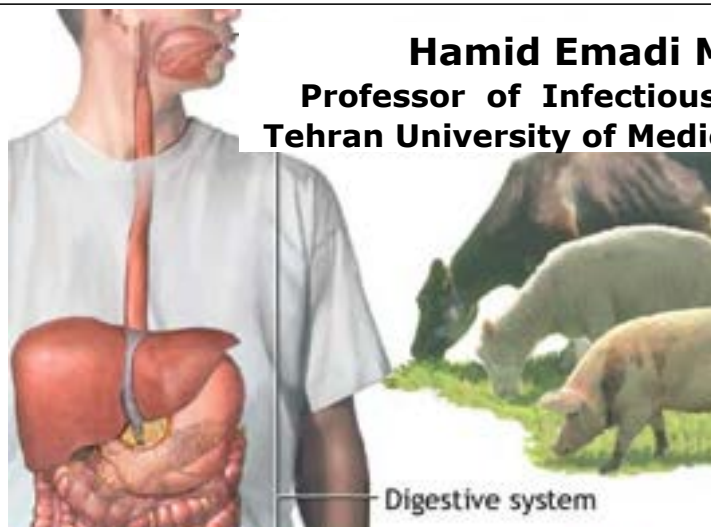




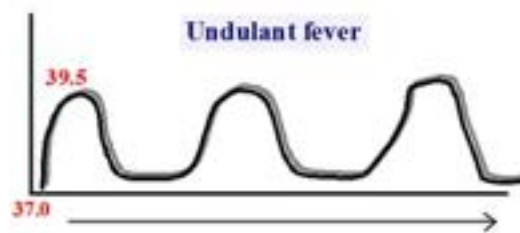
Brucellosis



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Digestive system

- Brucellosis is a bacterial zoonosis
- transmitted directly or indirectly to humans from infected animals
- The disease is known *undulant fever* because of its remittent character.



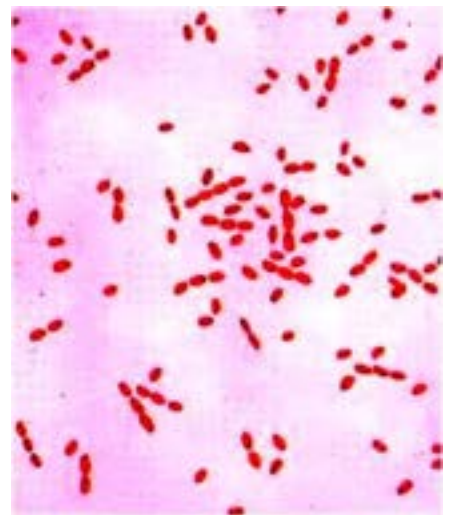
Etiologic Agents

- *B. melitensis*, which is the most common cause of symptomatic disease in humans and for which the main sources are sheep, goats, and camels;
- *B. abortus*, which is usually acquired from cattle or buffalo:

Etiologic Agents

- *B. suis*, which generally is acquired from swine
- *B. canis*, which is acquired most often from dogs
- *B. ovis*, which causes reproductive disease in sheep
- *B. neotomae*, which is specific for desert rodents
- *B. ceti* and *B. pinnipedialis* in marine mammals, including seals and dolphins

-
- All brucellae are small, gram-negative, rods or coccobacilli.
 - intracellular parasites





organisms are sensitive to

- The sunlight
- ionizing radiation
- moderate heat;

they are killed by

- boiling
- pasteurization

easily killed by a wide range of common disinfectants



Resistance to

- Freezing
- drying
- low temperatures

The organisms can survive for

- up to 2 months in soft cheeses
- for at least 6 weeks in dry soil
- at least 6 months in damp soil cool dark conditions.

