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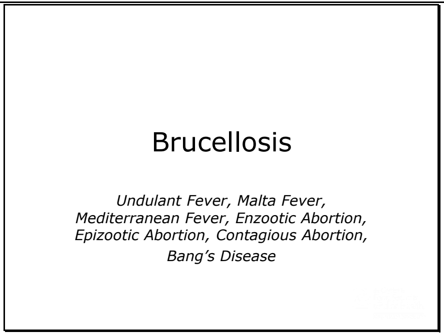
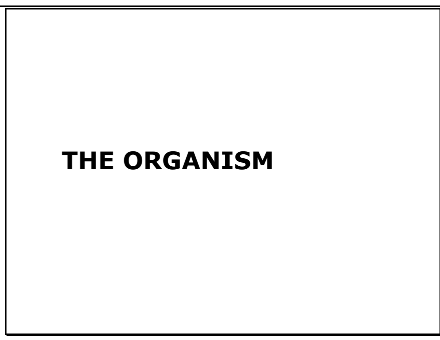


Slide 2

In today's presentation we will cover information regarding the organism that causes 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 brucellosis, as well as actions to take if brucellosis is suspected.

[Photos: (Top) Cow and calf. Source: Dr. Beth Carlson/North Dakota State Board of Animal Health/CFSPH; (Middle) Goat. Source: Wikimedia-commons; (Bottom) Feral hog with piglets. Source: Alabama Wildlife Damage Management]

Slide 3



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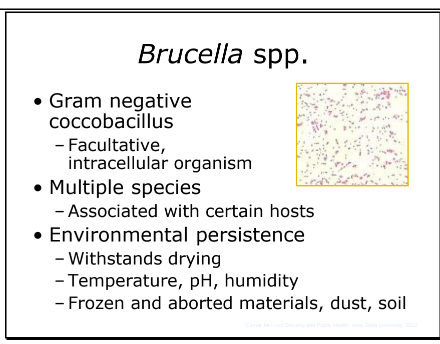

Brucellosis is caused by various species of the genus *Brucella*, Gram negative, facultative intracellular bacteria (coccobacillus or short rods). Each *Brucella* species is associated most often with certain mammalian hosts. The organism is able to withstand drying, particularly when organic material is present and can survive in dust and soil. In conditions of high humidity, low temperatures, and no sunlight, these organisms can remain viable for several months in water, aborted fetuses, manure, wool, hay, equipment and clothing. *Brucella* spp. can survive even longer at lower temperatures, particularly when it is below freezing.

[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

Species	Biovar/ Serovar	Natural Host	Human Pathogen
B. abortus	1-6, 9	cattle, bison, buffalo	yes
B. melitensis	1-3	goats, sheep	yes
B. suis	1, 2, 3	swine	yes
	2	European hares	yes
	4*	reindeer, caribou	yes
	5	rodents	yes
B. canis	none	dogs, other canids	yes
B. ovis	none	sheep	no
B. neotomae	none	rodents	no
B. maris *B. pinnipediae,* *B. cetaceae(?)*		marine mammals	yes?

Six named species occur in animals (*Brucella abortus*, *B. melitensis*, *B. suis*, *B. canis*, *B. ovis*, *and B. neotomae*). One or more unnamed species of *Brucella* have been found in marine mammals; formal names have been proposed but not yet accepted [*B. maris* proposed for all marine mammal strains; *B. pinnipediae* for pinnipeds (seals, sea lions, and walruses) strains; *B. cetaceae* for cetaceans (whales, porpoises, and dolphins) strains]. *B. abortus* usually causes brucellosis in cattle, bison, and buffalo. *B. melitensis* is the most important species in sheep and goats. *B. ovis* can cause infertility in rams. *B. canis* causes disease almost exclusively in dogs. *B. neotomae* is found in rodents, but has not been linked to disease. *B. suis* contains more diverse isolates which have broader host specificity. Some species of *Brucella* contain biovars which vary in their natural host. *B. suis* has 5 biovars, *B. melitensis* has 3 and *B. abortus* has up to 9 different biovars; the associated natural hosts for these biovars are shown in this table. Many *Brucella* species are pathogenic to humans (see above chart). Listed in decreasing pathogenicity to human are *B. melitensis*, *B. suis* (biovars 1,3, 4), *B. abortus*, and rarely *B. suis* biovar 2, *B. canis*, and marine mammal *Brucella*.

*Note: *B. suis* biovar 4 was formerly known as *B. rangiferi*.

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HISTORY

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The Many Names of Brucellosis

Human Disease
- Malta Fever
- Undulant Fever
- Mediterranean Fever
- Rock Fever of Gibraltar
- Gastric Fever

Animal Disease
- Bang's Disease
- Enzootic Abortion
- Epizootic Abortion
- Slinking of Calves
- 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 of Brucellosis

- 450 BC: Described by Hippocrates
- 1905: Introduced to the U.S.
- 1914: *B. suis*
  - Indiana, United States
- 1953: *B. ovis*
  - New Zealand, Australia
- 1966: *B. canis*
  - Dogs, caribou, and reindeer

In his book Epidemics, Hippocrates first described a condition of recurring fever and death with a duration of 4 months in 450 B.C. Undulant fever did not enter into the United States until 1905 through the shipping of 65 Maltese goats on the *S.S. Joshua Nicholson. B. suis* was isolated in 1914 by Traum in the U.S. from aborting swine in Indiana. *B. ovis* was isolated in 1953 from sheep with ram epididymitis in New Zealand and Australia. *B. canis* was discovered in 1966 from dogs, caribou, and reindeer.

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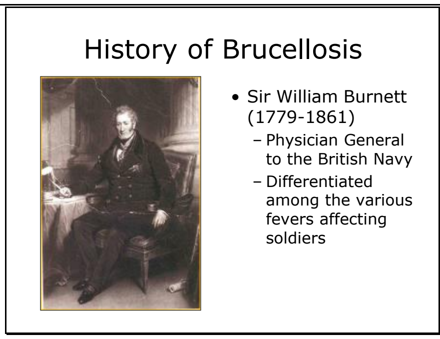

The island of Malta was given to the Knights of the Order of St. John in 1530, and contagious fevers were noted from that time well into the 19th century. During the 17th and 18th centuries there were numerous reports of undulant fevers from all over the Mediterranean and most were given local names (Mediterranean fever, Rock fever of Gibraltar, Cyprus fever, Danube fever). 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.

