Occupational Health Issues in Biological Laboratories

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Objectives

- Differentiate the appropriate medical surveillance requirements as they relate to the biosafety levels.
- Understand the need for a risk assessment to identify hazards in the laboratories that include working with animals and biological agents.
- Identify the appropriate post exposure prophylactics for optimal treatment outcomes and vaccines.
Why do we care about Biosafety?

Some unfortunate examples of disease outbreaks in research labs:

- SARS infects researchers in a lab in Singapore
- A US and a Russian scientist are infected by Ebola. One survives, one dies
- Polio virus escapes from two Indian labs
- Primate Lab – Herpes B exposure and death
- Anthrax exposure in a Houston lab due to aerosols leaked inside an unshielded centrifuge
- April 2012 death of lab employee in San Francisco working with *Neisseria meningitidis*, serotype B

Definitions to Remember

- **Biohazard**: An agent of biological origin that has the capacity to produce deleterious effects on humans, i.e. microorganisms, toxins and allergens derived from those organisms; and allergens and toxins derived from higher plants and animals.

- **Biosafety**: The containment principles, technologies and practices that are implemented to prevent the unintentional exposure to pathogens and toxins, or their accidental release.

- **Biosecurity**: Control of accidental and deliberate release of biohazardous material.
Pathogen Risk Assessment

- Pathogenicity/infectivity
- Virulence/lethality
- Infective dose
- Mode of transmission
- Resistance
- Therapy/Prophylaxes
- Survival in the environment
- Epidemic potential
- Geographic spread (endemic)

WHO Risk Group 1 & 2

**WHO Risk Group 1**
No or low individual and community risk

- A microorganism that is unlikely to cause human disease or animal disease. i.e. e. coli, animal cell lines

**WHO Risk Group 2**
Moderate individual risk, low community risk

- A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment.
- Laboratory exposures may cause serious infection, but effective treatment and preventative measures are available and the risk of spread of infection is limited. i.e. salmonella
WHO Risk Group 3 & 4

WHO Risk Group 3
High individual risk, low community risk
- A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another.
- Effective treatment and preventive measures are available. i.e. Francisella tularensis, Mtb

WHO Risk Group 4
High individual and community risk
- A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly.
- Effective treatment and preventive measures are not usually available. i.e. Marburg virus

Biosafety Levels
Biosafety Levels

<table>
<thead>
<tr>
<th>Agent Characteristics</th>
<th>Practices</th>
<th>Primary Barriers and Safety Equipment</th>
<th>Facility Design Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agents not known to consistently cause disease in healthy adults.</td>
<td>Standard Microbiological Practices Registration with IBC required for recombinant DNA work.</td>
<td>None required</td>
<td>Laboratory Bench and sink.</td>
</tr>
</tbody>
</table>
### Biosafety Level: 2

<table>
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<tr>
<td>Agents associated with human disease</td>
<td>BSL-1 practices plus limited access, biohazard warning signs, “sharps” handling, defined waste handling and medical surveillance policies.</td>
<td>Annually certified Class I or II BSCs or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infections materials.</td>
<td>BSL-1 plus autoclave access.</td>
</tr>
</tbody>
</table>

+ Routes of transmission include percutaneous injury, ingestion, mucous membrane exposure.  
+ Registration with IBC required for work with biohazard materials.  
+ Lab coats, impervious gloves, safety goggles and face shield as needed.

### Biosafety Level 3

<table>
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<th>Facility Design Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agents that are indigenous or exotic with potential for aerosol transmission, Disease poses serious or lethal consequences</td>
<td>BSL-2 practices plus controlled access, decontamination of all wastes, decontamination of lab clothing before laundering. Baseline serum measurements</td>
<td>Annually certified Class I or II BSCs or other physical containment devices used for all open manipulations of agents. Appropriate PPE to include impervious gloves and respiratory protection as needed.</td>
<td>BSL-2 plus physical separation from access corridors, self closing double door access. 10% of air with no circulation, laboratory under negative pressure.</td>
</tr>
</tbody>
</table>

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### Biosafety Level 4

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<thead>
<tr>
<th>Agent Characteristics</th>
<th>Practice</th>
<th>Primary Barriers and Safety Equipment</th>
<th>Facility Design Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dangerous exotic agents which pose high individual risk of aerosol-transmission. Laboratory infections are frequently fatal, for which there are no vaccines or treatments.</td>
<td>BSL-3 practices plus: Clothing change before entering; Shower on exit; All material decontaminated on exit from facility</td>
<td>All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body, air-supplied, positive pressure suit.</td>
<td>BSL-3 plus: Separate building or isolated zone; Dedicated supply and exhaust, vacuum; and decontamination systems</td>
</tr>
</tbody>
</table>
BSL Primary Barriers

BSL laboratories play a key role in the national effort to study, diagnose, treat, and ultimately prevent the spread of emerging and re-emerging infectious disease.

