



IPVS 2000

16th INTERNATIONAL PIG  
VETERINARY SOCIETY CONGRESS  
MELBOURNE AUSTRALIA

17-20 SEPTEMBER 2000

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Papers on Tiamutin presented  
at the 16th IPVS Congress

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As a world leading animal health company Novartis, manufacturer of Tiamutin, is proud to be a major sponsor of the 2000 IPVS Congress, source of so much new and significant research information.

Over the past 22 years Tiamutin, the original member of the pleuromutilin family of antibiotics, has evolved as the leading therapeutic product for “pneumo-enteric” diseases.

Tiamutin is highly effective against traditional pig diseases like swine dysentery and enzootic pneumonia, yet is still a valuable weapon in the fight against emergent diseases such as ileitis and mycoplasmal arthritis. Tiamutin is not only the long-proven aid for the pig farming industry but definitely an antibiotic “in step with time”.

It is our hope that these Proceedings – a collection of papers presented on Tiamutin at the 2000 IPVS – will be a reminder of Novartis Animal Health’s commitment to the global pig industry and assist you in your production related decisions.



## FOCUS

Susceptibility testing of 50 field isolates of *Brachyspira hyodysenteriae* (*B.hyo*) by a new broth dilution method to tiamulin and other antimicrobials.

## KEY FACTS

- Field isolates of *B.hyo* from 46 different farms in Sweden from 1997-2000 were studied at the National Veterinary Institute, Uppsala, Sweden. Two reference strains of *B.hyo* (B78 ATCC27164 and B204ATCC 31212) were also included.
- 6 antimicrobials were tested:-

Antimicrobials	Antibiotic group
tylosin erythromycin	macrolids
clindamycin	lincosamide
tiamulin valnemulin	pleuromutilins
virginiamycin	streptogramin

- Two fold serial dilutions of the antimicrobials were dried in tissue culture trays with 48 wells.
- Bacteria harvested from FAA plates were suspended in BHIS broth to a concentration of  $1 \times 10^8$  and  $5 \times 10^8$  CFU/ml. The optical density of all the suspensions was measured and correlated to population density by viable cell counts.
- From this suspension 300ml was transferred to 30ml BHIS broth to prepare a final inoculum concentration of  $1 \times 10^6$  –  $5 \times 10^6$  CFU/ml. Each well in the panels was filled with 0.5ml of the inoculum and the panels were incubated in anaerobic jars for 4 days on a shaker at 37°C. The MIC was determined as the lowest concentration of antimicrobial which prevented visible growth.

## BENEFITS

- The new broth dilution procedure is convenient and labour saving and can be performed at short notice in a standardised manner.
- The 50 field isolates and 2 standard strains of *B.hyo* were 100% sensitive to tiamulin. No resistance to tiamulin has been recorded for *B.hyo* in Sweden.
- The majority of isolates were sensitive to tiamulin in the mic range 0.031-0.125 mcg/ml.
- The majority of isolates tested were resistant to tylosin (mic > 256 mcg/ml) All isolates resistant to tylosin were also cross-resistant to erythromycin and clindamycin.

*Tiamulin® is a highly suitable antibiotic to effectively control swine dysentery and spirochaetal colitis.*

# ANTIMICROBIAL SUSCEPTIBILITY TESTING OF SWEDISH *BRACHYSPIRA HYODYSENTERIAE* ISOLATES BY BROTH DILUTION PROCEDURE

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## INTRODUCTION

Antimicrobial susceptibility testing of *Brachyspira hyodysenteriae*, the causative agent of swine dysentery, is mostly done by agar dilution. The most common medium used is Trypticase Soy agar supplemented with 5% bovine or ovine blood (1). Agar dilution is a rather complex method and we find the endpoints difficult to read using the inoculum size recommended for anaerobic bacteria in the National Committee for Clinical Laboratory Standards (NCCLS) (2). In order to facilitate susceptibility testing of *B. hyodysenteriae* a broth dilution method was evaluated (to be published). In this paper the method is described and the in vitro activity of six antimicrobial agents to 50 Swedish field isolates is presented.

## MATERIALS AND METHODS

Field isolates of *B. hyodysenteriae* isolated from 46 different farms between 1997 and 2000 were investigated. The isolates were identified according to a biochemical classification system and stored in liquid nitrogen (3). Thawed strains were grown on FAA-plates (Fastidious Anaerobe Agar, National Veterinary Institute, Uppsala, Sweden) in an anaerobic atmosphere for three days at 39-40°C. The following reference strains were included: *B. hyodysenteriae* B78<sup>T</sup> (ATCC 27164<sup>T</sup>) *B. hyodysenteriae* B204 (ATCC 31212).

The following six antimicrobial agents were used: tylosin, tiamulin, erythromycin, clindamycin, valnemulin, and virginiamycin. The compounds were dissolved and diluted according to the recommendations of the manufacturers. A panel for susceptibility testing of the six antimicrobial agents was designed. Two-fold serial dilutions of the antimicrobial agents were dried in tissue culture trays with 48 wells (Nunclon™ Multidishes, NUNC™, Denmark).

Bacteria harvested from FAA plates were suspended in BHIS broth (Brain Heart Infusion broth, Difco, supplemented with 10% fetal calf serum) to a concentration between  $1 \times 10^9$  and  $5 \times 10^8$  CFU/ml. The optical density of all the suspensions was measured (Secomam S.250 spectrophotometer, 620 nm, 5 mm path length) and correlated to population density by viable cell counts. From this suspension 300 ml was

transferred to 30 ml BHIS broth to obtain a final inoculum concentration of  $1 \times 10^6$ - $5 \times 10^6$  CFU/ml. Each well in the panels was filled with 0.5 ml of the inoculum. The panels were incubated in square-shaped GENbox anaerobic jars with GENbox anaerobic generator sachets (bioMérieux, Lyon, France) for four days on a shaker at 37°C. The MIC was determined as the lowest concentration of antimicrobial agent that prevented visible growth. The trays were covered with plastic lids. Four trays were the maximum number in one jar.

## RESULTS AND DISCUSSION

In our hands the broth method is convenient and labor saving with endpoints easy to read and with reproducible results. The panels are stored in airtight foil pouches with a desiccant. To our experience the shelf life is at least 6 months. The susceptibility testing may be performed at short notice in a standardized way.

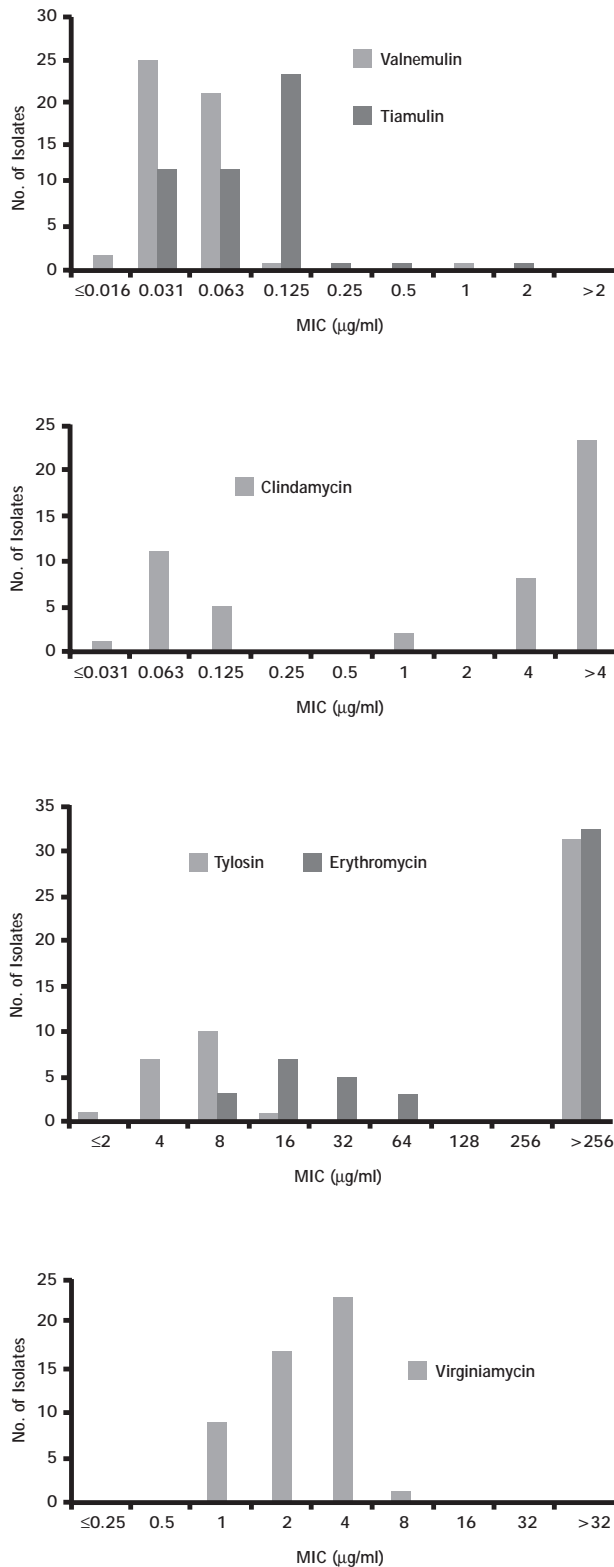
The results of the susceptibility testing are presented in Table 1 and Figure 1. No pleuromutilin resistance has yet been recorded for *B. hyodysenteriae* in Sweden. For different isolates the MIC of tiamulin was between 0 to 8 times higher than that of valnemulin.

Table 1. In vitro activity (MIC) of six antimicrobial agents for reference strains of *B. hyodysenteriae*.

Strain	MIC (µg/ml)					
	Tia	Val	ClI	Tyl	Ery	Vir
B78 <sup>T</sup> ATCC 27164 <sup>T</sup>	0.063	0.063	0.125	8	16	2
B204 ATCC 31212	0.063	0.031	4	>256	>256	2

All isolates resistant to tylosin were cross-resistant to erythromycin and clindamycin. This resistance is caused by a point mutation at position 2058 (*E. coli* numbering) in the 23S rRNA gene (4). Mutation or methylation of the equivalent position causes macrolide, lincosamide, and streptogramin B (MLS<sub>B</sub>) resistance in several bacterial genera (5). Virginiamycin is a combination of streptogramin A and B and the 2058 mutation will not affect the activity. This is supported by the virginiamycin MICs, which shows the distribution of a susceptible population (Fig 1).

Figure 1. Distribution of MIC of six antimicrobial agents for 50 Swedish field isolates of *B. hyodysenteriae*.

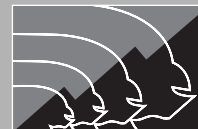


## ACKNOWLEDGMENTS

We thank Annica Landén and Margareta Horn af Rantzien for excellent technical assistance. This work was supported by the Swedish Council for Forestry and Agricultural Research.

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## FOCUS

Successful eradication of lincomycin-resistant *Brachyspira hyodysenteriae* (*B.hyo*) in a breeding-finishing unit using tiamulin medication and cleaning/disinfection.

## KEY FACTS

- Herd – An SPF unit with 450 breeders, 900 piglets, 1500 weaners and a finishing unit of approx 700 pigs. Annual production 2000 fatteners and approx 9000 x 30kg b.wt pigs.
- Though typical clinical signs of swine dysentery were seen, laboratory diagnosis by culture of faeces and rectal swabs was unsatisfactory.
- A FISH (fluorescent in situ hybridisation) technique using a specific oligonucleotide probe targeting 23S ribosomal RNA of *B.hyo* was used to detect *B.hyo* in colon tissue.
- *B.hyo* was successfully isolated from the colon of one pig and was demonstrated by the Danish Veterinary Laboratory to be lincomycin – resistant and tiamulin-sensitive.
- Prior to the commencement of the medication programme, the flooring was renewed, cleaned and disinfected.

