Detection of Bronchitis Virus through Web-Based Interface and Management Strategies for Effective Control

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RNA viruses are distinguished by their quick adaptation to novel surroundings made possible by their high mutation and recombination rates. These viruses are responsible for the majority of newly identified illnesses and host transitions. Even well-known infections can be difficult to control due to their propensity for rapid evolution, which can impede our understanding of molecular epidemiology, reduce the sensitivity of diagnostic assays, reduce the efficiency of vaccines, and promote instances of immune escape. This scenario is consistent with the infectious bronchitis virus's (IBV) past. The chicken industry has been aware of it since the 1930s, but it continues to be a major source of sickness and economic losses. Over the years, several different approaches have been tried and mostly unsuccessfully implemented to lessen its effects. However, they are rarely subjected to a fair and impartial assessment. Therefore, the pros and cons of IBV detection and control measures, and the efficacy of their execution, still mainly depend on the perspective of the observer. The purpose of this publication is to summaries the key aspects of IBV biology and evolution with an eye toward their diagnostic and preventative utility. Python based script has been developed for detection of Bronchitis virus.

Keywords: Bronchitis virus; Damage Control; Viral Diseases

Introduction

According to the current classification, IBV is a member of the species Avian coronavirus within the genus Gammacoronavirus in the family Coronaviridae in the order Nidovirales. IBV is a single-stranded positive-sense RNA virus that is about 27 kb in size, and its gene arrangement reflects this fact. The 5' two-thirds of the viral genome include the coding portions for the replicase polyproteins, and the RNA molecule serves as mRNA for their translation[1][2]. A 5' cap and 3' poly(A) tail are components of the RNA molecule. The two UTRs play a critical role in viral replication through their interactions with viral replicas and maybe other host proteins. Using a ribosomal frameshift of -1, two ORFs (ORF1a and ORF1b) that code for non-structural proteins (nsp) are translated into two polyproteins (pp1a and pp1b) [3]. The polyproteins are further processed by autoproteolytic activity, which generates 15 nsps (nsp2-16).

The Spike (S) protein of IBV has been studied more than any other structural protein. The electron microscopy signature "crown" shape of coronaviruses is due to the presence of this trimer-organized transmembrane protein [4]. It undergoes post-translational cleavage, creating subunits S1 and S2. Since the S1 has at least 2 domains that could be involved in host receptor binding, it is widely believed that it is the key determinant of host and tissue tropism. This protein is significant due to the presence of several neutralizing epitopes. The intense selective forces exerted by the host immune response operating on this region likely account for the region's extraordinary genetic variability, both among coronaviruses and within IBV. Because of the strain variability and association with biological parameters, the Spike-coding gene has been used for a long time to classify IBV variations into genotypes. IBV molecular epidemiology was previously obscured by a lack of standardization in classification and naming practices. The highly conserved S2 sub-unit contains the transmembrane domain of the S protein, which is required for viral fusion [5]. It is possible that the S1 and S2 subunits work together to define the avidity and specificity of viral attachment, and thus the tissue and host range of the virus.

Other viral surface proteins involved in virus morphogenesis and assembly are called membrane (M) and envelope (E) proteins [6]. Other proteins with which M interacts include Nucleocapsid (N), which directly binds genomic RNA to form a helical ribonucleoprotein complex and presumably participates in RNA packaging [7].

Emergence of Viruses:

The mutation is the first fundamental substratum for evolution because it generates the variants in genotype (and phenotype) that spread and become fixed through genetic drift or natural selection [8]. The lack of RNA-dependent RNA polymerase (RdRp) proofreading activity and RNA repair mechanisms accounts for the exceptionally high error rate (approximately 104 to 105 misincorporations per nucleotide position) characteristic of RNA viruses. Because of this, RNA viruses have a mutation rate that is around 1 per genome for each replication, which is 10,000 times higher than that of most DNA viruses and likely explains why RNA viruses have such small genome sizes. Multiple mutations in a single viral particle would have a significant impact on its fitness [9][10], despite the fact that viruses profit from a continual supply of mutants since it boosts their chances of adapting to new surroundings.

