Slide 1

Porcine and Rangiferine Brucellosis: *Brucella suis*

Enzootic Abortion, Contagious Abortion, Undulant Fever

Slide 2

Overview

- Organism
- History
- Epidemiology
- Transmission
- Disease in Humans
- Disease in Animals
- Prevention and Control
- Actions to Take

In today's presentation we will cover information regarding the organism that causes brucellosis in swine and its epidemiology. We will also talk about the history of the disease, how it is transmitted, species that it affects (including humans), and clinical and necropsy signs observed. Finally, we will address prevention and control measures for swine brucellosis, as well as actions to take if swine brucellosis is suspected.

[Photo: Sow and piglets. Source: Scott Bauer/USDA ARS]

Slide 3

THE ORGANISM

Slide 4

The Organism

- *Brucella suis*
  - Gram negative coccobacillus
  - Facultative intracellular pathogen
- Five biovars
  - 1, 2, 3: pigs
  - 4: reindeer and caribou
  - 5: rodents
- Can persist in the environment

In pigs, brucellosis is mainly caused by *Brucella suis*, a Gram negative coccobacillus or short rod. This organism is a facultative intracellular pathogen. Other *Brucella* species rarely found in pigs include *Brucella abortus* and *B. melitensis* . *B. suis* contains more diverse isolates than other *Brucella* species, and these isolates have broader host specificity. Five *B. suis* biovars have been identified. Biovars 1, 2 and 3 are maintained in pigs; European hares are also a reservoir for biovar 2. Biovar 4 mainly affects reindeer and caribou and is not normally found in pigs, although is genetically very closely related to biovar 1. Biovar 5 occurs in rodents in the former USSR. Biovar 5 is distinct from other *B. suis* biovars, and may be more closely related to marine mammal *Brucella* isolates. *Brucella* species can persist in the environment invariably depending on temperature, pH, and humidity.

[Photo: Micrograph of *Brucella* organisms. *Brucella* spp. are gram-negative in their staining morphology. *Brucella* spp. are poorly staining, small gram-negative coccobacilli (0.5-0.7 x 0.6-1.5 µm), and are seen mostly as single cells and appearing like "fine sand". Source: CDC Public Health Image Library #1901]

Slide 5

The Many Names of Brucellosis

Human Disease	Animal Disease
• Malta Fever	• Bang's Disease
• Undulant Fever	• Enzootic Abortion
• Mediterranean Fever	• Epizootic Abortion
• Rock Fever of Gibraltar	• Slinking of Calves
• Gastric Fever	• Ram Epididymitis
	• Contagious Abortion

Due to its illustrious history, brucellosis has many different names. The disease is commonly known as undulant or Malta fever in humans and Bang's disease in animals.

Slide 6

HISTORY

Slide 7

History of Brucellosis

- Early 1800s
  - Sir William Burnett differentiates fevers affecting seamen in the Mediterranean
- Late 1880s
  - Sir David Bruce isolates the cause of Malta fever, *Micrococcus melitensis*
  - Dr. Bernhard Band discovers cause of cattle abortion in Denmark, *Bacterium abortus* ("Bang's disease")

Sir William Burnett was a physician to the British Navy in 1810 and was the first person to differentiate between the various fevers affecting seamen in the Mediterranean. It is thought that Malta became such an important center for the study of undulant fever because many British troops were sent there to recuperate following the Crimean War (1853-1856), along with skillful medical doctors utilizing clinical thermometers to monitor the disease progression. The microorganism responsible for Malta fever was discovered by a British Army physician, Sir David Bruce, on July 9, 1887, which he called *Micrococcus melitensis*. It was isolated from the spleen of a British soldier who had died of the disease. He later established goats as the main reservoir for infection by identifying the organism in their blood, urine, and milk. A Danish physician and veterinarian, Bernhard Bang discovered *Bacterium abortus* in 1897 while investigating contagious abortion that had been affecting cattle in Denmark for over a century. He also discovered the organism affected horses, sheep, and goats. Thus the disease became known as "Bang's disease". The connection between animals and humans was discovered by Alice Evans, an American bacteriologist in the 1920s.

