Ileitis (porcine proliferative enteropathy) – treatment and control

David Burch, Veterinarian, Octagon Services Ltd, Old Windsor, Berkshire, UK

Ileitis or porcine proliferative enteropathy, to give it its full name, is a proliferative disease affecting the terminal part of the small intestine called the ileum. The disease is caused by an infective bacterial agent, *Lawsonia intracellularis*, which has adapted itself to live inside the epithelial cells in the crypts lining the small intestine (see Photo 1) but may also colonise the caecum and proximal large intestine or colon. The bacteria are transmitted by the faecal-oral route and once swallowed and passed into the small intestine, penetrate the cells lining the gut in a couple of hours, where they multiply and then can spread down to the ileum, which is their main predilection site. The bacteria are micro-aerophilic (i.e. don't like too much oxygen) hence the ileum is the ideal site for colonisation. The disease is widely spread throughout the world and in some countries, like the UK, 95% of farms are sero-positive (Mortimer and others, 2000).

Photo 1. Infected crypts containing silver-stained *L. intracellularis* in the cell lining

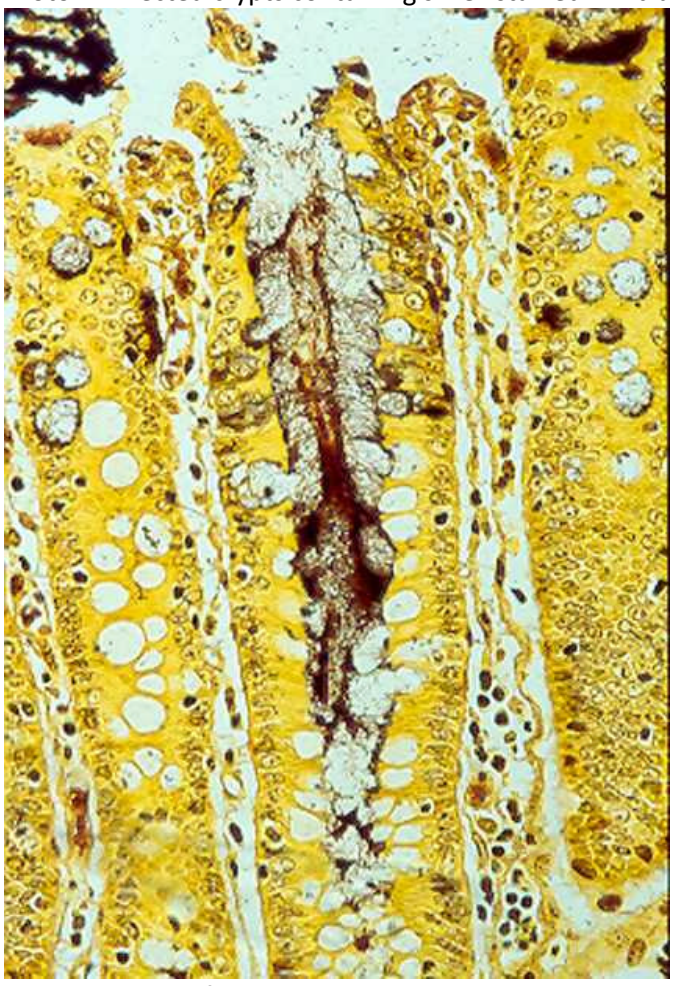


Photo courtesy of Jill Thomson

Once in the cells the bacteria cause proliferation of the cells, or thickening of the ileal wall. This thickening of the wall (so called 'hosepipe gut') (see Photo 2) can cause reduced absorption of nutrients in the intestine and hence its major economic effect on reducing growth rate and feed conversion efficiency. Commonly, this can also lead to diarrhoea, the most obvious clinical sign. In severe cases, it may lead to ulceration of the epithelial surface and colonisation by other bacteria and results in regional ileitis or even necrotic enteritis, especially if salmonellae are involved. In per-

acute cases, there can be a massive haemorrhage into the gut (proliferative haemorrhagic enteropathy or 'bloody gut') and commonly large pigs over 60kgs are found dead in the finishing shed. The carcases are very pale due to the haemorrhage and occasionally live pigs can be treated, especially by injection. The severity of the disease is dependent on the immune status of the pig, whether it has maternally derived antibodies (MDAs) or not, or it has started to develop its own immunity and the weight of infectious challenge (see Figure 1).

