Improving economic productivity by controlling immunosuppression: I

Merial, part of Boehringer Ingelheim, recently held its Poultry IBD summit in Atlanta, USA entitled 'Improving Economic Productivity by Controlling Immunosuppression'.

Dr Guilermo Zavala from the USA set the scene by reflecting on the current situation regarding the use of vectored vaccines in poultry. He stated that 'One of the most significant advances in poultry vaccinology in recent years has been the advent of recombinant vaccines for use in the hatchery and in the field. Recombinant vaccines have vast potential for disease protection in the classical sense, while eliminating, partially or completely, some of the unwanted consequences seen after the use of live attenuated vaccines'.

He then summarised the important characteristics of some of the most widely used recombinant vaccines in the poultry sector, including those for infectious bursal disease, infectious laryngotracheitis, avian influenza and Newcastle disease.

Infectious bursal disease

Infectious bursal disease (IBD) recombinant vaccines are possibly the prime example of a product that has performed extremely well and very consistently in the field. As well as being associated with an unusual preservation of the integrity of the bursa of Fabricius, these vaccines can improve economic performance in most situations.

Their use in the hatchery for commercial layers has replaced in many cases, but not all, the need for multiple vaccinations against IBD in the field. In some circumstances when vvIBD virus is a serious problem there might be a need to combine the use of recombinant IBD vaccines with conventional live attenuated virus vaccines for some time before attempting to adopt the exclusive use of recombinant vaccines. Overall, IBD recombinant vaccines have been extremely successful worldwide.

Infectious laryngotracheitis

Infectious laryngotracheitis (ILT) recombinant vaccines have become the only legal vaccine choice because of the possibility of other types of vaccines recrudescing from latency and regaining virulence.

HVT- and Fowl pox-vectored vaccines are commonly used in the hatchery without a need for field boosting with other products.

Regardless of the approach, it is critical to ensure proper biosecurity to allow recombinant (rHVT or rFPV) vaccines to fulfil their mission. Until recently, the tendency worldwide in broiler production has been towards ever younger broilers, which is highly compatible with the use of recombinant ILT vaccines.

However, recombinant vaccines against ILT have also performed well in long lived chickens, provided field challenge is low to moderate.

Avian influenza

Avian influenza (AI) recombinant vaccines should not be regarded as a fully preventative tool or as a sole solution for AI problems in the field. Recombinant AI vaccines are a very efficient tool for controlling AI, but their use should be complemented with a variety of other preventative actions.

Do not expect recombinant vaccines against AI to be fully protective in situations where field challenge is overwhelming, but their combined use with killed vaccines or other types of vaccines can provide very attractive economic results.

The most serious AI problems involve subtypes H5 and H7. Commercially recombinant vaccines against these subtypes are available in various areas of the world, using either an HVT or a FPV platform. Additional subtypes causing problems are H1 and H3 in turkeys and H6 and H9 in chickens, for which there are multiple killed vaccines in various countries.

Newcastle disease

In countries like the USA where IBV is the highest day-to-day concern, recombinant Newcastle disease (ND) vaccines are used to provide some protection against ND infections without interfering with IB vaccines so that airsacculitis condemnations are kept at a minimum.

In other countries where ND is the priority, recombinant ND vaccines are used to prime birds against ND, but this program should always be complemented with spraying broiler chicks with conventional live attenuated vaccines in the hatchery.

This approach has been extremely successful, even in countries where ND is a serious problem.

Recombinant vaccines reached the US market in the early 2000s and have taken over a very large portion of the market both in the USA and worldwide.

One of the major reasons for this is their ability to protect chickens through hatchery vaccinations without the need to vaccinate chickens in the field, which has taken a very important variable out of the overall vaccination scenario.

In addition, virtually all recombinant vaccines have added tremendous value in terms of safety because you no longer have to worry about vaccine reactions, reversion to virulence, loss of two or more points of FCR, loss of uniformity and the need for medication in some cases where vaccine reactions get complicated by secondary pathogens. Guilermo concluded by stressing that the first 10-15 years of recombinant vaccine use in the field had produced very good results and that almost certainly we are about to see even further advancements in recombinant vaccine development and use in the field.

The pathologist's perspective

Dr Frederic J. Hoerr from Virginia, USA then gave a pathologist's perspective of immunosuppression and disease interactions in commercial broiler operations.

Histopathology is the microscopic definition of an individual organ's pathology at a level of detail that is not possible at necropsy and this science can be integrated with production, examining multiple birds at various ages, or comparing normal to affected birds. This allows the assessment of the development and resolution of lesions, with consideration of severity and the length of time that the disease presents a stress for the flock.

With respect to the immune system, histopathology surveys can include not only organs of the immune system, primarily the bursa of Fabricius and thymus, but also the spleen, bone marrow and caecal tonsil when appropriate.

Continued on page 24

Continued from page 23

When the immune system pathology is examined relative to ongoing issues in the digestive or respiratory system, or skin or bone, it is possible to look at interactions of diseases as they develop relative to immune system injury.

IBD is the dominant immunosuppressive viral disease in broiler production. In broilers that are not vaccinated in endemic regions, infectious bursal disease virus infection can occur at a young age and cause permanent immunosuppression.

With modification of the disease by passive/maternal immunity and acquired vaccinal immunity, it is possible to delay the age of infection to an older age, and to influence the recovery of the bursa from lymphocytolytic infection.

