

History of Biosafety

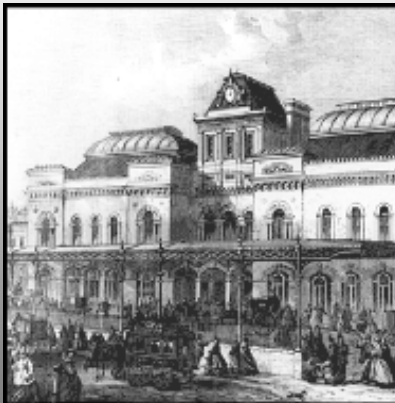
***“If you would understand anything,
observe its beginning and its
development.” Aristotle***

**Chesapeake Area Biological Safety Association’s
2009 Scientific Symposium
June 11, 2009**

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President, Proven Practices, LLC
www.provenpractices.com**

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A Beginning



- 1854 London cholera epidemic
- Edwin Chadwick and John Snow
- Water pollution and disease transmission
- Ignited “the sanitation revolution”

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A Beginning

Lessons Learned ¹

- Effective intervention does not always need accurate knowledge of disease causation
- Environmental measures may be more effective than changing individual behavior
- Always search for pragmatic solutions

BMJ readers chose “the sanitation revolution” as the top medical milestone since its inaugural publication in 1840.

¹ Mackenbach, J. Sanitation: pragmatism works. BMJ 2007; 334: s17

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In with the Germ Theory - Out with the Miasma Theory

- Pasteur established the germ theory in 1862
 - Demonstrated that fermentation is caused by the growth of microorganisms; published paper on lactic fermentation in 1857
- Isolation and culturing of bacteria
 - Robert Koch: *Bacillus anthracis* - 1877; tuberculosis bacilli - 1882; *Vibrio cholera* - 1883; *Corynebacterium diphtheriae* - 1881- 1884; *Salmonella typhi* - 1884 (Gaffky); *Yersinia pestis* - 1894 (Yersin)
 - David Bruce: *Brucella melitensis* - 1887

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In with the Germ Theory - Out with the Miasma Theory

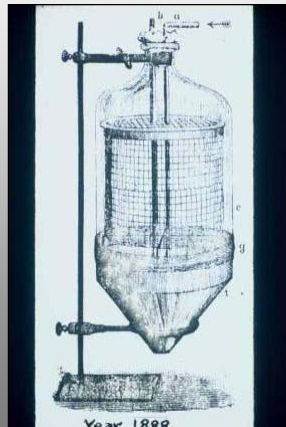
First Laboratory Infections

- 1885** Typhoid lab infection, unknown cause
- 1893** Tetanus lab infection by syringe
- 1894** Cholera lab infection by pipette
- 1897** Brucella lab infection by syringe
- 1898** Glanders lab infection by syringe
- 1899** Diphtheria lab infection by pipette

Adapted from Kisskalt, 1915; Riesman, 1898; Birt, 1899

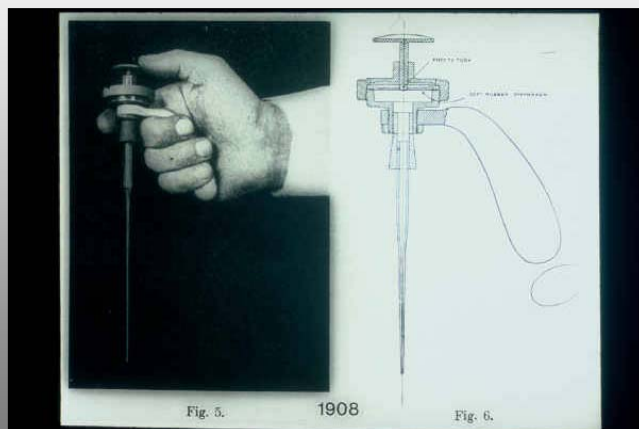
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Cotton for Exhaust Air for Anthrax Aerosol Challenge (Buchner)



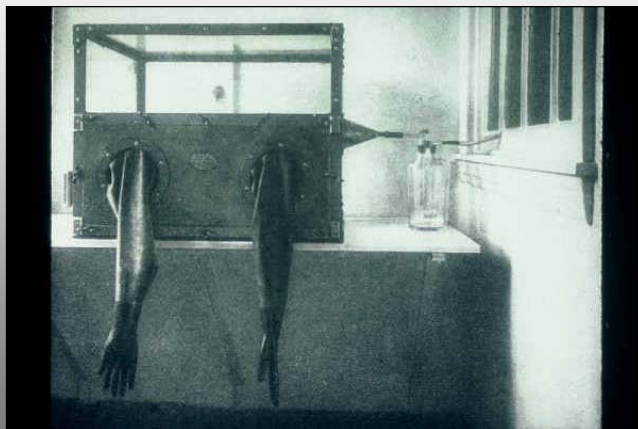
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What LAI encouraged the development of pipetting aids?



