

Comprehensive Insights into Infectious Bronchitis Virus in Poultry: Evolution, Immunopathogenesis, and Advances in Modern Vaccine Strategies

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Abstract: Infectious bronchitis virus (IBV) remains a major global threat to poultry production due to its high transmissibility, genetic diversity, and continuous emergence of new variants. This review summarizes the historical development, epidemiology, and molecular characteristics of IBV, with emphasis on its rapid evolution driven by mutation and recombination. The virus exhibits broad tissue tropism affecting respiratory, renal, and reproductive systems, resulting in significant economic losses. Host immune responses, including humoral and cellular immunity, play crucial roles in controlling infection, yet viral immune evasion mechanisms limit long-term protection. Classical vaccines face challenges due to antigenic drift and short-lived immunity. Therefore, modern vaccine strategies such as recombinant vector vaccines, DNA and mRNA platforms, nanoparticle-based systems, and yeast-based delivery approaches have been explored. These novel technologies aim to enhance cross-protection, durability, and mucosal immunity. Continuous surveillance and innovative vaccine development remain essential for effective control of IBV in poultry industries worldwide.

Keywords: Coronavirus, vaccine development, genetic diversity, recombinant vaccines

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Definition and historical background

Infectious bronchitis (IB) is a viral disease that affects poultry and is caused by infectious bronchitis virus (IBV). It is a fast-spreading disease that is extremely contagious and avian viruses. The first reports of avian viruses surfaced in the 1930s in the United States when young chicks began to develop a new respiratory disease. Since then, the infectious bronchitis virus has spread to all parts of the world that have poultry. IBV was discovered to be a corona virus of the genus Gamma coronavirus. IBV has maintained its importance in the field of infectious bronchitis viruses because it has the ability to mutate and recombine and is then able to form new distinct serotypes and genotypes making it even more complicated to manage and control (Guo et al., 2025; Strydom et al., 2025; Keep et al., 2025). Historical studies also demonstrated that IBV caused more than just respiratory illness; it was also able to inflict illness on the kidneys and the reproductive organs. The broad tissue tropism increased the economic

impact and made the disease a persistent challenge in poultry health management.

In the early stages, research for IB focused on the development of new methods of isolating and characterizing viral strains. The first vaccines for IB were developed in the mid twentieth century. However, these vaccines were also only effective for a very brief period because new variants were developing. The first genetic recombination studies were conducted in the 1950s and have shown the importance of developing new methods of viral surveillance. Infectious bronchitis virus is one of the first viruses shown to rapidly evolve in animal populations. The advancement of technology has also contributed to the development and refinement of the biology of IBV. The sequencing of the S1 gene has advanced greatly the knowledge on the antigenic variation. The studies provided insight on why vaccination may not offer cross-protection (Yan et al., 2023).

Recent studies use modern genomic analysis. Whole genome sequencing has provided the global diversity of IBV and identified dominant lineages GI-19 and QX across varying regions. Studies reconfirmed the role of recombination in forming new pathotypes. The historical trajectory IBV has endured explains why IBV continues to remain a threat almost a century later. The disease illustrates a veterinary challenge, as well as a model of the evolution of coronaviruses in the animal kingdom (Falchieri et al., 2024).

Economic and global impact on the poultry industry

IBV leads to severe economic impacts in the commercial production of poultry. The virus infects layer and breeder hens causing a decrease in egg quantity and quality. Broilers are also affected as their growth and feed conversion rates are impacted. While morbidity is very high and almost all birds in a flock can be infected, mortality is typically moderate. Financial impacts are felt greatly even when death rates are low. Increased vet costs, vaccinations, and trade bans are additional sources of loss. This is worsened by the global scale of poultry farming as billions of birds are raised annually (Guo et al., 2025; Strydom et al., 2025).

IBV Infection causes long term damage to the oviduct of hens which leads to the production of irregular eggs with thin shells and lower hatchability. This results in a lowered value of breeding stock and commercial layers.

The expenses associated with increased mortality and treatment requirements are increased by the nephropathogenic varieties of the virus. On the occasions when an outbreak occurs, significant culling, disinfection, and downtime for the farm are required. All of these factors contribute to the economic impact of poultry viruses, which is one of the largest in the world (Keep et al., 2025).

IBV is an important global trade barrier. Sudden outbreaks of IBV can lead to bans on the transport of live birds and poultry products. This is particularly detrimental to developing nations, as they have limited vaccine and diagnostic resources. IBV is endemic in many parts of the world and causes repeated economic losses. Even the best managed enterprises incur economic losses to control IBV, which demands vaccination and rigorous monitoring. Thus, IBV is a chronic economic problem for the world poultry industry (Yan et al., 2023; Falchieri et al., 2024).

