

Brucellae are obligate intracellular pathogen of animal & human. They are relatively inactive metabolically.

*B.melitensis* typically infects goats. *B. suis* infects swine. *B.abortus* infects cattle & *B. canis* infects dogs.

The disease in human (Brucellosis, undulant fever, Malta fever) characterized by an acute bacteremia phase followed by chronic stage that may extent for many years & involve many organs in the body.

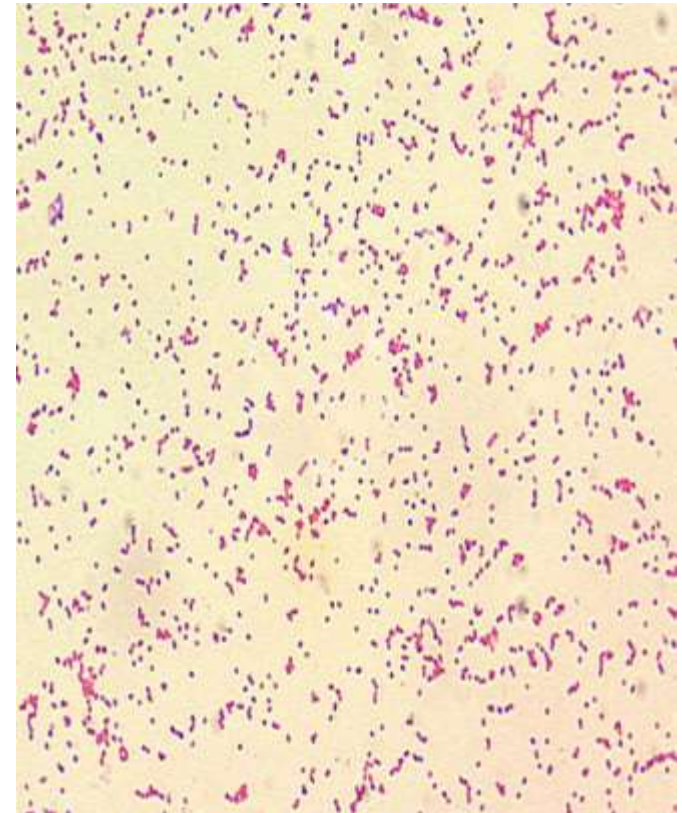
### **Morphology & identification:**

They are G negative short coccobacilli, aerobic, non-motile.

### **Culture:**

Small convex, smooth colonies on enriched media in 2-5 days. Fresh specimens from animal & human source are usually inoculated on trypticase soy agar or blood agar. *B.abortus* require 5-10% CO<sub>2</sub> for growth, while other species grow aerobically. Catalase & Oxidase tests are positive, H<sub>2</sub>S production & nitrate reduction tests are positive.

