Looking Beyond the Risk Group: Risk Assessment Challenges in Models of Emerging and Zoonotic Disease

University of Pittsburgh
Department of Environmental Health & Safety

Molly S. Stitt-Fischer, PhD, CPH, CBSP, (SM)NRCM
## Risk Groups, Biosafety Levels, and Research

<table>
<thead>
<tr>
<th>Risk Group</th>
<th><strong>Infectious Agent – Severity of Disease</strong></th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Typically does not cause disease in healthy adults</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>Can cause disease; Not airborne</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>Can cause serious disease; Airborne transmission</td>
<td>Sometimes</td>
</tr>
<tr>
<td>4</td>
<td>Serious, and often potentially fatal disease</td>
<td>No</td>
</tr>
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## Risk Groups, Biosafety Levels, and Research

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<th>Risk Group</th>
<th>BSL</th>
<th>Infectious Agent – Severity of Disease</th>
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<tbody>
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<td>No</td>
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</table>
Risk Group ≠ BSL
Risk Group \( \approx \) BSL
Risk Group  ?  BSL
Human pathogen?

Animal pathogen?

Transmission route?

Aerobiology, imaging, etc.?

Animal research?

Species?

Available facilities?

Personnel performing work?
Case Studies: Process and Potential Stumbling Blocks

• Juvenile baboon model of reemerging disease
  – *Bordetella pertussis* (pertussis; whooping cough)

• Host-pathogen interactions
  – *Batrachochytrium dendrobatidis (Bd)*
Pertussis: A Reemerging Disease

• Agent mainly causes disease in children and infants, but adults may develop symptoms as well.
Pertussis: A Reemerging Disease

- Agent mainly causes disease in children and infants, but adults may develop symptoms as well.
- Exposure of infants to agent can lead to severe disease and high mortality.

https://phil.cdc.gov/PHIL_Images/09132002/00036/PHIL_2121_lores.jpg
Pertussis: A Reemerging Disease

- Agent mainly causes disease in children and infants, but adults may develop symptoms as well.
- Exposure of infants to agent can lead to severe disease and high mortality.
- Agent is contagious and spreads from person-to-person through direct contact and/or inhalation of respiratory droplets.

https://phil.cdc.gov/PHIL_images/09132002/00036/PHIL_2121_lores.jpg
Pertussis: A Reemerging Disease

Pertussis global annual reported cases and DTP3 coverage, 1980-2016

Source: WHO/IVB database, 2017
194 WHO Member States
Data as of 19 July 2017
Pertussis: A Reemerging Disease

Reported NNDSS pertussis cases: 1922-2015

Source: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1980, passive reports to the Public Health Service

https://www.cdc.gov/pertussis/surv-reporting.html
### 2016 Provisional Pertussis Surveillance Report

<table>
<thead>
<tr>
<th>State</th>
<th>Incidence (per 100,000)</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>OKLAHOMA</td>
<td>3.1</td>
<td>121</td>
</tr>
<tr>
<td>OREGON</td>
<td>4.5</td>
<td>180</td>
</tr>
<tr>
<td>PENNSYLVANIA</td>
<td>11.4</td>
<td>1454</td>
</tr>
<tr>
<td>RHODE ISLAND</td>
<td>6.7</td>
<td>71</td>
</tr>
<tr>
<td>SOUTH CAROLINA</td>
<td>3.7</td>
<td>180</td>
</tr>
<tr>
<td>SOUTH DAKOTA</td>
<td>1.6</td>
<td>14</td>
</tr>
<tr>
<td>TENNESSEE</td>
<td>2.0</td>
<td>131</td>
</tr>
<tr>
<td>TEXAS</td>
<td>4.1</td>
<td>1119</td>
</tr>
<tr>
<td>UTAH</td>
<td>6.9</td>
<td>206</td>
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<tr>
<td>VERMONT</td>
<td>43.5</td>
<td>272</td>
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<tr>
<td>VIRGINIA</td>
<td>2.2</td>
<td>181</td>
</tr>
<tr>
<td>WASHINGTON</td>
<td>7.1</td>
<td>512</td>
</tr>
<tr>
<td>WEST VIRGINIA</td>
<td>1.3</td>
<td>23</td>
</tr>
<tr>
<td>WISCONSIN</td>
<td>2.1</td>
<td>1212</td>
</tr>
<tr>
<td>WYOMING</td>
<td>3.1</td>
<td>18</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>4.9</strong></td>
<td><strong>15737</strong></td>
</tr>
</tbody>
</table>