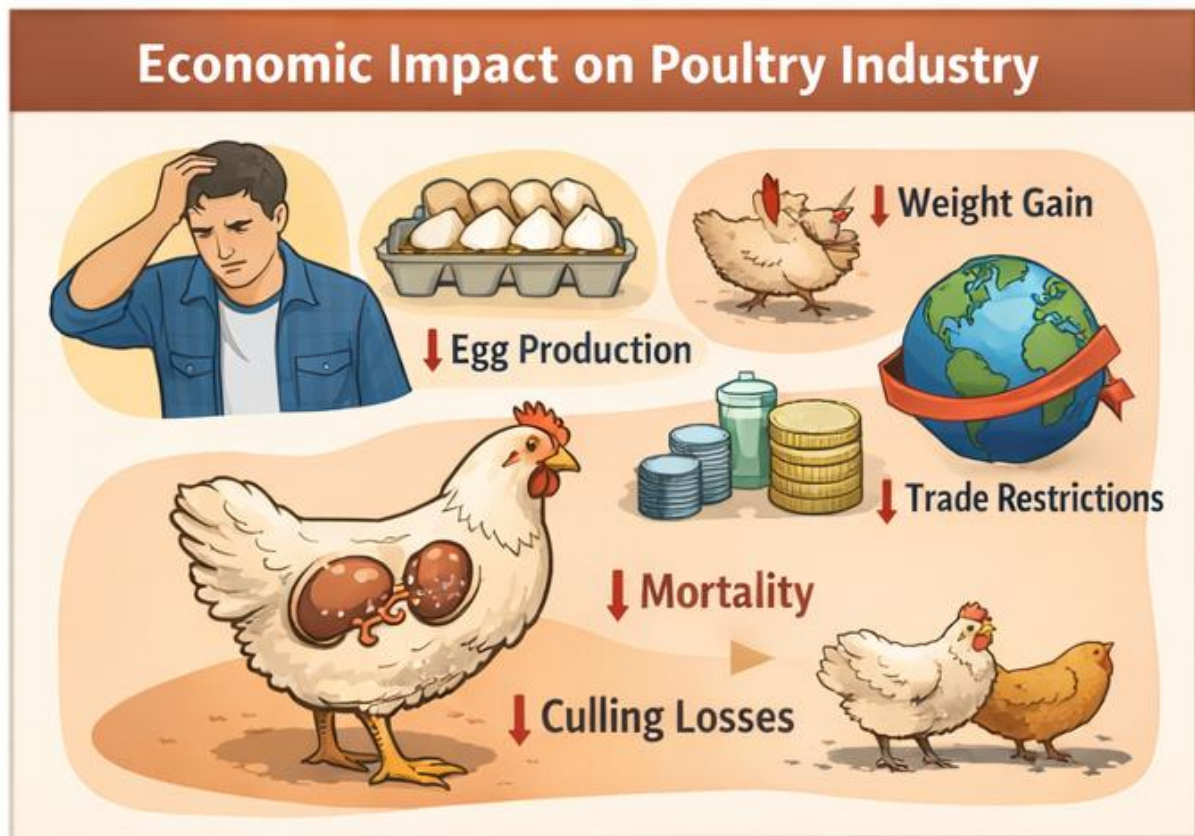


Figure 1: Economic Impact of IBV on Poultry Industry Occurrence and epidemiology of IB outbreaks worldwide

IB has been documented in almost all countries that produce poultry. The IB epidemiology is characterized by the repeated and consistent appearance of novel variants that replace or function in concert with existing strains. In Asia, strains of GI-19 (QX-like) have become the dominant strain. In Africa and the Middle East, multiple genotypes are in circulation and are found to co-infect the same flocks. The constant emergence of recombinant viruses also occurs in Europe. These differences in the distribution of IB demonstrate the viruses competence in tailoring itself to fit the challenges presented by the local environment and the host populations (Guo et al., 2025; Strydom et al., 2025).

IB epidemiology can be explained by the viruses' structure, which is made of RNA that is prone to constant and rapid changes in the order of the nucleotides (high mutation rate). These changes (mutations) can alter the pathogenic nature of the virus as a result of strand recombination. In less than 10 years, infection strains from South Asia and China have been documented with rapid frequency changes. These changes have also been documented in specific regions of Latin America that have exhibited challenges with vaccination in South Africa. The emergence of strains in Africa that are classic vaccine strain types has raised concerns as they appear to be a significant center for control (Keep et al., 2025).

IB epidemiology can also be explained by the nature and structure of viruses involved in IB and how they are influenced by the types of management systems in very different countries. Diverse IB strains are found in small-scale and backyard poultry production systems (contrary to larger-scale, commercial operations). Conversely, large-scale, commercial poultry flock operations are more likely to disseminate large amounts of highly-infectious strains, especially as bird populations trade. In addition to commercial poultry flocks and the trade of poultry birds other than IB-affected birds, the global trade of poultry products and the natural flight of wild birds are other modes of transmission of IB viruses. The global transmission of IB requires continued epidemiological surveillance and updated vaccination strategies (Yan et al., 2023; Falchieri et al., 2024).

Etiology: Infectious Bronchitis Virus (IBV)

Viral taxonomy and classification

IBV is classified as a virus in the genus of Gammacoronavirus, of the family of Coronaviridae. The Infectious Bronchitis Virus (IBV) is classified in the Nidovirales order along with other coronaviruses from the avian and mammal classes. The Nidovirales taxonomic classification systems contain systems based off structuring of genomes, replication strategies, and structural proteins (known as spike proteins). IBV is the only member of the Nidovirales family that is known to infect chicken and chicken-like birds. There is value in this classification systems as the diverse profiles of different serotypes and genotypes have differing antigenic profiles. The most extensively studied genotypes and serotypes worldwide include Massachusetts, 793B/4-91, and QX. The differing genotypes possess differing structural spike proteins as well as differing capabilities to protect in immune responses to different IBV lineages. This is further complicated by the fact that the IBV is constantly mutating and evolving. With that said constant and continual studies and surveillance of the IBV is of utmost importance (Lu et al., 2024).

The classification of serotypes is also practiced based off of the sequencing of the spike (S1) proteins. The S1 subunit is responsible for driving and causing the variation in antigen, and as a result this further complicates efforts to develop a vaccine. While genotypes, such as GI-19 (more commonly referred to as QX-like) which have dominated the avian viral infection world recently, other genotypes, such as Massachusetts, remain to be important. This is due to the fact that this genotype forms the basis and foundation for the most classical vaccines. There is a diverse number of genotypes, which shows clearly that IBV is evolving at rapid rates in response to the pressures from immune systems as well as the pressures caused by farming practices to control and manage the infection/virus. The IBV is constantly evolving, and this classification system demonstrates both the dynamics from a biological standpoint as well as the pressures from the sociological standpoint and with made demands that the classification be done for disease control (Wang et al., 2023; Yehia et al., 2020).

Positive confirmation of the co-infection of multiple serotypes of the IBV in a defined area has been observed. This co-infection increases the probability of the recombination of the virus as well as the emergence of novel lineages of the IBV. This means that the classification of the virus, in terms of its taxonomic classification, is constantly changing. The flowering of technology of the analysis of phylogenetics, as well as advance in the analysis of the entire genomes have been evidenced to help in the refinements to the classification systems of the IBV. The emergence of new lineages and unique lineages of the IBV is the evidence for the need for the classification systems to be updated on a continual basis (Hong et al., 2023). The virus IBV is an enveloped virus with a morphology that is spherical in nature with a diameter ranging from 80 to 120 nm.

