Bioterrorism: What It Is; What You Should Know

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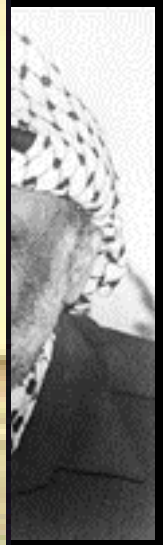
Biological
Terrorism
101

Close Encounter of the 1st Kind

Close Encounter of the 2nd Kind

Close Encounter of the 3rd Kind

Who is a Terrorist?



Who Needs to Know?

BIOLOGICAL
WARFARE

Biological Warfare

The intentional use of micro-organisms or toxins derived from living organisms to produce death or disease in humans, animals, or plants

History of Biological Warfare

- 14th Century: plague at Kaffa

History of Biological Warfare

- 18th Century: smallpox blankets

History of Biological Warfare

- 20th Century:
  - 1943: USA program launched
  - 1953: Defensive program established
  - 1969: Offensive program disestablished

HISTORY

History of Biological Warfare

- 20th Century:
  - 1974-1981: “Yellow Rain”
  - 1979: Sverdlovsk accident
  - 2002: Rouge Nations

BW Agents Destroyed by US

Lethal	**Incapacitating**	**Anti-crop**
B. anthracis	*B. suis*	Wheat stem rust
Botulinum toxin	VEE virus	Rye stem rust
F. tularensis	Staphylococcus enterotoxin B	Rice blast
	Q fever agent	

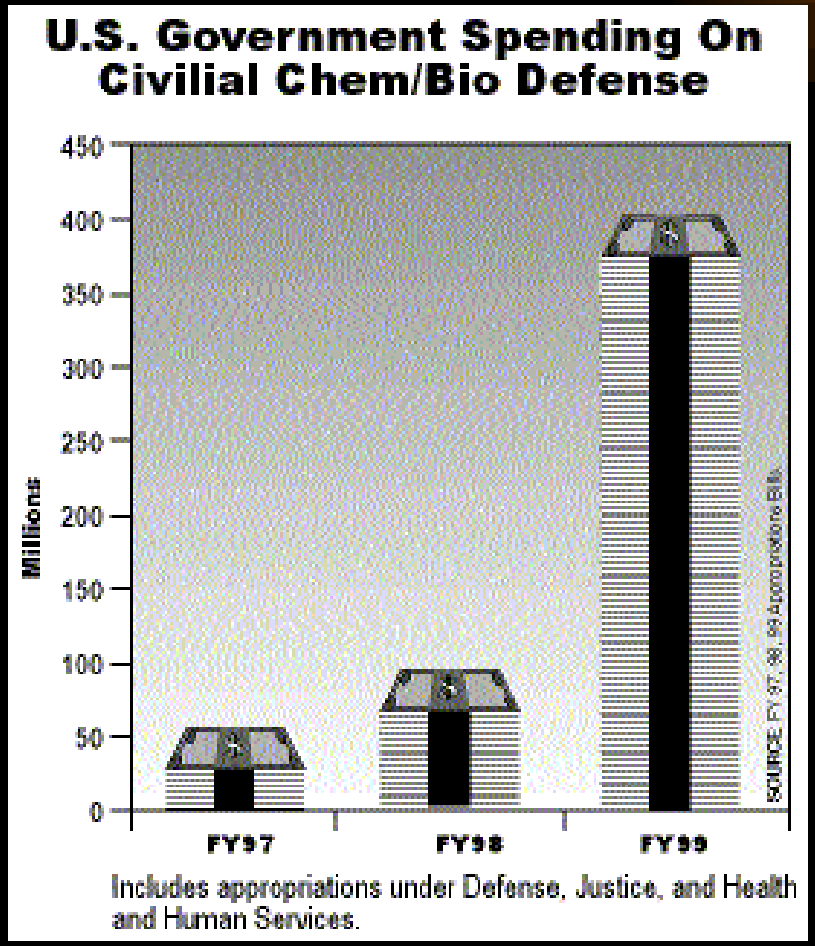
USSR "Hot" List

- Smallpox
- Plague
- Anthrax
- Botulism
- VEE
- Tularemia
- Q Fever
- Marburg Virus
- Influenza
- Melioidosis
- Typhus

Biological Terrorism

WOMAN KILLED
BY FUR COAT!
$316 full-length mink
COMES ALIVE and bites

Cost of Bioterrorism



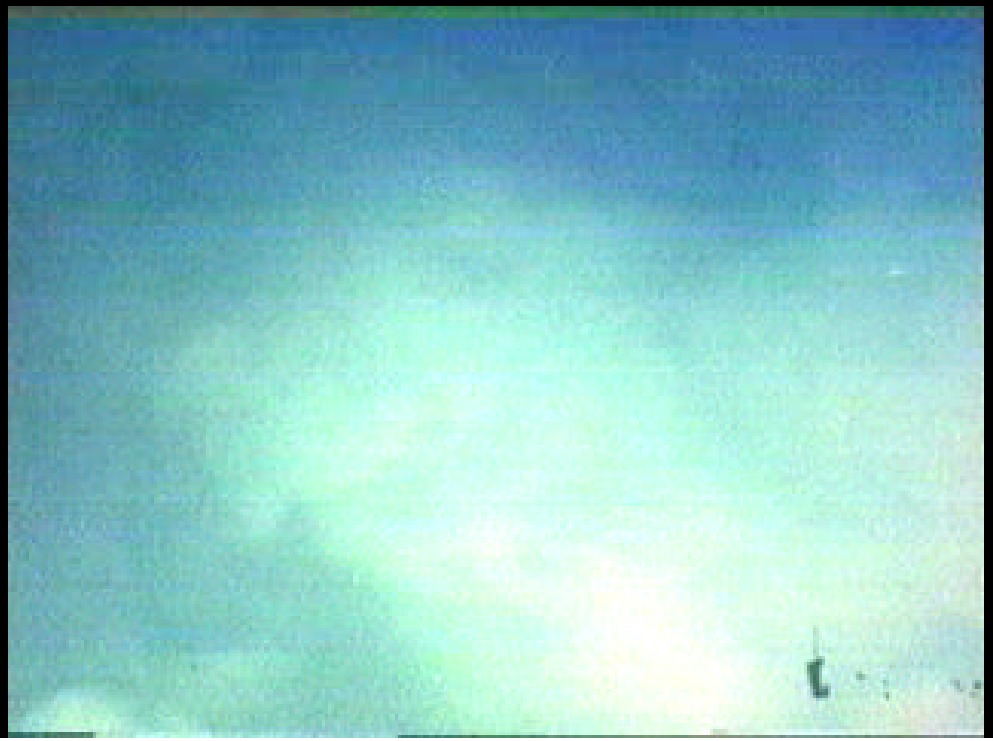
History of Biological Terrorism

1915	New Jersey	Glanders
1932	Japan	Cholera
1933	BC Pandey	Plague
1950	Mau Mau	Milk Bush
1964	M Suzuki MD	Salm & Shig
1970	E Kranz PhD	Ascaris
1978	Bulagria	Ricin
1981	Dark Harvest	Anthrax
1984	Rajneeshees	Salmonella
1990	Aum Shinri Kyo	Anthrax
1995	D Green MD	Ricin
1996	D Thompson	Shigella
1997	NZ Farmers	RCD

Agents Used by Bioterrorists

- Anthrax
- Plague
- *S. typhi*
- *S. typhimurium*
- *Shigella*
- Cholera
- *Y. enterocolitica*
- *Giardia*
- Schistosoma
- *Ascaris suum*
- Botulism
- HIV
- Yellow Fever
- Ricin
- Tetrodotoxin
- “Snake Venom”

Four Horsemen of the Apocalypse



CDC's "Short List"

- Report ALL suspected or confirmed illness due to these agents to health authorities immediately

CDC's "Short List"

- *Bacillus anthracis* (Anthrax)
- *Yersinia pestis* (Plague)
- *Francisella tularensis* (Tularemia)
- *Brucella* spp. (Brucellosis)
- *Burkholderia mallei* (Glanders)
- *Burkholderia pseudomallei* (Melioidosis)

CDC's "Short List"

- *Clostridium botulinum* toxin (Botulism)

CDC's "Short List"

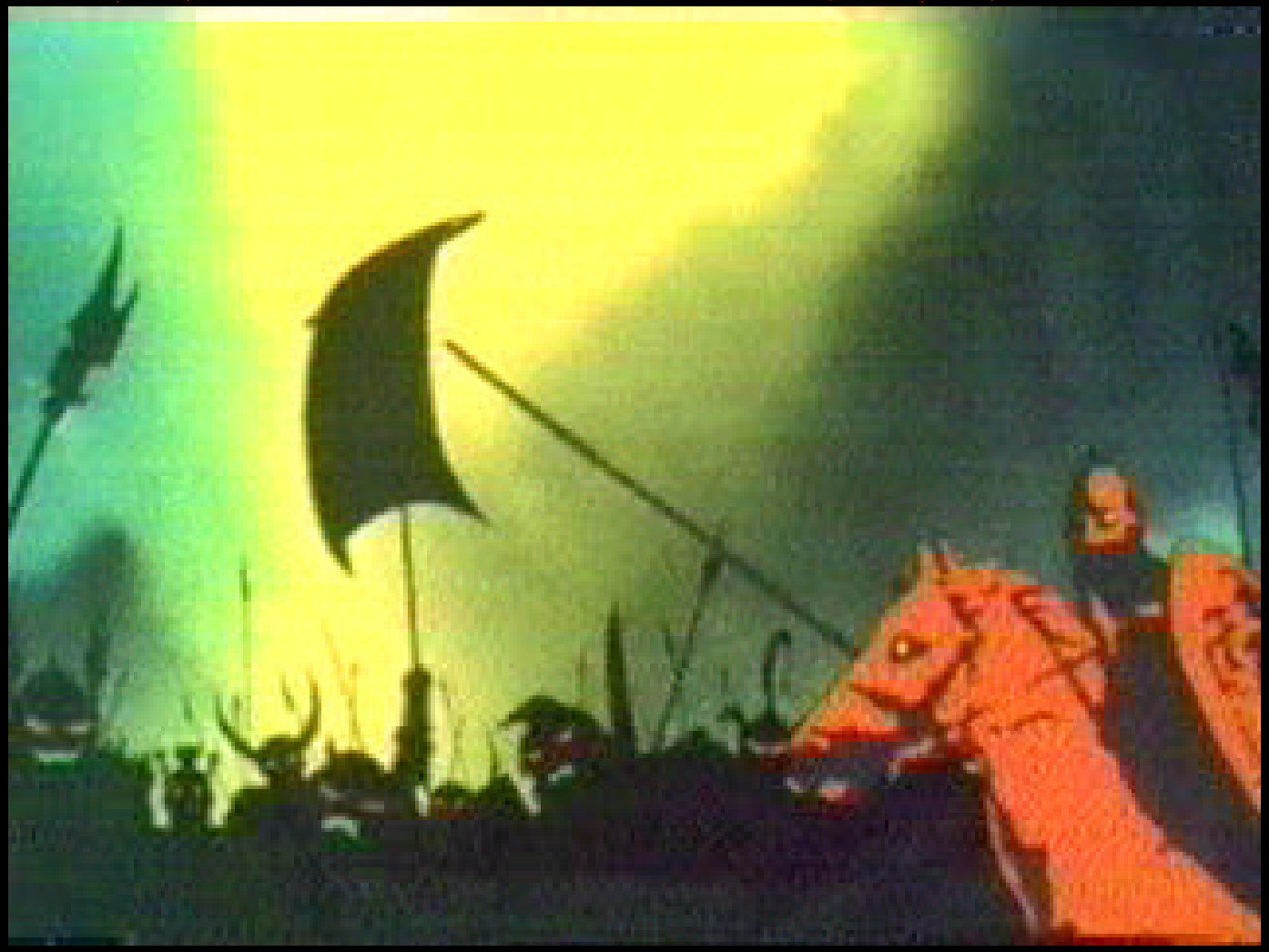
- Variola major (Smallpox)
- Filoviruses and Arenaviruses
  (Viral hemorrhagic fevers)

Why These Agents?