[Photo: Sir William Burnett. Source: U.S. National Library of Medicine – Images from the History of Medicine]

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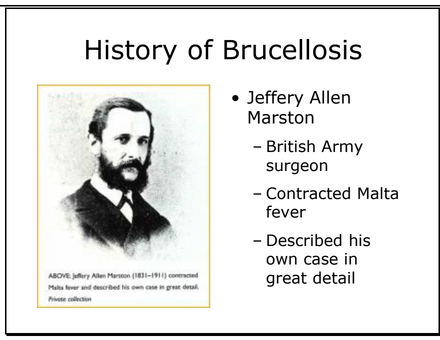

J.A. Marston was an army surgeon (British) who, after contracting the Malta fever, wrote the first detailed account of the disease (his own illness). He was afflicted with an irregular fever for 30 to 90 days, gastrointestinal symptoms, and muscle and joint pains.

[Photo: Jeffery Allen Marson. Source: The Wellcome Trust Illustrated History of Tropical Diseases]

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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 also identified that the organism grew best at higher temperatures and speculated that this accounted for the increased frequency of cases in hot summer months. He later established goats as the main reservoir for infection by identifying the organism in their blood, urine, and milk. This discovery helped explain the epidemiology of the disease. For example, officers were three times more likely to become ill because they drank more milk than private soldiers, and large numbers of cases were found in hospitals where milk was widely distributed.
[Photo: Sir David Bruce. Source: The Wellcome Trust Illustrated History of Tropical Diseases]

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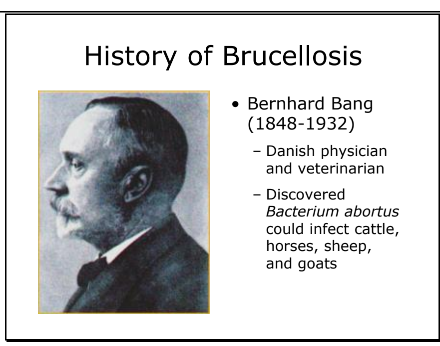

A Danish physician and veterinarian, Bernhard Bang discovered *Bacterium abortus* in 1897 while investigating contagious abortion that had been affecting cattle in Denmark for over a century. He also discovered the organism affected horses, sheep, and goats. Thus the disease became known as "Bang's disease". [Photo: Bernhard Bang. Source: The Wellcome Trust Illustrated History of Tropical Diseases]

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History of Brucellosis

- Alice Evans
  - American bacteriologist credited with linking the organisms in the 1920s
  - Discovered similar morphology and pathology between:
    - Bang's *Bacterium abortus*
    - Bruce's *Micrococcus melitensis*
- *Brucella* nomenclature
  - Credited to Sir David Bruce

The connection between animals and humans was discovered by Alice Evans, an American bacteriologist in the 1920s. The morphology and pathology of the organism was very similar between Bang's *Bacterium abortus* and Bruce's *Micrococcus melitensis*. The name of Sir David Bruce has been carried on in today's nomenclature of the organisms.

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EPIDEMIOLOGY

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Populations at Risk

- Occupational disease
  - Cattle ranchers/dairy farmers
  - Veterinarians
  - Abattoir workers
  - Meat inspectors
  - Lab workers
- Hunters
- Travelers
- Consumers
  - Unpasteurized dairy products

Brucellosis is predominantly an occupational disease of those working with infected animals or their tissues, but can also infect consumers of unpasteurized dairy products, and hunters who unknowingly handle infected animals. Illness in people can be very protracted and painful, and can result in an inability to work and loss of income. Travelers to areas with enzootic disease who consume local delicacies, such as goat, sheep, or camel milks or cheeses, may become infected.
[Photo: Bottles of raw milk. Source: Kyle McDaniel/Wisconsin State Journal]

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Brucella melitensis

- Distribution
  - Mediterranean, Middle East, Central Asia, Central America
- Incidence
  - Mediterranean, Middle East
    - 78 cases/100,000 people/yr
  - Arabic Peninsula
    - 20% seroprevalence; 2% active cases
- 100 to 200 U.S. cases annually
  - Unpasteurized cheeses

B. melitensis is particularly common in the Mediterranean. It also occurs in the Middle East, Central Asia, around the Arabian Gulf, and in some countries of Central America. This organism has been reported from Africa and India, but it does not seem to be endemic in northern Europe, North America (except Mexico), Southeast Asia, Australia, or New Zealand. There have been annual incidence reports of up to 78 cases per 100,000 people in the Mediterranean and Middle East. Greater than 550 cases have been reported from endemic areas that have no mandatory animal control measures. In some countries where animals are controlled, such as Southern Europe, incidence reports of 77 cases per 100,000 people are reported annually. A seroprevalence rate of 20% was identified on the Arabic Peninsula, with greater than 2% having active brucellosis Approximately 100 to 200 cases per year are reported in the U.S., most of those being in California and Texas in association with consumption of unpasteurized cheeses. Source: Koneman's Color Atlas and Textbook of Diagnostic Microbiology. Washington C. Winn, Elmer W. Koneman, Stephen D. Allen, William M. Janda, Paul Schrekenberger, Gail Woods.

[Photo: Goat and kid. Source: LT Hunter/wikimedia-commons-org]

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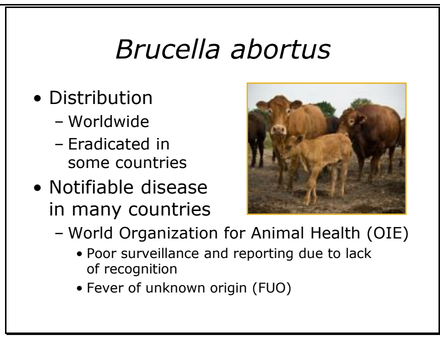

B. abortus is found worldwide in cattle-raising regions, except in Japan, Canada, some European countries, Australia, New Zealand, and Israel, where it has been eradicated. Eradication from domesticated herds is nearly complete in the U.S. *B. abortus* persists in wildlife hosts in some regions, including the Greater Yellowstone Area of North America. The actual incidence of infection may be 10-25% higher than recognized because cases may not be properly diagnosed (i.e., fevers of unknown origin).

[Photo: Cow and calf. Source: Bob Nichols/USDA]

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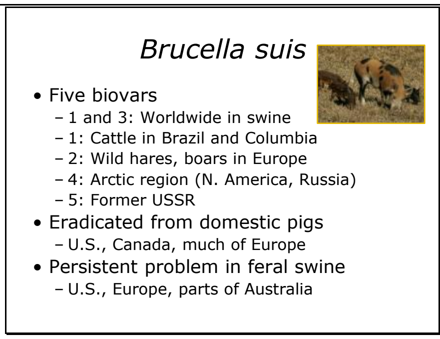

Five biovars of *B. suis* have been identified. Biovars 1 and 3 are considered to have worldwide distribution, while the others have limited geographic distribution. *B. suis* biovar 1 has also become established in cattle in Brazil and Columbia. *B. suis* biovar 2 is primarily found in Europe, and is enzootic in wild hares, posing a problem when swine have direct contact with this infected population. 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. Biovar 5 (murine brucellosis) occurs in the former USSR. *Brucella suis* has been eradicated from domesticated pigs in the U.S., Canada, many European countries, and other nations. Due to religious reasons, there are very low rates of incidence in the Middle East, North Africa, and India. 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.

