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Risk Assessment in the Clinical Microbiology Laboratory

Montana ASCLS Spring Meeting

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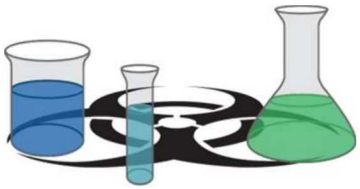

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Biorisk Assessment

- **According to the BMBL, 5th ed.**
  - "There is no standard approach for conducting a biological risk assessment, but some structure can be helpful in guiding the process." (Biosafety in Microbiological and Biomedical Laboratories, 5th ed., HHS Publication No. (CDC) 21-1112)
- **Risk assessments drive risk identification, prioritization, and mitigation measure determination**
  - Biosafety
  - Biosecurity

Overview

- **Define Risk**
- **Define Biosafety and Biosecurity, and components of each**
- **Discuss a structured process to conduct risk assessments**
  - Biosafety
  - Biosecurity
- **Risk Mitigation**
- **Risk Assessment Case Studies**
  - Ebola
  - Prions
  - Unknown Samples

Definitions

- **Biosafety**
  - Combination of equipment, practices and procedures, and PPE to minimize the likelihood of accidental exposure to biological material
    - **Protection of workers**

- **Biosecurity**
  - Combination of equipment and practices and procedures to minimize the likelihood of deliberate theft, diversion, exploitation of biological material, equipment, and expertise
    - **Protection of biological material**
    - **Protection of expertise**
    - **Protection of equipment**
    - **Protection of information**

Risk

- **Function of the likelihood an adverse event will occur and the consequences of the adverse event**
  - Risk = Likelihood * Consequences
  - Accidental exposures
  - Theft of biological material

- **Work with pathogens will always involve some level of biosafety and biosecurity risk**
  - Distinguish between “acceptable” and “unacceptable” risks
  - Risks must be prioritized
  - Cannot protect against every conceivable adverse event

- **Resources for risk mitigation are not infinite**
  - Risk mitigation is determined by risk assessment
  - Existing resources should be used efficiently

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BIOSAFETY

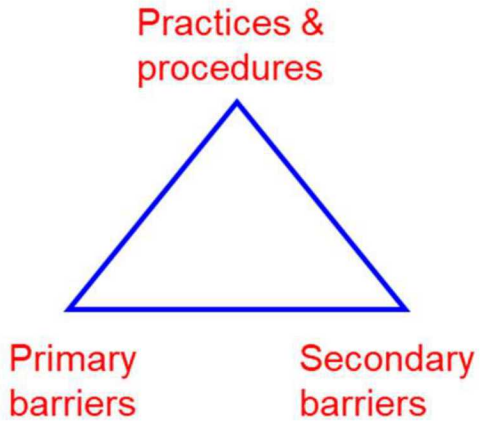
Biosafety Risk Assessment

1. **Characterize biological agents and activities**
   a. Evaluate biological agent characteristics and hazards
   b. Evaluate hazards of activities and procedures

2. **Evaluate scenarios**
   a. Create scenarios consisting of the specific agent and specific procedures
   b. Determine the likelihood of exposure based upon the procedure and the likelihood of infection based upon the agent as related to the method of exposure

3. **Characterize the risk**
   a. Evaluate the overall likelihood and consequences of each scenario
   b. Determine acceptable and unacceptable risks
   c. Prioritize

4. **Determine appropriate measures to mitigate the risks**
   a. Primary barriers, and secondary barriers
   b. Practices & procedures
   c. PPE