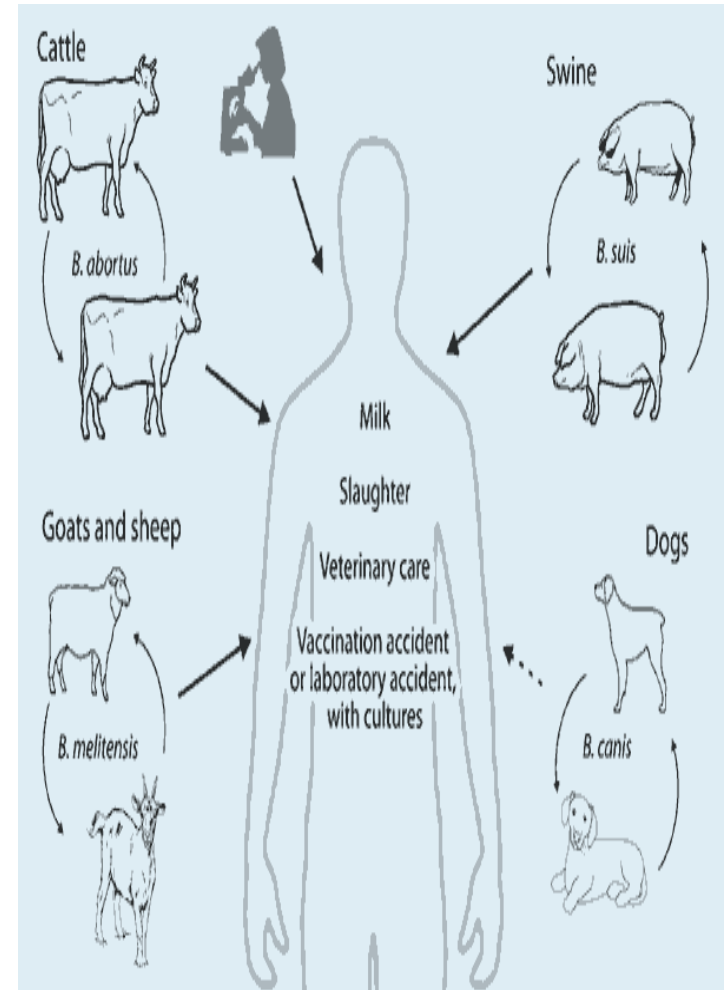
# **Brucellae (Brucella)**



Brucellosis is the most common bacterial zoonosis. Humans are the end hosts. The common route of infection in human are the intestinal tract (ingestion of infected raw milk), mucous membranes (droplet) & skin (contact with infected tissues of animals). Cheese and **cream** from infected milk is a common vehicle. Brucella may also transmitted through breast feeding. Transmission through respiratory route is rare. Vertical & blood transfusion transmission is also reported. Brucella rarely transmitted from human to human.

Brucellosis has a tendency toward chronicity and persistence. Brucellae have no classical virulence factors. LPS that cover the bacterium, The organism progress from the portal of entry via the lymphatics to bloodstream which distribute them to parenchymatous organs.