- Infectious via aerosol
- Organisms fairly stable in environment
- Susceptible civilian populations
- High morbidity and mortality
- Person-to-person transmission (smallpox, plague, VHF)
- Difficult to diagnose and/or treat
- Previous development for BW

ANTHRAX
PLAGUE
BRUCELLA
SMALLPOX

ANTHRAX



History of B. anthracis

- 1491 Exodus 5th plague
- 17th C “Black Bane”
- 1876 Koch’s Postulates
- 1881 Pasteur’s spore vaccine

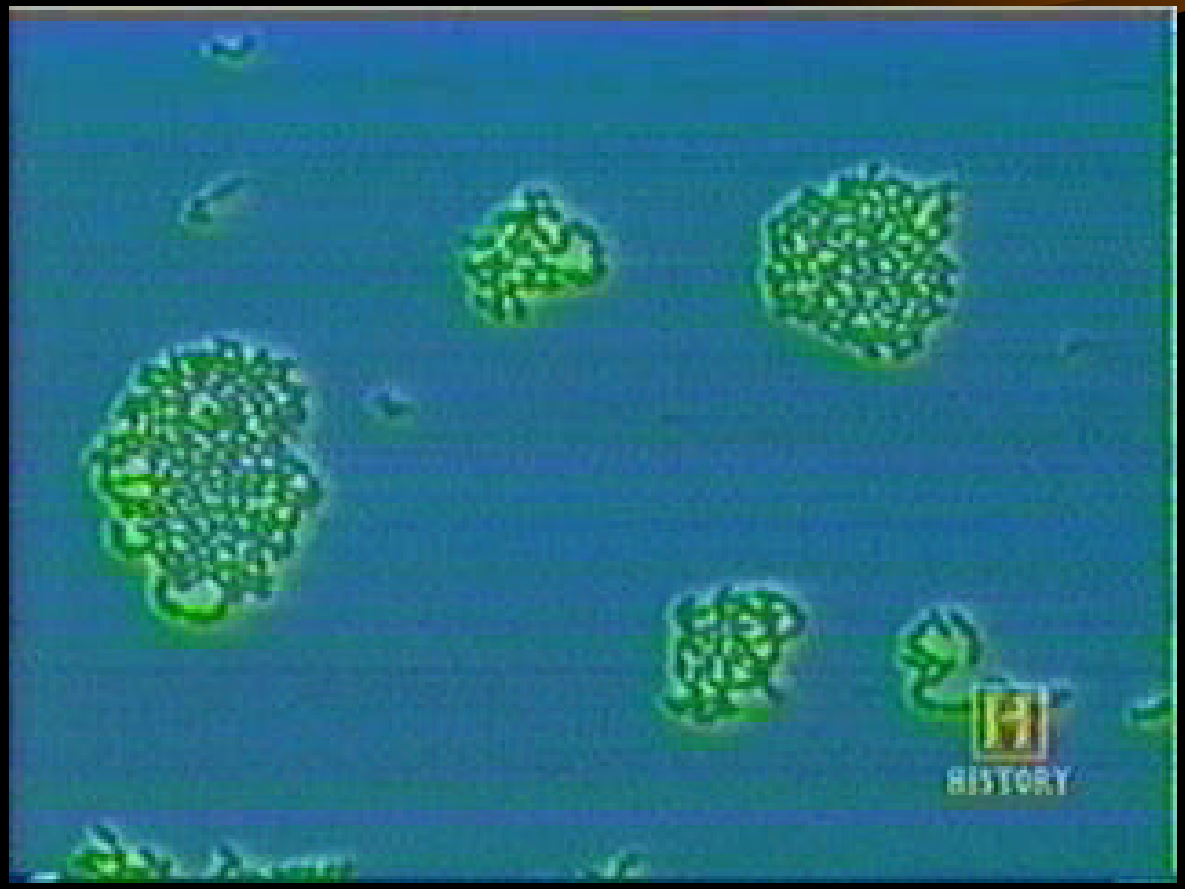
Anthrax Characteristics

- World-wide soil distribution
- Common disease of herbivores
- Cattle in USA vaccinated
- Man infected via animal products

Anthrax Characteristics

- Rapidly propagating organism

Anthrax Characteristics



Anthrax Epidemiology

- Normal flora in soil
- Herbivores infected during grazing
- Transmission to humans via:
  - contact with hides, hair, wool, bone
  - ingestion of contaminated meat
  - inhalation in industrial settings
  - biting flies
- Annual human incidence:
  - 20,000-100,000

Anthrax ***Bioterrorism***

- Delivery systems

MAIL

Anthrax Pathogenesis

- Spore enters skin, GI or lung
- Germinates in macrophage
- Transported to regional lymph nodes
- Local production of toxins
- Edema & necrosis
- Bacteremia & toxemia

Anthrax Virulence Factors

- Capsule
  - polysaccharide
  - poly-D-glutamate polypeptide
  - inhibits phagocytosis
  - protects against digestion
- Thermolabile toxin
  - Edema Factor (EF)
  - Protective Antigen (PA)
  - Lethal Factor (LF)

Anthrax Virulence

MODEL	ID50	TOXIN LD50	[BACTERIA] AT DEATH
Mouse	5 cfu	1000 U/kg	10M/ml
Monkey	3000 cfu	2500 U/kg	10M/ml
Rat	1M cfu	15 U/kg	10K/ml

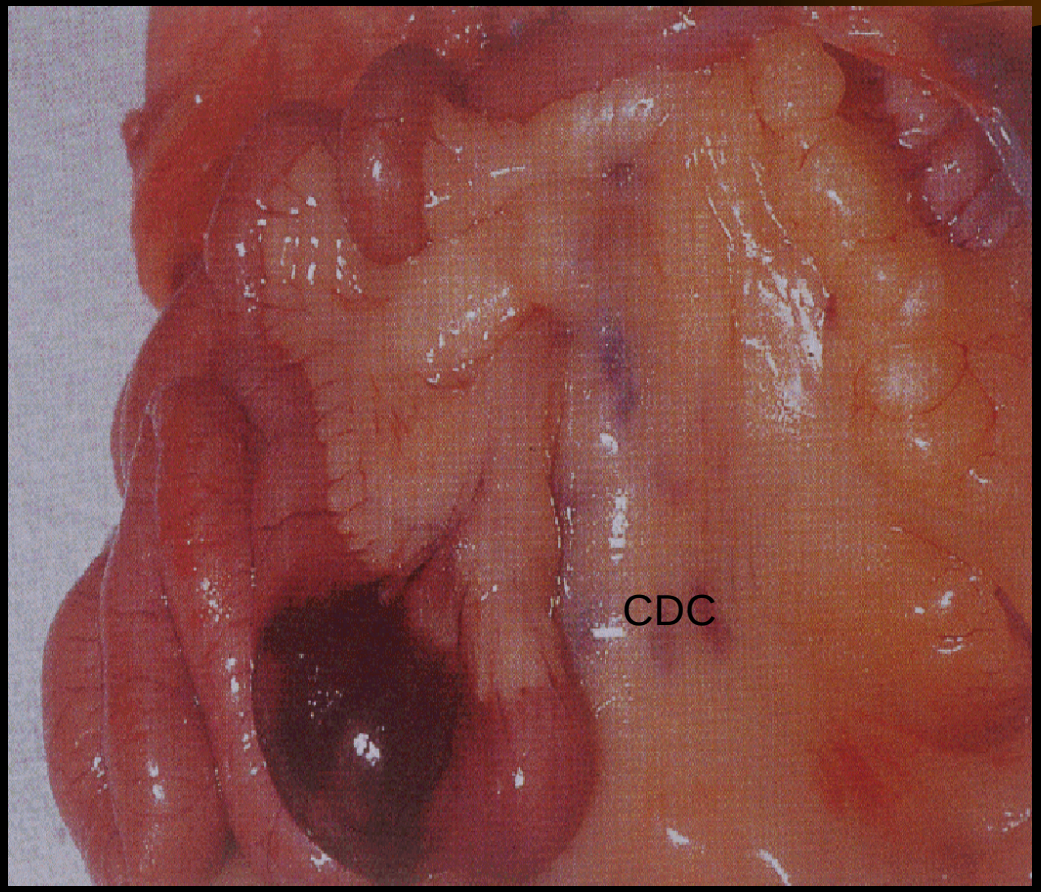
Anthrax

- Cutaneous
- Gastrointestinal
- Inhalation

Gastrointestinal Anthrax

- Very rare
- Ingestion of insufficiently cooked infected meat
- Mortality 25%-60%

Gastrointestinal Anthrax



Cutaneous Anthrax

- Malignant pustule
- 95% of cases
- Occurs most frequently on hands and forearms of persons working with infected livestock
- Black scab
  - anthrax: Greek for coal
- 25% mortality if untreated

Cutaneous Anthrax

- Minor scratch on skin or mucus membranes
- gelatinous edema at site
- papule develops within 12-36 hrs
- Papule rapidly changes to vesicle

Cutaneous Anthrax

- Vesicle rapidly changes to pustule (malignant pustule)
- Necrotic ulcer, intensely black with bright red border
- Lymphatic swelling after 7 days
- Septicemia & death

Cutaneous Anthrax

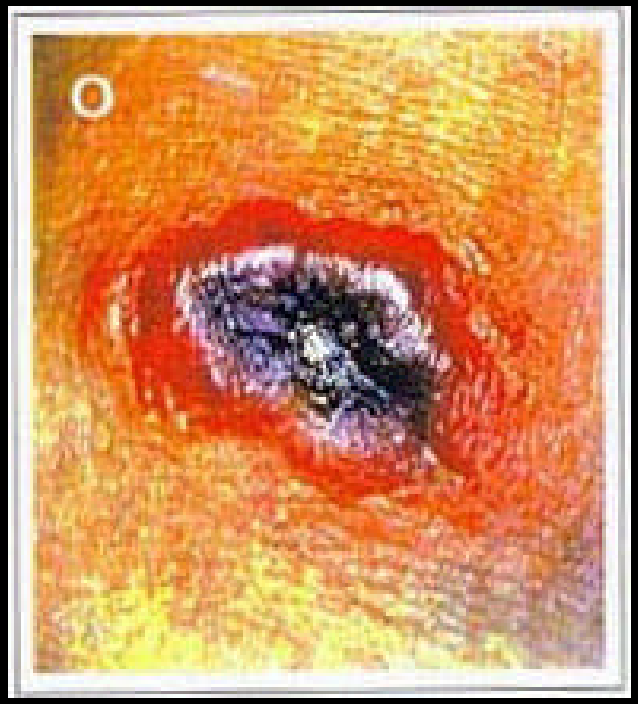
Cutaneous Anthrax

Cutaneous Anthrax

Cutaneous Anthrax

– Vesicle development, day 2

Eschar formation, day 4



Cutaneous Anthrax

Cutaneous Anthrax

Postal Employee

A

B

Cutaneous Anthrax

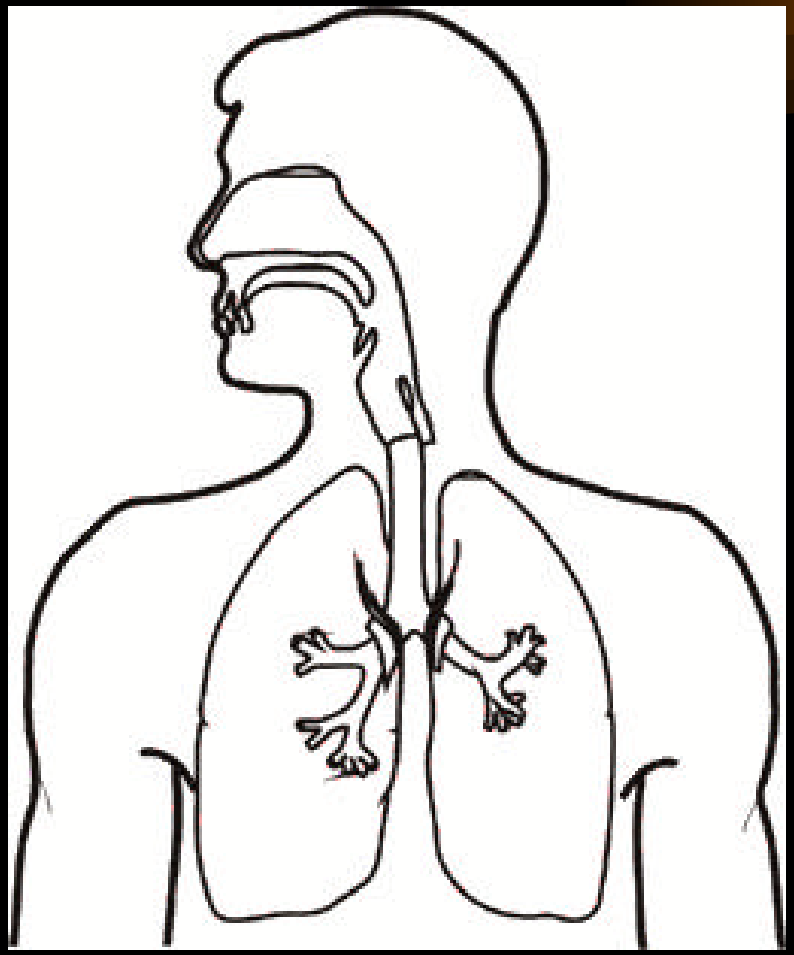
Cutaneous Anthrax

- Treatment
  - oral penicillin
  - oral tetracycline or ciprofloxicin if penicillin resistant

Inhalation Anthrax

- Woolsorter's disease
- Causes sever hemorrhage of lungs
- High bacteria load
- High mortality ~100%
- Post exposure treatment ineffective
- Pre-exposure prophilaxis highly effective

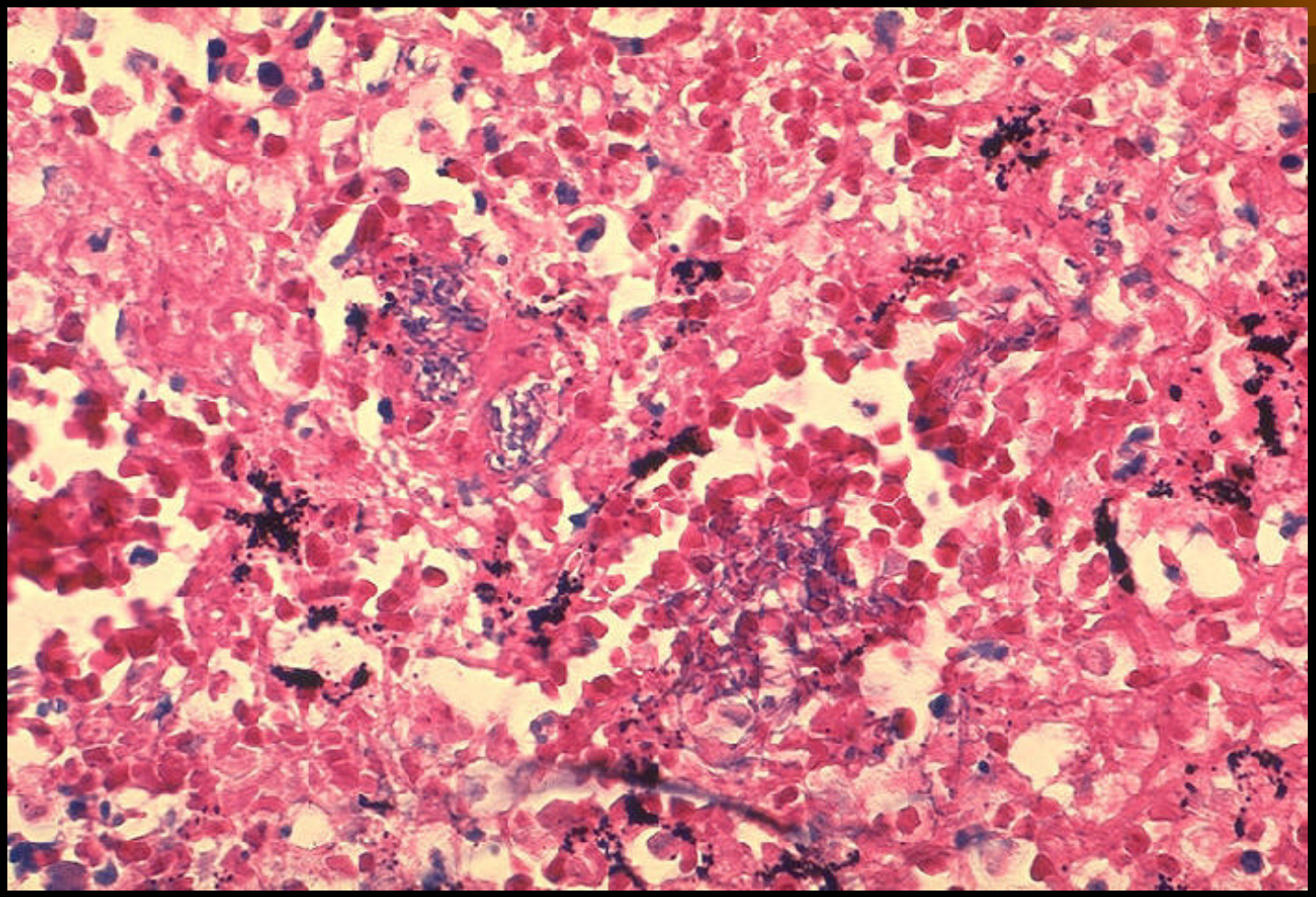
Inhalation Anthrax



Inhalation Anthrax

- Incubation period
  - 1-6 days
- Initial symptoms
  - malaise, fever, fatigue, non-productive cough, chest discomfort

