JOURNAL OF POULTRY RESPIRATORY PROTECTION

PRP

ISSUE 1

Protectotype

A new concept for protecting poultry against IB variants

16

ISP-PBU-598

ISSUE 1
JOURNAL OF POULTRY RESPIRATORY PROTECTION

Protectotype

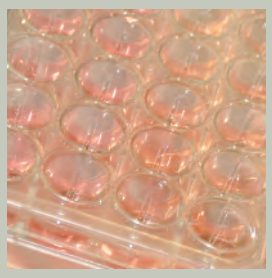
16

Control of infectious bronchitis (IB) remains challenging in poultry due to the emergence of variants. However, research shows that some IB virus serotypes are Protectotypes — meaning they cross-protect against other IB serotypes — and that the use of IB vaccines from more than one serotype can provide broad IB control. Protectotypes and the Protectotype protocol are the focus of this premier issue of *PRP*, the *Journal of Poultry Respiratory Protection*.

PRP

About the cover: How does one illustrate the Protectotype concept? What's a good metaphor for broad protection against variant IB strains? *PRP's* editorial staff struggled with that challenge for days. Then, while staring through the rain-splattered window of their warm, dry conference room, they found their image. It occurred to one editor that the beads of water coating the window were like IB variants — all very similar, but none exactly the same. "And the window is like a vaccine that's protecting us from them," another editor observed. Someone then grabbed a camera and started firing away. For a much clearer view of the Protectotypes and their applications in IB management, read this special issue of *PRP*.

Intervet
Schering-Plough Animal Health



ISSUE 1 JOURNAL OF POULTRY RESPIRATORY PROTECTION

IB variants and new strategies for control

Welcome to the premier issue of the *Journal of Poultry Respiratory Protection*, or *PRP*, a new magazine published by the Global Poultry Business Unit of Intervet/Schering-Plough Animal Health.

When we sat down to discuss the content of the first issue, it didn't take long for us to agree that the primary focus should be infectious bronchitis (IB), a disease of major importance in chickens of all types and ages. Despite the availability of quality vaccines developed to control IB, the disease continues to compromise animal welfare and cause serious economic losses for producers.

Far-reaching effects

The adverse effects of IB are also far-reaching. In broilers, for example, the disease causes respiratory infection and leads to secondary bacterial infections that result in high morbidity and variable mortality; it also results in increased condemnations at slaughter.

In layers and breeders, IB often results in poor egg production or infertility. Some strains of IB also cause severe kidney damage. (See our interview with Aris Malo, DVM, on page 9, for more details.)

Control of IB is challenging because there are many types of IB viruses besides the Massachusetts serotype first described in the early 1900s. Some IB virus variants, such as D207 (D274) and D212 (D1466), have been around since the 1960s. In the early 1990s, a major new variant — 4/91 — was identified and continues to be an important respiratory pathogen throughout Europe and other regions of the world. In France, it is still the dominant variant IB virus. More recently, two other IB virus variants that have emerged in Europe are Italian 02 and QX (D388).

Poultry producers have asked whether a new vaccine needs to be developed to combat each new strain of IB virus that surfaces. However, Jane Cook, BSc, PhD — a well-known IB expert — doesn't think so.

Strategic approach

In an article beginning on page 5, she notes that while various IB viruses differ antigenically, they still share many of the same antigens. Currently available vaccines should, therefore, protect against many IB viruses of different serotypes, she says. This strategic approach to vaccination is also more practical and less costly than developing a live-IB vaccine for each new variant that emerges.

As you consider new strategies for IB management, you might also want to become more familiar with what we call the "Protectotype" protocol. Both research and field experience show that using two existing IB vaccines based on different IB serotypes — for example, Nobilis IB Ma5, which is based on the original Massachusetts serotype, followed by Nobilis IB 4/91 — can provide broad protection against many IB variants. This, in turn, improves animal welfare and reduces the economic devastation that can occur due to IB outbreaks.

We hope this first edition of the *Journal of Poultry Respiratory Protection* enhances your understanding of IB variants and the tools that are available to control this costly disease. We'll explore other respiratory topics in the future. For more information, please contact your Intervet/Schering-Plough Animal Health representative or contact me at frederic.david@intervet.com.

FRÉDÉRIC DAVID, DVM

Global Marketing Director
Global Poultry Business Unit
Intervet/Schering-Plough Animal Health

Peer-reviewed website offers practical information on IB

This easy-to-navigate website...is designed for poultry veterinarians and specialists worldwide.

The first peer-reviewed website about infectious bronchitis (IB) in poultry — www. infectious-bronchitis.com — has been developed with the support of Intervet/Schering-Plough Animal Health.

