Treating and controlling mycoplasma infections

Mycoplasma infections can be a major cause of turkey losses. Mixed infections with other disease agents and resistance to some antibiotics complicates the control of these infections. However trials have shown tiamulin is active against all mycoplasma species found in turkeys.

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Table 1 - Comparison of mycoplasma infections in turkeys

Effect	Mg	Ms	Mm	Mi
Sinusitis	++	± (+) (+Mm)	± (+) (+Ms)	-
Pneumonia	++	±	-	-
Airsacculitis	++	+	+ (+) (+Ms)	(+)*
Synovitis	-	++	-	(+)*
Arthritis	-	++	-	(+)*
Chondrodystrophy	-	-	+	(+)*
Meningitis	+	+	-	-
Reduced egg production	++	±	-	-
Embryo mortality	+	±	+ (+) (+Mi)	+
Reduced Hatchability	+	±	+ (+) (+Mi)	+
Poor Growth	++	+	+	-
Poor feathering	-	-	+	+
Affects chickens	+	+	-	(+)*

Legend: ++ = severe; + = moderate; ± = mild; - absent; (+Mm) = mixed infection; (+)* = artificial infection.
Source: Kleven and others (1997)

Table 2 - Reported incidents of avian mycoplasmosis in the UK

Reports	1993	1996	1999	2000
Mg	15	24	21	9
Mm	1	2	0	0
Mycoplasma unspecified	20	32	16	27
Total incidents	36	58	37	36

Source: VIDA (2001)

The major mycoplasma infections in turkeys are *Mycoplasma gallisepticum* (Mg), *M. synoviae* (Ms), *M. meleagridis* (Mm) and *M. iowae* (Mi). In the past these organisms caused major losses in turkeys but over recent years eradication programmes, especially in North America and Northern Europe have successfully eliminated them from the pyramid breeding flocks. Occasionally breakdowns in breeders do occur and this has important implications in the subsequent progeny, as all of these infections can be transmitted vertically via the egg. Nor-mally flocks would be culled but at special times, when poults are being produced for the fresh meat markets around Thanksgiving and Christmas, medication may be a necessary option.

Growing flocks may also become infected, especially by Mg and Ms from outside sources. Wild birds such as pheasants, partridges, rooks and finches may all be potential reservoirs of infection as well as other neighbouring turkey and chicken farms. Mm and Mi, which are more host specific to the turkey and are primarily transmitted vertically from the breeding flock, are less frequently encountered but in some countries they remain endemic. Antimicrobial use has been the most common method of control, other than eradication, as vaccination other than killed vaccines for Mg and Ms have not been developed for turkey use and the live F strain live Mg vaccine will actually cause disease in turkeys (*Table 1*).

Infections in turkeys

***M. gallisepticum* – Infectious sinusitis:** Mg causes primarily a respiratory infection in turkeys inducing sinusitis, pneumonia, and airsacculitis. The birds show a nasal and ocular discharge, swollen paranasal sinuses, tracheal râles, coughing, laboured breathing, loss of condition and even death, especially if the infection is compounded with secondary bacteria such as *E. coli*. Usually outbreaks occur between 8-15 weeks of age. Up to 90% of birds may show signs. In breeding birds, there may be a drop in egg production. Occasionally an encephalitic form is seen in growing birds. A tenovaginitis may also develop and the organism can be found in the oviduct and semen of infected male birds, leading to infection in the egg and eventually of the young poult.

***M. synoviae* – Infectious synovitis:** Ms in turkeys is associated more with lameness rather than respiratory signs. A sinusitis may develop especially when compounded with Mm or a virus infection as well as an airsacculitis. Nervous signs have been described. Swellings of one or more joints are common and are filled with a fibrino-purulent exudate. Enlargement of the sternal bursa may occur. Growth may be depressed if severe but morbidity may be as low as 1-20% and mortality is usually low.

***M. meleagridis*:** Mm is the cause of an egg-transmitted disease where the primary lesion is an airsacculitis in the young bird but clinical respiratory signs may not be apparent. Other signs are leg malformations in the tarso-metatarsal bones, hock joint swelling and poor growth performance in the young bird between 1-6 weeks of age. Poults infected this way then become infected adults and if bred can pass Mm on via the egg. Birds can be infected horizontally both directly and indirectly. The organism may lodge in the genitalia of only about 5% of the birds infected by the respiratory route but are able to perpetuate the infection if reared for breeding. In adult birds airborne transmission is of little significance as it does not affect the genitalia and eggs are free from infection. Egg production and fertility is not affected but Mm does cause late embryo mortality and reduces hatchability by 5-6%. If the condition is complicated with Mi in breeders, then embryo mortality is significantly increased. If complicated with Ms in growing birds the severity of respiratory signs and airsacculitis increase and sinusitis may develop. Mi may also increase the severity of Mm air sacculitis in poults.

