

Overview of Bioterrorism Agents

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Prepare Pre-Event Respond Recover Mitigate

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Overview of Bioterrorism Agents

Objectives

- Identify the major biological threat agents
- Describe the natural transmission of Category A biological agents
- Describe clinical presentations of Category A biological agents
- Describe available treatments and prophylaxis options

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Overview of Bioterrorism Agents

Ideal Qualities for a Biologic Terrorist Agent

- High rate of illness among those exposed
 - High attack rate
- High rate of death among those who get ill
 - High case fatality rate
- Short time between onset of illness and death
 - Small window to start treatment
- Low level of immunity in the population

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Overview of Bioterrorism Agents

Ideal Qualities for a Biologic Terrorist Agent (cont)

- No effective or available treatment
- Can be transmitted person to person
- Easy to produce and disseminate
- Difficult to diagnosis either clinically or diagnostically (i.e. laboratory identification)

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Epidemiological Clues

What we look for...

- Large outbreak with high illness and death rate
- Single case of uncommon disease (e.g., Smallpox)
- Unusual symptoms or severity of illness
- Infection is non-endemic to region
- Unusual seasonal distribution
- Multiple simultaneous outbreaks in non-contiguous areas
- Sick or dying animals

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Bioterrorism Threats: Priority Biological Agents

- Bacterial**
 - Anthrax
 - Plague
 - Tularemia
 - Brucellosis
 - Q fever
 - Other
 - food borne pathogens
 - waterborne pathogens
- Viral**
 - Smallpox
 - Viral Hemorrhagic Fevers
 - Viral Encephalitis
- Toxins**
 - Botulism
 - Staph Enterotoxin B
 - Ricin toxin
 - Tricothecene mycotoxins



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Anthrax

- Gram positive spore forming bacterium *Bacillus anthracis*
- Primarily disease of herbivores which are infected by ingesting spores in soil
- Natural transmission to humans by contact with infected animals or contaminated animal products
 - "Woolsorter's disease"
- Three forms of disease
 - Cutaneous
 - Inhalational
 - Gastrointestinal (GI)



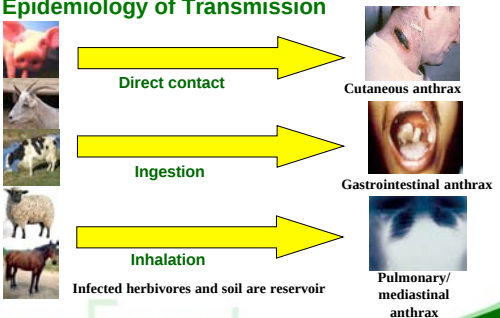
CDC: Gram stain of *B. anthracis*

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Epidemiology of Transmission



Infected herbivores and soil are reservoir

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Anthrax: Cutaneous

- Accounts for 80% of naturally occurring Anthrax cases
- Enters through openings in skin from abrasions, lacerations
- 20% progress to systemic form if untreated
- Most cases recover



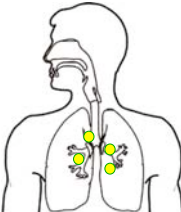
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Anthrax: Inhalational

- Inhalation of spores
- Incubation, 2-3 days (range up to 60 days)
- Spores engulfed by macrophages and transported to mediastinal and peribronchial lymph nodes
- Insidious onset: malaise, low grade fever, nonproductive cough
- Abrupt development of respiratory distress
- Hemorrhagic mediastinitis
- Hematogenous spread
- Meningitis in 50%, usually fatal

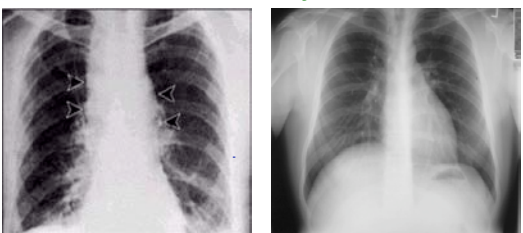


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Anthrax: Pulmonary/Mediastinal



Mediastinal widening from anthrax Normal chest x-ray

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Patient Care Inhalational Anthrax

