Salmonella choleraesuis in Pigs
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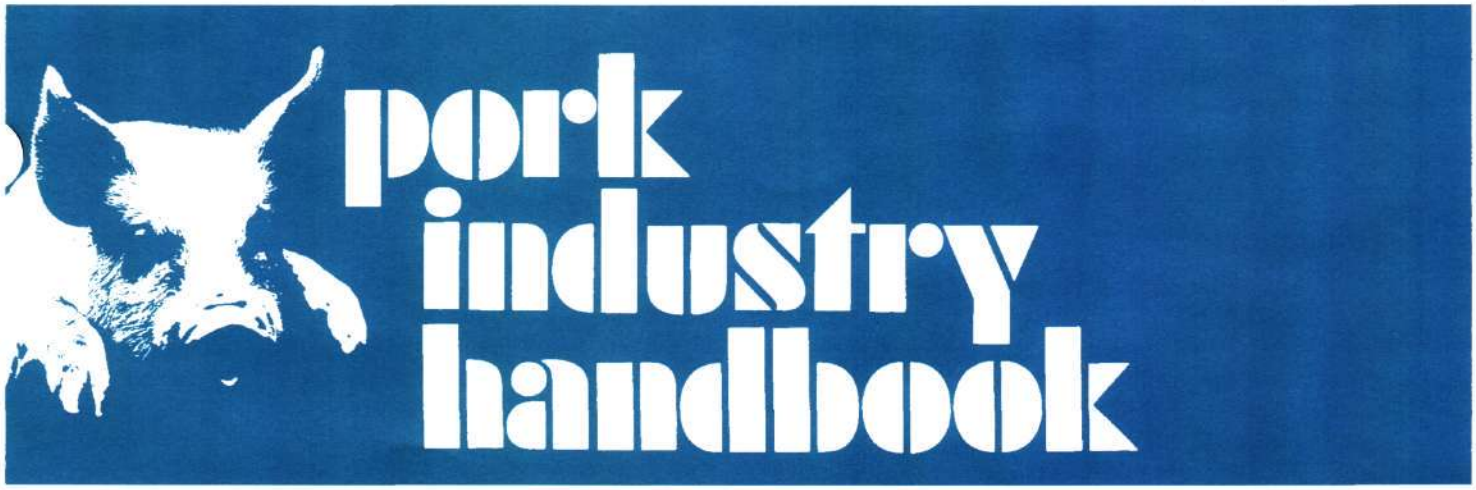

Michigan State University Extension

Salmonella choleraesuis in Swine

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Salmonellosis, the disease that may result from *Salmonella* infection, continues to have a significant economic impact on the national swineherd. Between 1975 and 1995, *S. choleraesuis* was one of the most common organisms isolated from cases of swine pneumonia and septicemia. It also was the most prevalent serotype (>90% of isolates) of all *Salmonella* isolated from diseased swine. In 1991, it was estimated that the disease caused by *S. choleraesuis* cost pork producers in the United States more than $100 million annually due to death losses, medication costs, and poor production efficiency of survivors. Since the mid-1990's, the prevalence of *S. choleraesuis*-associated disease has moderated. Currently, serotypes of *Salmonella* other than *S. choleraesuis* have increased in frequency and presently account for over 50% of the serotypes isolated from diseased swine.

In addition, concerns over *Salmonella*-contaminated pork products as a human health hazard add to processing and monitoring costs of pork products and may impact overall product demand. All *Salmonella spp.* are considered pathogenic for humans but *Salmonella choleraesuis* is rarely isolated from pork products.

Salmonellosis in swine occurs as either of two general clinical disease entities. Enterocolitis (diarrhea) may be caused by a broad range of *Salmonella* serotypes, including *S. choleraesuis,* but *S. typhimurium* is more common. Septicemia (affecting multiple organ systems) is due to *Salmonella choleraesuis*. *Salmonella* are notoriously diverse. This publication discusses only *S. choleraesuis* as a cause of disease in swine.

