
بسم الله
الرحمن الرحيم

Brucellosis

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Disease in Humans

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Epidemiology

- Brucellosis – zoonosis – all infections, derive directly or indirectly from animals exposure.

- Disease exists world-wide, esp. Mediterranean, Arabic Peninsula, Indian subcontinent, parts of Mexico and Central South America.

- B. abortus found mainly in cattle, but others spp. like buffalo, camels, can be affected.
- B. Melitensis primary affects goats and sheep. Camels can be important source in some countries.
- B. Suis biovars 1-3 in domestic and feral swine, cause abattoir-assoc. human disease.

Epidemiology (Cont'd.)

- B. Canis: Least common cause of human disease.
- Animals: Brucellosis, persisting for life.
- Brucellae localization in reproductive organs, accounts for major manifestations – abortion and sterility.
- Brucellae shed in large numbers in: Milk, urine,

Epidemiology (Cont'd.)

- Thus, Brucellosis constitutes occupational risk for: farmers, veterinarians, abattoirs and Laboratory personnel.

Routes of transmission to human include:

- Director contact with animals or their secretions,
  through cuts and skin abrasions.
- Infected aerosols inhaled or inoculated into eye
  conjunctival sac.
- Ingestion of unpasteurized dairy products.

Epidemiology (Cont'd.)

- Meat products: rare source of infection because: Meat is rarely eaten raw and organisms are present in low number of muscle tissue.
- Blood and bone marrow may transmit disease when ingested in some cultures.
- Human-to-human transmission: Unusual, but rare cases suspected to be sexually transmitted.

Epidemiology (cont'd.)

- One case reported recently, presumptively due to intra-uterine transmission.

- Aids patient, prone to infections by zoonoses, but Brucellosis occurred in very few of these patients.

- Brucellosis manifests similarly in: Neonates, children and adults.

Human Disease

- Can affect any organ or organ system
- All patients have a cyclical fever
- Variability in clinical signs
  - Headache, weakness, arthralgia, depression, weight loss, fatigue, liver dysfunction

Clinical Manifestation

- Symptoms of Brucellosis: non-specific, e.g. fever, sweats, malaise, anorexia, headache, backpain.
- Onset: acute or insidious, beginning within 2 to 4 weeks after inoculation.
- An "Undulant" fever pattern observed if patients go untreated for long periods.

- Some patients c/o malodorous sweat and peculiar mouth taste.
- Depression common and often out of proportion to severity of symptoms.
- In comparison to plethora of somatic complaints, physical abnormalities are few.
- Mild lymphadenopathy reported in 10 to 20% of cases.

Clinical Manifestation

- Splenomegaly or hepatomegaly in 20 to 30% of cases.

When CNS or heart involved, such cases: difficult to treat and outcome can be affected.

GIT 70% of patients with brucellosis

Clinical Manifestation (cont'd.)

- Chronic Brucellosis usually caused by persisting deep foci of infection, e.g. suppurative lesions in bone, joints, liver, spleen or kidneys.

- Some patients experience delayed convalescence after treatment, with persisting non-specific complaints of ill health, notably fatigue.

Clinical Manifestation (cont'd.)

- Relapse not usually caused by antibiotic resistance, because strains of brucellae isolated during relapse have antibiogram identical to original infecting strains.

Osteoarticular complications

reported in 20-60% of pts. infected with brucellosis.

Bone and joint lesions include:

- **Arthritis**
- **Spondylitis**
- **Osteomyelitis**
- **Tenosynovitis**
- **Bursitis**
- **Sacroileitis most commonly reported complication.**

Spondylitis, predominantly, involving lumbar spine

more common among elderly pts. and rarely associated with paraspinal abscess.

- **C.V.S.**

- Endocarditis occurs in less than 2% of cases,
but accounts for majority of brucellosis-related deaths

Aortic valve is affected more often than mitral valve

Renal involvement is rare- Orchitis occurs in up 20% of men with brucellosis.

