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“Occupational Infections”

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Classical Textbook Occupational Infections

Human Pathogens
Tuberculosis
Hepatitis B
HIV

Zoonotic Pathogens
Brucellosis
Anthrax

Occupational Infections

Epidemiology
  Occupational Setting
  Populations At Risk
  Route of Exposure
  Job Categories
Healthcare Facilities
  Bloodborne Pathogens
  Infectious aerosols
Biomedical Industry
  Bloodborne Pathogens
  Infectious aerosols
  Select Agents
What I won’t be talking about

Pneumoconioses due to accumulation of dusts in the lung and reactions
Fibrogenic (Silica (TBc association), Asbestos, Mica, Graphite,
Beryllium, Coal dust, Tale, Hard metals)
Non-Fibrogenic (Tin (Stannosis), Barium (Bariotosis),
Iron (Siderosis), Calcium (Chalitosis), Molydenum)
Organic Toxic Dust Syndrome
Cyanide
NOx (NO, Nitrogen dioxide (NO2), Nitrogen tetroxide (N2O4)
Sulfur Oxides (SO2)
Hydrogen Sulfide (H2S) from decomposition of organic material
Extrinsic Allergic Pneumonitis /Alveolitis to “Biologic Agent”
aka: hypersensitivity pneumonitis, Farmer’s lung, Bird-Feeders Lung
most often fungal spores from mold

Non-Infectious Aerosols
Fibers: silica, asbestos, nylon, etc.
Metals: lead, titanium dioxide, chromium, cadmium, etc.
Carbon: coal dust, combustion dusts, diesel fume, asphalt fumes, smoke particulates, etc.
Organic Solvents: metal working fluids, etc.
Synthetics: isocyanates (styrofoam), methylethyl ketone,
acetoin or diacetyl fumes in artificial butter
flavoring (broniolitis obliterans)
Pesticide surfactants, etc

What I won’t be talking about
Cuts and Crush injuries
Burns (thermal and chemical)
Repetitive Injuries (Hand, wrist, Back)
Slips on wet surfaces, Trips, Falls
Latex Allergy
Animal Dander Allergy
Noise Hazards (e.g. Cage Washing)
PPE Hazards (heat stress, dermatoses, etc)
Volatile Anesthetics
Chemical Hazards (disinfectants)
Epidemiology of Occupational Infections

- Who  Population at Risk
- What  Type of Infections
- Where  Occupational Setting
- How  Route of Exposure
- Why  Task of the OEM Specialist

Classic Hierarchy of Controls

1. Engineering and Environmental Controls
   - physical barriers, general and local ventilation, filtration, anterooms, negative pressure isolation, and temporary structures (triage tent ER facilities)
2. Administrative Controls and Work Practices
   - early identification and separation of cases; SOPs to reduce duration, frequency and severity of exposures to HCW, patients and visitors; education, drills
3. Personal Protective Equipment
   - gloves, gowns, goggles/eye shields, masks & respirators

NOTE: In infectious disease outbreaks, Administrative Controls (i.e. early identification of cases) is critical prior to the effective implementation of Engineering and Environmental Controls.

Population At Risk to Infectious Aerosols

Health Care Workers
  (Tbc, SARS, Avian flu, Ebola, Smallpox)
Laboratory Workers
  (Clinical Labs, Research Labs (Laboratory Animal Workers)
Patient Population
  (Hospital, Nursing Homes, Institutional)
First Responders
  (Police, Fire, EMS, Hazmat; FEMA; National Guard; Relief Volunteers )
Certain Occupations
  (Poultry Industry, Animal/Animal Product Handlers; Nano-technicians)
The General Public
  (Legionellosis; Plague; Histoplasmosis; Coccidioidomycosis; Avian Influenza, bioterrorist attacks)
Special Populations
  (Airline Passengers; Temporary Housing; Water Park; Prisoners)
Types of Occupational Infections

1. Human Infections (Bloodborne Pathogens, Tuberculosis)
   - Hospital / Medical Research
   - Institutions (CCC, Prisons, Mental Institutes)
   - First Responders (EMT, Biomedical Labs, Disaster)

2. Zoonotic/Arthropod-borne Infections (Brucella, Anthrax)
   - Veterinary Medicine
   - Farm/Ranch/Forestry/Hunters
   - Military Operations
   - Missionary/Relief Workers

3. BioMedical Research
   - Vaccine Development
   - Select Agents

4. Travel-associated Diseases

Occupational Settings

Institutions
- Military Recruits/Units
- Schools
- CCC
- Prisons
- Cruise Ship

Hospitals
- In-Patient
- Out-Patient
- First Responders

Medical Research
- Farm/Ranch/Forestry

Travel Associated Diseases

Routine Vaccination

Required Travel Vaccinations
- Yellow Fever
- Meningococcal (Haaj)

Recommended Travel Vaccinations
- Hepatitis A
- Typhoid Fever
- Hepatitis B
- Japanese Encephalitis
- Rabies
- Meningococcal
- Malaria
- Traveler's Diarrhea
Route of Exposure
Occupational Infections