The virus envelope is derived from host cell membranes and includes membranous structural proteins. With large spike glycoproteins on their surface, coronaviruses achieve a crown-like appearance. These spikes mediate receptor recognition and entry. Also present in the viral particle structure are small envelope (E) proteins and membrane (M) proteins, which stabilize the particle structure. Nucleocapsid (N) proteins encapsidate the RNA genome and play a role in replication and packaging. The IBV genome is positive-sense, single-stranded RNA of approximately 27 kilobases. It encodes both structural proteins and non-structural proteins. Because the RNA is capped and polyadenylated, it can function immediately as mRNA once it enters the host cells. Detailed studies of the SCCCD spike trimer and its conformational changes using electron cryo-microscopy, as well as a study of the virus's structural flexibility, show how the virus can alter its immune responses and accommodate to novel hosts (Sives et al, 2023)

Morphological stability is dependent on various environmental parameters. The envelope also makes IBV sensitive to heat, detergents, and lipid-solubilizing agents. With efficient spreading within favorable infection conditions to poultry, the virus can persist for a considerable period. Morphological studies of IBV inform vaccine development by identifying conserved structural sites, a necessity for controlling a virus that is rapidly changing at the genetic level (Lu et al, 2024)

The primary structural proteins of IBV are spike (S), membrane (M), envelope (E), and nucleocapsid (N). The S protein is cleaved into two S1 and S2 subunits. S1 mediates receptor binding, whilst S2 promotes membrane fusion.

The M protein plays a major role in the assembly of the viral component of the virus and is physiologically very abundant. The E protein is small but assists in the budding of the virus and its release. The N protein encapsulates the RNA in a helical fashion, constituting the helical nucleocapsid. These proteins allow the virus to replicate, spread, and provide a basic structure (Wang et al., 2023).

Recent molecular-based studies documented the role of the S protein in antigenic variability. Certain mutations in the receptor-binding domain are said to be under very strong selective pressure. These mutations lead to host tissue changes in the tropism and the host range. Accessory proteins are also said to be responsible for modulating the host response as well as increasing the viral persistence. It is noteworthy that the complete function of the structural as well as the non-structural proteins is of paramount importance in the engineering of novel vaccines and antiviral approaches (Sives et al., 2023; Hong et al., 2023).

Genetic variability and recombinant DNA technology in IBV

Genetic variability is one of the most pronounced characteristics of the evolution of IBV. The combination of a high rate of mutation and/or a high level of recombinant DNA technology leads to a high level of different genotypes. This positive feedback loop occurs during host co-infection with 2 or more different strains, also known as 'co-infection'. This results in the formation of 'novel viruses' that possess 'mosaic genomes'. Most strains emerging in nature as recombinants are said to possess novel and often more dangerous (pathogenic) immunity to the host. Most reports of surveillance have shown that the areas of China, Asia, Africa, and the Middle East are the most active in the recombination of IBV strains (Lu et al., 2024).

Recent studies have also documented recombinants that contain genetic material of QX-like strains along with one or more of the local lineages. Such events have resulted in the formation of viruses that possess greater tissue tropism (a greater ability to infect and invade host tissues) or exhibit greater pathogenicity (the ability to cause disease). The diversity and capacity of IBV for recombinant DNA must be monitored at all times.

Contemporary sequencing methods offer the ability to monitor these alterations live. Comprehending the mechanisms at play genetically assists in forecasting and averting significant outbreaks (Wang et al., 2023; Yehia et al., 2020).

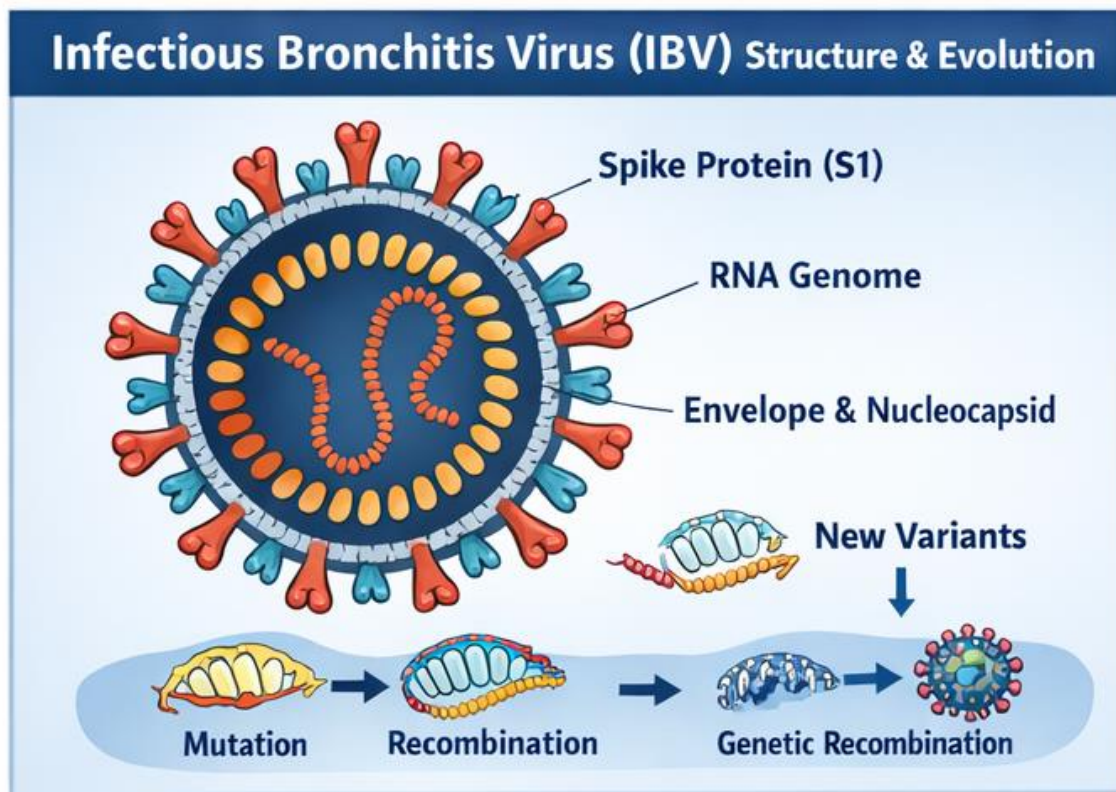


Figure 2: Overview of Infectious Bronchitis Virus (IBV) structure

Humoral Immunity (serum IgY, mucosal IgA)

