Slide 1

Canine Brucellosis:
Brucella canis

Contagious Abortion,
Undulant Fever

Canine brucellosis, caused by *Brucella canis*, is an important cause of reproductive failure, particularly in kennels. *B. abortus* causes abortions, stillbirths, epididymitis, orchitis and sperm abnormalities in dogs. Canine brucellosis can end the reproductive career of a breeding animal. *B. canis* is zoonotic, although disease appears to be rare in humans.

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 canine brucellosis 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 canine brucellosis, as well as actions to take if canine brucellosis is suspected.

[Photo: Dog and pup. Source: AVMA Photo Gallery]

Slide 3

THE ORGANISM

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The Organism

- *Brucella canis*
  - Gram negative coccobacillus
  - Facultative intracellular pathogen
- Other *Brucella* species that can affect dogs
  - *B. abortus, B. melitensis, B. suis*
- Can persist in the environment

In dogs, brucellosis is mainly caused by *Brucella canis*, a Gram-negative coccobacillus or short rod. This organism is a facultative intracellular pathogen. Other *Brucella* species occasionally associated with disease in dogs include *Brucella abortus*, *B. melitensis* and *B. suis*. Genetic and immunologic evidence suggests that all members of the genus *Brucella* are closely related, and some microbiologists have proposed that this genus be reclassified into a single species (*B. melitensis*), which contains many biovars. This proposal is controversial, and both taxonomic systems are currently in use. *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]

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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.

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HISTORY

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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.

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History of Brucella canis

- First isolated in 1966
  - Dogs, caribou, and reindeer
- Now known to be an important cause of economic loss in kennels

Brucella canis was first isolated in 1966 in dogs, caribou, and reindeer. It has been since been recognized as a cause of economic loss in kennels.

Source: Canine brucellosis. Wanke MM. Anim Reprod Sci. 2004 Jul;82-83:195-207.
[Photo: Dog kennel. Source: USDA APHIS Image Gallery]

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EPIDEMIOLOGY

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Geographic Distribution

- United States
- Canada
- Central and South America
- Some European countries
- Parts of Africa and Asia
- Free areas
  - Australia, New Zealand

B. canis has been reported from the United States (particularly the southern states), Canada, Central and South America (including Mexico) some European countries, Tunisia, Nigeria, Madagascar, Malaysia, India, Korea, Japan and China. *B. canis* is probably found throughout most of the world; however, New Zealand and Australia appear to be free of this organism.

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Species Affected

- Mainly dogs
- Experimental infection
  - Domestic livestock
  - Chimpanzees
- Humans
  - Laboratory workers
  - People in close contact with dogs

Dogs are the only species known to be affected by *B. canis*; however, antibodies to this organism have been found in other carnivores. Experimental infections can be established in domesticated livestock and chimpanzees; however, these species are considered highly resistant to natural exposure. *B. canis* is zoonotic, but human infections seem to be uncommon. Cases have been reported in laboratory workers and people in close contact with dogs.

[Photo: A veterinarian examining a dog. Source: AVMA Photo Gallery]

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TRANSMISSION

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Transmission in Humans

- Ingestion
- Contamination of mucous membranes and abraded skin
- Close contact required
  - Infected dogs
  - Bacterial cultures

Humans usually become infected with *Brucella* spp. by ingesting organisms or by the contamination of mucous membranes and abraded skin. Infection with *B. canis* seems to require close contact with infected dogs or contact with bacterial cultures.

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Transmission in Animals

- Contact with fetus/fetal membrane
  - Ingestion
  - Mucous membranes
  - Broken skin
- Venereal
- *In utero*
- Milk
- Fomites

B. canis occurs in the fetus, placenta, fetal fluids and vaginal discharge after an abortion or stillbirth. This organism can be found in vaginal discharges for 4 to 6 weeks after an abortion. High concentrations of *B. canis* are found in semen for up to two months after infection, and intermittent shedding of smaller quantities can occur for years. Although some dogs clear the infection after a year, others remain bacteremic for five years and possibly longer. *B. canis* is also found in urine, and low concentrations of bacteria may be excreted in saliva, nasal and ocular secretions, and feces. In dogs, *B. canis* is mainly transmitted by contact with the fetus and fetal membranes after abortions/stillbirths, or by venereal transmission. This organism primarily enters the body by ingestion and through the genital, oronasal and conjunctival mucosa, but transmission through broken skin may also be possible. *In utero* infections occur. Nursing puppies can be infected from milk, but the importance of this route is controversial. Other potential sources of infection include blood transfusions and contaminated syringes. *B. canis* can also be spread on fomites.