Systemic Anthrax



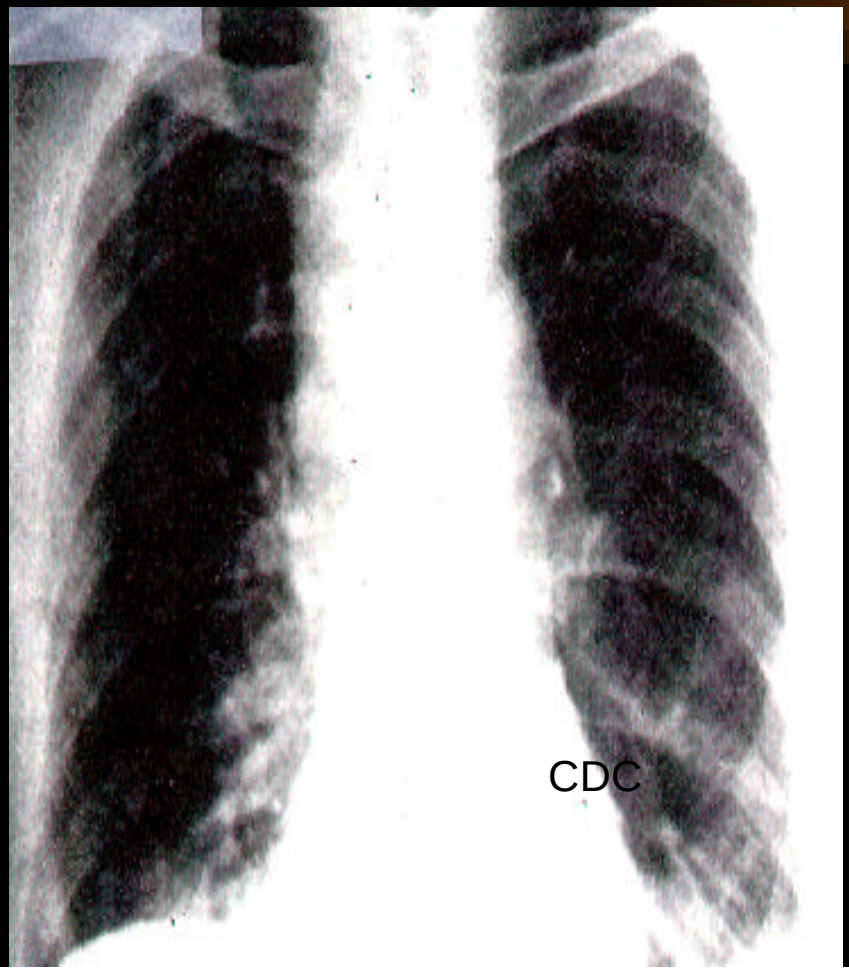
Lymph node

B. anthracis microcolony

Inhalation Anthrax

- Terminal phase
  - dyspnea, stridor, cyanosis, shock, chest wall edema, meningitis, widened mediastinum with effusion, no pulmonary infiltrates
  - death within 1-2 days