### Medication Programme

- During the 1st 2 weeks populated areas were cleaned twice daily using 0.1% sodium hypochlorite in wet areas and “Stalosan” powder in dry areas.
- Day 1 – All breeders medicated with Tiamutin® in-feed (6mg thf/kg b.wt) for 14 consecutive days. All piglets medicated with Tiamutin injectable (10mg thf/kg b.wt) intramuscularly. All weaners medicated with Tiamutin premix (200ppm thf) for 35 consecutive days.
- Day 2-6 – Continuation of Tiamutin medication programme for all breeding animals and weaners.
- Day 7 – All group housed sows moved to cleaned, disinfected and dry sectors and Tiamutin feed medication continued.
- Day 8 – All piglets medicated with Tiamutin injectable 20% at 10mg khf/kg b.wt i/m and feed medication continued.
- Day 9-13- Continuing feed medication with Tiamutin of all breeders and weaners.
- Day 14 – All piglets medicated with Tiamutin injectable (20%) (as on Day 8). All group housed sows moved to cleaned, disinfected, dry areas and feed medication continued.
- Day 15-20 – All breeders medicated with Tiamutin in feed (250ppm – 2.5mg/kg b wt) for 21 consecutive days. All weaners medicated with Tiamutin in feed. (200ppm)
- Day 21 – All group housed sows moved to cleaned, disinfected, dry sections and Tiamutin feed medication continued.
- Day 22-27 – All breeders medicated with Tiamutin 250ppm in feed. All weaners medicated with Tiamutin 200ppm in feed.
- Day 28 – All group housed sows moved to cleaned, disinfected and dry areas and feed medication continued.
- Day 29-35 – All breeders medicated with Tiamutin 250ppm in feed. All weaners medicated with Tiamutin 200ppm in feed.

### Monitoring

- After the eradication rectal swabs, faeces and euthanized weaners were examined over a 6 month period for *B.hyodysenteriae* and the herd was monitored clinically for 12 months.

## BENEFITS

- Swine dysentery could not be demonstrated either clinically or bacteriologically during the post-eradication observation period.
- Tiamutin medication in breeders, piglets and weaners combined with rigorous cleaning/disinfection procedures successfully eliminated lincomycin-resistant *B.hyodysenteriae* from a breeding/finishing unit.

*Tiamutin is active against B.hyo which have developed resistance to other antibiotics.*

# ERADICATION OF *BRACHYSPIRA (SERPULINA) HYODYSENTERIAE* IN A BREEDING TO FINISHING UNIT BY COMBINED TIAMULIN MEDICATION AND CLEANING/DISINFECTION.

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## INTRODUCTION

Swine dysentery (SD) is known to occur world-wide and the primary etiologic agent is considered to be *Brachyspira (Serpulina) hyodysenteriae*. The *B. hyodysenteriae* proliferates in the large intestine and initially causes mucoid diarrhoea, possibly with mucus and/or blood, eventually developing to watery mucohaemorrhagic diarrhoea. Swine dysentery reduces profitability due to increased mortality, decreased rate of feed conversion and growth and higher treatment expenses.

## MATERIALS AND METHODS

### HERD

In an SPF herd of 450 breeding animals, 900 piglets, 1500 weaners and a separate finishing unit of approximately 700 growing/finishing pigs an eradication programme for *Brachyspira hyodysenteriae* was carried out, combining cleaning/disinfection and tiamulin medication. The SPF unit has an annual production of 2000 fatteners and a sale of approx. 9000 x 30 kg pigs.

### DIFFICULTIES WITH LABORATORY CONFIRMATION OF DIAGNOSIS

Typical clinical signs of SD occurred among fatteners and in a finishing herd, buying 30 kg pigs directly from the SPF herd. It was however difficult to verify the diagnosis in the SPF herd by culture of *B. hyodysenteriae* as presented in Table 1.

Table 1 Date and number of samples taken to verify the SD-diagnosis

Date	Number of samples	Lab results
04.09.1998	faeces, n=20	<i>B. hyodysenteriae</i> not detected <sup>1</sup> Lawsonia intracellularis detected in 5 samples
20.10.1998	rectal swabs, n=5	<i>B. hyodysenteriae</i> not detected <sup>1</sup>
30.11.1998	faeces, n=20	<i>B. hyodysenteriae</i> not detected <sup>1</sup>
10.12.1998	rectal swabs, n=5	<i>B. hyodysenteriae</i> not detected <sup>1</sup>

(1. By culture)

In order to try to confirm the diagnosis, four weaners of about 20 kg with clinical symptoms of swine dysentery were transported to the Danish Veterinary Laboratory. The pigs were euthanised and necropsied. Fluorescent *in situ* hybridization (FISH) technique using a specific oligonucleotide probe targeting 23S ribosomal RNA of *B. hyodysenteriae* was used for

detection of *B. hyodysenteriae* in colon tissue (1). The result of the investigation is shown in Table 2.

Table 2 Post mortem investigation of 4 growing pigs

	Lesions	Fluorescent <i>in situ</i> hybridization	Culturing of <i>B. hyodysenteriae</i>
Pig no. 1	Catarrhal colitis	<i>B. hyodysenteriae</i>	Positive
Pig no. 2	Catarrhal colitis	<i>B. hyodysenteriae</i>	Negative
Pig no. 3	No lesions	Negative	Negative
Pig no. 4	No lesions	Negative	Negative

Two pigs had gross lesions in the colon typical for SD. The diagnosis was verified by FISH in which *B. hyodysenteriae* was detected in two of four weaners (20 kg). *B. hyodysenteriae* was successfully isolated by culture from the colon of one pig. The following culture showed the *B. hyodysenteriae* to be resistant to lincomycin but sensitive to tiamulin.

### PREPARATION FOR ERADICATION OF SD

Prior to starting the eradication programme the floors were mended, the number of sows was reduced by slaughter to obtain some free space in all sections to assure proper cleaning. Chronically sick animals were euthanised or removed from the unit area, medicated feed was ordered in advance to secure that medicine was available for the whole medication period. Special consideration had to be made to the group housed sows in two identical sections with electronic sow feeding (ESF). Both sections were cleaned and disinfected immediately prior to starting the medication programme during which all sows were housed in one section – the empty section being cleaned, disinfected and dried up for one week before the sows once again were moved to the clean section.

### DISINFECTION

The empty ESF section of the unit was extensively cleaned and disinfected.

During the first two weeks of medication populated areas were carefully cleaned and disinfected twice daily using 0.1% sodium hypochlorite in wet and *Stalosan* in dry areas.

### MEDICATION

#### Day 0:

Control of all preparations was carried out

**Day 1:**

All breeding animals were treated with tiamulin 600 ppm in feed, 2 kg/animal/day (6 mg/kg body weight/day) for 14 days. All piglets were treated with Tiamutin 20%, 0.1 ml/two kg (10 mg/kg body weight) i.m. All weaners were treated with tiamulin 200 ppm in the feed for 35 days

**Day 2 – 6:**

Continuing feed medication of all breeding animals and weaners

**Day 7:**

All group housed sows were moved to the cleaned, disinfected and dried up section and feed medication was continued.

**Day 8:**

All piglets were treated with Tiamutin 20%, 0.1 ml/two kg (10 mg/kg body weight) i.m. and feed medication was continued.

**Day 9-13:**

Continuing feed medication of all breeding animals and weaners

**Day 14:**

All piglets were treated with Tiamutin 20%, 0.1 ml/two kg (10 mg/kg bodyweight) i.m. All group housed sows were moved to the cleaned, disinfected and dried up section and feed medication was continued.

**Day 15 – Day 20:**

All breeding animals were treated with tiamulin 250 ppm in the feed, 2 kg/animal/day (2.5 mg/kg body weight/day) for 21 days. All weaners were treated with tiamulin 200 ppm in the feed.

**Day 21:**

All group housed sows were moved to the cleaned, disinfected and dried up section and feed medication was continued.

**Day 22-27:**

All breeding animals were treated with tiamulin 250 ppm in the feed, 2 kg/animal/day. All weaners were treated with tiamulin 200 ppm in feed.

**Day 28:**

All group housed sows were moved to the cleaned, disinfected and dried-up section and feed medication was continued.

**Day 29-35:**

All breeding animals were treated with tiamulin 250 ppm in the feed, 2 kg/animal/day. All weaners were treated with tiamulin 200 ppm in the feed.

**MONITORING**

After the eradication programme was carried out rectal swabs, samples of faeces and euthanized weaners were examined for *B. hyodysenteriae* during a period of six months. The herd was monitored for clinical signs of SD for one year. During the monitoring period an infection contact test was performed with sentinel SPF-gilts.

**RESULTS**

During the observation period SD could not be demonstrated, neither clinically nor bacteriologically (Table 3).

Table 3 Monitoring of the herd for six months after the eradication programme.

Date	Nature and number of samples	Lab results
03.05.1999	rectal swabs, n=19 + faeces, n=2 pigs, n=2 (FISH)	<i>B. hyodysenteriae</i> not detected <sup>1,2</sup>
26.05.1999	rectal swabs, n=20	<i>B. hyodysenteriae</i> not detected <sup>1</sup>
22.06.1999	rectal swabs, n=16 + faeces, n=6	<i>B. hyodysenteriae</i> not detected <sup>1</sup>
19.07.1999	rectal swabs, n=20 + faeces, n=2	<i>B. hyodysenteriae</i> not detected <sup>1</sup>
30.08.1999	rectal swabs, n=20	<i>B. hyodysenteriae</i> not detected <sup>1</sup>
08.10.1999	rectal swabs, n=20 + pigs, n=2 (FISH)	<i>B. hyodysenteriae</i> not detected <sup>1,2</sup>

(1. By culture, 2. By fish)

To replace the sows that had been slaughtered prior to the eradication programme 60 SPF-gilts were bought and introduced to the sow-herd in the group-housed unit approximately 2 months after finishing the eradication programme. These sentinels were carefully observed and monitored and still, one year after finishing the eradication programme, no clinical signs have been observed.

**CONCLUSION**

The eradication programme combining tiamulin treatment and cleaning/disinfection proved to be effective in the elimination of SD in a breeding to finishing unit (with group housing and ESF) although the eradication was carried out during winter-time.

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## B Eradication of endemic *Brachyspira pilosicoli* infection from a sow herd – a case report.

*M. Fossi and others.*



### FOCUS

Eradication of endemic *B.pilosicoli* infection from a sow herd with Tiamutin® premix.

### KEY FACTS

- *B.pilosicoli* and *B.innocens* were isolated from weaned pigs in a 60 sow herd in 1997. A severe post-weaning diarrhoea problem had persisted for several years and laboratory tests on rectal samples had confirmed the presence of *B.pilosicoli* and *B.innocens*. They were both found to be tiamulin-sensitive, MIC range (0.06-0.25µg/ml)
- The standard weaner feed (7-10 weeks of age) contained 50ppm carbadox or olaquinox until October 1998, Piglets received a creep feed containing the same additives until May 1999. Subsequently no antimicrobial feed additives were used on the farm.
- An eradication programme for *B.pilosicoli* using Tiamutin premix commenced at the beginning of August 1997. At that time the farm had 60 sows, 40 suckling piglets, 1 boar, 69 finishers (> 25kg b.wt) and 112 weaners (< 25 kg b.wt)
- On August 25th 1997 the piggery was totally emptied for 25 days during which time it was cleaned, washed and disinfected and all worn surfaces were repaired. Old wooden materials and old tools were burned. The automatic manure system was replaced and rodents were controlled with poisonous baits.

### Medication

- All feed was changed to Tiamutin medicated feed, 5 days before emptying the piggery. Tiamutin premix (200ppm thf) was given in the sow feed for 30 days, the piglets for 23 days and the finishers for 18 days.

### Management

- Sucking piglets were not injected with any antimicrobials. Dry sows and the boar were taken to a paddock near the piggery. Sows which had just farrowed or which were going to farrow during the eradication programme were taken to a building 20m from the piggery. All weaners were kept in the same building whilst finishers went to another building 100m from the piggery.

Post-eradication all 4 replacement stock were medicated with Tiamutin premix (200ppm thf) for 3 weeks in the quarantine area.

### Monitoring

- Post-eradication control samples for spirachaetes were last taken in December 1999, 7 months after the total withdrawal of antimicrobial feed premixes. The samples were cultivated by routine methods and *B.pilosicoli* specific PCR assays.

### BENEFITS

- *B.pilosicoli* was not identified in any of the samples taken post-eradication.
- The problem of post-weaning diarrhoea disappeared after the Tiamutin premix medication programme.

*Tiamutin is highly effective against mixed ileitis/spirochaetal colitis infections.*

# ERADICATION OF ENDEMIC *BRACHYSPIRA PILOSICOLI* INFECTION FROM A SOW HERD – A CASE REPORT

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## INTRODUCTION

*Brachyspira* (*B.*) *pilosicoli*, a causative agent of Porcine Intestinal Spirochetosis, is fairly prevalent in Finnish swine herds (1). The eradication of *B. pilosicoli* from swine herds has been estimated to be a difficult task due to the capability of this organism to inhabit many other mammalian species and birds, and due to its survival in natural water systems. To date, no scientific reports about attempts to eradicate *B. pilosicoli* from swine herds have been published. The aim of this study is to report a program to eradicate *B. pilosicoli* from a small farrowing herd in Finland.

