Volume 3, Issue 4, 2025

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

PATHOBIOLOGY AND CONTROL OF AVIAN MYCOPLASMOSIS: TRENDS IN DIAGNOSIS, TREATMENT, AND PREVENTION

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DOI: https://doi.org/10.5281/zenodo.15709270

Keywords
Mycoplasmosis, Avian, Vaccine, Pathobiology, Poultry Industry

Article History
Received on 13 May 2025
Accepted on 13 June 2025
Published on 21 June 2025

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Abstract

Avian mycoplasmosis, which is mainly caused by Mycoplasma gallisepticum (M G) and Mycoplasma synoviae (M S), remains an economical and health load to the poultry industry of the world. The review gives an in-depth coverage of the pathobiology and management of avian mycoplasmosis and gives current updates in diagnosis, treatment and prevention strategies of avian mycoplasmosis. We address the etiology and taxonomy of the most important pathogenic Mycoplasma species, bring to light their genetic details and their strategy of infection, not to mention adhesion, immune escape and cyto-toxicity. The section on epidemiology reports on prevalence in different parts of the world, route of transmission of the disease (vertical and horizontal), risk factors that influence disease spread in commercial as well as backyard flocks. Clinical presentations, lesions and how subclinical infections and carrier conditions are more critical are discussed as well. The review is a critical assessment of the modern diagnostic methods, starting with traditional culture and serologic methods through to more complex molecular-based methods, such as the polymerase chain reaction (PCR) or loop-mediated isothermal amplification (LAMP) assays, and their relative performance and applicability in the field. We enter into antimicrobial therapy, briefly describing some commonly encountered antibiotics, and discussing the rising problem of antimicrobial resistance and how it occurs and develops. In addition, the paper explores the current mechanisms of vaccination, like the live attenuated and inactivated vaccines and how newer technology, including the recombinant, subunit, and DNA vaccine, can be constructively applied. More importantly, the role of high biosecurity and management, such as environmental control, segregation of flocks, and surveillance programs are discussed, which is a fundamental element when dealing with an effective disease control. Lastly, we discuss some of the challenges that lay ahead, as diagnostic complexities of mixed infections, opportunity of genomics and proteomics in future vaccine development, the need of global surveillance and harmonization of policies and the overall perspectives of One Health. The proposed synthesis will provide the veterinarians, researchers and poultry producers with integrated measures that can curb the effect of avian mycoplasmosis, ensure the safety of the poultry industry as a source of food security in the world.

Volume 3, Issue 4, 2025

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

INTRODUCTION

1.1 Background and Significance of Poultry Production

Poultry production is one of the most dynamic and rapidly expanding sectors of agriculture worldwide. It serves as a major source of affordable animal protein, contributing significantly to food security, rural development, and national economies (Etim et al., 2024). According to the Food and Agriculture Organization (FAO), global poultry meat production has reached over 130 million metric tons annually, with developing countries playing an increasingly important role in meeting growing consumer demand. In regions such as South Asia and Sub-Saharan Africa, poultry farming not only provides income and employment opportunities but also plays a critical role in women's empowerment and nutritional supplementation (Shi et al., 2021).

However, the intensification of poultry farming has been paralleled by an increase in disease incidence, particularly infectious diseases that compromise productivity, health, and profitability. Respiratory diseases, in particular, have emerged as a major constraint to efficient poultry production, leading to severe economic losses through decreased growth rates, reduced egg production, increased mortality, and costs associated with treatment and prevention (Alsayed et al., 2023).

1.2 Overview of Avian Mycoplasmosis

Among the respiratory pathogens affecting poultry, avian mycoplasmosis stands out as a significant and persistent challenge globally. It is a chronic disease complex primarily caused by bacteria of the genus Mycoplasma, characterized by respiratory distress, synovitis, decreased feed efficiency, and overall poor flock performance (Xuan et al., 2020). The disease manifests in various forms depending on the species involved, the age of the birds, environmental conditions, and co-infections with other pathogens such as Escherichia coli or viral agents like Infectious Bronchitis Virus (IBV) (Qi et al., 2023).

The economic impact of avian mycoplasmosis is multifaceted, involving both direct losses such as increased mortality and decreased egg and meat production, as well as indirect losses including culling of infected flocks, trade restrictions, and increased use of veterinary antimicrobials (Qian et al., 2023).

1.3 Key Causative Agents

Table 1: The genus Mycoplasma comprises over 20 species that can infect birds; however, only a few are of major veterinary concern in poultry (Pai et al., 2023):

Species	Common Name	Primary Clinical Manifestations	Host Range
Mycoplasma gallisepticum	MG	Chronic respiratory disease (CRD), sinusitis	Chickens, turkeys, game birds
Mycoplasma synoviae	MS	Infectious synovitis, subclinical respiratory infections	Chickens, turkeys
Mycoplasma meleagridis	MM	Airsacculitis, poor hatchability in turkeys	Turkeys
Mycoplasma iowae	MI	Embryonic mortality, skeletal deformities	Turkeys, chickens (rare)

Among these, Mycoplasma gallisepticum (MG) and Mycoplasma synoviae (MS) are the most significant pathogens in commercial poultry, often causing persistent infections that are difficult to eradicate due to their ability to evade the host immune system and survive in latent forms.