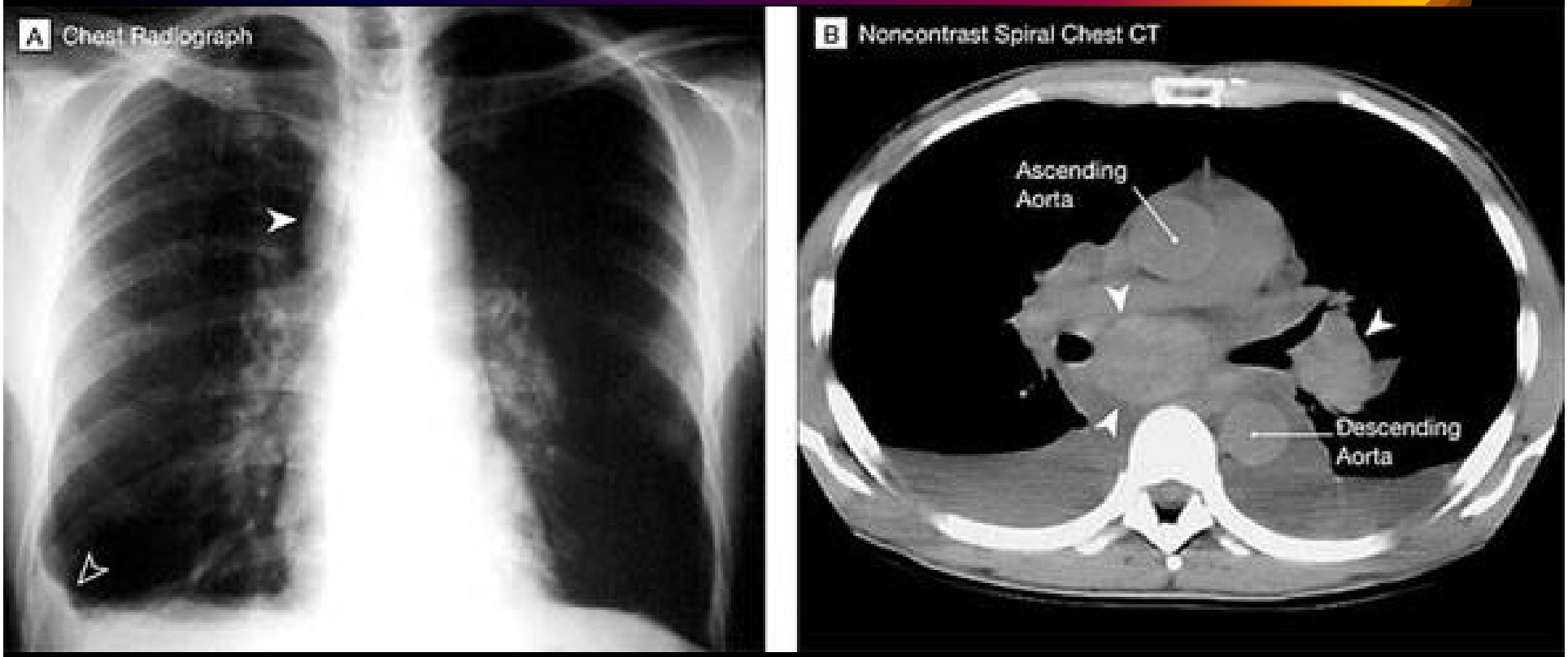
Inhalation Anthrax



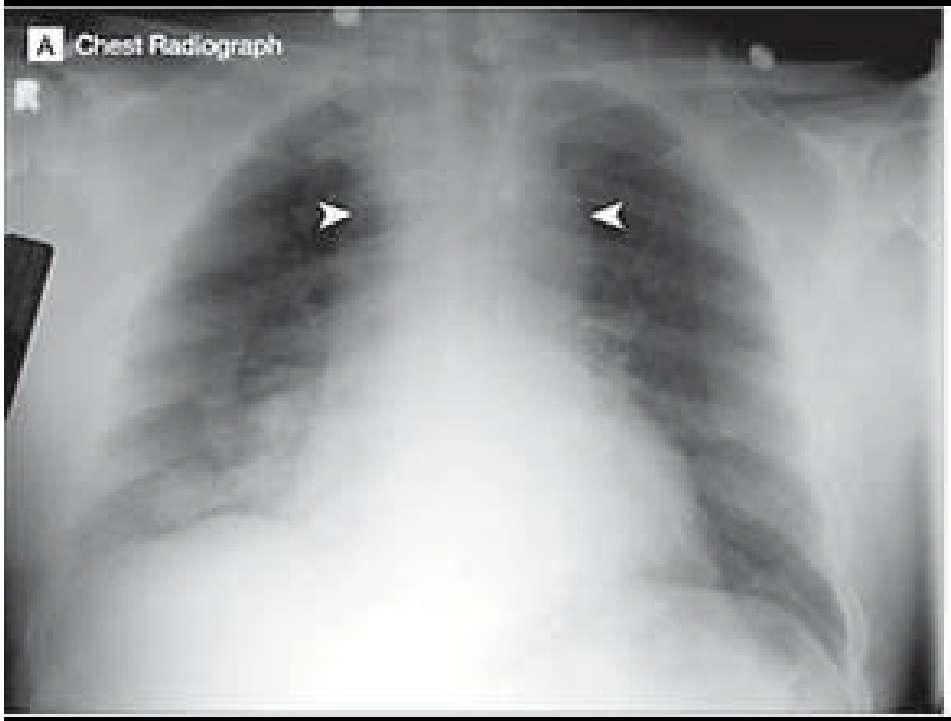
Inhalation Anthrax

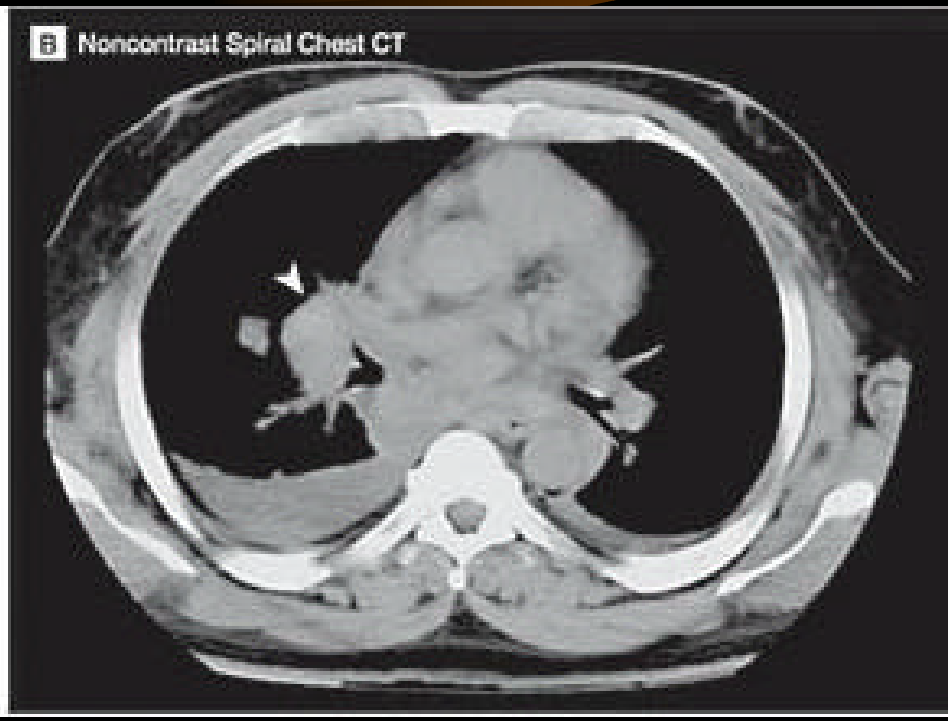
X-ray mediastinum

Inhalation Anthrax

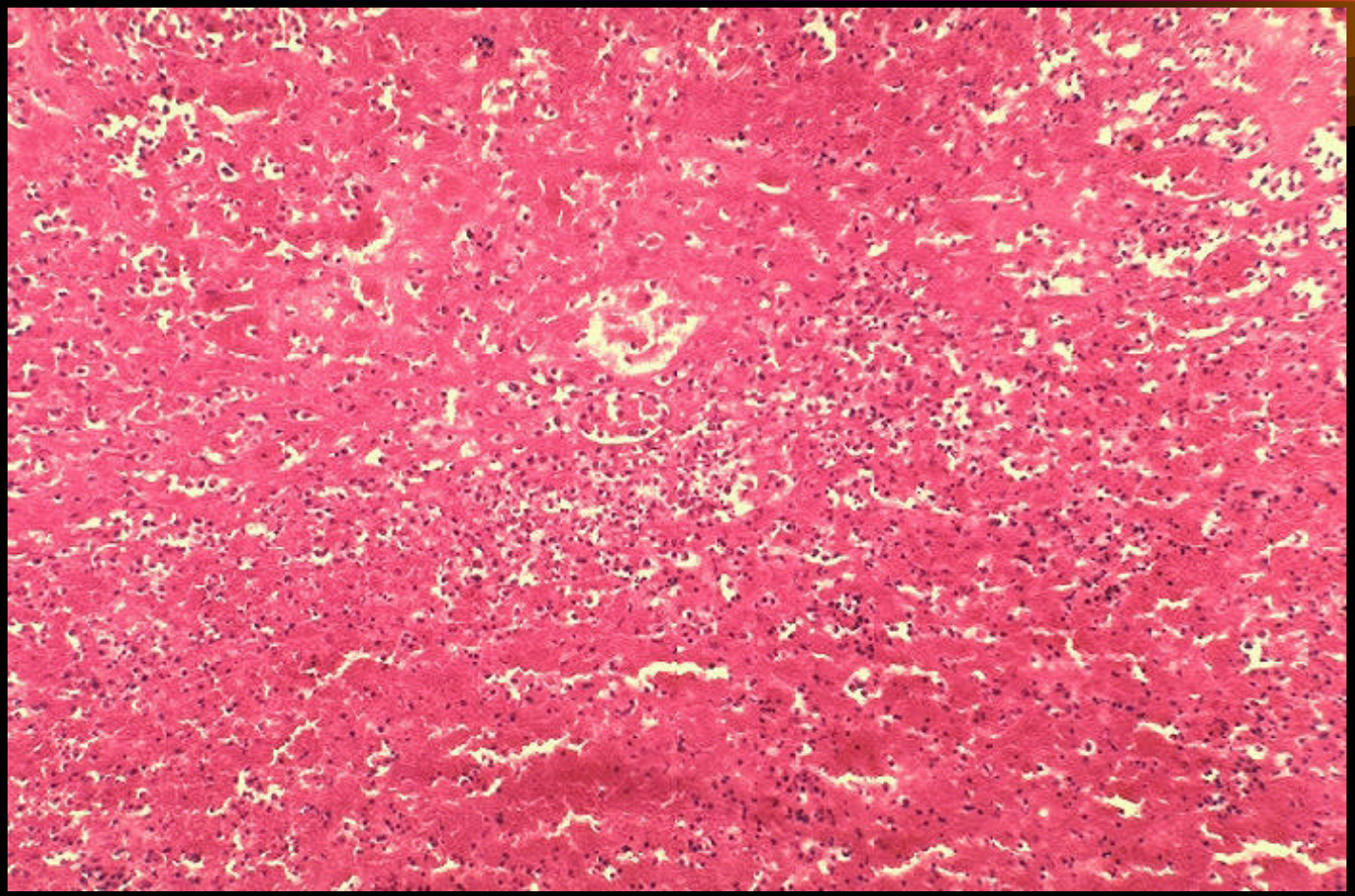


Inhalation Anthrax



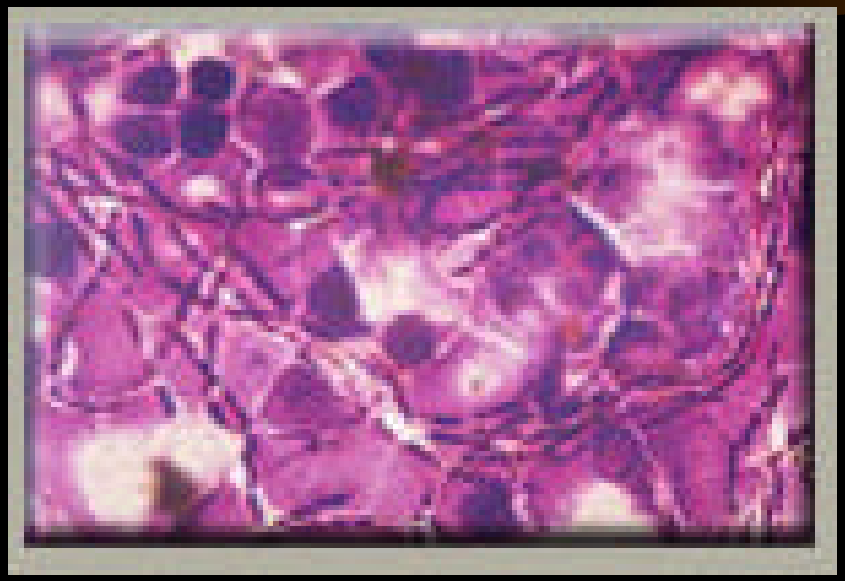


Systemic Anthrax



Occluded
blood vessel

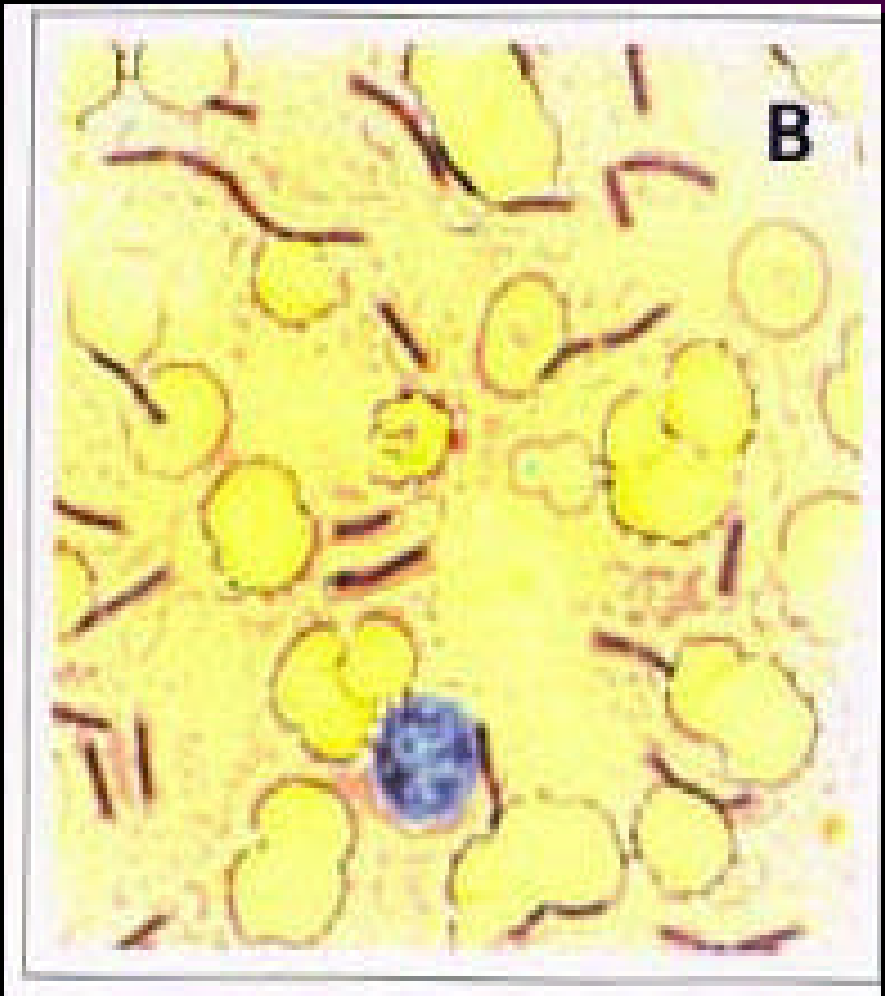
Systemic Anthrax



Direct Gram’s stain on peripheral blood

Systemic Anthrax

Systemic Anthrax

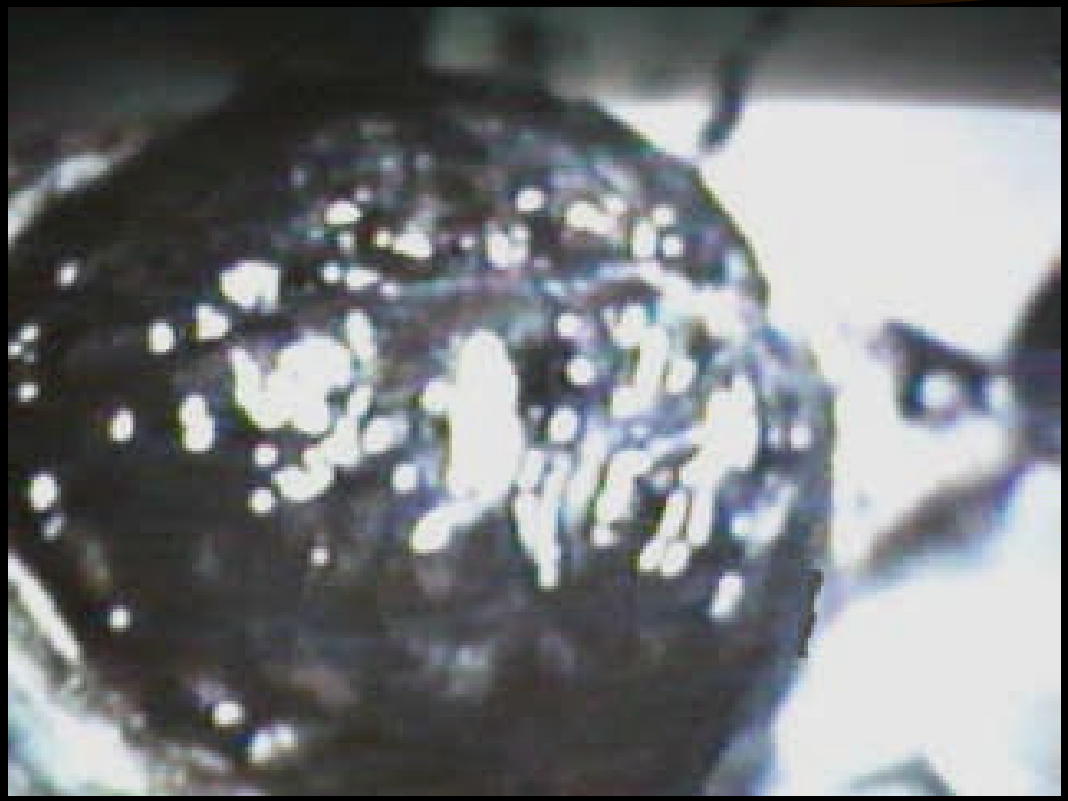


Encapsulated, *B anthracis* in peripheral blood smear. blue stain. Note: *in vivo,* the bacilli are in short chains

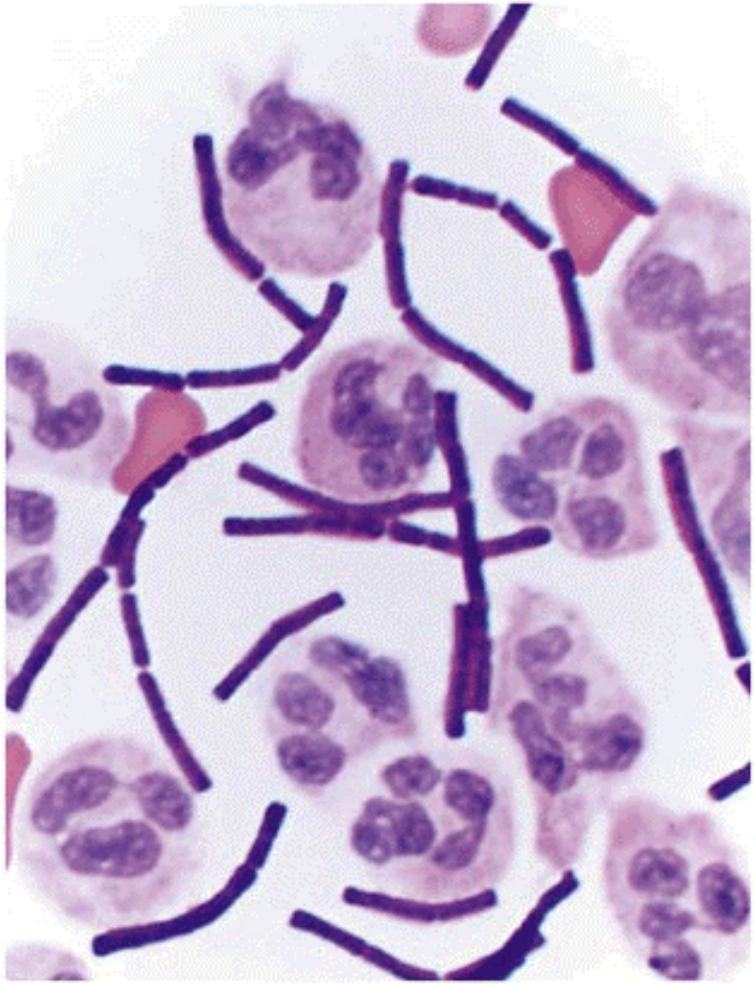
Polychrome methylene

Anthrax Bioterrorism

Anthrax Bioterrorism



Anthrax CSF



Inhalation Anthrax

- Diagnosis
  - history of exposure
  - painless pruritid papule
  - gram stain & culture
  - widened mediastinum
  - 4x titer rise via ELISA
  - Immunohistology

Inhalation Anthrax: Differential Diagnoses

- Dissecting aortic aneurysm
  - widened mediastinum
  - no fever
- Community acquired pneumonia (CAP)
  - if infiltrate (rare) or pleural effusion present
- Pneumonic Tularemia or Plague
  - pleural effusion
- Hantavirus pulmonary syndrome (HPS)

Inhalation Anthrax

- Treatment
  - Pre-exposure
    - vaccine
  - Post-exposure
    - penicillin 2M units IV q 2 h
    - ciprofloxacin 400mg IV q 8-12 h
    - doxycyline 200mg IV x 1; 100mg IV q 12 h
    - vaccine
  - Symptomatic
    - R.I.P.

Inhalation Anthrax

- Treatment
  - Post-exposure (terrorist) prophylaxis
    - **Adults**
      - ciprofloxacin 500 mg bid
      - levofloxacin 500 mg pd
      - ofloxacin 400 mg bid
      - doxycyline 100 mg bid
    - **Children**
      - ciprofloxacin 20-30 mg/kg q 12 h
      - levofloxacin not recommended
      - ofloxacin not recommended
      - doxycyline 5 mg/kg q 12 h

Prophylaxis continued until *B. anthracis* has been excluded.