1. Contact with Infected Living Animals
2. Contact with Contaminated Animal Product
3. Contact with Tick, Fleas, Mites
4. Contact with Human or Animal Waste
5. Contact with Infected Patient or Blood
6. Raised Dust Containing the Pathogen

Categories of Occupational Exposures

1. Contact with Infected Living Animals
   - Handling infected domestic animals (inhalation or percutaneous exposure)
   - Handling infected chickens or birds (fecal-oral or inhalation)
   - Bite or scratch by infected domestic animals (dog or cat)
   - Bite by skunk, raccoon, bat, fox, other carnivore, or woodchuck
   - Handling infected rodents (inhalation or percutaneous exposure)
   - Bite by rodents

2. Contact with Contaminated Animal Product
   - Handling infected animal carcasses or placental tissues
   - Handling raw goat hair, wool or hides from endemic area
Categories of Occupational Exposures

3. Contact with Tick, Fleas, Mites
   – Work in tick infested area in North America
   – Work in building infested with fleas or mites of rodents
   – Work in mite infested area of central, eastern or Southeast Asia

Categories of Occupational Exposures

4. Contact with Human or Animal Waste
   – Work or swim in contaminated water (percutaneous exposure)
   – Associate with dogs in endemic area
   – Care for children or animals infected with cryptosporidiosis

Categories of Occupational Exposures

5. Contact with Infected Patient or Blood
   – Handle contaminated needles or surgical instruments
   – droplet/airborne pathogens
   – Bloodborne pathogens
Categories of Occupational Exposures

6. Raised Dust Containing the Pathogen
   – Plow, dig or excavate soil in endemic area
   – Raise dust from bird roosts, chicken coops or bat-inhabited caves in endemic area
   – Raise dust of excreta from rodents

Applying Job Categories to this Epidemiological Approach to Occupational Infections

Handle infected domestic animals
(inhalation or percutaneous exposure)

<table>
<thead>
<tr>
<th>Animal breeder</th>
<th>Brucellosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal caretaker</td>
<td>Influenza</td>
</tr>
<tr>
<td>Animal scientist</td>
<td>Hendra &amp; Nipah virus</td>
</tr>
<tr>
<td>Farmer &amp; Rancher</td>
<td>Leptospirosis</td>
</tr>
<tr>
<td>Farm worker</td>
<td>Q fever</td>
</tr>
<tr>
<td>Lab animal worker</td>
<td></td>
</tr>
<tr>
<td>Veterinarian</td>
<td></td>
</tr>
</tbody>
</table>
### Handle infected chickens or birds

<table>
<thead>
<tr>
<th>Role</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal breeder</td>
<td>Influenza</td>
</tr>
<tr>
<td>Animal caretaker</td>
<td>Newcastle disease</td>
</tr>
<tr>
<td>Animal scientist</td>
<td>Psittacosis</td>
</tr>
<tr>
<td>Lab animal worker</td>
<td></td>
</tr>
<tr>
<td>Poultry farmer</td>
<td></td>
</tr>
<tr>
<td>Poultry handler</td>
<td></td>
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<tr>
<td>Veterinarian</td>
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</tbody>
</table>

### Bite or scratch by infected dog or cat

<table>
<thead>
<tr>
<th>Role</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal breeder</td>
<td>Brucellosis</td>
</tr>
<tr>
<td>Animal caretaker</td>
<td>Cat scratch fever</td>
</tr>
<tr>
<td>Animal scientist</td>
<td>Capnocytophaga infection</td>
</tr>
<tr>
<td>Farmer &amp; Rancher</td>
<td>Pasteurellosis</td>
</tr>
<tr>
<td>Farm worker</td>
<td>Plague</td>
</tr>
<tr>
<td>Lab animal worker</td>
<td>Rabies</td>
</tr>
<tr>
<td>Veterinarian</td>
<td>Tularemia</td>
</tr>
</tbody>
</table>

### Bite by skunk, raccoon, bat, fox, other carnivore, or woodchuck

<table>
<thead>
<tr>
<th>Role</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farmer &amp; Rancher</td>
<td>Rabies</td>
</tr>
<tr>
<td>Farm worker</td>
<td></td>
</tr>
<tr>
<td>Game warden</td>
<td></td>
</tr>
<tr>
<td>Hunter &amp; Trapper</td>
<td></td>
</tr>
<tr>
<td>Veterinarian</td>
<td></td>
</tr>
<tr>
<td>Wildlife biologist</td>
<td></td>
</tr>
</tbody>
</table>
### Bite by rodents

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farmer &amp; Rancher</td>
<td>Monkeypox</td>
</tr>
<tr>
<td>Farm worker</td>
<td>Plague</td>
</tr>
<tr>
<td>Game warden</td>
<td>Rat bite fever</td>
</tr>
<tr>
<td>Hunter &amp; Trapper</td>
<td></td>
</tr>
<tr>
<td>Veterinarian</td>
<td></td>
</tr>
<tr>
<td>Laboratory Workers</td>
<td></td>
</tr>
<tr>
<td>Wildlife biologist</td>
<td></td>
</tr>
</tbody>
</table>

