
Laboratory-Acquired Vaccinia Infection at a Small Research Institution

2007 ABSA Conference

Nashville, TN

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VACCINIA VIRUS:

Vexation;

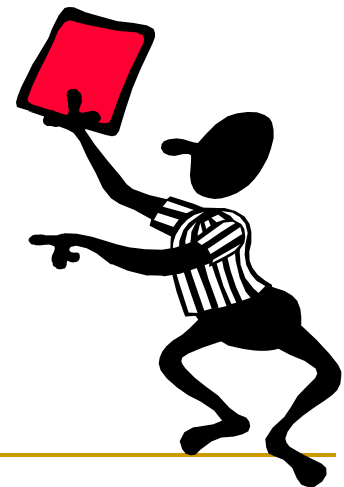
Vast Information; and

Vaccination

Vexation: Incident Chronology

■ Day 0

- Percutaneous injury w/needle used to inoculate research animals (PI, 46 yr. old male)
 - 10^7 pfu/mouse I.P. (12 mice)
- Recombinant Vaccinia virus (VVHA) expressing Influenza Hemagglutinin gene
 - WR TK- strain
- Work practice failures – PI modified protocol
 - Recap of needles (safely?)
 - Transport of sharps prior to disposal (floor to floor)
 - BSL2 PPE worn in hallway
 - Glove removal before biowaste disposal
 - Delay (slight) in treatment



Incident Chronology

- Day 1-2
 - No reaction
 - Day 3
 - Swelling at location of injury
 - Base of left thumb
 - Day 4
 - Increase in swelling, redness, fever, malaise
 - Tender axillary adenopathy
 - Lymphangitic streaking from thumb to wrist
 - First report to medical personnel
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Incident Chronology

- Day 4 (continued)
 - Examined by a physician
 - Secondary bacterial infection identified
 - Patient sent home/Dicloxacillin provided
 - Day 5
 - Lymphangitic streaking extended up arm
 - Family report to CDC
 - CDC call to YNHH
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Lesion at site of inoculation



Photo provided by Dr. Marie Landry – YNHH Clinical Virology

Lymphangitic streaking from thumb to axilla



Photo provided by Dr. Marie Landry – YNHH Clinical Virology

Incident Chronology

- Day 5 (continued)
 - Patient admitted to YNHH (sepsis)
 - Released on Day 6 w/ Augmentin
 - No patient care for MD for next 10 days
 - Vaccinia treatment options (for severe cases)
 - Mild case – not pursued
 - YNHH Virology Assessment
 - BSL2 cell culture (Rhesus monkey cells)
 - Positive at 48 hours
 - Sample sent to State CT DPH lab for PCR
 - Positive at 24 hours
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Vexation: Post-incident biosafety review

- Registration and approval process
 - Human pathogens
 - Non-exempt rDNA experiments
 - Biohazards in animals
 - Medical Clearance for Vaccinia
 - Immunization
 - Personnel risk evaluation
 - Emergency/Incident Response Protocols
 - Local, state and federal reporting requirements
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Post Incident Biosafety Review

■ Institutional Review

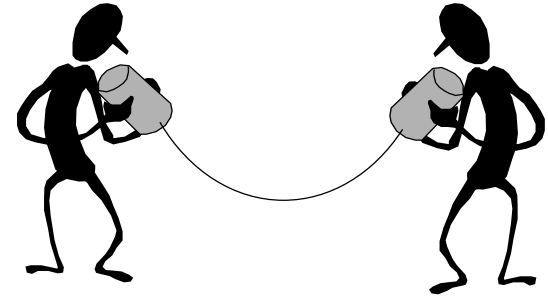
- Accepted generic BSL2 protocol from PI
 - “BSL2 practices will be followed”
 - BMBL/MSDS only a starting point
- No verification of:
 - Immunization w/in 10 years
 - Prior/recent work experience
 - Worker proficiency w BSL2/ABSL2 practices
- Lack of awareness of reporting requirements
 - State of CT DPH (reportable infectious disease)
 - NIH Office of Biotechnology Activities (NIH funded)