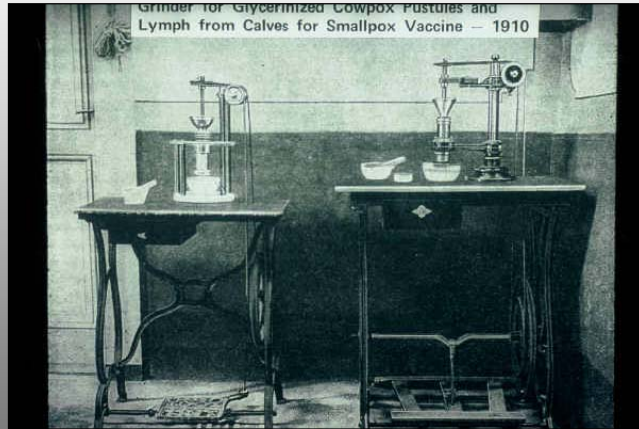
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Tuberculin Preparation



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Grinder for Glycerinized Cowpox Pustules



1910

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From “NIH: An Account of Research in its Laboratories and Clinics” 1984

Referring to George W. McCoy, Director of the Hygienic Laboratory (1915 - 1937)

“I have often pondered McCoy’s genius for choosing productive research people. He sought dedication and industry in young researchers and rarely imposed his decisions on them. Between the lack of laboratory training and the rather primitive conditions for handling infectious materials, there is little wonder at the frequency of serious disease among the workers.”

Sanford M. Rosenthal, M.D., Scientist Emeritus
Laboratory of Biochemical Pharmacology
National Institute of Arthritis, Diabetes, and Digestive and
Kidney Diseases

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Reports and Surveys of Laboratory Associated Infections

Surveys of Laboratory Infections

Kisskalt, K. 1915. Laboratory Infections with Typhoid Bacilli.
Zeitschrift fur Hygiene und Infektionskrankheiten 80:145-162

Meyer, K.F. and Eddie, B. 1941. Laboratory Infections Due to Brucella.
J. Infect. Dis. 68:24-32

Sulkin, S. E. and Pike, R.M. 1951. Survey of Laboratory-Acquired
Infections. *Amer. J. Public Health* 41:769-781

Pike, R.M. 1976. Laboratory-associated Infections: Summary and
Analysis of 3921 Cases. *Health Laboratory Science* 13:105-114

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Reports and Surveys of Laboratory Associated Infections

Multiple Laboratory Infections

Agent	Probable Source	LAI	Year
<i>Franciscella tularensis</i>	handling rodents	6	1920
<i>Brucella melitensis</i>	centrifuge	45	1938
<i>Coxiella burnetii</i>	centrifuge use	47	1947
VEE	dropped lyophile tubes	24	1959
Marburg virus	blood and organ	23	1968

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Reports and Surveys of Laboratory Associated Infections

Cause of 3921 Laboratory-associated Infections

Cause	Number	Percent
Aerosol	522	13
Accident	703	18
needle and syringe		
spills and sprays		
sharps injuries		
pipetting by mouth		
animal bite or scratch		
Essentially unknown	2696	69

Adapted from Pike 1976

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Fort Detrick Contributions to Biosafety 1943 - 1969

- **Occupational health program**
 - Health and safety of workers highest priority
 - Treat every infection as a LAI until proven otherwise
 - Reporting exposures was encouraged
- **Risk assessment**
 - Number and severity of LAI
 - Infectious dose for humans
 - Availability of specific therapy or effective vaccine

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Fort Detrick Contributions to Biosafety 1943 - 1969

- **Applied research**
 - Pioneered risk assessment studies
 - Developed and validated decontamination protocols
 - Evaluated microbial hazards and protocols
 - First microbial test of AAF 50 FG
 - Evaluated efficiency of HEPA filters for capturing viral particles

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Estimated Rate of Laboratory-acquired Infections Among Fort Detrick Personnel 1943 - 1969

Period	Personnel at Risk	Approximate Containment Level	LAI / Million Person-hours Worked
1943 - 1945	primarily military	P1	35
1954 - 1958	primarily civilian	P2	9
1960 - 1962	primarily civilian	P3	2
1960 - 1969	primarily civilian	P4	1

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Applied Research in Biosafety

Lessons from History and Epidemiology of Laboratory Infections

- When an agent that may cause disease is studied in the laboratory, it is logical to expect sooner or later that some laboratory worker will become infected with the agent.
- Analysis of outbreaks inside laboratory buildings with no primary or secondary barriers shows no infections outside the buildings in persons not associated with the laboratory.
- Class III BSC systems can operate without LAI in whole-body and head-only aerosol studies using repetitive procedures with stable, well trained, and well disciplined workers.

