

LAI Lessons Learned and the need for an LAI Reporting System

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Advocacy for LAI/Incident reporting system

Systematic, Informative-

nature of the incident, probable cause, lessons learned for stakeholders.

Build Awareness and Advocacy

- Trans-Federal Task Force Report on Biosafety and Biocontainment Oversight
- GAO report 10-850-design of safety reporting system.

▫ J.Kozlovak. *Applied Biosafety* 17(2)56-57

Evidence-based biosafety: a review of the principles and effectiveness of microbiological containment measures

- “Data on the containment effectiveness of equipment and laboratories are scarce and fragmented. **Laboratory-acquired infections (LAIs) are therefore important for evaluating the effectiveness of biosafety.**”
- Kimman, TG. et al. 2008. Clin Microbiol Rev. 21(3):403-25. ▪

Published LAI Survey Data

Pike and Sulkin: **mail** survey sent to 4,000 labs of various types: approx. 50% response. Reported: 4,079 laboratory-acquired infections from 1935 to 1978. 168 fatalities.

17% in 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

Pike , R M. 1979. Annu. Rev. Microbiol. 33:41-66.

Harding, L.H. and K.B,Byers. 2006. Epidemiology of laboratory-acquired infections. *IN Biological Safety Principles and Practices*. ASM Press. D. Fleming and D. Hunt, eds.

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

Year	Agent	#cases	Entity type	Lab Type
2004	Brucella melitensis	1	Registered	BSL2
2004	Coccidioides sp.	1	Registered	BSL3
2004	Francisella tularensis*	3	Registered	BSL2
2007	Brucella melitensis	1	Registered	BSL3
2007	Brucella melitensis	1	Exempt	BSL2
2008	Brucella melitensis	1	Registered	BSL3
2009	Francisella tularensis*	1	Registered	BSL3
2010	Brucella suis	1	Exempt	BSL2
2010	Brucella suis	1	Exempt	BSL2

Francisella tularensis

- **Strain verification &**
- **Follow BL2 with attenuated strains**

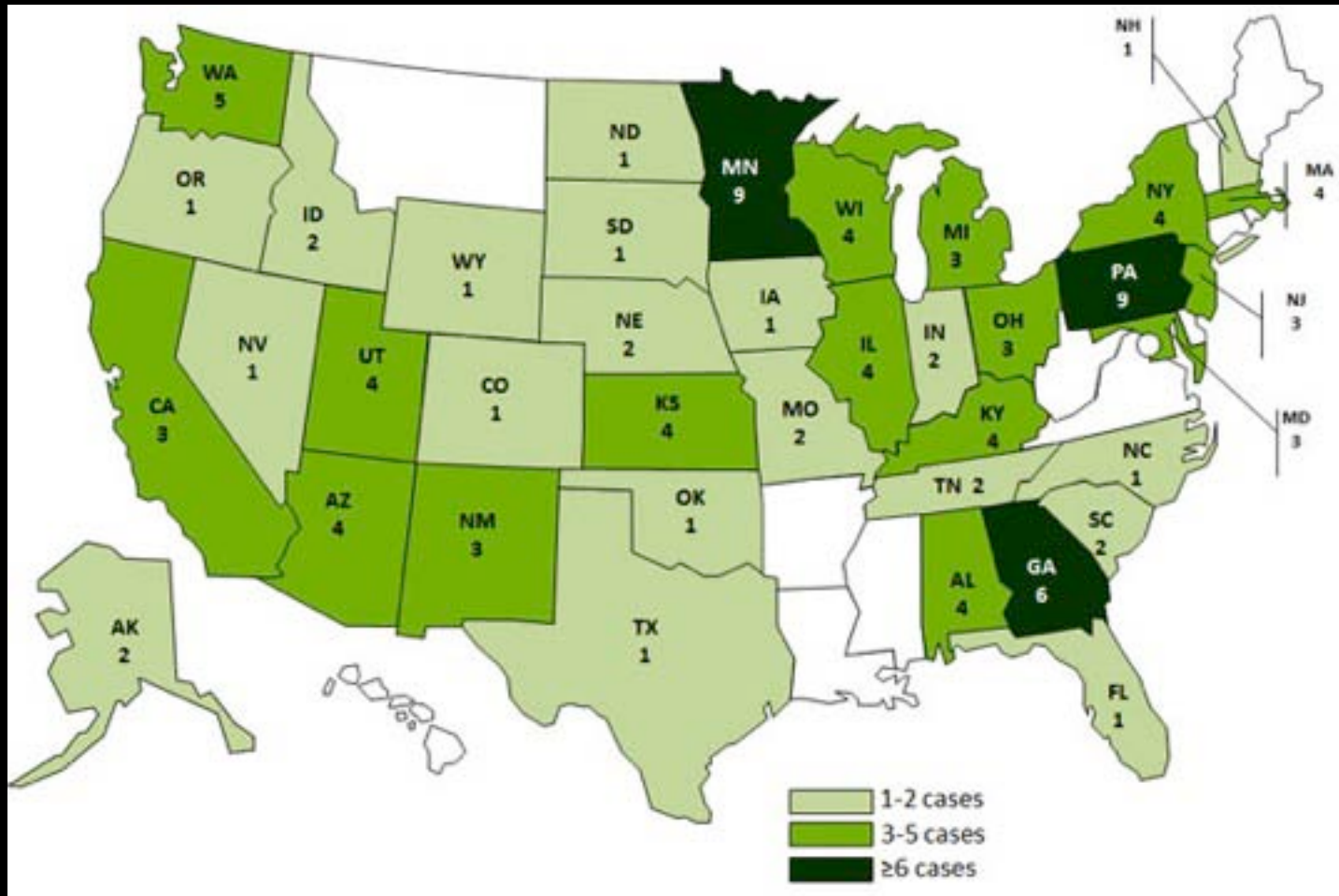
3 cases of pneumonia – traced to laboratory work with stocks contaminated with strain A *F. tularensis*.