Epidemiology

- Brucellosis is a zoonosis
- closely related to domesticated animals
- *B. melitensis* still pose a major public health problem in Mediterranean countries , Asia; and in parts of Africa



Brucellosis usually acquired by

- occupational or domestic exposure to infected animals or their products
- contaminated foods
- Dairy products, especially soft cheeses, unpasteurized milk, and ice cream



- 
-
- ingestion, inhalation, or mucosal or percutaneous exposure.
 - Accidental injection of the live vaccine
 - as biological weapons bioterrorism
 - Person-to-person transmission is extremely rare,
 - as is transfer of infection by blood or tissue donation



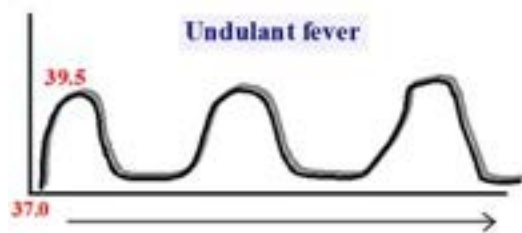
Clinical Features

- Brucellosis almost invariably causes fever, which may be associated with profuse sweats, especially at night



Clinical Features

- the fever of brucellosis shows an *undulating pattern* associated with musculoskeletal symptoms and signs in about one-half of all patients.



clinical syndromes

- **B. melitensis** tends to more acute and aggressive presentation
- **B. suis** with focal abscess
- **B. abortus** insidious in onset and more likely to become chronic.
- **B. canis** present frequently with acute gastrointestinal symptoms

- 
-
- The incubation period varies from **1 week to several months**
 - onset of fever may be abrupt or insidious.
 - In addition to fever and **sweats**, patients become increasingly **apathetic** and **fatigued**;
 - **lose appetite and weight** nonspecific myalgia, headache, and chills



presentation of brucellosis often fits one of three patterns

- febrile illness that resembles typhoid but is less severe;
- fever and acute monoarthritis, typically of the hip or knee, in a young child;
- long-lasting fever, misery, and low-back or hip pain in an older man.



In an endemic area (e.g., much of the Middle East), a patient with **fever and difficulty walking** into the clinic would be regarded as having brucellosis until it was proved otherwise



Diagnostic clues in the patient's history

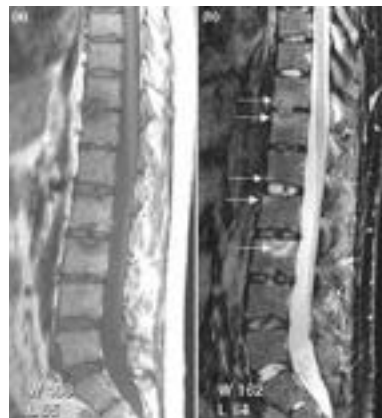
- travel to an endemic area
- a diagnostic microbiology laboratory
- consumption of unpasteurized milk products (including soft cheeses)
- contact with animals
- accidental inoculation with veterinary *Brucella* vaccines
- history of similar illness in the family (documented in almost 50% of cases).

Clinical Features

- The most common Focal features are musculoskeletal pain and physical findings in the peripheral and axial skeleton (40% of cases).



- Osteomyelitis more commonly involves the lumbar and low thoracic vertebrae than the cervical and high thoracic spine.



- Individual joints that are most commonly affected by septic arthritis are the knee, hip, sacroiliac, shoulder
- monoarthritis or
- polyarthritis



Radiology Spine: Differentiation of Brucellosis from Tuberculosis

	Tuberculosis	Brucellosis
Site	Dorsolumbar	Lumbar and others
Vertebrae	Contiguous	Multiple or contiguous
Diskitis	Early	Late
Body	Morphology lost early	Intact until late
Canal compression	Common	Rare
Epiphysitis	General: upper and lower disk regions, central, subperiosteal	Anterosuperior (Pom's sign)
Osteophyte	Unusual	Anterolateral (parrot beak)
Deformity	Anterior wedge, gibbus	Wedging uncommon
Recovery	Variable	Sclerosis, whole body
Paravertebral abscess	Common and discrete loss, transverse process	Small, well-localized
Psoas abscess	More likely	Rare

