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
B. abortus	1-6, 9	cattle	yes
B.melitensis	1-3	goats, sheep	yes
B. suis	1, 3	swine	yes
	2	hares	yes
	4	reindeer, caribou	yes
	5	rodents	yes
B. canis	none	dogs, other canids	yes
B. ovis	none	sheep	no
B. neotomae	none	Desert wood rat	no
B. maris (?)		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

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

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

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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

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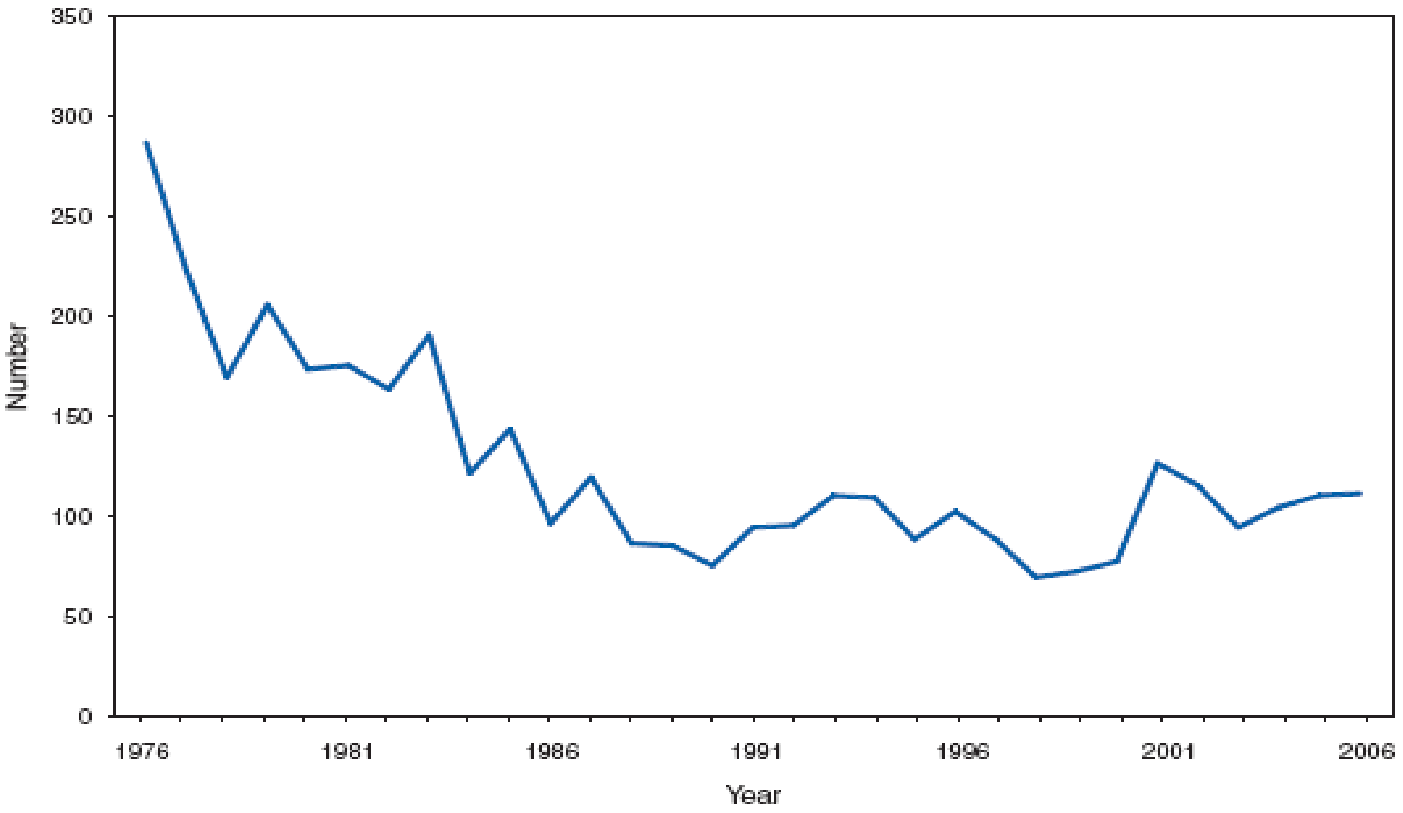
Brucella in Marine Mammals

- 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

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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

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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

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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