1.4 Purpose and Scope of the Review

Despite extensive efforts to control avian mycoplasmosis, the disease continues to pose substantial challenges to poultry health management. The emergence of antimicrobial resistance, limitations of current vaccines, and difficulties in early diagnosis contribute to the complexity of managing this disease effectively.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

This review aims to provide a comprehensive overview of the pathobiology and control of avian mycoplasmosis, with a particular focus on:

- Recent trends in the epidemiology of Mycoplasma infections
- Advances in diagnostic tools and molecular techniques
- Current treatment approaches and antimicrobial resistance concerns
- Preventive strategies including vaccination and biosecurity measures
- Future directions for research and disease management

By synthesizing the latest scientific findings and practical insights, this article seeks to support veterinarians, researchers, and poultry producers in developing integrated strategies for the effective control of avian mycoplasmosis.

2. Etiology and Taxonomy

2.1 Classification and Taxonomy of Avian Mycoplasmas

Mycoplasmas are wall-less, pleomorphic bacteria that belong to the class **Mollicutes**, within the phylum **Firmicutes**. They are among the smallest self-replicating prokaryotes, distinguished by their lack of a rigid cell wall, which contributes to their intrinsic resistance to beta-lactam antibiotics and their unique filtration properties (Mercer et al., 2019).

Table 2: The taxonomic hierarchy of Mycoplasma species relevant to avian infections is as follows:

Domain:	Bacteria
Phylum:	Firmicutes
Class:	Mollicutes
Order:	Mycoplasmatales
Family:	Mycoplasmataceae
Genus:	Mycoplasma

Within the genus Mycoplasma, over 20 species have been isolated from avian hosts, but only a few are recognized as economically significant pathogens in poultry. These species typically colonize the mucosal surfaces of the respiratory, reproductive, or synovial systems, leading to chronic infections that are difficult to eradicate.

2.2 Key Pathogenic Species

Table 3: Among the Mycoplasma species infecting birds, the following are of major veterinary importance in poultry:

Species	Abbreviation	Primary Disease(s)	Host(s)	Transmission
Mycoplasma gallisepticum	MG	Chronic respiratory disease (CRD), sinusitis	Chickens, turkeys, game birds	Vertical and horizontal
Mycoplasma synoviae	MS	Infectious synovitis, airsacculitis	Chickens, turkeys	Vertical and horizontal
Mycoplasma meleagridis	MM	Airsacculitis, poor hatchability	Turkeys	Primarily vertical
Mycoplasma iowae	MI	Embryonic mortality, reduced hatchability, skeletal issues	Turkeys (primarily)	Vertical

Mycoplasma gallisepticum (MG):

MG is the most pathogenic and economically damaging avian Mycoplasma species. It causes chronic respiratory disease (CRD) in chickens and infectious sinusitis in turkeys. MG is capable of both vertical (egg-mediated) and horizontal (aerosol, direct contact) transmission, making it highly persistent

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ISSN: (e) 3007-1607 (p) 3007-1593

and difficult to eliminate from infected flocks (Tahseen et al., 2019).

Mycoplasma synoviae (MS):
MS typically causes subclinical infections in the upper respiratory tract but can become systemic, leading to infectious synovitis. In co-infections or under stress, MS contributes to airsacculitis and lameness. Like MG, it spreads both vertically and horizontally (Rajamanickam et al., 2021).

Mycoplasma meleagridis (MM):
Primarily affecting turkeys, MM leads to airsacculitis and reproductive issues, including decreased fertility and hatchability. It is predominantly transmitted through eggs (Rotundo et al., 2024).

Mycoplasma iowae (MI):
Also turkey-specific, MI is associated with embryonic mortality and skeletal deformities. Though less common today due to improved hatchery management, it remains a concern in breeder flocks (Trajman et al., 2024).

2.3 Genetic Characteristics and Variability
Avian Mycoplasmas possess small genomes ranging from 600 to 1,000 kilobase pairs, encoding fewer than 1,000 proteins. Their limited biosynthetic capabilities render them dependent on host cells for essential nutrients, contributing to their parasitic lifestyle (Darraj et al., 2021).

Key genetic features include (Tjota et al., 2013)**:**
Lack of cell wall genes: Due to genome reduction, Mycoplasmas lack the genes responsible for cell wall synthesis, which explains their resistance to beta-lactam antibiotics.

High mutation and recombination rates: These facilitate antigenic variation, particularly in surface lipoproteins, allowing the pathogen to evade host immune responses and persist in chronic infections.

Phase variation: Many Mycoplasma species can switch surface antigen expression on and off, aiding immune evasion and complicating vaccine development.

Mobile genetic elements and horizontal gene transfer: Although rare, these contribute to genetic diversity and may influence antimicrobial resistance mechanisms.
Molecular studies using multilocus sequence typing (MLST), random amplified polymorphic DNA (RAPD), and whole-genome sequencing have revealed considerable intraspecies variability, particularly in M. gallisepticum field isolates. Such variability has significant implications for diagnostics, vaccine efficacy, and epidemiological tracing.