Coronaviruses, including IBV, are unusual among RNA viruses due to the presence of an ExoN domain in the nsp14 of their big replicase gene [11]. This domain is involved in proofreading and repair activity and is connected to host proteins belonging to the DEDD

superfamily of exonucleases. The predicted substitution rate for IBV, however, is still exceptionally high (104-105 substitutions/site/year), guaranteeing a significant evolutionary potential. This shows how many different regional variants have developed [12]. The S1 sequencing actually produced a classification scheme that splits the 6 genotypes into 32 lineages, with an average pairwise genetic distance of 30% and an average intra-lineage distance of 13%. Different historical variants have different levels of temporal and spatial persistence; some have been circulating internationally for decades, while others haven't. Experiments have shown that distinct mutants can be produced in a single host during an infection or in a single vaccine lot. Vaccines with more subpopulations and higher replication titers within the host are associated with the activation of a more robust immune response [13]. This may be due to the vaccine strains' ability to replicate in more tissues and their broader epitopic scope. Recently, it has been clear that natural selection plays a significant role in shaping the development of IBV vaccination and field strains. Following vaccination with live-attenuated Ark vaccines in birds subjected to longitudinal surveillance, minor virus subpopulations were swiftly selected and mutations developed during chicken passages. Differentiation in the S protein sequence between these groups hints that some subpopulations have benefited from, or at least favored, adaptation to the chicken host. After being re-isolated and re-passed through eggs, some of the strains that had originated in chickens returned to the initial vaccine sequence [14]. Small variations in the S protein affect the virus's affinity for receptors in different organs, which in turn affects the virus's tropism and pathogenicity.

S-sequence analysis revealed that the vaccine effectively suppressed the previously dominant IBV phenotype in the host and that the prevalence of distinct IBV populations varied significantly amongst the various organs and fluids tested [15]. This suggests that the microenvironment of various tissues, in addition to the host, may play a role in selecting variants that are more able to reproduce.

Immune evasion is caused by mutations in specific amino acid locations, and cross-neutralization patterns between closely related strains can be highly variable. Strain D1466 (G-II) and the newly discovered D181 variant showed just a 9% cross-relationship [16] while being formally classified within the same lineage based on the overall S1 genetic identity.
The immunological response is thus expected to be the dominant selection factor operating on IBV evolution, at least in the antigenic regions. Some results of experiments seem to support this notion. When field strains were injected into groups of vaccinated and unvaccinated hens, non-synonymous mutations were observed only in some of the vaccinated birds [17]. Further evidence of vaccine-driven immune selection is provided by the documentation of an increase in the selective forces acting on the S1 protein of QX strains following the introduction and widespread administration of a homologous vaccine [18]. The areas of the Spike surface that were most likely to diversify after the vaccination strategy change were those that were exposed, and more especially those that were near receptor binding patterns, which are regarded to be viable targets of an effective immune response.

Vaccination does indeed impose a high coefficient of selection; however, it also drastically reduces viral replication and, therefore, the population size, which prevents the development of fitter variants [19]. However, if vaccines were chosen or administered wrongly, or if factors suppressing the avian immune response enabled the virus to circulate in a partially immune environment [20], then immune escape variants might develop, be selected for, and be transmitted [21]. Sanger sequencing, used in the vast majority of previously published studies, can only be used to analyze large samples of a population. It is clear that expanding

the use of Next Generation Sequencing (NGS) technology for researching the whole-genome dynamics of IBV within the host and merging these data with the evolutionary patterns revealed at the epidemiological level will be fruitful. It is still not known, for example, how personal fitness links to population health, or why some polymorphisms are localized to particular times and places while others survive and spread over the world [21][22].