### Handle infected rodents

(ingestion or percutaneous exposure to infected rodent)

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farmer &amp; Rancher</td>
<td>Arenaviral infection</td>
</tr>
<tr>
<td>Farm worker</td>
<td>Hantavirus infection</td>
</tr>
<tr>
<td>Game warden</td>
<td>Lassa fever</td>
</tr>
<tr>
<td>Hunter &amp; Trapper</td>
<td>Leptospirosis</td>
</tr>
<tr>
<td>Veterinarian</td>
<td>Lymphocytic choriomeningitis</td>
</tr>
<tr>
<td>Wildlife biologist</td>
<td>Plague</td>
</tr>
<tr>
<td></td>
<td>Omsk hemorrhagic fever</td>
</tr>
<tr>
<td></td>
<td>Monkeypox</td>
</tr>
</tbody>
</table>

### Handle infected laboratory rats

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab animal worker</td>
<td>Hantavirus infection</td>
</tr>
<tr>
<td>Veterinarian</td>
<td>LCM</td>
</tr>
<tr>
<td></td>
<td>Rat bite fever</td>
</tr>
</tbody>
</table>
### Handle infected macaque monkeys

<table>
<thead>
<tr>
<th>Role</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab animal worker</td>
<td>B-virus infection</td>
</tr>
<tr>
<td>Veterinarian</td>
<td>SIV</td>
</tr>
</tbody>
</table>

### Handle infected animal carcasses or placental tissues

<table>
<thead>
<tr>
<th>Role</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal breeder</td>
<td>Anthrax</td>
</tr>
<tr>
<td>Animal caretaker</td>
<td>Brucellosis</td>
</tr>
<tr>
<td>Animal scientist</td>
<td>Crimean Congo HF</td>
</tr>
<tr>
<td>Butcher</td>
<td>Glanders</td>
</tr>
<tr>
<td>Farmer &amp; Rancher</td>
<td>Hendra &amp; Nipah virus</td>
</tr>
<tr>
<td>Farmworker</td>
<td>Influenza</td>
</tr>
<tr>
<td>Hunter &amp; Trapper</td>
<td>Leptospirosis</td>
</tr>
<tr>
<td>Lab animal worker</td>
<td>Newcastle disease</td>
</tr>
<tr>
<td>Meat packer</td>
<td>Plague</td>
</tr>
<tr>
<td>Slaughterer</td>
<td>Psittacosis</td>
</tr>
<tr>
<td>Veterinarian</td>
<td>Q fever</td>
</tr>
<tr>
<td></td>
<td>Rift valley fever</td>
</tr>
<tr>
<td></td>
<td>Tularemia</td>
</tr>
</tbody>
</table>

### Handle raw goat hair, wool or hides from endemic area

<table>
<thead>
<tr>
<th>Role</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grader &amp; Sorter</td>
<td>Anthrax</td>
</tr>
<tr>
<td>Freight handler</td>
<td></td>
</tr>
<tr>
<td>Packer</td>
<td></td>
</tr>
<tr>
<td>Drum head Importer</td>
<td></td>
</tr>
</tbody>
</table>
Work in tick infested area in North America

- Farmer & Rancher: Babesiosis
- Farmworker: RMSF
- Forester: Ehrlichiosis
- Groundskeeper: Lyme disease (Borrelia)
- Highway maintenance: Powassan virus encephalitis
- Hunter & Trapper: Relapsing fever
- Landscaper: Colorado tick fever
- Logging worker: STARI
- Rail track maintenance: Tick paralysis
- Tularemia

Work in building infested with fleas or mites of rodents

- Building cleaning worker: Murine typhus
- Pest control worker: Plague
- Rickettsialpox

Work in mite infested area of central, eastern or Southeast Asia

- Hunter & Trapper: Scrub typhus
- Laborer
Care for children or primates infected with hepatitis A

Child care worker  Hepatitis A
Lab animal worker
Veterinarian

Work or swim in contaminated water (percutaneous exposure)

Farm worker  Leptospirosis
Farmer & Rancher  Melioidosis
Sewer worker  Naegleriasis
Schistosomiasis

Care for children or animals infected with cryptosporidiosis

Animal handler (cattle)  Cryptosporidiosis
Child care worker
Associate with dogs in endemic area

Farmer & Rancher  Echinococcosis
Farm worker

Handle contaminated needles or surgical instruments

Dental worker  AIDS
Embalmers  Hepatitis B
Healthcare worker  Hepatitis C
Ebola -Marburg
Lassa fever
Crimean-Congo HF