Slide 8

History of *Brucella suis*

- 1914: *B. suis* first recognized
- 1972: National Brucellosis Eradication Program
  - *B. suis* now eliminated from commercial swine herds in U.S.
- Feral swine an emerging reservoir

B. suis was first isolated from aborting swine in the United States in 1914 by Traum. In 1972, the United States Department of Agriculture formed the National Brucellosis Eradication Program and it was subsequently expanded to cover commercial swine herds. After this, *B. suis* was virtually eliminated from domestic swine; however, the disease is still found in feral swine.

Photos: Wild pig (*Sus scrofa*) stop near the Kennedy Space Center Press Site on their daily foraging rounds. Source: National Aeronautics and Space Administration (NASA) via Wikimedia Commons at http://en.wikipedia.org/wiki/File:Wild_Pig_KSC02pd0873.jpg]

Slide 9

EPIDEMIOLOGY

Slide 10

Geographic Distribution

- Worldwide in swine-raising regions
- Eradicated from domestic pigs
  - U.S., United Kingdom, Canada, Europe
- Occurs in feral swine in many areas
- Sporadic outbreaks
  - South and Central America
  - Asia
  - Africa

In the past, *B. suis* was found worldwide in swine-raising regions. This organism has been eradicated from domesticated pigs in the U.S., Canada, many European countries, and other nations. However, it persists in wild and/or feral swine populations in some areas, including the U.S., Europe, and Queensland, Australia. Sporadic outbreaks are reported in domesticated herds or humans due to transmission from this source. *B. suis* continues to occur in domesticated herds in some countries of South and Central America (including Mexico) and Asia. Cases are occasionally reported in Africa.

Slide 11

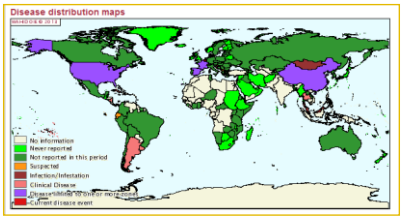
Geographic Distribution

- Biovars 1 and 3
  - Worldwide
- Biovar 2
  - Wild boar in Europe
- Biovar 4 (rangiferine brucellosis)
  - Arctic regions of N. America, Russia
- Biovar 5 (murine brucellosis)
  - Former USSR

B. suis biovars 1 and 3 are found worldwide, but other biovars have a limited geographic distribution. Biovar 2 occurs in wild boar in much of Europe. Biovar 4 (rangiferine brucellosis) is limited to the Arctic regions of North America and Russia, including Siberia, Canada, and Alaska. Biovar 5 (murine brucellosis) is found in the former USSR.

Slide 12

Geographic Distribution



This image, from the World Organization for Animal Health (OIE), shows the reported distribution of *B. suis* from January to June 2013. Red indicates a current disease event, purple indicates disease limited to one or more zones, dark green indicates disease not reported in this period, and light green indicates disease never reported. [Source: World Organization for Animal Health (OIE) WAHID at http://www.oie.int/wahis_2/public/wahid.php/Diseaseinformation/Diseasedistributionmap]

Slide 13

In the United States

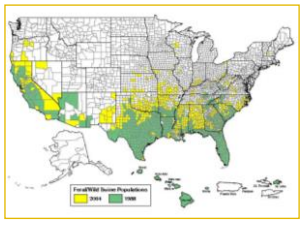


Figure 1—In 1998, feral swine could be found in parts of all the counties shown here in green. By 2004, wild pigs had increased their range to counties shown in yellow, while remaining in the green-colored areas as well. Note that wild pigs are now found in two counties in Iowa—America's #1 swine-producing State. (Map adapted from originals created by the Southeastern Cooperative Wildlife Disease Study, Athens, GA.) [Source: Feral/Wild Pigs: Potential Problems for Farmers and Hunters. United States Department of Agriculture Animal and Plant Health Inspection Service. Available at: *www.fs.usda.gov/Internet/FSE_DOCUMENTS/stelprdb5313597.pdf*]