Ciprofloxacin 400 mg intravenous every 12 hours for adults 10 -15 mg/kg intravenous every 12 hours for children	AND/OR	Doxycycline 100 mg intravenous every 12 hours for adults and children ≥ 8 yr and > 45 kg 2.2mg/kg every 12 hours for children < 8 yr (up to 200 mg/day)
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PLUS

- One or two additional anti-microbial agents effective against anthrax (e.g. imipenem, clindamycin, rifampin, macrolides)

Additional issues

- Penicillin should never be used as a monotherapy
- If meningitis is suspected, an antibiotic with good CSF penetration should also be administered (e.g. rifampin or chloramphenicol)
- Supportive therapy for shock, fluid volume deficit and airway management may be needed.
- Drainage of pleural effusions may improve clinical outcome

Anthrax Immune Globulin (AIG) can be used to neutralize anthrax toxin.

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Anthrax: Post-Exposure Prophylaxis

- Start 60 days of oral antibiotics ASAP after exposure
 - Ciprofloxacin or Levofloxacin
 - OR**
 - Doxycycline
 - OR**
 - Amoxicillin or Penicillin (if known PCN sensitive)
- Vaccine
 - Can be given post-exposure in conjunction with antibiotics

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Smallpox

- Variola* virus, two forms of the disease: minor and major
- Spread via respiratory droplets or aerosols expelled from the oropharynx
- May also spread via direct contact
- Patients are most contagious during the time at which the skin rash is present
- Approx. 30% of patients exposed go on to develop the disease
- Approx. 30% mortality with ordinary smallpox

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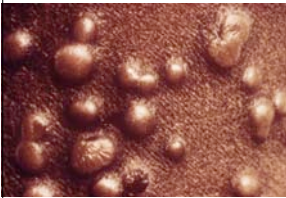
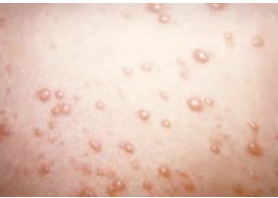
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Smallpox Characteristics

- **Febrile Syndrome** – occurring 1-4 days prior to rash.
- **Classic Smallpox lesion** – deep-seated, firm/hard, round, well-circumscribed; lesion may become umbilicated or confluent.

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Smallpox Rash	Chickenpox Rash
	

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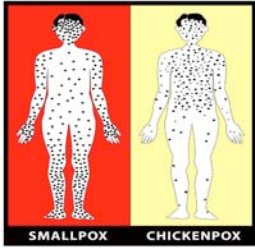
Smallpox Characteristics

- **Febrile Syndrome** – occurring 1-4 days prior to rash.
- **Classic Smallpox lesion** – deep-seated, firm/hard, round, well-circumscribed; lesion may become umbilicated or confluent.
- **Lesion in Same Stage of Development** – Evolve from macules _ papules _ pustules at the same time.
- **Centrifugal distribution** – First lesion on oral mucosa, face, or forearms.

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Smallpox vs. Chickenpox: Distribution



SMALLPOX CHICKENPOX

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Smallpox Characteristics

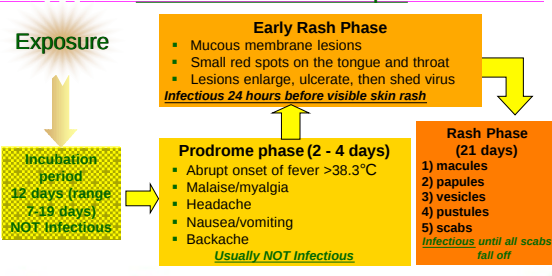
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- **Lesion in Same Stage of Development** – Evolve from macules _ papules _ pustules at the same time.
- **Centrifugal distribution** – First lesion on oral mucosa, face, or forearms.
- **Lesion on palms and soles**

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Clinical Timeline for Smallpox



Exposure

Incubation period
12 days (range 7-19 days)
NOT infectious

Prodrome phase (2 - 4 days)

- Abrupt onset of fever $>38.3^{\circ}\text{C}$
- Malaise/myalgia
- Headache
- Nausea/vomiting
- Backache