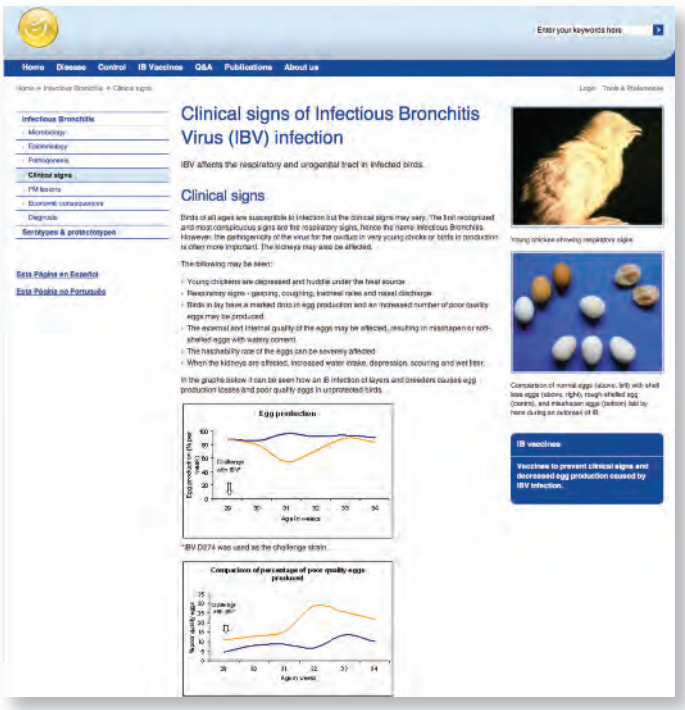
This easy-to-navigate website is available in three languages — English, Portuguese and Spanish — and is designed for poultry veterinarians and specialists worldwide. It provides information about the pathogenesis, microbiology, epidemiology and clinical signs of IB and provides a platform for peer-reviewed articles and current IB news items.

Viewers will also find articles about important IB variants that have emerged around the globe and explanations of IB Protectotypes — the IB serotypes that have an ability to cross-protect against other IB serotypes.

The "Control" section of the IB website includes information about live- and inactive-IB vaccines, application methods, vaccination programs and biosecurity. There is also a page devoted to common questions and answers about IB vaccination, and a "Publications" page with links to key IB studies.

On the "About us" page of the website, registered users can ask experts at Intervet/Schering-Plough Animal Health questions about IB.

The site reviewers are IB experts Jane Cook, BSc, PhD, an editor for the journal *Avian Pathology* and a consultant, and Mark Jackwood, PhD, a molecular virologist at the Poultry Diagnostic Research Center, University of Georgia, USA. Both have conducted extensive IB research and contributed information to the website.



www.infectious-bronchitis.com

ISSUE 1 JOURNAL OF POULTRY RESPIRATORY PROTECTION

Vaccination with two serotypes helps control IB in chickens

expertise

in 30 seconds

- Infectious bronchitis (IB) virus is highly infectious and affects chickens of all ages, type and breed in all countries where there is a developed poultry industry.
- Variants of IB virus continue to emerge.
- No single vaccine can effectively control all strains of IB viruses, but using currently available vaccines of two different serotypes in the program can very often provide protection against many different IB variants.

New variants of infectious bronchitis (IB) will continue to emerge, but currently available vaccine programs can control many of them, says poultry consultant Jane Cook, BSc, PhD, an authority on this highly infectious disease.

"Do we need a new vaccine for every different serotype or genotype that's found? I think the answer to that is most definitely no, we don't," says Cook, who is based in the UK.

Cross-protection against the different variant strains of IB virus that arise is much broader than the results of laboratory tests suggest, she says, emphasizing that using vaccines of two different serotypes is probably the best approach for producers who want good IB control.

IB causes disease and economic losses in all parts of the world that have a developed poultry industry. It affects chickens of all ages, type and breed and it is unlikely that this highly infectious disease will ever be eradicated, she points out.

In broilers, IB causes respiratory infection that is often complicated by secondary bacterial infection, leading to high morbidity and variable mortality; renal damage resulting in morbidity and mortality may also occur.

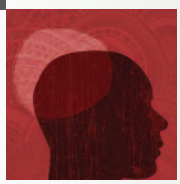
In layers and breeders, IB is associated with a drop in egg production — one that may never return to the pre-infection level. The virus also can lead to poor eggshell quality, color and internal egg quality (watery whites). Respiratory infection may occur, but its importance is minimal compared to the effect of IB on egg-laying performance, Cook says.

continued

"Do we need a new vaccine for every different serotype or genotype that's found? I think the answer to that is most definitely no, we don't."

