Ileitis (Porcine proliferative enteropathy). History and etiology

Roberto M. C. Guedes / Veterinary School, Universidade Federal de Minas Gerais
Belo Horizonte, MG – Brazil

INTRODUCTION

Porcine proliferative enteropathy (PPE), also known as ileitis, is an infectious enteric disease caused by the obligate intracellular bacterium *Lawsonia intracellularis*. The forms of presentation of the disease in pigs are haemorrhagic or acute, chronic and subclinical. As the most prevalent and economically important enteric disease in growing-finishing animals, it deserves frequent updating regarding its general aspects and updates.

> Ileitis is an example of a disease that you must learn how to live with.

As a result, the intention of this series of articles about the disease is to remind the reader about the relevance of its adequate understanding and, consequently, efficient control for improving herd performance.

HISTORY

Although the disease in pigs was first reported in 1931, research interest in PPE was minimal until the early 1970s, when a research group in the United Kingdom, lead by Dr. Gordon H. K. Lawson, started to report and study field outbreaks (Lawson & Gebhart, 2000). The early description of the disease was based on macroscopic and histological features, but it was also characterized as infectious with its experimental reproduction using an intestinal homogenate as an inoculum for susceptible animals (Biester & Schwarte, 1931). The presence of intracellular bacteria within proliferative lesions was described in 1973 by Rowland et al., using hyperimmune serum from an affected pig in an immunofluorescence preparation of affected intestine samples. It was not until 1993 that this intracellular bacterium, the aetiological agent, was cultured in vitro from pigs (Lawson *et al.*, 1993), and the disease was reproduced using a pure culture, fulfilling Koch's postulates (McOrist *et al.*, 1993). The causative intracellular bacterium of PPE was classified as a new genus and species in 1995, and named *Lawsonia intracellularis* in honor of Dr. Lawson (McOrist *et al.*, 1995a).

Jeff Knittel et al. (1998) developed the first serology test, indirect immunofluorescence assay, to detect specific serum IgG against *L. intracellularis*, and in 2002 Guedes et al. optimized the immunoperoxidase monolayer assay (IPMA) in 96 well plates. The onset and duration of humoral and cell-mediated immune response against *L. intracellularis* was studied by Guedes et al. (2003), using the IPMA and ELISPOT tests, respectively. Several different ELISA tests were developed in the following years (Boesen et al., 2005; Kroll et al., 2005; Nathues & Grosse, 2008; Wattanaphansak et al., 2008). However, only the blocking ELISA test (Nathues & Grosse, 2008) is commercially available worldwide. The IPMA test is only offered through the Diagnostic Veterinary Laboratory of the University of Minnesota, USA, and the Universidade Federal de Minas Gerais, Brazil.

The complete genome sequence of *L. intracellularis* was accomplished in Minnesota (Gebhart & Kapur, 2004), this allowing the use of a molecular technique, Variable Number of Tandem Repeats (VNTR), based on four hypervariable loci (Beckler et al., 2004). This technique allowed the conduction of molecular epidemiological studies, including the demonstration of interspecies transmission.

More recently, two publications have brought some light about the pathogenesis of *L. intracellularis*, demonstrating, for instance, no involvement of apoptosis in the mechanism of proliferation of infected enterocytes.

AETIOLOGY

It is not possible to culture *L. intracellularis* in conventional bacteriological media, and it can only be done in eukaryotic cells monolayers, such as intestine 407 cells, rat ileal enterocytes cell line (IEC-18) (Fig. 1), McCoy cells and others. As a result, the final classification of the organism had to be done by molecular taxonomic methods. Gebhart et al. (1993), using the recently developed molecular taxonomic method of the 16S rDNA sequence analysis (Weisburg *et al.*, 1991), showed that the sequences obtained from organisms purified from the ileal mucosa of four pigs were similar to those of Desulfovibrio desulfuricans (91% similarity). In another study, a sequence comparison showed a 92% similarity between Bilophila wadsworthia, a free-living anaerobic human pathogen, and *L. intracellularis* (Sapico et al., 1994). Finally, as mentioned above, in 1995 this intracellular bacterium, previously known as *Campylobacter-like* organism (CLO), Ileal symbiont *intracellularis* and Ileobacter *intracellularis*, was classified in a new genus as *Lawsonia intracellularis* (McOrist *et al.*, 1995a).

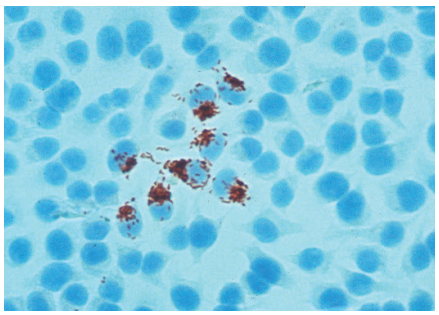

Figure 1. Rat intestinal epithelial cells, in blue, infected with *Lawsonia intracellularis*, in red, in vitro. Note the intracellular location of the bacteria and foci proliferation, demonstrating focal amplification of the infection.

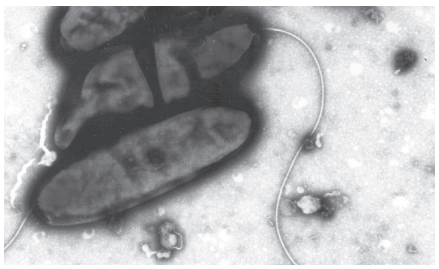

Figure 2. Electron microscopy of *Lawsonia intracellularis* preparation obtained from supernatant of in vitro pure culture flasks. Note the unipolar flagella. Courtesy of Dr. Connie J. Gebhart, University of Minnesota, USA.

L. intracellularis is a Gram-negative curved or sigmoid-shaped rod, 1.25 to 1.75 µm long and 0.25 to 0.43 µm wide. The bacterial wall has a trilaminar outer envelope, frequently separated from the cytoplasmic membrane by an electron-lucent zone. No fimbriae or spores have been detected. A long, single, unipolar flagellum, which is suspected to help bacterial movement in the intestine, and in the attachment and penetration in the enterocytes, has been observed by electron microscopy in three different cell culturegrown isolates (Lawson & Gebhart, 2000) (Fig. 2)

FINAL CONSIDERATIONS

Despite the first report of PPE dated 1931, knowledge about the disease has been growing slowly since the 1970s. In addition, not many research groups are working with this important disease, that requires greater efforts to improve the understanding of different aspects of the *L. intracellularis* infection. In the following articles, aspects related to PPE epidemiology, pathogenesis, clinical presentations, treatment and control, and the potential impact of antimicrobial restrictions on the incidence and severity of the infection with *L. intracellularis* will be discussed.

Figure 1. Rat intestinal epithelial cells (in blue, infected with *Lawsonia intracellularis*, in red, in vitro). N.B. the intracellular location of the bacteria and foci proliferation, showing the focal amplification of the infection.

Figure 2. Electron microscopy of a *Lawsonia intracellularis* preparation obtained from the supernatant of in vitro pure culture flasks. N.B. the unipolar flagella. Courtesy of Dr. Connie J. Gebhart, University of Minnesota, USA.