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## A COMPREHENSIVE REVIEW OF NEWCASTLE DISEASE IN POULTRY: PATHOGENESIS, DIAGNOSIS, VACCINATION AND CONTROL MEASURES

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### ABSTRACT

Newcastle disease (ND) remains one of the most consequential viral diseases of poultry because it combines rapid transmission, high mortality in susceptible flocks, major trade consequences and incomplete protection against infection despite widespread vaccination. This critical review synthesizes contemporary knowledge on ND pathogenesis, diagnosis, vaccination and control with emphasis on the interface between molecular virology and practical flock-level disease management. Virulent Newcastle disease virus (NDV), or avian orthoavulavirus 1, exhibits pathotype ranging from lentogenic to velogenic, with virulence strongly influenced by the fusion protein cleavage site and by host, management and immunologic context. The disease classically affects respiratory, digestive, neurologic, reproductive and immune systems, but field recognition is complicated by co-infections, vaccine reactions and variable signs across species and production systems. Laboratory confirmation is therefore essential. Current diagnostic best practice combines rapid molecular screening, virulence determination by F-gene cleavage-site analysis or validated virulent-specific real-time RT-PCR, virus isolation when epidemiologically necessary and sequencing-based surveillance to track genotype shifts. Vaccination remains central to control, but live and inactivated genotype II vaccines do not always prevent infection or shedding after challenge with divergent field strains, especially genotype VII lineages. Vector, recombinant, genotype-matched, mucosal and thermostable vaccines are promising, although implementation is constrained by cost, maternal antibody interference, cold-chain capacity and uneven coverage in backyard and smallholder systems. Durable control requires layered biosecurity, active surveillance, rational vaccination schedules, emergency response capacity, transparent compensation and regionally coordinated movement controls. The review concludes that ND control should move from vaccine-centered programs toward integrated risk-based systems that link genotype-informed surveillance, vaccine effectiveness monitoring and One Health-aware governance of poultry value chains.

**Keywords:** Newcastle disease; avian orthoavulavirus 1; poultry; pathogenesis; real-time RT-PCR; vaccination; genotype VII; biosecurity; disease control

### Introduction

Newcastle disease is a highly contagious viral disease of birds and an enduring constraint on poultry production, food security and international trade. The World Organisation for Animal Health (WOAH) describes ND as a severe disease of domestic poultry and other birds caused by virulent Newcastle disease virus; the disease is reportable because outbreaks can cause substantial

morbidity, mortality and market disruption (WOAH, 2024a, 2024b). In practical veterinary medicine, the disease is especially important because clinical suspicion requires rapid action: delayed diagnosis and delayed movement control can allow NDV to move between farms, live-bird markets and backyard flocks before laboratory confirmation is complete.

The etiologic agent is Newcastle disease virus (NDV), formally classified within avian orthoavulavirus 1. NDV isolates are often discussed according to biological pathotype: lentogenic strains cause mild or inapparent infection, mesogenic strains cause intermediate disease and velogenic strains cause severe systemic disease (Alexander, 2000; Merck Veterinary Manual, 2024). However, pathotype categories should not be treated as fixed clinical labels. As Cattoli et al. (2011) emphasized, field recognition is influenced by host species, age, immune status, route of exposure, management conditions and co-circulating pathogens. Consequently, a flock that appears to have ordinary respiratory disease can still require investigation for virulent NDV in endemic or high-risk settings.

The poultry industry has made major progress through vaccination, biosecurity and diagnostic modernization, but ND remains a continuous challenge rather than a solved problem. Dimitrov et al. (2017) argued that ND vaccines have reduced losses but have not eliminated infection, shedding, or periodic outbreaks. A key reason is that most conventional vaccines are based on historical lentogenic genotype II strains, whereas contemporary outbreaks in many regions are frequently associated with antigenically and genetically divergent field viruses, particularly genotype VII lineages (Dimitrov et al., 2019; Hu et al., 2022). This mismatch does not always abolish clinical protection, but it can reduce the ability of vaccination to limit virus replication and transmission.