3. Epidemiology
3.1 Global Prevalence and Distribution
Avian mycoplasmosis is a globally distributed disease affecting both commercial and backyard poultry operations. The two most prevalent and economically significant species, Mycoplasma gallisepticum (MG) and Mycoplasma synoviae (MS), are endemic in most poultry-producing countries, particularly in regions with intensive farming and inadequate biosecurity.

Developed countries such as the United States, United Kingdom, and parts of the European Union have made considerable progress in reducing prevalence through strict eradication, surveillance, and biosecurity programs. However, sporadic outbreaks still occur, especially in multi-age production systems and backyard flocks (Xuan et al., 2014).

Developing countries, including many in Asia, Africa, and Latin America, report high and persistent prevalence rates due to limited resources for diagnosis and control. The lack of routine surveillance and the frequent use of multi-species farms further facilitate disease maintenance and spread. Recent molecular surveillance studies indicate that MS may be underdiagnosed, often presenting as a co-infection or subclinical carrier state. The true burden of avian mycoplasmosis is therefore likely underestimated, especially in regions with limited diagnostic infrastructure (Yasuda et al., 2012).

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3.2 Transmission Routes

3.2 Transmission Routes of Avian Mycoplasma

The success of Mycoplasma species as persistent and economically significant pathogens in poultry is primarily due to their ability to utilize both **vertical** and **horizontal** modes of transmission, which facilitate rapid and sustained spread within and between flocks.

Vertical Transmission

Vertical transmission occurs when infected breeder hens pass the pathogen directly to their offspring through the egg. This route is particularly significant for Mycoplasma gallisepticum (MG), Mycoplasma synoviae (MS), and Mycoplasma meleagridis (MM), where the infection of the reproductive tract enables the bacterium to be incorporated into the egg yolk, albumen, or shell membranes. Chicks hatched from infected eggs may already be carriers, thereby introducing the pathogen into previously uninfected flocks and perpetuating infection cycles in integrated poultry systems (Masamune et al., 2010).

Horizontal Transmission

Horizontal transmission takes place through direct or indirect contact between infected and susceptible birds. The pathogen is shed via respiratory secretions and can be spread through airborne droplets (aerosols), contaminated equipment, feed, water, and **even** human clothing or footwear, making biosecurity breaches a common source of outbreaks. This route is especially efficient in environments with high stocking densities, poor ventilation, or inadequate hygiene practices, where close contact among birds enhances transmission rates (Zhao et al., 2015).

Both vertical and horizontal transmission routes play complementary roles in the silent persistence and endemic circulation of Mycoplasma in commercial and backyard poultry populations. Additionally, mixed infections with other respiratory pathogens—such as Escherichia coli, Newcastle Disease Virus (NDV), or Infectious Bronchitis Virus (IBV)—can not only intensify clinical manifestations but also promote more efficient horizontal dissemination, complicating diagnosis and control efforts (Zhao et al., 2021).

3.3 Risk Factors and Host Susceptibility

Table 4: Several environmental, managerial, and host-specific factors influence the epidemiology of avian mycoplasmosis:

Risk Factor	Impact
High stocking density	Increases stress and facilitates horizontal transmission
Poor ventilation and hygiene	Promotes respiratory disease outbreaks
Multi-age flock management	Enhances maintenance of infection cycles
Lack of vaccination	Leaves flocks susceptible to primary infection
Immunosuppression (e.g., IBD, stress)	Enhances severity and persistence of infection
Inadequate biosecurity	Allows reintroduction and spread of the pathogen
Co-infection with viruses or E. coli	Leads to more severe clinical outcomes

Host species and age also play a role. Young birds are more susceptible due to immature immune systems, while older birds may act as asymptomatic carriers. Turkeys are particularly sensitive to MG and MM, often exhibiting more severe respiratory distress than chickens.

3.4 Impact on Commercial and Backyard Flocks

The impact of avian mycoplasmosis varies with flock type, management system, and market orientation:

Commercial flocks: In layer and broiler operations, MG and MS infections lead to reduced growth rates, decreased egg production, poor feed conversion, and increased mortality. Breeder flocks face the added threat of vertical transmission, leading to widespread infection in offspring and compromised hatchability (Li et al., 2015).

Backyard and rural poultry: Backyard flocks often serve as reservoirs for Mycoplasma due to poor

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ISSN: (e) 3007-1607 (p) 3007-1593

biosecurity, lack of vaccination, and close proximity to wild birds. Though the economic losses per bird may be lower, the cumulative effect on food security and rural livelihoods can be substantial (Al-Aarag et al., 2019).

Trade implications:
Countries aiming for Mycoplasma-free certification face significant challenges when infected flocks are detected, often resulting in restrictions on the movement and export of live birds and hatching eggs (Chan et al., 2024).