Humoral immunity limits IBV to the blood and the lumen. Serum IgY neutralizes the virus after viremia and in the tissues. Mucosal IgA blocks viruses from attaching in the airway and the surface of the eyes. The type of vaccine administered affects these responses. Oculo-nasal and spray vaccinations stimulate more local IgA than parenteral vaccines. This is consistent with where the vaccine is administered in the upper respiratory tract (Al-Rasheed, Ball, & Ganapathy, 2021; Al-Rasheed, Ball, Manswr, Leeming, & Ganapathy, 2022).

Yolk-derived IgY reduces early clinical signs and viral loads in lymphoid tissues, providing partial, short-lived protection. Maternal antibodies delay until the host develops active immunity from the vaccine or infection. Field applications take advantage of this in planning priming doses (Isham, Hassan, Abd-Elsalam, Ranaweera, Mahmoud, Najimudeen et al., 2023; Isham, Hassan, Abd-Elsalam et al., 2023).

Adjuvants improve levels of functional antibodies. Molecules of the β -glucan type activate dendritic cells and enhance memory and recall responses. Mucosal cytokines adjuvants via lactic acid bacteria stimulate secretory IgA. These strategies enhance breadth and durability of responses when antigenic drift is present. They also decrease the amount of antigen necessary to develop protection (Larsen et al., 2020; Guo, 2020; Peng et al., 2020).

Cellular Immunity (CD4+, CD8+ T cells, cytokine responses)

Cellular immunity is mainly responsible for the clearance of infected cells. CD8+ T cells identify and eliminate cells with IBV peptides. CD4+ T cells provide assistance in antibody class switching and memory development. The mapping of IBV T-cell epitopes aids in the development of vaccines. It additionally directs studies that monitor memory in flocks post vaccination (Qin, Tu, Teng, Feng, Zhao, & Zhang, 2021).

Innate signals set the tone. stimulation of chicken dendritic cells via beta-glucan improves the ex-vivo antigen presentation and T cell recall. Mucosal cytokine adjuvants, in contrast, are shown to increase Th-associated cytokines across the portals of entry. A balanced Th1/Th2/Th17 profile is associated with reduced viral loads and improved mucosal integrity (Larsen et al., 2020; Guo et al., 2020).

Cellular immunity can be blunted by pathogenic variants. DMV/1639 has the capacity to replicate in lymphoid tissues and, in fact, does cause immunosuppression. Evidence suggests that lymphoid damage can diminish the action of downstream T cells. There are strain differences that influence cytokine patterns and the severity of lesions. There are also observed sexual differences among individuals subject to the same inoculum. These host and strain effect provide the explanation for the varied response among farms (Najimudeen, et al., 2023; Abd-Elsalam et al., 2024; Isham et al., 2023).

In poultry, the immune system is mucosal (the cecal tonsils and the Harderian gland).

The Harderian gland is regarded as one of the principal ocular-nasal inductive sites, and it also facilitates the presence of local IgA and memory cells that are tissue resident post spray or eye drop vaccination. Several studies describe either high or low viral loads at the induction site and the early clearance. The strong local immune gene expression during clearance, as well as the irritation to the mucosal surfaces, has been documented (Al-Rasheed et al., 2022).

The cecal tonsils function as the hub of the gut-associated lymphoid system. They serve to integrate the signals that are presented by the oral vaccines and the microbiota. It has been documented that at this site, maternal antibodies modulate the early replication of pathogens. Early control of replication is associated with reduced systemic spread and decreased lymphoid damage. The timing of oral priming is of great importance as it is the only means by which one can effectively manipulate the window to establish long-lasting mucosal immunity (Isham et al., 2023; Isham et al., 2023).

Pathogenic strains disrupt the function of these sites

Replication of DMV/1639 occurs within primary and secondary lymphoid organs including the Harderian gland and cecal tonsils, which results in transient immunosuppression due to the heightened potential of co-infections. Differences in mucosal tropism that are specific to the strain assist in clarifying the diverse field pictures and the performances of the vaccines (Najimudeen et al., 2023; Abd-Elsalam et al., 2024).

Immune Evasion Strategies of IBV

Infectious bronchitis virus targets the immune system. It causes replication of the bursa, thymus, and cecal tonsils, which causes transient immunosuppression. Lymphoid depletion weakens the body's immune response. Pathogenic strains lead to a more serious condition of immunosuppression and longer recovery times. This makes the condition more favorable for persistence and secondary infections (Najimudeen et al., 2023; Abd-Elsalam et al., 2024).

The virus alters mucosal microenvironments. Initial replication in the Harderian glands and turbinates occurs before peak IgA. Inflammation that causes damage to the mucosal barriers can be caused through the inflammatory response. This is further influenced by sex and age. With the appropriate use of targeted adjuvant strategies that stimulate dendritic cells and local T cells, some of this evasion can be countered (Al-Rasheed et al., 2022; Larsen et al., 2020; Guo et al., 2020).

Limitations of classical vaccines (Short Immunity, Antigenic Drift)

Classical vaccines have moving targets. IBV undergoes a process of evolution through mutations and subsequent recombination. Antigenic drift in S1 vaccines leads to erosion of the matching characteristics of the vaccines. The prevailing field protection wanes due to the emergence of new lineages. A short period of mucosal immunity exists following the live doses, which creates gaps in the rapidly growing population of broilers. Protection derived from inactivated vaccines also declines in layers late in the laying cycles. These scenarios require updates and strict schedules (de Wit et al., 2022; Nakanishi & Soma, 2023). Live vaccines also have the potential to place pressure on viral populations. They may

select for escape variants when the population coverage is incomplete.

