Haemophilus parasuis:
Research update on diagnosis, epidemiology, and control

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Haemophilus parasuis is still one of the main causes of nursery mortality in most U.S. herds.[1] Mortality rates due to *Haemophilus parasuis* can be as high as 10%,[2] which makes this agent one of the most costly pathogens in swine production. Although a few herds experience nursery mortality solely due to *H. parasuis*, disease caused by this agent may occur at the same time as other bacterial and viral infections. *Streptococcus suis* and Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) are two of the agents that are frequently isolated from pigs showing polyserositis due to *H. parasuis*.[3] The epidemiology of *Streptococcus suis* infection is very similar to *H. parasuis*, which may explain why these two agents often affect nursery pigs at 4 to 6 weeks after weaning.[4] PRRSV infection, however, has a very distinct role in *H. parasuis* infection. A recent study suggests that pigs colonized by a virulent *H. parasuis* strain are susceptible to development of pneumonia by this agent following PRRSV challenge.[5] Although the interaction between PRRSV and *H. parasuis* is now evident both experimentally and in the field, the mechanisms involved in such interaction are still unclear. The present article will discuss some of the features regarding diagnosis, epidemiology, and control of *H. parasuis* in the nursery.

Etiological agent (cause)

Haemophilus parasuis is the etiological agent (cause) of the syndrome currently known as "Glässer's disease". This organism is an early colonizer of the upper respiratory tract and may be normally isolated from the nasal cavity, tonsil, and trachea of healthy pigs. Although non-pathogenic strains predominate in the upper respiratory tract, some animals may harbor virulent strains that can cause systemic disease characterized by fibrinous polyserositis, arthritis, and meningitis.[1,6] Fifteen serovars of *H. parasuis* have been reported,[7] and there is extensively strain variation within serovar groups.[1]

Clinical signs and lesions

The clinical signs characteristic of *H. parasuis* infection are certainly not unique to this agent, and a differential diagnosis with other pathogens such as *S. suis* is necessary. The clinical presentation of *H. parasuis* systemic infection may vary with the virulence of the strain and the immune status of the pig. Three main presentations may be observed in the field: super-acute, acute, and chronic. Super-acute infections are characterized by sudden death with lack of clinical signs and gross lesions in most cases. Some animals may show a slight increase of fluids in the pericardial sac, pleural, and abdominal cavities. Fibrin may or may not be observed. In these cases, *H. parasuis* may be isolated from the blood, which confirms septicemia. Super-acute infections usually occur in naive herds (*H. parasuis*-free) or due to infection by a highly virulent strain. Acute infections are more commonly observed in the field and are characterized by

fibrinous polyserositis. Clinical signs will usually appear 2-3 days following infection. Affected pigs may present fever (> 40 º C), labored breathing (abdominal breathing), coughing, swollen joints, and central nervous system (CNS) signs, which are characterized by lateral decubitus, paddling, and trembling. When samples are properly collected, *H. parasuis* can be easily isolated from these animals. Acute infection may also be characterized by development of either pneumonia or CNS signs. These clinical presentations may be associated with specific groups of strains. Some strains seem to have a tropism to the brain, causing only CNS signs. Other strains may be found in lungs causing pneumonia without systemic infection. Further studies are necessary to clarify the association between specific strains and clinical presentations in the field. Chronically affected animals (6-7 weeks after weaning) are survivals of the peak of nursery mortality. These animals probably received antibiotic treatments and were able to survive systemic infection. In most chronically affected animals, *H. parasuis* can no longer be isolated from lesions. These animals usually present poor growth performance throughout late nursery and early finisher and may die from complications of fibrosis in the thoracic cavity.[3, 6]

Diagnosis and strain characterization

The diagnosis of *H. parasuis* systemic infection is based on the association between clinical history and isolation of the agent from characteristic lesions. Successful isolation of *H. parasuis* from clinical samples can be achieved by sampling acutely affected, non-treated animals. Isolation is easier when clinically affected animals are euthanized and fresh samples are submitted to a diagnostic laboratory as soon as possible. Sample collection may be performed using a sterile swab containing Stuart or Amies media.[15] It is very important to collect the fibrin on the surface of affected organs, as *H. parasuis* will be mostly concentrated in this material. Tissues may also be collected for isolation, and should be submitted in separate sterile bags to the laboratory. It is known that different strains can affect one pig at the same time. Special care should be taken to separate brain tissue or swabs from other samples, as some *H. parasuis* strains seem to have a tropism to the brain. When isolation is negative, polymerase chain reaction (PCR) may be used to detect the presence of *H. parasuis* in tissues and swabs.[8] PCR is useful to define the role of *H. parasuis* in nursery mortality, but isolation is still necessary for further characterization of strains by serotyping and genotyping. A new technique, more sensitive and specific, has been recently developed to serotype *H. parasuis*. Indirect hemaglutination (IHA) apparently reduces the percentage of non-typable isolates compared with traditional serotyping by agar gel precipitation test (AGPT).[9] Genotyping by Enterobacterial Repetitive Intergenic Consensus-based PCR or ERIC-PCR has been extensively used to characterize and compare *H. parasuis* field strains.[1, 10] This technique is more discriminatory than serotyping and can be used to detect prevalent strains in affected herds. Both techniques (serotyping and genotyping) are important for the development of control strategies.

