Biological Risk Assessment: The Foundation for the Practice of Safe Science

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Biological Risk Assessment: The Foundation for the Practice of Safe Science

- The Leadership of Arnold G. Wedum, M.D., Ph.D.
  - Director of Industrial Health and Safety at the U.S. Army Biological Research Laboratories, 1946 – 1979
  - Revered as the “Father of Microbiological Safety”
- Expert in the discipline of biological risk assessment
- Advisor in microbiological safety for the NIH and CDC

Laboratory-Associated Infections with Pathogens Now Classified as Select Agents

Period of LAI Report

Select Agents	1930 - 1978	1979 - 2004	2005 - 2009
Viruses			
Cercopithecine herpesvirus	21	10	
Crimean-Congo hemorrhagic fever	8		
EEE	4		
Ebola	1	4	
Marburg	25	2	
Hemorrhagic fever viruses	368	9	
Junin	21	1	

Source: National Research Council, *Protecting the Frontline in Biodefense Research; The Special Immunizations Program* 2011, and Harding and Byers 2006.

Laboratory-Associated Infections with Pathogens Now Classified as Select Agents - *Continued*

Period of LAI Report

Select Agents	1930 - 1978	1979 - 2004	2005 - 2009
Viruses			
Machupo	1	1	
Kyasanur forest disease	133		
Omsk hemorrhagic fever	5	4	
Russian spring and summer encephalitis	8		
Rift Valley fever	47	6	
Venezuelan equine encephalitis	146	1	

Source: National Research Council, *Protecting the Frontline in Biodefense Research; The Special Immunizations Program* 2011, and Harding and Byers 2006.

Laboratory-Associated Infections with Pathogens Now Classified as Select Agents - *Continued*

Period of LAI Report

Select Agents	1930 - 1978	1979 - 2004	2005 - 2009
Bacteria			
Coxiella burnetii	280	177	
Francisella tularensis	225	3	1
Rickettsia prowazekii	181	10	
Bacillus anthracis	40	1	
Brucella spp.	426	143	3
Burkholderia mallei		3	

Source: National Research Council, *Protecting the Frontline in Biodefense Research; The Special Immunizations Program* 2011, and Harding and Byers 2006.

Milestones in Biological Safety

1857 Pasteur discovers microbial fermentation

1876 Koch proves *Bacillus anthracis* etiology of anthrax

1887 Bruce isolates *Brucella melitensis*

1912 McCoy isolates *Pasteurella tularensis*

1946 Wedum leads biosafety program at Fort Detrick

Milestones in Biological Safety

1951 Sulkin and Pike report on laboratory-acquired infections

1957 Transportation of etiological agents (42 CFR 72)

1964 National Cancer Institute Special Virus Leukemia Program

1969 NIH first high-containment research laboratory (Building 41)

Milestones in Biological Research

Biohazards in Biological Research, the Proceedings of a Conference held at the Asilomar Conference Center, Pacific Grove, California, January 1973

- Laboratory infections introduced by experimental animals or animal cell culture
- The tumor viruses themselves - how dangerous are these agents?
- Hazards associated with modern research methodology
- What can be done to control biohazards in cancer research?

Milestones in Biological Safety

1974 National Cancer Institute Safety Standards for Research Involving Oncogenic Viruses

Moderate Risk Viruses

1) RNA Tumor Viruses
    a. Feline Leukemia
    b. Feline Sarcoma
    c. Woolly Monkey Fibrosarcoma
    d. Gibbon Ape Lymphosarcoma

Milestones in Biological Safety

Moderate Risk Viruses *(Continued)*

2) DNA Tumor Viruses
   a. *Herpesvirus saimiri*
   b. *Herpesvirus ateles*
   c. Yaba pox virus
   d. Epstein-Barr virus
   e. Non-defective Adeno-2 SV-40 hybrids
3) RNA and/DNA virus isolates from man with possible oncogenic potential

Milestones in Biological Safety

1975 Asilomar Conference on Recombinant DNA

- Discovery that genes from different species of bacteria could be recombined in the laboratory
- 1974 worldwide voluntary moratorium
- Assessing risks and containment
- Need for guidelines (published for public comment in 1978)

Milestones in Biological Safety

1976 CDC Classification of Etiologic Agents on the Basis of Hazard:

- **Class 1** – Agents of no or minimal hazard (under ordinary conditions of handling)
- **Class 2** – Agents of ordinary potential hazard (contained by ordinary lab techniques)
- **Class 3** – Agents involving special hazard (require special conditions for containment)
- **Class 4** – Agents that are extremely hazardous to laboratory personnel (require the most stringent containment)