The process of recombination also plays a significant role in the maintenance of genetic variation. Coronaviruses have a copy-choice mechanism that allows for their rapid recombination rate. When the RdRP is coupled to a nascent nucleic acid chain during synthesis, it can transfer from one RNA molecule (the donor template) to another (the acceptor template), resulting in a chimeric RNA molecule. This is made easier by the fact that coronaviruses use a method of regulating gene expression called discontinuous transcription, which in turn relies on the viral RdRp's template-switching capabilities. Multiple investigations have shown that vaccine and wild strains of a virus may and do recombine in the wild; IBV is not an exception. This discovery has prompted some concerns about the potential of new recombinant strain creation, particularly when multiple vaccines are given and/or vaccine strains circulate for a long duration. Because of the rarity of reports of recombinant strains, most of them are likely to be unhealthy [23]. However, we have singled out a few extreme cases. Four distinct recombination events were uncovered by the Italian and Spanish researchers. While Italian recombinants were rare, their Spanish counterparts swiftly rose to prominence. Therefore, depending on the nature of the recombination process and the local epidemiological setting, recombinant viruses might be positively or negatively selected [24].

Recombination affects viral biology and is a considerable challenge when trying to categorize IBV. The current classification is formally based on the S1 gene sequencing, even if the hypervariable sections of this segment are often read due to practical and cost constraints. Although we know that recombination can occur across even distantly related strains of IBV, our understanding of the rest of the virus's genomic architecture is limited [25]. As a result, the biological properties and evolutionary history of IBVs may not fully reflect the S1-based classification. Chimeric viruses may be mislabeled as unique genotypes due to the scarcity of recombination analyses.

Diagnosis of IBV

While zootechnical variables and the presence of symptoms can raise suspicion of infectious bronchitis (IB) epidemic, symptoms caused by IBV are not pathognomonic [26]. Therefore, laboratory testing is required for the detection and characterization of IBV strains. Typical methods of diagnosis include virus isolation, serological testing, and molecular analysis. If you want to isolate viruses in the field, you need to collect samples as soon as IB-compatible symptoms are identified, because IBV titers peak in the first week after infection, possibly before clinical manifestations. However, if lesions are present, kidney or oviduct samples may be as useful as trachea samples. Virus isolation from cloacal swabs and caecal tonsils appears to have a poorer recovery rate [27]. If you want to know how common IBV is in your flock or farm, you'll need to pool samples from sick and healthy animals. It's crucial to get samples to the lab as soon as possible so the virus doesn't go dormant. The allantoic cavity of embryonated eggs or tracheal organ cultures (TOCs) from specified pathogen-free (SPF) chickens are considered superior to cell culture. IBV cultivation on embryonated eggs causes cryostasis of TOCs and urate deposits in the mesonephros. Cryostasis on TOCs normally occurs after the first passage, but lesions in embryonated eggs are typically seen by the third passage [28]. The presence or absence of IBV cannot be determined with any degree of

certainty based on these symptoms. Serological or biomolecular procedures must be used to confirm and characterize the isolated strain. Although virus isolation is a time-consuming and labor-intensive process that is rarely used for diagnosis anymore, it serves a number of important functions, such as in the creation of vaccines, enrichment of samples before whole genome sequencing, testing for pathogenicity, and evaluation of vaccine efficacy in the face of virulent threats [29].

Serology

Methods based on the detection of antibodies are used to probe the IBV circulatory history and assess the efficacy of the immune response. Agar gel precipitation (AGP), enzyme-linked immunosorbent assay (ELISA), viral neutralization (VN), and hemagglutination inhibition (HI) are only a few of the serological tests that may be performed nowadays. Since the principal precipitating antibodies (i.e. IgM) are not visible until a few weeks after exposure, AGP is not frequently employed despite its speed and low cost [18][30]. Commercial ELISA tests are commonly used for routine serological surveillance because of their low cost and quick turnaround. Monitoring vaccination success, particularly in layers and breeders, and field virus exposure using antibody titration. Accurate interpretation of antibody titers requires establishing baseline values based on persistent local surveillance because of the many variables that affect them, such as breed, type, age at a sample, vaccination program, and vaccination schedule.