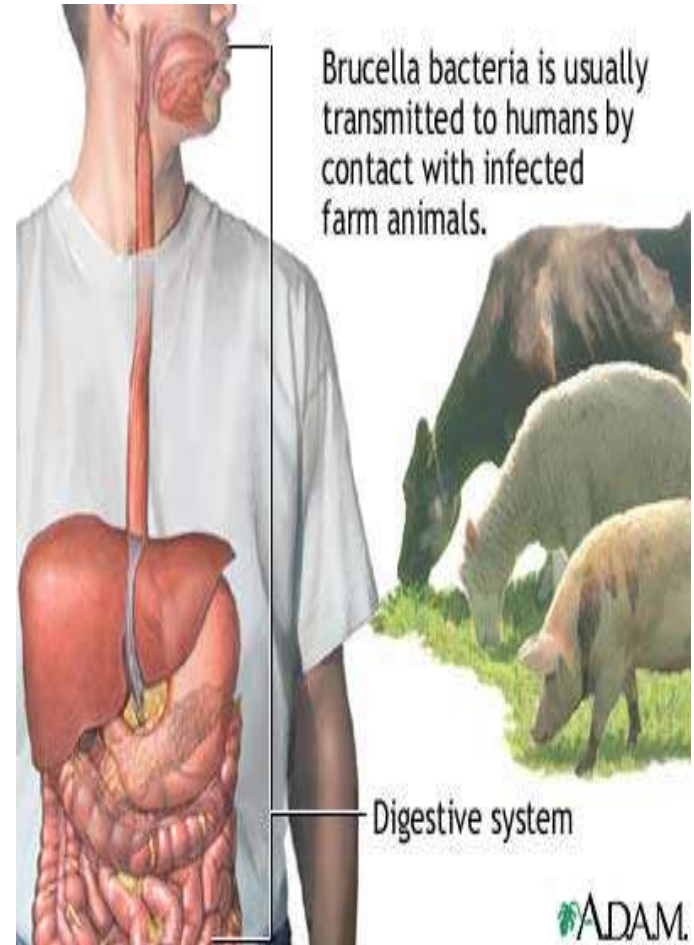
## Pathogenesis



# Pathogenesis

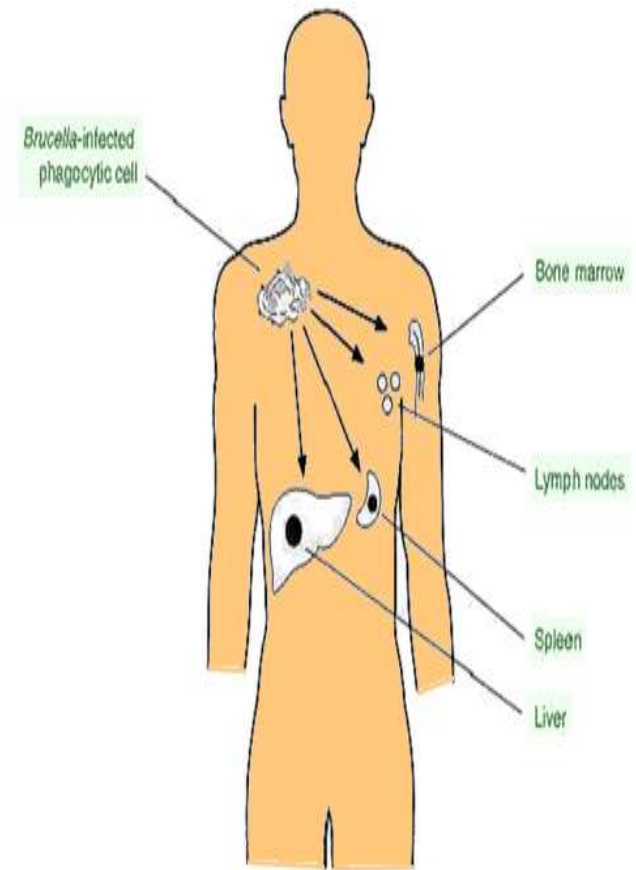
Brucellae can multiply within phagocytic cells. Granuomatous nodules within the lymphatic tissues, liver, spleen, bone marrow & other reticuloendothelial system may develop into abscesses. In such lesions the brucellae are typically intracellular. Osteomyelitis, meningitis & cholecystitis may occur. The granuloma consist of epithelioid & giant cells with central necrosis & peripheral fibrosis.

Brucellae infect humans have differences in pathogenesis. *B. abortus* usually causes mild disease without suppuration. *B. canis* also caused mild disease. *B.suis* infection tent to be chronic with suppurative lesions. *B.melitensis* infection is the most acute & severe. Placentas & fetal membranes of cattle, swine, sheep & goats contain **erythritol**; a growth factor for brucellae. Placentitis in these animals may lead to abortion. In human placenta, there is no **erythritol**.