JANE COOK, BSc, PhD

ISSUE 1 JOURNAL OF POULTRY RESPIRATORY PROTECTION



Vaccination with two serotypes helps control IB in chickens

continued from page 5

Understanding serotypes and testing

Different serotypes of IB appear either by spontaneous mutation or by recombination, which may occur when two different virus particles are in the same chicken cell at the same time, she says.

Connecticut, the first IB virus variant, was identified in the 1950s, and others followed. The traditional way to detect and identify IB variants was by isolating the virus, then by serotyping using cross-neutralization tests, which are expensive, time-consuming and difficult to do. However, since the advent of molecular methods for genotyping, such as the reverse transcriptase polymerase chain reaction (PCR) — a technology that gives results much more quickly than previously available diagnostic methods — many more variants have been identified.

Most variants do not survive, but some, such as Arkansas or 4/91, do survive and become economically important, Cook explains. However, because the techniques are so sensitive, caution must be applied when performing the test and when interpreting results.

A potential problem with molecular methods is illustrated by experience with the IB-variant Italian 02. This variant is easily detected by PCR testing, has a wide distribution and is often impossible to isolate, but it is rarely associated with disease. In contrast, the IB-variant QX is easily detected by PCR, can frequently be isolated and is associated with disease.

"So, we have a PCR technique that is very easy and widely used to detect these viruses," she explains, "but caution is required because sometimes a situation may arise where there is a much better correlation between isolation of the virus and disease than there is between genotyping by PCR and disease.

"PCR is a very useful technique, but interpretation needs a lot of care," she continues. "Basically, if you can't actually isolate the virus and you can't associate the PCR results with disease, then is the virus important?"

Two-serotype strategy

Cook suggests using two different types of vaccines for IB control — a recommendation she bases on independent, controlled studies that she and colleagues conducted.[1]

Investigators used an Ma5 vaccine, which is of the Massachusetts serotype and highly immunogenic, and the 4/91 vaccine, which is antigenically different from Ma5. They gave chickens either no vaccine, the Ma5 vaccine alone at 1 day of age, the 4/91 vaccine alone at about 2 weeks of age or the Ma5 vaccine at 1 day of age followed by 4/91 at 2 weeks of age. The birds were challenged at 5 weeks of age with different variants from different countries. Protection was determined by scoring ciliary activity in the tracheal epithelium.

Generally, birds that received both vaccines 2 weeks apart had the best protection against challenge with variant IB virus strains, she reports.

Spacing out vaccination

While it would be more convenient to give the two IB vaccines together at 1 day of age, Cook says this isn't always the most effective.

"If the challenge is homologous, then protection is good if the two vaccines are given together at 1 day old. But if the challenge is with a different serotype or genotype of virus, then it is beneficial to leave about 14 days between the two," she says.

However, if challenge is anticipated to occur at a very early age, or if the other vaccines included in the program make any other option difficult, application of both vaccines at 1 day old may well provide good protection.

"Sometimes," Cook adds, "you find a challenge strain where protection is not really good, even using this combined vaccine program. But I must say, they are rare, and on most occasions, you certainly see an enormous benefit from the use of these two vaccines in the program."

Asked why producers should use the Ma5 vaccine instead of the commonly used and less expensive H120-strain vaccine, Cook says, "H120 may control IB problems and, if so, well and good! If not, then it is worth trying Ma5, which is strongly immunogenic and provides good, broad protection. If IB is a major problem, the cost of an Ma5 vaccine becomes less of a factor to consider."

Cook also cautions that producers vaccinating against IB virus at 1 day of age should wait 7 to 10 days before vaccinating against avian pneumovirus because IB and pneumoviruses can compete for the same receptors in the respiratory tract and interfere with one another.

> "PCR is a very useful technique, but interpretation needs a lot of care."
>
> JANE COOK, BSc, PhD

Should you adopt a Protectotype strategy?

The practice of using vaccines of two different serotypes has become known to many scientists as the Protectotype strategy or protocol. For more information on this concept and how it relates to managing IB, see the interview with Aris Malo, DVM, beginning on page 9, and Portfolio on page 16.

[1] Cook, J.K.A., *et al.* Breadth of protection of the respiratory tract provided by different live-attenuated infectious bronchitis vaccines against challenge with infectious bronchitis viruses of heterologous serotypes. *Avian Pathology* 1999:28;477-485.

ISSUE 1 JOURNAL OF POULTRY RESPIRATORY PROTECTION

conversations

Q&A

Understanding IB: What you need to know

Aris Malo, DVM,* clears the air about IB variants,

the challenges of control programs and the value of using a Protectotype strategy with vaccines of different serotypes.