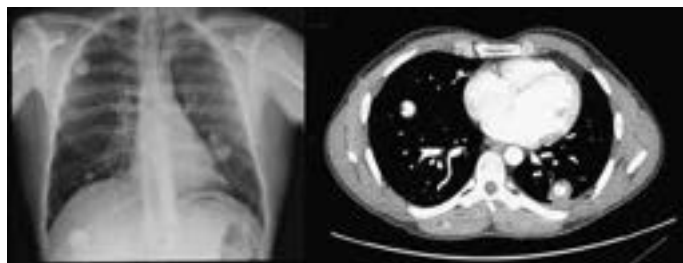
Parrot Beak



- Other systems may be involved in a manner that resembles typhoid



- About one-quarter of patients have a dry cough, usually with few changes visible on the chest x-ray, although pneumonia, empyema, intrathoracic adenopathy, or lung abscess can occur



- One-quarter of patients have
- hepatosplenomegaly
- Pancytopenia



- 10–20% have significant lymphadenopathy
- differential diagnosis :
- Epstein-Barr virus,
- *Toxoplasma*,
- cytomegalovirus,
- HIV
- *Mycobacterium tuberculosis*



- Acute epididymoorchitis
-

distinguished from

- mumps
- torsion
- Prostatitis

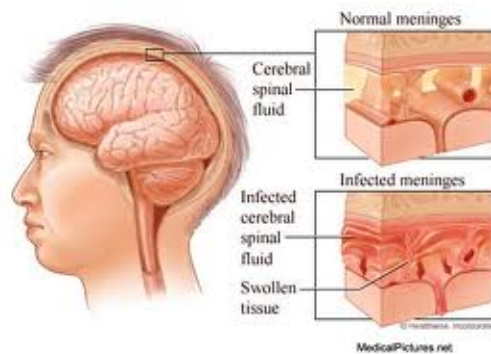


-
- There is an increased incidence of fetal loss among infected pregnant women
 - abortions is much less pronounced in humans than in farm animals
 - teratogenicity has not been described



Neurologic involvement

- depression
- lethargy
- lymphocytic meningoencephalitis that mimics neurotuberculosis

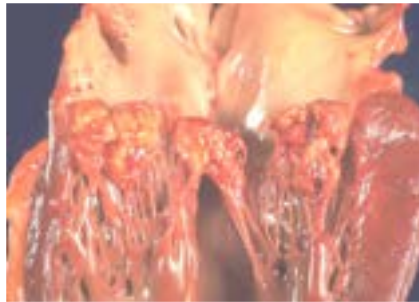


meningoencephalitis that mimics neurotuberculosis, atypical leptospirosis, or noninfectious conditions and that may be complicated by intracerebral abscess, a variety of cranial nerve deficits, or ruptured mycotic aneurysms



Endocarditis

- most often affecting the aortic valve (natural or prosthetic).
- Any site in the body may be involved in metastatic abscess formation or inflammation;



-
- the female breast and the thyroid gland are affected particularly often. Nonspecific maculopapular rashes and other skin.



DIAGNOSIS

The laboratory findings should be interpreted together with

- clinical manifestations
- exposure history
- occupation
- history of past infection

Culture

- Brucella are isolated from **blood, bone marrow, or other body fluids or tissues**
- time consuming,
- Biphasic (solid and liquid) **Castaneda**
- positive blood cultures ranges from %15 to %70 between the 7th and 21st day
- (BACTEC) shorten detected by the third day of incubation

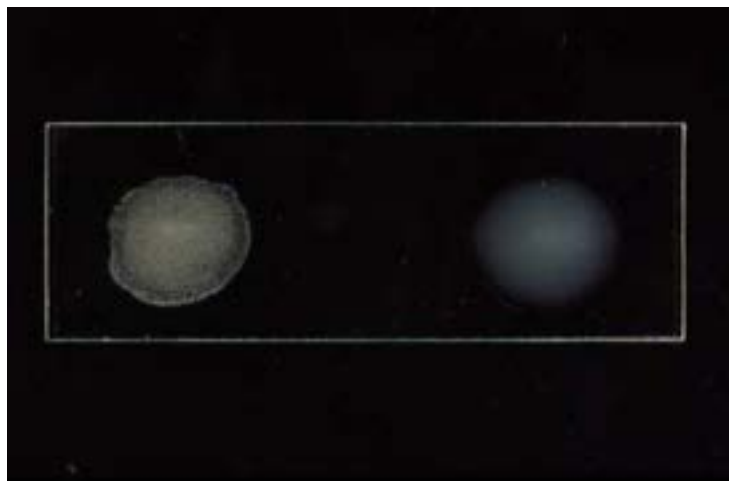


Serologic tests

- Serum agglutination (standard tube agglutination)
- ELISA (enzyme-linked immunosorbent assay)
- Rose Bengal agglutination
- Coombs test
- Immunocapture agglutination (Brucellacapt)
- 2-mercaptoethanol agglutination

