Laboratory-Acquired Infections in Research Settings: Published Reports as Sources of Preventive Strategies

New England Biosafety Association Symposium
Broad Institute, Cambridge MA
September 17, 2013

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LAI: what do we know?

Limitations in our data:

- No national reporting system for LAI, except for work with BSAT.
- Data useful for preventive measures is usually missing from media reports.

Scientific literature:

Pike and Sulkin: survey sent to 4,000 labs of various types: approx. 50% response. Reported: 4,079 laboratory-acquired infections from 1935 to 1978.

- 14% were from clinical laboratories
- 59% research laboratories

Harding and Byers: literature survey of LAIs from 1979-2005: 1,141 LAI and 24 deaths.

- 46% were from clinical laboratories.
- 50% were from research laboratories

Byers and Harding- working on update. 2033 LAI and 37 deaths...and counting.
Monitoring Select Agent Theft, Loss and Release Reports in the United States - 2004-2010

- 11 LAI with BSAT
- 10,000 individuals with access.
- No fatalities
- No secondary infections.

_Applied Biosafety_ 2012. 17(4) 171-180.
Laboratory-acquired infections caused by BSAT’s 2004-2010

<table>
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<tr>
<th>Year</th>
<th>Agent</th>
<th>#cases</th>
<th>Entity type</th>
<th>Lab Type</th>
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<td>2004</td>
<td><em>Brucella melitensis</em></td>
<td>1</td>
<td>Registered</td>
<td>BSL2</td>
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<tr>
<td>2004</td>
<td><em>Coccidiodes</em> sp.</td>
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<td><em>Francisella tularensis</em></td>
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<td>Exempt</td>
<td>BSL2</td>
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<tr>
<td>2010</td>
<td><em>Brucella suis</em></td>
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<td>Exempt</td>
<td>BSL2</td>
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</table>

*Applied Biosafety. 2012. 17(4) 171-180*
BSAT program - Anthrax Incident at USAMRIID

Researcher #1- set up culture (250 ml in 2-liter flask, loose screw cap covered with paper towels and gauze) placed on shaker.

Researcher #2- removed flasks from shaker, placed on cart, brought to BSC. Noticed dried media at top of flasks.

Researcher #1- opened flask–also noticed dried media stains on stopper, screw top, and neck of flask when discarding OUTSIDE the BSC.

PPE on both: scrubs, gloves – no respiratory protection. Reported incident.

• Considered low risk exposure, since researchers were immunized, but nose and throat swabs were taken.

• Positive throat culture from researcher who threw the contaminated paper towel in the trash outside the BSC. Both went on antibiotics.

Follow-up: respirators, flask inspection prior to removal from incubator, filtered flask stoppers.
F. tularensis Exposure

- Attributed to disposal of waste materials outside of bsc.
- Not immunized (she had some natural antibodies).
- USAMRIID requires PAPR if staff are not immunized – wore only “mask”.
- Did not receive antibiotics promptly, reported to routine health center, not occ. health, at peak of flu season.

http://www.fredericknewspost.com/archive/article 5e4539ea-7902-5b13-8d37-8c37-8c7b6ade7
USAMRIID *F. tularensis* Incident Follow-up

In-lab cameras were installed in all BSL3 and BSL4 laboratories between 2004-2007.
Strain Verification Mishap

- **Boston, MA.** Staff thought they were manipulating avirulent *F. tularensis* in a vaccine development study.

- 3 cases of pneumonia in lab staff were tularemia infections.

- Inadvertently handled virulent *F. tularensis*; the source was a stock culture cross-contaminated with a virulent strain.

http://www.bphc.org/programs/cib/environmentalhealth/biologicalsafety/Pages/Home.aspx
Laboratory-related orthopoxvirus exposures reported to CDC for assistance with medical response: 2005–2008

<table>
<thead>
<tr>
<th>#</th>
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<th>strain</th>
<th>incident</th>
<th>infection?</th>
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<tbody>
<tr>
<td>8</td>
<td>7-no 1-?</td>
<td>recombinant Western reserve</td>
<td>6 needlesticks, 2 eyesplashes</td>
<td>Yes -6 needlesticks No- 2 eyesplashes</td>
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<tr>
<td>5</td>
<td>2-yes 2-??</td>
<td>not known</td>
<td>2 animal care, 1 eyesplash, 1 tube leakage</td>
<td>No</td>
</tr>
<tr>
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<td>yes</td>
<td>monkeypox</td>
<td>1 needlestick</td>
<td>No</td>
</tr>
<tr>
<td>1</td>
<td>yes</td>
<td>rabbitpox</td>
<td>1 eyesplash</td>
<td>No</td>
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<tr>
<td>1</td>
<td>no</td>
<td>NYCBOH</td>
<td>1 eyesplash</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Case Report: Ocular Vaccinia Infection in Laboratory Worker, Philadelphia, 2004

http://www.cdc.gov/ncidod/eid/vol12no01/05-1126.htm
“Staff infrequently wore eye protection while performing experiments with vaccinia. Laboratory coat sleeves were not elasticized and did not always cover the wrist.”

