# **Brucella**

## **1. Definition, Taxonomy & Classification**

* **Brucellosis** (aka Malta, Crimean, Mediterranean, Rock, undulant, Bang’s disease).
* Caused by *Brucella* spp.: small, **Gram-negative coccobacilli**, **facultative intracellular pathogens** (within macrophages/reticuloendothelial system).
* non-motile, non-spore-forming, aerobic.
* *B. abortus* and *B. suis* may require 5–10% CO₂.
* Do not ferment sugars.
* **Closely related** to *Bartonella*

### **Human pathogenic species:**

* *B. melitensis*: goats, sheep, camels – **most virulent, most common worldwide**, acute presentation.
* *B. abortus*: cattle.
* *B. suis*: pigs, hares, reindeer.
* *B. canis*: dogs (milder human disease).
* Rare: *B. ceti*, *B. pinnipedialis* (marine mammals), *B. inopinata* (human isolate, e.g. breast implant).

## **3. Epidemiology**

* **Worldwide zoonosis**; most common zoonotic infection globally.
* **Endemic regions**: Mediterranean basin, Middle East, Africa, Latin America, Central and South Asia.
* UK: ~10 imported cases per year.
* Important occupational hazard: abattoir workers, vets, farmers, meat inspectors, lab staff.
* Human-to-human: rare (sexual, congenital, breast milk, transplant).
* **Ingestion**: unpasteurised dairy (milk, cheese) > pasteurisation.
* **Direct contact**: animal blood, tissues, aborted products > eliminated by animal vaccination).
* **Inhalation**: aerosols on farms, in labs > PPE
* Rare human-to-human.
* Worry re: bioterrorism

## **5. Pathogenesis**

* Enters via mucosa/skin → regional lymph nodes → bloodstream → reticuloendothelial organs.
* Intracellular survival: inhibits apoptosis, suppresses Th1/TNF-α responses.
* **Virulence factors**:
  + Smooth LPS (resists complement killing).
  + VirB type-IV secretion system (T4SS).
  + BvrR/BvrS two-component system.
  + Cyclic β-1,2 glucans.
  + Superoxide dismutase and urease (acid survival).
* Forms granulomas in liver, spleen, marrow.
* Persistence in granulomas → relapsing or chronic disease.

## **6. Laboratory Diagnosis**

### **Safety**

* **Hazard Group 3**. Highly infectious (10–100 organisms enough).
* Commonest lab-acquired infection. Work in BSL-3. Notify lab when suspected.

### **Specimens**

* Blood cultures (yield 15–70%).
* Bone marrow: **gold standard**
* Other: Tissue, synovial fluid, CSF

### **Culture**

* Slow-growing: 2–3 days up to 8 weeks (usually positive 7–21 days).
* Small convex non-haemolytic colonies.
* Chocolate agar, blood agar, Brucella broth.
* MALDI-TOF can identify (under BSL-3).
* Microscopy: Gram-negative coccobacilli, faint staining.
* Biochemical tests: Oxidase +, catalase +, urease + (rapid).
* Slide agglutination with specific antisera.
* Molecular : PCR assays increasingly used (esp. for focal disease, FFPE tissue).
* Serology
* **SAT (Standard tube agglutination test)**: titre ≥1:160 significant.
* **Rose Bengal test**: screening.
* ELISA (IgM vs IgG).
* Coombs anti-Brucella: useful in chronic disease.
* *B. canis* requires separate serology.

## **7. Clinical Features**

### **Incubation**

* Typically 2–4 weeks (range: 5 days – 6 months).

### **General symptoms**

* “Great imitator”: non-specific systemic illness.
* **Undulant fever**, night sweats (malodorous, “wet hay” smell), malaise, anorexia, arthralgia, myalgia, headache, weight loss.
* Lymphadenopathy, hepatosplenomegaly.
* Anaemia, leukopenia, thrombocytopenia possible.

### **Focal disease (~30%)**

* **Osteoarticular** (most common, up to 50%): sacroiliitis, spondylitis, peripheral arthritis.
* **Genitourinary**: epididymo-orchitis; female pelvic infections, abortion, infertility.
* **Hepatic**: hepatitis, granulomas, abscesses.
* **Cardiac**: endocarditis (<2% but major cause of death), myocarditis, pericarditis, mycotic aneurysms.
* **Neurological (10%)**: neurobrucellosis – meningitis, meningoencephalitis, myelitis, radiculopathy, cranial nerve palsy.
* **Respiratory** (rare): bronchitis, pneumonia, pleural effusion, TB-like miliary pattern.
* **Ocular**: uveitis, optic neuritis.
* **Cutaneous**: varied, vasculitic, psoriasiform lesions.
* **Pregnancy**: ↑ risk of miscarriage, preterm labour, congenital infection → avoid breastfeeding.
* **Children**: abdominal pain, arthritis more common. Chronicity rare.

## **8. Treatment**

### **Principles**

* Always **combination therapy** for ≥6 weeks.
* Aim: intracellular penetration, relapse prevention.

### **Uncomplicated brucellosis (WHO first-line)**

* **Doxycycline 100 mg PO BD × 6 weeks + Rifampicin 600–900 mg OD × 6 weeks**.
* Alternative: Doxycycline × 6 weeks + Streptomycin (or gentamicin 5mg/kg) 1 g IM daily × 2–3 weeks.

### **Complicated**

* **Spondylitis/osteomyelitis**: prolonged (3–6 months).
* **Neurobrucellosis**: Doxycycline + Rifampicin + Ceftriaxone (IV 1 month) for 4–6 months. Continue until CSF normalises.
* **Endocarditis**: Doxycycline + Rifampicin + Aminoglycoside; surgery often needed.
* **Pregnancy**: Rifampicin monotherapy (TMP-SMX if appropriate, but avoid near term).
* **Children <8 years**: Rifampicin + TMP-SMX.

### **Special note**

* Vaccine strain *B. abortus* RB51 is **rifampicin-resistant** → use doxycycline + TMP-SMX.

### **Relapse**

* Occurs in 5–15%. Risk: poor compliance, late diagnosis, focal disease. Retreatment with prolonged combos.

# **Key Exam Pearls**

* **Bone marrow culture > blood culture** for sensitivity.
* **B. melitensis** = most pathogenic.
* **Combination therapy (Doxy + Rifampicin)** always.
* **Endocarditis = main cause of mortality**.
* **Neurobrucellosis → triple therapy + prolonged duration**.
* **Lab hazard – inform lab**