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In an approach to investigating any suspected disease or disorder in swine production, a history should be gathered first. Important history to understand from caretakers includes: age of pigs affected, duration of clinical signs, morbidity rate, mortality rate, treatments administered, response to treatments, and any other important information regarding previous diagnoses or disease in the affected group of animals. This is also the time to examine any production records that have been kept on the affected group of swine as well as previous groups for comparison. Records include but are not limited to: where the animals originated from; number in the herd; age; daily mortality; number treated; name of treatment, route of delivery and dose; feed and water usage; high–low temperatures; and vaccinations received or administered. After examining the production records and obtaining a history, proceed with a visual examination of the herd. Typically, it is a biosecurity custom to observe youngest groups first; however, in cases of suspected infectious diseases, it may be best to begin with the healthiest group advancing in order of increasing severity or prevalence.

Often, a definitive diagnosis is not achieved without an extensive clinical and pathological investigation. A post-mortem examination, or necropsy, of affected pigs should occur last. Any pigs recently deceased of natural causes should be examined to establish trends, with the understanding that submission of tissues from these animals may not yield valuable diagnostic results. Tissues for diagnostic evaluation should be collected from clinically affected pigs that are euthanized immediately before necropsy. Sampling of five or more pigs may be required to obtain a valuable diagnosis. When investigating signs referable to the central nervous system (CNS), it is important to preserve brain and spinal cord tissue for microscopic evaluation in cases of neurological disease; therefore, blunt force trauma and brain penetration by captive bolt are not preferred methods of euthanasia. At minimum, fresh and formalin-fixed tissue samples should include: brain, tonsil, heart, lung, lymph nodes, spleen, kidney, liver, and intestine. Additional samples that may be beneficial for diagnosis include: premortem whole blood and ethylenediaminetetraacetic acid-chelated blood (for serum chemistry and complete blood count), spinal cord, intact stifle and hock joints (remove the leg at the hip), intact eyeball with optic nerve attachment, urine, feed, and water. Consult a diagnostic lab regarding any additional samples that may be required in determining an etiologic diagnosis. The etiologic diagnosis should be based on consistent history, signs, and pathology derived from a list of differential diagnoses that are most common or most likely to occur in that herd or production system.

A treatment, control, or prevention program should be formulated simultaneously. Before using any chemical, pharmaceutical, or biologic in swine intended for food, know the domestic use guidelines, importer requirements or producer-packer agreements regarding withdrawal times, residue and tolerance limits, prescribing guidelines, and prohibited substances.

Central Nervous System Diseases and Disorders

This section will focus on a practical approach to investigating signs of neurological disease in swine summarized in Table 1. It is important to determine if clinical signs are consistent with CNS or peripheral nervous system lesions (PNS). Common CNS signs in pigs include behavioral abnormalities (most commonly stupor), ataxia, loss of righting, seizures or
seizure-like activity (paddling), nystagmus, and blindness. Musculoskeletal disorders may clinically confuse or complicate perceived PNS signs and must be differentiated from each other.

*Streptococcus suis* is a gram-positive cocci with 35 reported serotypes. Observational studies implicate sows as carriers and piglets are colonized as they pass through the birth canal (Amass *et al.*, 1996). Disease occurs most frequently during the suckling and postweaning period. Commingling pigs from different herds, concurrent infection with porcine reproductive and respiratory syndrome (PRRS), and other stress factors may increase the risk of developing *S. suis* meningitis (Villani, 2002; Thanawongnuwech *et al.*, 2000). Variable morbidity and mortality: mortality depends on early recognition and treatment. Clinical signs of *S. suis* meningitis include paddling, recumbency, nystagmus, and seizure. Isolation of *S. suis* from the lung, nasal secretions, or tonsil from normal pigs is clinically insignificant. In contrast, *S. suis* isolation from cerebrospinal fluid (CSF), meninges, joints, endocardium, or serosal surfaces with or without lesions is relevant (Pijoan, 1994). Few to no gross lesions may be observed during necropsy. Early recognition of clinical signs followed by injection with an antimicrobial that *S. suis* is susceptible is the most effective means of treatment. Administering an antimicrobial that *S. suis* is susceptible to in the drinking water has been proposed to control morbidity (Villani, 2002). Antimicrobial susceptibility patterns for *S. suis* isolates from regional diagnostic laboratories can be used to assist in selection of an appropriate antimicrobial while diagnostic tests are pending; cefotiofur is effective (Halbur *et al.*, 2000). Commercial and autogenous vaccines are available but due to *S. suis* serologic diversity may not be effective (Halbur *et al.*, 2000).

*Haemophilus parasuis* (HPS), also called Glässer’s disease, causes bacterial meningitis, arthritis, and polyserositis similar to *S. suis*. Infections are not clinically or grossly distinguishable from *S. suis*. Definitive diagnosis is by bacterial isolation. However, HPS is a fastidious gram-negative rod and culture media must be supplemented with V factor for successful isolation. Owing to the difficulty in isolating HPS, Polymerase chain reaction (PCR) tests are a suitable alternative (Oliveira *et al.*, 2001). Like *S. suis*, isolation from the airways has little significance unless lesions are present (Hoefling, 1994). Antimicrobial susceptibility testing identifies cefotiofur or florfenicol that are typically effective first choice therapeutics (Oliveira, 2007b). Prevention may be achieved with medicated early weaning.

Edema disease results when a fimbrial (F18 or F4) and shiga-like toxin (StX-2e) positive strain of *Escherichia coli* successfully attaches to brush border receptors releasing toxin that damages blood vessels including those of the blood–brain barrier causing edema and encephalomalacia. Edema disease most commonly affects rapidly growing pigs, 2 weeks postweaning. Morbidity is moderate to high and mortality is high. Acute death of robust pigs, ataxia, eyelid swelling, and diarrhea are typical clinical signs (Rademacher, 2001). At necropsy, edema may be observed in the mesentery between the loops of the spiral colon and in the cardiac region of the gastric mucosa. Stomachs are usually full of feed. Bacteriologic isolation of a β-hemolytic strain of *E. coli* from affected pigs with meningoencephalitis is not sufficient for a diagnosis. Genotyping is necessary to confirm that the *E. coli* isolated was F18 or F4 and StX-2e positive and thus capable to induce such lesions. There is no effective treatment. Vaccination using an avirulent live culture of *E. coli* postweaning, thorough cleaning and disinfection between groups, and use of genetically resistance breeds that lack the fimbrial receptor are preventative (Fairbrother and Gyles, 2006).

Pseudorabies (PRV), also known as Aujezsky’s disease, is caused by a herpesvirus. PRV was eradicated from the US commercial swine herd in 2004 (USDA APHIS, 2008). Feral swine are potential reservoirs. Cattle, sheep, dogs, and cats can also be infected with PRV. High morbidity is due to large quantities of virus shed in saliva and nasal secretions for several weeks following infection. Mortality is inversely related to age approaching 100% in neonates. Clinical signs are also age dependent. Neonates may die without signs. Suckling and recently weaned pigs are those that commonly exhibit ataxia, tremors, excess salivation, and seizures. At necropsy, the brain appears congested and hemorrhagic. Necrotic foci occur in the spleen, liver, lung, lymph node, and specifically tonsils. Histopathologic lesions are characterized by non supplicative meningitis and intranuclear inclusion bodies. PCR, virus isolation (VI), immunohistochemistry (IHC), or fluorescent antibody can be used to confirm the diagnosis. No specific treatment is available. Vaccination and eradication are effective for control (USDA APHIS, 2008). In areas free of PRV, suspicion of the disease should be reported to state and federal agencies as required.

Congenital tremors result when hypomyelination or demyelination of the brain and spinal cord. Clinical signs are clonic muscle contractions that cause a general tremor of the entire body. Pigs are affected at birth but severity subsides with

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**Table 1** Common central nervous diseases and disorders of pigs

|                      | Preweaning | Postweaning nursery | Postweaning grow–finish | Adult |
|----------------------|------------|---------------------|-------------------------|-------|
| *Streptococcus suis* | ++         | ++                  | ++                      | ++    |
| HPS                  | +          | ++                  | +                       |       |
| Edema disease        | ++         | ++                  |                         | +     |
| PRV                  | ++         | +                   |                         |       |
| Congenital tremor    | ++         |                     |                         |       |
| Hypoglycemia         | ++         |                     |                         |       |
| Water deprivation    | ++         |                     |                         | ++    |

*Note: The first column provides the diseases. The remaining columns represent the respective phases of production. The frequency of the occurrence is + (occasional), ++ (common), and +++ (routine).*
Gastrointestinal System Diseases and Disorders

Gastrointestinal diseases and disorders can occur in all ages of swine as summarized in Table 2. Most digestive diseases are referable to the gastrointestinal tract and result in diarrhea and occasional vomiting. Diarrhea is the result of an intestinal dysfunction caused by malabsorption, excessive secretion, or effusion. Unfortunately, this is not an exclusive characterization of diarrhea and overlap occurs (Moeser and Blikslager, 2007). Rather, differentials for diarrhea should be referable to age at onset and site of infection.

