OPEN ACCESS

Haya: The Saudi Journal of Life Sciences

Abbreviated Key Title: Haya Saudi J Life Sci
ISSN 2415-623X (Print) | ISSN 2415-6221 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Review Article

Pasteurella multocida in Veterinary Medicine Emerging Resistance, Vaccination Challenges, and Control Approaches

Haider Ali[1], Muhammad Waseem[1], Abdul Khaliq[2], Muhammad Salman[1]*, Muhammad Abdullah Saad[1], Muhammad Asad Bashir[1], Muhammad Mahboob Ishaq[1], Awais Hameed[3]

[1]Faculty of Veterinary Sciences, Cholistan University of Veterinary and Animal Sciences, Bahawalpur, Pakistan
[2]Department of Allied Health Sciences, University of Health Sciences, Lahore, Pakistan
[3]Department of Bioinformatics and Biotechnology, Government College University, Faisalabad, Pakistan

DOI: https://doi.org/10.36348/sjls.2025.v10i08.010 | **Received:** 26.07.2025 | **Accepted:** 23.09.2025 | **Published:** 25.09.2025

***Corresponding author:** Muhammad Salman
Faculty of Veterinary Sciences, Cholistan University of Veterinary and Animal Sciences, Bahawalpur, Pakistan

Abstract

Pasteurella multocida is a Gram-negative bacterium of global veterinary importance, associated with a wide spectrum of diseases in livestock, poultry, rabbits, and companion animals. It can exist as a harmless commensal in the upper respiratory tract, but under favorable conditions acts as a potent pathogen, causing hemorrhagic septicemia in cattle and buffalo, progressive atrophic rhinitis in pigs, fowl cholera in poultry, and snuffles in rabbits. Pathogenesis is mediated by virulence factors including the polysaccharide capsule, lipopolysaccharides, adhesins, iron acquisition systems, biofilm formation, and the P. multocida toxin (PMT), which collectively promote colonization, immune evasion, and systemic infection. Advances in taxonomy and classification, from serotyping to multilocus sequence typing and whole-genome sequencing, have improved epidemiological understanding, though distinguishing virulent from commensal strains remains challenging. Antimicrobial resistance (AMR) is an emerging concern, particularly against tetracyclines and macrolides, threatening treatment efficacy in food-producing animals and increasing zoonotic risks. Vaccination remains central to control, with bacterins, toxoids, and autogenous vaccines widely used, though their cross-serotype protection is limited. Future perspectives highlight the need for next-generation vaccines, genomic surveillance, CRISPR-based diagnostics, and alternative therapies such as phage treatment. Integration of vaccination, antimicrobial stewardship, and biosecurity measures within a One Health framework will be essential to reduce disease burden, protect animal productivity, and safeguard public health.

Keywords: *Pasteurella multocida*, veterinary medicine, pathogenesis, host tropism, antimicrobial resistance, vaccines, zoonosis, biosecurity, One Health.

INTRODUCTION

Pasteurella multocida is a Gram-negative, facultative anaerobic coccobacillus that has been a significant bacterium in the field of veterinary microbiology, due to its importance as both a pathogen and commensal organism (Calderón Bernal *et al.,* 2022). For example, *P. multocida* was first recognized during research into fowl cholera and hemorrhagic septicemia in the late 1800's. As *P. multocida* was the agent causing these diseases and important causes of mortality in both poultry and livestock, it gained unknown notoriety as an important disease agent in this context (Chen *et al.,* 2023). As bacteriological techniques improved, researchers confirmed that *P. multocida* was the causative agent of a number of diseases of animals, but furthermore, found that it could exist in the upper respiratory tract of innocuous healthy animals without causing clinical signs (Cid *et al.,* 2019). Being both a harmless resident and a life-threatening invader makes *P. multocida* an important component of research into veterinary infectious disease and a continuous worry for animal health (Christensen *et al.,* 2004).

The wide host potentiality and variety of pathogens that *P. multocida* encompasses give it both clinical and economic significances. For instance, it plays a major role in Hemorrhagic Septicemia in cattle and buffalo, the acute form of which is invariably fatal and often endemic in tropical and subtropical regions (Cuevas *et al.,* 2020; Fegan *et al.,* 2024). The loss in productivity due to the various methods of controlling

hemorrhagic septicemia (like immunization) along with death losses are economic impacts (OIE,2021). In pigs, it takes part in the multifactorial disease processes in atrophic rhinitis and respiratory disease that decrease performance and carcass quality (Ferreira *et al.,* 2016). It causes fowl cholera in poultry, where these may complicate peracute (and fatal) outbreaks or chronic, insidious infections affecting egg production and general flock health (Deeb *et al.,* 1990; Gharib Mombeni *et al.,* 2021).

Snuffles have been defined as chronic upper respiratory disease in rabbits chiefly associated with *P. multocida*. The socioeconomic burden that this disease imposes leads to commercial implications restricting the efficiency of the rabbit industry and its use as a laboratory animal (Girma *et al.,* 2023; Gluecks *et al.,* 2017). Pet animals, specifically cats and dogs, are gaily carrying *P. multocida* within their flora and frequently suffer from opportunistic infections and diseases, which include respiratory disease, bite wounded infections, and rarely a very serious systemic disease (Hurtado *et al.,* 2018). Most likely, however, the zoonotic potential of this organism has been well established, with even documented cases of human infections due to bites and scratches from companion animals (Hurtado *et al.,* 2020; Kamal *et al.,* 2017).

This review will provide an up-to-date and comprehensive assessment of *P. multocida* infection in veterinary medicine, focusing on taxonomy, virulence factors, host susceptibility, and clinical manifestations (Lan *et al.,* 2019). It is equally essential to investigate how their pathogenesis can guide diagnostic efforts and modern strategies for disease prevention and control (Liang *et al.,* 2023). Historical viewpoints will be woven into the contemporary literature to illustrate the enduring and complicating facets of *P. multocida* , with particular implications for clinical and epidemiological endeavors into the future (Lin *et al.,* 2024).

Taxonomy and Classification

Over the last hundred years, taxonomy and classification of *Pasteurella multocida* has evolved significantly, due in part to developments in phenotypic methods and the use of molecular biology-based approaches which increases our understanding of this diverse pathogen (Liu *et al.,* 2019). Previously, classification of strains of *P. multocida* was entirely based on biochemical characteristics and the antigenic properties that led to designating biovars and serotypes (Oh *et al.,* 2019). Currently, there are five groupings or capsular serotypes (A, B, D, E and F) which are based, in part, on differences in capsular polysaccharide. It is worth noting that groupings (serogroups) reflect many factors beyond taxonomic, such as host ranges and disease considerations. For example, group A strains are often associated with fowl cholera in poultry and respiratory disease in rabbits and ruminants (Peng *et al.,* 2019). Serogroup B is associated with hemorrhagic septicemia in both cattle and buffalo, particularly in Asia and Africa (OIE, 2021). Group D strains are involved in progressive atrophic rhinitis of pigs, and group E strains are more commonly associated with hemorrhagic septicaemia in African cattle. Finally, group F strains, although seldom recognized, are primarily obtained from avian hosts. The serotyping exercise can still only give limited insight into epidemiologically useful information but it does not encompass the breadth of genetic diversity and virulence information associated with the species.

