Category A Agents

- ❑ Anthrax (*Bacillus anthracis)*
- ❑ Botulism *(Clostridium botulinum* toxin*)*
- ❑ Plague (*Yersinia pestis*)
- ❑ Smallpox (*Variola major*)
- ❑ Tularemia (*Francisella tularensis*)
- ❑ Viral hemorrhagic fevers (*filoviruses* – e.g. *Ebola, Marburg; arenaviruses*- e.g. *Lassa, Machupo*; bunyaviruses; and flaviviruses)

Category A agents characteristics *(CDC)*

1) Can be easily disseminated, and some are transmitted from person to person
2) Result in high mortality rates and have the potential for major public health impact
3) Might cause public panic and social disruption
4) Require special action for public health preparedness

Reporting Protocols & Resources

(ACP/ASIM)

If you suspect bioterrorism,
contact your local health department immediately!
Do not wait for confirmation.

Suspicious case ⇒ record data and order tests ⇒ report to local health dept. ⇒ alert clinical lab ⇒ arrange for consultations ⇒ discuss findings with all involved parties.

ACP ASIM Guide to Bioterrorism Identification

Epidemiological Clues of a Bioterroristic Attack

1. Unusual temporal or geographic clustering of illness
2. Unusual age distribution of common disease (e.g., an illness that appears to be chickenpox in adults but is really smallpox).
3. Large epidemic, with greater case loads than expected, especially in a discrete population.
4. More severe disease than expected.
5. Unusual route of exposure.
6. A disease that is outside its normal transmission season, or is impossible to transmit naturally in the absence of its normal vector.
7. Multiple simultaneous epidemics of different diseases.
8. A disease outbreak with health consequences to humans and animals.
9. Unusual strains or variants of organisms or antimicrobial resistance patterns.

None of these clues alone are pathognomonic of bioterrorist attack, but several taken together provide support for further investigation

Sentinel Clues for Category A Biological Agents

These agents are easily disseminated, may be transmitted from person to person, and can cause high mortality.

Pneumonia or Influenza-like Syndromes

- ❖ Chest pain, dry cough, possible nausea and abdominal pain, followed by sepsis, shock, widened mediastinum, hemorrhagic pleural effusions, and respiratory failure. A Gram-positive bacillus may be isolated. *Consider inhalation anthrax.*
- ❖ Gram-negative bacillus pneumonia associated with muco-purulent sputum, chest pain, and hemoptysis, particularly in an otherwise normal host. *Consider pneumonic plague.*
- ❖ A Gram-negative coccobacillus broncho-pneumonia associated with pleuritis and hilar lymphadenopathy, particularly in an otherwise normal host. *Consider tularemia.*

Cutaneous Ulcer or Ulceroglandular Syndromes

- ❖ A painless ulcer covered by a black eschar, surrounded by extensive non-pitting edema that is out of proportion to the size of the ulcer. Fever and regional lymphadenopathy may be present. *Consider cutaneous anthrax.*

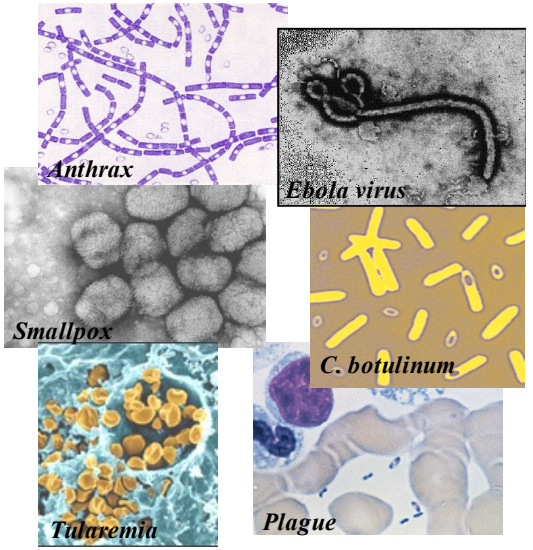
Fever and Rash Syndromes

- ❖ An abrupt, influenza-like illness with fever, dizziness, myalgias, headache, nausea, abdominal pain, diarrhea and prostration. Evidence of "leaky capillary syndrome" with edema or signs of bleeding ranging from conjunctival hemorrhage, mild hypotension, flushing, petechiae, and ecchymoses to shock and generalized mucous membrane hemorrhage and evidence of pulmonary, hematopoietic, renal and neurological dysfunction. *Consider viral hemorrhagic fevers.*
- ❖ A febrile illness with myalgias followed in two to three days by a generalized macular or papular-vesicular-pustular eruption, with greatest concentration of lesions on the face and distal extremities, including the palms. On any one part of the body (face, arms, chest) all lesions are the same stage of development (all papules, vesicles, pustules, or scabs). *Consider smallpox.*

