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Mycoplasma hyosynoviae, Mycoplasma hyorhinis and *Mycoplasma suis* overview: Disease basics, clinical presentations, diagnostics, treatments and prevention/ control strategies

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The intent of this paper and our presentation is to provide a broad overview of these three organisms, provide an update on recent published information and to provide some recent experiences, with the overall goal of stimulating further interest and discussion in this topic. The most recent chapter on mycoplasmal diseases in Diseases of Swine provides a broad overview of each of these organisms and was used as a foundation for the disease basics and clinical presentations sections of this paper (prepared by Thacker).[1] The diagnostic sections of this paper mainly focus on the recent development and application of PCR testing for these three organisms along with diagnostic case and survey experiences (prepared by Thacker). The prevention/control and treatment sections present recent information on these topics (prepared by Scheiber).

Mycoplasma hyosynoviae

Disease basics. *M. hyosynoviae* was first recognized in the late 1960's, is widespread worldwide and causes a non-purulent arthritis.[1] Isolation of the organism by culture is often complicated by *M. hyorhinis* overgrowth. Genetic diversity among isolates has been reported but the importance of this finding is unknown. The organism colonizes the upper respiratory tract and pigs can become long term carriers although shedding from these carriers is intermittent. Transmission can occur at any age but typically is observed after 4-8 weeks of age. From the upper respiratory tract, the organism spreads systemically to joints and other tissues over a 1-2 week acute phase. Sub-acute and chronic phases occur 3-16 weeks post-exposure. Arthritis can occur after an incubation phase as short as 4 days but the time period is typically longer.

Clinical presentations. Lameness, joint swelling and pain resulting in gait alteration are the main clinical signs observed and are most often observed in 3-5 month old pigs. Hind limb involvement is usually the most prominent but all joints can be involved. Signs persist for 3-10 days before subsiding although stiffness may persist beyond that time period. Rectal temperatures are either normal or slightly elevated due to pain response. Appetite may be slightly diminished but the ability to access the feeder may be influenced by high stocking density and large pen size. Direct mortality is low and morbidity can be variable. Some pigs will develop lameness that results in sufficient debilitation such that the animal has to be removed from the pen and may require culling from the herd or selling at a light market weight.

Detection of clinically affected pigs for treatment can be confounded by the number of pigs per pen. With early infections, pigs may exhibit signs for only a short period of time before "warming out" of the lameness. Therefore in barns with large numbers of pigs per pen, it is difficult for the staff to detect pigs that should be treated. Whether or not "large pen" housing schemes contribute to lameness has not been determined.

Diagnostics. Diagnosis requires identification of clinically lame pigs, detection of the organism in joint fluid and identification of microscopic lesions in synovial tissue.[2] Acutely-affected, non-treated pigs provide the best samples. The subtle clinical signs require careful inspection of the pigs and must take into consideration the short time that pigs may show lameness at this stage of disease as discussed above. Joint taps can be done on live anesthetized pigs but the need for examining the joint synovial tissue requires sampled pigs to be euthanized. Joint taps and tissue collection can be done at the farm if performed in a sterile manner but often it is best to send one entire limb per pig to the diagnostic laboratory for sample collection. Sampling at least 2-3 pigs is recommended. In my experience, the hock joint is the easiest to tap or open for collecting joint fluid and the joint fluid is typically clear and abundant. The stifle joint is harder to access, the fluid is brown colored, synovial tissue is more easily collected and grossly visible proliferation of the synovial tissue is more prominent. Detection rates from either joint are similar.

The main test for detecting *M. hyosynoviae* is PCR, which has replaced culture for the most part as the routine test. Culture is attempted and necessary for antibiotic sensitivity testing or production of autogenous vaccines. In some situation, culturing the sample before performing the PCR may improve detection.[3] Histological examination is fairly straightforward.

Prevention/control strategies. *M. hyosynoviae* is present in the tonsils of infected gilts and sows and can persist in a

carrier state indefinitely. The organism does not appear to infect pigs until 4 to 8 weeks of age[1] and *M. hyosynoviae* has not be isolated from pigs less than 4 weeks of age. There have been reports of increased pathogen transmission to piglets from younger sows[4] as with *M. hyorhinis*.[5] Therefore, acclimation of gilts and boars should be part of any prevention protocol. New start up herds then would be more likely to see *M. hyosynoviae* in the offspring in the finisher pigs. Also, swine herds that have a high turnover of sows would be more likely to see this disease.