Q How big of a problem is infectious bronchitis (IB)?

AM: IB remains a highly infectious, common and costly disease in commercial poultry around the world. The virus can spread through an entire flock in only 1 or 2 days, causing widespread morbidity and variable mortality.

Q What are the common manifestations of the IB virus?

AM: The disease starts in the respiratory tract and can cause respiratory signs such as gasping, coughing and nasal discharge, but the virus can also spread quickly throughout the bird, affecting the reproductive tract and kidneys.

Q What are the economic losses that occur due to IB?

AM: In broilers, producer losses from IB occur due to poor growth and feed conversion, secondary bacterial infections that require antibiotic treatment and increased condemnations at slaughter.

In layers and breeders, egg production and quality are adversely affected. Losses from kidney damage can occur in broilers, layers and breeders.

Q Why is IB so difficult to control?

AM: New IB serotypes are emerging all the time. The genetic makeup of the IB virus can be altered by spontaneous mutation or by recombination, which is the exchange of genetic information with another genome.

Many of the IB virus-variant strains that develop don't survive long enough to become a problem, but some do, and those are the ones we have to worry about — the surviving, pathogenic variants.

Q What new variants are the most important?

AM: One is the variant known as IB 4/91, which is found in many parts of the world, including Europe. Another is called QX — it's thought that this variant originated in China, then spread to Europe. It can lead to proventriculitis, severe kidney damage, permanent damage in the oviduct (resulting in so-called "false-layers") and poor egg production.

"Many of the IB virus-variant strains that develop don't survive long enough to become a problem, but some do, and those are the ones we have to worry about — the surviving, pathogenic variants." ARIS MALO, DVM

Q There's been much discussion lately about developing a "Protectotype" protocol. What do scientists mean by that? And how does it relate to IB-management programs?

AM: Some IB virus serotypes are able to cross-protect against other IB serotypes; these have become known as Protectotypes. There's a reason for this. New IB variants can arise due to very small changes in the makeup of the IB virus, but the rest of the virus' genetic makeup remains the same. This is why some cross-protection is thought to occur.

An example of a Protectotype protocol is one featuring the live vaccines Nobilis IB Ma5 and Nobilis IB 4/91. The Ma5 vaccine is based on the classical Massachusetts IB virus serotype, while the 4/91 vaccine is based on the 4/91 IB variant serotype. Used together, they can provide broad protection against an IB challenge.

Q What evidence is there that the Protectotype protocol works?

AM: Carefully designed studies have demonstrated the efficacy of the Protectotype protocol.

In one study, specific-pathogen-free chickens received Nobilis IB Ma5 at 1 day of age; it provided excellent protection against the USA Arkansas IB isolate and IB isolates from Brazil and Japan. Nobilis IB 4/91 used alone at 14 days of age protected against the same three isolates plus an IB isolate from Italy. However, the best cross-protection occurred when both vaccines were used and when Ma5 was administered before, rather than at the same time or following, the 4/91 vaccine.[1]

In 2008, Italian investigators concluded from their study that the use of these two vaccines may be "instrumental in reducing the economic impact of QX IB virus infections" on layer and broiler farms. [2]

Another study demonstrated that the 4/91 live strain used alone, and especially live Ma5 plus 4/91, protected well against a nephropathogenic IB virus (B1648) — a strain that attacks the kidneys.[3]

Q What about field experience with the Protectotype protocol?

AM: The results from studies are being proven true in the field.

A recent case occurred on two Middle Eastern broiler farms. One had been using only the Ma5 vaccine and the other was using H120 vaccine.

After the Protectotype protocol utilizing Nobilis IB Ma5 and Nobilis IB 4/91 was initiated, mortality on both farms declined and bodyweight improved.

More specifically, at one farm following just two cycles of the Protectotype protocol, mortality dropped from 35% to less than 8%. Furthermore, bodyweight increased from 1.406 grams to 1.600 grams — nearly 14% — and days until slaughter de-creased from 36.05 to 34 days.

Q Why not develop new vaccines for new strains that emerge?

AM: Developing a new vaccine for every significant IB variant that emerges would be impractical and costly, especially in today's regulatory environment. A recent survey conducted in the UK demonstrated that a wide variety of IB strains is circulating, and the situation is likely to be similar in other European countries.

Because existing vaccines can effectively control many IB strains, it makes more sense to use what's already available.

Q Could an IB H120 vaccine be used instead of an Ma5-strain vaccine as part of the Protectotype protocol?

AM: In some circumstances, an IB H120-strain vaccine may be adequate, but generally, field results have been better when the Ma5-strain vaccine is used.