Gastric ulcers are noninfectious and result when glandular mucosa specifically the pars esophagea is traumatized by gastric acid. Gastric ulcers have a wide variety of causes but are most commonly associated with small feed particle size (Ayles et al., 1996) and interruption of feed intake whether caused by disease or poor management. It is common to see signs consistent with gastric ulceration increase following an acute PRRS or influenza outbreak. Morbidity and mortality vary with the scope of the underlying cause. Clinical signs include regurgitation, vomiting, pallor or jaundice, and acute death. An acutely dead pig with blood in its stomach is indicative of an active ulcer and is sufficient evidence for a diagnosis. In chronic cases, ulceration causes hyperplasia resulting in stricture of the pars esophagea and regurgitation. Feeding a coarse ground diet for 3 weeks significantly decreases severity (Ayles et al., 1996) but is impractical in modern production facilities.

Rotavirus is a nonenveloped RNA virus with a double-layered capsid allowing it to remain stable and infective in the environment for months and intrinsically resistant to some disinfectants. Four serogroups infect swine: A, B, C, and E (the latter only reported from the United Kingdom). In addition, infections with particular serogroups vary by age: Type C mostly in suckling piglets and Type A predominately in nursery pigs (Stephenson et al., 2013). Type A is the most prevalent serogroup. Severity of disease decreases with age and is self-limiting. The virus infects and destroys villous enterocytes resulting in villous atrophy. In response, crypt cells fill in the gaps but, because they are incapable of absorption, suckling piglets quickly lose body condition and have a gaunt or wasted appearance. Neither clinical signs nor gross lesions are pathognomonic although loops of small intestine appear thin-walled with moderate to large amounts of watery contents. A histopathologic report of blunted villi and crypt hyperplasia is suggestive of rotavirus infection. Infection with rotavirus can be confirmed by PCR or electron microscopy (EM). Enzyme-linked immunosorbent assay (ELISA) is also available but limited to detection of serogroup A. IHC and EM detect rotavirus and confirm its role in pathology, but both tests lack

| Table 2 | Common gastrointestinal diseases and disorders of pigs |
|---------|-------------------------------------------------------|
|         | Preweaning | Postweaning nursery | Postweaning grow–finish | Mature |
| Gastric ulcer                    | +          | +                    | +++               | ++     |
| Clostridium difficile           | ++         | +                    |                   |        |
| Clostridium perfringens Type A (CpA) | ++         | +                    |                   |        |
| Clostridium perfringens Type C (CpC) | ++         | +                    |                   |        |
| Coccidiosis                      | ++         | ++                   |                   |        |
| Salmonellosis                    | ++         | ++                   |                   |        |
| Colibacillosis                   | ++         | ++                   |                   |        |
| Swine Dysentery                  | +          | ++                   |                   |        |
| Porcine proliferative enteropathy (PPE) (Ileitis) | +++       | +                    |                   |        |
| Rotavirus                        | ++         | ++                   |                   | +      |
| Transmissible gastroenteritis (TGE) | ++         | ++                   |                   |        |
| Porcine epidemic diarrhea (PED)  | ++         | +                    |                   | ++     |
| Whipworms                        | ++         | ++                   |                   | +      |

Note: The first column provides the diseases. The remaining columns represent the respective phases of production. The frequency of the occurrence is + (occasional), ++ (common), and +++ (routine).
sensitivity. Treatment is supportive by administration of oral rehydration solutions. Acidifiers and antibiotics are sometimes administered to control secondary bacterial infections. Treatment success is variable and depends on the degree of malnutrition. Prevention among neonatal piglets is through ingestion of lactogenic virus neutralizing antibody from the sow, which is stimulated by administering feedback of Rotavirus positive piglet feces or intestines (Arruda et al., 2011) or a modified-live commercial Type A vaccine no less than 3 weeks before farrowing. A modified-live commercial Type A vaccine is also available for pigs. It does not induce cross-protection for other serogroups and may be cost-prohibitive.

TGE is caused by TGEv, a coronavirus that is heat labile at temperatures above 21°C, prone to desiccation and photosensitization (Bay et al., 1952). The epidemic form causes acute disease in all age groups within as little as 18 h of infection. Morbidity and mortality is high, approaching 100%, in an epizootic outbreak. The severity of disease is age dependent but all ages will develop diarrhea (Moeser and Blikslager, 2007). Postweaning infections result in high morbidity but low mortality; the most significant economic losses at this time are caused by reduced average daily gain, market weights, and overall system efficiency. Necropsy reveals that the small intestine and colon are fluid filled, the small intestinal wall is thin almost translucent, and lacteals are empty. Necrosis and atrophy are observed throughout the length of the villus. The colon and cecum are spared. The endemic form occurs when susceptible animals are introduced to the herd or after maternal antibody wanes. Prior exposure to porcine respiratory coronavirus (PRCV) may cause false-positive antibody test results. A TGEv/PRCV differential ELISA is available. In an outbreak, sows are fed tissue of diarrheic pigs to stimulate herd immunity and new introductions of animals are stopped. After the exposure and a subsequent cool-down period of 4–6 months or after clinical signs cease, sentinel can be introduced and monitored for seroconversion (Saif and Sestak, 2006). Absence of seroconversion indicates successful elimination of TGEv. Commercial vaccines are available but should be used with caution and only when elimination is not an option.

PED is caused by PEDv, a coronavirus that causes signs and histopathologic lesions indistinguishable from TGEv. Unlike TGEv, PEDv is more environmentally resistant making elimination more difficult. The disease has been described in Europe, Asia, and, as of 2013, the United States. Prevalence of the enzootic form is approximately 50% (Chae et al., 2000). Morbidity approaches 100% and mortality is 80% or more in a naïve sow herd resulting in 3–5 weeks of production losses. Clinical signs appear within 12 h; piglets develop a watery, fetid diarrhea leading to dehydration, metabolic acidosis, and death before caretakers are able to humanely euthanize them. Vomiting also occurs. The severity of disease is age dependent but all ages will develop diarrhea. Postweaning infections result in a high morbidity but low mortality; most significant economic losses at this time are caused by reduced average daily gain, market weights, and overall system efficiency. Viral shedding occurs up to 10 days postinfection. Reproductive failure and inefficiency is a sequela of an outbreak (Olanratmanee et al., 2010). TGEv/PEDv differential PCR is available to confirm a presumptive diagnosis of PED. Serum can be submitted for ELISA or immunofluorescent antibody but collected no sooner than 3 weeks after diarrhea was observed. Immunoprophylaxis using egg antibody or hyperimmune serum and supportive care including electrolyte administration have been used for treatment. In an outbreak, sows are fed tissue and feces from diarrheic pigs to stimulate herd immunity (Olanratmanee et al., 2010). Hygiene is the key to reducing environmental contamination. Preventing introduction of virus into a herd with biosecurity alone may not be sufficient because the virus has been found in aerosol up to 10 miles from a positive farm (Goecke et al., 2013).

Porcine coccidiosis is most often caused by Isospora suis. Farm hygiene, specifically farrowing rooms, and sow infestation influence the persistence of disease; however, age at infection rather than infectious dose has the greatest impact on severity (Worliczek et al., 2009). The prepatent period is approximately 5 days. Morbidity is variable and mortality is low. Pasty diarrhea, unthriftiness and appearance of 7–21 day old pigs, and below average wean weight is suspicious for coccidiosis. On necropsy, the small intestine is thickened and the mucosal surface is necrotic and has an adherent pseudomembrane. Histopathologic examination of the affected portion of the intestine reveals larvae in the lamina propria. Sensitivity of fecal flotation is moderate. There is no effective treatment. Prevention is by oral administration of an anticoccidial (Maes et al., 2007). Heat treatment (flaming) of flooring may reduce environmental contamination. Concrete, rubber coated and plastic flooring in the farrowing crates are difficult to clean and disinfect so removal may be the only option.