Recombination with field strains has also been noted. Programs must manage trade-offs between breadth and risk mitigation. They must reduce the risk of simultaneous infection with multiple live genotypes. They must also limit unnecessary boosting that increases the risk of mixing (Guzmán & Hidalgo, 2020; Hassan et al., 2024).

There are also limitations due to operational constraints. Breaks in the cold chain reduce the effectiveness of live vaccines. Less than optimal spray application leads to inadequate tracheal infection. Oil adjuvants are labor intensive and require skilled personnel to administer. Farms with high personnel turnover have a challenging time adhering to strict timelines. Prime-boost vaccination is the most effective and has the best average outcome, however, it requires a high level of control. Continuous surveillance, rapid updates of circulating antigens, and robust biosecurity are essential to complement vaccination. These measures keep classical tools effective even in the face of virus drift and the emergence of new variants (Hassan et al., 2022; Ali et al., 2023; Buharideen et al., 2021).

Modern Vaccine Approaches

Recombinant vector vaccines (NDV, HVT, adenovirus)

Recombinant vaccines use safe carrier viruses to deliver IBV antigens. They induce all three arms of the immune response: cellular, humoral and mucosal. NDV vectors are water and spray vaccination compatible. They can be used in both hatcheries and farms and can be used in combination with NDV vaccination. HVT vectors integrate into the host, and therefore, induce prolonged immune responses. Adenoviral vectors can be designed to be multivalent due to the ability to incorporate larger plasmids. Reviews detail the various platforms, promoters, insertion sites and methods of vaccination (Wang et al., 2024; Wang et al., 2024). Preclinical data demonstrated robust respiratory immune responses and practical application in the field.

Results from preliminary safety evaluation indicate that the responses and stability of expressed inserts are satisfactory (Tan et al., 2024). The systems are designed to mitigate the drift issue by focusing on conserved areas and facilitating quick re-engineering.

Prior to application, the potential pre-existing immunity to the carrier must be evaluated. NDV maternal antibodies might hinder take in chicks, while HVT immunity takes effect best by in-ovo or day-old injection and provides long lasting immunity. Adenoviral vectors are applicable in situations where NDV interference is a concern. The optimal dose, route, and age are situated where the immunity is most robust. Prime schedules are customizable to align with the layers and breeder calendars. Additionally, the choice of vector is influenced by the cold-chain conditions and available labor on the farm (Wang et al., 2024; Tan et al., 2024). Monitoring is conducted with ELISA, neutralization, and challenge outcomes. Programs are designed to align inserts with the dominant regional genotypes to ensure high relevance.

Safety profiles are encouraging, but ongoing vigilance is essential. The backbones of the vectors are attenuated and well characterized, however, insert stability must be closely monitored throughout the passages. The recombination risk is lower than that of live IBV vaccines but remains a consideration. Field conditions, such as coinfections and dust, can severely limit efficacy. Multivalent constructs may encounter expression trade-offs among inserts. There are region- and species-specific differences in regulatory pathways. Practical recommendations involve small-scale pilot studies, strategic interval planning, and regular monitoring post-vaccination (Wang et al., 2024; Tan et al., 2024).

Principles and mechanisms of DNA vaccines

DNA vaccines involve the delivery of plasmids encoding the antigens of IBV. The host cells are responsible for transcribing and translating the gene. The resulting antigen is expressed on the MHC molecules and incites a response from CD4⁺ and CD8⁺ T cells in addition to stimulating antibody production.

Electroporation or molecular adjuvants can improve priming. Consensus-sequence designs aim at targeting the conserved S1 regions to expand coverage against drift (Zuo et al., 2021). Heterologous boosting using a viral vector amplifies both the breadth and the magnitude of the immune response (Chandrasekar et al., 2023). The platform is both modular and rapid to change when new variants are the new dominant strains.

Mechanistic studies indicate a balanced profile Th1/ Th2. DNA priming establishes a cellular baseline that allows the rise of the neutralizing antibodies. The boosts modify the effector composition and improve their longevity. Antigen design is important. S1 or S ectodomain that is stabilized helps improve the display of the conformational epitopes. Secretory leader sequences and codon optimizations enhance expression. Addition of the nucleoprotein can improve T-cell help and cross-reactivity (Zuo et al., 2021; Chandrasekar et al., 2023). The plasmid backbones are provided with strong promoters and poly-A signals to achieve high transcription levels in avian tissue.

The response site is shaped by the route of delivery. Intramuscular injection is simple and grants good uptake on farm. In-ovo is viable in large flocks when suitable devices are available. Needle-free alternatives result in less carcass damage in broilers. Adjuvants (e.g. CpG or cytokine cassette) can bias the response to cellular when desired. Schedules are combined with inactivated boosters in layers. Prime timing takes into account maternal antibody decay to prevent masking (Chandrasekar et al., 2023; Zuo et al., 2021).

Benefits of using DNA vaccines for the poultry industry

DNA vaccines are simple and stable, and they are easier to manufacture than live vaccines. They are more tolerant to temperature changes, do not recombine like live vaccines, and do not shed. They are also easier to redesign if S1 undergoes a drift. Regulators also have a better understanding of plasmid DNA, which makes it easier to provide the regulatory dossiers for plasmid DNA. These features fit rapid response and regional tailoring (Zuo et al. 2021, Chandrasekar et al. 2023). If S1 and N are included, DNA vaccines can be designed for B and T cell responses.

Challenges remain. Immunologic responses are not as strong without a booster, and large scale use of electroporation is not feasible on a commercial farm. Needles can create additional labor, and the risk of carcass trimming increases. Maternal antibodies do not neutralize plasmid DNA, and they could influence the perceived efficacy from field exposure. Achieving strong mucosal IgA could require a live component or viral vector. Field management heterogeneity could widen the performance range (Chandrasekar et al., 2023). Theoretical risk of insertion has not been observed in commercial field use, so safety risks around DNA vaccines are minimal.

Strategies aim to mitigate these problems. A heterologous prime-boost increases titers and the duration of the response. Optimized promoters and molecular adjuvants can increase the expression of the antigen. Using consensus-sequence antigens can extend centuries of cross protection and reduce the frequency of redesign. Integration with inactivated boosters is preferable for layers and breeders. Clear Standard Operating Procedures for the injection logistics can reduce the labor burden. Decision trees are helpful for aligning the platform, schedule, and farm resources (Chandrasekar et al., 2023; Zuo et al., 2021).