- G.U.T. cont'd.)

  - In women, rare cases salpingitis, cervicitis and pelvic abscess reported.

  - Principal brucellosis in animals is spontaneous abortion

Brucellosis can result in human abortions, but

unclear whether it is more frequent than with

other bacteremic infections.

Hematologic Complications

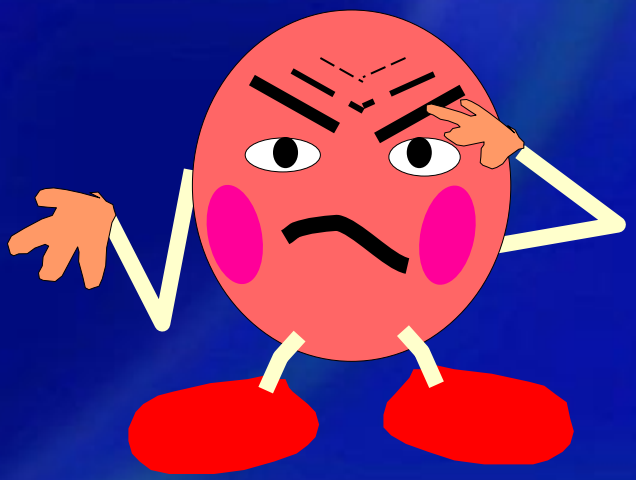
- Hematologic manifestations of brucellosis include: anemia, leukopenia, thrombo-cytopenia and clotting disorders.

- Granulomas found in B. marrow in up to 75% of cases, but they are small and indistinct.

Differential diagnosis

- Enteric fever
- Miliary TB
- Infectious mononucleosis
- Toxoplasmosis
- Acute rheumatic fever
- Malaria and relapsing f.
- Leishmaniasis

Diagnosis of Brucellosis



Diagnosis is based on :

- Clinical manifestations
- History of contact
- Laboratory changes

Clinical manifestations

The clinical Suspicion that the patient has brucellosis should be higher in :

- **Abattoir workers**
- **Veterinarians**
- **Others exposed to infected tissues or animal products**

Bacteriological Diagnosis

Laboratory changes
Bacteriologic tests

- Efforts to grow Br. Abortus from blood, usually fail (30% pos.)
- When the illness is due to Br. Suis or
- Br. Melitensis blood culture usually succeeded (85% pos.)

Laboratory changes
Bacteriologic tests

- Taking **bone marrow** is more rewarding
- Brucella can be isolated from **liver** taken by biopsy
- Human **semen** may be positive
- Blood or bone marrow cultures should be incubated for at least **6 weeks**

Laboratory changes
Bacteriologic tests

- Blood culture processed in radiometric detection systems may yield positive cultures in less than 10 days
- The culture of brucella organisms is potentially hazardous to laboratory personal

Serological Diagnosis

Laboratory changes
Serologic Tests

- Tube Agglutination
- 2ME Agglutination
- Coombs' test
- Complement fixation
- PCR ,esp. in relapse
- ELISA
- Rapid Agglutination
- Rose bengal test

Serologic Tests
IgG in brucellosis

- Begins to rise in the second week
- Remain elevated for > 1 year
- in treated patients falls by 6 months
- In unrecovered patients persists for a long time

Laboratory changes
Serologic Tests

Tests	Antibodies which can be detected
STA	IgM + IgG
2ME	IgG
COOMBS	If STA is negative and disease is chronic then only IgG

Standard tube agglutination test

False positive results

- F. tularensis
- Y. enterocolitica
- V. cholera
- Salmonella
- Vaccine against F. Y. V & S.
- Brucella skin testing
- Stenotrophomonas maltophila
- E. coli O157

Standard tube agglutination test

False negative results

- Agammaglobulinemia
- First week of disease
- Disease due to Br. Canis
- Chronic brucellosis
- Prozone phenomenon

