Brucellosis: still a problem in the Arab World

FASCMID & Tunisian Society of Clinical Microbiology and Infectious Diseases
Hammamet Yasmine 23 - 26 May 2012

Jamal Wadi Al Ramahi M.D.
Infectious Diseases Medicine

http://www.infectiologie.org.tn
1. Bruce or not Bruce, that is the question!? 
2. Epidemiology and prevalence 
3. Humans and Animals, they share suffering! 
4. Transmission, is it the same story? 
5. Organ system infections and pregnancy, are there any new data? 
6. Testing for brucella, shall we stick to what we already do? 
7. Brucella Man Combat, who is the winner so far?
History of Brucellosis

The Truth About Bruce and Brucellosis
Malta fever, Gibeltar fever, Bang fever

14 June 1905
Marston 1860, first accurate clinical description.
Bang, Described infectious abortion

We read with interest Dr Wyatt’s article (October 2005 JRSM) on Zammit’s discovery that brucellosis was transmitted by goat milk. We would like to add the names of some other people who were involved in the research.

First, Dr Carruana-Secluna, who accompanied Zammit to Chadwick Lakes, carried out a great deal of work for Sir David Bruce—he prepared the agar plates and the culture media and cultured the causative organism from the spleen samples of fatal cases. He never received proper recognition for his work and Sir David Bruce did not allow him to be co-author on any publications. Secondly, Surgeon Captain M. Louis Hughes assisted Bruce in his studies and first named the disease ‘undulant fever’. He also named the organism Micrococcus melitensis, although he was wrong about the source of infection, believing it to be resident in the soil and inhaled by the human. Hughes was killed in the Boer war at the age of 32.

Sir David’s wife Lady Bruce was a trained microbiologist, and took an active part in her husband’s research, including the exquisite illustrations to his papers.²

Finally, it is worth noting that Zammit was knighted—an honour given for his work.

Catherine Edwards

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E-mail: alismjawad1@hotmail.com
History of Brucellosis

The Truth About Bruce and Brucellosis

14 June 1905, Zammit and Scicluna, a Maltese doctor:

– found that 5/6 goats reacted to the blood test for brucellosis

– Greatest discovery; healthy goats could be carriers of the disease

– From September 1904 – April 1905 Zammit fed goats with Micrococcus melitensis to infect them

Journal of the royal Society of Medicine, 2006 February. Volume 99
Journal of the royal Society of Medicine, 2005;98:451–454
“After months of hard and disappointing work, Dr Zammit, a Maltese colleague, happened to examine the blood of a goat” Bruce said !!!!!

Finally, it is worth noting that Zammit was knighted an honour given for his work

Horrocks, a friend of Bruce undermined Zammit work as well

Some World Countries: Brucellosis Annual Cases per Million Of Population

[Bar chart showing cases per million of population in various countries.]
Worldwide incidence of human brucellosis
The first case of Brucella canis in Sweden: background, case report and recommendations from a Northern European perspective


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Arab World incidence of human brucellosis per million population
Arab Countries: Brucellosis Annual Cases per Million of Population

http://www.infectiologie.org.tn

Lancet Infect Dis 2006; 6: 91–99
Veterinary Microbiology 90 (2002) 81–110
Number of Cases of Brucellosis In Jordan over Two Decades as Published on MOH

Jordan Population ≈ 6000,000
Brucellosis cases in Jordan for the years 2001 - 2010

http://www.infectiologie.org.tn

www.moh.gov.jo
Epidemiology

Present all over the world, Primarily in animals:

- **B. abortus** Cattle
- **B. melitensis** goat, sheep 80 - 100% of Arabia Infections
- **B. suis** pigs
- **B. ovis** sheep, rams
- **B. canis** dogs
- **B. neotamae** rats

[References]