***M. iowae*:** Mi is primarily associated with embryo mortality and reduced hatchability but experimentally if injected into air sacs may cause airsacculitis and leg abnormalities. The organism is spread by vertical transmission and the severity of embryo mortality is variable and depends on the extent of the infection in the breeding birds. Transmission from bird to bird is primarily by the venereal route. There is little transmission horizontally in young poults and the majority remain culture negative.

After laying and insemination starts a high percentage of the birds become culture positive. The organism can be recovered from the cloacal and vaginal sites. Hatchability may be reduced by 2-5%. It can also complicate Mm infections and increase their severity.

The number of incidents of mycoplasmosis in poultry reported in the UK is quite low (*Table 2*). Reports are submitted to the Veterinary Laboratories Agency, part of the Department of the Environment, Food and Rural Affairs. Mm has not been reported in the UK in the last four years and Mi has been eliminated from major turkey breeder producers.

Antimicrobial sensitivity

The antimicrobial sensitivity of all the major mycoplasma species was reviewed by Valks and Burch (2002) between 1990-2000, comparing the sensitivity of tiamulin with other antimicrobials (*Table 3*).

Tiamulin is very active against almost all of the common mycoplasma species found in turkeys. Tylosin and oxytetracycline show clear signs of potential resistance for all four species of mycoplasma with some very high MICs recorded. Lincomycin has some resistance development for Mg, Mm and clearly for Mi. Enrofloxacin has some borderline resistant Mg and Mm strains but Ms and Mi would all appear to be sensitive.

Tiamulin is very well absorbed in the turkey and achieves high blood levels in comparison with other antibiotics such as tylosin (*Figure 1*).

Tiamulin has good tissue penetration and has an affinity for respiratory tissues such as the lung as well as concentrating in eggs. In studies in breeder turkey hens given tiamulin at 0.025% in the drinking water for 5 days, antimicrobially active residues of tiamulin could be found in eggs for 12 days after treatment. Levels well above the MICs of most turkey mycoplasmas (0.25µg/ml) are still found at 9 days and this approach was considered to offer potentially an excellent way to control the transmission of mycoplasmas via the egg (*Figure 2*). From these studies it was demonstrated also that tiamulin had no reported adverse effect on egg production, fertility or hatchability in turkey breeder birds (*Table 4*).

Prevention

Tiamulin has been intensively tested in artificial infection studies in young turkeys and shown to be highly effective in preventing and treating Mg infections. The difference between tiamulin and tylosin was clearly confirmed with tiamulin at 0.025% given for 5 days giving an excellent result in preventing air sac lesions developing in the birds (cure %), equivalent to tylosin at 0.1% at four times the concentration (*Figure 3*).

Treatment

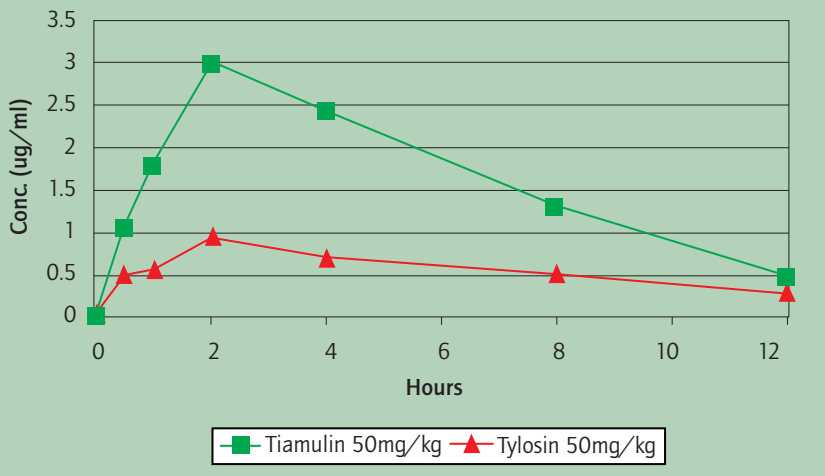
In treatment studies tiamulin given in the drinking water for 5 days also proved

Table 3 - Antimicrobial sensitivity ranges of various antimicrobials (µg/ml) against Mg, Ms, Mm and Mi, reported between 1990 and 2000

