ORIGINAL RESEARCH

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Evaluating a natural outbreak of porcine proliferative enteropathy and treatment with tylosin in the grow-finish phase

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Summary

Objective: To determine approximate time and severity of a porcine proliferative enteropathy (PPE) outbreak in a herd with a history of PPE; to compare average daily gain (ADG), average daily feed intake (ADFI), feed efficiency (F:G), and clinical impression of disease in clinically affected nonmedicated controls versus pigs medicated with 110 ppm (100 g per ton) of tylosin for 21 days followed by 44 ppm (40 g per ton) tylosin for an additional 21 days; and to follow pigs to market to determine effects of the outbreak on clinical PPE lesions detected at slaughter.

Methods: One hundred and twelve pigs with clinical signs of PPE were randomly assigned to either a control group receiving nonmedicated feed or to a medicated group receiving feed with 110 ppm (100 g per ton) of tylosin for 21 days. The feed of the medicated group was then changed from 110 to 44 ppm (100 g to 40 g per ton) tylosin for another 21 days. Then all pigs (in both medicated and control groups) were placed on 22 ppm (20 g per ton) tylosin (for growth promotion) until market. Average daily gain, ADFI, and F:G were compared for the first 21-day phase, the second 21-day phase, and throughout the 42-day trial period. Pigs were also rated with a clinical impression score (CIS) ranging from 0 = clinically normal to 3 = severely infected for the first 21-day phase.

Results: Clinical impression scores improved more rapidly in medicated pigs than in nonmedicated controls during the first 21 days. Growth performance, although it tended to be improved for ADG (P <.09) and F:G (P <.07), did not differ significantly between treatment groups in the first 21-day phase, in the second 21-day phase, or for the overall trial period.

Implications: Tylosin in this study was effective in treating PPE when administered at a dosage of 110 ppm (100 g per ton) for 21 days. There was no significant advantage to medicating pigs with 44 ppm (40 g per ton) tylosin for an additional 21 days. Ileal thickening at slaughter was observed in 26% of the pigs in this study, suggesting that palpation of ileal thickening at slaughter may detect previous PPE outbreaks.

Keywords: swine, porcine proliferative enteropathy, *Lawsonia intracellularis*, tylosin

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Porcine proliferative enteropathy (PPE) is a commonly recognized condition in grower-finisher pigs and breeding animals worldwide. Estimates of the prevalence of this disease in Spain[1] and Denmark[2] range from 29%–88%, and in Australia the disease is estimated to affect 15% of herds.[3,4] In the United States, Bahnson, et al.,[5] found palpable lesions of PPE in 35% of herds evaluated at the slaughter plant and in 5%–20% of the pigs in those herds. According to the NAHMS Swine '95 survey,[6] 6.5% of all swine operations and 18.5% of large operations (those marketing > 10,000 pigs per year) reported having experienced PPE outbreaks.

Little is known about the epidemiology and pathogenesis of PPE,[7] although clinical reports often refer to either an acute or a chronic infection, with clinical signs often inapparent in the chronic form.[8–10] The causative agent has recently been identified as an obligate intracellular bacterium—*Lawsonia intracellularis*.[11,12] Recent breakthroughs in antemortem diagnostics may contribute to our understanding of the course of PPE in herds experiencing problems.[5,12,13]

Few controlled studies have been reported that document the effects of a clinical outbreak of PPE on morbidity, mortality, or growth performance, nor have any studies evaluated the time of onset or risk factors possibly associated with clinical disease. Much of the difficulty in accurate clinical outbreak documentation has been related to the lack of readily available antemortem or confirmatory postmortem diagnostic tools.[12,13]

We conducted this clinical field trial to:

- evaluate a natural infection of PPE (i.e., time of onset and severity) by placing genetically similar pigs in a facility that had a history of PPE outbreaks in previous groups;
- compare average daily gain (ADG), average daily feed intake (ADFI), feed efficiency (F:G), and the clinical impression of the

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disease in nonmedicated controls versus pigs medicated with tylosin; and

- follow pigs to market to determine the effects of the outbreak on clinical PPE lesions detected at slaughter.

Materials and methods

Throughout this study (during the pretrial phase, the first 21-day phase, the second 21-day phase, and in the post-trial phase until slaughter), the pigs were fed a commercially pelleted corn–soybean-meal base ration containing 18% crude protein with 5% added fat offered on an ad libitum basis. All feed additives were incorporated by the commercial feed manufacturer and were within acceptable assay limits.