Detailed genetic studies conducted in Brazil have demon-strated that even though H120 and Ma5 are both from the Massachusetts IB serotype, they differ. The Nobilis IB Ma5 strain's S1 subunit of the spike gene was found to be structurally different compared to an H120 strain. It's thought that this finding explains why the Nobilis IB Ma5 strain appears to be more immunogenic than H120.[4]

As far back as the 1980s, a study conducted by Intervet/Schering-Plough Animal Health indicated that Ma5 may be more immunogenic than H120. (See Table 1.)

Aris Malo, DVM,*
clears the air about IB variants, the challenges of control programs and the value of using a Protectotype strategy with vaccines of different serotypes.

conversations Q&A

	4 days after challenge with IB strain M41		
Vaccine administered at 1 day of age	% of birds with clinical signs (n=10)	% of birds protected determined by viral re-isolation (n=10)	% of birds protected determined by ciliostasis (n=5)
H120	30%	60%	80%
Ma5	0%	90%	100%
Control	90%	0%	0%

TABLE 1. Results when chickens vaccinated with either Ma5 or H120 were challenged 5 weeks later with a different strain

Q What if I also need to vaccinate against Newcastle disease?

AM: Nobilis IB Ma5 will not interfere with the Nobilis Clone 30 Newcastle disease vaccine. If other live-IB vaccines are used, they should be given 1 week apart from additional respiratory disease vaccines to prevent interference, which occurs when both vaccines compete for the same receptor sites in the trachea.

Q Won't biosecurity and good husbandry practices keep IB under control?

AM: Biosecurity and good husbandry practices are crucial for control of IB but are seldom sufficient. They must be used along with IB vaccines — which must be administered properly to get the best results.

REFERENCES

[1] Cook, J.K.A., *et al.* Breadth of protection of the respiratory tract provided by different live-attenuated infectious bronchitis vaccines against challenge with infectious bronchitis viruses of heterologous serotypes. *Avian Pathology* 1999:28;477-485.

[2] Terregino, C., *et al.* Pathogenicity of a QX strain of infectious bronchitis virus in specific-pathogen-free and commercial broiler chickens, and evaluation of protection induced by a vaccination programme based on the Ma5 and 4/91 serotypes. *Avian Pathology* 2008:37; 487-493.

[3] Cook, J.K.A., *et al.* Protection of chickens against renal damage caused by a nephropathogenic infectious bronchitis virus. *Avian Pathology* 2001:30;423-426.

[4] Torres, C.A., Universidade de São Paulo, Brazil, *et al.* On the molecular basis of the higher protection by Nobilis IB Ma5 strain of IBV against infectious bronchitis when compared to H120. Article on file at Intervet/Schering-Plough Animal Health.

* *Aris Malo, DVM, is a technical service manager for Intervet/Schering-Plough Animal Health and is based in Boxmeer, the Netherlands.*

Molecular studies help explain better immunogenicity of infectious bronchitis strain Ma5 compared to H120

Recent molecular studies using state-of-the-art technology may explain why an infectious bronchitis (IB) vaccine based on the Ma5 strain provides better protection in poultry than a vaccine with an H120 strain.

"We've known, based on performance data from poultry producers, that protection against an IB field challenge is better when an Ma5 vaccine is used compared to the traditional H120 vaccine strain, even though both strains are from the Massachusetts IB serotype," says Laura Villarreal, DVM, technical manager, Intervet/Schering-Plough Animal Health, Latin America.

"Our aim was to discover if there is a molecular basis for this difference in performance," says the veterinarian, who was a co-investigator in a study led by Paulo Brandão, DVM, and Carolina Torres, DVM, Universidade de São Paulo.

Laura Villarreal, DVM: The IB Ma5 and H120 strains differ structurally.

Structural differences

Using sophisticated testing methods, including RNA extraction, real-time polymerase chain reaction and gene sequencing and analysis, the researchers found that the IB Ma5 strain in the vaccine Nobilis IB Ma5 has structural differences in the S1 subunit of the spike protein compared to an H120 IB strain.

The S1 subunit of the spike protein, Villarreal explains, is directly involved in the stimulation of neutralizing antibodies and, thus, protection.

Although changes in the S1 subunit can occur, she notes, the rest of an IB virus strain remains largely unchanged. This is why some strains of IB cross-protect against other IB strains.

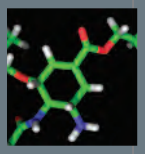
Remaining stable

"The differences found in the S1 subunit of the Ma5 strain are thought to be the result of amino acid mutations that might have actually helped the strain to become more immunogenic and more effective as a vaccine," Villarreal says.

"Even though both strains belong to the Massachusetts serotype, they had different selective pressures during their evolution," she adds.

