Brucellosis
Overview

- Organism
- History
- Epidemiology
- Transmission
- Disease in Humans
- Disease in Animals
- Prevention and Control
- Actions to Take
The Organism
Brucella spp.

- Gram negative, coccobacilli bacteria
- Facultative, intracellular organism
- Environmental persistence
  - Temperature, pH, humidity
  - Frozen and aborted materials
- Multiple species
<table>
<thead>
<tr>
<th>Species</th>
<th>Biovar/Serovar</th>
<th>Natural Host</th>
<th>Human Pathogen</th>
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<tr>
<td><em>B. abortus</em></td>
<td>1-6, 9</td>
<td>cattle</td>
<td>yes</td>
</tr>
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<td><em>B. melitensis</em></td>
<td>1-3</td>
<td>goats, sheep</td>
<td>yes</td>
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<tr>
<td><em>B. suis</em></td>
<td>1, 3</td>
<td>swine</td>
<td>yes</td>
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<tr>
<td></td>
<td>2</td>
<td>hares</td>
<td>yes</td>
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<td></td>
<td>4</td>
<td>reindeer, caribou</td>
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<td></td>
<td>5</td>
<td>rodents</td>
<td>yes</td>
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<td><em>B. canis</em></td>
<td>none</td>
<td>dogs, other canids</td>
<td>yes</td>
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<tr>
<td><em>B. ovis</em></td>
<td>none</td>
<td>sheep</td>
<td>no</td>
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<tr>
<td><em>B. neotomae</em></td>
<td>none</td>
<td>Desert wood rat</td>
<td>no</td>
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<td><em>B. maris (?)</em></td>
<td>none</td>
<td>marine mammals</td>
<td>?</td>
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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
History
History of Malta Fever

- 450 BC: Described by Hippocrates
- 1905: Introduction into the U.S.
- 1914: \textit{B. suis} Indiana, United States
- 1953: \textit{B. ovis} New Zealand, Australia
- 1966: \textit{B. canis} in dogs, caribou, and reindeer
Sir William Burnett (1779-1861)

- Physician General to the Navy
- Differentiated the various fevers affecting soldiers
Jeffery Allen Marston

• Contracted Malta fever
• Described his own case in great detail

ABOVE: Jeffery Allen Marston (1831–1911) contracted Malta fever and described his own case in great detail.

Private collection
Sir David Bruce (1855-1931)

• British Army physician and microbiologist

• Discovered *Micrococcus melitensis*
Bernhard Bang (1848-1932)

- Danish physician and veterinarian
- Discovered *Bacterium abortus* could infect cattle, horses, sheep, and goats
• Alice Evans, American bacteriologist
  – Credited with linking the organisms
  – Similar morphology and pathology between:
    ▪ Bang’s *Bacterium abortus*
    ▪ Bruce’s *Micrococcus melitensis*

• Nomenclature today credited to Sir David Bruce
  – *Brucella abortus* and *Brucella melitensis*
Transmission to Humans

- Conjunctiva or broken skin contacting infected tissues
  - Blood, urine, vaginal discharges, aborted fetuses, placentas
- Ingestion
  - Raw milk & unpasteurized dairy products
  - Rarely through undercooked meat
Transmission to Humans

- Inhalation of infectious aerosols
  - Pens, stables, slaughter houses
- Inoculation with vaccines
  - *B. abortus* strain 19, RB-51
  - *B. melitensis* Rev-1
  - Conjunctival splashes, injection
- Person-to-person transmission is very rare
- Incubation varies
  - 5-21 days to three months
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
Epidemiology
Who is at Risk?

- Occupational Disease
  - Cattle ranchers/dairy farmers
  - Veterinarians
  - Abattoir workers
  - Meat inspectors
  - Lab workers
- Hunters
- Travelers
- Consumers of unpasteurized dairy products
B. melitensis

- Latin America, Middle East, Mediterranean, eastern Europe, Asia, and parts of Africa
- Accounts for most human cases
  - In the Mediterranean and Middle East
    - Up to 78 cases/100,000 people/year
    - Arabic Peninsula 20% seroprevalence
- Recent emergence in cattle on Middle Eastern intensive dairy farms
B. abortus

- Worldwide
- Some countries have eradicated it
- Notifiable disease in many countries
  - Poor surveillance and reporting due to lack of recognition
  - Fever of Unknown Origin (FUO)
B. suis

- Biovars 1 and 3
  - Worldwide problems where swine are raised
- Free
  - United Kingdom, Canada
- Eradicated
  - Holland, Denmark
- Low Incidence
  - Middle East, North Africa
B. suis