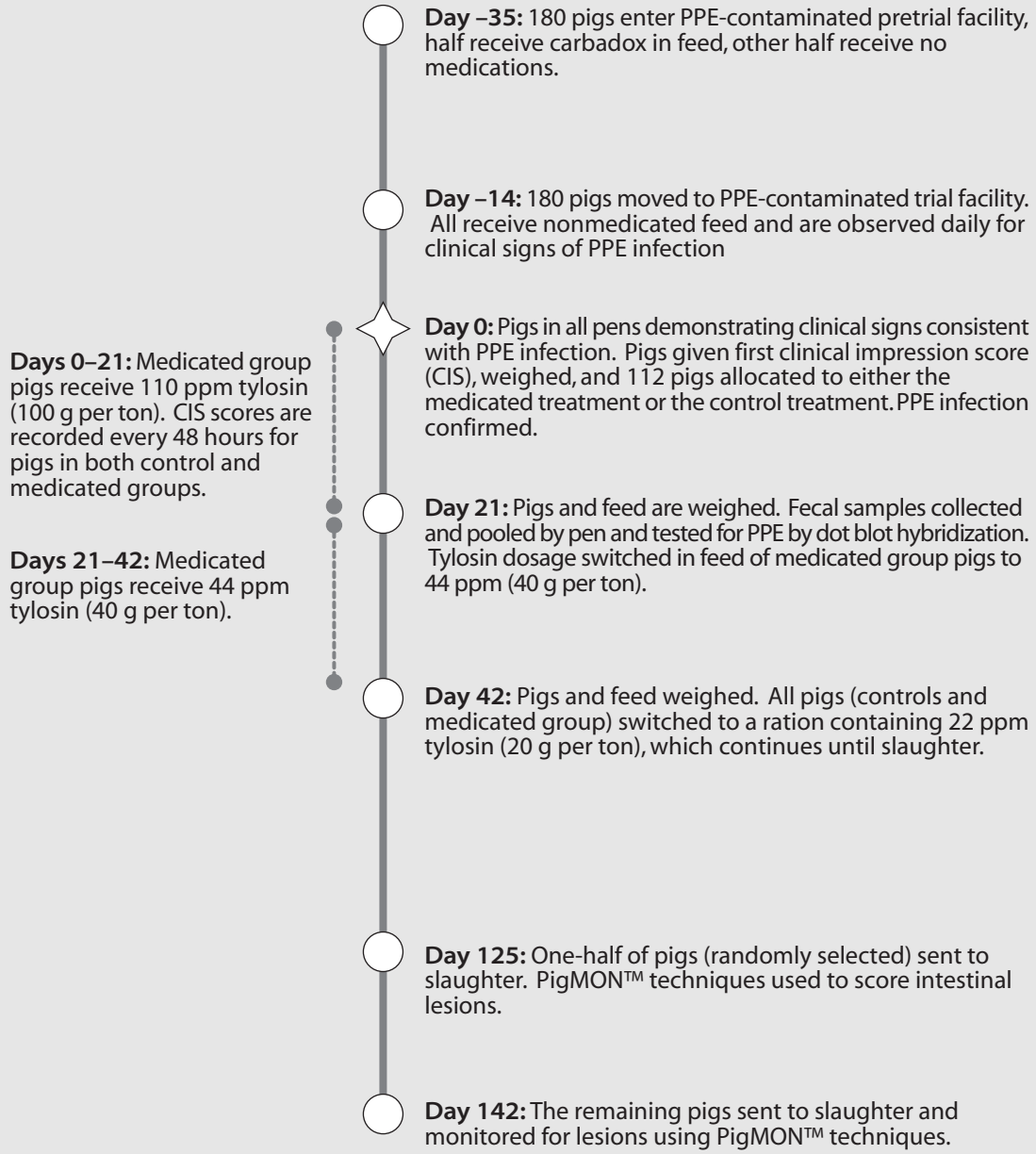
During the trial, affected pigs were only given feed medication; no injectable or water soluble antibiotics were administered.

Pretrial period

Immediately prior to the present study, 180 commercial crossbred pigs, each weighing approximately 19.5 kg (43 lb), were moved into a facility that had a history of clinical outbreaks of PPE (Figure 1). The pigs were placed in four large pens and ear tagged for identification.

Half the pigs received a nonmedicated base ration, and half were given the base ration to which 55 ppm (50 g per ton) of carbadox (Mecadox®, Pfizer, Inc.; Animal Health, Groton, Connecticut) had been added. The pigs remained in the pretrial facility for 3 weeks.

