OVERVIEW

• REVIEW PATHOGEN ENTRY AND POSSIBLE DESTINATIONS IN HOST

• GIVE EXAMPLES OF KNOWN, PROBABLE AND POSSIBLE LAI EXPOSURE ROUTES

• PROVIDE INFORMATION FOR EXPANDED RISK AWARENESS DISCUSSION WITH THOSE EXPOSED TO BIOHAZARDS

• INSPIRED BY ABSA MEMBERS
LAB ACQUIRED INFECTIONS 1930 -2015

• 1930 – 2015
• 7,325 LAIS (SYMPTOMATIC AND ASYMPTOMATIC)
• 210 FATAL LAI’S
  • SULKIN SE, PIKE RM. SURVEY OF LABORATORY-ACQUIRED INFECTIONS. AM J PUB HLTH. 1951; 41: 769-81.

WHAT IS KNOWN ABOUT EXPOSURE ROUTES?

Percutaneous  Facial Mucous Membranes  Ingestion

Inhalation  *Contact

*Contact involves self-inoculation through one of the known exposure routes
REVIEW OF LABORATORY INFECTIONS: IMPORTANT MESSAGES

- **80%** of the published laboratory acquired infections linked to an **unknown route of exposure**.
  - Aerosols most likely associated with unknown infections
  - Dr. Edward Sulkin & Dr. Robert Pike

GOLDEN AGE OF BIOSAFETY (1949 – 1979)

There can be **unnatural routes of exposure** in the laboratory setting that are generally not seen in nature.

(Sulkin 1960)
Infections with unidentified route of exposure

Non-traditional exposure route

**NON-TRADITIONAL EXPOSURE ROUTES**

GI Pathogens: Salmonella, Listeria, Shigella, Campylobacter, E. coli, etc.

NON-TRADITIONAL EXPOSURE ROUTES

GI Pathogens: Salmonella, Listeria, Shigella, Campylobacter, E. coli, etc.

Aerosol → Nasal mucociliary escalator → Throat → Gut

Aerosol → Tracheo-bronchial mucociliary escalator → Throat → Gut

NON-TRADITIONAL EXPOSURE ROUTES

West Nile Virus, Yellow Fever Virus, Rabies Virus, Influenza Virus, Neisseria meningitidis, Streptococcus pneumoniae

Aerosol → Nasal Cavity → Cranial Nerves → Brain
NON-TRADITIONAL EXPOSURE ROUTES
West Nile Virus, Yellow Fever Virus, Rabies Virus, Neisseria meningitidis, Sabia Virus, EEE, WEE, VEE

Aerosol  Lower Lung  Blood stream

Thomas, R.J., “Particle Size and Pathogenicity in the Respiratory Tract.” Virulence 4:8, 847-858; November 15, 2013.

RECOGNIZED VS. UNRECOGNIZED EXPOSURES:
PEOPLE REPORT WHAT THEY CAN “FEEL”

Feel splashes/splatter to face or skin
Feel needle sticks, lacerations, punctures, cuts, etc.
WHAT YOU CAN'T FEEL IS (PROBABLY) NOT REPORTED?

Ingestion

Inhalation

May also not feel exposure through micro-abrasions

GOLDEN AGE OF BIOSAFETY (1949 – 1979)

THE LABORATORY CAN BE MORE DANGEROUS THAN NATURE DUE TO THE ABILITY TO AMPLIFY AND CONCENTRATE PATHOGENS TO LEVELS NOT SEEN IN NATURE. ALSO, THE GROWTH AND PROPAGATION OF INFECTIOUS AGENTS IN LABORATORY SETTINGS ARE CONDUCTED REPEATEDLY WITHIN THE LABORATORY AS PART OF THE RESEARCH EFFORT, ENHANCING THE POTENTIAL EXPOSURE.

