CONTROLLING ILEITIS IN THE 'COLITIS' COMPLEX

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Summary

In this paper, the author takes a wide-ranging look at Proliferative Enteropathy (P.E.), covering in detail all salient aspects of this important, wide-spread disease. Its clinical manifestations and economic implications are fully recorded and extensive references made to the many trials into the use and efficacy of the various drugs currently employed in the control of this condition.

Introduction

Since the breakthrough in the identification, culturing in cells of *Lawsonia intracellularis* and reproduction of the disease by McOrist *et al* (1993), understanding of Proliferative Enteropathy (PE) or ileitis and its treatment has made major leaps forward. The proliferative lesions of ileitis are usually associated with the terminal ileum and may continue along into the caecum and colon. In severe cases, they may extend up to the jejunum. The disease primarily occurs in 6-16 week old grower pigs (20-50kgs) and the morbidity in the herd may be about 30%. Several national surveys have shown the prevalence of the disease to be about 30-40%. The disease causes a number of sub-clinical and clinical signs such as a depression or unevenness in growth rate, poor feed conversion efficiency and greyish coloured diarrhoea. The acute form Proliferative Haemorrhagic Enteropathy (PHE) or 'bloody gut' usually occurs in older pigs 60kgs and above.

At the farm level this is not the whole story, as other infectious diseases frequently compound the situation and may play a role in the development and severity of the 'grey diarrhoea' commonly encountered in growing pigs. Thomson *et al* (1998) described the incidence of potential pathogens found while investigating cases of 'colitis' or non-specific grey diarrhoea in growing pigs on 85 farms in Scotland. A number of bacteria were identified either by isolation or by histopathology. Fifty-four % of the cases were attributed to a single infection, 39% were due to mixed infections and 7% no pathogens could be found.

Brachyspira (Serpulina) pilosicoli was the most commonly identified (Table 1) followed by *Yersinia pseudotuberculosis*, then *L. intracellularis*, Salmonella, *B. hyodysenteriae* and atypical Brachyspira. *Escherichia coli* and *Clostridium perfringens* were occasionally recovered.

Table 1 – Causes of colitis and their incidence

Organism	**Single**	**Mixed**	**Total**	**%**
B. Pilosicoli	21	23	44	39
Atypical Brachyspira	7	2	9	8
B. hyodysenteriae	6	3	9	8
L. intracellularis	3	10	13	12
Salmonella	4	8	12	11
Y. pseudotuberculosis	4	13	17	15
E. coli	1	5	6	5
C. perfringens	0	2	2	2

The many different organisms, alone and in combination, make it difficult to diagnose clinically without good laboratory support.

The spirochaetal infections Brachyspira (Serpulina) accounted for 55% of the isolations, Lawsonia 12% and the others 33%.

Gresham *et al* (1998) described the difficulty of treating mixed infections of resistant *B. hyodysenteriae* and *S. typhimurium* as an extreme example.

Thomson *et al* (1998) observed that mixed infections tend to increase the severity of lesions associated with just single infections and this was particularly noticeable with *Y. pseudotuberculosis, S. typhimurium and B. hyodysenteriae.*

The selection of medication or combination of antimicrobials, is very important to control a potential mixture of pathogens, to achieve the best results. Ileitis is only a single but important component of this ‘colitis’ complex.

Antimicrobial activity

If the antimicrobial activity of various products is examined, it can be seen some can treat more than one infection and possibly even a combination approach may be more likely to give a more favourable response, depending on the organisms isolated. (Tables 2, 3, and 4).

McOrist *et al* (1995,1998*) reported on the activity of a large number of antimicrobials against *L. intracellularis* using a cell culture to propagate the organism. There were two approaches: to look at the extracellular minimal inhibitory concentration (MIC) where the bacteria were introduced to a cell culture bathed in antibiotic, or the intracellular method where an infected cell culture was treated with different concentrations of antibiotic and the MIC was the level that stopped bacterial growth (Table 2)

Table 2 - Antimicrobial activity against *L. intracellularis*

Antimicrobial	Minimum Inhibitory Concentration (Intracellular) (mcg/ml)
Tylosin	64
Tilmicosin	2
Tiamulin	4
Valnemulin*	2
Lincomycin	32
Spectinomycin	32
Apramycin	>128
Neomycin	>128
Chlortetracycline	1
Penicillin G	1
Amoxycillin	1
Ceftiofur	>8
Enrofloxacin	8

The intracellular MIC in most cases was equal or lower than the extracellular MIC, which was surprising, as the antibiotic has to penetrate into the cell, rather than just kill the bacteria in the antibiotic solution. In fact, the intracellular MIC is probably more representative of the situation that occurs when an animal is treated and would relate to the concentrations required of an antimicrobial to be achieved in the gut.