Antimicrobial	Mg (66)*	Ms (52)*	Mm (11)	Mi (86)
Tiamulin	0.006-0.39	0.006-0.5	0.025-3.13	0.006-0.125
Tylosin	0.006-400	0.006-50	0.78-50	0.05-100
Oxytetracycline	0.05-200	0.025-100	0.05-25	0.025-100
Lincomycin	0.125-6.25	0.05-1.56	0.05-25	0.05-100
Enrofloxacin	0.0125-2.0	0.025-1.56	0.1-3.13	0.005-1.0

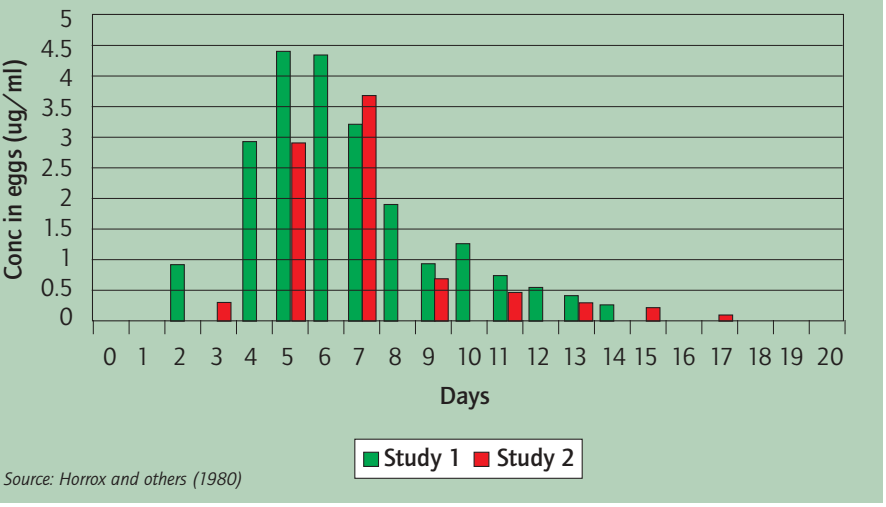
Legend: () no of isolates: * = turkey and chicken isolates.
Source: Valks and Burch (2002)

Figure 1 - Comparative pharmacokinetics of tiamulin and tylosin in turkeys



Source: Laber and Schutze (1976)

Figure 2 - Concentration of tiamulin in turkey eggs during and after 5 days treatment at 0.025% in drinking water



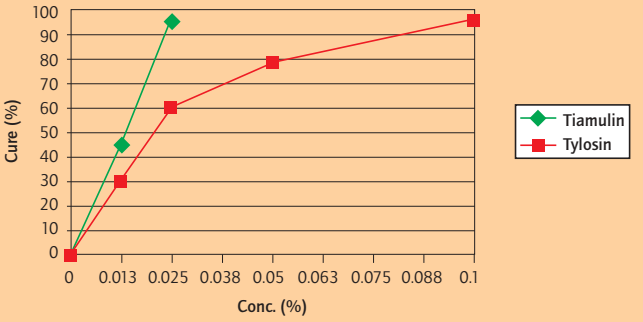
Source: Horrox and others (1980)

Table 4 - Hatchery production parameters of eggs set in both trials

	Study 1		Study 2	
	Tiamulin 0.025%	Untreated control	Tiamulin 0.025%	Untreated control
No. of eggs	1051	1175	722	830
Infertile (%)	5.6	4.9	1.8	2.17
Fertile (%)	89.5	89.4	94.6	95.06
Hatched of set (%)	79.16	79.16	86.29	86.99

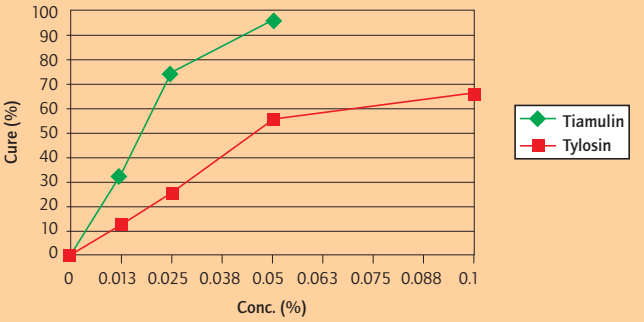
Source: Horrox and others (1980)

Figure 3 - Comparison of tiamulin and tylosin for the prevention of Mg



Source: Baughn and others (1978)

Figure 4 - Comparison of tiamulin and tylosin for the treatment of Mg



Source: Baughn and others (1978)

to be very effective in treating an Mg infection given directly into the air sac. Tiamulin gave substantially better clinical responses in comparison with tylosin and reduced the number of birds with air sac lesions (cure %) markedly (*Figure 4*).

