and public health. However, microorganisms like bacteria, viruses, fungi, and protozoa drive these infections, which cause diseases ranging from localized conditions to systemic illnesses. Moreover, pathogenesis complex mechanisms such as microbial immune evasion and host-pathogen interactions are highlighted due to advanced research that varies across species. Diagnostic techniques like morphological and functional imaging have enhanced disease detection, and treatment strategies are evolving due to the challenges posed by antimicrobial resistance. The dairy, poultry, and aquaculture industries are particularly vulnerable and require innovative approaches to mitigate microbial threats. Disease prevention strategies are biosecurity measures, vaccination, and immunostimulation, and these are alternatives to antibiotics that show promise in combating these infections. Consequently, the importance of a holistic approach to managing microbial diseases in animals, which ensures emerging technologies and interdisciplinary research, underscores both animal welfare and public health safety and this approach.

**KEYWORDS**
Microbial infections, Host-pathogen interactions, antimicrobial resistance, Veterinary diagnostics, Animal disease prevention, Zoonotic diseases

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## INTRODUCTION

Disease and illness are interconnected concepts with indirect differences. Patients experience illnesses while doctors diagnose and treat diseases (Caselli, 2021). A disease refers to a collection of signs and symptoms and can be described as a phenomenon involving structural or functional disorders or illnesses linked to a specific cause. It represents an abnormal condition that impacts an organism's body, which is often identified as a medical issue characterized by distinct symptoms and signs (Jomova et al., 2022). Diseases may arise from external sources, such as infectious agents, or internal dysfunctions, such as autoimmune disorders. Microorganisms, including microbes, are common causes of diseases. Microbial colonization of the body leads to infectious diseases. For instance, pneumonia can stem from diverse pathogens such as viruses, bacteria, protozoa, or fungi (Vojdani et al., 2022). Microbes are the oldest life forms on Earth. They are single-celled organisms that millions of people can fit on the tip of a needle, and they are visible only through a microscope (Mubeen et al., 2021).

Fossil evidence shows microbes have existed for over 3.5 billion years. However, organic matter wouldn't decompose, and oxygen levels would drastically diminish without their growth. These microscopic organisms are often termed microorganisms and are omnipresent and found in air, water, soil, rock, plants, animals, and the human body (Qin et al., 2020). Some thrive in extreme heat or cold, although others require or avoid oxygen. Microbes play roles in both plants and animals, including humans, and are significant contributors to infectious diseases. Animal models have been instrumental in advancing our understanding of osteomyelitis, offering insights into pathogen-host interactions that cannot yet be replicated in vitro (Yu et al., 2024). These models range from simple setups like metal implants placed in subcutaneous tissue or cortical bone to complex systems to simulate functional orthopaedic devices (Alaneme et al., 2022).

Non-implant infections are induced through methods like hematogenous inoculation into the tail vein, direct inoculation into vertebral bodies or intervertebral discs for vertebral osteomyelitis, or footpad inoculation in diabetic obese rodents to mimic diabetic foot infections. The microbial etiology of osteomyelitis varies by infection type (Masters et al., 2022).

*Staphylococcus aureus* and coagulase-negative staphylococci (CoNS), such as Staphylococcus epidermidis and Staphylococcus lugdunensis, are responsible for up to two-thirds of skeletal infections, with *S. aureus* being the most prevalent pathogen (Haddad et al., 2023). Methicillin-resistant *S. aureus* (MRSA) strains account for nearly 50% of *S. aureus* osteomyelitis cases, which highlights the challenge of antimicrobial resistance. Other pathogens include Enterococcus spp, *Pseudomonas aeruginosa*, *Escherichia coli*, and Cutibacterium acnes. Most cases are mono-microbial by polymicrobial infections, which are frequent and include trauma-related, fracture-related, and foot or ankle infections (Nasser et al., 2020).

Current clinical management is osteomyelitis classification, pathogen diagnosis, and treatment strategies. However, progress in prevention and eradication has been incremental, necessitating novel therapeutic approaches. Emerging technologies and insights into the host's immune response are the concept of susceptible versus protective immune proteomes, which offer hope for improving prevention and treatment outcomes in skeletal infections (Shafiei et al., 2021). Balancing profitability in the dairy industry with safeguarding water quality and the health of humans and animals posed significant challenges for farmers in the 1990s. Runoff contains sediment, pesticides, and nutrients such as phosphorus and nitrogen were identified as one of the most serious environmental threats to water quality from animal agriculture (Grout et al., 2020).

## 1. Impact of Pathogens on Public Health and Agriculture:

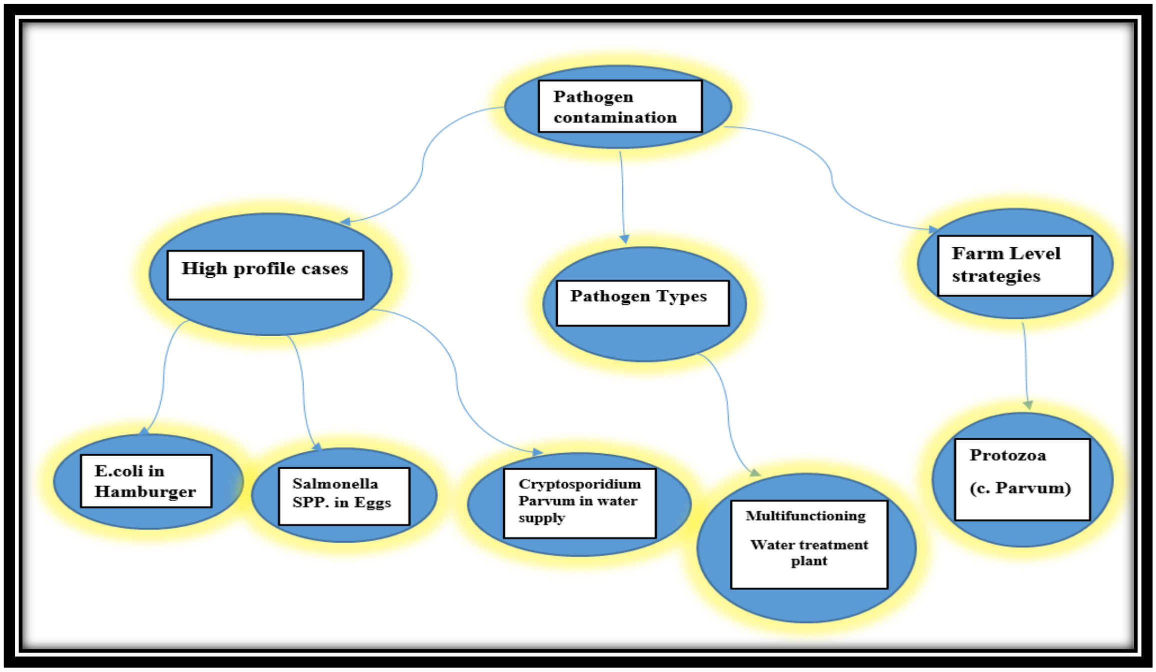

**Fig. 1.** Impact of pathogens on public health and agriculture

Recent research has elucidated key mechanisms underlying *S. aureus* pathogenesis, such as implant-associated biofilms, staphylococcal abscess communities (SACs), and invasion of the osteocyte lacuno-canalicular network (OLCN) is presented in fig. 1 (Gimza & Cassa, 2021). Additional studies have explored the role of other pathogens, including CoNS, *C. acnes*, and *Streptococcus agalactiae* in skeletal infections. Pathogens employ sophisticated immune evasion strategies by leading to the establishment of osteomyelitis and contributing to challenges in its treatment. Extensive research is being conducted on infectious diseases to uncover their causes, diagnostics, treatments, and prevention strategies (Masters et al., 2022). The National Institute of Allergy and Infectious Diseases (NIAID) is, a part of the National Institutes of Health (NIH), spearheads federal research on infectious diseases. NIAID-backed biomedical research develops critical tools such as diagnostic tests, advanced treatments, vaccines, and innovative methods to combat current and emerging microbial threats. (Greenwood et al., 2022).

## 2. Pathogenesis of Microbial Infections

Most living organisms are parasitic, and their response to the host relies on their immune systems to prevent infections or control parasites. The immune system is one of the most intricate biological systems that shows clear evidence of coevolution with parasites. Its efficiency is critical for the survival of long-lived multicellular organisms to enable them to outlast their short-lived and abundant parasites (Santiago et al., 2021). Recently, many research has also highlighted that several factors contribute to this variation or suboptimal response. For hosts, mounting a strong immune response can carry fitness costs. For parasites, maximum virulence can be counterproductive by killing the host prematurely, which may limit transmission opportunities. Additionally, genetic interactions between hosts and parasites where only certain parasite genotypes infect specific host genotypes and vice versa add another layer of complexity is enlisted in table 1. These genotype-specific interactions offer insight into the molecular mechanisms that underlie host resistance and parasite infectivity (Suthar et al., 2021).

**Table 1.** Association between the Host and Pathogens

| Aspects | Description |
|---|---|
| **Host immune system Interactions** | Close molecular interactions occur between parasites and the host immune system. |
| **Parasite Mechanisms** | Parasites evolve molecular-level mechanisms to counteract host defenses. |
| **Host Defense Strategies** | • Selecting parasite-free habitats<br>• Adjusting behavior to reduce exposure |
| **Parasite Adaptations** | Modify transmission pathways to enhance host encounters. |
| **Immune Evasion Tactics** | Parasites use a wide range of strategies, including:<br>• Entering host tissues<br>• Influencing immune signaling networks<br>• Avoiding immune responses |
| **Major Parasite Groups** | Bacteria<br>Viruses<br>Protozoa<br>Helminthes |
| **Host-Pathogen Interaction** | The dynamic and complex interactions between microbial invaders and their hosts, encompassing stages from invasion to dissemination. |

For example, it has been demonstrated that virulence factors of *Escherichia coli*, such as SPATE proteins (TagB, TagC, and Sha) can break down the cytoskeletons of bladder epithelial cells and break down mucin and gelatin (Navarro-Garcia, 2023). Similarly, a study on non-*E. coli* Enterobacterales from healthy individuals revealed low virulence and antibiotic susceptibility. Research on *Salmonella* enterica demonstrated that the pdxB-usg-truA-dedA operon aids intracellular survival and oxidative stress resistance (Rathnayake et al., 2021). Investigations into Aeromonas hydrophila identified the LahS global regulator as essential for biofilm formation, motility, and virulence. For stress tolerance and infection, the Dickeya genus of plant pathogens depends on proteins like Lon. In contrast, the Candidatus Phytoplasma mali effector PME2 localizes in host cell nuclei and affects apple proliferative disease (Wang et al., 2024).

Other research looked at fungal diseases where the SsNsd1 transcription factor affects pathogenesis and development, like Sclerotinia sclerotiorum. Additionally, studies showed how bacterial outer membrane vesicles (OMVs) contribute to interspecies communication and increased pathogen pathogenicity in species such as Candida albicans (Fang et al., 2022). Furthermore, it was shown that Bordetella pertussis's RNA chaperone Hfq is a crucial modulator of the expression of genes linked to virulence. Understanding microbial virulence pathways is crucial for agriculture, health, and the fight against antibiotic resistance, as this collection emphasizes (Casillo et al., 2024).

Foot-and-mouth disease (FMD), brucellosis, and tuberculosis are examples of microbial illnesses that are serious hazards to both human and animal health. Intracellular Brucella bacteria produce zoonotic infections in humans and reproductive problems in cattle, although brucellosis causes financial losses (Yao et al., 2023). The pathogen's capacity to infiltrate host cells, withstand intracellular conditions, and elude immune reactions all play a part in the development of the disease from acute to chronic phases. Although FMD is mainly investigated in cattle, it can also cause myocarditis and chronic syndromes in small ruminants and wildlife. *Streptococcus pneumoniae*, *S. aureus*, and *S. pyogenes* are typical causes of secondary bacterial pneumonia, which is frequently brought on by influenza virus infections. According to a study, it is essential to comprehend the molecular pathophysiology of these illnesses in order to create effective vaccines and therapies, especially for emerging and re-emerging pathogens (Roychoudhury et al., 2020).

## 3. Diagnosis of Microbial Infections

Despite significant progress in understanding microorganisms and the mechanisms of infection and inflammation, infections remain a leading cause of morbidity and mortality. Symptoms such as fever, pain, loss of appetite, and abnormal lab results may indicate infection, but imaging studies are often essential for confirmation and localization (Alshoabi et al., 2022). Diagnostic imaging can be categorized into two main types: morphological and functional.

Morphological imaging, such as radiographs, ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI), highlights structural changes in tissues caused by microbial invasion and the body's inflammatory response (Greco et al., 2023). In contrast, functional imaging, including nuclear medicine techniques, utilizes radioactive tracers to detect cellular or metabolic changes associated with infection. For instance, radiolabeled substances like indium-111 leukocytes and fluorodeoxyglucose (FDG) PET scans are widely used to pinpoint infection sites (Kuzma et al., 2021).

### 3.1. Morphological Imaging Modalities

#### 1. X-rays and CT scans

- X-rays and CT scans utilize X-rays to produce images. CT, in particular, measures X-ray attenuation, with denser structures appearing brighter.
- Infections alter normal tissue densities. For example, pyogenic pneumonia replaces air in the lungs with water-density exudate, turning the affected lung areas from black to gray on CT scans. Similarly, soft tissue infections like myositis blur fat planes and show increased tissue density due to inflammatory edema (Chin & Peh, 2021).

#### 2. Magnetic Resonance Imaging (MRI)

- MRI uses magnetic fields and radiofrequency energy to detect tissue changes. It is especially effective for diagnosing osteomyelitis, as inflammation changes the signal intensity of bone marrow due to increased water content (Aydıngöz & Yıldız, 2022).
- Contrast agents like gadolinium enhance inflamed areas, distinguishing between infected and non-infected tissues. For example, infected synovium in joints enhances markedly, aiding in the differentiation of synovitis from joint fluid (Kang et al., 2024).

#### 3. Ultrasound (Sonography)

- Ultrasound employs high-frequency sound waves to create images and is particularly useful for evaluating soft tissue infections and joint effusions (Poboży et al., 2022).
- While highly effective for detecting septic arthritis, ultrasound has limitations in diagnosing osteomyelitis, as it cannot image beyond the bone cortex. Subperiosteal abscesses may be identified using sonography and power Doppler imaging (Shahid et al., 2020).

### 3.2. Functional Imaging Techniques

Functional imaging leverages radiotracers to detect infection-related changes. For instance:

- FDG-PET Scans highlight increased glucose metabolism at infection sites.
- Indium-111-labeled leukocytes track white blood cell accumulation.
- Gallium scans and other radiolabeled markers target specific infection markers to provide precise localization.

By integrating these imaging modalities, clinicians can detect, localize, and monitor infections effectively, complementing clinical assessments and laboratory findings to optimize patient outcomes (Haselmann et al., 2022).

## 4. Treatment of Microbial Infections in Animals

The introduction of antibiotics nearly 50 years ago revolutionized the treatment of bacterial infections, while their subsequent use as feed additives for growth promotion (AMGP) enhanced the economic efficiency of livestock production. However, the rise of antibiotic-resistant strains has revealed that relying solely on antibiotics is insufficient to control bacterial infections (Sarkar et al., 2023). Although the use of newer antibiotics in animal production has addressed some clinical issues caused by resistant strains, this success has not been mirrored in human health. The growing prevalence of multi-resistant pathogens poses a significant threat to both human and animal health to necessitate specialized control measure (Ponzo et al., 2024). The use of antibiotics in animal agriculture has sparked major concerns, especially those that are essential for human health as like fluoroquinolones. Particular concerns have been raised regarding antibiotics used to promote growth (Ghimpețeanu et al., 2022).

The World Health Organisation (WHO) has advised against using antibiotics that are essential for treatment or that encourage resistance to other drugs as growth promoters-3-. These suggestions were reaffirmed by the European Commission's Scientific Steering Committee in 1999, which also underlined the significance of introducing disease-preventive techniques in cattle production to lessen reliance on antibiotics (Giampieri et al., 2022). Antibiotics' ability to suppress intestinal bacterial infections is the main factor responsible for their growth-promoting effects. Antibiotics' ability to suppress intestinal bacterial infections is the main factor that influences their growth-promoting effects. Infections such as necrotic enteritis in poultry must thus be treated using different methods-5 (Fig. 02) (Kulkarni et al., 2022).

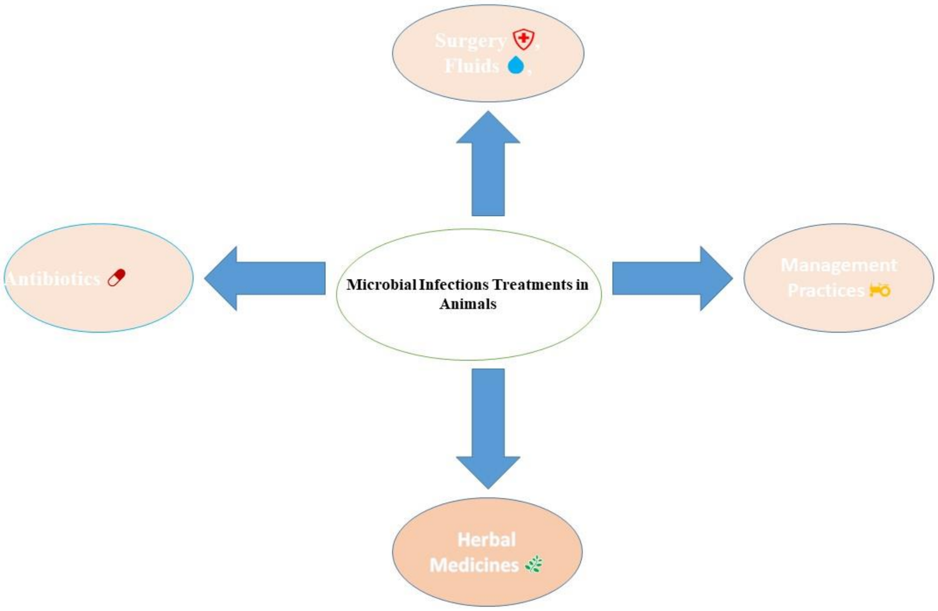

**Fig.02.** Microbial Infections in Animals

## 5. Concept for Disease Prevention

For a long time, antibiotics have been essential to prevent bacterial infections in aquaculture. The antibiotic-resistant bacteria emergence and aquatic habitat contamination are among the negative consequences of its use and overuse (Serwecińska, 2020). Therefore, there are alternate ways to improve disease resistance in farmed shrimp and fish that have become more and more important. Promising substitutes are a variety of feed additives that are demonstrated to increase fish immune response by functioning as immunostimulants (Hossain et al., 2024). Phytochemicals, chitin, β-glucans, and herbal immunomodulators are among the compounds that are shown to improve the immune system in aquatic research. Still, studies are being conducted to find stronger and more efficient immune-stimulatory substitutes (Nassar, 2022).

Active molecules like lactoferrin (LF) are glycoproteins linked to plasma iron-transport proteins and are found in considerable amounts in milk, especially bovine milk. An iron-binding site is located in each of the peptide chain's two lobes that make up LF's structure (Dyrda-Terniuk & Pomastowski, 2023). Lactoferrin has immunostimulatory qualities and strengthens the non-specific immune system, and it helps many fish and shellfish species become more resistant to disease. Due to its antibacterial, iron-absorptive, and antioxidant properties, bovine lactoferrin (BLF) is a common source of LF that is applied extensively in industry. Furthermore, BLF demonstrates anti-inflammatory, anti-parasitic, antiviral, and antifungal properties to render it a powerful defense for aquatic creatures against a variety of infections (Superti,2020).

## 6. Prevention and Control of Microbial Infections

The IOM's Convergence Model report was described in 2003, which suggested that infectious diseases are the result of a combination of biological, environmental, and host-related factors which create the perfect conditions for microbial pathogens to harm both humans and animals (Haldar et al., 2023). This "microbial perfect storm" is a rare and catastrophic event that may occur once in a century due to a unique combination of factors, and these factors also contribute to the rise of infectious diseases. Growing human populations have increased the global demand for animal protein, which has led to the intensification of animal farming. In high-density confinement systems, stress and overcrowding can promote the shedding of zoonotic pathogens (e.g., *Salmonella* in cattle) (Stevenson, 2023). The surge in demand for animal protein often leads to farming practices that compromise biosecurity, allowing the introduction of harmful pathogens that pose risks to both animal and human health (e.g., H5N1 avian influenza in Southeast Asia's free-ranging ducks and geese). Climate change is characterized by extreme weather events such as floods and droughts, which can affect the transmission vectors of diseases like the floodwater *Aedes* mosquitoes, which spread the Rift Valley fever virus to animals (Dash et al., 2021). International travel further accelerates the spread of infectious diseases by transporting infected animals, humans, and vectors across borders, as seen in the emergence of the West Nile virus in North America in 1999. Additionally, war and political instability can devastate societal structures and disrupt infrastructure that protects animal health. Human and agricultural encroachment into wildlife habitats also increases the likelihood of cross-species transmission of novel pathogens. Microbes are adept at evolving strategies to bypass immune defenses and infect animal cells (Meurens et al., 2021).

Outbreaks of infectious diseases in animals impose significant societal costs. For example, the 2001 foot and mouth disease outbreak in the United Kingdom led to the culling of 4.2 million cattle, sheep, and goats, with an estimated economic cost to the UK of over £6 billion. In this context, animal vaccination becomes essential for preventing emerging infections. However, the deployment of vaccines for emerging diseases requires careful consideration (Pandey & Upadhyay, 2022).. The existence of animals as reservoirs or vectors of zoonotic diseases offers significant opportunities for developing control strategies for zoonoses, which may not be applicable to human-to-human or environmental transmission. Vaccination in animals is a promising tool for controlling zoonotic diseases and may provide an alternative to drastic measures such as depopulation. In addition to preventing human disease, vaccinating reservoir species can protect non-human species from infections as well (Clemmons et al., 2021).

## 7. Emerging Challenges in Microbial Infections

Inadequate infection prevention and control (IPC) methods make germs more likely to spread because the antibiotics use puts ecological pressure on them. Various resistance mechanisms developed by bacteria can drastically reduce the number of available treatments and hasten the environmental spread of multidrug-resistant (MDR) organisms. The increase in IPC and careful antibiotic usage is critical to effectively combating AMR in hospitals (Oliveira et al., 2024).

The possibility that germs can spread occurs due to the ecological pressure that antibiotic usage places on bacteria and poor infection prevention and control (IPC) practices. By developing different resistance mechanisms, bacteria may rapidly disseminate multidrug-resistant (MDR) organisms across the environment and significantly limit the number of potential therapies (Catalano et al., 2022). Furthermore, bats are vulnerable to climate change, and they can transmit the virus to humans through pangolins as intermediary hosts. The pandemic has highlighted the importance of antimicrobial stewardship in preventing AMR; it worsened the AMR crisis by increasing antibiotic use and the incidence of drug-resistant secondary infections in hospitals (Khaznadar et al., 2023).

**Fig. 3.** Association of Climate changes and its AMR (Anti-microbial Resistance)

Both climate change and AMR have been exacerbated by human activities, which necessitates action to mitigate their impacts. However, the effects are not evenly distributed, with low- and middle-income countries bearing a greater burden because they often lack funded action plans to address AMR (Tang et al., 2023). People with pre-existing health conditions or those living in close proximity to the local environment are also more vulnerable to the impacts of climate change. The extent of climate change's effect on human health depends on individuals' sensitivity and their ability to adapt, which is influenced by social determinants of health (Ebi et al., 2021). While the link between AMR and climate change is now established due to the complex interactions between these two issues, it remains unclear and is highlighted in fig 3. Current research is still insufficient and controversial, indicating a need for targeted surveillance and interdisciplinary studies (Magnano et al., 2023).

## 8. Future Directions

Recent advances in diagnostic technologies and therapeutic approaches are revolutionizing the fight against bacterial infections. Rapid point-of-care diagnostics and next-generation sequencing enable personalized medicine approaches and optimizing antimicrobial therapy. Diagnostic tools, including bacteriophage-based bioassays, are emerging specificity and potential to combat antimicrobial resistance. Bacteriophage therapy is gaining renewed interest as a potential solution to antibiotic resistance despite historical controversy. Synthetic biology is improving bacteriophage-based diagnostics by modifying phages to transfer payloads into bacteria, which boosts antibiotic efficiency and improves biofilm removal. Moreover, these developments in phage-based systems revolutionize microbial diagnostics by providing near-real-time pathogen identification.

In the twenty-first century, international cooperation is combating new microbiological dangers. The globe is facing a number of infectious disease concerns, such as Zika and Ebola epidemics, due to an increase in antibiotic resistance danger (Baker et al., 2022). These problems occur through factors such as urbanization, population increase, and climate change. Coordinated global collaboration is necessary for effective solutions like initiatives from the human and animal health sectors. The global health system comprises many organizations and networks to make progress but still faces challenges in providing adequate protection against dynamic infectious disease threats (Topluoglu et al., 2023). The establishment of a multi-disciplinary Global Technical Council on Infectious Disease Threats gives suggestions to address these concerns and also implements the World Health Assembly's Global Action Plan on antimicrobial resistance. Further study and useful techniques are opening the door for these innovative diagnostic and treatment approaches to be successfully used in clinical settings because many challenges like regulatory barriers and host range restrictions are unsolved (Cao et al., 2024).

## 9. Conclusion

Microbial infection management in animals remains a complex challenge because of evolving pathogens, antimicrobial resistance, and environmental influences. The foundation for innovative diagnostic and therapeutic is established through understanding microbial pathogenesis and host immune responses. However, sustainable solutions necessitate combining preventive measures such as vaccination, biosecurity, and immunomodulators to reduce reliance on antibiotics. These infections' global impact, including on food safety and zoonotic disease transmission, can emphasizes the need for collaborative efforts across veterinary, medical, and environmental disciplines. Furthermore, addressing gaps in research these gaps can be addressed by enhancing surveillance systems, and fostering international cooperation will be critical in modifying the societal and economic burdens which are occurring in animals caused by microbial infections.

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# Immunological Frontiers in Combating Antimicrobial Resistance: Integrative Approaches in Veterinary Medicine

09

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## ABSTRACT

The ever-increasing risk of antimicrobial resistance (AMR) is a major concern to worldwide health and veterinary medicine is a key factor in its growth and its solution. This chapter dwells on the cutting-edge immunological measures designed and implemented in the fight against AMR in animal wellbeing. It highlights the integrative measures of using the traditional veterinary-based practices, alongside novelty Immunotherapeutics such as vaccines, monoclonal antibodies, immunomodulators, and host-directed structures. The chapter explains the ways that can be used to minimize antibiotic dependency by taking advantage of the developments in the field of immunology, including the knowledge of the innate and adaptive immunities as well as microbiome-immune environment communication and pathogen- specific tactics of immunoreaction. Further, it emphasizes the relevance of One Health approach in planning sustainable and effective immunological interventions considering the health of animals, people, and the environment. Seeking to offer in-depth review of the ongoing struggle against AMR to achieve animal welfare and human health through the use of immunological tools, this chapter can be thought of as a compilation of case studies and the latest research describing the movement towards the evolution of combating AMR in veterinary practice.

**KEYWORDS**
Antimicrobial Resistance, Immunomodulators, Vaccines, Immunotherapeutics, One health, Veterinary medicine

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## INTRODUCTION

One of the greatest threats to the health of both humans and animals around the world is antimicrobial resistance (AMR). Antibiotic resistance by bacteria is an age old feature of the bacteria that enables bacteria to live in the dynamic environment. Potent antimicrobial resistance has been characteristic of the pathogenic and indeed in any microorganism as it is an occurrence which aids the survival and evolution of such bacteria in such an elaborate environment (Sharma et al.,2018). The AMR threat is to a large extent, the symptom of overutilization and frequent abuse of antibiotics, which are prescribed quite unevenly, in unnecessary instances, or by providers, who cannot be considered competent. Moreover, in animals (food and companion animals and exotic species), the anti-microbial therapy is the agent that is chosen and spread with high and significant levels of this event. The authors of this source published their research as early as in 2016 (Velazquez-Meza et al., 2019). In bacteria, AMR is a bacterium that fails to respond to maximum doses of the most recently relevant clinical antimicrobial agents (Martins et al., 2024).

This came as a revelation to science community to some degree since way back in 1945 when Sir Alexander Fleming was awarded the Nobel Prize he cautioned about the threat that bacteria might grow resistant to antibacterial drugs (Horvat & Kovačević, 2025). It was soon even reported that the said wonder drug itself was not effective. This is how it started dictating the ineffectiveness of other curing drugs against the infectious organisms that then appear and are called drug resistance or AMR or antibiotic resistance and challenge the efficacy of the current regimens of therapeutic drugs. However, use of disinfectants and antibiotics without any discretion has led to world health issues never imagined. This issue was evident upon the occurrence of bacteria producing genes that made it live without antibiotic residue. The resistance genes render infections to spread under various environments thus restricting the treatment of infectious diseases leading to morbidity and mortality because a high population of resistant bacteria is multiplying in both humans and animals.

One of the major issues of contemporary healthcare practice and community health is the way, time of occurrence, and the outlook of the drug-resistant microbe (Leung et al. 2011; Laxminarayan et al. 2013). The risk and burden of AMR is not strange internationally. E.g., antibiotic-resistant organisms cause some 33,000 deaths annually in Europe and 4.95 million deaths globally out of which many become established as sources of EUR 1.5 billion worth of health system costs and productivity losses every year (European Commission. There can be a delay in treatment (EU Action on Antimicrobial Resistance et al.,2023). The estimated deaths due to resistance caused by AMR were found highest in sub-Saharan Africa and lowest in Australia and New Zealand. Besides this, Methicillin-resistant Staphylococcus aureus was estimated to cause half a million deaths, and the six pathogens (Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Acinetobacter baumannii, and Pseudomonas aeruginosa) contributed to 50 000-100 000 deaths (Murray et al.,2019).

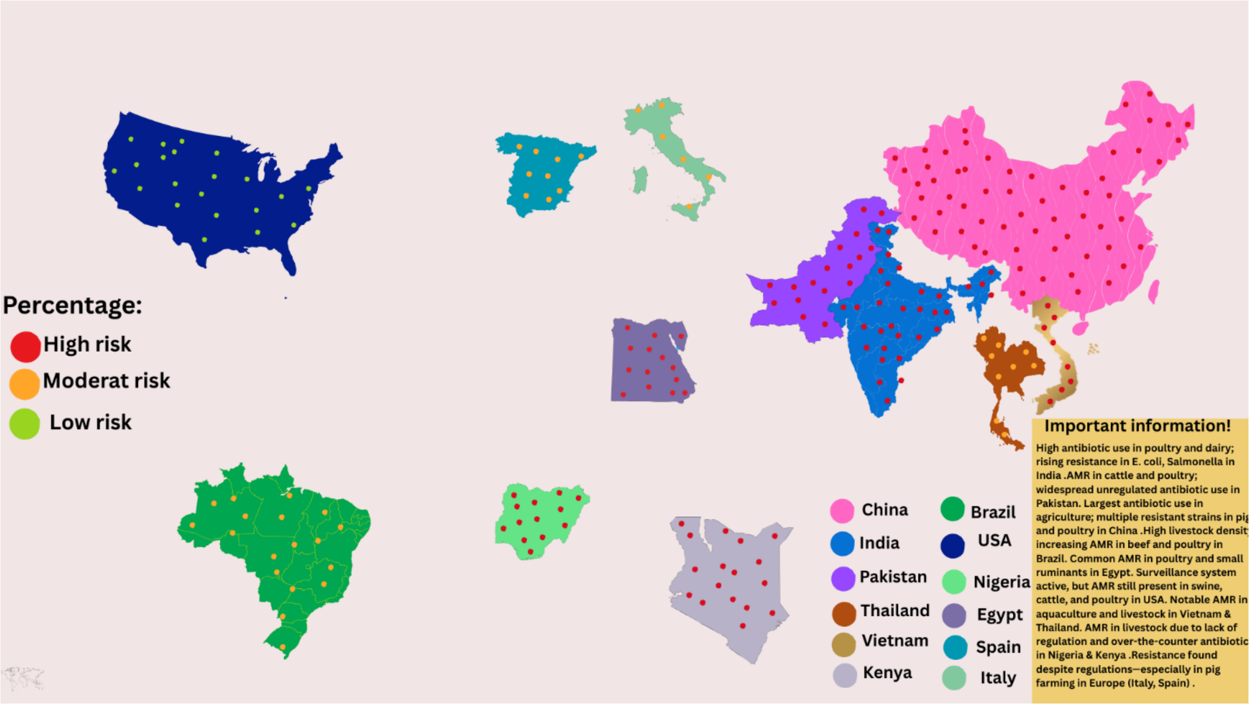
Antimicrobial resistance (AMR) is an international community issue linked to the human, animal and environmental component. ABR involves a multi-disciplinary, multi-sectoral and joint-response to human-animal-environment interface health risks that have been summed up as a One Health concept (Robinson et al., 2016). Current OH strategies on AMR primarily reflect on reductions in the use of antibiotics in livestock. In recent systematic reviews and meta-analyses, correlations were found between decreased use of antibiotics in food animals and decreased AMR in animals, and there is weak evidence of a partial decrease in humans (Hoelzer et al., 2017; Tang et al.,2017; Tang et al. 2017; Scott et al. 2018). The concept of One Health is well integrated in the global activities of reducing AMR. It will also entail addressing conflicting interests of different branches of the economy and institutions working with animal, human and environmental health. To agree on synergies and best solutions, such areas of priorities include key priorities of action, the best methods to measure and control AMR and infection as well as policies to govern the usage of antimicrobials.