This review critically evaluates the current knowledge base on ND pathogenesis, diagnosis, vaccination and control. The aim is not to provide an exhaustive virology textbook, but to integrate evidence into a practical framework for researchers, veterinarians, poultry health managers and policy makers. The central argument is that high-impact ND control depends on connecting molecular diagnostics and genotype surveillance with realistic field implementation: vaccination strategies must be interpreted alongside biosecurity, flock structure, live-bird market ecology, surveillance incentives and outbreak-response governance.

### Review approach and scope

This article was structured as a critical narrative review rather than a formal meta-analysis because the literature spans experimental pathogenesis, diagnostic validation, vaccine-challenge studies, surveillance reports and disease-control policy. Priority was given to peer-reviewed reviews, experimental studies, WOAHP guidance, veterinary diagnostic manuals and recent studies addressing molecular detection or vaccine performance. The review focused on chickens and commercial/backyard poultry while acknowledging wild birds, pigeons and other avian reservoirs where they influence poultry risk.

The synthesis was organized around five questions: (i) which viral and host factors explain NDV pathogenicity; (ii) how should clinical suspicion be translated into laboratory confirmation; (iii) why do vaccinated flocks still experience outbreaks; (iv) which vaccine platforms and control measures are most appropriate in different production systems; and (v) what research and policy gaps limit sustainable control. Because the requested article is intended for a high-impact review format, the discussion emphasizes limitations, controversies, translational barriers and future directions rather than simple description.

### Etiology, classification and epidemiology

NDV is an enveloped, negative-sense, single-stranded RNA virus. Its genome encodes structural and accessory proteins that mediate attachment, fusion, replication, immune modulation and assembly. The hemagglutinin-neuraminidase protein supports receptor binding and release, while the fusion protein is central to membrane fusion and is a major determinant of virulence because its cleavage activation governs whether replication remains localized or becomes systemic (Peeters et al., 1999; Panda et al., 2004).

NDV has one serotype but substantial genetic diversity. The single-serotype concept explains why conventional vaccines can often protect against mortality caused by heterologous genotypes. Yet genotype divergence still matters: sequence variation can influence diagnostic primer/probe performance, antigenic match, virus shedding after vaccination and outbreak tracing (Miller et al., 2010; Dimitrov et al., 2019). A unified genotype nomenclature has been proposed to standardize global communication, an important requirement because inconsistent naming historically complicated interpretation of surveillance data (Dimitrov et al., 2019).

Epidemiologically, ND is maintained through direct bird-to-bird contact, aerosolized secretions, fecal contamination, contaminated equipment, vehicles, personnel, live-bird markets and movements of infected or incubating birds. WOAHP (2024a) identifies ND as a globally important poultry disease and national case definitions, such as the 2025 USDA APHIS virulent NDV case definition, reinforce the need to align diagnostic interpretation with recognized virulence criteria (USDA APHIS, 2023). In endemic regions, risk is amplified by incomplete vaccine coverage, poor cold-chain management, mixed-age rearing, informal bird trade and insufficient separation between commercial and backyard sectors.

Wild birds and pigeons can contribute to NDV ecology, but the risk they pose to commercial poultry depends on contact networks and virus lineage. Brown and Bevins (2017) noted that wild-bird involvement in virulent NDV epidemiology is context dependent; for control programs,

the more immediate risk often comes from human-mediated movement of poultry, equipment, manure, eggs, crates and live-bird market traffic. Therefore, control

models that focus only on wildlife reservoirs may miss more tractable intervention points in poultry value chains