Droplet/airborne pathogens

Healthcare worker  Arenavirus/Filovirus
eating for sick patients  Lassa fever (?)
Crimean-Congo HF
Diphtheria
Influenza
Measles
Meningococcal
Monkeypox
Mumps
Mycoplasma infection
Parvovirus
Pertussis
Rubella
SARS
Tuberculosis
Varicella
<table>
<thead>
<tr>
<th>Raised dust of excreta from rodents</th>
<th>Building cleaning worker</th>
<th>Arenaviral infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Construction worker</td>
<td>Hantavirus infection</td>
</tr>
<tr>
<td></td>
<td>Dockworker</td>
<td>Lassa fever</td>
</tr>
<tr>
<td></td>
<td>Farmer &amp; Rancher</td>
<td>Leptospirosis</td>
</tr>
<tr>
<td></td>
<td>Farm worker</td>
<td>LCM</td>
</tr>
<tr>
<td></td>
<td>Game warden</td>
<td>Rat bite fever</td>
</tr>
<tr>
<td></td>
<td>Granary worker</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Groundskeeper</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heating &amp; AC worker</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hunter &amp; Trapper</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pest control worker</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Repair worker</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wildlife biologist</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Raised dust from bird roosts, chicken coops or bat-inhabited caves in endemic area</th>
<th>Bridge painter</th>
<th>Histoplasmosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Construction worker</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Demolition worker</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Farmer &amp; Rancher</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Farmworker</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gardener</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heating &amp; AC worker</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Roofer</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Plow, dig or excavate soil in endemic area</th>
<th>Archeologist</th>
<th>Coccidioidomycosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Demolition worker</td>
<td>Paracoccidioidomycosis</td>
</tr>
<tr>
<td></td>
<td>Farmer &amp; Rancher</td>
<td>Hantavirus (HCPS)</td>
</tr>
<tr>
<td></td>
<td>Farmworker</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Military Personnel (DMZ)</td>
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</tbody>
</table>
Healthcare Facilities

Bloodborne pathogens

<table>
<thead>
<tr>
<th>Healthcare worker caring for sick patients</th>
<th>AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Arenavirus (Lassa Fever)</td>
</tr>
<tr>
<td></td>
<td>Crimean-Congo HF</td>
</tr>
<tr>
<td></td>
<td>Ebola -Marburg</td>
</tr>
<tr>
<td></td>
<td>Hepatitis B</td>
</tr>
<tr>
<td></td>
<td>Hepatitis C</td>
</tr>
<tr>
<td></td>
<td>Lassa fever</td>
</tr>
<tr>
<td></td>
<td>West Nile virus infection</td>
</tr>
</tbody>
</table>

Proliferative Bioaerosols:
The “Classic” Infectious Aerosols

<table>
<thead>
<tr>
<th>Tuberculosis (the Prototypical Infectious Aerosol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avian Influenza</td>
</tr>
<tr>
<td>Influenza</td>
</tr>
<tr>
<td>SARS (Coronaviruses)</td>
</tr>
<tr>
<td>Aspergillus spp.</td>
</tr>
<tr>
<td>Legionella spp.</td>
</tr>
<tr>
<td>Varicella-zoster virus</td>
</tr>
<tr>
<td>Plague (Yersinia pestis)</td>
</tr>
</tbody>
</table>
Newly Emerging Diseases

Highly Virulent Avian Influenza
Pandemic Influenza viruses (H1N1, H5N1, etc.)
SARS/ MERS-CoV (Coronavirus)
Hemorrhagic Fevers (Marburg, Ebola, Lassa Fever, etc)
MDR Tuberculosis
MRSA
MDR C. difficile
ESBL-producing gram negatives (E.coli, etc.)
  Carbapenem-resistant Klebsiella pneumoniae (KPC)
  Carbapenem-resistant Enterobacteriaceae (CRE)
  New Delhi Metallo-beta-lactamase (NDM-1)
  Colistin-resistant Acinetobacter baumannii and Pseudomonas aeruginosa

Bioaerosol Generating Sources/Procedures in Hospitals

Patients >> HCWs
Routine and Emergency Intubations
Respiratory Therapy (Inducing Sputum)
Surgical Laser ablations
Surgery on extrapulmonary tbc
Hospital Construction Activities
Autopsy Procedures (electric saw and opening sites/containers of infectious materials whose internal pressures may be different from ambient pressures)
Decorative fountains and fish tanks in Patient Areas

Infectious Aerosols of Recent Public Health Concern

Acute Respiratory Outbreaks in Military Trainees in Russia and Malaysia
Anthrax Incident in Veterinary Research Lab
Animal Caretakers and Cage Washers
Fermentation Operations (e.g. in-process sampling)
In-Door Mold (Stachybotrys) in Post-Katrina New Orleans homes and Temporary Classrooms
Hantavirus Risk in Camping/Hiking Shelters in Public Parks; Cabins in West Virginia and NYC (2014)
SARS in Asia (2003)
Pertussis in USA (2010)
MERS-CoV in the Middle East (2012)
Legionellosis in Open Markets and Water Parks, and Decorative water fountains in Hospitals in the USA; Nursing Homes in Spain and a Factory in Portugal. (2014)
Measles in USA (2014)
### Severe Respiratory Illnesses

- Extensively Drug Resistant (XDR) Tuberculosis (Mycobacterium tuberculosis hominis)
- Severe Acute Respiratory Syndrome: SARS/MERS-CoV (Coronavirus)
- Avian Influenza (H5N1 Influenza virus)
- Bioterrorism
  - Smallpox (Variola major)
  - Inhalational Anthrax (Bacillus anthracis)