- <http://www.bphc.org/programs/cib/environmentalhealth/biologicalsafety/Pages/Home.aspx>

■ **Immunization**

- No incident. Not immunized.
- “worked with *F. tularensis* types A and B, also *Y. pestis*. Sputum PCR + for *F. tularensis*. Titer:1:40 2 weeks after illness; rose to 1:1280 by hospital admission day.
- No event; worked in BL3, used bsc &/or N100 half-face respirator when doing aerosolizing procedures: force filtering, loosening screw caps, centrifugation, or vortexing.”
- Lam, S.T., W. Sammons-Jackson, J. Sherwood, R. Ressler. 2012. Laboratory-acquired tularemia successfully treated with ciprofloxacin: a case report. *Infectious Disease in Clinical Practice* 20(3):204-207.

Multistate Outbreak of typhimurium infections associated with clinical and teaching labs. August 20, 2010 - June 29, 2011



<http://www.cdc.gov/salmonella/typhimurium-laboratory/011712/index.html>

109 infections in 38 states
4 of the LAI were
In children under 4

Lesson Learned:
Training
Tool Target to Students

**Supervisor
Responsibilities
listed:**
Advice to Laboratory
Directors, Managers,
and Faculty Involved
with Clinical and
Teaching
Microbiology
Laboratories

What You Work With Can Make You Sick

Follow safe lab practices—and don't bring germs home with you.



Always wash your hands with soap and water...

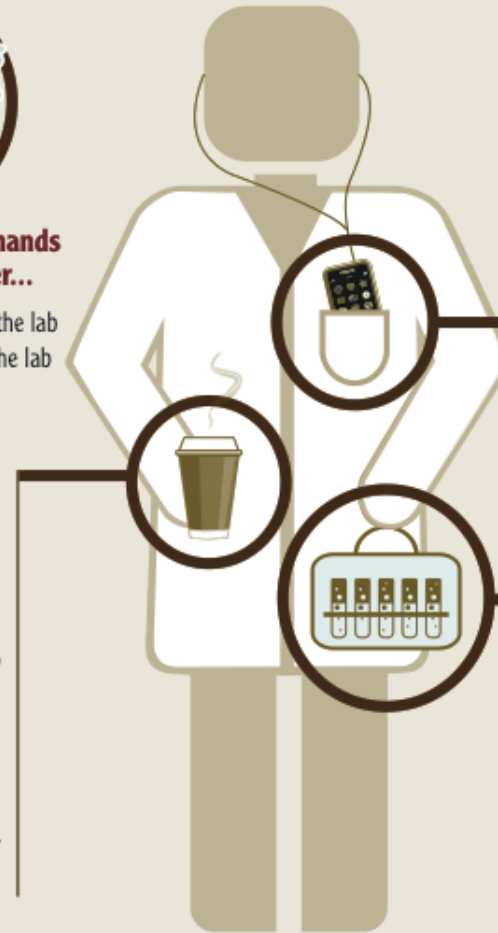
- ▶ Right after working in the lab
- ▶ Just before you leave the lab

Avoid contamination while in the lab.