History

Salmonella was among the first bacteria discovered, and it was first observed microscopically in 1880 in tissues from humans dying from typhoid fever. The causative organism, *Salmonella typhi,* was first isolated in 1884. The first isolation from animals was *Salmonella choleraesuis*, which was isolated in 1885 by Salmon and Smith from pigs that had died of hog cholera. *Salmonella choleraesuis* was considered to be the cause of hog cholera until 1904 when a virus was proven to be the etiologic agent.

Etiology

Salmonella are a genus of Gram-negative bacteria that contains more than 2,000 serovars, sometimes referred to as species or serotypes. These organisms are very common in animal populations and feces, residing in the intestinal tracts and feces of both warm- and cold-blooded animals. *Salmonella* are quite hardy and are able to survive for months in cool organic substrates in either aerobic or anaerobic environments. Since some *Salmonella* survive within animal cells (phagocytes), intestinal tracts, or feces for extended periods of time, the organism is unlikely to be eradicated. Fortunately, *Salmonella* are quite sensitive to disinfection with most common disinfectants, but only after thorough cleaning and removal of organic debris.

Salmonella choleraesuis causes the majority of cases of salmonellosis in pigs. *Salmonella typhimurium*, the other major cause of porcine salmonellosis in the United States, accounts for 30% of swine outbreaks. Infections of pigs with other *Salmonella* serovars frequently occur but are only occasionally causes of disease outbreaks.

Zoonotic Potential

Salmonella choleraesuis is considered to be host-adapted to pigs, meaning that infection and disease due to this organism is limited almost exclusively to pigs, and persistent infections can occur in pigs without signs of disease. Although infection of other species of animals (and humans) is rare, *S. choleraesuis*

can cause a generalized, life-threatening septicemia. People who have extensive contact with pigs are infected the least often. Most human infections occur in immuno-compromised (with drugs or disease) people who have no known direct contact with pigs. The most important serotypes for food-safety concerns are the myriad of serotypes other than *S. choleraesuis* that may infect pigs, usually asymptomatically.

Epidemiology

Ingestion of feces-contaminated materials is the most important route of infection for all *Salmonella*. With *S. choleraesuis*, pig feces and/or contact with infected pigs is the predominant route in contrast to other serotypes where environmental contamination, feedstuffs, and feces from other animal species (including birds) are often implicated. Feedstuffs are rarely, if ever, a source of *S. choleraesuis* infection for swine. During outbreaks, *S. choleraesuis* may be aerosolized for short distances within a room. Once infected, pigs can carry and intermittently shed *Salmonella* in their feces for extended periods of time and are therefore considered to be the major source of *Salmonella* infection between and within herds.

Salmonella choleraesuis is seldom isolated from the feces of healthy pigs. This has made it difficult to determine the initial source of infection in herds without a previous history of infection. *Salmonella choleraesuis* has been isolated from the neutrophils (white blood cells involved in bacterial killing) of healthy pigs, some even from herds with no history of salmonellosis. It appears that both healthy and sick pigs can harbor viable *S. choleraesuis* for extended periods of time. Undefined stresses may allow organisms to multiply and to be shed in feces or cause clinical disease. Pigs with acute diarrhea due to *S. choleraesuis* excrete several million organisms per gram of feces, theoretically sufficient to infect thousands of pigs. *Salmonella choleraesuis* has been shown to survive at least 24 days in the water overlay and at least 78 days in the sludge of a water and swine manure mixture. This same species was viable after being buried in an Indiana pasture for 451 days and for up to 120 days in cattle fecal slurry. It is clear that a single pig with diarrhea can contaminate the environment, infect its penmates, and provide a source of infection for future groups of pigs.

Like other *Salmonella* infections, *S. choleraesuis* outbreaks frequently are associated with "stress" factors such as commingling, overcrowding, transportation, inclement weather (environmental), feed changes, parasitism, poor sanitation, aflatoxin in the feed, or other concurrent infectious disease(s). Morbidity can range from a single animal to more than 50%. In many outbreaks, less than 10% of the group is affected, but a high proportion of affected pigs may die.