Annals of Saudi Medicine, Vol 19, No 5, 1999
Clinical Infectious Diseases 1995;21:283-90
J. Bacteriol. January 1965 vol. 89 no. 1 9-16

http://www.infectiologie.org.tn
Prevalence of brucellosis in livestock in different countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Species</th>
<th>Prevalence (%)</th>
<th>Brucella species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Algeria</td>
<td>Sheep</td>
<td>2.18</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Goat</td>
<td>12.00</td>
<td></td>
</tr>
<tr>
<td>Egypt</td>
<td>Buffalo</td>
<td>10.00</td>
<td>Br. abortus</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>23.30</td>
<td>Br. melitensis biovar 3</td>
</tr>
<tr>
<td></td>
<td>Donkey</td>
<td>7.30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Horse</td>
<td>5.88</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mule</td>
<td>71.42</td>
<td></td>
</tr>
<tr>
<td>Iraq</td>
<td>Sheep</td>
<td>15.00</td>
<td>Br. melitensis</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>3.00</td>
<td>Br. Abortus</td>
</tr>
<tr>
<td></td>
<td>Camel</td>
<td>17.20</td>
<td></td>
</tr>
<tr>
<td>Libya</td>
<td>Camel</td>
<td>4.10</td>
<td>Br. melitensis biovar 1.</td>
</tr>
<tr>
<td>Oman</td>
<td>Camel</td>
<td>8.00</td>
<td>Br. abortus</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>3.30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sheep</td>
<td>1.60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Goat</td>
<td>6.40</td>
<td>Br. melitensis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Br. melitensis biovar 2.</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>Camel</td>
<td>8.00</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>18.70</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sheep</td>
<td>6.50</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Goat</td>
<td>9.70</td>
<td></td>
</tr>
<tr>
<td>Sudan</td>
<td>Camel</td>
<td>6.95</td>
<td>Br. abortus</td>
</tr>
<tr>
<td></td>
<td>Camel</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>5.00</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sheep</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Goat</td>
<td>4.00</td>
<td></td>
</tr>
<tr>
<td>United Arab Emirates</td>
<td>Camel</td>
<td>2.00</td>
<td>Br. abortus</td>
</tr>
<tr>
<td></td>
<td>Cattle</td>
<td>1.30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sheep</td>
<td>2.00</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Goat</td>
<td>3.40</td>
<td></td>
</tr>
</tbody>
</table>

Livestock In Egypt

- Brucellosis prevalence were estimated:
  - Cattle 0.79%
  - Buffaloes 0.13%
  - Sheep 1.16%
  - Goats 0.44%

- It is estimated that 0.2% of households livestock has one seropositive animal
Human brucellosis cases in Saudi Aramco Health Care Population between 1983 and 2007

Bars: the number of new cases of per year
Line graph: the yearly rate of cases per 100,000 population

Monthly number of human brucellosis for the years 1983—2006 (Saudi Arabia)

- Total
- 1993-2006
- 1983-1992

Cases

Months

Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec

http://www.infectiologie.org.tn
Age and sex distribution of Human brucellosis

Bars: The number of new cases in each age group
Line graph: The rate of cases per 100,000 population in the age groups


http://www.infectiologie.org.tn
Human brucellosis in Lebanon, Retrospective studies of cases in Lebanon

- $N = 1137$
- Diagnostic criteria $\text{STA} \geq 1/160$ with symptoms suggestive of brucellosis
- Age distribution; ($> 60$ years) $40\%$, ($< 14$ years) $16\%$
- Male to Female: $1.01$
- Season: $69\%$ in spring and summer
- Acute in $65\%$, sub-acute in $33\%$, chronic in $2\%$
- *Kuwait: 400 cases acute in $77\%$, sub-acute in $12.5\%$, chronic in $10.5\%$

Clinical Manifestations

<table>
<thead>
<tr>
<th>Symptoms and Signs</th>
<th>Rates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>90</td>
</tr>
<tr>
<td>Chills</td>
<td>83</td>
</tr>
<tr>
<td>Sweating</td>
<td>87</td>
</tr>
<tr>
<td>Night Sweating</td>
<td>83</td>
</tr>
<tr>
<td>Back pain</td>
<td>84</td>
</tr>
<tr>
<td>Arthritis</td>
<td>40</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>23</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>15</td>
</tr>
</tbody>
</table>

Brucella Rates (%) of Symptoms and Signs in 140 Patients from Iran

Iranian Journal of Clinical Infectious Diseases. 2010;5(3):189-190
Transmission

<table>
<thead>
<tr>
<th>Occupation/avocation</th>
<th>Principal <em>Brucella</em> species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle rancher</td>
<td><em>B. abortus</em></td>
</tr>
<tr>
<td>Dairy farmer</td>
<td><em>B. abortus</em></td>
</tr>
<tr>
<td>Veterinarian</td>
<td><em>B. abortus</em> (B. abortus strain 19 and B. melitensis strain Rev-1 vaccines)</td>
</tr>
<tr>
<td>Abattoir worker</td>
<td><em>B. suis</em></td>
</tr>
<tr>
<td>Traveler (to areas with enzootic disease)</td>
<td><em>B. melitensis</em></td>
</tr>
<tr>
<td>Hunter (feral swine)</td>
<td><em>B. suis</em></td>
</tr>
<tr>
<td>Dog handler</td>
<td><em>B. canis</em></td>
</tr>
<tr>
<td>Laboratory worker</td>
<td><em>All Brucella species</em></td>
</tr>
</tbody>
</table>