Don't eat, drink, or put things in your mouth (such as gum)

Don't touch your mouth or eyes

Don't put on cosmetics (like lip balm) or handle your contact lenses



Don't carry dangerous germs from the laboratory home with you.

Leave personal items outside of the lab so you don't contaminate them: cell phone, car keys, tablet or laptop, MP3 player

Keep work items off of bench areas where you do experiments: backpacks, notebooks, pencils, pens

Leave lab supplies inside the lab.

If you must take supplies out of the lab, keep them in a separate bag so you don't contaminate anything else

Leave your experiment inside the lab so you can stay healthy outside the lab.



Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases

Analysis of teaching labs with and without Salmonella LAI

- Essentially same facilities, safety policies, procedures.
- Lesson Learned: Labs without LAI included symptoms in their training.
- Students more familiar with biosafety training materials.

“It’s time for a centralized registry of laboratory acquired infections” ...

A recent serious outbreak of *Salmonella* linked to clinical and teaching microbiology laboratories highlights the dangers of working with laboratory pathogens—but it is probably not an isolated occurrence. Without a better system for reporting infections resulting from laboratory exposures, we risk seeing more of these types of outbreaks.

Singh, K. 2011. *Nature Medicine* 17(8):919.

Lesson - Follow BL2 practices with attenuated strains

Fatal Laboratory-Acquired Infection with an Attenuated *Yersinia pestis* Strain --- Chicago, Illinois, 2009

MMWR Weekly

February 25, 2011 / 60(07);201-205

- Diabetic with inconsistent use of gloves with undiagnosed hemochromatosis, a genetic condition leading to iron overload in the tissues.
- Slide show that illustrates the issues:

<http://mrce.wustl.edu/mrce/ckfinder/userfiles/files/Lab%20Acquired%20Infections%202012.pdf>

[J Infect Dis.](#) 2012 Oct 1;206(7):1050-8. doi: 10.1093/infdis/jis433. Epub 2012 Aug 14. Hereditary hemochromatosis restores the virulence of plague vaccine strains.

Lesson learned: disclose occupational exposure

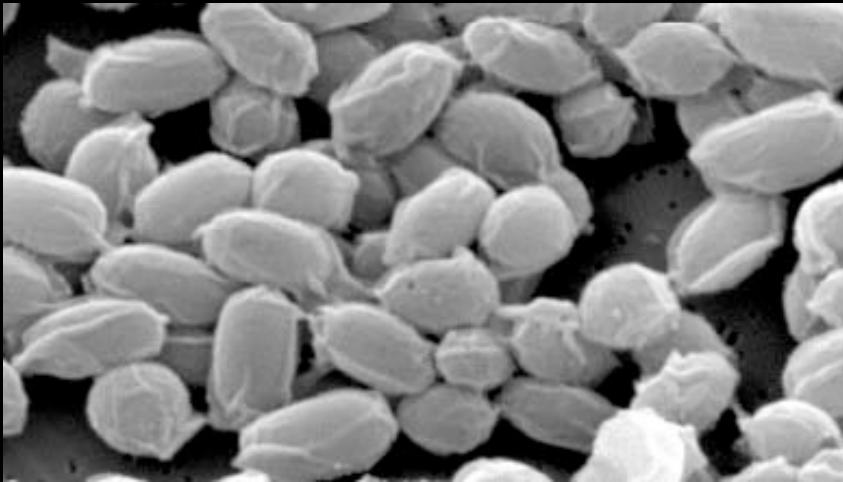
- Microbiologist hospitalized for 2 months before organism correctly identified. [1st US case glanders since 1945].
- Had insulin-dependent diabetes mellitus. Did not wear gloves when handling lab equipment. Was the risk factor the punctures from blood sugar testing or from increased susceptibility?
- Antibigram of lab strain provided answers for treatment that cured infection.