The sensitivity patterns of other bacteria found in the colitis complex are described below. (*B. hyodysenteriae* and *B. pilosicoli*, Moller *et al* 1996; *C.*

perfringens, Dutta and Devriese, 1980; Devriese *et al*, 1993; *E. coli* and Salmonella, Laperle *et al*, 1996; *Y. enterocolitica*, Fossler *et al*, 1996) (Tables 3 and 4).

Table 3 - Antimicrobial sensitivity of *B. hyodysenteriae, B. pilosicoli* and *C. Perfringens*

Antimicrobial	***B. hyodysenteriae* Range MIC (mcg/ml)**	***B. pilosicoli* Range MIC (mcg/ml)**	***C. perfringens* Range MIC (mcg/ml)**
Tylosin	128 - >128	2.0 - >128	<0.12 – 0.25
Tiamulin	0.125 – 1.0	0.0156 – 0.0625	0.25 – 4.0
Valnemulin	0.0156 – 1.0	0.0156	-
Lincomycin	64 - >128	0.5 – 128	0.12 - >128
Tetracycline	-	-	0.06 – 64
Penicillin	-	-	0.06 – 1.0

Table 4 - Antimicrobial sensitivity of *E. coli, Salmonella* and *Y. enterocolitica*

Antimicrobial	***E. coli* Sensitive (%)**	**Salmonella Sensitive (%)**	***Y. enterocolitica* Sensitive (%)**
Ampicillin	53	94	1
Apramycin	90	100	100
Cephalosporin	47	100	100
Enrofloxacin	99	94	100
Neomycin	53	89	100
Spectinomycin	31	56	0-99
Tetracycline	14	50	37-50
Trimethoprim/Sulpha	72	72	100

Antimicrobials tend to divide into two distinct groups, those that treat spirochaetal infections and those that treat *E. coli.* It is interesting that Lawsonia appears to be somewhere in between and can be treated by both groups. Some antimicrobials also have resistance problems such as tylosin against *B. hyodysenteriae* and tetracyclines against *E. coli*, so it is important to take these factors into account as part of the decision making process for medication selection.

Pharmacokinetics

The alimentary tract is a very dynamic organ. If the passage of an antimicrobial along its length is considered, either in food or water, it is diluted, attacked by acid, neutralized by bile and attacked by enzymes and bacteria.

Products may be absorbed, metabolized and re-excreted back into the intestine in a neutral or still microbiologically active form. Some products stay in the gut and, after the initial dilution, are then concentrated as they pass down and as nutrients and water are drawn out. An antimicrobial in feed is approximately diluted four-fold by the time it gets into the ileum and, if not absorbed or broken down, is concentrated in the faeces 2.5 times, the so-called 'curry effect.' One kg of food produces 0.4 kg of faeces (Burch, unpublished information).

For example, an inert antimicrobial, which started in the feed at 100ppm, would go down to 25ppm in the small intestine, then concentrate to 250 ppm in the faeces. If a product were 90% absorbed, the concentration would fall to 2.5ppm and concentrate to 25ppm in the faeces. It is very useful to know the approximate concentration of a substance at the site of infection to predict the likely efficacy; although several other factors can come into play. De Geeter *et al* (1980) described the concentrations of Lincomycin in various parts of the pig's intestine. Other information can sometimes be found in product literature or assessment reports on the EMEA web site (Anon, product information*; MRL assessment report**).

Table 5 - Relative absorption or gut levels of various antibiotics

Antimicrobial	**Approximate Absorption**	**Ileal Concentration (mcg/g)**	**Colon Concentration (mcg/g)**
Lincomycin 110ppm Lincomycin 220ppm	Moderate (50%)	48 25	35 101
Tiamulin 110ppm Tiamulin 220ppm	High (>90%)	- -	2.8* 8
Valnemulin 75ppm Valnemulin 200ppm	High (>90%)	- -	1.7* 5.2
Tylosin 100ppm	Low (<20%)	-	50(E)**
Chlortetracycline	Low (<20%)	-	-
Spectinomycin	Low (<10%)	-	-
Apramycin	Low (<10%)	-	-
Neomycin	Low (<10%)	-	-

Determining antimicrobial levels in the gut is quite difficult, especially using microbiological methods. Abstraction or recovery from intestinal contents can be very variable, giving wide variations in results (De Geeter *et al* 1980). Therefore, figures give an indication only; but can give some guidance to likely break points when estimating microbial sensitivity.