Slide 14

Populations at Risk

- Occupational disease
  - Laboratory workers
  - Abattoir workers
  - Farmers, herders
  - Veterinarians
- Hunters
- Travelers
- Consumers
  - Unpasteurized dairy products

B. suis biovars 1, 3 and 4 are important human pathogens. Human infections are usually the result of occupational exposure in laboratory workers, abattoir workers, farmers, herders, veterinarians and others who contact infected animals or tissues. Travelers to areas with enzootic disease who consume local delicacies, such as goat, sheep, or camel milk or cheese, may become infected.

[Photo: Herding pigs. Source: Kate Harvey/CFSPH]

Slide 15

Species Affected

- Domestic and feral pigs
- European hares
- Caribou and reindeer
- Moose, cattle, Arctic foxes, wolves
- Small rodents
- Cattle, small ruminants, horses, dogs, and other spillover hosts

Most species of *Brucella* are primarily associated with certain hosts; however, infections can also occur in other species, particularly when they are kept in close contact. *B. suis* biovars 1, 2 and 3 affect swine. Biovars 1 and 3 are found in both domesticated pigs (*Sus scrofa domesticus*) and wild or feral pigs. Biovar 2 currently occurs mainly in wild boar (*Sus scrofa scrofa*) and European hares (*Lepus capensis*); however, this biovar can be transmitted from these reservoirs to domesticated pigs, and spreads readily in these herds. Biovar 4 is maintained in caribou and reindeer (*Rangifer tarandus* and its various subspecies). Biovar 4 can also infect moose, cattle, Arctic foxes and wolves. Biovar 5 is found in small rodents. Various *B. suis* biovars have been reported occasionally in cattle, small ruminants, horses, dogs and other spillover hosts.

Slide 16

TRANSMISSION

Slide 17

Transmission in Humans

- Contamination of:
  - Mucous membranes
  - Abraded skin
- Ingestion
  - Unpasteurized milk
  - Bone marrow

Humans usually become infected by the contamination of mucous membranes and abraded skin, but they can also be infected by ingesting organisms. Because porcine isolates of *B. suis* can colonize the bovine udder, unpasteurized milk can be a source of infection for people. Biovar 4 (rangiferine brucellosis) is generally transmitted to humans by direct contact, through unpasteurized milk products and in bone marrow, which is a regional delicacy.

[Photo: Bottles of raw milk. Source: Kyle McDaniel/Wisconsin State Journal]

Slide 18

Transmission in Pigs

- Ingestion
  - Contaminated feed
- Venereal
- Fomites
- Minimally important routes
  - Inhalation
  - Via broken skin or conjunctiva

In pigs, *B. suis* occurs in the fetus, placenta, fetal fluids and vaginal discharges after an abortion or stillbirth. Pigs usually become infected when they ingest feed contaminated by birth or abortion products, or eat aborted fetuses and membranes. Venereal transmission is also common in swine. *B. suis* is shed in semen; both symptomatic and asymptomatic boars can excrete bacteria. *B. suis* can be also spread on fomites, particularly feed and water. Transmission could occur by inhalation, through the conjunctiva or via broken skin, but these routes seem to be of minimal epidemiological significance in pigs. Other species can be infected with *B. suis* after contact with infected pigs or other maintenance hosts.

[Photo: Sow and piglets. Source: www.public-domain-image.com]

Slide 19

DISEASE IN HUMANS

Slide 20

Disease in Humans

- May be asymptomatic
- If symptomatic:
  - Disease is variable
  - Often begins as acute febrile illness with influenza-like signs
- Spontaneous recovery possible
- Disease may wax and wane

Some *Brucella* infections are asymptomatic in humans. In symptomatic cases, the disease is extremely variable and the clinical signs may appear insidiously or abruptly. Typically, brucellosis begins as an acute febrile illness with nonspecific flu-like signs such as fever, headache, malaise, back pain, myalgia and generalized aches. Drenching sweats can occur, particularly at night. Some patients recover spontaneously, while others develop persistent symptoms that typically wax and wane.

