

**HHMI**

HOWARD HUGHES MEDICAL INSTITUTE

**RISK ASSESSMENT  
AND CONTAINMENT**

Presented by

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# 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 <sup>5</sup>     | Ingestion                   |
| ■ <i>Francisella tularensis</i>     | 10 <sup>8</sup>     | Ingestion                   |
| ■ VEEV                              | 1 <sup>(a)</sup>    | Subcutaneous                |
| ■ Influenza A2 virus                | <790 <sup>(b)</sup> | Nasopharyngeal              |
| ■ Measles virus                     | 0.2 <sup>(c)</sup>  | 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<br>from 6 runs | Airborne<br>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>Viabile 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

| <u>Agent</u>  | <u>Outbreaks</u> | <u>LAI</u> | <u>Period</u> |
|---|------------------|------------|---------------|
| ▪ <i>Coxiella burnetti</i>                          | 9                | 356        | <1965         |
| ▪ <i>Brucella sp.</i>                               | 8                | 160        | <1941         |
| ▪ LCM virus   | 3                | 81         | <1975         |
| ▪ <i>Rickettsia prowazekii</i> ;<br><i>R. typhi</i> | 3                | 59         | <1954         |
| ▪ Viral hemorrhagic fever<br>(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