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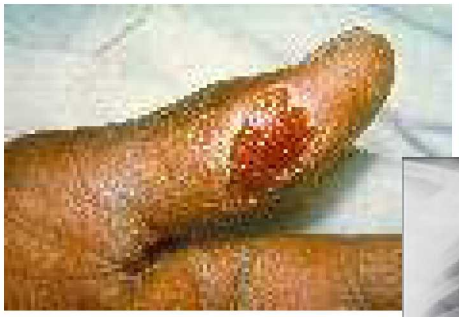
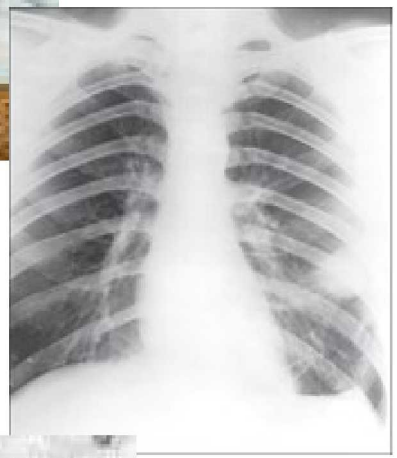
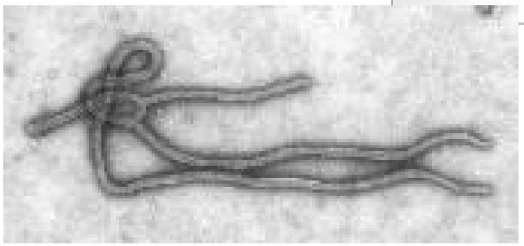
Biological Agent Characteristics

- **Effects and severity may vary**
  - Lethal
  - Incapacitating
- **ID_{50}: Number of organisms necessary to cause infection**
- **LD_{50}: Amount of agent necessary to kill 50% of animals tested**
- **Environmental stability**
- **Transmissibility**
- **Antibiotic resistance**
- **Route of entry**
  - Potentially result in different disease
- **Infectious (low ID_{50})**
- **Treatment availability**
- **Prophylaxis availability**
- **Endemic or exotic**
- **Host range**







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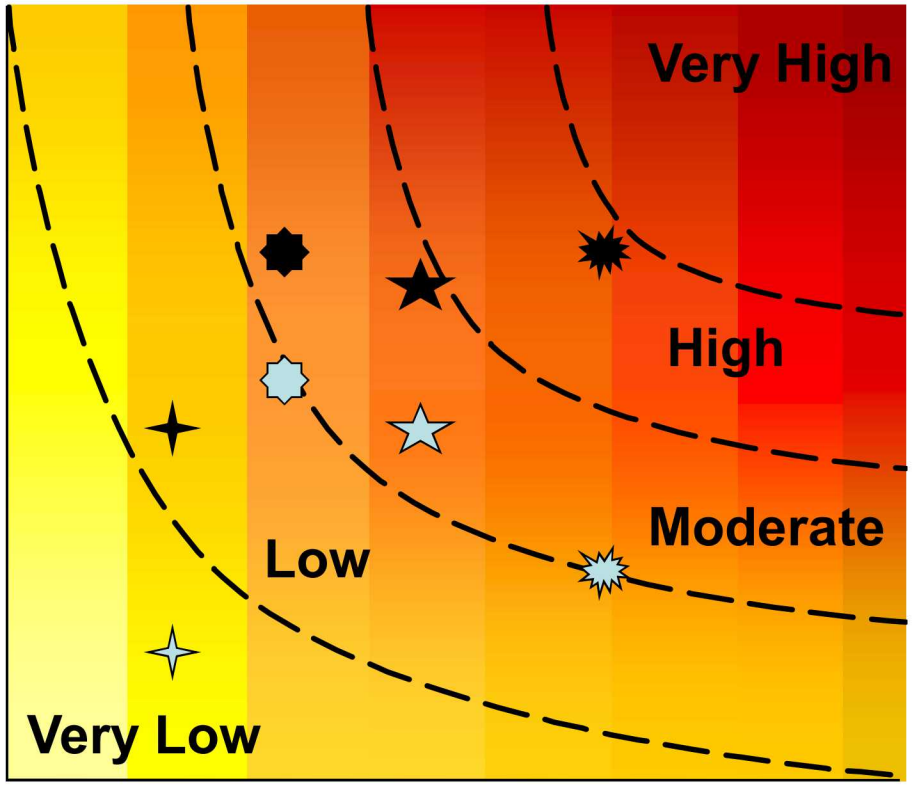
Activities and Scenarios

- **Identify scenarios for how exposures could occur**
- **Sample receipt**
  - Opening samples received by shipment
  - Sample collection procedures, such as blood or CSF
- **Sample manipulation**
  - Culture
  - Slide preparation
    - **Use of microtome for tissue preparation**
  - PCR
- **Biocontainment is the appropriate balance of practices & procedures, primary barriers and secondary barriers, and PPE necessary to mitigate risks**

