Marek's Disease

BIOPROPERTIES
The Vaccine Innovators

BIOPROPERTIES' Marek's Disease Vaccines

- BIOPROPERTIES provides high level troubleshooting and technical support
- Effective and proven product range for Australian poultry flocks
- Highest potency Rispens and HVT vaccines in Australia
- Supports MD research to improve our knowledge of MD
- Proven productivity gains in layers and broilers

Background

Marek's disease (MD) was historically recognised as a spastic paralysis of one or both legs due to infiltration of the peripheral nerves with cancerous and inflammatory white blood cells. While signs of paralysis associated with MD can still occur, MD presents more frequently as a cancerous disease that results in tumour (lymphoma) formation throughout most tissues (Figure 1).

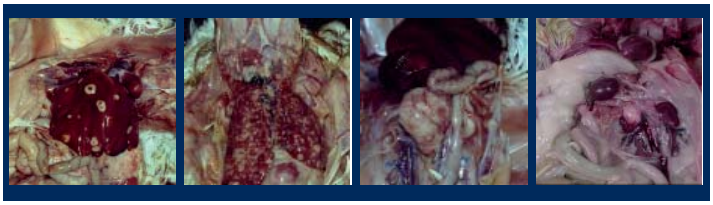

Figure 1. Gross MD lesions in various organs

Lymphoma development is most frequently seen in long-lived flocks such as layers and breeders. However, MD also occurs in short-lived broiler flocks in which it is usually associated with immunosuppression, poor feed conversion, increased mortality and reduced carcase yield.

Aetiology

Marek's disease is caused by a herpesvirus called Marek's disease virus (MDV). There are 3 serotypes of MDV that can infect commercial chickens including MDV 1, 2 and 3. Of these, only serotype 1 viruses induce MD as they encode a gene associated with tumour development.

The pathogenesis of MD has four key phases: i) early cytolytic, ii) latent, iii) late cytolytic, and iv) tumour development. The first two of these phases occur in all chickens after infection with MDV. The first phase involves early white blood cell destruction associated with virus multiplication (0-10 days after infection), which is then followed by a dormant or latent phase (10+ days after infection). Prolonged immunosuppression associated with the late cytolytic phase and tumour development only occurs in birds which are not protected by vaccination and have a susceptible genetic background. Tumours have been reported as early as 28 days after infection.

Transmission

Marek's disease is usually transmitted by inhalation of contaminated chicken dust (chicken dander). Approximately two weeks following infection, MDV multiplication transfers to the skin and feather follicles, resulting in shedding of cell-free virus into the environment. Virus particles are then inhaled or contaminate the environment. Contamination can remain in a shed for more than six months where it can infect susceptible chicks placed into that environment. Epidemiological studies have indicated that flocks within 1km of an infected farm are also susceptible to infection by airborne transfer. Consequently, a focus on tight biosecurity and high standards of hygiene can assist in MD control.

Protection

Marek's disease vaccines do not prevent infection with wild-type viruses, but rather the pathogenesis of disease is altered after infection depending upon the type of vaccine used. All chickens in a flock must be vaccinated to ensure protection from MD. Vaccination must be carried out prior to exposure to wild-type MDV (preferably 2-3 weeks). Vaccination is invariably carried out in the hatchery by injection at either 18 days of embryonation or at day-old. Horizontal transmission of MD vaccine viruses between flock mates either does not occur (MDV1 & HVT) or occurs poorly (MDV2). Thus each egg or chick must receive a full dose of vaccine to develop a protective immune response.

Mechanisms of Action

While the precise mechanism of protection induced by MD vaccines is not completely understood, there is evidence that two processes are involved.

The primary mechanism of protection is through direct anti-viral immunity. This limits replication of wild-type viruses after infection and therefore, limits the number of latently-infected cells that may subsequently undergo transformation (tumour formation). Thus this mechanism not only reduces the clinical effects associated with the early cytolytic phase of infection, it also reduces the risk of tumour development by simply reducing the number of cells that can potentially undergo transformation.

The second mechanism of protection is 'anti-tumour cell' immunity. As MDV1 vaccines are closely related to wild-type MDV, they can uniquely stimulate immunity against the protein responsible for tumour development (MEQ), which is expressed in latently-infected and transformed cells. Therefore, MDV1 vaccines such as Vaxsafe® RIS, can induce ongoing protection in long-lived birds, whereas MDV2 and HVT vaccines can not.

Finally, as vaccination reduces virus multiplication, it also reduces virus shedding and thus reduces environmental contamination / challenge to adjacent flocks (Figure 2).