Parameter	Commercial Flocks	Backyard Flocks
Biosecurity	High (ideal), but variable	Low
Surveillance and diagnosis	Routine in large operations	Rare or absent
Vaccination	Often implemented	Rare
Risk of vertical transmission	High in breeders	Moderate (depending on breed sourcing)
Role as reservoir	Lower (if managed well)	High
Economic impact per bird	High	Low per bird, but significant at household level

4. Pathogenesis and Clinical Manifestations

4.1 Mechanisms of Infection

The pathogenicity of avian Mycoplasma species, particularly Mycoplasma gallisepticum (MG) and Mycoplasma synoviae(MS), is closely linked to their unique structural and genetic characteristics. These bacteria lack a cell wall and possess a flexible membrane, allowing them to closely adhere to and invade host epithelial cells, especially in the respiratory and synovial tissues.
Key steps in pathogenesis include (McNally et al., 2023):

Adhesion to host cells: Surface lipoproteins (e.g., GapA, CrmA) mediate tight attachment to the ciliated epithelium of the respiratory tract. This adhesion is crucial for colonization and evasion of mucociliary clearance.

Immune evasion: Antigenic variation in surface proteins allows Mycoplasmas to avoid immune detection. Additionally, phase variation mechanisms help the pathogen modulate expression of virulence factors.

Cytotoxicity and inflammation: MG and MS can induce the release of reactive oxygen species (ROS), hydrogen peroxide, and pro-inflammatory cytokines (e.g., IL-1, IL-6, TNF-α), leading to tissue damage, cilia loss, and impairment of mucosal defenses.

Secondary infections: Damage to the respiratory epithelium predisposes birds to secondary bacterial infections, particularly with E. coli, leading to complicated respiratory disease complexes (Fenhua et al., 2021).

4.2 Disease Progression

4.3 Clinical Manifestations by Species

4.3.1 Mycoplasma gallisepticum (MG)

Mycoplasma gallisepticum is a highly pathogenic species that primarily affects chickens and turkeys:

In Chickens: MG is the causative agent of chronic respiratory disease (CRD), especially in broiler and layer flocks. Clinical signs include nasal discharge, coughing, sneezing, rales, reduced feed intake, and decreased egg production (Xu et al., 2017).

In Turkeys: MG causes infectious sinusitis, which is characterized by pronounced swelling around the infraorbital sinuses, ocular discharge, and respiratory distress.

Complications: Co-infections with Escherichia coli or respiratory viruses such as Infectious Bronchitis Virus (IBV) significantly worsen clinical outcomes, often resulting in severe airsacculitis, pericarditis, and even septicemia. These complications can increase mortality and economic losses (Lee et al., 2013).

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4.3.2 Mycoplasma synoviae (MS)

Mycoplasma synoviae is generally considered less virulent than MG, but its clinical impact can be significant under certain conditions:

Respiratory Form: MS often establishes **subclinical infections in the upper respiratory tract**, particularly in chickens. These infections frequently go unnoticed but contribute to pathogen persistence and spread (Baranzehi et al., 2020).

Systemic Form: Under stress or in the presence of immunosuppression, MS can become systemic and **localize in the synovial membranes**, leading to **infectious synovitis**. This form is characterized by joint swelling, lameness, breast blisters, and reduced mobility, particularly in broilers and breeders.

4.3 Clinical Signs in Different Poultry Species

Species	Pathogen	Primary Clinical Signs
Chickens	MG	Nasal discharge, coughing, rales, conjunctivitis, reduced growth and egg production
Turkeys	MG	Sinus swelling, respiratory distress, ocular discharge
Chickens/Turkeys	MS	Swollen joints, lameness, breast blisters, mild respiratory signs, eggshell deformities
Turkeys	MM/MI	Airsacculitis in embryos and poults, poor hatchability, skeletal deformities

Reproductive Impact: In laying hens, MS has been associated with **eggshell apex abnormalities (EAA)** a condition marked by weak, wrinkled, or misshapen eggshells at the apex, thereby compromising egg integrity, hatchability, and market value (Carreto et al., 2021).

4 Lesions and Pathological Findings

Postmortem examination of birds infected with Mycoplasma species reveals characteristic lesions that vary depending on the specific pathogen and the severity of the disease. In cases of Mycoplasma gallisepticum (MG) infection, the most prominent lesions include cloudy and thickened air sacs, indicative of airsacculitis, as well as inflammation of the trachea and bronchi (tracheitis and bronchitis). In turkeys, MG often causes accumulation of caseous exudate in the infraorbital sinuses, leading to marked facial swelling. In birds suffering from co-infections, especially with E. coli, additional findings such as pericarditis and perihepatitis may be observed, indicating systemic involvement (Narasimhan et al., 2013). Mycoplasma synoviae (MS) primarily affects the synovial joints, where yellowish, fibrinous exudate and thickening of the synovial membranes are commonly noted. These lesions result in joint swelling and lameness, often accompanied by mild airsacculitis. In the case of Mycoplasma meleagridis (MM) and Mycoplasma iowae (MI), which predominantly affect turkeys and embryos, lesions include thickened chorioallantoic membranes in developing embryos, skeletal deformities, and increased late-stage embryo mortality. These findings underscore the broad pathological spectrum of avian mycoplasmosis and its significant impact on both live birds and embryonic development (Zhou et al., 2021).

4.5 Subclinical Infections and Carrier States

A critical aspect of avian mycoplasmosis is the ability of birds to harbor the pathogen without showing overt clinical signs. These asymptomatic carriers act as a major source of infection for other birds, especially in multi-age farms and hatcheries. Stress, poor nutrition, or co-infections may reactivate latent infections, leading to outbreaks. Understanding the subclinical nature and latency of Mycoplasma infections is vital for effective control strategies, as apparent recovery does not equate to pathogen clearance (Huan et al., 2016).