Characterize the Risk



- Protect against unacceptable risk scenarios

- Develop mitigation measures and incident response plans for acceptable risk scenarios

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Biosafety Mitigation

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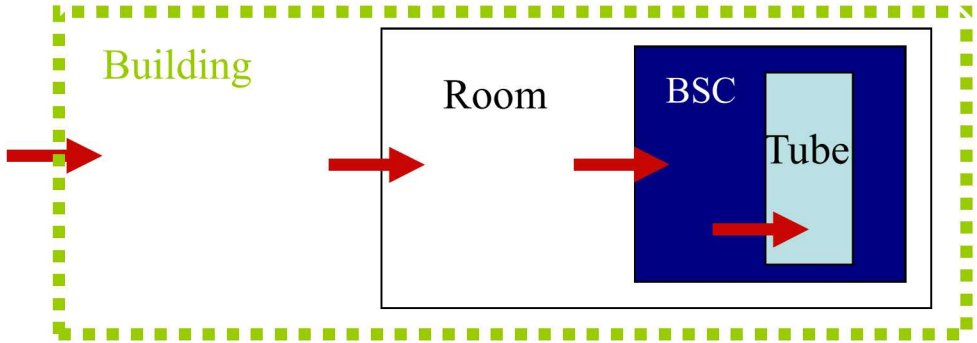
Biosafety: Engineering Controls

- **Primary barriers – contain the agent at the source**
  - Biological safety cabinet
  - Specialized lab equipment (centrifuges)

- **Secondary barriers – contain the agent within the room or facility *in case an agent escapes from the primary barriers***
  - Building & Room Construction
  - HVAC
    - **Directional airflow**
    - **Exhaust filtration**
  - Other Engineering Controls:
    - **Solid waste treatment**
    - **Wastewater treatment**



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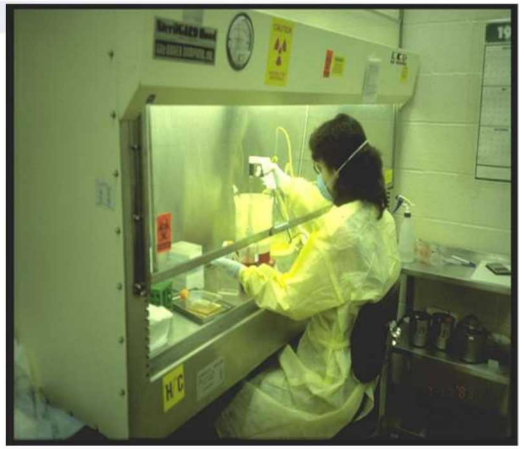
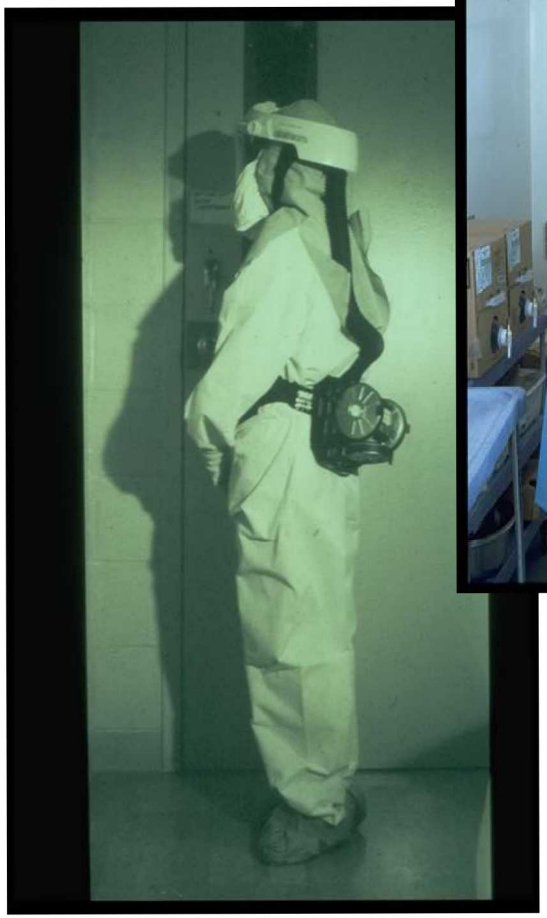
Biosafety: Standard and Special Procedures