Following the incorporation of molecular approches into veterinary microbiology, the taxonomy of *P. multocida*, was able to advance to higher genomic resolutions. Multi-locus sequence typing (MLST) provides an example of such advances with the ability to designate isolates to a successive sequence type (ST) based upon the allelic profiles of housekeeping genes (Puspitasari *et al.,* 2019). MLST has been especially useful for providing insights into transmission pathways, comparing isolates across geographic areas, and separating endemic from epidemic strains of the organism during investigations into outbreaks (Griffin *et al.,* 2010). While PFGE requires considerably more effort to, it does also give more high-resolution discrimination of isolates as it pertained to epidemiological investigation. Also, in recent years WGS had expanded our taxonomic understanding of *P. multocida* while also contributing vast amounts of knowledge on virulence genes, antimicrobial resistance determinants, and phylogenetic associations of this organism as well (Wilkie *et al.,* 2012). Although these high-throughput genomic approaches suggest that pathogenic potential is not evenly distributed across capsular types or STs, it appears that pathogenic potential is more complex than this and is contingent on many interactions among the genetic background of *P. multocida* , the host, and environmental conditions (Rímac *et al.,* 2017).

As a large barrier in the taxonomy of *P. multocida* is that many healthy animals have the organism colonising their upper respiratory tract and show no clinical signs, indicating that *P. multocida* is overall considered a commensal organism (Snyder & Credille, 2020). The strains that cause disease, however, typically express virulence factors such as the toxA gene that encodes dermonecrotic toxin in swine or genes for capsule biosynthesis in hemorrhagic septicemia strains that allow these strains to invade the tissue and produce immunological evasion (Harper *et al.,* 2006). The capacity to distinguish causative/downstream strains from commensals has important implications for diagnostic, surveillance, and vaccine development (Wang *et al.,* 2024).

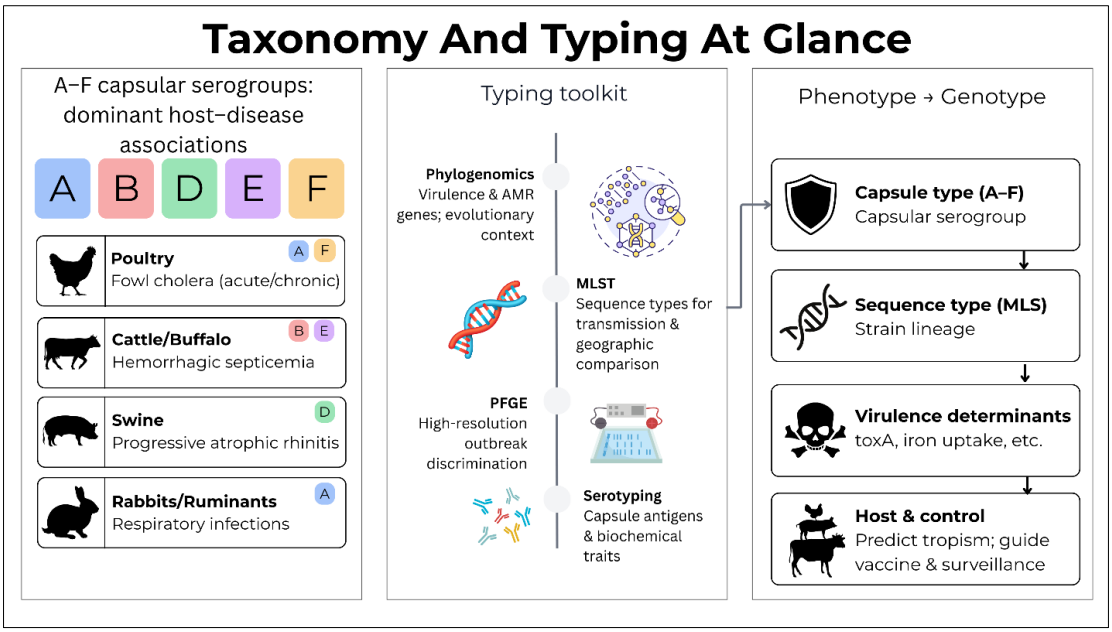

Figure 1: "Capsular serogroups of P. multocida and their dominant host–disease associations (A); evolution of typing approaches from phenotypic to genomic (B); integration of serotyping, MLST, and WGS for epidemiology and vaccine design (C)."

The interplay between taxonomy and host specificity underscores the clinical importance of precise classification. Certain serogroups and sequence types display strong host tropisms—serogroup B in bovines, or serogroups A and F in poultry supporting the notion that genetic background influences disease manifestation (Maes *et al.,* 2008). By utilizing both traditional serotyping and modern genomic analysis, the skills of veterinary microbiologists include better understanding of strain diversity patterns, disease development, and effective control of infection. Modern classification methods can be utilized for both identification of microorganisms and predictive modeling to manage animal health and develop intervention strategies (Wang *et al.,* 2022).

Pathogenesis Mechanisms

Pathogenicity is attributed to several factors, including virulence factors that aid in colonization of mucosal surfaces (*Pasteurella multocida*), immune evasion by the host, and systemic disease caused by many animal hosts. Certain virulence factors are specific to strains and serogroups, which can account for the differences in clinical syndromes among species (Harper *et al.,* 2006; Yehia *et al.,* 2023). A polysaccharide capsule is a true virulence factor in this armory, and it is the basis for categorizing *P. multocida* as essentially containing capsular serogroups.' The polysaccharide capsule is essential for immune evasion in *P. multocida* as it shields the organism from complement-dependent lysis, preventing neutrophil or macrophage-mediated phagocytosis, and provides them with an opportunity to survive in the systemic circulation that is crucial for host destruction and causes septicemia associated with hemorrhagic bacterial infections in cattle and buffalo. Notably, serogroups B and E often linked to acute systemic infections—possess particularly robust capsule-mediated defenses, whereas serogroups A and D are more commonly associated with localized respiratory diseases (Deeb *et al.,* 1990; Kubatzky, 2022).

Among the most potent virulence factors is the *Pasteurella multocida* toxin (PMT), a 146-kDa protein predominantly produced by serogroup D strains. PMT acts intracellularly by deamidating G-proteins, leading to the activation of Rho-family GTPases. This disrupts actin cytoskeleton organization, induces osteoclast differentiation, and amplifies proinflammatory responses (Townsend *et al.,* 2001). In swine, PMT is the principal agent of progressive atrophic rhinitis, driving nasal turbinate atrophy, facial deformities, and reduced weight gain. The pathophysiological consequences of PMT underscore its value as a diagnostic marker and a strategic target for vaccine development in porcine health management (GR, 1955).

Lipopolysaccharide (LPS), a key outer membrane component, plays multiple roles in pathogenesis, including resistance to complement, promotion of endotoxic shock, and facilitation of bacterial adhesion. Structural modifications in the LPS core and O-antigen can impact serum resistant, with some strains exhibiting an enhanced ability to escape complement-mediated killing. Due to its ability to induce disseminated intravascular coagulation, LPS can cause septicemic forms like hemorrhagic septicemia, which in turn causes fast death in susceptible animals (Wilkie *et al.,* 2012).

Attachment to the host's tissue is a crucial step in the pathogenesis of P. multocidum. There are many different types of adhesins, including filamentous hemagglutinin proteins, outer membrane proteins and type IV fimbriae that attach to respiratory epithelial cells (Zhao *et al.,* 2024). The characteristics that are important for attachment and colonization, as well as infection after settlement in poultry, rabbits, and companion animals.... The persistence and recurrence of fowl cholera are largely caused by adhesion and attachment in avian species, regardless of treatment or vaccination (Griffin *et al.,* 2010).