Slide 21

Treatment and Prognosis in Humans

- Possible complications
  - Arthritis, spondylitis, chronic fatigue, epididymo-orchitis
  - Neurologic signs
- Treatment with antibiotics
  - Relapses possible
- Low mortality
  - 2 to 5% (untreated cases)
  - Death from endocarditis, meningitis

Occasionally seen complications include arthritis, spondylitis, chronic fatigue, and epididymo-orchitis. Neurologic signs (including personality changes, meningitis, uveitis and optic neuritis), anemia, internal abscesses, nephritis, endocarditis and dermatitis can also occur. Other organs and tissues can also be affected, resulting in a wide variety of syndromes. Treatment is with antibiotics; however, relapses can be seen months after the initial symptoms, even in successfully treated cases. The mortality rate is low; in untreated persons, estimates of the case fatality rate vary from less than 2% to 5%. Deaths are usually caused by endocarditis or meningitis.

Slide 22

DISEASE IN ANIMALS

Slide 23

Disease in Swine

- Clinical signs
  - Abortion
  - Weak or stillborn piglets
  - Metritis
  - Epididymitis and orchitis
  - Abscesses
  - Sterility (may be permanent)
  - Swollen joints, tendon sheaths

In pigs, the most common symptoms are abortion, which can occur at any time during gestation, and weak or stillborn piglets. Weak piglets may die before weaning. Vaginal discharge is often minimal in pigs that abort, and abortions may be mistaken for infertility. Occasionally, some sows develop metritis. *B. suis* can also cause epididymitis and orchitis in boars. Abscesses and swelling are sometimes seen, and the testes may become sclerotic and atrophy during the final stages of disease. The lesions are often unilateral. Boars can also excrete *B. suis* asymptomatically in the semen, and sterility may be the only sign of infection. Swollen joints and tendon sheaths, accompanied by lameness and incoordination, can occur in both sexes. Less common signs include posterior paralysis, spondylitis, metritis and abscess formation in various organs. Although some pigs recover, others remain permanently infected. Fertility can be permanently impaired, particularly in boars. Some animals remain asymptomatic.

Slide 24

Disease in Other Animals

- Hares (biovar 2)
  - Nodules in internal organs
- Horses
  - Inflammation of:
    - Supraspinous bursa (fistulous withers)
    - Supra-atlantal bursa (poll evil)
- Caribou and reindeer (biovar 4)
  - Abortion, retained placenta, metritis
  - Lameness

In hares, *B. suis* biovar 2 infection is characterized by nodules in the internal organs, particularly the reproductive organs, as well as the subcutaneous tissues and muscles. Horses exposed to infected pigs can also be infected, although this occurs rarely. In horses, *B. suis* usually causes inflammation of the supraspinous or supra-atlantal bursa; this syndrome is known, respectively, as fistulous withers or poll evil. The bursal sac becomes distended by a clear, viscous, straw-colored exudate and develops a thickened wall. It can rupture, leading to secondary inflammation. In caribou and reindeer, *B. suis* biovar 4 can cause abortion and retained placenta in females. Metritis can occur, and may be accompanied by a bloodstained discharge. Mastitis is also seen. Orchitis can occur in males. Lameness may be seen in both sexes, as a result of arthritis, bursitis, tenosynovitis and/ or hygromas. Subcutaneous abscesses also occur.