**Table 1. Practical classification of Newcastle disease virus pathotypes and field implications**

| Pathotype                      | Typical severity in chickens | Common signs                                                                    | Laboratory/epidemiologic significance                                            | Control implication                                                                    |
|--------------------------------|------------------------------|---------------------------------------------------------------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| <b>Lentogenic</b>              | Low                          | Mild respiratory disease or subclinical infection; may be used as live vaccines | Can complicate interpretation where vaccine virus is detected by molecular tests | Maintain vaccination records; use sequencing or virulence assays if outbreak suspected |
| <b>Mesogenic</b>               | Moderate                     | Respiratory signs, reduced production, moderate mortality                       | May meet virulence concern depending on cleavage site and standards              | Rapid reporting, confirm virulence, intensify biosecurity                              |
| <b>Velogenic viscerotropic</b> | High                         | Severe depression, diarrhea, hemorrhagic intestinal lesions, high mortality     | Usually associated with virulent NDV requiring official control                  | Quarantine, movement controls, stamping out or emergency vaccination                   |
| <b>Velogenic neurotropic</b>   | High                         | Respiratory disease followed by tremors, torticollis, paralysis, high mortality | Clinical signs may appear after intense virus amplification                      | Immediate laboratory confirmation and tracing                                          |

(Alexander, 2000; Cattoli et al., 2011; WOA, 2024b).

### Pathogenesis and host response

NDV pathogenesis begins when susceptible birds are exposed through the respiratory, conjunctival, or oral-fecal routes. Initial replication commonly occurs in respiratory and intestinal epithelium, where local virus amplification may produce coughing, sneezing, rales, conjunctivitis, diarrhea and reduced feed intake. If the virus is lentogenic, replication may remain more localized; if the virus is virulent, systemic spread can involve the spleen, thymus, bursa of Fabricius, intestinal lymphoid tissue, central nervous system and reproductive tract (Susta et al., 2011; Merck Veterinary Manual, 2024).

The fusion protein cleavage site is one of the most important molecular determinants of virulence. Virulent viruses usually possess a polybasic amino acid motif that can be cleaved by ubiquitous host proteases, enabling systemic replication, whereas low-virulence viruses generally require trypsin-like proteases with more restricted tissue distribution (Peeters et al., 1999; de Leeuw et al., 2005). This principle explains why F-gene cleavage-site sequencing is central to virulence determination in diagnostic protocols (WOAH, 2024b). Nevertheless, virulence is not reducible to one motif alone; polymerase genes, accessory proteins, host immunity and infection route can shape disease outcome (Dortmans et al., 2011).

The immune response to NDV involves innate antiviral signaling, interferon responses, mucosal immunity, humoral antibodies and cellular immunity. Protection against clinical disease is often associated with antibodies

to the hemagglutinin-neuraminidase and fusion proteins, which is why hemagglutination inhibition titers are widely used as a practical proxy of flock immunity. However, antibody titer alone is an incomplete predictor of protection because mucosal immunity, cell-mediated responses, vaccine strain, administration quality and field challenge dose all influence outcomes (Kapczynski et al., 2013; Hu et al., 2022).

Virulent NDV can cause lymphoid depletion and immunosuppression, thereby increasing vulnerability to secondary infections and reducing flock performance even when mortality is not dramatic. In layers and breeders, ND can produce sudden drops in egg production, abnormal shells, reduced hatchability and long recovery periods. In broilers, losses may result from mortality, condemnation, poor weight gain and trade restrictions. Thus, pathogenesis should be interpreted not only as tissue injury but also as a production-system problem that interacts with economics, welfare and antimicrobial-use pressure.

### Diagnosis: from clinical suspicion to molecular confirmation

Clinical signs can support suspicion but cannot confirm ND. Respiratory disease, neurologic signs, greenish diarrhea, sudden mortality and egg-production declines are diagnostically important, but overlap with avian influenza, infectious bronchitis, infectious laryngotracheitis, mycoplasmosis, infectious bursal disease, fowl cholera and toxicologic events. Cattoli et al. (2011) therefore recommended laboratory confirmation as a core principle

of ND diagnosis, especially where virulent NDV or avian influenza would trigger regulatory action.