Meeting Regulatory Requirements

- Boston Public Health Commission
- OSHA®
- CDC
- National Institutes of Health
Hazardous and Potentially Hazardous Biological Agents

- Microorganisms which may cause disease in humans
- Microorganisms in human or non-human primate body fluids, tissues, or wastes (e.g., bloodborne pathogens)
- Bacterial, fungal, parasitic, chlamydial, rickettsial, viral, and prion disease agents
- Human or non-human cell culture (primary or continuous)
- Microorganisms in animals (e.g., zoonotic diseases)
- Items contaminated with animal or human body fluids, tissues, or wastes
- Plant and animal toxins
- Plant and animal allergens
Medical Surveillance: Programs and Components

Life Science Medical Surveillance Program

- Medical surveillance assessments programs:
  - Monitor the health status of employees who work in a hazardous setting.
  - Monitor the effectiveness of exposure prevention strategies.
Medical Surveillance Components

- Initial Medical History Questionnaire
- Focused physical Exam
- Health History
- Annual Medical History Questionnaire
- Additional Screening
- BSL 3 & 4 Specific Requirements
- Surveillance Card

Medical Surveillance Components

Initial Medical History Questionnaire

- Risk Assessment
  - BSL level
  - Animals contact
  - Biological agent
  - Other hazardous material; chemical, radioactive material, unfixed tissue, laser use

- Focused physical exam, if required.
Medical Surveillance

Health History

- Health History
  - Allergies and Respiratory system
    - Animal or environmental allergy
    - Asthma
    - Symptoms
  - Immune and Metabolic Systems
    - Diabetes
    - Heart disease
    - Immune system deficiencies
    - Seizure disorders
    - Medications

Medical Surveillance

Annual Surveillance Questionnaire

- Annual Health Status Questionnaire
  - Change in workplace exposure
  - Changes in health status, new medication
  - New onset of allergies
  - New vaccinations received
Medical Surveillance
Additional Screening

- Animal Allergy screening
  - Causative animals
  - Symptoms

- OSHA Respirator Questionnaire
  - Clearance for use of respiratory protection
    - N95
    - PAPR

Medical Surveillance
Additional Screening

- Obtain Laboratory testing, if needed
- Obtain Baseline serologies
  - TST or IGRA if working with NHP or M.Tb
- Reproductive hazard counseling
Medical Surveillance
BSL 3 & BSL 4

- Physical exam
- Psychological screening
- CBC w/ diff, Metabolic Panel, UA
- Audiometry and Vision Titmus testing
- Spirometry
- EKG
- Drug testing for NEIDL access
- Annually meets with clinician to review health history
  - May warrant additional testing

Medical Surveillance Card

- A Surveillance Card is provided for all laboratory workers.
- Workers are instructed to present this card to a Health Care provider in the event of an unexplained illness.
- Card contains medical contact information including the website where the Health Care provider can find information and treatment for biological agents listed on card.
Early Reporting:
Potential Exposures

The primary reasons to report a potential exposure immediately are to:

- Provide **optimal care** to the exposed worker
- Provide **strategic post exposure prophylaxis**
- Administer **vaccines**, if appropriate
- Analyze the **root cause** of the exposure
- Implement **appropriate surveillance**
Agent Information Sheets (AIS)

- Typical Agent Information Sheets provide the following details about an agent:
  - Description
  - Pathogenicity
  - Biosafety Information
  - Information for Lab Workers
  - Information for First Responders/Medical Personnel

- The following pages present a sample Yersinia Pestis Agent Information Sheet.
Agent Information Sheet

Agent:

Y. pestis causes a zoonotic disease of rodents and in humans can take the form of bubonic, septicemic or pneumonic plague.

Pathogenicity

Humans generally contract the disease through contact with infected rodents or their fleas.