Iron acquisition systems are also very important to *P. multocida 's* virulence, and especially to systemic spread. In the iron-poor environment of the host, *P. multocida* will employ siderophore-independent mechanisms such as transferrin- and hemoglobin-binding proteins, and TonB dependent transporters to utilize iron from host proteins ((Prescott *et al.,* 2022). This capability is especially important in hemorrhagic septicemia, where rapid replication in the bloodstream hinges on efficient iron uptake. The ability to acquire iron from bovine transferrin has been identified as a key factor in the explosive disease progression in cattle and buffalo (Ziagham *et al.,* 2024).

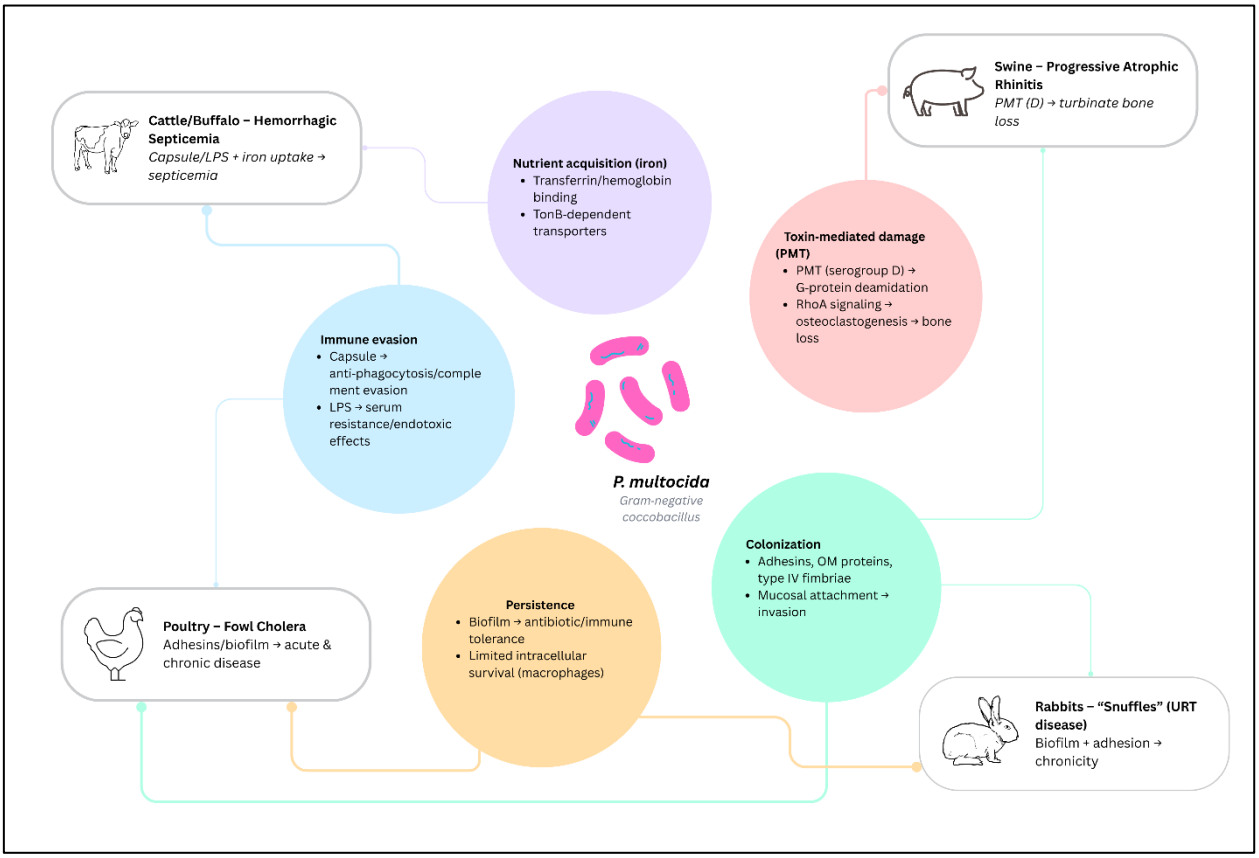

Figure 2: "Integrated model of P. multocida virulence: immune evasion (capsule, LPS), colonization (adhesins/fimbriae), nutrient acquisition (iron uptake), toxin-mediated damage (PMT), biofilm persistence, and limited intracellular survival; host-specific disease links highlighted."

Beyond these classical virulence traits, biofilm formation has emerged as a significant contributor to the persistence and chronicity of *P. multocida infections*. Biofilms confer resistance to antibiotics and immune effectors by creating a protective matrix around bacterial communities. In rabbits with snuffles, biofilm-mediated colonization of the upper respiratory tract is believed to underlie recurrent infections and poor treatment outcomes (Deeb *et al.,* 1990). Similarly, in poultry, biofilms may support long-term carriage and relapse of fowl cholera, even in vaccinated flocks.

Though *P. multocida is* not traditionally regarded as a facultative intracellular pathogen, increasing evidence suggests it can persist within host cells, particularly macrophages. Intracellular survival is facilitated by the capsule and LPS, which shield the bacterium from phagolysosomal killing. The information presented above suggests that this intracellular niche may facilitate the evasion of immune detection by the pathogen, allow for systemic infection to occur, and maintain latent carriage in asymptomatic hosts (Harper *et al.,* 2006).

In summary, *P. multocida 's* pathogenicity is likely due to its multiple virulence mechanisms that may work in tandem. Capsule and LPS can facilitate immunoevasion and septicemia, PMT can mediate bone

resorption and inflammation in pigs, adhesins can influence colonization and invasion, iron uptake systems can provide energy for bacterial replication during systemic disease, and biofilms and intracellular persistence offer improved resistance to treatment and microorganisms. These complex and diverse factors indicate broad host range and wide variety of clinical presentations for this organism, further emphasising studies of its pathogenesis that may inform vaccine development and diagnostics and therapeutics in veterinary science (Rímac *et al.,* 2017).

Host Tropism and Disease Manifestations

The remarkable host tropism of *Pasteurella multocida* is evident in the very broad range of disease syndromes that it can produce in different animal species. These clinical outcomes are dependent not only on the virulence factors of the bacterium, but also on host specific factors including immune competence, physiological state, and environmental stresses. The interaction between pathogen and host is critical to understanding the widespread veterinary and economic importance of *P. multocida* , which remains an endemic problem in most livestock and associated animals across the globe (Harper *et al.,* 2006). In cattle and buffalo, *P. multocida* is best known as the etiological agent of hemorrhagic septicemia, a fulminant, septicemic disease with high mortality in tropical and sub-tropical areas, most notably across Asia and Africa (OIE, 2021). Outbreaks usually occur during or directly after rainy seasons or periods of environmental stress that lead to exposure of animals to infection. Affected animals often present with pyrexia, submandibular edema, respiratory distress, and rapid deterioration, with death commonly occurring within 24 to 48 hours. Pathological findings include widespread serosanguinous effusions, edema, and hemorrhages, consistent with endotoxin-mediated vascular damage. The disease disrupts subsistence farming by reducing draft power and productivity, while emergency vaccination efforts and livestock losses contribute to significant economic burdens. Additionally, *P. multocida* is involved in the bovine respiratory disease complex commonly termed shipping fever where it acts synergistically with *Mannheimia haemolytica*, *Histophilus somni*, and respiratory viruses. In these cases, the bacterium invades the lower respiratory tract after viral priming, causing fibrinous bronchopneumonia, especially in stressed or transported animals. Though typically less acute than hemorrhagic septicemia, shipping fever imposes chronic economic costs through reduced weight gain, prolonged recovery, and increased antibiotic usage in feedlot systems (Kubatzky, 2022).

