Malta symposium focuses on Marek's disease

Recently Fort Dodge held its 3rd Poultry Partnership in Malta and it focused on Marek's disease. In this article we will review the material covered.

Fort Dodge's Herve Le Galludec began by reviewing the worldwide situation. The disease was first described by Jozsef Marek in 1907 as fowl paralysis, but it was another 60 years before the causative agent was identified as a herpesvirus by researchers at Houghton in the UK. Within two years of this the first effective vaccine was obtained by attenuating the HPRS-16 strain of the virus. At this time a naturally avirulent turkey herpesvirus (THV) was shown to give good protection and in 1972 Rispens described the use of an attenuated CVI988 strain as a vaccine.

Today three avian herpesviruses are recognised – Marek's disease herpesviruses 1 and 2 and turkey herpesvirus 1.

No sterilising immunity

Unfortunately, although vaccines give good protection, they do not provide a sterilising immunity and so reduced infection and shedding are common in vaccinated birds. As a consequence a continuous virus reservoir in vaccinated flocks provides the opportunity for the selection and adaption of new Marek's disease virus strains with the result that the virulence of field strains has increased since the 1960s.

This was initially countered by introducing the Rispens strain of the vaccine into Europe and in the 1990s the introduction of a bivalent vaccine based on Rispens and THV (serotypes1 and 3). In the USA a similar situation led to the evolution of a vaccination strategy based on serotypes 2 and 3.

The economic impact of Marek's disease is estimated to be $US1-2 billion per year. The reasons for outbreaks of Marek's disease in vaccinated flocks are summarised in Table 1.

Prof. Jean-Luc Guerin from Toulouse, France then focused on the disease's viral biology and epidemiology. Infection leads to an early cytolytic infection that is primarily in the B-lymphocytes and this is followed by a second wave of similar infection in activated T-lymphocytes and some of these cells may ultimately be transformed to produce tumours in one or more tissues – commonly liver, spleen, heart, kidneys and gonads.

- Increasing virulence of field strains
- Concurrent disease challenge with focus on immunosuppressive diseases
- Genetic resistance of birds
- Brand of vaccine
- Vaccine preparation, handling and administration

Table 1. Reasons for Marek's disease outbreaks in vaccinated flocks.

This cytolytic infection of B and T-lymphocytes may lead to cellular depletion and atrophy of the thymus and bursa of Fabricius resulting in temporary or permanent immunosuppression. Historically, Marek's disease was considered to be a disease of chickens, but recently the disease has been seen in turkeys.

Table 2. Factors that optimise vaccinal protection against Marek's disease.

- Early vaccination is essential as Marek's disease is ubiquitous and passive immunity from maternal antibodies does not give protection.
- Cleaning and disinfection and all-in, all-out management are critical to decrease environmental viral load.
- Good management practices are important, especially in the first four weeks.
- Control other immunosuppressive diseases such as Gumboro disease, reoviruses and chicken anaemia.
- Vaccine brand choice is important as some vaccines show lower replication rates leading to delayed and/or weak immunity.
- Vaccine handling.
- Vaccine administration.

Willem Wijmenga from Fort Dodge then considered Marek's disease immunity. The natural infection route of field infection is via the lungs by the inhalation of infected dust and dander.

After phagocytosis of the virus in the lungs, the virus is transported by blood and lymph to the lymphoid tissues. An early cytolytic infection of the B-cells occurs and as a reaction resting T-cells become activated. After about a week a latent infection becomes established and latent T-cells are now capable of producing lymphomas. After 10 days or so a fully productive infection starts as by now the virus has been taken to the feather follicles and cell free Marek's disease virus is shed with flakes of skin into the environment.

Vaccination stimulates both cellular and humoral responses but it does not evoke a sterilising immunity but it does reduce or prevent mortality, tumour development, clinical signs and immunodepression. Efficacy of vaccines is variable.