Usually NOT infectious

Early Rash Phase

- Mucous membrane lesions
- Small red spots on the tongue and throat
- Lesions enlarge, ulcerate, then shed virus

Infectious 24 hours before visible skin rash

Rash Phase (21 days)

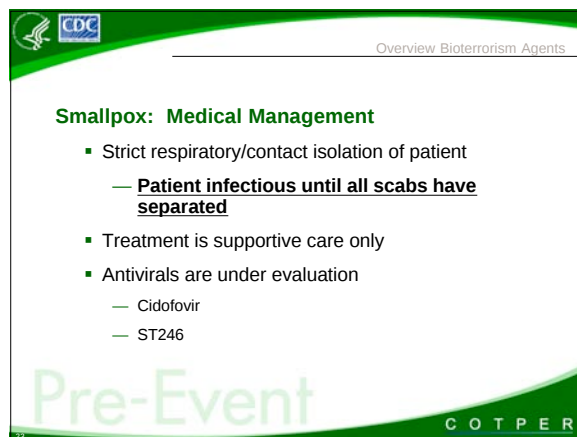
- 1) macules
- 2) papules
- 3) vesicles
- 4) pustules
- 5) scabs

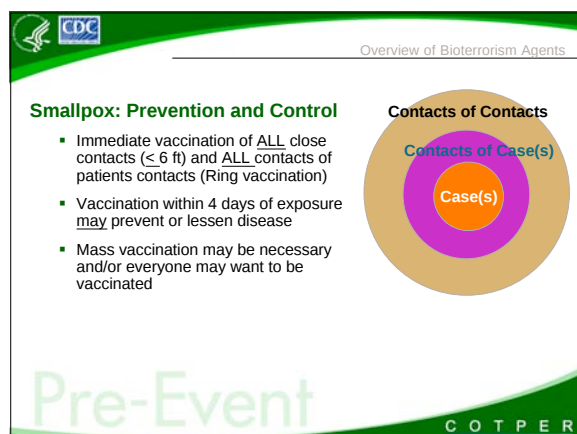
Infectious until all scabs fall off

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Smallpox: Current Vaccine

- Live vaccinia virus
- Because it is a live virus, there can be adverse events from vaccination
 - Occurs mostly in immunologically suppressed persons
- Immunity is **not** life-long, but having been vaccinated in the past may reduce morbidity and mortality



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Plague

- Plague is a severe bacterial disease of humans and animals produced by the gram negative nonsporulating bacillus *Yersinia pestis*
 - Bite of a rodent flea that is carrying the plague bacterium, or by handling an infected animal
- Hundreds of millions of people died when human dwellings were inhabited by flea-infested rats
- Modern antibiotics are effective, but without prompt treatment the disease can likely cause illness or death



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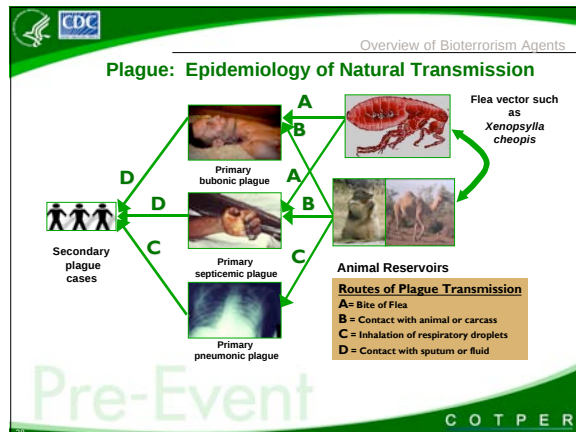
Overview of Bioterrorism Agents