Croat Med J. 2010; 51: 289-95
Clinical Infectious Diseases 2010; 51(2):e12–e15
Clinical Infectious Diseases 2007; 45:e135–40
Clinical Infectious Diseases 1995;21:283-90
The Lancet. (337) 8732. 5 January 1991, Pages 14-15

http://www.infectiologie.org.tn
The Many Faces of Human-to-Human Transmission of Brucellosis: Congenital Infection and Outbreak of Nosocomial Disease Related to an Unrecognized Clinical Case

Oded Mesner, Klaris Riesenberg, Natalia Biliar, Eliezer Borstein, Leah Bouhnik, Nehama Peled, and Pablo Yagupsy

Divisions of *Neonatology and Obstetrics and Gynecology, Institute of Infectious Diseases, and Clinical Microbiology Laboratory, Soroka University Medical Center, Ben-Gurion University of the Negev, Beer-Sheva, Israel

**Patient**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Description</th>
<th>Cesarean delivery</th>
<th>IM STR 2 weeks &amp; oral doxy 6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>39-year-old male neonatologist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>29-year-old female pediatric</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>33-year-old obstetrician</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>premature offspring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>32-year-old Bedouin woman</td>
<td>⭐⭐</td>
<td></td>
</tr>
</tbody>
</table>

**Timeline**

- **2006**
  - May: 1
  - June: 1
  - July: 1
  - August: 0
  - September: 0
  - October: 0
  - November: 0
  - December: 0

- **2007**
  - April: 0
  - May: 0
  - June: 0
  - July: 0

Gray bars, clinical symptoms
Red bars, antimicrobial therapy
Hatched bar, hospitalization period
Black stars, serological tests for patient 1.
Sexually Transmitted Brucellosis in Humans (Occupied Palestine)

- Sexual transmission in livestock through semen and vaginal secretions is well documented
- In a two cases report; a month after husband diagnosis, wives developed symptoms and signs of brucellosis
- Urine and semen from both husbands reveal the same B. melitensis biotype 1
- No other risk factors identified for both wives
- Semen commonly harbor Brucella spp in infected individuals.
  
- Vaginal secretion harbor commonly Brucella in infected individuals.
  
Re-infection & Relapse

- Relapses are uncommon in properly treated patients.

- Recurrent episodes in 5%, usually milder

- Look for focal disease

- Beware of hypersensitivity reaction that mimic the disease (Sx. occur in minutes to hours)

Clinical Infectious Diseases, 1995 August; 21:283-90
Relapse in a Spanish Study:

- N = 394
- Logistic regression analysis of risk factors associated with relapse studied in patients with brucellosis

86 patients relapsed
- Positive blood cultures 53
- Positive culture of specimen from sternum costal abscess 1
- Clinical relapse 32

*Suboptimal Therapy
Positive Blood Culture
≤ 10 days of disease before treatment
Male Sex
Platelets < 150 x 10^3

*TMP/SMZ. Rif/TMP. Dox/Rif (30 days)


http://www.infectiologie.org.tn
Clinical Syndromes/Complications

Characteristics of B. Vertebral Osteomyelitis

A descriptive, retrospective, observational study of 96 patients in Spain and 74 in Jordan

- Focal in 10.4% (Osteo-articular), mostly in adults age (µ ± SD; 49.5 ± 14.0 yrs)
- µ (diagnostic delay) = 12.7 weeks.
- Spinal pain, (94.8%), fever (91.7%)
- Paravertebral masses (45.8%), epidural masses (27.1%), and psoas abscesses (10.4%)
- 34-35% require additional surgical therapy
- If surgery was not needed, then FNA (p = 0.3) and TCB (p = 0.4) are comparable in sampling.
- Therapeutic failure may occur (12%)
- Attributable mortality (2.1%), severe functional sequelae (6.2%)
- No significant differences between patients treated with doxycycline-streptomycin and doxycycline-rifampicin.