[Photo: Feral sow with piglets. Source: www.public-domain-image.com]

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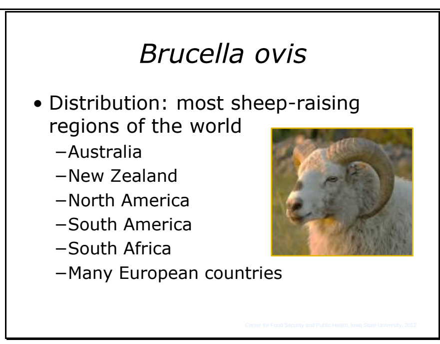

B. ovis probably occurs in most sheep-raising regions of the world. It has been reported from Australia, New Zealand, North and South America, South Africa, and many countries in Europe.

[Photo: Ram. Source: Martin Stoltze/Wikimedia Commons]

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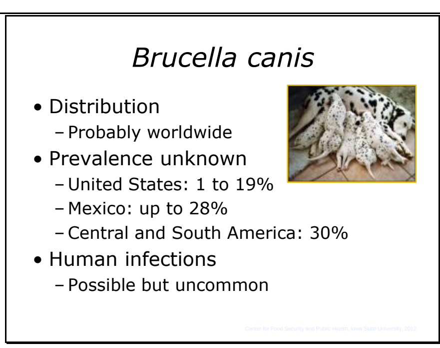

B. canis probably occurs throughout most of the world; however, New Zealand and Australia appear to be free of this organism. The prevalence of infection is unknown, although serosurveys of *B. canis* have found rates or 1 to 19% in the U.S., up to 28% in Mexico and 30% in Central and South America. Human infections with *B. canis* seem to be uncommon.

[Photo: Dam and pups. Source: Wikimedia Commons]

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Since 1994, *Brucella* strains have been isolated from a wide range of marine mammal populations (e.g., seals, sea lions, walruses, dolphins, porpoises, and an otter). Culture-positive or seropositive animals have been found in the North Atlantic Ocean, the Mediterranean Sea, and the Arctic, including the Barents Sea. Infected or exposed animals have also been found along the Atlantic and Pacific coasts of North America; the coasts of Peru, Australia, New Zealand, and Hawaii; and in the Solomon Islands and the Antarctic. As of July 2007, only four human infections with marine mammal *Brucella* have been reported.

[Photo: (Top) Ringed seal. Source: NOAA]

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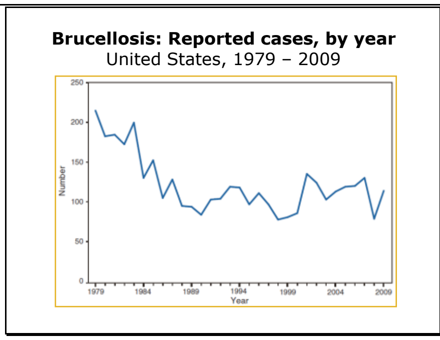

Because the U.S. control and eradication program for brucellosis has nearly eliminated *B. abortus* infections among U.S. herds, the risk of a human acquiring the infection, either from occupational exposure to domestic livestock or from consuming contaminated food products, is small. A summary of cases is published each year in the Morbidity and Mortality Weekly Report from the CDC. Today in the United States, most cases come from consuming contaminated imported unpasteurized milk products; there were 115 human cases reported to the CDC in 2009.

Graph: Summary of Notifiable Diseases 2009. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5853a1.htm.

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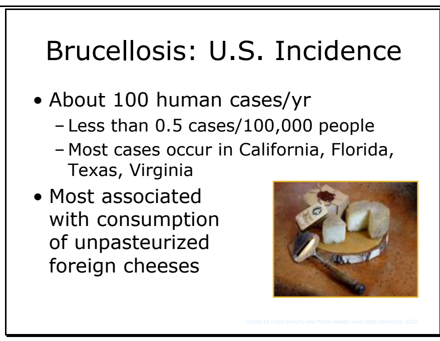

Incidence in the United States is less 0.5 cases per 100,000 people. Most cases are reported from California, Florida, Texas, and Virginia. There have been about 100 cases reported each year for the last 10 years.

[Photo: Goat cheese. Source: wikimedia.commons.org]

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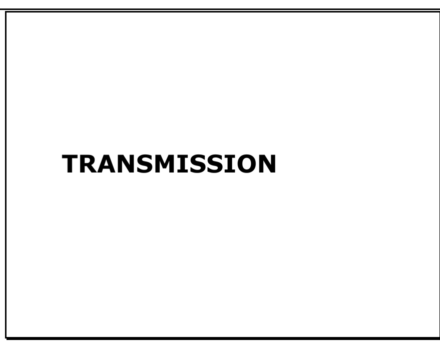

Slide 25

Transmission in Humans

- Ingestion
  - Raw milk, unpasteurized dairy products
  - Rarely through undercooked meat
- Mucous membrane or abraded skin contact with infected tissues
  - Animal abortion products
    - Vaginal discharge, aborted fetuses, placentas

Humans usually become infected with *Brucella* species by ingesting organisms or by the contamination of mucous membranes and abraded skin. Common sources of infection for people include: animal abortion products, ingestion of unpasteurized dairy products, ingestion of uncooked meat uncooked or undercooked meat or meat products, contact with laboratory cultures or tissue samples and accidental injection of live brucellosis vaccines.

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Transmission in Humans

- Aerosol
  - Laboratory, abattoirs
  - Pens, stables, slaughter houses
- Inoculation with vaccines
  - *B. abortus* strain 19, RB-51
  - *B. melitensis* Rev-1
  - Conjunctival splashes, injection
- Person-to-person transmission rare

In the laboratory and probably abattoirs, *Brucella* can be transmitted in aerosols. Inhalation of infectious aerosols can also occur while cleaning out an infected animal's pen, or in a slaughter house. The current vaccines available are strain 19 and RB-51 for *B. abortus* immunization and Rev-1 for *B. melitensis.* Self inoculation could occur by a needle stick of a vaccine when handling animals, or when infected tissue or body fluids splash onto the conjunctiva of the eye. Conjunctival splashes are more likely to get a larger dose than an injection of a vaccine. Person to person transmission is very rare but has been reported as the result of blood transfusions, bone marrow transplants, and sexual contact between lab workers and their spouse. Rare congenital infections seem to result from transplacental transmission or the ingestion of breast milk. Congenital infections might also occur if the infant is exposed to organisms in the mother's blood, urine, or feces during delivery.