Bubonic plague may occur 2-8 days after the bite of an infected flea with rapid onset of symptoms of high fever, severe malaise, headache, myalgias, and sometimes nausea and vomiting. Buboes (swollen and extremely painful infected lymph nodes) usually develop at the same time as symptoms are generally 1-10 cm in diameter. In natural infections these buboes usually develop in the femoral or inguinal lymph nodes because fleas generally bite on the legs. However a laboratory-acquired infection might be more likely to develop buboes in the cervical lymph nodes.

Septicemic plague occurs when the bacteria enters the bloodstream; it occurs in 10-20% of plague cases. This can occur with or without the formation of buboes. Without treatment septicemic plague is 100% fatal. With treatment there is a 30 to 50% survival rate.

Pneumonic plague occurs when the lungs become infected either from the bloodstream for from inhaling the bacteria. An infectious dose is 100 colony forming units. Patients with primary pneumonic plague develop symptoms within 1-4 days. Without treatment it is 100% fatal. When untreated there is a 60% mortality rate. Pneumonic plague is the only form of plague which is readily transmissible from person to person. From past plague epidemics the secondary infection rate is estimated to be 1.3 cases per primary case.

3. Biosafety Information
   a. Risk Group/BSL
      Risk Group 3
      Biosafety Level 3 Practices
   b. Modes of Transmission
      Handling infected tissues, airborne droplet, or manipulation of lab cultures
      
      | Transmission          |
      |-----------------------|
      | Skin Exposure (Needlestick, bite, or puncture) | Yes |
      | Mucous Membrane Splashing or Eye(s), Nose or Mouth | Yes |
      | Inhalation | Yes |
      | Ingestion | Unlikely |
   c. Host Range/Reservoir
      Wild rodents (rabbits, hares), and carnivores may be a source of infection to humans. Vectors include wild rodent fleas, especially the oriental rat flea (Xenopsylla cheopis), occasionally by human fleas (Pulex irritans)
   d. Symptoms
      Patients with bubonic plague present with local lymphadenitis with fever, chills, weakness, and headache. Septicemic patients can have bacterial blood stream infection leading to shock and death without necessarily presenting with buboes. With pneumonic plague, the first signs of illness are fever, headache, weakness, and rapidly developing pneumonia with shortness of breath, chest pain, cough, and sometimes bloody or watery sputum. The pneumonia progresses for 2 to 4 days and may cause respiratory failure and shock. Without early treatment, patients may die.
Agent Information Sheet
Biosafety Information (cont.)

ea. Incubation Period
   2 to 6 days, may be a few days longer in vaccinated individuals, for primary plague pneumonic, 1 to 6
days
f. Viability
   Susceptible to many disinfectants - 1% sodium hypochlorite, 70% ethanol, 2% gluteraldehyde, iodines,
   phenolics, formaldehyde. Sensitive to moist heat (121°C for at least 15 min) and dry heat (160-170°C
   for at least 1 hour)
g. Survival Outside Host
   Blood - 100 days; human bodies - up to 270 days

Agent Information Sheet

Information for Lab Workers

1. Laboratory PPE
   Gloves should be worn when handling field-collected or infected laboratory rodents and when there is the
   likelihood of direct skin contact with infectious materials; gown with tight cuffs and ties in back or the equivalent
   should be worn when manipulating cultures and specimens, a N95 should be worn when there is a risk of contact
   with aerosols.

2. Containment
   BSL-3/ABSL-3 practices, containment equipment, and facilities are recommended for all activities involving the
   handling of potentially infectious clinical materials and cultures. Additionally, all work including necropsies of
   potentially infected animals should be performed in a BSC with special care given to avoid the generation of
   aerosols.
   BSL-3 is recommended for activities with high potential for droplet aerosol production and for activities involving
   large-scale production or high concentrations of infectious materials.

3. Vaccination
   Previously formalin-killed vaccine, Plague Vaccine U.S.P., was available for use by persons who worked with
   Y. pestis in the laboratory setting. However, this was not protective against inhalation exposures and is no longer
   available. Research is underway for new vaccine targets. There is a vaccine available in other countries but not
   currently in the United States.
Agent Information Sheet

Information for First Responders/Medical Personnel

1. Public Health Issues
   Person-to-person transmission only occurs in pneumonic disease and generally with close contact or in patients with coughing spells and not through aerosolized particles or droplet nuclei. However, to prevent person-to-person transmission, patients with suspected pneumonic plague should be managed in isolation under respiratory droplet precautions. Respiratory droplet precautions include the use of fitted masks, gowns, gloves, and protective eyewear when providing direct patient care. Those without respiratory symptoms can be managed with standard precautions.
   Outside providers should call ROHP in case of either infection or exposure for further instructions.