Jamal Wadi et al. JRMS, 2011 June: 18 (2); 43-48
Juan D. Colmenero et al. CID 2008; 46:426–33

http://www.infectiologie.org.tn
Clinical Syndromes/Complications

Neurobrucellosis

- Pooled data $N_{\text{studies}} = 36$, $N_{\text{patients}} = 187$ neurobrucellosis cases were evaluated (Retrospective Study of Turkish and International database)

- Symptoms: Headache, fever, sweating, weight loss, and back pain

- Signs: Meningeal irritation, confusion, hepatomegaly, hypoesthesia, and splenomegaly

- Complications: polyneuropathy/radiculopathy, depression, paraplegia, stroke, and abscesses

- Duration of antibiotic therapy: 2-15 months (median 5 months)

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International Journal of Infectious Diseases (2009) 13, e339—e343 (Turkey)

*Trop Doct, October 2009: (39) 4; 233-235

**The Brazilian Journal of Infectious Diseases 2009;13(3):245

http://www.infectiologie.org.tn
Clinical Syndromes/Complications

Neurobrucellosis

- Serum and CSF STA may be negative and CSF culture positive
- BC +ve in 9 patients and from CSF 11
- Neck stiffness in 25/36 (69.4%) patients
- Spastic Paraparesis reported from India
- Incidence: Algeria is about 4% of cases. Kuwait 7% out of 400 cases
- Mortality was 0.5%

International Journal of Infectious Diseases (2009) 13, e339—e343 (Turkey)
*Trop Doct, October 2009: (39) 4; 233-235
**The Brazilian Journal of Infectious Diseases 2009;13(3):245
Clinical Syndromes/Complications

Cardiovascular

- *Isolated Myocarditis in Tunis, and plus asymptomatic pericardial effusion in Greece

- #Isolated Acquired QT prolongation and ventricular tachycardia (Turkey)

- Endocarditis < 2%, mostly lethal.

- Out of I,E (NVE) accounts for < 1%

- Diagnosis usually late

- Frequency of involvement; Aortic, Mitral & PVE

Trop Doct. 2009 Apr;39(2):123-4
*http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3037886/
#Journal of Cardiology Cases, 2011 October; 4 (2): e121-e125
Clinical Syndromes/Complications

Genitourinary Epididymo-orchitis

- May present as epididymo-orchitis, prostatitis, cystitis, pyelonephritis, interstitial nephritis, exudative glomerulonephritis, renal and testicular abscess, and seminal vasculitis

- BEO in Turkey; 18.8%, Iran 11.1%. Range (2-20%), Kuwait 8.5%

- Onset was acute in (81.8%), subacute in (14.8%), and chronic in one patient (3.7%).

- Pain and scrotal swelling (100%) and fever (96.7%)

- Dysuria, haematuria, frequency or urgency (22.2%)

http://www.infectiologie.org.tn
Specific signs and symptoms in 30 patients with Brucella epididymoorchitis (Iran)

<table>
<thead>
<tr>
<th>Findings</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scrotal pain and swelling</td>
<td>30</td>
<td>100</td>
</tr>
<tr>
<td>Fever (temp ≥ 38°C)</td>
<td>29</td>
<td>96.7</td>
</tr>
<tr>
<td>Sweating</td>
<td>25</td>
<td>83.3</td>
</tr>
<tr>
<td>Anorexia</td>
<td>25</td>
<td>83.3</td>
</tr>
<tr>
<td>Weakness</td>
<td>23</td>
<td>76.7</td>
</tr>
<tr>
<td>Myalgia</td>
<td>8</td>
<td>26.7</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>Back pain</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>Urinary frequency</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>Weight loss</td>
<td>4</td>
<td>13.3</td>
</tr>
<tr>
<td>Lumbosacral pain</td>
<td>4</td>
<td>13.3</td>
</tr>
<tr>
<td>Dysuria</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>3</td>
<td>10</td>
</tr>
</tbody>
</table>

Najafi et al. BMC Research Notes 2011, 4:286
http://www.biomedcentral.com/1756-0500/4/286
Clinical Syndromes/Complications

Distribution of BEO by months of the year (Turkey)

http://www.infectiologie.org.tn

Clinical Syndromes/Complications

Oophoritis

- In 1998 Uwaydah et al. Beirut, Lebanon, reported a Brucella-infected ovarian dermoid cyst which caused initial treatment failure in a patient with acute brucellosis. The patient defervesced abruptly after oophrectomy.

