Experience with the United States Department Of Agriculture (USDA) Center for Grain & Animal Health Research (CGAHR) Arthropod-Borne Animal Diseases Research Unit (ABADRU):

Looking at Rift Valley fever virus and Occupational Biosafety and Hazard Practices

Masters of Public Health Field Experience
Kansas State University

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Outline

• Introduction
• Overview of Rift Valley fever virus (RVFV)
• Overview of Occupational Biosafety
• Field Experience
  o Biosafety Training Module
  o Rift Valley fever virus and Bluetongue virus Module
• Assessment of Biosafety for Needle-free Delivery
  o Objectives
  o Materials and Methods
  o Results
  o Summary
  o Conclusion
• Acknowledgements
Introduction

• Zoonotic threat of Rift Valley fever virus (RVFV)
  o An Arthropod-Borne - Arbovirus
  o Medically and Agriculturally important in Africa (Hughes-Fraire, et al, 2011)
  o Causes outbreaks impact both human and animal health (Ikegami & Makino, 2011)
    • Bans on movement of animals and products

• Organizations and researchers
  o Concern of occupational biosafety (NICD, 2011)
  o Constitutes an important public health issue (Archer, et al, 2011)
  o Potential to be globally significant (Strauss & Strauss, 2008)
Overview

Rift Valley fever virus

- Isolated from lamb in Kenya, Africa’s Rift Valley (Daubney, et al, 1931)
- Responsible for severe disease in sub-Saharan Africa for over 70 years (Hartley, et al, 2011)
  - In 2010 (NICD, 2011)
    - 238 human infections, 26 deaths
    - 14,342 animal infections, 8,877 confirmed deaths
    - Subclinical cases difficult to quantify
- Rift Valley fever virus (Sindato, et al, 2011)
  - Family: Bunyaviridae Genus: Phlebovirus
  - Single stranded, negative RNA virus
  - Genome
    - Made up of S- M- and L- segments each containing a separate nucleocapsid within the virion

Adapted from Geisbert, et al, 2001
Overview
Rift Valley fever virus

- Epidemiology
  - As mentioned RVFV is a mosquito transmitted disease
    - Virus can be transmitted (vertically) from mother to eggs (Hartley, et al, 2011)
    - Humans and Ruminants amplify virus (Sindato, et al, 2011)
  - Humans also infect via (Hartley, et al, 2011)
    - Contact of infected blood or tissue
    - Inhalation of aerosol during slaughter of infected livestock
Overview

Rift Valley fever virus

• Human Health (Sindato, et al, 2011)
  o Incubation period 2-6 days

• Clinical Signs
  o Flu-like syndrome, hemorrhagic fever (37.8-40°C), strong headaches, body pain, dizziness, nausea, epigastric discomfort, photophobia-retinitis, anorexia, and hemorrhage from body cavities
  o <2% can progress from illness to death

• Recovery within 4-7 days
Overview
Rift Valley fever virus

• Animal Health (Spickler & Roth, 2006)
  o Incubation
    • 12-36 hours in newborn lambs
    • Up to 72 hours in sheep, cattle, and dogs

• Clinical Signs
  o Fever (40-42°C), anorexia, lymphadenopathy, weakness, nasal discharge, and usually death within 36 hrs

• Recovery
  o Lambs: 90-100% mortality
  o Cattle: 10-70% mortality
  o Abortion is typical in 90-100% of affected ewes and cattle
Overview of Rift Valley fever virus

- Diagnosis
  - RVFV treated as emergency (Archer, et al. 2011)
  - Dependent on virus or nucleic acid isolation (Clements, et al. 2007)
    - Via RT-PCR or isolation in mice or cell culture (NICD, 2011)
      - Vero E6 (African green monkey) cells
      - BHK-21 (baby hamster kidney) cells
  - Immunoassay
    - Antigen detection
    - Antibody detection
Overview
Rift Valley fever virus

- Prevention and control
  - Attenuated and Killed Vaccines
  - Vector control
    - Insecticides
    - Repellants
    - Clothing

- Treatment
  - None – supportive care
Overview
Rift Valley fever virus

  o West Nile virus (WNV) in 1999-present
    • Exotic arbovirus endemic in North America
    • Due to presence competent mosquito vector
  o Outbreaks confirmed in Yemen and Saudi Arabia in 2000
    • Turell, et al, 2008
      o Demonstrated the vector competence of North American mosquito species
        • Competent vector
          o Culex tarsalis
          o Aedes vexans from Louisiana and Florida
  o Hughes-Fraire, et al, 2011
    • Epidemic/economic model determined a potential loss of $120 million– $2.3 billion
Overview
Occupational Biosafety