Alternative products used as antibiotics alternatives are different in character but they fall to categories of vaccines, antibodies, pattern recognition receptors (PRRs), probiotics, bacteriophages, peptides, phytochemicals, metals and antimicrobial enzymes (The Pew Charitable Trusts. In this study, we tracked the pipeline of antibiotics in development across the world (Tracking the global pipeline of antibiotics in development 2020). Besides sanitation, vaccines and AMs have offered the backbone towards improvement of public health. It is true that AMR has appeared to be hastened with introduction of antibiotics and other AMs. The circumstances of the occupation of AMR have revealed that it is one of such paradoxes, in which free choice of use is in conflict with the dire necessity of use, and collective action on every level of taxonomic hierarchy, multi-sectoral integrated action is required to distinguish and initiate action on national and international levels. Repetitive misuse and overuse of such drugs in food animals contributes to the development of resistant culture that is later transferred to people either after consumption of food, contact with animals or in the environment (Angulo et al.,2005). The way the vaccines and antibiotics act are also different hence chance of developing resistance due to vaccination not likely to occur at all. Vaccines work better on a prophylactic basis when the pathogens have no chance to reproduce and enter into different tissues. This is necessary to reduce the probability to develop a resistance to a drug due to mutations in the pathogen genome (Bagnoli et al. The most likely among them is the vaccines that may potentially restrict the distribution of resistant bugs and the AMR that comes with them. Vaccine is a significant breakthrough in the history of immunology, especially since prophylactic treatment of patients in a global environment accelerates the growth of their life expectancy levels (Costanzo et al.,2022).

## The burden of AMR in veterinary medicine

By now antimicrobial resistance (AMR) has assumed one of the most critical global health care problems, and AMR countermeasures, including antimicrobial stewardship, infection prevention, and biosecurity initiatives, investing in research and development (R&D), and extended monitoring and surveillance have been more frequently implemented (Ghebreyesus et., 2019). More action and sources have become more imminent in the AMR not only because the social and economic cost of the threat AMR presents has been increasingly understood, but also because the cost of AMR has become more influential to both research and policy to deal with the challenge. In the past 2 decades, measurement has grown to as wide as bugs, attributable mortalities, economic casualties. The initiation of AMR began with the WHA declaration made in 1998 (World Health organization. 1998). The clinical and economic burden were clearly addressed throughout these calls to action however the recommendation was the pathogens coded by surveillance and reporting in the lab (Sharma et al., 2017).

In food-producing and companion animals, there is a common use of antibiotics in the treatment, meta phylaxis, prophylaxis and growth promotion. The use of antimicrobials in food animals (in form of medicated feed or water) is often to prevent disease and enhance growth performance in poultry, swine and cattle. The author emphasizes that these risks need to be countered with making better use, restrictions and monitoring to preserve efficiency of antimicrobials available (Ye et al., 2025). In comparison with others, antibiotics were subdivided into two sets CIAs and others. In the case of the current report, CIAs are categorised based on WHO classification of antibiotics (WHO 2011) based on their significance in human medicine and include (fluoro)quinolones, third- and fourth-generation cephalosporins, macrolides and glycopeptides. Besides the fact that they are used in large quantities with thousands of tones being consumed across the globe. Antibiotics are used in almost all the nations in the fight against the animal disease, maintenance of the animal health, and in the feed to enhance the animal growth and feeds perception (Stärk et al., 2006). Their mechanism of trying to be fed through animal secretions, mostly in manure and urine that contains antibiotic reductions in feeding of animals, get into drinking water and feeds will be adverse effects to the environment and soil contamination (Fig. 01).



**Important information!**

High antibiotic use in poultry and dairy; rising resistance in E. coli, Salmonella in India .AMR in cattle and poultry; widespread unregulated antibiotic use in Pakistan. Largest antibiotic use in agriculture; multiple resistant strains in pig and poultry in China .High livestock densit increasing AMR in beef and poultry in Brazil. Common AMR in poultry and small ruminants in Egypt. Surveillance system active, but AMR still present in swine, cattle, and poultry in USA. Notable AMR in aquaculture and livestock in Vietnam & Thailand. AMR in livestock due to lack of regulation and over-the-counter antibiotic in Nigeria & Kenya .Resistance found despite regulations—especially in pig farming in Europe (Italy, Spain) .

**Fig. 1.** Geographic hotspots of veterinary AMR cases.

It is calculated that sixty percent of all human infectious disease is zoonotic. The emergent and re-emerging zoonotic diseases are a grave issue to the human wellbeing today, as the recent outbreak of pig sourced H1N1 influenza A pandemic in 2009, and camel sourced Middle East Respiratory Syndrome Coronavirus (Munang'andu et al, 2024). In the current framework, the zoonotic agents are the infectious agents that tend to produce the diseases in humans as well as at least one other vertebrate animal species, where it replicated or is closely related. Also, the sprouting of killing zoonotic diseases has been shown to be a blow to local economies: on the one hand, causing extreme financial burden to the affected human population but also indirectly and negatively to trade and commerce with wealthier and consumer driven countries, who fear the risk of introduction of the disease to their population (Hegde, 2023).

Since past 20 years, there have been various diseases being added by rapid Globalization in food trade. Together with this growth, there is growing concern amongst the population, in regard to the widespread distribution of zoonotic diseases, food security, animal health and welfare and environmental pollution. The safety of animal foods is directly linked with animal health and herd management which directly depend on presence and availability of good relevant veterinary diagnostic and public health services. Increasing globalization of trade in animals is raising the necessity of animal health surveillance systems at the same time support by human and financial resources to the national veterinary services is being cut down in numerous countries worldwide. This puts a limit on all the elements of Veterinary services activity such as surveillance and observation (Aslam et al., 2021).

## The role of vaccine in AMR mitigation

Vaccine its origin is a Vaccinus, Latin word, meaning cow; the application of cowpox virus to the human body in order to trigger an immune response to the human version of the same disease (smallpox), as explained by Edward Jenner in the early days of the field, is an early example of the fusion of human and animal infectious disease disciplines. Trivalent vaccinations eliminate the burden of zoonotic infections among human beings and their domesticated pets respectively. However the vaccinated individuals in most cases are not the infecting, species but the one that is targeted, and there is dearth of experimentally implanted examples of how the path may be possible intervention strategy to illustrate how this can be done by vaccinating natural animals such as domesticated. we need vaccines that will not only prevent the occurrence of disease in both humans and economically important animals who may be the source of infection but will also interrupt chains of infection in nature (LeBlanc et al., 2006). Vaccines have been developed against several pathogens and currently dogs can be vaccinated against a variety of diseases and it is possible that in future new techniques of developing a vaccine may allow the protection of a dog against more infectious agents. Also, rabies causes high morbidity due to bites by rabid animals, most of which are highly disfiguring. The incidence of bite injury caused by suspect rabid dogs varies between 40 to 288 cases/ 100000 individuals (Prescott, 2008).

Specifically, where infections are spread primarily by infectious pathogens that are infected by members of a herd (for example with foot and mouth disease), herd resilience also encompasses additional factors: pathogen burden of the environment, infection predisposition and the duration and length of the infectious period of those who become infected. In the animal production sector, disease resilience has been categorized (conditionally) as the ability of an individual animal, a herd (animals' group) or a production unit (groups of herds) not to deteriorate performance in spite of being pressured by a pathogen pressure (Parasion et al., 2014). In this case, the term resilience will be defined more precisely as either invulnerability to the impacts of infectious pathogens or restoring oneself to a condition prior to an infecting pathogen. Such infections as those in which herd immunity can prove to be a significant factor in terms of defining the risk of an infection on susceptible individuals in the population; those which are transmitted directly between people (e.g. measles, rubella, varicella) and those where human beings are, or and important, reservoir of infection, (polio, malaria). It is unlikely that there is herd immunity (the contamination is not even transmitted human to human) and also it is also a fact that there is no important source of patient reservoirs in human pressure (proxies: tetanus, rabies) in nature which is a process requiring relatively long evolution time in the occurrence of bacterial AMR, and the over use of antimicrobials by or nearly 100 years has accelerated this natural cycle so incredulously to create bacterial AMR resistant Evolution and transmission of AMR Evolution and transmission of AMR is a complex process, due to action of intrinsic determinants and extrinsic drivers. As it seems, the ARGs and MGEs were combined together and concur in the bacterial chromosome as the intrinsic determinant of ARGs (Meeusen et al., 2007). The MGEs mainly consisted of plasmids, transposons, integrons etc, whose determinant actions were referred to the outlook mobilisation of ARGs. The extrinsic motivators are indirect and direct. Direct Factors and their Antimicrobials: selective pressures by chemicals in the ecological niches, e.g. antimicrobials (heavy metals and disinfectants), etc. The mediate factors involve social (national medicine policy, environmental protection policy, etc.), economical (intensive farming density, retail price of meat product etc.), drug (antimicrobial price, desinfectant utilization mode of hospital infection, etc.), health (food hygiene, environment hygiene etc.), climate (include temperature and humidity, pollution of environment, high wind, rain etc.) factors.

The impacts of vaccines on AMR as a result of all these effects can be further enhanced by indirect protection or herd immunity, which is generated when vaccinated persons are not infected or colonized and do not transmit the pathogen to others (Hinchliffe et al., 2018). And in doing so not only can infections and drug-resistant infections and antimicrobial use be decreased among the vaccinees but also among their contacts are sketched in fig. 02.

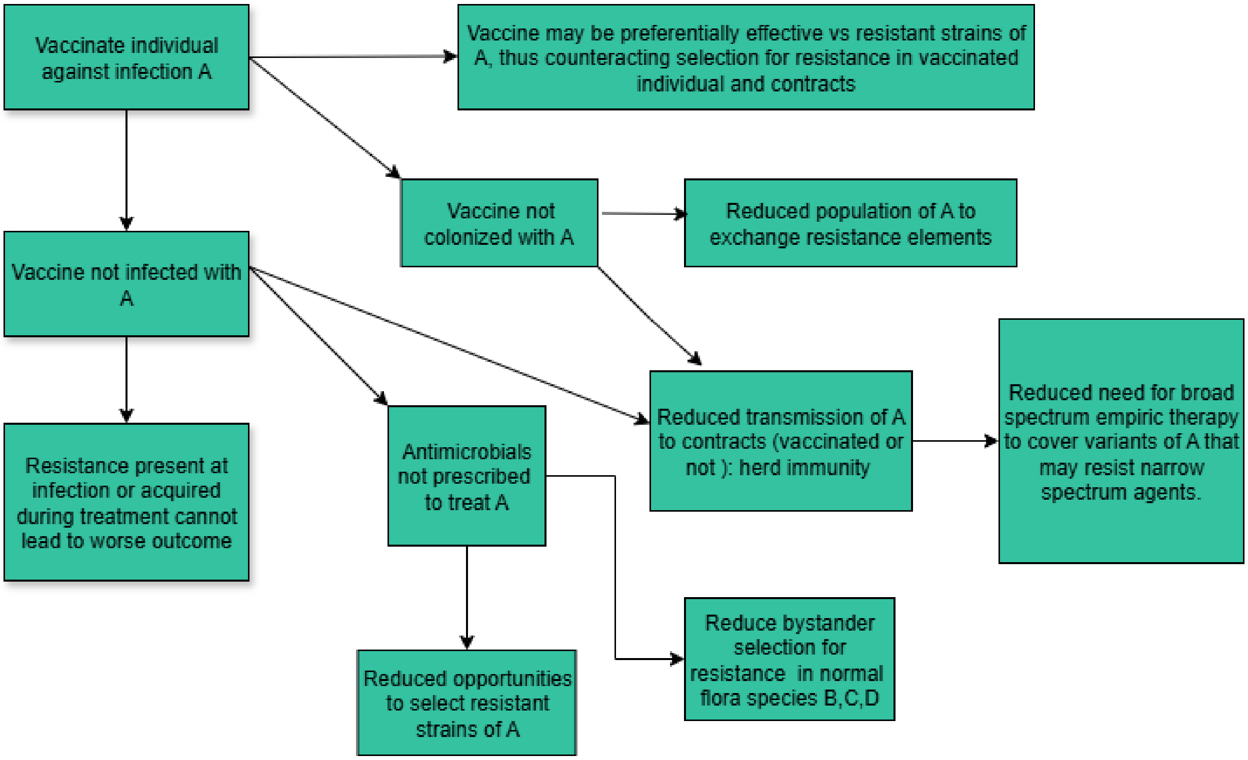


**Fig. 2.** Showing how vaccines reduce infection and antibiotic use.

Development of safe and effective vaccines is one of the most pressing challenges in human and veterinary medicine. Indeed, the development of new vaccines has largely been a process of empirical trial and error, with limited attention being given to theoretical considerations of the pathogenesis of, and immune response to, infectious diseases. It is important to determine the relevant pathway of protection for each infection and build a vaccine that will induce the appropriate pathway. Because one pathway is naturally down regulating the other, the magnitude of immune activation must be tuned to achieve optimal defense. There have been a variety of human and animal vaccines since Pasteur's administration of the live attenuated (non-virulent) fowl cholera vaccine more than a century ago. Fears of the safety of vaccines have occasioned the production of inactivated (killed) or chemically detoxified (so-called toxoid) vaccines for most of the early vaccines The basic principle is that the most effective route of vaccination is the route by which an individual acquires the infection (Keenan et al., 2025). Several pathways can be employed for vaccinating. They are the parenteral (i.e., i.d., s.c., or i.m.), transcutaneous and mucosal (oral, enteric, intranasal, respiratory, pulmonary, vaginal) mucus (Fig. 3).

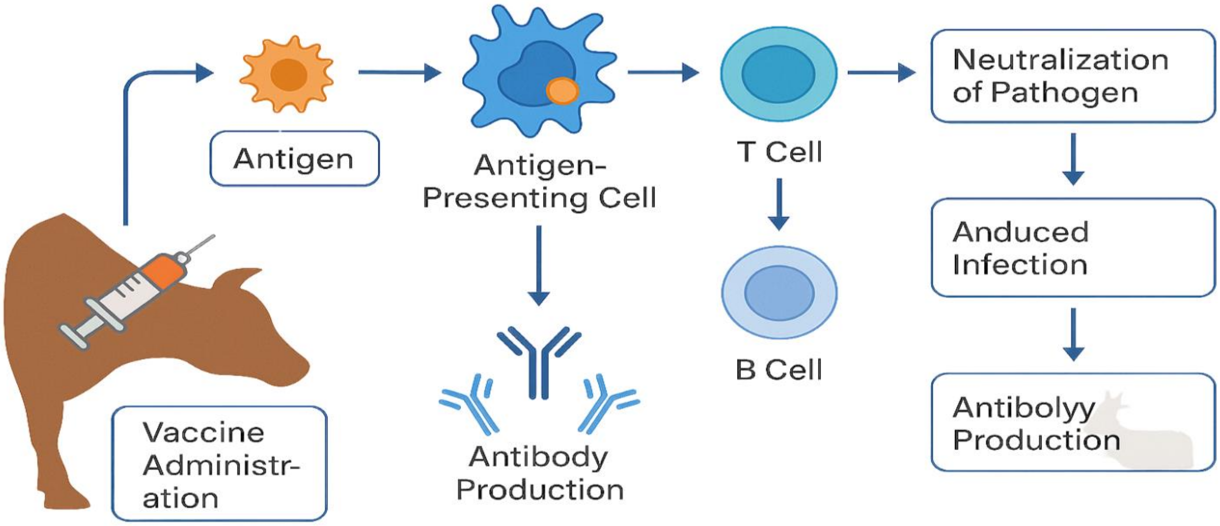


**Fig. 3.** Immune response mechanism triggered by a veterinary vaccine

## Immunomodulators: Enhancing Innate Immunity

Immunomodulators are those that are basically prepared so that the immune system can be further improved as well. The immune system naturally has a variety of cells at hand to detect and destroy foreign aggressors, but it gets weak unless boosted by immunomodulators. Gut microbiota plays an important role in the immune system. Therefore, probiotics filled to optimize the intestinal microbiota used in immuno prevents immuno (Monath, 2013). Plant polysaccharides are innate immunomodulators and they can modulate the acquired, adaptive and innate immune system by interacting with leukocytes, monocytes, macrophages and B- and T- lymphocytes. It is immunomodulation, you are messing with the immune system, and the stage of increasing and lowering the immune system. And restricted to immunopotentiation of just a single kind of antigen (i.e. vaccine) in formation of immunity in body to one disease (Refeld et al., 2020). A general immunity change is known as non-specific immunomodulation and this represents a change in host responsiveness to many antigens. One of the most alternatives to control the diseases is the immunomodulation with the additional advantage of improving the specific against the vaccines are illustrated in fig. 4).

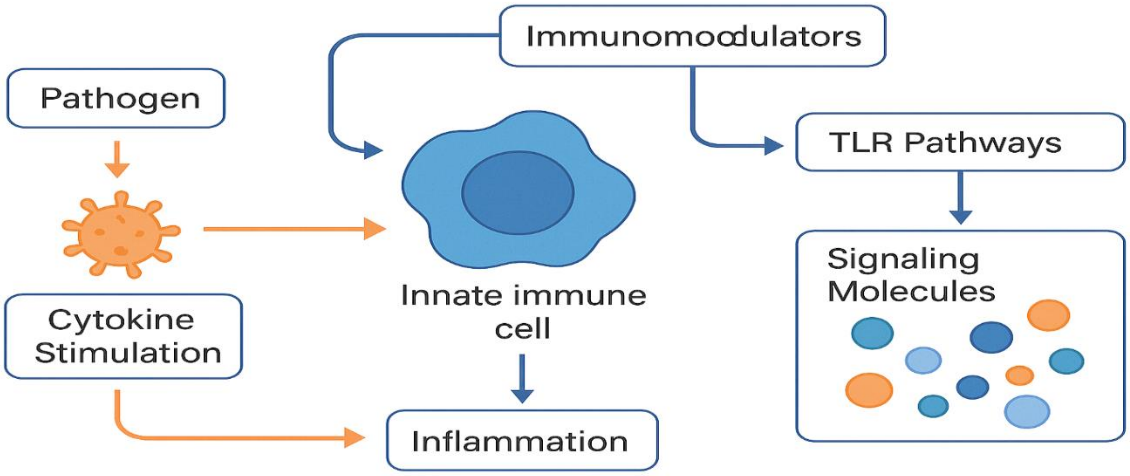


**Fig. 4.** Innate immune system and where immunomodulators act (e.g., cytokine stimulation, TLR pathways).

As a possible method of enhancing disease resistance in food animals without antibiotics, immunomodulation is possible. Among the most current and developing fields in immunomodulations is associated with such phenomenon as trained immunity, according which after priming, innate immune cells undergo, due to their epigenetic reprogramming encouraged by nonexclusive reshaping of the chromatin architecture and adaptation of metabolism, either high or low magnitudes of supplied stimuli (induction or tolerance, respectively). There are various ways of disease and antibiotic control in farm animals, however, in most infectious diseases of farm animals, there have been lacking, effective ways of intervention. Immunomodulation is one of the ways in which an innate immunity of a host may be activated/sensitized to protect against infection. Vaccines are strong immunomodulators and methods of inducing use of adaptive immune system are well known to infectious disease experts. The goal of innate immunomodulation is to enhance the immunological condition of the host and disease resilience to enhance the wellbeing of animals and production efficiency (Palma et al., 2020).

The immunomodulators are a wide network of agents that have capability of altering immune response, either stimulating or causing suppressive conditions, with sensational effects on therapeutic and prophylactic medicine. They can be divided in two broad categories namely as immunostimulants, immunosuppressants, immunoadjuvants, and biological response modifiers (BRMs) (Kumar et al., 2022). Immunostimulants (like IL-2, BCG vaccine and levamisole), which activate components of the immune system (such as macrophages and natural killer cells), have become favorites in the treatment of immunodeficiency disorders and neoplasia. In comparison, the immuno ( cyber ) suppressant drugs including cyclosporine, glucocorticoids and azathioprine which targets T-cell growth or inflammatory cytokines play an essential role in the therapy of automated disorders in addition to a reduction in the generation of transplant rejection (Kumar et al., 2022). As a vaccine component, immunoadjuvants enhance antigen-specific response through an interaction with the antigen presenting cells as well as prolonging exposure of the antigen. BRMs aid immune responses, and can incorporate monoclad antibodies, and interferons that are useful in cancer and viral diseases. The mechanism of these immunomodulators is multisided, at the level of signaling by cell, the modulation of cytokines, interaction with the immune checkpoint. They are widely utilized and along with cancer and adjuvants of vaccines in veterinary and human medicine practices, chronic infections and autoimmune diseases can already be discussed. Due to the broad therapeutic potential, their classification and the mechanics of action require better understanding so that they can be able to maximize their safe and selective use in clinic (Kumar et al., 2022).

**Table. 01.** Common immunomodulators used in veterinary species

| Immunomodulator | Type | Mechanism of action | Veterinary application | Species |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| **Interleukin-2 (IL-2)** | Cytokine | Stimulates proliferation of T cells and NK cells | Viral infections, cancer therapy | Dogs, cats, horses |
| **Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF)** | Cytokine | Enhances differentiation and activity of macrophages and neutrophils | Immune recovery post-infection or chemotherapy | Dogs, cattle |
| **β-glucans** | Natural polysaccharide | Activates macrophages via pattern recognition receptors (e.g., Dectin-1) | Improves resistance to infections | Fish, poultry |
| **Levamisole** | Synthetic compound | Stimulates T-cell and macrophage activity | Parasitic infection control, general immunity | Cattle, sheep |
| **Lactoferrin** | Iron-binding glycoprotein | Binds iron to inhibit bacterial growth; modulates cytokine production | Mastitis treatment, gut health | Cattle, poultry |
| **Toll-Like Receptor (TLR) agonists** | Synthetic or microbial | Mimic pathogen-associated signals to activate innate immunity | Vaccine adjuvants, immune priming | Multiple species |
| **Plant-derived compounds (e.g., Echinacea, Aloe vera)** | Natural phytochemicals | Modulate cytokine production and enhance phagocytosis | Immune boosting supplements | Horses, dogs, poultry |
| **Mycobacterium phlei extract** | Bacterial derivative | Stimulates innate immunity and non-specific resistance | Respiratory infections | Cattle, horses |

| | | | | |
|---|---|---|---|---|
| **Probiotics (e.g., Lactobacillus spp.)** | Microbial | Enhance gut immunity, modulate mucosal immunity | Gastrointestinal health | Poultry, ruminants |
| **Zinc and Selenium** | Trace elements | Support immune enzyme function, antioxidant defense | Immunity support, deficiency correction | All livestock and companion animals |

The general term immunostimulants can bottle up a very gigantic amount of naturally present and synthetic materials that can stimulate their immune system and more specifically innate immune systems which are the first line of defense against infections. The Toll-like receptor (TLR) agonists or the microbial-derived products turn out to be potent agents in activating the macrophages, dendritic cells, and natural killer cells (Shahbazi & Bolhassani, 2016).

All countries share common concern over FADs prevention and control. The benefits of improved animal identification systems in case of FAD outbreaks are sum of costs avoided through improved animal identification systems. These merits are that it prevents the diffusion of a FAD, there is the easy trace-back in case of infected animals, a minimum production loss occur through the presence of a disease, and a cost to Government is reduced as a result of control, intervention and elimination and of last importance is the reduction of trade losses that may occur (Caneschi et al., 2023) Epidemiology is a good new facet and method of investigation to expound and quantify the complimentary risk factors giving rise to a disease. In the meantime, health management or production medicine is described as an all-inclusive, preventive or performance-based, database-dependent and economically designed system of preventing diseases and performance excellence. The health management has been described as the health, productivity, and disease prevention of animals in the economic perspective of the owner and industry and acknowledging the animal welfare, food safety, public health, and the sustenance of the environment (Disney et al., 2001).

### Phage Therapy: A Targeted Approach

Bacteriophages, or bacterial viruses, have life cycles that are closely dependent on the bacterial cells that they colonize. Because of their mode of action, which is based on their absence of a specific enzymatic system, bacteriophages cannot survive on their own outside a host cell. Phages exist in almost all the natural ecosystems, and their presence has also been detected in the bodies of both animals and humans, such as those in the oral cavity, the gastrointestinal tract, and the respiratory system, and even in urine and serum (Chauhan et al., 2024). They play a role both in maintaining the homeostasis of natural ecosystems (Fig. 05).

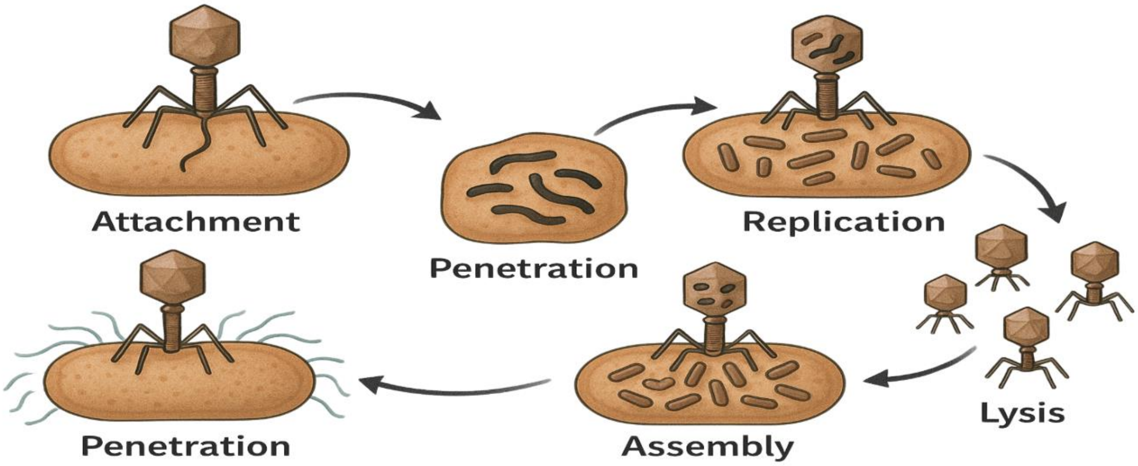


**Fig. 5.** Lifecycle of a bacteriophage and how it attacks bacteria.

Bacteriophages, phages, are a group of viruses that infect and multiply in the bacterial cell, and their life cycle consists of an orderly sequence of events, including adsorption, injection, replication of virus component, assembly, and cell lysis. First, phages bind to receptors on the bacterial surface; it is an extremely specific event and determines the host specificity. Upon the attachment the phage injects its genetic material (DNA or RNA) into the host cell, while the protein coat remains outside (Sharma et al., 2017). Within the host, the phage genomic material takes over the bacterial machinery to reproduce its nucleic acids and to produce viral proteins (Borie et al., 2014). This is succeeded by the construction of fresh phage progeny in the bacterium. In the end, the most lytic phages encode enzymes (endolysins, holins, etc) that digest the cell wall and catastrophically destroy the cell, and progeny virions escape to infect other host cells (Singer et al., 2003). Some phages, such as temperate phages, can integrate their genetic material into the chromosome of their host bacterium and continue to leave their DNA in silence until the phage is induced to make new particles. This bidirectional lifecycle makes bacteriophages not only bacterial killers, but also the genetic vectors that participate in the horizontal gene transfer Expressed as antibacterials and horizontal gene transfer under certain circumstances (Sharma et al., 2017). The specificity and accuracy of these mechanisms is the inspiration for their use in phage-based therapies and other antimicrobial strategies. Phage particle Phage particles are composed of nucleic acid (genetic material) and of proteins as the main structural matter of phages and with enzymatic characteristic. There are also filamentous phages, and icosahedral phages with tails, non-tailed phages, and numerous phages that have a lipoprotein envelope or that have lipids in the particle shell Ohashi & Ushida, 2009).

Environmental conditions and phage resistance are the important aspects to be considered in the phage therapy. Extrinsic factors affect the stability of bacteriophages. For long-term storage in solution or dry state, bacteriophages are kept at neutral pH (6–8). Phage replication is generally reduced at lower pH (4–6). In most cases, temperature influence on phage survival is low. The majority of them are able to live at temperatures between 40 and 90 °C, and some phages, such as the one infecting Lactococcus, even can resist pasteurization temperature (Klous et al., 2016). There are several potential benefits for phage therapy in the treatment of bacterial infections. And they can do so even against bacteria that are resistant to them, as good murderers should. Mastitis is just one of the bovine diseases for which phage therapy has been suggested as a remedy. Metritis is an acute systemic illness of the cow in first three weeks postpartum and has been associated with adverse reproductive effects (Doeschl-Wilson et al., 2021: Ferriol-González & Domingo-Calap, 2021). The most overwhelmingly abused use of antibiotics, however, may be in livestock, which poses a major threat. Treatment of predominantly cattle and swine infections with phages has been proven to be successful. Lytic phage-infected bacteria cannot recover viability. Few, in contrast, are bacteriostatic only (thus potentially permitting the development of bacterial resistance) (Griffin, 2002; Șonea et al., 2024)).

Use of bacteriophage (s) in the treatment of bacterial infections has many difficulties. Bacteriophage product manufacturing and characterization as well as designing and implementing early clinical trials designed to confidently demonstrate product safety and tolerability are essential prerequisites for progressing to trials designed to demonstrate efficacy and clinical benefit (Urban-Chmiel & Pyzik, 2025). The overall success of phage therapy is quite sensitive to the safety of phage preparations in terms of manufacturing and formulation. Phages would have to be developed on a large scale and under Good Manufacturing Practices (GMP) good practice validated by the regulators to be widely usable in clinical practice (Reindel & Fiore, 2017; Loponte et al., 2021).

## Probiotics and Gut Immunity

The gut microbiota, the most abundant symbiotic interfacing ecosystem with the host, has been demonstrated to exert crucial effects on the preservation of gut homeostasis. The microbiota-companying in the gut ble4-forther(gut-GM) in animals is closely associated at relevance to hosts, diets, and gut mucosal and immune system. The mammalian gut is the largest immune organ in the body and contains cells of both nonhemopoietic (epithelia cells (2), pencells (3), goblet cells (4)) and hemopoietic origin (macrophages (5), dendritic cells (3), T cells (6)), and is also a residence of trillions of microbes collectively known as the microbiota (7) (Wynn, 2009).

The complex gut microbiome is not an inert organ, or a set of 'passenger' microorganisms, however, the intestinal community is an active ecosystem that forms an integral part of vertebrate immunity and physiology. Gut microbiota offers several health benefits such as nutrient metabolism and absorption, play in the construction of the host intestinal epithelial barrier, in the development and function of the host immune system, and in the competition with pathogenic microbes to avert their harmful expansion (Shahbazi & Bolhassani, 2016). The GM is known as the community of microorganisms residing in a specific environment along the GI tract, which consists of bacteria, fungi, protozoa, archaea and yeasts. Because more than 98% of nonhost derived genetic sequences in the gut are bacteria, the term and the majority of studies on this topic have focused on bacteria in the GI tract (Fig. 6) (Jandhyala SM et al., 2015).