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Transmission in Animals

- Ingestion of infected tissues or body fluids
- Contact with infected tissues or body fluids
  - Mucous membranes, injections
- Venereal
  - Swine, sheep, goats, dogs
- Fomites

In animals, transmission usually occurs by contact with the placenta, fetus, fetal fluids, and vaginal discharges from an infected animal. Animal are infectious after either an abortion or full-term parturition. Most or all *Brucella* species are also found in semen. Males can shed these organisms for long periods or lifelong. The importance of venereal transmission varies with the species. It is the primary route of transmission for *B. ovis; Brucella suis* and *B. canis* are also spread frequently by this route. *B. abortus* and *B. melitensis* can be found in semen, but venereal transmission of these organisms is uncommon. Some *Brucella* species have also been detected in other secretions and excretions including urine, feces, hygroma fluids, saliva, and nasal and ocular secretions. In most cases, these sources seem to be relatively unimportant in transmission; however, some could help account for direct non-venereal transmission of *B. ovis* between rams. *Brucella* can be spread on fomites including feed and water.

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DISEASE IN HUMANS

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Disease in Humans

- Incubation period
  - Variable; 5 days to three months
- Multisystemic
  - Any organ or organ system
  - Cyclical fever
- Flu-like illness
  - May wax and wane
  - Chronic illness possible

Brucellosis in humans can involve any organ or organ system, and have an insidious onset with varying clinical signs. The incubation period in humans is variable and can range from 5 to 21 days up to three months. This often adds to the difficulty of diagnosis due to the latency of clinical signs.

The one common sign in all patients is an intermittent/irregular fever of variable duration, thus the term *undulant fever*. The acute form (<8 weeks from illness onset) is characterized by symptomatic, nonspecific, or flu-like symptoms, including fever, malaise, anorexia, headache, myalgia, and back pain. Drenching sweats can occur, particularly at night. Splenomegaly, hepatomegaly, coughing, and pleuritic chest pain are sometimes seen. Gastrointestinal signs, including anorexia, nausea, vomiting, diarrhea, and constipation, occur frequently in adults but less often in children. In many patients, the symptoms last for two to four weeks and are followed by spontaneous recovery. Others develop an intermittent fever and other persistent symptoms that typically wax and wane at 2 to 14 day intervals. Most people with this undulant form recover completely in three to 12 months. A few patients become chronically ill. Relapses can occur months after the initial symptoms, even in successfully treated cases.

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Complications of Brucellosis

- Most common
  - Arthritis, spondylitis, epididymo-orchitis, chronic fatigue
- Neurological
  - 5% of cases
- Other
  - Ocular, cardiovascular, additional organs and tissues

Complications are seen occasionally, particularly in the undulant and chronic forms. The most common complications are arthritis, spondylitis, epididymo-orchitis and chronic fatigue. Neurological signs occur in up to 5% of cases. They may include personality changes, meningitis, encephalitis and peripheral neuropathy. Uveitis, optic neuritis and papilledema have been reported. Endocarditis is one of the most serious complications, and is often the cause of death in fatal cases. Many other organs and tissues can also be affected, resulting in a wide variety of syndromes including nephritis, dermatitis, vasculitis, lymphadenopathy, deep vein thrombosis, granulomatous hepatitis, cholecystitis, osteomyelitis, anemia, leukopenia and thrombocytopenia. Abscesses can occur in internal organs.

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Congenital Brucellosis

- Variable symptoms
  - Premature delivery
  - Low birth weight
  - Fever
  - Failure to thrive
  - Jaundice
  - Hepatomegaly
  - Splenomegaly
- Abortion risk unclear

The symptoms of congenital brucellosis are variable. Some congenitally infected infants are delivered prematurely, while others are born at full term. Common symptoms include low birth weight, fever, failure to thrive, jaundice, hepatomegaly and splenomegaly. Some newborns with congenital brucellosis have respiratory difficulty or severe respiratory distress, hypotension, vomiting and other signs of sepsis. Other infants may be asymptomatic or have only mild symptoms at birth. Whether brucellosis can lead to spontaneous abortion in humans is controversial.

Photo: Newborn with jaundice. Medline Plus (A service of the U.S. National Library of Medicine National Institutes of Health).

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Diagnosis in Humans

- Isolation of organism
  - Blood, bone marrow, other tissues
- Serum agglutination test
  - Four-fold or greater rise in titer
  - Samples 2 weeks apart
- Immunofluorescence
  - Organism in clinical specimens
- PCR

Microscopic examination of stained smears can be useful for a presumptive diagnosis, particularly if the direct examination is supported by other tests. They are not truly acid-fast; however, they are resistant to decolorization by weak acids, and stain red against a blue background with the Stamp's modification of the Ziehl-Neelsen method. Other organisms, such as *Coxiella burnetii,* can resemble *Brucella*. In humans, the definitive diagnosis is by culture or serology. *Brucella* species can sometimes be isolated from the blood early in the infection; bone marrow is often positive at this stage. Occasionally, bacteria can be recovered from the cerebrospinal fluid, urine, or tissues. Most *Brucella* species form colonies within a few days, but isolates from seals grow slowly and may take 7 to 10 days to become visible on selective media. *Brucella* isolates can be identified to the species and biovar level by phage typing and cultural, biochemical, and serological characteristics. Most human infections are diagnosed by serology. Tests used include serum agglutination, a modified Coombs' (antiglobulin) technique, ELISAs, and immunoblotting (Western blotting). Serologic diagnosis is complicated by previous exposures and other factors; a definitive diagnosis usually requires a fourfold rise in titer. Immunostaining can sometimes demonstrate the presence of *Brucella* spp. in a clinical specimen. PCR techniques can also be used for diagnosis. PCR has begun to gain popularity in the diagnosis of brucellosis due to the high specificity and sensitivity of the test, as well as the quick turn around of results. Chronic brucellosis can be extremely difficult to diagnose if the serologic results are equivocal and the organism cannot be cultured.