## MATERIALS AND METHODS

*B. pilosicoli* and *B. innocens* had been isolated from weaned pigs in one herd with 60 sows in 1997 (Table 1). A severe post-weaning diarrhoea problem had persisted for several years in this farrowing herd raising also some finishing pigs. Rectal samples had been taken from pigs older than 7 weeks and the samples had been sent to the laboratory in transport media. The samples were cultivated and incubated by routine methods. The *Brachyspira* isolates were classified with biochemical tests (2). The species specific polymerase chain reaction (PCR) was used to confirm the species of *B. pilosicoli*. The strains of *B. pilosicoli* and *B. innocens* present were found to be sensitive to tiamulin (range of MIC values 0.06–0.25 µg/ml).

The area around the farm in southern Finland consisted mainly of forests and some small fields, and there were no lakes or rivers within a few kilometres around the farm. A neighbouring all in – all out swine finishing unit with 300 finishing pigs was situated about 300 metres from the farm. All the pigs were kept in one building with no compartments. All manure was collected in the solid form. The standard feed for weaned pigs 7–10 weeks old contained 50 ppm olaquinox or carbadox until October 1998. The piglets were fed creep feed with 50 ppm olaquinox or carbadox as feed additive until May 1999, after which no antimicrobial feed additives were used on the farm.

The eradication measures for *B. pilosicoli* were planned and run on the herd at the beginning of August 1997, when there were 60 sows, 40 sucking piglets, 1 boar, 69 finishing pigs (over 25 kg) and 112 weaned piglets (under 25 kg) on the farm. The piggery unit was totally emptied on August 15th for

25 days. During this time it was cleaned, washed and disinfected (Virkon® 1%), and all worn surfaces were repaired. Old wooden materials and old tools were burned. The automatic manure system was replaced by a new one. The solid manure was transported to the fields and the manure pit was disinfected with lime. Rodents were controlled with poison baits before and during the eradication procedure.

Five days before emptying the piggery, all feed was changed to medicated feed. Tiamulin 200 ppm (Tiamutin®) was used in the feed which was given to the sows as the only feed for 30 days, the piglets for 23 days and the finishing pigs for 18 days. Sucking piglets were not injected with any antimicrobials. Dry sows (n=46) and the boar were taken to a paddock next to the piggery. The sows which had just farrowed or were going to farrow during the eradication program were taken to an old barn (3 sows) or to a shed next to it (11 sows) situated 20 meters from the piggery unit. All weaned piglets were kept in the same shed. The finishing pigs were transported to another shed about 100 meters from the piggery unit. None of the piglets or finishing pigs were returned to the piggery unit after the eradication, but they were all sold from the sheds by December. Between September 10th and October 3rd the sows and the boar were taken from the paddock into the clean piggery unit. After the eradication, all replacement stock of four animals was medicated with tiamulin (Tiamutin) 200 ppm in their feed for three weeks in the quarantine.

After the eradication, control samples for anaerobic spirochetes were taken four times (Table 1). The last samples were taken in December 1999, seven months after the total withdrawal of antimicrobial feed additives on the farm. The samples were cultivated by routine methods. After 14 days of incubation, the primary plates from the last three samplings were studied also with *B. pilosicoli* specific PCR assays targeting 16S rDNA and 23S rDNA. The *Brachyspira* isolates were classified biochemically (2). Six *B. pilosicoli* and two *B. innocens* isolates before the eradication and five *B. innocens* isolates after the eradication were subjected to pulsed-field gel electrophoresis (PFGE).

## RESULTS AND DISCUSSION

The eradication program seemed to have succeeded. *B. pilosicoli* was not identified in any of the samples taken after the eradication. Clinically, the problem with post-weaning diarrhoea disappeared. The macrorestriction profiles of six *B. pilosicoli* isolates in PFGE were identical. This supports the presumption that *B. pilosicoli* was a major factor for diarrhoea in this herd. After the eradication, only a few litters have needed medication because of diarrhoea, even though no antimicrobial feed additives have been used on the farm. *B. innocens*, a harmless commensal, was isolated from each batch of samples with high frequency (Table 1). The results from PFGE study suggested that at least one genotype of *B. innocens* could persist in the herd. All *B. pilosicoli* and *B. innocens* isolates prior to and after the eradication were sensitive to tiamulin in vitro.

A long medication period, intensive cleaning and repairing of the premises, dry and warm season and the low density of pig herds in the neighbourhood were likely to promote the success of this eradication. The relatively long soil frost period in the Finnish winter might reduce the pressure of *B. pilosicoli* reinfection from the environmental sources. Unlike *B. hyodysenteriae*, it might not always be cost-effective to eradicate *B. pilosicoli* (3), because it can be found also in non-diarrhoeic herds (1). However, in some problem herds eradication programs are likely to be beneficial. Further eradication trials should be conducted, before any probability of successful eradication of *B. pilosicoli* can be assessed.

Table 1: The rectal samples taken from piglets older than 7 weeks and cultivated for *Brachyspira* before and after the eradication program of *B. pilosicoli* in a farrowing herd.

Date	N of samples	N of samples pos. for <i>B. pilosicoli</i>	N of samples pos. for <i>B. innocens</i>
Apr 1997	20	4 <sup>a</sup>	5 <sup>a</sup>
Apr 1997	20	5 <sup>a</sup>	5
May 1997	20	4 <sup>a</sup>	9 <sup>a</sup>
Aug 1997: eradication program			
Apr 1998	20	0	6 <sup>a</sup>
Nov 1998	49 <sup>c</sup>	0 <sup>b</sup>	39 <sup>a</sup>
Mar 1999	42	0 <sup>b</sup>	26
May 1999: withdrawal of all antimicrobial feed additives			
Dec 1999	45	0 <sup>b</sup>	36

1-3 isolates per sampling were subjected to PFGE study

<sup>a</sup> Negative also with two *B. pilosicoli* specific PCR assays

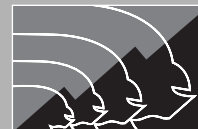
<sup>c</sup> Includes 4 pathological samples from 4 finishing pigs weighing about 110 kg

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C(i) A double-blind, randomised placebo controlled, clinical trial to investigate the efficacy of tiamulin in the control of porcine proliferative enteropathy (PPE) and porcine colonic spirochaetosis (PCS) under field conditions.

*J. Haugegaard and others.*



## FOCUS

A GCP trial to assess the efficacy of Tiamutin® premix (150ppm thf for 14 days) in the control of combined PPE (*L.intracellularis*, L.i) and spirochaetal colitis (*B.pilosicoli*, B.p) infection under field conditions.

## KEY FACTS

- 120 cross-bred pigs from a swine dysentery free (SPF) herd where the presence of L.i and B.p had been confirmed were moved to the study facility.
- The 120 pigs (av.wt 19.0kg) were identified by ear tags and divided into 2 groups of 60 pigs each by weight and allocated to 6 pens.
- Approx. 50% of the pigs in both groups had diarrhoea when examined clinically on the first day of the study and faecal sampling revealed a high frequency of L.i and B.p in both groups.
- One group received Tiamutin premix medicated feed (150ppm t.h.f.) whilst the other group received feed medicated with placebo. Both groups were medicated for 14 days.
- The pigs were extensively monitored clinically and microbiologically for a total of 21 days and the study ended on day 21. Faecal analysis by PCR from selected pigs with and without diarrhoea, for L.i was conducted. In tissues L.i was detected by PCR and immunohistochemistry.
- B.p was examined by culture and identified by haemolysis and indole and hippurate hydrolysis tests.
- At the end of the trial 9 pigs were euthanized and evaluated for gross and histological lesions in the large and small intestines.

## BENEFITS

- In the Tiamutin premix medicated group clinical score and diarrhoea improved rapidly. (in the placebo group diarrhoea and clinical scores worsened during the first 9 days of the study)
- The average daily weight gain in the Tiamutin medicated group, over 21 days, was 14.9% better than the placebo group (979g vs 852g) whilst the feed conversion ratio was improved by 7.5% in the Tiamutin medicated group (1.75 vs 1.89)
- In the placebo group gross and microscopic lesions, characteristic of Li. and B.p infections were present.
- The study clearly demonstrated that Tiamutin premix (150ppm for 14 days) was highly effective for the treatment of an acute outbreak of combined PPE/spirochaetal colitis infection and successfully prevented the associated economic losses.

*Tiamutin premix provides excellent activity against classical swine dysentery, spirochaetal colitis and PPE.*

# A DOUBLE-BLIND RANDOMIZED PLACEBO-CONTROLLED CLINICAL TRIAL TO INVESTIGATE THE EFFICACY OF TIAMULIN IN THE CONTROL OF PORCINE PROLIFERATIVE ENTEROPATHY (PPE) AND PORCINE COLONIC SPIROCHAETOSIS (PCS) UNDER FIELD CONDITIONS

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## INTRODUCTION

Porcine Proliferative Enteropathy (PPE) caused by *Lawsonia intracellularis* and Porcine Colonic Spirochaetosis (PCS) caused by *Brachyspira pilosicoli* are commonly recognised diseases in grower – finisher pigs world-wide. In Denmark both infections usually occur simultaneously in chronically infected herds and may aggravate the growth performance (1). The objective of the study was to investigate the efficacy of tiamulin in the control of naturally and simultaneously occurring PPE and PCS. The study was conducted according to the Good Clinical Practice Guidelines.

## MATERIALS AND METHODS

Immediately prior to the present study, 120 cross-bred pigs from a SPF herd, free from swine dysentery (*Brachyspira hyodysenteriae*), where the presence of *L. intracellularis* and *B. pilosicoli* had been confirmed, were moved into the study facility. 120 pigs, average weight approx. 19 kg, were identified by ear tags, divided into two groups of 60 pigs by weight and allocated to six pens according to the stratified randomised scheme. Approximately 50% of the pigs in both groups had diarrhoea on examination at the first day of the study, and faeces samples confirmed a high frequency of *L. intracellularis* and *B. pilosicoli* in both groups. One group of pigs was fed ad libitum with feed medicated with tiamulin 150 ppm while another group received feed with placebo. Feeds both with tiamulin and placebo were prepared in the feed mill. Due to technical problems under pelleting, the feed with placebo was contaminated with 8.8 ppm tiamulin. Investigators did not know which pens received which treatment. Both groups were treated for 14 days. The pigs were monitored for 3 weeks and the study was ended on day 21. During the study all pigs were individually scored three times a week for general appearance (range 0-3), general condition (range 0-3), consistency of faeces (range 0-3), and weight was measured four times during the study. Feed consumption was recorded per pen. Faeces from randomly selected pigs and from pigs with diarrhoea were examined for *L. intracellularis*. *L. intracellularis* was detected in faeces by PCR and in tissue immunohistochemically and by PCR (2, 3). *Brachyspira* spp., *E. coli* and *Salmonella enterica* were examined by culture. *B. pilosicoli* was identified on basis of haemolysis and indole- and hippurate-hydrolysis tests (4). During the study pigs that died or

were euthanized due to humanitarian reasons were necropsied. At the end of the trial nine pigs were euthanized and evaluated for gross and histological lesions in the small and large intestines for confirmation of infections. Tiamulin in vitro activity against isolated *B. pilosicoli* was determined. Statistical analysis: Weight gain was analysed by t-test. Clinical impression score and faecal score were analysed by a Chi-Square test.

## RESULTS

Results of the study are shown in Table 1 and Figure 1. Clinical score and diarrhoea improved rapidly in tiamulin medicated pigs. In the placebo group diarrhoea and clinical scores increased during the first 9 days treatment compared to day 0. Average weight gain improved significantly in the tiamulin group and was 355 g higher than that of the placebo for the period day 0 to 7 and was 179 g higher for the periods days 0 to 21. The pigs were affected by PPE and PCS, which was confirmed during the study by frequent detection of *L. intracellularis* and *B. pilosicoli* in the faeces samples and by the presence of evident lesions in ileum and colon in the dead or euthanized pigs in the placebo group during the study. Gross and microscopical lesions were characteristic of infections with *L. intracellularis* and *B. pilosicoli*. *B. hyodysenteriae* and *Salmonella enterica* were not isolated from any of the faeces samples. This study shows that tiamulin was highly effective for treatment of acute outbreak of simultaneously occurring PPE and PCS and prevented economic loss associated with these diseases.