(LANGMUIR 1960)
UNKNOWN BIOHAZARDS

WHY A CONSISTENT APPLICATION OF GOOD MICROBIOLOGICAL PRACTICES IS CRITICAL

- NEW PATHOGENS (MIMIVIRUS)
- OUTBREAK PATHOGEN STRAINS (E.COLI 0157:H7)
- FIRST "REPORT" OF INFECTION IN HUMANS WITH EXISTING PATHOGEN (KEYSTONE VIRUS 2018 FLORIDA)
- MORBIDITY NEWLY RECOGNIZED IN AN EXISTING MICROORGANISM (MERKEL POLYOMA VIRUS)
- INTRODUCTION OF BIOHAZARDS TO LOW RISK LABS (TRANSFERRIN, MYCOPLASMA, VIRUS IN TISSUES)
- VETERINARY RISKS (VET SCHOOL, CLINICS, FIELD SETTINGS – CRYPTOSPORIDIUM INFECTIONS)
- NON-PATHOGENIC MICROBES ASSISTING WITH PATHOGENICITY OR SPREAD OF DISEASE (FUSOBACTERIUM NUCLEATUM)
- WHEN GOOD GENES GET INTO BAD PLACES (DR. GARY FUJIMOTO)

REFERENCES

GOLDEN AGE OF BIOSAFETY
(1949 – 1979)

The majority of laboratory procedures have the potential to generate aerosols in the size range that can remain suspended in air and also reach the lower lung, where they can either be inhaled and cause infection or enter the bloodstream via the alveoli and cause infection in another location of the body.

(Reitman and Wedum 1956 and Kenney and Sabel 1968)

ROUTE OF EXPOSURE TREES

INHALATION

- Facial mucous membranes
- Cranial nerves from nose to brain
- Mucociliary escalators - gut

INHALATION

- Lung (Epithelial cells, other)
- Blood (alveoli, lymphatic system)
- Contact (from contaminated surfaces)
GOLDEN AGE OF BIOSAFETY
(1949 – 1979)

FROM DR. ARNOLD G. WEDUM, CONSIDERED THE “FATHER OF BIOLOGICAL SAFETY” IN THE U.S., WE LEARN THE IMPORTANCE OF “CONFINING AEROSOLS AS CLOSE AS POSSIBLE TO THEIR POINT OF GENERATION.”
(WEDUM 1960)

NASAL CAVITY TO BRAIN VIA CRANIAL NERVES

INFLUENZA A VIRUS, HERPES VIRUSES, POLIOVIRUS, PARAMYXOVIRUSES, VESICULAR STOMATITIS VIRUS, RABIES VIRUS, PARAINFLUENZA VIRUS, ADENOVIRUSES, JAPANESE ENCEPHALITIS VIRUS, WEST NILE VIRUS, CHIKUNGUNYA VIRUS, LACROSSE VIRUS, Bunyaviruses, Streptococcus pneumoniae, Neisseria meningitidis, Burkholderia pseudomallei, Listeria monocytogenes, Lymphocytic CHORIOMENINGITIS VIRUS, Naegleria Fowleri, EEE, VEE, WEE

INGESTION

• DR. THOMAS HAMM (PLEA TO NHP STAFF NOT WEARING GOGGLES: “S_IT EATERS”)
• NASAL LACRIMAL DUCT
• MUCOCILIARY ESCALATORS
  • NASOPHARYNGEAL
  • TRACHEAL BRONCHIAL

• 3 WAYS YOU CAN INGEST A PATHOGEN

ROUTE OF EXPOSURE TREES

INGESTION

VIA EATING, DRINKING OR CONTACT

VIA NASAL LACRIMAL DUCT

VIA MUCOCILIARY ESCALATOR
INGESTION LIKELY UNRECOGNIZED

• NOT COGNIZANT OF HAND TO FACE CONTACT
• POOR WORK PRACTICES IN SHALLOW WATER (JIM WELCH)
• LACK OF RECOGNITION OF POSSIBLE ROLE OF AEROSOLS FROM CONTAMINATION TO HOST ENTRY
• CAN’T “FEEL” THE EXPOSURE
• COMPETING RISKS OUTSIDE OF LAB
  • CDC: 48 MILLION FOODBORNE ILLNESSES ANNUALLY
  • MANY SELF MEDICATE AND DON’T REPORT
  • OVER 250 FOODBORNE PATHOGENS