- **Introduction** (CDC, 2009; Harding & Byers, 2006)
  
  - Biosafety
    - Consistent application of safety measures
  
  - Biohazard
    - Biological agent or condition that causes a hazard
  
  - Biosecurity
    - Designed to prevent misuse of microorganisms
Overview

Occupational Biosafety

• History
  o Biosafety limited to last 150 years

  • Empirical practices go to ancient times (Block, 2001)
    o The Odyssey – Homer (Rieu, 1952)
    o Susruta – Hindu Physician
    o Black Plague Middle Ages
    o Venice Magistry, 1438
    o Many others...
Overview

Occupational Biosafety

• Laboratory acquired infections (LAI) (CDC, 2009)
  o Due a break down in microbiological practices

• Risk of LAI
  o Transmission hazards
    • Mouth pipettes, syringe and needle, spills and splashes, etc…
  o Reported late 1880’s
    • Brucellosis, glanders, diphtheria, cholera, tetanus, & Typhoid fever
  o Epidemiological review
    • Kisskalt, 1915
Overview

Occupational Biosafety

- Studies of LAIs

  - Pike & Sulkin (1935-1978)
    - 4,079 reported infections
    - 168 fatalities

  - Harding & Byers (1979-2005)
    - 1,141 reported infections
    - 24 fatalities

*Not all LAIs reported
Overview
Occupational Biosafety

- **BSL-1**: Student training/teaching labs
  - Agents are well-defined and characterized
    - Not known to cause disease

- **BSL-2**: Clinical/diagnostic labs
  - Agents are considered moderate-risk agents
    - Associated with human disease (varying severity)
  - Open bench
    - Standard microbiological techniques
      - Probability of splashes and aerosols is low

- **BSL-3**: Research/production facilities
  - Agents may be indigenous or exotic
    - Associated with serious and potentially lethal infections
    - Potential for respiratory transmission
      - High transmissibility by aerosols

- **BSL-4**: Dangerous/exotic laboratories
  - Agents pose high individual risk of life-threatening disease
    - Vaccine or therapy may not be available
Field Experience

• Organization History
  - Arthropod-Borne Animal Disease Research Unit (ABADRU)
  - Moved from Laramie, WY → Manhattan, KS
    • Cooperative with K-State researchers
    • Biosecurity Research Institute (BRI)
  - Study animal diseases transmitted by arthropods
    • Bluetongue virus (BTV)
    • Vesicular Stomatitis virus (VSV)
    • Epizootic Hemorrhagic Disease virus (EHDV)
    • Rift Valley fever virus (RVFV)

• Importance
  - Public health and U.S. livestock

Public Health
Field Experience

- **Role & Objectives**
  - USDA ABADRU
    - Rift Valley fever virus
    - Zoonotic disease research
    - Occupational hazard guidelines
    - Laboratory biosafety
Field Experience

Student Activities

• Mouse work
  - *Culicoides sonorensis*
  - Immunologic response from feeding

• Lab work
  - Methods and procedures
  - Occupational hazards and biosafety
Field Experience

Student Activities

• Frontier Field Trip
  o U.S.-Mexico Border Port of Entry (USPOE) in Santa Teresa, NM
    • Border control interdiction and trade security
    • Immigration Policy Border Communities Conference
    • NM Border Authority
    • U.S. Customs and Border Protection (USCBP)
    • Food and Drug Administration (FDA)
    • New Mexico Department of Agriculture, at the Chihuahua Regional Cattle Union Livestock Facilities
Field Experience

Student Activities

- **Product**
  - Biosafety Training PowerPoints

- **Need**
  - No tutorials specific to the BSL-2 Laboratory

- **Use**
  - Provide safety information
  - Knowledge to be proactive during training period
  - Completion of presentation
    - Quiz to provide certificate of completion
Field Experience

Student Activities

• **Product**
  - Virus Overview Training PowerPoint
    - Rift Valley fever virus
    - Bluetongue virus

• **Benefit**
  - Student and temp-works need basic virology
  - Understand why the ABADRU research is important

• **Use**
  - Health impact and risks of viruses
  - Self-vigilance to increase biosafety
  - Completion of presentation
    - Quiz to provide certificate of completion
Field Experience

Student Activities

• Product
  o Preliminary evaluation of P50 Microdose NeedleFree Injection System© in BSL-2 laboratory

• Benefit
  o Increase worker biosafety
  o Improve the immunologic response from vaccines
  o Reduce the need to raise *Culicoides sonorensis* (midge) strains for research