Photo 2. Progressive thickening of the intestinal wall as the disease progresses down to the ileum causing thickening and folds in the mucosa

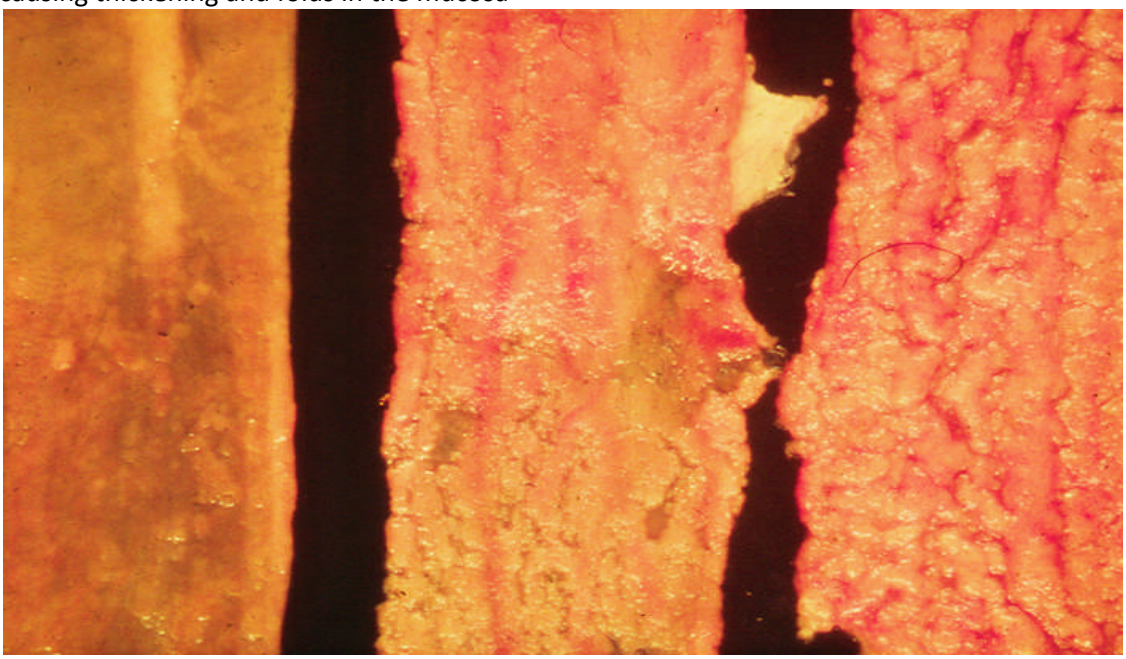
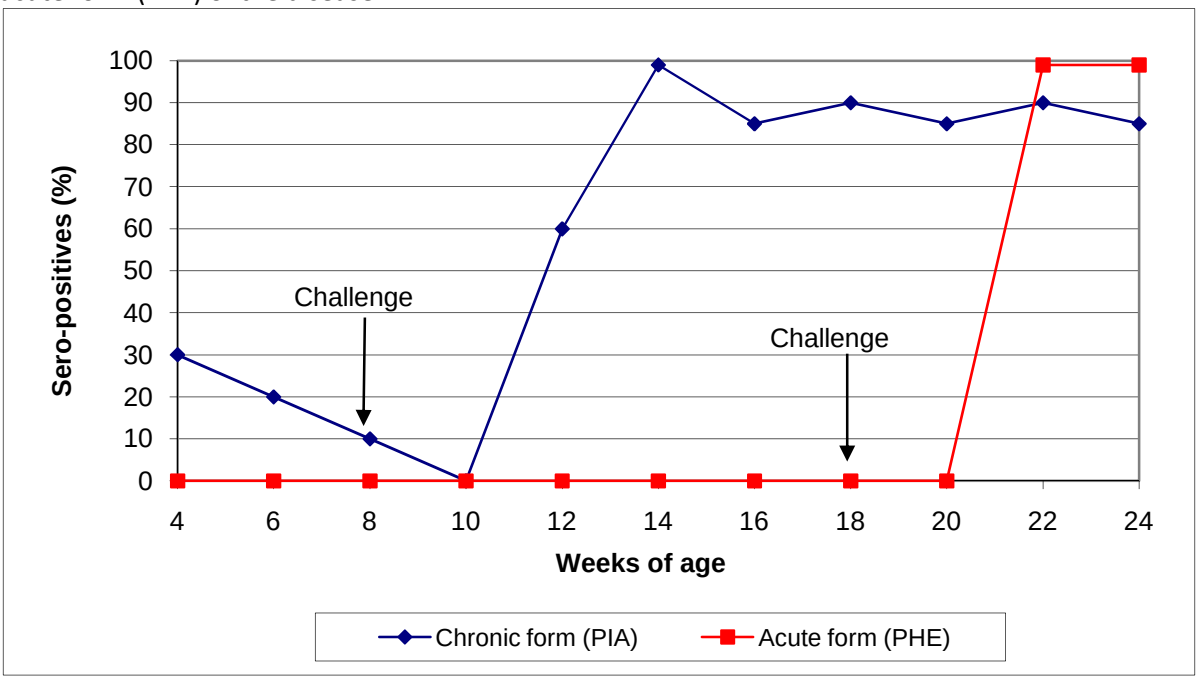