Anthrax Vaccine

- History
  - 1881 Pasteur's Duplex vaccine
  - 1937 Sterne's Live Spore vaccine
    - veterinary use
    - human use in former USSR

Anthrax Vaccine

- History
  - 1963 V770 Cell-free Filtrate vaccine
    - current usage by armed forces
    - produced by BioPort, Lansing, MI
    - FDA-licensed since 1970
  - 1990's Candidate vaccines
    - recombinant PA
    - *B. subtilis* cloned with PA gene

Anthrax Vaccine

- Current US vaccine
  - schedule:
    - 0.5 ml SQ at 2 and 4 weeks
    - 6, 12 and 18 months
    - yearly booster required

Anthrax Vaccine

- Current US vaccine
  - response:
    - 83% serologically positive after 3 doses
    - 100% serologically positive after 5 doses
    - 100% protective in animals

Anthrax Vaccine

- Current US vaccine
  - adverse reactions:

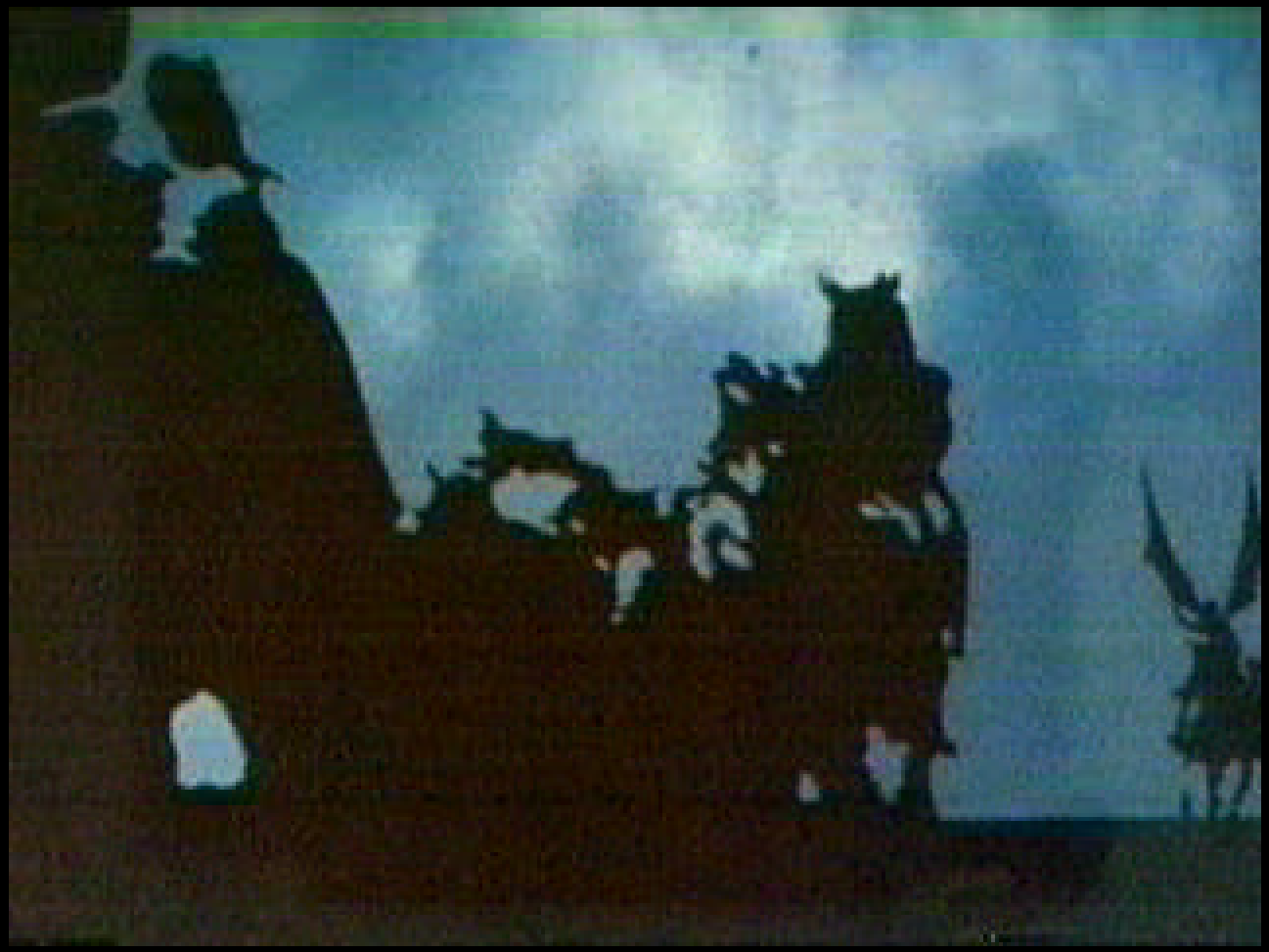
• 1st dose	n=1274	48	3.8%
• 2nd dose	n=1228	48	3.9%
• 3rd dose	n=1177	28	2.4%
• booster	n=5799	224	3.9%

Anthrax: Specimen Selection

- Inhalation: Blood and Sputum*
- Cutaneous: Vesicles and Eschar
- Gastrointestinal: Stool and Blood

*may be negative in early stages

PLAGUE



Plague: Epidemiology

- Natural vector - Rodent flea
- Mammalian hosts
  - rats, squirrels, chipmunks, rabbits, and carnivores
- Enzootic or Epizootic
- About 10-15 cases/year U.S.
  - Mainly SW states
  - Bubonic most common form

Plague: Clinical Forms

- Bubonic
  - Inguinal, axillary, or cervical LN most common
  - 80% can become bacteremic
  - 60% mortality overall if untreated

Plague: Clinical Forms

- Primary or secondary septicemic
  - 100% mortality untreated

Plague: Clinical Forms

- Pneumonic
  - From aerosol or septicemic spread to lungs
  - Person-to-person transmission by respiratory droplet
  - 100% mortality untreated

Plague: Bubonic

- Incubation: 2-6 days
- Sudden onset headache, malaise, myalgia, fever, tender lymphnodes
- Regional lymphadenitis (Buboes)
- Cutaneous findings
  - possible papule, vesicle, or pustule at inoculation site
  - purpuric lesions - late

Plague: Bubonic

Source: USAMRICD

Plague: Bubonic

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- Regional lymphadenitis (Buboes)
- Cutaneous findings
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  - purpuric lesions - late

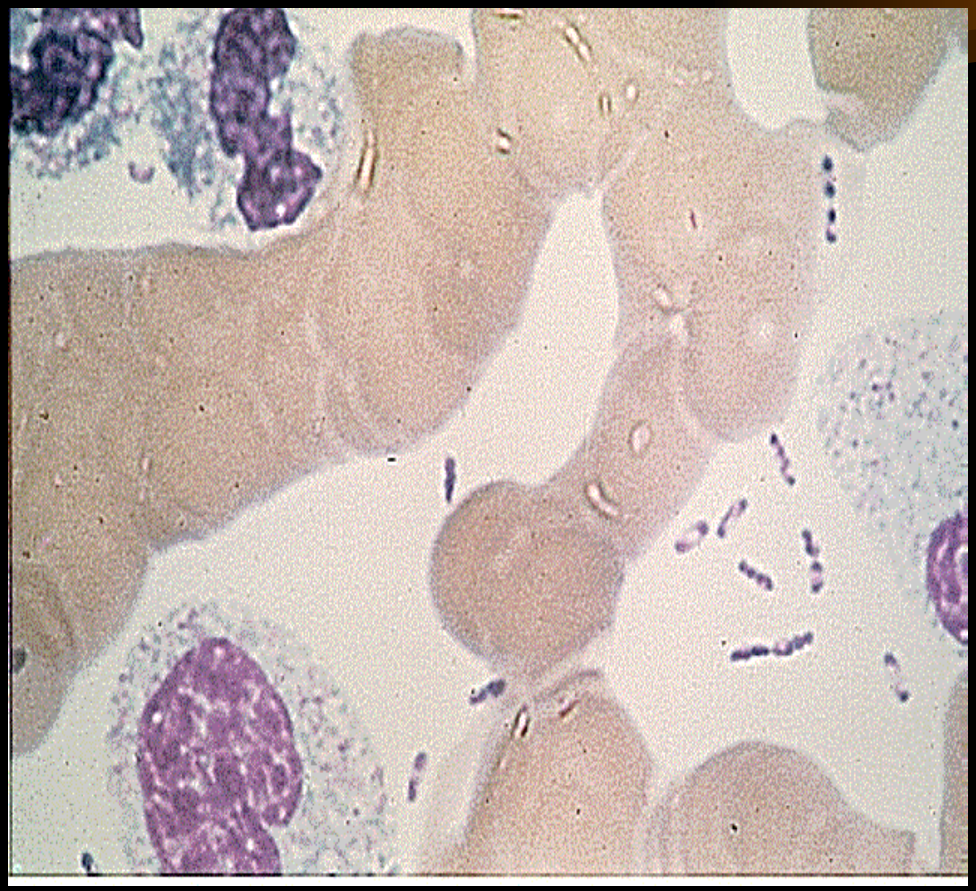
Plague: Differential Diagnosis

- Bubonic
  - Staph/streptococcal adenitis
  - Glandular tularemia
  - Cat scratch disease

Plague: Septicemic

- Primary or secondary
  - Secondary from bubonic or pneumonic
- Severe endotoxemia
- Systemic inflammatory response syndrome
- Shock, disseminated intravascular coagulation, acute respiratory distress syndrome

Plague: Septicemic



Plague: Differential Diagnosis

- Septicemic
  - Other gram-negative sepsis
  - Meningococcemia

Plague: Septicemic

Ecchymosis from systemic plague

Plague: Septicemic

Ecchymosis from systemic plague

Plague: Septicemic

Ecchymosis from systemic plague

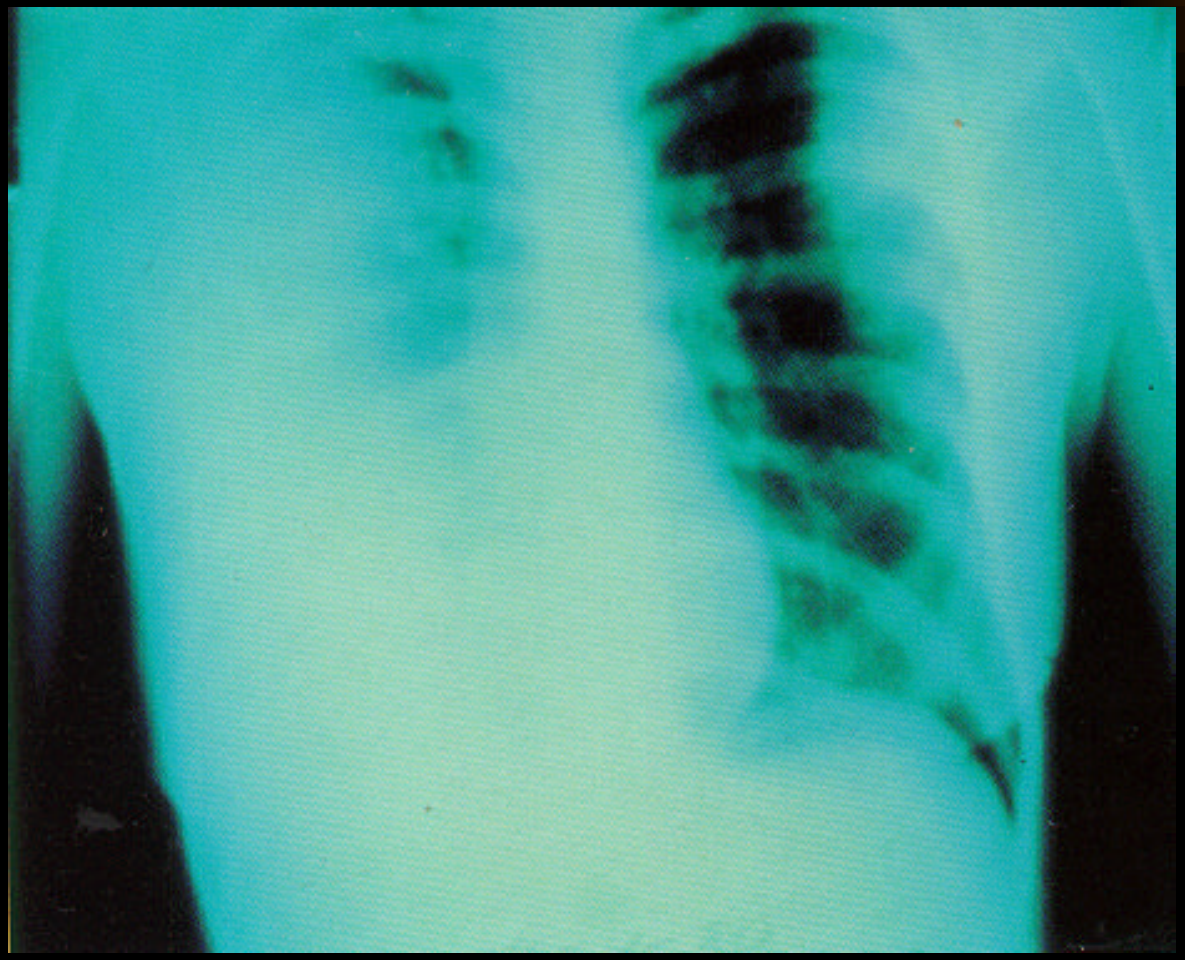
Plague: Pneumonic

- Incubation: 1-3 days
- Sudden onset HA, malaise, fever, myalgia, cough
- Pneumonia progresses rapidly to dyspnea, cyanosis, hemoptysis
- Death from respiratory collapse/sepsis

Plague: Pneumonic

Rock squirrel *in extremis*

Plague: Pneumonic



Source: USAMRICD

Plague: Differential Diagnosis

- Pneumonic
  - Bioterrorism threats
    - Anthrax
    - Tularemia
    - Melioidosis
  - Other pneumonia's
  - Hemorrhagic leptospirosis

Plague: Medical Management

- Antibiotic therapy
  - Gentamicin or Streptomycin
  - Tetracycline's
  - Sulfonamides
  - Chloramphenicol (meningitis/pleuritis)
- Supportive therapy
- Isolation and droplet precautions for pneumonic plague until sputum cultures negative
- Antibiotic resistant strains have been documented

Plague: Prophylaxis

- Bubonic contacts
  - If common exposure to fleas or infected animals, consider oral Doxycycline, Tetracycline, or TMP/SMX for 7 days
  - Other close contacts, fever watch for 7 days (treat if febrile)

Plague: Prophylaxis

- Pneumonic plague contacts (respiratory/droplet exposure)
  - Consider oral Doxycycline, Tetracycline, or TMP/SMX
  - Continue for 7 days after last exposure