• Use in a controlled research facility
  o Administer modified live vaccines (such as MP-12)
  o Live Rift Valley fever virus
Assessment of Biosafety for Needle-free Intradermal Delivery

- Occupational biosafety
  - Workers in bioresearch laboratories
    - Zoonotic agents
- Simulate transmission method of arthropod vectors
- Risks and safety (Deng, et al., 2012; Mitragotri, 2005)
  - Compared to traditional needle and syringe
- Risks of aerosol generation (Zehrung, & Kristensen, 2009)
Objectives

To characterize potential risks of the P50 Microdose NeedleFree Injection System® for intradermal injection of infectious agents or modified live vaccines in BSL-2 and BSL-3 laboratories

To evaluate differences in surface splatter and wetness for test dose and pressure combinations
Materials & Methods

• Donated Boer goat forelimbs with intact hide
  o Stored in a sealed bag at -20°C

• P50 Microdose NeedleFree Injection System©
  o Compressed CO₂ as a power source
Materials & Methods

• Two Solutions
  o 5% Crystal Violet
  o Germ Juice®

• Doses/pressure
  o 50 µL/100 psi
  o 100 µL/90 psi
  o 250 µL/90 psi
## Results

### Germ Juice® Solution

<table>
<thead>
<tr>
<th>Limb Location</th>
<th>Right Front</th>
<th>Data Points</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wetness (mm) 50 uL/100 psi</td>
<td>22 21 19</td>
<td>23* 27* 27*</td>
<td>23.2</td>
</tr>
<tr>
<td>Pooling (y/n) 50 uL/100 psi</td>
<td>0 0 0</td>
<td>0* 0* 0*</td>
<td>0.0%</td>
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<tr>
<td>Surface splatter (mm) 50 uL/100 psi</td>
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<td>20* 22* 25*</td>
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</tr>
<tr>
<td>Wetness (mm) 100 uL/90 psi</td>
<td>27 33 25</td>
<td>22* 28* 28*</td>
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<tr>
<td>Pooling (y/n) 100 uL/90 psi</td>
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<tr>
<td>Surface splatter (mm) 100 uL/90 psi</td>
<td>25 20 20</td>
<td>26* 24* 29*</td>
<td>24.0</td>
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<tr>
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<tr>
<td>Wetness (mm) 250 uL/90 psi</td>
<td>35 33 35</td>
<td>36* 40* 52*</td>
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<td>1* 1* 1*</td>
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<tr>
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<td>. . .</td>
<td>1* 1* 1*</td>
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</tbody>
</table>
## Results

### Crystal Violet Solution

<table>
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<th>Data Points</th>
<th>Mean</th>
</tr>
</thead>
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<tr>
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<td>50 uL/100 psi</td>
<td>25 21 22</td>
<td>34* 25* 26* 25.5</td>
</tr>
<tr>
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<td>. 0* 0* 0.0%</td>
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<td>Wetness (mm)</td>
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<tr>
<td>Surface splatter (mm)</td>
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<td>25* 20* 21* 19.3</td>
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<td>Wetness (mm)</td>
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</tr>
<tr>
<td>Surface splatter (mm)</td>
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<td>27* 24* 37* 14.7</td>
</tr>
<tr>
<td>Aerosolization (y/n)</td>
<td>250 uL/90 psi</td>
<td>. . .</td>
<td>. 1* 1* 1* 100.0%</td>
</tr>
</tbody>
</table>
Results

Wetness (Germ Juice®)

Surface Splatter (Germ Juice®)
Results
Results
Results
Results
Results
Conclusion

• Advances in technology
  o Evaluate the safety
  o Practical application

• Success of the device
  o Subcutaneous and intramuscular injections
  o Accuracy of intradermal delivery
  o Interest for research purposes

• More data points needed
  o Statistical difference
  o Other devices

• Safety of device
  o Needle-less use
  o Aerosolization
Summary

• **Gains**
  - Knowledge
  - Understanding
  - Risks and hazards

• **Disciplines**
  - Public health
  - Animal health
Acknowledgements

This capstone field experience was possible due to the support of

- USDA, CGAHR, ABADRU
  - Dr. Scott McVey, Dr. Mark Ruder, Dr. Chris Lehiy, Dr. Barb Drolet, Kyle Schweisthal, Lindsey Reister, Kruger Bryant, and Joanne Gresens
  - As well as other staff and student workers

- K-State’s Comparative Medicine Group (CMG)
  - Dr. Tracy Miesner

- K-State College of Veterinary Medicine
  - Dr. Patricia Payne, Dr. Robert Larson, and Dr. Justin Kastner

- K-State University/New Mexico State University Frontier Program
References

References

Questions

Thanks to my brother Levi Roof