Vaccination Against Infectious Bronchitis in Chickens: An Evolving Challenge

Infectious Bronchitis (IB) is a highly contagious respiratory disease of poultry, that causes widespread economic losses within the industry. Vaccination is key to the effective control of IB, but IBV has an inherently high mutation rate, and the continual emergence of new serotypes makes this challenging. For successful IB control, alternatives to homologous vaccines are necessary and protectotyping is one such concept that has been suggested.

Infectious bronchitis is caused by the Infectious Bronchitis Virus (IBV), a Gammacoronoavirus belonging to the Coronaviridae family, and it was first reported in 1931.[1] IBV affects the respiratory, urinary and reproductive systems and clinical signs depend on the tissue tropism of the infecting virus. Coughing, sneezing, tracheal rales and ocular discharge are commonly seen, and the disease tends to be more severe in young birds. In addition, mortality rates are higher in those strains with a renal tropism (nephropathogenic strains), or where secondary infection occurs.

Structure of the Infectious Bronchitis Virus

IBV is an enveloped, single stranded RNA virus. Three virus-specific proteins (the spike, membrane and nucleocapsid glycoproteins) are encoded by the IB viral genome, and it is the spike protein that is particularly important when it comes to both infectivity of the virus and vaccine efficacy.

The spike proteins are comprised of two glycopolypeptides, termed S1 and S2, and they project from the surface of the virus, enabling attachment to the cell surface and entry into host cells. The S1 glycoprotein determines serotype and enables binding of the virus to the host cell receptor. It contains a number of epitopes (or antigenic determinants) to which antibodies attach, and indeed it is known that most haemagglutination inhibition (HI) and serum neutralisation antibodies are directed against this glycoprotein.[2]

Serotype and the S1 Glycoprotein: An Evolving Threat

While biosecurity measures are important, control of IB is focused on vaccination. However, despite widespread use of vaccines dating back to the 1950s, the disease continues to circulate widely, with a devastating impact on the poultry industry.

The lack of progress in disease control, is largely due to the inherently high mutation rate of IBV, which results in continuous genetic and antigenic changes of the circulating virus, and the emergence of new strains or serotypes.[3] The majority of these genetic mutations occur in the S1 glycoprotein, and new serotypes can result from very few changes in the amino acid sequence. In the face of this constant change, successful control of IBV by vaccination is challenging.

Homologous Vaccines and Infectious Bronchitis Control

Having a homologous, serotype-specific vaccine to protect against different serotypes as they arise is the ideal scenario. With an S1 glycoprotein amino acid sequence homologous to the circulating serotype, such vaccines may give full protection. However, given the remarkable ability of IBV to mutate and the continual emergence of new serotypes, it would be impossible to develop such a vaccine against all new strains. Even if it was possible, many of these variant serotypes disappear from circulation and may no longer be of significance by the time a vaccine was ready for use.

Heterologous Vaccines and Cross Protection

No single vaccine can protect against all emerging serotypes; however it has been shown that a heterologous vaccine virus may provide cross protection. In other words, the vaccine confers protective immunity against an IB serotype that shares cross-reacting antigens with the vaccine virus. This is possible, because despite the frequent mutations in the S1 protein that result in new serotypes, the majority of the viral genome, including some of the S1 epitopes, remains unchanged. In addition, the S2 protein, which genetically is much more stable than S1, also has epitopes that may be involved in the production of protective antibodies.

The Protectotyping Concept

Due to the constantly changing picture in the field, an alternative to the use of homologous vaccines is necessary if IB control is to be successfully achieved. Protectotyping is one such concept that has been suggested.[4]

Treatment group	Vaccine regime		Challenge (day 28)	Challenge dose	Number of birds
	Vaccination (day zero)	Booster (day 14)			
T01	None	None	None		25
T02	None	None	IBV QX	$4LOG_{10}$ EID_{50}/bird	25
T03	IB-Var 2	IB-H120			25
T04	IB-Var 2 + IB-H120	None			25
T05	IB-Var 2 + IB-H120	IB-H120			25

