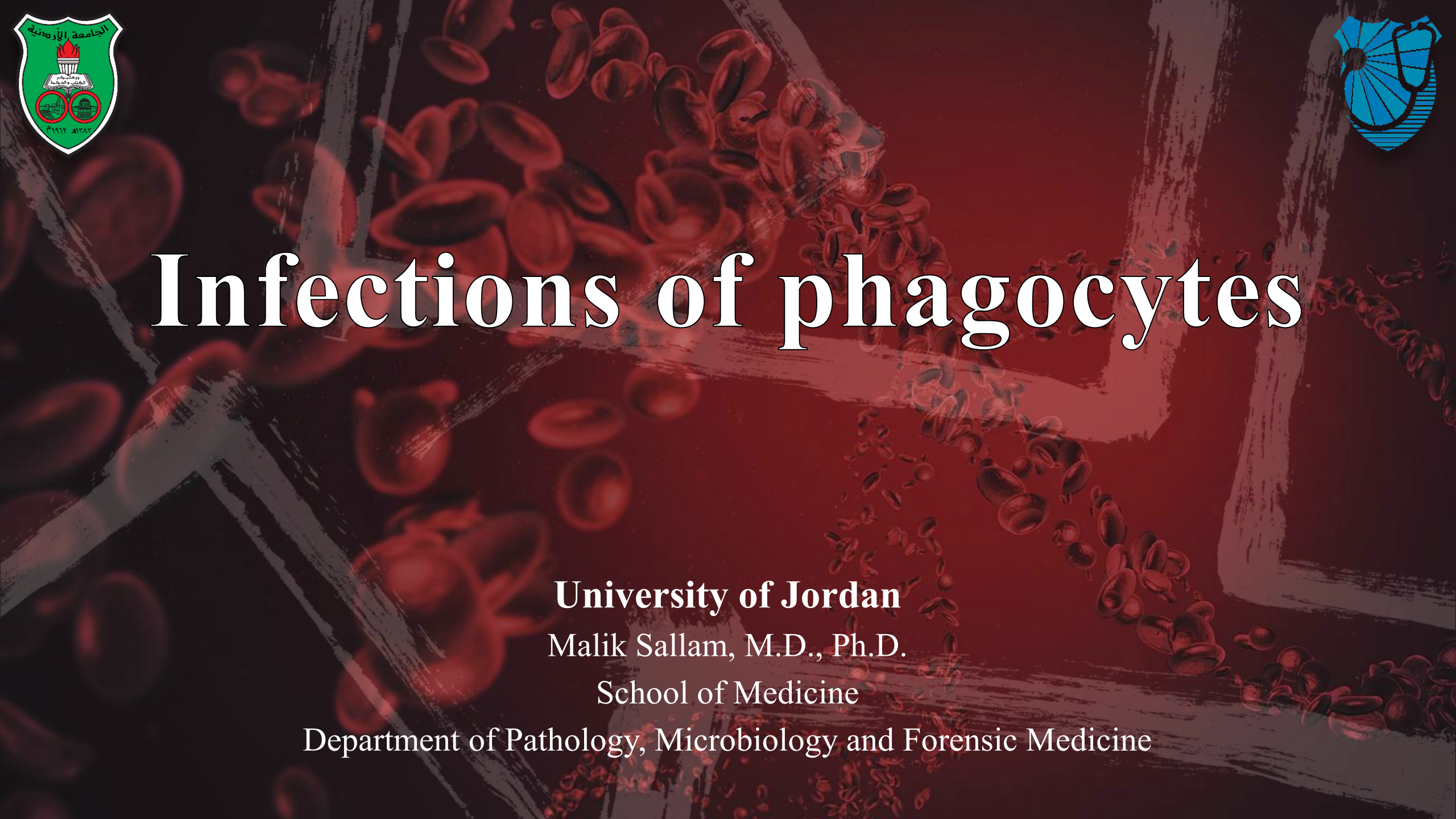


Infections of phagocytes

University of Jordan

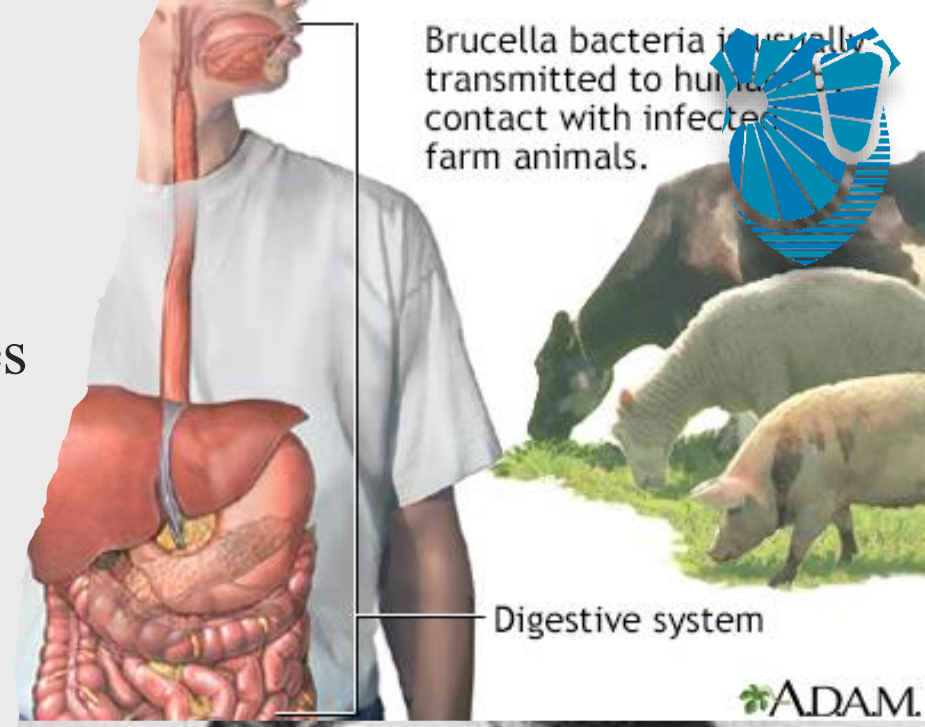
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Brucella – Overview

- Brucellosis is a **zoonotic infection** caused by *Brucella* species which is Gram-negative, non-motile, facultative intracellular coccobacilli.
- Transmitted through **ingestion of unpasteurized dairy products or via direct contact or aerosol exposure (e.g., slaughterhouse, veterinary, or lab work)**.
- Main human pathogens:
  - *B. melitensis* (sheep, goats) – most virulent
  - *B. suis* (pigs) – highly pathogenic
  - *B. abortus* (cattle) – moderate
  - *B. canis* (dogs) – least pathogenic
- Named after Sir David Bruce; infection historically known as **Malta or undulant fever**.





Brucella - Epidemiology

- Global burden: 1.6-2.1 million new human cases yearly.
- High-risk regions: Middle East, Central Asia, and parts of Africa.
- Jordan: Common in rural young adults and livestock workers.
- Seasonal peaks in spring/summer due to animal exposure.

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Serological prevalence of *Brucella* spp. at the livestock-human interface in Jordan

Ehab A. Abu-Basha [a,*,1], Zuhair Bani Ismail [a,1], Lea Widemann [b,1], Yasmin Daradkeh [a], Omar Al-Omari [a], Alaa Fahmawi [c], Mais Lakaideh [a], Belal Sha'fout [c], Haia Mellhem [a], Leen Al-Bayari [a], Hani Talafha [a], Zaidoun Hijazeen [d], Bilal Al-Omari [a], Jean DeMarco [b], William B. Karesh [b]

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Brucella – Pathophysiology

- Incubation: 3 days to several weeks.
- Entry: Ingested bacteria invade intestinal mucosa and taken up by macrophages
- The bacteria then spread to lymphoid tissues.
- Intracellular survival: Brucella evades immune response by inhibiting bactericidal mechanisms and complement activation.
- Then, *Brucella* spreads via lymphatic and hematogenous routes to liver, spleen, kidneys, joints, or breast tissue.
- Course: Causes localized or systemic infection; may persist for months to years (chronic brucellosis).