Prompt reporting of possible LAI- *B. cereus* case study.

- day1-Researcher scratched skin lesion - hand must have been contaminated.
- Day 2-swelling; reported to PI. Decided to wait to report until next day.
- Day 3- Met with PI. Went to hospital. Surgery. Necrotizing fasciatis.
- Decontamination of labs, purchase of additional bsc's, retraining of lab staff in this shared facility, removal of *B. cereus* from BL2 space. Cost:\$633,000.

Lesson: inactivated infectious material coming into the facility?

2003- 5 to 7 lab workers in Oakland, CA, handled “inactivated” anthrax – that wasn’t inactivated.



GOOD NEWS: No infections

Reinforces:

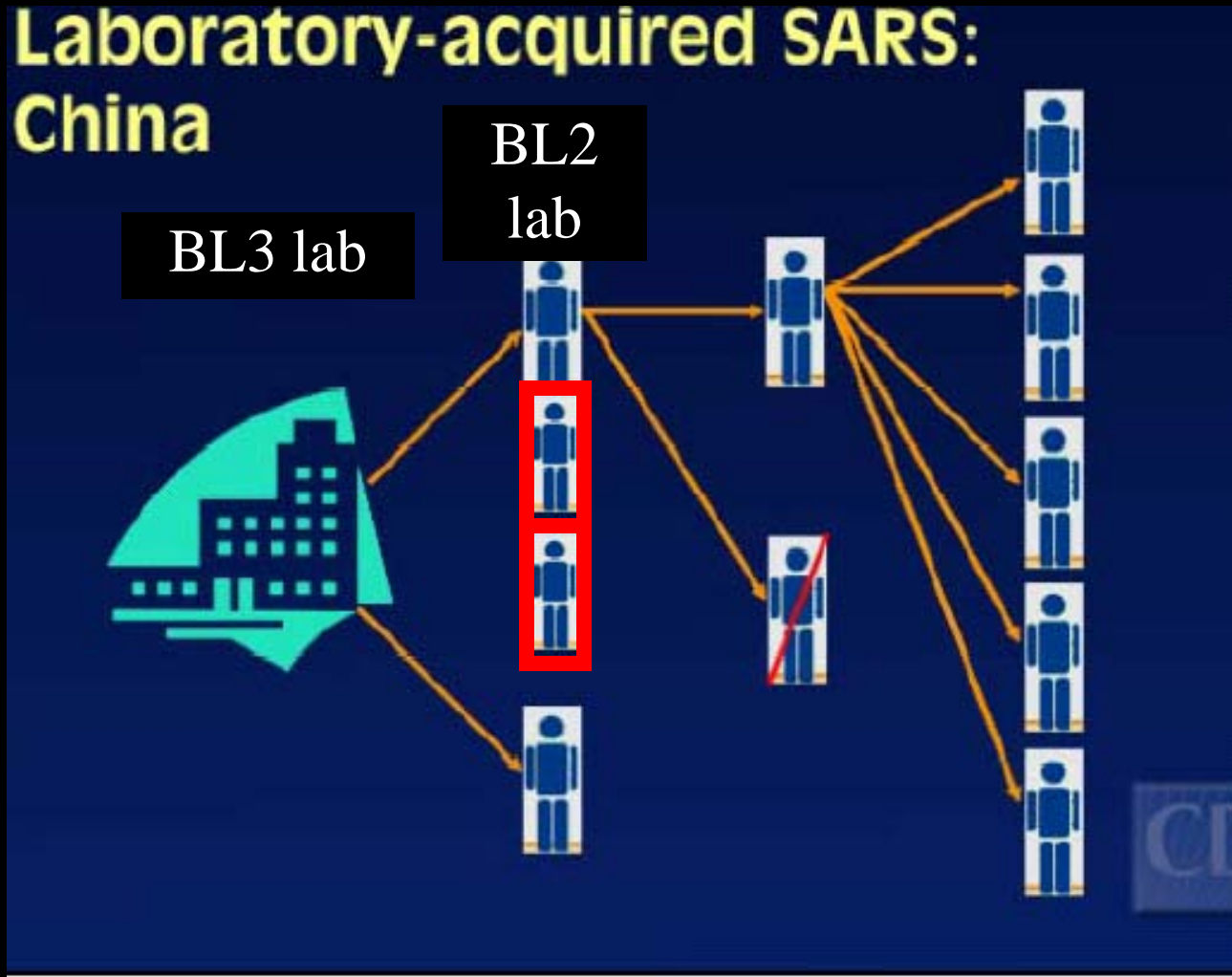
- good handling practices

Verification procedures

AP News

<http://renew.com/general53/>

Lesson



Samples removed for analysis at Biosafety Level 2-inactivation conditions not verified.