In swine, *P. multocida* contributes to two economically important diseases: progressive atrophic rhinitis and enzootic pneumonia. Progressive atrophic rhinitis, largely caused by toxigenic serogroup D strains producing *P. multocida* toxin (PMT), affects young pigs by inducing turbinate bone resorption. Clinical signs include sneezing, nasal discharge, epistaxis, facial deformities, and growth retardation. Microscopic examination typically reveals turbinate atrophy, inflammation, and osteoclastic activity (Maddock *et al.,* 2025). This disease significantly impairs feed efficiency and carcass quality, leading to production losses. *P. multocida* is also a key player in enzootic pneumonia, usually in co-infection with *Mycoplasma hyopneumoniae*. In this multifactorial condition, *P. multocida* colonizes the damaged respiratory epithelium, contributing to bronchopneumonia marked by cranioventral lung consolidation and mucopurulent exudate. Chronic respiratory illness in intensive swine operations undermines growth performance and necessitates extended antimicrobial regimens (Maes *et al.,* 2008).

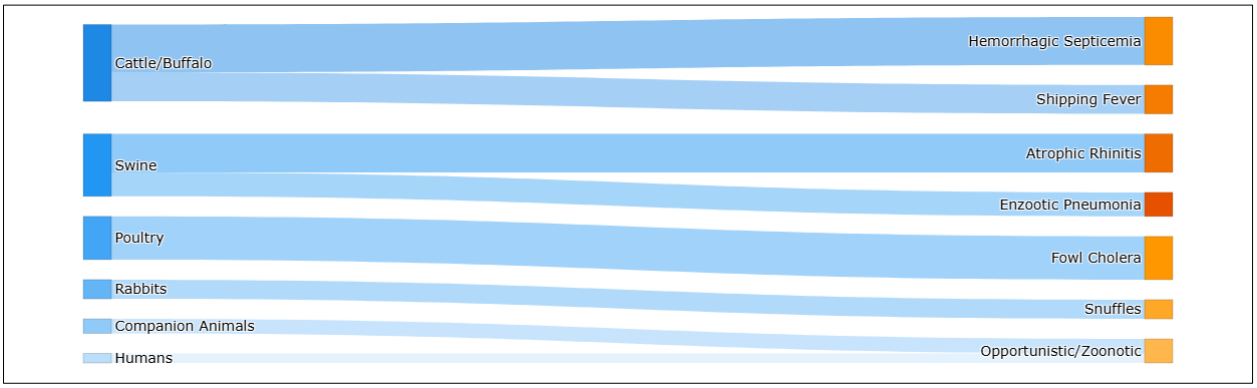

Figure 3: "Host–pathogen landscape of P. multocida, linking animal species to dominant clinical syndromes and production impacts."

Poultry are highly susceptible to fowl cholera, one of the most significant bacterial diseases in commercial flocks. Caused predominantly by serogroup A strains, fowl cholera may present acutely, with sudden mortality, septicemia, and cyanosis, or as a chronic infection involving localized abscesses, sinusitis, arthritis, and reproductive tract involvement. Lesions often include fibrinous pericarditis, perihepatitis, and air sacculitis (Michael *et al.,* 2012). The persistence of *P. multocida in* poultry populations is partly due to its

ability to form biofilms and establish asymptomatic carrier states, complicating eradication efforts. Recurrent outbreaks result in decreased egg production, compromised flock longevity, and heavy reliance on vaccination and antimicrobial control, posing a particularly steep burden in resource-limited poultry systems (Christensen *et al.,* 2004).

In rabbits, *P. multocida* is the primary pathogen responsible for "snuffles," a chronic upper respiratory tract disease prevalent in commercial rabbitries and laboratory colonies. Infection is often triggered by stress, inadequate ventilation, or poor husbandry, allowing virulent strains to colonize the nasal passages. Affected rabbits show mucopurulent nasal discharge, sneezing, and conjunctivitis; in advanced stages, the infection may spread to the middle ear, lungs, or bloodstream. Histologically, snuffles is characterized by suppurative rhinitis, sinusitis, and bronchopneumonia (Deeb *et al.,* 1990). Biofilm formation and intracellular persistence are thought to contribute to the relapsing nature of infection, which hampers treatment success. The disease adversely affects reproductive performance, diminishes the scientific validity of experimental animals, and causes substantial losses in commercial breeding.

P. multocida is usually a commensal organism in companion animals (dogs and cats) and exists in the oropharynx and upper respiratory tract. It can act as an opportunist when there is immune compromise or co-infection. *P. multocida* is associated with upper respiratory infections in cats including rhinitis, conjunctivitis, and pneumonia. In dogs, it is often involved in respiratory illness and is also introduced into wounds. A serious zoonotic threat exists with *P. multocida*. Why? The bacterium is frequently transmitted to humans through cat bites and scratches, leading to rapidly progressive cellulitis, abscesses, or septicemia (Michael *et al.,* 2012). In veterinary medicine, clinicians and pet owners must be aware of the potential danger of *P. multocida* in cats when it becomes exacerbated by antimicrobial stewardship.

Ultimately, *P. multocida* displays several traits related to host specificity, as it shows that this organism can be commensal in some hosts and a pathogen in others. *P. multocida* can cause explosive septicemia in ruminants and chronic respiratory disease and toxigenic diseases in porcines. However, the former is more severe. Why? At times, this pathogen can cause severe epizootic infections in poultry, chronic upper respiratory disease in rabbits, and a range of zooplankton infestations in companion animals. All animal species face significant clinical and economic consequences, including mortality, morbidity, reduced production, and public health.

Diagnosis and Laboratory Identification

Accurate diagnosis and laboratory confirmation of infections with *Pasteurella multocida* is important to differentiate true pathological situations from asymptomatic carriers for the purposes of implementing control measures in different hosts. Recent molecular diagnostics provide improved accuracy, but conventional methods are important, particularly for fieldwork, and in countries with limited resources, where accurate and cheap, rapid methods are important (Harper *et al.,* 2006).

Microscopic examination of clinical specimens such as blood, nasal exudates, or tissue impressions can offer immediate, though non-specific, clues. *P. multocida* typically appears as small Gram-negative coccobacilli demonstrating bipolar staining often described as a "safety-pin" morphology when visualized using Giemsa or Wright's stain (Oehler *et al.,* 2009). Culture on blood agar yields smooth, non-hemolytic colonies that are oxidase- and catalase-positive, indole-producing, and non-motile. These classical biochemical traits provide a presumptive identification and remain useful in primary diagnostic workflows. However, phenotypic similarities with other *Pasteurellaceae* family members can complicate interpretation, particularly in mixed infections or in healthy carriers.

Molecular diagnostics have revolutionized *P. multocida identification* by enhancing sensitivity, specificity, and turnaround time. Polymerase chain reaction (PCR) assays targeting species-specific genes, such as *kmt1*, allow rapid confirmation of suspected isolates (Petruzzi *et al.,* 2017). Multiplex PCR techniques further enable simultaneous capsular typing by amplifying capsule biosynthesis genes (e.g., *capA*, *capB*, *capD*, *capE*, and *capF*), thus facilitating strain differentiation and providing essential epidemiological data (Townsend *et al.,* 2001). Quantitative PCR (qPCR) adds another layer of diagnostic sophistication by enabling direct detection and quantification of bacterial DNA from clinical samples, often bypassing the need for culture. This is particularly advantageous during outbreaks or in vaccinated populations, where rapid differentiation between vaccine-derived and wild-type strains is necessary.