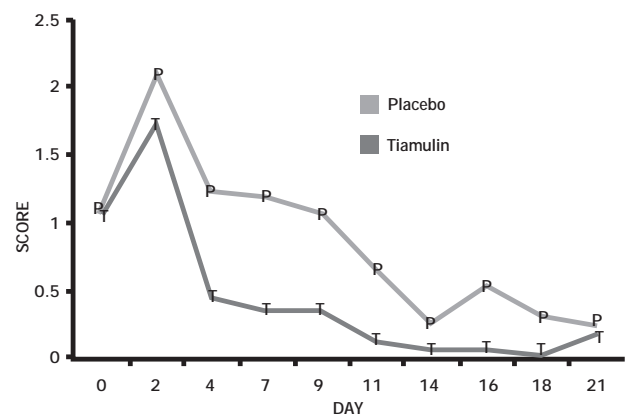


Figure 1. Mean faecal scores in Tiamulin and Placebo groups \*  
\*Score 2 and 3 = Diarrhoea  
Score 0 and 1 = No diarrhoea

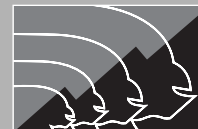
Table 1. Clinical scores, weight gain and feed conversion rate

	Placebo	Tiamulin	p-value
Avg. daily weight gain (grams)			
Day 0 to 7	658	1013	<0.001
Day 0 to 21	852	979	<0.001
Feed conversion rate	1.89	1.75	nd *
Avg. body condition score (0-3)			
Day 0 to 14	0.33	0.08	0.03
Day 0 to 21	0.31	0.05	0.02
Avg. faecal score (0-3)			
Day 0 to 21	1.47	0.96	< 0.01

\* not done

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## FOCUS

Successful eradication programme for *Lawsonia intracellularis* (L.i) and *Brachyspira pilosicoli* (B.p) infection with Tiamutin® water soluble medication and management procedures.

## KEY FACTS

- 2 x 35 sow units were used in this test. Herd A was a closed, AI/AO farrow to finish herd. The sows farrowed in batches and the pigs reared in the same pen from birth to slaughter. Herd B had a continuous production of growers for sale at 25kg b.wt. This herd had purchased a few breeders from a multiplier post the eradication programme being completed. These animals were medicated with Tiamutin before being taken into the herd.
- Bacteriological examinations of faecal samples from growers confirmed the presence of L.i and B.p in Herd A and L.i/*Brachyspira innocens* (III b) in Herd B pre-eradication.
- Eradication programme

### Pigs

Animals younger than 10 months were removed from the herds to reduce infection pressure and to provide clean areas for the Tiamutin medicated pigs. During the medication programme the herds consisted of sows, gilts and piglets born during the medication programme.

### Antibiotic treatment

All sows were medicated with Tiamutin water soluble at a level of 60ppm tiamulin h f to provide a dosage of approx. 8mg tiamulin h f/kg b.wt/sow/day for 3 weeks. (Antibiotics are not used in animal feeding stuffs in Norway)

Following the end of the medication period the sows were moved into cleaned and disinfected pens. Sucking piglets born during the medication period received Tiamutin injection intramuscularly (15mg thf/kg b.wt) once per week for 3 consecutive weeks, the first being given at 3-7 days of age.

### Disinfection

Prior to the medication period all pigs were removed from the farrowing to slaughter units in Herd A and from the farrowing unit in Herd B. All rooms for pigs were thoroughly cleaned by power washing and disinfected by 27% "Virkon S" and calcium hydroxide. Repairs to flooring and walls were also made. During the medication period all areas in the units were cleaned and disinfected daily. An intensive rodent control programme was implemented.

- Post-eradication monitoring.

Laboratory tests were conducted at the National Veterinary Institute, Oslo. In Herd A rectal swabs and rectal faecal samples from approx. 40 pigs were collected 2-3 weeks post-weaning and 1-2 weeks pre-slaughter.

In Herd B rectal swabs and faecal samples were collected from 105 pigs at 2-3 weeks post-weaning until the time at which they reached 25kg b. wt.

## BENEFITS

- The eradication programme was completed in July 1998 in Herd A and in August 1998 in Herd B. To date, >24 months post-completion of the programme, there have been no clinical problems and antibiotics have not been required to control diarrhoea.
- L.i and B.p can be successfully eradicated from certain pig herds by a combination of Tiamutin medication and management procedures.

Results of sampling programme.

	Herd A		Herd B.	
	Pre-eradic	Post-eradic.	Pre-eradic.	Post-eradic.
L.i	10/32	*2/324	7/30	0/105
B.p	12/32	0/324	0/30	0/105
* may be false positives (PCR) since all 241 subsequent samples have been negative.				

*Tiamutin is unrelated to human use antibiotics and does not share patterns of cross-resistance with them – a prudent choice.*

# AN ATTEMPT TO ERADICATE *LAWSONIA INTRACELLULARIS* AND *BRACHYSPIRA SP.* FROM SWINE HERDS

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## INTRODUCTION

*Lawsonia intracellularis* (*L. intracellularis*) and *Brachyspira pilosicoli* (*B. pilosicoli*), the causative agents of porcine intestinal adenomatosis and porcine intestinal spirochaetosis, respectively, are commonly identified in faecal samples from pigs in Norwegian herds (1,2). Both infections may cause serious economical losses due to diarrhoea, increased mortality, reduced daily weight gain and poor feed conversion efficiency, especially in weaner pigs, growers and young fattening pigs (3,4). The clinical symptoms can be controlled by the use of antibiotics and appropriate management practices. To our knowledge, no eradication programme has been described for these infections.

The objective of this field trial was to eradicate *L. intracellularis* and *Brachyspira sp.* from pig herds by a combination of medication and management procedures, and to keep the herds free from the infections after eradication.

## MATERIALS AND METHODS

### HERDS

The eradication programme was carried out in two conventional herds with a history of medication of weaned and grower pigs due to diarrhoea and poor growth rate. Bacteriological examinations of faecal samples from grower pigs had confirmed the occurrence of *L. intracellularis* and *B. pilosicoli* in herd A, and *L. intracellularis* and *B. innocens* group IIIb in herd B (Table 1).

Herd A is a 35-sow, closed farrowing to finishing herd with two "farrowing to slaughter" (FTS) -units, each with 15 pens. In this system, based on the Swedish FTS-model, the sows farrow in batches, and the pigs are reared in the same pen from birth to slaughter. Each unit is managed in an all in/all out manner.

Herd B is a 35-sow herd with a continuous production of growers for sale at 25 kg. This herd has bought some few breeding animals from a multiplier herd also after the time when the eradication programme was completed. These breeding sows have been medicated for 14 days with tiamulin (Tiamutin®) before they have been taken into the herd.

### ERADICATION PROGRAMME

The eradication programme for *L. intracellularis* and *Brachyspira sp.* was carried out according to the following general strategy:

## PIGS

Animals younger than 10 months should be removed from the herds to reduce the infectious pressure, and to provide clean areas for medicated pigs. During the medication programme the herds consisted of sows, gilts and piglets born during the medication programme.

## MEDICATION

All sows were medicated with tiamulin 60 ppm in the drinking water for 3 weeks to provide a dosage of approximately 8 mg tiamulin/kg body weight per day. Following medication for some days, the sows were moved into cleaned and disinfected pens. In herd A, 9 gilts younger than 10 months were medicated for 4 weeks. Suckling piglets born during the medication period were medicated by injection with 15 mg tiamulin/kg IM once a week for 3 weeks. The first injection was given when the piglets were between 3 to 7 days old. In herd B some growers were kept in a separate room during the eradication period, treated with tiamulin in drinking water, and removed from the herd as soon as they reached 25 kg.

## DISINFECTION

Prior to the medication period, all pigs were removed from the FTS units in herd A and from the farrowing unit in herd B. All rooms for pigs were thoroughly cleaned by power washing and disinfected with 2 % Virkon S® and Ca (OH)<sub>2</sub>. Repairs to flooring and walls were also undertaken. During the medication period, all areas in the units, including the yards, were cleaned daily and disinfected as described above. An intensive control programme for rodents was also performed.

## MONITORING AFTER ERADICATION

From each batch of pigs in herd A, rectal swabs (Transwab®) and faecal samples from the rectum of about 40 pigs were collected 2 – 3 weeks after weaning and 1 – 2 weeks before slaughter. In herd B rectal swabs and faecal samples were collected from 105 pigs. The time of collection ranged from 2 – 3 weeks after weaning and up to the time when the pigs were 25 kg body weight.

## LABORATORY TESTS

Rectal swabs were submitted in a transport medium to the National Veterinary Institute of Norway, and examined for *L. intracellularis* by a PCR-technique (1) and for *Brachyspira sp* by culture (2).

## RESULTS

The eradication programme was completed in July 1998 in herd A, and in August 1998 in herd B. To date, about 20 months after completing the eradication programmes, there have been no clinical problems and antibiotics have not been used to control diarrhoea. Antibiotics are not used as feed additives in Norwegian swine herds. The results from the bacteriological monitoring programme are shown in Table 1.

Table 1. Number of positive samples in relation to number of samples examined «before» and «after» the eradication programme was carried out.

Herd	L. intra.	B. pilo.	B. in. IIIb	B. mur.	Other B. sp
A «before»	10/32	12/32	7/32	3/32	4/32
A «after»	2*/324	0/324	0/324	43/324	0/324
B «before»	7/30	0/30	24/30	0/30	1/30
B «after»	0/105	0/105	30/105	0/105	0/105

\*Two fattening pigs from the first batch of pigs born after eradication.

In herd A, *B. pilosicoli* has not been found in faecal samples from pigs born after the eradication. *B. murdochii* has, however, been regularly found in faecal samples both from newly weaned pigs and from fattening pigs about one week before slaughter. In herd B, *Brachyspira* sp. were not found in the first samples taken after the eradication. *B. innocens* IIIb was, however, isolated from many of the samples taken about 18 months after the eradication.

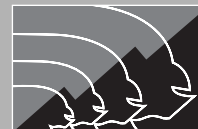
## DISCUSSION

This field trial indicates that *L. intracellularis* and *B. pilosicoli* may be successfully eradicated from a pig herd by a combination of medication and management procedures. The two positive PCR reactions for *L. intracellularis* in faecal samples from fattening pigs in herd A are difficult to explain. They may have been false positive since all the 241 subsequent samples from pigs in the same herd have been negative.

The removal of weaned pigs, growers, fattening pigs and breeding animals younger than 10 months is thought to be important to reduce the infectious pressure during the eradication period. Further field trials are needed to obtain more knowledge of the safety of the eradication method, and to determine the most important factors influencing the outcome of the eradication programme.

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## FOCUS

In-feed tiamulin for the control and treatment of PPE. due to induced *L.intracellularis* (L.i) infection.

## KEY FACTS

- 48 healthy 5 week old pigs of mixed breed and sex were used in the study, and assigned to 16 pens (3 pigs/pen) consisting of 8 blocks in 2 groups balanced for weight and gender.
- Artificial infection achieved with pure culture of L.i inoculated intra-gastrically on day-9 prior to initiation of treatment and in control group.
- Treatments Control: unmedicated Treated: 38.5ppm tiamulin h.f in-feed for 4 consecutive weeks after symptoms first became evident.
- Medicated feed provided to treated group when  $\geq 50\%$  of pens had pigs with clinical symptoms of PPE.
- Clinical monitoring of all pigs (diarrhoea, body condition) occurred periodically throughout the study.
- Faecal shedding of L.i and productivity were also regularly monitored.
- At autopsy (37 days post-infection) PPE specific gross and histological lesions were quantified and intestinal tissues were cultured for L.i.

## BENEFITS

- The artificial infection was confirmed to be L.i only – all pigs were free from *Brachyspira spp*, *Salmonella spp* and *E.coli*.
- After 4 weeks feed medication statistically significant reductions developed in the prevalence and severity of gross and histological PPE specific lesions between treated and control groups:-

	Treated gp	Control gp
Gross lesions	4%	33%
Histological lesions	9%	33%

- The shedding of L.i was significantly reduced in the treated group (0%) compared to 19% in the controls after 4 weeks of medication.
- Statistically significant performance improvements in average daily gain (ADG) and feed conversion ratio (FCR) of 29.1% and 14.6% respectively were seen in the treated group compared to the controls after 4 weeks of medication.
- Tiamulin administered in feed at 38.5ppm for 4 consecutive weeks to pigs already infected with L.i, successfully treats and controls the clinical, pathological and negative productivity effects of P.P.E.