RNA vaccines

Research on using mRNA as a vaccine platform for poultry is new. The mRNA is encapsulated in lipid nanoparticles and contains a polyadenylated cap. After the nanoparticle enters the cell, the mRNA drives antigen expression in the cell and therefore does not require transport to the nucleus.

This results in rapid and strong responses from both B and T cells. Targets of IBV work are S1 and N. The use of consensus sequences has been documented to broaden coverage across multiple genotypes (Xiao et al., 2025). Protection from multiple avian coronaviruses in challenge models was documented in early studies.

The composition of nanoparticles can be used to modify the delivery and reactogenicity of the LNPs, while the lipid concentration can be used to determine the endosomal escape and tissue tropism. LNPs, specifically those tailored towards avians, are believed to possess improved uptake and reduction of local reactions. The incorporation of potent formulations allows for dose sparing, and rapid design cycles provide the opportunity for quick modifications to the LNPs in response to the emergence of new variants. Due to this, along with the ability of mRNA to be tailored to specific outbreaks and for precision matching in regions with rapid drifts, mRNA has the potential to be used for outbreaks (Xiao et al., 2025). Proof-of-concept reports indicate neutralization breadth and reduced endemic shedding of the virus.

Research is also evaluating mRNA with nanoparticles specifically for IBV. Neutralizing antibodies and reduction of clinical signs were observed with prototype vaccines. These vaccines combine the rapidity of RNA synthesis with the convenience of non-replicative platforms. Advances in lipid chemistry have improved the cold-chain requirements. On-farm applications for IBV vaccines will require simple administration tools and validated stability profiles in the poultry environment (Sakhrie et al., 2025; Xiao et al., 2025).

Vaccines based on nanoparticles and virus-like particles (VLPs) Nanoparticles provide antigens in such a way that the geometry presents multiple copies of the same antigen, and this can cross-link B-cell receptors to facilitate the formation of a germinal center. Self-assembling particles such as AP205 are able to present S1 or RBD epitopes from IBV. When AP205 VLPs were used as a booster following a protein prime, a breadth of response was observed. In chickens, the neutralizing response to IBV was broad and supported the claim that the vaccinated chickens shed less virus. Bacterium-like particles also provide strong innate stimulation and have the potential for good mucosal stimulation (Zhang et al., 2023).

Nanoparticle and virus-like particle (VLP) vaccines

They are correctly assembled and show a good presentation of conformational epitopes. Protection and good safety are demonstrated in challenge studies in SPF chickens. Process papers describe optimization of expression and assembly to maximize both yield and potency (Sepotokele et al., 2023; Sepotokele et al., 2023). New S1 inserts can be updated to these systems rapidly. They also lessen the need for egg-based manufacturing.

RNA cargo also extends to nanoparticle platforms. IBV antigens are delivered by LNP-mRNA with speed and flexibility (Xiao et al., 2025). Other reports demonstrate protective neutralization in vivo from induced nanoparticle mRNA (Sakhrie et al., 2025). Altogether these modalities provide modular toolkits for drift and recombination. They also complement classical schedules as boosters. Practical deployment will be balanced with the needs of broilers, layers, and breeders while also keeping cost, cold-chain, and control feasibility (Zhang et al., 2023; Sepotokele et al., 2023) for the optimal dose, route, and timing.

General characteristics of *Saccharomyces cerevisiae* (GRAS, safety)

Saccharomyces cerevisiae has GRAS status. Extensive use in food and pharma. Simple cultivation. Simple engineering. Gut stress and intestinal passage are easily tolerated. Antigens are presented in a non-pathogen manner. Safe, non-pathogen replication. Non-virulence gene shedding. Stable genomic vaccine construct (Austriaco, 2023; Hedin et al., 2023) Argument supporting safety is probiotic human data. *S. boulardii* adds evidence. Low adverse event rates when used correctly. Biocontainment tools also reduce risk in engineered strains (Hedin et al., 2023; Kwak et al., 2024). Safety is supported by human probiotic data.

Simplicity of manufacturing

Yeasts have several versatile properties. They utilize simple media. They ferment in standard-sized fermenters. They comply to GMP (Good Manufacturing Practices) guidelines. They support heat-stable formats when dried. They tolerate oral formulation which assists programs in resource-limited settings.

This reduces the burden of cold-chain logistics. It also facilitates mass dosing to entire flocks or herds (Austriaco, 2023; Kwak et al., 2024). Modular design of platforms also allows rapid iteration to improve functionality. New targeting antigens can be added by routine cloning. Expression of the antigen can be surface-displayed or intracellular. There can also be secreted forms. This variety allows rapid adaptation to antigenic variation.

The combination of design elements is highly favorable from both practicality and regulatory perspectives. The history of GRAS (Generally Recognized as Safe) status significantly reduces the length of regulatory risk assessments. The oral route of infection simplifies deployment of the waste stream, and the treatment of waste stream is also simple the risk of spills is minimized by auxotrophs and kill switches. There have been advancements in targeting strategies that have improved localization and reduced off-target spread (Heavey et al., 2024). In combination, these factors create a safe and highly adaptable chassis for veterinary and human use vaccines (Austriaco, 2023; Hedin et al., 2023; Kwak et al., 2024).