Risk Assessment: Infectious Agent
<table>
<thead>
<tr>
<th><strong>Bacteria</strong></th>
<th>Genus</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH: 2</td>
<td>Bordetella</td>
<td>pertussis</td>
</tr>
<tr>
<td>BMBL*: 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia/New Zealand: 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Belgium: 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Germany: 2 notes: AR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EU: 2 notes: V</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Singapore: 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Singapor Schedule:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Switzerland: 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UK: 2 notes: Vaccine available</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human Pathogen: y Animal Pathogen: n Plant Pathogen: n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Select Agent CDC: Ⅱ Select Agent USDA: Ⅱ</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Containment Recommendations

BSL-2 practices, containment equipment, and facilities are recommended for all activities involving the use or manipulation of known or potentially infectious clinical material and cultures. ABSL-2 practices and containment equipment should be employed for housing experimentally infected animals. Primary containment devices and equipment, including biological safety cabinets, safety centrifuge cups or safety centrifuges should be used for activities likely to generate potentially infectious aerosols. BSL-3 practices, containment equipment, and facilities are appropriate for production operations.
Risk Assessment: Animal Model
What will our research entail?

Pertussis disease and transmission and host responses: insights from the baboon model of pertussis

Marta Y. Pinto, Tod J. Merkel

Journal of Infection (2017) 74, S114–S119

Airborne Transmission of Bordetella pertussis

Jason M. Wartel, Joel Beren, and Tod J. Merkel

1Division of Bacterial, Parasitic and Allergenic Products, Center for Biologics Evaluation and Research, and 2Division of Veterinary Services, Center for Biologics Evaluation and Research, FDA, Bethesda, Maryland

The Journal of Infectious Diseases 2012;206:902–6
Risk Assessment: Treatments or Vaccines Available?
Vaccines and Work Practices: What should we recommend?

- An FDA-approved vaccination is available for *Bordetella pertussis*
  
  - The University has a required vaccine program for other high risk pathogens
  
  - Should we require personnel to be boosted? Recommend?
  
  - Is vaccination enough given baboons develop severe disease?
Vaccines and Work Practices: What should we recommend?

- Is there a possibility that fomites or worker exposure could lead to family and/or community risk?
  - High impact to infants and children
  - Work with baboons infected with *Bordetella pertussis* at ABSL-3
Are we being too conservative?

- Ask a peer review committee for their feedback on recommendations
Are we being too conservative?

No.
Case Study #2: What are factors to consider for work with an agent that is not infectious to humans?
Risk Assessment: Biological Agent Information
Batrachochytrium dendrobatidis (Bd)

- Chytrid fungus severely affecting amphibian species worldwide
  - Over 700 species have shown decline

Batrachochytrium dendrobatidis (Bd)

- Chytrid fungus severely affecting amphibian species worldwide
  - Over 700 species have shown decline
- More species extinct than any other infectious disease known
  - At least 200

Batrachochytrium dendrobatidis (Bd)
- Spread via pet trade/research/testing

African clawed frog
*Xenopus laevis*

North American bullfrog
*Lithobates catesbeianus*
Batrachochytrium dendrobatidis (Bd): Natural Hosts

Aquatic salamander
*Cryptobranchus alleganiensis*

Northern leopard frog
*Lithobates pipiens*

Louisiana crayfish
*Procambarus clarkii*

Everglades crayfish
*Procambarus alleni*
Risk Assessment: Research Planned
Research Plan: Field studies

• Field studies
  – Established SOPs to avoid cross contamination during sample collection
    • New nitrile gloves, separate sterile container for each animal or sample collected

https://toxics.usgs.gov/photo_gallery/photos/armi/ARMI_b_boreas_SpruceLK_CWA_1.jpg
Research Plan: Field studies

• Field studies
  – Established SOPs to avoid cross contamination during sample collection
    • New nitrile gloves, separate sterile container for each animal or sample collected
  – Does this translate to the lab?

https://toxics.usgs.gov/photo_gallery/photos/armi/ARMI_b_boreas_SpruceLK_CWA_1.jpg
Research Plans: In the lab

- Culture \( Bd \) and intentionally infect animals

http://www.michigan.gov/images/leopard_frog_102908_7.jpg
Research Plans: In the lab

- Culture *Bd* and intentionally infect animals

- Maintain research colonies of uninfected animals in common facility
Risk Assessment: Research Plans

- Do we have capacity to house infected animals in shared facility?
Risk Assessment: Research Plans

• Do we have capacity to house infected animals in shared facility?