Figure 1. Comparison of *Lawsonia intracellularis* antibodies in growing pigs in the chronic (PIA) and acute form (PHE) of the disease



Maternally derived antibodies in the milk appear to be protective to suckling piglets and circulating MDAs in weaned pigs also appears to offer some protection. Generally, hygiene is also good in flat-

deck weaner accommodation and nurseries, but infection and increased exposure builds up during this stage. Lesions and clinical signs can be induced usually within 7-21 days following artificial infection and then the pig develops its own immunity over the subsequent 3 weeks, which gives it complete protection and the lesions start to regress on their own. The organism is shed during this period via the faeces so they remain infectious to other pigs but also the organisms can be detected mainly by PCR (polymerase chain reaction) test. Post-mortem examination and histology on the ileum (see Photo 1) using Warthin-Starry (silver) stain are confirmatory of the disease and the severity that is present. In artificial infections studies, severe lesions can extend up the ileum for over a metre in length and in very severe cases mortality can be induced.

In an overview of 17 artificial infection and field trials, interesting comparative data on uninfected controls, untreated infected controls and treated pigs can be analysed to demonstrate the effects of the disease and response to treatments with antibiotics.

Table 1. Comparison of the results from 17 treatment of ileitis studies including artificial infection and field results

Parameter	No of trials First group	Infected untreated control	Uninfected control	Treated
ADG (g)	8	304	503 (+65%)	512 (+68%)
FCE	8	2.79	1.79 (-36%)	1.82 (-35%)
Mortality (%)	1	13	0 (-13)	0 (-13)
	Second group			
ADG (g)	9	422	-	570 (+35%)
FCE	7	3.06	-	2.26 (-26%)
Mortality (%)	4	31.0		10.6 (-20.4)

In the artificial infection studies with the uninfected controls the effects the disease can have, are quite considerable with the pigs having a 65% better average daily gain (ADG) than the infected pigs and having improved feed conversion efficiency (FCE) of 36%. There was mortality in one trial in the infected untreated controls and this did not occur in the uninfected controls or in the treated groups. Importantly, the treated groups' results were similar to the uninfected controls, demonstrating the efficacy of most treatments, whether in feed or drinking water. In more field infections where there were no uninfected controls and the duration of trial was sometimes longer, treatment still improved ADG on average by 35% and FCE by 26%. Mortality was substantially reduced by two thirds in those studies, where there was mortality.

In a way, it is surprising how severe the disease can be in badly affected farms. In general, it is considered much less severe on most farms but during the acute phase, when pigs are being challenged, it explains why productivity can be so seriously affected if untreated.