Figure 1



Study timeline

Natural infection

Two weeks before the trial began, 180 of the pigs were moved into the study facility, which also had a history of previous PPE outbreaks. The pigs were commingled into nine pens and placed on nonmedicated feeds. Pigs were observed daily for the clinical signs of a natural infection of PPE.

By the first day of the trial (day 0), some pigs had diarrhea in all pens. On day 0, the day the clinical outbreak of PPE was first observed, pigs were given a clinical impression score (CIS) of disease severity based on a scale from 0–3, so that:

- 0 = clinically normal (Figure 2);
- 1 = pigs exhibiting decreased abdominal fill and semi-solid fecal material (Figure 3);
- 2 = pigs with semi-liquid feces and exhibiting signs of weight loss (Figure 4); and
- 3 = pigs with liquid feces and a rough hair coat that were gaunt to moribund (Figure 5).

One hundred twelve pigs were assigned to one of eight pens of 14 pigs per pen, so that each treatment had pigs from all four of the CIS categories. To achieve a stocking density equivalent to what is standard in commercial herds, pigs were equally allocated among the pens according to weight, gender, and whether or not they had received medicated feed during the pretrial phase.

The pens of pigs were randomly assigned to one of two treatment groups:

- Four pens served as controls, and received the same base ration as in the pretrial phase. No medication was added for the 42-day trial period.
- The other four pens of pigs received the same base ration as the controls. During the first 21-day phase of the trial, (phase 1, days 0–21), 110 ppm (100 g per ton) of tylosin was added to the base ration. For phase 2 (days 21–42 of the study), these pigs received a base ration to which 44 ppm (40 g per ton) of tylosin was added to the base ration.

Three pigs were not allotted to pens because they were judged to be too severely infected to compete with penmates for feed. Two of the three pigs were humanely euthanized and underwent postmortem examinations. The third pig was treated and removed from the study.

The pigs were fed the treatment rations for 42 days. Starting on day 43, all pigs (including the controls) were fed the base ration to which 22 ppm (20 g per ton) tylosin was added as a growth promotant until slaughter (half of the pigs were slaughtered on day 125 and the remaining half on day 142 of the study).

Clinical impression scores were recorded for individual pigs every 48 hours for days 0–21 only by one unblinded rater.

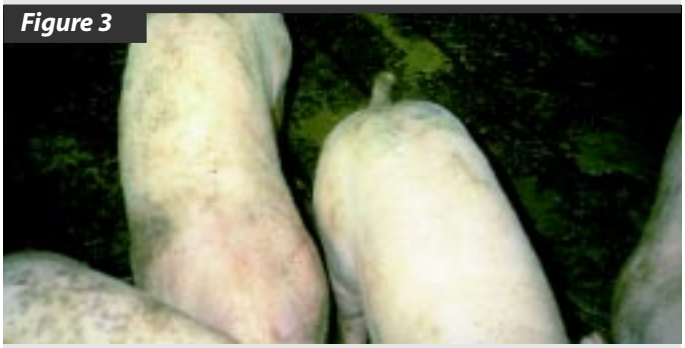
Confirmation of PPE infection

Fecal samples were collected randomly from several pens at day 21, pooled by pen, and evaluated for the presence of the PPE organism