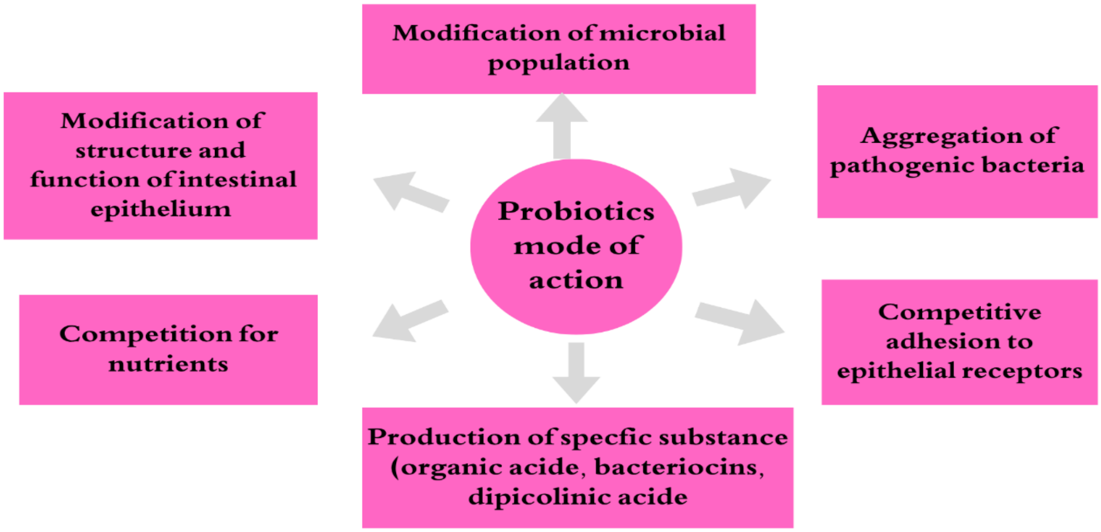


**Fig. 6.** Explaining the mechanism of how probiotics support immunity.

The term probiotics can be defined as live microorganisms which upon administration in sufficient quantity accords a health benefit to the host (Aslam et al., 2024). Ideally, probiotics made use of in an ailing patient were those whose species was of the sick patient and the probiotics should not be pathogenic, survive gastric acid and occurrence of intestinal enzymes, attachment to the intestine, and chance to alter the immune response of the host (Musa et al., 2009). The authors reviewed the modes of action of probiotics, which was referred to as immunobiotics due to the immunomodulatory properties of probiotics, in view of employing them to the veterinary sphere (Negash, 2022). The authors also mention that the manifestation of the effects of immunobiotics is primarily through the regulation of the response of the host and bowel homeostasis. The probiotics act upon gut associated lymphoid tissue (GALT) and primes the innate and acquired immunity. Among the most important mechanisms include activation of macrophages, dendritic cells and natural killer (NK) cells and stimulation of the synthesis of cytokines including interleukins and interferons, which are very crucial in signal and immune operations. Also, immunobiotics alter the release of Toll-like receptors (TLRs), which are major receptors that detect pathogen microorganisms and initiate immune responses. In addition, they take part in Th1/Th2 immune response regulation and in stimulation of intestinal barrier performance by tightening tight junctions and secretion of mucins to prevent the attachment and infection of pathogens. Such pleiotropic functions provide rationale of using immunobiotics not just in the preservation of gut health but also in curb infections as well as overall boost of animal immunity (Refeld et al., 2020). Probiotics come in a variety of formulations - pelleted feed, fermented feed, capsules, paste, powder and granules. The hypothesis has lately been put forward that the inactivated" bacteria too possess the probiotic effect, i.e. immune-modulating effect and thus must be classified under the category of probiotics in the broad sense immune-modulating organisms with relatively high adhesion power to the bowel wall, will overwhelm the pathogens adhesion (Pires et al., 2020; Ravichandran et al., 2024).

Handling of embryos and post hatch immuno-physiology of the gastrointestinal (GI) tract: Some of the enhanced stressors can be encountered in a modern broiler production complexes e.g. changes or imbalances in the feed, transportation, in hatchery processing and in high stocking densities all of these stressors impact negatively on the colonization of the GI tract with a post hatching pathogenic enteric bacteria population due to the existence of a compromised immune system and hence affect the birds health and the poultry food safety (Pinch The competition with the pathogens can be achieved by use of adherence sites and nutrient substrate and production of toxic or immune-activating metabolites by the endogenous intestinal microflora (Smith, 2010; Turner, 2018).

## Integrative Strategies for Sustainable AMR Control

Preventive and control measures used in public health practice to minimize and contain the effects of the disease include good hygiene, adoption of bio-security measures, vaccination as well as other methods of enhancing immunity. Now as an example of these actions, and of their potential impact on the reduction of AMR, we shall be having World Bank (van Wietmarschen, 2020), are used to mean an intervention, which reduces AMR indirectly, and an intervention that reduces AMR directly, respectively. As an example, interventions that decrease the burden on human health in relation to pathogens (eg, water, sanitation, hygiene; WASH), although they do not cause a direct effect on AMR, are still significant in AMR approaches, as there is a chance of indirectly causing an effect on AMR and creating AMR co-benefits (Kogut & Arsenault, 2016; De Briyne et al., 2014). Through AMR a combined effort by the health services, agriculture and environment management, as well as the policy structure is needed as a response to the public health effects of AMR. Since AMR is the problem that affects human, animal and environmental health, it is necessary to approach it in the light of one health and planetary health concepts that include inter-relatedness of these systems (Kolawole et al., 2023) (Fig. 7).

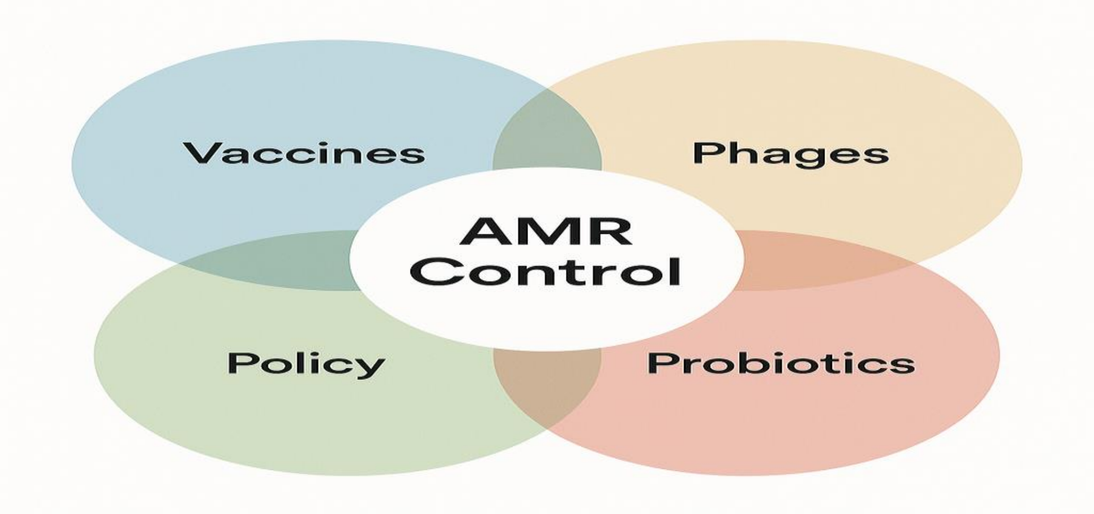


**Fig. 7.** Systems showing integration of vaccines, phages, probiotics, and policy in AMR control.

Also, community activation and broadcasting of the value of responsible AMU is required to induce a behavioral change leading to unnecessary prescriptions (ASML et al., 2015). Not only is research and innovation important for developing new AMAs and novel interventions, it is also essential for discovery of new non-antibiotic agents and alternative interventions for such research and innovation to thrive. Although vaccines and bacteriophage therapies are promising approaches to reduce dependency on conventional antibiotics, bacteriocins, particularly bacteriocins synthesized by bacteria are also identified as a very promising alternative option that require exploration (Cleaveland et al., 2006). In addition, strengthening surveillance networks worldwide will help to better monitor trends in AMR and to respond timely to AMR threats (Byrne et al., 2020).

Educational programs directed toward both healthcare providers and the lay public are essential for promoting responsible antibiotic use. Studies have shown that such interventions can result in marked reductions in antibiotic prescribing (Lloyd, 2006; White & Hughes, 2019). Legislation in veterinary medicine should only allow the use of antibiotics on veterinary prescription and eliminate the use of antibiotics as growth promoters in animals (Wilkinson et al., 2018). Countries should exchange surveillance data, best practices, and approaches to the regulation of, and resistance to, antibiotics. International organizations like WHO and FAO are crucial in the AMR agenda setting, through creating settings where interventions can be standardized globally (Murugaiyan et al., 2022; Costanzo & Roviello, 2023).

The WHO, and others, are formulating guidelines on the growing problem of antimicrobial resistance (WHO 2015). They are calling for One Health participation of all parties in all disciplines because – no one will be spared of AMR irrespective of our state of health. However, effective implementation of these plans has been difficult due to the battle for resources to properly support these plans, this was reported by WHO in 2019 (WHO Putting plans into action for antimicrobial resistance (AMR)). The financial limitations do not allow the full implementation of strategies to alleviate AMR at a worldwide level. The consequences of AMR are not confined to public health but extend to global socio-economic development (Velazquez-Meza et al., 2022).

Innovative approaches to tackling AMR cut across healthcare settings and need varied responses, such as public education and awareness programs, improved infection control, and the incorporation of antimicrobial stewardship in clinical care (Fong & Fong, 2017). Surveillance and reporting mechanisms are essential for follow-up of antibiotic consumption and resistance trends and for rapid decision making (LeBlanc et al, 2006). The linkage of an education to a policy, stewardship programs and internationalization is central in a bid to minimize these risks around AMR and therefore effectively protect public health for the generations to come (Gupta & Sharma, 2022).

## Conclusion

Veterinary immunology is a critical and future-oriented way of addressing the investment of the impending issue of antimicrobial resistance (AMR). These strategies equally minimize the use of antibiotics by strengthening the host immune response using vaccines, immunostimulants, probiotics and phage therapy, whilst effectively preventing and controlling the infection diseases. In contrast to the selective pressure by antibiotics that lead to resistance, the immunological interventions induce resilience to disease developing in animals, but they do not promote resistance. They are instrumental in protecting animal health and animal productivity, but also are important in preserving the effectiveness of the current use of antimicrobials, which is part of the solution to AMR.

Furthermore, the application of these measures in a One Health context guarantees a comprehensive plan of action, since human, animal and ecological health cannot be separated. In order to be successfully implemented, the approaches based on immunology should be promoted, alongside with the work of strong surveillance systems, specific investigations, awareness of people, and evidence-based veterinary policies. To put these innovations into practice, it is required to bring veterinarians, researchers, farmers and policymakers together. Since the problem of AMR continues increasing around the world, the introduction of immunological frontiers into veterinary practice is a lasting and scientifically valid option, a necessity to warrant animal health, food security, and human health at global level.

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## 10

# Zoonotic Diseases

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## ABSTRACT

This chapter describes the history, major outbreaks, public health impact, classification of zoonotic diseases on the basis of types of pathogens, risk factors to community, host-pathogen interaction, diagnosis, differential diagnosis, prevention from zoonotic diseases, one health approach to control zoonotic diseases, emerging zoonotic threats, economical and ethical concerns and future directions of zoonoses. With six out of ten known infectious illnesses being zoonotic, zoonotic diseases caused by pathogens that spread from animals to humans, represent a serious global public health concern. These illnesses, which include parasitic, bacterial and viral infections, have historically caused catastrophic outbreaks like the Black Death and remain a threat because of things like urbanization, climate change, and increased human-animal interactions. Ecological, climatic, and socioeconomic factors all affect zoonotic disease epidemiology; high-risk environments include biodiverse places with dense populations of people. Transmission risks are significantly increased by occupational exposure, especially for veterinarians, livestock workers, and wildlife handlers. Early detection is crucial, and the diagnosis is made using both conventional (culture, microscopy, serology) and innovative (PCR, NGS, fast testing) techniques. Vaccination (e.g., rabies in dogs), antimicrobial stewardship, public health education, and wildlife management are essential for prevention. To lessen the growing hazards posed by zoonoses, future research goals include mRNA-based vaccinations, AI-driven predictive analytics, and enhanced international surveillance networks.

**KEYWORDS**
Zoonoses, Risks, Zoonotic diseases, Transmission, Control.

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## INTRODUCTION

Zoonoses, also referred to as zoonotic illnesses, are infections caused by infectious agents that enter humans from an animal host and start a chain of pathogenic events. The terms "zoonoses" and "zoonosis" both refer to diseases that can be transmitted from animals to humans, but they differ grammatically (Singh et al., 2023). Zoonosis refers to a single zoonotic disease, for example: Rabies is a zoonosis transmitted through animal bites. Zoonoses refer to multiple zoonotic diseases, for example: COVID-19 (Parwanto 2023), Ebola, and Lyme disease are all zoonoses.

Sometimes, when people engage with animals that are carrying infectious agents, they can contract these germs from the animals. People who interact with animals, such as those who assist in abattoirs (Sattar et al., 2023), handle meat, or maintain cleanliness in slaughterhouses, may come into contact with the disease-causing bacteria. Today six out of every ten known infectious diseases are zoonotic.

When an infectious agent grows more severe and pathogenic to humans, it can also cause human-to-human transmission, making zoonotic diseases worse. Any pathogen that may pass from animals to people, such as a virus, prion, fungus, bacteria, or parasite, is the cause of an infectious disease. Since humans rely on animals for sustenance, it is crucial to comprehend zoonotic diseases, reverse zoonosis also known as anthroponosis, which occurs when an animal contracts an infection by ingesting a pathogen from humans (Al Noman et al., 2024).

### Historical context and major outbreaks:

The word "zoonoses" originates from an ancient Greek word ζῷον *(zoon)* which means 'animal' and νόσος *(nosos) means* 'sickness' or 'illness' (Agnelli and Capua 2022). Zoonotic diseases are of immense importance due to their lethal and fatal impact on human life. *Yersinia pestis* is the bacteria that causes Black Death (Jedwab et al., 2022), the first zoonotic illness to be recognized. Some zoonotic infections have a severe effect on human health in addition to causing a significant loss in food-borne animals like cattle, sheep, goats, and cows, among others.

The majority of zoonotic illnesses have significant rates of morbidity and mortality (Baumgartner 2021). For example, some bacterial zoonoses include anthrax, salmonellosis, TB, Lyme disease, leptospirosis, and brucellosis. Rabies, avian influenza, COVID-19, AIDS, Ebola, and rabies are examples of viral zoonoses. According to a 2010 study, 60% of human infections are zoonotic (Rahman et al., 2020), with 70% of these pathogens originating from wildlife species that have a serious negative impact on humans. Throughout historical history, there have been three significant zoonotic plague outbreaks, notably the Justinian plague (Bystrický 2023), which is estimated to have killed 25 million people. In the 14th century, a second plague pandemic, known as the Black Death or Great Plague, affected 60% of Europe's population. In the 19th century, China experienced the third plague, which had an impact on the economy and killed 10 million people globally (Xu et al., 2011).

## Global burden and public health impact:

Humans and vertebrates can naturally contract illnesses from zoonotic diseases. According to the WHO, 60% of the infectious diseases that have been documented in the literature are zoonotic, and the emergence of new infections indicates that 60% of them are zoonotic. Eight of the 200 zoonotic illnesses are classified as neglected zoonotic diseases (NZD) (Hossain et al., 2023). Because the zoonotic disease affects both humans and livestock, the nation bears a double financial burden from treatment costs, medical expenses, and preventative efforts. According to a dataset produced between 1980 and 2013, 65% of infections were identified as zoonotic diseases, which together accounted for 56% of outbreaks worldwide, whereas 44% of outbreaks were linked to diseases particular to humans.

According to a 2023 projection, zoonoses cause 2.7 million human fatalities and 2.5 billion human diseases globally each year (Samadi 2024). The substantial risk that zoonosis poses to human health has prompted various organizations, including the Centers for Disease Control and Prevention (CDC), the Global Health Security Agenda (GHSA), and the One Health approach, to step up their efforts and joint initiatives.

## Classification of Zoonotic Diseases:

Zoonotic diseases can be classified on the basis of types of causative agents as follows:

## Bacterial Zoonoses:

When a bacterial zoonotic disease is spread from animal to human through direct and indirect contact and excessive antibiotic use allows bacteria to persist in food that humans eat and become infected, it is known as bacterial zoonoses (Cantas and Suer 2014). Furthermore, bacterial zoonotic infections, in particular, may resurface after being thought to be eradicated or under control, raising public health concern (Wesey and Daniel 2025). Global climate change, excessive or inappropriate use of antibiotics, and large farm settings could all contribute to this. Leptospirosis (Ahmad et al., 2023), which is mostly brought on by Leptospira interorgan, is one of the most prevalent bacterial illnesses. When a person becomes yellow, they may experience kidney failure and bleeding, which are two of the infections known as Weil's disease. Leptospira interorgan can also induce severe pulmonary hemorrhage syndrome, which is characterized by extensive lung bleeding.

A genus of bacteria called Brucella is the cause of the infectious zoonotic disease known as brucellosis (Alharbi et al., 2022). The main animals affected by brucellosis are cattle, sheep, goats, pigs, and dogs. Consumption of raw milk and unpasteurized cheese can spread it. While epididymitis, orchitis, and placentitis are among the numerous signs and symptoms in an infected animal, abortion is primarily regarded as clinical. Because of the animals' activity, it can spread from one herd to another or from one location to another. Because of its aerosolization mode of transmission, brucellosis is most frequently obtained in laboratory (Di Bonaventura et al., 2021).

The 1980s saw the emergence of Lyme disease (Mahajan 2023), a zoonotic vector-borne illness brought on by the bacteria Borrelia burgdorferi. Joint discomfort, fever, some neurological issues, and the development of an enlarged lymph node are possible signs and symptoms. Hard ticks are typically the main vectors, and small rodents are their natural reservoirs.

## Viral zoonoses:

Viral zoonotic disease is the term for an illness caused by a virus that spreads from an animal to a human. Worldwide, viral zoonoses has grown to be a significant issue (Marie and Gordon 2023). Mammals, birds, and reptiles are among the amplifying host range of certain zoonotic viruses, which are classified as emerging and reemerging illnesses. There are three ways that viral zoonoses can spread: nosocomial, vector-borne, and direct. Since the genome sequence of viruses is made up of both DNA and RNA, RNA viruses are probably less stable than DNA viruses, increasing the likelihood that they may reappear. Regular and prolonged human-animal contact may raise the possibility of viral zoonotic illness development.

Among the most prevalent viral zoonotic illnesses Ebola virus (Hussein 2023) is responsible for severe hemorrhagic fever, fruit bats were thought to be the primary reservoirs, a filamentous RNA virus that causes severe hemorrhagic illness. Human-to-human transmission of the Ebola virus is thought to be possible.

Dogs are the primary reservoirs for rabies, a zoonotic illness that is contracted by direct contact with an infected animal. The rabies virus, which is spread by an infected animal's bite or saliva, attacks the central nervous system and results in neurological disorders. Compared to dogs, cats are more prone to become infected. Transmission by aerosols is uncommon (Dutta and Research 2014). The prevalence of rabies all around the world is shown in fig. 1.

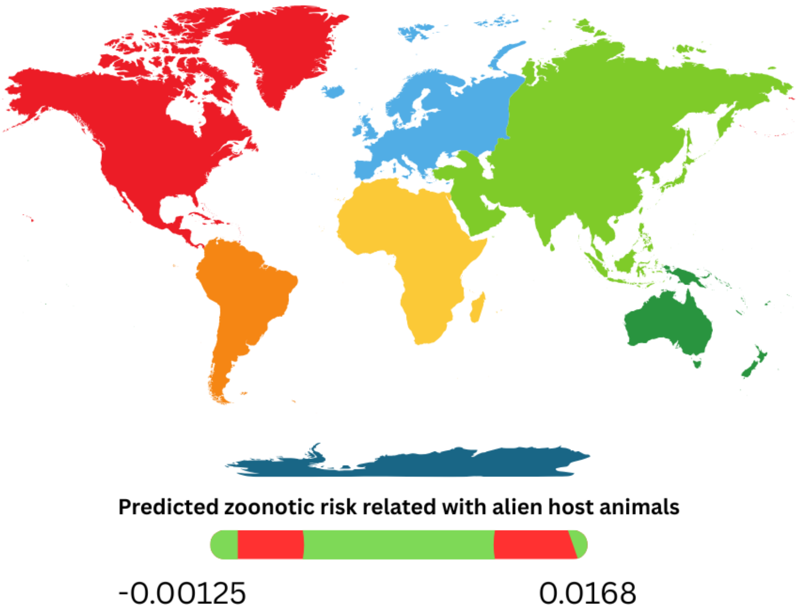

**Fig. 1.** The prevalence of rabies all around the world

The influenza virus is a segmented RNA virus that is categorized by the glycoproteins on its surface called NA Neuraminidase and HA Haemagglutinin (Chauhan and Gordon 2022). The genes 18HA and 11NA need to be identified. Numerous viral combinations fall under this category, such as the 1918 Spanish flu, or H1N1. The migrating waterfowl and wild ducks serve as the natural reservoirs. As of the current century, only two NA genes (N1 and N2) and three HA genes (H1, H2, and H3) are still in use in humans. Antigenic drift and antigenic shift have made this virus a substantial and persistent global public health threat (Adlhoch et al., 2022). Through reassortment, some strains of the low pathogenic influenza virus may have the capacity to infect people and change into highly pathogenic influenza viruses.

The coronavirus, a zoonotic disease which can infect both humans and animals (Holmes 2022), was discovered in the middle of the 1960s. When the COVID-19 outbreak happened in Wuhan, China, in 2019, four people from a seafood wholesale market where wild (snakes) and domesticated (poultry and bats) animals were sold illegally were reported as having contracted the virus (Holmes 2022). The remaining cases were thought to have been human-to-human transmission. Droplets from coughing or sneezing, when inhaled deeply by an infected individual, and surfaces of public transportation, restaurants, and other public locations (toilet, elevator, bus stops) can all spread it.

## Parasitic zoonoses:

Parasitic zoonoses is the name of the contagious parasitic diseases that spreads from animals to people. The majority of parasite diseases are found in wildlife, and intimate contact between people and wild animals can result in the development of parasitic infections (Omeragic et al., 2022). A key factor in the spread of parasites is food and water. For instance, only two genotypes of the zoonotic parasite disease echinococcosis significantly affect humans (Bagchi and Bagchi 2022). E. granulosus is the primary cause of cystic echinococcoisis in humans, while E. multilocularis is the primary cause of alveolar echinococcosis, another parasite illness that mostly affects the human alveolar region. Cats can contract toxoplasmosis (Daher et al., 2021), but humans can contract disease by coming into direct or indirect contact with cats. It can be transferred to offspring when a person gets infected early before pregnancy or during pregnancy. So, there is an intensive need to understand animal parasites to avoid humans getting infected.

Because of their constant contact with dogs and cats, livestock animals, which primarily consist of mammals (cattle, goats, and sheep), might contain viruses that can be transferred to people. Viruses like the rabies virus, which is spread by animal bites, and bacterial infections like salmonella, brucella, and E. coli are primarily found in livestock. The One Health concept draws attention to the substantial continuous efforts being made in the public health and veterinary fields to reduce the danger of zoonotic illnesses like rabies (Acharya et al., 2021).

### Epidemiology:

Regions with high biodiversity and dense human population are recognized as hotspots for the emerging zoonotic diseases (de Thoisy et al., 2021). Zoonotic diseases cover a wide range of geographic distribution mostly influenced by ecological, climatic and socio-economic factors. The predicted zoonotic risks all around the world is demonstrated in fig. 2 (Zhang et al., 2022).

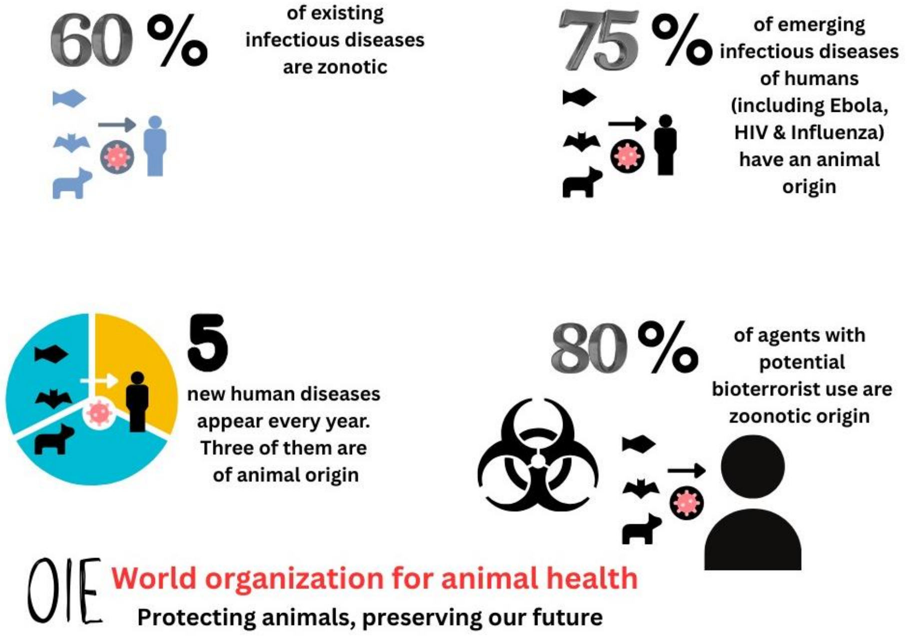

**Fig. 2.** The predicted zoonotic risks all around the world.

### Climate change and zoonotic disease emergence:

Climate change has a major impact on the emergence and spread of zoonotic diseases (Ojeyinka et al., 2024). The increasing spread of vector-borne diseases is caused by the expansion of the habitat of vectors such as ticks, fleas, and mosquitoes brought about by climate change and global warming. More than half of the pathogenic human diseases that have been made worse by climate change and exacerbated by climatic risks like heat, floods, and droughts were identified in a 2022 study (Ripple et al., 2022). The majority of research demonstrates the intricate connection between climate change and a higher risk of infectious disease spread.

### Urbanization and human-animal interface:

The natural ecosystem is severely disrupted by rapid urbanization and deforestation, which also causes ecological imbalance and brings people and wildlife into close contact, raising the danger of zoonotic transmission. Asia's significant increase in urbanization leads to overuse of land, habitat encroachment, and biodiversity loss. The ecology has evolved due to these man-made causes, altering the natural barriers that previously prevented the spread of pathogens (Dubey et al., 2023).

The main cause of deforestation is agricultural growth and infrastructure development, which is intricately linked to zoonotic transmissions like the Nepah virus when fruit bat habitat overlaps with pig farms, forming a bridge to humans. These significant environmental changes (Esposito et al., 2023) not only facilitate the pathogen evolution and host switching but also enhance the risk of the emergence of novel zoonotic pathogens and established the new transmission cycles.

### Occupational risks:

People that are in close contact with animals such as veterinarians, livestock farmers, abattoir workers and wildlife handlers have significantly increased risk of zoonotic pathogens. They are regularly exposed to biological hazards such as animal bites, inhalation of infectious aerosols and close contact with mucosa or secretions.

Similarly, workers in meat processing industries and livestock employees are at considerable risk of zoonoses such as brucellosis, Leptospira and bovine tuberculosis. This occupational risk necessitates effective biosafety protocols, regular surveillance and implementations of suitable educational interventions to mitigate the burden of zoonotic pathogens in high-risk population (Adam-Poupart et al., 2021).

## Host-pathogen interactions:

The host pathogen interaction involves microbial adhesion, invasion and subsequent response of host cellular pathway (Ferreira et al., 2021). When zoonotic pathogen gets entry into host cells, they use different surface proteins or some virulence factors that help in bacterial survival and evade from host immune response. Many zoonotic pathogens can manipulate host cell signaling systems like NK and MAPK that enhance the intracellular survival, replication and dissemination of the bacteria (Escudero-Pérez et al., 2023). These types of hosts- pathogen interaction often result in systemic or localized inflammatory response characterized by pro-inflammatory cytokines IL-1β, TNF-α, IL-6), initiates innate immune response(macrophages) and adaptive immunity including B and T cell immunity.

## Immune evasion mechanisms:

Recent research is carried out to comprehend immune response against zoonotic infections (Tang et al., 2023). To persist infection within the host, zoonotic pathogen adopts various immune evasion strategies such as antigenic drift and shift, inhibition of phago-lysosome fusion, interference with antigen presentation to APC and secretion of immune modulating signals. For example, Brucella evade from immune system by residing into modified vacuole that avoids lysosomal degradation and prevent from intracellular killing. Similarly, some viruses like Ebola and Nepah virus exhibit some proteins that inhibit the signaling of INF that are responsible component for antiviral immunity. Such type of immune evasion mechanisms may result in chronic infection, delay immune response that ultimately facilitates further transmission.

## Zoonotic spillover and adaptation to humans:

Zoonotic spillover is facilitated by ecological, behavioral and environmental factors and is a cross-species transmission of pathogen from animal reservoir to human (Ellwanger et al., 2021). Successful spillover requires a zoonotic pathogen to overcome interspecies barrier and could be able to adapt according to human physiology and immune defense system. This process is facilitated by the different mechanisms such as genetic variation, recombinant assortment, antigenic drift and shift. Moreover, an influenza virus that infects animals earlier undergoes antigenic drift and shift resulting in reassorting strain that is capable of human infection (Sánchez et al., 2021). The evolutionary dynamic that facilitates zoonotic adaptation influenced by host-pathogen interaction, immune selection criteria and ecological interphase complexity.\

## Severe zoonotic infections:

Certain zoonotic diseases are characterized by high morbidity and mortality rates especially when early diagnosis and therapeutic interventions are delayed. Rabies is caused by rabies lyssavirus, and nearly fatal once clinical symptoms appear which include fever, abnormal behavior and hydrophobia. Ebola and Marburg virus manifest systemic symptoms include viral hemorrhagic fever with high mortality rates. Some of the emerging zoonotic diseases include plague sandfly fever and Monkeypox pose significant public health challenges. Climate change, global travel and environmental factors contribute to the rapid transboundary spread of zoonotic agents. Therefore, rapid diagnostic system, surveillance system and international organizations like one health approach may contribute to mitigate the impact of severe zoonotic threats.

## Long-term complications:

Some zoonotic infections may lead to log term sequelae contributing to patient morbidity and health care burden at later stages. Lyme disease is caused by *borrelia burgdorferi* primarily transmitted via Ixodes spp. Ticks may evolve into chronic neurological disorder if not diagnosed and treated properly. Moreover, a subset of patients develops a post treatment Lyme disease syndrome characterized by persistent symptoms including cognitive impairment (brain fog), arthralgia, musculoskeletal discomfort and fatigue. The pathophysiology of the PTLDS remains incompletely described so it is hypothesized to involve immune dysregulation and neural injuries. Rabies result from rabies *lyssavirus* infection followed by the variable incubation period manifesting neurological symptoms (Nath et al., 2024). Rabies viruses target the central nervous system via peripheral nerve causing diffuse encephalomyelitis. Its clinical manifestation includes hydrophobia, aerophobia, progressive paralysis and autonomic dysfunction. These long-term significant complications highlighted the critical need of rapid diagnosis, illustrative patient management strategies to mitigate the drastic impact of zoonotic infections on human health.

## Diagnosis:

There are several methods and approaches used for the diagnosis of zoonotic diseases. The traditional methods which have been the cornerstone for detecting pathogenic agents including zoonotic diseases. The culture methods include culture, microscopy and serology. Each method has its strengths and limitations. Culture is used for isolating and identifying bacterial and fungal pathogens responsible for zoonotic infections. The methodology includes sample collection, media selection, incubation conditions, colony morphology, biochemical identification, and antimicrobial susceptibility testing.

Microscopy is a rapid and widely available method (Oeschger et al., 2021), often used as a preliminary step in zoonotic disease detection. This includes Light, Fluorescence and Electron microscopy. Serological testing detects antibodies or antigens in a patient's blood, identifying past or present infection with zoonotic pathogens.

Modern molecular diagnostic techniques, which provide quick, precise, and extremely sensitive identification, have greatly enhanced the diagnosis of zoonotic infections. Targeted genetic material is amplified using methods such as Polymerase Chain Reaction (PCR), whereas quantitative PCR (qPCR) precisely detects and quantifies the amount of pathogen present. By sequencing whole pathogen genomes, Next-Generation Sequencing (NGS) offers a comprehensive perspective (Suminda et al., 2022). Rapid diagnostic tests (RDTs) and point-of-care (POC) instruments are also crucial in low-resource and on-site settings because they provide prompt results without requiring complex lab facilities (Hobbs et al., 2021). In order to monitor zoonotic disease outbreaks and improve early warning systems, the One Health framework which links the health of people, animals, and the environment—is essential.

## Prevention and Control:

A comprehensive approach that incorporates immunization, public health campaigns, prudent use of antibiotics, and efficient management of both cattle and wildlife is needed to control and prevent zoonotic infections. The risk of disease transmission from animals to people is greatly reduced by vaccination, making it an essential preventive intervention (Van Herten & Bovenkerk, 2021). For instance, rabies vaccinations for dogs and wild animals as well as anthrax vaccinations for livestock have shown promise. Reducing the spread of illnesses requires public health measures such separating infected animals, culling when required, and improving hygiene standards (Carpenter et al., 2022). Additionally, educating the public on safe food habits, proper animal care, and cleanliness helps to prevent illness. Antimicrobial resistance (AMR) poses a serious challenge in treating zoonotic infections. Therefore, adopting antimicrobial stewardship programs, together with alternatives like probiotics, vaccines, and improved livestock management, can help reduce dependency on antibiotics (Zahmanova et al., 2022). Lastly, the key to reducing the danger of zoonotic disease outbreaks is effective wildlife and livestock management, which includes disease surveillance, controlled farming methods, and reducing human-wild animal contact.

## One Health Approach to Zoonotic Diseases:

To combat zoonotic illnesses, an effective One Health approach requires collaboration across several disciplines, such as human health, veterinary medicine, and environmental research (Erkyihun & Alemayehu, 2022). Collaboration between physicians, veterinarians, environmental experts, and decision-makers improves disease prevention and control tactics and allows for the early identification of emerging zoonotic hazards. Through improved disease monitoring, resource efficiency, timely interventions, improved global health preparedness, early detection, and a reduction in human-animal disease transmission, this integrated framework promotes healthier ecosystems and improved public health (Ghai et al., 2022). The WHO, OIE, and FAO are key international organizations that define worldwide standards and develop policies for zoonotic disease control (Bhatia, 2021). These organizations develop comprehensive plans for surveillance, immunization programs, and emergency response. Recent incidents such as the 2024 dengue warning in mainland France, the 2023 dengue fever cases in Lombardy, Italy, and the 2024 Marburg virus outbreak in Rwanda (Mohanty et al., 2024) demonstrate the One Health approach's practical success.