In Frederic's experience, administering vectored Gumboro vaccine on day one proceeds without any histopathological lesions to the bursa and begins to establish acquired immunity.

These factors then become important in minimising clinical immunosuppression, and the overall influence of infectious bursal disease.

Chicken infectious anaemia

Chicken infectious anaemia (CIA) virus is a common immunosuppressive cohort to infectious bursal disease. The classical form of CIA involves vertical transmission of virus from a seronegative hen.

The chick hatches with no maternal immunity, and experiences severe damage to blood-forming elements in the bone marrow and to lymphocytes in the lymphoid tissues, primarily the thymus.

This leads to anaemia, leukopenia, thrombocytopenia and the clinical blue wing syndrome. In most broiler operations, maternal immunity to CIA virus exists to some degree, and the classical form of CIA is mostly prevented.

The common problem observed today with CIA infection occurs following the decline of maternal immunity. In this situation, broilers experience a secondary infection with CIA virus that can result in severe lymphocytic depletion in the thymus in a subpopulation. In this situation, the bone marrow is substantially spared, in contrast to the neonatal infection in an immunologically naïve chick.

The occurrence of simultaneous IBD and CIA can cause lesion patterns supportive of combined B- and T-lymphocyte immunodeficiency. This situation is variably expressed clinically as inclusion body hepatitis, gangrenous dermatitis, coccidiosis, and respiratory disease.

Additional viral diseases that are associated with the development of lymphocytic depletion in the bursa and thymus include viral enteritis, viral arthritis (reovirus tenosynovitis), Newcastle disease, and Marek's disease.

These observations are based on lesions observed in histopathology surveys of broiler production programs, but are also supported by experimental studies of the individual diseases. Experimental studies of mycotoxicosis have revealed that commonly encountered mycotoxins can also cause immunosuppression.

Frederic concluded by stressing that understanding the age of onset and the severity of immunosuppression can provide insight to the application of mitigation strategies to improve immunity such as vaccination.

Viral interaction

Prof. Karel Schat from Cornell University in the USA then continued the theme of viral interaction by reflecting on the effect on birds of CIA and its interaction with IBD.

CIA virus was recently classified a member of the Anelloviridae and has a single-stranded circular DNA genome and, because the virus does not code for the enzymes needed for DNA replication, CIA virus can only replicate in dividing cells.

Target cells for CIA virus infection are haemocytoblasts in the bone marrow, T lymphocyte precursors and mature

antigen-specific T cells undergoing cell division.

Infection of these target cells results in apoptosis with important consequences for innate and acquired immune responses.

Apoptosis of the haemocytoblasts, precursors for red blood cells, heterophils, and thrombocytes, causes a decrease in heterophils and thrombocytes. Because both cell types are important phagocytic cells and producers of cytokines, a decrease can lead to increased bacterial infections and gangrenous dermatitis.

The effects on the thymocytes often lead to severe thymus atrophy and a lack of mature helper T (Th) cells and cytotoxic T lymphocytes (CTL). Naïve and memory Th cells and CTL responding to vaccination or infection undergo cell division and become susceptible to CIA virus resulting in a decrease in Th-dependent antibody responses and CTL-mediated lysis of target cells.

Virus-neutralising (VN) antibodies are crucially important for the control of CIA virus infection.

Most broiler chickens have maternal VN antibodies against CIA virus either as a consequence of natural exposure or vaccination of the parent flock and are protected against infection until two to three weeks of age. However, subclinical infections are frequently occurring after maternal antibodies have waned.

Any immunosuppressive event influencing the development of acquired humoral immunity against CIA virus will prolong the replication of the virus causing increased damage to the immune system.

Exposure to mycotoxins, excessive stress, and/or infection with IBD virus, including vaccination with intermediate plus vaccine strains, are examples that can negatively influence the development of anti-CIA virus IgY. IBD virus infection or vaccination with 'hot' strains will lead to increased cell death of bursacytes, thus negatively influencing the development of immune responses to other pathogens including CIA virus.

However, VN antibodies are also important for the protection against and recovery from IBD virus infection.

Any decrease in Th cell activity due to CIA virus infection will negatively influence the development of anti-IBDV IgY antibodies.

It has been shown that Ark-type infectious bronchitis outbreaks in vaccinated broiler flocks coincided with lymphocyte depletion in the bursa and/or thymus.

Subsequent experimental work in commercial broilers confirmed that dual infection delayed recovery in broilers compared to single infections.

A major problem in understanding the importance of subclinical immuno-suppressive infections is the lack of simple assays to demonstrate immunosuppression.

Nonetheless there are enough indications that CIA virus infection combined with IBD virus infection or vaccination causes economical important damage.

Protection against CIA virus

Protection of broilers against CIA virus induced immunosuppression by vaccination will be an important tool to increase productivity. However, vaccination with a live vaccine has two problems.

First, maternal antibodies will interfere with vaccine virus replication for at least two to three weeks of age similar to the problems with IBD vaccines.

The second problem is that a live CIA vaccine will need to replicate in order to induce an adequate immune response.

Replication of CIA virus will cause apoptosis in cells of the immune system and therefore may interfere with immune responses, which could be a problem in short-lived broilers.

The solution for a CIA virus broiler vaccine will need to be based on recombinant or immune complex vaccines, an approach that has been successfully introduced for IBD control. ■

Part II of this article will be published in the next issue of International Poultry Production