Specimen choice influences diagnostic yield. Oropharyngeal/tracheal and cloacal swabs are commonly used in live birds; spleen, brain, trachea, lung, intestine and cecal tonsils may be collected from dead birds depending on signs and stage of disease. Samples should be kept cold, transported rapidly and accompanied by vaccination history, flock age, clinical chronology, mortality pattern and epidemiologic links. Poor sample quality can produce false reassurance, particularly when only late-stage or heavily degraded materials are submitted.

Molecular assays now dominate frontline diagnosis. Real-time reverse-transcription PCR provides rapid, sensitive detection and can be designed either as broad APMV-1/NDV screening or as virulent-pathotype targeting. WOA (2024b) notes that outbreaks with compatible signs and positive screening PCR may require direct sequencing of the F-gene cleavage site or virus isolation/classical analysis if virulent-specific assays are negative or inconclusive. Recent multiplex rRT-PCR development illustrates the continuing need to detect genetically diverse class II viruses while differentiating virulent and non-

virulent pathotypes in the same workflow (Song et al., 2026).

Virus isolation in embryonated chicken eggs and hemagglutination-based assays remain important in reference laboratories, vaccine-seed evaluation and confirmatory work. However, isolation is slower, requires biosafety capacity and may not be suitable as the sole basis for urgent field decisions. Sequencing has become increasingly valuable because it resolves genotype, supports phylogeographic tracing, monitors diagnostic target drift and helps evaluate whether vaccine strategy is aligned with circulating lineages (Miller et al., 2010; Dimitrov et al., 2019).

Point-of-care and isothermal amplification technologies are attractive for resource-limited settings. Loop-mediated isothermal amplification and recombinase-aided amplification can reduce turnaround time and instrument dependence and recent reviews describe rapid detection as a priority for early control (Shan et al., 2022). Yet field deployment requires strict attention to validation, contamination control, sample preparation, operator training and integration with official confirmation. A test that is fast but poorly governed can generate either panic or complacency.

