The use of tylosin for mycoplasmosis and necrotic enteritis control

Huvepharma recently hosted a symposium in Istanbul to coincide with the launch of Pharmasin (tylosin) in Europe. This article looks at some of the presentations from that event which are relevant to the poultry sector.

Dr Anne Ferberwee reviewed the situation with regard to Mycoplasma gallisepticum and M. synoviae in commercial poultry. There are some 24 species of mycoplasma capable of infecting birds but the two most important ones are M. gallisepticum and M. synoviae. Natural hosts for these two mycoplasmas are shown in Table 1.

M. gallisepticum and M. synoviae have a global distribution but, while breeders endeavour to keep their stocks M. gallisepticum free, the same can not always be said for M. synoviae. These two mycoplasmas can survive on human hair and in human noses for 1-3 days and for 2-4 days on quite a few fomites but for 6-18 weeks in egg material. They are able to avoid the bird's immune system with the result that infection may not be countered and seroconversion may not always occur.

Mycoplasma can spread horizontally from bird to bird by direct contact or indirectly via fomites or vertically via the eggs so that an infected breeder hen can produce infected progeny.

In M. gallisepticum infection clinical signs can range from none to very severe, which typically include sneezing, tracheal râles, nasal discharge, swollen infra-orbital sinuses and conjunctivitis.

Table 1. Natural hosts for Mycoplasma gallisepticum (Mg) and M. synoviae (Ms).

Animal	Mg	Ms
Chickens	+	+
Turkeys	+	+
Pheasants	+	+
Partridge	+	+
Peafowl	+	-
Quail	+	+
Parrot	+	-
Ducks	+	+
Geese	+	+
Wild birds	+	+
Pigeons	-	+

Pathogen	Ms	Ms + IB D1466	Ms + IB M41
Number affected	4/19	6/18	11/20
Affected (%)	21	33	55

Table 2. Synergism between M. synoviae and infectious bronchitis (all infections administered as aerosols).

Infection	None	Ms	IBV D1466 & MS
Mean (egg/hen/day)	0.75	0.49	0.54
EAA (%)	0	7	4

Table 3. Synergism between M. synoviae in eggshell apex abnormalities (EAA).

In M. synoviae infection the clinical signs depend on the strain involved – respiratory strains tend to show mild or no respiratory signs, arthropathic strains show lameness and swollen joints, whereas strains affecting the oviduct can induce eggshell apical abnormalities, drops in egg production and increased numbers of broken shells.

With M. synoviae synergism can occur with infectious bronchitis infection (see Table 2).

When it comes to commercial impact mycoplasma infections increase condemnation and culling rates and depress growth. The seriousness of this is often dependent on whether or not co-infections such as Newcastle disease, infectious bronchitis, E. coli and, especially in turkeys, M. meleagridis are present.

The problem of egg shell apex abnormalities associated with M. synoviae first appeared at about the turn of the century. This condition has a variable age of onset and affects white and brown layers housed under a variety of conditions. Again this is a condition in which synergism with infectious bronchitis occurs (see Table 3).

Eggshell apex abnormality can also be seen in eggs from broiler breeder flocks but these are less susceptible than table egg layers (2 vs. 14-22%) and the problem occurs later. Table 4 summarises the economic impact of this condition.

Anne then went on to consider the treatment of diseases caused by mycoplasma. Treatment could centre around the use of antibiotics such as tetracyclines, macrolides, quinolones and pleuromutilins.

Antibiotic treatment reduces the mycoplasma population, albeit temporarily, controls clinical signs and gets into the egg. However, this is often countered by the need for repeat treatments and the issues of resistance and residues. Control can involve the use of inactivated vaccines. These are safe, effective against air sacculitis and egg drop but countered by the fact that they are expensive, have a limited effect against colonisation, induce positive serology and can only be administered in rear.

Live vaccines on the other hand are easy to use, inexpensive and the vaccinal strain can replace the field strain on a farm. However, live vaccines, especially the F strain, can in their own right induce respiratory disease, induce positive serology and be adversely affected by antibiotics.