Swine dysentery (SD) is a spirochete of the genus Brachyspira that is an oxygen-tolerant anaerobe giving it the ability to survive for long periods of time in manure, pits, and lagoons (Schwartz et al., 2012). Rodents, particularly mice, are known vectors and can serve as reservoirs. Brachyspira hyodysenteriae is the species known for causing SD. Other species of Brachyspira have been recently described in dysentery-like disease (Burrough, 2012). Incubation is 10–14 days but disease occurs in a 3–4 week cycle. Administration of tiamulin or lincomycin in the feed or water may alter the time to onset of signs after exposure. Morbidity is high and mortality is low to moderate characteristically causing disease in only the finisher and mature groups. Economic significance is mostly lost performance due to reduced daily gain and feed conversion. The specific mechanism of pathogenesis is not well understood but the spirochete does not invade the lamina propria. Clinical signs are the presence of mucohemorrhagic diarrhea containing flakes of frank blood or appearing as a generalized brick red to rust color. Lesions are mostly observed in the spiral colon where epithelial sloughing and mucosal invasion cause necrosis resulting in the formation of a pseudomembrane. The colonic walls may be thickened due to vascular congestion and mucosal hyperplasia. Bacterial culture produces strong β-hemolysis. PCR test for confirmation and speciation is recommended for any isolate with characteristic growth. Introduction of infected pigs and contaminated equipment or facilities are the source of infection. Pleuromutins, like tiamulin, and the lincomamide, lincomycin, are effective for treatment. However, if the environment remains contaminated, clinical signs will recur. Depopulation has resulted in
successful eradication (Harms, 2011). Medicated elimination that combines thorough pulse medication with tiamulin, cleaning and disinfection, and employment of an aggressive rodent control program is also effective (Burrough and Sexton, 2013).

*Escherichia coli* is a gram-negative rod that infects all ages of swine but must express virulence factors to cause diarrhea. *Escherichia coli* colonize the small intestine by fimbria that binds receptors on the villous surface of enterocytes. Enterotoxigenic *E. coli* (ETEC) then produce toxin(s) that increase osmolality leading to diarrhea (Moese and Blisklager, 2007). ETEC is subdivided by fimbria, toxin, and age of pig affected. Neonatal diarrhea (ND) is most common in pigs 0–7 days of age. The onset of postweaning diarrhea (PWD) caused by F18 is delayed, occurring 5–14 days postweaning, compared to that caused by F4 and its severity is indirectly related to wean age. Clinical signs are profuse diarrhea, rapid dehydration leading to emaciation, or death due to metabolic acidosis. Fluid filled and hyperemic sections of jejunum and ileum may be present at necropsy but few consistent gross lesions occur. Intestinal contents have a distinctly alkaline pH. Isolation of large numbers of *E. coli* and with dense layers of rod-shaped bacteria covering villi seen on histopathology in samples from pigs with diarrhea is sufficient for diagnosis of *E. coli* but not ETEC. Genotyping is necessary to determine fimbria and toxin types, which are essential to confirm diagnosis of ETEC. Treatment of affected pigs/litters/groups includes administration of antibiotics and oral rehydration solution or electrolytes to correct hyperkalemia (Kiers et al., 2006). Control and prevention of ND is by passively derived lactogenic immunoglobins from vaccinated females (Kohler, 1974). Prevention of PWD include selection of genetically resistant breeds lacking K88 and F18 receptors, administration of an oral avirulent live culture to stimulate active immunity or competitively exclude field strains (Genoves et al., 2000), feeding 2500 ppm zinc oxide postweaning and probiotics. Immunity and exclusion is unique to each fimbria; vaccines should include the prevalent genotype(s) causing the diarrhea.

*Clostridium perfringens* Type A (CpA) is a gram-positive bacillus and inefficient sporulator. Sows are regarded as the source of neonatal infection. Frequency of CpA diarrhea is on the rise in the USA. In uncomplicated cases, mortality is low whereas morbidity is high and below average weaning weights result. Cases of CpA diarrhea are associated with the expression of α and β2 toxin. CpA is cultured from the stomach and upper third of small intestine but does not bind intestinal epithelium causing few to no histologic lesions. Because of its ubiquitous nature and prevalence among health pigs, CpA may be an opportunistic and its role as a primary cause of neonatal enteritis is not definitive. Large numbers (3+ or 4+) of gram-positive bacilli cultured from feces or intestinal contents of diarrheic pigs is suggestive of CpA. Genotyping by PCR to confirm presence of cpb2 gene in CpA isolates and rule out other causes of ND are supportive to the diagnosis (Bueschel et al., 2003). Treatment has variable success rates and is limited to administration of empirically selected antibiotics and oral rehydration solutions to affected piglets. Control of CpA enteritis is best accomplished by preventing other causes of ND. Following a thorough cleaning, sporidal disinfectant should be applied to farrowing crates and equipment between litters and be allowed to dry before reloading. Feeding of bacitracin to sows has resulted in significant increases in weaning weights (Schultz, 2007). A commercial CpA toxoid vaccine is available (Hammer et al., 2005). Autogenous whole cell vaccines are also in use. If vaccine is unavailable, feedback might be considered but should be pursued with caution (Robbins and Byers, 2013a).

CpC is a gram-positive bacillus and inefficient sporulator. Sows are regarded as the source of infection. Pathogenesis of type C is due to expression of β toxin leading to necrosis of intestinal epithelium resulting in hemorrhagic diarrhea or acute death of piglets less than 3 days of age. Gross necropsy reveals hemorrhagic and blood-filled loops of small intestine. A pseudomembrane may form on the luminal surface, and intestinal mucosa is edematous. Gross and histopathologic lesions in the presence of large numbers (3+ or 4+) of gram-positive bacilli cultured from feces or intestinal contents warrant a presumptive diagnosis. Genotyping by PCR to confirm presence of the cpb gene is confirmatory (Songer and Uzal, 2005). Treatment of affected piglets is unrewarding due to the rapid and debilitating course of this disease. Prevention is accomplished by vaccination of gestating females with a commercial toxoid and ensuring piglets consume sufficient colostral antibodies to result in protection.

*Clostridium difficile* is a gram-positive bacillus that easily sporulates making it environmentally resistant to many disinfectants. *Clostridium difficile* associated diarrhea leads to a 10–15% reduction in wean weights (Songer and Uzal, 2005). Although more than a third of piglet diarrhea involves *C. difficile*, it is the better known to cause healthcare-associated infections among humans. The pathogenesis of *C. difficile* infections is in response to the expression of toxins A and B. A watery diarrhea occurs in 1–7 day old piglets. Mesocolonic edema may be observed at necropsy. *Clostridium difficile* is difficult to culture and can be isolated from healthy piglets. Therefore, volcano lesions on histologic exam and confirmation of toxins in fecal contents by antigen ELISA are diagnostic. Treatment is ill-defined but is likely similar to that for CpA enteritis, because it is likely to be initiated based on clinical signs, which are similar. Autogenous vaccines are used to aid in prevention but efficacy is unclear.

PPE, commonly referred to as ileitis, is the general categorization of infections caused by *Lawaonia intracellularis*, an obligate intracellular bacterium. Because the bacteria cause lesions in the ileum, PPE is also referred to as ileitis. Seroprevalence in grow–finish herds can reach 100%. PPE can further be divided into four clinical forms (Kroll et al., 2005). Porcine intestinal adenomatosis (PIA) is most common in 6–20 week pigs and causes little mortality. Porcine hemorrhagic enteritis (PHE) affecting pigs 28 weeks of age and older including breeding swine and can be associated with increased mortality and dark, bloody stools. Necrotic enteritis (NE) and subclinical ileitis, the most common form, occur among postweaning pigs. In all forms, transmission is by the fecal–oral route. Crypt enterocytes infected with *L. intracellularis* become hyperplastic. The altered ratio of villous and crypt enterocytes leads to malabsorption and subsequent increases in feed conversion and time to reach market weights. PIA results in variable degrees of thickened ileum that can be found at necropsy. The ileal lumen may contain a blood clot in PHE.
or pseudomembrane in NE. When diarrhea ranging in color from normal (PNA, NE, and subclinical) to dark-red or black (PHE) is observed, PHE should be considered as a possible cause. Subclinical ileitis usually causes no clinical signs (Gebhart, 2007). Histopathologic lesions containing intracellular S-shaped organisms are suggestive of Lawsonia infection but IHC should be used to confirm diagnosis. PCR is helpful to detect infection and is highly specific but moderately sensitive. Cross-sectional or longitudinal serologic profiles using a widely available ELISA is the best tool for determining timing of exposure. Treatment is with effective antibiotics, such as tylosin, administered by injection or in the feed or water. Control is by administration of a commercially available modified-live oral vaccine before infection or feeding antibiotics when infection is known to occur. Vaccination should take place at least 8 weeks before seroconversion (Walter et al., 2004).