Field-to-laboratory diagnostic pathway for suspected Newcastle disease

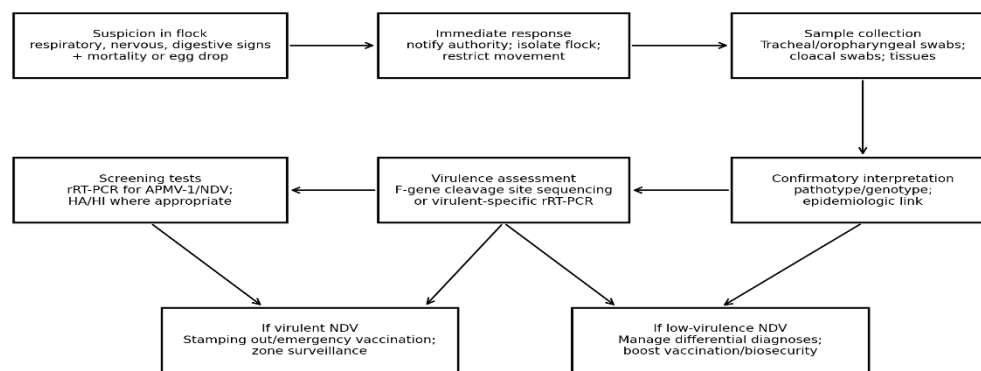


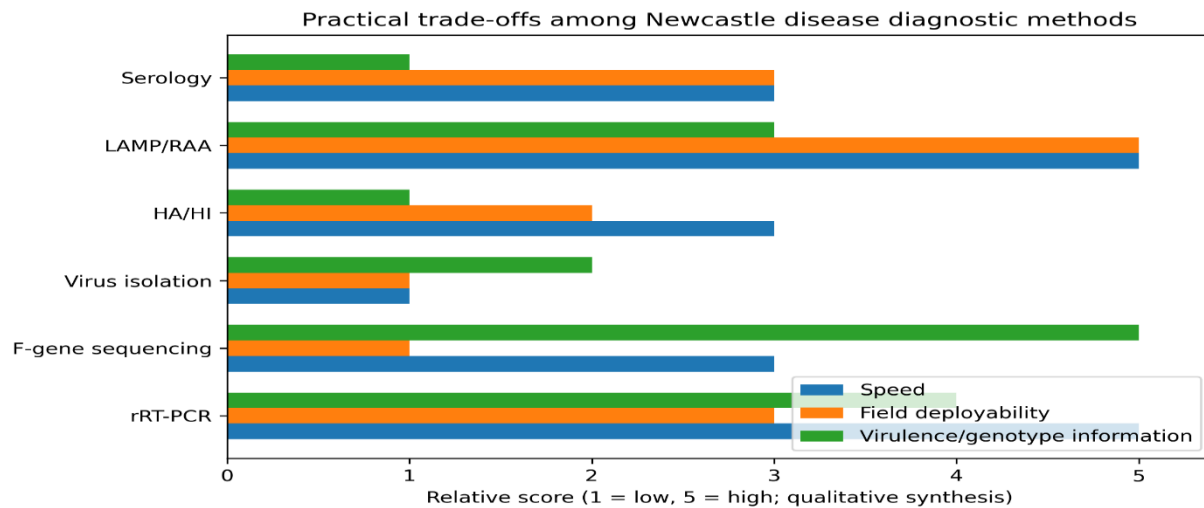
Figure 2. Field-to-laboratory diagnostic pathway for suspected Newcastle disease.

Table 2. Diagnostic methods for Newcastle disease and their critical strengths and limitations

| Method              | Best use                                    | Strengths                                        | Limitations                                                       | Critical interpretation point                       |
|---------------------|---------------------------------------------|--------------------------------------------------|-------------------------------------------------------------------|-----------------------------------------------------|
| Clinical assessment | Triggering suspicion and immediate response | Fast, inexpensive, useful for flock-level triage | Non-specific; overlaps with avian influenza and other diseases    | Never use alone for official confirmation           |
| rRT-PCR screening   | Rapid detection of NDV/APMV-1 RNA           | Sensitive, high throughput, rapid turnaround     | Primer/probe mismatch possible; vaccine strain detection possible | Interpret with vaccination history and epidemiology |

|                                        |                                            |                                                   |                                                               |                                                                 |
|----------------------------------------|--------------------------------------------|---------------------------------------------------|---------------------------------------------------------------|-----------------------------------------------------------------|
| <b>Virulent-specific rRT-PCR</b>       | Rapid risk classification                  | Useful during outbreaks and surveillance          | May miss divergent viruses if targets drift                   | Negative result may still require F-gene sequencing             |
| <b>F-gene sequencing</b>               | Virulence and genotype determination       | Directly supports pathotype inference and tracing | Slower and requires sequencing capacity                       | Cleavage-site motif must be interpreted under official criteria |
| <b>Virus isolation + HA/HI</b>         | Reference confirmation and virus recovery  | Provides live isolate for characterization        | Slow, laborious, biosafety demands                            | Useful when molecular results are inconclusive                  |
| <b>Serology/HI titers</b>              | Monitoring flock immunity and vaccine take | Low cost, practical for programs                  | Cannot distinguish infection from vaccination without context | Trend and coverage matter more than single titer                |
| <b>LAMP/RAA and other field assays</b> | Rapid local screening                      | Potentially deployable near farms/markets         | Validation and contamination control are major issues         | Positive results should feed into confirmatory network          |

(Cattoli et al., 2011; Shan et al., 2022; WOA, 2024b).



**Figure 3. Practical trade-offs among diagnostic methods.**

### Vaccination: achievements, limitations and next-generation directions

Vaccination is the cornerstone of ND control in most poultry-producing regions. Conventional live lentogenic vaccines such as LaSota, B1, VG/GA and related strains are widely used because they are inexpensive, scalable and capable of stimulating local and systemic immunity. Inactivated oil-emulsion vaccines are commonly used in breeders and layers to increase antibody duration and protect production. These tools have dramatically reduced mortality, but they do not guarantee sterile immunity (Dimitrov et al., 2017; Hu et al., 2022).