- **Appropriate covering on work surface assists clean-up**
- **Appropriate disinfectant**
  - Chemical
  - Concentration
  - Contact time
- **Handwashing**
- **Procedures that minimize aerosol generation**

Biosafety: PPE Examples



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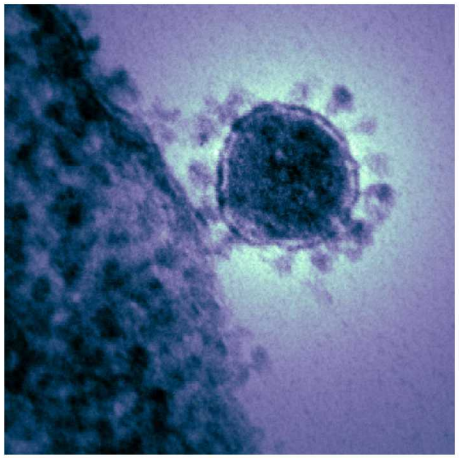
Severe Acute Respiratory Syndrome (SARS)

- In 2003, SARS infected over 8,000 people and killed approximately 800
- Cases in Pacific Rim and Canada
- Laboratory acquired SARS outbreaks
  - Singapore—September 2003
  - Taiwan (China)—December 2003
  - Beijing and Anhui (China)—March 2004



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Laboratory-Acquired SARS Outbreak in China, March-April 2004

- Occurred in Beijing and Anhui Province, linked to the National Institute of Virology, China CDC
- The source of the outbreak was failed or incomplete inactivation of SARS-CoV (cold inactivation)
- Involved two verified chains of SARS-CoV transmission
  - Three generations, resulting in 9 cases
- Serological analysis on the laboratory staff revealed three more seroconverted cases

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Laboratory-Acquired SARS Outbreak in China, March-April 2004

- A (female research student) 25 March
  - 2nd → B (A's mother) → death
  - 2nd → C (nurse attending A)
    - 3rd → D (C's mother)
    - 3rd → E (C's aunt)
    - 3rd → F (C's father)
    - 3rd → G (retired doctor sharing hospital room with C)
    - 3rd → H (G's daughter-in-law)
- I (male laboratory researcher) 17 April

SARS IgG (+) J (female laboratory worker in BSL-3 laboratory)
K (female laboratory worker developed pneumonia)
L (male laboratory worker, A's supervisor)

China CDC

Common Problems

- Bad practice in laboratory management
- Poor supervision of less experienced professionals
- A lack of accountability for occupational health and safety
- A lack of biosafety policy
- A lack of biosafety procedures and staff training in biosafety practice
- A lack of internal and external quality assurance

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Summary of Biosafety Level Requirements

Table 3. ***Summary of biosafety level requirements***

	BIOSAFETY LEVEL			
	1	**2**	**3**	**4**
Isolation[a] of laboratory	No	No	Yes	Yes
Room sealable for decontamination	No	No	Yes	Yes
Ventilation:				
— inward airflow	No	Desirable	Yes	Yes
— controlled ventilating system	No	Desirable	Yes	Yes
— HEPA-filtered air exhaust	No	No	Yes/No[b]	Yes
Double-door entry	No	No	Yes	Yes
Airlock	No	No	No	Yes
Airlock with shower	No	No	No	Yes
Anteroom	No	No	Yes	—
Anteroom with shower	No	No	Yes/No[c]	No
Effluent treatment	No	No	Yes/No[c]	Yes
Autoclave:				
— on site	No	Desirable	Yes	Yes
— in laboratory room	No	No	Desirable	Yes
— double-ended	No	No	Desirable	Yes
Biological safety cabinets	No	Desirable	Yes	Yes
Personnel safety monitoring capability[d]	No	No	Desirable	Yes

[a] Environmental and functional isolation from general traffic.
[b] Dependent on location of exhaust (see Chapter 4).
[c] Dependent on agent(s) used in the laboratory.
[d] For example, window, closed-circuit television, two-way communication.