ROUTE OF EXPOSURE TREES

Facial Mucous Membranes

- Blood, Lymph
- CRANIAL NERVES - FROM NOSE TO BRAIN
- GUT (from eye, nose or mouth)
**HAND TO FACE CONTACT (HFC) ARTICLE**

- 72% of researchers touched face at least once
- Average of 2.6 HFCs/hr
- HFC found “common” among BSL-2 lab workers
- Possibly an overlooked route of exposure for unknown LAIs


**ROUTE OF EXPOSURE TREES**

- Skin (Local infections)
- Blood stream
- Facial mucous membranes

Percutaneous
PERCUTANEOUS EXPOSURES

Needle sticks, lacerations, punctures, bites

Unhealed wounds

Breaks in skin, cuticles, poison ivy, eczema, dermatitis

Acne, other micro-abrasions

GLOVE - LEAK RATE - FACTS

<table>
<thead>
<tr>
<th>Glove Leak Rates</th>
<th>Exam Gloves</th>
<th>Surgical Gloves</th>
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</thead>
<tbody>
<tr>
<td>Before Use (FDA)</td>
<td>2.5%</td>
<td>1.5%</td>
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<tr>
<td>After Use</td>
<td>*21 – 35%</td>
<td><strong>15.2%</strong></td>
</tr>
</tbody>
</table>

**Double gloving: leak rates for inner gloves when double gloved - 1.17% (98.83% Effective!)

*Boyle, B & Boyle, T, “Loss of Glove Integrity During Laboratory Animal Care Providers Daily Tasks,” Lenape Regional High School, Medford NJ, Science Fair Poster Presentation, 2017

## BIOSAFETY FOUNDATION GAME

<table>
<thead>
<tr>
<th></th>
<th>Don’t eat, drink or smoke</th>
<th>Confine Aerosols</th>
<th>Eliminate or work safely with sharps</th>
<th>No mouth pipetting</th>
<th>Disinfection</th>
<th>Wear PPE</th>
<th>Wash Hands</th>
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<tr>
<td><strong>Inhalation</strong></td>
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<td><strong>Mucous Membranes</strong></td>
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## HOW RESEARCHERS TYPICALLY ANSWER

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<tr>
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MISCONCEPTIONS (OR MISINFORMATION)?

• MY GOWN WON’T PROTECT ME, I ONLY HAVE TO WORRY ABOUT SHARPS.”
• I CAN’T GET INFECTED WITH SALMONELLA FROM FACIAL CONTACT
• VIBRIO CHOLERAE SHOULD NOT BE CLASSIFIED AS A HUMAN PATHOGEN IN THE USA (WE CAN TREAT IT)
• I’M WORKING WITH ATTENUATED VACCINIA, SO I DON’T NEED AN IMMUNIZATION. MY FIRST EXPOSURE WILL BE MY IMMUNIZATION.
• I DON’T NEED EYE PROTECTION: I’M USING A BIOSAFETY CABINET; I’M ONLY WORKING WITH GI PATHOGENS; I’M ONLY WORKING WITH SMALL VOLUMES OF LIQUIDS

EXPECTED RESPONSES

<table>
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### FOUNDATION GAME AUGMENTED

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### SUMMARY

- ROUTES OF EXPOSURE HAVE NOT CHANGED
- CONTROLLING BIOHAZARDS REMAINS THE AIM
- GOOD MICROBIOLOGICAL WORK PRACTICES WILL HELP PREVENT EXPOSURES
- THE IMMUNE SYSTEM IS DIVINE, EXCEPT WHEN IT’S NOT
- CONSIDER THE PROBABLE, POSSIBLE AND UNRECOGNIZED EXPOSURE ROUTES IN RISK ASSESSMENT AND BIOSAFETY TRAINING (ALONG WITH THE KNOWN EXPOSURE ROUTES AND SIGNS & SYMPTOMS OF DISEASE)
- ADDRESS LABORATORIAN MISCONCEPTIONS WITH FACTS
"WE ARE ALL THE SAME"