*Tiamulin possesses potent intracellular activity vs L.intracellularis.*

# EFFECTIVENESS OF TIAMULIN IN FEED FOR CONTROL AND TREATMENT OF PORCINE PROLIFERATIVE ENTEROPATHY (ILEITIS) DUE TO *LAWSONIA INTRACELLULARIS* INFECTION

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## INTRODUCTION

Porcine Proliferative Enteropathy (PPE, ileitis) is a common enteric disease of grow-finish swine which may result in poor growth rate, diarrhoea, and stunting or may be manifested as sudden death or bloody diarrhea in late finishing pigs and replacement gilts(1). The causative organism, *Lawsonia intracellularis* (LI)(2) is a fastidious and obligately intracellular bacterium. The inoculation of pigs with pure cultures of LI has allowed successful reproduction of disease without the confounding effect of other potentially pathogenic microflora and variability of infective dose inherent in crude inoculum preparations(2). Tiamulin (Denagard™) is a member of the pleuromutilin family of antibiotics, which are selectively reserved for use in food producing animals and are not used in human medicine. Tiamulin achieves high tissue levels in both the enteric and respiratory tracts. Tiamulin has good in vitro activity against gram positive bacteria, mycoplasmas, anaerobes, spirochetes (e.g. *Brachyspira/Serpulina* spp.), and selective gram negative activity including *Actinobacillus pleuropneumoniae*, *Haemophilus parasuis*, *Pasteurella multocida* and *Lawsonia intracellularis*(3).

## OBJECTIVE

The objective of this study was to evaluate the effectiveness of 35 g/t (38.5 ppm) tiamulin hydrogen fumarate (thf) in feed of swine for control and treatment of PPE due to LI infection.

## MATERIALS AND METHODS

Forty-eight healthy 5-week-old pigs of mixed breed and sex were assigned to 16 pens (3 pigs/pen) comprising 8 blocks of two treatment groups balanced for body weight and gender. Treatments were assigned to pens within blocks randomly. The CONTROL group was infected and nonmedicated. The TREATED group of pigs was infected followed by medication with thf at 38.5 ppm for four weeks after symptoms of PPE became evident. On day -9 both treatment groups were inoculated intragastrically via stomach tube with a pure culture of LI. Medicated feed was provided to the TREATED group when  $\geq$  50% of pens had pigs with clinical symptoms of PPE

on day 0. Clinical signs (diarrhoea, body condition), fecal shedding of LI, and productivity were monitored periodically throughout the study. Both treatment groups were necropsied 37 days post-infection. PPE-specific gross and microscopic lesions were quantified and intestinal tissues were cultured at necropsy. Blinding measures were utilized.

## RESULTS AND DISCUSSION

The only lesions observed in any pigs by gross and microscopic examination were those of PPE. All pigs were free of *Brachyspira(Serpulina)* spp, *Salmonella* spp, and *E. coli* by culture, verifying the presence of an uncomplicated LI infection. The prevalence and severity of gross and microscopic PPE-specific lesions were significantly reduced in the TREATED group. Faecal shedding of LI was significantly reduced in the TREATED group after two weeks on medication (P=0.0312). Clinical signs were significantly reduced in the TREATED group after 7-10 days of medication and remained significantly reduced throughout the rest of the study. The rate and efficiency of weight gain of the TREATED group tended to be greater by 14 days on medication (P=0.071) and was significantly greater by 21 days (ADG P=0.007, G/F P=0.010). Two CONTROL pigs died of PPE while all TREATED pigs survived.

Tiamulin has been reported to possess good *in-vitro* activity against LI(3) and to be effective in treating, controlling or preventing PPE in three separate pure culture LI challenge models(4-6), a field study with the naturally occurring disease(7), and in clinical use by swine practitioners(8-10). This study demonstrates the ability of tiamulin in feed to treat and control the clinical, pathological, and negative productivity effects of PPE in pigs experiencing an outbreak.

Table 1. Effects of tiamulin against PPE after 4 weeks feed medication

	CONTROL	TREATED	P value
% pigs with PPE gross lesions	33 %	4 %	0.0206
% pigs with PPE microscopic lesions	33 %	9 %	0.0557
% pigs with fecal LI shedding	17 %	0 %	0.0500
Average daily weight gain (g), DO-28	409	528	0.007
Average daily feed intake (kg), DO-28	0.76	0.84	0.029
Gain/Feed, DO-28	0.540	0.631	0.010

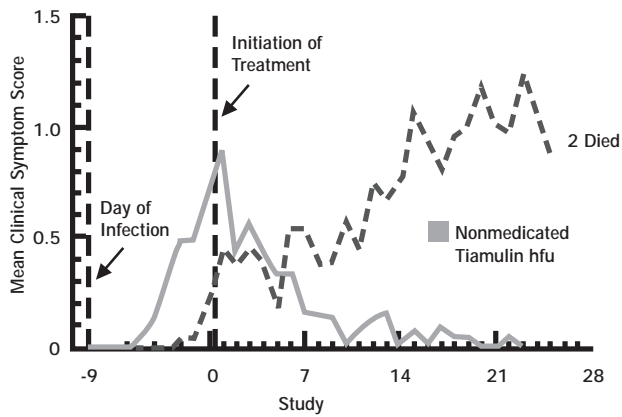


Figure 1. Mean daily clinical symptom scores by treatment group

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D(ii) Effectiveness of tiamulin in drinking water for treatment and control of porcine proliferative enteropathy (ileitis) due to *Lawsonia intracellularis* infection.

*D. Walter and others.*



## FOCUS

Tiamulin 60ppm in drinking water for 5 days for the treatment and control of porcine proliferative enteropathy (ileitis) due to induced L.i infection.

## KEY FACTS

- 48 healthy 6 week old pigs of mixed breed and sex were used in the study and assigned to 16 pens (3 pigs/pen) consisting of 8 blocks in 2 groups balanced for weight and gender.
- The control group was infected and non-medicated and the treatment group was infected and medicated with tiamulin h.f. (60ppm) in water for 5 consecutive days when clinical symptoms became apparent in some pigs in  $\geq 50\%$  of pens.
- Infection was induced on day 0 by intragastric inoculation of a pure culture of L.i.
- Medication was provided for days 8-13 of the study followed by a 10 day post-medication observation period.
- Clinical signs (diarrhoea, body condition) faecal shedding of L.i and productivity were monitored throughout the study.
- At autopsy 23 days post infection, PPE-specific gross and histological lesions were quantified and intestinal tissues were cultured.

## BENEFITS

- The artificial infection with L.i was confirmed to be L.i only – all pigs were free from *Brachyspira spp.*, *Salmonella spp* and *E coli*.
- The prevalence and severity of gross and histological PPE specific lesions in the tiamulin medicated group were significantly reduced – (from 58% and 92% in the controls to 12% and 21% respectively in the medicated group)
- Faecal shedding of L.i was significantly reduced in the tiamulin medicated group (from 71% in the unmedicated controls to 12%)
- Statistically significant performance improvements in average daily gain (ADG) and feed conversion efficiency (FCE) of 25.7% and 16.4% respectively were seen in the treated group compared to the controls, over the combined treatment and post-treatment periods.
- Tiamulin (60ppm) in drinking water for 5 consecutive days successfully controls the clinical, pathological and negative productivity effects of PPE.

*Tiamulin in drinking water at 60ppm for 5 days controls both ileitis and swine dysentery.*

# EFFECTIVENESS OF TIAMULIN IN DRINKING WATER FOR TREATMENT AND CONTROL OF PORCINE PROLIFERATIVE ENTEROPATHY (ILEITIS) DUE TO *LAWSONIA INTRACELLULARIS* INFECTION

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## INTRODUCTION

Porcine Proliferative Enteropathy (PPE, ileitis) is a common enteric disease of grow-finish swine which may result in poor growth rate, diarrhoea, and stunting or may be manifested as sudden death or bloody diarrhoea in late finishing pigs and replacement gilts(1). The causative organism, *Lawsonia intracellularis* (LI)(2) is a fastidious and obligately intracellular bacterium. The inoculation of pigs with pure cultures of LI has allowed successful reproduction of disease without the confounding effect of other potentially pathogenic microflora and variability of infective dose inherent in crude inoculum preparations(2). Tiamulin (Denagard™) is a member of the pleuromutilin family of antibiotics, which are selectively reserved for use in food producing animals and are not used in human medicine. Tiamulin achieves high tissue levels in both the enteric and respiratory tracts. Tiamulin has good *in-vitro* activity against gram positive bacteria, mycoplasmas, anaerobes, spirochetes (e.g. *Brachyspira/Serpulina* spp.), and selective gram negative activity including *Actinobacillus pleuropneumoniae*, *Haemophilus parasuis*, *Pasteurella multocida* and *Lawsonia intracellularis*(3).

## OBJECTIVE

The objective of this study was to evaluate the effectiveness of 60 ppm tiamulin hydrogen fumarate (thf) for 5 consecutive days in drinking water of swine for treatment and control of PPE due to LI infection.

## MATERIALS AND METHODS

Forty-eight healthy 6-week-old pigs of mixed breed and sex were assigned to 16 pens (3 pigs/pen) comprising 8 blocks of two treatment groups balanced for body weight and gender. Treatments were assigned to pens within blocks randomly. The CONTROL group was infected and non-medicated. The TREATED group of pigs were infected followed by medication with thf at 60 ppm for 5 consecutive days after symptoms of PPE became evident. On day 0 both treatment groups were inoculated intragastrically via stomach tube with a pure culture of LI. Water medication was provided to the TREATED group when ≥ 50% of pens had pigs with clinical symptoms of PPE. Medication was provided from days 8-13 followed by a 10-day post-medication observation period. Clinical signs (diarrhoea, body condition), faecal shedding of LI, and productivity were monitored periodically throughout the study. Both treatment groups were necropsied 23 days post-

infection (10 days after cessation of medication). PPE-specific gross and microscopic lesions were quantified and intestinal tissues were cultured at necropsy. Blinding measures were utilized.

The only lesions observed in any pigs by gross and microscopic examination were those of PPE. All pigs were free of *Brachyspira(Serpulina)* spp, *Salmonella* spp, and *E. coli* by culture, verifying the presence of an uncomplicated LI infection. The prevalence and severity of gross and microscopic PPE-specific lesions were significantly reduced in the TREATED group. Faecal shedding of LI was significantly reduced in the TREATED group. Clinical signs were significantly reduced in the TREATED group by the third day of medication and remained significantly reduced throughout the study. The rate and efficiency of weight gain of the TREATED group was significantly greater for the combined treatment and post-treatment periods.

Tiamulin has been reported to possess good *in-vitro* activity against LI(3) and to be effective in treating, controlling or preventing PPE in three separate pure culture LI challenge models(4-6), a field study with the naturally occurring disease(7), and in clinical use by swine practitioners(8-10).

Table 1. Effects of tiamulin against PPE 10 days after cessation of treatment

	CONTROL	TREATED	P value
% pigs with PPE gross lesions	58 %	12%	0.0002
% pigs with PPE microscopic lesions	92 %	21%	<0.00005
% pigs with fecal LI shedding D23	71 %	12%	<0.00005
Average daily weight gain (g), D8-23	510	641	0.007
Gain/Feed, D0-28	0.528	0.633	0.010

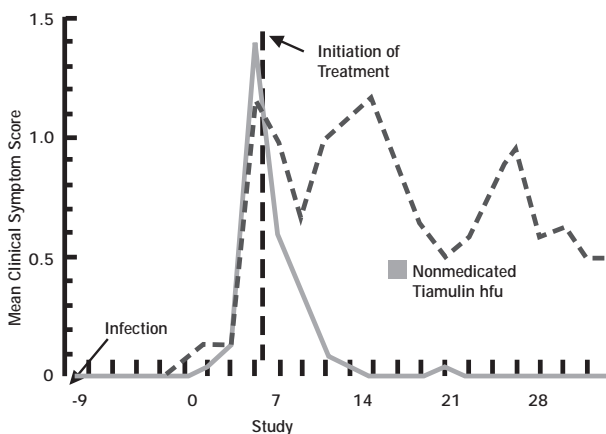


Figure 1. Mean daily clinical symptom scores by treatment group

This study demonstrates the ability of tiamulin in drinking water to treat and control the clinical, pathological, and negative productivity effects of PPE in pigs experiencing an outbreak.

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## E Performances of commingled segregated early weaning pigs in a testing system.

A. Broes, R. Boutin and R. Ethier.



## FOCUS

Performance of SEW pigs in a testing station, using, inter alia, tiamulin in drinking water – Canada.

