

UNDERSTANDING OF COLITIS IN SWINE IMPROVED



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INTRODUCTION

Porcine colonic spirochaetosis (PCS), also known as intestinal spirochaetosis, is an endemic infectious disease in all major pig-producing countries of the Americas, Europe and Asia. It was first identified over two decades ago in the United Kingdom.¹

Clinically, PCS is characterized by transient to persistent diarrhoea that results in decreased performance and a lack of uniform weight gain among grower-finishers. PCS risk factors include commingling pigs with a different health status, abrupt dietary change and environmental faecal contamination. A diagnosis of PCS requires demonstration of the spirochaete in association with epithelial damage and colitis.

Over the last decade, major advances in the field of intestinal spirochaetal research, particularly molecular detection methods, have led to recognition of *Brachyspira pilosicoli* as the cause of PCS. *B. pilosicoli* is now recognized as a significant contributing cause of reduced performance in pigs raised under intensive management practices worldwide. In addition, an apparent re-emergence of PCS in the European Union may be due in part to regulatory policies banning in-feed use of antimicrobial agents for promoting growth and feed efficiency in healthy pigs.

The economic impact of PCS is not well documented. However, control of PCS is

essential in systems using multiple sites and all-in/all-out management practices.

EPIDEMIOLOGY

Currently, there are five spirochaetal species within the genus *Brachyspira* (formerly *Serpulina*) that are known to colonize the hindgut of pigs (Table 1). Two are pathogenic for pigs: *B. pilosicoli*, the cause of PCS^{1,2} and *B. hyodysenteriae*, the cause of swine dysentery.

Table 1. Intestinal *Brachyspira* species affecting pigs.

Taxon	Host Association
<i>B. hyodysenteriae</i>	Swine dysentery
<i>B. intermedia</i>	Uncertain
<i>B. innocens</i>	Commensal
<i>B. murdochii</i>	Commensal
<i>B. pilosicoli</i>	Porcine colonic spirochaetosis

The prevalence of *B. pilosicoli* varies in surveys (Table 2). In a 1998 field survey of ten US farms, 50% had *B. pilosicoli* infection among grower pigs with diarrhoea.³ However, a later survey conducted from 1998 to 1999 indicated that 2% of 50 farms had PCS.⁴ Surveys in Brazil and Finland showed a high prevalence on farms where growers were fed rations without antimicrobial agents, but a low prevalence when antimicrobial agents were in the nursery diet.

Varying results are probably due to differences in the use of antimicrobials together with differences in laboratory techniques and sample selection (Table 2).



In contrast to large-scale prevalence surveys, the within-herd epidemiology of *B. pilosicoli* has only recently been examined.⁵ The prevalence on a >2,000-sow farm and an 80-sow farm in Western Australia was 2.4% and 12.2%, respectively. On both farms, infection was largely confined to grower-finishers and was significantly associated with diarrhoea. These findings are consistent with large-scale surveys where classification of faecal specimens as diarrhoeic or normal have been reported (Table 3).

Table 2. Diagnostic surveys of *Brachyspira pilosicoli* in intestinal specimens obtained from pigs in different countries.

Country	Year of Survey	No. Herds Examined	Prevalence (%)	Comments
UK	1992-1996	85	32.9	Primary cause
			18.9	Mixed infection
Sweden	1996	15	46.7	Randomly selected
Sweden	1996-1997	894	18.0	With diarrhoea only
Finland	1997	50	28.0	Randomly selected high health
Denmark	1997-1999	79	19.0	Randomly selected without diarrhoea
Brazil	1998	17	41.2	With diarrhoea only
S. Korea	1999-2001	398	10.1	With diarrhoea only
Spain	2000-2002	225	4.9	With diarrhoea only

Table 3. Prevalence of *B. pilosicoli* in intestinal specimens obtained from grower pigs with and without a history of diarrhoea.

Country	Year of Survey	No. Herds Examined*	Prevalence (%)	
			Diarrhoea Present	Diarrhoea Absent
Denmark	1995-1996	72/26	13.9	0.0
Finland	1997	42/8	31.0	12.0
Sweden	1996	7/8	85.7	12.5

*With diarrhoea/without diarrhoea.

Isolation of *B. pilosicoli* from pigs without clinical signs of diarrhoea in field surveys⁵ and the results of experimental challenge studies^{3,6,7} indicate that the rate of infection exceeds the prevalence of pigs with diarrhoea. Although the

duration of infection in individual pigs with a specific strain lasted at least 2 weeks, evidence of reinfection in individual pigs with genetically distinct strains was also found. Detection of genetic diversity among *B. pilosicoli* strains present on a farm suggested variable biological properties, including virulence and susceptibility to antimicrobial agents that could affect the success of PCS intervention strategies.