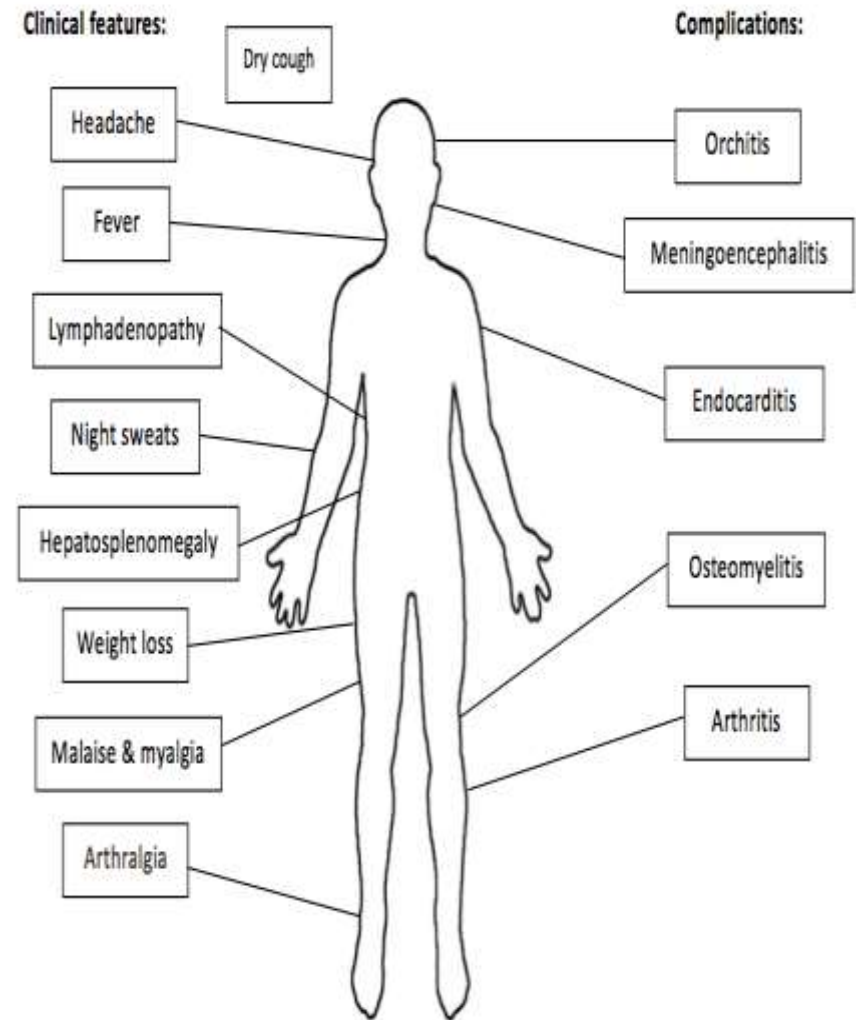
Brucellosis has a wide spectrum of clinical manifestations, depending on the stage of the disease & the organs & systems involved. . The incubation period is 1-6 weeks. The onset is insidious with malaise, fever, weakness, aches & sweats. Fever usually rise afternoon & its fall during night is accompanied by drenching sweat. Fever is the most common feature followed by osteoarticular involvement (Sacroiliitis, spondilitis, peripheral arthritis & osteomyelitis). Spleen & LNs are enlarged (Splénomegaly). Hepatitis may be accompanied by jaundice (Hepatomegaly). Hepatosplenomegaly observed in one third of patients. Lymphadenopathy in 10%, & osteoarticular manifestation in 50% of patients. Anemia affecting 25%, leukopenia or leukocytosis also reported. The most osteoarticular findings in children is monoarticular arthritis (Knee or hip), while in adults, Sacroiliitis is most frequent.

## Clinical findings



Following the initial infection, chronic stage may develop characterized by weakness, aches, pain & low grade fever. Brucellae can not be isolated from patient at this stage, but the Ab titer may be high. Accurate diagnosis of brucellosis continues to challenge clinicians because of its non-specific clinical features, slow growth rate in blood culture, and complexity of its sero diagnosis.

## Clinical findings





**Specimens:** Blood, biopsy materials (LNs, bone marrow) for culture & serum for serological tests.

**Culture:** Blood culture is the gold standard in diagnosis of brucellosis, & its sensitivity depends on the stage of the disease & previous antibiotic treatment.

Blood or tissues specimens are inoculated in trypticase soy broth & on thionine-tryptose agar & incubated in 10% CO<sub>2</sub> & should be observed & subcultured for at least 3 weeks before being discarded as negative. Brucellae are non-hemolytic, G negative coccobacilli, oxidase +, urease +, non-lactose non-glucose fermentor & obligate aerobic. Suspected colonies should be typed by H<sub>2</sub>S production & agglutination with antisera.

**Serology:** IgM Abs rise during the 1<sup>st</sup>. week of acute illness, peaked at 3 months & may persist during chronic phase. High IgM may persist for upto 2 years.

