Rift Valley Fever, What’s the Big Deal?

Feed the Future Innovation Lab: Control of Rift Valley Fever in Agriculture.

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In collaboration with:

The University of Texas Medical Branch, Galveston, TX
Sokoine University of Agriculture, Morogoro, Tanzania
MCI Sante-Animale, Morocco

IL Director Meeting, Malawi: April 20, 2015
Rift Valley fever, the disease

- **Location**
  - Sub-Saharan Africa
  - endemic to epidemic

- **Spread to Egypt, Saudi Arabia, Madagascar**

- **Disease & abortions in sheep, cattle & goats**

- **Zoonotic**

- **Amplified by ruminants**

- **Mosquito vector (vertical & horizontal)**

- **Outbreaks, start fast but short duration**

- **Usually not diagnosed until human involvement**
Rift Valley fever, the cost

• OIE Reportable (stops export)
• Pregnant Sheep- 100% abortions
• Sheep, cattle 10-30% mortality
• Disrupts food, milk supplies, loss of jobs
• 5-40% Case Fatality rate in humans (clinically diagnosed)
• 5-10% blindness
Rift Valley fever, the big deal

- Egypt 1977
  - 18,000 – 1,900,000 infected, CFR 3% - ?

- Saudi Arabia 2000
  - Cattle exports from Horn to Saudi down 42%

  - Total national impact of $32 MM
  - Producers- prices ↓ 20% ; loss of livestock↓ 22% at cost $ 9.3 MM
  - Traders decreased 40-50%

- Tanzania 2007
  - CFR 28%

- South Africa 2010
  - CFR in 10-15% range, mostly responders (ca 230)
Rift Valley fever, the cause

- Phlebovirus (arbovirus, mosquito spread Aedes & Culex spp.)
  - RNA virus
  - 3 Segments Large, Medium, and Small (L, M, S)
  - Genetically conserved (>95%)
- Highly infectious (may be as low as 1 pfu)
- No licensed human countermeasures (experimental)
- Animal vaccines
  - Smithburn neurotropic (SNS), live attenuated*
  - Clone-13 (deletion of IFN suppressor NSs from S segment), live attenuated*
  - MP-12 (multiple SNP in L and M) experimental
Rift Valley fever, the outbreak

Mosquito Eggs

H₂O

Adult

Blood meal host (?)

Rain

Harvest animals

Epizootic outbreak

Amplifier

Aerosols & Mosquitos

Humans

Disease

benign hemorrhagic ocular encephalitis
Rift Valley fever, prevention

• Smithburn neurotropic- (SNS) aborts pregnant sheep
• Clone-13 (NSs-deletion of IFN suppressor)
  - Licensed in So. Africa but meeting with reluctance
  - Can phenotypically revert to virulence

Experimental

• MP-12 (U.S. Army, USAMRIID)
  - Efficacious, protects cattle and sheep in challenge studies
  - Single dose, persistent antibody (years)
  - Successful human Phase 2 clinical trial completed

- MP-12 Deleted (MP-12-NSm-del) DIVA
  - Safe in pregnant sheep
  - Protects against virulent RVFV challenge
Rift Valley fever, the project

- **License MP-12-Deleted for Use in Africa**
  - Select manufacturer (MCI-Sante Animale, Mohammedia, Morocco)
  - Develop manufacturing process (<$0.25 USD/dose, est.)
  - Prepare licensing dossiers
  - Needle free delivery system

- **Develop DIVA Diagnostic Test**
  - Distinguish infected from vaccinated animals
  - Western blot and Elisa preliminary results
  - Convert to pen-side test

- **Determine the safety of deletion vaccines (NSs)**
  - Test reassortment in lab culture
  - Isolate phleboviruses from Africa and test reassortment in culture and bovine hepatocyte model
Capacity building

• Train in classical/molecular virology techniques
• Support 3 Ph.D. students
• Renovation to create first tissue culture lab in country
• Major location for reassortant studies
Laboratory Renovation
MCI Sante Animale - Morocco
Questions
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Bioject Devices

B-2000

ID Pen

Jupiter Jet

Zeta Jet

Zeta Jet Syringe (0.5 ml)
BoFish Large Animal Nasal Delivery System

- Reloadable mechanically actuated nasal dispenser
- Single use nasal applicator tip designed for precision dose delivery into nares of cattle, sheep, horses or livestock
- Dispensed dose is delivered as a spray or stream and can be calibrated to a specific volume ranging from 100 μL to 300 μL
- No priming required
- Dispenser is sterilizable using standard disinfection agents