Brucellosis:
Preventing Animal & Human infections

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Brucellosis

• Due to *Brucella abortus*, *melitensis* or *suis*
  – Gram negative bacteria (*α*-proteobacteriaceae)
  – Mammals facultative intracellular pathogens

• Geographical distribution
  – Mediterranean countries, near- and middle east
  – Distributed worldwide

• Clinical signs in animals (non pathognomonic)
  – abortions, sterility, unthrifty offspring
  – orchitis & epididymitis
  – joints may be affected, causing lameness and sometimes paralysis (pigs)
Human Brucellosis Worldwide

From Pappas et al., The Lancet Inf. dis., 2006, 6:91-99
Human Brucellosis in Europe

From Pappas et al., The Lancet Inf. dis., 2006, 6:91-99
### Brucella: species & biovars

<table>
<thead>
<tr>
<th>Species</th>
<th>Biovars</th>
<th>Preferred natural host</th>
<th>Main geographical area</th>
<th>Pathogenicity for man</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>B. melitensis</em></td>
<td>1, 2, 3</td>
<td>Sheep, Goats, Wild ongulates</td>
<td>Mediterranean countries Middle &amp; Near East</td>
<td>High</td>
</tr>
<tr>
<td><em>B. abortus</em></td>
<td>1, 2, 3, 4, 5, 6, 7, 9</td>
<td>Bovines, Wild ongulates</td>
<td>Europe, Americas, Africa, Asia</td>
<td>Moderate</td>
</tr>
<tr>
<td><em>B. suis</em></td>
<td>1</td>
<td>Suids</td>
<td>Americas, Asia, Oceania</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Suids, Hares</td>
<td>Central &amp; Western Europe</td>
<td>Very low</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Suids</td>
<td>USA, China</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Reindeer</td>
<td>USA, Canada, Russia</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Wild rodents</td>
<td>Russia</td>
<td>High</td>
</tr>
<tr>
<td><em>B. neotomae</em></td>
<td></td>
<td>Desert wood rat</td>
<td>USA</td>
<td>Unknown</td>
</tr>
<tr>
<td><em>B. ovis</em></td>
<td></td>
<td>Sheep (males)</td>
<td>Mediterranean countries</td>
<td>No</td>
</tr>
<tr>
<td><em>B. canis</em></td>
<td></td>
<td>Dogs</td>
<td>USA, South America Central Europe</td>
<td>Low</td>
</tr>
<tr>
<td><em>B. ceti</em></td>
<td></td>
<td>Cetaceans</td>
<td></td>
<td>High / Unknown</td>
</tr>
<tr>
<td><em>B. pinnipedialis</em></td>
<td></td>
<td>Pinnipeds</td>
<td></td>
<td>High / Unknown</td>
</tr>
<tr>
<td><em>B. microti</em></td>
<td></td>
<td>Common vole</td>
<td>Central Europe</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
Brucellosis: the global cycle

- Wild Ruminants, Rodents, Carnivores, Swine

- B. melitensis
- B. abortus
- B. suis

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Abortions
Endometritis
Orchitis in rams
Orchitis in pigs
Wild ruminants – *e.g.* in the EU

- **Chamois** (*Rupicapra rupicapra*)
- **Alpine ibex** (*Capra ibex*)
Domestic animals are the main reservoir…

*Preventing human brucellosis means primarily…*

*…Preventing and/or controlling the animal reservoir*
Brucellosis is a "multi-species" infectious disease…

- different animal species
- different Brucella species

…..to be considered
Epidemiology of Brucellosis….

- Cattle, sheep, goats or pigs, ...
  ...and wildlife

- Frequently in contact... in many areas
Abortion is the main sign of brucellosis...

But, most infected females give birth normally...

In both cases, huge and durable excretion of Brucella
Brucella are excreted primarily in:

- Abortion & normal delivery materials
- Vaginal secretions
- Semen
- Milk and colostrum
Survival of *Brucella* out of their host is long (compared with most other non-sporing pathogenic bacteria, under suitable conditions)

*Brucella* survive on/in many materials

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Epidemiology of Brucellosis....
Epidemiology of Brucellosis….