However, the investigators found no differences in the clones of both strains used for sequence analysis, which indicates that the strains tested were stable and would remain stable in a vaccine formulation.

Moving forward, investigators will perform *in vivo* studies to expand on the findings of the current study, Villarreal says.



ISSUE 1 JOURNAL OF POULTRY RESPIRATORY PROTECTION

Respiratory vaccine 'failure' often due to poor application

expertise

in 30 seconds

- Outbreaks of respiratory disease could very well be due to problems with vaccine application, not vaccine failure.
- Proper vaccine application in large flocks can be challenging, even for skilled professionals, and can be affected by a variety of factors such as ventilation and lighting.
- Producers should refrain from mixing their own vaccine combinations because it could lead to poor results.

Outbreaks in chicken flocks vaccinated against respiratory diseases could very well be the result of improper vaccination application — not vaccine failure, cautions Sjaak De Wit, DVM, PhD, at GD Animal Health Service, Deventer, the Netherlands.

Producers want the application of vaccines to be convenient, fast, inexpensive and effective, but these are challenging goals — especially in large flocks because vaccination is often performed under difficult conditions that many times include hot weather, high humidity and long hours.

To underscore his point, De Wit cites a small-scale field study conducted at the University of Utrecht, designed to assess the efficacy of vaccine application. Inexperienced veterinary students and a professional vaccination team injected 16.5-week-old birds with an inactivated vaccine. Their skill was determined by obtaining hemagglutination inhibition titers from birds.

The percentage of birds missed by the professional team was much higher than the percentage missed by students, who were nervous but tried hard to do a good job. The take-away message from the study: "Checking for quality is a good thing. It won't cost you money; it will bring you money," De Wit says.

IB field vaccination

Experiments have also shown that proper field application can be difficult to achieve with live infectious bronchitis (IB) virus vaccines. In a Dutch study, investigators who used an eyedropper to administer an IB vaccine to six groups of commercial broilers achieved a protection level of 89% to 100%. However, protection of birds from the same six flocks that had received the same vaccine at the same dose by spray or drinking water ranged from 0% to 86%.

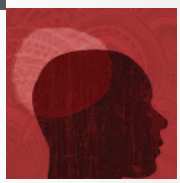
"Most surprising were the differences seen on the same farm," De Wit says.

continued

photo: Dr. Sjaak De Wit at his lab in Deventer. "There are several things going on in chicken houses that influence the efficacy of vaccination."


ALTRA20
OLYMPUS
CKX41
OLYMPUS

ISSUE 1 JOURNAL OF POULTRY RESPIRATORY PROTECTION



Respiratory vaccine 'failure' often due to poor application

continued from page 13

At one farm, protection was 0% in one house and 50% in another, even though the same veterinarian vaccinated all of the birds. At another farm, birds in one house showed only 10% protection but in a second house 86% were protected. At the third farm, birds in one house showed 37% protection but in a second house the protection level was 73%.

"We concluded that there are several things going on in chicken houses that influence the efficacy of vaccination," which prompted another field trial, he says.

In the study, investigators used an IB-vaccine spray to immunize 360 flocks — including broilers, broiler breeders, broiler grandparents and layer pullets — at around 14 days of age. Immunoglobulin M (IgM) testing indicated that only 46% were responding, a level significantly lower in broilers and pullets than in broiler grandparents, De Wit says, adding that it appears that the bigger the flock, the lower the rate of vaccine response.

"We also saw a very, very significant relationship between sampling time and IgM response," he continues. "If sampling for IgM was conducted later, the response to the vaccine was higher. Basically, that means that there's a lot of spreading of the vaccine through the flocks.

"The good news is that spreading compensates for birds that were missed when vaccinating, and the bad news is that if the vaccine had been applied correctly in the first place, spreading wouldn't be needed," De Wit adds, noting that a complete overview of the study was published in the April 2010 issue of *Avian Pathology*.[1]

House conditions affect vaccine response

A better vaccine response occurred if the ventilation system was turned off while spraying the vaccine. However, some veterinarians don't like to spray a vaccine with the ventilation system off because it causes the temperature to go up, which stresses birds. In this trial, the IgM response was 15% lower if the ventilation system was on during vaccine application, he says.

A better vaccine response also occurred when lights in the house were on during vaccination — the response was 78% with lights on, compared to 37% if the house was dark, De Wit continues.

This fieldwork also showed that when higher temperatures of water were used to reconstitute and spray the vaccine, the IgM responses were significantly lower, he says.

Other reasons for poor vaccine efficacy can be an incorrect dosage, poor water quality if the vaccine is administered in water, the presence of another virus or interference from other vaccines, he notes.