"Do what you can;
With what you have;
In the place that you are;
In the time that you have"

Nkosi Johnson
"We Are All The Same" by James Wooten

REFERENCES


• CENTERS FOR DISEASE CONTROL. 1977. RABIES IN A LABORATORY WORKER, NEW YORK. MMWR 26(22): 183-184


REFERENCES


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• SULKIN SE, PIKE RM. SURVEY OF LABORATORY-ACQUIRED INFECTIONS. AM J PUB HLTH. 1951; 41: 769-81.
REFERENCES


• THOMAS, R.J., "PARTICLE SIZE AND PATHOGENICITY IN THE RESPIRATORY TRACT." VIRULENCE 4:8, 847-858; NOVEMBER 15, 2013.


## Overview of a few Laboratory Acquired Infections (LAIs)

**Benjamin Fontes, CBSP, MPH – Yale University EHS**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Exposure Route</th>
<th>Notable impact</th>
<th>Factors</th>
<th>Risk Assessment or Risk Management failures</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmonella typhimurium</td>
<td>U ING</td>
<td>SO</td>
<td>NASS, IBOA, PWP</td>
<td>1, 2, 3, 4, 5, 6</td>
<td>1, 2, 3, 4, 5, 6</td>
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<tr>
<td>Salmonella typhimurium</td>
<td>U ING</td>
<td>SO, F</td>
<td>NASS, IBOA, PWP</td>
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<td>Salmonella typhimurium</td>
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<tr>
<td>Lassa Fever virus</td>
<td>U AER-L</td>
<td>SI, F</td>
<td>NASS, IBOA, PWP</td>
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<tr>
<td>Rabies virus</td>
<td>U AER-L, AER-MM</td>
<td>F</td>
<td>PWP</td>
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<tr>
<td>Rabies virus</td>
<td>U AER-L, AER-MM</td>
<td>F</td>
<td>PWP</td>
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<td>Neisseria meningitidis</td>
<td>U AER-L</td>
<td>F</td>
<td>NASS, PWP, NIMM</td>
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<tr>
<td>Yersinia pestis (attenuated)</td>
<td>U AER-L</td>
<td>F</td>
<td>NASS, PWP</td>
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<td>Sabia virus</td>
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<td>NASS, PWP</td>
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<tr>
<td>Salmonella typhi and S. agona</td>
<td>U ING</td>
<td>SO, F</td>
<td>IBOA, PWP</td>
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<tr>
<td>Hepatitis B virus</td>
<td>U SK</td>
<td>F</td>
<td>PWP, NIMM</td>
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<td>Bacillus cereus</td>
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<td>SI</td>
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<tr>
<td>Pathogen</td>
<td>Storage</td>
<td>Test</td>
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<td>Numbers</td>
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<td>Shigella sonnei</td>
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<td>SARS-CoV</td>
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<td>Macacine Herpesvirus 1 (B-virus)</td>
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<td>Vaccinia virus VA</td>
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<td>Shigella dysenteriae</td>
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<td>HIV</td>
<td>SK</td>
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<td>IBOA, PWP</td>
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<td>HIV &amp; Hepatitis C virus</td>
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<td>Multiple F</td>
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<td>Borrelia burgdorferi</td>
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<td>Brucella Melitensis</td>
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<td>Cryptosporidium parvum</td>
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**TABLE Legend**
Quick Overview of the 6 P's of Risk Assessment and Risk Management

1-Pathogen
Policy that requires registration for possession, use, storage and transfer of biohazards and regulated biological materials including human pathogens. The PI and the IBC must conduct a formal risk assessment of the proposed research with biohazards and a review also of the standard operating procedures developed to work safely with the biohazard.