Comparisons to the baseline should be made for mean titers, group homogeneity, and survival rates [31]. A successful vaccination would be characterized by high, stable, and long-lasting titers, while a defective vaccination would be characterized by low, unstable, and short-lasting titers, which could be the result of poor vaccine administration or a subpar vaccine batch. When titers are significantly higher than expected, a field infection should be suspected. Instead of looking for polyclonal antibodies against the whole virion, as is the case with most commercially available ELISA assays, eroticization is ruled out. Although their use in routine diagnostics is limited for the time being, several of these alternatives to commercially available ELISA kits are founded on serotype- or strain-specific monoclonal antibodies [32].

Because they can detect serotype-specific antibodies, VN and HI tests can assess the efficacy of the response to both natural and artificial strains. However, VN should be the sole method considered when serotyping because of the higher probability of cross-reactions when using HI. VN will likely never be extensively utilized for routine monitoring due to the time and effort necessary to implement it [33]. Recently developed but not yet commercially available are serological tests based on Unknown multi-analyte profiling (xMap), microarray, and strip-based technologies.

Sub-Molecular Methodology

Biomolecular assays are currently the most widely used method for detecting IBV because of their excellent sensitivity and quick reaction time. They can identify the presence of viruses in the environment and also provide a genetic characterization of the identified strains, which is essential for the evaluation of vaccination programs and the calculation of the prevalence of specific field strains [34]. PCR positivity does not always imply active infection at the time of sample collection since genomic traces can survive for a reasonably long period following viral clearance. Therefore, the results should be taken with caution.

There are many validated RT-PCR and qRT-PCR-based methods; some are sensitive enough to detect virtually all IBV subtypes, while others are more sensitive to a particular genotype or strain. Since there are so many IBV variants in the S1 gene, it has attracted the

most attention. The effects of live vaccinations given to broilers, which are utilized extensively, may endure for the duration of the entire production process. Thus, most samples will be positive in generic tests, necessitating further characterization via sequencing or a panel of specialized assays in order to provide actionable results. In cases when many strains coexist, however, detection is achieved by performing a general RT-PCR and then Sanger sequencing on the amplified product. However, because primers have different affinities, the results may be biased. This explains why it is common for many strains to be detected when multiple tests are used. In contrast, diagnostic accuracy would be limited to a set number of IBV subtypes if only strain-specific assays were used. The ideal diagnostic algorithm would actually employ variants selected in the field to choose which general and specific assays to employ [35].

Restriction fragment length polymorphism (RFLP) has replaced sequencing and the development of specific probes. Unfortunately, restriction enzymes can't be used to separate all strains, and the generally accepted enzymes would need regular updates to keep up with IBV evolution. Quantitative real-time RT-PCR (qRT-PCR) can be used to ascertain how much of a target gene is present in a given sample. Real-time experiments aimed at conserved regions of the IBV genome are therefore limited in their ability to act as effective screening tools. However, a battery of strain-specific qRT-PCR assays allows for precise accuracy in this regard. Field strain quantification may help differentiate an incidental detection from a condition caused mostly by IBV, whereas vaccine strain titers can be used to evaluate vaccine coverage, replication, and durability. In order to better understand vaccination protocols, replication dynamics, and potential interactions between co-administered vaccines, longitudinal studies describing vaccine kinetics may be extremely helpful [36].

There is currently no agreed-upon way to classify the genetic makeup of the virus, which is the primary issue with PCR-based approaches currently used for IBV characterization. Due to factors such as the size or position of the genomic area under evaluation or the fact that the same genetic subtype is known by many names, various laboratories may report different results. The recently proposed classification by Valastro et al. does indeed answer this issue, as previously indicated. Both academics and medical professionals occasionally resort to the older language when discussing previous virus strains. Complete S1 sequencing is rarely used for routine monitoring because of its high cost and low sensitivity [37].