Brucellosis – Clinical Features

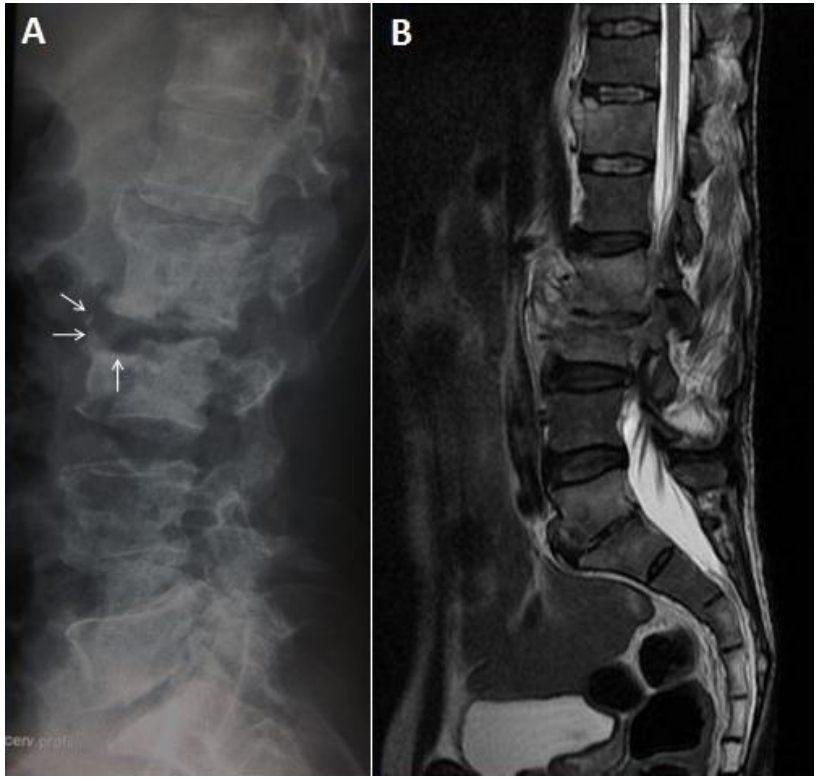
- Systemic: **Cyclical fever**, malaise, fatigue, sweating, headache, arthralgia, myalgia, and anorexia.
- Musculoskeletal: Sacroiliitis, osteomyelitis, spondylodiscitis, and septic arthritis.
- GI & Hepatic: Hepatosplenomegaly, hepatic granulomas/abscesses, and abdominal pain.
- Genitourinary: Epididymo-orchitis and miscarriage in females.
- Neurologic & Cardiac: Neurobrucellosis (meningitis, myelitis), endocarditis (rare but fatal).
- Dermatologic/Ocular: Erythema nodosum, uveitis, keratoconjunctivitis.
- Mortality: Up to 2% of cases.



Brucella – Diagnosis

- Blood culture definitive but slow (≥1 week). Bone marrow culture has a higher yield; handle under biosafety.
- Serology: ELISA & Rose Bengal are used.
- PCR: Rapid & sensitive.
- Imaging: **Pedro Pons sign** (lumbar erosion) in spondylodiscitis.
- Biopsy: Bone marrow/liver may show granulomas or abscesses.