- Harvard Medical School reported similar case to Marwan Uwaydah in 2007.
Clinical Syndromes/Complications

Others

- **Gastrointestinal**
  - GI Sx. Relatively uncommon but reported at a rate of 67% in Saudi Arabia and 20% in pediatric patients
  - Abnormal LFTs in 30-60%
  - Diffuse and granulomatous hepatitis.
  - Splenic calcification.

- **Pulmonary (Kuwait):** Cough in about 20%. Anormal CXR in about 16%

- **Hematological:** Anemia, leukopenia, thrombocytopenia common in adult and pediatric patients

- **Cutaneous:** E. nodosum, papules, rubeoliform, scarlitiniform, and eczematous rash.
Hemophagocytic Syndrome in a Child with Brucellosis

Nivedita Mondal • R. Suresh • N. Srinivas Acharya •
Ira Praharaj • B. N. Harish • S. Mahadevan
The Effects of Maternal Brucellosis on Pregnancy Outcome

- Prospective study: Taif, S.A. and Mansoura University Hospital
- Primary Measure: Outcome of pregnancies complicated by Brucella infection.
- August 2005 - December 2007
- The incidence was 12.2% (55/450) among pregnant women

STA was performed on 450 pregnant women

35 had symptoms and signs of the disease

- **Group 1**
  - (N = 55)
  - 35 Symptomatic
  - 20 Asymptomatic
  - STA >1/160

415 had no symptoms or signs of brucellosis

- **Group 2**
  - (N = 395)
  - 395 pregnant women
  - Had no Symptoms and STA positive

- 20 pregnant women Had no Symptoms and STA positive

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Outcome of Pregnancies Complicated by Brucella Infection based on STA positivity and level (Saudi/Egypt)

Percentage of abortion, IUFD and preterm labour of the two studied groups

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Abortion</th>
<th>IUFD</th>
<th>Preterm labour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 STA &gt; 1/160 N = 55</td>
<td>12.2</td>
<td>0.002</td>
<td>0.3</td>
</tr>
<tr>
<td>Group 2 STA negative N = 395</td>
<td>P = 0.01</td>
<td>P = 0.002</td>
<td>P = 0.3</td>
</tr>
</tbody>
</table>

The relation of the tested parameters based on brucella titer

<table>
<thead>
<tr>
<th>Abortion</th>
<th>IUFD</th>
<th>Preterm labour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1a STA &gt; 1/160 N = 34</td>
<td>P = 0.03</td>
<td>P = 0.4</td>
</tr>
<tr>
<td>Group 1b STA &lt; 1/160 N = 21</td>
<td>P = 0.09</td>
<td></td>
</tr>
</tbody>
</table>

Occurrence of spontaneous abortion and intrauterine death, according to trimester of pregnancy, in 92 women with acute brucellosis in Saudi Arabia

<table>
<thead>
<tr>
<th>Trimester of pregnancy</th>
<th>No. of patients</th>
<th>No. (%) of spontaneous abortions</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>23</td>
<td>12 (52)</td>
</tr>
<tr>
<td>Second</td>
<td>44</td>
<td>28 (64)</td>
</tr>
<tr>
<td>Third</td>
<td>25</td>
<td>2 (8) a</td>
</tr>
<tr>
<td>Total</td>
<td>92</td>
<td>42 (46) a</td>
</tr>
</tbody>
</table>

(P < 0.0001) (P < 0.001)

a These were or included intrauterine fetal deaths

M. Y. Khan, Manuel W. Mah, and Z. Memish. CID 2001; 32:1172–7
Laboratory Diagnosis

1. Rose bangal test (RBT)
2. SAT (STA)
3. Coombs test brucella (non-agglutinating antibodies)
4. Counter immune electrophoresis proteins test
5. ELISA
6. Immune capture brucella
7. Fluorescence polarization assay
8. Lateral flow immunochromotography assay (IgM, IgG)
9. Blood culture


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**RBT** versus (Serum agglutination, Coombs, competitive ELISA, Brucellacapt, lateral flow immunochromatography for IgM and IgG detection and immunoprecipitation with Brucella proteins) *