• How would our other researchers feel about that?
Risk Assessment: Logistics

- Can we renovate or otherwise modify existing research space to accommodate housing of infected animals?

Risk Assessment: Logistics

• We will still need to house uninfected animals in the common housing area

Risk Assessment: Logistics

- We will still need to house uninfected animals in the common housing area
  - Emphasize strict traffic patterns
  - Uninfected animals first
  - No re-entry to common housing area after work in laboratory space

Risk Assessment: Logistics

• Use engineering controls and standard microbiological practices and PPE for culture of pathogen and handling of infected animals

https://www.cdc.gov/about/facts/cdcfastfacts/cdcfacts.html
Risk Assessment: Logistics

• Already familiar with use of BSCs for cultures

https://www.cdc.gov/about/facts/cdcfastfacts/cdcfacts.html
Risk Assessment: Logistics

- Already familiar with use of BSCs for cultures
- Lab coats?? Why would we need those?

https://www.cdc.gov/about/facts/cdcfastfacts/cdcfacts.html
https://ecos.fws.gov/ServCat/DownloadFile/15727?Reference=16196
Risk Assessment: Logistics

- Waste disposal, transport, and storage of cultures
  - Biological waste storage and -80 freezers require personnel to walk past clean *Xenopus* facility
Risk Assessment: Logistics

- Waste disposal, transport, and storage of cultures
- Secondary containers and surface disinfection
Risk Assessment: Personnel

• Undergraduate student researchers
  • Lack of research experience
  • Participation in laboratory and/or field work as part of courses
Risk Assessment: Personnel

- Undergraduate student researchers
  - Can they recognize the importance of adhering to strict SOPs?
- Required, documented training by PI

https://upload.wikimedia.org/wikipedia/commons/5/5d/Downtown_Pittsburgh_from_Duquesne_Incline_in_the_morning.jpg
Lessons Learned: What is a Risk Assessment?

### Section 1: Natural Assessment Conclusion

**Proposed Title:** Standards of Performance Evaluation and Review

**FIPS Name:** Job Location: **TBD**

**Project Name:** Design and Leverage: **TBD**

**Leads:**
- **Title:** Manager of Environmental Health
- **Email:** Email Address
- **Phone:** 312-222-3210

**Animal Species Used:**
- **Species:** Rodents

**Implementation Review Required:** Yes

**Required Participants:** N/A

**NOTE:** For Implementation Review to be successful, the PI must submit the appropriate documents (GSL, HSL, Radiation Safety) by the annual deadline. If not submitted, a meeting plan is required. Failure to perform this notification may result in other actions to protect individuals.

### Summary

- **Description:** The Risk Assessment is a systematic process for identifying and evaluating potential hazards to human health and the environment.

### Use of Agents in Summary

- **Species:** Rodents
- **Description:** The Risk Assessment is a systematic process for identifying and evaluating potential hazards to human health and the environment.

### Section 2: Use of Biological Agents

**Agent:**
- **Name:**
- **Species:** Rodents
- **Description:** The Risk Assessment is a systematic process for identifying and evaluating potential hazards to human health and the environment.

### Section 3: Use of Chemical Agents

**Agent:**
- **Name:**
- **Species:** Rodents
- **Description:** The Risk Assessment is a systematic process for identifying and evaluating potential hazards to human health and the environment.

### Notes

- **Notes:**
  - The Risk Assessment is a systematic process for identifying and evaluating potential hazards to human health and the environment.
  - Failure to perform this notification may result in other actions to protect individuals.

*For additional information, please visit the University’s website.*
### Lessons Learned: What is a Risk Assessment?

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<th>Title</th>
<th>Description</th>
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<td>11: Hazard Assessment</td>
<td>Overview</td>
<td>Introduces the concept of risk assessment and its importance.</td>
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**University of Pittsburgh Department of Environmental Health and Safety**

http://kitegy.com/
Lessons Learned: A good investment

• Conversations with researchers and peer review committees are worth the time in the long run
  – Demonstrate that you are a resource
Lessons Learned: A good investment

- Conversations with researchers and peer review committees are worth the time in the long run
  - Demonstrate that you are a resource
Lessons Learned: What other risks should be considered?

• Take time to evaluate and communicate non-traditional risks
Acknowledgements

Environmental Health and Safety:
Rebecca Lingenfelter, MPH, Associate Biosafety Officer
Katy Board, MS, RBL Biosafety Officer and ARO
Jay Frerotte, MBA, Director and RO