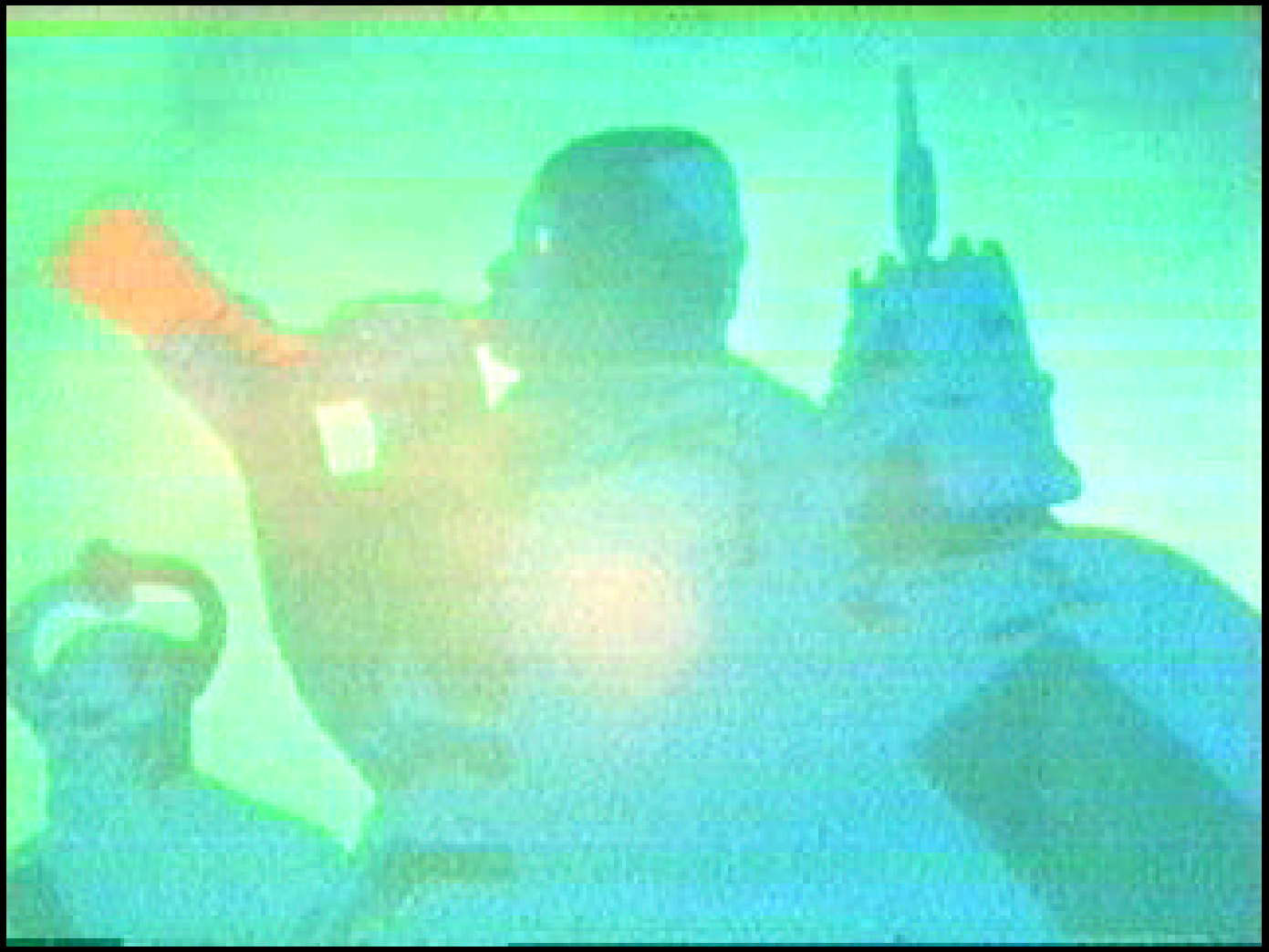
Plague: Prophylaxis

- Vaccine no longer manufactured in U.S.

Plague: Specimen Selection

- Specimen selection is important
  - Bubo - lymph node aspirate
  - Blood - organisms may be intermittent. Take three specimens 10-30 minutes apart
  - Pneumonic
    - Sputum/throat - use Wayson and DFA stain
    - Bronchial washings - Wayson and DFA stain
- Inoculate routine plating media and make thin smear for DFA
  - Wayson to be used only if DFA is unavailable

BRUCELLA



Brucellosis: History

- 1887 Bruce
  - malta fever, *Brucella melitensis*
- 1897 Bang
  - cattle abortion, *Brucella abortus*
- 1914 Traum
  - *Brucella suis*

Brucellosis: History

- In 1954, *B. suis* became the first agent weaponized by the U.S. in the early days of its offensive biological warfare program
- Infective inhalation dose = 10 -100 bacteria

Brucellosis: Epidemiology

- A zoonotic disease caused by any of 4 *Brucella* sp.: *abortus, melitensis, suis, and canis*
- Highly endemic in Peru, Mexico, Spain, Greece, Iraq, Iran, Jordan, and Kuwait
- But relatively rare in the U.S. with approximately 100 cases/yr

Brucellosis: Epidemiology

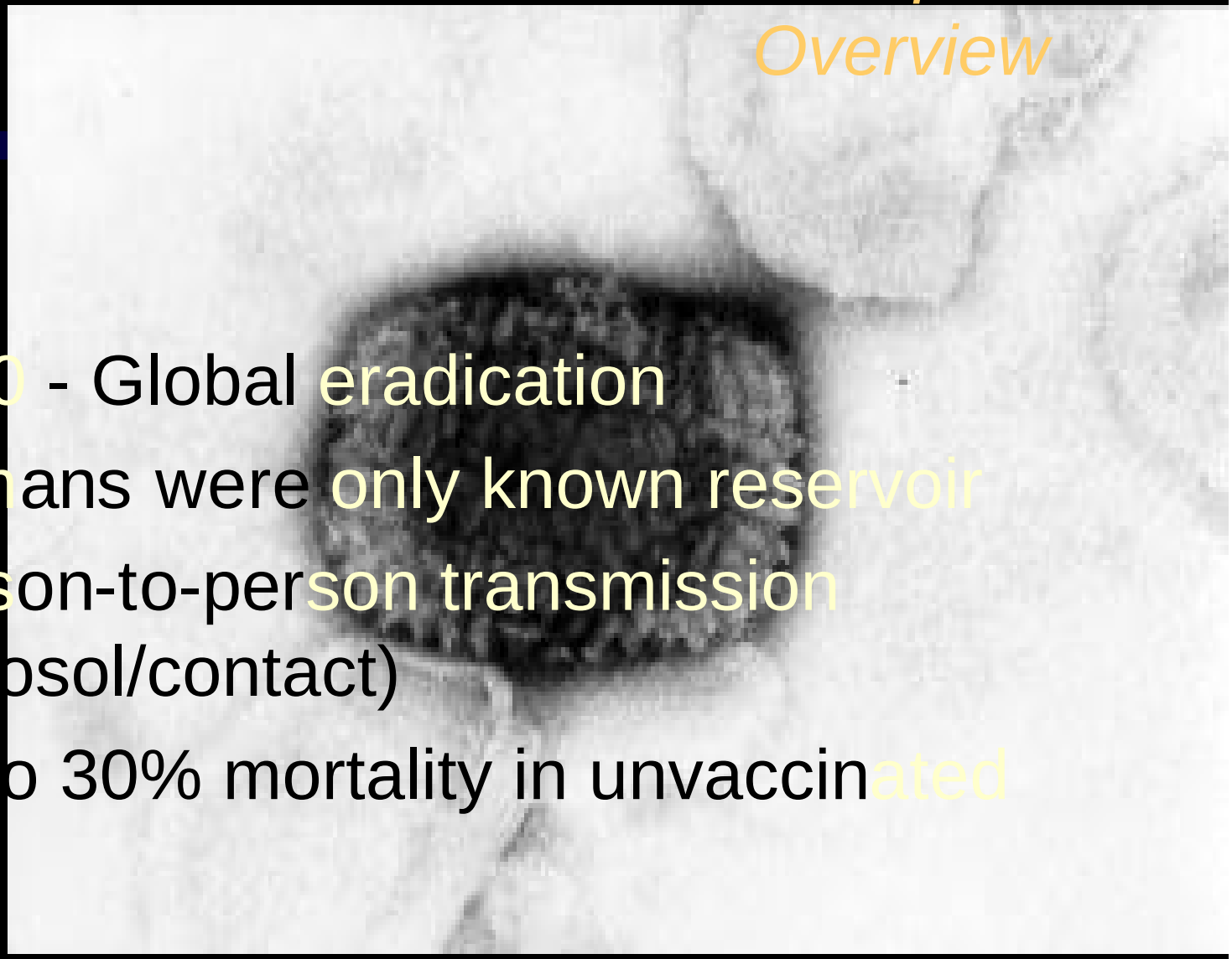
- Unpasteurized dairy products
  - The most common mode of transmission
- Direct skin contact
  - Occupational hazard for farmers, butchers, veterinarians, and laboratory personnel
- Aerosols
  - Highly infectious

Brucellosis: Clinical Features

- Infective dose = 10 -100 organisms
- Incubation period = 5 days - > 6 months
- Duration of illness = weeks to months
- Fever, profuse sweating, malaise, headache and muscle/back pain.
- Person to person transmission = no?
- Mortality = <5%
- Persistence of organism = very stable

SMALLPOX

Smallpox: Overview



- 1980 - Global eradication
- Humans were only known reservoir
- Person-to-person transmission (aerosol/contact)
- Up to 30% mortality in unvaccinated

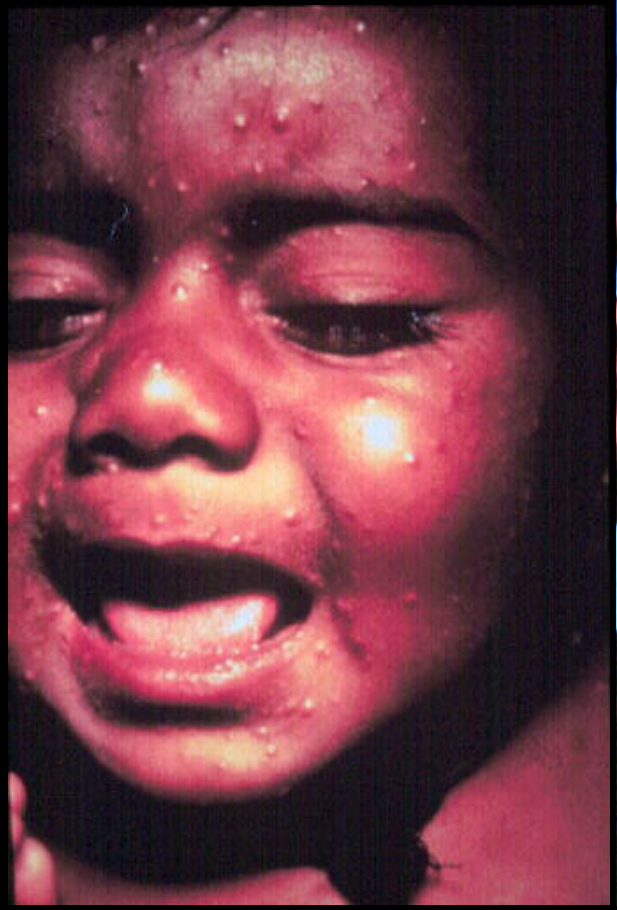
Smallpox: Clinical Features

- Prodrome (incubation 7-17 days)
  - Acute onset of fever, malaise, headache, backache, vomiting, occasional delirium
  - Transient erythematous rash

Smallpox: Clinical Features

- Exanthem
  - Begins face, hands, forearms
  - Spread to lower extremities then trunk over ~ 7 days
  - Synchronous progression: macules --> vesicles --> pustules --> scabs
  - Lesions on palms /soles

