The Bioterrorism Research Handbook

What to do before & after experiments
Organized Sections

- Physical description of agents
- Pathophysiology – How it infects
- Symptoms & Signs – How the disease looks
- Pre Research - tests on the researcher
- Post Exposure – if the researcher is infected
- Treatment of infection
- Post Research tests of researcher
ANTHRAX

- Name - *Bacillus anthracis*
- Gram positive chains of boxcar bacilli
- Spores in soil worldwide and in furs & hides
- Invades: Skin -> itchy vesicle -> black scab -> jelly edema -> swollen lymph nodes
- Mouth -> swollen neck nodes -> gut -> bloody vomiting and diarrhea -> perforation
- Lung -> pneumonia -> hemoptysis -> death
Case Fatality Rate

- **If Untreated**
  - From skin -> 5-20%
  - By mouth -> 25-60%
  - Lung -> 45-99%
Pre - Research

- Vaccinate
- Test serum for antibodies (Serology)
Post Exposure

- If you suspect infection GET:
- Culture blood, sputum, throat, for anthrax
- Gram stain of growth -> gm neg. boxcars
- Serum for rising titer of antibodies
- Chest x-ray if cough or SOB -> pneumonia -> widening mediastinum, pleural effusion
Anthrax Treatment

- Penicillin G - IV or IM until edema down
  Or Doxycycline
  Erythromycin
  Ciprofloxacin
- Give one antibiotic even if immunized
- Use any TWO for lung
  Spores in lungs can germinate after 50 days
Post Research Surveillance

- Serum for antibodies
- Infection may be subclinical
- Be alert for delayed symptoms by spores germinating long after experiments cease
BOTULISM

- Clostridium botulinum makes a TOXIN
- “The most poisonous one known to man”
- One gram can kill a million people
- Clostridium grows without air – hence makes its toxin after the can is sealed.
- Spores are worldwide in all soil.
- A common growth in intestines.
Vectors of Botulism Toxin

**FOOD** - insufficiently boiled before canned. Must boil 20 min at 250 F

**BIOTERRORIST ROUTE**

**WATER, FOOD** - tainted with toxin

**AEROSOL**
Toxin blocks nerve function at neuromuscular junction -> paralysis

Never contagious
Signs & Symptoms of Botulism

- Descending paralysis
- Facial muscles -> blurred vision, drooping eyelids, can’t smile, no expression
- Tongue -> can’t chew, swallow, talk, dry mouth
- Weak shoulders first, then arms, hands.
- Diaphragm paralysis -> can’t breathe
- Internal -> hypotension, constipation
Pre Research testing

- Pulmonary function baseline
- Vaccine is in clinical testing
Treatment of Botulism

- Give BIG – Botulism immune globulin
- Give Botulism anti-toxin
- Ventilator assistance for up to months
- Test food, water, stool for toxin
- IV fluids, cathartics, enemas to flush out.
- Avoid Magnesium which potentiates neuromuscular blockade.
BRUCELLOSIS

- Genus *Brucella*
  - species: *abortus*, *melitensis*, *suis*, *canis*
- *Gram negative rod*
- *Vectors*: milk, cheese, meat, animal fluids
Pathophysiology of Brucellosis

- Bacteria invades: Skin, Eyes, Mouth, Nose
- Survives as a parasite inside WBC’s thus avoiding antibodies and antibiotics in the blood
Signs & Symptoms of Brucellosis

- Slow headache, low fever, chills, weakness
- Sweat smells like new mowed hay
- Skin -> swollen local lymph nodes
- Eye -> unilateral red & sore, pus, uveitis
- GI -> anorexia, pain, vomiting, diarrhea
- Lung -> pneumonia, pleural effusion
- Myalgias, arthralgias, nephritis, meningitis
Pre-Research testing

- Serum for antibody baseline

BIOTERRORIST ROUTE

- Bacteria in Food, water or as an aerosol
Post exposure tests

- Serology for rise in antibodies
- Culture blood, skin, eyes
- Liver biopsy of granulomas
- Lymphocytes in CSF
- X-ray after long term – anterior vertebrae have “parrot beaked” osteophytes & osteoporosis
Treatment of Brucellosis

- Doxycycline PLUS
  - One of following:
    - Trimethoprim-Sulfamethoxisole
    - Gentamycin
  - For relapses add Rifampin
Post Research testing