## Emerging Zoonotic Threats:

Population growth, fast urbanization, deforestation, industrial farming, ecological disturbances, antibiotic resistance, inadequate biosecurity in animal production systems, and greater international mobility are some of the interrelated factors that contribute to the emergence of zoonotic diseases (Saba & Balwan, 2021). These elements increase the connection between people, animals, and the environment, which gives viruses greater chances to spread over species boundaries. The risk of disease transmission is further increased by unhygienic conditions in live animal marketplaces and ineffective waste management. Furthermore, ecosystems and wildlife migration pathways are impacted by climate change, which may expand the range of disease-carrying vectors. World Health Organization (WHO)-designated high-priority pathogens, like the Nipah virus and Middle East Respiratory Syndrome Coronavirus (MERS-CoV), are particularly concerning because of their detrimental effects on health, high death rates, and dearth of effective treatments (Dong & Soong, 2021). Large-scale epidemics could be caused by these diseases, especially in places with weak healthcare systems and insufficient disease surveillance. Pandemic preparedness and response require a worldwide coordinated strategy that includes rapid diagnostics, early detection systems, vaccine research, and extensive public education. Integrating human, animal, and environmental health is emphasized by the One Health paradigm (Kelly et al., 2020), which is essential for thorough disease monitoring and prevention. Rapidly identifying, reducing, and responding to zoonotic disease risks and future pandemics requires improving healthcare infrastructure, funding scientific research, and cultivating international collaborations.

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## Ethical, Economic and Social Implications:

Zoonotic diseases have a significant financial impact on both global and local economies. High medical costs, large losses in the livestock, poultry, and agricultural sectors, as well as interruptions to global trade and tourism, are all common outcomes of outbreaks (Conrady & Health, 2021). Rapid response systems, vaccine research, and disease monitoring all demand significant investments from both public and commercial entities. Beyond the short-term expenses, zoonotic outbreaks often have a long-term financial impact that jeopardizes food security, safety, and economic stability. It is frequently necessary to make difficult moral choices in order to control these outbreaks, particularly when it comes to managing animal reservoirs (Buikstra et al., 2020). Mass culling of ill or high-risk animals is one popular technique that, although it effectively stops the spread of disease, raises questions over animal welfare and the effects on biodiversity. Ecological disruptions may result from such actions. As an alternative, more ethical and sustainable methods concentrate on protecting biodiversity by limiting human contact with wildlife, vaccinating animals, and maintaining natural habitats. Preventing zoonotic outbreaks also requires public awareness and education. Communities can be educated about risky behaviors, proper animal care, cleanliness, and the advantages of vaccination through focused and transparent communication. The danger of zoonotic disease transmission can be significantly lowered by encouraging behavioral changes, such as improved biosecurity farming techniques, responsible domestic animal care, and less involvement in wildlife trafficking (Layton et al., 2017).

## Future Directions and Research Priorities:

Predictive modelling is one of the most promising topics for future study on zoonotic diseases. By combining environmental, ecological, and genetic factors, improved computer tools are being developed to predict the spread of illnesses within populations, directing risk assessments and intervention plans. By utilizing more trustworthy datasets and combining machine learning and artificial intelligence (AI) to analyze complicated data, ongoing research attempts to increase the accuracy of these models (Bag et al., 2024). It is anticipated that these developments will aid in the creation of early-warning systems that are able to identify outbreaks before they become major world emergencies. Developing viable vaccinations and therapeutic treatments for zoonotic illnesses is another of the field's main priorities. Researchers are developing universal or broad-spectrum vaccinations that can provide defense against a variety of zoonotic pathogens in different species. Furthermore, it's critical to develop immune-based therapies, antibiotics, and targeted antivirals to combat zoonotic infections. Biotechnology advancements like PCR, qPCR, Next-Generation Sequencing (NGS) (Satam et al., 2023), and mRNA technology are expected to play a major role in the creation of these medical remedies.

Effective early response also requires improving monitoring systems that track epidemics, monitor human and animal health, and encourage international data sharing. Future initiatives will focus on enhancing frameworks for data sharing, honing monitoring instruments, and enhancing global cooperation and communication between countries, organizations, and stakeholders. Researchers are now looking into the use of mRNA vaccine technology for preventing zoonotic diseases as a result of its success during the COVID-19 pandemic. Researchers are now exploring universal vaccines that can protect against a wide range of zoonotic pathogens, which could provide a quicker response to new threats.

## Conclusion:

Animal-to-human transmission of zoonotic illnesses, which account for 60% of all known infectious diseases, is a serious worldwide health concern. Deadly epidemics like the COVID-19 pandemic, rabies, and plague have shown how these illnesses may annihilate entire populations throughout history. Because human activities like deforestation, urbanization, climate change, and extensive livestock farming disturb ecosystems and increase human-animal pathogen interaction, zoonotic spillover events are becoming more frequent. Exposure risks are especially high for high-risk groups, such as farmers, veterinarians, and wildlife handlers.

These diseases are difficult to diagnose and manage; they call for sophisticated molecular tools, careful use of antibiotics, and immunization campaigns. Effective surveillance and outbreak response have been demonstrated to depend on the One Health approach, which unifies environmental, animal, and human health initiatives. Looking ahead, preventing future zoonotic pandemics will demand a careful balance between scientific innovation, ecological conservation, and international cooperation. By addressing the root causes of pathogen transmission and strengthening global health systems, we can mitigate the ongoing threat posed by zoonotic diseases to both human and animal populations worldwide.

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# Advanced Diagnostic Techniques for Early Detection of Animal Diseases

11

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## ABSTRACT

Early detection of diseases in animals is crucial for preventing outbreaks and effectively managing animal and public health. Many approaches to traditional diagnostic techniques often rely on the clinical symptoms that appear in advanced stages of infection. Recent advances in diagnostic techniques have led to the development of more rapid and effective tools for pathogen detection involving PCR, LAMP, Real-time PCR and NGS offers high specificity and sensitivity. Serological tests like ELISA is helpful for effective screening and surveillance. Nanotechnology and CRISPR-based diagnostics enhance detection capabilities for rapid and ultrasensitive outcomes. Accuracy can be improved by analyzing data through AI. Advanced diagnostic tools play a vital role in the intervention of diseases detection early, reducing economic losses in preventing zoonotic diseases and livestock industry. However, some challenges are faced in advanced technologies like cost, skilled persons and infrastructure. Continued research on these technologies is essential for its widespread use in veterinary practice.

**KEYWORDS**
Early diagnosis, Veterinary diagnostics, Molecular diagnostics, Serology, Imaging techniques, Artificial intelligence.

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## 1. INTRODUCTION:

The early detection of animal diseases is a cornerstone of modern veterinary medicine and animal husbandry. It plays a vital role in safeguarding animal health, ensuring food security, and preventing the spread of zoonotic diseases which pose significant risks to public health. Since the world's population is increasing and more animal products are being consumed, it is particularly important to discover diseases as early as possible. Finding an infestation early can lower overall expenses, as it requires less heavy treatment and saves time compared to late intervention. Due to this, effective control measures can stop infections from one animal to other animals or even to humans (OIE, 2020).

### 1.1 Importance of Early Disease Detection

Detecting animal diseases early is necessary to protect the productivity and health of livestock and wildlife animals. Animal diseases often lead to big economic issues in farming, reduce biodiversity and may threaten people's health by causing zoonotic diseases. Among wild animals, brand-new diseases may cause trouble for threatened species and nature. If diagnosis happens early, action can be swift which stops outbreaks from getting severe and further spreading.

Zoonotic diseases that can spread from animals to humans demonstrate their spread early in populations. In human almost 60% infectious diseases are zoonotic and 75% infections are of animal origin. Spillover and the chance of a pandemic can be reduced greatly if animal reservoirs are identified and treated early such as in the case of COVID-19 Ebola and avian influenza (Rabinowitz & Conti, 2013).

### 1.2 Limitations of Traditional Diagnostic Methods

For decades, medical professionals have used clinical observation, serological tests and culturing microbes to detect diseases. Although these methods are helpful in many cases, they are not always suitable for catching disease at an early stage. A disease may not show any physical signs until major damage has occurred, and blood tests may not detect infections early when antibody levels are low. Moreover, for large scale screening these techniques are not suitable due to time consumption (OIE, 2020).

### 1.3 Advancements in Diagnostic Technologies

Recent advancements in molecular biology, genomics, proteomics and bio informatics have revolutionized animal disease diagnostics. Using PCR, NGS and CRISPR diagnostics, it is possible to spot viruses or bacteria at the molecular level. These approaches can detect a minute amount of genetic material from microorganisms and permitting the discovery of infections. Detection of infectious agents in wildlife and livestock is often done using PCR tests, which are fast and highly sensitive (Zhang & Li, 2019).

By next-generation sequencing (NGS), more details information can be obtained in the genomes of pathogens for better diagnosis. This technology makes it possible to discover new pathogens, analyze changes in pathogens and identification of genes conferring antibiotic resistance. Diagnostics based on CRISPR-Cas, especially SHERLOCK and DETECTR, are highly sensitive in finding small amounts of nucleic acids associated with early stages of disease (Zhang & Li, 2019).

## 2. Overview of the challenges in diagnosing animal diseases

Properly diagnosing diseases in animals is very important for both veterinary care and animal health management. Accurate and timely diagnosis helps in managing, preventing and safeguarding against zoonotic diseases. However, there are many obstacles to overcome when diagnosing animal diseases including technological issues, logistical difficulties, and technical limitations. These obstacles can impede early detection and effective disease management, resulting in significant consequences for animal health, food security, and biodiversity (Vidic et al., 2017).

### 2.1 Technical Limitations of Diagnostic Methods

One main issue in diagnosing animal diseases is that current diagnostic techniques have many limitations. Traditional methods such as clinical observation and serology tests often help to find the disease in its early stages. In numerous scenarios these methods have proven more effective. Often, animals will start showing symptoms when the disease is well-advanced which means response cannot happen fast enough. Moreover, for large scale screening these techniques are not suitable. (OIE, 2020).

### 2.2. Economic Barriers

Another significant challenge is the high cost of advanced diagnostic equipment and reagents, especially in limited resource places. The requirement of equipment, unique chemicals and expertise means that PCR and NGS are outside the reach of many veterinary laboratories and clinics in developing areas (Bissonnette & Bergeron, 2010). Since there is not enough software or training resources for laboratories so it is very difficult to conduct big-scale diagnoses.

### 2.3 Complexity of Pathogen Diversity and Evolution

It is challenging to diagnose animal diseases because pathogens are evolving and becoming increasingly diverse. The rapid change in viruses and bacteria makes it possible for new strains to appear and may go undetected by existing diagnostics. For example, the influenza virus undergoes significant mutation causing new strains of the virus to appear regularly and avoid both immune responses and diagnostic tests (Zhang & Li, 2019). Co-infections can make it difficult to diagnose infections where more than one pathogen infects a host at the same time. Sometimes, pathogens join the infection which can hide one pathogen and change the way the disease expresses itself highlighting the need for diagnostic tests that can simultaneously detect multiple pathogens.

The best example of evolution and pathogen diversity is COVID- 19 that is caused by severe acute respiratory syndrome coronavirus 2(SARS-COV-2). It is believed that SARS-COV-2 is originated from a zoonotic spillover and its intermediate host is bats. (Zhou et al., 2020). The global spread, continued mutation and zoonotic origin of SARS-COV-2 illustrates its evolution and pathogens diversity by understanding the need for integrated One Health approach, human, animal and environmental health strategies to control emerging pathogens (Fontanet et al., 2021).

### 2.4 Lack of Standardization and Training

Another reason for challenges in diagnosing diseases is that there are no consistent guidelines for veterinarians. Variability in laboratories testing methods can be extremely different, causing problems in the consistency of findings and explanations. Standardizing protocols and quality checks guarantees that diagnostic tests will be reliable and can be done in the same way. In addition, it is often necessary to have detailed knowledge and training to understand the results of some diagnostics which are not available. Providing veterinary professionals with training on advanced diagnostics and understanding difficult results is important for dealing with this issue. Equipment training for veterinary surgeons should involve training programs from academic institutions and participation from industry (OIE, 2020).

### 2.5 Challenges in Wildlife and Biodiversity Conservation

Detecting wildlife diseases is a challenge because it is difficult to collect samples and there are no specific tests for wild animals. As wildlife is distributed unevenly and is not always accessible, it is hard to keep track of their health and find signs of new diseases. Furthermore, many diagnostics designed for domestic animals may not suitable for wildlife leading to inaccurate findings. Disease spread in wild animals may negatively impact the diversity of species and the well-being of their ecosystems. For example, chytridiomycosis has significantly reduced the populations of many amphibians worldwide. Early detection of such diseases is important for conservation efforts and preventing loss of biodiversity (Rabinowitz & Conti, 2013).

## 3. Diagnostic Methods

### 3.1 Traditional Diagnostic Methods

Traditional diagnostic methods are the usual techniques veterinarians rely on to identify and diagnose illnesses in animals. For decades veterinary diagnostics depends on lab testing, observation and analyses of microbes because they are easy to use and affordable. They lack high sensitivity needed for early diagnosis. Patient's history, clinical signs, and tests are used together to make a diagnosis. Examples of Traditional Diagnostic Methods are:

- ➢ Clinical Examination
- ➢ Serological test

### Clinical examination

Clinical evaluation is a primary and common diagnostic strategy in veterinary medicine. It involves examining an animal's body behavior and background to find signs of sickness.

### Serological test

Although veterinary experts use clinical examination to begin, they normally need additional lab tests and techniques to confirm a diagnosis. Despite its limitation, it is still very important for vets, mainly where advanced laboratory tools are not accessible.

### 3.1.1 Components of Clinical Examination

Clinical examination in animals typically involves the following components:

### i. History Taking

Documenting the complete history of the animals include age, sex, breed, animal species, disease symptoms and its treatment, diet animals' exposure, vaccination status, environmental changes and exposure to potential toxins. For example**,** A farmer notes that one of his cows seems lethargic, produces less milk and has been coughing for several days. By using these details, the veterinarian can consider infections and metabolic concerns as possible causes (OIE, 2020).

### ii. Physical Examination

The physical examination requires a careful check of all the animal's body systems. Important steps included in this process are general appearance like (animal posture, behavior and animal condition) its vital signs including heart rate, measuring temperature, respiratory rate and systematic examination such as cardiovascular, musculoskeletal, gastrointestinal and respiratory systems. For Example**,** A veterinarian examining a dog with lameness may palpate the limbs, check joint swelling, and assess gait to localize the source of pain (Rabinowitz & Conti, 2013).

### iii. Observation of Clinical Signs

Clinical signs are easily noticed symptoms of illness by behavioral changes (aggression, lethargy or change in appetite) by physical abnormalities (swelling, lesions and discharge) and by physical impairments including difficulty in breathing and diarrhea. **For example,** A chicken with ruffled feathers, nasal discharge and sneezing could indicate that it has avian influenza or infectious bronchitis (OIE, 2020).

### 3.2. Benefits of Clinical Examination

- **Accessibility:** Clinical examination does not require specialized equipment, making it accessible in all settings.
- **Cost-Effective:** It is less expensive than advanced laboratory tests.
- **Immediate Results:** Veterinarians can make an initial diagnosis from the symptoms observed during the examination, enabling quick action (Mackay et al., 2002).

### 3.3. Role of Clinical Examination in Disease Diagnosis

Disease diagnosis begins with clinical examination and decisions about additional diagnostic tests are based on its finding. For example:

- A cow with fever, coughing, and nasal discharge may undergo serological tests to confirm bovine respiratory syncytial virus (BRSV) infection.
- A dog with lameness and joint swelling may require radiographs analysis to diagnose arthritis or Lyme disease (Mackay et al., 2002).

## 4. Serology in Traditional Diagnostic Methods:

Serology is a standard method for detecting antibodies or antigens in the serum of an animal to diagnose different infectious diseases. It's a crucial test in veterinary medicine, mainly for detecting old or current infections. Serological tests utilize the immune system response to detect infection by looking the production of antibodies after contact to specific antigens. These testing methods are primarily used for tracking diseases, outbreaks detection and checking vaccine responses. Despite new molecular techniques are available, serology remains valuable because it is easy to use, inexpensive and provides information about the immune system of animals (OIE, 2020).\

### 4.1 Principles of Serology

Serological tests depend on the interaction between antigens and antibodies. The finding of certain antibodies or antigens in the serum shows the exposure of particular pathogen. Serological tests can measure the presence or absence of antibodies (qualitative) or they can measure their quantity.

### 4.1.1 Types of Serological Tests

### 4.1.2 Enzyme-Linked Immunosorbent Assay (ELISA)

ELISA is commonly used for serological tests. This is done by using enzymes to detect the binding of antigen and antibody. An ELISA test can be designed to detect either an antibody (indirect ELISA) or an antigen (sandwich ELISA). For example, ELISA is used to detect antibodies against Brucella abortus in cattle in order to diagnose brucellosis (OIE, 2020).

### 4.1.3 Agglutination Tests

Agglutination tests reveal if red blood cells or bacteria are sticking together after being mixed with specific antibodies. Rapid testing is convenient, but may not catch every mild case. An example is the Rose Bengal test, a kind of agglutination test applied to cows, horses, sheep and goats for brucellosis detection (Mackay et al., 2002).

### 4.1.4 Complement Fixation Test (CFT)

CFT test detects whether antibodies can combine with antigens to begin the immune response. Diseases caused by bacteria, viruses and parasites can be diagnosed by CFT. For example, CFT is helpful for detecting foot-and-mouth disease (FMD) in livestock because it looks for antibodies against the FMD virus (OIE, 2020).

### 4.1.5 Immunofluorescence Assay (IFA)

When antibodies bind to antigens, the complex becomes visible under a fluorescence microscope by using certain fluorescent dyes. This technique detects the virus accurately. For example, IFA can detect Leptospira antibodies in both dog and livestock samples (Fig. 1) (Rabinowitz & Conti, 2013).

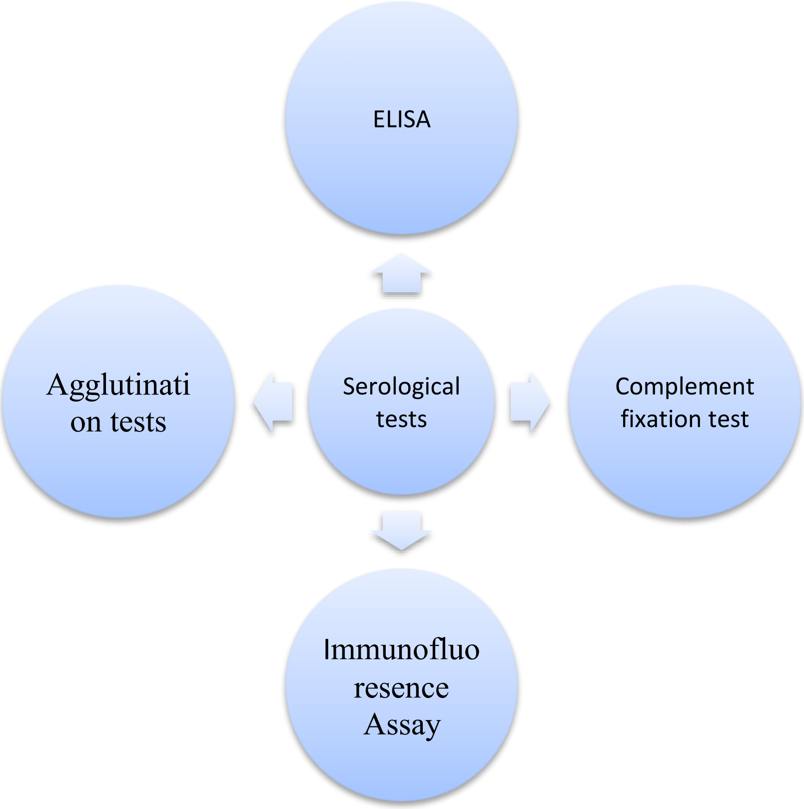

**Fig. 1:** Types of serological tests

### 4.2. Applications of Serology

#### 4.2.1. Disease Diagnosis

Serological tests enable the identification of infections in animals caused by bacteria, viruses or parasites. Example: Lyme disease in dogs is diagnosed using ELISA which detects antibodies in response to *Borrelia burgdorferi* (OIE, 2020).

#### 4.2.2. Disease Surveillance

Due to their sensitivity, serological methods are crucial for detecting and monitoring animal diseases. To detect avian influenza in birds, serological surveys are performed (Mackay et al., 2002).

#### 4.2.3. Vaccination Monitoring

Serological tests are used to detect if vaccines have triggered a good immune response. For example, after vaccinating cattle against the bovine viral diarrhea virus (BVDV), the level of antibodies is measured to prove that the animals are protected (Zhang & Li, 2019).

### 4.3 Benefits of Serology

- Serological tests are commonly provided and can be performed at most animal health laboratories.
- They are less costly than molecular diagnostics.
- Serology provides information about past exposure to pathogens and the immune responses.
- Serological tests are often applied to screen and monitor large populations (OIE, 2021).

## 5. Limitations of traditional methods in terms of sensitivity, specificity and time.

Veterinary diagnostic efforts for years have mainly depended on clinical observation, blood and tissue tests and culturing pathogens. These methods often lack specificity and sensitivity but they are widely used because of their cost-effectiveness. A lack of instruments in veterinary medicine can result in difficulties in keeping animals healthy, controlling diseases, recognizing diseases, diagnosing them and treating them quickly (García-Yoldi et al., 2006).

### 5.1 Sensitivity Limitations

Sensitivity describes how well a test can detect animals that are affected by disease. By using traditional methods, diseases cannot be detected early, as these methods rely on observable symptoms and antibody response that usually develop after the initial signs of a disease.

### 5.2 Specificity Limitations

Specificity describes a test ability to identify the presence of illness without false positives. As multiple pathogens can cause similar symptoms so traditional methods may fail to give a specific diagnosis.

### 5.3 Time Limitations

Conventional diagnostic methods can take a lot of time and delay the treatment. This can be a significant problem during outbreaks where rapid identification of new cases quickly helps to control the disease.

### 5.4 Impact of Limitations on Disease Management

The fact that traditional methods cannot be performed quickly or with perfect accuracy has a great impact on disease management:

- **Delayed Diagnosis:** Late detection can lead to the spread of disease within and between animal populations. For example, a patient with acute stage TB may exhibit mild symptoms such as fatigue and cough. Traditional sputum testing might not detect delaying treatment, low bacterial levels and increasing the risk of transmission in communities.
- **Misdiagnosis:** False positives or negatives can result in inappropriate treatment or failure to control outbreaks. For example, if a diabetic patient is utilizing glucose strips for monitoring and has a high kidney threshold for high glucose excretion, he may get false negative results and their blood sugar level will be uncontrolled.
- **Economic Losses:** Delayed or incorrect diagnosis can result to significant economic losses in livestock production due to decreased productivity and trade restrictions (Gallardo et al., 2015).

## 6. Molecular Diagnostic Technique

“Molecular diagnostic techniques” are used to examine and find genetic material in host organisms at a molecular level. These methods allow early diseases detection, as these methods produce specific, sensitive and fast results before any symptoms are noticeable. Molecular diagnostics help precisely to identify infections, modify gene testing and control disease progression that has changed the field of veterinary medicine. Advances in medicine are helping out infectious diseases, genetic disorders and pathogens that are emerging today. Some useful molecular testing procedures for early disease in animals are explained below.

### 6.1 Polymerase Chain Reaction

A technique that increases the level of specific DNA segments, making it possible to find pathogens even when they are present in low numbers. Due to its high sensitivity and specificity, it is best for finding out viral, bacterial and parasitic infections. The virus that causes African Swine Fever Virus (ASF) is now detected earlier in pigs due to PCR enabling more effective measures (Gallardo et al., 2015). RCR is helpful in:

#### 6.1.1. Zoonotic Disease Surveillance

PCR plays important role in the early detection of diseases caused by *Leptospira spp.*, *Coxiella burnetii* (Q fever) and *Bacillus anthracis* (anthrax), helping to stop human infections (Müller et al., 2013).

#### 6.1.2. Detection of Viral Diseases

PCR is crucial for detecting viral infections in animals, For example, foot-and-mouth disease virus (FMDV), African swine fever virus (ASFV) and avian influenza virus (AIV). Real-time PCR is used for finding highly contagious viruses because it is highly sensitive and specific. For this reason, RT-PCR is usually used to identify the rabies virus in animals suspected of infection (Dürr et al., 2008).

#### 6.1.3. Bacterial and Parasitic Infections

PCR can be used to detect bacteria that cause diseases in livestock such as *Mycobacterium bovis* (tuberculosis), Salmonella and Brucella PCR is also used to identify infections by parasites. For example, *Trypanosoma evansi* which causes surra in horses and camels (Desquesnes et al., 2001).

### 6.2. Immunohistochemistry

With IHC, animal diseases are more easily detected at the initial stage. By utilizing antibodies, the process can identify antigens in the tissue, revealing the presence of pathogens, unique proteins or disease factors. In veterinary medicine, IHC is best for diagnosing cancer, autoimmune disorders and infections (Rupprecht et al., 2017).

#### 6.2.1. Applications of IHC in Animal Disease Detection:

**a) Infectious Diseases**

IHC is frequently used to detect infections in animals caused by viruses, bacteria or parasites. For example, this technique is used to detect rabies virus in the brain and the avian influenza virus in poultry (Swayne et al., 2013).

**b) Cancer Diagnosis:**

IHC is used to determine tumour markers existence, so it become easier to organize and classify the different tumours in animals. For instance, it was tested to detect mammary tumours in dogs (Sassi et al., 2010).

**c) Autoimmune Diseases:**

IHC can search for immune complexes and auto-antibodies in dog tissues, aiding in the discovery of diseases such as lupus (Pedersen, 1999).

### 6.3 Imaging Techniques

Radiography, ultrasonography and CT have become essential for veterinarians in their day-to-day diagnostics. With imaging technologies doctors can see inside the body enabling earlier detection of diseases.

### 6.4 Radiography

In radiography, X-rays enables to examine the inside of the body. It is used to check for fractures, tumours and conditions of the lungs in animals. Radiography has helped veterinarians to find early detection of Osteosarcoma in dogs for timely treatment (Withrow et al., 2013).

### 6.5 Ultrasonography

Ultrasound imaging uses sound waves at a very high frequency to show the detailed structure of the body's organs. Ultrasonography helps in detecting reproductive, heart and abdomen diseases. By using ultrasonography, it is possible to detect complications in pregnancy at an early stage in cows by improving their reproductive results (Ginther et al., 2016).

### 6.6 Computed Tomography (CT)

CT uses complex imaging to create clear cross-sectional pictures inside the body. CT helps a lot in recognizing brain tumours and injuries in the spinal cord. In dog early detection of nasal tumors through CT imaging allows veterinarians to use targeted treatment (Lana et al., 2006).

### 6.7. Real-Time PCR and Quantitative PCR (qPCR)

Another term used is quantitative PCR (qPCR) makes it possible to track DNA quantity during the PCR process. It facilitates in monitoring how diseases develop and in assessing the effects of treatments. In this way, detecting BVDV in cattle with Real-Time PCR allow for proper action to be taken quickly and helped to avoid expensive consequences (Nonnecke et al., 2014).

### 6.8. Quantitative PCR (qPCR)

With qPCR, it is easy to determine the exact copies of a particular DNA sequence in a sample. qPCR can be used in:

#### 6.8.1 Detecting Animal Diseases

Viral infections like avian influenza and Newcastle disease can be detected by using qPCR. Test results of qPCR can help detect the presence of bacterial diseases, among them, brucellosis and tuberculosis. The disease progression can be observed with qPCR by quantifying target DNA as it changes over time (Huang et al., 2022).

### 6.9 Next-Generation Sequencing (NGS)

NGS enables to read every sequence in a genome at the same time. This technology is very useful for the discovery of new pathogens, to study how they develop and detect genes that resist antimicrobial drugs. NGS has enables the researchers to discovered several new types of Avian Influenza Virus (AIV) in poultry and are able to produce effective vaccines against them (Huang et al. 2022).

#### 6.9.1 Pathogens analysis and identification

With NGS, it becomes possible to detect familiar and unknown pathogens in animals by reviewing their genetic sequences. NGS make possible to spot new infectious diseases that might be missed by other systems. NGS technology was used to find the African swine fever virus and avian influenza virus found in both livestock and poultry. Genome sequencing by researchers to tracks the pathogens evolution and spread aids in the prevention of severe infections (Tran et al., 2022).

#### 6.9.2 Using Metagenomics to Analyze Microbial Communities

By using NGS, we can monitor the microbes in different tissues (including feces and blood) of animals. It enables to find both dangerous and helpful microorganisms, making it possible to know how some diseases are caused. The study by Huang et al. (2022) revealed that inspecting samples by metagenomic sequencing lets them spot bacterial and viral pathogens in pigs, making diagnosis and treatment more efficient.

#### 6.9.3 Recognizing and documenting antimicrobial resistance (AMR).

NGS helps veterinarians to identify genes that cause antimicrobial resistance in bacteria and helps them to make the right decisions for treatment and stop the spread of AMR.

For example, by NGS, it became clear that E. coli and Salmonella in livestock contain resistance genes which made it simple for farmers to treat the animals with antibiotics (Munk et al., 2018).

#### 6.9.4. Early diagnosis of genetic disorders

NGS identifies genetic changes associated with inherited diseases within animal populations. This is very useful in avoiding genetic disorders in breeding animals for these programs. Whole-genome sequencing (WGS) identifies mutations related to Bovine Leukocyte Adhesion Deficiency (BLAD) and Progressive Segmental Semi-Rigid Syndrome (PSS) (Bickhart et al., 2017).

## 7.Immunodiagnostic Techniques

### 7.1 Enzyme-Linked Immunosorbent Assay (ELISA)

ELISA is a widely used laboratory test in immunology. ELISA detects antigens or antibodies in serum, milk or many other fluids. Many diseases can be detected and managed early, for example, brucellosis, foot-and-mouth disease and avian influenza. ELISA technology facilitates health workers to detect *Brucella abortus* in animals, enabling treatment to begins early (Legesse et al., 2023).

### 7.2: Lateral Flow Immunoassay (LFIA)

LFIA or rapid test kits enables to spot pathogens detections. For example, LFIA kits are available to help quick detection of African swine fever in wild boars (Gallardo et al., 2019).

### 7.3 Immunohistochemistry (IHC)

IHC applies antibodies to find specific antigens in tissue, thus revealing where pathogens are found in the sample. In studies, IHC has helped to detect BVDV antigens in tissues stored in formalin (Su, 2023).

### 7.4 Flow Cytometry

Flow cytometry helps to analyze cells with the aid of fluorescently labelled antibodies to find pathogens. It can be used to find out immune responses and identify pathogens living inside cells such as *Mycobacterium bovis*. Flow cytometry has helped to examine the immune cell responses of cattle ill with tuberculosis (Neill et al., 2005).

## 8.Future Trends and Innovations

### 8.1. Emerging Technologies (e.g., CRISPR, Nanotechnology)

Using emerging technologies such as CRISPR and nanotechnology is expected to improve the early detection and diagnosis of diseases in animals. By using advanced techniques diagnosis is more accurate, quick and efficient which helps take care of animals and control diseases (Kitsiou et al., 2017). See what these technologies are doing to influence the future:

#### 8.1.1 CRISPR-Based Diagnostics

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) is a genome editing tool adopted for use in diagnostics. Examples of its role in animal disease detection are:

**i. Rapid Pathogen Detection:** Systems like SHERLOCK and DETECTR depend on CRISPR sequence recognition to highlight specific DNA or RNA sequences of pathogens from any animal sample. Consequently, diseases such as African swine fever, avian influenza and foot-and-mouth disease can be detected earlier.

**ii. Portable and Affordable Testing:** CRISPR based diagnostics technology can be applied to portable devices so that testing can take place anywhere, beyond laboratories.

**iii. High Specificity and Sensitivity:** CRISPR technology enables specific identification of closely related pathogens, supporting proper diagnosis and suitable treatment.

### 8.2. Nanotechnology in Diagnostics

For diagnosis nanotechnology applies materials with dimensions less than 100 nm offering potential to detect animal diseases in several ways.

i. **Nano-sensors:** They can identify disease biomarkers such as proteins, DNA and metabolites even when their levels are very low, helping diagnose diseases before any symptoms become noticeable. For example, by using nano-sensors we can observe mastitis in dairy cattle and problems with breathing in poultry.

**ii. Imaging with Nanoparticles:** Nanoparticles with various functions can aid MRI or fluorescence imaging to help find infections in animals accurately.

**iii. Drug Delivery Through Targeting:** Nanotechnology benefits therapy may assist in detecting diseases by delivering specific agents specifically to the tissues or cells needed.