Serotyping and virulence gene profiling play an important role in determining the pathogenic potential of a strain. While indirect hemagglutination serotyping of capsular serogroup remains a viable method, PCR-based capsular typing methods are favored because of their fast-turnaround and reproducibility. To differentiate between pathogenic and commensal strains of *P. multocida,* it is useful to identify the presence of virulence-associated genes such as toxA (PMT), hgbA and also cDNA sequenced to code for outer membrane proteins. This can be applied to companion animals, including those that are commonly found in healthy dogs and cats, and may also contract opportunistic infections when exposed to such bacteria (Wilkie *et al.,* 2012).

Diagnostic modalities exhibit both positive and negative aspects of each diagnostic technique. Besides speed and specificity, molecular diagnostics has several advantages over traditional cultures or biochemical tests in terms of anti-microbial susceptibility testing and vaccine strain development. Best practices in diagnostic medicine are best applied from a veterinary perspective through the combination of phenotypic identification and molecular identification assays. The identification, treatment options, and disease monitoring and control programs in various species are all aided by this.

Antimicrobial Resistance Patterns

Antimicrobial resistance (AMR) in *Pasteurella multocida* has become a growing concern in veterinary medicine, mirroring the extensive use of antimicrobials in animal agriculture and the organism's capacity to acquire and disseminate resistance determinants. Historically, *P. multocida has* been considered largely susceptible to a broad spectrum of antibiotics. Penicillin and other β-lactams have traditionally served as the mainstays of therapy, particularly in companion animals and for systemic infections in livestock (Wilkie *et al.,* 2012). In food-producing animals, tetracyclines and macrolides valued for their oral bioavailability and suitability for metaphylaxis through feed or water have been widely employed. For small animals, penicillin and amoxicillin-clavulanate remain effective first-line agents, especially for treating bite-related infections (Weber *et al.,* 1984). However, mounting reports of antimicrobial resistance among isolates from cattle, pigs, and poultry are raising serious concerns over treatment efficacy and the narrowing of therapeutic options.

Geographic variation in resistance profiles is evident, yet certain trends remain consistent, particularly in regions with high-intensity animal farming. Tetracycline resistance is the most frequently reported, reflecting its long-standing use for both therapeutic and non-therapeutic purposes (Michael *et al.,* 2012). Increasing resistance to macrolides, including tilmicosin and tylosin, is also emerging, especially in isolates associated with bovine and swine respiratory disease. Although resistance to penicillin and other β-lactams remains comparatively rare, sporadic cases of reduced susceptibility often mediated by β-lactamase production have begun to surface, underscoring the adaptive potential of *P. multocida* under antimicrobial pressure (San Millan & MacLean, 2017).

At the genetic level, resistance in *P. multocida is* mediated by a variety of well-characterized mechanisms. Typically, tetracycline resistance is conferred by tet genes that code for efflux pumps, or ribosomal protection proteins. Resistance for macrolides is correlated with erm genes which cause the 23S rRNA to become methylated, decreasing drug affinity (Kubatzky, 2022). In contrast, β-lactam resistance has been less prevalent and is associated with bla genes coding for β-lactamases that hydrolyze penicillins and similar drugs. Such resistance determinants are often located on mobile genetic elements such as integrative and conjugative elements (ICE) and plasmids which allows for horizontal transfer in the Pasteurellaceae family and via wider microbial communities especially in shared agricultural environments (Townsend *et al.,* 2001). Changing the selective pressure exerted by repeated antimicrobial usage largely mass prophylactic use, poor dosing, and antibiotic use for growth promotion contributes substantially to the emergence and continued presence of resistant strains of *P. multocida.* Animal infections can become increasingly difficult to treat and with the organism being associated with domestic pets and able to be transmitted to humans through bites or scratches, the zoonotic implications are concerning. Finally, the increasing importance of AMR in *P. multocida clearly* highlights the importance of antimicrobial stewardship and basic resistance detection, and the potential use of alternative control strategies such as vaccination and better husbandry to decrease the need for antimicrobials used in veterinary medicine.

Vaccines and Control Strategies

The increasing problem of antimicrobial resistance in *Pasteurella multocida* infections has generated renewed interest in vaccination, and non-antimicrobial control measures as part of the prevention of disease in veterinary medicine. Vaccination against *P. multocida* has a long history, with inactivated whole-cell bacterins being one of the first measures employed for the protection of livestock. These bacterins are still used widely in cattle, buffalo, pigs, and poultry; the recognition that they offered moderate protection against homologous strains by stimulating a systemic antibody response and contributed to lessen the incidence of septicemia and bacteremia (OIE, 2021). Bacterins are often functional, but the amount of cross-protection between different capsular serogroups is poor. A vaccine developed from one serotype may not confer adequate immunity against others a significant limitation in regions where multiple serogroups co-circulate. As a result, strain selection becomes a critical factor in vaccine formulation and regional disease control programs (Tang *et al.,* 2009).

Toxoid vaccines represent a more targeted approach, particularly in the prevention of progressive atrophic rhinitis in swine. Detoxified preparations of *P. multocida* toxin (PMT), often used in combination with *Bordetella bronchiseptica* antigens, are administered to piglets to reduce nasal turbinate atrophy and prevent the facial deformities associated with the disease (GR, 1955). These toxoid-based vaccines aim to neutralize the primary pathogenic mechanism of toxigenic strains, thereby limiting clinical disease and economic losses in intensive pig production systems.

In recent years, subunit and recombinant vaccines have gained research attention, offering a promising alternative to traditional bacterins. These

formulations typically include purified outer membrane proteins, adhesins, or capsule-associated antigens, sometimes delivered as recombinant proteins or DNA vaccines (Tang *et al.,* 2009). The goal is to elicit broader cross-protective immunity that extends across serotypes and is less dependent on whole-cell antigens. While these experimental vaccines have shown encouraging results in controlled studies, challenges related to production scalability, cost-effectiveness, and field performance have slowed their commercial uptake.