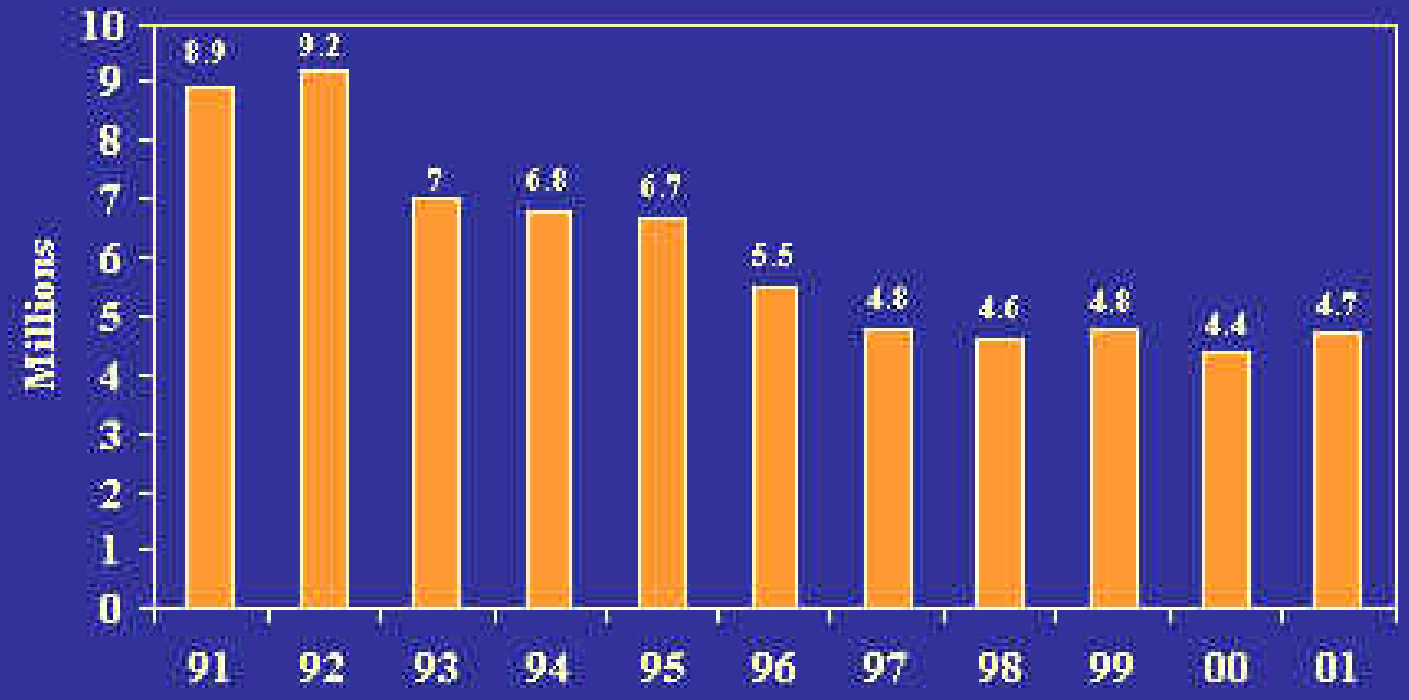

Figure 11

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

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

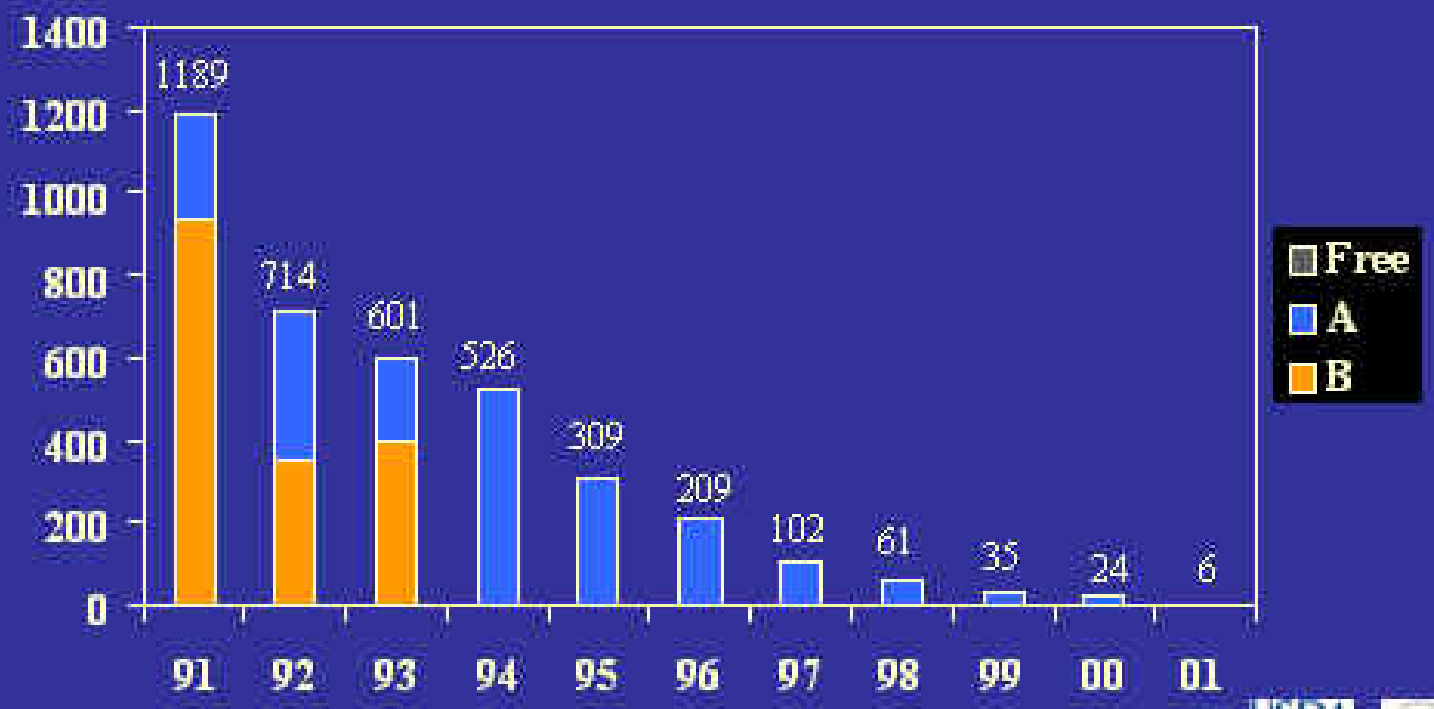

Figure 5 http://www.aphis.usda.gov/vs/nahps/brucellosis/status_rpt/figure05.jpg

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

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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

Acknowledgments

Development of this presentation was funded by grants from the Centers for Disease Control and Prevention, the Iowa Homeland Security and Emergency Management Division, and the Iowa Department of Agriculture and Land Stewardship to the Center for Food Security and Public Health at Iowa State University.

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