Transmission (*in animals*)

Entry point Mucous membranes & skin
Conjunctivae, nasopharynx & respiratory tract, oral route, genitalia

- Vertical transmission (*in utero*): congenital infection

- Horizontal transmission
  - Direct
    - Infected aerosols
    - Consumption (or licking) of infected materials and milk
    - Contact
  - Sexual transmission
  - Indirect (water, manure, materials, shoes,...)
Epidemiology of Brucellosis is complex...

Lots of transmission routes, most of them being almost impossible to control...
Brucellosis is a herd/flock disease...

- the epidemiological unit is the herd, the flock or the group including all epidemiologically-related sensitive animals
- the individual prevalence has no significance for control monitoring
Brucellosis Control /eradication strategies ....

Tools & strategies...
Brucellosis Control /eradication strategies ….

Tools & strategies…
Control of animal brucellosis: The tools

• Test and isolation/slaughter
  ✓ Partial or full depopulation
• Control of animal movements
• Vaccination

…and adequate

✓ Political will
✓ Budget
✓ Vet. Services / Lab. infrastructure
✓ Animal/herd identification
✓ Good quality vaccines
Diagnostic tools

• Direct:
  – Detection of the *Brucella* and/or their specific components (genes)
  *Unequivocal diagnosis*

• Indirect
  – Measure of the immune response
  *Essential in surveillance, control and eradication programs.*
Isolation (or PCR) & Typing of *Brucella*

- **Advantage:** unequivocal diagnosis
- **Disadvantage:** long and expensive, limited to equipped and experienced labs.
  - *The first laboratory-acquired infection in the world!!!*

- Not applicable at all stages of an eradication program (too many breakdowns)

- Essential in the last stages:
  - Diagnosis confirmation
  - Trace-back and forward tracing
Serological tests

All tests sensitive to antibodies induced by all S-Brucella species and biovars (B. abortus, melitensis and suis)

- RBT
- iELISA (serum and bovine milk)  
  Generally used as screening tests
- CFT
  Generally used as a complementary test

Brucellin skin test

- Highly specific  
  Generally used as a complementary test
Diagnosis of brucellosis

- No single test able to...
  - identify all infected animals, or
  - certify all free animals

- Tests repetitions / associations (parallel/series) modify considerably the results predictive values (-ve/+ve)
- Predictive values (-ve/+ve) linked to prevalence
- Choice of tests and interpretation strategy should always be based on epidemiological reality
Vaccination increases resistance to infection and decreases abortion risk

- Thus, decreases the spread of infection
- Thus, decreases individual and herd/flock prevalence
- Thus, decreases incidence in human populations

But,

- insufficient on its own to eradicate
- vaccine-induced serological/cell-immune reactions
Vaccination (S19 & Rev.1)

Sub-cutaneous or conjunctival route at standard dose

- Cattle (females): S19
  - 3-6 months: SC 5-10x10^{10} CFU/dose
  - Adults: SC 0.3-3x10^{9} CFU/dose (*non pregnant, lactating or late pregnancy*)
  - Both: CR 5-10x10^{9} CFU/dose (twice)

- Sheep & Goats: Rev.1
  - 3-6 months: SC 0.5-2x10^{9} CFU/dose
  - Both: CR 0.5-2x10^{9} CFU/dose (*non pregnant, lactating or late pregnancy*)
Brucellosis Control /eradication strategies ....