Prevention should center on controlling stocking density, trauma to joints in transport, trauma to joints from feeders, penning and drinkers, nutritional imbalances and other viral infections which lower immunity. Timed feed or water medication 2-3 weeks prior to the onset of clinical signs with antibiotics such as tiamulin, chlortetracycline, tylosin, and lincomycin have been used with varying results.[4] In addition to timed feed and water medication, antibiotic injections of enrofloxacin and tulathromycin to piglets have been used with varying success.[4] It is important to remember that there are no antibiotics approved for *M. hyosynoviae* and the antibiotics have to be used off-label.[5] A vaccine specific for *M. hyosynoviae* was investigated in Denmark and induced a high level of specific serum IgG in all animals one week post booster.[6]

Treatment. *M. hyosynoviae* is a chronic condition slow to show clinical signs. There have been reports with in vitro studies that demonstrate that enrofloxacin, lincomycin, tetracycline and tiamulin are active against *M. hyosynoviae* while tylosin provided variable results. In a study in Denmark of nine infected herds, lameness resolved independent of antibiotic therapy.[1] Aspirin seems to reduce the swelling and lameness during clinical disease.[4] Schultz reported on *M. hyosynoviae* susceptibility in twenty field isolates to eighteen antibiotics and found strong activity by tylosin, tiamulin, gentomycin, florfenicol, danofloxacin and enrofloxacin.[7] Treatment must be implemented early in the disease to reduce chronic lameness that result in market losses.

Mycoplasma hyorhinis

Disease basics. The role of this organism in causing clinical disease is often questioned because of its ubiquitous distribution in swine worldwide.[1] *M. hyorhinis* can be detected in the upper respiratory tract of nearly every pig regardless of age. It is also a common contaminant of both human and animal origin tissue/cell cultures and commercial kits are available for routine monitoring of these cultures in nearly all laboratories. As mentioned above, this organism tends to overgrow culture attempts for other mycoplasmas including *M. hyosynoviae* and *M. hyopneumoniae*. The organism colonizes the upper respiratory tract and Eustachian tubes quickly after exposure. From there, pneumonia, arthritis, polyserositis, eutachitis and otitis may occur. Infection in the ear may impair the mucociliary apparatus of ciliated cells. The mechanism for systemic spread to serosal surfaces is unknown. Typically disease occurs in pigs less than 8 weeks of age or during the nursery phase of production. Because of the ubiquitous nature of *M. hyorhinis*, correlation of finding the organism and disease causation is often questioned except for when it is detected in tissues that require systemic dissemination like joints and body cavities.

Clinical presentations. The clinical signs of *M. hyorhinis* can be similar to *M. hyosynoviae* with regard to lameness. Clinical signs due to polyserositis include mild fever, reduced appetite, lethargy, reluctance to move, postural changes and abnormal breathing pattern. Often these clinical signs are subtle, which confounds accurate selection of pigs for treatment or sample collection. Conjunctivitis has been reported as well. Signs may persist for 1-2 weeks and most pigs recover although some pigs may eventually succumb to the disease or require culling.

Diagnostics. The gross lesions are primarily polyserositis in one or more serosal surfaces (pericardium, pleura and peritoneum). These gross lesions are similar to those caused by *Hemophilus parasuis* and *Streptococcus suis*. Detection of the organism is now done routinely by PCR although culture is necessary for antibiotic sensitivity testing and autogenous vaccine production.[2] Culturing the samples first to increase the number of organisms and then conducting the PCR may enhance detection.[3]

Prevention/control strategies. Prevention should start with acclimation of incoming gilts and boars with finishing size pigs. Gilts and young parity sows appear to be the source of infection and the shedding period of *M. hyorhinis* appears to be extensive.[5] *M. hyorhinis* has been considered a secondary invader[8] and as such controlling stressors such as stocking density, temperature fluctuations, ventilation, and feed and water availability are important considerations. Infectious agents such as swine influenza virus (SIV), porcine reproductive and respiratory syndrome virus (PRRS) and porcine circovirus type 2 (PCV2) that depress immune function are contributing factors.[9] There has been one report of a vaccine for *M. hyorhinis* from South Korea. This study showed no clinical signs of *M. hyorhinis* in vaccinated animals compared to non-vaccinated animals.[10]

Treatment. There are no antibiotics specifically labeled for *M. hyorhinis* and therefore all antibiotic usage would be considered off-label.[5] Treatment of clinically affected animals is usually unsuccessful due to the chronic nature of the disease.[1] Antibiotics that have shown efficacy include chlortetracycline, lincomycin, tiamulin, amoxicillin, tylosin and florfenicol.[11-14] Treatment must be instituted early in the course of the disease and injectable antibiotics have

provided the best results. Feed and water antibiotics can help reduce the incidence of the disease if administered before the onset of clinical signs.