The major practical problem is the gap between protection from clinical disease and prevention of infection or shedding. Vaccinated birds may survive virulent challenge but still replicate and shed virus, especially when vaccine application is poor, maternal antibodies interfere with early vaccination, booster schedules are not completed, or field viruses differ genetically from vaccine strains. This

problem is particularly important in endemic regions because apparently healthy vaccinated birds can contribute to silent transmission, maintaining NDV pressure in multi-age farms and markets.

Genotype mismatch is a persistent debate. Because NDV has one serotype, classical vaccine strains can prevent disease even against heterologous genotype challenge. However, challenge studies and reviews suggest that genotype-matched or antigenically closer vaccines can reduce shedding and improve performance under some conditions (Miller et al., 2010; Dimitrov et al., 2017; Hu et al., 2022). Evaluation of genotype VII-mismatched commercial vaccines has reinforced that survival protection may coexist with measurable virus shedding, which matters for population-level control (Hassanzadeh et al., 2024).

Viral-vector vaccines, especially herpesvirus of turkey vectors expressing NDV fusion antigen, offer advantages

in hatchery administration, compatibility with mass vaccination and reduced vaccine-virus spread. Recombinant and reverse-genetics approaches enable rational design of genotype-matched vaccines and safer vaccine backbones. Nevertheless, vector immunity, onset of protection, local regulatory approval, cost and integration with existing infectious bursal disease, Marek's disease and infectious bronchitis schedules require careful planning. A technologically impressive vaccine can still fail if it is misapplied in a poorly managed vaccination program.

Thermostable vaccines are strategically important for village poultry and smallholder systems, where cold chains are unreliable and the economic consequences of ND can be severe for household nutrition and income. However, thermo-stability alone does not solve coverage, booster compliance, community trust, or surveillance gaps. Successful vaccination programs require training, farmer incentives, correct administration routes, monitoring of serologic coverage and periodic updating of schedules in response to field challenge.

**Table 3. Vaccine platforms for Newcastle disease: advantages, limitations and appropriate use contexts**

| Platform                                     | Examples/use                                         | Advantages                                                                      | Limitations                                                                             | Best-fit context                                  |
|----------------------------------------------|------------------------------------------------------|---------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|---------------------------------------------------|
| <b>Live lentogenic</b>                       | LaSota, B1, VG/GA-like vaccines                      | Low cost, mass application, mucosal immunity                                    | Can be neutralized by maternal antibody; reactions if mishandled; may not stop shedding | Broilers, routine endemic-zone programs           |
| <b>Inactivated oil-emulsion</b>              | Killed NDV vaccines in layers/breeders               | Longer antibody duration, safe, useful boosters                                 | Requires injection; labor intensive; weaker mucosal immunity                            | Breeders, layers, high-value flocks               |
| <b>HVT/fowlpox-vectored</b>                  | Vector vaccines expressing F protein                 | Hatchery administration, no live NDV shedding, compatibility with some programs | Cost, vector immunity, slower onset, regulatory constraints                             | Integrated commercial systems                     |
| <b>Genotype-matched recombinant</b>          | Reverse-genetics or recombinant genotype VII designs | Potentially reduced shedding against matched challenge                          | Development and approval costs; lineage drift still possible                            | Regions with dominant divergent virulent lineages |
| <b>Thermostable live</b>                     | Village poultry-oriented vaccines                    | Improved access where cold chain is weak                                        | Coverage and booster logistics remain challenging                                       | Backyard and smallholder poultry                  |
| <b>Experimental mucosal/nanoparticle/DNA</b> | Research-stage platforms                             | Potential for targeted immunity and rapid updating                              | Limited field validation and scale-up evidence                                          | Future outbreak-ready vaccine research            |

(Dimitrov et al., 2017; Hu et al., 2022).