Which strategy...
The epidemiological situation is almost never homogeneous in a given country/region

Different epidemiological / livestock contexts within a country/region

⇒

Different & adapted control / eradication strategies to be implemented

⇒

Primary goals of a control programme:
Knowledge of situation & definition of Epidemiological units of intervention
Decision tree for brucellosis control in animals

1. Is brucellosis present in a certain area/country?
   - Yes:
     - Are there adequate means / expertise / vet. services?
       - Yes: (survey/prevalence/epidemiological units)
         - high prevalence: Mass vaccination
         - Intermediate prevalence: Combined young animal vaccination and test/slaughter
         - Low prevalence: test/slaughter
       - No: Surveillance/test-and-slaughter/movement control
   - No: Surveillance/test-and-slaughter/movement control
First objective in endemic areas
  ⇒ Control of the infection

Final objective ⇒ Eradication

Mid / short-term objective
  ⇒ Regularly decrease the prevalence

Progressive strategy
The basic control program: mass vaccination

**Main objective:**
- Reduction of the prevalence to an acceptable level
  \((i.e.\ minimising\ disease\ impact)\)
- The highest level of immunity in the highest possible number of animals in the shortest possible time interval

**Tools required:**
- Minimal infrastructure and budget
- Good vaccines (quality control / cold chain)
Control strategy based on mass vaccination
(S19/Rev.1)

- Immunisation of the whole population in only one intervention
- Reinforcement of immunity in previously vaccinated animals
  If repeated at regular intervals
  ⇒ the most economic and effective way to control the disease in endemic areas

Also applicable to control outbreaks in eradication programmes (emergency vaccination) if depopulation unfeasible
Mass vaccination – conditions of success / drawbacks

- Good quality vaccines (and cold chain)
  - **S19**
    - 🌟 replacement cows & non pregnant adults
    - 😞 lactating adults ➔ 0.1-2% udder infection
    - 😞 pregnant ➔ 0.1-2% abortions
    - 😞 bulls ➔ fertility?
  - **Rev.1**
    - 😞 all animals but pregnant ➔ abortions

  ➢ Problems minimised by the use of conjunctival route and seasonal breeding ➔ late pregnancy/calving/lambing/lactation/pre-breeding season

- To be applied to the whole population
- To be maintained (10-12 years) and repeated every 2 years (FAO in Tunisia & Morocco – WHO in Mongolia)
Eradication Programmes

- Combined strategy (vaccination / T & S)
- Exclusive T & S (no vaccine)

"Iceberg" Conditions: tests and vaccines are the emerged part!!
- Adequate design and organisation
- Available means / expressed needs / Political long-term will
- Effective involvement of professionals (breeders)
- Control of animal movements / permanent individual identification
- Continuity – Repetition – Long term

– Moreover,
the better the results are..., ....the more severe the control policy should be...
Otherwise...no or little progress...
Combined program: Young replacement vaccination / T&S adults

• When?
  – Low to moderate herd/flock prevalence < 5-10%
  – Important risk factors (movements, outbreaks)
  – If ICEBERG conditions fulfilled

• Allows eradication & protection of herds/flocks

• Requirements for success
  – Regular vaccination of all replacement (3-6 months old)
  – Regular (at least annual) sero-testing of all adult animals
  – Rapid culling of positive animals (depopulation if needed)
  – Retest positive herds at short intervals (every 2 months)
  – Sufficient means for:
    • the surveillance of the whole population – herd certification
    • adequate rapid culling / slaughter compensation
Eradication by exclusive Test & Slaughter

• When?
  – Very low herd/flock prevalence < 5%
  – Very low risk factors (movements, outbreaks)
  – If ICEBERG conditions fulfilled (excellent Vet. Serv. organisation)

• Allows eradication but not the protection of herds/flocks

• Requirements for success
  – Vaccines prohibited
  – Regular (at least annual) sero-testing of all adult animals in all herds
  – Qualification of herds/flocks (OIE)
  – Partial depopulation of positive herds/flocks is risky
  – Depopulation of positive herds/flocks when possible
  – Sufficient means for:
    • Surveillance of the whole population – herd certification
    • Adequate rapid culling / slaughter compensation
    • Movement control / Epidemiological investigations

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Surveillance

• **When?** Eradication achieved / no permanent risk factors left

• **Regular surveillance**
  – Of the whole population
  – Of a representative sample
    • To detect new outbreaks as soon as possible
    • To prevent reintroduction of infection from foreign sources

• **Avoid commercial movements** from herds re-qualified after partial depopulation

• **Animal introduction** only from truly free herds of free regions
Control, surveillance & Eradication of animal Brucellosis…

Epidemiology is the main key…

- A sound knowledge of the situation is required before deciding of a strategy
- Adequate epidemiological parameters are required for evaluating the results and monitoring the program…
- Changes in strategy should always be based on epidemiological evidences
Control, surveillance & Eradication of Brucellosis…

Diagnosis is the 2nd key…

- *Tests associations* (series or parallel)
  - to increase the result predictive values
- *Test result interpretation*…always in relation with:
  - risk-factors
  - status of the herd, the area, the country
Don’t forget the iceberg!