## KEY FACTS

- 10 batches comprising approx. 4,000 pigs have been investigated.
- Pigs weaned between 10 & 16 days of age came from 20-30 herds of variable health status but were free from the clinical signs of significant diseases. Most of them were infected with *M.hyo* and PRRSV.
- On arrival they were allocated according to origin and weight and received (at label dosages)
  - 1 injection of ivermectin
  - 1 injection of ceftiofur or
  - 1 injection of oxytetracycline
  - 180ppm tiamulin in water for the 1st 4-5 days  
(in the last 5 batches vaccinations against *M.hyo* were given.)
- Feed medication in nursery diets.

Medication	Dosage	Day	Cost per pig
oxytetracycline	330ppm	1st 10 days	0.04\$ Can
carbadox	55ppm	days 11-17	0.04\$ Can
chlortetracycline	770ppm	days 18-38	0.38\$ Can
carbadox	55ppm	days 39-56	0.23\$ Can

## BENEFITS

- In nursery (7 week period) *E.coli* diarrhoea noted only sporadically
  - ADG 450g
  - FCR 1.54
  - Mortality 1.67%
- In grower/finisher section (av.91 days) (28.5-107kg) no antibiotics in food were used in any batches, few disease problems.
  - ADG 876g
  - FCR 2.57
  - Mortality 2.46%
- Rigorous SEW medication protocols including tiamulin in water, can permit commingling of pigs from numerous sources with few disease problems, excellent growth performance and minimal medication costs during the grow/finish phase.

*Routine use of Tiamutin® soluble or injectable is a valuable component of SEW protocols designed to reduce or eliminate enteric and respiratory infections associated with bacteria, spirochaetes and mycoplasmas.*

## PERFORMANCES OF COMMINGLED SEGREGATED EARLY WEANING PIGS IN A TESTING STATION.

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Since 1994, the Centre de développement du porc du Québec inc. (CDPQ) is operating a testing station as part of its genetic improvement programs. In the present paper we will summarize the growth and health performances of the first ten batches of pigs that were tested.

Testing facilities consist in a building with a nursery and a growing-finishing sections both with a capacity of about 400 pigs. The whole building is operated "all in, all out". Piglets originated from 20 to 30 herds. These herds had quite different health status, most of them being infected with several pathogens such as PRRSV or *M. hyopneumoniae* (*M. hyo*). The proportion of infected herds varied from batch to batch. However at the time when the piglets were chosen, the herds had to have been free of clinical signs of significant diseases in the breeding and nursery sections. Sows and nursing piglets received no additional treatment to those regularly chosen and applied by each producer.

Selected piglets (2 to 6 per litter, usually females and castrates) were weaned between 10 and 16 days of age. They were introduced into the nursery section within one or two days. On arrival they were allocated according to their origin and weight. They were injected once with Ivermectin (Ivomec®) and received one shot of Ceftiofur (Excenel®) or Oxytetracycline (Biomycine®). They were also medicated with 180 ppm Tiamulin (Denagard™) in the drinking water during the first 4 to 5 days. In the last 5 batches piglets were vaccinated against *M. hyo* (Respire® or Ingelvac *M. hyo*®). Nursery diets were supplemented with different antimicrobials. Several drug combinations and dosage were used. A typical feed medication protocol is described in Table 1. Curative treatments were administered by injection or

eventually through drinking water when required.

The nursery phase performances are presented in Table 2. Health problems varied from batch to batch. However, the most significant and consistent problems were related to infections with *Streptococcus suis* (meningitis, septicemia, arthritis) and/or *Haemophilus parasuis* (arthritis, polyserositis, bronchopneumonia). Exudative epidermatitis was observed in two batches. Systemic (septicemia, polyserositis) or digestive (diarrhoea) *Escherichia coli* infections were noted sporadically. One batch (7) experienced a significant problem of PRRS (fever, pneumonia). Although the morbidity and the mortality rates in this batch remained low, the growth performances were affected.

Piglets were transferred to the growing-finishing section usually after 7 weeks in the nursery. Only pigs required for the trial were transferred. These were randomly assigned within sex on the basis of weight blocks in a balanced design. The floor was fully slatted and about one m<sup>2</sup> was allocated per pig. The growing-finishing diets were pelleted and distributed ad libitum. No antimicrobials in the feed were used in any of the batches. Curative treatments were administered by injection or eventually through drinking water when required.

Table 1. Typical feed medication protocol used in the nursery phase

Drug	Dosage	Cost/pig
Oxytetracycline	330 ppm during the first 10 days	0,04\$
Carbadox	55 ppm during the next 7 days	0,04 \$
Chlortetracycline	770 ppm during the next 20 days	0,38 \$
Carbadox	55 ppm during the next 17 days	0,23\$

Table 2. Performances of the nursery and growing-finishing phases

	Nursery phase										Growing-finishing phase						
	Number of piglets	Age at start (days)	Weight at start (kg)	Age at transfer (days)	Weight at transfer (kg)	ADG (g)	FC	Mortality (%)	Preventive drug cost/pig	Curative drug cost/pig	Number of pigs	Age at slaughter	Weight at slaughter	ADG (g)	FC	Mortality (%)	Curative drug cost/pig
1	450	12,2	4,5	66,2	29,6	466	1,54	1,78	2,35\$	0,10\$	384	159,7	106,6	835	2,76	2,68	0,12\$
2	431	12,5	4,5	66,1	27,9	436	1,43	2,78	2,35\$	0,09\$	332	153,8	106,3	886	2,80	1,50	0,00\$
3	374	12,1	4,4	65,6	28,8	456	1,57	1,34	2,35\$	1,17\$	306	157,7	105,7	845	2,69	4,34	0,17\$
4	444	11,9	4,4	65,5	29,0	459	1,48	2,20	2,72\$	0,10\$	361	154,6	107,5	892	2,56	0,82	0,01\$
5	460	12,5	4,7	66,2	29,6	470	1,42	1,30	2,72\$	0,01\$	360	156,5	108,6	879	2,55	2,47	0,01\$
6	369	12,5	4,1	69,6	28,1	421	1,64	1,08	4,21\$	0,02\$	363	159,0	107,4	896	2,59	2,20	0,02\$
7	363	13,1	4,4	68,3	24,9	371	1,58	1,10	4,21\$	0,07\$	359	165,2	106,0	842	2,38	4,18	0,14\$
8	318	12,9	4,4	67,9	28,1	431	1,59	2,20	4,28\$	0,02\$	311	156,1	108,1	918	2,48	1,93	0,24\$
9	334	12,4	4,4	67,8	26,4	536	1,6	1,80	3,68\$	0,02\$	328	160,4	107,7	887	2,35	3,35	0,06\$
10	408	12,3	4,8	68,2	31,9	467	NA	0,98	3,68\$	1,56\$	386	NA	NA	NA	NA	2,07	0,50\$
av	395	12,4	4,5	67,0	28,5	450	1,54	1,67	3,18\$	0,32\$	349	158	107	876	2,57	2,46	0,13\$

Performances of the growing-finishing phase are presented in table 2. Few disease problems were encountered during this phase. Most of the batches demonstrated a self limiting episode of loose stools during the first month after the transfer. One batch (3) experienced higher mortalities which were essentially associated with *Streptococcus suis* endocarditis and/or gastric ulcer. Another batch (7) also demonstrated a high mortality rate several of which were due to acute deaths of undetermined origin. Leg weakness was observed in most of the batches, particularly those with purebred animals.

No evidence of *Sarcoptes scabiei* infections was observed at slaughter. Few if any lesions of hepatic milk spots (*Ascaris suum*) were noted. Respectively 2/10 and 6/10 batches were considered to be free of PRRSV or *M. hyo.* based on serology and/or slaughter check. Examinations for *Actinobacillus pleuropneumonia* (App) and toxigenic *Pasteurella multocida* (Pm) were conducted in 3 batches. Reactors against several App serotypes were observed using an ELISA assay in all them. However clinical signs of pleuropneumonia were not observed in any of the 10 batches and the rate of pleuritis remained quite low. No evidence of toxigenic Pm infection was found using an ELISA and/or a PCR assay in the same 3 batches. However in each of them several animals had nose score >3 using the PigMON scoring system. The *Salmonella* status of the last 3 batches was investigated by serology (ELISA). Two demonstrated low to moderate prevalence of reactors and the 3rd had no reactor. Finally, *Lawsonia intracellularis* infection was investigated in the last two batches using serology (IFAT). One batch demonstrated no reactor and the other had low prevalence of reactors.

Our results demonstrate that rigorous segregated early weaning protocols can allow commingling of pigs from numerous different sources with relatively few disease problems, excellent growth performances and minimal medication costs during the growing-finishing phase. Moreover, they demonstrate that such protocols may succeed, although not consistently, in producing animals free from important pathogens. We consider that the major key success factors consist in the absence of active infectious diseases in the source herds, a strict selection of piglets, the introduction of piglets within a short time period, the AI/AO management of the facilities, and a well adapted medication protocol in the nursery section.

## F(i) Eradication of *Mycoplasma hyopneumoniae* in two newly infected herds.

*K. Damgaard and others.*



## FOCUS

Eradication of acute *Mycoplasma hyopneumoniae* (*M.hyo*) infection in two recently infected SPF herds using oral tiamulin medication in feed/water.

## KEY FACTS

- 2 herds were used in the test.

Herd 1. Established in September '92. In Feb '93 clinical signs were seen and 8 out of 10 blood samples were positive for *M.hyo* antibodies. An eradication programme commenced in March '93.

Herd 2 Established in April '93 with infected and non-infected gilts. An acute outbreak of *M.hyo* infection occurred in animals 4-11 months of age and an eradication programme commenced in August '93.

- The eradication programme had 2 phases.

### Phase 1

In order to reduce the excretion of *M.hyo* all animals in herd 1 were medicated with tiamulin in feed at a dose of approx. 8mg/kg b.wt for 14 consecutive days and in herd 2 only gilts with signs of pneumonia were medicated with tiamulin in water at a dose of 8mg/kg b. wt/ day for 7 consecutive days.

### Phase 2

In both herds gilts between 4 & 11 months were divided over time into 2 groups. Animals over 10 months of age were totally separated from younger gilts in the cleaned and disinfected area.

In herd 1 young and older gilts were at the same unit but were kept in isolated rooms.

In herd 2 young gilts were located at a unit 500m distant from the older gilts.

### Medication

Herd 1 gilts > 10 months received tiamulin via feed at 8mg/thf/kg b.wt/day for 14 consecutive days.

Herd 2 gilts 7 days in water and for 7 days in feed at 8mg/thf/kg b.wt/day.

When the next group of gilts reached 10 months of age they were separated from the younger gilts, moved to another room and medicated with tiamulin (as above).

- Post-eradication monitoring involved clinical and serological testing monthly.

## BENEFITS

- Eradication of *M.hyo* has been very successful.

In herd 1 all blood samples for 7 years post-eradication have been negative for *M. hyo* antibodies.

In herd 2 all blood samples were negative for *M.hyo* antibodies for 2 years (prior to an *Actinobacillus pleuropneumoniae* breakdown and restocking)

- Eradication of *M.hyo* from acutely infected herds is feasible using tiamulin medication and age segregated gilt management.

*Tiamutin® is particularly convenient for control of M.hyo infections since it is available in injectable, water soluble and premix formulations.*

# ERADICATION OF MYCOPLASMA HYOPNEUMONIAE IN TWO NEWLY INFECTED HERDS

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1 Danvet K/S, 2 Danish Bacon and Meat Council, 3 Practitioner, 7950 Erslev, 4 Leo Animal Health, 5 Novartis Animal Health

## INTRODUCTION

In Denmark it has been possible for approx. 7 years to eradicate *Mycoplasma hyopneumoniae* in chronically infected herds using without restocking. (Zimmermann et al, Bækbo et al, 1994)(1, 2). The method was based on the assumption that spreading of disease by *M. hyopneumoniae* in chronically infected farrowing to finishing units mainly takes place between younger pigs after weaning and to a smaller extent from older immune breeding animals to progeny. It is furthermore believed to be easier to eliminate *M. hyopneumoniae* from older animals than from younger animals by treatment with antimicrobials. Therefore the general strategy was: Removing young animals less than 10 months old from the *M. hyopneumoniae* infected units, and then oral medication of the remaining breeding animals over 10 months old with antimicrobial. In the Danish breeding system SPF gilts are sold for at a better price than gilts with *Mycoplasma hyopneumoniae* infection. In already established breeding SPF herds reinfection means economical losses. Unfortunately some breeding herds get reinfected during establishment, because the herd, which supplies the gilts, gets reinfected. Depopulation and restocking is expensive and will not preserve valuable genetic material. The Zimmermann model therefore is of great interest in Denmark. This paper presents two clinical trials, where a modified *M. hyopneumoniae* eradication programme has been carried out in two acutely infected herds. Both herds were newly established SPF breeding herds, and they were both reinfected through by gilts from the same breeding SPF herd which had been infected with *M. hyopneumoniae* just before the gilts were sold.

