



FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative



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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



Rift Valley fever, the disease

- Location

- Sub-Saharan Africa
- endemic to epidemic

- Spread to Egypt, Saudi Arabia, Madagascar

- Disease & abortions in sheep, cattle & goats

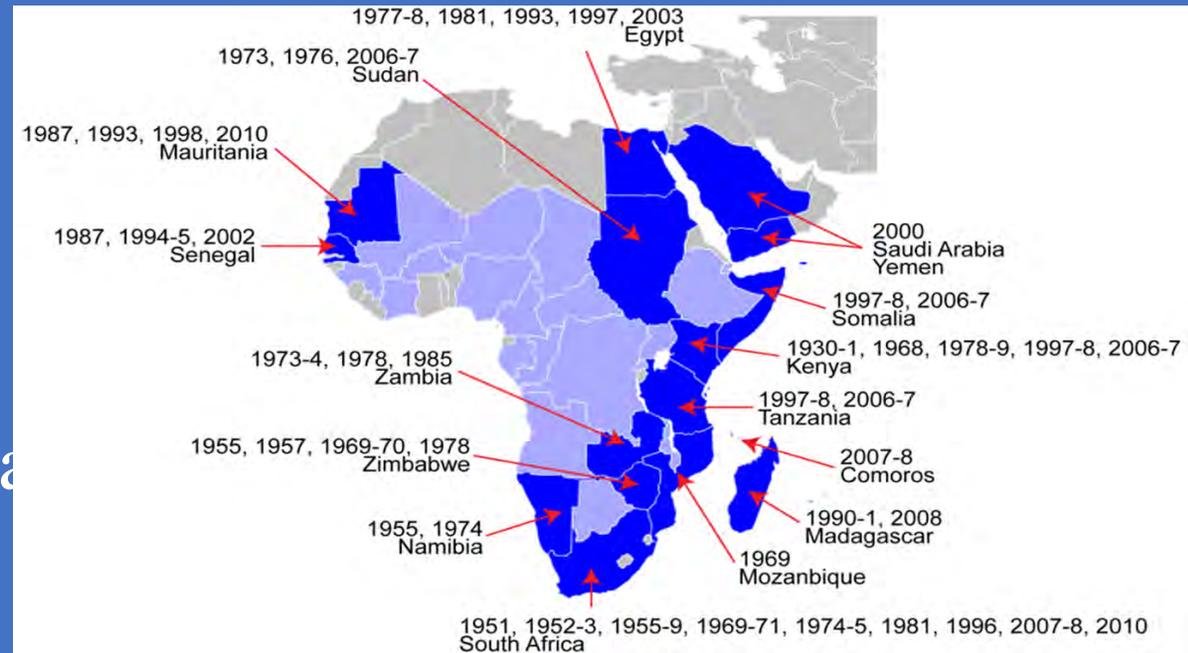
- Zoonotic

- 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

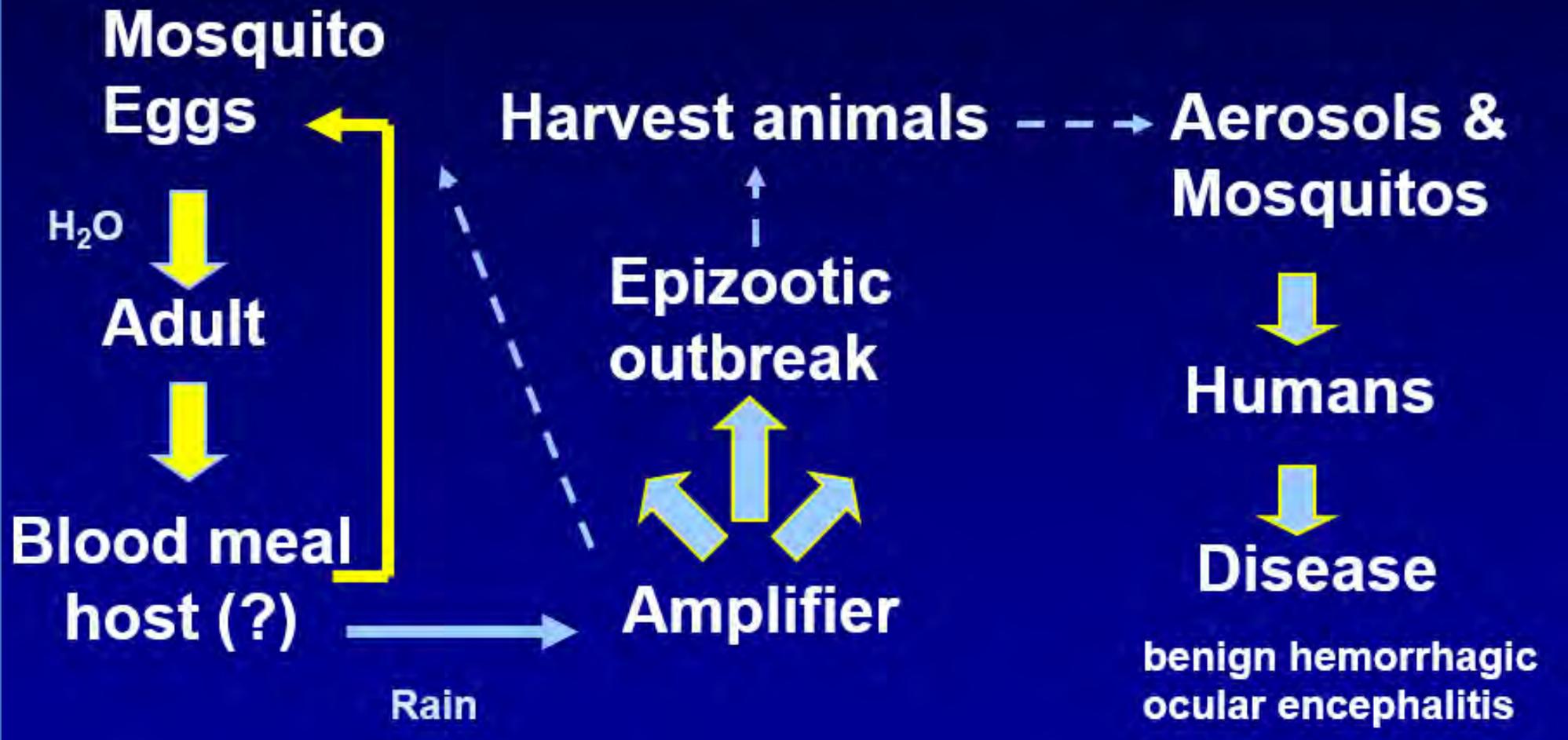
Rift Valley fever, the big deal

- Egypt 1977
 - 18,000 – 1,900,000 infected, CFR 3% - ?
- Saudi Arabia 2000
 - Cattle exports from Horn to Saudi down 42%
- Kenya 2006/7 (*Am. J. Trop. Med. Hyg.*, 83(Suppl 2), 2010, pp. 52–57)
 - 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



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 RVEFV 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

Sokoine University of Agriculture

School of Veterinary Medicine

Morogoro, Tanzania

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 Santé Animale - Morocco



Questions



Attenuation by Deletion vs Mutations

	Virulence		S	M	L	Sheep At
ZH-501	+					+
MP-12	-		MP-12	MP-12		+
	-				MP-12	nt
	-		MP-12			nt
R-566	-	Δ NSs	MP-12	MP-12		-
	-	Δ NSs	MP-ΔNSm	MP-12		-
MP-12 ΔNSm	-		MP-ΔNSm	MP-12		+
Clone 13	-	Δ NSs				+
CDC	+		Δ NSm			+
	-	Δ NSs	Δ NSm			+

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