### 8.3. The combination of CRISPR with Nanotechnology

Employing both CRISPR and nanotechnology significantly enhanced diagnostics capabilities.

**8.3.1. CRISPR-Nano Hybrid Systems:** CRISPR is delivered in cells with the help of nanoparticles that improves our ability to detect pathogens.

**8.3.2. Screening for Multiple Diseases:** When paired with nanomaterials, CRISPR can help detect a range of infections in a short period at a lower cost.

### 8.4. Opportunities offered by both telemedicine and remote diagnostics

Telemedicine and remote diagnostics may make it easier to get treated, cost-less and better outcomes by following ways:

#### 8.4.1. Enhanced Accessibility and Equity

Telemedicine eliminates the barriers of distance in underprivileged and rural regions. It was used widely during the COVID-19 epidemic to make sure treatment did not stop. Remote diagnostics make it possible for patients to speak to a specialist from a distance (Bashshur et al., 2016).

#### 8.4.2. Cost-Effectiveness

By reducing hospital stays and travel, medicine lowers expenses for patients and the healthcare system. In the management of chronic diseases, for example, long-term savings offset initial infrastructure costs. (Doraiswamy et al., 2021).

#### 8.4.3. Chronic Disease Management

Remote monitoring with wearable technology improves diabetes and hypertension outcomes. Continuous data transfer lower emergency rates and make proactive treatment possible. A study found that patients with heart failure who utilized remote monitoring experienced a 25% reduction in re-admissions (Kitsiou et al., 2017).

### 8.5. Biosensors, Artificial Intelligence and Data science as upcoming trends in diagnostics

Animal diagnostics future lies on biosensors, AI and data science because they play important role enabling more accurate and earlier disease detection in humans and animals. AI algorithms will analyze data to detect anomalies and disease prediction in animal behavior (Li et al., 2020). Data science plays a crucial role in this ecosystem by analyzing massive quantity of heterogenous data (kumar et al., 2023). Biosensors will play important role in advanced diagnostics to monitor animals' health. AI integration and powerful diagnostic platform will be created by data science. Simultaneously, more sensitive, smarter and smaller biosensors will enable point-of-care diagnostics that are suitable and portable for use in resource-limited areas. Specific biomarkers like pathogens, nucleic acids and proteins can be detected by these sensors (Singh et al., 2021).

### 8.6. Ethical considerations and regulatory challenges

Here are some ethical considerations and regulatory challenges associated with advanced diagnostic techniques for disease detection early.

#### Ethical Considerations

**8.6.1. Animal welfare:** Invasive treatments had been used in advanced diagnostic techniques, which make animals feel stressed and uncomfortable. Minimizing injury and ensuring animal care crucial.

**8.6.2. Privacy of data:** Collecting data from the latest diagnostic efforts may include people's genetic information and necessary for farmers and animal owners to have privacy with their data.

**8.6.3. Equity and Access:** Due to limited resources, some farmers and animal caretakers are unable to use modern diagnostic methods. Everyone deserves equal opportunities to the benefit of technology.

**8.6.4. Use of Advanced Diagnosis:** The energy consumption and chemicals used in advanced diagnostics have a greater environment impact than traditional methods. Efforts should make to reduce the harmful effects of these technologies.

### 8.7. Regulatory Challenges

**8.7.1. Validation and Verification:** To confirm their accuracy, sensitivity and specificity, advanced diagnostic methods must be checked. Strong processes and regulations must identify if these advanced systems meet the tough standards.

**8.7.2. Standardization:** There are several types of advanced ways to test patients that use many methods, chemicals and tools. If all experiments are done the same way, then the results from one lab will match those from another.

**8.7.3. Quality Control and Assurance:** Accuracy is maintained by inspecting and monitoring advanced methods.

**8.7.4. Labeling and Proof of Statements:** The use of advanced methods in diagnosis required companies to clearly label their products and prove their claims. Every product on the market must have correct labels and its marketing must include valid evidence from science.

**8.7.5.** Intellectual property and protection from liability may be considered when using newer diagnosis ways. Handling these issues with rules and guidelines helps to motivate developers to bring in innovative new technologies.

### 8.8. Regulatory Frameworks

**8.8.1. The International Organization for Standardization (ISO)** determines standards for standard and molecular diagnostic tests.

**8.8.2 The OIE (World Organization for Animal Health)** sets rules and guidelines to guarantee proper testing for animal disease with a focus on molecular testing.

**8.8.3. The US Department of Agriculture (USDA)** is responsible for checking animal diseases in the US.

**8.8.4. The European Medicines Agency (EMA)** is in-charge of setting rules for testing animals' diseases in the EU.

### Conclusion:

Cross sector collaboration by One Health approach and advanced diagnostic techniques is necessary for early detection of illnesses matters because it significantly impacts environment, welfare and animals' health. Modern approaches and high-technology equipment are being applied by conservationists to take care of endangered animals to detect emerging diseases that could affect the diversity of species. If the signs of avian influenza, bovine tuberculosis and foot-and-mouth disease are noticed before reducing losses, it supports proper feeding and stops losses for farmers. However, in areas where resources are unlimited, hospitals do not use these methods due to their high cost, require expert training and complex results. Cross-collaboration is required among researchers, veterinarians, policy makers and those involved in animal industries to handles these issues and promote advanced diagnostics in many situations. By this collaboration we can improve health outcomes, mitigate the disease impact on economy and human health. Thus, in advanced diagnostic one health framework is necessary to control disease, biodiversity, food security and health.

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# A methodological framework for geospatial analyses of livestock census data – A case study from Punjab, Pakistan

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## ABSTRACT

Background: Livestock census is a vital tool for planning disease control programs and other interventions. Conducting a livestock census is a resource-intensive, technologically demanding, and logistically challenging process. Geographic information systems (GIS) based analyses are required to uncover spatial patterns within census data. The main aim of the study was to develop a methodological framework for geovisualization and geospatial analyses of livestock census data. Methods: As a case study, we used district-level data of cattle and buffalo populations from the livestock census 2006, Punjab, Pakistan. We applied spatial techniques that have been previously used in human population census analyses. Key Findings: Dorling cartogram illustrated disparities in the spatial distribution of the bovine population and density. Those disparities were also evident when k-means clustering was applied on both variables. There was evidence of spatial autocorrelation at the province level but local spatial clusters and outliers were not statistically robust. With automatic zoning procedure (AZP)-a clustering approach, we aggregated the thirty-six districts of Punjab into five spatially contiguous regions based on similarity in cattle and buffalo population densities. Practical Implications: The study demonstrated the use of spatial analyses to support evidence-based planning and policies using livestock census data. Given the limitations of the study, no policy recommendations were made. However, the proposed methodological framework may be adapted when up-to-date and better quality livestock data become available. The spatial analysis techniques used in this study are also applicable to disease-related datasets, making this study relevant to veterinary preventive medicine.

**KEYWORDS**
Livestock census; GIS; Pakistan; spatial cluster; automatic zoning procedure

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## INTRODUCTION

Livestock species have several economic, social, and cultural functions. They play a pivotal role in food security and rural livelihood particularly in low- and middle-income countries. In these countries, millions of families along the value chain are directly or indirectly dependent on livestock for their livelihood. The livestock sector contributes to the national gross domestic product, value added in agriculture, and export earnings (Bettencourt et al., 2015). In the coming decades, the livestock sector is projected to grow rapidly in developing countries due to rising demand for animal-derived products (Du et al., 2025). Livestock production also presents notable challenges. Greenhouse gas emissions from livestock are contributing to climate change. Livestock may also place pressure on natural resources, for example, through overgrazing. They play a role in the emergence of zoonotic diseases, spread of food-borne diseases and the development of antimicrobial resistance (Bava et al., 2024; Gilbert et al., 2018; Robinson et al., 2014). For data-driven planning and policy making, regular livestock censuses are essential, as they provide quality data on available livestock resources and help identify trends in populations. (Mapitse & Letshwenyo, 2011) carried out a questionnaire-based study highlighting the importance, design and challenges of conducting livestock census in African countries. The researchers emphasized the need for livestock censuses to support disease surveillance and control, as well as other objectives including resource allocation, enhancing rural livelihood, breed improvement, and strengthening the role of women in livestock production. The census data are also important for the effective design and implementation of animal identification and traceability systems. Moreover, the World Organization for Animal Health (WOAH, previously called OIE) encourages member countries to share animal population data in their annual reports. From the perspective of veterinary preventive medicine, livestock census data are highly relevant, as the distribution, diversity and density of various species of livestock influence the risk of zoonotic and food-borne diseases. Census data provide the necessary denominators for epidemiological analyses. Moreover, livestock density is a risk factor for several diseases, and is used in spatial multi-criteria decision analyses. Internationally, efforts have been made to create gridded maps of livestock densities. However, the utility of these maps becomes limited when input census data are outdated and/or of doubtful quality (Serra et al., 2020).

Geovisualization and geospatial analyses can reveal spatial patterns in census data that remain hidden in summary tables and graphs. They can also help capture disparities in the distribution of livestock population. This spatial insight into the data is critical for policy-making, resource allocation, and targeted interventions. While spatial analyses have been extensively applied to human population data (Dykes & Unwin, 1998; Walker, 2023), their use in livestock census data remains comparatively limited, yet equally important. The main aim of this chapter is to provide a methodological framework for spatial analyses of livestock data using techniques that have been proven beneficial in human population studies. A secondary objective is to familiarize veterinary preventive medicine practitioners with spatial analysis techniques that can be applied to census data as well as disease related datasets.

## Methodological Framework

### Data sources and Preprocessing

We used district-level data from the Punjab livestock census 2006 (Pakistan Bureau of Statistics, 2006). The data were joined with the shapefile of the districts of Punjab, Pakistan. For each district, cattle and buffalo densities (number per km²) were calculated using the district area. We also calculated the total bovine population (cattle + buffalo) for each district (in millions). The data management and analyses were performed in RStudio version 2025.5.0.496, mainly with the rgeoda package version 0.1.0. K-means analysis was done in GeoDa version 1.22. Readers seeking more details are referred to (Anselin, 2024a, 2024b).

### Mapping Spatial Distribution of Bovine population and Density using Dorling Cartogram

A Dorling cartogram is a type of map in which each spatial unit is represented as a circle sized by an attribute value and placed to preserve approximate location and neighbor relationships. The circles are drawn around the centroids of spatial units. This transformation improves visual clarity. It is a powerful visualization tool to facilitate resource allocation, such as estimating the demand for vaccines and the provision of other support services while planning a vaccination campaign. We customized the cartogram so that circle size represented the bovine population, and the color tone represented density. This dual representation allowed quick visual assessment of resource needs. If population density in a district was relatively low, it suggested the need for more logistical support due to small-scale farming and a dispersed population.

### K-means Clustering of Bovine Population and Density

The k-means is a popular unsupervised machine learning clustering algorithm. It aims to partition data into a specified number (k) of clusters. It starts with k initial seeds, whose values are called centroids. Each data point is assigned to one of the seeds based on similarity (usually Euclidean distance). The initial clusters are refined, which includes recalculation of centroids based on the mean of data points in each cluster, and reassignment of data points based on distances from new centroids, until convergence is achieved. The k-means clustering was implemented on the bovine population and density separately. The optimum number of clusters was determined based on the ratio of between to total sum of squares (where a higher ratio, closer to 1, indicates better separation between clusters). To maintain a balance between this ratio and interpretability, the number of clusters was set at six. The analysis was conducted in GeoDa version 1.22, which selects initial seeds using the k-means++ algorithm. The algorithm iteratively ensures that the initial clusters are well spread out based on Euclidean distance.

### Analysis of Spatial Autocorrelation

Spatial autocorrelation refers to the tendency of similar values to occur near one another in geographic space. A common measure of spatial autocorrelation is the Moran's I coefficient, which resembles the correlation coefficient, although it is computationally different. The Moran's I statistic ranges from -1 to +1. Global spatial autocorrelation gives evidence for the presence of clustering at the provincial level, whereas Local Moran's I explores where spatial clusters and outliers are located. These techniques require defining a spatial weight matrix that includes neighborhood data. For this, we used Queen contiguity, in which any two districts are considered neighbors if they share a border or a corner. We tested global autocorrelation, for both population and density. Local Moran's I was applied to population density only, because a moderate evidence of clustering at the provincial level was detected. A false discovery rate (FDR) correction was applied to ensure robustness of the clusters and outliers. The Local Moran's I divided the districts into four classes. High-high cluster means the district had high population density,and the average population density of its neighboring districts was significantly higher compared to the provincial average. Low-low cluster means the district had low population density, and the average population density of its neighboring districts was significantly lower compared to the provincial average. High-Low means the district had a high value, but the average of its neighboring districts was significantly lower compared to the provincial average. Low-high means the district had a low value, but the average of its neighboring districts was significantly higher compared to the provincial average.

### Spatial Clustering Using Automatic Zoning Procedure (AZP)

The Automatic zoning procedure (AZP) is a spatial clustering method that groups spatial units, such as districts, into zones also called regions. The spatial units in each zone are homogeneous (similar in data values) as well as contiguous (geographically connected). AZP is a heuristic (shortcut) regionalization technique designed to provide approximate solutions to NP-hard problems. The AZP begins with randomly selected seeds, which grow by adding neighboring spatial units with similar values. The initial zones are then iteratively refined to increase within-cluster homogeneity while preserving spatial contiguity. The refinement involves swapping-that is moving a neighboring spatial unit from zone B (donor) to zone A (recipient) if the move improves homogeneity of zone A without breaking contiguity of zone B. Tabu search is an enhanced version of AZP in which successful swaps are recorded in a Tabu list, and back-swapping is blocked for a specified number of runs, known as the Tabu length. The automatic regionalization with Initial seed location (ARiSeL) algorithm improves the initial cluster solution by selecting "smart" seeds using k-means++ logic. To avoid sub-optimal results, Tabu search can also be configured to allow non-improving swaps, helping the algorithm to escape local traps. We implemented AZP with Tabu search to cluster the thirty-six districts of Punjab into twelve zones, based separately on similarities in cattle and buffalo densities. A customized R function was developed to explore different settings for the number of zones (5 to 12, in increments of 1), Tabu length (5 to 50, in increments of 5), and number of construction re-runs, i.e., *inits* (5 to 40, in increments of 5), selecting the combination that maximized the ratio of within-cluster sum of squares to total sum of squares. The final AZP settings consisted of twelve regions, a first-order queen contiguity matrix, and a Tabu length of 5 with 5 inits for cattle density and 10 inits for buffalo density.

### Results

This study presents a framework for geovisualization and geospatial analyses of livestock census data. As an example, we used a subset of data from the Punjab livestock census held in year 2006. Selected geospatial techniques were implemented to explore spatial patterns of the bovine population and density across Punjab, Pakistan. The analyses generated valuable insights and posed challenges, which are discussed in the limitations section. Below, we describe the analysis outputs along with their policy relevance.

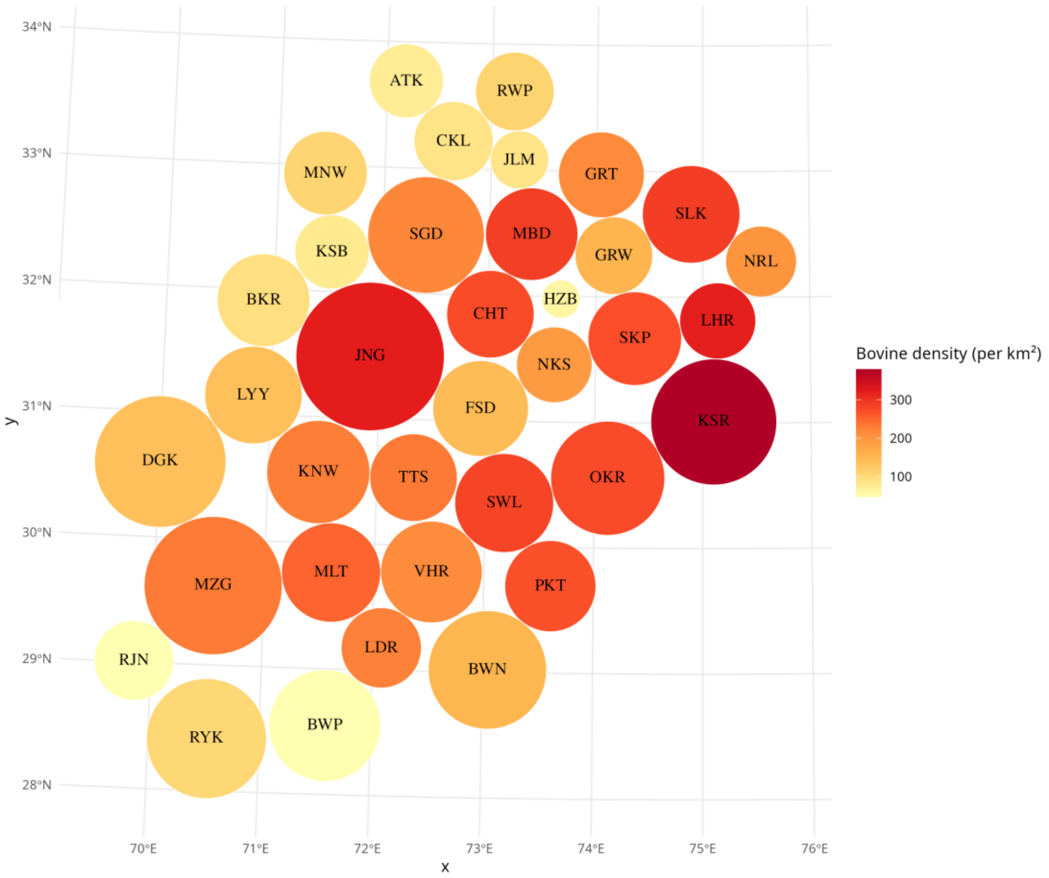

**Fig.1.** Dorling cartogram of bovine population in millions in districts of Punjab, Pakistan. Circle sizes represent population, while circle colors indicate bovine density using a sequential yellow–orange–red scale. Districts are labeled with three-letter abbreviations.

Fig. 1 illustrates the Dorling cartogram where circle size and color represent population and density, respectively. Each district is represented by a circle, whose size is scaled by its population, whereas the color tone indicates its population density. Considering both variables together, one may notice four categories of districts: i) high population and high density, ii) low population and low density, iii) high population but low density (sparse distribution), and iv) low population but high density. For resource allocation, such as planning a mass vaccination campaign, the cartogram facilitates decision-making. One may quickly assess, which districts need more doses based on population size, and which need more logistical support based on density. The cartogram effectively addresses the invisibility of low-density areas in conventional maps.

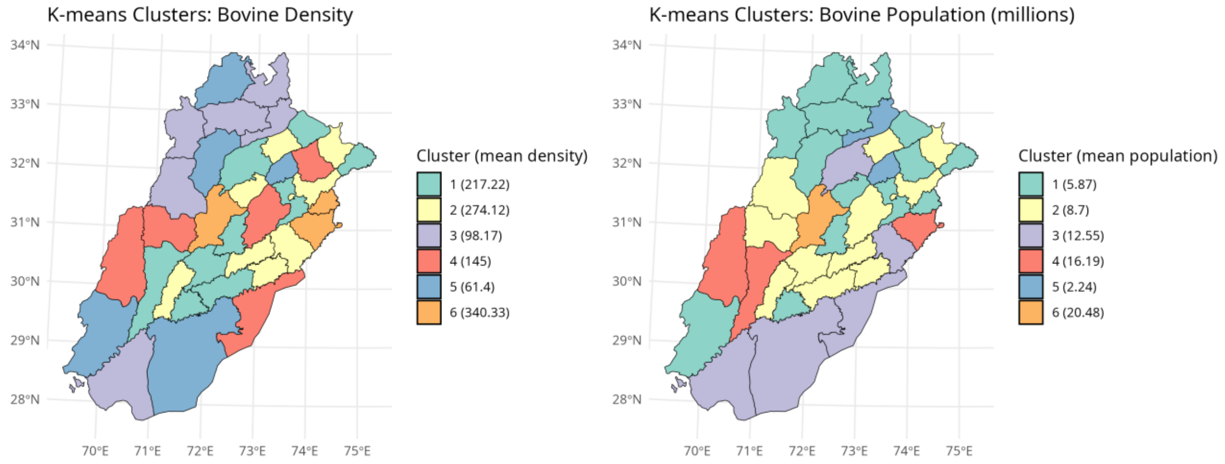

**Fig. 2.** K-means clusters of bovine density (left) and bovine population (right) across various districts of Punjab, Pakistan. Each cluster is represented by a distinct color, which does not indicate magnitude or rank. The cluster centers, representing the average of each cluster, are shown in parentheses in the legend.

Fig. 2 presents the results of K-means clustering. For both variables, the ratio of within-cluster sum of squares to between-cluster sum of squares (WSS/BSS) exceeded 96%, indicating strong separation between clusters. The cluster centers, represented by the mean values of districts in each cluster, reveal marked disparities in the spatial distribution of population and density. Additionally, the number of districts within each cluster was uneven, reflecting the heterogeneous distribution of these variables across the province. Within-cluster sum of squares values varied across clusters, indicating that, although districts belong to the same cluster, their values show some variation.

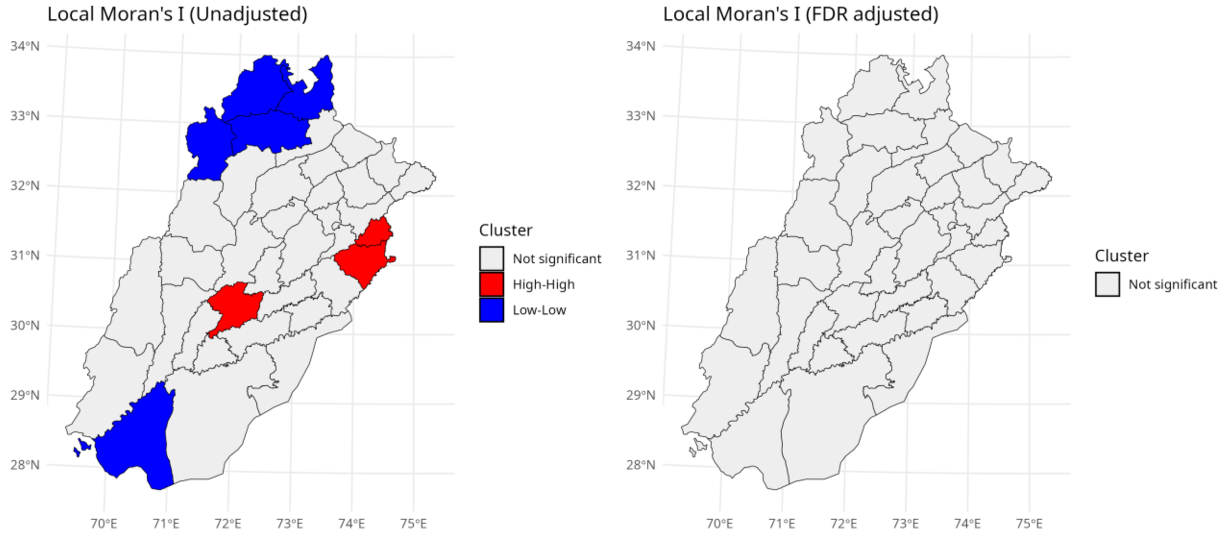

**Fig. 3.** Local Moran's I cluster and outlier maps of bovine population density across districts of Punjab, Pakistan, without false discovery rate (FDR) correction (left) and with FDR correction (right).

Fig.3 illustrates the spatial clustering of bovine population across Punjab districts using Local Moran's I statistic. The global Moran's I value of 0.31 indicates a moderate and statistically significant overall spatial autocorrelation, reflecting some clustering in bovine distribution. The left map presents the unadjusted Local Moran's I results, highlighting statistically significant clusters of high bovine density (High-High, shown in red) and low bovine density (Low-Low, shown in blue). However, after applying false discovery rate (FDR) correction to account for multiple testing, these local clusters lost statistical significance, as can be seen in the map on the right side. The global Moran's I confirms the presence of spatial clustering overall, prompting further investigation into cluster locations. The lack of robustness in local clusters following FDR adjustment is discussed, with potential reasons for these findings.

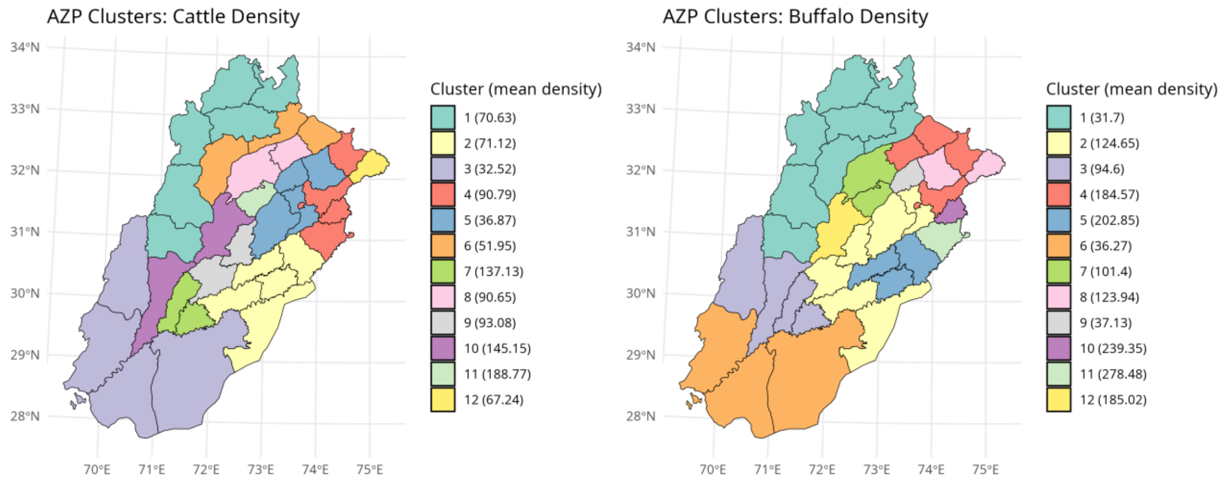

**Fig. 4.** AZP clusters of cattle density (left) and buffalo density (right) in Punjab, Pakistan. Distinct colors denote clusters, with centers (averages) in parentheses. Both variables achieved a within-cluster sum of squares (WSS) to total sum of squares (TSS) ratio of ~0.96, which is close to 1 and indicates good fit.

AZP with Tabu search clustering was applied separately to cattle and buffalo density data for the thirty-six districts of Punjab (Fig. 4). A twelve-region solution was selected. The ratio of within-cluster sum of squares (WSS) to total sum of squares (TSS) was approximately 0.96 for both variables (0.959 for cattle density, 0.958 for buffalo density), indicating that about 96% of the variation was explained by the clusters. The ratio closer to 1 is indication goodness-of-fit. For cattle density, the WSS ranged from 0.00 to 0.52, while for buffalo density it ranged from 0.00 to 0.50, reflecting high internal homogeneity of the clusters. Spatial validation metrics such as balance, compactness, connectedness and shape were not considered here, as they lie beyond the scope of this chapter. While the present analysis focused on cattle and buffalo densities, the AZP and other cluster analysis can be extended to other livestock species or attributes to support disease control, breeding programs, and resource allocation.

## Discussion

The study demonstrates the importance of spatial analysis to uncover geographic patterns in livestock census data that remain obscured in tabular summaries, graphs, and even traditional maps. We used multiple techniques that enabled comprehensive exploration. These geographic techniques were selected based on literature supporting their successful implementation in human census data analysis (Laaribi & Peters, 2019; Walker, 2023). When applied to updated and high-quality data, these techniques may inform polices for livestock health and extension services. The Dorling cartogram enabled us to understand the disparities in bovine population. It was possible to identify districts that have a sparse population and may therefore need additional resources when planning veterinary services .

We observed spatial variability in population as well as density. The possible reasons for this disparity could be agro-climatic conditions, agroecological zones, peri-urban and cooperative farming near urban areas, availability of land as a source of fodder and forage, irrigation system, dominant type of livestock husbandry and culture, demography, socioeconomic conditions, and shifting patterns of livelihood. (Pradhanang et al., 2015). Previously reported spatial determinants used for mapping cattle densities (Du et al., 2025; Robinson et al., 2014) may also help explain the observed variation in bovine population and density in our study.

For exploratory analysis, spatial autocorrelation at the province level was detected through the Moran's I coefficient, which is a formal technique to generate evidence of clustering of districts with similar values. It is followed by, or in some cases run in parallel with, Local Moran's I to find the location of spatial clusters and outliers. When applied to our data, we found that local clusters and outliers became non-significant when a false discovery correction was applied to account for multiple comparisons. It indicates that local patterns were weak, inconsistent, or spurious. The local patterns whether detected or not also depend on the resolution of the data. To explain it further, district-level data may obscure local patterns, and in such cases, sub-district level data may be preferred. This is also called the modifiable area unit problem. Also, a mix of high and low values in surrounding districts may hide the local patterns if any. In addition, queen and rook contiguity spatial weights have the limitation that districts at the borders of a province have fewer neighbors, a phenomenon known as the edge effect. (Malik et al., 2016) used livestock census data for Punjab, Pakistan, and calculated the Simpson diversity index and applied Bray-Curtis cluster analysis to identify similarities in livestock composition. We implemented AZP, which is a spatially constrained clustering method that creates regions. The regionalization may have several purposes, such as service planning (Aydin et al., 2021; Beconytė et al., 2023; Cockings, 2013; Grady & Enander, 2009). The AZP method creates regions from spatial units by incorporating both attribute values and spatial location similarities, thereby facilitating the decision-making process through coherent regionalization rather than scattered clusters. This study demonstrates its utility for livestock census data, with practical implications for enhanced planning and implementation of livestock services.

Our study also has several limitations. The data used in this study are outdated and might have quality issues (Pica-Ciamarra et al., 2014; Sadiq, 2018). Previous authors have raised concerns about the quality of census data and the reliability of projected estimates, which often do not take into account vital statistics such as crude birth, fertility, and death rates. This concern is further heightened given the increased incidence of bovine infertility, illegal slaughter of female animals and the mass sacrifice of livestock during the annual Eid-ul-Adha festival (Khan et al., 2013). Another possible source of bias is that density estimates may become less reliable if areas unsuitable for livestock, such as those occupied by rivers, protected areas, and urban centers are not excluded. The AZP results are sensitive to the initial seed selection and parameter settings. Moreover, it gives only a good local optimal solution (Anselin, 2024c). For AZP, we determined the number of regions based on the ratio of within-cluster sum of squares to total sum of squares, without considering spatial characteristics of the created regions, such as compactness. Therefore, we remain uncertain about the appropriateness of the 12-region solution. For AZP, goodness-of-fit was appropriate, but within-cluster homogeneity was relatively higher for a few clusters. The validity of our maps may be evaluated considering ground realities. Panel evaluation is another suggested method for assessing the appropriateness of output maps for planning and policy-making. Integrating spatial analysis with spatial covariates would further strengthen inference. One difficulty, we encountered was that the district shapefile was outdated, as some tehsils were upgraded to district status over time. Due to this reason, data for the tribal areas of Dera Ghazi Khan, Rajanpur, and Cholistan had to be excluded from analyses. The limitations of the study, data, and methods have been explicitly acknowledged, which makes them less relevant when considering the objectives of the study.

In conclusion, this study provided a practical approach to uncover spatial variations and patterns in livestock census data. For demonstration purpose, we used data about cattle and buffalo populations. The techniques may also be used for other species and disease-related data. Spatial exploration and analyses of livestock data together with other data such as human and other resources can support evidence-based decision-making in veterinary preventive medicine, guiding targeted interventions/extension services, resource allocation, and policy formulation, unless up-to-date and better-quality livestock data become available. The 7th national agriculture census in Pakistan has been conducted and reported (Government of Pakistan, Finance Division, 2025; Government of Pakistan, Ministry of Planning Development & Special Initiatives, Islamabad; Pakistan Bureau of Statistics, 2025). It has been reported to use international best practices and the latest technology. The methodological framework presented in this study may be applied to similar census datasets. It is also recommended to explore additional clustering techniques preferably with better resolution data such as sub-district level data.

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# Zoonoses and Socio-economic impact

13

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## ABSTRACT

Zoonotic diseases that are naturally spread from animals to humans. Pathogenic organisms (prions, viruses, fungi, parasites, and bacteria) are responsible for zoonoses. Transmission of this infection through direct contact with sick humans or animals, ingestion of contaminated objects exposure during processing and preparation. These pathogenic substances that are widely present everywhere in world. The distribution of zoonotic diseases that are significantly influenced by various factors including climate change, ecological changes, socioeconomic factors, intensive livestock farming practices, inadequate monitoring systems and disease surveillance, socioeconomic and public health impacts, and natural factors. Vector-borne diseases are susceptible to shifting environmental conditions because of variation in temperature, humidity, and vector demographics. The rise of zoonotic infectious poses a serious threat to human and animal health. Understanding the factors that contribute to the onset of these diseases is necessary for the implementation of effective control and prevention measures. It is necessary to comprehend the aspects in order to prevent zoonotic disease emergence, re-emergence, transmission, and spread in cattle and human populations and to modify control strategies to reduce the high risk.