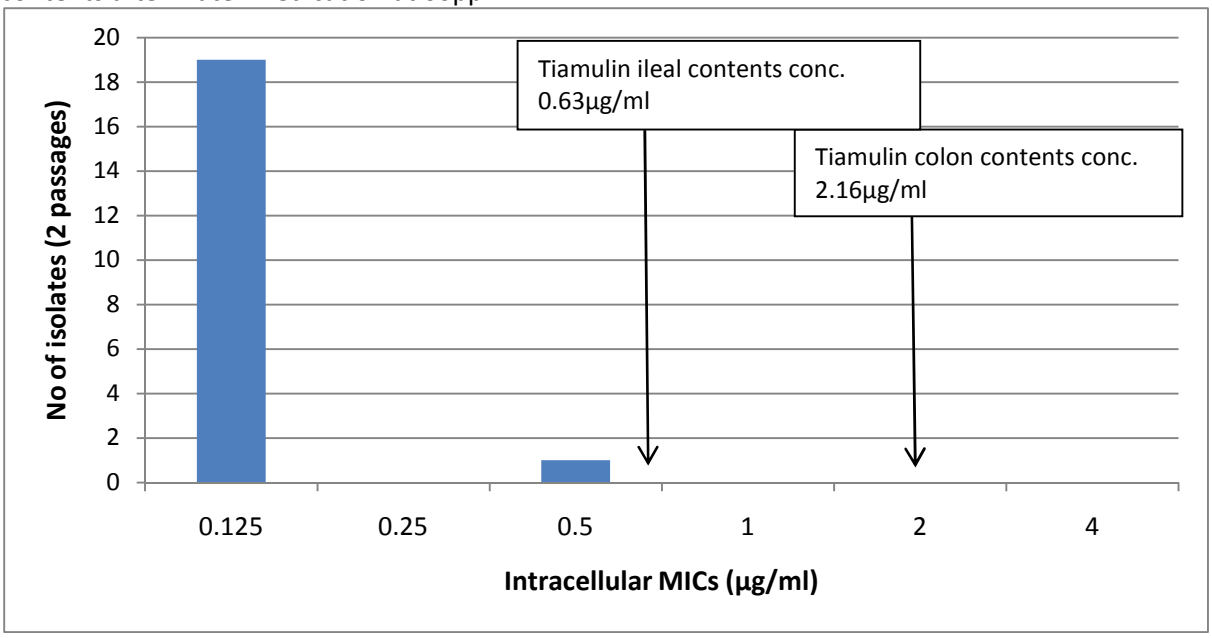
Vaccination of 3 week old piglets and above with a live vaccine has proven very effective in giving protection from 3 weeks post-vaccination in some countries, like the US, but in Europe uptake has been comparatively low. This begs a number of questions: - is antibiotic medication more commonly given at weaning in the feed or drinking water in the EU, is it difficult to administer the vaccine in the drinking water, or is it just more convenient to medicate via the feed? On some farms there are mixed infections with *Brachyspira* species, *E. coli* etc and therefore it is more common to use antimicrobial medications or combinations to control the problems.

The major approach to treatment and control has been the use of antimicrobial drugs. There is limited data regarding the susceptibility of *L. intracellularis* to antibiotics, because of the need to

grow the organism in cell cultures and testing to determine intracellular minimum inhibitory concentrations (MICS) is very complex and laborious in comparison with say *E. coli*. Recent data was developed using 10 isolates (US - 6 and EU - 4) (Wattanaphansak et al, 2009), which has given a better insight into which antibiotics are effective against *L. intracellularis*.

There is much interest in determining clinical breakpoints for the use of antibiotics, so that they may be used more effectively and responsibly. Much of my own work is towards that end. I look at the concentration of the drug achieved in the target tissues, in this case the ileum and colon contents and compare these with the MICs of the bacteria that I am interested in. With regard to *L. intracellularis*, I utilise the ileal contents concentration of an antibiotic and the intracellular MIC as I find this gives the best predictive results. This is called pharmacokinetic (drug concentration in the tissue) pharmacodynamic (MIC of the drug against the bug) integration. An example is the intracellular MICs of tiamulin against *L. intracellularis* and the ileal contents concentration (see Figure 2).