Ileitis treatment trials

Most of the trial data can be divided into artificial challenge studies, where either cell cultures (McOrist's model) or ground up mucosa from the small intestine is used. In many of the American studies, the latter is preferred and high doses of corticosteroid are given at the time of infection as a 'stressor'. This often results in a high level of disease with very severe and extensive lesions that can induce a high mortality (over 50%) in the untreated controls (Winkelman, 1999). This may be considered over severe in comparison with the natural infection seen in grower pigs and gives medications a very severe test also. The McOrist model gives a more typical representation of the disease.

Growth rate and feed conversion efficiency (FCE) are the main parameters measured. Clinical signs may be recorded and diarrhoea scored. At autopsy, the presence of lesions is recorded and, more recently, their extent measured. Histology confirms the presence of the lesion and the organism with silver staining (Warthin-Starry method) the most common. Polymerase Chain Reaction (PCR) techniques have also been applied to identify the presence of *L. intracellularis*.

Soluble products

1. *Tylosin Tartrate*

McOrist *et al* (1998a) described a challenge study (8-9 pigs/group) where the pigs were infected and, when clinical signs started to develop (14 days post infection (PI)), they were treated with tylosin at 0, 2.5, and 10mg/kg bodyweight (BW) for seven days. They were observed for a further seven days and then autopsied at about four weeks PI.

Table 6 - Treatment of ileitis - artificial challenge (AC)

Treatment Group	No. Pigs Gross Lesions (%)	Gross Lesion Score (0-5)	Affected Ileal Area (%)
Uninfected Control	0	0	0
Tylosin 0mg/kg	78	3.1	54
Tylosin 2.5 mg/kg	55	1.6	26
Tylosin 5 mg/kg	11	0.05	1.1
Tylosin 10mg/kg	11	0.05	1.1

There was a very good dose titration affect with 5mg/kg BW and above treating the disease very well.

In a further AC study, Pauling *et al* (1999) administered tylosin at 83ppm in water (8.7mg/kg BW) to pigs that had been infected with ground up mucosa. Clinical signs of diarrhoea developed in about 10% of the pigs 10 days PI and they were medicated for 7 days and then necropsied. There were 36 pigs per treatment group.

Table 7 - Treatment of ileitis – AC

Treatment Group	**ADG (g) Day –1 - 17**	**FCE Day –1 - 17**	**Ave. Affected / Pen (%)**	**Histological Ileal Lesions (%)**
Uninfected Control	332	1.65	3	0
Untreated Control	77	4.48	36	71
Tylosin 8.7mg/kg	151	2.34	11	28

There was a very good clinical response to treatment, with diarrhoea stopping in three days.

2. *Tiamulin*

The first description of tiamulin's use was by Jennings (1980) where he described the successful treatment for ileitis with Tiamulin in the drinking water at 60ppm, the standard level for the treatment of swine dysentery, followed up by tylosin and sulphadimidine at 100ppm in the feed.

Joens *et al* (1996) reported on a challenge using a cell culture of *L. intracellularis*. Tiamulin was given at 180ppm in the drinking water for 5 days immediately after challenge followed by tiamulin at 38.5 ppm in the feed. Initially, there was almost no diarrhoea for 10 days in the Tiamulin treated group, whereas in the infected group they were starting to break down with diarrhoea. In the following two weeks, the disease developed fully in the controls and the Tiamulin treated pigs' level of diarrhoea also increased. Tiamulin at 180 ppm in water was very effective in controlling ileitis; but did not totally eliminate the infection, and tiamulin at 38.5ppm did not fully prevent the disease clinically.

Table 8 - Prevention and control of ileitis – AC

Treatment Group	Mortality (%)	ADG (g)	Ave. Daily Diarrhoea Score (0-3)	No. Pigs Gross Lesions Small Int. (%)
Untreated Control	33	34	1.43	9/12 (75)
Tiamulin 180ppm Water, 38.5ppm Feed	17	96	0.34	4/12 (33)

This was a very severe challenge with a high mortality; although no other infectious agents were identified. The pigs were treated with cimetidine prior to infection.