“At one point in this experiment, a 96-well plate containing small amounts of vaccinia–infected mammalian cells was removed from the biosafety cabinet and hand-carried to another room, where the lid of the plate was removed, and the cells were examined for fluorescence.

The student did not wear eye protection during this phase of the experiment; whether she wore gloves is unclear.”

http://www.cdc.gov/ncidod/eid/vol12no01/05-1126.htm
Ocular Vaccinia LAI: Lapse in use of BSC

• “Laboratory staff routinely vortexed tubes containing live virus outside of the biosafety cabinet.”
• “Instances occurred in which samples with low titers of live virus were removed from the biosafety cabinet, transported to other parts of the facility, and manipulated.”
• “Waste pipettes were not disinfected before removal from the biosafety cabinet.”

http://www.cdc.gov/ncidod/eid/vol12no01/05-1126.htm
Lab had not worked with it in 5 years.

Student working in a research laboratory with a non-Orthopoxvirus Chordopoxvirus (NOC) that does not infect humans. No current work in the lab with vaccinia or cowpox; student declined vaccination.

Student developed a lesion on finger on right hand in July, 2010. Looked like vaccinia; occ. health remembered immunizing some former lab members. Student said it wasn’t in use.

Mice injected with NOC in July - no incident - PPE worn in animal facility - 4 out of 5 developed “unanticipated” lesions – bumps with central area of necrosis.

Where did the cowpox come from?

- Brighton strain of cowpox not used for 5 years.
- Shared freezer with cowpox and NOC
- All staff had access to it – some boxes had NOC and cowpox.
- “Labels difficult to read with frost”.
- Cowpox DNA contaminated viral stocks. (Not grown by LAI).
- 15% of environment swabs positive for cowpox DNA -pipettors, freezer handle, inside & outside of freezer boxes.
Biosafety Practices in the NOC Lab

• PPE use in the lab: labcoats (rarely).
• Gloves only when working in BSC, but contaminated gloves moved in and out.
• Gloves not always worn when moving live virus or cell culture to incubator or freezer.
• Gloves very painful and difficult to wear once lesion and swelling developed in LAI.
• In animal facility, complied with ABL2 PPE and disposed of in animal room.
Hindsight is 20-20

- Student used NOC stock contaminated with cowpox in laboratory work and used it to inject mice.
- Luckily, there were no individuals in the lab at increased risk for severe complications (immunocompromised, eczema, pregnancy).
- CDC contacted in October. Serum and biopsy samples analyzed. Hemagglutinin of LAI virus sequenced - identified as Brighton strain of cowpox.
LAIs with *N. meningitidis*

- 2 reports in 2000: **MMWR 51**(07):141-144.
- Isolated approx. 3,000x/year in the US.

- CDC sent query to professional organizations to inquire about laboratory-acquired infections.

N. Meningitidis LAIs

• 16 cases of probable laboratory-acquired meningococcal disease occurring worldwide between 1985 and 2001 were identified, including six U.S. cases between 1996 and 2000.

• Nine cases (56%) were serogroup B; seven (44%) were serogroup C.

• Eight cases (50%) were fatal. All cases occurred among clinical microbiologists.

• 50% fatality rate for LAI compared to community fatality rate of 10%.

Sevjar, 2005. J. Clin Micro. 43(9) 4811
Another LAI with *N. meningitidis*

OSHA report on meningitis fatality in San Francisco laboratory worker. There is no vaccine for the serotype B, which caused the fatal infection, but violations were issued due to failure to:

1) require work with live pathogen in the biosafety cabinet,
2) provide training on the signs and symptoms of disease so that medical attention can be received promptly,
3) provide available vaccine to laboratory staff.

Clinical Laboratory Procedures...bench or BSC?

CDC advice:

START in the biosafety cabinet with cultures from sterile sites — Blood, cerebrospinal fluid, inner ear.

Biosafety Cabinet for culture of sterile sites: blood, CSF, inner ear.

CDC NPHL image #8406, CDC Meningitis and Special Pathogens Branch
- Experience is **not** necessarily a factor
- Working on the open bench **is** a factor

**Experience of infected staff varies:**

- 1 fatality - first isolate in that lab in 4 years.
- 1 fatality - state lab worker who worked with approx. 4 isolates/month.