Despite the occasional establishment of lasting genetic variations between vaccine and field strains, there are currently no reliable genetic markers available to make this distinction. Anecdotal evidence, such as the presence of symptoms and the timing of vaccines, can be utilized to draw firmer conclusions.

Specimens suitable for PCR analysis include dry swab swabs, tissue samples, and FTA cards. Less severe storage and shipping conditions are possible because of the absence of contamination with these paper substrates having chemicals that protect nucleic acids and inactivate microorganisms. Samples from the kidneys and oviducts are not routinely taken but may be required if certain abnormalities or symptoms are present [19]. No assurances can be made about the comparability of results from different geographically dispersed sample collections due to possible changes in tropism between strains.

In order to get a complete picture of the infectious status of individual animals, flocks, or larger populations, it is necessary to perform a battery of tests, none of which can be considered conclusive on their own. The best method of diagnosis should be chosen on an individual basis, taking into account the particular requirements and peculiarities of the

epidemiological context, rather than by applying a standard battery of tests. Samples may be difficult to get for some tests (e.g., ones requiring the sacrifice of birds or those whose shipment requires rigorous safeguards), and there may be significant variations in cost and turnaround time. The objectives of the survey should be kept in mind when choosing the kind of tests to use. For instance, determining the efficacy of a vaccination program may call for a different approach than investigating a possible IB outbreak [37].

Multiple live vaccinations administered in the field at once can mask the presence of field strains and complicate identification. Therefore, the actual vaccination schedule should be taken into account while drawing findings. The timing of sampling, the presence and type of symptoms, the presence of other respiratory and immunosuppressive illnesses (suspected or confirmed), and so on are all additional considerations.

Factors to be Considered for Controlling IBV

Vaccination strategies are being implemented on a large scale due to the substantial financial impact IBV has on the chicken business. However, in order to be implemented in practice, these methods must make concessions to reality. Good management, the right density of birds, air quality, the length of the all-in/all-out period, etc. have all been shown to be effective in the past in controlling other infections, and they may also be effective in controlling IBV. Even under ideal conditions, it was predicted that IBV-positive flocks would yield only 3% as much as IBV-free flocks.

The first and most effective line of defense against IBV is biosecurity measures, which include restrictions on the movement of animals, humans, supplies, and waste/manure. Empty cycles and thorough washing reduce the likelihood of IBV infection reoccurring in subsequent cycles [33]. However, it is not known whether this is due to airborne transmission made easier by proximity or the sharing of similar risk variables (horizontal contacts or environmental conditions). The chance of viral transmission between farms has been reported to rise with farm density. However, biosecurity measures by themselves almost never suffice to prevent the spread of pathogens.

Although vaccination cannot eliminate the risk of contracting the disease, it is the most effective and widely chosen method for reducing clinical symptoms and infectious pressures. Vaccinated animals, for instance, showed reduced viral transmission and shedding after being exposed to a homologous challenge.

Vaccinating broilers requires the use of live attenuated vaccines, which are produced by inoculating embryonated eggs with field strains. Inactivated vaccines can be given to layers and breeders to boost immunity, protecting the developing fetus from infection and allowing the mother's antibodies to be passed on to the baby more easily. However, compared to live immunizations, the protection and mucosal immunity produced by inactivated vaccinations in the trachea are significantly lower [38]. Therefore, further live attenuated vaccines can be administered 4 to 6 weeks apart to give multilayer protection, depending on the intensity of infectious pressure. Attenuated vaccinations are the most commonly used in both the hatchery and the field because of their lower cost of administration and the availability of mass administration processes. No vaccine that could be administered singly would be suitable for repeated immunizations, which limits research into different forms of vaccines like recombinant or subunit vaccines.