From: WHO LBM 3rd edition

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BIOSECURITY

Laboratory Biosecurity Risks

- **Likelihood**
  - Of an adversary targeting and successfully acquiring a specific biological agent from the laboratory
- **Consequences**
  - Of disease from malicious release of the specific biological agent
- **Risks**
  - Deliberate release of biological material resulting in
    - **Exposure to the human community**
    - **Exposure to the animal community**
- **This method can be used to assess and help protect against other security risks (E.g. theft of equipment or sabotage)**

Biocrime Example: Diane Thompson, October 1996

- **Location: Hospital in Dallas, TX**
- **Perpetrator: Diane Thompson**
  - Clinical laboratory technician
- **Objective: Possibly revenge against former boyfriend and cover-up by infecting co-workers**
- **Organism: *Shigella dysenteriae* Type 2**
  - Acquired from clinical laboratory
- **Dissemination**
  - Contaminated pastries in the office break room
  - Infected 12 of her coworkers
- **Outcome**
  - Arrested, convicted, 20 year sentence

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Bioterrorism Example: Anthrax, October 2001

- **Location:**
  - Numerous sites in the US
- **Perpetrator:**
  - Bruce Ivins accused
- **Objective:**
  - Unknown
- **Organism:**
  - *Bacillus anthracis*
- **Dissemination**
  - 7 letters sent through postal system
  - 22 confirmed cases of anthrax
    - **11 Cutaneous**
    - **11 Inhalational (5 Deaths)**
- **Outcome:**
  - FBI unveils evidence against Ivins who died prior to indictment

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Biosecurity Risk Assessment

1. **Characterize biological agents and threats**
   a. Evaluate pathogens and toxins at a facility (asset assessment)
   b. Evaluate adversaries who might attempt to steal those pathogens or toxins (threat assessment)

2. **Evaluate scenarios**
   a. Create scenarios consisting of “specific adversaries” attempting to steal and misuse a specific biological agent
   b. Determine how the various scenarios could be perpetrated (vulnerability assessment)

3. **Characterize the risk**
   a. Evaluate likelihood and consequences of each scenario
   b. Determine acceptable and unacceptable risks

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Asset Characterization

- **Determining the ease or difficulty of malicious use (likelihood) should involve assessing the following:**
  - Difficulty of acquiring the agent
  - Difficulty of processing the agent into a suitable quantity in a suitable form
  - Difficulty of disseminating the agent to cause harm
- **Determining the potential consequences of the malicious use of a particular agent or toxin should involve assessing the following:**
  - Physical impact of an attack on a population
  - Impact of an attack on the economy
  - Impact of changes in public perception
  - Impact on facility operations