Salmonellosis causing gastrointestinal disease in swine is most commonly associated with the species Typhimurium. *Salmonella* Typhimurium is commonly isolated from swine. Isolation of multidrug resistance strains of *S. Typhimurium* from swine at slaughter have garnered attention from public health and food safety professionals and it is this that make this infection significant for the pork industry (Foley et al., 2008). Some European Union member states have implemented meat-juice serologic monitoring at slaughter to assess on-farm Salmonella control programs. Pathogenesis of *S. Typhimurium* is similar to *Salmonella choleraesuis* by invading enterocytes and subsequently macrophages leading to an infectious carrier state. Initial infection causes inflammation and cytokine release that result in watery, yellow diarrhea containing fecal particles. Button ulcers may be visible on the mucosal surfaces of the colon and cecum on gross necropsy examination and, on histopathology, can be found to extend into the lamina propria. Bacterial isolation without using enrichment media and the presence of histopathologic lesions is consistent with a diagnosis of Salmonella enteritis. Treatment is with antibiotics administered symptomatically to diarrheic pigs. Antibiotic susceptibility of the isolate should be considered before initiating treatment. Rearing pigs on slatted floors, decreasing stocking density, and acidification of digesta are effective in reducing the prevalence of Salmonella infections in swine (Funk and Gebreyes, 2004; Boyen et al., 2008). Cross-protection with *S. choleraesuis* vaccine has been reported and reduces carcass colonization (Husa et al., 2009).

Whipworm infestations of swine are the result of *Trichuris suis* infection. Pigs kept on pasture, in outdoor lots, or facilities with a history of *T. suis* diagnosis are at greatest risk for disease (Pittman et al., 2010a). The prepatent period is 6–7 weeks. The egg is not immediately infective, which requires 3–4 weeks in the environment. The infectious larva hatches from the egg and invades enterocytes in the small intestine and cecum. The entire life cycle of *T. suis* is completed in the intestine. Ulcerations in the mucosa and damage to capillary blood supply of intestinal epithelium lead to hemorrhage, anemia, and hypoalbuminemia. Clinical signs are depressed weight gain, increased feed conversion, bloody diarrhea, ill thrift, and death. Adult worms imbedded in the ileum, cecum, or proximal colon are sufficient for diagnosis of whipworms. Eggs are intermittently shed and thus not a reliable method of diagnosis (Pittman et al., 2010a). Treatment and control are synonymous and require administration of an effective anthelminetic like fenbendazole. Prevention is by steam sanitation and drying; however, eggs are resistant to common disinfectants and remain infective for years.

### Integument System Diseases and Disorders

The porcine integument or skin, like that of other domestic species, serves as a protective barrier between fragile internal tissues and harsh external hazards. Skin is comprised of layers (from external to internal): epidermis, dermis (superficial and deep), and subcutis. Blood vessels, hair follicles, sebaceous glands, and muscles are found in the dermis. Notably, the pig’s skin does not contain sweat glands; therefore, modern swine facilities are outfitted with evaporative cooling systems for thermal regulation in hot climates. Skin diseases and disorders can be the result of viral or bacterial infections, parasitic infestations, immunologic reactions, and idiopathic or iatrogenic causes that are summarized in Table 3 by their various macroscopic and microscopic lesions.

Greasy pig is a skin disease of swine caused by a toxin produced by *Staphylococcus hyicus*. A break in the skin is the typical sequela. Gilt litters reportedly have a higher incidence of this disease, presumably due to deficient maternal immunity. All ages of pigs may be affected but suckling and nursery pigs are most likely to develop disease. Affected pigs develop focal crusts on the face, neck, and axillary region, and the crusts may coalesce as the disease progresses. Affected areas are greasy to touch and may appear black due to dirt adhering to it. If pigs are untreated or fail to respond to treatment, the trunk and extremities may become involved. Pyrexia and lethargy can be observed in severe cases and are followed by growth reduction. Gross appearance of affected skin is rarely confused with other skin conditions of swine. Submission of formalin-fixed skin sections that include the junction of affected and unaffected layers of epidermis and dermis for histopathologic examination is needed for a diagnosis. The pathognomonic histologic lesion is exudative epidermitis.

#### Table 3

| Common integument diseases and disorders of pigs |
|-----------------------------------------------|
| **Crust** | **Papule** | **Plaque** | **Pustule** | **Necrosis** | **Erythema** | **Scar** | **Scale** | **Vesicle** |
| Greasy pig | X | X | X |   |   |   |   |   |
| Erysipelas  | X |   |   | X |   |   |   |
| Porcine dermatopathy and nephropathy syndrome (PDNS) | X | X |   | X |   |   |
| Sarcoptic mange | X |   |   | X |   |   |

*Note: The first column provides the diseases. The remaining columns represent the type of lesion that occurs.*
The *S. hyicus* can be cultured from the surface of clinically normal skin sections. Treatment includes topical application of antimicrobials or disinfectants. Unaffected pigs with direct contact with affected pigs should also be treated to control spread. In cases where pigs exhibit systemic signs, administration of an injectable antimicrobial and anti-inflammatory is warranted. In the United States, no antimicrobials are labeled for the treatment, control or prevention of *S. hyicus* so all antimicrobial therapy is extra-label. Prevention should focus on facility hygiene and include a soap degreaser and disinfectant regimen to reduce contamination. In addition, scarification of the skin of breeding age females with the farm-specific *S. hyicus* strain can reduce disease incidence in suckling pigs (Murray and Rademacher, 2008).

Erysipelas or diamond skin disease is caused by a soil-borne gram-positive bacterium, *Erysipelothrix rhusiopathiae*. This zoonotic pathogen is transmitted by migratory fowl, turkeys, and pigs. Humans may become sickened when direct contact with blood from affected animals contaminates an open wound (Brooke and Riley, 1999). The finding of lesions at slaughter results in partial or complete carcass condemnation (Bender et al., 2011). The disease is most common in growing, finishing, and breeding age swine. Bacterial emboli lodge in blood vessels causing vasculitis, thrombosis, and ischemia leading to lameness, abortions in gestating females, and raised, red to purple rhomboid skin lesions for which erysipelas is best known. Skin biopsies from the affected area should include epidermis and dermis, but histologic lesions are only supportive. Bacteriologic isolation or PCR identifying *E. rhusiopathiae* confirms the diagnosis. Treatment with β-lactam antibiotics including penicillin is effective. Commercial bacterins and avirulent live cultures are available for prevention (Wood, 1984) or in the face of outbreaks to prevent the chronic form.

PDNS has been associated with Porcine circovirus type 2 (PCV2) infection, but any disease process resulting in ischemia could cause result in PDNS. The condition is characterized by red to purple discoloration of skin that begins on the caudal surface of the hind limbs and the ventral surface of the abdomen resulting from ischemia. On necropsy, gross examination of the kidney cortex may be speckled with pinpoint, white foci caused by infected blood vessels. Pig of any age can be affected with PDNS, but it is more commonly observed during growing and finishing stages. Submission of fresh and formalin-fixed skin sections that include the junction of affected and unaffected layers of epidermis and dermis is required. There is no specific treatment or prevention; rather, diagnose the underlying cause to determine appropriate therapy (Figure 1).

Sarcoptic mange is the result of an allergic reaction to the saliva of ectoparasites, *Sarcoptes scabiei*. Mange may also be caused by *Demodex phylloides*. Mortality is low and morbidity is moderate. Economic losses are the result of reproductive inefficiency, growth reduction, and carcass condemnation. Infection and subsequent clinical signs in the breeding herd, most notably an incessant scratching, develop following the purchase of infested genetic replacements. In addition, growing pigs placed in facilities that previously housed infected swine or facilities that reuse straw bedding or have solid wood partitions may also become infested. The mite is rare in modern, high-health swine operations. The burrowing mite causes red pustules and flaking skin. Individual pigs may develop signs in as few as 3 weeks but a herd may not show signs for several months. In the chronic stage, thick crusts develop at the corners of and inside the ears. Examination of a scraping from the crusts will reveal the mite (Averbeck and Stromberg, 1993). An ELISA test is used to determine prior exposure and determine success of eradication programs. Treatment can be applied topically using an antiparasitic, such as amitraz, to temporarily alleviate clinical signs. Control and eradication programs utilize feeding or injection of ivermectins (Mohr, 2001).

**Musculoskeletal System Diseases and Disorders**

The musculoskeletal system is comprised of tendons, ligaments, muscles, and bones. Disorders and disease of this system are typically characterized by lameness. Lameness is any deviation in normal locomotion including favoring a limb or failure to bear weight on the limb. Neurologic conditions, which also cause changes in locomotion, may be ruled out by postmortem examination of articular surfaces and diagnostic testing. Investigation of musculoskeletal diseases and disorders should always start with the claws that are easily traumatized causing pain resulting in lameness. Flooring and genetics also influence the incidence of lameness. Common musculoskeletal diseases and disorders of swine can be divided into osteopathies and myopathies and summarized in Table 4.

