Genus: Brucella

Causative agent of undulant fever. This disease is also called “Malta Fever” Undulant fever can be also called “ Brucellosis”.

Species of genus Brucella:

Brucellae are characteristically located intracellularly.

Morphology The typical m.o. are predominantly gram negative coccobacilli, and stain irregularly. They are aerobic and nonmotile m.o.
Culture: Brucellae are adapted to intracellular compartment of cells (fastidious). So, their requirments are complex including a.a., sugars, salts, and vitamines. The best media used for the cultivation of these m.o. are: 1. Trypticase soy agar. 2. Castaneda biphasic medium (broth & agar). 3. Blood agar & blood culture media. 4. MacConkey’s agar 5. Brucella selective medium 6. Thionine tryptose agar. 7. Serum dextrose agar. 7. Glucose dextrose agar.
The growth characteristics: 1. B. abortus requires 5-10% CO2 for growth, whereas the other species grow in air. 2. nonhaemolytic, slightly yellowish in young cultures but brownish in old ones . 3. Also, the colonies from young cultures the m.o. are capsultaed when stained are vireulent, whereas from old culture the m.o. are uncapsulat-ed and are avirulent.
Biochemically: a) Brucellae can utilize carbohydrates, but with no acid and gas production (not fermenter), b) H2S is produced only by B. abortus and B. suis, most species reduce nitrate to nitrite, oxidase positive, and are sensitive to acid and heat

Antigenic Structure:

1. Two lipopolysaccharides antigens (A & M) are present in different proportions among the different species.

2. Superficial L antigen resembles the Vi antigen (virulence) of Salmonella.

Pathogenesis & Pathology:

The common routes of infections in humans are:

1. Intestinal tract (ingesion)

2. Mucous membrane (droplet)

3. Skin (contact with infected animal or human).

4. Conjunctiva (rare; airborne).

5. Breast milk (lactating woman).

- The m.o. progress from the portal of entery, via lymphatic channels and regional L.N., to the thoracic duct and the bloodstream,
- distributes them to the parenchymatous organs.
- Granulomatous nodules that may develop into abscesses form in lymphatic tissue, liver, spleen, bone marrow, and other parts of the RES. In such lesions the m.o. is intracellularly.
- Osteomyelitis, meningitis,orchitis, arthritis, vertebral collapse or cholecystitis may occur

Histological reaction in brucellosis :

1. consists of proliferation of mononuclear cells, exudate of fbrin, coagulation necrosis, and fibrosis. The granulomas consist of epithelioid and giant cells, with central necrosis and peripheral fibrosis.
2. B. abortus usually causes mild disease without suppurative complications; non-caseating granulomas of the RES are found.
3. B. melitensis infection is more acute, severe and causes granulomatous lesions.
4. These two species are common in Iraq.
5. erythritol (a growth factor for Brucella). The proliferation of m.o. in pregnant animals leads to placentitis and abortion (economic loss). There is no erythritol in human .

Clinical Finding:

1) The I.P. Of brucellosis is 1- 6 weeks. The onset is insidious, with malaise, fever, weakness, aches, and sweat.
2) The fever usually rises in the afternoon; its fall during the night is accompanied by drenching sweat.
3) There may be GI and nervous symptoms. L.N. enlarge, and the spleen becomes palpable.

4) Hepatitis may be accompanied by jaundice.

5) Deep pain and disturbances of motion, particularly in vertebral bodies suggest osteomyelitis. The manifestations may suside in weeks or months , although localized lesions and symptoms may continue.

Following the initial infection, a chronic stage may develop; characterized by weakness, aches and pains, low grade fever, nervousness or depression and other nonspecific manifestations including psychoneurotic symptoms.

The diagnosis of "chronic brucellosis" is difficult to establish. Because Brucellae usually can not be isolated from such patients except in only 2% of them.

Diagnostic Laboratory Tests:	**The serological tests used for diagnosis of brucellosis are:**
A. Specimens: Blood and biopsy material B. Culture C. Serology: 1) IgM antibody levels rise during the FIRST week of acute illness, peak at 3 months, and may persist during chronic disease. Even with approperiate treatment, high IgM may persist up to 2 years. 2) IgG antibody levels rise 3 weeks after onset of acute disease, peak at 6- 8 weeks and remain high during chronic disease. 3) IgA levels parallel the IgG levels; could be blocking antibody .	1. **Agglutination test** (tube or slide); usig: a. Heat-killed phenolized smooth standerized brucella antigens. b. Rose bengal antigens (stained red). The significant titre = 1/160 or higher. Cross reaction may occur with cholera vaccine, S.typhi /paratyphi , or Yersinia. a) **2. 2-Mercaptoethanol** test; 2-ME can destroy IgM and leaves IgG. This may be used to differentiate between current /recent brucellosis from previous /old brucellosis. **b)** Also, is useful in chronic active brucellosis. **3. Blocking antibodies**; These are IgA antibodies that interfere with agglutination by IgG & IgM and cause false negative result (prozone phenomena). 4. Skin test (Brucellergen or Brucellin); it is DHS reaction to I.D. Injection of a protein brucella extract. 5. ELISA , RIA or Immunofluorescent ; for Ab detection.

Immunity:

Resistance to subsequent attack may be produced. Both cellular and humoral immunities are induced.

Treatment:

Combined anti-microbial drugs are used, taking in consideration that the m.o. is an intracellular one:

1. Ampicillin or tetracycline with Streptomycin give good result. Cotrimoxazole may be added.
2. Refampin with doxycycline gives 97% cure rate. Also, an aminoglycoside drug could be added.

Treatment should be continued for at least 6 weeks and for bone or joint infections the treatment continues for at least 8 weeks.

For neuro-Brucellosis chloramphenicol or ampicillin could be used with other drugs.

Epidemiology, Prevention & Control:

1. Brucellae are animal pathogens transmitted to humans accidentally.
2. Eradication of brucellosis in animals by immunization
3. Immunization of humans is experimental, but was attempted in individuals at high risk of getting brucellosis.
4. Pasteurization of milk and milk products and reduction of occupational hazards are also important steps.