## MATERIALS AND METHODS

**Herd 1:** Was established in September 1992 with 180 gilts. In November 1992 gilts from the acutely infected breeding herd were introduced. In February clinical symptoms were observed and 8 out of 10 blood samples showed antibodies against *M. hyopneumoniae*. The number of gilts with clinical symptoms increased over the next month. On 1.March clinical symptoms were declining, and the eradication programme was started. The age of the animals varied from 4 to 11 months. **Herd 2:** Unit was established with approx. 360 gilts in April 1993 with infected and non-infected gilts from the same breeding SPF herd previously infected with *M. hyopneumoniae* and the breeding herd infected

with *Mycoplasma* 5 months earlier. After introduction mingling of infected and non-infected gilts an acute outbreak of *Mycoplasma hyopneumoniae* took place. In August 1993 the eradication programme was started. The age of the animals varied from 4 to 11 months.

The diagnosis in both herds was confirmed on the basis of clinical symptoms and serological tests. The test used was a highly sensitive and specific monoclonal blocking ELISA (Sørensen et al3).

The eradication programme was carried out in two phases.

**Phase 1:** As acute pneumonia occurred among the gilts in both herds it was necessary first to reduce the excretion of *M. hyopneumoniae* from the acutely infected gilts, and therefore all animals in herd 1 were treated orally with Tiamutin® in the feed at a dosage of approx. 8 mg/kg body weight/day for 14 days, and in herd 2 only gilts with signs of enzootic pneumonia were treated with tiamulin in the water (8 mg/kg body weight) for 7 days.

**Phase 2:** In both herds gilts between 4 and 11 months were gradually divided into two groups. Animals over 10 months were totally separated from younger gilts in the cleaned and disinfected area during the following 3-4 months. In herd 1 both young and old gilts stayed at the same unit but were kept in isolated different rooms. In herd 2 the young gilts were located at a separate unit 500 m away from the old gilts. In herd 1 gilts older than 10 months were treated for 14 days with tiamulin via feed at a dosage of 8 mg/kg body weight/day. In herd 2 gilts were treated for 14 days with tiamulin, in the first 7 days in the water and then for 7 days in the feed with the same dosage. This process was repeated stepwise. When the next group of younger gilts reached the age of approx. 10 months they were again separated from the younger gilts and moved to another room and treated with tiamulin for 14 days as described above. The eradication programme was finished after 3-4 months when all remaining gilts had reached approx. 10 months and were treated with tiamulin for 14 days. Additionally in herd 1 in this transition period the piglets born were treated on day 2 and day 10 after birth with tiamulin (10 mg/kg body weight i.m.) In this period internal barriers between medicated older gilts and younger non-medicated gilts were established to avoid transmission of *M. hyopneumoniae* infection from the youngest gilts to the older medicated animals.

In Herd 1 all 180 gilts were kept on the same location during the eradication programme. Gilts less than 10 months were kept in barn A. 40 gilts more than 10 months were kept in barn B. All the gilts in both barn A and B were treated with Tiamutin Premix 2% for 14 days in a doses of 8 mg/kg bodyweight. After 10 days of treatment all gilts in barn B were moved to the farrowinghouse (D). Treatment was continued here for the next 4 days. Farrowing started two days before treatment was finished. Four weeks later another 40 gilts more than 10 months old were moved to barn B and treated for 14 days with Tiamutin Premix 2%. Afterwards they were moved to the farrowinghouse (D). The next day the first born piglets were weaned to the weaning accommodation beside the farrowinghouse and barn B. Approximately four weeks later another 40 gilts more than 10 months old were moved to barn B and treated for 14 days with Tiamutin Premix 2%. Afterwards they were moved to the farrowinghouse (D). Another 4 weeks later the last group of gilts were treated with Tiamutin Premix. They were all older than 10 months. They stayed in barn A during treatment. Afterwards they were moved to the farrowinghouse (D) or the pregnant sows house (E). All piglets born during the eradication period were injected with Tiamutin inj. 0,1 ml/piglet at day 3 and 0,2-0,3 ml/piglet at 3 weeks of age. Barn B was cleaned and disinfected between every group of gilts. As soon as barn A was emptied, growers were moved from the weaning accommodation to barn B.

Barn A was cleaned and disinfected, before introduction of gilts born during the eradication period and 20 SPF gilts from another breeding herd. Careful instructions were given to be sure that no *Mycoplasma* was brought from the non eradicated area to the SPF area. Three sites of entrance were established during the eradication period. Persons were not allowed to go from the non-medicated part to the medicated part to the non medicated part.

They had to be very careful during feeding because the two parts were connected through the mill.

In Herd 2 180 gilts and 25 pregnant sows were placed on farm 1. All gilts more than 8 months old and the sows stayed on farm 1. Younger gilts were moved to farm 2, located 500 meter away. On farm 1 all gilts were treated with Tiamutin sol. 12.5%, in a dose of 120 ppm for 7 days. For the next 7 days they were treated with Tiamutin Premix 2% in a dose of 6 mg/kg bodyweight. Immediately after treatment the first farrowing took place. The gilts on farm 2 were divided in to three groups. As the gilts were more than 9.5 months old, they were treated with Tiamutin Premix 2% in a doses of 6 mg/kg bodyweight for 7 days. Then they were moved to farm 2. They were kept isolated and were treated with Tiamutin premix for another 7 days before introduction to the older gilts and sows.

After the eradication programme monitoring of both herds was carried out with clinical testing and serological testing, both herds were clinically tested

every month by the veterinarians from the Danish Slaughter House. Furthermore 20 blood samples every month were tested at the Danish Slaughter House Laboratory in Roskilde. Young pigs and newly introduced SPF gilts were blood tested for antibodies to *M. hyopneumoniae*.

## RESULTS

The eradication has been very successful. Both herds have achieved their SPF declaration again after 1 year of blood testing. In Herd 1 all blood samples for the last seven years have been free of *Mycoplasma hyopneumoniae* antibodies. In Herd 2 all blood samples were negative for *M. hyopneumoniae* in the period of 2 years (Table 1). Later on Herd 2 was infected with *Actinobacillus pleuropneumoniae* and restocked.

Table 1. Serological (ELISA) monitoring of the 2 herds after eradication programme for *M. hyopneumoniae* infection was carried out

	Post eradication period (years)	Antibody to <i>M. hyopneumoniae</i> No. of examined pigs Positive/negative
Herd 1	7	0/1680
Herd 2	2	0/480

## DISCUSSION

It has been shown, that it is possible to eradicate *M. hyopneumoniae* from acutely infected herds. Medical treatment of all animals in the acute phase was important to reduce the excretion of *M. hyopneumoniae* (Phase 1). Later on by stepwise and strictly isolating the younger gilts from older gilts over 10 months (Phase 2), it was possible to eliminate *M. hyopneumoniae* from the herds, even though the animals were located at the same farm.

In Herd 1 there was close contact between older medicated animals older than 10 months and non-medicated younger animals, only separated by a wall between rooms. We presume that the eradication was successful because all animals were acutely infected and immunised at the same time. Furthermore they were all treated for a longer period at the beginning of the eradication program. After treatment clinical symptoms were almost absent and thereby the amount of *Mycoplasma* spread through the air was reduced. It is important that both pig producers were highly professional and motivated. The Producer has to be very careful in his daily work and has to avoid any direct and indirect contact between older and younger animals.

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## FOCUS

Eradication of acute *M.hypopneumoniae* (*M.hyo*) infection from a 2 site 390 sow herd with Tiamutin® premix and avoidance of restocking.

## KEY FACTS

- The herd involved was a recently restocked 2 site multiplying herd. At the time of infection site I consisted of 390 young sows, (av. wt. 180kg) 527 sucking piglets and no weaners.
- There was continuous production in the farrowing and dry sow housing but the nurseries were built for AI/AO production.
- At site II there was continuous production and gilts and finishers were raised in a 1000 head facility.
- All animals were acutely infected and coughing and the diagnosis of *M.hyo* infection was confirmed by clinical, serological (ELISA) and post mortem investigations.
- The rationale of the eradication scheme was to prevent infection of piglets by sows and to prevent infection of pigs on site I by those from site II.
- To ensure colostral excretion of antibodies against *M.hyo* all sows were vaccinated twice with 2ml "Stellamune" Mycoplasma – 1 x one week pre-medication and, once in the middle of the medication period.

### Medication and vaccination programme

Week 1 All pigs vaccinated with Stellamune Mycoplasma.

Week 2. Breeding stock remained at site I. Sows expected to farrow in week 3, all sows with sucking piglets and all weaners were transferred to site II. Then farm separated into 2 sections  
site I – Tiamutin medicated  
site II - no medication.

Breeding stock medicated with Tiamutin premix 2% to deliver 6mg tiamulin h.f./kg b.wt/day for 21 consecutive days. Nurseries were cleaned and disinfected.

Week 3. All pigs on sites I and II were vaccinated with Stellamune Mycoplasma.

Week 4. The first farrowings occurred at site I.

Week 5. The 21 day period of Tiamutin premix medication ended.

Week 11. Site II was emptied, cleaned and disinfected.

Week 14 The first growers were moved from site I to the cleaned and disinfected site II.

## BENEFITS

- The validity of the Swiss method for the eradication of *M.hyo* (Zimmerman, W. and others 1989) was corroborated.
- During the post-eradication period the investigations on the progeny revealed no evidence of *M.hyo* infection:-

	No.of tests	No +ive
ELISA blood tests	210	0/210
Autopsies	4	0/4
Slaughter	20	0/20

- The Tiamutin medicated herd regained its Danish S.P.F. (specific pathogen-free) status since *M.hyo* had been successfully eliminated.

*Tiamutin® injectable reaches high concentrations in lung tissue and is valuable against acute Actinobacillus pleuropneumoniae infections, in addition to M.hyo infections.*

# ERADICATION OF *MYCOPLASMA HYOPNEUMONIAE* FROM AN ACUTELY INFECTED DANISH 2-SITE 390 SOW HERD WITHOUT RESTOCKING

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## INTRODUCTION

Swiss veterinarians (4) have documented a method for eradication of *M. hyopneumoniae* without restocking. The method requires adequate medication during a farrowing free period and all animals to be at least 10 months of age. This method has been well implemented in Norway and Denmark (1,2). The method implies that the herd is chronically infected by the start of the eradication, which means that excretion of *M. hyopneumoniae* is on a low level. In this eradication attempt a farrowing free period of five weeks was initiated five weeks after outbreak of *M. hyopneumoniae* infection, while all animals were still coughing.

## MATERIALS AND METHODS

The herd was a recently restocked 2-site multiplying herd, the two sites being 49 meters apart. At the time of infection Site I consisted of 390 young sows weighing 180 kg in average, 527 suckling piglets and yet no weaners. There was continuous production in the farrowing and dry sow housing, whereas the nurseries were built for a weekly all in/all out production. No younger animals ever had to pass directly by older animals at Site I. Site II, where the gilts and finishers were raised in a 1000 head facility, had a continuous production too. By the time the herd was infected by *M. hyopneumoniae* Site II was empty. The diagnosis was confirmed by clinical, serological (ELISA) and post mortem investigations.

## RISK ASSESSMENT

In this case not only young animals excreted *M. hyopneumoniae* but also sows, because all animals were acutely infected and coughing. Sows expected to farrow during the medication period, all sows with suckling piglets and all weaners were transferred to Site II before medication. The focus of this eradication was to prevent that sows infected piglets and to prevent that infected pigs in Site II reinfected Site I. Hence the pigs were sold by the age of 10 weeks. To reduce the risk of sows shedding *M. hyopneumoniae* after the farrowing free period medication was extended from the usual two to three weeks. To ensure that all sows excreted antibodies against *M. hyopneumoniae* in colostrum, it was decided that all sows should be vaccinated twice with 2 ml Stellamune® Mycoplasma. The first vaccination was done one week before medication was initiated. Because of lack of time the second vaccination

therefore was done in the middle of the medication period. The youngest gilts for the nucleus (30 – 100 kg) were raised at Site I, separated from older animals. They were isolated in one room during the medication period and the following four months.

