

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

Species	Biovar/ Serovar	Natural Host	Human Pathogen
<i>B. abortus</i>	1-6, 9	cattle	yes
<i>B. melitensis</i>	1-3	goats, sheep	yes
<i>B. suis</i>	1, 3	swine	yes
	2	hares	yes
	4	reindeer, caribou	yes
	5	rodents	yes
<i>B. canis</i>	none	dogs, other canids	yes
<i>B. ovis</i>	none	sheep	no
<i>B. neotomae</i>	none	Desert wood rat	no
<i>B. maris (?)</i>		marine mammals	?

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: *B. suis* Indiana, United States
- 1953: *B. ovis* New Zealand, Australia
- 1966: *B. canis* in dogs, caribou, and reindeer



Professor FEG Cox. *The Wellcome Trust, Illustrated History of Tropical Diseases*

Sir William Burnett (1779-1861)

- Physician General to the Navy
- Differentiated the various fevers affecting soldiers

Professor FEG Cox. *The Wellcome Trust, Illustrated History of Tropical Diseases*



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

Private collection

Jeffery Allen Marston

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



Sir David Bruce (1855-1931)

- British Army physician and microbiologist
- Discovered *Micrococcus melitensis*



Professor FEG Cox. *The Wellcome Trust, Illustrated History of Tropical Diseases*

Bernhard Bang (1848-1932)

- Danish physician and veterinarian
- Discovered *Bacterium abortus* could infect cattle, horses, sheep, and goats