### Control measures: integrating biosecurity, surveillance and outbreak response

ND control is most durable when vaccination is embedded within a broader risk-management system. Biosecurity is the foundation: control of farm entry, dedicated clothing and footwear, cleaning and disinfection of vehicles and equipment, rodent and wild-bird exclusion, appropriate disposal of carcasses and litter, downtime between flocks and separation of age groups can reduce challenge pressure. When biosecurity is weak, vaccines are forced to compensate for repeated high-dose exposure and the apparent failure may be misattributed to the vaccine rather than the system.

Surveillance must cover more than mortality reporting in commercial farms. Live-bird markets, backyard flocks,

fighting birds where relevant, pigeon networks and informal traders can maintain infection outside conventional farm records. Molecular surveillance can identify genotype replacement, detect incursions and evaluate whether vaccination programs are aligned with circulating viruses. Dimitrov et al. (2019) highlighted the value of standardized genotype nomenclature precisely because global control depends on comparable sequence-based information.

Outbreak response depends on the regulatory setting and poultry density. In countries or compartments free from virulent NDV, rapid stamping out, quarantine, movement restrictions, trace-back/trace-forward investigation, zoning and surveillance are often prioritized. In endemic regions, emergency vaccination, market closures, risk-based movement restrictions and intensified biosecurity may be

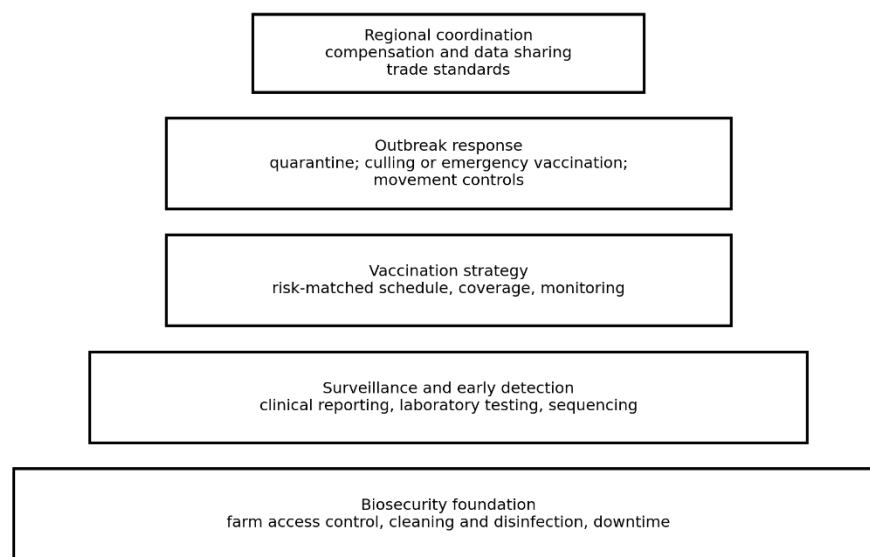
more feasible than blanket culling. Compensation policies are not merely economic tools; they influence whether farmers report early or hide disease until spread is advanced.

Differentiating infected from vaccinated animals is more difficult for ND than for some other diseases because conventional vaccines and field viruses are within one serotype and serology cannot easily separate vaccination from infection without additional design. This limitation strengthens the case for molecular surveillance, vaccine-history documentation, sentinel monitoring in some

systems and periodic evaluation of virus shedding after challenge in vaccine-effectiveness studies.

International trade adds a further layer of complexity. Official disease status, compartmentalization, veterinary certification and compliance with WOA standards affect market access. However, trade-oriented control can fail ethically and epidemiologically if it excludes smallholders. Backyard poultry often sustains livelihoods and household nutrition; therefore, equitable ND control should include affordable vaccines, community-based animal health workers, accessible diagnostics and locally meaningful communication.

