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January 1998

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Duhamel, Gerald; Mathiesen, Michelle R.; Kinyon, Joann M.; Murphy, Dorothy; and Walter, Don, "Activity of Four Antimicrobial Agents Against Porcine *Serpulina pilosicoli* Isolates From the Midwestern United States" (1998). *Nebraska Swine Reports*. 146.

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Activity of Four Antimicrobial Agents Against Porcine *Serpulina pilosicoli* Isolates From the Midwestern United States

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Summary and Implications

Porcine colonic spirochetosis (PCS) is a non-fatal, diarrheal disease affecting pigs during the growing and

*finishing stages of production. The disease is caused by *Serpulina pilosicoli*, a newly recognized species of intestinal spirochetes. Because *Serpulina pilosicoli* is transmitted by the fecal-oral route, control measures aimed at reducing environmental contamination, including sanitation and antimicrobial therapy, should be investigated. We determined the antimicrobial susceptibility of seven porcine *Serpulina pilosicoli* isolates recovered from pigs*

*in the midwestern United States against four antimicrobials commonly used for control of swine dysentery, a disease caused by the related spirochete, *Serpulina hyodysenteriae*. All the isolates were susceptible to carbadox and tiamulin, whereas the percentages of isolates susceptible, intermediate and resistant were 66.6, 16.6 and 16.6 percent with lincomycin, and 50 percent susceptible and 50 percent resis-*

(Continued on next page)



tant with gentamicin. This information is consistent with field observations about the efficacy of the respective antimicrobials for control of PCS.

Introduction

Porcine intestinal spirochetes consist of at least three species in the genus *Serpulina*; *Serpulina hyodysenteriae*, the agent of swine dysentery, *Serpulina innocens*, a non-pathogenic spirochete of the swine colon and the newly recognized *Serpulina pilosicoli*, the agent of porcine colonic spirochetosis (PCS). Clinical signs of *Serpulina pilosicoli* infection consist of transient-to-persistent watery to mucoid green to cement gray cow-manure-like diarrhea without blood, usually occurring 10 to 14 days after mixing grower pigs from different sources. While up to 50 percent of the pigs may show diarrhea, morbidity varies greatly from farm to farm and the factors responsible for this variation are not completely understood. Although the diarrhea associated with PCS usually subsides, the concurrent depression of weight gains results in unevenness within affected groups. This is a major problem in all in/all out management systems in which PCS causes disruption of pig flow by both extending the marketing period and increasing the number of pigs with lighter weights.

Because transmission of *Serpulina pilosicoli* is by the fecal-oral route, control measures aimed at reducing environmental contamination, including sanitation and antimicrobial therapy, should provide adequate disease control. Since *Serpulina pilosicoli* is a newly identified intestinal spirochete, determining the antimicrobial susceptibility of this organism so disease-specific control strategies can be implemented is important. In this study, we determined the antimicrobial susceptibility of seven porcine *Serpulina pilosicoli* isolates against four antimicrobials commonly used to treat swine dysentery. The *Serpulina pilosicoli* were isolated from pigs on farms in the midwestern United States.

Materials and Methods

A total of seven isolates of *Serpulina pilosicoli* were obtained from rectal swabs or colonic scrapings taken from pigs on farms in Iowa ($n = 2$), Missouri ($n = 3$) and Nebraska ($n = 1$). All the isolates were from different farms except isolates UNL-53 and UNL-54, which were both obtained from one farm in Missouri (Table 1). After isolating the spirochetes by anaerobic culture on selective medium, representative isolates were characterized using a polymerase chain reaction amplification method specific for *Serpulina pilosicoli*. The minimal inhibitory concentrations (MIC) of carbadox, gentamicin, lincomycin and tiamulin against the *Serpulina pilosicoli* isolates were determined by an agar dilution method.

Results

The MIC of carbadox, gentamicin, lincomycin and tiamulin against each *Serpulina pilosicoli* isolate is presented in Table 1. Because isolates UNL-53 and UNL-54 were obtained

from the same farm and had the same MIC values, they were considered one for the calculations of the MIC of each antimicrobial effective against 50 percent (MIC_{50}) and 90 percent (MIC_{90}) of the isolates (Table 2). From available literature data on the antimicrobial susceptibility breakpoints of *Serpulina hyodysenteriae* for each antimicrobial, we estimated all of the *Serpulina pilosicoli* isolates were susceptible to carbadox and tiamulin. However, the percentages of isolates susceptible, intermediate and resistant were 66.6, 16.6 and 16.6 percent with lincomycin, and 50 percent susceptible and 50 percent resistant with gentamicin.