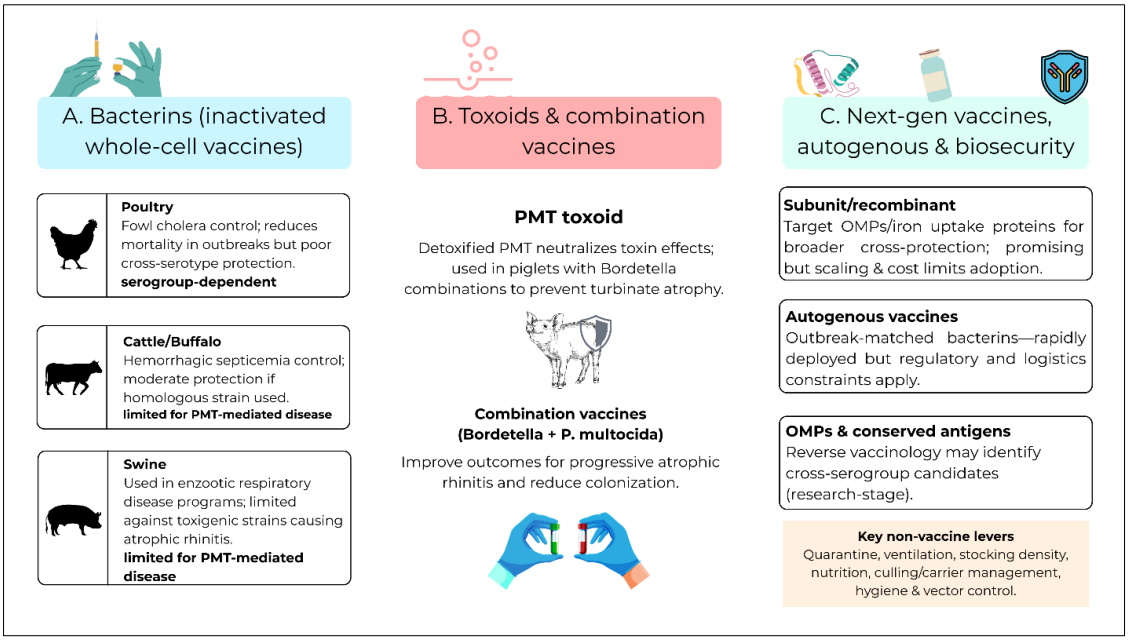

Figure 4: "Current vaccine modalities and their coverage limitations, with integrated biosecurity measures for durable control."

In situations where rapid protection is needed such as during outbreaks of hemorrhagic septicemia autogenous vaccines are sometimes employed. These are bacterins formulated from the specific strain isolated during the outbreak, providing a precise antigenic match for the affected herd or flock. Though useful in emergency settings, autogenous vaccines are constrained by the time required for preparation and the need for regulatory compliance, limiting their feasibility to endemic areas with recurrent disease episodes (Maes *et al.,* 2008).

Nevertheless, vaccination alone cannot fully control *P. multocida infections* without concurrent implementation of sound management and biosecurity practices. It is important to resolve environmental stressors-principally overcrowding, poor air quality, and nutrient imbalances-to reduce susceptibility of the host. A reduction in transmission risk requires the implementation of quarantine policies, strict sanitation procedures, and ongoing vector control measures. The identification and management of animals carrying carryover infections through culling or segregation is a crucial advantage to vaccination in species like poultry and rabbits, where chronic diarrheal carriers are prevalent.

At last a successful control program requires integration, which includes targeted vaccination, responsible use of antimicrobials, and integrated implementation of biosecurity measures. The implementation of a comprehensive, system-level approach is essential for both improving animal health and productivity and decreasing the selective pressure that leads to antibiotic resistance. The collaborative approach adheres to the One Health principles, promoting sustainable livestock farming while managing risks to both animals and humans. Define.

Zoonotic Considerations

The zoonotic outcomes of *Pasteurella multocida* highlight the intricate and multifaceted connection between animal and human health within the One Health system. While *P. multocida* is generally a harmless commensal flora present in the upper respiratory tract and oral cavity of feline, canines or other companion animals, it may be an important pathogen in humans when transmitted through bites, scratches, or close contact. When cats are transmitted, bites can be a problem due to their ability to cause deep puncture wounds that allow bacteria to enter subcutaneous tissues, leading ultimately to cellulitis, abscesses, or septic arthritis with rapid progression (Weber *et al.,* 1984). Also, it is possible for severe or untreated infections caused by *P. multocida* to result in systemic infections such as septicemia, endocarditis, or meningitis (usually in patients with immunosuppression). Despite the infrequent and severe impact of *P. multocida* invasion, it underscores the necessity for prompt identification and treatment, typically with a -lactam antibiotic.

In this regard, the key aspects of human and animal health can be integrated into their response framework emphasizing the need to include relevant surveillance and intervention measures and communication mechanisms that cross both livestock and human health sectors.

Effective approaches to mitigating the zoonotic risk of *P. multocida* are multifaceted in nature. In veterinary contexts, reducing the prevalence of this pathogen within the community involves three avenues: routine health assessments and monitoring, appropriate vaccinations, and prudent veterinary prescriptions for antimicrobials in pets. Education in public health contexts can aid in reducing zoonotic risks by teaching responsible pet ownership, safe handling, and timely treatment for bites or scratches. The convergence of these approaches can be utilized to manage the incidence of *P. multocida* in the community, which aligns with the One Health Principles and promotes animal welfare by minimizing danger to vulnerable individuals.

Future Perspectives

The research on *Pasteurella multocida* in the future must incorporate advanced biotechnological techniques and epidemiological knowledge regarding its dual role as a commensal and pathogen. The primary concern will be genomics surveillance, utilizing whole-genome sequencing and molecular epidemiology to conduct advanced analysis of strain diversity, antimicrobial resistance genes, and virulence gene content. With the ability to create global genomic databases, researchers can provide early warning signs of new pathogenic lineages and their potential identification at the origin of an outbreak, as well as establish control or eradication programs for specific areas by analyzing serogroup distribution across different regions. Moreover, scientists will have the chance to explore the evolutionary mechanisms behind the commensal pathogen transition that can be utilized for better risk assessment.

The need for vaccine development, especially for broad-spectrum or even universal vaccines that provide protection against multiple serogroups and host species, remains a priority. Advances in reverse vaccinology and epitope mapping are facilitating the identification of conserved antigens, such as outer membrane proteins and iron acquisition systems, which could form the basis of next-generation vaccines. Coupled with novel delivery platforms such as nanoparticle-based formulations and mucosal vaccines, these innovations may overcome the limitations of current bacterins and toxoids, offering durable and cross-protective immunity in diverse production systems.

Equally promising are novel diagnostic technologies that leverage gene-editing tools. CRISPR-based diagnostics, such as CRISPR-Cas12 and Cas13 platforms, have the potential to deliver rapid, point-of-care detection of *P. multocida* with high specificity, even in mixed microbial communities or vaccinated herds. These systems could revolutionize outbreak management by enabling early identification of pathogenic strains before clinical disease becomes widespread.

Antimicrobial therapies are being evaluated as a potential alternative to traditional treatments for infections caused by *P. multocida*. As an illustration, bacteriophage therapy is being studied to specifically target targeted bacteria, such as *P. multocida* in order to preserve their commensal microbiome. Small-molecule inhibitors of virulence factors, which aim at capsule biosynthesis, PMT activity, or iron acquisition pathways, could be used to decrease toxicity and pathogenicity. The use of strategies that decrease virulence factors could limit the impact of microbial toxicity without causing significant selective pressure for bacterial resistance. Our overall objective is to manage diseases effectively through sustainable means, given the rise in antimicrobial resistance. The upcoming strategies outline a future direction agenda that incorporates genomics, biotechnology and new therapeutics.

CONCLUSION

The canonical name *Pasteurella multocida* continues to be one of the most significant bacteria relevant to veterinary medicine, due to its variety of taxa, large host range, and host-specific ability to cause disease that can range from acute septicemia in cattle and buffalo to chronic respiratory disease in swine, poultry, rabbits, and companion animals. Pathogenicity is mediated by multiple virulence factors, such as capsule, lipopolysaccharide, adhesins, and the effective *P. multocida* toxin, and hosts have evolved specific diseases by associating numerous virulence factors in their pathogenesis. Improved diagnostic capabilities, including culture and biochemical assays, as well as new molecular approaches, such as PCR and whole genome sequencing, have improved our capacity to detect pathogenic strains of *P. multocida*, but the distinction between commensal and virulent strains still remains elusive. The emergence of antimicrobial resistance, particularly against tetracyclines and macrolides, underscores the need for prudent antimicrobial stewardship and the strengthening of vaccination programs. Current vaccines, including bacterins, toxoids, and autogenous preparations, provide partial protection, but limitations in cross-serotype coverage highlight the need for next-generation, broadly protective formulations. Effective control must extend beyond vaccination to include rigorous biosecurity, herd management, and surveillance. Looking ahead, the integration of genomic epidemiology, innovative vaccine platforms, and novel therapeutic approaches such as phage therapy will be essential. Sustained collaboration between veterinary and public health sectors within a One Health framework will ultimately be pivotal in mitigating the impact of *P. multocida* on

animal productivity, zoonotic risk, and global food security.