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## 1. INTRODUCTION

The development and spread of some infectious diseases are significantly influenced by humans, environmental factors and animals (Thompson, 1992). Animals are the source of the majority of human infectious diseases. Over 60% of newly discovered human infections are zoonotic, according to the 2010 publication "Asia Pacific strategy for emerging diseases" (WHO, 2010). Over 70% of these viruses originate from wildlife. In recent decades, animal-based foods have been directly linked to newly discovered human diseases (Slingenbergh, 2013). The term "zoonoses" derives from the Greek words "zoon," which means animal, and "nosos," which means sick. A zoonosis is any illness or infection that can spontaneously spread from vertebrate animals to humans or from humans to animals, according to the World Health Organization (WHO, 2020). Zoonotic pathogens account for 61% of human pathogens (Taylor et al., 2001). Zoonotic disease incidence and prevalence are a significant global public health issue, according to statistics (Sanyaolu, 1992). Estimates indicate that between 58% and 61% of all infectious diseases that affect people worldwide are caused by zoonoses (Woolhouse et al., 2005*).* Zoonoses are more common and prevalent in developing nations, which is explained by a lack of proper infrastructure, control mechanisms, and knowledge about their importance and dispersion. The method of control, clinical symptoms, social factors, environmental variables, behavioral factors, the socio-economic impact of such diseases, and the mechanism of transmission are some of the elements that increase the burden of zoonotic diseases in the United States (Leslie, 1992; Smolinski, 2003). According to WHO, One Health approach in which we study public health related issues in animals, human and their surrounding environment (Chakraborty et al., 2021). The One Health approach to zoonoses frame work are consist of five pillars such as food safety, security, water contamination, anti-microbial resistance and bond between human and animals. Major contribution of One Health in protection of humans, animals, environment and surveillance etc (Saldanha et al., 2020)

### 1.1 Major Zoonotic Pandemics in Modern History

In history, SARS is not first zoonoses that caused a pandemic more than 767 million cases and 7 million deaths confirmed (WHO Coronavirus (COVID-19)). First zoonotic disease was plague in Athens that killed 1 lac human (Littman, 2009). SARS

(2002-2004) outbreak lasted for two years. Most viral strain SARS-CoV-1 that are originally from Guangdong, province of south China. (Wang and Eaton, 2007) reported this type of corona virus transmit from bats to humans through civets (intermediate hosts). Emerging Zoonoses in the 21st Century Recent outbreaks highlight ongoing risks: "COVID-19" (2019–present): "likely" SARS-CoV-2 of bat origin, with more than 7 million deaths (WHO, 2023). Second strain SARS-CoV-2 was known as Wuhan virus or COVID -19 that are the largest pandemics of history (WHO, 2023).

Rasing of camels in Iran is significant direct contact between camels and farmers; camels used for milk and meat production and their smuggling and importation in neighbouring countries like Pakistan and UAE also a source of zoonotic diseases. (Pour Reza, 2013) reported that campylobacteriosis endemic disease in Iran that was present in sheep, chicken and camel comes from different regions especially from central Iran.

## 2. Classification of Zoonoses

Numerous microorganisms can cause zoonotic illnesses. Zoonoses are categorized according to their etiology: bacterial zoonoses (like anthrax, salmonellosis, tuberculosis, brucellosis); viral zoonoses (like herpes virus, rabies, viral hepatitis, COVID-19); parasitic zoonoses (toxoplzmosis, Giardiasis, Cytosporiodiosis, Malaria); Fungal zoonoses (Aspergillosis, Histoplasmosis, Cryptococvosis, Blastomycosis) (Batt, C. A., 2014). The visual representation of the microorganisms causing zoonotic illness is shown in fig 1.

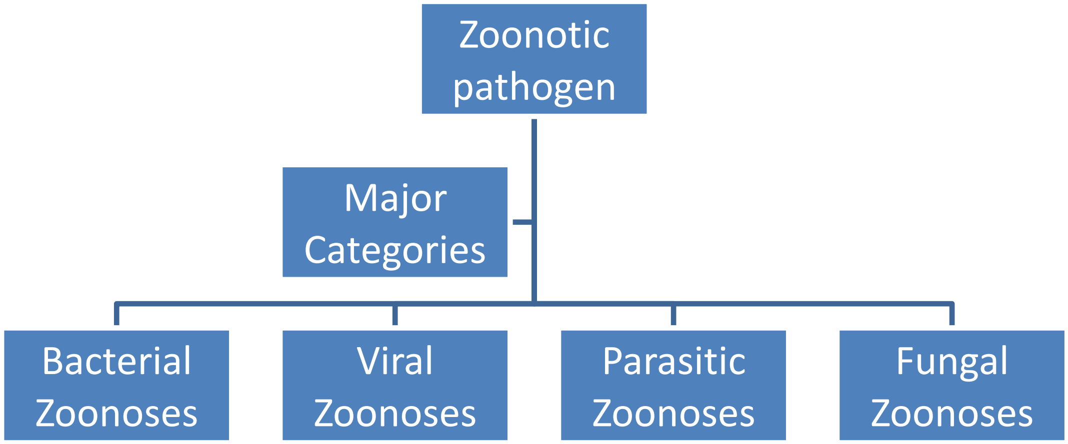

**Fig. 1.** Microorganisms causing zoonotic illnesses

### Bacterial Zoonoses:

This type of zoonoses can be occur by bacteria. Bacteria are single celled organisms that release toxins in host organisms. All bacterial zoonoses have different incubation period, mode of transmission and host organisms (Table 1).

**Table 1:** Bacterial Zoonoses their transmission mode, affected organism and symptoms, host organism, specie, genus, incubation period and treatment.

| Disease | Genus species | Host organisms | Mode of transmission | Symptoms and organ effected | Treatment | Incubation period |
|---|---|---|---|---|---|---|

| | | | | | | |
|---|---|---|---|---|---|---|
| Anthrax | *Baccillus anthrancis* | Cattle, pig, sheep,Mink, Horse, bison | Inhalation of anthrax spores, contact with infected animals faeces. | Cough, fever,headaches, skin,chest pain and GIT. | Doxycycline, Amoxycillin, Ciproflloxacin | 1-7 days after exposure |
| Brucellosis | *Brucella( B.melitensis, B.abortus, B.suis, B. canis)* | Goat, dog, sheep,swine, | Contact of infected animal by mucous membrane or skin, tissue, body fluid include blood contact. | Fever, joint and back pain,weight loss.spleen, heart, gall bladder cause abscess and lesion | Tetracycline,streptomycin, sulphonamides mostly used combination of antibiotics. | 1-15 weeks |
| Tuberculosis | *Mycobacterium tuberculosis* | Human, rodents, cattle and non-human primates | Inhalation of aerosol droplet, bites,contaminated equipment. | Fever, fatigue, bone marrow, chronic kidney disease, lung and respiratory problem | Streptomycin, Isonazide,Ethambutol, Rifampin | 2-5 weeks |
| Salmonellosis | *Salmonella enterica,Salmonella bongori* | Rodents, dogs, csts, monkeys , reptile, pigs, chicken, fish. | Transfer by direct or indirect contact such as unpasteruized milk,raw eggs etc. May be possible by transfer from human to human | Headaches,high fever, spleen enlargement and enteritis. | Ampicillin, Chloramphenicol, Neomycin. | 6 hours-3days |

**Viral Zoonoses:**

This type of zoonoses in which viruses have a small piece of genetic information and it’s also used host machinery and produce multiple copies of themselves (Table 2).

**Table 2.** Viral Zoonoses their incubation period, affected organ and symptoms, host organism, specie, genus, transmission mode and treatment.

| **Disease** | **Genus’s species** | **Host organisms** | **Mode of transmission** | **Symptoms and organ effected** | **Treatment** | **Incubation period** |
|---|---|---|---|---|---|---|
| Herpes virus | Herpes virus Type1 cause blister, cold. Type 2 cause genital herpes. | Human and non-human primates | Latent infection in host and frequently shed without overt lesion. | Vesculiar lesion. Lips, mouth,eyes,skin etc | Valcyclovir arrest the virus but does not eliminate it from host. | 5 days -1 month |

| | | | | | | |
|---|---|---|---|---|---|---|
| Rabies | Rhabdoviridae.<br>Genus Lyssavirus | Cats, horses, cattles, foxes,raccoons. Natural reserviors such as bats. | Contact with animals bites, saliva or tissue. | Nervousness, convulsion, dilation of pupils, headaches. Nervous system effected. | Anti-rabies vaccine. | 3-8weeks |
| Viral hepatitis | Hepatitis A, B, C, D, E. | Human and non-human primates (monkey, celebs, ape, chimpanzee.) | Direct contact with infected equipment or animals. | Vomiting, nausea, jaundice, mild fever. Liver damage. | Hepatitis A,B,C vaccines are availables | 3-6 weeks |
| COVID | Alpha corona virus species alpha corona virus 1( canine coronavirus, Feline corona virus) | Natural reserviors such as bats | Transfer by direct or indirect contact Transfer from human to human,objects and animals. | Fever, chills, shortness of breath, sore throat, change of taste and smell. Lung, liver, kidneys and brain. | Novarax COVID-19 vaccine, Pfizer vaccine, SARS vaccine. | About 6 days |

### Parasitic Zoonoses:

This type of zoonoses in which protozoa (single-celled organisms), ectoparasites (lice and mites) and parasitic worms also responsible for these diseases (Table 3).

**Table 3:** Parasitic zoonosis their genus incubation period, host organism affected organ and symptoms, specie, transmission mode and treatment.

| **Diseases** | **Genus's species** | **Host organism** | **Mode of transmission** | **Symptoms and organ affected** | **Treatment** | **Incubation period** |
|---|---|---|---|---|---|---|
| Toxoplasmosis | *Toxoplasma gondii* | Host specificity lack. Carnivores, birds, undulates, rodents and primates | By taking under cooked meat, water or food,oocytes ingestion in milk, contact with soil containg contaminated cat feces | Sore throat,pneumonitis, fever,encephalitis and mayocarditis, skeletal muscles, eyes and brain | Sulfonomide pyrimethamine | 10 to 23 days |
| Giardiasis | *Giardia lamblia* | Monkeys and dogs | By contaiminated water drinking, by eating contaimiated food, person to person contact | Asymptomatic to nausea, severe diarrhea, high fever, anorexia and fatigue, small intestine | Furazolidone,hydrochloride,tinidazole,quinacrine,metronidazole and albendazole | 3 to 25 days |
| Cytosporiodiosis | *Cryptosporidium; C.parvum, C. hominis* | Cattle, birds, reptiles, fishes, human | Fecal-oral route,direct contact with infected peoples and animals, by | Watery diarrhea,stomach cramps,vomoting, fever, nausea, small intestine | Healthy immune system person recover on their own within a month, | 1 to 12 days |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | drinkind containinated water | | medication like nitazoxanide is used | |
| Malaria | *Plasmodium; P.vivax, P.ovale, P.malariae* | Anopheles mosquito | Mosquito bite | Headache, chill, muscle pain, bloody stools, juandice,fever, coma, sweating, convulsions, blood, spleen and liver | Chloroquine,malorone,primaquine | 10 days to 4 weeks |

### Fungal Zoonoses:

This is a fungal infection that can be transferred from animals to humans. Fungal spores play important role in this zoonoses (Table 4).

**Table 4:** Fungal diseases their genus incubation period, organ and symptoms, host organism affected specie, transmission mode and treatment.

| **Diseases** | **Genus species** | **Host organism** | **Mode of transmission** | **Symptoms and organ affected** | **Treatment** | **Incubation period** |
|---|---|---|---|---|---|---|
| Aspergillosis | *Aspergillus* spp. | Domestic animals and birds | By inhailing Aspergillus spores | Respiratory problems | Antifungal medication | Few days to several months |
| Histoplasmosis | var. *capsulatum Histoplasma capsulatum* | Dogs, rats Cats, dogs, rabbits, and | Inhalation of fungal spores | Often asymptomatic, fever, chest pain,hematologic disturbances productive weight loss, | Amphotericin B or itraconazole | 3 to 17 days |
| Cryptococcosis | *Cryptococcus neoformis* | Cats,goats,birds ,dogs, cattle,sheep horses, and wild animals | By fungal spores inhalation | Meningitis,headache fever, ,neck stiffness, malaise, nausea, photophobia, cough and vomiting | Fluconazole, flucytosine | Between 2 and 13 months |
| Blastomycosis | *Blastomyces dermatitidis* | Mostly cat and dogs common in ferrets,horses, deer, wolves, African lions, bottle-nosed dolphins, and sea lions | Inhalation of airborne fungal spores | Fever,subacute meningitis, gait Abnormalities, , pneumonia, verrucous skin lesions and seizures | Antifungal medication | 3 weeks to 3 months |

## 3. Mode of Transmission

Like the diseases themselves, zoonotic disease transmission can vary greatly (Rahman et al., 2020). Even if organisms are spread through their usual methods, the majority can be obtained through unconventional means, making it more difficult to defend against illnesses. The transmission mechanisms are numerous and ubiquitous to the majority of activities that humans must engage in in order to exist (Daszak et al., 2000). These activities include drinking contaminated water or by using contaminated water to wash food. The "zoonotic pool" of organisms that could potentially harm humans is rapidly expanding, as are their modes of transmission, as a result of our growing presence on the planet and our increasing interactions with animals (Fig. 02) (Daszak et al., 2000).

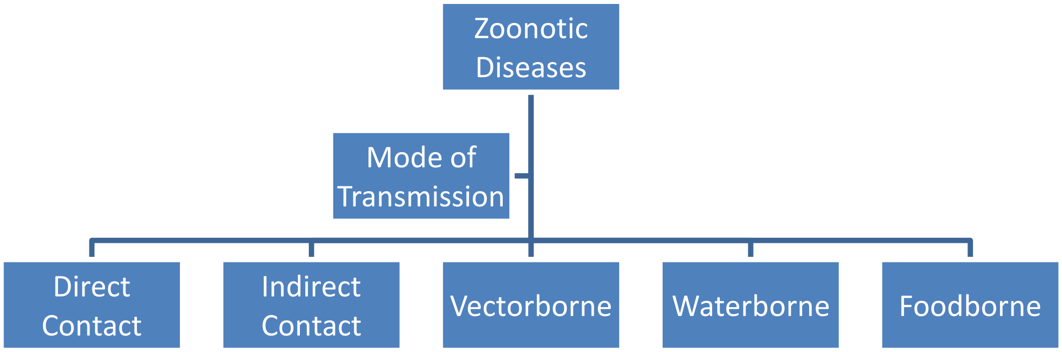

**Fig. 2.** Different mode of transmission in zoonotic disease

### 3.1 Direct Contact:

Exposure to infected animal bodily fluids (such as saliva or blood, for example) through direct contact.

### 3.2 Indirect contact:

Indirect Contact – Contact with contaminated surfaces or environments (e.g., leptospirosis).

### 3.3 Waterborne

Water is one of the global zoonotic disease sources that is growing at the fastest rate. Water used for sanitation or drinking that is tainted might spread infection. Due to our dependence on water, humans are particularly susceptible to watery zoonotic infections. Paratyphoid fever and typhoid and are frequently spread through the consumption of food or water contaminated with the excrement of an acutely ill person (WHO, 2001; Newton, 2015).

### 3.4 Food borne

Unsanitary conditions and improper cooking techniques could lead to contamination because some zoonotic diseases can only be transmitted through food. Foodborne illness is one of the most common causes of acute illness (Maddox-Hyttel et al., 2006). Microorganisms like Clostridium, Staphylococcus, and Salmonella are the most common culprits in food poisoning. When salmonella is still alive in reservoirs like eggs, livestock, or poultry, it typically infects food. However, inadequate food preparation or unhygienic slaughterhouses may spread it (Rose, 1999). When fish or shellfish are not consumed promptly and decomposition is permitted, toxins such ciguatera can be produced, which can lead to fish poisoning) (Control of communicable diseases manual (2000).

### 3.5 Vector borne

A vector is another significant way that zoonotic infections are spread. Because they are so prevalent and require blood to survive, mosquitoes are capable of easily transmitting diseases; frequently, individuals are unaware that they have been bitten until an illness strikes. Through vector transfer, mites, fleas, and ticks are all significant contributors to zoonotic illnesses. Some of the most common diseases spread by vectors include ehlichia, West Nile virus, tularemia, and plague (Petersen et al., 2016). Viral hemorrhagic fevers caused by yellow fever, dengue, and Rift Valley frequently result in sequelae (Cassadou et al., 2014), including bruising, bleeding, rashes, and malaise. While some zoonotic illnesses are not spread from person to person, they can nonetheless spread from person to person and produce epidemics in human populations (Wood et al., 2016). Various mode that are responsible for the transmission of diseases to other organisms through direct or indirect contact, waterborne, food-borne and vector-borne mode of transmission. Direct contact most common route of infection in organisms (Petersen et al., 2016).

## 4. Factors responsible for zoonotic diseases emergence:

The development of zoonotic diseases in human and cattle populations can be influenced by a variety of factors, broadly categorized as biological, ecological, and socioeconomic factors. The interaction of human, animal, and environmental factors that result in the transmission and spread of infectious zoonotic diseases (Fong, 2017).

### 4.1 Ecological changes:

Humans have caused changes to ecosystems by damaging forests, growing farms and building more cities (Fong, 2017). Human, cattle and wildlife populations became fragmented, changed where they lived and altered their behavior as a result of this process which also helped zoonotic diseases thrive more easily. According to Garcia Pena et al., (2016) these adaptations facilitated infections spreading between various species and drew them closer to one another.

### 4.2 Climate changes:

Climate change has affected the spread of diseases carried by flies, ticks and mosquitoes as well as their biological and mechanical brothers. Because of this, the routines and spread of population groups of people and animals changed. This boosted the risk of spreading diseases, according to Barry et al., 2018). Higher temperatures make the living conditions of disease-spreading insects and animals better. With rising temperatures, the spread of zoonotic pathogens is changed and mosquitoes are more likely to transmit diseases such as dengue and malaria (Imran et al., 2023). Disease outbreaks happen more rapidly and with more power at higher temperatures, since it takes a shorter time for the disease to incubate and spread. That might lead to more disease spreading and the possibility of bigger outbreaks. Changes in weather can impact how hosts and infection's function and act. The alteration in how the host and pathogen interact can produce changes in the occurrence, severity and patterns of spreading diseases (Petersen et al., 2016).

### 4.3 Socioeconomic factors:

Social problems like poverty, not being able to afford healthcare and poor veterinary services can lead to more diseases and their spread. Following some traditions such as preparing animal products or using them in medicine, might raise the risk of acquiring zoonotic infections. Bad hygiene and insufficient care for sanitation allow zoonotic diseases to quickly spread and linger among humans and animals. If no actions are taken, poverty, hunger and not enough access to healthcare facilities will make both the onset and spread of zoonotic diseases more problematic (Cassadou et al., 2014; Wood et al., 2016).

### 4.4 Intensive livestock farming practices:

Basically, by having large amounts of livestock concentrated in one place and planting only one species of crop, infectious diseases spread more quickly among animals. Lots of stress for the animals and thin biosecurity measures are found in these systems and these factors can have bad effects on their immune systems, efficiency and likelihood of catching diseases. According to (Cascio et al., 2011) some animal breeds with particular productivity characteristics are frequently preferred in intensive farming and frequently squeeze into congested spaces in intensive husbandry. These factors, such as overcrowding, stress, inadequate biosafety and an unsanitary environment, impair an animal's immune system and make them more susceptible to illness (320 ZOONOSIS). Furthermore, animals may be exposed to a variety of poisons found in plant and animal wastes when they are fed them. In addition to introducing new microbial pathogens to the human and animal community, this could transmit zoonotic infections (Craddock and Hinchliffe, 2015).

### 4.5 Inadequate diseases surveillance and monitoring system:

Early and precise pathogen detection is necessary to prevent outbreaks from spreading to a large area. Poor healthcare infrastructure, a lack of qualified staff, and a lack of testing facilities can cause zoonotic infections to be undetected or receive the incorrect diagnosis. Effective control efforts are also frequently impeded by the absence of accurate data on illness prevalence and distribution (Cascio et al., 2011). In livestock populations, pathogens cause zoonotic diseases that spread silently throughout animal populations without showing symptoms yet they can still infect people (Alvi et al., 2023b). Infectious diseases modeling tools like Global Livestock Environmental Association Mode to detect mode of transmission vector. Billion people are affected by zoonotic infectious diseases, which cause about 60% of human and domestic animal deaths annually. It is estimated that 75% of newly emerging infectious diseases. Microbial diseases can be passed on to humans through a variety of terrestrial and marine vertebrate animals (Usmani et al., 2007). Laboratory scientists, public health professionals, and medical and veterinary scientists all need to work together to investigate emerging and novel zoonotic diseases. Sub-typing method tools and well-equipped labs are needed to identify disease outbreaks and characterize the transmission channels (Hadorn & Stärk, 2008). New technologies (bio-informatics and genomics sequencing) that are helpful for preventing future outbreaks (Halliday et al., 2012; Koopman, 2013). Advanced technologies helped us for early detection of new diseases and Global surveillance. These methods are essential for controlling and detecting emerging diseases. Global surveillance system includes network (Global Outbreak Alert), event-based system (SARS, Global Public Health Intelligence Network), web tools (Google) and social media (Fig. 3) (Sharanetal,2023).

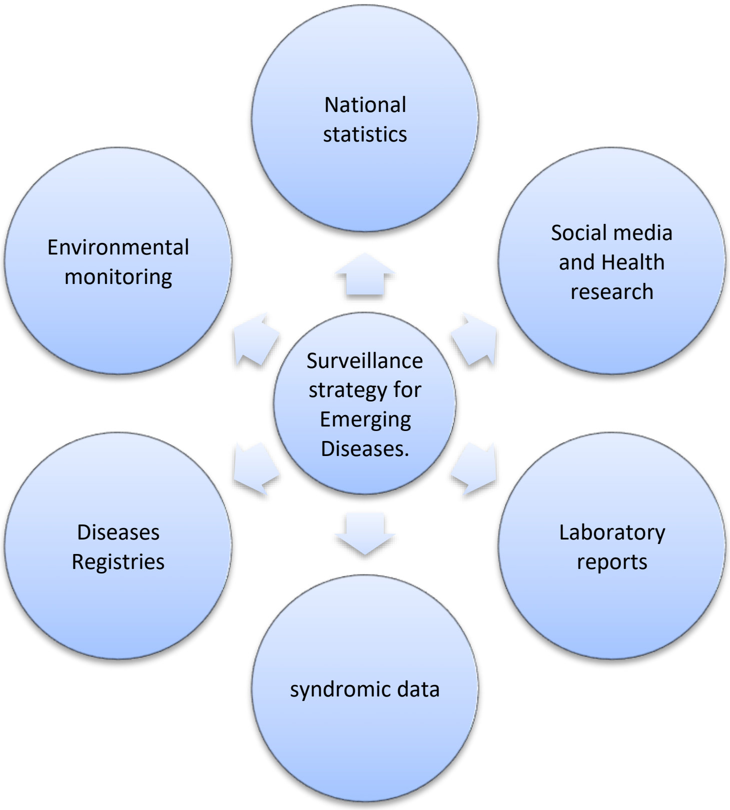

**Fig. 3:** This figure represents a framework for surveillance,monitoring and multiple data source for detection of diseases.

### 4.6 Impact on Global Socio-economic and Public Health:

Global socioeconomic and public health are significantly impacted by the development and zoonotic diseases reemergence. Out of 175 known developing diseases, 132 have been designated as emerging zoonotic infectious diseases (Alvi et al., 2022). Emerging zoonotic diseases have high impact on global socio-economic and public health in the world i-e COVID-19, Nipah virus, Mpox virus, MERS (Middle East respiratory syndrome), SARS (severe acute respiratory syndrome) and recent COVID-19 (coronavirus disease 2019) infection are the most significant emerging zoonotic diseases. According to Mosnier et al., (2020) has identified that approximately 71.8% of these zoonotic diseases originate in wild animals and account for nearly 60.3% of all novel diseases. Several zoonotic diseases have critical public health like as Mpox also called monkeypox virus. Firstly, it occurred in human (1970). Petesen et al., (2019) reported that Mpox endemic to west and central Africa. Due to rapid transmission, this virus gained international attention from WHO. Rodents and non-human primates are animal vector of Mpox virus. (Petersen et al., 2019; Peiris and Poon, 2021; Bunge et al.,2022; Zinnah et al., 2024). Nipah virus also zoonotic and effect different organ in human such as brain and respiratory system. Transmission to human from bats, pigs and contaminated objects. Nipah virus caused huge human death rate especially those areas where lack of necessities (Sharma et al., 2019). Avian influenza virus comes from Orthomyxoviridae. Waterfowl is vector animal of avian influenza virus. Antigen-specific antibodies are produced by animals in endemic areas that cause severe fever (Kimble et al., 2024; Subedi et al., 2024). COVID-19 transfer by direct or indirect contact Transfer from human to human, objects and animals. Natural reservoirs such as bats. Middle East Respiratory Syndrome (MERS), a recently discovered human-infectious viral zoonotic virus, was first discovered in camels in Saudi Arabia in 2012 (Chaisiri et al., 2017). The MERS coronavirus (MERS CoV) is the virus that causes this infection, which has serious effects on public health, slows production, and kills many people. Despite the fact that infected dromedaries show no symptoms, this disease has a morbidity incidence of roughly 60% and a fatality rate of 7–14% in humans. However, the infected dromedaries only had minor respiratory symptoms. According to research, MERS CoV can seriously infect an animal's lower respiratory tract (Saldanha et al., 2020).

## 5. Prevention and control

To lower the risk of zoonoses in various industries, the best recommendations for authorized organizations in that region are to develop a plan for disease mitigation. Structure of Operations between the Human Health and Livestock Sectors Strong coordination between the human health and cattle health sectors is essential for combating the rapid emergence of zoonotic diseases in the strategic plan. According to Rahman et al., 2020), this partnership will improve communication, networking, and connections between the public and private sectors. Combining Diagnostic Skills for New Pathogens Laboratory services should be enhanced with diagnostic capabilities in order to effectively detect zoonotic diseases in the region. For speedy analysis, both inland and arid laboratory networks can speed up sample transport (Belay et al., 2017). In recent years, the number of zoonotic disease outbreaks has increased. The objective is to prevent and limit the spread of these diseases because it is nearly impossible to predict when and where the next outbreak will occur. To accomplish this, a strategy must be developed that enables prompt action at the first sign of an outbreak. The primary foundations for managing and preventing zoonotic diseases are mutual recognition, research, and collaboration. Transfers of technology, information, communication, and education will also aid in prevention and control (Chomel, 2003). To enable timely detection and response to outbreaks, global surveillance and reporting systems must still be improved. In fact, these research gaps highlight the necessity of ongoing funding for zoonotic disease research in order to protect public health and avert future pandemics. To prevent zoonotic infections, public health officials, veterinarians, and other experts must collaborate. This includes actions including early identification and monitoring, animal immunization programs, safe food preparation and handling, and public education and awareness campaigns. The strategy of One Health focuses on uniting professionals from different areas, including public health, environmental science, veterinary medicine and medicine specializing in humans. Sharing of data and resources is important as well as the creation of unified surveillance systems for tracking diseases that spread between animals and people (Elsohaby & Villa, 2023).Prevention from zoonoses by adopting these steps like as vaccinated against infection, wear full protected from bugs bites, wear gloves during handling of any group of species, cook food properly, always wash yours hand before eating, drinking etc and last one avoid direct contact with infected organisms (Elsohaby & Villa, 2023).

## 6 Challenges and Future directions:

According to Naser et al., (2024), major challenges that faced in zoonotic diseases are antimicrobial resistance. In agriculture and health, antimicrobial resistance major threat due to over use of drugs that cause pathogen resistance. Asha et al., (2024) & Rahman et al., (2024) reported that *E. coli* and Salmonella already have resistance pathogen. Accordingly, the One Health approach should emphasize on how to control antimicrobial resistance pathogen through bio-security governance and new policy. They should be improved by legal and regulatory framework from international organization collaboration including WHO and IHR. Future direction in which should followed new technologies like next generation sequencing and genomics surveillance (WHO, 2023).

## 7. Conclusion:

Zoonotic diseases are becoming common threat in worldwide due to environmental and social factors. Effective prevention and well control strategy requires for the One Health approach especially in animals, human and environmental health. Although zoonotic diseases are screened, controlled and prevented, they still occur in humans because they can spread through contaminated hands and via pests. For early detection and effective surveillance system require good tools and molecular diagnostics techniques used for preventing future outbreaks such as antimicrobial resistance. Rapid diagnostics techniques are helpful for vaccine development against infection. Increased global organization, good bio-security, public education will be essential for preventing zoonosis outcomes.

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# Zoonotic spillovers the interface of wildlife livestock and human health

## 14

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## ABSTRACT

Zoonotic diseases, caused by pathogens transmitted between animals and humans, are a significant public health concern, accounting for approximately 60% of human infectious diseases and 75% of emerging infectious diseases. Zoonotic spillovers occur when pathogens cross species barriers, often due to ecological disruptions, wildlife trade, and close interactions between humans, livestock, and wildlife. Key spillover events include historical examples such as the Black Death, 1918 influenza, and more recent pandemics like HIV/AIDS and COVID-19. Live animal markets, wildlife hunting, intensive wildlife farming, and domestic animals as intermediates are major pathways for zoonotic spillovers. Several drivers, including deforestation, globalization, intensive farming, urbanization, and climate change, contribute to the increased risk of zoonotic emergence. The One Health approach, integrating human, animal, and environmental health, is crucial in mitigating these risks. With growing global interconnectedness, it is vital to implement effective measures to prevent and control zoonotic diseases, reduce habitat loss, regulate wildlife trade, and adapt to the challenges posed by climate change.

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## INTRODUCTION

The term zoonosis is derived from the Greek words zoon (animal) and nosos (disease), meaning "disease from animals." The World Health Organization (WHO) defines zoonoses as diseases and infections that are naturally transmitted between vertebrate animals and humans (WHO, 2020).

Over 200 zoonotic diseases have been identified.

They can be caused by a wide variety of pathogens:

Viruses (rabies, SARS, influenza, COVID-19)

Bacteria (anthrax, brucellosis, plague)

Parasites (toxoplasmosis, leishmaniasis)

Fungi (dermatophytosis, sporotrichosis)

Prions (bovine spongiform encephalopathy or "mad cow disease")

Zoonotic diseases account for:

~60% of all human infectious diseases (Jones et al., 2008).

~75% of emerging infectious diseases (EIDs) (Karesh et al., 2012).

Zoonoses are diseases that are naturally transmitted between animals and humans, representing more than 60% of all infectious diseases in humans and about 75% of emerging pathogens (Jones et al., 2008; Karesh et al., 2012). Zoonotic spillover occurs when a pathogen maintained in a reservoir host successfully crosses the species barrier and establishes infection in humans, often through an intermediate host or direct contact (Plowright et al., 2017).

Historically, zoonotic spillovers have shaped human societies. The Black Death (Yersinia pestis) in the 14th century caused millions of deaths across Europe, originating from rodent-flea-human cycles (Benedictow, 2004). The 1918 influenza pandemic is believed to have emerged from avian reservoirs and killed over 50 million people worldwide (Taubenberger & Morens, 2006). More recent examples include HIV/AIDS, traced to simian immunodeficiency virus in primates, and COVID-19, likely originating from bat coronaviruses with a possible intermediate host (Andersen et al., 2020).

Given globalization, climate change, and expanding human populations, the risk of zoonotic spillovers has dramatically increased, demanding integrated approaches like One Health, which unites human, animal, and environmental health for disease prevention (Zinsstag et al., 2011).

### Zoonotic Spillovers: The Interface of Wildlife, Livestock, and Human Health

Zoonotic diseases are infections that naturally transmit between animals and humans. Approximately 60% of all infectious diseases in humans are zoonotic, and nearly 75% of emerging infectious diseases originate in animals (Jones et al., 2008). Spillover events occur when pathogens cross the species barrier, often due to ecological disruption, wildlife trade, or close contact between humans, livestock, and wildlife (Plowright et al., 2017). The figure highlights the major pathways for zoonotic spillovers, including live animal markets, wildlife hunting, intensive wildlife farming, and domestic animal interactions.

### Live Animal Markets

Live animal markets are hotspots for zoonotic spillovers due to the congregation of multiple wild and domestic species in confined spaces. Stress, poor hygiene, and close animal-human contact increase the risk of pathogen transmission. Notable examples include:

- SARS (2002–2003): Originated from civet cats sold in markets in China, with bats as the natural reservoir (Guan et al., 2003).
- COVID-19 (2019): Linked to a seafood and live animal market in Wuhan, suspected bat origin with possible intermediate hosts (Zhou et al., 2020).
- Avian Influenza (H5N1, H7N9): Spread from poultry to humans, often in markets with live birds (Chen et al., 2005).

Live animal markets act as mixing vessels, facilitating viral reassortment and new strains capable of infecting humans.