2. Diagnostic/Surveillance
   Monitor for symptoms; organism can be isolated in blood or clinical specimen cultures-presumptive diagnosis is made by visualizing bipolar staining; avoid, gram-negative organisms in sputum or material aspirated from bubo; FA and ELISA test; PHA using Fraction-1 antigen.

Agent Information Sheet

Information for First Responders/Medical Personnel (cont.)

3. First Aid/Post Exposure Prophylaxis
   Doxycycline is the prophylactic agent of first choice, given in an adult dose of 100 mg twice daily for 7 days. Antibiotics can be used for chemoprophylaxis against plague in laboratory workers thought to have had an infective exposure within the previous 7 days. Alternative drug is Ciprofloxacin 500 mg BID or levofloxacin 500 mg daily for 7 days.
   Perform one of the following actions:

<table>
<thead>
<tr>
<th>Skin Exposure (Needlestick or scratch):</th>
<th>Immediately go to the sink and thoroughly wash the wound with soap and water for 15 minutes. Decontaminate any exposed skin surfaces with an antiseptic scrub solution.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucous Membrane</td>
<td>Exposure should be irrigated vigorously.</td>
</tr>
<tr>
<td>Splash to Eye(s), Nose or Mouth:</td>
<td></td>
</tr>
<tr>
<td>Splash Affecting Garmets:</td>
<td>Remove garments that may have become soiled or contaminated and place them in a double red plastic bag.</td>
</tr>
</tbody>
</table>

4. Treatment
   Antibiotic therapy in early stages (8 to 24 hours after onset of pneumonic plague); secondary infection or suppurative bubo may require incision and drainage. Gentamycin is the antibiotic of choice or doxycycline in patients who are aminoglycoside allergic. Chloramphenicol should be used in settings where high tissue penetration is required such as myocarditis, meningitis or sepsis.

5. References
   CDC: [http://www.cdc.gov/plague/transmission/index.html](http://www.cdc.gov/plague/transmission/index.html)
Herpes B Exposure

- A clinician and researcher at MEEI went to MGH with fever, HA, and rigors
- Reports:
  - Being scratched by a Macaque research monkey 9 days prior on the dorsum of L hand.
  - Washing the wound for few minutes but did not report the injury.
  - No neck pain, or difficulty with concentration.
- PE: Scar longitudinal between 3rd and 4th MC L hand 3 cm. Negative for vesicular lesions, erythema, signs of infection, or rashes
Herpes B Exposure (cont.)

Labs:
- LP's performed weekly with Herpes B negative on PCR
- Elevated WBC’s seen on CBC

Imaging:
- 2 MRI’s were normal

Treatment:
- Started on IV acyclovir and ganciclovir on presentation to the ED
- Completed a 4 week course of IV antivirals

Diagnosis:
- On week 3 LP again performed with PCR of CSF positive for Herpes B and Ab (+)
- Daily valacyclovir 1 gram for life

LCMV Exposure

- Researcher was injecting mice with concentrated LCMV
- Wearing PPE that included a Tyvek suit she dropped a syringe onto her right quadriiceps
- 7 days post exposure the researcher develops a low grade fever, muscle ache, fatigue for 5 days
- Sought treatment for her symptoms with her PCP, she did not report the incident or her work in a laboratory
LCMV Exposure (cont.)

- At PCP office CBC performed with WBC 2,500 with 70% lymphocytes no treatment given
- Reports 10 day post exposure to Occupational health with acute serum IgM, IgG
- Serology repeated 3 weeks later
- Acute serology IgM 1:1250, IgG1:512
- Convalescent serum IgM 1:256, IgG 1:1250 -- 3 weeks later

Neisseria meningitidis

- 25-year-old research associate at the Veterans Affairs (VA) Medical Center in San Francisco
- Working with serotype B, for which there is no current immunization
- Complained of headache and nausea with the onset of symptoms
- His condition deteriorated quickly, and he died 17 hours after his symptoms first appeared.
Summary

Safety in the workplace is a direct result of:

- Awareness of risk
  - Ask questions
  - Bring potential risk issues to PI
- Adherence to protocols
- Education regarding:
  - Agents in use
  - Vaccine availability
  - Prophylaxis
  - Timely post exposure treatment

Questions?
References

- Centers for Disease Control and Prevention: [www.cdc.gov](http://www.cdc.gov)