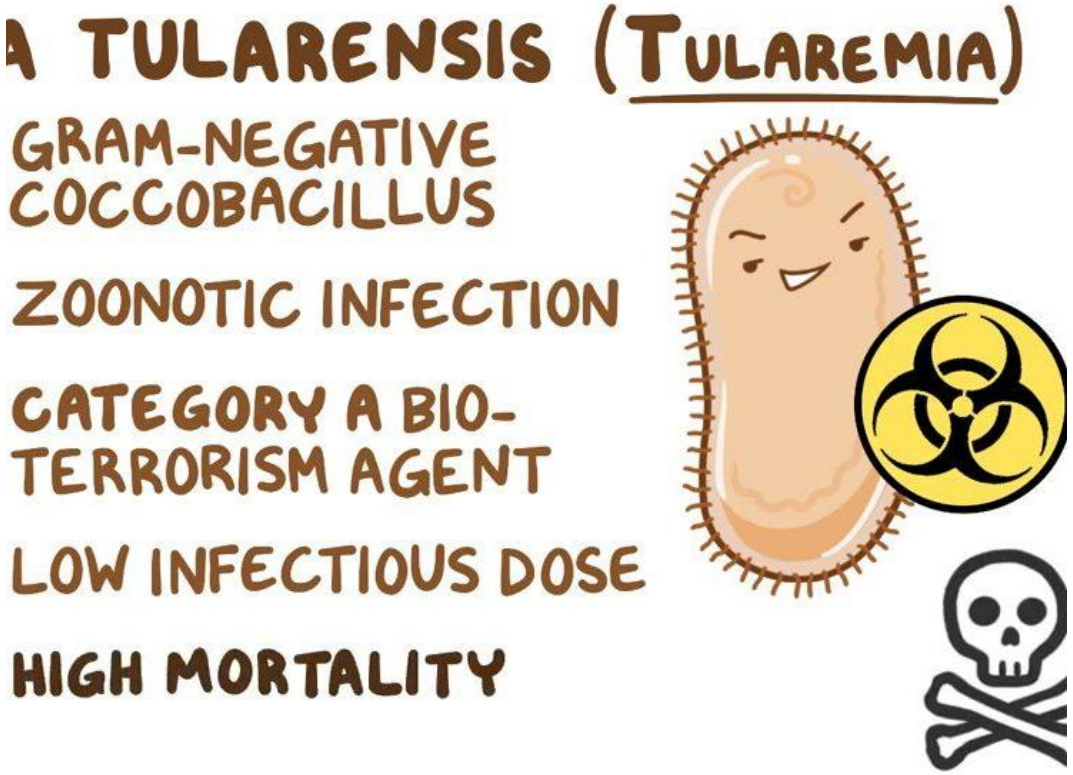
Source: Eljebbouri, Brahim, and Abad Cherif El Asri. "Pedro Pons' sign." The Pan African medical journal vol. 17 177. 7 Mar. 2014,

Brucellosis – Management

- Standard regimen: Doxycycline + Rifampin × **6 weeks** (uncomplicated).
- Severe focal disease: Add Gentamicin or Streptomycin × 2-3 weeks, then continue Doxycycline + Rifampin × **6 weeks**.
- Supportive: Antipyretics, analgesics; corticosteroids (for neurobrucellosis).
- Prevention: Annual herd vaccination.

Tularemia: Overview & Epidemiology

- Caused by *Francisella tularensis*, a Gram-negative coccobacillus.
- Zoonotic transmission via tick/fly bites, inhalation, ingestion, or direct animal contact.
- Very low infectious dose: 10-25 organisms.
- Found across the Northern Hemisphere, especially in warmer months.
- Clinical forms: Ulceroglandular, glandular, oropharyngeal, pneumonic, and typhoidal.



Tularemia: Clinical Features, Diagnosis & Management

- Symptoms: Fever, malaise, lymphadenopathy; ulceroglandular form most common. Other forms: pneumonia, GI or systemic involvement.
- Diagnosis:
- Serology: Titer >1:160 or fourfold rise.
- Culture: From blood, lymph, or ulcer (slow growth, **high biosafety risk**).
- Early negative serology does not rule out tularemia.
- Treatment: IV gentamicin (7-14 days) for moderate–severe cases. Fluoroquinolones (e.g., ciprofloxacin) for mild disease.
- Surgery: Incision and drainage may be needed for lymph nodes.