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Treatment and Prognosis

- Rarely fatal if treated
  - Case-fatality rate <2% (untreated)
  - Antibiotics necessary
  - Death usually caused by endocarditis, meningitis
- About 5% of treated cases relapse
  - Failure to complete treatment
  - Infections requiring surgical intervention

Brucellosis is rarely fatal if treated; in untreated persons, estimates of the case fatality rate vary from less than 2% to 5%. Antibiotics are usually the mainstay of treatment; long-term treatment may be required. Some forms of localized disease, such as endocarditis, may require surgery. Deaths are usually caused by endocarditis or meningitis. Although recovery is common, disability is often pronounced depending on the localization of infection and response to treatment. Approximately 5% of treated cases will relapse weeks to months after therapy has ended due to the failure to complete the treatment regimen or infection that requires surgical drainage. Antibiotic resistant strains of *Brucella* have been reported, but the clinical importance of that fact is not well understood.

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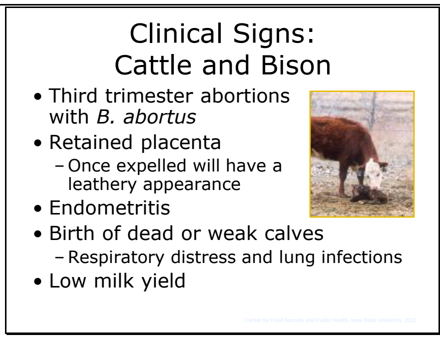
ANIMALS AND BRUCELLOSIS

Slide 35



Brucellosis causes abortions in the third trimester of pregnancy when unvaccinated cattle are exposed to the infectious organism. It is stated that greater than 80% of cattle will abort if exposed during this critical time of gestation. The organisms enter through the mucous membranes and can cause inflammation of the placenta. Abortion can occur within 2 weeks or up to 5 months following infection. The overall appearance of the placenta is a leathery look. The intercotyledonary area is thickened and has a wet appearance. The fetus may look normal if aborted acutely after infection, or autolytic if not expelled for a period of time. The pregnancy may end with a stillborn or weak calf. Often, retained placentas and decreased milk yield follow. Once a cow has aborted from infection, subsequent gestations are normal, after a period of temporary sterility. Only 5% have residual sterility. Most cows will shed the organisms in the milk and uterine discharges for life following infection. Infections in nonpregnant females are usually asymptomatic. [Photo: Cow and calf. Source: USDA]

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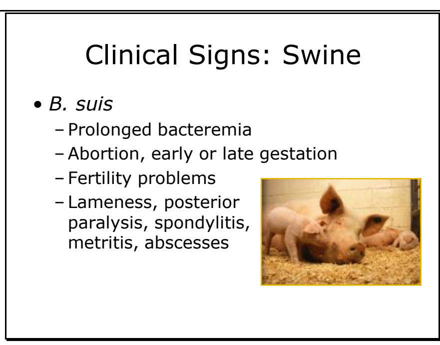
The primary causal agent of abortion in sheep and goats is *B. melitensis,* which has similar signs to *B. abortus* in cattle. Abortion generally occurs late term or results in stillbirths or weak lambs/kids. The organisms enter through the mucous membranes and can cause inflammation and retention of the placenta. Sheep and goats usually abort only once, but reinvasion of the uterus and shedding of organisms can occur during subsequent pregnancies. Acute orchitis and epididymitis can occur in males, and may result in infertility. Arthritis is seen occasionally in both sexes. Many non-pregnant sheep and goats remain asymptomatic.

B. ovis affects sheep but not goats. It can cause abortions, placentitis, and neonatal death. The most important clinical signs are epididymitis and orchitis resulting in fertility problems. It is venereally transmitted, and rams can shed the organism for over four years. Semen quality deteriorates rapidly and often inflammatory cells are present. Epididymal enlargement can occur unilaterally or bilaterally and the tunics become thickened and develop adhesions. Fibrous atrophy of the testes is permanent. If no outward clinical signs are palpable, semen must then be repeatedly cultured to catch intermittent shedders. Abortions, placentitis and perinatal mortality can be seen in ewes but are uncommon. Systemic signs are rare.

[Photo: Sheep and lambs. Source: Stephen Ausmus/U.S. Department of Agriculture]

Slide 37



Pigs are primarily affected with *B. suis* which causes a long lasting bacteremia. Localization of the infection can vary, and thus, so do the clinical signs. Abortion can occur up to 80% of the time; when abortions occur early in gestation, infected animals often go undetected and are rebred. Temporary or permanent sterility is common and is sometimes the only sign. Boars can have unilateral or bilateral orchitis affecting their fertility. Other signs include lameness, posterior paralysis, spondylitis, metritis, and abscess formation in various locations of the body.
[Photo: Sow and piglets. Source: Scott Bauer/USDA ARS]

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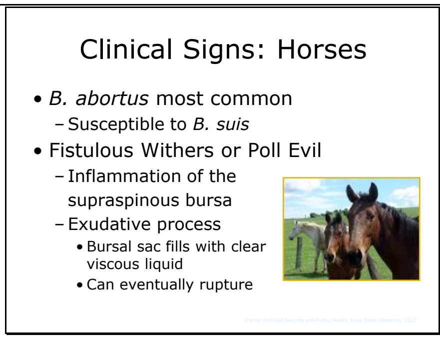

Horses are susceptible to *B. abortus* or *B. suis* from infectious or traumatic origin. Clinically, these animals have an inflammation in the supraspinous bursa or supra-atlantal bursa; this is referred to as Fistulous Withers or Poll Evil, respectively. The bursal sac becomes distended by a clear, viscous, straw-colored exudate and develops a thickened wall. It can rupture, leading to secondary inflammation. In chronic cases, nearby ligaments and the dorsal vertebral spines may become necrotic. *Brucella*-associated abortions are rare in horses.

[Photo: Horses. Source: U.S. Department of Agriculture]

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Dogs are susceptible to infections with *B. melitensis*, *B. abortus*, and *B. suis*, but the major cause of abortion in this species is *B. canis*. Generally, dogs will abort in the last trimester of pregnancy (seventh to ninth week of gestation) and have prolonged vaginal discharge. Bacteremia often occurs up to eighteen months post-exposure. Other clinical signs include stillbirths, failure to conceive/early embryonic death, lymphadenitis, epididymitis, periorchitis, and prostatitis.

