



Overview

- Definition
 - A zoonotic disease caused by the gram-negative *Brucella* species transmitted to humans from livestock, causing a flu-like illness with potentially lethal complications of endocarditis or neurobrucellosis
 - Reservoirs include cattle, sheep, goats, and pigs
 - High-risk occupations: abattoirs, veterinarians, animal handlers, and microbiology laboratory workers
 - Uveitis (80%) is the most common ocular manifestation, usually occurring during acute brucellosis
- Symptoms
 - Blurry vision
 - Floaters
 - Photopsia
- Laterality
 - Unilateral or bilateral
- Course
 - Ocular disease occurs in chronic brucellosis and typically resolves after an appropriate course of antimicrobial therapy
- Age of onset
 - All age groups
- Gender/race
 - No gender predilection
 - Common in the Mediterranean, Arab gulf, India, Central America and South America, Asia, and sub-Saharan Africa
- Systemic association

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- Council of State and Territorial Epidemiologists (CSTE) definition: “An illness characterized by acute or insidious onset of fever and one or more of the following: night sweats, arthralgia, headache, fatigue, anorexia, myalgia, weight loss, arthritis/spondylitis, meningitis, or focal organ involvement (endocarditis, orchitis/epididymitis, hepatomegaly, splenomegaly)”
- Acute brucellosis
 - Average incubation: 1–4 weeks (but highly variable, ranging from 5 days to 6 months)
 - Often subclinical with mild flu-like illness with no sequelae
 - Symptomatic disease presents with fever, anorexia, weight loss, headache, arthralgia, and malaise, with focal organ involvements
 - Musculoskeletal: spondylitis and arthritis, especially of the sacroiliac joints and large joints of the lower extremities, osteomyelitis of the vertebrae, tibia, and especially knee
 - Heart: endocarditis (most common cause of death)
 - Central nervous system (CNS): meningoencephalitis (change in mental status, seizure, coma, neurologic deficits, nuchal rigidity)
 - Gastrointestinal (GI): hepatic abscess, hepatomegaly, splenomegaly
 - Genitourinary: orchitis/epididymitis
 - Pulmonary: multiple syndromes
 - Hematologic: cytopenia, disseminated intravascular coagulation
 - Dermatologic: variable morphologies of rashes
- Chronic brucellosis (defined as >1 year of symptoms following diagnosis)
 - Can be persistent localized infection (e.g., bone or eye disease) or relapse following treatment
 - Some patients attribute symptoms to chronic brucellosis without objective evidence of infection

Exam: Ocular

Anterior Segment

- Episcleritis
- Diffuse or nodular scleritis
- Nummular keratitis
- Chronic granulomatous or non-granulomatous iridocyclitis

Posterior Segment

- Multifocal choroiditis, either in geographic pattern or in circumscribed nodules, is most characteristic of posterior segment disease
- Vitritis of varying severity
- Optic disc edema or hyperemia
 - Retrobulbar optic neuritis, chiasmal arachnoiditis

- Cystoid macular edema
- Retinal vasculitis
- Retinitis with edema and hemorrhage
- Exudative retinal detachment

Exam: Systemic

Findings are variable and nonspecific

- Hepatosplenomegaly (most common physical finding), lymphadenopathy
- Right upper quadrant abdominal tenderness
- Knee swelling, sacroiliac tenderness
- New or changing murmur (endocarditis), pericardial rub (pericarditis)
- Nuchal rigidity, Kerning sign, and Brudzinski sign (meningitis)
- Tender, swollen and erythematous scrotum (orchitis)

Imaging

- FA
 - Optic nerve staining or leakage
 - Multiple hyperfluorescent lesions with late leakage
- ICG
 - Multiple hypofluorescent and hyperfluorescent lesions, early
 - Multiple hyperfluorescent spots with associated large areas of hypofluorescence, late
- Visual field
 - Bilateral blind spot enlargement or visual field constriction

Laboratory and Radiographic Testing

- Fluid culture for identification of *Brucella* species (e.g., blood, aqueous, vitreous)
- Standard agglutination test (SAT)—most commonly used
 - “Gold standard” test that uses an antigen derived from *B. abortus* to detect both Immunoglobulin G (IgG) and Immunoglobulin M (IgM) agglutinating antibodies
 - Titers exceeding 1:160 are considered significant for brucellosis in endemic areas (1:80 in non-endemic areas)
 - Interpretation of serologies can be challenging in endemic areas and in patients who have been treated previously
 - This test does not detect antibodies to *B. canis*, which requires *B. canis* serology for diagnosis
- Enzyme-linked immunosorbent assay (ELISA)
 - ELISA and SAT both cross-react with other bacteria

- ELISA and SAT can both give false-negative results early in infection and in immunocompromised patients
- Polymerase chain reaction (PCR)
- Anterior chamber tap or vitreous tap with Goldmann-Witmer coefficient analysis

Differential Diagnosis

- Tuberculosis
- Syphilis
- Sarcoidosis
- White dot syndromes
- Lyme disease
- Outer retinal toxoplasmosis
- Diffuse unilateral subacute neuroretinitis (DUSN)
- Septic choroiditis
- Viral retinitis
- Presumed ocular histoplasmosis syndrome (POHS)
- Vogt-Koyanagi-Harada (VKH) syndrome
- Sympathetic ophthalmia

Treatment

- Adults and children >8 years
 - Oral doxycycline 2–4 mg/kg/day (maximum 200 mg/day) in two divided doses or oral tetracycline 30–40 mg/kg/day (maximum 2000 mg/day) in four divided doses, *PLUS*
 - Rifampin 15–20 mg/kg/day (max 600–900 mg/day) in one or two divided doses
 - This combination is given for a minimum of 6 weeks
- Pregnancy patients and children <8 years
 - Oral TMP-SMZ (trimethoprim, 10 mg/kg per day, maximum 480 mg/day; and sulfamethoxazole, 50 mg/kg per day, maximum 2400 mg/day) divided in two doses for 4–6 weeks, *OR*
 - Rifampin with ceftriaxone
 - TMP-SMZ should be avoided during the last week of pregnancy before delivery due to risk for kernicterus
- Cases complicated by endocarditis or meningitis
 - Add streptomycin (20–40 mg/kg per day, maximum 1 g/day divided in two doses) or gentamicin (5 mg/kg per day divided in one–three doses) to the above regimen for the first 2 weeks, then extend the regimen for 4–6 months
 - Surgical intervention for deep-tissue abscesses

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- About 10% of patients have relapsing infection despite systemic antimicrobial therapy, due to evasion by intracellular organisms
 - Topical and systemic corticosteroids are appropriate once antimicrobial therapy has been commenced

Referral/Co-management

- Infectious disease
- Cardiology
- Neurology