LAI with *N. meningitidis*:
DROPLET Transmission

43 cases of LAI *N. meningitidis* in literature—

- **ONLY** 1 microbiologist infected
- 40 worked on the open bench (catalase assays, made suspensions, etc.) 2 worked behind a plastic shield; 1 in a defective biosafety cabinet.
- None were immunized.
- **Immunization** recommended — decreases risk of A, C, Y and W-135 (not B).
SARS-BSL3: lesson in validation of inactivation conditions
SARS-BSL3 lesson: Require verification of inactivation

• BAD NEWS: 5/18/2004
  – Biosafety Level 2 laboratory in Beijing, China, analyzed SARS samples inadequately inactivated before removal from BL3 lab.

• WORSE NEWS:
  – Exposure resulted in:
    • 2 laboratory-acquired infections,
    • 2 secondary infections (mother, nurse)
    • 5 tertiary infections.
    • One secondary infection was fatal.
SARS-BSL3 lesson: Require verification of inactivation

Modified image from: http://www.wpro.who.int/sars/docs/update/update_07022004.asp
Is inactivated infectious material coming into the facility?

Case study: BAD NEWS

6/10/2003- 5 to 7 lab workers in Oakland, CA, handled “inactivated” anthrax— that was viable.

GOOD NEWS: No one infected.

CDC MMWR (2005) 54(12):301.
1979-2004 literature survey:

**Zoonotic infections:** 171 overt infections with 2 fatalities
144 seroconversions.

Compare with: infections from experimentally infected animals:
11 symptomatic, no asymptomatic.

Harding and Byers, 2006. Epidemiology of Laboratory-acquired infections. in *Biological Safety, Principles and Practices*, 4th Ed. ASM Press
Q fever:
• 177 symptomatic and 1 death

ADD:
• 3 asymptomatic in 2006

Orf:
• 2 incidences

www.cdc.gov/.../classic_orf_finger.htm
Wild Rat and Mouse Zoonoses: 1979-2004

Hantavirus: 155

Belgium (Desmyter, 1983)

France (Dournon, 1984)

Japan (Kawamata, 1987; Umenai, 1979)

United Kingdom (Lloyd, 1984; Lloyd & Jones, 1986)

Singapore (Wong, 1988)

Mouse: 8 LCMV (Dykewicz, 1992)

1 LCMV (Braun, 2004)
LAI via Research Procedure: Sonication

- Researcher followed published procedure for isolation and purification of proteins from *Orientia (Rickettsia) tsutsugamushi*.
- No biosafety precautions were listed in the publication.
- Infected cells were disrupted with a grinder and the rickettsial membranes broken up with a sonicator on the open bench, even though a biosafety cabinet was present in the laboratory.
"We report a case of scrub typhus pneumononitis in a laboratory worker who apparently acquired it through the respiratory tract. The patient was suffering from fever, cough and dyspnea. He had both cervical and axillary lymphadenopathy, and hepatomegaly. A chest X-ray showed interstitial infiltrates. A diagnosis of scrub typhus was established upon isolation of *Orientia tsutsugamushi*"
LAI from Sonication of *C. trachomatis*

2 out of 5 lab staff working with *Chlamydia trachomatis* were hospitalized despite the fact that biosafety had arranged for access to a BSL3 facility.

Problem: sonication occurred in hallway outside BSL3.


Lab worker sonicated uv inactivated *C. trachomatis* for 2 years without incident.

- UV step eliminated; procedure continued until staff member hospitalized 2 months later.
- Infectious disease physician hospitalized 3 days after sonicating *C. trachomatis* on the open bench.

Sonication for Enzyme Studies

• Lab tech routinely sonicated gram-negative clinical isolates from a local hospital to extract aminoglycoside-inactivating enzymes.
• Unfortunately, 1 isolate identified as *Ps. cepacia* was actually *Ps. pseudomallei* (now *Burkholderia mallei*).
• Tech was hospitalized with acute meliodosis.

Unique to Research: Experimental aerosolization studies

Vaccine studies: Use of aerosol-generating devices to expose animals to aerosol challenges.

Case Study: 3 staff members became PPD positive after use of Madison aerosol chamber. Leaky valve: staff not wearing respirators. Described on Sunshine Project website.

Case Study: Staff member exposed to Brucella when decontaminating same type of chamber during a training session. Described in GAO report
Reducing sharps exposures...

Your ideas..
- Products
- Procedures

Pls. share!
Anonymous reporting of LAIs in the literature, with accompanying detailed information on associated laboratory conditions and practices, can facilitate the implementation of policies and procedures to prevent LAI in the future.