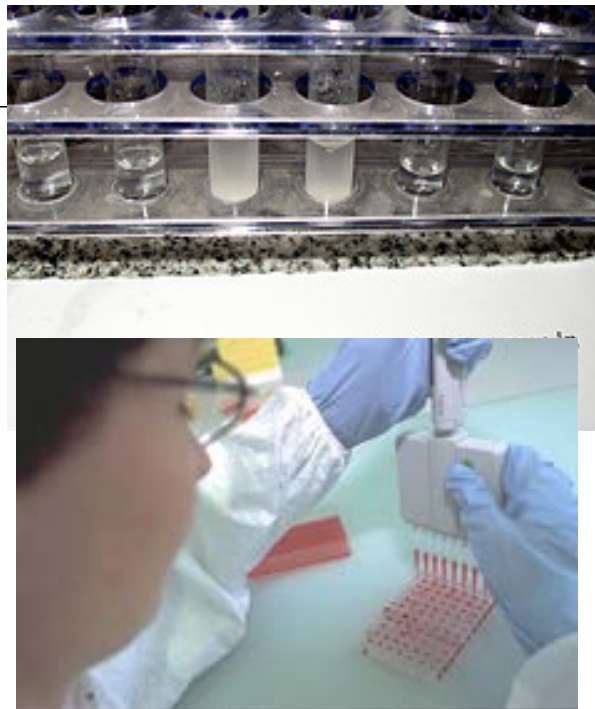
Slide Agglutination Test

- Rose Bengal plate agglutination test is often used as a rapid screening test



Serum agglutination testing (SAT)

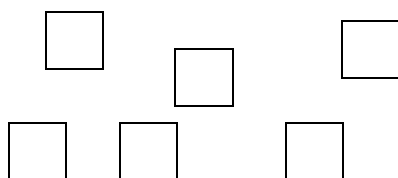
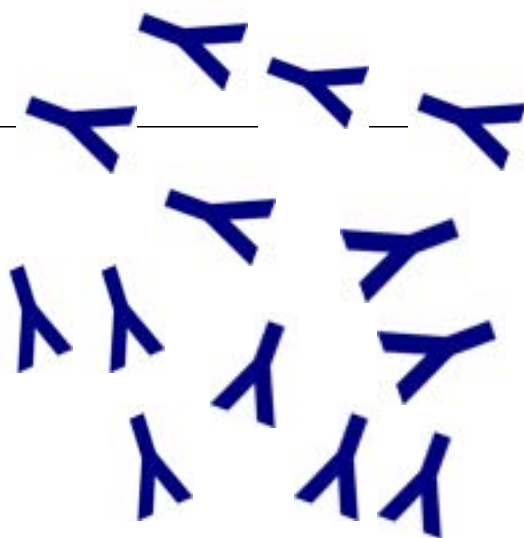
- There are no absolute thresholds for confirmatory titers.
- In general, positive titers consist of 1:160 in nonendemic regions and 1:320 in endemic areas

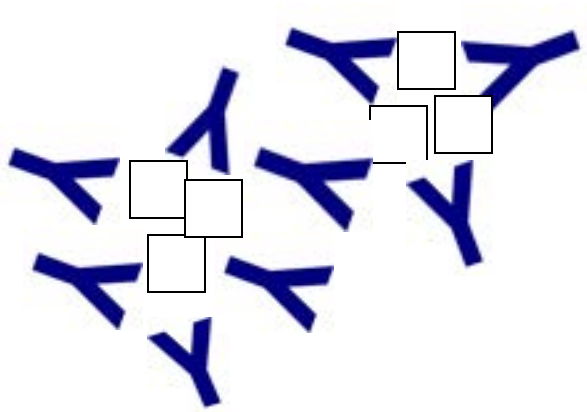


آزمایش باست آماده ای (کامل)

