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Formatting
Tina Smith Graphics
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CD-ROM
David Brown
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Logo Design
Ruth Cronje, and Jan Swanson;
based on the original design by Dr. Robert Dunlop

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2011 Allen D. Leman Swine Conference
Differential diagnosis of finishing pig diarrhea

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General recommendations

The selection of pigs for testing, whether for serology or necropsy, is the most important step in obtaining an accurate and timely diagnosis. The majority of the veterinarian’s time should be spent observing pigs, taking temperatures, and obtaining complete histories prior to collecting samples or performing euthanasia.

Sampling pigs that have been treated for days or weeks with antibiotics will be unrewarding if your goal is to isolate pathogenic bacteria. Likewise, sampling only pigs that are chronically ill will skew the diagnostic picture, resulting in isolation only of common secondary or opportunistic pathogens and having histopathological lesions masked by scarring or regeneration rather than the inciting lesion.

In some situations, sample selection is straightforward—such as in acute, severe outbreaks of TGEV. In other, more complex situations such as porcine respiratory disease, many agents may be involved. Diagnostic sample selection may involve testing pigs at recurring intervals in order to define all the agents involved. Sampling carefully to include acutely affected pigs will be the greatest help to the producer, the pathologist, and the veterinarian seeking treatment or prevention strategies.

Finisher pig diarrhea: Pathogens, brief pathogenesis, and laboratory procedures

Brachyspira spp.

Swine Dysentery is caused by the spirochete Brachyspira hyodysenteriae. B hyodysenteriae is one of the most pathogenic of the several species in the genera and when grown in vitro is strongly hemolytic. Also of clinical significance are Brachyspira pilisicoli (weakly hemolytic in vitro) and a recently discovered species, a novel strongly hemolytic (NSH) Brachyspira sp. yet to be properly named and fully characterized. Interestingly, the clinical signs, gross and microscopic lesions of colitis caused by B hyodysenteriae, B pilisicoli, and NSH can be strikingly similar but there are diagnostic tests that can distinguish them.

In cases of Brachyspira hyodysenteriae, the diarrhea is usually described as mucoid and bloody. The lesions can be found the colon, cecum, and rectum but the small intestine is usually spared. The mucosa is usually thickened and can be covered with a pseudomembranous necrotic layer. Microscopically, the acute phase of the disease is characterized by mucous and goblet cell hyperplasia and the presence of neutrophils in the superficial lamina propria. As the disease progresses, there are large accumulations of fibrin, mucous, cell debris and blood in the mucosa. The superficial mucosa may be necrotic but deep ulceration, as is present with Salmonella Typhimurium, is not typical. There is colonization of the mucosa with large spirochetes that can be detected in the acute phase but are more prominent in the subacute to chronic phases. In this diagnostician’s experience, the range of lesions is vast but the majority are usually mild, superficial inflammation of the mucosa with mucosal and goblet cell hyperplasia being the most common histopathological findings.

Porcine intestinal spirochetosis (Brachyspira pilisicoli) and the NSH Brachyspira sp. infections can cause postweaning and grow-finish pig diarrhea. Pigs have loose feces and become gaunt. The diarrhea is usually self-limiting. Decreased rate of gain results and thus a proper diagnosis is recommended to prevent and control further losses. Grossly, the colon is flaccid and fluid filled, the mesenteric lymph nodes are enlarged, and ulceration may or may not be present. Histopathology findings include a mild catarrhal, erosive or ulcerative colitis that is usually confined to the mucosa and submucosa. As with B hyodysenteriae, there are mucous filled crypts, spirochetes within the colonic epithelium.

The diagnosis of Brachyspira sp. can be done by isolation or PCR detection of the bacteria in feces or colon, immunohistochemistry of the spirochetes in the large intestine, presence of typical clinical signs or lesions, and/or exclusion of the other causes of grow-finish diarrhea. Definitive diagnosis of Brachyspira sp. requires differentiation of the species isolated by sequencing or PCR. A multi-plex PCR is available that can detect and differentiate B pilisicoli and B hyodysenteriae. The other Brachyspira spp. are identified by NOX-gene sequencing of the isolate. Isolation of Brachyspira sp. requires special media and extra time (up to 6 days or more), so PCR and isolation can be done in tandem to speed up the diagnosis. That said, PCR on feces is difficult and feces is a complex...
matrix to work with for PCR thus rendering PCR on original material such as feces or colon slightly less sensitive than a combination of culture and PCR. The saprophytic Brachyspira spp. isolated may or may not be clinically significant, especially if other co-infections are identified in the same tissues, pigs, or herds. In the absence of other known causes of diarrhea, the finding of Brachyspira spp. should be interpreted with knowledge of clinical signs, pig movement, antibiotic therapy, nutritional changes, water quality, and environmental conditions before considering them pathogenic and significant.