[Photo: Dam and pups. Source: Alexandra Belyaev/Wikimedia Commons]

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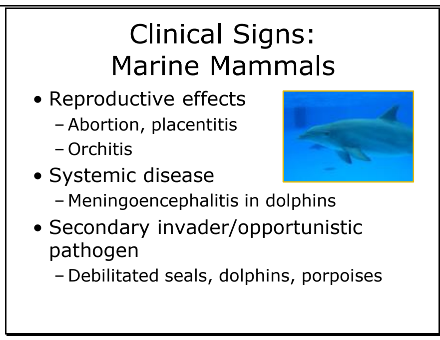

There is little information on the effects of brucellosis in marine mammals. Reproductive disease is difficult to assess in wild animals, but *Brucella* has been isolated from the reproductive organs of some marine species. In rare cases, infections have also been linked to lesions or clinical disease. *Brucella*-associated abortions and placentitis were reported in two captive bottlenose dolphins. Lesions consistent with a possible abortion were also reported in a wild Atlantic white-sided dolphin. *Brucella*-associated epididymitis has been reported in porpoises, and orchitis from suspected brucellosis was reported in minke whales.

Brucella infections have been linked with systemic disease in a few marine mammals. *Brucella*-associated meningoencephalitis was reported in three stranded striped dolphins. Other signs of *Brucella*-associated systemic disease have been seen mainly in Atlantic white-sided dolphins; the lesions included hepatic and splenic necrosis, lymphadenitis and mastitis. *Brucella* has also been identified as a possible secondary invader or opportunistic pathogen in debilitated seals, dolphins and porpoises. It has been isolated from several subcutaneous abscesses. In addition, this organism has been found in organs with no microscopic or gross lesions, and in apparently healthy animals.

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Elk generally lose their first pregnancy after becoming infected with *B. abortus*, but do not have problems with retained placenta or infertility as cattle do. Elk infection has been documented in Alaska, Canada, and mainland United States. It is thought that moose are very susceptible to infection with *Brucella abortus*, unlike other wildlife. Seropositive free-ranging moose have not been found in North America, and it is often thought this is due to the rapid death that follows once they become infected. Predators act as vectors to spread the disease, but are resistant to infection. Spread of *Brucella* bacteria can occur when predators come across an aborted fetus or other tissues and drag them to a new location, contaminating a larger area for susceptible species to become infected.

[Photo: (Top) Elk. Source: Washington Department of Fish and Wildlife; (Bottom) Moose. Source: Ryan Hagerty/U.S. Fish and Wildlife Service via Wikimedia Commons]

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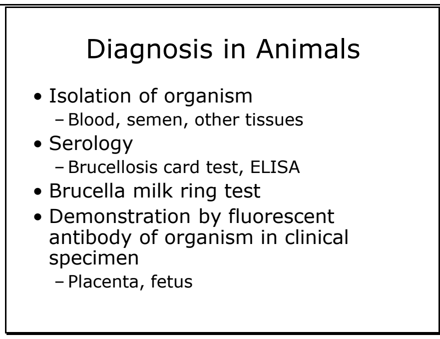

Brucellosis can be diagnosed by culture, serology, or other tests. Microscopic examination of smears stained with the Stamp's modification of the Ziehl-Neelsen method can be useful for a presumptive diagnosis. Organisms may be found in abortion products, vaginal discharges, milk, semen, or various tissues. This test is not definitive, however, since other organisms, such as *Chlamydophila abortus* and *Coxiella burnetii*, can resemble *Brucella*. Direct examination may not detect the small numbers of organisms present in milk and dairy products. Blood cultures are often used to detect *B. canis* in dogs. In canines, bacteremia (which may be intermittent) can persist for up to five years and possibly longer. *B. canis* requires a specific test as it does not have a smooth lipopolysaccharide cell wall. Genetic techniques can also be used for biotyping. The vaccine strains (*B. abortus* strains S19 and RB51, and *B. melitensis* Rev 1) can be distinguished from field strains by their growth characteristics and sensitivity to antibiotics and other additives.

Brucellosis is often diagnosed by serology. Serological tests are not completely specific and cannot always distinguish reactions due to *B. melitensis* from cross-reactions to other bacteria, particularly *Yersinia enterocolitica* O:9. Serology is commonly used at slaughter plants and when marketing cattle. The Brucella milk ring test is used on pooled milk samples and fluorescent antibody of the organism in the placenta and fetus for abortion cases.

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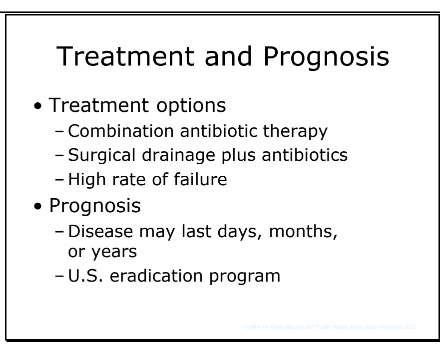

There is no practical treatment for infected cattle or pigs, but long-term antibiotic treatment is sometimes successful in infected dogs. Prolonged treatment with clinically effective antibiotics is necessary to penetrate these facultative, intracellular pathogens. Combination therapy has shown the best efficacy for treatment, but due to the expense incurred and the high rate of failure, it often is not practical. Some dogs relapse after treatment. Surgical drainage, if appropriate, along with antibiotics may be of some use. With the indemnity program, owners often opt for depopulation instead of treatment. The disease may last days to years depending on the species and type of infection. In the United States, animals are often serologically tested and carriers of brucellosis are eliminated.

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Although Brucellosis is not a prevalent disease in the United States, certain wildlife species can serve as a source of infection to domesticated animals, especially cattle. This is especially a concern in the Yellowstone area where cattle can come into contact with roaming bison or *Brucella* contaminated soils and fetal tissues. *B. abortus* was first detected in bison in 1917 in Yellowstone National Park.

[Photo: Waterfall at Yellowstone National Park in Wyoming, United States. Source: Erik Marr/wikimedia-creative commons.org]

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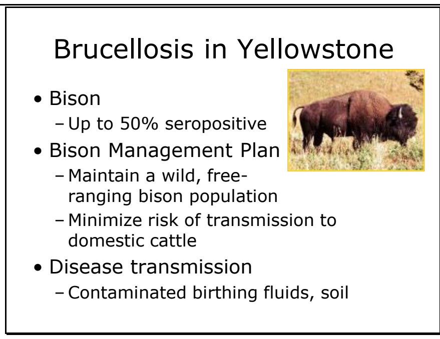

Up to 50% of bison in Yellowstone test positive for brucellosis. Concern exists that bison leaving the park will transmit the disease to cattle in surrounding states. Currently, a bison management plan is in place; it's goals are to maintain a wild, free ranging bison population while minimizing the risk of transmitting brucellosis from bison to domestic cattle on public and private lands adjacent to Yellowstone. The bison management plan is not considered to be a brucellosis eradiation plan. Bison are likely to spread disease to herdmates by direct contact with birthing fluids and contaminated soil and vegetation during calving.