Q Fever - Overview

- Q fever is an acute zoonotic febrile illness caused by ***Coxiella burnetii***, a gram-negative **intracellular** bacterium.
- Discovered in 1935 among Australian meat workers. Classified in the US as a reportable disease and **a potential bioterrorism agent**.
- Transmitted by **inhalation of aerosols** from animal placenta, urine, feces, or contaminated dust/straw. The reservoirs: Cattle, sheep, goats, also cats, dogs, wild birds, rodents. Other modes of transmission: raw milk, blood transfusion, autopsy exposure, or during delivery of infected women.



Q Fever – Overview

- Risk Groups: Farmers, veterinarians, slaughterhouse workers.
- Immunocompromised, pregnant women, patients with valvular heart disease or vascular grafts.
- Higher incidence in spring and early summer (birthing season).
- Outbreaks linked to urban goat/sheep farming (e.g., Netherlands 2007-2010).

Ladbury *et al. BMC Infectious Diseases* (2015) 15:372
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BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Integrating interdisciplinary methodologies for One Health: goat farm re-implicated as the probable source of an urban Q fever outbreak, the Netherlands, 2009

Georgia A. F. Ladbury[1,2*†], Jeroen P.G. Van Leuken[1,3†], Arno Swart[1], Piet Vellema[4], Barbara Schimmer[1], Ronald Ter Schegget[5] and Wim Van der Hoek[1]

Q Fever – Clinical Features, Diagnosis, Management

- Acute Q fever: high fever, headache, myalgia, atypical pneumonia, hepatitis, rash common.
- Chronic Q fever: culture-negative endocarditis, hepatitis, osteomyelitis. Post-Q fever fatigue syndrome: prolonged fatigue, myalgia, cognitive issues (about 20%).
- Diagnosis: Serology (indirect immunofluorescent antibody test). PCR for early detection or endocarditis.
- Treatment:
- Acute: doxycycline 100 mg twice daily × 14 days.
- Chronic (endocarditis): doxycycline + hydroxychloroquine for 18–24 months.
- Vaccine available in Australia for high-risk workers.



CSD – Etiology

- *Bartonella henselae* is a **Gram-negative** bacillus bacterium that is the cause of cat-scratch disease (CSD)
- Spread to humans through a cat's scratch or bite, especially from kittens
- Causes lymphadenopathy
- More severe systemic disease, occur in immunocompromised individuals