5. Economic Impact

Avian mycoplasmosis poses a significant economic burden to the poultry industry worldwide, affecting both commercial and backyard operations. The impact is multifaceted, involving direct and indirect losses that compromise productivity, profitability, and market access.

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5.1 Direct Losses

The most immediate and visible economic consequence of avian Mycoplasma infections is **direct production losses**. Mortality rates can increase notably, especially when infections are complicated by secondary pathogens or poor management. Infected flocks often suffer from reduced growth rates, poor weight gain in broilers, and decreased egg production in layers and breeders (Casciaro et al., 2019). Chronic respiratory disease caused by Mycoplasma gallisepticum (MG) results in lowered egg numbers and poor egg quality, while Mycoplasma synoviae (MS) can cause lameness and reduced mobility, further diminishing productivity. In turkeys, infectious sinusitis and embryo mortality due to Mycoplasma meleagridis(MM) directly reduce hatchability and flock replacement rates (Fan et al., 2021).

5.2 Indirect Losses

Indirect economic losses arise from **poor feed conversion efficiency**, as infected birds consume more feed but convert it less effectively into body mass or eggs. Prolonged illness increases the duration of production cycles and delays market readiness, raising operational costs (Pace et al., 2014). Additionally, **treatment and control expenses** add a significant financial burden. These include costs of antimicrobials, vaccination programs, enhanced biosecurity measures, labor, and diagnostic testing. The necessity for repeated treatments and the risk of antimicrobial resistance can further complicate management strategies and increase expenditure (Mercer et al., 2019).

5.3 Impact on Trade and Biosecurity

Avian mycoplasmosis also has broader implications for **international trade and biosecurity**. Many countries maintain strict import regulations to prevent the introduction of Mycoplasma species into disease-free zones. Detection of these pathogens can lead to trade restrictions, quarantine measures, and loss of market access, particularly for breeding stock and hatching eggs. Endemic infection complicates national control programs and necessitates ongoing surveillance, raising the costs for regulatory bodies and producers alike (Kim et al., 2022).

Economic Impact of Avian Mycoplasmosis

Impact Category	Description	Examples
Direct Losses	Mortality, reduced growth and egg production	Increased death rate, fewer eggs produced
Indirect Losses	Poor feed conversion, treatment costs, delayed production	Higher feed intake per unit weight gain, medication expenses
Trade and Biosecurity Impact	Restrictions on exports, quarantine costs, surveillance expenses	Export bans, costs of testing and certification

Understanding these economic repercussions highlights the importance of effective diagnosis, control, and prevention strategies to mitigate the impact of avian mycoplasmosis on poultry production systems globally.

6. Diagnostic Approaches

Accurate and timely diagnosis of avian mycoplasmosis is essential for effective disease management, control, and prevention. Various diagnostic techniques are employed, ranging from conventional culture and serological assays to advanced molecular methods. Each method has its advantages and limitations with respect to sensitivity, specificity, cost, and practicality in different settings (Mercer et al., 2019).

6.1 Conventional Methods

6.1.1 Culture Techniques

Isolation and culture of Mycoplasma species remain the gold standard for definitive diagnosis. Samples commonly collected include tracheal swabs, synovial fluid, or tissues from affected birds. The organisms are fastidious, requiring specialized media supplemented with sterols and incubation in a microaerophilic environment at 37°C for up to several weeks. Culture allows for subsequent identification, antimicrobial susceptibility testing,

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and epidemiological typing. However, it is time-consuming, labor-intensive, and has relatively low sensitivity due to the fragile nature of Mycoplasmaand contamination risks (Zhou et al., 2021).

6.1.2 Serology

Serological tests detect host antibodies against Mycoplasma antigens, providing evidence of exposure rather than active infection. The **Slide Plate Agglutination (SPA)** test is rapid and inexpensive but may give false positives due to cross-reactivity and cannot distinguish between current and past infections. The **Enzyme-Linked Immunosorbent Assay (ELISA)** offers higher sensitivity and specificity and is widely used for flock-level surveillance and monitoring vaccination efficacy. However, serology is less useful in early infections before antibody development and in differentiating between infection and vaccination responses (Fan et al., 2021).

6.2 Molecular Diagnostics

6.2.1 Polymerase Chain Reaction (PCR) and Real-Time PCR

Molecular techniques based on PCR have revolutionized Mycoplasma diagnostics by providing rapid, sensitive, and specific detection directly from clinical samples. Conventional PCR amplifies pathogen-specific DNA sequences, while real-time PCR adds quantification and reduced contamination risk through closed-tube systems. These methods enable differentiation between Mycoplasma species and strains, essential for epidemiological investigations and control strategies (Baranzehi et al., 2020).

6.2.2 Loop-Mediated Isothermal Amplification (LAMP) and Emerging Techniques

LAMP is an emerging molecular technique that amplifies DNA under isothermal conditions, eliminating the need for expensive thermocyclers. It is highly sensitive, rapid, and suitable for field diagnostics, especially in resource-limited settings. Other novel approaches include CRISPR-based detection and next-generation sequencing, which promise enhanced specificity and detailed pathogen characterization but require further validation for routine use (Lee et al., 2013).