Post-weaning E coli

The onset of diarrhea from E coli varies from a few days placed in nursery until several weeks post placement. Pigs more than 10-weeks-old can be affected and occasionally pigs as old as 14 weeks have had pathogenic, toxigenic E coli disease. The death loss may vary from minimal to 25-30% or more. Liquid yellow to bloody diarrhea is a common clinical sign. Stomach and colon edema, the hallmarks of edema disease caused by shiga-toxin producing E coli, are infrequent if not rare gross lesions. More frequently, at necropsy there will be a reddened intestinal mucosa with liquid red content, empty GI tract, and mesenteric lymph nodes usually not enlarged. Microscopically, the enterocytes are lined by small rod-shaped bacteria, reactive peyer’s patches. In cases of edema disease, there is necrosis of small arteries and encephalomalacia (which explains the neurological signs that can be seen). Bacteriology is often fruitful and growth of beta-hemolytic E coli with either K88 or F18 pilus genes are the most likely pathogens identified. Non-hemolytic E coli can also possess the necessary pilus and toxin genes for pathogenicity, therefore PCR screening of both non-hemolytic and beta-hemolytic isolates is often done in cases with characteristic clinical signs and lesions. To more completely identify the possible mixed infections in a pig or herd, it is often recommended to test several or all E coli isolates from the intestines.

Escherichia coli infections in swine are common and can be difficult to control. Characterization of the isolates by PCR can be helpful in determining whether or not they are causing the reported clinical signs of disease in the herds and may be useful for the veterinarian when designing herd specific E coli control and prevention programs. PCR characterization has been demonstrated as more sensitive than FA, thus FA is rarely used at the U of MN VDL for E coli pilus typing.

Lawsonia intracellularis

The bacterium Lawsonia intracellularis causes enteritis of varying names including necrotic enteritis, regional ileitis, acute hemorrhagic proliferative enteritis, chronic proliferative enteritis, and porcine proliferative enteropathy. The incubation period is usually 2-3 weeks, with the chronic form usually presenting in pigs 6 to 20-weeks old. The acute hemorrhagic form is usually found in young adult or replacement age gilts and boars. The clinical signs vary from a severe, hemorrhagic diarrhea with sudden death to a more subtle, subclinical diarrhea resulting in and increase in “failure-to-thrive” pigs with inappetance and loose stools ranging from normal color to blood flecked.

Gross lesions in pigs infected with Lawsonia intracellularis are striking. In the chronic form, the organs affected are usually distal ileum and colon. There is a thickened intestinal mucosa with or without necrotic debris and mesenteric lymph nodes may or may not be enlarged. In the acute form, lesions are present in the ileum, colon, and even sometimes in the jejunum. The mucosal thickening is present but can be segmental. There are bloody intestinal contents represented as liquid red to tarry/black feces.

Histopathology for Lawsonia intracellularis is definitive with numerous bizarrely branching and hyperplastic crypts in the ileum being the most prominent feature. The pathogen is identified by PCR or IHC. Regardless of the detection method, the sensitivity is higher early in the infection. PCR has identified feces as positive from pigs as early as 6-weeks-old. Experimentally feces may be positive as early as 7 days post infection. Immunohistochemistry on intestine can be more sensitive than PCR and this may be due to the complex nature of feces as sample for PCR extraction.

Serology for Lawsonia intracellularis is also a useful diagnostic tool. Experimentally 99% of infected pigs seroconvert at 3-weeks post infection. Pigs remain positive for 2 more weeks and then antibodies wane to non-detectable orseronegative. Experimentally seroconversion may be as early as 14 days post exposure. However, in the field, seroconversion is generally only detectable in 5 to 50% as the infection is slow moving.

Post mortem diagnosis is usually straightforward as long as the prosector submits multiple sections of small intestine and colon.

Salmonella enterica spp.

Salmonella Typhimurium is the Salmonella spp. most commonly identified in pigs from weaning to 4 or 5 months of age. Salmonella Choleraesuis has been identified in pigs from weaning to less than 5 months typically. Clinically, pigs with salmonellosis have lethargy, inappetance, fever, and dyspnea. Diarrhea is watery, lasts 3-7 days, and may be recurring or intermittent. In cases of Salmonella enteritis, one may see blood and necrotic debris over several weeks.

Gross lesions of systemic salmonellosis include pneumonia, cyanotic skin (“purple pigs”), hepatomegaly,
Diseases II

Diseases II

Transmissible gastroenteritis virus (TGEV)

TGEV was thought to be eliminated by transitioning swine herds into large, multi-site, unidirectional flow operations is transmissible gastroenteritis virus (TGEV). This change in production management, in addition to biosecurity enhancements such as heating and drying trucks, has not prevented TGEV from occurring on a seasonal basis. In fact, TGEV has even become endemic in some herds. Traditionally, TGEV is characterized by extremely high morbidity in naïve animals and high mortality in newborn pigs, which can cost producers thousands of dollars in lost production and added diagnostic and treatment costs.