*Mycoplasma hyosynoviae* colonizes upper airways and tonsils resulting in a carrier state. Transmission is vertical from sow to pigs and lateral between pigs (Ross and Spear, 1973). *M. hyosynoviae* is most often diagnosed during the grow–finish phase. Morbidity is variable but mortality is low. Clinical signs are a stiff gait and difficulty in standing, most often the stifle or elbow and less frequently the hock, hip, and shoulder. Signs often occur 2–3 weeks after a stressful event; lesions begin to resolve 7 weeks postinfection. The affected joint contains yellow or blood-tinged effusion with moderate

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**Figure 1** PDNS, skin, grow-finish pig. Hemorrhagic pustules, coalescing areas of erythema, crusts present on hind limbs and abdomen. Courtesy Dr. Glen Almond.
Table 4  Common musculoskeletal diseases and disorders of pigs

|                  | Preweaning | Postweaning nursery | Postweaning grow–finish | Adult |
|------------------|------------|---------------------|-------------------------|-------|
| Mycoplasma hyosynoviae | ++         | ++                  | ++                      | ++    |
| Mycoplasma hyorhinis   | ++         | ++                  | ++                      | ++    |
| Erysipelas            | ++         | ++                  | ++                      | ++    |
| Osteochondrosis (OC)  | ++         | ++                  |                         |       |
| Ricketts             | ++         | ++                  |                         |       |
| Mulberry heart disease (MHD) | ++ | ++                  |                         |       |
| Splayleg             | ++         | ++                  |                         |       |

Note: The first column provides the diseases. The remaining columns represent the respective phases of production. The frequency of the occurrence is + (occasional), ++ (common), and +++ (routine).

villous proliferation but is not always observed despite lameness and does not necessarily correlate with presence of histopathologic lesions. Aseptic collection of synovial fluid by needle aspiration or sterile swab or submission of the affected joint intact is recommended for diagnosis. PCR is the most sensitive test; culture requires special media and lacks sensitivity (Gomes Neto et al., 2012). Histopathologic examination of formalin-fixed synovium reveals nonsuppurative fibrinous polyarthritis and lymphoplasmacytic perivascular synovitis. ELISA is also available. Lincomycin has historically been an effective therapeutic choice (Burch and Godwin, 1984). Treatment should be initiated when lameness is first observed; however, spontaneous resolution is common. No commercial vaccines are available.

Mycoplasma hyorhinis is a ubiquitous bacterium that is an early colonizer of upper airways. Transmission is vertical from sow to pigs and then between pigs postweaning (Rovira, 2009). Infection can progress to polyarthritis, polyserositis, and otitis in the pre- or postweaning phases; arthritis develops postweaning. Clinical signs include lameness, arthritis, and fever that develop 3–10 days after septicemia occurs and persists for 10–14 days (Gomes Neto et al., 2012). Disease may become chronic resulting in ill thrift, reduced growth, and death. Articular surfaces may be eroded. In cases of lameness, synovial fluid and formalin-fixed synovium can be submitted. Alternatively, the entire affected leg can be submitted; disarticulate above the infected joint keeping the affected joint intact. Submission of fibrin or fibrin covered tissue(s) should be included for PCR testing to differentiate M. hyorhinis from other bacteria that form fibrin on serosal surfaces like HPS and S. suis (Rovira, 2009). Histopathology reveals fibrinosuppurative inflammation in affected tissues. Treatment is empirical.

Erysipelas is the result of a chronic E. rhusiopathiae infection causing arthritis and endocarditis that follows the initial septicemia. Lameness and joint swelling is mostly noticeable in hock and carpal joints. Lameness may also occur in stifle and elbow but swelling cannot be appreciated. Synovial fluid appears serosanguinous and can be submitted for testing by bacterial culture or PCR. Alternatively, the entire affected leg can be removed to prevent contamination; disarticulate the leg above the infected joint. Histopathologic examination of formalin-fixed synovium reveals a proliferative synovitis. Other lesions that occur are nonsuppurative fibrinous polyarthritis and erosion of cartilage that can progress to pannus and ankylosis. Treatment with β-lactamase antibiotics including penicillin is effective. An anti-inflammatory is added to a treatment program for pain management. Commercial bacterins or avirulent live cultures are available for control and prevention.

OC is the result of a delay in ossification of articular cartilage, and represents the most common lesion among culled sows. Morbidity is most often reported in adult and breeding age pigs (Dewey et al., 1993). Mortality is variable and is the result of humane euthanasia because the animal becomes nonambulatory. OC causes lameness, pain, and joint swelling. A noninfectious lameness most often affects the distal part of the humerus or femur. Lesions are typically bilateral and symmetrical. Diagnosis is made by ruling out other causes of lameness.

Ricketts occurs as a result of phosphorus deficiency, vitamin D deficiency, or secondary to iron toxicity but is not caused by dietary calcium deficiency. The condition should be suspected when there is an increase in nonambulatory pigs and broken bones during the finishing stage particularly at and immediately before marketing. Occasionally, joint swelling in the nursery stage is observed. Rachitic rosary (enlargement of costochondral junctions) and soft bones are observed on necropsy. If rickets are present, a bone ash analysis of the second rib will be below normal. Feed analysis can identify low levels of vitamin D or phosphorus. Low levels of vitamin D or phosphorous serum chemistry also will occur (Madson et al., 2012). Supplementation of vitamin D is the only reported treatment and response that may be considered diagnostic. Prevention includes proper diet formulation for the stage of production.

MHD is a noninfectious disease of muscle caused by deficiency of vitamin E or selenium. It can occur if pigs are fed grain grown in selenium deficient soils (Dewey, 2006). Clinical signs are limited to acute death of large, robust pigs. On necropsy, the heart muscle has a mottled appearance. Feed analysis, response to vitamin E supplementation, and ruling out other causes support diagnosis of vitamin E/selenium deficiencies like MHD (Hooser, 1996). Supplementation with selenium is impractical in the United States because of environmental regulations, and overzealous supplementation may cause toxicosis.

Splayleg is a noninfectious, congenital condition resulting from delayed myofibril development with no known cause. Splayleg has low morbidity and mortality as long as it is identified and corrected before it leads to starvation or being crushed by the sow. Treatment includes the use of nonslip
flooring in farrowing crates and application of harness or tape that holds the rear legs under the pig until it is strong enough to walk on its own.

**Reproductive System Diseases and Disorders**

Reproductive failure occurs when insemination fails to result in pregnancy or pregnancy fails to produce viable pigs due to infectious and noninfectious causes summarized in Table 5. Reproductive failure should be considered when a low conception or farrowing rate, irregular returns to estrus, abortions, stillbirths, or mummies persist at an abnormal rate. Infertility occurs when fewer than four embryos are present at the time of maternal recognition of pregnancy resulting in a regular return to estrus and reduced conception rate for that breeding group. Irregular returns to estrus result from embryonic death or early term abortion after implantation but before calcification of the fetuses. Embryonic death of some or all of the embryos will result in low total born or irregular return to estrus, respectively. Early term abortion also will reduce farrowing rates. Mummies and stillborns can occur any time after calcification of the fetuses. The normal rates for mummies and stillborns are <0.5 and <1 pig per litter, respectively. Late-term abortions are classified as those occurring after 70 days of gestation. Total abortion rate should remain <2% of a breeding group. These are general guidelines; thus, familiarity with the herd's normal reproductive performance is the most sensitive means to identify a reproductive problem.

PRRS is, at this time, known only to occur among swine. The estimated cost of PRRS to the US pork industry is US$664 million annually (Holtkamp et al., 2013). PRRS usually results when susceptible swine are infected with either the Leylystad or North American strains of PRRS virus (PRRSv), a member of the Arteriviridae family. Viremia lasts up to 42 days, but shedding of infectious virus can last much longer (Murtaugh and Genzow, 2011). PRRSv is most commonly transmitted by introduction of infected swine or contaminated fomites, use of contaminated semen, and aerosol. The pathogenesis of the reproductive form is believed to be arteritis of fetal umbilical cords during gestation (Lager and Halbur, 1996). Swine may show no signs when reinfected with a homologous strain. Conversely, infection with a heterologous strain will reproduce lesions and disease but is usually less severe than that of naive swine (Murtaugh and Genzow, 2011). Clinical signs of PRRS in a breeding herd start with an epidemic of abortions followed by an increase in low viable piglets, stillbirths, and mummies. Abortions result due to fetal death or pyrexia of the gestating female. Sows and gilts may be anorexic, pyrexic, or lethargic. Periparturient females may become agalactic. In severe outbreaks of PRRS, sow mortality also increases. In utero infection of feti can result in persistently infected piglets (Rossow, 1998). Prewean mortality commonly increases and may remain above the herd average for weeks. Diagnosis can be made by submitting lung, spleen, and lymph node from fetuses or low viable piglets. Whole fetuses can also be submitted but should be refrigerated to prevent autolysis. Lesions are not pathognomonic so confirmatory testing such as PCR, IHC, or VI should be conducted. Tissues and thoracic fluid from stillbirths, aborted, or mumified feti can be submitted but may result in false negatives. Serum collected from aborted sows or low viable piglets and tested for PRRSv by PCR is another option for diagnosis. PRRSv ELISA indicates previous exposure but is not useful in a previously exposed herd. Treatment of PRRS is supportive. Anti-inflammatories to reduce fever and antibiotics for control and treatment of secondary bacterial pneumonia may be necessary. The most common methods for control include depopulation–repopulation and herd closure and rollover, also called load-close-homogenize, using commercial vaccine or herd-specific live virus exposure (Corzo et al., 2010). Periods of closure vary based on facility capacity but a minimum of 180 days is recommended. Commercial modified-live and killed vaccines are available but do not prevent infection and should be used in accordance with label and domestic guidelines.