Paralytic Syndromes

- ❖ A paralytic illness characterized by symmetric, descending flaccid paralysis of motor and autonomic nerves, usually beginning with the cranial nerves. *Consider botulism.*

Bioterrorism Guide: Category A Agents



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CATEGORY "A" AGENTS OF BIOTERRORISM

DISEASE INCUBATION PERIOD (BSL)	MICROBIOLOGY	CLINICAL SYNDROME	DIFFERENTIAL DIAGNOSIS	ISOLATION PRECAUTIONS/ MODE OF TRANSMISSION	SAMPLE/ DIAGNOSTICS	RECOMMENDED THERAPY (Alternatives may be available)	POST-EXPOSURE PROPHYLAXIS
ANTHRAX *Inhalational/GI:* 1-7 days (up to 60 days). *Cutaneous:* 1-12 days (BSL 2)	*Bacillus anthracis*: Spore-forming, encapsulated, Gram-positive bacillus that grows aerobically in long chains. Non-motile, non-hemolytic, catalase-positive. *Spores are actual infective agent.*	**Inahlational**: non-specific "flu-like" illness with fever, nausea, emesis, cough, +/- chest discomfort, without coryza or rhinorrhea → abrupt onset of respiratory distress. CXR: mediastinal widening. **Cutaneous**: pruritic, painless papule→ vesicle→ulcer→edematous black eschar. +/- massive edema, regional adenopathy, fevers, evolving over 3-7 days. **GI:** abdominal distress, nausea, emesis, fever, dysphagia, diarrhea, GI ulcers, regional edema & lymphadenitis	**Inhalational Anthrax, Tularemia and Pneumonic Plague:** Bacterial and mycoplasmic pneumonias, SARS, mediastinitis, coccidiomycosis, Q fever, psittacosis, influenza, Legionella, staphylococcal or streptococcal diseases, tuberculosis, and cat-scratch fever **Cutaneous Anthrax:** Human Orf, early boils, arachnid bites, vaccinia **Septicemic Plague:** Meningococcemia, Gram-negative streptococcal, pneumococcal or staphylococcal sepsis and SARS	Standard / Contact with animal tissue, hides, hair, wool, or bone meal.. Cutaneous infections require contact with damaged skin. GI infections may arise from ingestion of *B. anthracis* spores. Person-to-person transmission rare.	Nasal swab, blood culture, pleural fluid, BAL, sputum, serum, skin lesion, mediastinal lymph node biopsy or aspirate/ Culture, RT-PCR, serologic testing, Direct Fluorescence Antibody (DFA) assay, Gamma-phage lysis, Time-resolve Fluorescence (TRF) Assay, Immunohistochemistry (IHC) & ELISA	**Inhalational & GI**: *Adults*: *Cipro 400 mg IV BID* **AND** 1-2 antibiotics with in vitro activity: (e.g. Rifampin, vanco, penicillin, ampicillin, chloramphenicol, etc), changing to oral therapy when stable. *60 total days of treatment* *Children*: Same as above with appropriate dose adjustments. **Cutaneous:** *Cipro 500 mg PO BID x 60 days*	**Inhalational**: *Adults*: Cell-free vaccine at 0, 2 & 4 weeks if 18-59 years old **WITH** *Cipro 500 mg PO BID* **OR** (if susceptible) *Amox 500mg PO TID x 60 days* *Children*: Same as above with appropriate dose adjustments.
PLAGUE 1-6 days (BSL 2/3)	*Yersinia pestis:* small, non-motile, non-spore forming Gram-negative bacillus, with bipolar staining- "safety-pin" ovoid appearance	**Septicemic**: Sepsis, DIC, purpura, ecchymoses, acral gangrene, GI symptoms, hypotension, acute renal failure and other signs of shock. **Pneumonic**: Cough, fever, dyspnea, hemoptysis, +/- shock, & organ failure, +/- cervical bubo, GI symptoms. Advanced disease with purpuric skin lesions & necrotic digits. Chest x-ray with pulmonary infiltrates or consolidation		Droplet if pneumonic and drainage/secretions if bubonic, until 3 days of successful treatment/ Inhalation of respiratory droplets or contact with infected animals	Throat swab, blood /sputum culture, sputum smears, serum, bubo aspirate, CSF, lesion scraping, LN aspirate Culture, 4-fold change in antibody titer, DFA, RT-PCR, antigen detection, PHA, serology, TRFIA	*Adults*: *Streptomycin 1g BID* **OR** *Gentamicin 1mg/kg TID* **OR** *Tetracycline 0.5g QID* **OR** *Chloramphenicol* 12.5mg/kg QID x 7-10 days* *Children*: Same as above with appropriate dose adjustments. **required for plague meningitis*	*Adults*: *Tetracycline 1g* **OR** *Doxy 100 mg PO BID* **OR** *Cloramphenicol 30mg/kg PO QID x 7 days* *Children*: Same as above with appropriate dose adjustments.