- Studied patients:
  - 208 sera were tested from **patients** with brucellosis proved by **bacteriological isolation**
  - 20 **contacts** with no brucellosis
  - 1559 sera of persons with no **recent contact** or brucellosis symptoms
- Using modified RBT titre > $\frac{1}{4}$ none of contacts or Rev 1 was positive
- *Other tests failed to discriminate** contacts or Rev 1 injected individuals
- **RBT** > $\frac{1}{4}$ does not need confirmation by other* (usually more expensive, sophisticated and time consuming) tests
- **RBT** is as good as sophisticated tests and recommended as the first test

doi:10.1371/journal.pntd.0000950

http://www.infectiologie.org.tn
STA (SAT)

- Positive; IgG ≥ 1/160 or four fold increase in titer

B. abortus Ag React with

- B. Abortus Ab.
- B. melitensis Ab.
- B. suis Ab.
- Not B. canis Ab.

Titer of 1/160 may persist for up to 1.5 yrs.

JCM, June 1980, p. 691-693
2-ME STA
For initial diagnosis and follow up

- The 2ME disrupts disulfide bonds, making IgM inactive and permitting only brucella agglutination by IgG

- 2ME test is evidence of an active infection and the need for antibiotic therapy

- Not sensitive at the outset of illness

| Number of patients by titers and by time after onset of brucellosis |
|------------------|-------|-------|-------|-------|
| ≥ 1/160          | Months| First week| 6     | 9     | 12    | 18    |
| STA             | 53/53 (100%)| 75     | 62    | 55    | 44    |
| 2-ME            | 24 (45%)  | 22     | 12    | 8     | 4     |

Adopted and modified: JCM, June 1980, p. 691-693
Comparison of SAT and ELISA IgG/IgM tests in patients with positive Brucella blood cultures

<table>
<thead>
<tr>
<th></th>
<th>SAT</th>
<th>ELISA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive (titre ≥320)</td>
<td>IgG</td>
</tr>
<tr>
<td></td>
<td>Negative (titre &lt;320)</td>
<td>IgM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IgG+IgM</td>
</tr>
<tr>
<td>Positive blood cultures (n = 68)</td>
<td>65 3</td>
<td>31 37</td>
</tr>
<tr>
<td>Controls (n = 70)</td>
<td>0 70</td>
<td>2 68</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>65/68 = 95.6%</td>
<td>31/68 = 45.6%</td>
</tr>
<tr>
<td>Specificity</td>
<td>70/70 = 100%</td>
<td>68/70 = 97.1%</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>100%</td>
<td>45.2%</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>99.7%</td>
<td>97.1%</td>
</tr>
<tr>
<td>Positive IgG or IgM</td>
<td>62 4</td>
<td>62/66 = 94.1%</td>
</tr>
<tr>
<td>Negative IgG and IgM</td>
<td>2 68</td>
<td>68/70 = 97.1%</td>
</tr>
<tr>
<td>Note: Predictive value calculation assumes seroprevalence of active Brucellosis in Saudi Arabia is 5%.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ELISA and CNS Brucellosis

Sera from patients in different stages of brucellosis as well as sera and CSF from patients with CNS brucellosis and controls, were tested by ELISA for Brucella-specific IgG, IgM and IgA.

<table>
<thead>
<tr>
<th>Test</th>
<th>IgG</th>
<th>IgM</th>
<th>IgA</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELISA Serum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>97</td>
<td>100</td>
<td>98</td>
</tr>
<tr>
<td>Subacute</td>
<td>100</td>
<td>86</td>
<td>100</td>
</tr>
<tr>
<td>Chronic</td>
<td>100</td>
<td>33</td>
<td>100</td>
</tr>
<tr>
<td>n = 296</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 44</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ELISA CSF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 45</td>
<td>100</td>
<td>20</td>
<td>85</td>
</tr>
<tr>
<td>STA (MDA) and RBT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>98</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subacute</td>
<td>84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic</td>
<td>61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STA(MDA) RBT</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B. Melitensis (SA) and Culture</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ELISA was negative in the CSF specimens from patients with brucellosis without CNS involvement (n = 66), or meningitis other than Brucella (n = 62), and no meningitis (n = 144).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Thus, ELISA is the test of choice in the diagnosis of patients with brucellosis, especially those with chronic or CNS infection.

George Araj et al. APMIS, 1988 January; 96 (1-6), pages 171–176
Treatment

• Single agent treatment carries 10 – 40 % chance of relapse

• WHO, 1981 regimen
  – Tetracycline 2 gm/day for 6 weeks
  – Streptomycin 1 gm / day for 3 weeks.