Vexation: Post-incident biosafety review

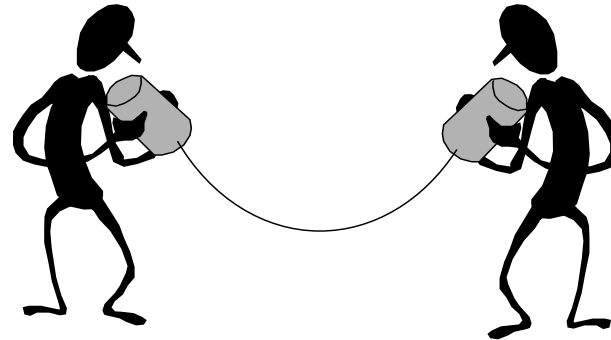
- Principal Investigator
 - Healthcare duties and research
 - Limited staff
 - Initiation of BSL2 experiments after delay
 - Unsafe procedures involving sharps
 - Recapping needles, PPE worn outside ABSL2 lab, hand transport of sharps outside lab, glove removal w/needles in hand
 - Failure to discard sharps in immediate vicinity of use
 - Accident in location w/out sink/eyewash (hallway)
 - Failure to immediately report exposure to employee health
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Recommendations



- Combined authorization program
 - Employee Health
 - Verification of prior immunization
 - For researchers and animal handlers
 - Contraindications
 - Immunizations provided w/ counseling on infection control
 - Signs/symptoms, breaks in skin
 - Exposure response/reporting posters/cards created
 - Written approval letter
 - Describes site-specific protocol requirements
 - CC'd to all involved
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Recommendations



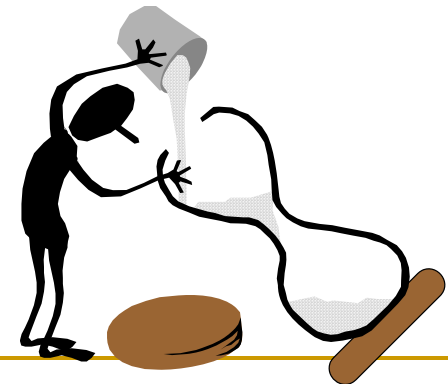
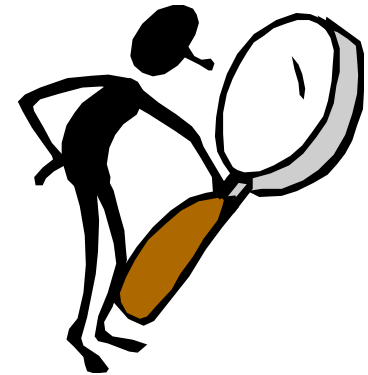
- IACUC/IBC/EH&S
 - Class training and recent field experience verified
 - PI risk assessment and SOP confirmed
 - Onsite proficiency observation and certification
 - Confirm PI selection of safe sharps (i.e. retractable needles/syringes)
 - Availability
 - Training & evaluation
 - Start-up meeting w/ animal care, PI, EH&S
 - Emergency response cards or posters
 - Oversight & monitoring
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Vast Information for Risk Assessment

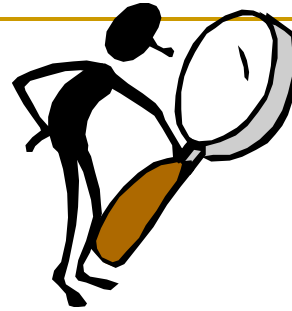
- 5 P's of Risk Assessment and Risk Management

- Pathogen
- Procedures (proposed manipulations)
- Personnel
- Protective Equipment and (work) Practices
- Place (proposed facilities)

- Ensure sufficient time allotted



Vast Information



■ 5 P's of Risk Assessment and Risk Management

□ Pathogen

■ RG2 agent

□ Recombinant strain (Influenza HA gene)

- WRTK- strain grows to high titer

■ Routes of exposure

□ Percutaneous

□ Mucous membranes

■ Prior LAI's

□ Unknown route of exposure in recent LAI's

□ Infections from attenuated strains

□ Infections from recombinant strains



Vast Information – Prior Vaccinia LAI's

❑ Ocular Vaccinia infection

- ❑ Unknown route (some procedures outside containment)
- ❑ Unvaccinated researcher
 - Lewis et al 2006 (Emerging infectious diseases, Vol 12, No. 1, January 2006 p 134 – 137)