USAMRIID-Role of Preventive

- Vaccines in SA Research
- U.S. offensive biological warfare program (from 1943 to 1969). Safety measures (including BSCs) without vaccination failed to sufficiently prevent illness from agents with lower infective doses in this high-risk research setting.
- Infections continued with tularemia (average 15/year), Venezuelan equine encephalitis (1.9/year), and Q fever (3.4/year) but decreased dramatically once vaccinations became available (average of 1, 0.6, and 0 infections per year, respectively).

Rusnak, JM et al. 2004. Risk of occupationally acquired illnesses from Biological threat agents in unvaccinated laboratory workers. *Biosecur Bioterror*.2(4):281-93.

Laboratory-related orthopoxvirus exposures reported to CDC, 2005–2008

#	meet ACIP ?	strain	incident	infection?
8	7-no 1-?	recombinant Western reserve	6 needlesticks 2 eyesplashes	Yes -6 needlesticks No- 2 eyesplashes
5	2-yes 2-??	not known	2 animal care 1 eyesplash 1 tube leakage	No
1	yes	monkeypox	1 needlestick	No
1	yes	rabbitpox	1 eyesplash	No
1	no	NYCBOH	1 eyesplash	Yes
16		MacNeil Virology 385 (2009) 1-4.		5 hospitalizations

Misunderstanding of Respiratory Protection

- **Case study:** 2 staff members collect nasal swabs from influenza-infected pigs.
- 1 LAI infected with 4 strains; 2nd LAI with: 2 strains.
- LAI's infected with strains identical to strains used to inoculate pigs.
- Staff wore dust masks, not respirators, for the procedure.
- Note: Oddly, authors state infections occurred despite Animal Biosafety Level 3 procedures!

J. Infect. Dis. 1997. 175:7-15.

Brucella: lack of 2y container case study

- Polystyrene tube containing B. abortus broke during transport from 1 lab to another.
- Wearing mask, gloves, applied disinfectant. Lab evacuated w/in 45 mins. Cleaned up after 60 mins.
- 6 weeks post event: 3 staff diagnosed w/ Brucellosis.
- Serologic study began: 9 more staff (incl. 1 office worker) seropositive- treated prior to development of clinical illness.

Research with Animals-LAI

- 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 & Byers

LAI associated with NHP: 1979-2004



CHV-1: 10 LAI
1 fatality, 1 secondary
Ebola, new strain: 1 chimpanzee autopsy in
field.

Asymptomatic Ebola-related Filovirus: 42

Simian Type D retrovirus (SRV): 2

SIV: 2

Spumavirus, or simian foamy virus: 18

LAI associated with Sheep:1979-2004



- Q fever:
- 177 symptomatic and 1 death
- (Graham, 1989)

- +
- 3 possible asymptomatic in 2006
- (GAO report)

LAI assoc. with rodents: 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)



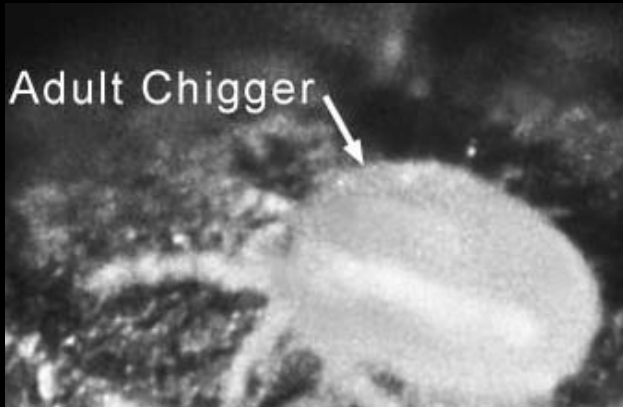
Mouse: 8 LCMV (Dykewicz, 1992)
1 LCMV (Braun, 2004)

Medical Management-USAMRIID

1989 to 2002 evaluated 234 persons (78% vaccinated) for exposure to 289 infectious agents revealed 5 confirmed infections (glanders, Q fever, vaccinia, chikungunya, and Venezuelan equine encephalitis).