### Biomedical Industry

### Institute of Medicine’s 2002 List of Candidate Infectious Aerosols for Biological Terrorism/Warfare

- Smallpox
- Monkeypox
- Nipah (Paramyxovirus)
- Viral encephalitides (VEE, WEE, Chikungunya)
- Tick-borne encephalitis virus
- “Eradicated” polio and measles
- Influenza A 1918 strain (Avian Flu)
- Hong Kong H5N1
- Others (Plague, Q Fever, Anthrax, Brucella)
Bioterrorism / “Select Agents” Research

- Anthrax (Bacillus anthracis)
- Pneumonic plague (Yersinia pestis)
- Tularemia (Francisella tularensis)
- Smallpox (Variola major)/ Monkey Pox / Vaccinia
- Botulinum exotoxin (Clostridium botulinum)
- Hemorrhagic Fevers (Ebola/Marburg)

Medical Surveillance in Biomedical Research

- Workplace Evaluation
  - Pregnant Workers
  - Immunosuppressed Workers
- Biological Surveillance
  - Prior immunity (rubella, rabies, Hep B, Hep A)
  - PPD / QuantiFERON TB Gold
  - Toxoplasmosis (female workers)
- Pre-Exposure Immunization
  - Bloodborne Pathogens (HIV, SIV, Hep B, Hep C)
  - Rabies
  - Rubella
  - Select Agents (Anthrax, Botulinum, Smallpox, Tularemia, RVF, etc)
- Post Exposure Prophylaxis
  - Bloodborne Pathogens
  - Simian Retroviruses
  - B virus
  - Select agents that do not vaccine preventable (ricin, VHF, toxins)

Preventive Measures in the Biomedical Research Industry

- Universal Precautions
- Hand Washing
- Elimination of unnecessary use of needles
- Use of sharps container
- Appropriate personal protective equipment including face shields, safety gloves, arm protectors, respirators, and goggles
- Mandatory vaccination programs
- Use of the minimum quantities of agents
- Work Practices to reduce aerosolization

Note: growing problem of hypersensitivity in laboratory animal handlers
Infection Hazards to Laboratory Animals Handlers

Common Vaccinations
- Tetanus
- Rabies (if indicated)
- MMR (non-human primate work)
- Vaccinia (Smallpox, Monkey Pox, Vaccinia-Chimeric Vaccine Research)

Vaccinations for specific research protocols
- Anthrax
- Clostridum botulinum
- Yellow Fever
- Japanese B Encephalitis
- Influenzae (Avian Flu, Swine Flu, SARS)
- BCG

Laboratory-acquired Infections
1930’s and 1940’s

The first studies of the occupational hazards to bacterial, fungal and rickettsial agents in laboratories were published in the 1930’s and 1940’s.

Laboratory-acquired Infections
1950 - 1975

Laboratory works were shown to have higher rates of Brucellosis, Q fever, typhoid fever, viral hepatitis and tuberculosis compared to the general population.

20% of cases were attributed to documented accidents (mouth pipetting and needle sticks) and exposure to infectious aerosols was considered to be the plausible but unconfirmed source of infection in the remaining
Laboratory-acquired Infections
1970’s and 1980’s

There was a marked decline in bacterial and rickettsial infections and with a lesser decline in Viruses and fungi.

At the same time there was growing attention focused on laboratory exposure to Hepatitis B virus and WV.

In the 1990’s, attention focused on laboratory exposure to recombinant DNA, chimeric virus development using vaccinia virus, and carcinogenic material/tissues.

Laboratory-Acquired Infections
21st Century

Since 2000, attention has focused on disease agents without current effective antidotes or treatments

“SELECT AGENTS” (e.g. ricin, hemorrhagic viruses)

MDR Bacteria (TBc, C. difficile, ESBL, MRSA)

Multidrug resistant HIV

Pandemic Viruses (Avian Flu, SARS, MERS)

Prions (biologically active)

Nanoparticles (biologically active)

Top Ten Laboratory-Acquired Infections
1979-2004

Total of 1,141 laboratory-associated infections in literature review

<table>
<thead>
<tr>
<th>Organism</th>
<th>Cases</th>
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<tbody>
<tr>
<td><em>Mycobacterium tuberculosis</em></td>
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<tr>
<td>Arboviruses</td>
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<tr>
<td><em>Coxiella burnetti</em></td>
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<td><em>Hantavirus</em></td>
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<tr>
<td><em>Brucella</em></td>
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<tr>
<td>Hepatitis B</td>
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<tr>
<td>Shigella spp.</td>
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<tr>
<td>Salmonella spp.</td>
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<tr>
<td>Hepatitis C</td>
<td>32</td>
</tr>
<tr>
<td><em>Neisseria meningitidis</em></td>
<td>31</td>
</tr>
</tbody>
</table>

Bold = AEROSOL transmissions
Business Travel Associated Diseases

Routine Vaccination (Tdap, IPV, MMR, Influenza, Pneumococcal)
Required Travel Vaccinations
  Yellow Fever
  Meningococcal (Haaj)
Recommended Travel Vaccinations
  Hepatitis A/ Hepatitis B
  Typhoid Fever
  Japanese Encephalitis
  Rabies
  Meningococcal
  Malaria Prophylaxis
  Traveler’s Diarrhea
  Altitude Sickness
  Motion Sickness (Sorcerer II, Antarctic Expeditions)
  Sunburns