Weaned pigs less than 5 months of age are most often affected. However, market weight and adult pigs occasionally may be affected. Suckling piglets infrequently develop clinical disease due *to S. choleraesuis*. The reason for the resistance of nursing piglets is not known; but is thought to be due to maternal immunity acquired via colostrum and milk. Disease can occur in suckling pigs in those herds previously naïve to *S. choleraesuis* infection. Abortions also may result from infection of pregnant sows.

The Disease

Disease due to *S. choleraesuis* consists of acute septicemia (generalized infection of blood and organs) and/or enterocolitis (diarrhea). Acute septicemia without enterocolitis is by far more common. *Salmonella choleraesuis* is the only species that commonly results in acute septicemia in pigs. *Salmonella typhimurium*, and a few other species, usually cause enterocolitis, with septicemia a possible but minor feature.

Oral infection of pigs with *S. choleraesuis* leads to colonization of palatine tonsil and lymphoid tissues of intestine (Peyer's patches). The organism can survive within phagocytes (macrophages and neutrophils) which serve as vehicles to distribute the organism throughout the body. Tissue localizations of infection then occur, the most common being liver (hepatitis), spleen (splenomegally), lymph nodes, lung (pneumonia), brain (encephalitis) and joints (synovitis). There, the organism destroys local tissues, causes inflammation, and persists.

Septicemic *S. choleraesuis* infection can result in death without forewarning signs. More commonly, affected pigs are off feed, lethargic, have a shallow cough, high fevers, and their breathing is difficult (thumping) giving the impression of pneumonia. Some pigs can have neurologic involvement (down and paddling) and pregnant sows may abort. The ears, tail, nose, feet, and abdomen usually become light red to dark purple. Pigs that survive three or four days develop yellow diarrhea containing flakes of fibrin or, less frequently, blood. Animals that recover usually have decreased weight gain and stunting.

Diagnosis

Postmortem examination reveals purplish discoloration of the extremities and abdomen, swelling and hemorrhage of lymph nodes, and frequently small hemorrhages in many tissues. The lungs are often fluid-filled, do not collapse, have interlobular edema, and usually are diffusely red with small hemorrhages. The spleen usually is swollen and dark blue-black in color. The liver is swollen and blood-filled, and in some cases, contains pinpoint white foci. The inner lining of the stomach is dark red to black. Pigs dying of acute septicemia generally have no lesions in the intestine. If the disease course has been prolonged or in those pigs with diarrhea, often there are irregular ulcers and fibrin in the large, and sometimes small, intestine. Rarely, there are shallow, oval ulcers throughout the colon. A few pigs also will have tissues that appear yellowish (jaundice or icterus).

Septicemic *S. choleraesuis* must be differentiated from other acute diseases of swine, such as septicemia due to *Erysipelothrix rhusiopathiae, Streptococcus suis*, or *Actinobacillus suis,* edema disease due to *Escherichia coli,* pleuropneumonia caused by *Actinobacillus pleuropneunoniae,* mulberry heart disease, hog cholera, and more recently, PMWS (post-weaning multisystemic wasting syndrome, thought to be due to porcine circovirus). Diarrhea due to *S. choleraesuis* must be differentiated from *S. typhimurium*, swine dysentery, porcine proliferative enteritis (ileitis *or Lawsonia intracellularis*), whipworm (*Trichuris suis*) infestation, and hog cholera (classical swine fever).

The clinical signs combined with postmortem lesions are suggestive of *S. choleraesuis* infection, but by themselves, they are not diagnostic. Microscopic lesions, especially focal areas of necrosis in the liver and macrophagic interstitial pneumonia, provide a presumptive diagnosis.