History

- 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

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



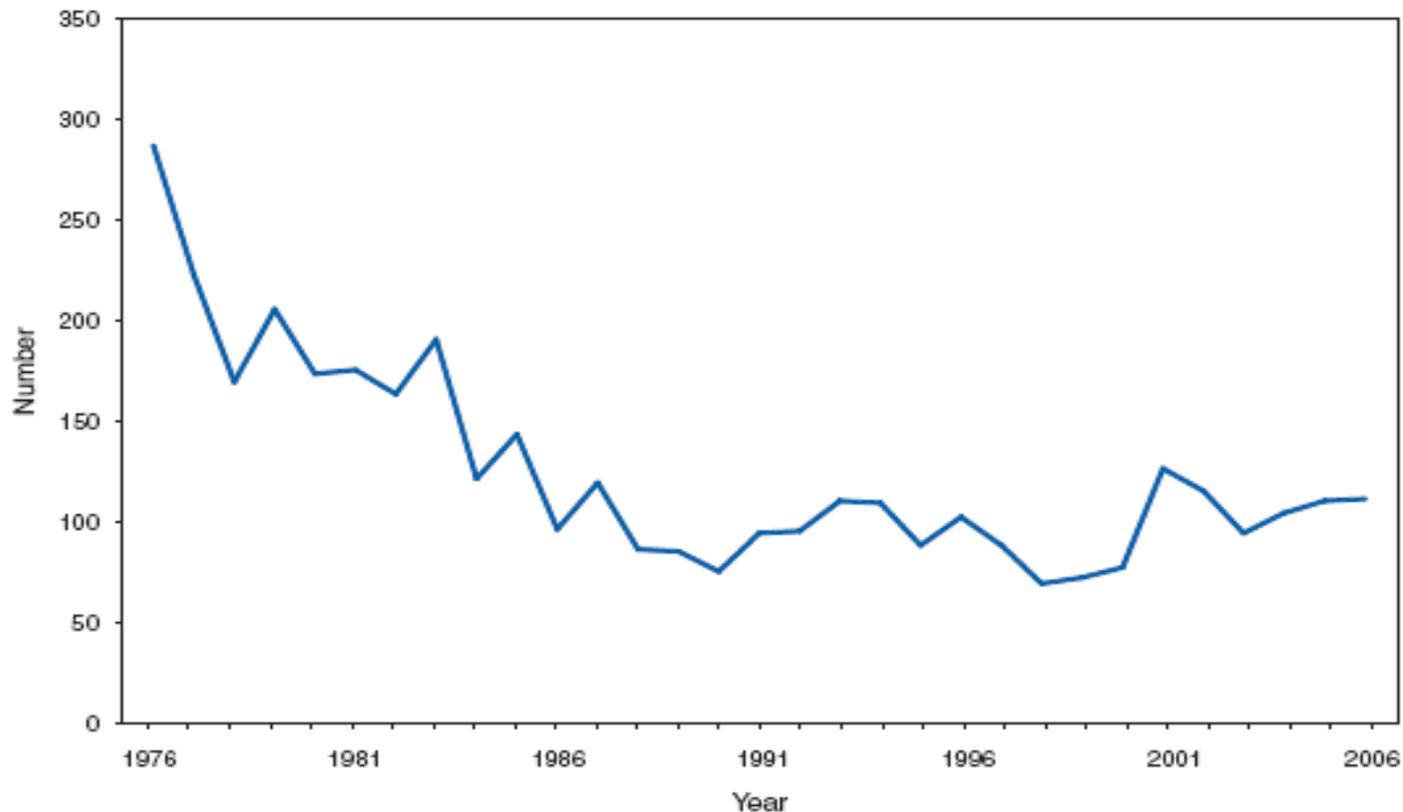
Brucella in Marine Mammals

- 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



Brucellosis in U.S.: 1975-2006

BRUCELLOSIS. Number of reported cases, by year — United States, 1976–2006



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% seropositive
- 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