De Wit cautions producers against making their own vaccine combinations because it could result in poor results. "It's much better to rely on data from the vaccine manufacturers than to mix up vaccines yourself," he says.

An increased incidence of respiratory outbreaks can also occur if something changes in the field. "Maybe the field pressure has gone up, there's a different virus or it's more aggressive or another variant," he says. "But very often, if you have done some research, [you discover that] the virus has not changed and the application of the vaccines was not very good," he says.

In the end, it's common for a producer with more outbreaks of respiratory disease to say that the vaccine didn't work. "But I think that, in general, it would be wise to ask if the application is really as good as you assumed it was," De Wit says.

[1] De Wit, J.J., *et al.* Efficacy of infectious bronchitis virus vaccinations in the field: association between the α-IBV IgM response, protection and vaccine application parameters. *Avian Pathology* 2010:39(2);123-131.

Two IB vaccines of different serotypes help producers implement 'Protectotype' strategy

Field experience and studies demonstrate that infectious bronchitis (IB) variants can be controlled by using two vaccines of different serotypes, or what many specialists now call a Protectotype strategy.

Research has demonstrated that some IB vaccine viruses can induce effective cross-protection against strains from serotypes other than those of the vaccines used, explains Aris Malo, DVM, global technical director for Intervet/Schering-Plough Animal Health.

A combination that is proving to be effective in the field is Nobilis IB Ma5 and Nobilis IB 4/91, an approach that Malo calls "a Protectotype protocol." Nobilis IB Ma5 is based on the Massachusetts serotype, while Nobilis IB 4/91 is built on the IB-variant 4/91 serotype — one of the most common IB virus variants in Europe, the Middle East, Asia and Africa.

Extensive field monitoring

Evidence that the Protectotype concept works when these vaccines are utilized comes from x-OvO, a diagnostic services company headquartered in the UK. Richard Currie, DVM, president of x-OvO, says his company's extensive field monitoring of Nobilis IB Ma5 and Nobilis IB 4/91 shows that "the combination of these two vaccines provides extremely broad protection against a wide variety of IB-variant viruses."

Any vaccine coverage, he explains, will favor the selection of immunological escape mutants that will naturally "escape" the protective response of that vaccine.

"By using a vaccine, you are encouraging the variation that will lead to the generation of a new variant," he explains. "However, because the Ma5 and 4/91 combination gives the broadest protection, it is less likely than other vaccine combinations to select immunological escapes since it is more likely to completely neutralize any challenge."

continued

"...because the Ma5 and 4/91 combination gives the broadest protection, it is less likely than other vaccine combinations to select immunological escapes since it is more likely to completely neutralize any challenge."

RICHARD CURRIE, DVM

ISSUE 1 JOURNAL OF POULTRY RESPIRATORY PROTECTION

Two IB vaccines of different serotypes help producers implement 'Protectotype' strategy

2 IB

portfolio

Monitoring of the vaccines by x-OvO has also involved confirming the exact genetic sequence of the vaccine strain circulating on farms and has demonstrated that both vaccines are stable. "We have shown that the viral sequences of these two vaccines remain consistent, despite widespread cycling through the chicken population on farms," he says.

Long track record

Malo says that Nobilis IB Ma5 has been available worldwide for over 20 years and Nobilis IB 4/91 for more than a decade. Both vaccines, which are manufactured by Intervet/Schering-Plough Animal Health, can be administered by coarse spray, eye drop or in drinking water, although the eye-drop and coarse-spray methods are preferable because they better stimulate local immunity.

In one study, administration of the Ma5 vaccine alone at 1 day of age provided excellent protection against the Arkansas IB isolate from the US and IB isolates from Brazil and Japan. The IB 4/91 vaccine used alone at 14 days of age protected against the same three isolates plus an IB isolate from Italy. Cross-protection was best, however, when birds received both vaccines, Malo says.

In a study published in the October 2008 issue of *Avian Pathology,* Italian investigators concluded that the use of Nobilis IB Ma5 and Nobilis IB 4/91 "may be instrumental in reducing the economic impact of QX IB virus infections" on layer and broiler farms.

Strategic combinations

The Ma5 vaccine can also be used with the live Newcastle disease vaccines such as Nobilis Clone 30. In layers, the Ma5 and IB 4/91 vaccines have been shown to be effective "primers" for an inactivated-IB Massachusetts booster before the onset of lay, he says.

Recent experience on two poultry farms in the Middle East demonstrated that after using IB vaccine protocols for broilers that featured three vaccines — Nobilis IB Ma5, Nobilis IB Ma5 + Clone 30 and Nobilis IB 4/91 — bodyweight increased and mortality from IB virus and days until slaughter decreased, Malo adds.