## MEDICATION AND VACCINATION

**Week 1:** All animals vaccinated with Stellamune® Mycoplasma.

**Week 2:** The breeding stock was left at Site I. Sows expected to farrow in Week 3, all sows with suckling piglets and all weaners were transferred to Site II. After that the farm was separated in two: Site I, which was tiamulin treated and Site II which was not treated. The breeding stock was treated with 57 gram Tiamutin® Premix 2% per sow per day corresponding to tiamulin 6 mg/kg body weight/day for 21 days. Nurseries were cleaned and disinfected.

**Week 3:** All animals on both Site I and II were revaccinated with Stellamune® Mycoplasma.

**Week 4:** The first sows were farrowing at Site I.

**Week 5:** Three weeks of Tiamutin® medication ended.

**Week 11:** Site II was emptied, cleaned and disinfected.

**Week 14:** The first growers were moved from site I to the cleaned and disinfected Site II.

## RESULTS

As appears in Table 1 during the observation period 7 x 20 ELISA blood test from sentinels at Site II and 7 x 10 from sentinels at Site I (altogether 210) were examined for antibodies against *Mycoplasma hyopneumoniae*. All negative. Also four finishers weighing 35 - 70 kg had been autopsied during the observational period. At the end of the period 20 finishers were examined at the abattoir. None of these 4 + 20 animals showed any signs of infection with *M. hyopneumoniae*.

Table 1: Extent of conducted examinations in offspring for *M. hyopneumoniae*.

	Extent	Pos / Neg
ELISA blood tests	210	0 / 210
Autopsies	4	0 / 4
Slaughter controls	20	0 / 20

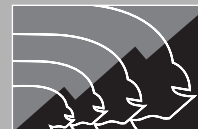
## DISCUSSION

The ELISA method used has a negative predictive value on a herd level of 99 – 100 % provided 20 blood tests (3). Provided 30 blood tests, it is higher. With the described extent of serial blood testing it is very much unlikely that an infection with *Mycoplasma hyopneumoniae* is overlooked. According to the Danish SPF demands the herd regained its SPF status.

When even this eradication strategy, conducted under acute course of infection could be successful, it corroborates the assumption that the Swiss method is very safe.

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## FOCUS

Pulse dosing regime with in-feed tiamulin®/chlortetracycline combination in finishers affected with mycoplasmal pneumonia.

## KEY FACTS

- A commercial 3 site production system in the mid west of the USA, which had experienced reduced performance in finishers 8-12 weeks post-placement into finishing units, was used.
- 1,092 single source pigs (av. wt. 29.0kg) from a commercial 3 site system were individually identified, blocked by weight into 42 pens and randomly allocated into 3 treatment groups for the 16 week study.
- Medication
  - Treatment 1.**  
Continuous in-feed medication.  
i)38.5ppm tiamulin h.f & "Aureomycin" CTC 22mg/kg b.wt  
Pulse dosed: weeks 2, 4, 7, 10 and 13.  
**PLUS**  
ii)110ppm CTC in feed during weeks 3, 5/6, 8/9, 11-12
  - Treatment 2**  
Pulse. Identical to treatment 1 without additional CTC (110ppm) between pulse doses of tiamulin/CTC.
  - Treatment 3**  
No medication.
- Pigs were weighed and feed consumption recorded bi-weekly. Two pigs from each pen were serially bled bi-weekly and tested for antibodies to selected pig pathogens – PRRS virus, swine influenza virus and *M.hyo*.

## BENEFITS

- There were statistically significant differences between treatments 1 / 2 and 3 in average daily gain, feed intake, feed conversion efficiency and mortality. There were no significant differences between the two medicated groups.
- 14% of pigs tested were seropositive to *M.hyo* at the start of the study. In treatment 1 a significant rise in titre to *M.hyo* occurred at 16 weeks, when continuous medication had been withdrawn. However in treatments 2 & 3 this rise occurred at week 12.
- The titre responses suggest that the pigs in treatment group 3 (no medication) and treatment group 2 (pulse medication) received adequate natural exposure to *M.hyo* during the non medicated period(s) to generate an active immune response.
- Treatment group 1 (continuous medication) pigs received an inadequate exposure to *M.hyo* which proved insufficient to stimulate an immune response until the continuous medication was withdrawn.
- The results in treatment group 1 suggested that continuous in-feed medication may prevent the stimulation of an active immunity against mycoplasmal pneumonia, leaving pigs immunologically naïve and potentially susceptible to subsequent re-exposure to *M.hyo* on withdrawal of medication.
- In this study "pulse dosing" with tiamulin/CTC premix protected growth performance in finishers whilst permitting the development of an active immune response against *M.hyo* which could provide long term protection.

*The tia/CTC premix combination provides synergistic action against bacterial/mycoplasmal respiratory pathogens.*

# METAPHYLACTIC ANTIMICROBIAL STRATEGY IN FINISHING PIGS WITH NATURALLY OCCURRING MYCOPLASMA PNEUMONIA

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## INTRODUCTION

The effectiveness of tiamulin or the tetracycline derivatives for the control of porcine bacterial and mycoplasmal pneumonia is markedly enhanced when the two antibiotics are given concurrently, an effect commonly referred to as “synergy”(1). Non-traditional medication strategies such as pulse dosing with this combination of antibiotics have been shown to be effective for controlling a variety pig diseases(2,3). Pulse dosing is the practice of providing a limited number of short-term medication “pulses” at therapeutic doses separated by non-medicated intervals. A fundamental hypothesis of pulse dosing is that intermittent therapeutic antimicrobial medication may allow natural exposure to endemic pathogens while abbreviating the infection incubation process before a clinical disease outbreak and the associated biologic and economic costs are incurred. Acquired active immunity may be stimulated which could provide long-term protection once the short-term protection of medication is discontinued.

A commercial three-site pork production system in the Midwest had been experiencing reduced performance 8-12 weeks post-placement into finishing units due at least in part to infectious respiratory disease. This study was conducted to determine a) if feed medication could reduce the commonly observed decrease in performance in mid-late finishing; b) if there are differences in the effectiveness of pulse versus continuous feed medication; and c) if exposure to infectious agents may be associated with the reduced performance in this herd.

## MATERIALS AND METHODS

The research barn was a tunnel-ventilated finishing facility with natural ventilation capability containing forty-four pens on totally slatted floors. The barn was managed in an all-in, all-out manner and was one of ten barns on a continuous flow finishing site. One thousand ninety two (1092) single-source barrows averaging 29 kg body weight from a commercial three-site system were individually weighed and identified, blocked by weight into 42 pens, and randomly allotted to one of 3 treatment groups for the 16 week trial. Treatment 1 (“Continuous”) was Denagard™ (tiamulin hydrogen fumarate-thf) 38.5 ppm plus Aureomycin™ granular (chlortetracycline-CTC) 22 mg/kg body weight pulse-dosed in feed on weeks 2, 4, 7, 10 and 13. One hundred ten (110) ppm CTC was provided in feed during weeks in between pulse-doses (no medication weeks 1 and 14-

16). Treatment 2 (“Pulse”) was identical to treatment 1 without CTC in between pulse doses. Treatment 3 (“Controls”) received no feed medication. Pigs were weighed and feed consumption was recorded bi-weekly. Two pigs from each pen were serially bled biweekly and tested for antibodies to selected pig pathogens.

## RESULTS AND DISCUSSION

There were significant differences in body weight ( $P < .0001$ ), feed intake ( $P = .004$ ), and feed conversion efficiency ( $P = .02$ ) between the control group and the two medicated groups. There were no significant differences between the medicated groups. Both medicated groups had significantly lower mortality rates than the control group ( $P = < .001$ ). There was no significant difference in mortality rate between the medicated groups.

Pigs were seronegative to PRRS at the initiation of the study and seroconverted by week 4. There was also a significant rise in measured antibody titers against swine influenza virus at week 12. As expected there were no differences in seroconversion to viral pathogens detected between treatments since antibiotics do not affect viruses. Fourteen (14) percent of the pigs tested were seropositive to *M. hyopneumoniae* at the initiation of the study. A significant rise in *M. hyopneumoniae* titers occurred beginning at 12 weeks in both treatment groups 2 and 3, and at 16 weeks for treatment group 1.

The performance parameters from the two medicated groups were averaged and then compared to the control group for economic analysis, consistent with the statistical results. Economic advantages were due to greater weight gain and reduced mortality which more than offset the cost of medication under most feed cost and market hog price scenarios. As an example, the use of feed medication was projected to be profitable when finishing feed costs were \$0.132/kg and market hog prices were >US\$0.48/kg liveweight. If market hog prices were US\$1.00/kg liveweight the projected additional profit per pig space was US\$3.91 compared to controls.

There were significant differences between treatment groups in serologic response to *M. hyopneumoniae*. Adequate exposure for detectable changes in serologic response occurred between weeks 8-12 for treatments 2 and 3, but was delayed in treatment 1 until weeks 14-16 when continuous medication had been withdrawn.

This suggests that the pigs on no medication or pulse medication received adequate natural exposure to *M. hyopneumoniae* during the nonmedicated period(s) to generate an active immune response. The continuously medicated group received inadequate *M. hyopneumoniae* exposure to stimulate an immune response until the continuous medication was withdrawn late in the study (weeks 14-16). Continuous medication may prevent stimulation of active immunity against mycoplasmal pneumonia leaving animals immunologically naïve and potentially susceptible to subsequent re-exposure to *M. hyopneumoniae* when medication is withdrawn. Continuous feed antibiotic medication has also been shown to decrease the prevalence of seroconversion to *Lawsonia intracellularis* in experimentally infected pigs(4). Pulse dosing protected growth performance similar to continuous medication while permitting an active immune response which may potentially provide long-term protection against endemic disease.

Table 1: Performance of finishing pigs with natural disease exposure on pulse versus continuous feed medication

	1 (Continuous)	2 (Pulse)	3 (Control)
Start weight, kg	28.65	28.64	28.66
End weight, kg	116.3 a	116.0 a	112.8 b
Average daily gain, g	772 a	767 a	704 b
Average daily feed intake, kg	2.26 a	2.25 a	2.15 b
Feed/Gain	2.94 a	2.93 a	3.05 b
Mortality, %	0.55 a	1.92 a	5.22 b

$P \leq 0.05$

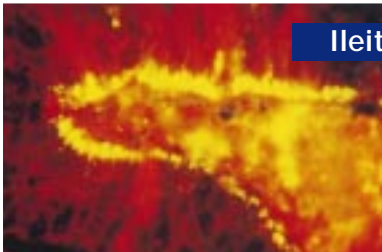
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## NOTES

# tiamutin®

the productivity protector...

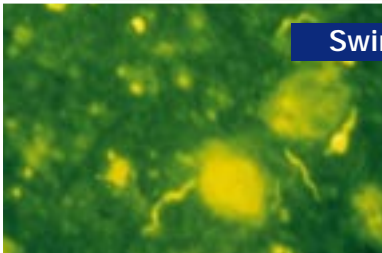


## Ileitis

Tiamulin premix (38.5ppm) controls the clinical and pathological effects of P.E. when given both prior to infection\* and when clinical signs are present\*\*.

\*SCHWARTZ, K., et al. (1999) *Swine Health & Production*. 7. 1, p5-11

\*\*WALTER, D. H., et al. (2000) *Proc. 31st Ann. Mtg Amer. Ass. Swine Pract., Indianapolis, USA*. p215-217



## Swine dysentery

Tiamulin controls strains of *B. hyodysenteriae* which are tylosin and lincomycin-resistant.

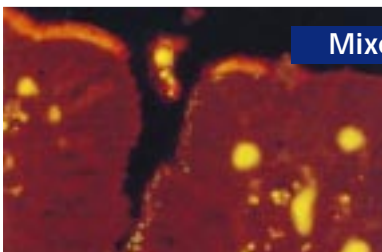
AITKEN, I. A., et al. (1999) *Veterinary Record*. 144.



## Spirochaetal colitis

Tiamulin is >200x more active in-vitro against *B. pilosicoli* than tylosin and 94x more active than lincomycin.

OXBERRY, S. L. & HAMPSON, D. J. (1998) *Proc. 15th IPVS Congress, Birmingham, England*. p132



## Mixed spirochaetal/ileitis infections

Combined *B. pilosicoli* and ileitis infection can be successfully treated with tiamulin premix.

MØLLER, K., et al. (1998) *Proc. 15th IPVS Congress, Birmingham, England*. p139



*Tiamutin is a pleuromutilin antibiotic developed expressly for use in animals. It is not chemically related to human use antibiotics and does not share patterns of cross-resistance with them.*

**a prudent choice**

...effectively combats all these key enteric diseases