False-negative results in STA test

Prozone & postzone phenomenon

آنتي ژن	آنتي بادي	واكنش
مناسب	مناسب	به درستي صورت مي گيرد
مناسب	زياد	واكنش پروزون (با رقيق كردن آنتي بادي اصلاح مي‌شود)
زياد	مناسب	پست زون (با رقيق كردن آنتيژن، رفع مي‌شود)

Serologic Tests

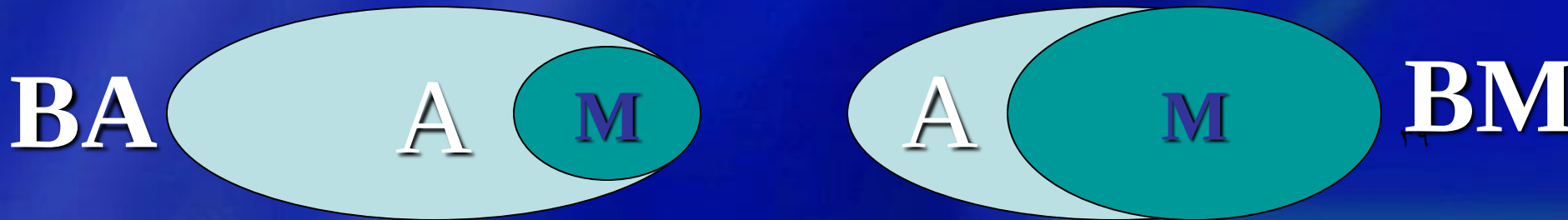
تفسير آزمون‌هاي سرمي

چرا در كشور ايران، عيارهاي كمتر از ١:١٦٠ تست رايت را به شرط وجود علائم باليني منطبق بر بروسلوز حاد يا تحت حاد، باارزش تلقي مي‌كنيم؟

Serologic Tests

A and M antigens

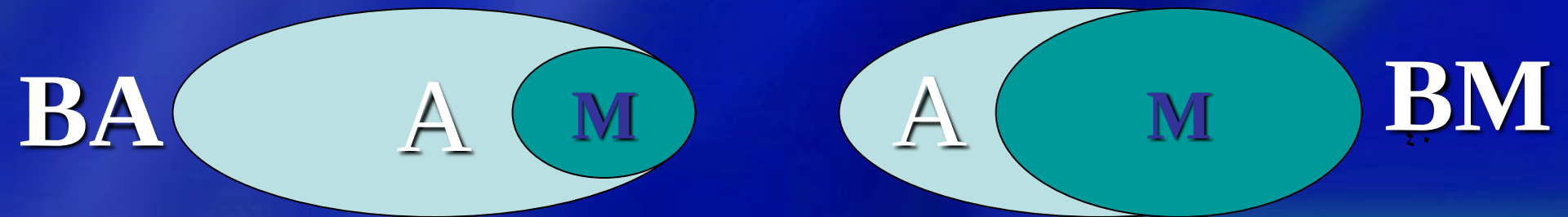
- Antigen A and M are common to the three main brucella species
- In the Br. Abortus, there is more A antigen than M antigen
- In the Br. Melitensis there is more M antigen than A antigen



Serologic Tests

A and M antigens

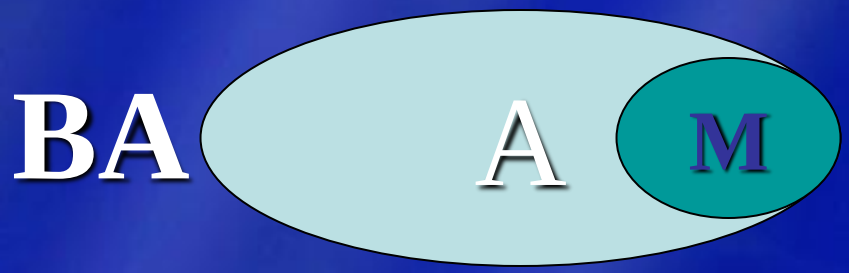
- In IRAN We have human brucellosis nearly always due to Br. Melitensis but use Br. Abortus antigen
- Br. Abortus antigen in our laboratories shows lower agglutinin titers