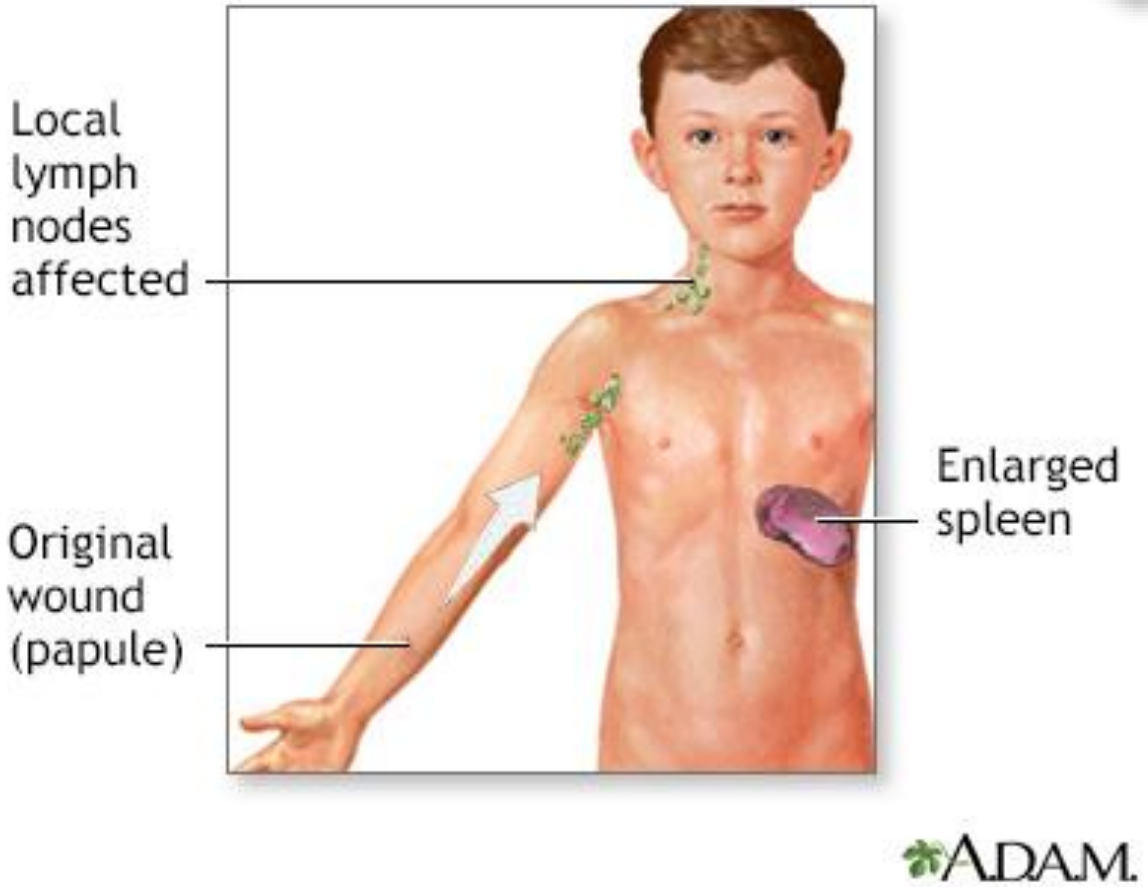
CSD – transmission and manifestations



- *Bartonella henselae* causes different diseases based on immune status
- Transmission: Cat scratch or bite, especially from kittens
- Typical presentation: papules in the scratch site, swollen lymph nodes (lymphadenopathy), high fever
- Usually self-limited illness

CSD – Clinical Features

- Key sign: Tender lymphadenopathy at scratch/bite site that appears 1-2 weeks after inoculation
- Disease Course: Common cause of chronic lymphadenopathy. May spread to eye, liver, spleen, CNS
- Histology: Granulomas with central microabscesses. Similar changes in skin lesion and regional nodes



CSD – Pathophysiology

- *B. henselae* enters through cat scratch/bite and then phagocytized by macrophages (not killed). Then, it is transported to regional lymph node
- Macrophages release IL-1 & TNF-α which recruit neutrophils & macrophages leading to lymph node swelling. IL-1 causes fever & activates T-helper cells followed by granuloma formation.
- Activated T-helper cells release more TNF-α which stimulates macrophages resulting in nitric oxide (NO) production which kills bacteria. Inflammation resolves and node regresses.

CSD – Diagnosis

Clinical
- Cat exposure and tender lymphadenopathy

Serology
- Positive = Diagnosis supported
- Negative = Does NOT rule out CSD

Radiology
- Ultrasound to guide needle aspiration

Pathology
- Lymph node biopsy with combined application of the IHC and WS

CSD – Treatment and Prevention

- In mild cat-scratch disease, supportive care with antipyretics, anti-inflammatory agents, and warm compresses is often sufficient.
- For moderate cases, a 5-day azithromycin course may reduce pain but does not shorten illness.
- Immunocompromised patients should always receive antibiotics to prevent severe disease.
- Severe or disseminated cases may require rifampin, TMP-SMX, or ciprofloxacin.
- Prevention includes avoiding cat scratches/bites, handwashing after handling cats, prompt wound cleaning, trimming cat nails, and flea control.

Thank You…
Wishing you all the best!
See you in the RS ☺