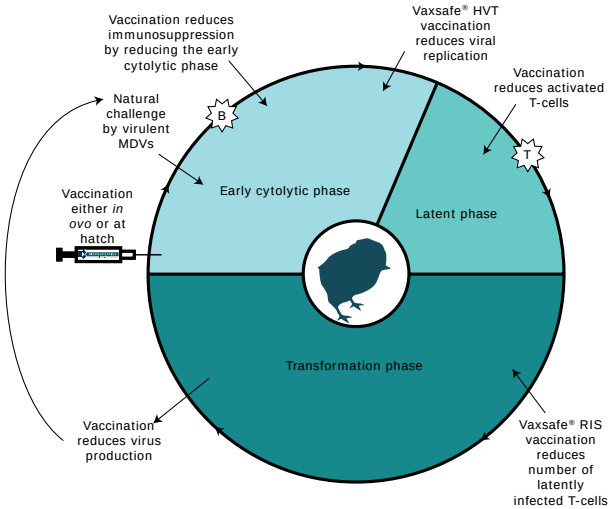

Figure 2. Vaccination: Mechanisms of Action

Vaccination Options

Vaccines have been developed from all three serotypes of MDV. Serotype-1 vaccines, such as Vaxsafe® RIS (Strain CVI988) or Rispens, are closest in their genetic structure to wild-type viruses and therefore offer the greatest level of protection. This is thought to be due to the stimulation of anti-viral and anti-tumour immunity. Serotype-2 vaccines tend to offer lower levels of protection when used on their own. Serotype-3 vaccines or Herpesvirus of turkeys (HVT), such as Vaxsafe® HVT, also offer lower levels of protection compared to serotype-1 vaccines when used alone, but when used in combination with serotype-2 vaccines, offer excellent protection to short-lived birds such as broilers, as they reduce early virus replication (Table 1).

Table 1. MD vaccine type and relative efficacy

MDV Serotype	Relative Efficacy Against MDV Pathotypes			Bird Type	
	V	V V	V V +	Layers / Breeders	Broilers
HVT (FC126)	+++	+	+	+	+
MDV2 (SB1)	+	-	-	-	+
HVT & MDV2 (HVT & SB1)	+++	+++	+	++	+++
MDV1 (Rispens)	+++	+++	+++	+++	+

+ indicates relative efficacy against pathotypes and bird type

BIOPROPERTIES' Vaccines

BIOPROPERTIES imported Rispens and HVT master seeds into Australia in 1997 from which commercial vaccines were manufactured locally. At that time, there were heavy losses from MD in meat breeder and commercial layer flocks. Losses in the layer industry alone reached an average of 21.5% to 80 weeks of age at the peak of the outbreak in 1996, with an excess of 2.1m layers placed to compensate for the losses and together costing the industry an estimated $50m per annum in replacement birds alone. The introduction of Vaxsafe® RIS and Vaxsafe® HVT brought 'overnight' relief to farmers, leading to a reduction in pullet placement in 1998 of 14% below predicted, due to increased liveability provided by the vaccination program. In field trials conducted with all major broiler companies within Australia, significant improvement in liveability was obtained against existing vaccination programmes. This led to improved productivity of the entire industry.

BIOPROPERTIES has continuously provided the highest potency Rispens and HVT vaccines available to the Australian poultry industry. The registered end of shelf life titres are 4,000 and 8,000 pfu per dose, respectively. Due to the strong 'dose response' relationship observed with Marek's vaccines, higher dosage is associated with earlier onset of protection, higher levels of protection, and longer duration of protection.

High product quality and reliable product supply will ensure ongoing sustainable control of MD for the Australian industry.

Is your flock worth the risk of not using BIOPROPERTIES' Marek's vaccines?

Vaccine Potency

The term 'potency' is used to describe the titre or infectivity of MD vaccines. Manufacturers of MD vaccines have reported the potency of their vaccines in different formats. There is, however, one generally accepted assay method that reports the number of virus-infected cells contained in the product. This is termed the 'plaque-assay', and the results are reported as 'plaque-forming units' or pfu. There is a direct correlation for most vaccines between the potency or pfu count and the protection offered against Marek's disease.

Vaxsafe® RIS and Vaxsafe® HVT are produced with very high virus titres (vaccine potency) to ensure maximum protection against MD in birds, including disease caused by the more virulent field strains that are now circulating globally. A lower titre vaccine, or under dosing, may induce a lower level of immunity that may well encourage the generation of more virulent field strains (Witter 1998).

Alternative assay systems that are occasionally used include the 'Tissue-culture infective dose 50%' ($TCID_{50}$) assay and 'Bird infective dose 50%' (BID_{50}) assay. The potency from these assays can be mathematically converted to pfu, for example: 1000 $TCID_{50}$ = 690 pfu.