Slide 25

Morbidity and Mortality

- *B. suis* eradiated from domesticated swine in most developed countries
  - Found in U.S. feral swine
- Biovar 2: European wild boar
- Morbidity high in naïve herds
  - High abortion rates
  - Non-specific infertility in endemic herds
- Mortality rare in adult pigs

B. suis has been eradicated from domesticated swine in some countries, including the U.S. However, this infection still occurs in wild and feral pigs in some areas, including the U.S., and can spread to domesticated herds. Biovar 2 is thought to be widespread in wild boar in Europe, although infections are not always associated with gross lesions. Domesticated pigs reared outdoors are at highest risk of infection by biovar 2. The morbidity rate varies with the length of time *B. suis* has been in the herd. When this organism is first introduced into a herd, there may be a significant increase in returns to service, abortions and stillbirths, weak piglets, lameness/ arthritis, posterior paralysis and other signs. The pre-weaning mortality rate usually increases. In endemic herds, brucellosis may appear as non-specific infertility, a slightly

reduced farrowing rate, and irregular estrus cycles. In domesticated pigs, the abortion rate from *B. suis* varies widely, from 0% to 80%. Natural resistance to *Brucella suis* exists among swine, and pigs can be bred to increase their resistance to infection. Deaths are rare except in the fetus and newborn.

Slide 26

Differential Diagnosis

- Aujeszky's disease
- Leptospirosis
- Erysipelas
- Salmonellosis
- Streptococcidiosis
- Classical swine fever
- Porcine parvovirus

Porcine brucellosis can be difficult to diagnose and is usually recognized as a herd problem rather than a disease of individual swine. Porcine brucellosis should be suspected when reproductive failure in sows, orchitis in boars and lameness, arthritis or paralysis occur together in a herd. In herds where *B. suis* has become endemic, the symptoms can be subtle and this classical presentation may not be seen. Other diseases causing abortion, orchitis, arthritis, posterior paralysis and lameness should be considered. In pigs, the differential diagnosis for abortion includes a number of other diseases including Aujeszky's disease, leptospirosis, erysipelas, salmonellosis, streptococcidiosis, classical swine fever and porcine parvovirus infection.

Slide 27

Collecting Samples

- Testes
- Vaginal swabs or semen
- Fetal organs
- Placenta
- Adult necropsy
  - Spleen, genital lymph nodes, liver, uterus

B. suis biovars 1, 3 and 4 are highly pathogenic for humans; samples should be collected and handled with all appropriate precautions. A variety of samples can be collected for culture and microscopic examination. Vaginal swabs, semen or blood samples can be submitted from live animals. Testicles can be submitted after castration. The placenta or aborted/ stillborn fetuses can also be cultured. At necropsy, *B. suis* can be isolated from lymph nodes and various organs including the spleen, liver and reproductive organs (uterus, testis, epididymis, seminal vesicles, bulbourethral glands).

[Photo: Blood collection on a pig. Source: Alex Ramirez/Iowa State University, CFSPH]

Slide 28

Laboratory Diagnosis

- Culture and identification
  - Phage typing
  - Biochemical characteristics
  - Genetic techniques (e.g., PCR)
- Serology
  - Best for herd surveillance
  - Cross-reactions may occur
  - ELISA, buffered *Brucella* antigen tests, complement fixation

A definitive diagnosis can be made if *B. suis* is cultured from an animal. *Brucella* spp. can be isolated on a variety of plain media, or selective media such as Farrell's medium or Thayer-Martin's modified medium. Enrichment techniques can also be used. *Brucella* colonies usually become visible after two days growth. *B. suis* is a smooth (S) form, like *B. abortus*. *B. suis* can be identified to the species and biovar level by phage typing and cultural, biochemical and serological characteristics. Polymerase chain reaction (PCR) techniques are available in some laboratories. In swine, serology is generally considered to be more reliable for identifying infected herds than individual pigs. Serological tests are not completely specific and cannot always distinguish reactions due to B. suis from cross-reactions to other bacteria, particularly Yersinia enterocolitica O:9. Serological tests used in swine include indirect or competitive enzyme-linked immunosorbent assays (ELISAs), the buffered Brucella antigen tests (rose bengal test and buffered plate agglutination test) and complement fixation. A fluorescence polarization assay has been developed. Supplemental serological tests used in cattle may also be used in swine.