TGEV can be diagnosed several ways. Virus can be detected in intestinal sections by fluorescent antibody examinations on flash-frozen tissues and immunohistochemistry (IHC) on fixed sections of intestine. The IHC test, while good, is subject to false negative results for several reasons. False negative results by IHC could occur due to inadequate numbers of sections examined, post-mortem autolysis, and prolonged fixation. Also, IHC is time consuming, requiring fixation of at least 12 hours and another 8 hours of tissue processing. To overcome this diagnostic hurdle, A TGEV PCR test was developed at the University of Minnesota Veterinary Diagnostic Laboratory to aid in the antemortem and post-mortem diagnosis of TGEV infection.

The TGEV PCR test detects a portion of the S-gene (surface glycoprotein) that by analysis should be unique to TGEV and not react with the closely related coronavirus known as Porcine Respiratory Coronavirus. The sensitivity of the TGEV PCR on a TGEV isolate (optimal sample under optimal conditions) is less than 1 TCID50 per milliliter. Fecal samples negative for TGEV were spiked with known dilutions of the TGEV virus isolate. The fecal samples along with a swab from each fecal sample were sent to the virology lab for standard processing and then tested for TGEV by PCR. The sensitivity of the fecal samples and the corresponding fecal swab was the same. Sensitivity on tissue cases was done by comparing the current “gold standard” test, the TGEV IHC. Two hundred and sixty five cases were evaluated. Forty cases were positive by IHC and PCR. Six cases were PCR positive and IHC negative. Of these six cases, each had a clinical history of diarrhea and evidence of villous atrophy. TGEV seroconversion was demonstrated in two of these 6 cases. Specificity of the TGEV PCR was tested against the following isolates with no cross reactivity: PRCV, PRRSV (NA and EU), PCV1, PCV2, SIV H1, SIV H2, SIV H3, PRV, PCMV, HEC, EMC, BVD, PPV, porcine adenovirus, porcine enterovirus, bovine coronavirus, porcine rotavirus (EM positive feces), Lawsonia intracellularis, APP, A suis, Bordetella bronchiseptica, Mycoplasma hyorhinus, Salmonella cholerasuis, Pasteurella multocida, Salmonella typhimurium, Brachyspira hyodysenteriae, Clostridium perfringens and E coli (beta and non-hemolytic). Samples suitable for TGEV PCR are small intestine, feces or fecal swabs.

Since the implementation of the TGEV PCR test, the number of TGEV positive cases has increased. The cases have all been confirmed by immunohistochemistry, clinical signs of diarrhea on the farm, and eventual seroconversion when follow-up was permitted. Thus, perhaps TGEV didn’t go away but was under detected. The widespread prevalence of porcine respiratory coronavirus (PRCV) appears to provide some immune protection against severe clinical signs of TGEV. Therefore, TGEV infections appear milder than those in the past. Because current cases of TGEV appear to have mild clinical manifestations and are frequently found as co-infections in diarrheic pigs with E coli, Salmonella sp., Lawsonia intracellularis, coccidiosis, and rotavirus, the TGEV can be missed if a PCR test is not used. Missing a TGEV diagnosis or discounting it because it doesn’t present like it did long ago with 100% morbidity and > 50% mortality can be a costly mistake.

Yersinia spp.

Yersinia spp., specifically Y enterocolitica, is a rare but possible enteric pathogen of finisher age pigs. It is usually a diagnosis of exclusion and cultures are done after more common pathogens have been successfully ruled out. A culture of Yersinia enterocolitica is accompanied by characteristic clinical signs and lesions before a diagnosis is made.

Stomach ulceration

An upper gastrointestinal disease such as an ulcerated stomach may be misinterpreted as bloody diarrhea. Rather,
digested blood is passed through the colon and this is termed melena. Because melena is dark red and tarry stool that may look like diarrhea, any post-mortem examination of a finisher pig should include examination of the stomach for ulceration of the pars esophagea.

**Parasites (Trichuris suis)**

Whipworms cause large intestine ulceration and necrosis that needs to be differentiated from *Brachyspira spp.*, *Salmonella spp.*, ileitis, and *Yersinia spp.* A fecal floatation examination for oocysts will suffice as does a history, or lack thereof, of outdoor housing.

**Sulfates/water quality/nutrition**

I am not a nutritionist nor do I play one on TV. Nevertheless, poor water quality and/or improperly mixed feeds can be a cause of diarrhea in finisher age pigs. These conditions are considered possibilities or causes of diarrhea usually only after all infectious agents have been eliminated. Water assessments and nutritional analyses are available to assist the veterinarian in a diagnosis of feed or water related diarrhea.

**General conclusions**

As with most disease entities of swine, they are can be multi-factorial and require a bit of diagnostic savvy and patience to accurately diagnose. In the case of *Brachyspira spp.* or nutritional causes of diarrhea, the diagnosis can be slow or only made by exclusion.