Vaccine "breakthroughs" were not unexpected (enzootic Venezuelan equine encephalitis, localized vaccinia) or presented with mild symptoms (Q fever).

Case study: transmission route, symptoms can change.



- Procedure: 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.

RESULT

- “We report a case of scrub typhus pneumonitis 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*”

Lesson: Key Safety Step Eliminated

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

- UV inactivation step eliminated -
- Procedure continued until staff member hospitalized 2 months later.

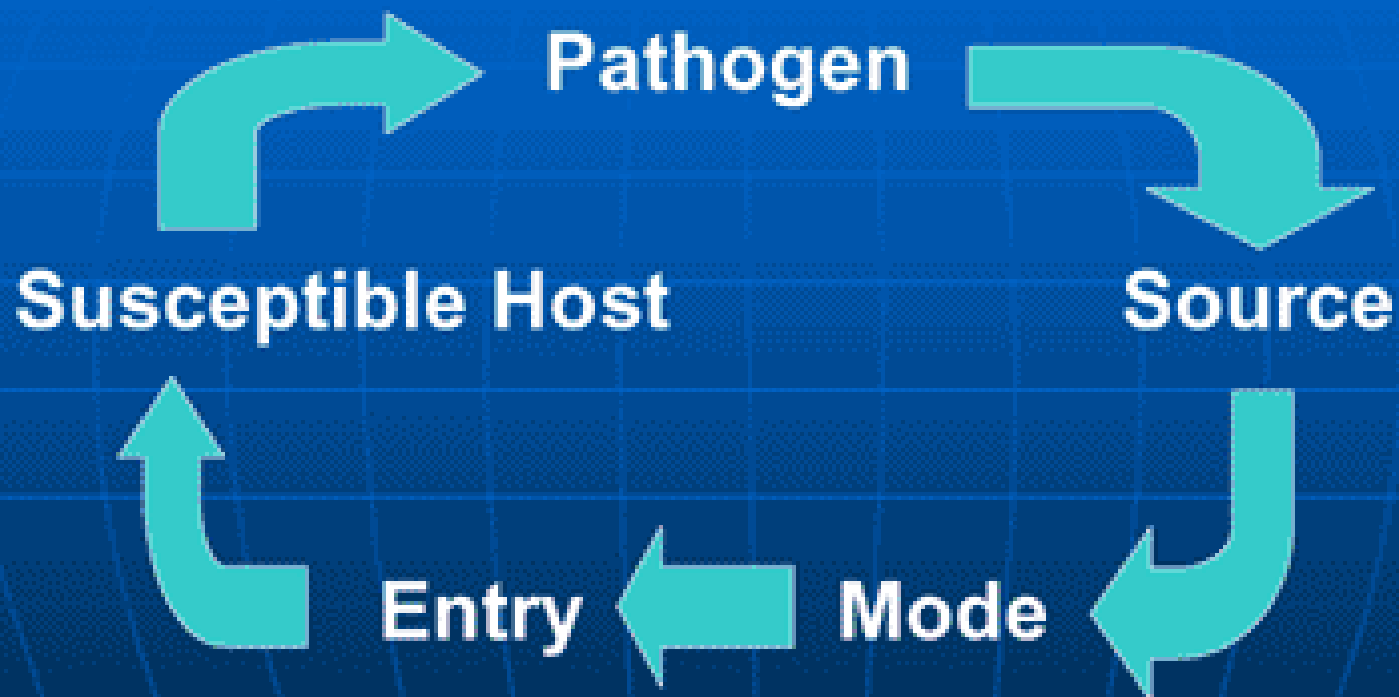
- Bernstein, D. et al. 1984. NEJM 311: 1543-1546.

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 melioidosis.
- Schlech, W. 1981. NEJM **305**, 1133-1135.

LAI happen when...

Chain of Infection



DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION



Summary: Reports and Investigations of Laboratory-Acquired Infections (LAI) are invaluable.

- Reporting LAI is a contribution to prevention efforts.
- Case studies of LAI are guideposts for evidence-based biosafety practice.
- Better reporting would provide the relevant data.