Bite Wounds

Domesticated and laboratory animals
  commonly Eikenella corrodens and Pasteurella multocida
Pig bites are the worst for secondary wound infections
  Augmentin 875 mg BID x 10 days
  (if allergic to PCN, use Levaquin)
Macaque Non-human Primates
  B-virus, SIV, SHIV, simian retroviruses

Simian “B Virus”

Cercopithecine herpesvirus 1, an alphaherpesvirus endemic in macaque monkeys, and the only one of nearly 35 identified non-human primate herpesviruses that is highly neurotropic and neurovirulent in humans.

B virus has caused 46 human infections since 1933, and results in an extremely high mortality rate (~80%) if untreated, five of those in the last 15 years.

Timely antiviral intervention is an effective means of reducing B virus-associated morbidity and preventing a fatal outcome.
**Simian “B Virus”**

Ocular, oral - genital secretions, CNS tissues, CSF fluid are infectious

Infection in humans is associated with breach of primary skin or mucosal in humans inadvertently exposed by handling macaque monkeys generally used in biomedical research.

**Route of Exposures for Animal Care Takers**
- Bites, scratches
- Secretions into the eye or mucous membranes
- Open wounds from handling dirty cages
- Fomites, contaminated particulates or surfaces, have served as source of virus infection

Note: Exposure to peripheral blood has NOT been reported to associated with human infection

**Simian “B Virus”**

Flu-like symptoms which progresses to encephalitis (usually fatal if untreated in humans)

Incubation period 2 days to 5 weeks

Rarely see herpetic lesions at exposure site

Recurrent encephalitis reported in 25 survivors

**Simian “B Virus”**

B-Virus Post-Exposure Prophylaxis Protocol
- Cohen et al, Recommendations for Prevention of and Therapy for exposure B Virus, Clinical Infectious Diseases, 2002. 35; 1191-1203

Protocol
- Immediate cleansing / irrigation of wound
- Viral wound culture (AFTER the cleansing/irrigation)
- 14 days of Valcyclovir (Valtrex) 1000mg po TID
- Herpes B titer at baseline, in 2-4 weeks, and in 3 months if symptomatic (Georgia State Univ. Lab)
Simian Immunodeficiency Virus (SIV)

HIV-like retrovirus of NHP

Causes an asymptomatic infections in humans

Limited human studies suggests that SIV infection does NOT result in an AIDS-like syndrome

Simian Immunodeficiency Virus (SIV)

Post-exposure prophylaxis utilizes enhanced USPHS 28 Day HIV PEP Protocol (25% failure AZT- Regimens)

Current Recommended Regimens
Insentress (Raltegravir) 1/daily and Truvada BID
Truvada 1/daily and Kaletra BID
Atripla 1/daily (if not pregnant) -> 50% Dizzy
Initial and follow-up CMP, CBC, U/A 2-4 weeks
SIV testing at 0, 6 weeks, 3 months and 6 months

What we have seen ….
What you have read ….

What we fear ….

Smallpox  Anthrax  Avian Influenza
SARS  West Nile Virus  MDR TBc

BioSafety Level ?
Agents by Biosafety Levels

BSL 1
- Bacillus subtilis, Canine Hepatitis, E. Coli, attenuated Vaccine strains

BSL 2
- Hepatitis B, Hepatitis C, Influenza, Lyme Disease, Salmonella, HIV, scrapie

BSL 3 (~60 operational in USA)
- Anthrax, BSE, mumps, WNV, SARS, Smallpox, TBC, typhus, Yellow Fever

BSL 4 (~12 operational in USA)
- Bolivian Fever, Dengue Fever, Marburg virus, Ebola, Hanta virus, Lassa virus or other hemorrhagic diseases.

BSL 5 (fictional)
- “Andromeda Strains;” “Wildfire;” NASA extraterrestrial samples

BSL-1 Laboratory
- Typical university research laboratory or microbiology teaching lab
- Few restrictions on who may enter
- Lab connects directly with the remainder of the building
- Few specialized safety features
  - lab coats
  - hand washing before and after work in the lab
  - decontamination of bench tops before and after use
  - restrictions on food and drink
  - sterilization of all materials in contact with microorganisms.
- Work space with sealed seams and a crevasse-free surface to lessen the chances that microorganisms will survive on surfaces.
- Work is done on open-air bench tops without Biosafety Cabinets.
- Laboratory personnel are trained in the simple techniques necessary to prevent contamination of the experiment or themselves.
bacteria and viruses that cause only mild disease to humans, or are difficult to contract via aerosol in a lab setting:

*C. difficile*, most Chlamydiae, hepatitis A, B, and C, orthopoxviruses (other than smallpox), influenza A, Lyme disease, *Salmonella*, mumps, measles, scrapie, MRSA, and VRSA.
BSL-2 Laboratory

