

***Mycoplasma gallisepticum* and Chronic Respiratory Disease in Poultry: A Comprehensive Review**

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Abstract *Mycoplasma gallisepticum* (MG) is one of the most significant pathogens in poultry medicine, responsible for chronic respiratory disease (CRD) in chickens and infectious sinusitis in turkeys. As a member of the class Mollicutes, MG is distinguished by its lack of a cell wall, small genome, and parasitic lifestyle. Infections cause substantial economic losses in the global poultry industry through reduced productivity, increased mortality, and costs of treatment and prevention. This review summarizes current knowledge on MG, including its history, taxonomy, morphological and molecular characteristics, pathogenic mechanisms, epidemiology, clinical manifestations, immune responses, diagnostic strategies, antibiotic resistance, control measures, and vaccination. Future perspectives are also outlined, emphasizing genomic insights, host-pathogen interactions, and novel therapeutics.

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Introduction Mycoplasmas are unique prokaryotes, representing the smallest free-living organisms. They lack a rigid cell wall, possess reduced genomes, and depend heavily on host-derived nutrients (1). Among avian mycoplasmas, MG is of particular importance, causing CRD in chickens and sinusitis in turkeys, both of which impair flock performance and increase susceptibility to secondary infections such as *Escherichia coli* (2). Despite decades of research, MG remains globally prevalent, and avian mycoplasmosis is listed by the World Organisation for Animal Health (WOAH) as a notifiable disease due to its transboundary and economic impact (3).

Historical Background

The study of mycoplasmas dates back to Pasteur's observations in 1843 of organisms linked to bovine pleuropneumonia. Subsequent isolation of these agents by Nocard and Roux in 1898 and their filterability led to initial misclassification as viruses (4). The term mycoplasma derives from Greek—mykes (fungus) and plasma (formed)—reflecting their fungal-like growth. Molecular studies in the 1960s clarified their identity as wall-less prokaryotes distinct from bacterial L-forms (5). Avian mycoplasmas, including MG, were later recognized as major causes of poultry respiratory disease (6).

Taxonomy and Evolutionary Perspectives

MG belongs to the class Mollicutes ("soft skin"), characterized by wall-less, pleomorphic organisms. Mollicutes evolved from low-GC Gram-positive ancestors (Firmicutes) via reductive evolution, losing genes for biosynthetic pathways and increasing host dependence. While 16S rRNA analyses suggest monophyly, whole-genome sequencing has provided higher resolution, confirming their close relationship to Gram-positive bacteria (6).

Morphology and Cultural Characteristics

MG cells are extremely small (300–800 nm), pleomorphic, and bounded by a cholesterol-rich plasma membrane that stabilizes osmotic pressure and mediates host interactions (7). On culture media, MG forms "fried-egg" colonies, but growth is slow (3–10 days) and requires serum and complex nutrients. MG is facultatively anaerobic and forms biofilms, enhancing persistence and antimicrobial tolerance (8).

Genome Organization and Molecular Biology

The MG genome (~1.0–1.1 Mb, ~31% GC content) encodes ~700–800 proteins. A hallmark is surface antigenic variation: the pMGA multigene family encodes variable immunodominant proteins. Key adhesins GapA and CrmA are essential for attachment to host epithelium. MG also exhibits gliding motility, aiding colonization of respiratory mucosa. Recently, CRISPR-Cas9 has been

explored for functional genomic studies to identify virulence-related genes (9).

Pathogenesis and Virulence Factors

Adhesins such as GapA and CrmA mediate tight adherence to ciliated epithelial cells, initiating colonization. Frequent phase variation of surface lipoproteins allows MG to evade host immunity. TLR2-mediated recognition of MG lipoproteins triggers cytokine release, inflammation, and lesions. Coinfections with *E. coli* or respiratory viruses exacerbate disease severity (10).

Clinical Manifestations

Chickens: Chronic respiratory disease with coughing, nasal discharge, airsacculitis, reduced feed conversion, egg drop, and poor hatchability (11).

Turkeys: Infectious sinusitis with sinus swelling, ocular/nasal discharge, and growth retardation. Economic impact: Subclinical infections reduce productivity even without overt mortality (12).

Immune Responses

Innate immunity: MG lipoproteins activate TLR2, inducing pro-inflammatory cytokines. Adaptive immunity: Both humoral and cellular immunity develop but are insufficient for clearance due to antigenic variation. Immune evasion: Antigenic variation, biofilm formation, and immune modulation enable persistence (13).

Epidemiology

MG is distributed worldwide in commercial and backyard poultry; >50 wild bird species serve as reservoirs. Transmission occurs vertically (transovarian) and horizontally (aerosol, fomites, direct contact) (14). Latent carriers perpetuate flock infections and complicate eradication.

Diagnostic Methods

Culture: Gold standard but slow and technically demanding. Serology: ELISA (sensitive), HI and RSA (rapid but less specific). Molecular: PCR/qPCR for rapid detection; MLST and WGS for epidemiology and vaccine differentiation. Recently, LAMP assays have been highlighted as rapid and cost-effective diagnostic alternatives (15).

Antibiotic Resistance

Macrolides, tetracyclines, and fluoroquinolones remain widely used. Mutations in 23S rRNA (macrolides) and gyra/parC (fluoroquinolones) drive resistance. Resistance prevalence varies regionally, with increasing fluoroquinolone resistance reported (16).

Vaccination Strategies

Live Attenuated Vaccines: F strain (effective but transmissible); ts-11 and 6/85 (safer but less immunogenic). Inactivated Vaccines: Safe but confer shorter protection.

Recombinant/Subunit Vaccines: Promising approaches under development (17).

Challenges: Antigenic variation, limited cross-protection, and surveillance complications.

Economic Impact

MG causes direct losses via reduced egg production, hatchability, and growth, plus indirect costs of medication, vaccination, and culling. Global annual losses are estimated at >\$780 million (18). Trade restrictions further amplify economic burdens.

Prevention and Control

Strict biosecurity, including all-in/all-out management, sanitation, and wild bird exclusion, remains critical. Monitoring programs such as NPIP in the U.S. enforce regular testing and control (19). Antimicrobial stewardship and vaccination are essential components of integrated management.

Emerging Research & Future Perspectives

Genomic Insights: WGS identifies virulence determinants and resistance markers. Host-Pathogen Interaction Models: Omics-driven studies reveal mechanisms of persistence and immunity (20).

Novel Therapeutics: Nanoparticles, immunomodulators, and recombinant vaccines hold promise for future sustainable control. CRISPR-Cas9 applications are emerging as tools for studying gene function and vaccine development (21-29). A One Health perspective integrating wild bird reservoirs and farm management is essential.

Conclusions

MG remains a globally significant pathogen in poultry, with major economic and trade implications. Effective control requires integration of biosecurity, vaccination, prudent antimicrobial use, and advanced molecular diagnostics. Future research should focus on next-generation vaccines, omics-based host-pathogen studies, and One Health approaches addressing wild reservoirs.

Conflict of interest

Authors declare no conflict of interest.

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