PPV is sometimes described by the acronym SMEDI (stillborns, mummies, embryonic death, and infertility). PPV is an enzootic infection of swine breeding herds in the United States. The virus is ubiquitous and is transmitted through ingestion of infected feces, afterbirth, or fetal tissue. The disease most commonly affects gilts and younger parity sows (Christianson, 1992). The pathogenesis is through damage to

**Table 5**  Common reproductive diseases and disorders of pigs

| Diagnosis                  | Embryonic death | Abortion | Mummies | Stillbirths | Infertility | Weak born pigs | Low total born |
|----------------------------|-----------------|----------|---------|------------|-------------|----------------|---------------|
| PRRS                       | ++              | +++      | +++     | +++        | ++          | +++            | ++            |
| Porcine parvovirus (PPV)   | ++              | ++       | +++     | +++        | ++          | +++            | ++            |
| Porcine circovirus type 2 (PCV2) | ++             | +        | +++     | +++        | ++          | +++            | ++            |
| Leptospirosis              | ++              | ++       | +       | ++         | +++         | +++            | ++            |
|                            | (Pomona)        | (Bratislava) |        |            |             |                |               |
| PRV                        | ++              | +++      | ++      | ++         | +           | ++             | ++            |
| Brucellosis                | ++              | +++      | ++      | ++         |             | ++             | ++            |
| Carbon monoxide (CO) poisoning | ++        | +        | ++      | ++         |             | ++             | ++            |
| Zearalenone                | ++              |          | ++      | ++         |             | ++             | ++            |
| Swine Erysipelas           | ++              | +++      |         | ++         |             | ++             | ++            |
| Autumn abortion syndrome (AAS) and seasonal infertility | ++ | +++ | | | | |

Note: The first column provides the diseases. The remaining columns represent the clinical signs. The frequency of the occurrence is + (occasional), ++ (common), and +++ (routine).
the placental epithelium resulting in fetal death. Clinical signs of PPV range from low total born, mummies of various sizes, irregular returns to estrus, and females diagnosed pregnant but fail to farrow. Diagnosis is based on vaccination history, clinical signs, and PCR testing of mummified fetuses. PPV ELISA may provide diagnostic value if acute and convalescent serum samples are used. There is no effective treatment for PPV; however, commercial killed vaccines are available and very effective. Exposure of unbred females to tissue or cull sows from a seropositive herd has been used for immunization when vaccine is unavailable.

Leptospirosis is caused by infection by spirochete bacteria. *Leptospira* species may be zoonotic (*Leptospira canicola, L. icterohemorrhagiae*), swine-adapted (*L. pomona* and *L. bratislava*), or incidentally infect swine (*L. grippotyphosa* and *L. hardjo*). Infection has been associated with exposure of swine to contaminated soil or untreated surface water, and exposure to urine from infected vectors, such as rodents. Infected swine can become carriers resulting in chronic disease. The pathogenesis is due to bacteremia resulting in transplacental infection followed by fetal death. Clinical signs include pyrexia, low conception rate, abortion, stillbirths, and low viability pigs resulting in increased prewean mortality. Diagnosis is made using dark field microscopy or IHC performed on tissues, particularly kidney, of aborted feto or stillbirths. Paired or matched serology for hemagglutination inhibition (HI) testing may be useful if suspected. Treatment with antibiotics, such as chlortetracycline, may be pursued (Henry et al., 1993). Commercial killed bacterins are available to aid in prevention and control of disease but not infection or viremia (Madson et al., 2009a). Gilts and low parity sows are affected most often, whereas boars show no clinical signs. PCV2-associated reproductive failure may occur in conjunction with PPV. Infection results in variable lengths of viremia. PCV2-reproductive failure is due to transplacental infection of fetuses. Clinical signs depend on the stage of gestation when the infection occurs. Embryonic death, early term abortions, stillbirths, mummies, low total born, or low viable pigs can result from infection. Mummies may vary in size, like PPV, and measuring crown to rump length is useful to determine the time when that fetus was infected. PCV2-reproductive failure is diagnosed by the presence of viral antigen confirmed by IHC or deoxyribonucleic acid confirmed by PCR along with the presence of lesions in fetal tissue notably myocardial mineralization. PCR testing of fetal thoracic fluid is sufficient to diagnose in utero infection of piglets (Madson and Opiensnig, 2011). Commerical killed baculovirus vectorized vaccines are available and effective for prevention of disease but not infection or viremia (Madson et al., 2009b).

PRV or Aujeszky’s disease virus was eradicated from the US commercial swine herd in 2004; a comprehensive review is available (USDA APHIS, 2008). PRV is a member of the Herpesviridae family and, like other herpesviruses, infection can result in a carrier state or latency within nervous tissue with the potential for recrudescence. The pathogenesis of PRV results from viremia, and then replication and necrosis of epithelial tissue including the placenta (Christianson, 1992). The period of viremia gives PRV time to cross the placenta and cause fetal death. Clinical signs following acute infection include embryonic death, abortion, mummies, and stillborns. Necrotic foci can be found in fetal spleen, liver, lung, and lymph node. Histopathology is not definitive; IHC is required to confirm presence of antigen. Diagnosis may also be made through serology; a commercial ELISA test is available and can differentiate between exposure to the gene-deleted vaccine and wild-type virus used extensively in the US eradication. Commercial PRV vaccines are available but only should be used in accordance with federal guidelines.

Brucellosis is a zoonotic infection caused by the bacteria, *Brucella suis* biovars 1 and 3. *Brucella suis* is transmitted through direct contact with susceptible swine, ingestion of infected tissue, or fluids including milk and contaminated semen. Pathogenesis of *B. suis* is initiated when the mucosal epithelium is penetrated, thereby resulting in bacteremia that commonly persists for 5 weeks and results in placental abortion among other lesions. Clinical signs of infection in gilts and sows include abortion with or without vaginal discharge, whereas boars have reduced libido and fertility. Bacteriologic isolation of *B. suis* from vaginal discharge or tissue confirms diagnosis. Serology reflects prior exposure (or vaccination) to *B. suis* but not for diagnosis of acute disease. The US commercial swine herd is Brucellosis free.

Swine erysipelas (SE) is a zoonotic, gram-positive bacterium, which is ubiquitous among swine. *Erysipelothrix rhusiopathiae* is the sole causative species. Carrier swine shed the bacteria in saliva, nasal discharge, and feces. Infection may result from direct contact with carriers, exposure to infected facilities or soil (Wood, 1984). A bacteremia lasting several days precedes lesions. Reproductive failure is most often due to abortion but infertility and low total born following high fevers or endometritis at the time of breeding is also possible.
Clinical signs including rhomboid skin lesions, high fevers, lethargy, inappetence, withdrawal, and response to treatment with penicillin of affected sows and gilts are suggestive of acute and subacute SE. Serology is available; availability is by veterinary diagnostic laboratory (VDL) and value is limited when vaccine is in use. Bacterial culture and histopathologic examination of fetal tissue is unrewarding for diagnosis of SE but is helpful to rule out other causes of abortion. In chronic SE, culture of *E. rhusiopathiae* from vulvar discharges was successful (Gertenbach and Bilkei, 2002). Treatment involves injections of antibiotics and anti-inflammatory agents. Commercial vaccines are available and effective.

CO poisoning induces hypoxia resulting in an increased number of stillborns (Hooser, 1996). Concentrations of >250 ppm are toxic. Malfunctioning heating units or poorly ventilated farrowing rooms are the cause. Diagnosis is done by ruling out infectious causes of stillbirths. Fetal blood or thoracic fluid can also be measured for CO concentrations.

Zearalenone is a luteotropic mycotoxin produced by *Fusarium roseum*. It binds estrogen receptors resulting in irregular returns to estrus, signs of estrus in prepubertal gilts, and reduced litter size (Hooser, 1996). Diagnosis is by detection of elevated levels in feed samples. However, definitive diagnosis is rarely possible because the contaminated feed has long been consumed by the time reproductive failure occurs.