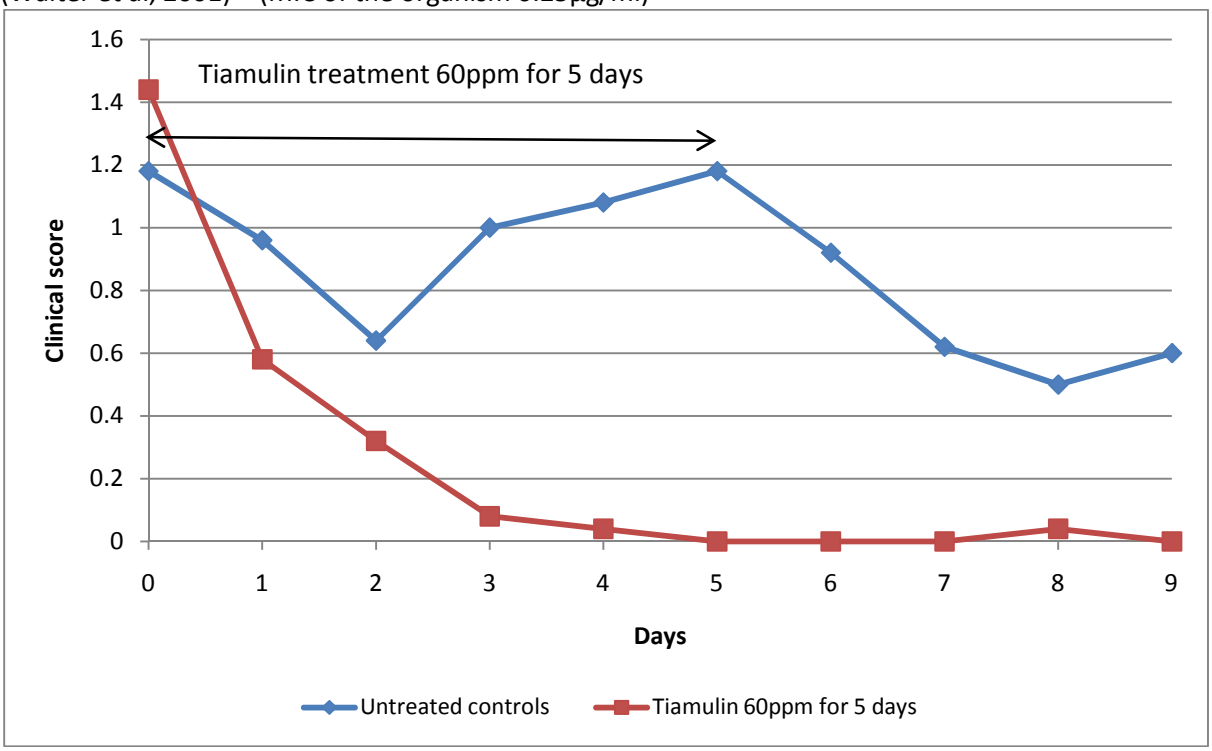
Figure 2. Susceptibility patterns for tiamulin against *L. intracellularis* and drug concentrations in gut contents after water medication at 60ppm



Treatment can be administered by injection for speed, water medication will also give a rapid response (see Figure 3) or by feed and usually a good response can be achieved.

In-feed medication can be given preventively at lower doses and inclusion levels to inhibit the development of the disease but allow for immunity to develop. However, care must be taken that sufficient levels are used to ensure efficacy. Metaphylactic medication (high level treatment) is also commonly employed to treat the animals on arrival in a finishing shed to clear up any sub-clinical infection. If the pigs have already been exposed and have started to build up immunity then there should be a good control from future infectious challenges. If they are immunologically naive on arrival then it is possible for the infection to develop later and may cause the per-acute, sudden death form.

Figure 3. Clinical response to tiamulin in the drinking water against an artificial ileitis challenge (Walter et al, 2001) – (MIC of the organism 0.25µg/ml)



Although *L. intracellularis* is widespread throughout the world, it is only in certain situations that disease is expressed. This is primarily due to immunity and the degree of challenge, which is also dependent on floor type, hygiene and pig-flow management. In the UK the use of solid floor systems and straw facilitate the spread of the infection and on serology 95% of the herds are infected but a much lower proportion express major disease problems. Fortunately there is a reliable vaccine and sufficient medications to control the disease and eradication, although very difficult, can be achieved.

References:

Mortimer, L., Green, L. and Hodge, A. (2000) Serological prevalence of Lawsonia intracellularis across UK and Irish pig herds. Proceedings of the 16th International Pig Veterinary Society, Melbourne, Australia, p 110.

Walter, D., Knittel, J., Schwarz, K., Kroll, J. and Roof, M. (2001) Treatment and control of porcine proliferative enteropathy using different tiamulin delivery methods. Journal of Swine health and production, 9, 3, 109-115.

Wattanaphansak, S., Singer, R.S. and Gebhart, C.J. (2009) In vitro antimicrobial activity against 10 North American and European *Lawsonia intracellularis* isolates. Veterinary Microbiology, 134, 305-310.