Present Status of MD

Broiler condemnation rates at slaughter have fallen in the US to <0.01% when vaccinated with bivalent serotype-2 and -3 vaccines, even when placed onto used litter. Further, Rispens is controlling vv+ MDV in long lived birds throughout the world at present. Combined, these observations indicate a reasonable level of confidence that the existing vaccines will contain the disease for some time to come.

In Australia, MD control is currently at unprecedently low levels. Long-lived flocks are a more sensitive indicator of vaccine efficacy, and it is now common to achieve <4% mortality to end of lay in commercial layers. This achievement has only been realised due to the high quality BIOPROPERTIES Rispens vaccine combined with a high quality technical servicing programme and an industry commitment to early biosecurity and optimised vaccination.

This achievement should not relax our goal of maximising early biosecurity, down-time intervals and vaccination efficacy, as these practices will reduce the risk of driving further virus evolution of virulence in this country.

BIOPROPERTIES is committed to both monitoring the current field situation and funding research to improve our understanding of MD control. Through these approaches, BIOPROPRERTIES seeks to maintain its number one status in MD vaccine production and technology in Australia.

Marek's Disease

Troubleshooting & Technical Support

There are many technical aspects involved in Marek's vaccine transport, storage, preparation and administration. The effects on vaccine efficacy of inefficiencies in these processes are cumulative. Further details on these effects are contained in the respective product brochures and leaflets. While there may not be a specific incident of failure that leads to inadequate protection, the entire process up to and including vaccine delivery may require auditing to identify inefficiencies. Additionally, administration of the vaccine does not induce immunity immediately. It takes at least 2-3 days before the vaccine virus commences replication, and a further 7 days before the immune response strengthens. Protection is not induced until around 2 weeks after vaccination, and does not reach maximum levels until around 4 weeks after vaccination. Therefore, biosecurity (protection from field challenge) is essential during the early rearing period, but exposure to challenge should be avoided until beyond 3-4 weeks of age.

In a recent hatchery survey in the Netherlands it was found that the potency of Rispens vaccine, recovered from reconstituted or unthawed ampoules, was significantly below the minimum release titre of that vaccine. Indeed all ampoules tested in two of the hatcheries were below the threshold, while vaccine recovered from other hatcheries had pass rates of between five and 77%. These findings confirmed an association between inadequate vaccine virus handling and preparation, and the occurrence of clinical disease. They also reinforce the need for care and attention to detail in transport, handling and preparing vaccine for use.

Additionally, recent investigations into the effect of vaccine administration devices in Australian hatcheries found a significant reduction in the cell count (between 20% and 80%) at the needle point compared to that of the prepared vaccine. These losses are due to the pressure and shear forces applied to the cells contained in the vaccine, which if not carefully monitored can lead to significant reduction in the dosage delivered. This effect can also be minimised by ensuring equipment is properly maintained and correctly operated at all times.

BIOPROPERTIES offers the highest quality service in all aspects from production, research and development, and technical servicing in the field. This backing and service is unmatched in Australia. BIOPROPERTIES has taken the view that all Marek's disease vaccines are vulnerable to breakdown in any vaccinated flock in the event of challenge with highly virulent strains. A vaccination breakdown can be a result of poor handling of the vaccine, under-dosing, lack of attention to detail during vaccine preparation and administration, equipment malfunction or early challenge. As the market leaders in Marek's disease vaccine and vaccine technology, BIOPROPERTIES' service staff conduct periodic audits of essential vaccine handling and administration procedures directly in the hatchery. This servicing is not only a quality check on the efficiencies of operation, but also provides a training forum to ensure key hatchery staff are well equipped with background knowledge on the subject to ensure the correct procedures are followed and correct decisions are made in the event a part of the procedure varies from normality. Customers can be assured that BIOPROPERTIES' hatchery audits are associated with implementation of the highest standards in vaccine handling, preparation and administration.

Vaccine Use

A full description of the storage, handling and method of administration of Vaxsafe® RIS and Vaxsafe® HVT is described in the product leaflet that accompanies the vaccine and in technical brochures on each product.

References & Further Reading

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BIOPROPERTIES
The Vaccine Innovators

Registered Office/Distribution
36 Charter Street, Ringwood
VIC 3134 AUSTRALIA

T +61 3 9876 0567
F +61 3 9876 0556
www.bioproperties.com.au

Manufacturing Division
11-15 Moores Road, Glenorie
NSW 2157 AUSTRALIA

T +61 2 9652 0087
F +61 2 9652 0914