A field infection study (Tsinas *et al* 1998) was carried out on a farm with a history of the disease. Tiamulin was given in the drinking water at 60ppm for 3 days at weaning at 21 days of age followed by feed medication at 35ppm from day 25-140 and the pigs were sent for slaughter on day 161. Eight pigs from each treatment group were then randomly selected and autopsied.

Table 9 - Prevention and control of ileitis – field infection

Treatment Group	Mortality (%) Day 21-161	ADG (g) Day 21-161	FCE Day 21-161	Diarrhoea Score Ave.	Lesions (%) Day 161
Untreated Control	20.8	573	2.94	2.81	7/8 (88)
Tiamulin 60ppm Water, 35ppm In Feed	10.4	725	2.53	1.59	1/8 (13)

There was quite a high disease level on this farm; but tiamulin given in water at 60ppm followed in feed at 35ppm appeared to control ileitis very well.

3. *Lincomycin/Spectinomycin (L/S)*

As a combination this is of interest as both substances have reported activity against *L. intracellularis* and the MICs are the same at 32mcg/kg. Which component is more active is debatable; but the broad spectrum of activity provided by the two products could be of value for 'colitis' control. Winkelman *et al* (1998), using an artificial infection model of ground up mucosa followed by injections of prednisolone, tested L/S for the treatment of ileitis. Medication was started seven days after infection at 10mg/kg BW (ratio 1L:2S) in the drinking water for 21 days and neomycin was administered at

22mg/kg BW for 14 days. No autopsy or lesion details were provided. There were 25 pigs in the treated groups

Table 10 - Treatment of ileitis – AC

Treatment Group	**ADG (g) Day 1 - 35**	**FCE Day 1 - 35**
Uninfected Control	980	2.14
Unmedicated Control	460	3.73
Lincomycin/Spectinomycin 10mg/kg BW	960	2.01
Neomycin 22mg/kg BW	800	2.43

L/S was reported to have a good treatment effect and certainly improved the performance of the pigs to the level of the uninfected controls. At least one mortality occurred in each treatment group, thought to be due to an *E. coli* infection. Neomycin was partially effective by comparison.

McOrist *et al* (2000) recently reported on the results of six field trials involving over 800 pigs carried out in Europe with L/S soluble administered at 10mg/kg BW in the drinking water (21ppm L and 42ppm S) for the treatment of ileitis. Farms with a history of ileitis were chosen and *L. intracellularis* was confirmed by a specific PCR assay. The pens were allocated to one of three treatment groups, untreated, L/S at 10mg/kg for seven days or for 14 days and followed through until 21 days.

Table 11 - Treatment of ileitis – field trials

Treatment Group	**ADG (g) Days 0-14**	**Pigs with Normal Faeces**		
		Day 0	Day 7	Day 14
Untreated Control	540	44.3	38.2	44.1
L/S 10mg/kg 7Days	650	51.6	76.6	63.4
L/S 10mg/kg 14Days	680	51.5	70.2	73.8

Both treatments gave significant improvements in growth rate and diarrhoea control; although there was no significant difference between the treated groups. Numerically the 14-day medication was better.

Water administration does have some advantages over feed medication in that there is usually a quicker response. However, in-feed medication still remains very popular and convenient for the farmer, especially for prophylaxis of potentially susceptible animals on farms with a history of the disease.

In-feed medication

1. *Tylosin*

Tylosin 100ppm or chlortetracycline 300ppm have been the traditional treatments in practice for ileitis or when there was an upsurge in 'bloody gut' or PHE on a farm. Since the discovery and culture of *L. intracellularis*, much more work has been carried out on tylosin, culminating in its registration in the EU and US for ileitis.

McOrist *et al* (1997) described an artificial infection study using his cell-culture model. One group was used for treatment with tylosin 100ppm in feed 7 days after challenge for 21 days. Two groups were used for prevention and were medicated four days before infection with tylosin at 100ppm or 40ppm for a further 16 days. This was then reduced to 40ppm and 20ppm tylosin respectively for 12 days until the trial finished and the pigs were autopsied.