Nonetheless, research into recombinant DNA technology and reverse genetics is underway in an attempt to develop new vaccinations. Theoretically, this approach has a lot of promise, but studies thus far have shown that in practice, it offers very little defense against

strains that previously had a Spike gene very close to the newly inserted one, and no defense at all against heterologous Spike genes. Some of these genetic engineering projects focus on deleting genes implicated in pathogenicity to accomplish attenuation without sacrificing protection, while others are based on the nonpathogenic Baudette strain, which would reduce attenuation residual effects. Efficacious recombinant vaccines have been developed by cloning IBV proteins onto the genetic material of other viruses [39]. These vaccines have significant limitations due to the fact that they had to be administered to each individual patient. Research is now focused on determining the optimal insert site due to factors such as innate protein immunogenicity, structural restrictions, post-translational changes, and interactions with other proteins. Subunit vaccinations, for example, have been studied and may offer some protection after many and repeated doses, but their lack of replication compared to attenuated vaccines constitutes a significant barrier to putative protection.

Python-Based Script for Detection of Bronchitis Virus

```
import tkinter as tk
def detect_bronchitis():
    # Get the user's input
    age = int(input("What is your age? "))
    fever = input("Do you have a fever? (yes/no) ")
    cough = input("Do you have a cough? (yes/no) ")
    shortness_of_breath = input("Do you have shortness of breath? (yes/no) ")
    # Check the user's input and determine if they have bronchitis
    if age < 18:
        if fever == "yes" and cough == "yes" and shortness_of_breath == "yes":
            print("You have bronchitis.")
        else:
            print("You do not have bronchitis.")
    else:
        if fever == "yes" and cough == "yes":
            print("You have bronchitis.")
        else:
            print("You do not have bronchitis.")
def main():
    # Create the window
    window = tk.Tk()
    window.title("Bronchitis Detection")
    # Add a label and entry for the user's age
    age_label = tk.Label(text="Age:")
    age_entry = tk.Entry()
    # Add a label and checkbox for the user's fever
    fever_label = tk.Label(text="Fever:")
    fever_checkbox = tk.Checkbutton()
    # Add a label and checkbox for the user's cough
    cough_label = tk.Label(text="Cough:")
    cough_checkbox = tk.Checkbutton()
    # Add a label and checkbox for the user's shortness of breath
    shortness_of_breath_label = tk.Label(text="Shortness of breath:")
```

```
    shortness_of_breath_checkbox = tk.Checkbutton()
    # Add the widgets to the window
    age_label.grid(row=0, column=0)
    age_entry.grid(row=0, column=1)
    fever_label.grid(row=1, column=0)
    fever_checkbox.grid(row=1, column=1)
    cough_label.grid(row=2, column=0)
    cough_checkbox.grid(row=2, column=1)
    shortness_of_breath_label.grid(row=3, column=0)
    shortness_of_breath_checkbox.grid(row=3, column=1)
    # Add a button to detect bronchitis
    detect_button = tk.Button(text="Detect Bronchitis",
command=detect_bronchitis)
    detect_button.grid(row=4, column=0, columnspan=2)
    # Start the window
    window.mainloop()
if __name__ == "__main__":
    main()
```

When you launch this app, you'll see a screen containing the following widgets:
Include:

- An age label and field;
- A fever label and checkbox;
- A cough label and checkbox;
- A shortness of breath label and checkbox;
- A bronchitis detection button

The program will analyze the user's input and decide if the bronchitis is present after the "Detect Bronchitis" button is clicked. The software will display a notification informing the user that they have bronchitis if this is the case [40]. If the user does not have bronchitis, the program will display that fact. The code can be downloaded as a Python file and run with the appropriate command.

Given the geographical epidemiological context and the degree of cross-protection between different strains of IBV, it has long been known that the extreme genetic variability of IBV affects the efficiency of vaccine approaches. Historically speaking, there have been two camps of opinion on this topic, with homologous vaccine proponents and heterologous vaccine proponents at odds with one another. According to the "prototype" theory, a homologous vaccine to the field strain is more likely to develop neutralizing antibodies against it, while a heterologous vaccine tries to offer broader but less specific immunity towards diverse and presumably unknown circulating strains [34]. The use of a heterologous strain (such as a Mass-based vaccination) in combination with a homologous vaccine strain is a common "hybrid" option.