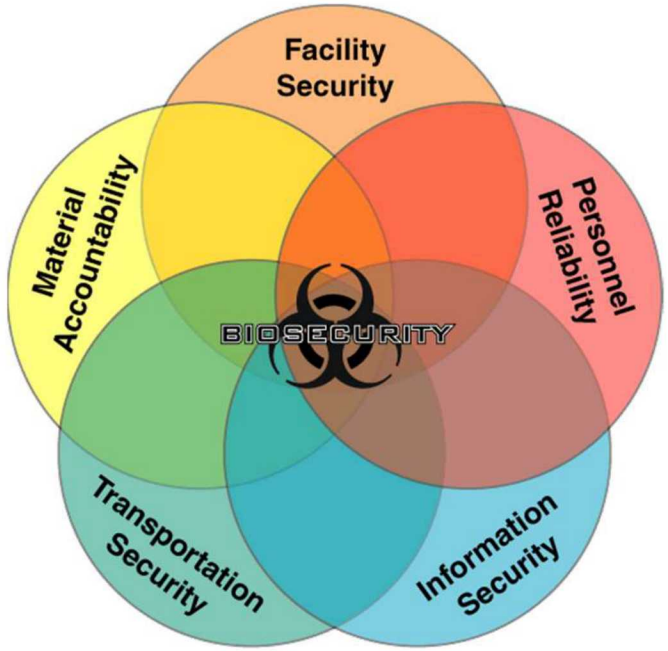
Scenarios

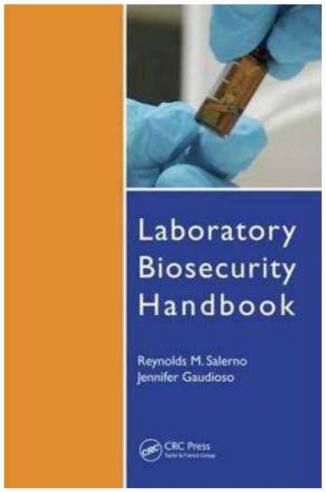
- **Scenarios are used to help detect vulnerabilities in the biosecurity management program**
- **Consider**
  - Assets
  - Facility
  - Adversary type
  - The method the adversary could use to:
    - **Attempt to steal or divert the biological agent**
    - **Subsequently misuse the agent or toxin**

Biosecurity Systems – A Comprehensive Approach

- **Biosecurity system components**
  - Physical security
  - Personnel security
  - Material handling and control measures
  - Transport security
  - Information security
  - Program management practices

- **Each component implemented based on results of risk assessment**





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Indicators

- **Nefarious activity may be difficult to detect**
  - Evidence of equipment use outside of routine activity
  - Evidence of suspicious activities such as media consumption exceeding routine activity
- **Suspicious behaviors**
  - Outsider threat
    - **Unusual deliveries**
    - **Attempts to penetrate the laboratory**
    - **Hanging around the laboratory**
    - **Increased interest in laboratory or location where biological materials are stored**
  - Insider threat
    - **Change in behavior**
    - **Susceptibilities to coercion**
    - **Efforts to get access to areas not required for job**

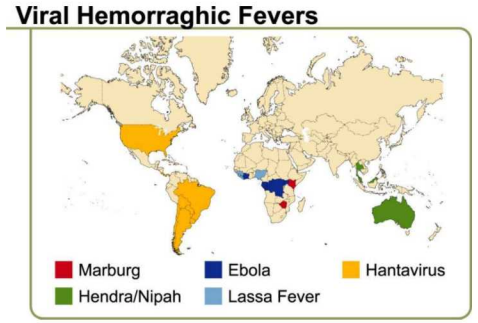
Disease Patterns as Indicators

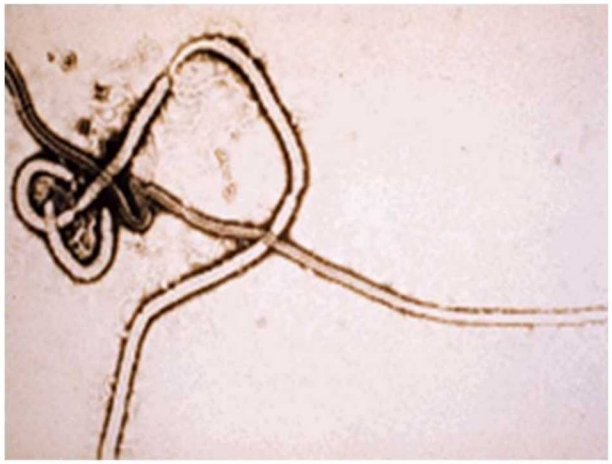
- **Increase in patients with similar symptoms and disease in the same stage**
- **High mortality rate among victims having common home, work, or activity locations**
- **Concurrent human and animal illness with same causative agent**
- **Abnormal disease distribution**
  - New geographic location
  - Unusual time of year
- **Diagnosis of a disease with potential or historical bioterrorism usage**

CASE STUDIES

Ebola Virus Risk Assessment

- Zoonotic
- Host Range
  - Humans and nonhuman primates
- Relatively unstable (enveloped viruses)
- ID_{50}: 1 – 10 virions
- Mortality varies
  - 50 – 90%
- Generally only supportive treatment
  - New Ebola vaccine
- BSL4 organism
  - Exotic