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Applied Research in Biosafety

Lessons from History and Epidemiology of Laboratory Infections

- Research using repetitive procedures is less hazardous than research requiring frequent changes in technique and equipment.
- In the absence of effective vaccination, it is not possible to do basic research using Class I BSCs with a highly infective agent without LAI.

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Biosafety Outreach

Fort Detrick (1943 - 1969)

- Created the Biological Safety Conference in 1955
- Provided guidance to federal agencies in support of the development of biosafety programs and guidelines
- Published papers on biosafety practices, risk assessments, and applied research projects
- Dr. Wedum was a mentor to whoever asked for his guidance

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Arnold Gerhard Wedum, Ph.D, M.D. 1903 - 1976



18th Biological Safety Conference in
Lexington, Kentucky, 1975

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Honor Roll

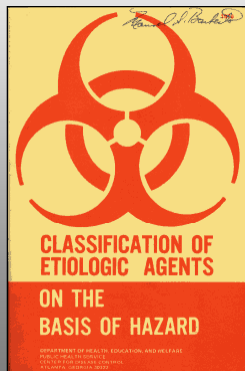
Mentors on Whose Shoulders Biosafety Flourished

- Arnold Wedum
- Everett Hanel
- Briggs Phillips
- Manny Barbeito
- Jerry Tulis

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Biosafety Guidelines

Classification of Etiological Agents on the Basis of Hazard



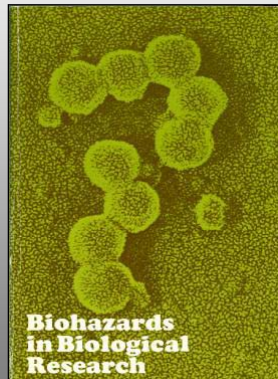
1969

- Four classes of hazard (1, 2, 3, 4)
- A fifth class (5) of animal agents with USDA restrictions
- Scientific judgment of PI (risk assessment)
- Competence and physical containment

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Biosafety Guidelines

**Asilomar Conference
January 22 - 24, 1973**



Experiments of Concern:

- SV40-lambda hybrid (Paul Berg)
- Non-defective adenovirus-SV40 hybrids (Andrew Lewis)

Proceedings of a Conference held at the
Asilomar Conference Center, Pacific Grove, CA

Edited by:
Hellman, National Cancer Institute
M.N. Oxman, Harvard Medical School
R. Pollack, Cold Spring Harbor Laboratory

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Biosafety Guidelines

**NCI Safety Standards for Research Involving
Oncogenic Viruses**



1974

- Three classes (low, moderate, high) of potential hazard
- PI and Individual responsibility
- Practices, safety cabinets, and facilities
- Medical surveillance

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Biosafety Guidelines

Asilomar Conference on Recombinant DNA Molecules February 24 - 27, 1975

Organizing Committee:

Paul Berg; David Baltimore; Sydney Brenner; Richard
Roblin III; Maxine Singer

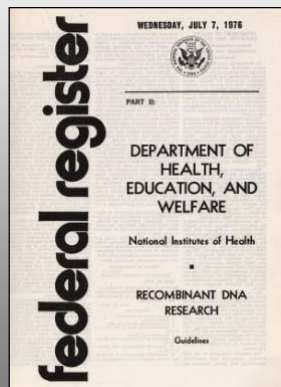
Conference Agenda:

- Review progress in rDNA research
- Consider potential biohazards
- Consider ethical and legal concerns
- Draft a conference summary paper with recommendations

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Biosafety Guidelines

NCI Recombinant DNA Research Guidelines



1976

▪ Containment

- Physical: P1; P2; P3; P4
- Biological: EK1; EK2; EK3

▪ Experimental Guidelines

- Risk assessment
- Selecting containment

▪ Roles and Responsibilities

- Principal investigators
- Institutions
- Institutional Biohazard Committee

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Biosafety Guidelines

Biosafety in Microbiological and Biomedical Laboratories



1984 1st Edition

- Advisory recommendations
- Voluntary code of practice
- Goal of upgrading operations
- Guide for laboratory construction or renovation
- Application to laboratories based on risk assessment