- Some additional safety features for more hazardous microorganisms
- Lab personnel are trained in the handling of specific disease-causing microorganisms and more care is taken when handling the microbes
- Special protective clothing such as a facemask is worn, and biological safety cabinets are present for procedures like blending and centrifugation that can aerolize of organisms
- Lab access is restricted and the doors remain closed when experiments are in progress.
- There are no specific ventilation requirements. Air enters and exits the lab via the building's ventilation system. Windows can be opened.
- People who are known to have a less efficiently operating immune system are not allowed inside the laboratory.
- All workers are tested regularly for evidence of infection, and/or can be vaccinated against the microbes they work with.
BSL 3

For various bacteria, parasites and viruses that can cause severe to fatal disease in humans but for which treatments exist:


Large Scale Operations BSL 2 agents (>10 Liters)

Recombinant and synthetic Nucleic Acid Molecules research

NIH/NIAID Bldg 33

Hardened Level 3 Facility at NIH

Poxvirus
Drug resistant TB
Tularemia
Food and Waterborne Pathogens
Viral Hemorrhagic Fevers (Ebola, etc.)
Avian Influenza
SARS (Coronavirus)
Bacteria Vaccine (non-GMP)

BSL-3 Laboratory

- Lab designed for work with infectious microorganisms that can easily become airborne (e.g. the bacteriology lab in a Hospital).
- All work with the microorganisms be done within biological safety cabinets or by personnel wearing protective clothing (i.e., gowns, scrub suits, coveralls, gloves).
- Increased restrictions for access to the lab.
- Double doors, which are sealed around their edges. Outside door must be fully closed before the inside door to the BSL-3 lab is opened.
- Ventilation systems in the BSL-3 lab are independent from the rest of the building's ventilation system.
- The air should flow from corridors to experimental work areas (negative pressure) where the microorganisms are being studied.
- The air from the laboratory is filtered before being exhausted directly to the outside and not into the general building circulation.
- The floors and walls are impermeable to fluids, and chemical resistant. While windows are permitted, they cannot be opened.
- All equipment and personnel are monitored and annually re-certified.
BSL 4

For dangerous arboviruses and exotic Arenaviruses and Filoviruses that pose a high individual risk of aerosol-transmitted laboratory infections, agents which cause severe to fatal disease in humans for which vaccines or other treatments are not available:

Bolivian and Argentine hemorrhagic fevers, Marburg virus, Ebola virus, Lassa virus, Crimean-Congo hemorrhagic fever, and various other hemorrhagic diseases.

Herpes B Virus
Highly Virulent Avian Flu (H7N9)
MERS-CoV
Variola major (Smallpox)
### BSL 4 Containment Laboratories Worldwide

(62 as of 2015)

<table>
<thead>
<tr>
<th>Country</th>
<th>Count</th>
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<tbody>
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<tr>
<td>Argentina</td>
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</tbody>
</table>

### FIELD BSL 4 (Ebola Virus Disease)

Vikers Aircraft Transport Isolator (VATI)
BSL 4 Containment Facilities in USA
Operational Facilities
USAMRIID in Fort Detrick, MD (Renovated 2011)
CDC in Atlanta, GA (two buildings operational)
NIAID’s Integrated Research Facility in Fort Detrick, MD
NIAID's Rocky Mountain Laboratories in Hamilton, MT
NIH’s BSL-4 lab 12735 Twinbrook Pkwy, Rockville, MD
NIH’s BSL-4 lab 12735 Twinbrook Pkwy, Rockville, MD
Southwest Foundation for Biomedical Research in San Antonio, TX
UTMB's Shope Laboratory in Galveston, TX
Georgia State University in Atlanta, GA (smaller "glovebox" facility
The Division of Consolidated laboratory Services lab (part of the
Department of General Services of the Commonwealth of Virginia) in
Richmond, VA (so-called "surge" BSL-4 capacity)
The Infectious Disease Unit (IDU) of the Oklahoma Animal Disease
Diagnostics laboratory (OADDL) at Oklahoma State Univ

Department Homeland Security
National Biodefense Analysis and Countermeasures Center (NBACC) in Fort Detrick, MD (completed 2008)
BSL 4 Containment Facilities in USA
Under Construction

Boston University’s National Emerging Infectious Diseases Laboratory (NEIDL) in Boston, MA (initially 2012 – but ?) (community protesting construction)

DHS’s National Bio and Agro-defense Facility (NBAF) in Manhattan, KS (2015 – 2023) (will replace (PIADC) Plum Island Facility)

BSL-4 Laboratory

- Designed for work with microorganisms that pose a dire health threat (i.e., Ebola virus, Bacillus anthracis, Marburg virus, and Hantavirus)
- Two hallmarks of the microorganisms under study is their ability to be easily transmitted to an from people via the air and from person to person.
- The laboratory is designed to be a secure facility to prevent the release of these microorganisms into the environment and protects the researchers from infection.
- Only highly trained and certified personnel are allowed into the laboratory.
- Entry to the Level 4 area requires passage through several checkpoints and only after the person has been vaccinated against the microorganism under study.
- All work in the level 4 lab is done in a pressurized and ventilated suit; the air for breathing is passed into the suit through a hose and is filtered so as to be free of microorganisms.
- Standard operating procedures are in place for every technique and operation and all work done in the laboratory is documented.
- The laboratory is completely isolated from the rest of the rooms in the building.
- Since 2001, security against sabotage or deliberate damage has been added as a design feature (e.g. perimeter illumination and fence, guards, security gates, observation cameras, and multi-levels of secured access.)
Case Study: Vaccinia infections