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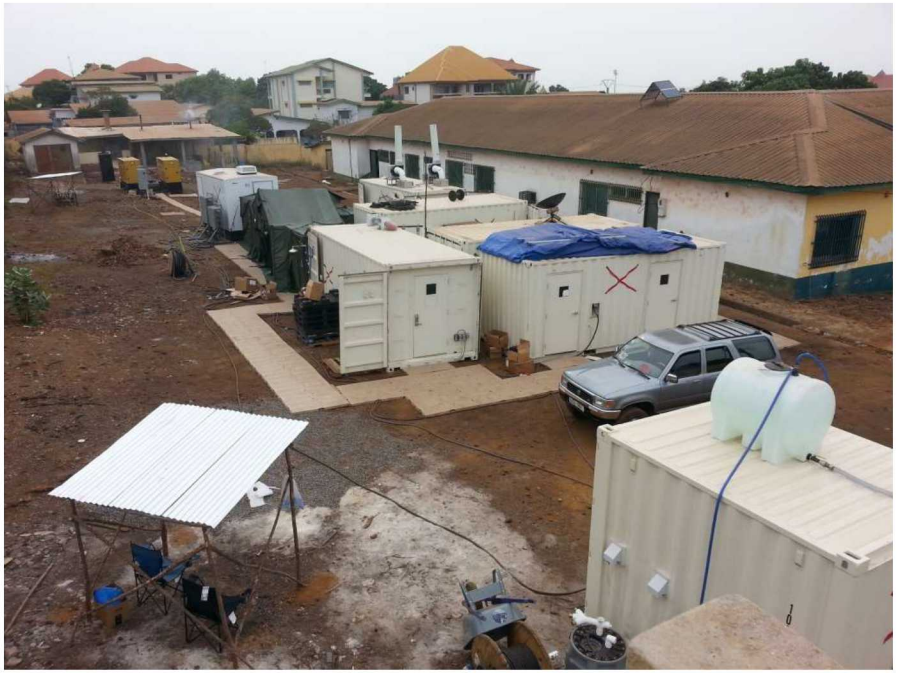
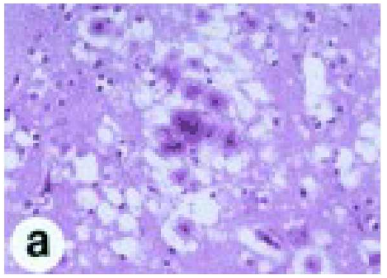
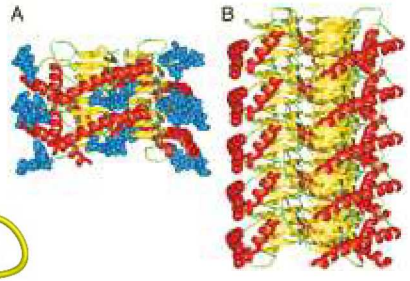
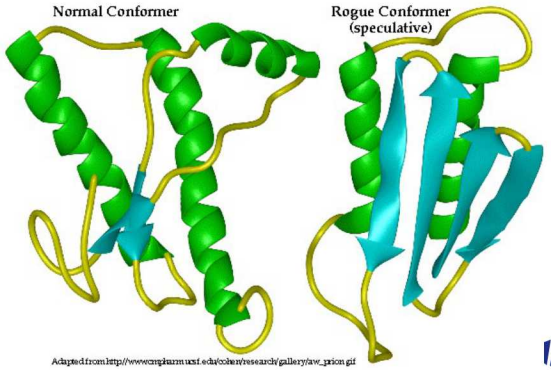


Prions Bovine Spongiform Encephalopathy

- Transmissible spongiform encephalopathy
  - Mad cow disease
  - Variant Creutzfeldt Jakob disease (vCJD)
- Incubation period: Years
- Extremely stable
- ID_{50}: Unknown but thought to be one prion protein
- Unilaterally fatal
- No treatment







Adapted from http://www.cmpharm.ucsf.edu/cohen/research/gallery/aw_prion.gif

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Unknown Samples

- **What do you know about the sample?**
- **What do you know about the patient?**
- **What other information can help you determine risks associated with the sample?**
- **What are considerations for biosecurity?**
  - Is this disease-causing agent unique?
  - Is it possible that the disease results from a deliberate release?


Thank you!