Table 1

Figure 1

Protectotyping involves combining vaccine virus strains that are antigenically different into a vaccination programme. Typically, a classical strain is combined with a variant strain, producing a synergistic effect and an increased level of protection than if the two strains were used separately. Studies have shown that this approach, using two or more live attenuated vaccines, can successfully confer protection against heterologous serotypes.[5]

An element of trial-and-error may be used in the field to determine the optimum vaccine or combination of vaccines. However, identifying serotypes that are prevalent in the region and using these antigenically dominant strains in a vaccination programme will maximise the chances of success, as there is likely to be significant cross-protection between emerging serotypes.

A Protectotyping Case Study: Evaluation of IB-H120 and IB-Var 2 Infectious Bronchitis Vaccines

A study[6] was carried out on 150 specific pathogen free (SPF) chickens to evaluate two live attenuated vaccines, MEVAC IB H-120 and MEVAC IB-Var 2 (Figure 1). Birds were allocated to one of five treatment groups (Table 1), and vaccines were administered by eye drop. Apart from control group T01, all birds were challenged on day 28 by administration of IBV strain QX by eyedrop.

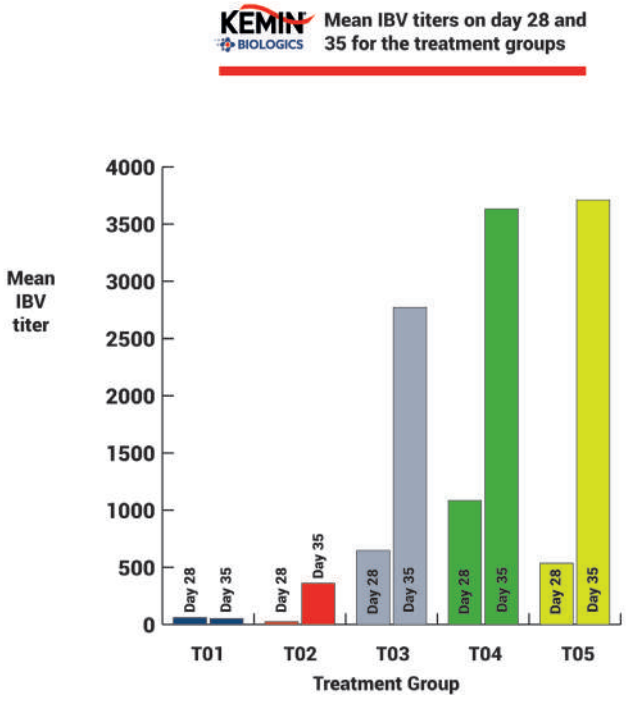

Figure 2

A number of parameters were evaluated to assess vaccination efficacy:

- **Serological Response to Vaccination: ELISA Testing**
  Mean IBV titers increased significantly in all vaccinated groups, with the highest titers in treatment groups T04 and T05 (Figure 2).

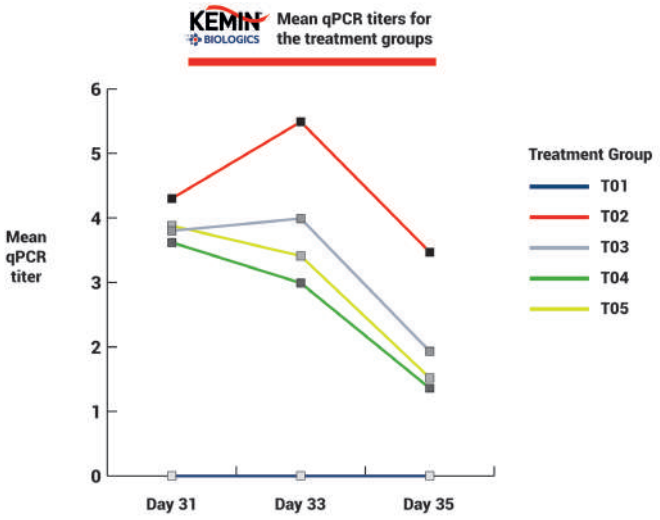

Figure 3

- **Serological Response to Vaccination: Haemagglutination Inhibition (HI) Testing**
  Haemagglutination is a reaction that causes clumping of red blood cells in the presence of some viruses, including the IBV. The reaction is inhibited in the presence of HI antibodies. At days 14 and 28, all birds apart from those in the control groups had HI antibodies against the challenge virus, IBV QX.