❑ rDNA Vaccinia infection

- ❑ Breaks in skin of hands, failure to wear gloves
 - ❑ Gene that inhibits leukocyte adhesion (enhanced risk?)
 - ❑ Last immunization 28 years earlier
 - ❑ 12 month delay between experiments
 - Mempel et al 2003 (Journal of investigative Dermatology, Vol 120, NO. 3, March 2003, p 356 – 358)
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Vast Information – Prior Vaccinia LAI's

- Severe lesions after needlestick
 - Surgical excision of necrotic tissue required
 - 26 yr. old, vaccinated in childhood
 - Moussatche et al 2003 (Emerging Infectious Diseases, Vol 9, No. 6, June 2003 p 724-726)
 - Recombinant Vaccinia infection in research lab – 2002
 - Secondary bacterial infection that required hospitalization
 - No exposure route identified – contaminated surfaces?
 - Unvaccinated employee
 - Health and Safety Executive Newsletter 32, online @ www.hse.gov.uk/biosafety/gmo/acgm/acgm32/paper8.htm
-

Vast Information – Prior Vaccinia LAI's

- rDNA Vaccinia LAI identified from ER visit
 - Last vaccination 40 years prior
 - Long history of eczema, cut on finger previous week
 - Failure to wear gloves (exacerbated eczema)
 - No known accident
 - **No awareness of signs/symptoms of the disease**
 - Canada Communicable Diseases Report, Volume 29-15, 1 August 2003
 - Vaccinia infection from sexual contact with recently vaccinated person
 - Change of bandage by recently vaccinated person prior to romantic contact
 - Egan et al, J Clin Microbiology, Nov. 2004, p 5409-5411.
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Vast Information for Risk Assessment

- 5 P's of Risk Assessment and Risk Management

- Pathogen

- Environmental stability

- Viable virus in dried scabs

- Extended survival in aqueous solutions

- Survives up to 2 weeks dried on surfaces, fabric

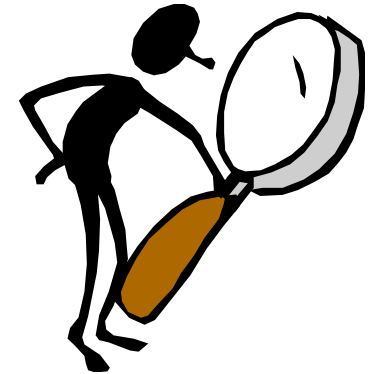
- Communicable disease

- Many “categories” of personnel at elevated risk

- Pre- and post exposure prophylaxis

- Immunization (initial, booster @ 10 yr)

- VIG



Vast Information for Risk Assessment

■ 5 P's of Risk Assessment and Risk Management

□ Procedures

■ Cell culture

- Equipment, locations, transport

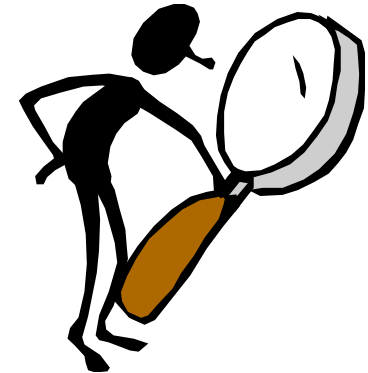
■ Animals (mice)

□ Sharps

- Safe sharps, use, disposal
- Bites, scratches

□ Shed in urine

- Bedding, cage, biosafety cabinet contamination

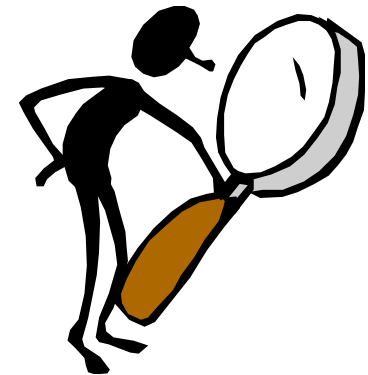


Vast Information for Risk Assessment

■ 5 P's of Risk Assessment and Risk Management

□ Personnel

- Contraindications for immunization for work w/ agent
 - Skin conditions and disorders
 - Conditions & medications that may suppress immunity
 - Pregnant or breastfeeding mothers
 - Diagnosis of heart disease
 - Allergies to vaccine components
 - Close contacts w/conditions
- Adherence to vaccine infection control requirements
- Prior BSL2 work experience (lab/animal)