REFERENCES

- Calderón Bernal, J. M., Fernández, A., Arnal, J. L., Sanz Tejero, C., Fernández-Garayzábal, J. F., Vela, A. I., & Cid, D. (2022). Molecular epidemiology of Pasteurella multocida associated with bovine respiratory disease outbreaks. *Animals*, *13*(1), 75.
- Chen, N., Jiang, D., Liu, Y., Zhang, Z., Zhou, Y., & Zhu, Z. (2023). Preparation of Escherichia coli ghost of anchoring bovine Pasteurella multocida OmpH and its immunoprotective effect. *BMC Vet Res*, *19*(1), 192. https://doi.org/10.1186/s12917-023-03743-9
- Christensen, H., Angen, Ø., Olsen, J. E., & Bisgaard, M. (2004). Revised description and classification of atypical isolates of Pasteurella multocida from bovine lungs based on genotypic characterization to include variants previously classified as biovar 2 of Pasteurella canis and Pasteurella avium. *Microbiology*, *150*(6), 1757-1767.
- Cid, D., Fernández-Garayzábal, J. F., Pinto, C., Domínguez, L., & Vela, A. I. (2019). Antimicrobial susceptibility of Pasteurella multocida isolated from sheep and pigs in Spain - Short communication. *Acta Vet Hung*, *67*(4), 489-498. https://doi.org/10.1556/004.2019.048
- Cuevas, I., Carbonero, A., Cano, D., García-Bocanegra, I., Amaro, M. Á., & Borge, C. (2020). Antimicrobial resistance of Pasteurella multocida type B isolates associated with acute septicemia in pigs and cattle in Spain. *BMC Veterinary Research*, *16*(1), 222.
- Deeb, B. J., DiGIACOMO, R. F., Bernard, B., & Silbernagel, S. (1990). Pasteurella multocida and Bordetella bronchiseptica infections in rabbits. *Journal of Clinical Microbiology*, *28*(1), 70-75.
- Fegan, J. E., Waeckerlin, R. C., Tesfaw, L., Islam, E. A., Deresse, G., Dufera, D., Assefa, E., Woldemedhin, W., Legesse, A., Akalu, M., Bayissa, B., Nguyen, Q. H., Ng, D., Ahn, S. K., Schryvers, A. B., Tefera, T. A., Moraes, T. F., & Gray-Owen, S. D. (2024). Developing a PmSLP3-based vaccine formulation that provides robust long-lasting protection against hemorrhagic septicemia-causing serogroup B and E strains of Pasteurella multocida in cattle. *Front Immunol*, *15*, 1392681. https://doi.org/10.3389/fimmu.2024.1392681
- Ferreira, T. S., Moreno, L. Z., Felizardo, M. R., de Gobbi, D. D., Filsner, P. H., de Moura Gomes, V. T., Moreno, M., & Moreno, A. M. (2016). Pheno- and genotypic characterization of Pasteurella multocida isolated from cats, dogs and rabbits from Brazil. *Comp Immunol Microbiol Infect Dis*, *45*, 48-52. https://doi.org/10.1016/j.cimid.2016.02.004
- Gharib Mombeni, E., Gharibi, D., Ghorbanpoor, M., Jabbari, A. R., & Cid, D. (2021). Toxigenic and non-toxigenic Pasteurella multocida genotypes, based on capsular, LPS, and virulence profile typing, associated with pneumonic pasteurellosis in Iran. *Vet Microbiol*, *257*, 109077. https://doi.org/10.1016/j.vetmic.2021.109077
- Girma, S., Getachew, L., Beyene, A., Tegegne, D. T., Tesgera, T., Debelo, M., Debano, J., Teshome, D., Abdisa, K., Wirtu, A., Tekle, M., Abera, B., Tafess, K., Dandecha, M., Abayneh, T., Getachew, B., Tufa, T. B., & Tolera, T. S. (2023). Identification of serotypes of Mannheimia haemolytica and Pasteurella multocida from pneumonic cases of sheep and goats and their antimicrobial sensitivity profiles in Borana and Arsi zones, Ethiopia. *Sci Rep*, *13*(1), 9008. https://doi.org/10.1038/s41598-023-36026-2
- Gluecks, I. V., Bethe, A., Younan, M., & Ewers, C. (2017). Molecular study on Pasteurella multocida and Mannheimia granulomatis from Kenyan Camels (Camelus dromedarius). *BMC Vet Res*, *13*(1), 265. https://doi.org/10.1186/s12917-017-1189-y
- GR, C. (1955). Studies on Pasteurella multocida. I. A hemagglutination test for the identification of serological types. *American Journal of Veterinary Research*, *16*(60), 481-484.
- Griffin, D., Chengappa, M., Kuszak, J., & McVey, D. S. (2010). Bacterial pathogens of the bovine respiratory disease complex. *Veterinary Clinics: Food Animal Practice*, *26*(2), 381-394.
- Harper, M., Boyce, J. D., & Adler, B. (2006). Pasteurella multocida pathogenesis: 125 years after Pasteur. *FEMS microbiology letters*, *265*(1), 1-10.
- Hurtado, R., Carhuaricra, D., Soares, S., Viana, M. V. C., Azevedo, V., Maturrano, L., & Aburjaile, F. (2018). Pan-genomic approach shows insight of genetic divergence and pathogenic-adaptation of Pasteurella multocida. *Gene*, *670*, 193-206. https://doi.org/10.1016/j.gene.2018.05.084
- Hurtado, R., Maturrano, L., Azevedo, V., & Aburjaile, F. (2020). Pathogenomics insights for understanding Pasteurella multocida adaptation. *Int J Med Microbiol*, *310*(4), 151417. https://doi.org/10.1016/j.ijmm.2020.151417
- Kamal, N. M., Zamri-Saad, M., Masarudin, M. J., & Othman, S. (2017). Interaction between Pasteurella multocida B:2 and its derivatives with bovine aortic endothelial cell (BAEC). *BMC Vet Res*, *13*(1), 186. https://doi.org/10.1186/s12917-017-1109-1
- Kubatzky, K. F. (2022). Pasteurella multocida toxin–lessons learned from a mitogenic toxin. *Frontiers in Immunology*, *13*, 1058905.
- Lan, W., Xiao, X., Jiang, Y., Jiang, L., Zhao, X., Yu, Z., Zhu, B., Li, C., Bian, L., & Wang, Z. (2019). Comparative pharmacokinetics of florfenicol in healthy and Pasteurella multocida-infected Gaoyou ducks. *J Vet Pharmacol Ther*, *42*(3), 355-360. https://doi.org/10.1111/jvp.12761
- Liang, W., Xiao, H., Chen, J. Y., Chang, Y. F., Cao, S. J., Wen, Y. P., Wu, R., Du, S. Y., Yan, Q. G., Huang, X. B., & Zhao, Q. (2023). Immunogenicity

and protective efficacy of a multi-epitope recombinant toxin antigen of Pasteurella multocida against virulent challenge in mice. *Vaccine*, *41*(14), 2387-2396. https://doi.org/10.1016/j.vaccine.2023.02.070