IgG Abs rise about 3 weeks after onset of acute disease, peaked 6-8 weeks & remain high during the chronic phase.

## Laboratory diagnosis:



Abs tend to persist in patients long after recovery; so in endemic areas, high background values could occur that may affect the diagnosis.

### **Agglutination test (Rose Bengal test):**

- **Rapid slide agglutination test:**

- **Tube agglutination test:** Through 2 folds serial dilution.

IgG agglutinin titer above 1:80 indicate active infection (Cholera vaccine may develop agglutinin titer to brucellae).

**Prozon phenomenon:** If the test is negative with the presence of highly suggestive clinical picture, this is probably due to the presence of **bloking Antibodies** (it appears during the subacute stage of infection & persist for many years independent of disease activity). This can be detected by adding antihuman globulin to the Ag-serum mixture

. 2. ELISA: which can differentiate between IgG, IgM, & IgA Abs.

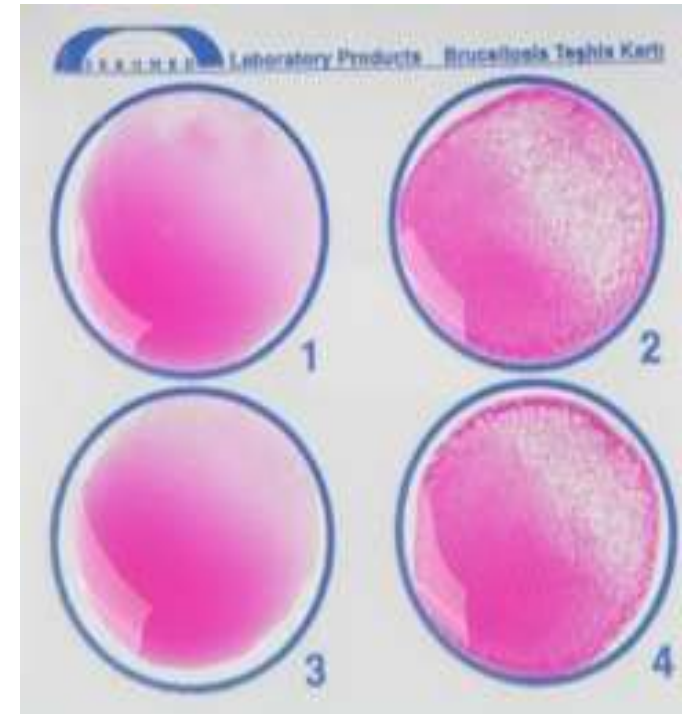
3. IFAT test: using fluorescent materials conjugated with specific Abs.

4. 2 mercaptaethanol test: The addition of 2ME destroy IgM & leaves IgG for agglutination reaction.