Figure 2

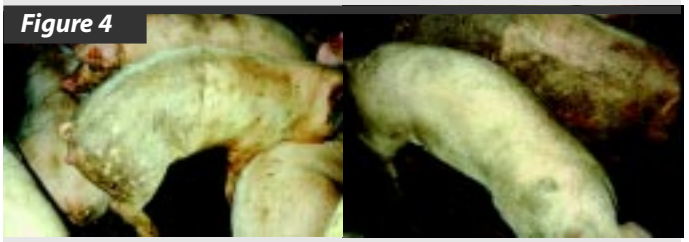
CIS = 0: Clinically normal pigs

Figure 3



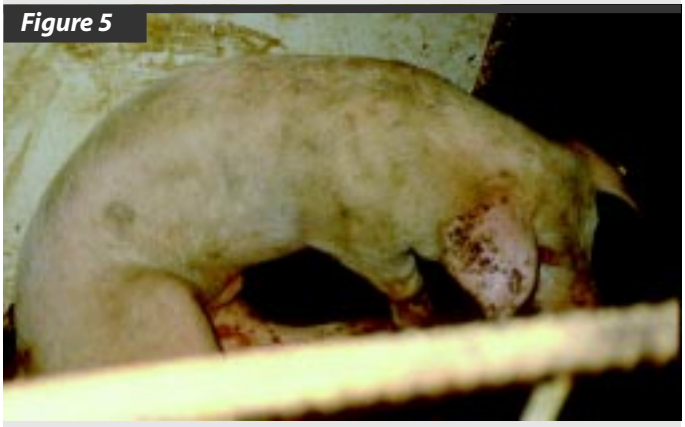
CIS = 1: Pig in middle showing decreased abdominal fill. Semi-solid to liquid feces can be seen in pen. (Pig on right appears clinically normal; CIS = 0.)

Figure 4



CIS = 2: Pigs showing signs of weight loss, semi-liquid feces, pig in left photo straining to defecate

Figure 5



CIS = 3: Pig with liquid diarrhea, gaunt and moribund (euthanized)

using dot blot hybridization (Dr. Gary Jones conducted sample evaluation at the University of Minnesota, Department of PathoBiology, St. Paul, Minnesota). In addition, feces and intestinal tissues were cultured according to standard bacterial culture procedures at the Ohio Department of Agriculture State Veterinary Diagnostic Laboratory for the presence of *Salmonella* spp. and *Serpulina* spp.

In addition to the two pigs deemed too ill to participate in the study, one other pig was euthanized and submitted for postmortem examination. Intestines from all three pigs were observed for gross lesions. Intestinal lesions were also histologically analyzed using hematoxylin and eosin (H & E) and Warthin-Starry stains (Dr. Harold Stills conducted the histopathology and silver staining at The Ohio State University, Department of Preventive Medicine, Columbus, Ohio).

Growth

Feed and water were provided *ad libitum* during the trial. The pigs and feed were weighed at the beginning of phase 2 (when the tylosin levels were switched) and at day 42. The pigs were again weighed on the day they were shipped to market.

Average daily gain (ADG), average daily feed intake (ADFI), and feed efficiency (F:G) were calculated for both treatment groups for phase 1, phase 2, and the entire trial.

Slaughter checks

At slaughter, the accurate identity of 101 pigs was established and those pigs were evaluated for lesions of PPE: ileal thickening and the presence of PPE lesions, using PigMON™[14] procedures. The inspector was not aware of the identity of the pigs or treatment group at the time of slaughter evaluation.

Statistical analysis

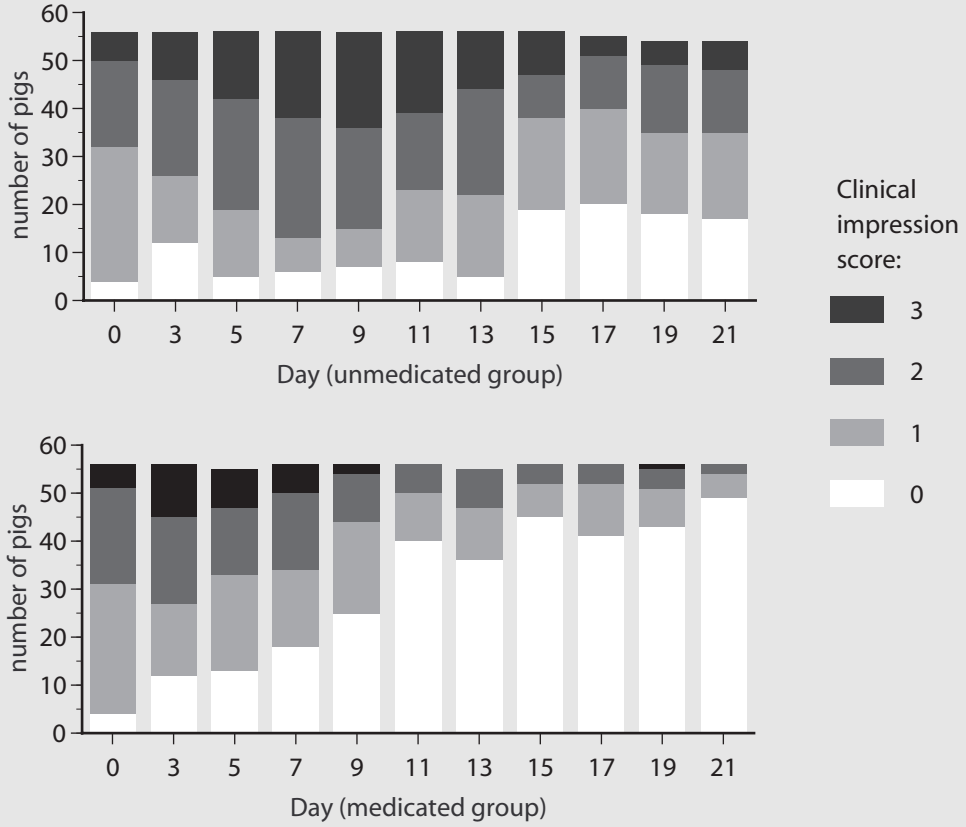
Pen means for ADG, ADFI, and F:G for:

- phase 1,
- phase 2, and
- the entire 42-day study period

were analyzed for treatment effects after adjusting for initial weight and block effects (least squares means).[15,16]

Clinical impression scores were analyzed using regression and ANOVA. Scores for each pig were regressed against time and slopes were estimated for each pig (profile analysis). To determine whether the mean CIS for the medicated versus the control pigs were different, slopes were analyzed for treatment differences after adjusting for block effects.

Figure 6



Daily record of number of pigs assigned to each clinical impression score (CIS) category in first 21 days

Results

Clinical signs of enteric disease were observed in pigs 2–3 weeks after they were moved to the study facility; however, no differences attributable to previous treatment (carbadox) were observed.

Natural infection

Natural infection with PPE was confirmed by the following observations:

- gross intestinal lesions were characteristic of infection with *L. intracellularis*;
- lesions were also consistent with those characteristic of PPE by histologic examination using hematoxylin and eosin (H & E) and Warthin-Starry stains;
- microbiologic examination of tissue from small and large intestines and fecal samples failed to culture *Salmonella* spp. or *Serpulina* spp.;
- fecal samples from five of the nine pens were positive by dot blot hybridization for *L. intracellularis*.

Clinical impression scores

The average clinical impression score for the nonmedicated pigs (1.51) was higher (P=.0002) than the average score for the medicated pigs (0.75) (Figure 6). The distribution of pigs in each CIS category (0, 1, 2, and 3) was very nearly the same at the start of the trial (Figure 6). However, as the trial continued, the CIS of the pigs receiving tylosin at 110 ppm (100 g per ton) decreased more quickly than those of the unmedicated controls (P=.002). Further examination shows that the CIS of many of the nonmedicated pigs never returned to 0, while by the end of day 11, the CIS of tylosin-treated pigs were back to normal.

Growth performance

From phase 1 of the trial, the ADG (P=.09) and F:G (P=.07) of pigs in the medicated groups tended to differ from that of the controls (Figure 7). Average daily feed intake did not differ significantly between the medicated and control groups (P=.32).

For phase 2 of the trial, none of the growth performance parameters differed between medicated- and control-group pigs (ADG: P=.25; ADFI: P=.17; F:G P=.78) (Figure 7).

Growth performance for the entire 42-day trial also did not differ significantly between the medicated- and control-group pigs (ADG: P=.11; ADFI: P=.32; F:G: P=.13) (Figure 7).