### Wildlife Hunting

Bushmeat hunting and consumption bring humans into direct contact with blood and body fluids of wild animals. High-risk pathogens include:

- HIV/AIDS: Believed to have originated from simian immunodeficiency virus (SIV) in primates, transmitted through hunting and butchering (Sharp & Hahn, 2011).
- Ebola virus: Linked to handling of infected bats, gorillas, and other primates during hunting (Leroy et al., 2004).

These diseases highlight the role of cultural practices and food insecurity in zoonotic emergence.

### Intensive Wildlife Farming

Wildlife farming involves breeding wild species (such as deer, civets, porcupines, and ostriches) for meat, fur, or traditional medicine. These systems often mimic intensive livestock farming, creating environments conducive to pathogen amplification.

- COVID-19: Farmed wildlife species have been implicated in the transmission chain (Zhou et al., 2020).
- Rabies: Wildlife farming and trade can spread rabies in exotic carnivores (Nel, 2013).
- Avian Influenza: Farmed ostriches and wild birds are known reservoirs (Sims & Peiris, 2013).

Thus, wildlife farming increases human exposure to novel pathogens by artificially sustaining dense populations of exotic animals.

### Domestic Animals as Intermediate Hosts

Domestic animals often serve as bridges for zoonotic pathogens between wildlife and humans. Examples include:

- Nipah virus: Fruit bats transmitted the virus to pigs, which subsequently infected humans in Malaysia (Chua et al., 2000).
- Hendra virus: Bats transmitted the virus to horses, which then infected humans in Australia (Field et al., 2007).
- Avian Influenza: Domestic poultry facilitate sustained outbreaks with spillover into humans (Peiris et al., 2007).

**Livestock and pets increase the frequency of human-animal interactions, making them critical intermediates in zoonotic disease ecology.**

Drivers of Zoonotic Spillovers

Several factors contribute to the rising incidence of zoonotic spillovers:

- Deforestation and habitat loss → increases contact between humans and wildlife.
- Globalization and trade → rapid movement of animals and pathogens across borders.
- Intensive farming practices → amplify disease risk in both livestock and wildlife.
- Climate change → shifts in animal migration and vector distribution (Becker et al., 2020).

These drivers emphasize the need for a One Health approach, integrating human, animal, and environmental health to prevent pandemics.

### The Ecology of Spillover Events

Spillovers occur at the intersection of ecological, biological, and social systems. Wildlife serves as the largest reservoir of emerging pathogens, with bats, rodents, and birds being primary hosts (Allen et al., 2017). These species often harbor viruses without clinical illness, making them silent carriers.

Environmental factors play a major role:

- Deforestation and habitat loss bring wildlife closer to human settlements (Keesing et al., 2010).
- Agricultural expansion introduces livestock as amplifying hosts, creating bridges for pathogen transmission (Gibb et al., 2020).
- Climate change alters vector distributions, rainfall patterns, and migratory routes, influencing pathogen spread (Carlson et al., 2021).

For example, Nipah virus outbreaks in Bangladesh are linked to human consumption of date palm sap contaminated by fruit bats during dry seasons, demonstrating how ecological behavior directly facilitates spillover (Rahman et al., 2012).

Wildlife–Livestock–Human Interface

The majority of zoonotic spillovers occur in contact zones where wildlife, livestock, and humans interact.

- Wildlife to Livestock: Pathogens like Nipah virus (fruit bats → pigs) or avian influenza (wild birds → poultry) spill into livestock populations, where they amplify before reaching humans (Chua et al., 2000).
- Wildlife to Humans: Direct transmission occurs through hunting, bushmeat consumption, and wildlife trade, e.g., Ebola outbreaks linked to bushmeat handling (Leroy et al., 2005).
- Livestock to Humans: Intensive farming and global livestock trade facilitate large-scale transmission, e.g., H1N1 “swine flu” pandemic in 2009 (Smith et al., 2009).

Agricultural intensification has been identified as one of the strongest drivers of zoonotic emergence. Overcrowded farming practices reduce genetic diversity, enhance pathogen mutation rates, and create conditions for viruses to adapt to humans (Gilbert et al., 2017).

Drivers of Zoonotic Spillovers

Several socio-ecological drivers increase the risk of zoonotic spillovers:

### Deforestation and Land-use Change

Deforestation, agricultural expansion, and habitat fragmentation force wildlife, domestic animals, and humans into closer contact, creating opportunities for pathogens to jump species.

**Mechanism:** When forests are cleared for agriculture, logging, or settlements, wildlife lose their natural habitat. This stresses animals, weakens their immunity, and pushes them closer to human settlements, where transmission becomes more likely.

**Examples:**

**Nipah virus (Malaysia, 1998):** Deforestation and fruit orchard expansion attracted fruit bats near pig farms. The bats transmitted Nipah virus to pigs, which then infected humans (Chua et al., 2002).

**Malaria:** Deforestation in the Amazon and Southeast Asia has expanded mosquito breeding grounds, increasing malaria transmission (Yasuoka & Levins, 2007).

**Impact:** Land-use change is one of the strongest predictors of new zoonotic disease emergence worldwide.

### 2. Wildlife Trade and Bushmeat Hunting

Hunting, butchering, and trading wildlife for food, medicine, or luxury markets expose humans directly to blood, saliva, and other infectious materials.

**Mechanism:** Handling and consumption of bushmeat brings hunters and consumers into contact with novel pathogens. Wet/live animal markets further amplify risks by mixing different species in stressful, unsanitary conditions.

**Examples:**

**HIV/AIDS:** Originated from simian immunodeficiency viruses (SIV) when humans hunted and butchered primates in Central Africa (Sharp & Hahn, 2011).

**Ebola virus:** Linked to hunting and handling of fruit bats, gorillas, and chimpanzees (Leroy et al., 2004).

**SARS-CoV (2002–2003):** Traced to wildlife (civets and bats) sold in live animal markets in China (Wang et al., 2006).

**Impact:** The global legal and illegal wildlife trade is a multi-billion-dollar industry and a recognized hotspot for zoonotic spillover.

### 3. Urbanization and Population Growth

Rapid urban expansion and dense human populations increase exposure to both domestic and wild animals while creating environments favorable to vectors.

**Mechanism:** Poor sanitation, overcrowding, and peri-urban livestock keeping amplify transmission opportunities. Cities also attract synanthropic animals (rats, bats, pigeons) that act as reservoirs.
**Examples:**
**Leptospirosis:** Spreads in urban slums due to rat infestations and poor drainage (Costa et al., 2017).
**Dengue, Zika, and Chikungunya:** Spread by *Aedes aegypti* mosquitoes, which thrive in densely populated urban areas with stagnant water storage (Bhatt et al., 2013).
**Rabies:** Urban stray dogs remain a major source of rabies transmission in many developing countries.

**Impact:** By 2050, ~68% of the world's population will live in cities (UN, 2019), increasing risks of urban zoonoses.

### 4. Climate Change

Climate change alters ecosystems, vector ranges, and animal migration, creating new conditions for pathogen spillover.

**Mechanism:** Rising temperatures, changing rainfall, and extreme weather events shift the habitats of vectors (mosquitoes, ticks) and reservoir species. This brings them into contact with new host populations, including humans.
**Examples:**
**West Nile Virus:** Spread to new regions of Europe and North America due to warmer climates favoring mosquito survival (Kilpatrick, 2011).

**Lyme Disease:** Warmer winters allow ticks (*Ixodes scapularis*) to expand northward in North America, increasing Lyme disease incidence (Ogden et al., 2014).

**Rift Valley Fever:** Climate-driven heavy rains and flooding in Africa have triggered repeated outbreaks (Anyamba et al., 2009).

**Impact:** Climate change is a "threat multiplier" for zoonoses, as it interacts with deforestation, urbanization, and globalization to accelerate disease emergence.

### 5. Globalization and Trade

Globalization has significantly increased the movement of people, animals, and animal products across borders, thereby creating new opportunities for zoonotic pathogens to spread rapidly. The global trade in wildlife, livestock, meat, and animal-derived products often bypasses strict sanitary controls, making it easier for novel pathogens to cross international borders.

#### Wildlife Trade

The international wildlife trade (both legal and illegal) is one of the most critical pathways for zoonotic spillover. Exotic animals sold in live animal markets or trafficked across countries can carry pathogens that are novel to humans. For instance:

- The SARS-CoV outbreak (2002–2003) was linked to civet cats sold in Chinese wildlife markets (Wang et al., 2006).
- The global demand for exotic pets, such as reptiles, amphibians, and primates, increases the risk of spreading pathogens like *Salmonella* and *Herpes B virus*.

#### Livestock and Agricultural Trade

The expansion of global meat and dairy trade has also facilitated the spread of zoonotic diseases:

- Bovine Spongiform Encephalopathy (BSE), also known as mad cow disease, spread due to international cattle and meat trade in the 1980s–1990s.
- Avian Influenza (H5N1 and H7N9) has been spread through the movement of poultry across regions and countries (Kilpatrick, 2011).

#### Tourism and Human Travel

With globalization, human travel has become faster and more widespread, enabling zoonotic diseases to spread globally in days. For example:

- COVID-19, originating in Wuhan, China, spread worldwide within weeks due to international air travel.

- The Zika virus outbreak (2015–2016) spread from South America to other continents through travelers (Musso & Gubler, 2016).

## Conclusion

Zoonotic diseases represent a growing threat to global health, particularly in the context of increasing human-wildlife interactions and environmental changes. As pathogens continue to cross species barriers, the need for a comprehensive, integrated approach like One Health becomes more urgent. This approach can help mitigate risks and improve prevention strategies by addressing the complex relationships between humans, animals, and the environment. Effective management of zoonotic risks is critical to reducing future pandemics.

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# Introduction to Vector-Borne Zoonotic Diseases

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## ABSTRACT

Vector-borne zoonotic diseases (VBZDs) represent a significant and ongoing public health challenge, accounting for over 17% of all infectious diseases globally and causing more than 700,000 deaths annually. These diseases, which are transmitted to humans through arthropod vectors such as mosquitoes, ticks, and sandflies, often involve non-human animals as reservoirs for pathogens. The complex interplay between vectors, pathogens, animal reservoirs, and environmental factors underscores the ecological foundation of VBZDs, making them difficult to predict and control. Climate change, urbanization, and land use are all major drivers of disease transmission, expanding the range of vectors and creating conditions that favor pathogen spread. This chapter provides an in-depth exploration of the ecology of VBZDs, analyzing the key vectors, environmental factors, and host interactions that shape disease dynamics. It highlights several prominent diseases, including malaria, dengue, Zika, Lyme disease, and West Nile virus, and examines the ecological and societal factors that influence their spread. Additionally, the chapter discusses current and emerging control strategies, including insecticides, vaccines, biological control methods, and innovative technologies like genetic engineering and digital surveillance. The future of VBZD control hinges on integrated, multidisciplinary approaches that combine epidemiology, environmental science, public health policy, and community engagement to mitigate the global burden of these diseases.

**KEYWORDS**
Vector-borne diseases, zoonotic diseases, ecology, climate change, disease control, public health

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## INTRODUCTION

Vector-borne zoonotic diseases (VBZDs) are infectious conditions transmitted between animals and humans through the bites of arthropod vectors such as mosquitoes, ticks, fleas, sandflies, and triatomine bugs. The term “zoonotic” refers to the ability of a pathogen to cross the species barrier between animals and humans, while “vector-borne” specifies that transmission depends on an intermediary organism that carries the pathogen from host to host. Together, these diseases illustrate one of the most complex and consequential intersections of ecology, microbiology, and public health

Vector-borne zoonotic diseases represent one of the most persistent and complex public health challenges in the modern world. These diseases are caused by pathogens transmitted to humans through vectors such as mosquitoes, ticks, fleas, and sandflies, often with non-human animals acting as reservoirs. The World Health Organization (WHO, 2020) estimates that vector-borne diseases account for over 17% of all infectious diseases globally, leading to more than 700,000 deaths annually. Beyond mortality, they contribute significantly to morbidity, long-term disability, and economic instability, especially in low- and middle-income countries where healthcare resources are already limited (Githeko et al., 2014; Rocklöv & Dubrow, 2020). Because many of these pathogens cross the boundary between animals and humans, they embody a One Health challenge, linking human, animal, and environmental health in complex ways.

Zoonotic pathogens carried by vectors include viruses, bacteria, protozoa, and helminths, and their impact is often magnified in regions with poor infrastructure, rapid urbanization, and ecological disturbances. Diseases such as malaria, dengue fever, Lyme disease, Zika virus infection, and West Nile virus continue to illustrate the devastating effects of vector-borne transmission. The dynamic interaction between pathogens, vectors, reservoir hosts, and the environment underpins their persistence and spread. This ecological interplay underscores why public health responses often fall short if they fail to integrate multidisciplinary perspectives that account for climate, land use, vector biology, and human behavior (Gubler, 2011).

The significance of these diseases goes beyond mortality and morbidity. They impose severe economic burdens, disrupt livelihoods, and strain healthcare systems. For example, dengue alone causes an estimated annual global cost of USD 9 billion due to healthcare expenditures and lost productivity (Shepard et al., 2016). Moreover, zoonotic spillover events such as Zika in Brazil (2015–2016) and West Nile virus in the United States (1999–2002) demonstrate how quickly vector-borne zoonoses can become public health emergencies. These outbreaks are further exacerbated by globalization, increased travel, and the effects of climate change, which expand the range of both vectors and pathogens (Rocklöv & Dubrow, 2020).

The consequence of vector-borne zoonoses lies not only in their impact on human health but also in the ecological dynamics that drive their transmission. Unlike infections spread directly between individuals, these diseases depend on a web of interactions among vectors, animal reservoirs, humans, and the environment. For instance, the distribution and feeding behaviors of *Anopheles* mosquitoes directly shape malaria epidemiology, while land use changes and deforestation have been strongly associated with zoonotic spillover of arboviruses and parasitic diseases (Patz et al., 2004; Kilpatrick & Randolph, 2012). Climate change further complicates this picture by altering vector habitats, expanding their geographical ranges, and changing the timing and intensity of disease outbreaks (Campbell-Lendrum et al., 2015).

The increasing globalization of trade and human mobility has also accelerated the spread of vector-borne diseases beyond their traditional endemic zones. The rapid dissemination of chikungunya and Zika viruses across the Americas in the past two decades highlights how quickly these pathogens can move in a connected world (Musso & Gubler, 2016). Moreover, the rise of urbanization, inadequate sanitation, and water management have created favorable conditions for vectors such as *Aedes aegypti* to thrive in densely populated cities, fueling recurring dengue epidemics (Bhatt et al., 2013).

Given these challenges, vector-borne zoonotic diseases demand a multidisciplinary lens that integrates epidemiology, ecology, environmental science, and public health policy. Understanding their ecological foundations is vital to designing sustainable control strategies that can adapt to shifting environments and evolving pathogens. As this chapter will show, the ecology of vector-borne diseases is inseparable from their control, and both must be addressed in tandem to reduce the global burden and prepare for future threats

Malaria, dengue, Zika, Lyme disease, Rift Valley fever, and plague are only a few names on a long list. Each has its own story, but all share a common thread: they rely on a vector for transmission and often originate in animals before spilling over into humans. Together, they account for more than 17% of all infectious diseases globally and cause more than 700,000 deaths each year. These numbers, however, only scratch the surface. Beyond mortality, vector-borne zoonoses cripple economies, strain health systems, limit agricultural productivity, and disrupt communities.

The importance of these diseases cannot be separated from their ecology. Unlike infections that spread directly from person to person, vector-borne zoonoses depend on a chain of events involving climate, geography, vector biology, animal reservoirs, and human activity. A change in rainfall patterns can alter mosquito breeding grounds. Deforestation may bring people closer to wildlife reservoirs. Urban growth can create hotspots where vectors thrive. In other words, these diseases are shaped not only by microbes but also by the landscapes and societies in which they exist.

This chapter explores that intertwined reality. We will journey through the ecological underpinnings of transmission, examine case studies that show their public health impact, discuss the control measures that have been tried (and sometimes failed), and look ahead at where research and policy might lead us. The goal is to make sense of a complex but crucial topic, in a way that is both rigorous and relatable.

## 2. Ecology of Vector-Borne Zoonotic Diseases

The ecology of vector-borne zoonotic diseases is defined by the intricate relationships among vectors, pathogens, reservoir hosts, and the surrounding environment. Unlike directly transmitted infections, VBZDs depend on external conditions that determine whether a pathogen can persist, expand, or disappear from a particular region. This ecological complexity makes VBZDs not only challenging to predict but also highly responsive to environmental and societal change. Understanding these dynamics is essential for designing effective control strategies.

### 2.1 Overview of Vectors

Vectors are living organisms that transmit infectious pathogens between humans or from animals to humans. Arthropods are the most significant vectors due to their abundance, global distribution, and blood-feeding behavior. The primary groups include mosquitoes, ticks, fleas, sandflies, and triatomine bugs.

- Mosquitoes (*Culicidae*) are responsible for transmitting malaria (*Plasmodium spp.*), dengue virus, chikungunya virus, yellow fever virus, Zika virus, and West Nile virus. The genus *Anopheles* is the sole vector for malaria, while *Aedes aegypti* and *Aedes albopictus* are globally important for arboviruses. *Culex* species act as vectors for Japanese encephalitis and West Nile virus (Becker et al., 2010).
- Ticks (*Ixodidae* and *Argasidae*) transmit bacterial pathogens like *Borrelia burgdorferi* (Lyme disease), viral pathogens such as tick-borne encephalitis virus, and parasites like *Babesia microti*. Their long lifespan and ability to feed on multiple hosts across life stages make them particularly effective vectors (Sonenshine & Roe, 2014).
- Fleas, particularly *Xenopsylla cheopis*, transmit *Yersinia pestis*, the causative agent of plague. Their close association with rodent populations makes them persistent threats in areas with poor rodent control (Gage & Kosoy, 2005).

- Sandflies (*Phlebotominae*) are vectors of *Leishmania* parasites, causing leishmaniasis. They thrive in warm, humid environments and are closely associated with both wild and domestic animals (Ready, 2013).
- Triatomine bugs ("kissing bugs") in Latin America transmit *Trypanosoma cruzi*, the parasite causing Chagas disease. Their behavior of feeding around human dwellings highlights the connection between ecology, poverty, and disease risk (Coura & Viñas, 2010).

These vectors differ in biology, feeding behavior, and environmental tolerance, yet their unifying ecological feature is dependence on both host availability and environmental suitability.

### 2.2 Habitat and Environmental Factors

The distribution and abundance of vectors are shaped by environmental conditions:

**Climate:** Temperature influences vector survival, breeding, and the extrinsic incubation period (EIP) of pathogens. Warmer conditions shorten the EIP of malaria parasites in *Anopheles* mosquitoes, making them infectious more quickly (Paaijmans et al., 2009). Rainfall patterns affect mosquito breeding sites, while humidity impacts vector longevity.

**Land use and deforestation:** Human-driven ecological changes bring people, livestock, and wildlife into closer contact. Deforestation in the Amazon, for example, has been linked to malaria outbreaks due to changes in mosquito breeding habitats (Olson et al., 2010).

**Urbanization:** Rapid, unplanned urban growth fosters *Aedes aegypti* populations through water storage practices and waste accumulation. Poor drainage systems create breeding sites, while high human density amplifies transmission potential (Gubler, 2011).

**Agricultural practices:** Irrigation and livestock farming can increase breeding grounds for mosquitoes and expose humans to zoonotic reservoirs. Japanese encephalitis virus persists in rural Asia partly because of rice paddies and pig farming (Solomon, 2006).

### 2.3 Life Cycles of Significant Vectors

The biology of vectors strongly influences transmission dynamics:

- Mosquitoes undergo complete metamorphosis: egg, larva, pupa, and adult. Aquatic larval stages depend on standing water, while adults require blood meals for reproduction. Each species has unique host preferences, influencing which pathogens they can carry.
- Ticks pass through larval, nymph, and adult stages, feeding on different hosts at each stage. This multi-host lifecycle facilitates pathogen transfer between wildlife reservoirs and humans (Gray et al., 2009).
- Fleas have life stages linked to host nests and bedding. Their survival is tied to rodent populations, which in turn are influenced by climate and food availability.

The synchrony between vector development and pathogen replication is critical; transmission is possible only when both are aligned ecologically.

### 2.4 Reservoir Hosts

Reservoir hosts are animals that maintain pathogens in nature, providing continuous sources of infection for vectors. They vary widely depending on the disease:

- Rodents are reservoirs for plague (*Y. pestis*), hantaviruses, and arenaviruses. Their adaptability to human settlements makes them dangerous allies for vectors.
- Birds sustain arboviruses such as West Nile virus and St. Louis encephalitis virus, acting as amplifying hosts for *Culex* mosquitoes (Komar, 2003).
- Domestic animals, like dogs and cattle, serve as reservoirs for diseases such as visceral leishmaniasis and Rift Valley fever.
- Wildlife, including deer (for Lyme disease) and primates (for yellow fever and Zika), play pivotal roles in maintaining pathogens in ecosystems.

Understanding these ecological reservoirs is essential, as targeting vectors alone may not interrupt transmission if reservoirs remain abundant.

### 2.5 Human Behavior and Ecology

Human activities complete the ecological picture: migration, travel, deforestation, agricultural expansion, and settlement patterns all reshape vector habitats. For example, international tire trade facilitated the spread of *Aedes albopictus* globally, while war and displacement often lead to outbreaks due to disrupted control infrastructure (Patz et al., 2000).

## 3. Major Vector-Borne Zoonotic Diseases

Vector-borne zoonotic diseases (VBZDs) represent some of the most pressing public health concerns in the 21st century. They account for more than 17% of all infectious diseases worldwide and cause over 700,000 deaths annually (WHO, 2020). Unlike diseases that spread directly from person to person, VBZDs depend on the ecology of vectors and reservoirs, which makes them more complex and harder to control. This section explores several of the most significant VBZDs, highlighting their epidemiology, transmission cycles, clinical features, and impacts on both humans and animals.

### 3.1 West Nile Virus (WNV)

West Nile virus is a mosquito-borne flavivirus first identified in Uganda in 1937. Initially confined to Africa, the Middle East, and parts of Europe, WNV became a global concern after its introduction into North America in 1999, where it rapidly spread across the continent (Petersen et al., 2013).

**Transmission:** WNV is primarily transmitted by *Culex* mosquitoes. Birds act as the main reservoirs, amplifying the virus through frequent mosquito–bird cycles. Humans and horses are incidental, “dead-end” hosts because they do not produce sufficient viremia to perpetuate transmission (Komar, 2003).

**Epidemiology:** Outbreaks in the United States have resulted in thousands of cases and hundreds of deaths, with neuroinvasive disease being the most severe outcome. In Europe, cases are often seasonal, linked to warm summers that extend mosquito activity (Chancey et al., 2015).

**Clinical impact:** Most infections are asymptomatic, but about 20% of patients develop febrile illness, and less than 1% progress to neuroinvasive disease such as meningitis, encephalitis, or acute flaccid paralysis (Sejvar, 2016).

**Public health impact:** WNV exemplifies how globalization, climate change, and migratory birds can facilitate the rapid spread of VBZDs into new regions.

### 3.2 Lyme Disease

Lyme disease, caused by the bacterium *Borrelia burgdorferi*, is the most common tick-borne disease in North America and Europe. First recognized in the 1970s in Lyme, Connecticut, it has since become a major public health challenge.

**Transmission:** The bacterium is transmitted by *Ixodes* ticks (blacklegged or deer ticks). Small mammals, particularly the white-footed mouse (*Peromyscus leucopus*), act as key reservoirs, while deer serve as important hosts for adult ticks (Steere et al., 2016).

**Epidemiology:** Each year, approximately 300,000 cases are reported in the United States alone (CDC, 2020). Climate change, reforestation, and suburban expansion have contributed to its geographic spread (Eisen & Eisen, 2018).

**Symptoms:** Early symptoms include fever, fatigue, and the hallmark erythema migrans (“bull’s-eye”) rash. Untreated infections may progress to arthritis, neurological disorders, and carditis (Stanek et al., 2012).

**Impact:** Lyme disease illustrates the tight ecological relationship between wildlife, vectors, and human land-use patterns. Its rising incidence highlights how environmental change drives disease emergence.

### 3.3 Zika Virus

The Zika virus outbreak in the Americas (2015–2016) highlighted the devastating potential of mosquito-borne arboviruses.
**Transmission:** Zika virus is transmitted primarily by *Aedes aegypti* and *Aedes albopictus*. Unlike many VBZDs, it can also be spread sexually and vertically from mother to fetus (Musso & Gubler, 2016).

**Epidemiology:** First identified in Uganda in 1947, Zika was relatively obscure until major outbreaks occurred in Micronesia (2007), French Polynesia (2013), and Brazil (2015). The Brazilian outbreak was particularly alarming due to thousands of cases of congenital Zika syndrome, including microcephaly (Mlakar et al., 2016).

**Clinical features:** Most infections are mild, presenting with fever, rash, joint pain, and conjunctivitis. The most significant consequences are neurological complications such as Guillain–Barré syndrome and severe birth defects in newborns.

**Public health relevance:** The Zika epidemic underscored the importance of surveillance, rapid diagnostic tools, and global preparedness against emerging vector-borne viruses.

### 3.4 Chikungunya

Chikungunya virus, an alphavirus transmitted by *Aedes* mosquitoes, causes explosive outbreaks characterized by fever and debilitating joint pain.

**Epidemiology:** First described in Tanzania in 1952, chikungunya has spread across Africa, Asia, the Americas, and Europe. In 2005–2006, a major outbreak on Réunion Island infected nearly 40% of the population, illustrating its epidemic potential (Burt et al., 2017).

**Transmission:** Like dengue and Zika, it is transmitted by *Aedes aegypti* and *Aedes albopictus*. Its global spread has been facilitated by international travel and the invasive expansion of *Aedes albopictus*.

**Symptoms:** Chikungunya is notable for causing severe polyarthritis, which can persist for months or years, severely impairing quality of life (Simon et al., 2011).

**Impact:** While rarely fatal, the disease exerts a heavy economic and social toll due to long-term disability among affected individuals.

### 3.5 Dengue Fever

Dengue is one of the fastest-spreading mosquito-borne viral diseases, with an estimated 390 million infections annually across more than 100 countries (Bhatt et al., 2013).

**Transmission:** Dengue virus (DENV) is transmitted by *Aedes aegypti* and *Aedes albopictus*. Humans are the primary reservoir hosts, which sets dengue apart from zoonotic viruses like WNV or yellow fever.

**Clinical spectrum:** Dengue infections range from asymptomatic to severe dengue, formerly known as dengue hemorrhagic fever, characterized by plasma leakage, shock, and multi-organ failure (WHO, 2019).

**Geographic spread:** Once confined to Southeast Asia, dengue has become endemic in Latin America, the Caribbean, and Africa. Climate change and rapid urbanization have driven its expansion.

**Public health burden:** Dengue outbreaks overwhelm health systems, with repeated epidemics causing major economic costs in tropical and subtropical regions.

### 3.6 Malaria

Though technically a parasitic rather than viral disease, malaria remains the most deadly vector-borne disease globally.

**Pathogen and vector:** Caused by *Plasmodium* parasites and transmitted by *Anopheles* mosquitoes, malaria is endemic in over 90 countries (WHO, 2021). *Plasmodium falciparum* is the deadliest species, while *P. vivax* has the widest geographic distribution.

**Epidemiology:** In 2020, there were 241 million malaria cases and 627,000 deaths, mostly among children under 5 years old in sub-Saharan Africa (WHO, 2021).

**Clinical symptoms:** Fever, chills, anemia, and organ dysfunction characterize malaria, with severe disease leading to cerebral malaria, respiratory distress, and death.

**Public health significance:** Despite progress through bed nets, insecticides, and antimalarial drugs, resistance in both parasites and mosquitoes remains a critical challenge.

### 3.7 Other Notable Diseases

**Yellow fever:** A mosquito-borne viral hemorrhagic fever that continues to cause deadly outbreaks in Africa and South America, despite the availability of an effective vaccine (Monath & Vasconcelos, 2015).

**Rift Valley fever:** A zoonotic viral disease transmitted by mosquitoes and direct contact with infected animals, causing both livestock losses and human illness (Ikegami & Makino, 2011).

**Leishmaniasis:** Transmitted by sandflies, this parasitic disease causes cutaneous and visceral forms, affecting millions worldwide (Alvar et al., 2012).

**Chagas disease:** Caused by *Trypanosoma cruzi* and spread by triatomine bugs in Latin America, it leads to chronic heart and digestive disease in millions of people (Rassi et al., 2010).

These diseases collectively illustrate the diversity of VBZDs, ranging from mosquito-borne arboviruses to tick-borne bacteria and parasitic infections. They thrive at the intersection of ecology, climate, human activity, and globalization. The recurring theme is that VBZDs are not isolated problems but interconnected global threats requiring sustained public health vigilance.

## Ecological Dynamics of Transmission

### Vectors as the Central Actors

At the heart of vector-borne zoonotic diseases are the vectors themselves. A mosquito, tick, or sandfly may seem insignificant, but its biology dictates whether a disease can spread or not. Each vector species has its own feeding habits, lifespan, breeding requirements, and susceptibility to pathogens. These traits influence whether transmission occurs in rural villages, dense urban centers, or forest edges.

Take *Aedes aegypti*, the mosquito notorious for spreading dengue, Zika, and chikungunya. Unlike many other mosquitoes, *Aedes aegypti* thrives in urban environments, breeds in small water containers, and prefers feeding on humans multiple times in a single cycle. These habits make it a near-perfect transmitter of viruses in crowded cities. In contrast, *Anopheles* mosquitoes, which spread malaria, are more tied to rural environments with access to fresh water pools.

Ticks tell a different story. Unlike mosquitoes, which live for weeks, ticks can live for years, feeding only occasionally but transmitting pathogens like *Borrelia burgdorferi* (the cause of Lyme disease) or *Crimean-Congo hemorrhagic fever virus*. Their long life and multiple host cycles make them resilient transmitters, deeply embedded in ecological webs.

### The Role of Animal Reservoirs

Vectors rarely transmit diseases in isolation; most zoonoses require an animal reservoir. Reservoir hosts are animals in which pathogens naturally circulate without causing major disease. Rodents are perhaps the most famous example, serving as reservoirs for plague and hantaviruses. Birds play a critical role in the spread of West Nile virus. Livestock can amplify Rift Valley fever outbreaks.

This animal-human connection is where ecology becomes vital. When humans encroach on new habitats, trade in wildlife, or expand farming into previously wild areas, they increase their contact with reservoirs. Every step into new ecological territory can create opportunities for zoonotic spillover.

### Climate and Environmental Drivers

Climate change is one of the most powerful forces shaping vector-borne diseases. Warmer temperatures expand the habitats of mosquitoes and ticks. Rainfall and humidity influence breeding sites. Droughts can paradoxically increase transmission when households store water in containers that become mosquito breeding grounds.

For example, highland regions of East Africa once considered too cool for malaria transmission are now seeing outbreaks as temperatures rise. Similarly, warming winters in North America and Europe have allowed ticks carrying Lyme disease to expand their range.

Urbanization and land-use change also play pivotal roles. Crowded cities with poor sanitation provide breeding grounds for *Aedes* mosquitoes. Deforestation in the Amazon has been linked to increased malaria cases as people move into areas rich with *Anopheles* mosquitoes. Irrigation and dam building, while boosting agriculture, often create perfect habitats for vector breeding.

### Human Behavior and Socioeconomic Factors

Disease ecology is never just about biology—it is about people. Housing quality, water management, agricultural practices, travel, and health-seeking behavior all affect disease transmission. Poverty often magnifies risk: inadequate housing lets in mosquitoes, lack of access to healthcare delays treatment, and limited resources restrict control programs.

Migration and global travel further complicate matters. A traveler infected with Zika in Brazil can arrive in Florida within hours, where local mosquitoes may spread the virus. Refugee crises often place vulnerable populations in conditions ripe for vector-borne outbreaks.

## Case Studies of Notable Diseases

### Malaria: A Persistent Scourge

Malaria remains the most recognized vector-borne disease, transmitted by *Anopheles* mosquitoes and caused by *Plasmodium* parasites. Despite decades of control efforts, it continues to cause more than 200 million cases annually, with the greatest burden in sub-Saharan Africa.

The ecology of malaria is tied to both mosquito and human factors. Mosquito species vary in their competence, with some transmitting far more efficiently than others. Human immunity, shaped by repeated exposure, also influences disease severity. Control measures such as insecticide-treated bed nets, indoor residual spraying, and antimalarial drugs have saved millions of lives, but resistance—in both mosquitoes and parasites—remains a looming challenge.

### Dengue and the Rise of Urban Arboviruses

Dengue fever illustrates the growing importance of urbanization in shaping disease. Once considered a tropical nuisance, dengue has exploded into one of the most rapidly spreading mosquito-borne diseases worldwide, affecting more than 100 countries.

Its main vector, *Aedes aegypti*, thrives in cities, breeding in everything from discarded tires to flowerpots. Global travel spreads the virus between regions, while weak infrastructure amplifies outbreaks. The 2015–2016 Zika epidemic followed a similar pattern, with devastating consequences for pregnant women and their babies.