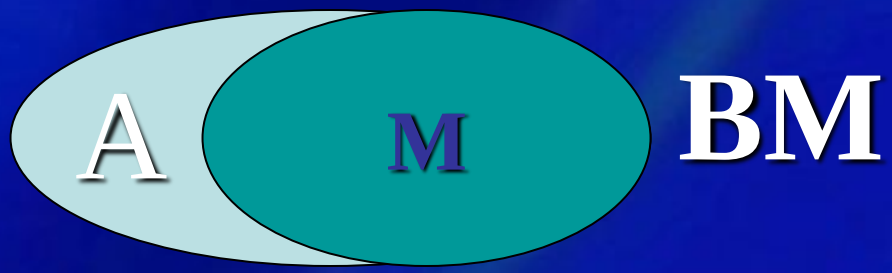


Serologic Tests

A and M antigens

- In IRAN We must accept titers lower than 1:160 if there is signs and symptoms compatible with brucellosis





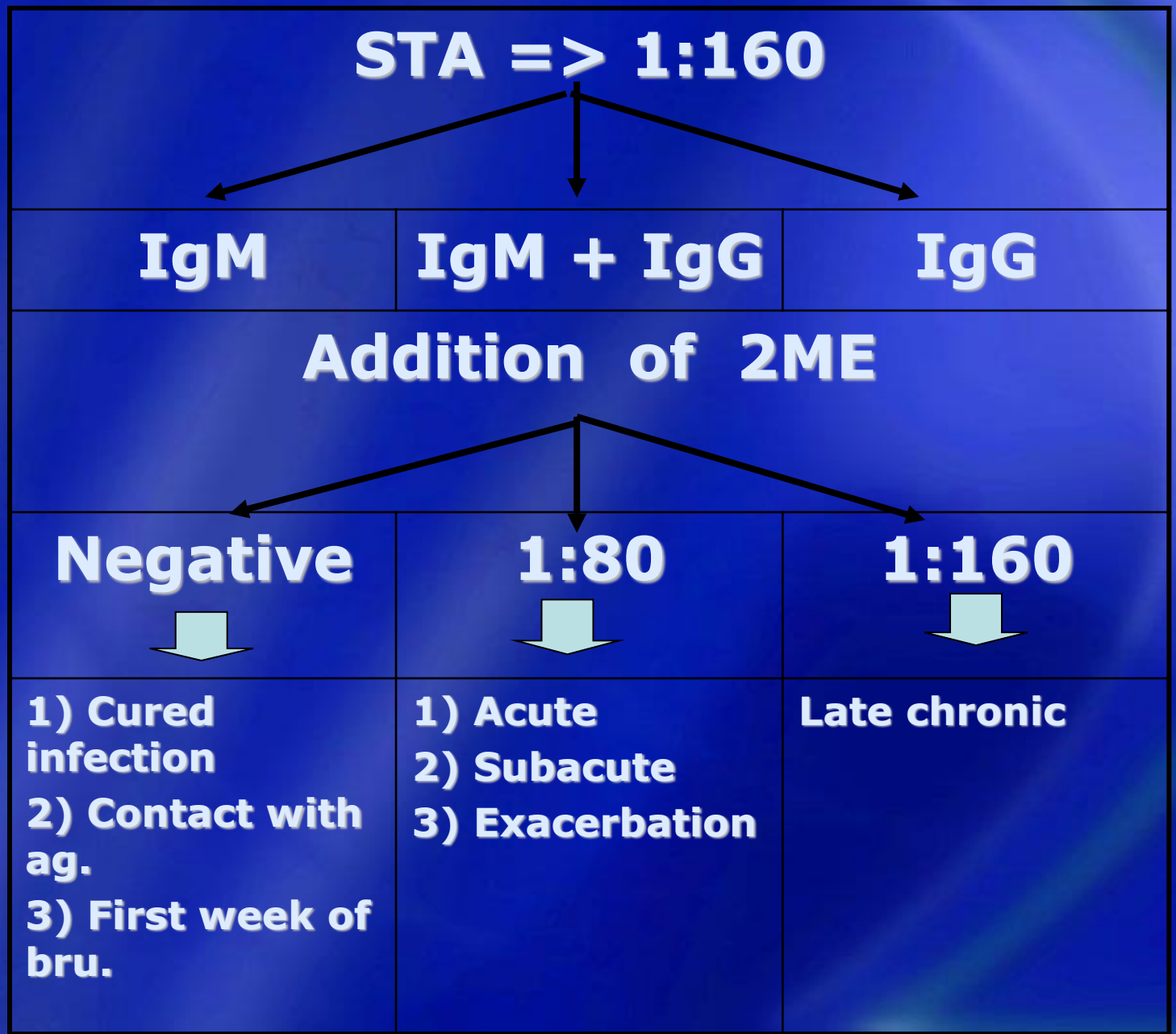
Serologic Tests
Coombs test

- **If STA is negative and there are symptoms and signs compatible with chronic brucellosis, then combs titer of => 1:40 should be considered positive**
- **Coombs test is not recommended when STA test is positive**

Serologic Tests
Rose Bengal plate test

- Is an agglutination test in which the brucella cells are bound to a dye
- Is quick and easy to read
- It is a useful screening test

Interpretation of STA and 2ME tests



Treatment of Brucellosis

Antimicrobial therapy:

- Shortens the course of illness
- Lessens morbidity
- Reduce the incidence of complications

Antimicrobial Regimens

- **Doxycycline + Rifampin**
- **Tetracycline + Rifampin**
- **Tetracycline + Streptomycin**
- **Co-trimoxazole + Rifampin**
- **3.G. Cephalosporines + Ritampin**

- ***Rifampin + Doxycycline is the treatment of choice (WHO)***

Brucellosis
Occupational exposure

- Antibiotics (doxycycline and rifampin for B-19 and REV-1, or doxycycline alone for RB-51) for 3 weeks
- At the end of that time you should be rechecked and a second blood sample should be collected.