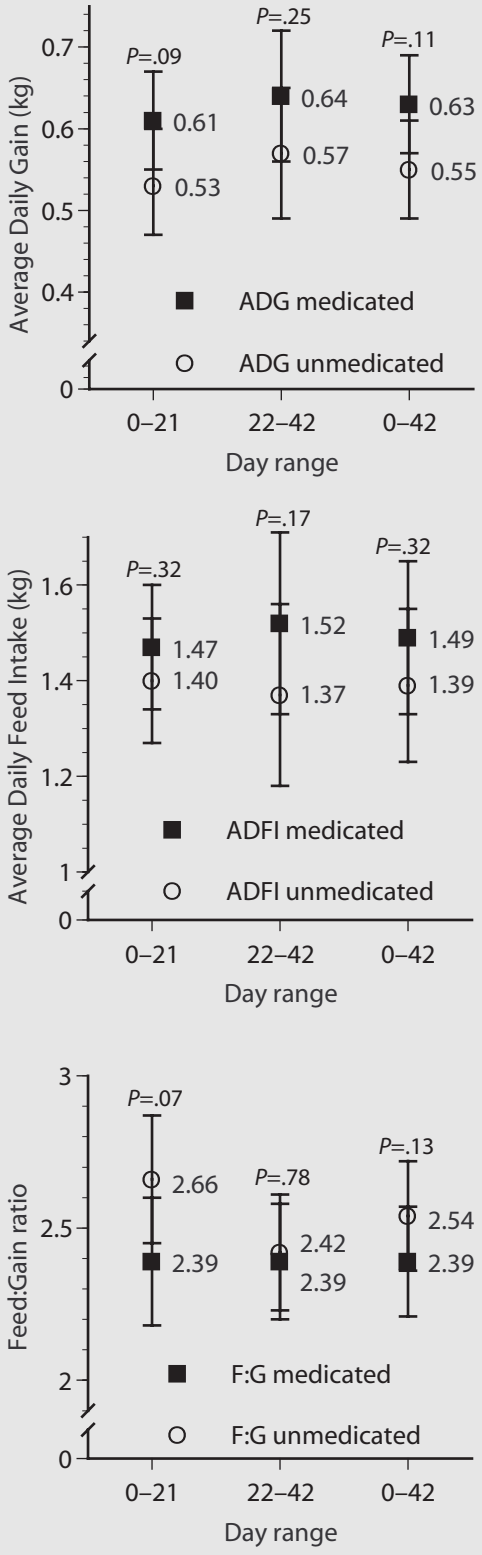
Slaughter lesions

The prevalence of palpable PPE lesions at slaughter did not differ between medicated groups (26%) and controls (26%).

Discussion

The initial intent of this study was to allow pigs to break with PPE, sacrifice those affected, and freeze the affected tissues for use in future studies. After the pigs were received, however, it was decided that a

Figure 7



Least-squares means for performance variables

natural outbreak and treatment study would be more applicable clinically. Once this was decided, carbadox medication was removed from the feed, and all pigs were moved to the trial facility and placed on a nonmedicated ration. The trial facility was designed for individual weighing of pigs, feed, and feeders and allowed us to include more experimental units.

Thus, we were able to make some observations on the effects of carbadox in controlling PPE when incorporated into the base ration at the pretrial facility. In this study, pigs introduced into facilities with a history of previous PPE outbreaks began to show clinical signs of disease 4–6 weeks after arrival. Feeding and withdrawal of carbadox had no observable impact on preventing a PPE outbreak.

The PPE observed in this trial may be more severe than is typically seen clinically, for several reasons. PPE had been diagnosed historically at both the pretrial and trial facilities, but possible differences in exposure by site based on cleaning and hygiene, and resultant organism load may have occurred. The stress of moving pigs a second time into the trial facility may have decreased the pigs' ability to resist the infection. Pigs in this study appeared to be infected with the chronic form of PPE based upon gross lesions at necropsy. Other investigators have found that clinical signs of PPE vary by site, age of pigs involved, and clinical form of the disease.[8–10]

Although we didn't detect statistically significant differences between tylosin-medicated and control group pigs, the growth performance of the medicated pigs was consistently improved over nonmedicated controls. Differences in ADG and F:G between the medicated and control groups were calculated based on pen measures rather than on an individual pig basis; if we had had a larger sample size, it is possible that we would have been able to detect statistically significant differences between medicated and control group pens.

Detecting lesions of ileitis in 26% of the pigs evaluated at slaughter was somewhat surprising compared to published estimates.[5,10,13] Most other estimates of herd prevalence were based on samples from the general population and not selected from pigs known to be exposed. The lack of differences in lesion prevalence at slaughter between treatment groups in our study may be because tylosin (22 ppm) was included in the feed of pigs in both medicated and control groups from day 42 to market. This may have helped to resolve lesions in those pigs in the finishing phase. Our observations suggest that lesions due to PPE may be present at slaughter in pigs known to be infected, even in those that received tylosin during the growing phase. However, estimates at slaughter based on ileal palpation are not highly accurate[14] and we may not have been able to ascertain actual differences between the treatment groups at slaughter due to limitations in sample size, number of pigs evaluated, and the healing of lesions from the time of exposure to evaluation.

Implications

- Tylosin administered at 110 ppm (100 g per ton) was an effective dose for treating PPE in this study.
- Average daily gain and F:G tended to be improved in pigs during the period when they received tylosin at 110 ppm (100 g per ton), but not during the phase when they received tylosin at 44 ppm (40 g per ton).
- No treatment differences were noted in percent of pigs exhibiting ileal thickening at slaughter. Although slaughter evaluation is neither a sensitive nor a specific indicator of herd infection with PPE, it may be one parameter to include on a more routine basis when screening for overall herd health at slaughter.
- Additional research on the use of tylosin in prevention, control, and treatment of PPE is warranted.

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