Tiamulin has been extensively studied in the field and has been shown to effectively treat Mg, Ms, Mm and mixed Mm and Ms infections in growers and breeders.

Dosing programmes

Prevention of mycoplasmosis in growers – (receiving tiamulin compatible anticoccidials such as lasalocid or diclazuril).

Tiamulin is normally given for the first 3 days of life at 0.025% in the drinking water and then repeated every 4 weeks depending on the severity of the challenge (*Figure 5*). If monensin is used as the anticoccidial then tiamulin cannot be used because the two products interact. Only after 7 days withdrawal can tiamulin be introduced in a regular program.

In some cases secondary bacterial invaders complicate mycoplasmosis such as *E. coli*. *Pasteurella multocida* and more recently *Ornithobacterium rhinotracheale* have been identified as major causes of respiratory problems in a turkey flocks. Tiamulin on its own has been shown to be highly active against O. *rhinotracheale* with an MIC range of ≤0.012-0.25µg/ml.

A broader spectrum product such as chlortetracycline or doxycycline can be used in combination with tiamulin and a synergistic activity has been reported against mycoplasma and some bacteria such as *P. multocida (Figure 6*).

In Denmark, preventive trials using the combined products, tiamulin at 70ppm and chlortetracycline at 200ppm, were particularly effective in controlling a mixed infection of mycoplasma and *E.coli* (*Figure 7*).

For treatment the concentration in feed was increased to 150ppm tiamulin and 450ppm chlortetracycline. Overall, tiamulin offers the veterinarian and turkey producer an effective alternative to combat mycoplasmosis in turkeys and combined with tetracyclines, an effective and economic broad-spectrum control of many mixed mycoplasmal and bacterial infections.

Conclusions

Mycoplasma infections can still be a major cause of losses in turkeys. Mixed infections with *E. coli, O. rhinotracheale* and *P. multocida* increase the severity of the infection, reducing growth and feed conversion efficiency and increasing mortality.

Eradication and vaccination programs cannot always keep out mycoplasma infections in turkeys. Resistance to antimycoplasmal antibiotics has been reported, especially to tylosin, oxytetracycline and lincomycin.

Tiamulin is active against all mycoplasma species found in turkeys and achieves sufficient blood, tissue and egg levels, well above the MICs needed to control these infections.

Turkey breeders can be treated with tiamulin; fertility and hatchability are not adversely affected.

Tiamulin is 2-4 times more active than tylosin for the control of mycoplasma infections in turkeys. Pulse dosing programs with 0.025% tiamulin for 3 days each month has proven effective in the prevention of mycoplasmosis in growing birds.

Recent field experience has shown that combinations of tiamulin at 70ppm and chlortetracycline at 200ppm in feed, broadens the spectrum of control to bacterial infections, whilst effectively and economically controlling underlying mycoplasmal infections.

References available on request.

Figure 5 - Dosage scheme for tiamulin in growers

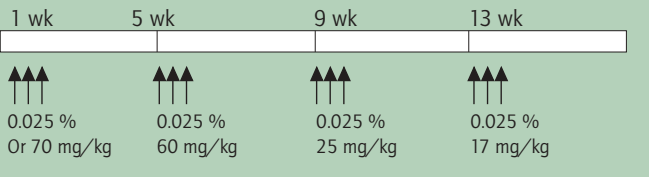
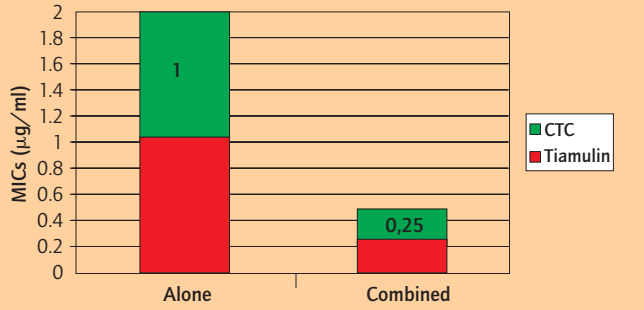


Figure 6 - Synergistic activity of tiamulin and chlortetracycline alone and in combination



Source: Burch and others (1993)

Figure 7 - Program using tiamulin and chloretracycline combined