Diagnostic tests
Vaccines

Political long-term will
Strategy adapted to real situation
Adequate means
Individual identification
& movement control
Control pressure – Periodic test repetition
Commitment of professionals
The Prevention of Brucellosis in Humans

- Control of the animal reservoir
- Preventive measures
Brucellosis in humans

- Accidental and almost dead-end host
- *B. melitensis* is the most important cause worldwide
- Most cases from direct exposure
  - Primarily an occupational risk
- Non-occupational cases due to raw milk/milk products consumption
- Geographical distribution depends upon:
  - local food habits
  - milk processing methods
  - animal husbandry types
  - climatic conditions
  - standards of personal and environmental hygiene
Brucellosis in humans: the sources
Brucellosis in humans: infection routes

- **Conjunctivae** by aerosols or fingers
- **Inhaled aerosols**
  - Slaughterhouse procedures
  - Laboratory accidents
  - Veterinary manipulations
- **Ingestion**
  - Dairy products
  - Contaminated fingers
- **Abraded skin**
  - Veterinarians
  - Abattoir workers

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Human brucellosis: Prevention/key points

Based on occupational and food hygiene

• Vaccination impossible
• All dairy products should be prepared from heat-treated milk
• Consumption of raw milk or raw-milk products should be avoided / discouraged
• Offal (kidney, liver, spleen, udder & testes) should be adequately cooked
• Special precautions should be taken by
  – Abattoir workers, veterinarians, breeders, ...
  – Laboratory personnel
• Physicians and health workers should be aware of the possibility of brucellosis
• Public health education should emphasize food hygiene and occupational hygiene
Human brucellosis: Control in populations

- Control
  - Diagnosis (case definition) and treatment
  - Educational activities in at-risk groups
  - Heat-treatment of milk and dairy products

- Surveillance
  - Evaluation of the health state of human populations (surveys, notification system)
  - Identification of risk factors (cases investigation)
## Human brucellosis (France 2002-2012)

<table>
<thead>
<tr>
<th>Origines probables des cas traités au CNR</th>
<th>Année</th>
<th>Total 2002-2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contamination liée à un pays étranger</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Péninsule Ibérique</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Italie (Sud)</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Balkans/Turquie</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Caucase (Arménie)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Maghreb</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Proche &amp; Moyen Orient</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Asie (Inde et/ou Golfe persique)</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Asie (Chine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Afrique (hors Maghreb)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Amérique du Sud (Pérou, Argentine)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mexique</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>USA ?</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Contamination en zone d’endémie française</td>
<td></td>
<td></td>
</tr>
<tr>
<td>à B. suis 1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(Polynésie Française - Wallis &amp; Futuna)</td>
<td></td>
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<tr>
<td>Polynésie (B. canis)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Contamination en France métropolitaine</td>
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<tr>
<td>Contamination en laboratoire</td>
<td>-</td>
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<tr>
<td>Sanglier ou lièvre France (B. suis 2)</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Rechute ou contamination France (B. abortus ou B. melitensis)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Non renseigné</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>24</td>
</tr>
</tbody>
</table>
Human brucellosis: Prevention / conclusion

• Health education and information
  (introduction of basic hygienic measures)
• Detection & Treatment of human cases required...

…….But main and most efficient measures for reducing the human cases is…
…..by controlling the infection in animals!!!
Merci de votre attention  Thank you for your attention....
Vielen Dank für Ihre Aufmerksamkeit.
Спасибо за внимание  хвала за вашу позорност...