6.3 Comparative Evaluation

Diagnostic Method	Sensitivity	Specificity	Turnaround Time	Cost	Field Applicability
Culture	Moderate (low if sample quality poor)	High	Weeks	Moderate	Limited (requires lab facilities)
SPA Serology	Moderate	Low to moderate	Minutes	Low	High (rapid screening)
ELISA	High	Moderate to high	Hours	Moderate	Moderate (lab required)
Conventional PCR	High	High	Hours	Moderate to high	Moderate (requires PCR lab)
Real-Time PCR	Very high	Very high	1–3 hours	High	Limited (advanced lab needed)
LAMP	High	High	<1 hour	Low to moderate	High (suitable for field use)

Molecular methods generally outperform conventional techniques in sensitivity and specificity but are costlier and require technical expertise. Serological tests remain useful for flock-level monitoring, while culture is indispensable for strain isolation and antimicrobial testing. The choice of diagnostic approach depends on the objectives (screening, confirmation, epidemiology), available resources, and the epidemiological context.

7. Antimicrobial Therapy and Resistance

Effective antimicrobial therapy plays a crucial role in managing avian mycoplasmosis, especially given the

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ISSN: (e) 3007-1607 (p) 3007-1593

chronic nature of the infection and its impact on poultry health and productivity. However, increasing antimicrobial resistance among Mycoplasma species poses significant challenges for treatment efficacy.

7.1 Commonly Used Antibiotics

Several classes of antibiotics are routinely employed to treat Mycoplasma infections in poultry, targeting bacterial protein synthesis or nucleic acid replication (Narasimhan et al., 2013):

- **Macrolides:** Tylosin is one of the most widely used antibiotics against Mycoplasma. It inhibits protein synthesis by binding to the 50S ribosomal subunit and is effective in reducing clinical signs and bacterial shedding.
- **Tiamulin:** A pleuromutilin antibiotic, tiamulin is highly effective against Mycoplasma spp. and often preferred due to its potent activity and relatively low toxicity.
- **Tetracyclines:** Drugs such as doxycycline and oxytetracycline are also used, targeting the 30S ribosomal subunit to inhibit protein synthesis. They are broadly effective but resistance is emerging.
- **Fluoroquinolones:** Enrofloxacin and other fluoroquinolones inhibit bacterial DNA gyrase but are generally reserved due to concerns over resistance and withdrawal periods.
- **Lincosamides and Chloramphenicol:** Occasionally used but less common due to toxicity and regulatory restrictions.

Treatment aims to reduce clinical symptoms and bacterial load but usually does not completely eradicate the pathogen, leading to carrier states and recurrence.

7.2 Trends in Antimicrobial Resistance

Recent studies indicate an increasing trend of antimicrobial resistance (AMR) in Mycoplasma isolates from poultry worldwide. Resistance development is driven by:

- Prolonged and subtherapeutic use of antimicrobials.
- Lack of strict regulatory controls and misuse in some regions.
- Horizontal gene transfer and mutations.

Resistance to macrolides and tetracyclines is of particular concern, with reports showing reduced susceptibility that complicates treatment. This trend threatens the effectiveness of current therapy regimens and necessitates ongoing surveillance and prudent antimicrobial stewardship.

7.3 Mechanisms of Resistance in Mycoplasma spp.

Mycoplasma species develop resistance through several molecular mechanisms, including:

- **Target site modification:** Mutations in ribosomal RNA genes (e.g., 23S rRNA for macrolides, 16S rRNA for tetracyclines) reduce antibiotic binding affinity.
- **Efflux pumps:** Active transport systems that expel antibiotics from the bacterial cell, lowering intracellular drug concentration.
- **Enzymatic inactivation:** Although less common in Mycoplasma, some isolates produce enzymes that degrade or modify antibiotics.

Due to their minimal genomes and lack of a cell wall, Mycoplasma rely heavily on target site mutations and efflux mechanisms for resistance, making molecular detection of resistance markers vital for guiding therapy.

Common Antibiotics Used in Avian Mycoplasmosis and Resistance Issues

Antibiotic Class	Examples	Mode of Action	Resistance Concerns
Macrolides	Tylosin	Inhibit 50S ribosomal subunit	Increasing mutations in 23S rRNA
Pleuromutilins	Tiamulin	Inhibit protein synthesis	Emerging resistance but less common
Tetracyclines	Doxycycline, Oxytetracycline	Inhibit 30S ribosomal subunit	Rising resistance via 16S rRNA mutations
Fluoroquinolones	Enrofloxacin	Inhibit DNA gyrase	Restricted use due to resistance and safety concerns
Lincosamides	Lincomycin	Inhibit protein synthesis	Limited use, resistance reported

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ISSN: (e) 3007-1607 (p) 3007-1593

The increasing antimicrobial resistance emphasizes the need for integrated control strategies, including vaccination, improved biosecurity, and responsible use of antimicrobials, to sustain the efficacy of treatments for avian mycoplasmosis.