Vast Information for Risk Assessment

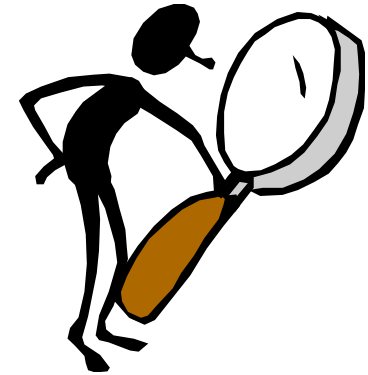
- 5 P's of Risk Assessment and Risk Management

- Protective equipment

- Effective use of the biosafety cabinet
 - Gloves
 - Limitations & use
 - Spread of contamination
 - Sharps containers

- Place

- Basic BSL2 lab design info (secondary containment)



Smallpox Vaccine Information – CDC

www.cdc.gov/smallpox

- Attenuated live virus vaccine
 - Recommended for lab workers
 - Directly handling poxvirus cultures
 - Research animals infected w/ poxviruses
 - Considered for
 - HCW caring for infected patients (smallpox)
 - Don't exclude vaccinated HCW's from duty
 - Train, strict adherence to infection control
 - Keep vaccination site covered/wash hands
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Smallpox Vaccine Information – CDC

www.cdc.gov/smallpox

■ Vaccine contraindications

□ For those vaccinated, household contacts, romantic contacts

■ Eczema

□ History/active

■ Current/active chronic skin conditions

□ Atopic dermatitis, impetigo, etc.

■ Impaired immune function

□ HIV, leukemia, lymphoma, generalized malignancy, therapy with immunosuppressive agents

■ Pregnant women

Smallpox Vaccine Information – CDC

www.cdc.gov/smallpox

- Vaccine contraindications
 - Allergies to vaccine components
 - Those who experience anaphylactic reactions
 - Latex allergies?
 - Vaccination produces a local infection
 - Shedding until scab separates from skin
 - Max viral shedding: days 4 – 14 post vaccination
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Smallpox Vaccine Information – CDC

www.cdc.gov/smallpox

- Adverse Reactions
 - Rashes, Fever
 - Serious reactions in past (1/1,000)
 - May require hospitalization
 - Severe reactions in past (52/1,000,000)
 - Deaths (2/1,000,000)
 - Recent adverse event rates (revaccination/primary vaccination)
 - Encephalitis: (2/1,000,000 / 12.3/1,000,000)
 - Generalized Vaccinia – bloodstream
 - (1/40,000 / 1/1,700)
 - Eczema vaccinatum – systemic dissemination
 - (3/1,000,000 / 38.5/1,000,000)
 - Vaccinia necrosum – can be fatal in immunocompromised (1/1,000,000)
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Researcher Misconceptions

- Attenuated strain (WR Tk-)
 - Healthy workers won't get infected, this is what they use for the smallpox immunization.

Wrong – literature shows numerous LAI's with this strain

 - Other genes associated with virulence are still present
 - Passaged in mouse neural cells (neurovirulent)?
 - Attenuation shown in lab animal model, never tested on humans
 - This is not the Vaccination strain!
 - Can a lower BSL be used?
 - No. Only the NYVAC strain may be lowered in containment to BSL1
-

Researcher Misconceptions

- Attenuated strain (WR Tk-)
 - Recombinant strains safer
 - LAI's with rDNA strains of Vaccinia well documented.
 - Next exposure will be 1st immunization
 - No. Next exposure could result in a LAI for you.
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Researcher Misconceptions

- Attenuated strain (WR Tk-)
 - This is not like Rabies virus, where you can die.
 - There are very serious consequences of infection for you and others.
 - Inadvertent inoculation
 - Skin rashes (extensive lesions, including ocular)
 - Eczema Vaccinatum, Vaccinia Keratitis
 - Encephalitis
 - Congenital Vaccinia
 - Generalized Vaccinia (bloodstream)
 - Progressive Vaccinia (Vaccinia Necrosum)
 - Communicable disease
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Case Study Example

BL2 rDNA – Vaccinia/Influenza

■ Location A

- Small research entity

■ Registration(s)