[Photo: Fomites. Source: Danelle Bickett-Weddle/CFSPH]

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DISEASE IN HUMANS

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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.

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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.

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DISEASE IN ANIMALS

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Clinical Signs

- Incubation period: 2 to 3 weeks
- Pregnant dogs
  - Late-term abortion, stillbirths
  - Vaginal discharge
  - Weak pups that die soon after birth
- Males
  - Abnormal sperm
  - Epididymitis, scrotal edema, orchitis

Dogs usually become bacteremic two to three weeks after infection. *B. canis* can cause abortions and stillbirths in pregnant dogs. Most abortions occur late, particularly during the seventh to the ninth week of gestation. Abortions are usually followed by a mucoid, serosanguinous or gray-green vaginal discharge that persists for up to six weeks. Early embryonic deaths and resorption have been reported a few weeks after mating, and may be mistaken for failure to conceive. Some pups are born live but weak; these pups often die soon after birth. Other congenitally infected pups can be born normal and later develop brucellosis. Clinical signs occur during subsequent pregnancies in some dogs, but not in others. The sperm may have morphological abnormalities and reduced viability in some infected males. Epididymitis, scrotal edema and orchitis may also be apparent. Scrotal dermatitis can occur due to self-trauma. Unilateral or bilateral testicular atrophy can be seen in chronic infections, and some males become infertile.

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Clinical Signs

- Lymphadenitis
- Other general signs
  - Lethargy
  - Decreased appetite
  - Behavioral abnormalities
  - Stiffness, lameness, or back pain
- Many dogs asymptomatic
- Chronic infections possible

Lymphadenitis is common in infected dogs. The retropharyngeal lymph nodes may enlarge after oral infection, and the superficial inguinal and external iliac nodes after vaginal infection. Generalized lymphadenitis is also common. Other symptoms that are occasionally reported include lethargy or fatigue, exercise intolerance, decreased appetite, weight loss and behavioral abnormalities (loss of alertness, poor performance of tasks); however, most affected dogs do not appear seriously ill. Occasionally, discospondylitis of the thoracic and/or lumbar vertebrae can cause stiffness, lameness or back pain. Uveitis, endophthalmitis, polygranulomatous dermatitis, endocarditis and meningoencephalitis have also been reported. Fever is rare. Many infected dogs remain asymptomatic. Dogs with brucellosis may recover spontaneously, beginning a year after infection, but recovery is more common after 2 to 3 years, and some dogs remain chronically infected for at least five years.

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Postmortem Lesions

- Lymph node enlargement
  - Retropharyngeal, inguinal, generalized lymphadenitis
- Splenomegaly
- Hepatomegaly
- Scrotal dermatitis, epididymitis

The lymph nodes are often enlarged in affected animals. The retropharyngeal and inguinal lymph nodes are often involved, but generalized lymphadenitis also occurs. The spleen is frequently enlarged, and may be firm and nodular. Hepatomegaly may also be seen. Scrotal edema, scrotal dermatitis, epididymitis, orchitis, prostatitis, testicular atrophy and fibrosis occur in some infected males, and metritis and vaginal discharge may be seen in females. Aborted puppies are often partially autolyzed and have evidence of generalized bacterial infection.