The benefits of vaccination against eggshell apex abnormalities are shown in Table 5.

In concluding, Anne said mycoplasma infections are still a problem because of the organism's ability for intracellular survival, there are reservoirs of infection, limited vaccine efficacy, antibiotic resistance and eradication failures.

Economic impact	
On the farm	
Egg production (%)	-2-3
Losses due to egg breakages (%)	+2-3
Downgrading (%)	+2-3
Increased labour	??
At the packing station	
Increased labour	??
Egg losses during transit (%)	≤10

Table 4. Economic impact of eggshell apex abnormalities.

Prof F. Van Immerseel from Ghent University in Belgium reflected on necrotic enteritis in broilers. When it comes to gut health nutrition (quality, toxin freedom, enzymes, low viscosity, influence of additives on gut microbiota and nutritional changes), the composition of the gut microbiota

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(microflora), gut health (villus structure, epithelial cell proliferation, lesions/erosions and epithelia cell damage) and inflammation all come into play.

He reckons that necrotic enteritis costs the industry some $2 billion a year. Although Clostridium perfringens is key to the aetiology of necrotic strains producing *netB* toxin are the key (see Table 6).

It is also interesting to note that Clostridium perfringens strains isolated from a necrotic enteritis flock are highly clonal, whereas those from healthy broilers are genetically heterogeneous and that virulent strains of Clostridium perfringens inhibit other strains, thereby facilitating their overgrowth in the chicken gut. Control centres around killing the causative bacterium (amoxicillin, lincomycin, tylosin), preventing predisposing factors such as coccidiosis challenge and, possibly, vaccination with a *netB* toxoid. He also highlighted the possible protective effects of ionophore anticoccidials and certain feed additives such as butyric and lauric acids and essential oils.

Dysbacteriosis he considers to be more of a dysbiosis of the microbiota that can be controlled by antibiotics, managing feed composition and using products that are antibacterial, anti-inflammatory and change the composition of the microbiota. When it comes to prevention products like acids, essential oils and prebiotics are useful.

	Non-vacc.	Vacc.
Mean egg/hen/day	0.48	0.54
Eggshell apex abnormalities (%)	22.9	11.9

Table 5. Vaccination against M. synoviae in the control of eggshell apex abnormalities.

Strain	Birds with lesions (%)	*netB*
7	0	-
8	0	-
17	0	-
48	11.11	+
56	48.15	+
61	55.56	+

Table 6. Necrotic enteritis specific toxin.

Tylosin	Relative antimicrobial activity
A	1.00
B	0.83
C	0.75
D	0.35

Table 7. Relative activities of tylosin subunits.

Pascal Richez from TransPharm, France, then discussed some pertinent properties of the macrolide antibiotic tylosin. Tylosin actually has four subunits – tylosin A (which accounts for>80% of the product), B, C and D. Their relative activities are shown in Table 7.

This shows a difference between tylosin A and B although some studies show these two subunits to have similar activities.

Pharmacokinetically tylosin has good water solubility and is absorbed well from the large intestine and in the body is widely distributed in the tissues by ion tapping and tissue protein binding. In chickens tylosin has an oral half-life of 15-30 minutes and has a systemic bioavailability of 60-70%.

Tylosin ends up with higher concentrations in the tissues than in the blood with the highest concentrations in lungs, liver, kidneys and heart. Clearance is fast resulting in low residues in edible tissues.

Tylosin is active against mycoplasma and a wide range of Gram positive bacteria including Staphylococcus Spp. In the EU the indications for tylosin in poultry are for the treatment and prevention of mycoplasma infections and the prevention of necrotic enteritis in chickens and for sinusitis in turkeys.

In concluding, Pascal said that tylosin has been used for 40 years and is the drug of choice for a number of diseases. Tylosin is well suited to water application and despite extensive use resistance levels are acceptable.

However, he still cautioned prudent use. He also highlighted that some recent research suggests that tylosin has some anti-inflammatory properties. ■