- Low Levels
  - United States and Australia
  - Persistent problem in feral swine
- Biovar 1
  - Established in cattle in Brazil and Columbia
- Biovar 2
  - Enzootic in wild hares in Europe
B. ovis

- Most sheep-raising regions
  - Australia
  - New Zealand
  - North America
  - South America
  - South Africa
  - Many European countries
**B. canis**

- Poorly understood
- 1-19% prevalence in United States
- Rarely causes disease in humans
**Brucella** in Marine Mammals

- Culture-positive or seropositive animals
  - North Atlantic Ocean
  - Mediterranean Sea
  - Arctic, including Barents Sea
  - Atlantic and Pacific coasts of North America
  - Coasts of Peru, Australia, New Zealand, Hawaii, Solomon Islands, Antarctic
The incidence of brucellosis has remained stable in recent years, reflecting an ongoing risk for infection with *Brucella melitensis* and *B. abortus* acquired through exposure to unpasteurized milk products in countries with endemic brucellosis in sheep, goats, and cattle and *B. suis* acquired through contact with feral swine in the United States.
Brucellosis

- United States
  - Approximately 100 cases per year
  - Less than 0.5 cases/100,000 people
  - Mostly California, Florida, Texas, Virginia
  - Many cases associated with consumption of foreign cheeses
Disease in Humans
Human Disease

- Can affect any organ or organ system
- All patients have a cyclical fever
- Variability in clinical signs
  - Headache, weakness, arthralgia, depression, weight loss, fatigue, liver dysfunction
Human Disease

- 20-60% of cases
  - Osteoarticular complications
    - Arthritis, spondylitis, osteomyelitis
- Hepatomegaly may occur
- Gastrointestinal complications
- 2-20% of cases
  - Genitourinary involvement
    - Orchitis and epididymitis most common
Human Disease

- Neurological
  - Depression, mental fatigue
- Cardiovascular
  - Endocarditis resulting in death
- Chronic brucellosis is hard to define
  - Length, type and response to treatment variable
  - Localized infection
- Blood donations of infected persons should not be accepted
Human Disease

- Congenitally infected infants
  - Low birth weight
  - Failure to thrive
  - Jaundice
  - Hepatomegaly
  - Splenomegaly
  - Respiratory difficulty
  - General signs of sepsis (fever, vomiting)
  - Asymptomatic
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
Treatment of Choice

- Combination therapy has the best efficacy
  - Doxycycline for six weeks in combination with streptomycin for 2-3 weeks or rifampin for 6 weeks
- CNS cases treat 6-9 months
  - Same for endocarditis cases plus surgical replacement of valves
Prognosis

- May last days, months, or years
- Recovery is common
- Disability is often pronounced
- About 5% of treated cases relapse
  - Failure to complete the treatment regimen
  - Sequestered infection requiring surgical drainage
- Case-fatality rate: <2% (untreated)
  - Endocarditis caused by *B. melitensis*
Animals and Brucellosis
Clinical Signs: Cattle & Bison

- Third trimester abortions with *B. abortus*
- Retained placenta
  - Once expelled will have a leathery appearance
- Endometritis
- Birth of dead or weak calves
  - Respiratory distress and lung infections
- Low milk yield
Clinical Signs: Sheep & Goats

- *B. melitensis* causes late term abortions
  - Retained placenta
  - Birth of dead or weak lambs/kids
- Goats - articular and periarticular hygroma localizations
- *B. ovis* causes abortions, fertility problems
  - Orchitis, epididymitis
  - Abnormal breeding soundness exam
  - Organisms present in semen
Clinical Signs: Swine

- *B. suis*
- Prolonged bacteremia
- Abortion, early or late gestation
- Fertility problems
  - Sows temporary
  - Boars, unilateral or bilateral orchitis
- Lameness, posterior paralysis, spondylitis, metritis, abscesses
Clinical Signs: Horses

- *B. abortus* most common
  - Susceptible to *B. suis*
- Fistulous Withers or Poll Evil
  - Inflammation of the supraspinous bursa
  - Exudative process
    - Fills with clear viscous liquid
    - Can eventually rupture
Clinical Signs: Dogs

• Susceptible to
  – *B. melitensis*, *B. abortus*, and *B. suis*

• *B. canis* causes abortions
  – Last trimester of pregnancy
  – Prolonged vaginal discharge
  – Bacteremia
  – Failure to conceive, stillbirths, prostatitis, epididymitis
Clinical Signs: Wildlife

- Elk
  - Abortions, no retained placenta
- Moose
  - Debilitated, death
- Predators not clinical, but are vectors
  - Coyotes, crows, vultures, bears
    - Aid in disease spread by carrying infected tissues away from abortion site
Diagnosis in Animals