TULAREMIA 1-14 days (BSL 2/3)	*Francisella tularensis:* Small, Gram-negative non-spore forming, aerobic, non-motile Coccobacillus requiring cysteine for growth	**Inhalational**: Acute fever with pharyngitis, pleuropneumonitis, bronchiolitis +/- hilar lymphadenopathy, and variable progression to respiratory failure. CXR: peribronchial infiltrates progressing to multilobar bronchopneumonia, pleural effusion, and hilar adenopathy		Standard/ No person-to-person transmission, but can be acquired environmentally	Throat swab, blood culture, serum, respiratory secretions, ulcer exudate/ DFA, Culture, ELISA assay for serum antibodies (in 2nd week), RT-PCR, antigen detection	*Adults*: *Streptomycin 1 g BID IM* **OR** *Gentamicin 5 mg/kg QD IM or IV x 10-14 days* *Children*: Same as above with appropriate dose adjustments	*Adults:* *Doxy 100 mg* **OR** *Cipro 500 mg BID PO x 14 days.* *Children*: Same as above with appropriate dose adjustments.
BOTULISM 6 hr-10 days (BSL 2)	Toxins (A-G) of *Clostridium botulinum:* spore forming, obligate anaerobe, Gram-positive bacillus	Acute onset of afebrile, symmetric, descending flaccid paralysis that begins in bulbar muscles. Findings include dilated pupils, dry mucous membranes with difficulties in swallowing and speaking; but no loss of consciousness.	Polio, tick paralysis, chemical intoxication, Guillain-Barre, myasthenia gravis	Standard/ Ingestion or inhalation of *C. botulinum* toxins or colonization of GI tract by ingested spores.	Nasal swab, wound tissue smear, serum, stool, gastric aspirate, vomitus/ Mouse bioassay, culture, antigen detection ELISA for A, B, E toxin, PCR	Supportive care and polyvalant (equine type AB or ABE) *botulinum* antitoxin (ASAP) - contains antibodies against toxin types A, B, E. One 10mL vial by slow IV infusion.	Close observation. At the first signs of illness, administer antitoxin.
SMALLPOX 7-19 days (BSL 4)	*Variola*: large, 300 nm, DNA virus with a dumbbell shaped core, and complex membrane system	Systemic toxicity: Prodrome of high fever, headache, back ache, prostration, chills, vomiting, abdominal pain, followed by synchronous, deep-seated rash beginning on face & extremities, progressive: papular → vesicular → pustular.	Atypical varicella or measles, influenza, secondary syphilis, molluscum contagiosum, meningococcemia, monkeypox, vaccinia, and scabies	Standard, contact and airborne/ Commonly spread through respiratory droplets or skin inoculation	Fluid of skin lesion, scab, Serum during febrile illness Cell culture, RT-PCR, negative stain electron microscopy, antigen detection, serology	Supportive care: Treat secondary bacterial infection Cidofovir effective in vitro; animal studies ongoing	Vaccination of close contacts and those living in the immediate vicinity within 4 days of exposure
Viral Hemorrhagic Fever (VHF) 4-21 days (varies with virus) (BSL 4 except Dengue; 3)	*Filoviridae, Arenaviridae, Bunyaviridae, Flaviviridae*: RNA viruses	Acute influenza-like illness → signs of increased vascular permeability: edema, hypotension, petechiae, conjunctival hemorrhage → generalized mucous membrane bleeding, shock, multiorgan failure	Leptospirosis, Meningococcemia, typhus, malaria, rickettsial disease, thrombocytopenic purpura, hemolytic uremic syndrome	Standard, contact and airborne/ Person-to-person transmission rare, usually vector-borne.	Nasal swab, serum, CSF/ Rapid antigen capture ELISA, acute sera antibody, RT-PCR, viral culture	Supportive care: Ribavirin (IND) for possible Arena or Bunyavirus. Ribavirin 30 mg/kg IV (max 2 g) load, then 16 mg/kg IV (max 1 g/ dose) QID x 4 days, then 8 mg/kg IVTID x 6 days (max 500mg/dose)	Medical surveillance for symptoms. If fever ≥ 101 ° F, start Ribavirin 500mg PO QID x 10 days for possible Bunyavirus or Arenavirus