Table 12 - Treatment and prevention of ileitis – AC study

Treatment Group	ADG (g)	FCE	Pigs Diarrhoea (%)	Pigs Gross Lesions (%)	Ave. Histological Lesion (%)
Uninfected Control	275	1.49	0	0	0
Untreated Control	250	1.60	38	63	50
Tylosin100ppm 7-28 Days	304	1.41	0	0	0
Tylosin 100/40ppm	300	1.47	0	0	0
Tylosin 40/20ppm	279	1.49	0	0	0

From this study, tylosin 100ppm for 21 days proved very effective in the treatment of ileitis and low levels down to 40/20ppm prevented the development of lesions. This is very interesting as these levels were the former growth promoting levels and highlight the medicinal benefits derived from some growth promoters in the past.

Field trials examining tylosin at 100ppm for the prevention and control of ileitis were reported on by Moore and Zimmerman (1996). Seven trials were carried out; but only four were used for evaluation as gross lesions were identified in the controls at slaughter. From epidemiological surveys on each farm, they could predict when clinical outbreaks were likely to occur and

medication with tylosin was introduced 5-7 days before and continued for 21 days. At the end of the 21-day medication period, all the unmedicated control pigs were necropsied to establish the presence of lesions and *L. intracellularis*.

Table 13 - Prevention and control of ileitis – field trials

Treatment Group	**ADG (g) Day 0 - 21**	**FCE Day 0 - 21**
Untreated Controls	823	2.911
Tylosin 100ppm	1008 (22%)	2.648 (- 9%)

There were significant improvements in performance and clinical parameters; but no information on lesions in the treated group was reported. It was concluded that tylosin at 100ppmis was effective in the prevention and control of ileitis.

2. Chlortetracycline (CTC)

In an artificial infection study, McOrist and Morgan (1998) reported on the use of chlortetracycline at 300 and 600ppm in comparison with tylosin at 100ppm in the prevention of ileitis. Pigs were put onto medication 4 days prior to infection and treated for a further 21 days PI.

Table 14 - Prevention of ileitis – AC study

Treatment Groups	**ADG (g)**	**FCE**	**Gross Lesions (%)**	**Incidence of Diarrhoea (%)**
Uninfected Control	290	1.52	0	0
Unmedicated Control	240	1.83	100	57
Tylosin 100ppm 21 Days	280	1.5	0	0
CTC 300ppm 21 Days	440	1.39	0	0
CTC 600ppm 21Days	450	1.47	0	0

Chlortetracycline at 300 and 600ppm was completely effective in preventing the development of lesions and was comparable with tylosin 100ppm the positive control. In growth terms, there was a marked improvement with CTC.

Winkelman (1998) described an artificial infection study using his model of ground up mucosa with 125 pigs. CTC was administered at 22mg/kg

BW (approx.440ppm) in feed from 4 days before infection and continued for 14 days (prevention); CTC was then given at 110ppm until the end of the study at day 35. The second group was given CTC at 110ppm from 4 days before infection until day 35. The third group was treated with 22mg/kg BW for 14 days when clinical signs appeared and this was followed up with CTC 110ppm until day 35. At the end, the pigs were autopsied and the intestinal lesions measured and scored. Apparently there were no significant differences between the CTC treatment groups, so unfortunately their figures were combined and averaged.

Table 15 - Treatment and prevention of ileitis – AC study

Treatment Group	ADG (g)	FCE	Gross Lesions (%)	Histological Lesions +ve (%)
Untreated Control	310	3.04	36	45
CTC Combined Groups 110 – 440ppm	490	2.23	7	24

Insufficient results were presented; but it would appear that CTC is improving the performance of pigs and reducing the effects of the disease.

3. *Lincomycin*

Winkelman *et al* (1998) compared Lincomycin at 220ppm with CTC at 550ppm as a positive control in an artificial infection study using ground up mucosa and high levels of corticosteroid as a 'stressor.' Treatment was started 7 days after infection and continued for 21 days.

Table 16 - Treatment of ileitis – AC study

Treatment Group	ADG (g) Day 0 – 28	FCE Day 0 - 28
Uninfected Control	980	2.14
Untreated Control	460	3.73
Lincomycin 220ppm	990	2.02
CTC 550ppm	1000	1.95

Lincomycin was reported as being an effective treatment of ileitis; although no lesion data was provided. From the performance results, they were better than the infected and uninfected controls and approaching those of the positive control CTC 550ppm.