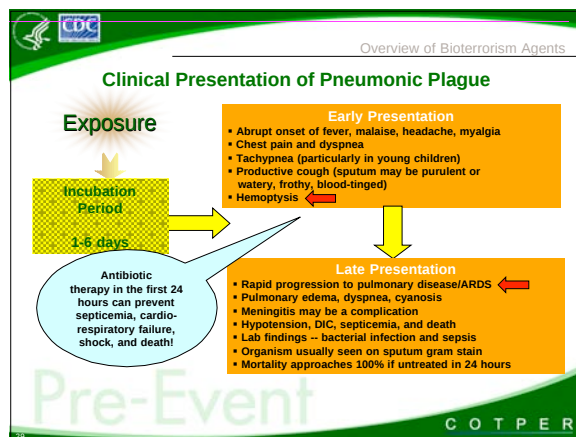
Types of Plague

- Three types:
 - Bubonic
 - Septicemic
 - Pneumonic




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Plague: Patient Care

Early antibiotic treatment* is paramount to patient survival

Adults: Streptomycin 1 gm IM b.i.d. for 10 days;
Chloramphenicol 25 mg/kg IM or IV 4 times daily for 10 days;
Gentamicin 5 mg/kg IM or IV once daily for 10 days;
Doxycycline 100 mg IV b.i.d. or 200 mg IV once daily for 10 days;
Ciprofloxacin 400 mg IV b.i.d. for 10 days;

Children: Streptomycin 15 mg/kg IM twice daily for 10 days (max 2 gm/day);
Chloramphenicol 25 mg/kg IV 4 times daily for 10 days (max 4 gm/day);
Gentamicin 2.5 mg/kg IM or IV 3 times daily for 10 days;
Doxycycline 2.2 mg/kg IV twice daily for 10 days (max dose 200mg/day);
Ciprofloxacin 15 mg/kg IV twice daily for 10 days (max 1 gm/day)

*CDC recommends initiating treatment with two drugs believed effective against *Y. pestis* until antimicrobial susceptibility data is available on isolates.

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Plague: Prophylaxis

- Pneumonic plague contacts (transmitted via droplets)
 - Oral Doxycycline or Ciprofloxacin
 - For 7 days after last exposure
- Vaccine no longer manufactured

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Botulism

Caused by toxin from *Clostridium botulinum*

- Colorless, odorless and tasteless
- Lethal dose for 70kg human is 1ng/kg
 - Botulinum toxin is the most lethal neurotoxin known to man
 - Dispersal of aerosolized toxin, 1 gm of aerosolized toxin could kill up to 1.5 million people
- Seven toxin types
 - Human disease: A, B, E, and F
 - Animal disease: C, D, and G

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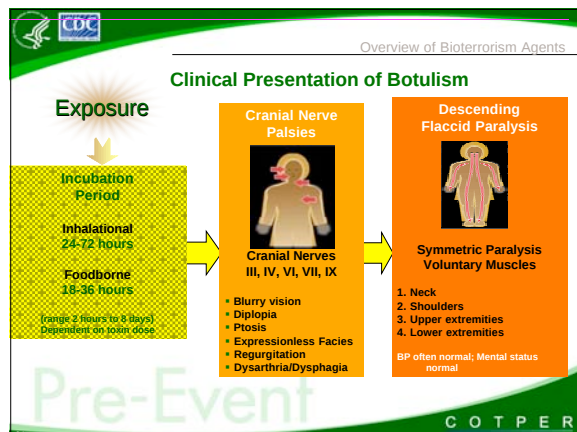
Botulism: Epidemiology of Natural Transmission

The diagram illustrates the epidemiology of natural transmission of Botulism through a cycle of four main stages:

- C. botulinum in the soil, flora and fauna:** The organism is naturally present in the environment.
- Colonization and toxin production in an open wound:** The organism enters a wound and produces toxin.
- Toxin production in foods prepared or stored at ambient temperature:** The organism grows and produces toxin in food.
- Botulism:** The toxin causes acute, symmetric, descending flaccid paralysis with bulbar palsies in humans.

Arrows indicate the flow of transmission between these stages, showing how the toxin can be ingested, enter through a wound, or be produced in the gut of susceptible infants and adults.