8. Vaccination Strategies

Vaccination represents a cornerstone in the control of avian mycoplasmosis, helping to reduce disease incidence, severity, and economic losses. Different vaccine types and approaches have been developed and deployed worldwide, each with distinct advantages and limitations.

8.1 Available Vaccines

Live Attenuated Vaccines

Live vaccines contain weakened strains of Mycoplasma gallisepticum (MG) or Mycoplasma synoviae (MS) that replicate in the host without causing full-blown disease. These vaccines induce robust and long-lasting immunity by stimulating both humoral and cell-mediated immune responses.

- Common live vaccines include the **F strain** and **ts-11 strain** for MG, widely used in broiler breeders and layers.
- Live MS vaccines are also available but less commonly applied due to variability in protection.

Advantages of live vaccines include good immunogenicity and potential for mucosal immunity. However, risks include residual pathogenicity, possible reversion to virulence, and interference with serological diagnostics.

Inactivated (Killed) Vaccines

Inactivated vaccines are prepared from chemically or physically killed Mycoplasma organisms, often combined with adjuvants to enhance immune responses. These vaccines are safer but generally less immunogenic than live vaccines and usually require multiple doses or boosters.

Inactivated vaccines are mainly used where live vaccines are contraindicated or as part of combined vaccination programs.

8.2 Efficacy and Limitations

Vaccine efficacy depends on factors such as vaccine strain, administration route, flock health status, and environmental conditions. Live vaccines tend to offer better protection against respiratory disease and reduce shedding, thereby lowering transmission risk.

Limitations of current vaccines include:

- Incomplete protection against all field strains, especially with genetic variability among Mycoplasma isolates.
- Potential interference with serological surveillance due to vaccine-induced antibodies.
- Risk of vaccine strain persistence or spread.
- Challenges in vaccinating large flocks under field conditions.

8.3 Emerging Vaccine Technologies

Recent advances aim to develop safer and more effective vaccines using modern biotechnology approaches:

- **Recombinant Vaccines:** These utilize specific antigenic proteins expressed in vector systems, focusing on immunodominant components of Mycoplasma to induce targeted immunity.
- **Subunit Vaccines:** Composed of purified proteins or peptides, subunit vaccines reduce risks associated with live organisms and allow differentiation between infected and vaccinated animals (DIVA).
- **DNA Vaccines:** Encoding Mycoplasma antigens to stimulate both humoral and cellular responses, though still largely experimental.
- **Nanoparticle-Based Vaccines:** Designed for improved delivery and sustained antigen release, enhancing immune activation.

These emerging technologies hold promise for overcoming current vaccine limitations but require further research and field validation.

8.4 Regional Perspectives on Vaccine Use

Vaccine adoption varies widely by region due to differences in disease prevalence, poultry production systems, regulatory frameworks, and economic factors.

- In intensive commercial poultry sectors of North America and Europe, live MG vaccines are routinely used with strict biosecurity and monitoring.
- Developing countries with extensive backyard and smallholder flocks face challenges such as limited vaccine availability, cold chain issues, and lack of vaccination programs.

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- Some countries implement national control programs integrating vaccination with diagnostics and biosecurity to manage mycoplasmosis.

Regional tailoring of vaccination strategies is essential to maximize impact and sustainability.

9. Biosecurity and Management Practices

Effective biosecurity and management practices are fundamental components in preventing and controlling avian mycoplasmosis. These measures reduce the introduction and spread of Mycoplasma pathogens within and between poultry flocks, complementing vaccination and treatment efforts.

9.1 Environmental Control and Hygiene

Maintaining a clean and hygienic environment is critical to minimize pathogen load and transmission risks:

- **Regular cleaning and disinfection:** Poultry houses, equipment, feeders, and waterers must be thoroughly cleaned and disinfected between production cycles using effective agents against Mycoplasma.
- **Ventilation:** Proper airflow reduces the accumulation of airborne pathogens and humidity, limiting respiratory disease spread.
- **Litter management:** Frequent replacement or treatment of litter helps prevent pathogen buildup.
- **Rodent and pest control:** Rodents and wild birds can act as mechanical vectors; controlling their presence reduces contamination.
- **Water and feed quality:** Ensuring clean and uncontaminated water and feed limits indirect transmission routes.

9.2 Flock Management and Quarantine Measures

Prudent flock management strategies help contain infection and protect uninfected birds:

- **All-in/all-out production:** Synchronizing flock placement and removal reduces cross-contamination between age groups.
- **Segregation of age groups:** Separate housing for breeders, layers, and broilers prevents pathogen spread.
- **Quarantine of new stock:** Newly introduced birds should be isolated and tested before integration into the main flock to prevent introduction of Mycoplasma.
- **Monitoring and early detection:** Regular health checks and rapid response to suspected infections limit outbreaks.
- **Limiting farm access:** Restricting visitors, vehicles, and equipment reduces external contamination risk.

9.3 Role of Surveillance Programs

Surveillance and monitoring programs are vital for early detection, control, and eradication of avian mycoplasmosis:

- **Serological and molecular testing:** Routine flock screening identifies infected or carrier birds for timely intervention.
- **Trace-back investigations:** Identifying sources and routes of infection enables targeted biosecurity improvements.
- **Data recording and reporting:** Systematic documentation supports risk assessment and epidemiological studies.
- **Integration with national control programs:** Coordinated efforts enhance regional disease management and trade compliance.