[Photo: Dog, scrotum. Scrotal edema and congestion. Source: Armed Forces Institute of Pathology/CFSPH]

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Morbidity and Mortality

- All dogs susceptible
  - Prevalence unclear
    - Up to 30% reported in S., Central America
    - Up to 6% in Southern U.S.
  - Most common in stray/feral dogs
- Death is rare
  - Fetus, neonate most affected
- May cause significant reproductive losses in breeding kennels

All breeds of dogs are susceptible to canine brucellosis. The prevalence of infection is unknown. A seroprevalence rate of 30% has been reported in Central and South America. In one survey of the southern U.S., approximately 6% of dogs had antibodies to *B. canis.* Infections are particularly common in stray and feral dogs. Although death is rare, except in the fetus and neonate, significant reproductive losses can be seen, particularly in breeding kennels. Up to 75% fewer puppies may be weaned from affected kennels.

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Differential Diagnosis

- Beta-hemolytic streptococci
- *Escherichia coli*
- *Mycoplasma*, *Ureaplasma*
- *Streptomyces*
- *Salmonella*, *Campylobacter*
- Canine herpesvirus
- *Neospora caninum*
- *Toxoplasma gondii*

Canine brucellosis should be considered when abortions and stillbirths are seen, particularly late in gestation, or when male dogs develop epididymitis and testicular atrophy. Some infected dogs are asymptomatic or have only nonspecific signs such as lymphadenitis. The differential diagnosis includes beta-hemolytic streptococci, *Escherichia coli*, *Mycoplasma*, *Ureaplasma*, *Streptomyces*, *Salmonella*, *Campylobacter*, canine herpesvirus, *Neospora caninum* and *Toxoplasma gondii*.

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Laboratory Diagnosis

- Serology
  - Rapid slide agglutination, indirect fluorescent antibody, AGID, ELISA
  - Cross-reactions may occur
    - Other *Brucella* spp., Gram negatives
- Culture and identification
  - Definitive diagnosis
- PCR

Serology can be used for a presumptive diagnosis. Serological tests for *B. canis* include rapid slide agglutination (card or RSAT) tests, tube agglutination, an indirect fluorescent antibody (IFA) test, agar gel immunodiffusion and enzyme-linked immunosorbent assays (ELISA). Cross-reactions between *B. canis* and other Gram-negative bacteria can occur in some tests, particularly agglutination tests. A definitive diagnosis can be made if *B. canis* is cultured from an animal. *Brucella* can be cultured 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. *B. canis* colonies are naturally rough (R) or mucoid (M). Repeated cultures may be necessary to detect *B. canis*. Polymerase chain reaction (PCR) assays are available in some laboratories.

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PREVENTION AND CONTROL

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Recommended Actions

- Notification of authorities
  - Federal
    - Area Veterinarian in Charge (AVIC)
      http://www.aphis.usda.gov/animal_health/area_offices/
  - State
    - State Animal Health Officials (SAHO)
      www.usaha.org/Portals/6/StateAnimalHealthOfficials.pdf

Canine brucellosis is reportable in some states. State and/or federal authorities should be consulted immediately for specific guidance if brucellosis is suspected.

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Prevention and Control

- Kennels and breeding programs
  - Remove infected dogs
  - Individual caging
  - Repeated testing
- No vaccine
- Antibiotics
  - May be useful
- Neuter

Canine brucellosis is usually introduced into a kennel in an infected dog or semen. This disease is controlled by sanitation and the removal of infected dogs. Housing in individual cages reduces the spread of the organism. Repeated testing and the removal of seropositive or culture-positive animals, combined with quarantine and testing of newly added dogs, have been used to eradicate brucellosis from some kennels. There is no vaccine for *B. canis.* Long-term antibiotic therapy has been used successfully to treat some dogs, but some animals relapse. Neutering can be used as an additional control measure.

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Prevention and Control

- Education about risk of transmission
  - Veterinarians, animal husbandry clubs, laboratory workers, and dog breeders
- 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 come into contact with infected animals or tissues from infected animals. These include veterinarians, members of animal husbandry clubs, laboratory workers, and dog breeders. 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.

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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]

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Additional Resources

- Center for Food Security and Public Health
  - www.cfsph.iastate.edu
- Centers for Disease Control and Prevention (CDC): Brucellosis
  - http://www.cdc.gov/ncidod/dbmd/diseaseinfo/brucellosis_g.htm

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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.

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Last updated: January 2012