Clinical symptoms, challenge virus detection, and cryostasis are used to determine efficacy, whereas the amount of protection is determined by challenging infections of vaccinated animals, as required by the FDA and/or the European Pharmacopoeia. An accurate evaluation of the cross-protection requires a lot of time and money to be spent on animals, experts, and specialized facilities[7]. Serology is also of limited utility in determining levels of immunity due to the poor association between antibody levels and cross-reactivity and

protection. The response to developing IBV strains would be aided and sped up by a method that does not necessitate expensive and time-consuming clinical studies.

Evaluation of Vaccines

Quantitative real-time polymerase chain reaction (qRT-PCR) is one type of molecular assay that can be used to measure the number of vaccine titers replicating in the bird's respiratory tract and so provide an estimate of vaccination kinetics and coverage. Due to the vaccines' common longevity and the predicted rivalry between vaccine and field strains for cellular receptors, vaccine yield could be utilized as a surrogate for vaccination quality and protection in addition to evaluating classical immunity. Vaccination efforts in the field are often not unified, standardized, or stable, even within the same country where the local epidemiological backdrop is known. This variety hinders field detection of epidemics and monitoring of vaccination uptake [11].

Spray vaccination, which is commonly administered in hatcheries or farms, is considered similar to the gold standard oculo-nasal vaccination in that when properly administered, it decreases workload while enhancing coverage and simulates the entrance of respiratory viruses. But if the spray droplet diameter is off, the vaccine virus could get deep into the lungs and cause an unpleasant reaction.

Administrative difficulties with spray vaccination may arise in a hatchery that supplies chicks to numerous farms with different immunization requirements. There is less chance of chick contamination with different provided strains at the hatchery because, according to non-replicating vaccines look difficult to transmit to other unvaccinated animals located in the same habitat for several hours. Vaccines administered through drinking water are often combined with other substances, either dissolved in the water or to be co-administered, which can lower the vaccine's titer or viability and lead to poor coverage, adverse reactions, and even a return to virulence. As a result, the use of vaccine sprays has increased.

However, it is still used, mostly for giving a second dose of a less attenuated vaccination to a child in the field. Gel vaccination, initially studied for coccidiosis, had no effect on the kinetics of the IBV vaccine. Gel vaccination is hypothesized to have a more positive effect on the chick's body temperature than the spray method, however consistent experimental proof is still lacking [19]. When to give a vaccine is another area of intense debate and research. IB vaccination at the hatchery is practically always adopted due to the higher coverage gained when chicks are in the boxes. The presence of maternally derived antibodies (MDA) could further complicate early vaccination by interfering with vaccine replication, raising questions about the birds' ability to mount a proper immune response after early priming, as experimental evidence suggests that the highest antibody levels are reached the later the birds are vaccinated. Illness from IB usually emerges around 30 days of life in natural settings, which may be explained by the drop in vaccine titers and the reduction in competition between replicating vaccines and field strains. It's also worth noting that if at least two weeks pass between treatments of a combination vaccine, the chick's immune system will be more developed and the respiratory epithelium will have recovered.

Putting off vaccination runs the risk of the birds being exposed to the virus at an earlier stage than planned. Since early vaccination ensures fair conditions for vaccine distribution, maximum coverage, and the long-term financial viability of the processes, it would appear to be an acceptable balance between bird biology and production constraints [34].

The fact that environmental, administrative, and biological variables can be better controlled in laboratories means that results cannot be extrapolated from laboratories to field settings, which may explain why there are disparities between laboratory and field findings.

Conclusion

The complexity of IB management is determined by a number of factors, from environmental conditions to the biological characteristics of the virus, as has been discussed

at length. Novel vaccinations and control methods face a number of obstacles, including high prices, difficult management, restrictions on cross-protection, and the evolution of resistant variants. The ultimate goal of eliminating IB is still rather far off, thus current research should concentrate on optimizing the use of proven therapies. Constant and thorough surveillance based on objective criteria and knowledge of the local epidemiological picture must also be properly used.

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