### Lyme Disease: An Expanding Threat

In temperate regions, Lyme disease provides an example of how environmental change shapes zoonoses. Caused by the bacterium *Borrelia burgdorferi* and spread by *Ixodes* ticks, Lyme disease has expanded dramatically in North America and Europe over the past few decades. Reforestation, changing land use, and warming temperatures have expanded tick habitats, while suburban sprawl brings humans into closer contact with them.

### Rift Valley Fever: The Livestock Connection

Rift Valley fever, transmitted by mosquitoes but amplified in livestock, highlights the animal-human interface. Outbreaks often occur after heavy rainfall or flooding, which boosts mosquito populations. Livestock infections spill over to humans, causing fever, blindness, or even hemorrhagic disease. The economic impact on agriculture is as significant as the health burden, with trade restrictions and livestock deaths undermining livelihoods.

### Plague: A Historic Reminder

Although often considered a relic of the past, plague remains present in parts of Africa, Asia, and the Americas. Carried by fleas that infest rodents, it exemplifies the complex ecology of zoonoses: reservoir hosts, flea vectors, and environmental changes all align to create outbreaks. The famous Black Death may be history, but its ecological lessons remain relevant.

## 4. Control Measures

Vector-borne zoonotic diseases (VBZDs) cannot be eliminated by targeting pathogens alone; rather, their control requires a focus on the ecological systems that sustain vectors and reservoirs. The strategies employed vary from classical methods such as insecticides and vaccination campaigns to innovative technologies such as genetically modified mosquitoes and digital surveillance systems. Effective control depends not only on science but also on policy, socioeconomic contexts, and public participation.

### 4.1 Preventive Strategies

Vaccination remains the most reliable preventive tool for several VBZDs. The yellow fever vaccine, developed in the 1930s, is among the most successful vaccines in history, conferring lifelong immunity in most individuals (Monath & Vasconcelos, 2015). Despite its effectiveness, vaccine coverage remains uneven, and outbreaks continue in under-vaccinated populations. Dengue has also seen progress with the development of the *Dengvaxia* vaccine, though its use is limited by safety concerns in seronegative individuals (Hadinegoro et al., 2015). Malaria vaccines, such as RTS,S/AS01, represent important breakthroughs, yet their protective efficacy is modest (WHO, 2021).

Personal protective measures form another line of prevention. In malaria-endemic regions, the distribution of insecticide-treated nets (ITNs) has significantly reduced infection rates (Bhatt et al., 2015). Similarly, repellents, protective clothing, and bed nets are widely promoted for travelers and communities in high-risk areas.

Education and awareness campaigns help communities understand how human behaviors — such as water storage practices, outdoor activities during peak mosquito hours, or improper use of pesticides — influence disease risk. In Brazil, community education during the Zika epidemic was key in mobilizing preventive action (Lowe et al., 2018).

### 4.2 Vector Control Methods

Vector control is the cornerstone of VBZD management, especially when vaccines or treatments are absent.

**Chemical control (insecticides):** For decades, insecticides such as DDT and pyrethroids have been the backbone of mosquito control. Indoor residual spraying (IRS) has proven highly effective against malaria vectors (Pluess et al., 2010). However, insecticide resistance is an escalating challenge, with resistant *Anopheles* and *Aedes* populations reported worldwide (Ranson & Lissenden, 2016).

**Biological control:** Natural enemies such as larvivorous fish (*Gambusia affinis*) and copepods have been used to reduce mosquito larvae in breeding sites. Bacterial agents like *Bacillus thuringiensis israelensis* (Bti) selectively kill mosquito larvae without harming other organisms (Becker, 2000).

**Environmental management:** Habitat modification, including draining stagnant water, improving irrigation practices, and covering water containers, disrupts breeding grounds. Singapore's dengue control program has successfully relied on community-driven environmental management (Ooi et al., 2006).

**Innovative technologies:** Cutting-edge methods are reshaping vector control. Wolbachia-infected *Aedes* mosquitoes, released in several countries, reduce the capacity of mosquitoes to transmit dengue, Zika, and chikungunya (Hoffmann et al., 2011). Gene-drive mosquitoes, designed to spread traits such as sterility, are being tested as a future strategy (Alphey, 2014). Digital tools, including GIS mapping and smartphone-based surveillance, also allow health authorities to identify and respond to hotspots in real time (Eisen & Eisen, 2011).

### 4.3 Role of Public Health Policies

National and international policies provide the framework for sustainable control of VBZDs.

**Integrated Vector Management (IVM):** Endorsed by the World Health Organization, IVM promotes the rational use of resources by combining multiple control tools tailored to local conditions. It emphasizes cross-sector collaboration, community involvement, and environmental stewardship (WHO, 2012).

**Surveillance systems:** Robust disease and vector surveillance is essential for early detection and response. The U.S. West Nile virus program integrates mosquito surveillance with bird and human case reporting, allowing targeted interventions (Hadfield et al., 2019).

**Legislation and regulation:** Policies regulating pesticide use, land development, and water management directly influence vector habitats. In many regions, weak enforcement undermines control efforts.

**International collaboration:** Diseases such as Zika and malaria transcend borders, requiring cooperation through global initiatives like the Roll Back Malaria Partnership or the Pan American Health Organization's arbovirus programs.

### 4.4 Community Engagement

Control strategies succeed or fail depending on the participation of affected communities. Without community buy-in, even the best-designed interventions collapse.

- During dengue outbreaks, households that eliminate breeding sites (e.g., emptying containers, cleaning gutters) have been shown to reduce local mosquito populations significantly (Caprara et al., 2009).
- Citizen science approaches, where individuals contribute to mosquito monitoring through apps or local sampling, are enhancing surveillance capacity (Palmer et al., 2017).
- Trust and communication are vital. In cases where communities have resisted spraying or vaccination campaigns, misinformation has often played a role (Larson, 2018). Building trust requires sustained engagement rather than reactive, crisis-driven messaging.

The control of VBZDs requires a multi-pronged approach that combines preventive strategies, robust vector control, strong public health policy, and community participation. While traditional tools like insecticides and bed nets remain important, resistance and ecological challenges demand innovation. Vaccines, novel biological control strategies, and digital technologies are expanding the toolbox, but success hinges on integration, sustainability, and the willingness of communities and policymakers to act collectively.

## 6. Future Directions and Research Needs

The control of vector-borne zoonotic diseases has made important progress over the past century, yet the global burden remains high. Malaria alone causes over 200 million cases annually, while arboviruses like dengue, Zika, and chikungunya continue to expand into new regions (WHO, 2023). Climate change, rapid urbanization, and global travel create conditions that enable vectors and pathogens to spread more widely than ever before. To address these evolving threats, future directions must focus on innovation**,** integration, and sustainability in both research and policy.

### 6.1 Emerging Threats

New challenges are reshaping the epidemiological landscape of VBZDs:

**Climate change:** Rising temperatures and shifting rainfall patterns alter vector habitats, extending the geographic range of mosquitoes and ticks into temperate zones. For example, *Aedes albopictus*, once limited to Asia, is now established across Europe and North America (Kraemer et al., 2019).

**Urbanization and population growth:** Rapid, unplanned urban expansion fosters environments with poor sanitation and water storage, fueling dengue and Zika outbreaks.

**Insecticide and drug resistance:** Increasing resistance in mosquito populations and pathogens threatens to undermine decades of control efforts (Ranson & Lissenden, 2016).

**Zoonotic spillover events:** Land-use changes and deforestation heighten contact between humans, domestic animals, and wildlife reservoirs, raising the risk of new zoonotic diseases (Allen et al., 2017).

### 6.2 Innovations in Vector Control

Research is advancing new methods that move beyond reliance on insecticides:

**Genetic engineering:** Gene-drive technologies have the potential to suppress mosquito populations or reduce their ability to transmit pathogens (Alphey, 2014). Ethical and ecological questions remain, requiring careful regulation and public dialogue.

**Wolbachia-based biocontrol:** The use of *Wolbachia*-infected *Aedes* mosquitoes, which block virus transmission, has shown promising results in Indonesia, Australia, and Brazil (O'Neill et al., 2018).

**Nanotechnology and new repellents:** Advances in nanomaterials are improving the durability and effectiveness of insecticides and personal protection tools (Patil et al., 2017).

**Digital surveillance and AI:** Satellite imagery, climate modeling, and machine learning algorithms are increasingly used to predict outbreaks and guide targeted interventions (Kraemer et al., 2020).

### 6.3 Research Needs

To keep pace with changing disease dynamics, future research should prioritize:

- Integrated eco-epidemiological models that combine climate, ecological, and human behavior data to better forecast outbreaks.
- Vaccines for neglected arboviruses such as chikungunya and Rift Valley fever.
- Sustainable alternatives to insecticides, including biological and environmental management strategies.
- One Health approaches linking human, animal, and environmental health to address zoonotic spillover more effectively (Destoumieux-Garzón et al., 2018).
- Community-driven innovation, ensuring that interventions are adapted to cultural and socioeconomic contexts, not just scientific feasibility.

### 6.4 Policy Directions

Science alone cannot control VBZDs; robust policy frameworks are essential:

**Strengthening health systems:** Ensuring rapid outbreak response, particularly in low-income countries where surveillance and infrastructure remain weak.

**International collaboration:** Pathogens and vectors cross borders; thus, global data-sharing and coordinated interventions are indispensable.

**Investment in R&D:** Funding agencies and governments must support long-term research rather than reactive crisis-driven funding cycles.

**Public engagement:** Transparency and community involvement are critical for building trust in new technologies like gene drives or Wolbachia.

## Conclusion

Vector-borne zoonotic diseases are more than a biomedical challenge; they are an ecological reality shaped by the interactions of humans, animals, vectors, and the environment. Their control requires not just technical tools but an understanding of these interactions, sustained commitment, and a recognition that our health is bound to the health of the ecosystems we live in.

By exploring their ecology, examining their impact, and considering both traditional and innovative control strategies, we see both the complexity of the challenge and the possibility of progress. The path ahead lies in combining scientific knowledge with practical action, bridging communities with policy, and preparing for a future where these ancient diseases may yet find new forms.

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# Blood Transfusion Practices and Advancements in Veterinary Medicine

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## ABSTRACT

Blood transfusion is a method in which one animal (the recipient) receives blood products (whole blood or components) from another animal (the donor) of the same species, with proper precautions taken to reduce risks such as immune reactions or disease transmission. Understanding species-specific blood volumes and blood group systems is essential. This review provides an updated overview of the history, blood volume, blood groups, and transfusion practices in veterinary medicine, with a focus on species-specific challenges and the importance of blood banks in enhancing transfusion safety.

**KEYWORDS**
Blood volume, Blood groups, veterinary medicine Practices,

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## INTRODUCTION

Blood transfusion is defined as the intravenous infusion of blood r its components, which has become more common in veterinary medicine and is considered an important aspect of lifesaving and advanced treatment for critically ill patients (Battaglia & Steele, 2020). Historically, blood transfusions relied only on the transfusion of whole blood. However, with advancements in component therapy of blood, such as RBCs, frozen plasma, and platelet-rich plasma, clinicians have been given the ability to employ these components according to the patient's needs (Everts et al., 2020).

The successful transfusion of blood from one dog to another was first reported in 1665 by Richard Lower. With the advancement in techniques and equipment development after 1950, blood transfusion became more popular in veterinary medicine (Van Zundert et al., 2021). The 20th century was known for the discovery of anticoagulants and preservatives for blood products, the description of human blood groups, and the development of compatibility assays. Transfusion therapy has increasingly become more practicable in small animal treatment (Pol D, 2020). Better access to blood products through on-site donors, the purchase of blood bank products, external donor programs, or the availability of blood component substitutes and infectious pathogen screening have increased the safety of transfusion therapy for canine patients (Prittie, 2021). The safe use of whole blood or blood component therapy, on the other hand, necessitates knowledge of blood groups and antibody prevalence, as well as the methods for reducing the risk of adverse reactions, such as the use of appropriate donors and screening assays that aid in the detection of serological incompatibility (Gelendi et al., 2025). Although blood transfusions may be life-saving, they are not a definitive treatment for disease but play a critical role in patients with acute blood loss, improving oxygenation capacity and the patients' ability to overcome the underlying diseases. Researchers have proposed the possibility of separating the whole blood into its fractions for the most efficient use (Abubakar and Haque, 2020). The ability to separate the blood into fractions (Apheresis) has helped improve the storage period and to specifically use the blood constituents depending on the requirement. The hematological parameters, such as hemoglobin, hematocrit, and total erythrocyte count, should be evaluated concurrently with physical examination findings to determine whether the patient requires a transfusion or not (Roney et al., 2023). The type of anemia, blood group, blood parameters, animal size, and blood products to be transfused all influence blood transfusion. Advanced screening facilities, testing blood groups, and cross-matching of blood have made the process accurate. Due to the several antigenic combinations in the blood groups of animals, there is no universal donor in animals (Baruah et al., 2022).

### Indications

The various components of blood can be used in different conditions, as indicated below:

### Fresh whole blood

Fresh Whole Blood that is less than 8 hours old and has not been refrigerated, and has all cellular and fluid components of blood (Hess and Alessandro, 2022). Stored Whole Blood is blood that is more than 8 hours old. It can be stored at 33.8-42.8 °F (1 - 6 °C) for a maximum of 28-35 days.

- Treatment for anemia with thrombopathy or severe thrombocytopenia and disseminated intravascular coagulation (Kalpatthi and Kiss, 2020).
- Animals with severe trauma requiring massive transfusion.
- Animals with acute hemorrhagic anemia.
- Animals suffering from blood-related protozoal diseases like Anaplasmosis, Babesiosis
- Animals suffering from anemia with hypoproteinemia. For intravascular volume expansion and oxygen support (Shepard and Brainard, 2022).

### Packed RBCs

Contains concentrated RBCs with a PCV of 80 percent. Depending on the anticoagulant used, it can be stored for 28 – 35 days.

- Animals with symptomatic anemia, including anemia due to hemorrhage, hemolysis, renal disease, and decreased production of RBCs (bone marrow suppression) (Tvedten, 2022)
- Helps to increase RBC concentration in animals that require oxygen support
- Packed blood cells are preferred for administration to animals with normovolemic anemia, such as occurs with chronic anemia or hemolytic anemia, and when the donor plasma contains alloantibodies to the recipient's red blood cells (Tvedten, 2022).

### Platelet rich

Plasma (Platelet concentrate) is obtained by centrifuging fresh blood at a rate slower than that used for the production of packed cell volume and plasma. Difficult to store. It can be used within 48 hours if kept away from light at room temperature. Should not be refrigerated.

- Consistently administered to animals with life-threatening hemorrhage due to marked thrombocytopenia (Walton, 2021).
- To animals with hemorrhage secondary to congenital or acquired thrombopathy.

### Cryoprecipitate

Cryoprecipitate is the cold, insoluble portion of plasma that precipitates after Fresh Frozen Plasma has been thawed slowly in the refrigerator at 33.8 to 42.8 °F (1 – 6 °C) (Kaplan, 2021). It has a slushy consistency. It can be stored at -4 to -22 °F (-20 to 30 °C).

Used in the treatment of Hemophilia A (factor VIII deficiency), Von Willebrand Disease, and hypofibrinogenemia (as it contains von Willebrand Factor, factor VIII, and fibrinogen).

### Important indicators of the need for transfusion

- Anemia of various diseases, like due to infection or acute/ chronic hemorrhage (Satniyazovna, 2022).
- Bleeding disorders such as thrombocytopenia or coagulopathies.
- Poisons like warfarin.
- Hypoproteinemia is usually of parasitic or infectious origin (Dubey et al., 2024).
- Burns.
- Intolerance of minimal exercise (nursing, walking).
- Parasitism, toxicosis, or immune-mediated anemia.
- Decline in hematocrit with exacerbation of abnormalities on physical examination, transfusion should be considered in any animal with a hematocrit below 20% (0.20 L/L) (Dubova et al., 2020).

### Blood volumes of animals

Blood and Blood Volumes of Animals. Blood is the vascular connective tissue composed of fluid parts termed plasma and of corpuscles, viz, erythrocytes or red blood cells, leucocytes or white blood cells, and platelets (Alimov, 2023). The shape and size of red blood cells vary in different animals, e.g., a Dog's RBC is a typical biconcave disk, whereas the Goat's RBC is more spherical. RBC shape in Camel is elliptical, in Deer it is sickle-shaped. Humans and animals have blood volumes of 7% to 9% of their body weight. When there is a reduction in the blood volume, transfusion is generally required (Table 1) (Mudge, 2022).

**Table 1.** Reduction in the blood volume and transfusion.

| Animals | Blood volume | Average body wt. (kg) | Total Blood Volume (ml) |
|---|---|---|---|

| | (ml/ kg) | | |
|---|---|---|---|
| Cattle | 55 | 300 | 16500 |
| Goat | 66 | 20 | 1320 |
| Sheep | 66 | 35 | 2310 |
| Dog | 86 | 25 | 2150 |
| Cat | 55 | 5 | 275 |
| Pig | 65 | 60 | 3900 |
| Horse | 76 | 450 | 34200 |
| Monkey (Rhesus) | 54 | 8 | 432 |
| Rabbit | 56 | 4 | 224 |
| Guinea pig | 75 | 1.2 | 90 |
| Ferret | 75 | 2 | 150 |

### Blood groups

Every species has specific cell surface antigens on its RBC, which differ, leading to the development of the blood groups in animals (Thiagarajan et al., 2021). In animals, there is a combination of blood factors leading to the terminology of the Blood grouping system rather than blood groups (Table 2).

**Table 2.** Combination of blood factors leading to the terminology of the Blood grouping system rather than blood groups in animals

| Animals | Blood volume (ml/ kg) | Average body weight (kg) |
|---|---|---|
| Cattle | 11 | A, B, C, F, J, L, M, R, S, T, Z |
| Sheep | 7 | A, B, C, D, M, R, X |
| Goat | 5 | A, B, C, M, J |
| Horse | 8 | A, C, D, K, P, Q, U, T |
| Pig | 11 | A-O, C, F, G, H, I, J, K, L, N, O |
| | 15 | |
| Dog | 9 | DAE1.1, 1.2, 3, 4, 5, 6, 7, 8, Dal antigen |
| Cat | 4 | A, B, AB, Mik antigen |
| Chicken | 13 | A, B, C, D, E, H, I, J, K, L, N, P, R |

### Blood typing

It is a technique by which the surface antigen of the erythrocytes can be identified (Ji W et al., 2020). The principle of all veterinary blood typing methods is a visible hemagglutination reaction between patient RBC surface antigens and known reagent monoclonal or polyclonal antisera. It works well to screen the blood donors of the animals before cross-matching and transfusion (Aravindh and Jacob, 2021). They are determined in the laboratory, and even blood-typing kits like card-based agglutination assay, immunochromatographic cartridge, and gel column diffuse assay are available in the market.

A card-based agglutination assay, an immune-chromatographic cartridge, and a gel column diffusion assay are all commercially available blood typing kits (Khan and Sharma 2021). Antisera are lyophilized and placed in reaction wells on blood typing cards. Positive and negative control wells are included on the dog cards, while an auto control well is included on the cat cards. The availability of blood typing reagents for extended blood typing is limited (Li and Guo 2022). The procedure is simple, and the results can be obtained in less than 2 minutes without the use of any additional equipment. The auto control well on the cat typing card, as well as separate cards for dogs, provides for auto-agglutination testing. Auto-agglutination resembles a positive reaction and may make correct typing impossible (Malla, 2023). The immune chromatographic kits use a plastic cartridge device and take around 2 minutes to complete. Simple preparation of a cell suspension and manipulation of the device to appropriately position the response strip in the suspension are all that is required for testing. By using capillary action, erythrocytes can migrate up the membrane (Wang et al., 2022). The antibody impregnated in the strip traps erythrocytes that are positive for the antigen in question, resulting in a visible line. Erythrocytes that do not have the antigen do not create a line and pass through the antibody. The strip is also impregnated with control material, which must read positive in order for the test to be valid (Alonzo et al., 2022).

### Crossmatch

Cross-matching reveals the serological compatibility or incompatibility between donor and recipient (Sidhu and Shah 2020). Blood typing tests reveal the blood group antigens on the red blood cell surface. However, cross-matching reveals the serological compatibility or incompatibility between donor and recipient. The major crossmatching uses the crossmatching of the donor's erythrocyte with the recipient serum, whereas the minor matching is just the reverse (Qiu et al., 2023). The end reaction to being noticed is hemolysis and agglutination. There are several in-house cross-matching tests, like Alvedia, Rapid Vet H Major for both feline and canine species. Since cats possess antigens against the blood type they lack, mismatching is more common and often fatal. Therefore, cross-matching must be done in cats for every successful transfusion (Humm and Chan, 2020).

### Major cross-match test

It searches for alloantibodies in the recipient's plasma against donor cells, whereas the minor cross-match test looks for alloantibodies in the donor's plasma against the recipient's RBCs (Khan and Sharma, 2021). The following is a simple major and minor cross-match protocol.

i. Centrifuge (1000 x g or 3400 rpm) donor blood from an EDTA vial (purple top) or citrated vial (blue top).
ii. Washing RBCs: Resuspend 0.25 mL of RBCs in 2 to 4 mL of saline; centrifuge for 1 min, remove supernatant, and repeat the procedure twice; remove supernatant (Solomon, 2020).
iii. Resuspend 0.1 to 0.2 mL of RBCs in approximately 4.8 mL of saline to obtain a 2% to 4% RBC solution.
iv. In 3 tubes identified as "Major," "Minor," and "Control," add the following:

| | Major cross-match | Minor cross-match | Control Patient |
|---|---|---|---|
| Recipient | 2 drops plasma | 1 drop RBC solution | 1 drop patient RBC solution + 2 drops patient plasma |
| Donor | 1 drop RBC solution | 2 drops plasma | 1 drop donor RBC solution + 2 drops donor plasma |

v. 2 drops plasma Incubate tubes for 15 min at 37°C.
vi. Centrifuge tubes for 15 s.
vii. Reading results: Note plasma color and record any hemolysis. Then gently resuspend the red cell button in the overlying plasma layer, noting the presence of agglutinating clumps (Spada, et al 2020). Next, place a drop of re-suspended RBCs on a slide, apply a coverslip, and read at 10X and 40X. If the crossmatch is compatible, the RBCs should be individually distributed. Hemolysis (compared to control) or agglutination is seen with an incompatible cross-match (Kretsch et al., 2023).

viii. Rouleaux, a physiological plasma-related phenomenon, may sometimes be observed. In order to distinguish this from agglutination, centrifuge the tubes again for 15 s, remove the serum, and add 2 drops of saline; then centrifuge the tubes once more and reexamine the RBC suspensions (Skrajewski-Schuler, 2023).

## Selection of a donor

### Canine

Donors should be typed and screened for general health and for endemic infectious diseases (Jones, 2020). The donor selected for blood collection should be an adult (2-8 years), healthy, weighing more than 30 kg, with a PCV 40% for dogs and or more, fully vaccinated, and free of various diseases such as heartworm infection, tick-borne diseases (*Ehrlichia canis, Babesia, Borrelia burgdorferi, Rickettsia rickettsii*), and brucellosis. Ideally, the donor should have taut neck skin that permits easy access to the jugular vein (Saluja et al., 2022). Moreover, dogs that have thick skin (Rottweilers) or skin folds on the neck (Bassett hound, Mastiffs) are less preferred than long-necked dogs (Greyhounds). The ideal donor should have a good temperament, fit in condition, and no previous history of transfusion or pregnancy. Regular blood donors should be sufficiently tractable to allow donation with either manual restraint or light sedation, especially if they are client-owned (Khan and Sharma, 2021). Blood can be collected from an uncooperative dog using sedation or general anesthesia, but regular blood donors should be sufficiently tractable to allow donation with either manual restraint or light sedation. The commonly used sedatives for canine transfusion are shown in Box 1 (Guillaumin and Kofron, 2023). Bacteremia-prone dogs should not be utilized as donors. Wounds, abscesses, surgical implants, widespread skin lesions, advanced periodontal disease, and diarrhea are examples of these. Blood should also not be collected from dogs whose collection sites have been affected by pyoderma (Nafie et al., 2023). Dogs with immune-mediated illnesses, cancer, organ failure, and other systemic conditions should not donate blood because of the possibility of undesirable stress on the donor and detrimental consequences on blood quality. Heartworm prophylaxis is required for donor dogs residing in heartworm-endemic areas, although it is debatable whether these treatments should be administered right before the donation (Smith-Blackmore, 2021). Flea treatments may be given to donor dogs regularly, although this is not recommended right before donation. Donors should not be on any drug therapy because of the potential for negative effects on the recipient and blood quality. The donors who donate regularly should receive a well-balanced, high-performance diet that may be supplemented twice weekly with oral ferrous sulfate if the donor is bled every 4 to 6 weeks (GUPTA, 2024).

### Feline

A blood donor must be large (>4 kg) and non-obese, have a calm disposition, and be between the ages of 1 and 8 years (preferably 1 to 5 years), should be healthy (indoor, fully vaccinated cats are preferred), and clinically sound (Ghosh, 2021). In practice, this necessitates several (initial and ongoing) assessments: Thorough clinical examinations and a thorough donor history should be obtained; Haematology (complete blood count) and biochemistry (urea, creatinine, total protein/albumin/globulin, ALT, ALP, blood glucose, Na, K, Cl) should be confirmed to be normal. The donor cat should be checked for blood-borne infectious illnesses (FeLV-, FIV-, and Haemoplasma-negative important; Bartonella screening) (Mesa-Sanchez et al., 2021). Before each donation, the donor's Packed Cell Volume (PCV) should be assessed, and donors with approximately 35% are considered ideal donors. Before each donation, the donor's blood pressure should be normal (120-180 mmHg). Low blood pressure, which can be aggravated by anesthesia and blood donation, can be associated with occult heart disease and other disorders (Meng and Arendt, 2021). To rule out occult heart disease, all cats should have an echocardiogram conducted before donation. Feline blood donors should have a pleasant temperament for simple handling and confinement, but it is more vital that they do not get stressed or sad. The more pleasurable the experience, the more relaxed and cooperative feline donors will be throughout future donation visits (Taylor et al., 2024). Feline pheromone diffusers or sprays, the use of the donors' own blankets, and a peaceful, relaxing setting can improve the quality of the visit while also promoting a relaxed donation process for the donors (Martín-Santana et al., 2021). Sedation of feline blood donors is now widely acknowledged as a prerequisite for blood collection, implying that temperament is solely examined to safely provide sedation. Feline blood donor health assessments to be performed before each blood collection (Vascellari et al., 2022).

## Anticoagulants

The two anticoagulants used for both administration and storage are Citrate-Phosphate-Dextrose-Adenine (CPDA-1) and Acid-Citrate-Dextrose (ACD). Citrate is present in the solutions used to collect blood and acts as an anticoagulant by binding calcium (Hess and D'Alessandro, 2022). These preservatives help red blood cells (RBCs) maintain viability during storage by supporting their glycolytic energy metabolism, including adenosine triphosphate (ATP) synthesis. Since CPDA-1 maintains higher levels of 2,3-disphosphoglycerate (2,3-DPG) and ATP in collected blood, it is considered a better anticoagulant (Bujok et al., 2022). Blood can be stored in the CPDA-1 system for approximately 35 days, while blood stored with ACD typically lasts for 21 days. For every 7 mL of blood, 1 mL of anticoagulant (either CPDA-1 or ACD) can be used. Heparin is not usually preferred for blood transfusions because it enhances antithrombin activity, leading to inactivation of thrombin, although 5 U per mL of blood is sufficient (Downey et al.,2020). The shelf life of CPDA is 28 days; however, adding SAGM (saline, adenine, glucose, mannitol) extends the shelf life to 42 days.

### Blood collection

### Open system

It refers to the system where the microbial-free environment is not guaranteed, and so the shelf life of blood is spontaneously reduced. It is preferred in cats since only a small amount of blood is generally transfused and can be collected by syringe (Taylor et al., 2021).

### Closed system

In this system, the sterility of the blood is maintained. This is suitable for the processing and storage of blood and blood products. It holds well in the case of canines (Abrams et al., 2022).

### Volume of blood to be administered

The amount of blood to be transfused depends on the clinical status of the recipient, but rules of thumb are available. For acute hemorrhagic anemia, the volume of blood lost should be estimated, and a combination of isotonic, polyionic fluids or isotonic saline and whole blood or packed red cells should be administered (Chohan and Davidow, 2024). The intent is to fully restore blood volume and ensure that the hematocrit is sufficient to meet the needs of the animal— it does not need to be restored immediately to pre-hemorrhage levels. For normovolemic anemia, and for hypovolemic anemia after restoration of circulating blood volume, the volume of transfusion can be calculated as:

Transfusion volume (mL) = Body weight of recipient (kg) × 80 mL/kg × [(desired recipient PCV – actual recipient PCV)/donor PCV]

where 80 mL/kg is the normal circulating blood volume (i.e., the dilution space of the transfused red cells)

- The median volume of whole blood transfused to horses with hemorrhagic or hemolytic anemia in one study was 15 mL/ kg BW with a range of 5 to 26 mL/kg (Divers et al., 2022).
- Healthy, adult donors can provide up to 20% of their blood volume at one time.

### Blood collection procedure

The donor is positioned in lateral recumbency on the blood donation table, and the venipuncture site (jugular vein) is clipped and prepared with surgical scrub to minimize the chances of bacterial contamination (Bernadette, 2020). A local anesthetic cream can be applied.

- The donor is allowed to settle down and secured properly on a lateral recumbency.
- The jugular vein is punctured with a needle provided with the bag.
- The progress of blood collection is monitored via the blood collection monitor (Patelet al., 2021).
- Once the desired amount is collected, the blood line is re-clamped close to the needle and the needle is removed from the donor.
- Pressure is applied digitally or with a pressure wrap on the venipuncture site until haemostasis is achieved (Palmer, 2022).
- The collected bag is labelled with the date of collection, product type, donor PCV (or Hb), blood group, donor identification, and date of expiry.

### Blood administration to the recipient

Blood should be transfused, preferably using a commercial blood infusion set with an in-line microfilter (Figure 4). A long (85 cm) blood infusion set with a dripping chamber and a short infusion set for small dogs to connect with syringes are available (Frost, 2020). Microfilters with 170 µm pores are commonly used to remove clots and larger red cell and platelet aggregates. Finer filters with 40 µm pores will remove most platelets and microaggregates but tend to clog after 100 ml. Sufficient gravity flow is necessary for easy administration (Hadde and Chen, 2021). The preferred route of transfusion is slow intravenous, but sometimes intramedullary (or intraosseous) infusion at the trochanteric fossa (or other sites) may be used when no venous access can be obtained, while intraperitoneal administration is not recommended because absorption time is delayed and RBCs can be damaged in the peritoneal cavity (Wu et al., 2022). The initial infusion rate should be approximately 0.25 ml/kg for the first 30 minutes, after which it can be increased if no reactions occur. The entire volume should be administered within 4 hours to prevent functional loss or bacterial growth. Blood is transfused using a commercially available blood infusion set with an in-line microfilter (Baillargeon and Mace, 2023). A long (85 cm) blood infusion set with a dripping chamber is preferred. Clots and larger red cell and platelet aggregates are routinely removed using microfilters with 170 µm pores. Most platelets and microaggregates are removed with finer filters with 40 µm pores. Concurrent administration of fluids other than normal saline should be avoided to prevent erythrocyte lysis or coagulation (Bacal et al., 2021). Therefore, during transfusion, fluids containing calcium or glucose, as well as those that are hypotonic or hypertonic, should not be administered through the same intravenous line. Food should also not be provided during a transfusion (Raval et al., 2022).

## Blood Banks

The demand for animal blood is fast-growing through the years as there is increased pet adoption. Facilitates the effective use of blood in the recipients and also avoids several cross-reactions

- It provides convenient access to blood and also relieves the suffering of the animals (Rinwa et al, 2024).
- It gives immediate action in finding a correct match for the animal without any further delay.

The enormous advancement in the veterinary field has seen researchers developing blood banks for pets. The first canine-to-canine blood transfusion was done as early as the year 1665 (Aravindh and Jacob, 2021). Since then, whole blood and blood products have been used to treat many diseases and also for surgery in veterinary medicine. In the year 2007, a successful blood bank was established in the United Kingdom. In India, it has gained importance at the local, regional, and national levels due to the need for blood during various emergencies (Mammen et al., 2021). India's first blood bank for dogs was started by the Tamil Nadu University of Veterinary and Animal Sciences (TANUVAS). They further developed a mobile app called Blood4Pet to provide continuous blood to the needy pets. This app can connect the client with the resource person and significantly contributes to saving the life of the needy pet at an economical cost (Tauseef et al., 2024).

## Conclusion

Transfusion medicine is a vital, life-saving practice in veterinary care for critically ill animals. Although it carries certain risks, evidence-based screening, matching, and administration protocols greatly reduce complications. It is essential to monitor each transfusion carefully. Future directions should aim at refining compatibility testing, improving blood storage, and increasing the availability of veterinary blood banks.

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