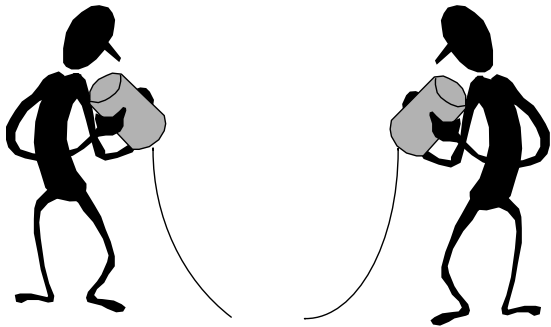
- IACUC
- IBC

■ Location B

- Large research institution

■ Registration(s)

- IACUC
- IBC
- YARC Haz. Agent
- OEHS RTUIA-Animals
- State of CT Human Pathogen



Case Study Example

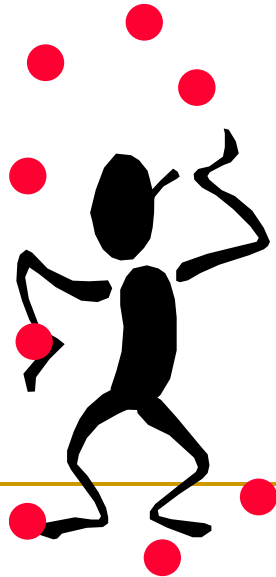
BL2 rDNA – Vaccinia/Influenza

- Location A
 - Review of Training
 - IACUC Orientation
 - Animal Handling
 - Location B
 - Review of Training
 - IACUC Orientation
 - Animal Handling
 - OEHS Classes
 - Biosafety, BBP, Chem
 - Researcher Experience Form
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Case Study Example

BL2 rDNA – Vaccinia/Influenza

- Location A
- Specific SOP created
 - None
 - PI general statements only (“will follow BSL2”)
- Location B
- Specific SOP created
 - Entry, exit, supplies
 - Protective clothing
 - Biosafety cabinet use
 - Safe sharps (devices/use)
 - Decontamination
 - Emergency response



Case Study Example

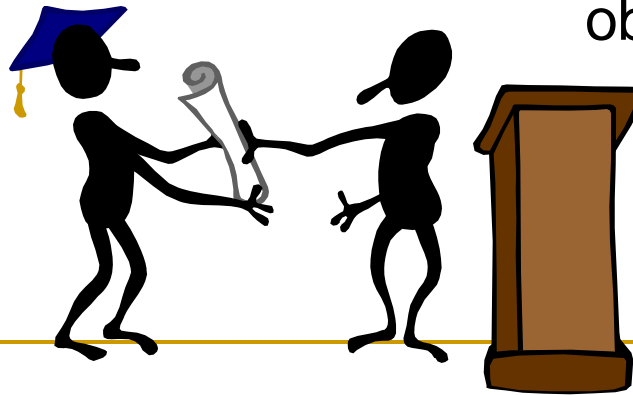
BL2 rDNA – Vaccinia/Influenza

- Location A
 - Additional Requirements
 - Medical Surveillance
 - Health history form
 - Location B
 - Additional Requirements
 - Medical Surveillance
 - Health history form
 - Vaccinia immunization consult
 - Employee Health review
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Case Study Example

BL2 rDNA – Vaccinia/Influenza

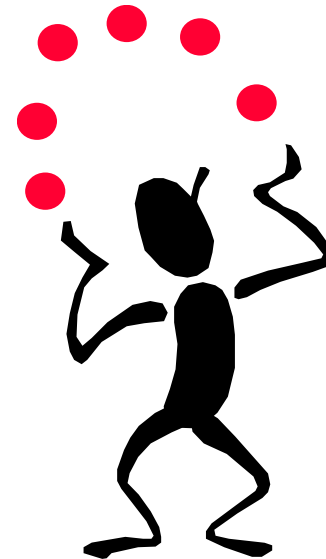
- Location A
- Training/Inspection
 - Facility orientation
- Location B
- Training/Inspection
 - Facility orientation
 - State CT Inspection
 - ARC/EHS/VCS start-up meeting w/ researcher
 - Researcher work practice observation



Case Study Example

BL2 rDNA – Vaccinia/Influenza

- Location A
- Implementation
 - Vaccinia needlestick
 - No incident report
 - Vaccinia LAI and bacterial sepsis
 - Hospitalization
 - Report to State CT
 - Report to NIH OBA
- Location B
- Implementation
 - No incidents to date



“I go where I’m towed to.”

- Tell ‘em (researchers) where you are going to tow them
- Tow them there (There = Safe Research)
- Tell why you’ve towed them there