Slide 29

PREVENTION AND CONTROL

Slide 30

Recommended Actions

- Notification of authorities
  - Federal Area Veterinarian in Charge (AVIC)
    http://www.aphis.usda.gov/animal_health/area_offices/
  - State veterinarian
    http://www.aphis.usda.gov/emergency_response/downloads/nahems/fad.pdf

B. suis infections are reportable in the U.S. State and/or federal authorities should be consulted for specific guidelines.

Slide 31

Prevention and Control

- Prevent introduction
  - Test, obtain animals from brucellosis-free areas
- Herd eradication
  - Test, depopulate, slaughter, genetics
- General infection control
  - Disinfection
  - Hygiene

B. suis is most likely to be introduced into a herd in an infected animal. Semen could also be a source of infection. Any addition to herds should be verified to come from a brucellosis-free state, country, or herds. If the animal cannot be verified, testing should be conducted before introduction. This organism can be eradicated from a herd by test and slaughter procedures, or by depopulation. Some programs exist to retain desirable genetics in the herd that will increase the herds resistance to *B. suis*. Transmission is also reduced by immediate disposal of the placenta, contaminated bedding and other infectious material, followed by thorough cleaning and disinfection. Infections in other species are prevented by controlling *B. suis* in swine.
[Photo: Piglets. Source: USDA ARS]

Slide 32

Prevention and Control

- Education about risk of transmission
  - Laboratory workers, abattoir workers, farmers, herders, veterinarians
- Wear proper attire if dealing with infected animals/tissues
  - Gloves, masks, goggles

Educate those at greatest risk about the routes of transmission of brucellosis. Those who have the greatest occupational exposure are people who can come into contact with infected animals or tissues from infected animals. These include laboratory workers, abattoir workers, farmers, herders, veterinarians and others who contact infected animals or tissues. Properly protecting yourself, if you are an "at risk" individual, by wearing gloves, masks, goggles, and coveralls to prevent exposure to tissues and body secretions of infected animals can help.

Slide 33

Prevention and Control

- Readily killed by most disinfectants
  - Hypochlorite
  - 70% ethanol
  - Isopropanol
  - Iodophores
  - Phenolics
  - Formaldehyde/glutaraldehyde
- Quaternary ammonium compounds not recommended

Brucella species are readily killed by most commonly available disinfectants including hypochlorite solutions, 70% ethanol, isopropanol, iodophores, phenolic disinfectants, formaldehyde, glutaraldehyde and xylene; however, organic matter and low temperatures decrease the efficacy of disinfectants. Alkyl quaternary ammonium compounds are not recommended. Autoclaving [moist heat of 121°C (250°F) for at least 15 minutes] can be used to destroy *Brucella* species on contaminated equipment.

[Photo: Disinfectant bottles. Source: Dani Ausen/CFSPH]

Slide 34

Additional Resources

- Center for Food Security and Public Health
  - www.cfsph.iastate.edu
- CDC Brucellosis
  - http://www.cdc.gov/ncidod/dbmd/diseaseinfo/brucellosis_g.htm
- USDA APHIS Swine Brucellosis
  - http://www.aphis.usda.gov/animal_health/animal_dis_spec/swine/

Slide 35

Acknowledgments

Development of this presentation was made possible through grants provided to the Center for Food Security and Public Health at Iowa State University, College of Veterinary Medicine from the Centers for Disease Control and Prevention, the U.S. Department of Agriculture, the Iowa Homeland Security and Emergency Management Division, and the Multi-State Partnership for Security in Agriculture.

Authors: *Kerry Leedom Larson, DVM, MPH, PhD, DACVPM; Anna Rovid Spickler, DVM, PhD; Sarah Viera, MPH*
Reviewer: *Glenda Dvorak, DVM, MPH, DACVPM*

Last updated: January 2012