- **Viral Shedding: qPCR on Tracheal Swabs**
  There was a clear reduction in viral shedding for all treatment groups, showing that the vaccines were able to inhibit the replication of the IBV QX challenge virus in the respiratory tract. Treatment group T04 showing the strongest reduction of all groups (Figure 3).

- **Ciliostasis Scoring**
  Tracheal cilia form part of the mucociliary apparatus, a defence mechanism to help protect the body against respiratory pathogens such as IBV. Loss of cilia negatively impacts the body's natural defences against IBV and when assessing vaccinated birds, the lower the score, the better the level of protection provided by the vaccination regime.

  Mean total ciliostasis scores were lowest in treatment group T05, vaccinated with a combination of IB-Var2 and IB-H120 at day zero and IB-H120 at day 14 and in addition 64 percent of birds in this group showed normal ciliary activity over both days on which scoring was carried out.

- **Tracheal histopathology**
  Infection of the nasal and tracheal mucosa by IBV causes loss of ciliated epithelium[3] and impaired mucociliary clearance.

Tracheal lesions were assessed according to set histological parameters, including loss of cilia, epithelial degeneration, epithelial atrophy, the presence of exudate and congestion of capillaries. The parameters were then

scored from zero to three, based on severity and location, with a score of zero where no lesions were present, up to a maximum of three for severe or diffuse lesions. For vaccinated birds, the lowest scores were observed in the T05 group (Figure 4).

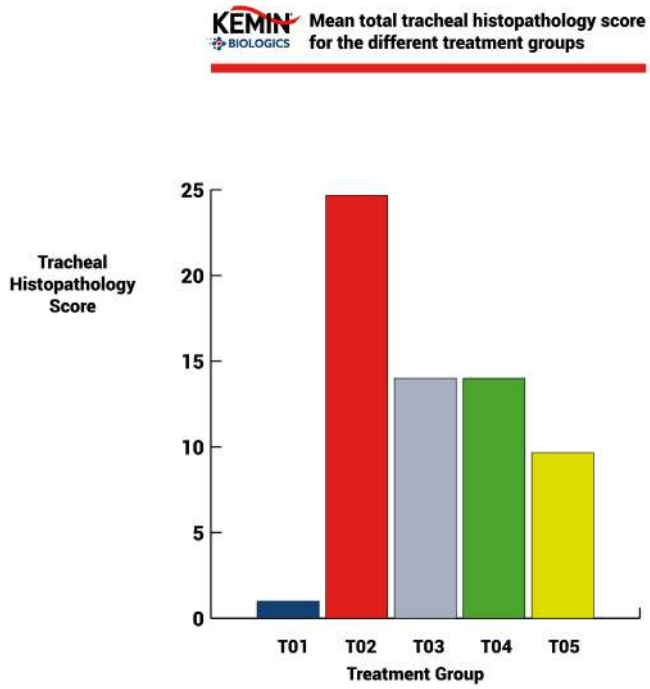

Figure 4

This study demonstrates the benefits of protectotyping. Even though IB QX was not included in the vaccine virus portfolio, a combination of variant (IB Var2) and classical (MEVAC H120) vaccine strains, provided good protection against challenge.

In Conclusion

No one combination of vaccines will provide complete protection against all IB serotypes. However, after identifying the serotypes that are prevalent in a region, protectotyping, in which antigenically different live attenuated virus strains are included in a vaccination programme, can be used to provide broad coverage through cross-protection. Greatest success is achieved where a classical strain (such as IB-H120) is used in combination with a variant strain (such as IB-Var 2). This approach is likely to play a key role in the control of infectious bronchitis both now and in the future.

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