AAS and seasonal infertility is a noninfectious cause of reproductive failure. The declining photoperiod and temperature fluctuations during the fall months result in declining progesterone levels. High-ambient temperature experienced during lactation and the postweaning period are suspected but not confirmed as a cause. Diagnosis is done by ruling out infectious causes and careful assessment of management, facilities, and reproduction records (Rueff, 2000). Modern facilities that utilize gestation crates and evaporative cooling systems may improve but not prevent infertility during the fall months (Leman, 1992).

### Respiratory System Diseases and Disorders

The respiratory system can be simply divided into upper and lower portions. The upper portion includes the nasal cavity and sinuses, throat, trachea, and bronchi for air conduction. The lower portion is the lung comprised of bronchioles and alveoli responsible for air exchange. The respiratory system is commonly involved in numerous infectious diseases of swine summarized in Table 6. The most notable infectious agents are the viral pathogens, PRRS and PCV2, which cause primary pathologic lesions to both the respiratory and the immune system. This damage to the immune system often leads to respiratory or systemic disease incited by secondary infectious agents. Such mixed respiratory infections can occur at any age, and, when they occur in growing and finishing pigs, are termed porcine respiratory disease complex (PRDC). Multifactorial respiratory disease can obscure histopathologic lesions complicating the diagnostic process.

APP is a host-adapted, fastidious, and gram-negative encapsulated rod that is transmitted vertically from sow to piglet. Morbidity and mortality are strain-specific; virulence varies with expression of Apx toxins. Inhalation of strains of APP expressing Apx toxins results in lung lesions within 24–36 h. The disease is economically significant because mortality occurs during the later part of the finishing phase, usually just before slaughter. Clinical signs of fever, lethargy, dyspnea, and acute death are common. Pigs found dead may have a frothy, blood-tinged discharge from the nose and mouth. Focal hemorrhage occurs in the diaphragmatic lung lobe, which is firm, and its appearance is likened to that of a bull’s eye. Fibrinous, necrotizing bronchopneumonia containing streaming leukocytes is a key histopathologic feature. Bacterial culture is difficult and requires nicotinamide adenine dinucleotide (NAD)-supplemented media so diagnosis is traditionally made on finding characteristic postmortem and histopathologic lesions. A PCR test is also available. In an outbreak, the entire population should receive antimicrobial therapy parentally. Unlike many other gram-negative bacteria, APP is sensitive to a variety of antimicrobials; at Iowa State University VDL >90% of isolates were sensitive to cefotior, enrofloxacin, florfenicol, tiamulin, tilmicosin, and tulathromycin. Prevention is aimed at eliminating carrier swine through depopulation or by pulse medication (Marsteller and Fenwick, 1999).

*Actinobacillus suis* causes a hemorrhagic, necrotizing pneumonia during nursery and grow–finish phases. *Actinobacillus suis* infection has similar clinical signs and pathologic appearance to APP. Affected pigs are frequently observed in a dog-sitting position with elbows abducted. Unlike APP, lung lesions are random in their distribution and petechial

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**Table 6  Common respiratory diseases and disorders of pigs**

| Disease                          | Preweaning | Postweaning nursery | Postweaning grow–finish | Adult |
|---------------------------------|------------|---------------------|-------------------------|-------|
| *Actinobacillus pleuropneumoniae* (APP) | +          | ++                  | +                       | ++    |
| *Actinobacillus suis*            | +          | +++                 | +                       | ++    |
| Atrophic rhinitis (AR)           | +          | +++                 | +                       | ++    |
| *Ascaris suum*                   | +          | ++                  | +                       | +     |
| *Mycoplasma hyopneumoniae* (MH)  | +          | +                   | ++                      | +     |
| Porcine circovirus associated disease (PCVAD) | +     | ++ (PMWS)          | +                       | +++   |
| PRRS (respiratory form)          | +          | +++                 | +                       | ++    |
| *Salmonella cholerasuis*         | +          | +                   | +                       | ++    |
| Swine influenza (SIV)            | +          | ++                  | +                       | ++    |

Note: The first column provides the diseases. The remaining columns represent the respective phases of production. The frequency of the occurrence is + (occasional), ++ (common), and +++ (routine).
hemorrhages may be seen in other organs due to the septicemia that follows A. suis infection (Yaeger, 1995). A PCR test is available to help differentiate disease from APP and HPS (Oliveira, 2007a). Like APP, outbreaks should be treated by parental delivery of an antimicrobial; however, treatment of only those individual pigs with clinical signs is usually sufficient. Autogenous vaccines can be used for control but response is variable because most pigs are already seropositive at the time of vaccination.

Ascaris suum, the swine roundworm, is the most common parasitic infection of swine. The reduced growth performance and liver condemnations are responsible for economic losses (Stewart and Hoyt, 2006). The prepatent period is 40–53 days. Adult roundworms are present in the manure but it is the migration of larvae through the lungs, occurring 8–10 days after ingestion of an infective egg that causes respiratory signs. A persistent cough and dyspnea result due to verminous pneumonia. The liver develops whitish spots, called ‘milk spots’ that are the cause of condemnations but resolve within 25 days (Stewart and Hoyt, 2006). The presence of eosinophils is suggestive of a parasite infestation. Treatment and control is accomplished using anthelmintics: dichlorvos, fenbendazole, levamisole eliminate adults and larvae; piperazine kills only adults. Proper cleaning and disinfection particularly removing fecal material between groups reduces potential for exposure but it is virtually impossible to get rid of A. suum once a premise is infested (Pittman et al., 2010b). It is necessary to prevent access to contaminated soil.

AR is described in two forms: progressive (PAR) and non-progressive (NPAR). PAR is caused by toxigenic strains of Pasteurella multocida, whereas NPAR is the result of toxigenic strains of Bordetella bronchiseptica. In both forms, the bacteria attach to cilia in the nasal passages and the cytotoxin production causes hypoplasia of nasal turbinates. Clinical signs include sneezing, deviated snouts, and, in cases of PAR, bloody nasal discharge occurring in a large number of grow–finish pigs. Mortality is low but the reduced growth that results due to AR makes it economically important. Because the cytotoxins are responsible for AR, isolation of either bacterium from nasal passages is not sufficient for diagnosis. In addition, B. bronchiseptica and P. multocida colonize the lung leading to bronchopneumonia causing cough and dyspnea in pigs post-weaning, often part of PRDC (Hansen et al., 2010). Therefore, examination of nasal turbinates at slaughter is the recommended method for diagnosis of AR (Gatlin et al., 1996). Transmission is vertical; therefore, prefarrow vaccination of sows can protect piglets up to 16 weeks of age. If vaccination does not prevent AR, depopulation of the herd may be necessary.

HPS is also called Glässer’s disease. There are 15 serovars identified and prefer to colonize the nose (MacInnes et al., 2007). HPS may not actually result in pneumonia but does cause signs of respiratory disease including nasal discharge and dyspnea. In addition, fever, lethargy, and acute death are observed. On necropsy, one or all of the pleural, pericardial, epicardial, and peritoneal serosal surfaces become covered in fibrin. Effusion commonly occurs. Histopathologic lesions are described as fibrinopurulent. Definitive diagnosis is by bacterial isolation on culture media supplemented with V factor. Owing to the difficulty in isolating HPS, PCR testing is now available (Oliveira et al., 2001). Isolation from the airways in the absence of lesions has little significance (Hoelling, 1994). Cefotiofur, enrofloxacin, or tulathromycin delivered parenterally to affected animals are effective therapeutic drugs. Use of water-soluble antimicrobials is for control. Maternal immunity, medicated early weaning, and controlling infections with PRRS, PCV2, and influenza postpone or prevent disease onset (Rapp-Gabrielson et al., 2006). Commercial and autogenous vaccines are available but may experience limited efficacy due to serologic diversity; controlled exposure to low dose, live virulent culture is another option (Oliveira et al., 2004) (Figure 3).