CLINICAL SIGNS

Clinical signs of PCS are typically seen 10 to 14 days after pigs with different health status have been moved from the nursery into a grower facility where they are mixed and fed a grower ration.^{3,5,8,9} At this stage, pigs are about 10 to 16 weeks of age and usually weigh more than 20 kg.

In experimental infection studies, the incubation period ranged from 3 to 20 days depending on the strain and number of *B. pilosicoli* inoculated.

Uncomplicated *B. pilosicoli* infection is characterized by diarrhoea with the consistency of wet cement, sometimes containing mucus, but usually without blood. Although diarrhoea is usually transient and typically resolves in 7 to 10 days, clinical signs may last 3 to 6 weeks as infection moves between individuals within pens.

Mixed infections with other enteric pathogens, most often *Lawsonia intracellularis* and *Salmonellae*, account for persistent problems accompanied by more severe reduction in growth performance and increased mortality.⁸⁻¹¹

PCS has several economic consequences, particularly for multisite, all-in/all-out production systems (Figure 1).

Figure 1. Economic consequences of PCS

- Increased feed costs/decreased feed efficiency
- Lack of uniform weight gain
- Increased days to reach market weight / extra facility time
- Disruption of normal pig flow through production units
- Holding back underweight pigs, which compromises hygiene
- Marketing pigs at less than optimal weight
- Reduced profitability

PATHOLOGY AND PATHOGENESIS

In pigs experimentally infected with *B. pilosicoli*:

- The infection rate is between 80% and 100%.
- The incidence of diarrhoeal disease is 33% to 67%.
- Infection persists for up to 6 weeks post-inoculation before natural recovery.
- From 30% to 50% of pigs have asymptomatic infection.

Gross and histological changes are limited to the large intestine. The caecum and spiral colon may be distended with gas, and the contents may be loose and contain excess mucus.

Damage to tissues and local inflammation (Figure 2) reduce the colon's ability to absorb nutrients, including water and electrolytes.

Because the hindgut of pigs has a 2- to 4-fold reserve capacity for daily reabsorption of fluids and electrolytes in the lumen, diarrhoea might not occur until three quarters of the surface area is lost. Thus, clinical signs of diarrhoea are seen only when the infection affects most of the colon, but with less severe colitis, depression of weight gain is seen.

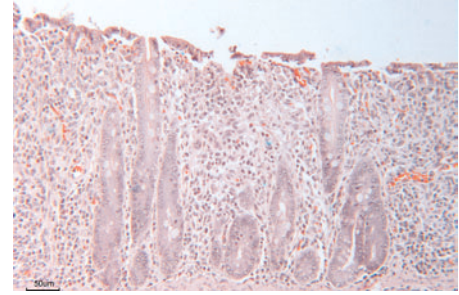


Figure 2. Light photomicrograph of an hematoxylin and eosin stained section of distal spiral colon taken from a pig 21 days after inoculation with *Brachyspira pilosicoli*. Note the severe colitis characterized by attenuation of the surface epithelium accompanied by a loss of crypt columns, hyperplasia of the remaining crypt epithelium and diffuse infiltration of the subepithelial tissue by large numbers of inflammatory cells.

RISK FACTORS FOR *B. PILOSICOLI* INFECTION

The pathogenesis of PCS is incompletely understood, but is likely to involve the interplay between *B. pilosicoli*, the host and the environment. Recent studies have begun to identify risk factors that affect the prevalence and severity of PCS.^{12,13} Environmental factors that may predispose to *B. pilosicoli* infection include stressors such as transport, crowding, commingling and re-sorting, improper ventilation and wide temperature fluctuations. However, the most significant one may be environmental contamination.¹⁴

The source of gilts, solid-floored pens with bedding and bowl and trough drinkers are significant risk PCS factors, whereas respiratory diseases are not.¹³ Since experimental transmission of *B. pilosicoli* is accomplished by oral inoculation of naive pigs,^{3,6,7,15} and pigs with PCS shed *B. pilosicoli* in faeces, the most important source of environmental contamination is likely to be clinically and perhaps subclinically infected pigs.

B. pilosicoli can survive several days at room temperature and for months at 4°C in faeces and manure-contaminated soil^{16,17} as well as fresh water.¹⁸ Therefore, improving hygiene and limiting access to manure-contaminated environments are important management strategies for reducing PCS spread and maintenance.

DIET AND PCS

A decrease in the prevalence of PCS has been reported when rations were changed from pelleted to meal form.^{19,20} It could be that inadequate average particle size in some pelleted diets or some unknown alteration of feedstuffs during the pelleting process shortens the transit time of feedstuffs through the gastrointestinal tract. This in turn could increase the concentration of carbohydrates that normally would not reach the hindgut, eventually leading to enhanced volatile fatty acid production (VFAs).

Enhanced VFA production can lower hindgut luminal pH and cause epithelial damage, a condition known as “colonic acidosis,”²¹ which has been proposed as a predisposing factor for colonization of *B. pilosicoli* and development of clinical PCS.^{22,23} Diet composition should be considered when evaluating PCS.