Definitive diagnosis requires isolation and identification of the organism. In most cases, *S. choleraesuis* can be readily isolated from unmedicated septicemic pigs by directly culturing lung, liver, spleen, kidney, or lymph nodes onto blood agar

plates and incubating overnight. Isolation from the intestine or feces often is unrewarding even with enrichment techniques. If attempted, enrichment with tetrathionate or Vassiliadis broth is preferred because selenite broth inhibits the growth of *S. choleraesuis*. Biochemical and serological tests are used to provide identification of genus and species.

An antimicrobial susceptibility test should be obtained to provide guidelines for antimicrobial treatment and control.

Serology tests are generally not available, lacking both sensitivity and specificity for disease diagnosis. Serology tests (mixed-ELISA) may be used to determine if a herd has had a recent *Salmonella* infection but are not specific for *S. choleraesuis*.

Treatment

When treating an outbreak of any disease, the goals are to cure clinically ill pigs and to prevent the spread of the disease to other pigs. With salmonellosis, the attainment of these goals can be difficult because *Salmonella spp.* are often resistant to many of the antibacterial agents approved for use in swine. Also, *S. choleraesuis* can survive within the host's cells, and few antibacterial drugs are able to enter animal cells. In many outbreaks, less then 10% of the pigs are affected, so the effectiveness of treatment is difficult to evaluate.

In human medicine, antibacterial agents are used to treat septicemic salmonellosis but usually are not used for enterocolitis because antibacterial therapy does not decrease the severity of illness and may actually increase the duration and magnitude of *Salmonella* shedding in the feces. Experimentally, antibacterial therapy in swine does not appear to increase the severity of the disease nor the duration of *Salmonella* shedding by clinically affected animals. Antibacterial therapy is viewed by many as beneficial for *Salmonella* enterocolitis and more certainly of benefit for septicemia.

Since *S. choleraesuis* usually causes septicemic disease in pigs, antibacterial therapy is warranted in most outbreaks. The use of systemic (able to enter the bloodstream) antibacterials to treat septicemic salmonellosis is widely practiced and is perceived to decrease the severity of the disease and to increase survival rate. Injectable products often are required for pigs that are clinically affected. Mortality in pigs with purplish discoloration is high, but early treatment combined with separation of animals to small hospital pens will increase survival rate. Antibacterial agents should initially be selected on the basis of susceptibility of the majority of *S. choleraesuis* isolates in the geographic area. Bacterial isolation and antimicrobial sensitivity testing in a particular disease outbreak will allow adjustments in therapy. Anti-inflammatory agents may be of benefit in severely affected pigs.

Oral medication (feed or water) begun early in an outbreak may decrease the numbers of new cases by decreasing organism shedding and increasing the dose required to infect healthy penmates. Oral medications are not sufficient to treat disease since affected pigs rarely eat and often do not consume sufficient water for adequate doses of medication to be delivered.

Management practices to reduce the exposure of pigs to *S. choleraesuis* are important in any outbreak. The most important step is to remove and isolate all sick pigs because they shed large numbers of organisms. Thorough cleaning of the pens and water bowls, covering any gutters that connect adjacent pens and the elimination of traffic from affected to non-affected groups are important. Recycling of flush water should be halted. Efforts to reduce and eliminate any stress factors are essential. Pens should be kept dry, clean, and well-ventilated. Pigs should be protected from weather extremes and overcrowding, and should be provided with high quality food and fresh, palatable water.

Prevention and Control

Currently, there are no practical methods to accurately identify asymptomatic carriers of *S.choleraesuis*, therefore, neither eradication nor prevention of introduction are consistently possible. Most carrier pigs apparently shed the organism in their feces only infrequently, thus making fecal culture unreliable. Isolation from tonsils, neutrophils, or blood has not been proven reliable. Blood tests can detect antibodies to *Salmonella* but these tests are rarely used because they cannot differentiate between infection with various serotypes of *Salmonella* nor between animals that have eliminated the organism from their system and those which have not. These tests are not specific for *S. choleraesuis*, but there is optimism that ELISA technology will eventually aid identifying infected individuals and/or herds in the future.