Key Biosecurity and Management Practices

Practice	Purpose	Key Actions
Environmental Hygiene	Reduce pathogen load and transmission	Cleaning, disinfection, ventilation
Flock Segregation and Quarantine	Prevent introduction and spread of infection	Isolation of new stock, age group separation
Surveillance and Monitoring	Early detection and control	Regular testing, health monitoring
Access Control	Minimize external contamination	Restricted farm entry, equipment sanitation

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Implementing comprehensive biosecurity and flock management practices remains a cost-effective and approach to control avian mycoplasmosis and maintain flock health.

10. Emerging Challenges and Future Directions

The control of avian mycoplasmosis faces evolving challenges as the poultry industry grows and pathogens adapt. Advances in science and coordinated global efforts offer promising pathways to improve management and mitigate impacts.

10.1 Diagnostic Challenges in Mixed Infections

One of the foremost challenges in diagnosing avian mycoplasmosis is the frequent occurrence of mixed infections with other respiratory pathogens such as Escherichia coli, infectious bronchitis virus (IBV), and avian influenza virus (AIV). These co-infections complicate clinical presentation, mask typical signs, and interfere with diagnostic accuracy. Conventional diagnostics may fail to detect co-pathogens or differentiate overlapping symptoms, leading to underdiagnosis or misdiagnosis. This underscores the need for multiplex molecular assays and integrated diagnostic platforms capable of simultaneous detection of multiple agents with high sensitivity and specificity.

10.2 Role of Genomics and Proteomics in Vaccine Development

Modern 'omics' technologies—genomics, transcriptomics, and proteomics—are revolutionizing vaccine research for avian mycoplasmosis. Whole-genome sequencing of Mycoplasma strains provides insights into genetic variability, virulence factors, and antimicrobial resistance genes, enabling the design of targeted vaccines. Proteomics helps identify immunodominant antigens and potential subunit vaccine candidates with better safety profiles. These approaches accelerate the development of next-generation vaccines that can offer broader protection, reduce adverse effects, and support differentiation between infected and vaccinated animals (DIVA). Integrating omics data with bioinformatics tools is pivotal for rational vaccine design and personalized disease management.

10.3 Need for Global Surveillance and Policy Harmonization

Avian mycoplasmosis has significant implications for international poultry trade and food security. However, disparate surveillance efforts, reporting standards, and regulatory policies across countries hinder effective global control. Establishing harmonized surveillance networks and data-sharing platforms would enable early outbreak detection, monitor antimicrobial resistance trends, and guide coordinated interventions. Moreover, international policy alignment on vaccination, antibiotic use, and biosecurity protocols is critical to mitigate cross-border transmission and promote sustainable poultry production.

10.4 One Health Implications

While avian mycoplasmosis primarily affects poultry, the One Health paradigm—recognizing the interconnectedness of human, animal, and environmental health—highlights broader implications:

- **Zoonotic Potential:** Although rare, some Mycoplasma species have zoonotic relevance, necessitating vigilance to prevent potential spillover.
- **Antimicrobial Resistance:** The use of antibiotics in poultry contributes to the global AMR burden, impacting human and animal health alike.
- **Environmental Impact:** Waste and effluent management from poultry farms can influence pathogen dissemination and ecosystem health.

Addressing avian mycoplasmosis within a One Health framework encourages multidisciplinary collaboration, sustainable antimicrobial stewardship, and integrated disease management strategies. Overcoming the emerging challenges in avian mycoplasmosis requires advances in diagnostics, innovative vaccines, global cooperation, and holistic health approaches. Continued research and policy support will be essential to safeguard poultry health, food security, and public health worldwide.

11. Conclusion

Avian mycoplasmosis remains a pervasive and economically significant disease in poultry

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ISSN: (e) 3007-1607 (p) 3007-1593

worldwide, caused predominantly by Mycoplasma gallisepticum, Mycoplasma synoviae, and other related species. This review highlights the multifaceted nature of the disease, including its complex pathogenesis, varied clinical manifestations, and challenges in diagnosis and treatment. The dual modes of transmission and persistence of chronic infections underscore the difficulty in eradicating the pathogen from poultry populations.

Effective management of avian mycoplasmosis necessitates an integrated approach combining accurate and timely diagnostics, prudent antimicrobial therapy mindful of rising resistance, strategic vaccination, and stringent biosecurity measures. Advances in molecular diagnostics and emerging vaccine technologies offer promising tools to enhance disease control. However, limitations such as diagnostic challenges in mixed infections, variability in vaccine efficacy, and the threat of antimicrobial resistance demand ongoing research.

Future efforts should focus on leveraging genomics and proteomics for vaccine innovation, expanding global surveillance networks, and harmonizing policies across regions to ensure sustainable poultry health. Moreover, adopting a One Health perspective will be crucial in addressing the broader implications of mycoplasmosis control, including antimicrobial resistance and environmental health.

In conclusion, sustained investment in research, improved biosecurity, and coordinated policy development are essential to mitigate the impact of avian mycoplasmosis, safeguard poultry production, and contribute to global food security.

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