Genetic resistance

Genetically resistant chickens respond better to vaccination and there is renewed interest in genetic resistance to infection according to Matthias Voss from Lohmann Tierzucht GmbH. He cited heritability estimates from 3 to 37% in the literature but in practice these are usually below 10%.

Kenton Kreager from Fort Dodge and formerly from Hy-Line then gave a clinical perspective of Marek's disease in pullets and layers. Evolution of Marek's disease in the USA has followed a cyclical pattern with a new 'very virulent' virus emerging every 10 years or so.

More recently, in the 1980s, this has been further complicated by lymphoid leucosis – a three way interaction of layer genotype, the presence of exogenous leucosis virus and the use of a serotype 2 vaccine exacerbated the expression of clinical leucosis and made the eradication of leucosis a priority.

This lead to licensing of European Rispens vaccines in the USA which dramatically reduced the incidence of Marek's disease and these continue to work well today.

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Currently, nearly all layers in the USA receive THV/Rispens and very little Marek's disease is seen. At the moment in ovo vaccination is expensive since half the doses are wasted on male chicks.

Paul McMullin from the UK then shared his experiences of clinical outbreaks of Marek's disease in layers. Typically, outbreaks are seen in layers and most cases are associated with elevated mortality, low weights and weak birds with occasional wing or leg paralysis.

Skin and ocular forms of the disease are rarely seen.

Affected flocks show a range of tumours but invariably show very large spleens that can be as large as ten times normal as well as enlarged livers, discrete tumours in livers and spleens and heart, ovarian and/or proventricular tumours.

The majority of cases are identified at 20-26 weeks of age and excess mortality typically continues to 35-40 weeks. Vertical transmission is not important and the virus can survive long periods (65 weeks or more) at ambient temperature and is resistant to quaternary ammonium and phenolic disinfectants.

It is likely that the virus is present on many farms but the disease is seen more frequently in poultry dense areas and stress plays a role.

Interestingly the investigation of such outbreaks by PCR has confirmed the diagnosis of Marek's disease but it has also confirmed the presence of vaccinal virus in pooled spleens.

- Decreases the risk of a chick not being injected
- Gives more uniform response and a higher peak of replication
- Increases the protection of birds in case of strong field challenge

Table 3. Observations on two vaccinations at day old.

Dr Harm Geerligs from Fort Dodge then looked at vaccine technology. He reported on several recent studies that confirmed the effectiveness of the current vaccines, in some cases even if the challenge occurred five days after vaccination.

He reported on different ways of producing the vaccine other than the traditional route through chicken embryo fibroblasts and several continuous cell lines have given promising results.

Continuous cell lines minimise the number of aseptic handling during production and open up the possibility for production in bioreactors.

Other work is with novel Marek's disease viral strains and vaccines based on bacterial artificial chromosomes as DNA vaccines have been tested with promising results.

Real time PCR developments were considered by Dr Susan Baignent from Compton in the UK. These have given us the ability to confirm and quantify concurrent virus infections with field and vaccinal strains although they can be expensive.

Paul Grignon Dumoulin from Hendrix Genetics, France, then highlighted how they had used PCR technology to confirm the effectiveness of the vaccination protocols.

Interestingly, they noted no real benefit from intramuscular vaccination when it was compared to vaccination in the neck and no differences in vaccination were seen between two lines of floor and cage reared birds.

Double vaccination gave almost the same results as standard vaccination but a better homogeneity in results was seen.

Eduardo Loedel Soca from Scotland then reflected on Marek's disease vaccination of broilers which varies by country. Field data from an extensive trial in Spain over almost three years showed a benefit from HVT vaccination in broilers in terms of biological and economical performance.

In reviewing vaccination protocols Herve Le Galludec highlighted the factors that optimise the resulting protection. These are detailed in Table 2.

He also cited some recent studies with two vaccine injections at day of age and his conclusions are shown in Table 3. ■