The OIE Reference Laboratory: Networks for Brucellosis

By John McGiven
Brucellosis

- Brucellosis is caused by the intracellular pathogen *Brucella*
- First discovered by Bruce in 1887. First diagnostic test developed in 1897 (SAT)
- They are Gram negative cocobacillary rods with a cell wall including LPS, peptidoglycans and OMPs
- The Genus includes six classical species with rough and smooth strains (*B. abortus, B. melitensis, B. suis, B. canis, B. ovis* & *B. neotomae*), and marine mammal species (*B. cetaceae* & *B. pinnipediae*)
- *Brucella* species have primary hosts but may cross host species boundaries and *Brucella* is considered zoonotic
- Symptoms of infection are variable, dependent on infective strain and host species but include abortion in cattle and recurrent fever in humans
Prevalence of Human Brucellosis (2006): 500,000 new cases/year (WHO)
Global Status of Bovine Brucellosis (OIE 2004)

- Bovine Brucellosis infected
- Bovine Brucellosis never reported
- Bovine Brucellosis has been eradicated

Data not available
Global Status of Sheep & Goat Brucellosis (OIE 2004)

- S&G Brucellosis infected
- S&G Brucellosis never reported
- S&G Brucellosis eradicated
- S&G Brucellosis reported in the past
- Data not available
Global Status of Porcine Brucellosis (OIE 2004)

Porcine Brucellosis infected countries

Porcine Brucellosis never reported

Data not available
The Role of the OIE Reference Laboratory (examples)

- To function as a centre of expertise and standardisation (e.g. development and distribution of International Standard Sera)
- To store and distribute to National Laboratories biological reference products used in diagnosis and control (e.g. anti-sera, phages)
- To develop new procedures for diagnosis and control (e.g. MLVA typing)
- Provision of scientific and technical training for personnel from OIE Member Countries
- Provision of confirmatory testing facilities to OIE Member Countries
- Coordination of collaborative scientific and technical studies (e.g. ‘Bruceladder’ PCR validation)
- Publication and dissemination of any information which may be useful to Member Countries of the OIE (e.g. OIE Manual)

**Networks are vital to achieve these important functions effectively**
Challenges

- Eradication of disease (lack of clinical signs other than abortion)
- Maintenance & demonstration of disease freedom
- Diagnosis: serology, cellular immunity, molecular, cultural
- Epidemiology: cultural, molecular
- Vaccination: Rev 1, S19, RB51
- Mechanisms of host preference
- Mechanisms of virulence
Networks for Brucellosis: Aims

- Development of new assays/methods
- Validation and Harmonisation
- Developing and applying standards
- Publications (6 peer reviewed OIE collaborative publications in 2007)
- Confirmatory testing
- Exchange of reagents
- Exchange/transfer of expertise
- Capability building
OIE Reference Laboratories

- VLA (UK): officially brucellosis free (OBF) since 1985, sea mammal brucellosis, automated HT serosurveillance, homogeneous assays.
- AFSSA (France): bovine brucellosis free, some caprine/ovine brucellosis (in south) and *B. suis* in wild boars, skin test in use, EU CRL
- FLI (Germany): livestock free of brucellosis but *B. suis* in wild boars, discovery of new *Brucella* species in in voles
- IZS (Italy): bovine brucellosis (buffalo herds in south) and caprine/ovine brucellosis, Cheese (mozzarella) PCR.
- CFIA (Canada): Livestock free of brucellosis but wildlife reservoir (elk, moose), expertise with FPA
- SENASA (Argentina): bovine brucellosis present, vast national herd vaccinated (S19), canine brucellosis, large laboratory network
- Kimron Vet. Inst. (Israel): caprine/ovine brucellosis and *B. melitensis* in cattle, Rev 1 vaccination programme in national flock
- NVRQS (Rep. Korea): Widespread brucellosis in national herd (4,715 infected herds in 2006). No vaccination. High throughput serosurveillance – e.g. annual testing of all beef cattle.
Visitors to *Brucella* OIE lab at VLA Weybridge
European Community Reference Laboratory
AFSSA, Paris
Brucellosis 2008 International Research Conference (310 delegates from ~ 60 countries)
Networking doesn’t always work
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International MLVA ring trial (COST Action 845)

- MLVA powerful tool for epidemiology at international and local levels
- Harmonisation required to reap greatest benefit (internet database [http://mlva.u-psud.fr/](http://mlva.u-psud.fr/)) so the same loci are used
- OIE laboratories in UK (VLA), Germany (FLI) and France (AFSSA) agreed best methodology and established ring trial
- Eight loci chosen for first ring-trial to allow basic speciation
- Sixteen laboratories participated (mainly from Europe) & all attended a training workshop beforehand
- All laboratories identified the correct species
- The next ring trial is open to all interested laboratories
International Standard anti-Brucella melitensis Serum

- Serum produced by VLA with international collaboration
- All OIE Reference laboratories for brucellosis participated plus expert laboratories from Spain (CITA) & Belgium (VAR) & Portugal (INRA)
- Study design to establish ISaBms criteria agreed by all participants and all participated in testing
- Minimum thresholds for analytical sensitivity have been set for RBT, mRBT, iELISA, cELISA & FPA
- Data will be published by authors from all participating laboratories
- International Standard anti-Brucella suis Serum was also produced (CFIA, Canada) and standardised in the same way
Collaborative projects

- EU framework 7 project to improve diagnosis of porcine brucellosis required collaborative proposals to qualify for funding. Joint project submitted by Denmark, UK (VLA) & France (AFSSA)
- Cooperation between Argentina (SENASA) & UK (VLA) to develop *Brucella* PCR from whole blood and serum
- VLA & State Central Veterinary Laboratory in Mongolia working to evaluate use of cELISA for routine serology
R. Korea NVRQS & VLA Collaboration

- R. Korea has a high prevalence of brucellosis but a strong desire and capability to tackle the problem
- VLA have been instrumental in aiding the application of NVRQS to become an OIE Reference Laboratory for Brucellosis.
- NVRQS are planning for the tail end of their eradication campaign and are already looking to address FPSRs
- VLA are already in this position and have experience and research programmes to address the FPRS issue
- Sharing resources and conducting collaborative research to improve PPV of serology in low prevalence populations and to improve epidemiology
The project has been a success!!
Turkey – OIE twinning project

- Formal agreement between Pendik Veterinary Control and Research Institute, VLA & OIE to undergo twinning programme
- Brucellosis (B. abortus and B. melitensis) endemic in turkey
- The VLA have provided training in cultural, molecular, and serological analysis
- Includes extensive training on reagent production & standardisation (OIE Manual of Diagnostic Tests and Vaccines)
- Several exchange visits have occurred
- Spin-off opportunities for both laboratories, e.g. provides effective environment for test validation comparing a free area (UK) to an endemic one (Turkey)
Networking is fun!
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All our partners within the networks

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Thank you