[Photo: Bison. Source: Scott Bauer/USDA]

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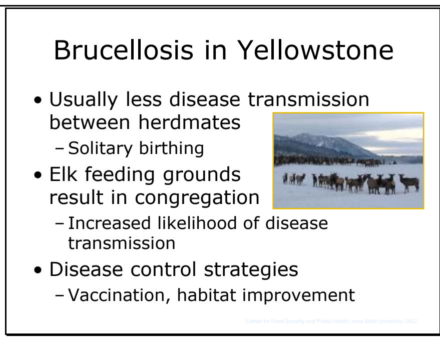

Elk are less likely to spread brucellosis than bison; they prefer to calve separately from other animals. However, elk feeding grounds cause congregation and may lead to increased disease transmission. Vaccination of elk in feeding grounds and habitat improvement (to keep elk away from cattle) have been used to combat brucellosis in elk.

[Photo: Elk feeding ground. Source: U.S. Fish and Wildlife Service]

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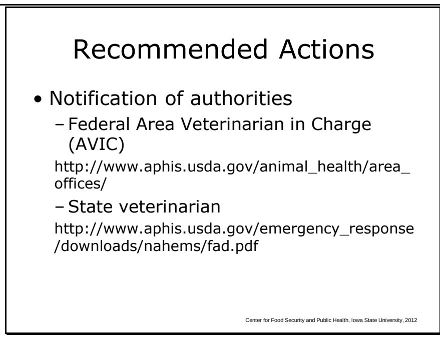

Brucellosis is a reportable disease. State and/or federal authorities should be consulted for specific guidelines.

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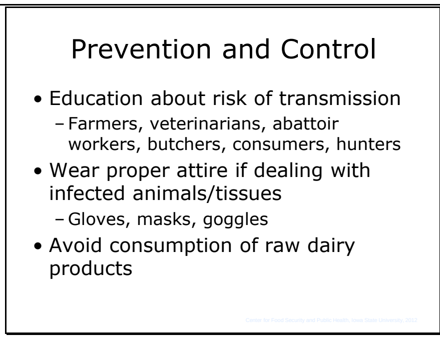

Education for those at greatest risk about the routes of transmission of is an important prevention measure to reduce the occurrence of brucellosis in humans. Properly protecting yourself, if you are an “at risk” individual, by wearing gloves, masks, goggles, and coveralls to prevent exposure to tissues and body secretions of infected animals can help. Pasteurization or boiling milk and avoidance of eating unpasteurized dairy products will also help decrease human exposure to brucellosis.

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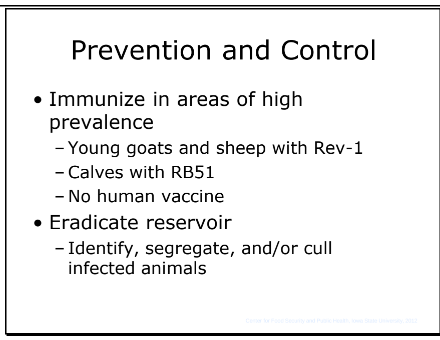

Vaccinating calves at 4 to 12 months of age with RB51 for *B. abortus* and goats and sheep with Rev-1 for *B. melitensis* has helped eliminate infection in these animals, thus decreasing possible exposure to humans. At this time, RB51 is being tested for efficacy in bison. Elimination of livestock reservoirs is the most effective means to reduce cases of disease in people, so strict adherence to federal laws for identifying, segregating and/or culling infected animals is essential to success.

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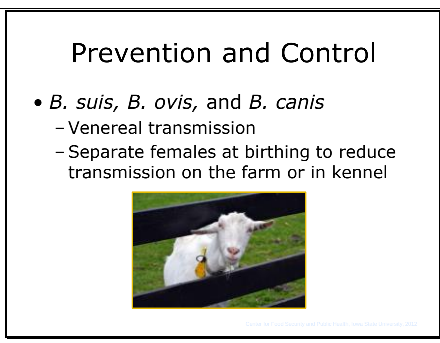

When it comes to preventing and controlling the venereal transmitted organisms (*B. suis*, *B. ovis*, and *B. canis*) it is important to separate females during birthing to reduce exposure and transmission to susceptible animals on the farm or in the kennels.

[Photo: Goat. Tim Strater/Wikimedia Commons]

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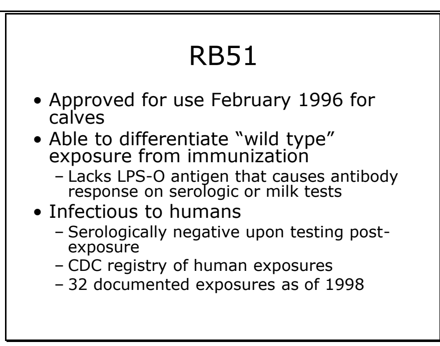

Vaccination has become an important control measure for brucellosis in the United States. RB51 was approved for use by APHIS in February 1996 and for use in the eradication program in March. It was the first new vaccine for brucellosis in 50 years, and it is given only to calves 4-12 months old. This attenuated strain is less virulent in cattle so they will shed fewer organisms if they become infected via vaccination. There are two major advantages with RB51: one is the ability to protect via vaccination and the other is the ability to differentiate those animals infected with the wild type virus. However, because vaccination with RB51 does not induce an antibody response, assessment of human exposure is also difficult. RB51 is considered infectious for humans and only federally accredited veterinarians should administer the vaccine. The CDC keeps a registry of all human exposures, and they can be notified at (404) 639-3158. As of 1998 there have been 32 documented exposures. Of those, three reported inflammation at the inoculation site, and one had intermittent fever, chills, headache, and myalgia.

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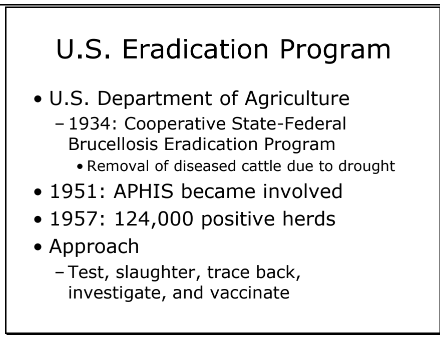

The USDA started the Cooperative State-Federal Brucellosis Eradication Program in 1934. An increasing public health concern and drought conditions made it necessary to reduce cattle herds, so the diseased were the first eliminated. The Program also implemented testing, quarantine, and elimination standards that are still followed today. In 1951, the National Brucellosis Program was initiated by the Animal and Plant Health Inspection Service and made it mandatory that all states comply. In 1957, there were more than 124,000 cattle herds known to be infected. The approach was to test herds and remove positives, depopulate if necessary, vaccinate new animals, and trace back reactors through the market identification program to the herds of origin.