PCS DIAGNOSIS

Although diagnostic capabilities for detecting pathogenic *Brachyspira* species have greatly improved over the last decade, recognition of several spirochaete species in colonic specimens of pigs, in turn, has increased the complexity of PCS diagnosis by veterinary diagnostic laboratories.

A presumptive clinical diagnosis of PCS is made on the basis of reduced growth performance and

increased prevalence of diarrhoea, particularly among growers. Clinical improvement in response to management changes, including antimicrobial therapy with drugs that have known activity against *Brachyspira* spirochaetes, is only suggestive of PCS. Confirmation of PCS requires identification of *B. pilosicoli* in association with colitis.

Because mortality with uncomplicated PCS is rare, examination of colonic tissues obtained at necropsy is usually not practical. Consequently, *B. pilosicoli* is most often diagnosed by collecting faecal swabs from live pigs with diarrhoea or from fresh, undisturbed loose stools on the floor of premises using established protocols (<http://vbms.unl.edu/irlsc/>).

Pigs that have not received antimicrobial therapy for 7 to 10 days before sampling are likely to provide more accurate results than pigs being treated during sampling.

Research and experience from several sources indicate the following:

- Between 10 and 30 faecal swabs are usually adequate to demonstrate the presence of *B. pilosicoli* infection on most farms.
- Faecal swabs should be placed in transport media for enteric specimens, such as Amies' transport medium containing activated charcoal.
- For necropsy examination, obtain specimens from more than one pig and more than one location along the length of the large intestine of individual pigs. Specimens should be fixed in 10% neutral buffered formalin and processed for histopathological examination.

- For accurate detection of *B. pilosicoli* by bacteriological examination, send chilled intestinal specimens or faecal swabs to a reference diagnostic laboratory by overnight courier.

Pathological Examination. Gross changes are often mild or not specific to PCS.^{7,24} However, mucosal colonization by *B. pilosicoli* is visible by routine histopathological examination of formalin-fixed and paraffin-embedded sections of caecum and spiral colon.

The presence of *Brachyspira* spirochaetes can be confirmed by using immunohistochemical (IHC) staining or fluorescent *in situ* hybridization (FISH) of deparaffinized tissue sections.

The presence of epithelial attachment of spirochaetes alone is not a reliable indicator of PCS. Demonstration of large clusters of *Brachyspira* spirochaetes inside dilated crypt lumina in association with colitis is more consistently seen.

Bacteriological Examination. PCS diagnosis by bacteriological examination is a challenge due to several factors, such as the wide variation in the number of spirochaetes present in intestinal specimens after infection. Nevertheless, culture of spirochaetes on selective agar media is the primary method for demonstrating *B. pilosicoli* in intestinal specimens. Surface growth and haemolysis are usually seen within ten days from the time of inoculation.²⁵

B. pilosicoli is easily differentiated from the strongly haemolytic *B. hyodysenteriae*, but cannot be differentiated from the other *Brachyspira* species of spirochaetes on the basis of haemolytic phenotype alone.

PCR-based Identification Methods. Polymerase chain reaction (PCR) assays that amplify

specific gene sequences have become widely available in veterinary diagnostic laboratories for definitive identification of *B. pilosicoli*. In particular, the method known as PCR restriction fragment length polymorphism (PCR-RFLP) allows identification of all *Brachyspira* species potentially present in pigs without having to run separate PCR assays.

Serology. A standardized serological test for PCS is not currently available. This has hampered further understanding of the role of herd immunity in PCS control.

CONCLUSIONS AND FUTURE PERSPECTIVES

PCS is now a well-recognized infectious cause of colitis in growing pigs worldwide. Clinical expression of PCS appears to be due to several factors such as significant environmental exposure to *B. pilosicoli*, coinfection with other enteric pathogens and the presence of certain predisposing dietary factors that allow spirochaetal colonization and disease. It also appears that regulatory policies in some areas that limit use of in-feed antibiotics may be responsible in part for an apparent re-emergence of PCS.

Although the economic impact of PCS is not well documented, it is known that PCS leads to growth retardation, increased feed costs due to decreased feed efficiency in infected pigs and a lack of uniform weight gain that increases days to market.

The availability of highly sensitive and specific molecular diagnostic methods for identifying *B. pilosicoli* has greatly improved our ability to understand the epidemiology and pathogenesis of PCS. A greater understanding of the cause

of PCS and the risk factors associated with the disease can foster development of intervention strategies aimed at increasing the productivity and welfare of pigs raised under intensive management practices.

Not yet known is whether PCS has public health significance or if it is a zoonotic problem. The role of *B. pilosicoli* in humans is currently under study.

For more information about antimicrobials that are effective against PCS, see the second article in this series, entitled "In Vitro and In Vivo Efficacy of Antimicrobial Agents for Control of Porcine Colonic Spirochaetosis."

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