5 cases of occupational exposure to Vaccinia that resulted in hospitalization

CDC investigation of the cases identified four preventable causes for these significant occupationally-related Vaccinia infections

1. The employee’s refusal to receive vaccination
2. The laboratory failure to vaccinate their employees
3. Failure to revaccinate individuals with inadequate response to an initial vaccinia vaccination
4. Failure to re-vaccinate (booster) exposed employees at 10 years.

Ref: MMWR 2008 (Vol. 57, No. 15)

Case Study: Sabia Virus

A centrifuge bottle containing Sabia virus cracked during centrifugation in a large floor-model centrifuge.

The centrifuge was opened, the cracked bottle removed, and bleach was added to the spilled culture. PAPR available; not worn. Sabia transmitted by aerosol to researcher.

Case study: scrub typhus

Researcher isolating proteins of Orentia (Rickettsia) tsutsugamushi (scrub typhus)

Biosafety cabinet present in lab, BUT its use was not written into published procedure.

Infected cells were disrupted with tissue grinder out on the open bench.

First documented case of scrub typhus transmitted by aerosol route.

Subsequent spread in the community by insect vector
Case study: Neisseria meningitidis

2 fatalities in clinical lab staff in 2001; CDC launched web and email survey to determine whether extent of problem. Found 16 probable cases worldwide occurred 1985 and 2001. 6 US cases between 1996 and 2000. Nine cases (56%) were serogroup B; seven (44%) were serogroup C. Eight cases (50%) were fatal—or 50% (compared to 10-15% fatality in community-acquired infections.) All cases occurred among clinical microbiologists. In 15 cases (94%), isolate manipulation was performed without respiratory protection on the open bench. J. Clin Micro. 43(9) 4811-4814.

Case study: Tuberculosis

3 positive PPD tests occur simultaneously in a clinical micro lab. Check X-rays taken, INH offered.

Investigation: “faulty” biosafety cabinet—continuous re-circulation; no exhaust.

One refused post-exposure treatment was later diagnosed with endometrial tuberculosis; culture yielded M. tuberculosis.

Case Study: Brucella

8 out of 26 microbiologists were infected with Brucella melitensis. 5 positive blood cultures for B. melitensis, biotype 3. After 1 confirmed case, did serology on lab staff; 8 had evidence of serologic evidence of infection; 7 had clinical illnesses between May and September. No laboratory isolation for 3 years….?????? Extensive investigation….. 6 weeks before the outbreak, a frozen brucella isolate from a patient hospitalized 3 years earlier had been thawed and subcultured—out on the open bench. infected staff had all worked in lab during manipulation implies an aerosol exposure. Journal of Clin Micro 1991 29(2) 287-290.
Case Study: Brucella

Experimental aerosolization vaccine studies:

Use of aerosol-generating devices to expose animals to aerosol challenges.

3 staff members seroconverted after use of Madison aerosol chamber.

Leaky valve: staff not wearing respirators.

Staff member exposed to Brucella when decontaminating same type of chamber during a training session.

Case Study: Brucella

2 staff members collect nasal swabs from infected pigs.

Staff wore dust masks, not respirators, for the procedure.

Lab worker infected with strains identical to strains used to inoculate pigs.

1 LAI infected with 4 strains; 2nd LAI with 2 strains.

Note: Oddly, authors state infections occurred despite Animal Biosafety Level 3 procedures!

Case Study: SARS:

Biosafety Level 2 laboratory 5/18/2004 in Beijing, China, analyzed Coronavirus-CoV (Severe Acute Respiratory Syndrome or SARS) samples inadequately inactivated before removal from BL3 lab.

Resulted in:

2 laboratory-acquired infections
2 secondary infections (mother, nurse)
5 tertiary infections

1 secondary infection was fatal.
Case Study F. tularensis

Strain verification to determine if inactivated infectious material coming into the facility?

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

Inadvertently handled virulent F. tularensis; cross-contamination may have occurred from rabbit blood used in culture media.

3 cases of tularemia pneumonia in lab staff

References

Laboratory-acquired Infections


Meyer, KF, Eddie BL. Laboratory infections due to Brucella, J Infect Dis, 68: 24-32, 1941


Occupational Infections, Library of Medicine, 2012; http://www.haz-map.com/infect.htm

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Occupationally-associated HIV PEP

CDC. Update: provisional USPHS recommendations for chemoprophylaxis after occupational exposure to HIV. MMWR 1996;45:468-72.


CDC. Updated U.S. Public Health Service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for post-exposure prophylaxis. MMWR 2001;50 (No. RR-11):1--52.

References
Occupationally-associated HIV PEP


NIH 2015 Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents developed by the DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents; A Working Group of the Office of AIDS Research Advisory Council (OARAC)