



HOWARD HUGHES MEDICAL INSTITUTE

RISK ASSESSMENT AND CONTAINMENT

Presented by

W. Emmett Barkley

Director, Office of Laboratory Safety
Howard Hughes Medical Institute

September 21, 2004

RISK ASSESSMENT

- Identifying risk factors
- Evaluating the likelihood for exposure
- Evaluating the potential consequences of an exposure
- Evaluating the capability of safeguards to control risks

IDENTIFYING RISK FACTORS

- Agent hazards
- Protocol hazards
- Susceptibility to disease of at-risk persons

AGENT HAZARDS

- Pathogenicity
- Virulence
- Infectious dose
- Route of transmission
- Agent stability
- Host range

INFECTIOUS DOSE FOR 25 TO 50% OF HUMAN VOLUNTEERS

<u>Agent</u>	<u>Dose</u>	<u>Route of Inoculation</u>
■ <i>Francisella tularensis</i>	10	Inhalation
■ <i>Coxiella burnetii</i>	10	Inhalation
■ <i>Mycobacterium tuberculosis</i>	<10	Inhalation
■ <i>Salmonella typhi</i>	10 ⁵	Ingestion
■ <i>Francisella tularensis</i>	10 ⁸	Ingestion
■ VEEV	1 ^(a)	Subcutaneous
■ Influenza A2 virus	<790 ^(b)	Nasopharyngeal
■ Measles virus	0.2 ^(c)	Intranasal spray

(a) Minimum infectious dose; Guinea pig infective unit

(b) Minimum infectious dose

(c) Medium infectious tissue culture dose in children

PROTOCOL HAZARDS

- Agent concentration
- Manipulations that produce droplets and aerosols
- Manipulations involving sharps
- Manipulations with high potential for spills and splashes
- Exposure to zoonotic diseases of experimental animals
- Alteration of agent hazards

RISK FACTORS ASSOCIATED WITH EXPERIMENTAL RECOMBINATION OF INFECTIOUS AGENTS

- Virulence
- Host range
- Compromise use of effective treatments
- Vigilance

HUMAN SUSCEPTIBILITY TO DISEASE

- Wide variation in infectious dose
- Reduced immunological competency
- Availability of vaccines, treatments
- Occupational medical evaluation

LIKELIHOOD OF EXPOSURE

- Person conducting protocol
- Other person in same lab
- Person not associated with the lab

MOST FREQUENTLY DOCUMENTED REPORTS OF LABORATORY-ASSOCIATED INFECTIONS - 1930 to 1999

<u>Agent</u>	<u>Laboratory-associated Infections</u>
■ <i>Brucella sp.</i>	507
■ <i>Coxiella burnetii</i>	456
■ <i>Mycobacterium tuberculosis</i>	417
■ Hepatitis viruses	380
■ <i>Salmonella sp.</i>	324
■ <i>Francisella tularensis</i>	225
■ Hantavirus	169
■ Venezuelan equine encephalomyelitis virus	150
■ (Influenza A2 virus)	(15)

AEROSOL RISK FACTORS

- Infectivity
- Viability
- Aerosol concentration
- Particle size

AEROSOL AND SURFACE RECOVERY FROM 10 PIPETTING OPERATIONS OF 10^9 /ML *B. SUBTILIS* (AVERAGE TIME 3 MIN; 1 ML PIPETTE; 2 ML BULB PIPETTER)

Summary Data from 6 runs	Airborne CFU	Settled CFU	
		Hands	Area
■ Lowest count	388	6,900	550
■ Average count	1,820	52,800	1,970
■ Highest count	5,110	228,000	3,700

Adapted from Chatigny, 1979

ESTIMATED AEROSOL EXPOSURE DOSE FROM PIPETTING OPERATION

<u>Individual Exposed</u>	<u>Good Technique</u>	<u>Poor Technique</u>
■ Person pipetting	25	1,200
■ Person in the room	<1	30

Assumptions:

Concentration	10^9 / ml
Time of operation	3 min.
Room volume	1,000 cu.ft.
Breathing zone around operator	27 cu.ft.
Breathing rate	1/3 cu.ft. / min.
Uniform diffusion of aerosol in room	

ESTIMATED AEROSOL EXPOSURE DOSE FROM OTHER OPERATIONS

<u>Operation</u>	<u>Viable Particles</u>
■ Blender lid opening after stop	1200
■ Sonic homogenizer (max aeration)	1200
(min aeration)	6
■ Streaking petri dish	<1
■ Dropping flask culture	360
■ Splash on centrifuge rotor	120

OUTBREAKS OF LABORATORY-ASSOCIATED INFECTIONS (LAI) WITHIN INSTITUTIONS

Agent	Outbreaks	LAI	Period
■ <i>Coxiella burnetti</i>	9	356	<1965
■ <i>Brucella sp.</i>	8	160	<1941
■ LCM virus	3	81	<1975
■ <i>Rickettsia prowazekii</i> ; <i>R. typhi</i>	3	59	<1954
■ Viral hemorrhagic fever (renal syndrome)	1	113	1962

Adapted from Wedum, 1976

CONTAINMENT

- Microbiological practices
 - Technical proficiency
 - Sterile technique
 - Washing hands
 - Good habits
- Primary barriers
 - Biological safety cabinets
 - Personal protective equipment

CONTAINMENT (*CONTINUED*)

- Facility safeguards

 - Access control

 - Directional air flow

- Hybrid containment

 - Adding BSL-3 safeguards to BSL-2

 - Adding BSL-4 safeguards to BSL-3