- Serum by ELISA for antibodies
- There may be subclinical infection
EBOLA VIRUS

- An RNA Filovirus
- Long spaghetti like virus
- Case Fatality Rate 50 – 90 %
- Vectors – animals, people of African Congo

BIOTERRORIST ROUTE

- Food, water, aerosol
Signs & Symptoms of Ebola Virus

Abrupt frontal headache with high fever 103-4F
Rash spreads to arms and bleeds
Bleeding from nose, gums, eyes, vagina
Blood in vomit, urine, stool
Internal bleeding -> hepatosplenomegaly
Death from anemia, hypotension, shock  OR
Recovery-> skin peeling, alopecia, psychosis
Pre & Post exposure testing

Pre and Post

Serology for antibodies

Post

- Culture of blood, urine, throat, rectum
- Liver biopsy for Electron Microscopy of virus
- Leukopenia, thrombocytopenia
Treatment for Ebola Virus

- Quarantine
- Supportive fluid replacement
- Transfusion whole blood
- Broad spectrum antibiotic prophylaxis
LASSA FEVER

Lassa virus – an RNA Arenavirus
Reservoir – Equatorial African mouse
Vectors – Rodent feces, aerosol, human blood, urine, saliva, sexual partner

Bioterrorist Route
Aerosol, food, water
Signs & Symptoms of Lassa Fever

- Fever and shaking chills, Headache, Myalgia
- Flushing face -> sore throat, white pharynx
- Painlessly swollen face & neck nodes
- GI–anorexia, nausea, pain, vomiting, diarrhea, bleeding from nose, gums
- Rash, cough, tachycardia, confusion, shock
- Recovery -> oculogyric crisis, 25% deaf bald
Pre & Post Research testing

- Serum for antibodies
- Lassa viral infection is often asymptomatic
MARBURG VIRUS

- An RNA filovirus
- Case Fatality Rate = 25% after 2 weeks
- Reservoir: Ugandan African green monkeys
- Vectors: Infected mammals, aerosol

BIOTERRORIST ROUTE

- Water, food, aerosol
Pathophysiology

- Marburg Virus infects widespread organs, liver, spleen, pancreas, adrenals, thyroid, kidneys, testes and brain, heart and lungs.
- These are necrotizing to tissue causing hemorrhage widespread.
Signs & Symptoms of Marburg Virus

- Abrupt frontal headache & fever of 103-4°F
- Red eyes, palate, tonsils
- Sore throat and enlarged neck nodes
- Rash spreading to extremities turns bloody
- Bleeding of eyes, throat, urine, bowel, vagina
- Internal bleeding of liver, spleen, face, genitalia. Death by DIC and shock
Pre & Post Research Testing

Serum for antibodies

- ELISA test measures specific Marburg IgG
- Marburg IgM means recent infection
Post Exposure Testing

- Culture blood, urine, throat, rectum

**Serum shows**

- Low lymphocytes and platelets
- Low serum protein
- High serum nitrogen metabolites (azotemia)
- High amylase, liver transaminasases (AST, ALT)
Treatment for Marburg Virus

- Quarantine
- IV fluids and whole blood
- Broad spectrum antibiotic prophylaxis
PLAGUE

- The black death of the Middle Ages
- 1/3 of Europe died
- Organism: *Yersinia pestis*
- Gram negative, pleomorphic bacillus
- Reservoir: Wild Rodents worldwide
- Vectors: Rodent fleas, ticks and lice
Pathophysiology

- **Bubonic** - flea bites injecting bacteria in saliva
- Bacteria makes fibrinolysin, coagulase and endotoxin causing tissue necrosis
- Eaten by WBC’s a protective capsule makes for an intracellular parasitic form.
- Infected WBCs migrate to swell lymph nodes where exploding bacteria burst through skin
- These are the black buboes of the Plague.
- **Pneumonic** – inhaled spores-> rapid fatal pneumonia
Signs & Symptoms of Plague

- Headache, fever, chills & weakness
- Very tender skin at swollen groin and axilla
- Nodes drain, petichiae, gangrene digits, penis
- Lung -> cough, dyspnea, hemoptysis, tachypnea, multi-lobar consolidation.
- CNS -> meningitis, delirium, coma
- CV -> hypotension, tachycardia, shock, death
Pre & Post Research testing

- Vaccine is in clinical testing
- Serology for antibodies.
Post Exposure testing