Epidemiology

Colonization of piglets by *H. parasuis* occurs a few days after birth, possible through nose to nose contact with sows and gilts. The weaning age appears to influence colonization of piglets by *H. parasuis*. Pigs weaned at 14 days tend to have lower levels of colonization compared with piglets weaned at 28 days.[11] Piglets that are colonized in the farrowing house in the presence of maternal immunity may develop active immunity against virulent strains and be protected

against systemic infection after weaning and commingling. Piglets that are not colonized prior to weaning are naive animals that may develop systemic infection when commingled with colonized pigs.[12] Systemic infection usually happens around 4 to 6 weeks after weaning, when maternal immunity is no longer protective.

Another interesting feature of the epidemiology of *H. parasuis* is the fact that no matter how many sources are commingled in the nursery, only a few prevalent strains (usually 2-3) will predominate in the herd.[1] Several within herd studies using genotyping by ERIC-PCR have confirmed this fact.[1, 2, 4, 13] Although many herds are affected by the same serovar group, each herd has a different prevalent strain. This was observed in herds affected by strains from serovars 2, 4, and 12.[1]

Co-infection with other pathogens

As mentioned before, *S. suis* has a very similar within-herd epidemiology compared with *H. parasuis*. Both organisms are early colonizers of the respiratory tract and the hypothesis for colonization dynamics for *S. suis* appear to be similar to that described for *H. parasuis*.[4,12] Disease in the nursery caused by *S. suis* seems to be also associated with the commingling of colonized and non-colonized piglets. Systemic infection by *H. parasuis* and *S. suis* occur at the same time in the nursery, and sometimes, these organisms may co-infect nursery pigs. Clinical signs are very similar. It is very common to isolate *S. suis* from pigs showing fibrinous polyserositis and *H. parasuis* from pigs showing only CNS signs without other systemic lesions. *Streptococcus suis* is mostly isolated from dead pigs, while *H. parasuis* is easily isolated from clinically affected, non-treated, euthanized pigs. Testing of clinical samples by PCR to detect *H. parasuis* may help on the differential diagnosis with *S. suis* infections.[3]

For many years, field experiences have suggested that PRRSV and *H. parasuis* may have a synergistic role in nursery mortality. However, several studies failed to prove the interaction between these two agents.[14] A recent study demonstrated that sentinel pigs that were housed in the same airspace as pigs challenged by the intra-tracheal route with a virulent *H. parasuis* strain developed pneumonia by this agent following PRRSV challenge. This study is the best evidence to date that these two agents may in fact interact.[5] The mechanisms involved in the interaction between PRRSV and *H. parasuis* are still unclear. One hypothesis is that the destruction of alveolar macrophages (innate immune response) by PRRSV allows potentially virulent *H. parasuis* strains to proliferate in the lung and cause pneumonia.

Control

The correct diagnosis of *H. parasuis* systemic infection in the nursery and the evaluation of the within-herd epidemiology are critical for control of mortality caused by this agent. Sample collection from clinically affected, non-treated, euthanized pigs is very important. If isolation is not accomplished, PCR can help to define if *H. parasuis* is involved in nursery mortality. When isolation is accomplished, further characterization of isolates by serotyping and genotyping is recommended.[3] Both commercial[16] and autogenous[17] products may be used to control nursery mortality. Selection of isolates to be included in autogenous vaccines should be based on the following factors: serovar, genotype (identification of prevalent strains), site of isolation (systemic isolates from pericardium, pleura, peritoneum, joints, or brain), and date of isolation

(isolates recovered within the past 2 years are preferred). Vaccination schedules vary with the peak of mortality in each herd. When systemic infection by *H. parasuis* is observed 1-3 weeks after weaning, sow vaccination at 4 and 2 weeks prior to farrowing may be an option. Some herds opt to vaccinate sows and piglets. Although there are some concerns regarding maternal immunity interference in piglet vaccination, a few studies suggest that better results may be achieved when sows and piglets are vaccinated. The majority of swine herds experience the peak of mortality due to *H. parasuis* infection at 4 to 6 weeks after weaning. This period corresponds to the decrease of maternal immunity. In these cases, piglet vaccination at weaning and 2 weeks later may control mortality. [1, 3, 6, 16.]

Recently, controlled exposure of 5-day old piglets to a low dose of live, virulent *H. parasuis* using the oral route has been used as an alternative measure to control nursery mortality caused by this agent. Although this technique may reduce nursery mortality by 50%[2,4] and protect pigs against homologous challenge,[5] it does have some inherent risks specially in herds with active PRRSV infection. A recent study demonstrated that sentinel pigs from the negative control group that were housed in the same air space as pigs challenged with *H. parasuis* developed pneumonia by this agent following PRRSV challenge. These results suggest that PRRSV may predispose pigs harboring virulent *H. parasuis* strains to develop systemic infection by this agent.[5]

Summary

The correct diagnosis of *H. parasuis* systemic infection in the nursery is critical for the control of this costly pathogen. It is very important to consider the differential diagnosis with *S. suis* infections and to evaluate the role of PRRSV concurrent infections in the nursery. Detection of *H. parasuis* in clinical samples may be performed by PCR, although isolation is still recommended for further characterization of isolates by serotyping and genotyping. Control measures should be designed based on the timing of mortality in each specific herd. Definition of serovars and the number of strains involved in nursery mortality are also important for selection of control measures. Controlled exposure should be used with caution, since clinical signs may occur in exposed piglets and systemic infection by the *H. parasuis* strain used for exposure may happen following stressful events such as weaning. When using this alternative control measure, one should keep in mind that pigs from herds experiencing active PRRSV infection in the farrowing house and in the nursery may be at greater risk of systemic infection by *H. parasuis*.

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