شماره لوله	۱	۲	۳	۴	۵	۶	۷	۸	۹	۱۰	۱۱
سرم فیزیولوژی (میلی لیتر)	۰/۹	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵
سرم بیمار (میلی لیتر)	۰/۱ →	۰/۵ →	۰/۵ →	۰/۵ →	۰/۵ →	۰/۵ →	۰/۵ →	۰/۵ →	۰/۵ →	۰/۵ →	—
آبشی ژن (میلی لیتر)	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵	۰/۵
وقت یا تیترو نهانی سرم	۱/۲۰	۱/۴۰	۱/۸۰	۱/۱۶۰	۱/۳۲۰	۱/۶۴۰	۱/۱۲۸۰	۱/۲۵۶۰	۱/۵۱۲۰	۱/۱۰۲۴۰	—

ساعت در 37 درجه بماند و در مقابل شاهد 48-72





Tube Agglutination Test

Agglutination

No agglutination



1/20

1/40

1/80

1/160

1/320

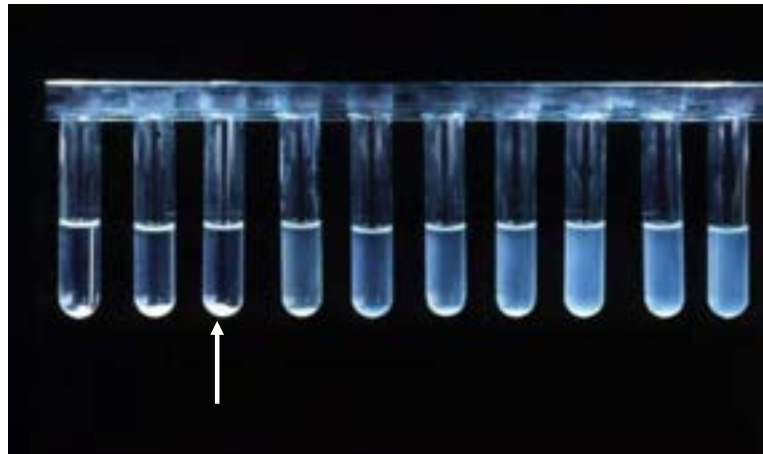
1/640

Neg. ctrl



In this case, the titre is 1/80

Tube Agglutination Test



0

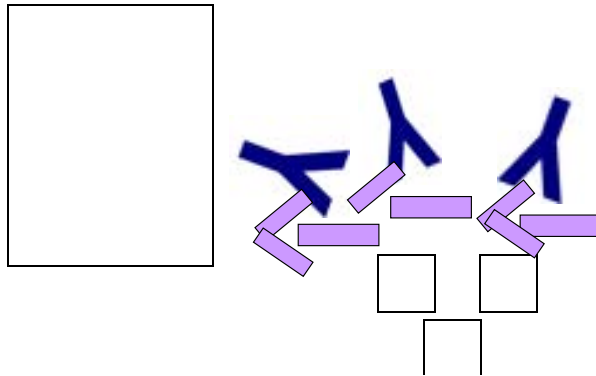
The Coombs and Immunocapture agglutination (Brucellacapt)





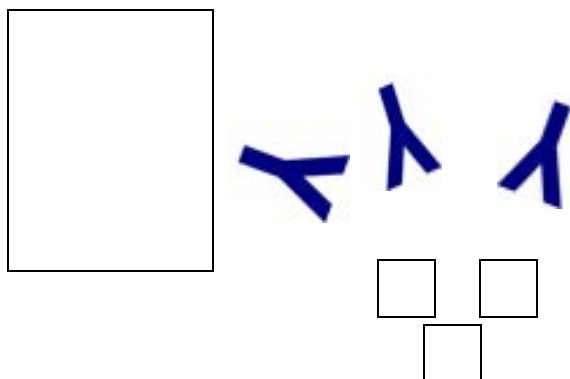
The Coombs and Immunocapture agglutination (Brucellacapt)