Currie sees one other advantage to the use of Nobilis IB Ma5 and Nobilis IB 4/91: flexibility. Having two individual vaccines with different serotypes enables veterinarians to time administration of each so that vaccine-strain replication is optimal when the challenge is highest. In contrast, bivalent products administered at a single time point rely on an extended duration of immunity, which can be "very variable" in a field situation, he says.

A practical example of this would be concern among veterinarians that hatchery administration of a bivalent vaccine may not give adequate protection toward the end of the commercial broiler's lifespan, particularly in birds grown for 6 weeks or longer. Administration of the Nobilis combination program, with IB 4/91 administered at day 14 of age, will often relieve concerns about maintaining adequate protection during this critical economic period of the broiler's life, Currie says.

For more information about the Protectotype strategy with Nobilis IB Ma5 and Nobilis IB 4/91, contact your Intervet/Schering-Plough Animal Health representative or go to www.infectious-bronchitis.com.

for the record

> When infectious bronchitis occurs in a laying flock, production usually drops to near zero within a few days. Four weeks or more may be required before the flock returns to production. Some flocks never regain an economical rate of lay.

POULTRYHUB.ORG
November 9, 2010

> Infectious bronchitis is considered the most contagious of poultry diseases. When it occurs, all susceptible birds on the premises become infected, regardless of sanitary or quarantine precautions.

MSUCARES.COM
October 14, 2010

> Many [IB] serotypes are recognized, and a number of new or variant serotypes have been reported, which pose problems in immunization and diagnosis. If possible, selection of vaccine should be based on knowledge of the prevalent serotype(s) on the premises.

THE MERCK VETERINARY MANUAL

EXECUTIVE EDITOR: Frédéric David, DVM
TECHNICAL ADVISOR: Aris Malo, DVM
MANAGING EDITOR: Joseph Feeks
NEWS EDITOR: Diana Delmar
FIELD EDITORS: Steven Fox, Phil Stewart
ART DIRECTOR: Susanna Ronner
PROOFREADER: Ruth Misiewicz

The *Journal of Poultry Respiratory Protection* is published by Intervet/Schering-Plough Animal Health, Boxmeer, the Netherlands. The editors welcome your ideas and suggestions for future news articles. Please send correspondence to Journal of PRP, PO Box 9000, PMB 239, Edgartown, MA 02539-9000, USA.

Fax: +1.508.627.5555
Email: JFeeks@prworks.net

This magazine contains information on veterinary products based on international registration dossiers and may refer to products that are either not available in your country or are marketed under different trade names. In addition, the approved indications as well as the safety and efficacy data for a specific product may be different depending on local registrations and approvals. For more information, read the product labeling that applies to your country or contact your local Intervet/Schering-Plough Animal Health representative.

Nobilis IB Ma5, Nobilis IB 4/91, Nobilis Clone 30, Nobilis Clone 30+Ma5 and Protectotype are trademarks owned by Intervet International B.V. or affiliated companies or licensors and are protected by copyrights, trademark and other intellectual property laws. © 2011, Intervet International B.V. All rights reserved.

As the IB virus changes, we'll help keep you covered

Vaccinating with Nobilis® IB Ma5 and Nobilis® IB 4/91 ensures robust protection to get your birds off to a flying start. Thanks to the highly immunogenic strains in Nobilis IB Ma5 and Nobilis IB 4/91, the unique combination ensures comprehensive defense — not only against classical Massachusetts and IB 4/91 strains, but also against newer variants.[1] Speak to your vet about vaccination with Nobilis IB Ma5 and IB 4/91.

Nobilis® IB Ma5 and Nobilis® IB 4/91

Ref: 1. Intervet Poultry Focus Technical Bulletin, June 2006. Nobilis® IB Ma5 is a live vaccine containing Avian Infectious Bronchitis virus strain IB Ma5. POM-VPS. Nobilis® IB 4/91 is a live, freeze dried virus vaccine containing Infectious Bronchitis strain 4/91. POM-V. Additional information and advice is available from your veterinary surgeon. Nobilis is the property of Intervet International B.V. or affiliated companies or licensors and is protected by copyrights, trademark and other intellectual property laws. Copyright © 2009 Intervet International B.V. All rights reserved. This advertisement contains information on veterinary products based on international registration dossiers and may refer to products that are either not available in your country or are marketed under a different trade name. In addition, the approved indications as well as safety and efficacy data for a specific product may be different depending on local regulations and approvals. For more information, read the product labeling that applies to your country or contact your local Intervet/Schering-Plough Animal Health representative.