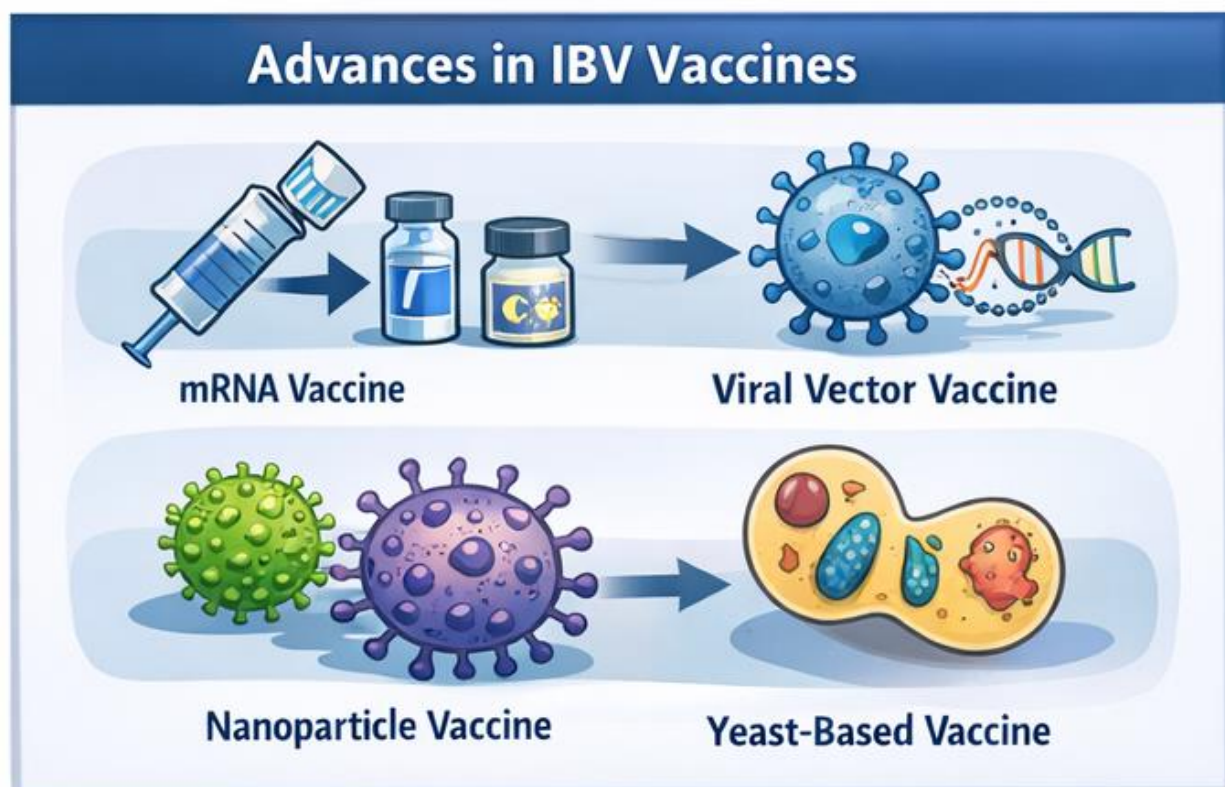


Figure 3: Advances in IBV Vaccine Technologies

Immunostimulatory cell wall components (β -glucans, mannans)

β -1,3/1,6-glucans, and mannans make up a significant portion of yeast cell walls, which are rich in these components. These ligands activate pattern-recognition receptors. Dectin-1 classifies β -glucanes. Mannans are bound by complement and lectins. This causes an immune response by trained immunity and cytokine release. Innate immune cells become more responsive, and their responses can last a long time after initial exposure. This is known as long-term memory and it aids in immune response after repeated exposure to an antigen (Vuscan et al., 2024; Mata-Martínez, 2022).

Mechanistic studies explain the pathways involved. Dectin-1 activates Syk, CARD9, and NF- κ B. The trained state can as a result of epigenetic rewiring. Metabolic alterations lean towards glycolysis and the mevalonate pathways. These alterations elevate cytokine production following repeated antigen exposure. They also enhance cross-protective immunity against different heterologous pathogens (Mata-Martínez,

2022). Both in vitro and in vivo studies correlate. Both dendritic cell and macrophage responses are stronger in vitro while in vivo rodent models demonstrate that both systemic and mucosal responses exist (Son et al., 2024).

These functional IMUC outcomes have been utilized in applied studies for vaccine development. Yeast particles may carry both an antigen and an adjuvant. This co-delivery enables improved antigen-presenting cell uptake. The oral route takes advantage of M-cell and Peyer's patches targeting. Surface display allows gut immune exposure to the contained epitope. Spore or whole-cell formats maintain β -glucan shell integrity, which allows for targeting and cargo protection through the stomach (Si et al., 2025; Austriaco, 2023). These characteristics demonstrate the reason yeast vectors function well without additional adjuvants.

Whole yeast Adjuvant (WRY) vaccine

The WRY vaccine uses yeast as a vector and the WRY platform to express the target antigens. The antigens can either be intracellular or surface located. The heat-killed form maintains the property of immunostimulant. The live form additionally offers the benefits of transient colonization and secretion. Both forms activate mucosal and systemic immune responses. The oral route is practical and inexpensive.

There have been multiple expressions of protective immunity (Austriaco, 2023; Li et al., 2023). There is confidence in veterinary case offerings. Oral WRY poultry studies have documented distinctive serum IgY and mucosal response.

Details of the design are critical. Consensus sequence modifications are broadening the improvement. Signal peptides can adjust localization. Yield is increased with stronger promoters. Discreet and surface-plasmon resonance (SPR) display exposes different conformational epitopes. Intracellular plasma cytosolic stores safeguard antigens until phagocytosis occurs. Each selection influences the Th1/Th2 axis and longevity of the effect (Li et al., 2023; Austriaco, 2023). Scalable production is achievable. Liquids in the batch can be dried into powder. Improved stability enhances farming operational logistics. A single dose can be administered through feed and water.

Containment and safety are critical. Auxotrophic strains have a limited survival outside of host organisms. Kill steps lead to a production of immunologically useable, but non-viable organisms. There are positive records concerning the use of a probiotic backbone. Monitoring occurs through serology and challenge readouts. The field translation focuses on the dose, schedule, and the age of the recipient at first administration. The documented results have demonstrated the presence of robust cellular immune response and a high antibody response with a simple regimen (Austriaco, 2023; Kwak et al., 2024; Li et al., 2023).

Yeast is used to deliver information (plasmid packaging, DNA transfer)

Yeast can be used to deliver DNA vaccines in the form of edible carriers. The yeast cells contain the plasmids that are intended to be delivered. Once the yeast is ingested by the antigen-presenting cells, the plasmid DNA is released and subsequently, the DNA is expressed by the host cells, and the corresponding antigen is then presented on MHC. This promotes T-cell help and antibody production. The system integrates vector and adjuvant within a single microsphere (Silva et al., 2021). This system lessens the dependence on needles and electroporation.