Anti Human Globuline



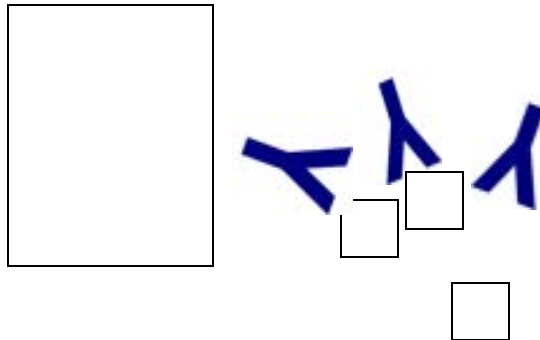
The Coombs and Immunocapture agglutination (Brucellacapt)

Anti Human Globuline



The Coombs and immunocapture agglutination (Brucellacapt)

Anti Human Globuline



2-MercaptoEthanol (2-ME)

The 2-mercaptoethanol (2-ME) agglutination test measures IgG antibodies only, and is a good marker to follow disease activity after initiation of therapy



2ME ☐
IgG ~~IgM~~



ELISA

- ELISA is the second most common serologic method utilized in evaluating patients with suspected Brucella infections.
- ELISA is rapid, objective, highly sensitive and specific; it measures IgM, IgG, and IgA



PCR

- The peripheral blood-based polymerase chain reaction to detect bacteremia, to predict relapse, and to exclude "chronic brucellosis."
- more sensitive and is certainly quicker than blood culture



Treatment

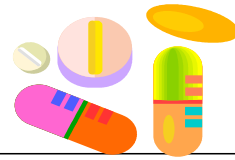
- Combination therapy
- Long course therapy



Treatment

- For adults with acute nonfocal brucellosis (duration, <1 month), a 6- 8 week course of therapy incorporating at least two antimicrobial agents is required.
- Complex or focal disease necessitates 3 months of therapy.

DRUGS



- Tetracyclines (Doxycycline)
- Aminoglycoside (Gentamycin, Streptomycin)
- Rifampin
- Trimethoprim- sulfamethoxazole
- Fluoroquinolones!!
- 3rd generation cephalosporins

World Health Organization recommendation

- rifampin (600–900 mg/d) plus
- doxycycline (100 mg twice daily) for 6 - **8** weeks





Treatment

- Patients who **cannot** tolerate or receive tetracyclines (children, pregnant women) can be given high-dose **TMP-SMX** instead (two or three standard-strength tablets twice daily for adults, depending on weight).



Treatment

- use of an aminoglycoside such as gentamicin (for at least 2 weeks) instead of streptomycin.
- neurologic requires prolonged treatment (i.e., for 3–6 months), usually with ceftriaxone
- endocarditis is treated with at least three at least 6 months,



prophylaxis after exposure

- rifampin plus doxycycline
- for 3 weeks after a low-risk exposure (e.g., a nonspecific laboratory accident)
- for 6 weeks after a major exposure to aerosol or injected material.
- doxycycline monotherapy of the same duration may be substituted.

- 
-
- Rifampin should be omitted after exposure to vaccine strain **RB51**, which is resistant to rifampin but sensitive to doxycycline.



Prognosis and Follow-Up

- Relapse occurs in up to 30% of poorly compliant patients.
- Thus patients should ideally be followed clinically for up to 2 years to detect relapse
- Fewer than 1% of patients die of brucellosis. When the outcome is fatal, death is usually a consequence of cardiac involvement



Prevention

- Vaccines based on live attenuated *Brucella* strains, such as *B. abortus* strain 19BA or 104M, have been used in some countries to protect high-risk populations
- only short-term efficacy and high reactogenicity.
- Subunit vaccines have been developed but are of uncertain

-
- The veterinary prevention is a national commitment to testing and slaughter of infected
 - control of animal movement
 - and active immunization of animals
 - pasteurization of all milk products before consumption is sufficient to prevent non-occupational animal-to-human transmission