Fort Detrick Risk Assessment Paradigm

- Number and severity of laboratory infections
- Infectious dose for humans
- Infection from procedure or equipment
- Hazards peculiar to the animal species
  - Infection of cagemate by inoculated animal
  - Excretion of the infectious agent in urine, feces, or saliva host susceptibility
- Practices and procedures of laboratory workers
- Available specific therapy or effective vaccine

BMBL 5th Ed. Risk Assessment Paradigm

- Identify agent hazards
  - Capability to infect and cause disease
  - Severity of disease
  - Availability of vaccines and effective treatments
- Identify laboratory procedure hazards
  - Agent concentration and suspension volume
  - Equipment and procedures that generate aerosols
  - Procedures involving animals: potential for bites and scratches; exposure to zoonotic agents
- Determine biosafety level and additional necessary safeguards

BMBL 5th Ed. Risk Assessment Paradigm

- Evaluate the proficiencies of staff regarding safe practices and the integrity of safety equipment
- The Lab Director or PI is responsible for:
  - Ensuring that laboratory workers have acquired the technical proficiency in the use of microbiological practices and safety equipment
  - Safety equipment
- Review the risk assessment with a biosafety professional, subject matter expert, and the IBC

NIAID Category A Priority Pathogens

Category A agents pose the highest risk to national security and public health. Can be easily disseminated or transmitted from person to person. Result in high mortality rates and have the potential for major public health impact. They might cause public panic and social disruption, and require special action for public health preparedness.

Category A Priority Pathogens

- *Bacillus anthracis*
- *Clostridium botulinum* toxin
- *Yesinia pestis*
- *Variola major* and other related pox viruses
- *Francisella tularensis*

NIAID Category B Priority Pathogens

Category B pathogens pose the second highest priority organism/biological agents. They are moderately easy to disseminate, result in moderate morbidity rates and low mortality rates, and require specific enhancements for diagnostic capacity and enhanced disease surveillance.

Category B Priority Pathogens

- Burkholderia pseudomallei
- Chlamydia psittaci
- Brucella species
- Staphylococcal enterotoxin B
- Typhus fever
- Epsilon toxin of Clostridium perfringens
- Burkholderia mallei
- Coxiella burnetii
- Ricin toxin
- Food- and Waterborne pathogens

Risk Assessment of Emerging Infectious Disease Agents

To assess the risk of a new disease, find out what is known about it:

- Has the agent been identified?
- Is it related to a known and characterized infectious agent? Use as a default.
- Is morbidity and mortality worse than with the related agent? If yes, consider it a higher risk.
- Determine the potential routes of infection based on clinical history. Aerosols are of greatest risk.

Risk Assessment of Emerging Infectious Disease Agents

- Increased use of exotic animals for pets and as food sources allows pathogens to jump from animal reservoirs to humans
- Close contact with imported exotic pet rodents was the origin of a US outbreak of monkeypox
- SARS coronavirus went from exotic civet cats imported for meat in China to human hosts

Risk Assessment of Laboratory-created Agents

Recombinant DNA

- Guidelines developed and constantly revised to address new technologies and concerns
- Risk Assessment guidelines in Section II
- Risk Groups in Appendix B
- Appendix B-V lists low risk animal viruses and retroviruses used as vectors

Risk Assessment of Laboratory-created Agents

Synthetic Genomics

- Synthetic genomics is the stringing together of short fragment of DNA called oligonucleotides (a short chain of nucleotides, the building blocks of DNA).
- “Oligos” may be made in a research laboratory or ordered from a central supplier.
- Synthetic genomics is a dual-use technology offering potential benefits (vaccines, drugs, efficient manufacture and contributions to basic research), but bioterrorists could use this technology to synthesize pathogens.
- Probably no more of an actual risk than with rDNA, but could lead to unforeseen results.

Risk Assessment of Laboratory-created Agents

Experiments of Concern

Seven experiments of concern, according to the 'Fink Report,' would require special review / approval:

- Demonstrate how to render a vaccine ineffective
- Confer resistance to therapeutically useful antibiotics or antiviral agents
- Enhance the virulence of a pathogen or render a non-pathogen virulent
- Increase transmissibility of a pathogen
- Alter the host range of a pathogen
- Enable the evasion of diagnostic / detection modalities
- Enable the weaponization of a biological agent or toxin

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