- Lin, L., Bi, H., Yang, J., Shang, Y., Lv, Q., Zhang, D., Huang, X., Zhao, M., Wang, F., Hua, L., Chen, H., Wu, B., Wang, X., & Peng, Z. (2024). Pasteurella multocida infection induces blood-brain barrier disruption by decreasing tight junctions and adherens junctions between neighbored brain microvascular endothelial cells. *Vet Res*, *55*(1), 104. https://doi.org/10.1186/s13567-024-01351-5
- Liu, Q., Hu, Y., Li, P., & Kong, Q. (2019). Identification of Fur in Pasteurella multocida and the Potential of Its Mutant as an Attenuated Live Vaccine. *Front Vet Sci*, *6*, 5. https://doi.org/10.3389/fvets.2019.00005
- Maddock, K. J., Stenger, B. L., Pecoraro, H. L., Roberts, J. C., Loy, J. D., & Webb, B. T. (2025). Hemorrhagic septicemia in the United States: molecular characterization of isolates and comparison to a global collection. *Journal of Veterinary Diagnostic Investigation*, 10406387251342528.
- Maes, D., Segales, J., Meyns, T., Sibila, M., Pieters, M., & Haesebrouck, F. (2008). Control of Mycoplasma hyopneumoniae infections in pigs. *Veterinary microbiology*, *126*(4), 297-309.
- Michael, G. B., Kadlec, K., Sweeney, M. T., Brzuszkiewicz, E., Liesegang, H., Daniel, R., Murray, R. W., Watts, J. L., & Schwarz, S. (2012). ICE Pmu1, an integrative conjugative element (ICE) of Pasteurella multocida: analysis of the regions that comprise 12 antimicrobial resistance genes. *Journal of antimicrobial chemotherapy*, *67*(1), 84-90.
- Oehler, R. L., Velez, A. P., Mizrachi, M., Lamarche, J., & Gompf, S. (2009). Bite-related and septic syndromes caused by cats and dogs. *The Lancet infectious diseases*, *9*(7), 439-447.
- Oh, Y. H., Moon, D. C., Lee, Y. J., Hyun, B. H., & Lim, S. K. (2019). Genetic and phenotypic characterization of tetracycline-resistant Pasteurella multocida isolated from pigs. *Vet Microbiol*, *233*, 159-163. https://doi.org/10.1016/j.vetmic.2019.05.001
- Peng, Z., Wang, X., Zhou, R., Chen, H., Wilson, B. A., & Wu, B. (2019). Pasteurella multocida: Genotypes and Genomics. *Microbiol Mol Biol Rev*, *83*(4). https://doi.org/10.1128/mmbr.00014-19
- Petruzzi, B., Briggs, R. E., Swords, W. E., De Castro, C., Molinaro, A., & Inzana, T. J. (2017). Capsular polysaccharide interferes with biofilm formation by Pasteurella multocida serogroup A. *MBio*, *8*(6), 10.1128/mbio. 01843-01817.
- Prescott, J. F., MacInnes, J. I., Van Immerseel, F., Boyce, J. D., Rycroft, A. N., & Vázquez-Boland, J. A. (2022). *Pathogenesis of bacterial infections in animals*. Wiley Online Library.
- Puspitasari, Y., Annas, S., Adza-Rina, M. N., & Zamri-Saad, M. (2019). In-vitro phagocytosis and intracellular killing of Pasteurella multocida B:2 by phagocytic cells of buffaloes. *Microb Pathog*, *131*, 170-174. https://doi.org/10.1016/j.micpath.2019.04.012
- Rímac, R., Luna, L., Hurtado, R., Rosadio, R., & Maturrano, L. (2017). Detection and genetic characterization of Pasteurella multocida from alpaca (Vicugna pacos) pneumonia cases. *Trop Anim Health Prod*, *49*(6), 1325-1328. https://doi.org/10.1007/s11250-017-1309-5
- San Millan, A., & MacLean, R. C. (2017). Fitness costs of plasmids: a limit to plasmid transmission. *Microbiology spectrum*, *5*(5), 10.1128/microbiolspec. mtbp-0016-2017.
- Snyder, E., & Credille, B. (2020). Mannheimia haemolytica and Pasteurella multocida in Bovine Respiratory Disease: How Are They Changing in Response to Efforts to Control Them? *Vet Clin North Am Food Anim Pract*, *36*(2), 253-268. https://doi.org/10.1016/j.cvfa.2020.02.001
- Tang, X., Zhao, Z., Hu, J., Wu, B., Cai, X., He, Q., & Chen, H. (2009). Isolation, antimicrobial resistance, and virulence genes of Pasteurella multocida strains from swine in China. *Journal of Clinical Microbiology*, *47*(4), 951-958.
- Townsend, K. M., Boyce, J. D., Chung, J. Y., Frost, A. J., & Adler, B. (2001). Genetic organization of Pasteurella multocida cap loci and development of a multiplex capsular PCR typing system. *Journal of Clinical Microbiology*, *39*(3), 924-929.
- Wang, J., Sun, S., Chen, D., Gao, C., Sang, L., & Xie, X. (2024). Pathogenic and genomic characterization of rabbit-sourced Pasteurella multocida serogroup F isolates recovered from dead rabbits with respiratory disease. *Microbiol Spectr*, *12*(4), e0365423. https://doi.org/10.1128/spectrum.03654-23
- Wang, J., Sun, S., Chen, Y., Chen, D., Sang, L., & Xie, X. (2022). Pathogenic and genomic characterisation of a rabbit sourced Pasteurella multocida serogroup F isolate s4. *BMC Vet Res*, *18*(1), 288. https://doi.org/10.1186/s12917-022-03381-7
- Weber, D. J., Wolfson, J. S., Swartz, M. N., & Hooper, D. C. (1984). Pasteurella multocida infections: report of 34 cases and review of the literature. *Medicine*, *63*(3), 133-154.
- Wilkie, I. W., Harper, M., Boyce, J. D., & Adler, B. (2012). Pasteurella multocida: diseases and pathogenesis. *Pasteurella multocida: Molecular Biology, Toxins and Infection*, 1-22.
- Yehia, N., Salem, H. M., Mahmmod, Y., Said, D., Samir, M., Mawgod, S. A., Sorour, H. K., AbdelRahman, M. A. A., Selim, S., Saad, A. M., El-Saadony, M. T., El-Meihy, R. M., Abd El-Hack, M. E., El-Tarabily, K. A., & Zanaty, A. M. (2023). Common viral and bacterial avian respiratory

infections: an updated review. *Poult Sci*, *102*(5), 102553. https://doi.org/10.1016/j.psj.2023.102553

- Zhao, G., Tang, Y., Dan, R., Xie, M., Zhang, T., Li, P., He, F., Li, N., & Peng, Y. (2024). Pasteurella multocida activates apoptosis via the FAK-AKT-FOXO1 axis to cause pulmonary integrity loss, bacteremia, and eventually a cytokine storm. *Vet Res*, *55*(1), 46. https://doi.org/10.1186/s13567-024-01298-7
- Ziagham, A., Gharibi, D., Mosallanejad, B., & Avizeh, R. (2024). Molecular characterization of Pasteurella multocida from cats and antibiotic sensitivity of the isolates. *Vet Med Sci*, *10*(3), e1424. https://doi.org/10.1002/vms3.1424