Engineering options further expands the range of applications. The uptake by dendritic cells is markedly enhanced with the presence of certain surface ligands. The release of the plasmids is further aided by the use of autolysis circuits. A high-expression plasmid backbone is used in the construction of the stabilized plasmid. The cellular immune response is enhanced by the co-delivery of certain cytokine cassettes. Spore display reveals resilience to hostile gastric circumstances. It protects payloads until they reach the intestines (Si et al., 2025; Silva et al., 2021). Such tools advance the reliability of yeast

DNA delivery for farm protocols

Safety mechanisms are improving. For example, biocontainment circuits are used to limit the persistence of an organism, while auxotrophic dependencies are used to control the spread of an organism. Probiotic strains such as *S. boulardii*, add a clinical element of familiarity. Targeting systems send yeast to inflamed tissue as desired, increasing the effect locally while decreasing the dosage (Heavey et al., 2024; Hedin et al., 2023). For these reasons, yeast presents a viable chassis for the large-scale delivery of DNA vaccines (Silva et al., 2021).

Chitosan is an example of a mucosal adjuvant; it is also one of the better known examples. Its biocompatibility and mucoadhesiveness allows it to extend the antigen's residence time on the mucosa. It causes the transient opening of junctions in the epithelial layer and protects antigens from being degraded. When broilers are vaccinated with nanoparticles containing chitosan, the enteric pathogens in the broilers are significantly reduced, and the antibody and cellular responses to the vaccine are enhanced (Acevedo-Villanueva et al., 2022). The next generation of these systems will contain various adjuvants and improved particle engineering. Such systems are expected to increase demands for the replacement of viral infections and reduce the shedding of viruses in challenged animals (Suresh et al., 2025).

The first step for increasing the effectiveness of vaccines using β -glucans, is the training of the innate immune system. This is accomplished by the binding of β -glucans to the receptor, dectin-1, which is located on the surface of myeloid cells. Such binding will result in a change in the cells metabolism, as well as the epigenetic regulation of the cell. The next time the cell is stimulated, it will inappropriately respond with a strong burst of cytokines. Such cells will also provide adequate support to B cells and will improve the quality of the antibodies produced. Supplementation with β -glucans in chickens, enhances the response to a vaccine, and also alters the expression of genes in the spleen (Cao et al., 2023). β -glucans can be included in oral and intranasal vaccines with great safety.

In avian cells, CpG motifs activate TLR9, an immune receptor.

Vaccines would be more effective if their mechanism of action was known, however it is much more favorable to include broad T1 and Cytotoxic T cell responses, and integrate them with nanoparticles, and proteins. Some literature mentions other more remote options, emulsions, liposomes, and polymer systems. Each of the above along with other adjuvants, if balanced with inflammation, fits more inflammation into memory responses. Field use requires formulations that are stable and readily dispersible to fit hatchery and farm workflows (Bodman-Harris et al., 2024; Suresh et al., 2025).

Assessment of Experimental Vaccines

Immunological evaluations

ELISA is the dominant technology for IBV vaccine studies. Systemic protection is demonstrated with serum IgY, and mucosal protection is demonstrated with IgA in tears or in tracheal washes. Both need to be present in well-constructed studies. Such studies involve multiple sampling from baseline and multiple post vaccination and challenge time periods. Field studies track the Delta of IgY to judge the success of the vaccine. Research studies are conducted to compare antigens for the scope of the binding (Hassan et al., 2022; Ali et al., 2023; Jung et al., 2022). Respiratory IgA is the major antibody for that system. It is associated with a reduction in shedding of viral particles and a reduction in the severity of lesions. Harderian and tracheal secretions are the tissues of choice for an intranasal or intratracheal spray. Handling of samples that are often and are assumed to be sterile will not be contaminated to avoid viral degradation and false lows (Nakanishi & Soma, 2023; Bhuiyan et al., 2021).

Neutralization assays determine the presence of functional neutralizing antibody and provide the titer that in vitro will block infection. There are classical, and more modern versions such as plaque reduction. They There are classical, and more modern versions such as plaque reduction. Both require use of matched cell systems and standardized criteria to ensure comparability. Cross neutralization panels investigate the breadth of neutralization and provide a more complete picture of from the variants present

compared to the neutralization against a single variant.

Compared to single-platform schedules, prime-boost strategies have been reported to have broader neutralization breadth (Hassan et al., 2022; Ali et al., 2023). Research about the QX-like line and DMV/1639 clearly states that matched antigens increase titer levels. Neutralization is lower and declines occur more rapidly with mismatched boosters (Nakanishi & Soma, 2023; Shao et al., 2020).

Tools specific to cell-mediated immunity are necessary. ELISpot works by counting cells that secrete specific cytokines, which in this case are antigens. Each IFN- γ spot represents one that is supportive of Th1 and cytotoxic cells. Including spots of IL-4 and IL-17 adds to the Th2 and Th17 cell context. T cell subsets are classified by specific CD markers and intracellular cytokines using flow cytometry. QPCR or multiplex beads, in addition to protein readouts, are complementary to cytokine profiling. These assays demonstrate how responses are shifted due to the use of a different platform and/or adjuvants. It has been shown that DNA or vector primes elevate cellular immunity. Inactivated boosters reinforce the components of humoral immunity (Zhang et al., 2023; Sepotokele, Wandrag, Smith, O'Kennedy, & Abolnik, 2023; Bhuiyan et al., 2021). It has been shown that a balanced response of antibodies and cellular immunity is correlated to improved responses in challenge models (Hassan et al., 2022; Ali et al., 2023).

Conclusion

Infectious bronchitis virus (IBV) poses a continuously evolving and serious threat to the global poultry industry because of its high rate of genetic evolution and immune escape. Classical vaccines confer a limited degree of protective efficacy due to antigenic drift and the emergence of novel variants. Consequently, the combination of surveillance and the development of novel vaccine technologies will be fundamental in the sustainable and effective management of IBV.

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