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Biosafety Training

- Safe practices in research involving oncogenic viruses and rDNA molecules (NIH 1972 - 1979)
- Train-the-trainer course on fundamentals for safe microbiological research (NIH / ASM 1977 - 1978)
- Instructors' Guide for Biosafety Training (NIH 1983)
- American Biological Safety Association (1984)
- National Biosafety & Biocontainment Training Program (NIH 2004)

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Regulatory Oversight for Biosafety Laboratory Practices

- **Interstate Shipment of Etiological Agents**
 - DOT 42 CFR Part 72 (1957)
- **Occupational Exposure to Bloodborne Pathogens**
 - OSHA 29 CFR Part 1910.1030 (1991)
- **Possession, Use, and Transfer of Select Agents**
 - CDC 43 CFR Part 73 (2005)
 - APHIS 9 CFR Part 121, and 7 CFR Part 331 (2005)

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Public Health Security and Bioterrorism Preparedness and Response Act of 2002

- **Sense of Congress**
 - Recognizes existing role of university programs in developing biodefense products and solutions
 - Accelerating university programs will contribute significantly to defense against biological threat or attack
 - Encourages additional resources to expand and maximize effectiveness of university programs
 - Encourages Secretary of DHHS to recognize importance of university programs when making awards and grants in accordance with this Act

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Public Health Security and Bioterrorism Preparedness and Response Act of 2002

- **Regulations for the transfer, possession and use of select agents**
 - Risk assessment (including children and vulnerable populations)
 - Ensure appropriate training and skill in handling select agents
 - Containment laboratories
 - Security measures commensurate with the risk such agent or toxin poses to public health and safety (including the risk of use in domestic or international terrorism)
 - Procedures to protect the public safety
 - Availability of select agents for research, education and other legitimate purposes

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Evolution of Protections for Research Animals, Biomedical Research and Health Care Personnel, and Human Subjects

Animal Care and Use	Biological Safety	Protection of Human Subjects
1940 - 1959		
1950 Animal Care Panel	1942 Fort Detrick BW program 1947 NIH Memorial Laboratory 1955 First Biological Safety Conference	
1960 - 1969		
1963 Guide for Laboratory Animal Facilities and Care 1965 AAALAC 1966 Animal Welfare Act (PL-89-544) 1969 Animal Care Panel became AALAS	1964 NCI Biohazard Safety Program 1966 Biohazard Symbol 1969 CDC Classification of Etiological Agents on the Basis of Hazard	1960 The Nuremberg Code 1964 Declaration of Helsinki 1966 NIH issues policies for the protection of human subjects; establishes IRBs

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Evolution of Protections for Research Animals, Biomedical Research and Health Care Personnel, and Human Subjects

Animal Care and Use	Biological Safety	Protection of Human Subjects
1970 - 1979		
1974 PRIM&R 1979 PHS Policy requires institutional committees to oversee animal research	1971 Nixon terminates US BW program 1972 BW Convention 1975 Asilomar Conference on rDNA Molecules 1976 NIH rDNA Guidelines creates IBC	1974 National Research Act (PL 93-348) mandates IRBs and National Commission for the Protection of Human Subjects 1978 Belmont Report
1980 - 1989		
1985 Amendments to the AWA mandates IACUC 1985 Health Research Extension Act (PL 99-158) sets guidelines for animal care	1984 Biosafety in Microbiological and Biomedical Laboratories (BMBL) 1984 rDNA gene transfer guidelines	1980 Institutional Review Board Guidebook 1984 rDNA gene transfer guidelines 1989 Amended Declaration of Helsinki

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Evolution of Protections for Research Animals, Biomedical Research and Health Care Personnel, and Human Subjects

Animal Care and Use	Biological Safety	Protection of Human Subjects
1990 - 2009		
1992 IACUC Guidebook - ARENA and OPRR 1996 Guide for the Care and Use of Laboratory Animals 7th Edition 1997 AAALAC International 2002 IACUC Guidebook, 2nd Edition	1991 Bloodborne Pathogens Rule 2002 Public Health Security and Bioterrorism Preparedness and Response Act (PL-107-188) 2004 Fink Report 2006 NSABB 2009 BMBL 5th Edition	1993 OHRP IRB Guidebook 2009 OHRP Research Community Forums

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