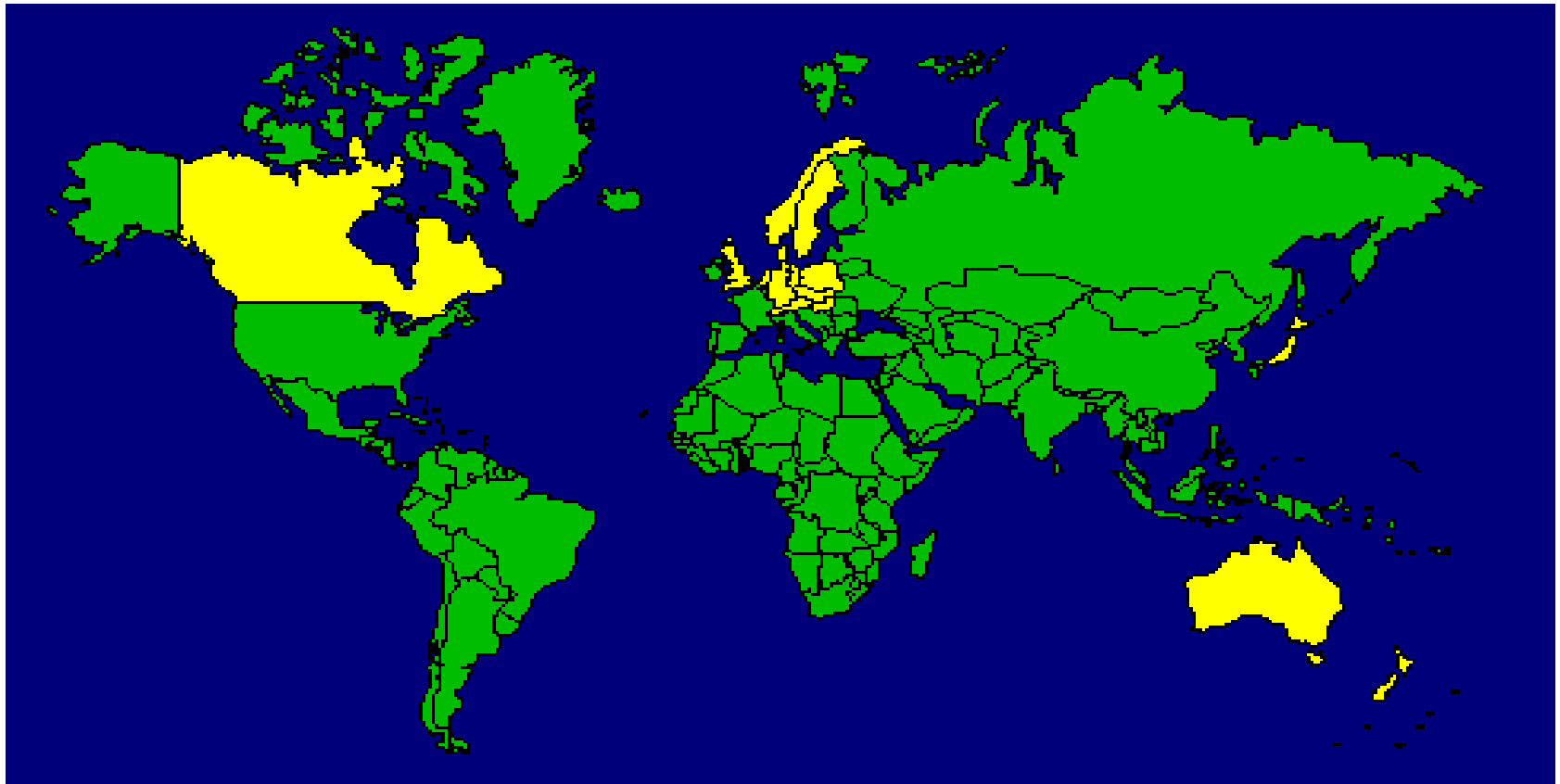
5. Molecular diagnosis by PCR

6. Intradermal skin test.

## **Laboratory diagnosis:**



# Global situation of Brucellosis



Free of *Brucella abortus* and *B. melitensis*





# Epidemiology and prevention

- Brucellosis is worldwide with some exceptions, with over half a million new cases annually. Brucellosis is endemic in many developing countries including Iraq. Brucellae are animal pathogen and an important cause of veterinary morbidity and mortality yielding important economic losses. It transmitted to human by accidental contact with infected animal, feces, urine, milk or tissues. Unpasteurized milk is the common source of infection. The three main human pathogens; *B.melitensis*, *B. abortus* & *B. suis*. Due to occupational risk, brucellae are more common in men. The majority of infection remains asymptomatic (latent). Brucellosis in humans is rarely fatal.
- **Prevention**
  - ☐ Education to avoid consuming unpasteurized milk and milk derivatives.
  - ☐ Barrier precautions for hunters and professionals at risk (butchers, farmers, slaughterers, veterinarians).
  - ☐ Careful handling and disposal of afterbirths, especially in cases of abortion.
  - ☐ Serological or other testing of animals; immunization of herds/flocks may be envisaged; eliminate infected herds/flocks.