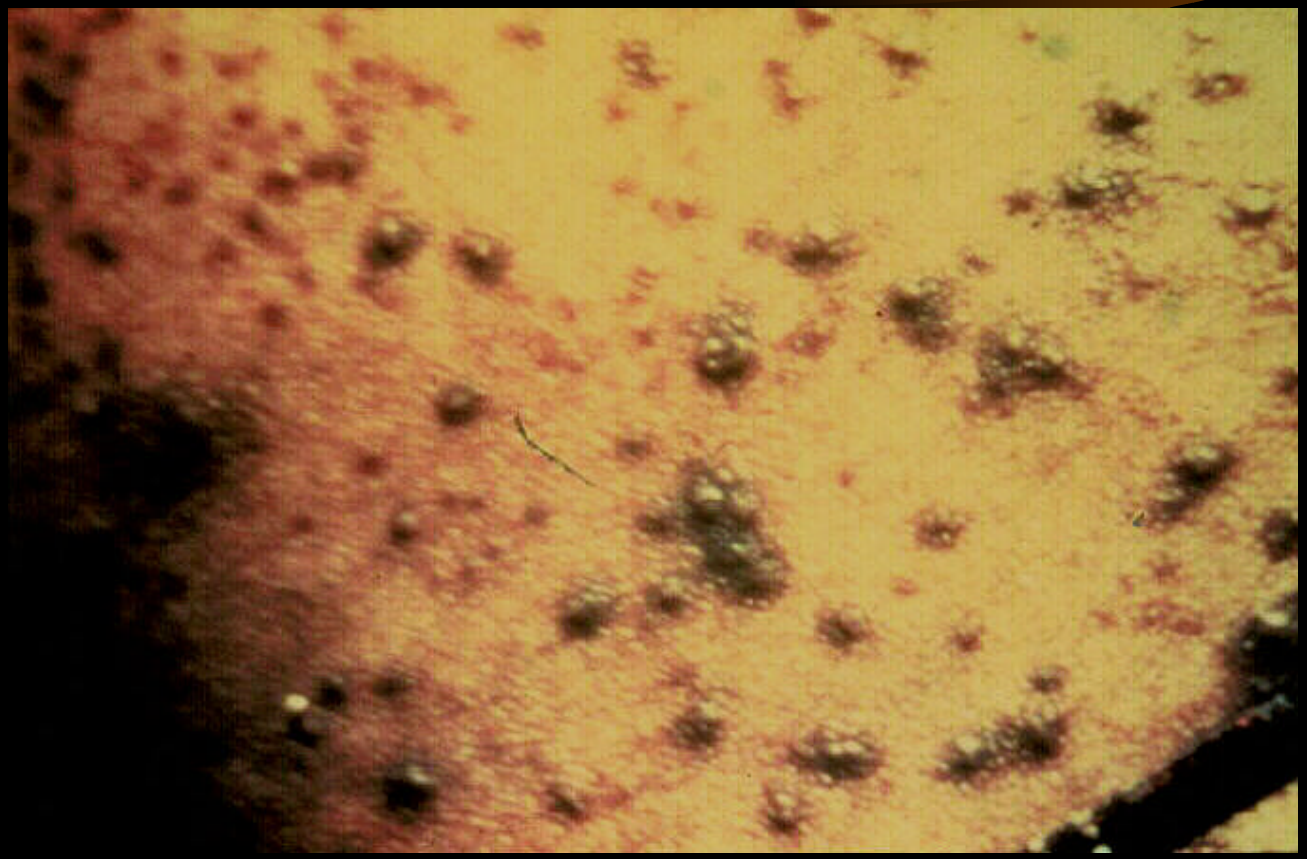
Smallpox: Clinical Features



Smallpox: Clinical Features

Smallpox: Clinical Features

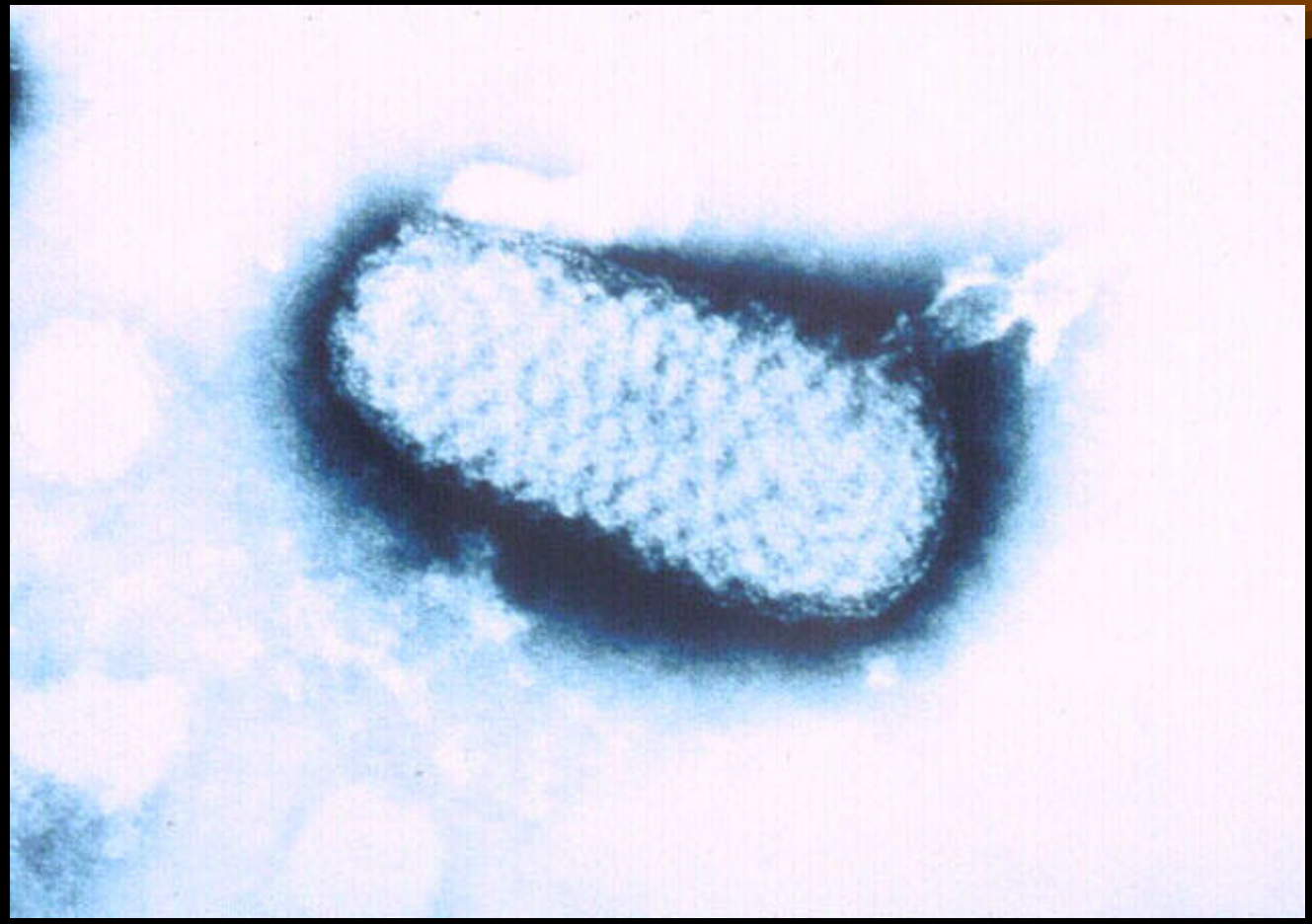
Smallpox: Clinical Features



Variola
Smallpox virus

- The family *Poxviridae* consists of eight genera and a few unclassified species
- Two species are human viruses
  - Variola virus (genus *Orthopoxvirus*)
  - Molluscum contagiosum virus (genus *Molluscipoxvirus*)
- *Orthopoxvirus* includes vaccinia (a lab virus), monkeypox, cowpox, and buffalopox

Variola
Smallpox virus



Smallpox virus

- Stored stocks to be retained until 2002 by U.S. and Russia
  - Undeclared virus could be anywhere
- No cases in over 20 years
- Controversial decision
- Immunity lost in U.S. population
  - Highly vulnerable to infection

Smallpox: Complications

- Encephalitis (1 in 2,000 cases)
- Keratitis, corneal ulceration
  - Blindness in 1% of cases
- Infection in pregnancy
  - High perinatal fatality
  - Congenital infection

Smallpox vs. Chickenpox

	Variola	Varicella
Incubation	7-17 days	14-21 days
Prodrome	2- 4 days	minimal/none
Distribution	centrifugal	centripetal
Progression	synchronous	asynchronous
Scab formation	10-14 d p rash	4-7 d p rash
Scab separation	14-28 d p rash	<14 d p rash

Smallpox: Current Vaccine

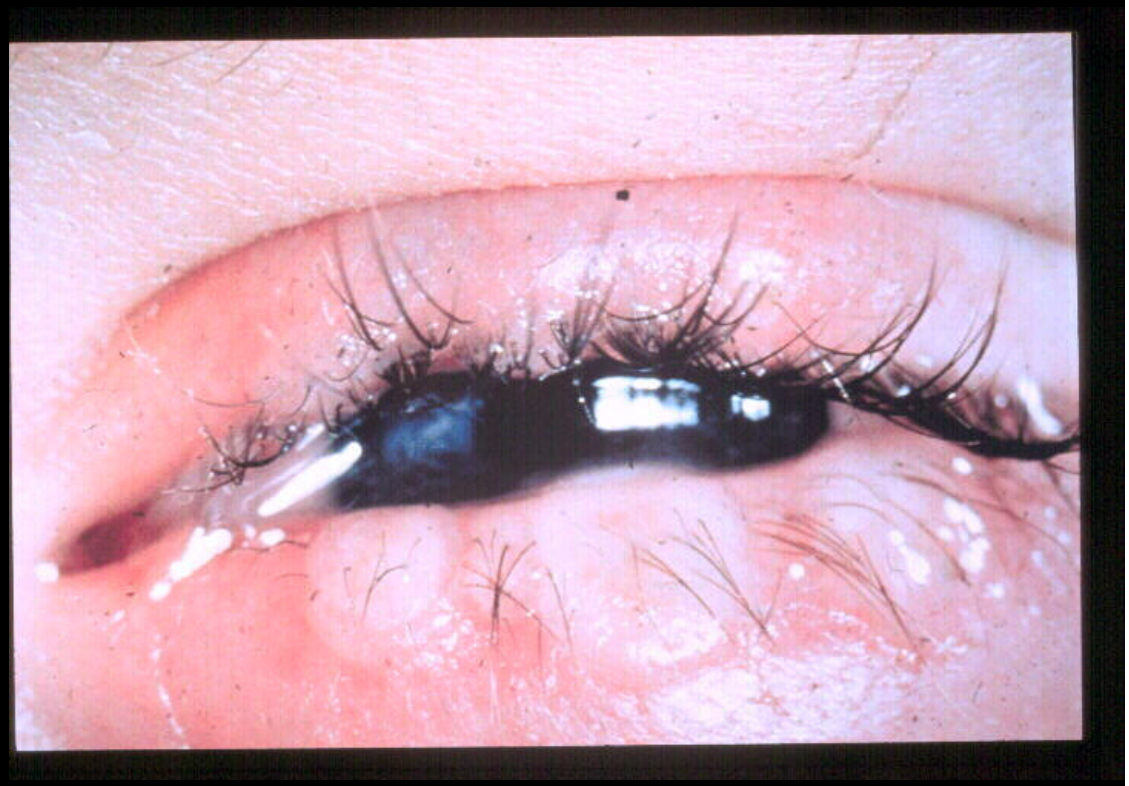
- Made from live Vaccinia virus
  - 15.4 million doses in US Stores
- Intradermal inoculation with bifurcated needle (scarification)
  - Pustular lesion or induration surrounding central lesion (scab or ulcer) 6-8 days post-vaccination
  - Low grade fever, axillary lymphadenopathy
  - Scar (permanent) demonstrates successful vaccination
  - Immunity <u>not</u> life-long

Smallpox: Current Vaccine

Smallpox: Current Vaccine

Smallpox: Vaccination Complications

- Most common
  - Inadvertent inoculation (skin, eye)



Smallpox: Vaccination Complications

- Less Common
  - Generalized vaccinia

Smallpox: Vaccination Complications

- Less Common
  - Post-vaccination encephalitis (2.8/million)
  - Fetal vaccinia
  - Eczema vaccinatum (4.5/million)

Smallpox: Vaccination Complications

- Less Common
  - Vaccinia necrosum (0.7/million)

Smallpox: Vaccination Complications

- Primary vaccination - 1 death/million
- Revaccination - 0.2 deaths/million

Smallpox: Vaccinia Immune Globulin (VIG)

- Treatment of adverse reactions (AR)
  - Approximately 25AR's/100,000 vaccinations
  - AR rate may be increased due to higher immunocompromised population

Smallpox: Vaccinia Immune Globulin (VIG)

- Post-exposure prophylaxis
  - Pregnant patients (VIG + Vaccinia vaccine)
  - Eczema (VIG + Vaccinia vaccine)
  - Immunocompromised patients, No consensus (VIG alone vs. VIG + Vaccinia vaccine?)

Smallpox: Vaccinia Immune Globulin (VIG)

- Current supplies limited

Smallpox: Medical Management

- Strict respiratory/contact isolation of patient
  - Patient infectious until all scabs have separated
- Notify public health authorities <u>immediately</u> for suspected case
- Identification of contacts within 17 days of the onset of case's symptoms

Smallpox: Management of Contacts

- Immediate vaccination (or boosting) of ALL potential contacts including health care workers
  - Vaccination within 4 days of exposure may prevent or lessen disease
  - 17 day observation for fever or rash
- Passive immunization (VIG)
  - Potential use for contacts at high risk for vaccine complications (pregnancy, dermatoses, immunosuppression)

The Wild Bunch

The Rest of CDC's *Hot List*

Tularemia

Francisella tularensis

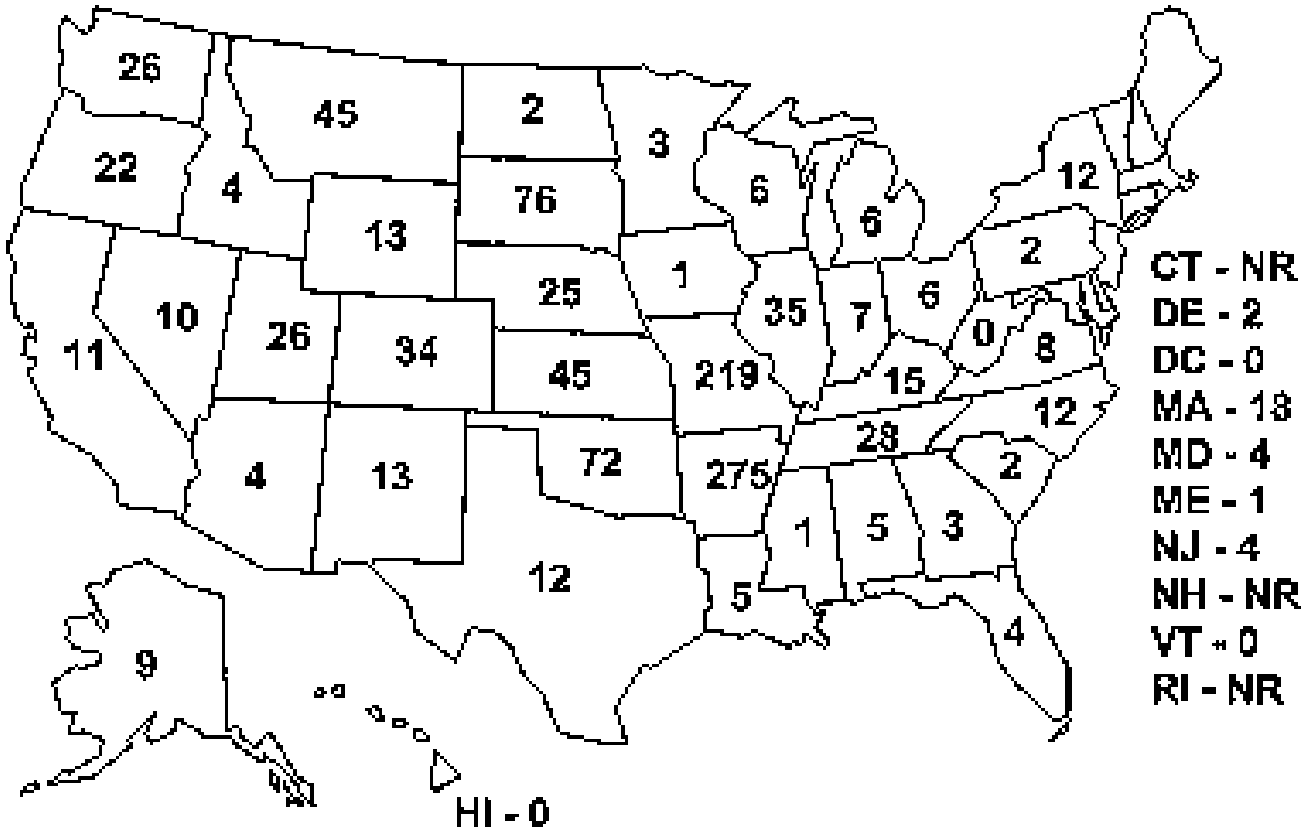
"A Rose by Any Other Name"