MH is known to infect pigs in production systems worldwide causing reduced growth performance and mortality. The disease is classified as enzootic pneumonia or a component of PRDC. Both manifestations of MH cause paralysis of the mucociliary escalator resulting in a severe cough and dyspnea known as thumping. Vertical and lateral transmission can occur; but, owing to its slow rate of transmission between pigs, the disease primarily occurs in grow–finish pigs (Meyns et al., 2004). In addition, time of colonization with MH and disease severity are directly related (Fano et al., 2007). On necropsy, well-demarcated (red to purple lobular consolidation occurs in the apical) diaphragmatic, and accessory lung lobes is visible. Histopathologic lesions characteristic of MH is bronchopneumonia with lymphocytic perivascular, peribronchial, and peribronchiolar cuffing. Because MH is difficult to isolate, PCR is the most sensitive method of detection. ELISA is available and is helpful in establishing herd status but must be interpreted in the context of vaccination as tests do not distinguish between antibodies produced subsequent to vaccination or field infection. Treatment of affected pigs with parental antimicrobials like enrofloxacin, tulathromycin, or lincomycin or administration of water-soluble lincomycin, tiamulin, or tetracyclines to affected groups is effective in outbreaks. Control can be achieved through pulse-medication in feed of chlortetracycline (Thacker et al., 2006) beginning

Figure 3 Epicarditis, heart, nursery pig. Fibrin gives surface a granular appearance, caused by HPS infection. Note the enlarged (draining) mediastinal lymph nodes located cranial to the base of the heart and the excess thoracic fluid (reddish-brown) indicative of septicemia. Courtesy Dr. Glen Almond.
1 week before the historical onset of disease (Maes et al., 2008). Commercial vaccines are whole cell bacterins marketed to reduce lesions but do not prevent disease or slow transmission rate. Simultaneous infection with PRRSv reduces efficacy of MH vaccination (Thacker et al., 2000; Thacker, 2000). Eradication from the herd is preventative but practically difficult to accomplish.

PCVAD is any disease process where PCV2 infection results in lesions and includes PMWS (Ellis et al., 1998) and PDNS. Infection with PCV2 is widespread. Morbidity and mortality is variable, often dependent on the occurrence of secondary infections and their virulence. Survivors of PCVAD remain stunted, owing to the economic significance of this collection of diseases. Clinical signs include wasting, dyspnea, depression, ill thrift, and diarrhea. Lungs are wet, heavy, and fail to collapse; pulmonary edema and lymphadenopathy also can be found at necropsy. Histopathology results include presence of interstitial pneumonia, lymphoid depletion, enteritis, nephritis, and dermatitis. For a diagnosis of PCVAD the following must occur: PCV2 antigen within characteristic lesions and lymph nodes are depleted (Sorden, 2008). IHC is used to confirm presence of PCV2 antigen within the histopathologic lesion. PCR has little value in diagnosing PCVAD unless the herd is considered free. Commercial vaccines are very effective and available with flex labels for administration to sows and pigs and as 1 or 2 doses (Chae, 2012). Nonvaccinated, subclinically infected pigs have poorer weight gain compared to their vaccinated counterparts (Kristensen et al., 2011); therefore, it is part of most vaccination protocols by US pork producers (Figure 4).

PRRS is the result of infection with the Leylstad or North American strain of PRRSv. The estimated cost of PRRS to the US pork industry is US$664 million annually (Holtkamp et al., 2013). PRRSv is the most commonly diagnosed viral respiratory pathogen at VDLs (Gauger, 2009). Infection is observed to increase susceptibility to other infections, particularly opportunistic bacteria. This apparent increased susceptibility to secondary and opportunistic infections is the result of the pathologic process in which PRRSv recruits and replicates in pulmonary alveolar macrophages, and then disseminates systemically (Rossow, 1998). Clinical signs are nonspecific including fever, lethargy, and dyspnea but not cough. Signs also depend on the type of secondary infection(s) present. Lungs fail to collapse and appear heavy, wet, and gray on postmortem examinations. Lymphadenopathy is caused by hyperplasia of germinal centers. Intestinal pneumonia, alveoli are lined with hyperplastic type II pneumocytes and contain necrotic debris, whereas the lining of bronchi and bronchioles is normal (Rossow, 1998). Vasculitis also occurs. PCR is the most sensitive method for confirming infection. Owing to the genetic diversity of PRRSv, sequencing of the ORF5 region is a common adjunct to PCR testing. Sequences are then used to create dendrograms for use by production systems pursuing PRRS control and epidemiologic investigations (Murtaugh, 2012). PRRSv ELISA is helpful for establishing herd status; National Animal Health Monitoring Service reports that a large percentage of US herds are seropositive. Treatment is limited to maintaining pig comfort, minimizing stress, and controlling secondary infections. Commercial modified-live vaccines (MLV) are available and administration during the nursery phase significantly reduces mortality and improves growth performance during the grow–finish phase of production (Robbins et al., 2013b). MLV vaccines do replicate and should not be used in negative populations.

Salmonella cholerasuis is the swine-adapted Salmonella from the C1 serogroup and, unlike S. Typhimurium, is not a food-borne pathogen. Ingestion or inhalation of the bacteria causes a septicemia resulting in low to moderate morbidity with high mortality within 1–2 days of infection that occurs postweaning, predominately during the grow–finish phase (Baskerville and Dow, 1973). Signs include high fevers ( > 40 °C), lethargy, dyspnea, acute death, and cyanotic extremities and abdomen. The latter makes it impossible to differentiate clinically from classical swine fever virus (CSFv). Pleuropneumonia, interlobular edema, mediastinal, and tracheobronchial lymphoedema, and occasionally white foci in the liver are apparent postmortem (Turk et al., 1993). Acute histopathologic lesions that form in the lung are purulent bronchitis, lobular necrosis, and abscession, whereas paratyphoid nodules are observed in the liver. Isolation is best achieved from the draining lymph nodes, lung, or liver using selective culture media. Serogrouping and typing is necessary for species identification and diagnostic confirmation. Owing to the rapid onset of disease, parental treatment is recommended. Salmonella cholerasuis isolates are commonly susceptible to ceftiofur. Increased hygiene particularly eliminating access to waste and vaccination is preventive (Husa et al., 2009).

SIV is more accurately described as influenza, to encompass the infections occurring in swine, avian, and human species. Influenza virus is classified by its hemagglutinin and neuraminidase proteins; the three predominant strains in pigs are H1N1, H1N2, and H3N2. Rapid transmission and onset are characteristic, in the experimental inoculation of one nonvaccinated nursery age pig resulted in 10.66 more becoming infected (Romagosa et al., 2011). Virus is shed for 3–5 days and uncomplicated lesions resolve 28 days post-infection (Graber, 2007). Nasal discharge, fever, and lethargy occur but resolve quickly. Cough and dyspnea can last up to 2

Figure 4 Pulmonary edema, lung, grow–finish pig. Interlobular edema associated with PCVAD, ventral portion of apical and diaphragmatic lung lobes is consolidated (purple) due to secondary bacterial infection. Courtesy Dr. Glen Almond.
weeks postinfection. PCR and VI detect virus for diagnosis of clinical cases. ELISA and HI detect antibodies; ELISA is helpful in establishing herd status, whereas HI is best for vaccination timing and measuring postvaccination titers (Allerson et al., 2008). Necrotizing bronchitis, bronchiolitis, and alveolitis as lesion resolves affected areas appear vacuolated. Pigs recover quickly so treatment should focus on maintaining pig comfort, minimizing stress, and controlling secondary infections. All licensed vaccines are killed; commercial and autogenous products are in use in the United States. Vaccination reduces lung lesions and rate of transmission, but does not prevent infection and is complicated by antigenic shift and drift. In the United States, it is typical to vaccinate the sows rather than pigs to control disease and infection (Allerson et al., 2013).

### Diseases That Affect International Trade

Trade diseases are those listed by the OIE. When one of these diseases is suspected or confirmed, it results in closure of international market access, which would be economically devastating to import–export businesses. The primary method for managing diseases that affect trade is to prevent their introduction.

Foot-and-mouth disease (FMD) is caused by a picorna-virus, FMDv, which causes mucosal lesions exclusively in cloven hoofed species. Clinical signs are excessive salivation, anorexia, and lameness causing high morbidity but low mortality. Gross lesions are vesicles at cutaneous junctions, on the snout, or in the oral cavity. Similar lesions can be caused by Seneca Valley virus, vesicular stomatitis, swine vesicular disease, and vesicular exanthema of swine; therefore, any blister in swine warrants diagnostic investigation. FMDv is highly transmissible within and between species.

African swine fever (ASF) is caused by ASFv, currently classified as an Iridovirus. Soft ticks can act as reservoirs or vectors. Current outbreaks are reported throughout Eastern Europe and Russia that have been associated with improper garbage feeding. The virus damages blood vessels resulting in clinical signs and gross lesions consistent with septicemia; including red to purple skin discoloration and enlarged spleen, liver, and lymph nodes. Excess blood and fluid in body cavities may occur.

Classical swine fever, historically referred to as hog cholera, is caused by CSFv, a pestivirus, eradicated from the United States in 1972. Transmission is associated with infected feeding, uncooked or undercooked garbage containing pork or pork by-products to swine. The virus remains infectious for months when refrigerated and years when frozen. Clinical signs are nonspecific and are easily confused with S. choleranus. The virus replicates rapidly in tonsils, which makes it the ideal tissue to collect for diagnosis of CSFv.

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