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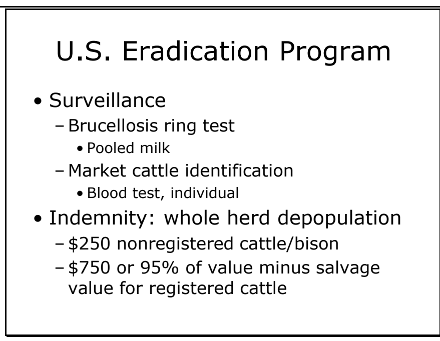

There are two primary surveillance procedures to locate infection without having to test each animal in every herd. Milk from dairy herds is checked two to four times a year by testing a small sample obtained from creameries or farm milk tanks for evidence of brucellosis, also known as the brucellosis ring test. Bison herds and cattle herds that do not produce milk for sale are routinely checked for brucellosis by blood-testing animals sold from these herds at livestock markets or at slaughter. The blood agglutination test is used to pinpoint infection within a herd. USDA APHIS is moving towards reduced brucellosis surveillance in the coming years. Should a herd test positive, it must then be depopulated. Financial compensation to the producer varies by offering a fixed rate, which is $250 per animal for cattle or bison that are not registered, or $750 per head for registered cattle, minus their salvage value. The appraisal option has been introduced based on fair market value for registered cattle, and producers are then offered 95% of that value, again, minus the salvage value.

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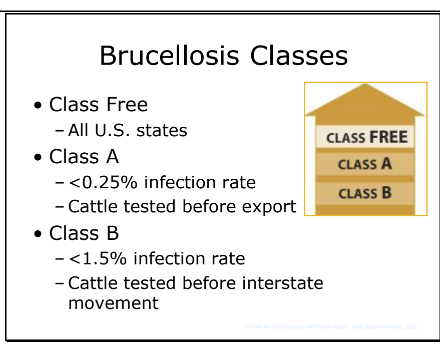

For management purposes, three bovine brucellosis classes have been defined: Free, A, and B. Currently all 50 states, Puerto Rico, and the U.S. virgin Islands are officially designated as Brucellosis Class Free. However, occasional cases still occur, mostly in the Greater Yellowstone Area.

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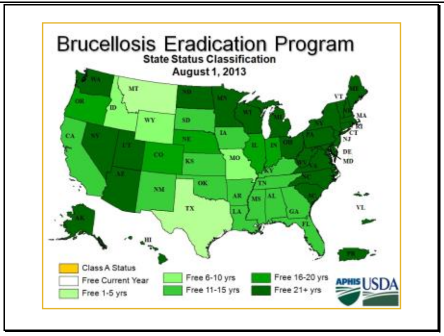

This map shows the status classification of each state for bovine brucellosis.

[Source: USDA APHIS. Bovine Brucellosis Monthly Report-Maps. http://www.aphis.usda.gov/animal_health/animal_diseases/brucellosis/downloads/monthly_rpt.pps]

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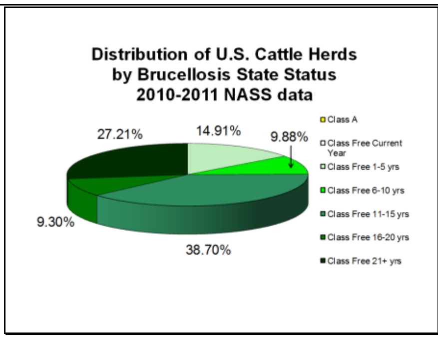

This chart shows the distribution of U.S. cattle herds by brucellosis state status.

[Source: USDA APHIS. Bovine Brucellosis Monthly Report-Maps. http://www.aphis.usda.gov/animal_health/animal_diseases/brucellosis/downloads/monthly_rpt.pps]

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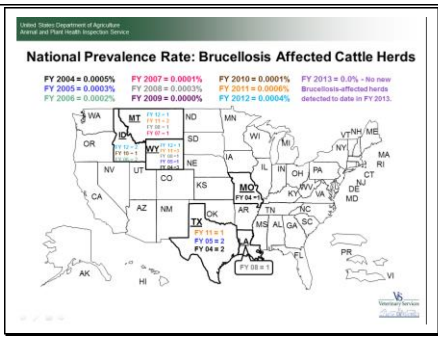

This map shows the national prevalence of brucellosis in U.S. cattle herds.

[Source: USDA APHIS. Bovine Brucellosis Monthly Report-Maps. http://www.aphis.usda.gov/animal_health/animal_diseases/brucellosis/downloads/monthly_rpt.pps]

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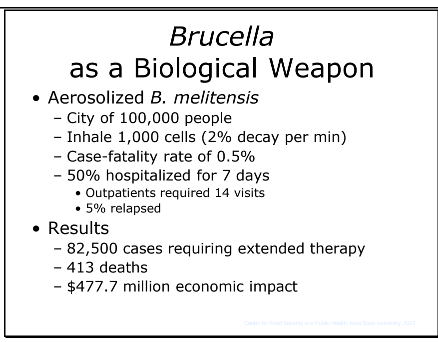

A bioterrorism scenario has been evaluated using an aerosolized *Brucella melitensis* agent spread along a line with the prevailing winds with optimal meteorological conditions. It assumed that the infectious dose to infect 50 (ID_{50}) percent of the population would require inhalation of 1,000 vegetative cells. The decay of the organism is estimated to be at 2% per minute without affecting viability and virulence. The scenario also assumed, depending on the persons closeness to the point of origin, one would inhale one to ten ID_{50}. The case fatality rate was estimated to be 0.5% with 50% of the people being hospitalized and staying on average, seven days. If not hospitalized, they often made fourteen outpatient visits and received oral doxycycline for 42 days, and parenteral gentamicin for 7 days. Relapses occurred at 5% and required 14 outpatient visits in one year. In looking at the economic impact of such a threat, one must consider the cost of premature human death, and all the costs related to hospitalization and outpatient visits. The minimum cost of exposure would be around $477.7 million per 100,000 persons exposed.

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Additional Resources

- USDA APHIS VS Brucellosis Disease Information
  - http://www.aphis.usda.gov/animal_health/animal_diseases/brucellosis/
- Center for Food Security and Public Health
  - www.cfsph.iastate.edu
- CDC Brucellosis
  - http://www.cdc.gov/ncidod/dbmd/diseaseinfo/brucellosis_g.htm

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Acknowledgments

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