Mycoplasma suis

Disease basics. This organism was known as *Eperythozoon suis*, and considered to be a rickettsial organism, until genetic analysis revealed that it was more appropriately classified in the family Mollicutes, hence the name change to *M. suis*.[1] The disease was first described in 1932 as a syndrome characterized by icteroanemia, respiratory distress, weakness and fever. In 1950, the organism (*E. suis*) was described as being the cause of this syndrome. Since, then the role of *M. suis* in causing clinical disease has been highly questioned. Serological surveys done in the US in the 1970's revealed a wide distribution. The organism is spread by direct exposure (licking wounds, cannibalism) or mechanical transmission (insects, needles, instruments, snares) of blood. In utero transmission has been reported. Experimental transmission is difficult and requires splenectomized pigs. Clinical signs following IV inoculation of splenectomized pigs can occur within 2 days and a severe bacteremia occurs thereafter. *M. suis* infects erythrocytes. The old dogma was that the organism adhered to the outer surface of erythrocytes. However, recently it has been shown that *M. suis* is capable of invading the erythrocytes by an endocytosis-like process.[15]

Anemia and associated icteremia due to erythrocyte destruction are the main causes of clinical disease. Work done at Michigan State University suggested that the anemia was due to an autoimmune-like response to the altered surface antigens of the infected erythrocytes.[16] Anemia is mainly a factor in young pigs. The organism has a high requirement for glucose in vitro and one mechanism for developing clinical disease may be hypoglycemia.[17] Hypoglycemia may be a factor in pigs that are influenced by their energy status such as lactating sows (high requirement, return to estrus after weaning), gestating sows (limit fed, compounded by other factors such as ambient temperature that influence energy needs), pre-pubertal gilts (high requirement, impact on puberty onset) and growing pigs.

Clinical presentations. The clinical signs of *M. suis* infection are vague at best and are highly influenced by other factors including concurrent disease, nutritional status and environment. Visible anemia and icterus are observed mostly in young pigs. Older pigs may exhibit fever, decreased appetite and lethargy, all resulting in poor growth. Thacker et al. reported a case in a breeding age boar that exhibit fever and was off feed.[18] Because blood was collected for performing a CBC in this teaching hospital setting, detection of the organisms was possible. However, CBCs are rarely done in swine practice so the role of *M. suis* in individual breeding age animals displaying non-specific illness is unknown.

Diagnostics. Serological testing by an indirect hemagglutination assay was relatively common in the 1970's and 1980's. This test is not done commonly at the present time. ELISAs have been developed but are not commonly available in the US. Work done at MSU suggested that the test mainly detected antibodies against red blood cell antigens and not the organism.[19] Detecting the organism in blood smears is possible with severe cases but the smears should be made directly from the collected blood prior to mixing with anti-coagulant. The common anti-coagulant, EDTA, kills the organism so making the smear from EDTA preserved blood may provide false negative results. PCR assays have been available for a number of years and are now the main method for detecting the organism.

Prevention/control strategies. Mechanical transmission of *M. suis* by needles and instruments must be minimized by changing needles when processing between litters and using two sets of instruments for tail docking, castration and teeth.[1,20] One set of instruments should be in a disinfectant while one set is being used on a litter. When vaccinating the sow herd, needles should be changed at least every 10 sows. Controlling mange and lice is a must in a prevention and control program as is hygiene. Fly and mosquito control is also necessary. Blood from farrowing or injuries can transmit the organism. If the swine herd is *M. suis* free, then gilts and boars should be purchased from a known *M. suis* free herd. Negative status can be assumed if serological or PCR tests from serum of piglets on sows are negative.[1]

FDA has not approved any product for the control or treatment of *M. suis*. Since the withdrawal by FDA of the organic arsenicals (which were the only products proven to eliminate *M. suis*),[13] *M. suis* infection has been on the increase. De Busser reported that treating all sows 6 weeks pre-farrowing and all neonates at day 1 of age with oxytetracycline parenterally and medicating the sow feed every 3 months with oxytetracycline at 600 ppm for 7 days controlled the infection but did not eliminate the organism. This protocol reduced the number of anemic pigs and pre-weaning mortality but did not reduce repeat breeders.[21,22]

Treatment. The treatment of choice at this time is oxytetracycline at a dose of 20-30 mg/kg administered parenterally and supportive therapy of iron dextran to help recovery and minimize mortality.[1,21]

Summary

Our presentation will mainly focus on clinical cases and situations that we have encountered with these organisms over the past 40 years. The recent increased interest in these organisms begs the question regarding what has changed; the bugs, the pigs, the people or how we raise the pigs. Hopefully this paper and ensuing discussions will shed some light on the situation.

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