• WHO 1986, and current regimen
  – Doxycycline 200 mg/day For 6 weeks
  – Rifampicin 600 – 900 mg/day For 6 weeks

• Ciprofloxacin; quick response but monotherapy has high rate of relapse (KFSH-Saudi Arabia)

Clinical Infectious Diseases 1995;21:283-90
M. Badawi et al, AAC, 1992 Jan; p. 150-152
Treatment

• Pregnancy: Rifampicin ± TMP-SMX

• Children:
  • More than 8 years:
    - Doxy 100 mg BID for 6 weeks + (Gentamicin iv 2-3 wks OR Streptomycin 1 gm IM QD for 2-3 wks)
    - Doxy + Rifampicin 600-900 mg/day for 6 wks
    - TMP-SMX DS p.o QID for 6 wks + Gentamicin for 2 wks.
  • Less than 8 years: TMP-SMX 5 mg/kg p.o. BID + Gentamicin for 2 wks.

  • TMP-SMX + rifampicin OR doxycycline + rifampicin (Turkey)


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Efficacy and Tolerability of Antibiotic Combinations in Neurobrucellosis: Results of the Istanbul Study

- Retrospective study, Adult patients (N = 215), 28 hospitals from 4 different countries

- **Ceftriaxone does not accumulate in phagocyes**, should it be added to Brucella treatment?
  - Protocol ONE = ceftriaxone, rifampin, and doxycycline (4.40 ± 2.47 months)
  - Protocol TWO = TMP-SMX, rifampin, and doxycycline (6.52 ± 4.15 months)
  - Protocol THREE = the patients started with P1 and transferred to P2 when ceftriaxone was stopped

- Ceftriaxone-based treatment period was shorter (P = 0.002), efficacy was found to be better (P = 0.017) and less relapse plus failure (P = 0.020)

- Seemingly, ceftriaxone-based regimens are more successful and require shorter therapy than the oral treatment protocol.

Hakan Erdem et al. AAC. March 2012; 56 (3): 1523-1528
Endocarditis

- Medical therapy

- Valve replacement and medical treatment

- Antimicrobial therapy: (Tetra, Strep, & TMP-SMX) OR (Rifampicin, TMP-SMX for 6 – 9 months)

Trop Doct. 2009 Apr;39(2):123-4
Combating Brucellosis in Human

Education and Changing the deeply rooted habits:

- Milk and its products
- Domestic farm animals slaughtering education
- Abattoir workers
- Farmers handling animals
- Laboratory personnel
Combating Brucellosis in Animals

Jordan (MOA) since 2003

- Logistics to prevent animal diseases (away from Urban areas, water, highways ... etc)
- Veterinarian services is a must in any animal barn
- Areas for infected animal isolation
- Areas to burn dead animals
- Barns for animals feed
- Screening of imported animals
Trends of Seroprevalence of Human and Animal Brucellosis in Turkey, 1930s–2000s

Zeki Yumuk. International Journal of Infectious Diseases 2012 April: 16((4); e228–e235

http://www.infectiologie.org.tn
Survey of Brucellosis among Sheep, Goats, Camels and Cattle in Kassala Area, Eastern Sudan

Mokhtar, M. Omer, Abdelhamid A. Abdelaziz, Sarah, M.A. Abusalab and Abbas M. Ahmed
Laboratory of Kassala Veterinary Research, Animal Resources Research Corporation, Ministry of Science and Technology, Sudan

Abstract: This study is conducted to estimate the prevalence of brucellosis in different animals species in Kassala area, eastern Sudan during 2004 up to 2006. The study aimed to provide a documented information on the prevalence of the disease with a view to assisting veterinary authorities in diseases control policies and planning research priorities in the region. The serum samples were collected from sheep, goat, camels and cattle, then tested in by Rose Bengal Plate test. The study showed that the prevalence of brucellosis is increased during the last years among different animal species.
Percentage of Animals Tested Positive Between 2004 - 2006

Animals sera were tested by RBST

To Wrap Up

- In many Arab countries brucella is still occurring at an unacceptable rates
- Guidelines for laboratory diagnosis are needed
- Efforts to combat brucellosis is not enough on the official scale
- Outreach people; educate them about their animals themself
- Treatment regimens should not be perplexed
- Educating physicians about brucellosis and about treatment and follow up
- Ministries of Health and Agriculture should work closely on this zoonotic infection

http://www.infectiologie.org.tn