In a further study, Winkelman *et al* (1998a), using his artificial infection model, looked at Lincomycin at 22, 44, and 110ppm in comparison with tylosin at 110ppm for the prevention of ileitis. The pigs were put onto treatment 4 days

before infection and medication continued for 35 days. In an additional paper, Winkelman (1999) described the same trial but included the lesion scores.

Table 17 - Prevention of ileitis – AC study

Treatment Group	Mortality (%)	ADG (g)	FCE	Lesion Length (cms)	Lesions in Ileum (%)
Untreated Control	52	95	5.55	160	84
Lincomycin 22ppm	20	182	2.85	-	-
Lincomycin 44ppm	4	232	2.56	84	72
Lincomycin 110ppm	8	241	2.38	79	60
Tylosin 110ppm	16	168	3.13	109	76

All lincomycin levels had a marked impact on mortality and performance, with Lincomycin 110ppm giving the best overall results. Forty-four ppm also appeared to be similarly effective. Lincomycin 22ppm had similar results to tylosin 110ppm. This was a particularly severe test of any medication as the model induced a 52 *per cent* mortality in the controls. Lesions were very extensive, even in the treated groups.

4. *Tiamulin*

McOrist *et al* (1996), in one of the first artificial challenge studies, tested tiamulin at 50ppm for the prevention of ileitis, given 2 days before infection and, for a further 21 days PI, tiamulin at 150ppm was given 7 days PI for the treatment of ileitis and for another 14 days. At autopsy, the intestines were examined grossly and histologically for lesions.

Table 18 - Treatment and prevention of ileitis – AC study

Treatment Group	ADG (g)	Gross Lesions (%)	Microscopic Lesions (%)	Lesion Score (%)
Uninfected Control	314	0	0	0
Untreated Control	248	86	100	42
Tiamulin 50ppm	362	0	0	0
Tiamulin 150ppm	295	0	0	0

In this milder, more representative model, tiamulin 50ppm was completely effective in preventing lesions and tiamulin at 150ppm was effective at treating the disease.

Moller *et al* (1998) described the treatment of a mixed field infection of ileitis and *B. pilosicoli* (BP) with tiamulin at 150ppm in the feed for 21 days, in comparison with an untreated control. At the end of the trial, 39/124 pigs were autopsied and the intestines examined for lesions, cultured for *B. pilosicoli* and tested by PCR for *L. intracellularis.*

Table 19 - Treatment of ileitis and colitis – field trial

Treatment Group	ADG (g)	FCE	Ave. Diarrhoea Score (0-3)	LI Detection (%)	BP Detection (%)
Untreated Control	445	2.23	0.14	49	36
Tiamulin 150ppm	585	1.91	0.03	3	5

This study confirmed that tiamulin at 150ppm was very effective in treating ileitis and colitis caused by BP; although it did not completely eliminate the organisms involved.

Schwartz *et al* (1998), in the US, carried out an artificial infection study, using cell cultures containing *L. intracellularis*. They tested tiamulin at 55 and 38.5ppm in the prevention of ileitis. The pigs were treated 7 days before infection and for an additional 28 days PI when they were autopsied.

Table 20 - Prevention of ileitis – AC study

Treatment Group	Mortality (%)	ADG (g)	FCE	Ileitis Lesions (%)	Micro Lesions (%)	Diarrhoea Score
Uninfected Control	0	581	2.08	0	0	3.1
Untreated Control	13	499	2.13	63	88	28.9
Tiamulin 38.5ppm	0	640	1.96	0	25	0
Tiamulin 55ppm	0	622	1.99	0	25	0.4

Both tiamulin treatment levels prevented the development of lesions to a greater extent as well as improved performance; demonstrating, in a more representative challenge model, that even at 38.5ppm tiamulin prevented ileitis.

Kyriakis *et al* (1994), in a field study on a farm with a history of PE, tested tiamulin at 100ppm for seven days in weaner pigs 23 days of age. This was followed by 50ppm for another week (to day 38) and then 30ppm to day 130. The pigs were slaughtered on day 155.

Table 21 - Prevention and control of ileitis – field trial

Treatment Group	Mortality (%)	ADG (g)	FCE	IS + ve at Slaughter (%)
Untreated Control	18	568	2.926	94
Tiamulin 100ppm 50ppm, 30ppm	7	778	2.565	6

Tiamulin appears to have had a very marked effect on performance and reduced the incidence of ileitis well, thus providing a good preventive effect under adverse field conditions.