2-Procedures
Identify all of the proposed procedures, supplies and equipment that will be used in the protocol and ensure that this is part of the risk assessment review and assignment of the final biocontainment level and SOPs created for the work. All procedures and all work locations, including animal experiments must be part of this review. Evaluation of sharps risks, aerosol risks, splash and splatter containment, etc. and the commensurate containment needed is part of this process.

3-Personnel
A medical surveillance review is required to determine what pre- and post-exposure prophylaxis may be indicated, a review of the signs and symptoms of disease caused by the biohazard and all clinical manifestations must be completed with all involved in the project (researchers to animal handlers, etc.) The PI and IBC must also ensure that all involved have relevant work experience, training, education, awareness and comfort for the proposed research. If needed a competency work practice evaluation should be conducted. Researchers must be reminded to not work with breaks in the skin, to have changes in their health evaluated and to report any potentially related symptoms or illnesses to Occupational Health.
4-Practices
The work practices that will be used as part of the SOP to work safely and contain the pathogen must be developed, reviewed and approved by the IBC. These SOPs should be part of the institution’s overall Biosafety Manual to create a site-specific biosafety manual. Some registration forms can guide the PI to develop site-specific work practices.

5-Protective Equipment
This part of the Risk Management side of Biorisk Management involves personal protective clothing and equipment and the use of engineering controls. Individuals require training on the use of both. Both must be evaluated to ensure that they are present, adequate, in good condition and used appropriately.

6-Place
Facility or lab design is the final part of the Risk Management side and this is the required evaluation by the IBC and Biosafety Officer to ensure that all work locations are appropriate for the proposed research. High traffic areas, large open areas, directional airflow and labs that open directly to public access corridors are some of the factors that must be critically evaluated to ensure that the proposed research will not lead to high risk situations for those performing the work and those outside the lab.
<table>
<thead>
<tr>
<th>Pathogen LAI</th>
<th>Reference</th>
</tr>
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</table>
[https://www.cdc.gov/salmonella/typhimurium-labs-06-14/index.html](https://www.cdc.gov/salmonella/typhimurium-labs-06-14/index.html)  
[https://www.cdc.gov/salmonella/typhimurium-07-17/index.html](https://www.cdc.gov/salmonella/typhimurium-07-17/index.html) |
[https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6335a2.htm](https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6335a2.htm) |
<p>| Yersinia pestis 2009 | <a href="https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6007a1.htm">https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6007a1.htm</a> |
| Salmonella agona, Salmonella typhi, 1980 | <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC273903/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC273903/</a> |
| Hepatitis B virus, 1985 | Personal communication in Clinical Chemistry laboratory |
| Shigella sonnei, 1996 | <a href="http://jcm.asm.org/content/35/12/3163.full.pdf">http://jcm.asm.org/content/35/12/3163.full.pdf</a> |
| Macacine Herpesvirus | <a href="https://www.cdc.gov/mmwr/preview/mmwrhtml/00056008.htm">https://www.cdc.gov/mmwr/preview/mmwrhtml/00056008.htm</a> |</p>
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<th>Year</th>
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<td>1, 1997</td>
<td>Dengue infection, 2014</td>
<td><a href="https://my.absa.org/LAI">https://my.absa.org/LAI</a></td>
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<td>Vaccinia virus, CT VA Hospital, 2005</td>
<td><a href="https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5715a3.htm">https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5715a3.htm</a></td>
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<td>Vaccinia virus, PA, 2004</td>
<td><a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3291406/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3291406/</a></td>
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<td>Vaccinia virus, VA, 2008</td>
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<td>Shigella dysenteriae, 1996</td>
<td><a href="https://jamanetwork.com/journals/jama/fullarticle/417894">https://jamanetwork.com/journals/jama/fullarticle/417894</a></td>
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<td>Borrelia burgdorferi 1996</td>
<td>Personal communication, bite of infected nymph tick</td>
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