- The same recommendations hold true for spraying vaccine in the eyes (6 weeks of treatment in this case) or spraying onto open wounds on the skin

Chronic brucellosis

- **The patient with chronic brucellosis presents a difficult therapeutic problem**
- **Long courses (2-6 months) of treatment may be required for patients with chronic brucellosis**

Pregnant women

- Toxicity of tetracycline is established
- Streptomycin is contra-indicated
- There is no evidence that Rifampin and Co-trimoxazole are harmful to developing human fetus

Indications for Corticosteroides

- Prevention of Herxheimerlike reactions
- Sever toxemia
- Thrombocytopenia and related bleeding
- Severe debility

Surgical treatment

- Osteomyelitis
- Paravertebral abscess
- Suppurative lesions
- Brucella endocarditis
- Aneurysmal aortitis

Prognosis

- **Brucellosis appropriately treated within the first month of symptom onset is curable**
- **Patients are frequently unable to work for up to 2 month**
- **With early antimicrobial therapy cases of chronic brucellosis are rare**

- **Prvention & Control**

- **Education about risk of transmission**

Farmer,veterinarian,abattoir worker, butcher,consumer,hunter,public

- **Wear proper attire,if dealing with infected animals/tissues**
- **Gloves, masks, goggles**

- **Avoid consumption of raw dairy products**
- **Immunize animals in areas of high prevalence**
- **NO HUMAN VACCINE**
- **Eradicate reservoir**

-infected animals