- Isolation of organism
  - Blood, semen, other tissues
- Serology
  - Brucellosis card test, ELISA
- Brucella milk ring test
- Demonstration by fluorescent antibody of organism in clinical specimen
  - Placenta, fetus
Treatment of Animals

- Combination antibiotic therapy has the best efficacy
- Surgical drainage plus antibiotics
- Often expensive
- High rate of failure
- Indemnity program from government
Prognosis

• Disease may last days, months, or years
• Eradication program in the United States often leads to slaughter of certain species
  – Cattle, bison, horses, sheep, goats, swine
Yellowstone National Park
Bison in Yellowstone

- Goal = Brucellosis free by 2010
- Can leave the park to winter feed in Wyoming
- Up to 50% sero-positive
- Congregate at calving
Elk in Yellowstone

- Exposed to *B. abortus* via winter feeding grounds
- Isolate themselves at calving
  - Clean the area
  - Remain separate from herd for a few days
- Less disease transmission between herdmates
Prevention and Control
Prevention and Control

- Education about risk of transmission
  - Farmer, veterinarian, abattoir worker, butcher, consumer, hunter, public
- Wear proper attire if dealing with infected animals/ tissues
  - Gloves, masks, goggles
- Avoid consumption of raw dairy products
Prevention and Control

- Immunize in areas of high prevalence
  - Young goats and sheep with Rev-1
  - Calves with RB51
  - No human vaccine

- Eradicate reservoir
  - Identify, segregate, and/or cull infected animals
Prevention and Control

- *B. suis, B. ovis, and B. canis*
  - Venereal transmission
  - Separate females at birthing to reduce transmission on the farm or in kennel
RB51

- Approved for use February 1996 for calves
- Able to differentiate “wild type” exposure from immunization
  - Lacks LPS-O antigen that causes antibody response on serologic or milk tests
- Infectious to humans
  - Serologically negative upon testing post-exposure
  - CDC registry of human exposures
  - 32 documented exposures as of 1998
U.S. Eradication Program

- U.S. Department of Agriculture
  - 1934: Cooperative State-Federal Brucellosis Eradication Program
    - Removal of diseased cattle due to drought
- 1951: APHIS became involved
- 1957: 124,000 positive herds
- Approach
  - Test, slaughter, trace back, investigate, and vaccinate
U.S. Eradication Program

- Target date for eradication was December 31, 1998
- Surveillance
  - Brucellosis ring test
    - Pooled milk
  - Market Cattle Identification
    - Blood test, individual
- Indemnity for whole herd depopulation
  - $250 nonregistered cattle/bison
  - $750 or 95% of value minus salvage value for registered cattle
U.S. Eradication Program

- Fiscal Year 2001
  - 4.7 million calves vaccinated
  - 9.9 million cattle tested under the Market Cattle Identification program
  - 3 brucellosis herds depopulated
    - Indemnity paid = $211,153
    - An additional $47,700 for purchase of animals or diagnostic purposes
Calves Vaccinated

Figure 11

http://www.aphis.usda.gov/vs/nahps/brucellosis/status_rpt/figure11.jpg
Number of Reactor Herds from 1991-2001 According to State Classification

Figure 5

http://www.aphis.usda.gov/vs/nahps/brucellosis/status_rpt/figure05.jpg
Brucellosis Classes

- **Free**
  - Feb 1, 2008 – U.S. class-free in cattle

- **A**: No more than 0.25% infection rate and cattle must be tested before export

- **B**: Infection rate of no more than 1.5% and must be tested before interstate movement
B. abortus Exposure

• 1997: Kansas State University
  – 14 month old heifer admitted to hospital with calving complications
    ▪ Vaccinated with RB51 at 8 months
    ▪ 10 times the dose for known pregnant cattle
  – 9 humans exposed
  – Treated with doxycycline
    ▪ No clinical signs
Brucella as a Biological Weapon

• Aerosolized *B. melitensis*
  – City of 100,000 people
  – Inhale 1,000 cells (2% decay per min)
  – Case-fatality rate of 0.5%
  – 50% hospitalized for 7 days
    ▪ Outpatients required 14 visits
    ▪ 5% relapsed

• Results
  – 82,500 cases requiring extended therapy
  – 413 deaths
  – $477.7 million economic impact
Internet Resources

- USDA APHIS VS Brucellosis Disease Information
  - www.aphis.usda.gov/animal_health/animal_diseases/brucellosis/
- WHO Fact Sheet Brucellosis
  - www.who.int/mediacentre/factsheets/en/
- Center for Food Security and Public Health
  - www.cfsph.iastate.edu
- BruNet Publication
  - www.moag.gov.il/brunet/public.htm
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