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Botulism: Medical Management

- Early administration of antitoxin
- Supportive care
 - Monitoring respiratory function
 - Providing mechanical ventilation
 - May be needed for weeks or months

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Botulism: Antitoxin

- Preferably within 24 hours of symptom onset
- Type of antitoxin based on type of botulism
 - Bivalent antitoxin specific to serotype A and B,
 - Monovalent antitoxin specific to serotype E, and
 - Heptavalent antitoxin specific against serotypes A, B, C, D, E, F, and G
- 1 vial per person
- Acts by binding free systemic toxin
 - Does not reverse paralysis already present

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Viral Hemorrhagic Fevers (VHF)

- Hemorrhagic fever viruses (RNA) belong to four taxonomic families:
 - Filoviridae (Ebola/Marburg)
 - Arenaviridae (Bolivian HF)
 - Bunyaviridae (Congo-Crimean HF)
 - Flaviviridae (Dengue)
- Natural vectors – virus dependent
 - Rodents, mosquitoes, ticks
- No natural occurrences in U.S.

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VHF as a Biological Weapon

- These viruses are considered suitable weapons because:
 - they have a low infectious dose
 - they cause high morbidity and mortality
 - they cause fear and panic in the general public
 - effective vaccines are either not available, or supplies are limited



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Clinical Timeline for VHF

Exposure

Incubation Period
2-21 days (depending on the virus)

Early Manifestations

In general:

- High fever
- Headache
- Myalgia
- Arthralgia
- Anorexia
- Varying degrees of nausea, vomiting and diarrhea

Later Manifestations

External/Internal Hemorrhage

- Ecchymosis
- Petechiae
- Bleeding from puncture site
- Bleeding from nose and gums
- Hemorrhagic conjunctivitis
- Gastrointestinal bleeding
- Severe vaginal bleeding
- Pleural effusion
- Renal Failure
- Shock

Laboratory Findings

- Leukopenia or leukocytosis
- Thrombocytopenia
- Elevated Liver Function Tests
- Anemia or Hemoconcentration
- Prolonged PT, PTT

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Clinical Presentation of VHF



Ecchymosis



Petechiae



Melena

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VHF Clinical Management

- Aggressive supportive care with intravenous fluids, colloids, blood products as needed
- Specific therapy (ribavirin) may be helpful in bunyaviruses and arenaviruses
- Avoid IM injections or invasive procedures (due to bleeding)
- Strict aerosol precautions (i.e. respiratory isolation)

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Sources of Information

- Centers for Disease Control (CDC)
 - www.cdc.gov
- CDC Emergency Preparedness
 - www.emergency.cdc.gov
- CDC Quarantine and Isolation
 - www.cdc.gov/nclodod/dp/index.htm

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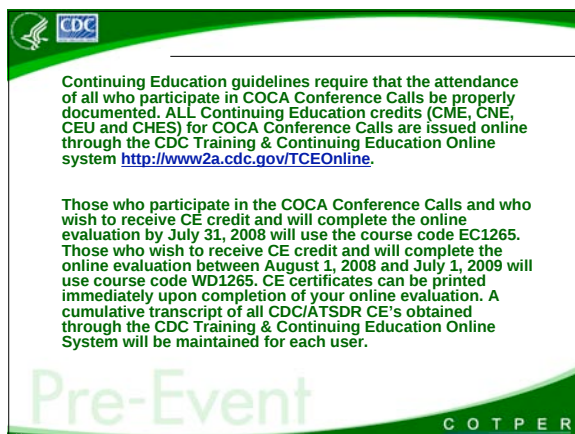


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Questions?

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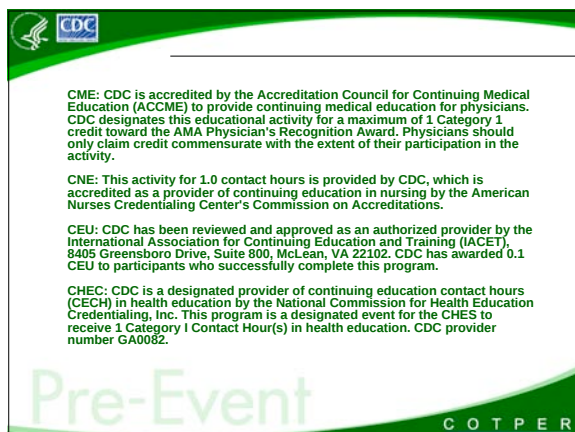


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