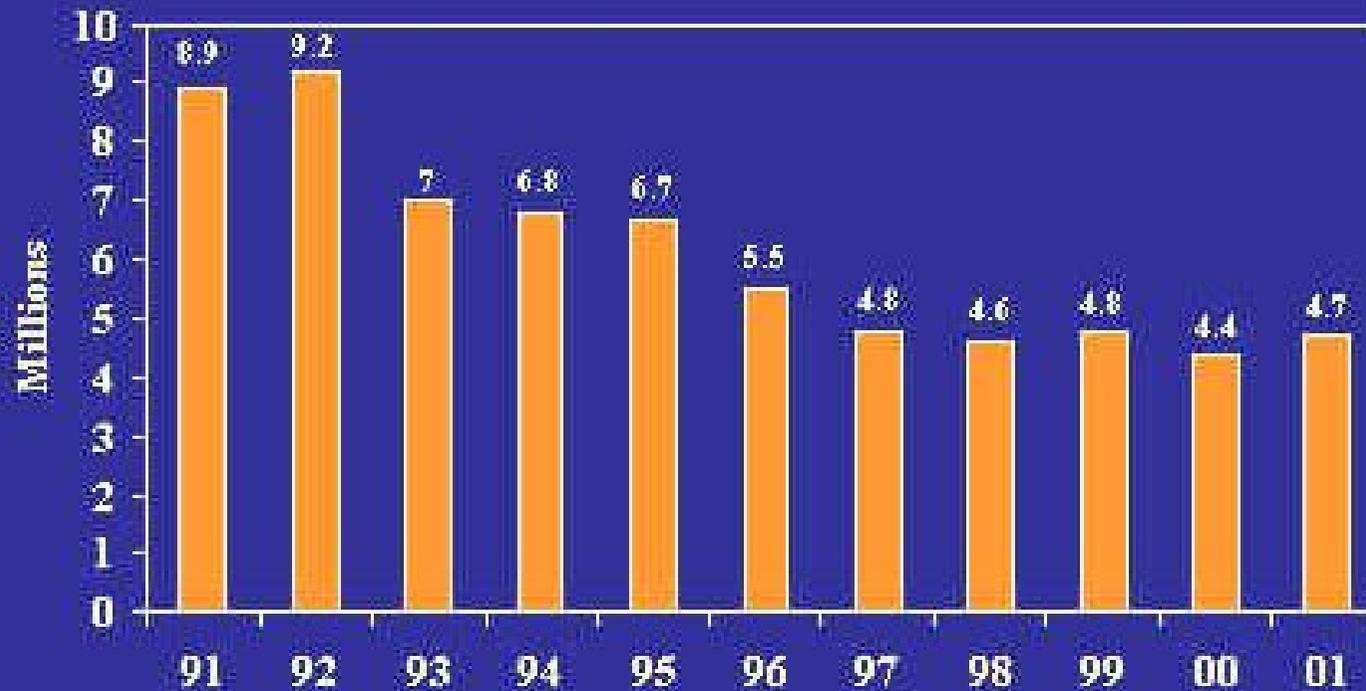


Figure 11

http://www.aphis.usda.gov/vs/naahps/brucellosis/status_rpt/figure11.jpg



Number of Reactor Herds from 1991-2001 According to State Classification

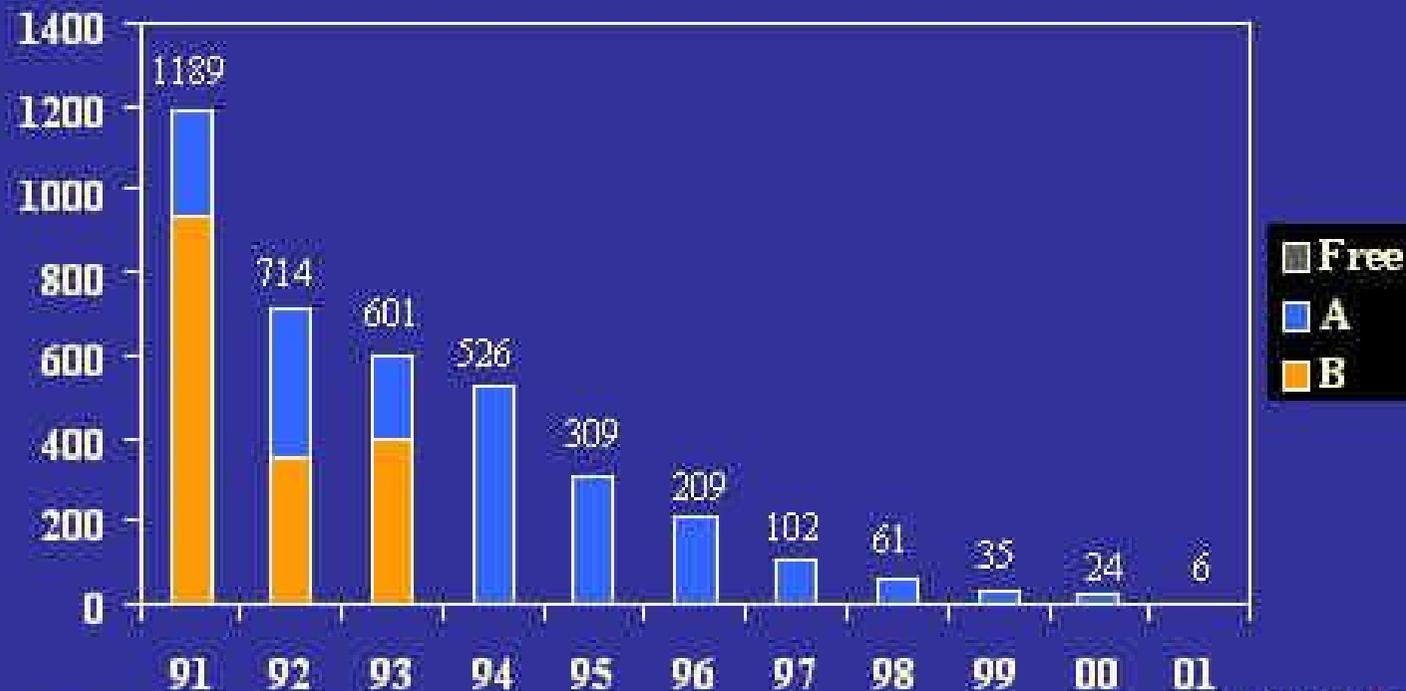


Figure 5

http://www.aphis.usda.gov/vs/naahps/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