- Culture blood, skin, sputum
- Stained with Giemsa or Wayson stain shows bipolar “safety-pin” morphology
- Fluorescent antibody stain
- Rising serology titer
- Passive Hemaglutination Antigen test (PHA)
Treatment of Plague

- Early empiric treatment lowers mortality from 100% to 10%
- 1st choice Gentamycin & Tetracyclines
- Trimethoprim-Sulfamethoxazole
- Quinolones
- Chloramphenicol for meningitis
SMALLPOX

- Variola major
- An Orthopox DNA 200nm brick shaped virus
- Case Fatality Rate 30%
- Reservoir: *Homo Sapiens* - last case 1977
- Last US vaccination 1972 (restarted in military)
- Stored in “safe” vaults in Atlanta and Moscow
- Vectors: direct contact, aerosol stable 2 days
Pathophysiology

- Inhaled virus incubate and multiply 1-2 wks
- Viremia results in intracellular haloed inclusions called Guarnieri bodies
- Vascular endothelial cells swell and leak
- Liver, spleen and lymph nodes enlarge.
- Vesicles or pox appear on skin.
- Pox fill with virus to bursting, then scab over
Pre Research testing

- Vaccinate by multiple pricks of skin with virus
- Use live Acambis vaccine
- Immunity wanes after 5 years.
- Lifetime immunity to severe infection.

Post research testing

- Serum for antibodies (serology)
Signs & Symptoms of Smallpox

- Sudden fever of 101-6 F & severe headache
- Severe back & abdominal pain, conjunctivitis
- Chills, vomiting, malaise & prostration
- 2-3 days fever drops -> maculopapular rash
- Turns to tense, clear vesicles of face, mouth, forearms
- Vesicles cloud & spread to trunk, legs, palms, soles
- Fevers rises until pox burst, scab and scar.
- 30% death by encephalitis, myocarditis, osteomyelitis
Post exposure testing

- Rising serum antibodies by DFA, IFA, PCR
- Precipitation of antigen with immune serum
- Culture of vesicle to BL-4 containment lab
- Electron Microscopy finds brick shaped virus
- Nucleic Acid base testing
Treatment of Smallpox

- Quarantine
- Vaccinia Immune Globulin 0.6 ml/kg
- Methisone interferes with viral replication
- Cidovir (Vestide)
- Antihistamines for itch
TULAREMIA

- Organism - *Francisella tularensis*
- Gram negative coccobacillus
- Survives for weeks in soil, water, hay, fur
- “The Most infectious bacteria”
- Vectors: meat, tick, flea, flies & biting insects

**Bioterrorist Route**

- Aerosol, water, food
Pathophysiology

- Invades by multiple sites
- Skin, Eyes, Mouth, Nose
- From gut and lungs to blood and lymphatics
- Survives intracellularly as a parasite in WBCs
- Avoids antibodies and antibiotics in serum
- Spreads body wide causing necrosis
- NOT spread person to person.
Pre – Research testing

● Serum for antibody baseline
● Vaccinate with live attenuate bacteria now in clinical trials
● Antibodies may cross react with Brucellosis
Signs & Symptoms of Tularemia

- Sudden fever to 104 F, chills, sweats
- Skin->rash, papule, pustule, sore itchy ulcer base turns black, lymph node swells & drains
- Eye->unilateral redness, soreness, pus, ulcer
- Mouth->sore ulcers, tonsillitis, adenopathy
- GI->ulcers, cramps, vomiting, diarrhea, peritonitis
- Lung->dry cough, pneumonitis, pleurisy, SOB
- Blood->undulating fever, lethargy, shock
- Brain-> headache, meningitis, lymphocytes in CSF
Post Exposure testing

- Culture blood, skin, sputum on buffered charcoal & yeast extract media or glucose-cystine blood agar media
- Serum antibody titer – rise x4 = infection
- WBC’s normal or elevated
- Chest x-ray– ovoid infiltrate, hilar adenopathy
Treatment of Tularemia

- Choose any two for intracellular resistance
  - Doxycycline
  - Gentamycin
  - Rifampin
  - Chloramphenicol for meningitis
  - Streptomycin
- Tendency to relapse.
Post Research testing

- Serum antibodies titers
- Be alert for latent emergence of infection
- Rise in titer signifies relapse
References

7. www.CDC.gov Center for Disease Control, US Dept. of Health & Human Services, Atlanta GA
9. Mercy Regional Health Center Laboratory Billing Director - Rhonda Steele