Prevention of clinical disease relies heavily on good management and husbandry practices. All-in/all-out management systems by age and building with thorough sanitation between groups is most desirable. Pigs of different ages or sources should not be commingled. Thorough cleaning and disinfection are important before adding new pigs to empty pens or buildings.

In the early 1990's, a very effective modified-live, avirulent vaccine (MLV) was introduced to prevent and control *S. choleraesuis* infections. There are now at least three such products that can be administered intranasally, intramuscularly, or orally to pigs as young as one week of age. If properly administered, these products control disease well with a single vaccination, are safe, and have duration of immunity that can provide protection until pigs are marketed. Since these vaccines contain live organisms, the producer must be certain that it is not used while pigs are consuming antimicrobials or water treated with medications or chlorine. The effectiveness of these products are in no small part responsible for the decrease in prevalence of clinical *S. choleraesuis* infections witnessed over the past decade. It is not unusual to see a favorable response (decreased duration and severity of the outbreak) by vaccination of affected groups of pigs. Most producers will then choose to vaccinate the next group of pigs entering the facility to help break the cycle of infection. In those environments or flows of pigs where likelihood of infection or disease is high, vaccine is applied to all pigs produced. In other situations, vaccine can be used intermittently to effectively control disease in the production system.

Several killed vaccines for *S. choleraesuis* are also available commercially. Experimental evidence indicates that either killed or endotoxin-based products increase the number of *Salmonella* organisms required to cause illness, but vaccinated animals do not become completely resistant to either infection or disease.

Clinical observations indicate that vaccination reduces but does not always eliminate salmonellosis in the herd. Pork producers should keep in mind that immunity can be overwhelmed by large numbers of organisms in herds with poor sanitation. Concurrent diseases (e.g. pseudorabies, PRRS) at the time of vaccination will also decrease effectiveness. Therefore, management efforts to provide a reduced-stress

environment and to reduce fecal shedding and exposure are still important in controlling *S. choleraesuis* in a vaccinated herd.

The prophylactic use of antibacterial agents in the feed may decrease the incidence of clinical disease but does not prevent infection or eliminate *S. choleraesuis*. This practice is expensive, encourages antibiotic resistance, and is generally regarded as the least desirable option for prevention and control. If used prophylactically, feed grade antibacterial additives should be used at treatment rather than at growth promoting levels for short periods of time (pulse doses). To decrease the risk of drug resistance, the same antibacterial drug should not be fed continuously.

Summary

1. Salmonella infection of swine remains a huge concern and economic burden for United States pork producers because of the disease in pigs which may result as well as the hazard presented to humans by infected pork products.
2. The primary cause of salmonellosis (disease) in swine is *Salmonella choleraesuis.*
3. *Salmonella choleraesuis* is transmitted by direct contact and by feces or feces-contaminated materials from clinically infected or carrier pigs. Feed and other animals are not a source of infection.
4. A tentative diagnosis is based on clinical signs and postmortem lesions. Confirmation requires histopathologic examination of tissues and bacterial isolation of the organism.
5. Systemic antibacterial drugs provide the most effective treatment in an acute outbreak of septicemic *S. choleraesuis* infection. Affected pigs should be injected. Antibiotics administered via feed or drinking water may be used to help reduce new infections and reduce the number of clinically affected pigs.
6. Initial selection of antibacterial drugs is based on prior knowledge of the sensitivity of *S. choleraesuis* isolates in a given area and by antimicrobial sensitivity testing of the offending organism.
7. Good management practices that reduce exposure to the organism and reduce stress on animals are very important in treating and controlling the disease.
8. Current methods do not enable detection of carrier pigs making it extremely difficult to prevent the introduction of *S. choleraesuis* into a herd.
9. Vaccination, in conjunction with good management practices, is extremely useful in reducing incidence and severity of outbreaks and may eliminate clinical disease entirely.

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