#### Integrated prevention and control layers for Newcastle disease



#### *Integrated prevention and control pyramid for Newcastle disease. Vaccination is essential*

**Table 4. Control measures by production setting**

| Setting                         | Dominant risk                                         | Core prevention package                                                              | Surveillance priority                                                      | Common weakness                                    |
|---------------------------------|-------------------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------|
| <b>Integrated broiler farms</b> | High density and rapid movement between farms         | Hatchery vaccination, all-in/all-out, vehicle control, cleaning/disinfection         | Mortality triggers, routine PCR in suspect flocks, sequencing of positives | Biosecurity breaches during catching and transport |
| <b>Layers and breeders</b>      | Long production cycle and production losses           | Live priming plus inactivated boosters, serologic monitoring, strict visitor control | HI titer coverage, egg drop investigation, rapid molecular confirmation    | Uneven booster timing and multi-age exposure       |
| <b>Backyard/village poultry</b> | Low cold-chain reliability and informal bird exchange | Thermostable vaccination, community campaigns, market hygiene education              | Syndromic reporting and affordable confirmatory testing                    | Low coverage and delayed reporting                 |

|                          |                                               |                                                                          |                                                          |                                                  |
|--------------------------|-----------------------------------------------|--------------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------|
| <b>Live-bird markets</b> | Mixing of sources and continuous introduction | Market rest days, cleaning, species separation, movement records         | Environmental and bird swab surveillance with genotyping | Economic pressure against closures               |
| <b>Outbreak zones</b>    | Rapid farm-to-farm spread                     | Quarantine, tracing, movement controls, culling or emergency vaccination | Active surveillance around infected premises             | Hidden infection when compensation is inadequate |

### Critical gaps and future directions

The next phase of ND research and control should address the following high-priority gaps:

- i. Genotype-informed vaccine evaluation: Challenge studies should report not only survival and clinical scores but also virus shedding, transmission potential, production outcomes and cost-effectiveness under realistic field schedules.
- ii. Better correlates of protection: HI titers remain useful but incomplete. Integrated measures of mucosal immunity, cellular response and shedding reduction would improve vaccine-program evaluation.
- iii. Diagnostics for decentralized systems: Rapid assays need rigorous validation across genotypes, sample types and field conditions, followed by governance pathways that connect positive screens with official confirmation.
- iv. Live-bird market epidemiology: More quantitative work is needed on how bird turnover, market rest days, species mixing and informal trade networks shape NDV persistence.
- v. Smallholder implementation science: Thermostable vaccines, community vaccinators and reporting incentives should be evaluated as delivery systems, not only as biological products.
- vi. Sequencing equity: Global genotype surveillance remains biased toward countries with laboratory capacity. Regional sequencing hubs and shared nomenclature would improve early warning and vaccine-strain decisions.

A major conceptual shift is needed. ND should not be viewed as a vaccine-preventable disease in the narrow sense; it is a systems disease in which immunology, diagnostics, animal movement, market design, governance

and farmer incentives interact. High-impact research should therefore combine molecular virology with field epidemiology and implementation science.

### Conclusion

Newcastle disease continues to threaten poultry health because NDV combines genetic diversity, efficient transmission and the capacity to cause severe multisystem disease. The fusion protein cleavage site remains a central virulence marker, but field pathogenesis is shaped by host immunity, vaccination history, management, co-infections and exposure intensity. Laboratory confirmation is essential and the most defensible diagnostic strategy links rapid molecular screening with virulence assessment, sequencing and epidemiologic interpretation.

Vaccination has transformed ND control but has not eliminated outbreaks. Conventional live and inactivated vaccines remain indispensable, while vector, recombinant, genotype-matched and thermostable vaccines offer important opportunities. The central limitation is not only vaccine technology; it is the mismatch between vaccine programs and real-world implementation. Sustainable control requires layered biosecurity, active surveillance, integrated live-market management, transparent outbreak response and policies that include smallholders rather than treating them as peripheral.

The future of ND control should be genotype-informed, surveillance-driven and implementation-focused. A high-performing program will monitor circulating viruses, evaluate vaccine effectiveness against shedding and transmission, deploy diagnostics close to risk points and align farmer incentives with rapid reporting. In this integrated model, molecular science becomes operationally useful because it directly informs vaccination, movement control and outbreak prevention.

## Declarations

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**Consent for publication:** Not applicable.

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