Discussion

The results from this study indicate the pattern of antimicrobial susceptibility of midwestern porcine *Serpulina pilosicoli* to antimicrobials used for treatment of swine dysentery was similar to that of *Serpulina hyodysenteriae*. Because of this, control measures known to be effective for swine dysentery, including stress reduction, sanitation and medication of

Table 1. Minimal inhibitory concentration values ($\mu\text{g/ml}$) of four antimicrobials against *Serpulina pilosicoli* isolated from pigs on farms in the midwestern United States

Isolate	Origin†	Carbadox	Gentamicin	Lincomycin	Tiamulin
UNL-5	Iowa	<0.0005	1.0	25.0	0.50
B1555a	Iowa	<0.0005	1.0	12.5	0.05
UNL-53	Missouri	0.015	10.0	75.0	0.10
UNL-54	Missouri	0.015	10.0	75.0	0.10
UNL-55	Missouri	0.005	10.0	25.0	0.05
B359	Missouri	<0.0005	1.0	12.5	0.20
UNL-8	Nebraska	0.005	10.0	50.0	0.05

†All isolates are from different farms except for isolates UNL-53 and UNL-54 which are from the same farm.

Table 2. Minimal inhibitory concentration (MIC) values of four antimicrobials against *Serpulina pilosicoli* isolates obtained from pigs on farms in the midwestern United States

Antimicrobial	Drug concentration range ($\mu\text{g/ml}$)	MIC_{50}	MIC_{90}
Carbadox	<0.0005 - 0.015	<0.0005	0.015
Gentamicin	1.0 - 10.0		1.0 10.0
Lincomycin	12.5 - 75.0		25.0 75.0
Tiamulin	0.05 - 0.50		0.05 0.50



water and feed with *Serpulina hyodysenteriae*-specific antimicrobials should be effective against PCS caused by *Serpulina pilosicoli*.

Koch's postulates for *Serpulina pilosicoli* have been fulfilled using gnotobiotic pigs and conventional pigs. Following initial association with the cecal and colonic mucus gel, the spirochetes attach to the colonic enterocytes, residing in the brush border of the colonic cells where they damage the microvilli, causing reduced surface area and perhaps loss of absorptive function. Clinical signs of absorption failure or diarrhea may be seen when the reserve capacity of the large intestine is compromised sufficiently. With time, the disease progresses to a stage in which the balance between infection and host response determines whether the pig remains persistently infected or eliminates the spirochetes. Pigs persistently infected with *Serpulina pilosicoli* develop chronic inflammation of the large intestine. The following altered intestinal function is thought to result in reduced growth rate.

Serpulina pilosicoli can be isolated from the large intestine of challenge-inoculated pigs for up to six weeks post-inoculation, even though diarrhea may have ceased. This suggests transmission of PCS is from shedding of *Serpulina pilosicoli* in the feces of persistently infected pigs. Some pigs infected with *Serpulina pilosicoli* may recover naturally without medication, but they have reduced average body weight gain when compared with noninfected control pigs. Carrier-shredder pigs are an important reservoir of *Serpulina pilosicoli* on infected farms and the movement of these pigs is the most likely means of transmission of *Serpulina pilosicoli* between farms.

Management systems favoring fecal-oral recycling, such as open-flush gutters and recycled lagoon water, appear to promote maintenance and transmission of PCS. Thus, in all in/all out multi-site production systems, transmission is most likely from co-mingling susceptible and carrier-shredder pigs or from the contaminated environment. In continuous flow production systems, spirochetes are most likely transmitted when younger *Serpulina pilosicoli*-naive pigs come into contact with feces of older pigs. The possibility also exists that hosts other than pigs, such as dogs, rodents and wildlife, including birds, act as sources of PCS infection, emphasizing the need for biosecurity.

Diarrheal disease and reduced performance associated with *Serpulina pilosicoli* have been reported from all major swine producing countries in North America, Europe and Australia. We estimated a 50 percent prevalence rate of *Serpulina pilosicoli* infection in finisher facilities within a multi-site production system in the United States; a finding not unlike the prevalence of *Serpulina hyodysenteriae* several years ago, before control measure for this spirochete became widely available.

The results of antimicrobial susceptibility of midwestern isolates of porcine *Serpulina pilosicoli* suggested carbadox and tiamulin may be suitable for control of PCS. Conversely, the susceptibility of the isolates to lincosamycin and gentamicin was variable. Although field information is consistent with these laboratory results, the applicability of specific antimicrobials in controlled challenge studies would be helpful in making cost-effective recommendations for prevention or treatment of PCS. When response to treat-

ment is poor, (i) error in dosage and/or inadequate delivery of antimicrobials, (ii) combination of agents with different antimicrobial susceptibility or (iii) poor control of environmental contamination may be involved. Eradication of *Serpulina pilosicoli* with antimicrobial therapy and sanitation with or without depopulation is probably possible, but it might not be cost-effective. When PCS occurs concurrently with other cause(s) of diarrhea, such as viruses, other bacteria, intestinal parasites or other non-infectious causes, mortality is high. In these cases, thorough laboratory diagnostic investigation is needed in order to achieve adequate control.

It is known that *Serpulina pilosicoli* has a broader host range than *Serpulina hyodysenteriae*. Spirochetes similar to *Serpulina pilosicoli* have been seen in the intestines of humans, non-human primates, dogs, guinea pigs, opossums, mice and birds often with clinical signs or lesions of colonic spirochetosis. Because *Serpulina pilosicoli* has been isolated from humans with lesions similar to PCS and human *Serpulina pilosicoli* can colonize in pigs and produce colitis, it may be zoonotic and have public health significance.

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