Walter *et al* (2000) tested tiamulin at 38.5 ppm for the treatment of ileitis in a cell-culture model infection. Pigs were infected and then, 9 days later when clinical signs were developing, they were put onto the tiamulin medication for 28 days and then autopsied.

Table 22 - Treatment and control of ileitis – AC study

Treatment Group	ADG (g)	FCE	PE Lesions (%)	LI Shedding Day 28
Untreated Control	409	1.85	37.5	17.4
Tiamulin 38.5 Days 0-28	528	1.59	8.7	0

This low level prolonged (21 days) application of tiamulin at 38.5 ppm appeared to have a treatment effect on the lesions of PE and prevented shedding of LI.

5. *Valnemulin*

Valnemulin, a recently introduced pleuromutilin, was tested for its activity against ileitis by McOrist *et al* (1998), using his cell-culture model. A dose-titration study was carried out, looking at 25, 37.5, 50ppm valnemulin for prevention and 75 and 125ppm valnemulin for treatment. For prevention, the pigs were put on medication 2 days before infection and, for treatment, they received medicated feed 7 days PI until the end of the study at 21 days PI.

Table 23 - Treatment and prevention of ileitis – second AC study

Treatment Group	ADG (g)	FCE	Gross Lesions (%)	Micro Lesions (%)
Untreated Control	271	1.54	0	0
Uninfected Control	195	2.00	71	100
Valnemulin 25ppm	286	1.47	29	46
Valnemulin 37.5ppm	257	1.52	20	22
Valnemulin 50ppm	262	1.56	0	9
Valnemulin 75ppm	248	1.58	0	0
Valnemulin 125ppm	267	1.50	0	0

There was a very good preventive dose-titration effect with regard to lesion scores for 25-50ppm valnemulin. Both treatment levels completely eliminated the infection and 75ppm and above proved to be an effective treatment. This is the first major study with valnemulin and further trial work is underway. Field experience for the treatment and control of a mixed infection of Lawsonia and *B. pilosicoli*, where tylosin was reported to have failed, (Evans, personal communication), was very positive.

Table 24 - Summary of trials

Solubles

Product	Treatment of Ileitis Dose Rate	Conc. In Drinking Water (ppm)
Tylosin	5 - 10 mg/kg BW for 7 days	85
Tiamulin	6 - 18 mg/kg BW for 5 Days	60 – 180
Lincomycin/ Spectinomycin	10 mg/kg BW for 7-14 Days	63

Feed Premixes

Product	Treatment of Ileitis (ppm)	Prevention of Ileitis (ppm)
Tylosin	100 –110	40 – 110
Chlortetracycline	300 - 600	100 – 300
Lincomycin	220	44 – 110
Tiamulin	38.5 – 150	30 – 50
Valnemulin	75 – 125	25 – 50

Conclusions

Much trial work has been carried out over recent years to prove new and existing products for the treatment and prevention of ileitis, primarily for regulatory purposes. If this is related to the 'colitis' complex of mixed infections, the best treatment for ileitis is only one component and the other conditions need to be examined before the veterinarian selects the optimum product, or combination of products, to resolve the problem diagnosed on the farm. Table 25 should help in that decision.

Table 25 - Selecting products for the control of the colitis complex

Antimicrobial	**Ileitis**	***B. hyo.***	***B. pil.***	***C. perf.***	***E. coli***	**Salm.**	***Yersi-nia***
Tylosin	Good	Poor	Mod.	Good	Poor	Poor	Poor
Lincomycin	Good	Mod.	Good	Good	Poor	Poor	Poor
Tiamulin	Good	Good	Good	Good	Poor	Poor	Poor
Valnemulin	Good	Good	Good	Good	Poor	Poor	Poor
Chlortetracycline	Good	Poor	Poor	Poor	Poor	Mod.	Mod.
Spectinomycin	Good	Poor	Poor	Poor	Mod.	Mod.	Mod.
Apramycin	Poor	Poor	Poor	Poor	Good	Good	Good
Neomycin	Mod.	Poor	Poor	Poor	Good	Good	Good
Trimethoprim/S	Poor	Poor	Poor	Mod.	Good	Good	Good
Amoxycillin	Poor	Poor	Poor	Good	Mod.	Good	Mod.
Penicillin	Poor	Poor	Poor	Good	Poor	Poor	Poor

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