- Plague-like disease in rodents (California)
- Deer-fly fever (Utah)
- Glandular tick fever (Idaho and Montana)
- Market men's disease (Washington, DC)
- Rabbit fever (Central States)
- O'Hara's disease (Japan)
- Water-rat trappers disease (Russia)

Tularemia: Overview

- Disease of Northern Hemisphere
- In U.S., most cases associated with rabbits/hares and ticks
- About 200 cases/year in U.S.
  - most in South central and Western states
  - majority of cases in summer, some in winter
- Low infectious dose
  - 1 to 10 organisms by aerosol or intradermal route
- No person-to-person transmission

Reported Cases of Tularemia 1990-1998



Tularemia: Clinical Forms

- Ulceroglandular
  - Ulcer with regional adenopathy
- Glandular
  - Regional adenopathy without skin lesion
- Oculoglandular
  - Painful purulent conjunctivitis with adenopathy

Tularemia: Clinical Forms

Scalp Ulcer

Tularemia: Clinical Forms

Ulceroglandualr

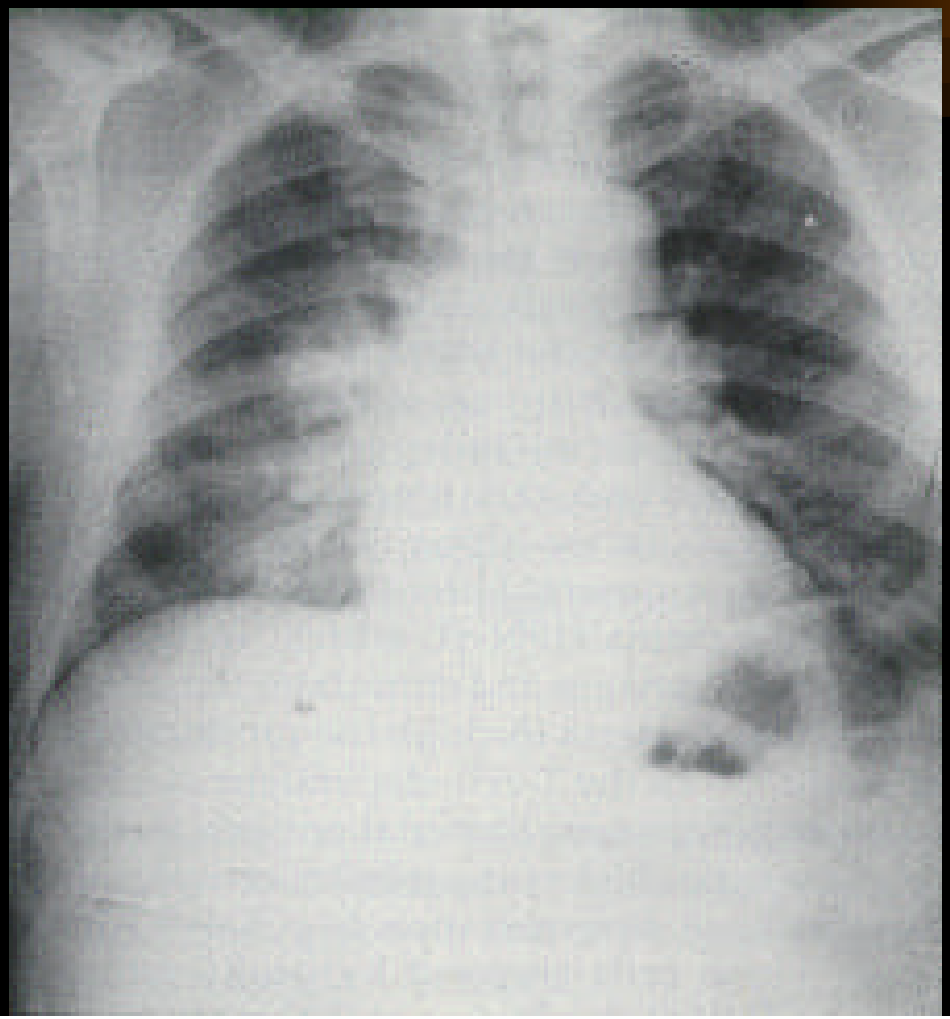
Tularemia: Clinical Forms

- Typhoidal
  - Septicemia, no adenopathy
  - Possible presentation for BT
- Pneumonic (primary or secondary)
  - Possible presentation for BT

Tularemia: Pneumonic

- Incubation: 3 to 5 days (range 1-21 days)
- Abrupt onset fever, chills, headaches, myalgia, non-productive cough
- Segmental/lobar infiltrates, hilar adenopathy, effusions
- Mortality 30% untreated; < 10% treated

Tularemia: Pneumonic



USAMRICD

Pneumonic Tularemia: Differential Diagnoses

- Community acquired pneumonia (CAP)
  - Atypical CAP (Legionella, Mycoplasma)
  - Streptococcal pneumonia, Influenza, *H. influenza*
- Other Zoonoses
  - Brucellosis
  - Q Fever
  - Pneumonic plague
  - Histoplasmosis
  - Inhalation Anthrax
  - Hantavirus pulmonary syndrome

Tularemia: Treatment/Prophylaxis

- Treatment
  - Streptomycin or Gentamicin
  - Tetracycline's
- Prophylaxis
  - Fever watch for 7 days (preferable)
  - Doxycycline or Tetracycline for 14 days if febrile
- Vaccine investigational, not available

Gram Negative Coccobacilli

- Most likely
  - *Acinetobacter* (ox.neg)
  - *Actinobacillus* (sticky)
  - *H. aphrophilus*
  - *Bordetella,* Grp. IV (inert, urea pos)
  - *Pasturella* (nonsticky, Mac pos**)**
- Least likely
  - DF-3
  - *Brucella* (Urea pos in seconds - minutes)
  - *Francisella* (Urea neg)

F. tularensis
Rapid Method Results

- Not on the data base of MicroScan or Vitek or API
- Should not be worked with in the Level A lab

Francisella tularensis
Technical Hints

If you see:

- Tiny, gram-negative coccobacilli from blood, lymph node aspirate, or respiratory specimens
- Blood isolates that will grow slowly on chocolate agar but [illegible] or not [illegible] all on blood agar in 24 hours
- Faint gr[illegible] in [illegible] ne in other broth

Refer

Melioidosis

Burkholderia pseudomallei

Melioidosis

- Acute pulmonary infection
- Can remain latent for years
- Months of antimicrobial treatment may not eradicate disease
- Histologically and clinically resembles tuberculosis

Melioidosis

- *Burkholderia* (formerly *Pseudomonas*) *pseudomallei*, GNB
- Found in soil, stagnant water, ponds, rice paddies, etc.
- Market produce in endemic areas
- Can cause disease in sheep, goats, swine, horses and seals
- Endemic in southeast Asia and northern Australia

Melioidosis

- Most widespread in Thailand
  - 19% of all hospitalizations
  - 40% of deaths due to community-acquired septicemia
  - 80% of children sero-positive by age 5

Melioidosis

- Drug of choice: ceftazidine
- Treat at least 30 days
- 60-150 days recommended for pulmonary disease
- 6-12 months for extrapulmonary disease

Melioidosis

- Mortality rate
  - untreated: 95%
  - treated but septic: > 50%
  - treated localized disease: 20%
  - overall: 40%

Glanders

Burkholderia mallei

Glanders

- Natural disease of horses, donkeys and mules
- Transmitted to humans via aerosols or dust or contact with infected animals
- 3-6 day incubation

Glanders

- Symptoms - equine
  - initially, slight nasal discharge
  - nasal discharge becomes mucopurulent
  - enlargement of submaxillary lymphnodes
  - cutaneous nodules
    - head, neck, back & legs
  - after 7 days, nodules open & discharge creamy pus
  - nasal mucosa have deep ulcers, esp over nasal septum
  - healing results in characteristic star-shaped scar

Glanders

- Symptoms - human
  - Incubation period - 3 to 6 days
  - Cough, nasal discharge, acute or chromic pneumonia
  - Multiple purulent cutaneous eruptions
  - 95% fatality rate, untreated

Glanders

- Treatment
  - Sulfadiazine, doxycycline, rifampin, trimethoprim-sulfamethoxazole, ciprofloxacin

Clostridium botulinum

Botulism

Botulism: Overview

- Caused by toxin from *Clostridium botulinum*
  - toxin types A, B, E, most commonly associated with human disease
  - most potent lethal substance known to man (lethal dose 1ng/kg**)**

Botulism: Overview

- *C. botulinum* spores found in soil worldwide
- Approximately 100 reported cases/year in the U.S.
  - infant most common (72%)
  - food borne not common
- No person-to-person transmission

Botulism: Clinical Forms

- Foodborne
  - toxin produced anaerobically in improperly processed or canned, low-acid foods contaminated by spores
- Wound
  - toxin produced by organisms contaminating wound
- Infant
  - toxin produced by organisms in intestinal tract
- Inhalation botulism
  - No natural occurrence, developed as BW weapon

Botulism

- There are seven types of *botulinum* toxin:
  - Types A, B, E and in rare cases, F cause disease in humans
  - Types C and D cause disease in birds and mammals
  - Type G, identified in 1970, has yet to be confirmed as a cause of illness in man or animals

Foodborne Botulism

- Infective dose: 0.001 ?g/kg (type A, LD_{50})
- Incubation period: 18 - 36 hr (6hr to 10 d)
- Dry mouth, double vision, droopy eyelids, dilated pupils
- Generalized, progressive descending bilateral muscle weakness & paralysis
- Respiratory failure and death
- Mortality 5-10%, up to 25%

Botulism: Clinical Presentation

- Incubation: 18 to 36 hours (dose dependent)
- Afebrile, alert, oriented; normal sensory exam
  - Early nausea, vomiting, diarrhea
- Cranial Nerve symptoms
  - Ptosis, blurry/double vision, difficulty swallowing/talking, decreased salivation

Botulism: Clinical Presentation

- Motor symptoms (progressive)
  - Bilateral descending flaccid paralysis --> respiratory paralysis
- Death 60% untreated; <5% treated

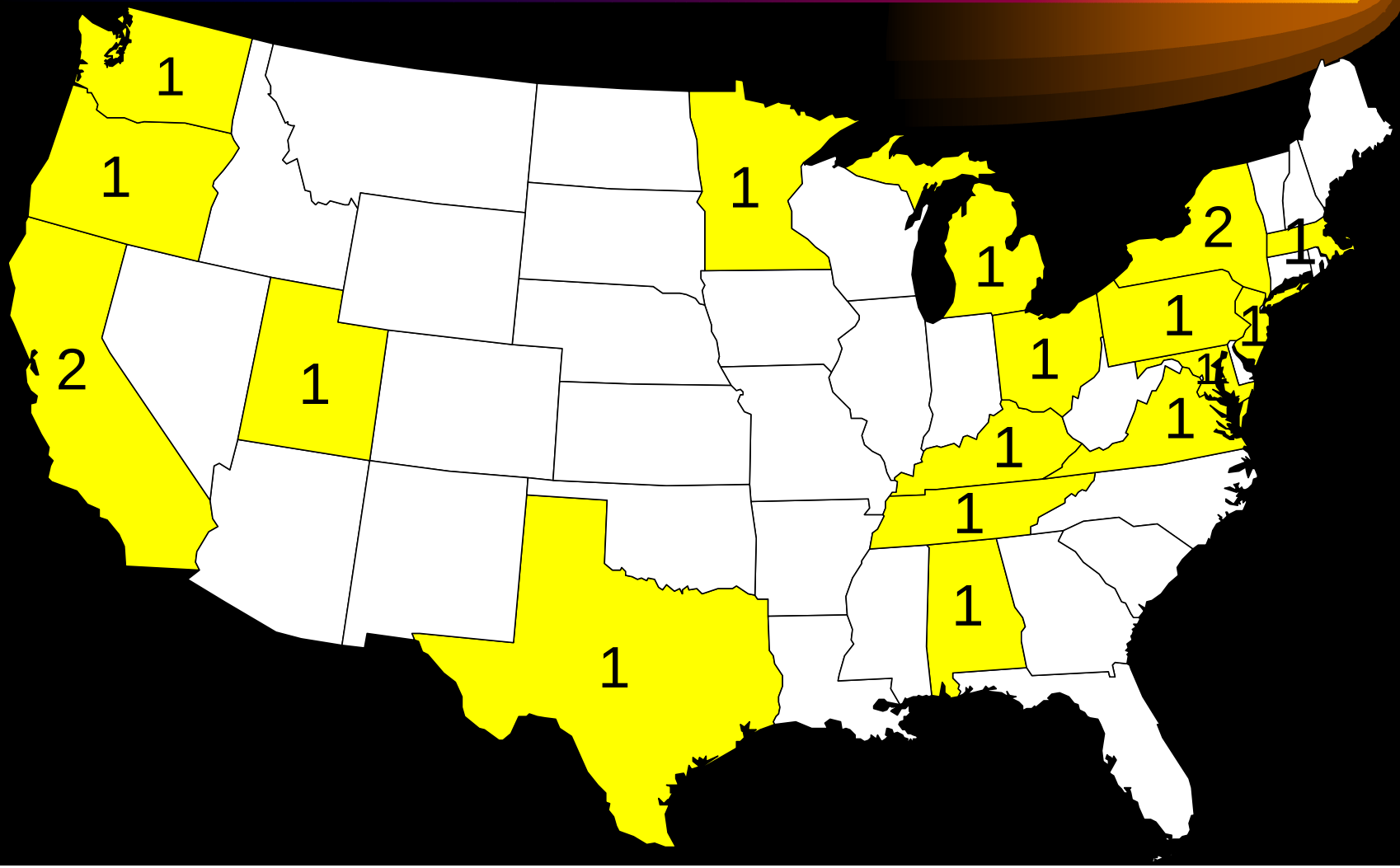
Botulism: Differential Diagnoses

- Neuromuscular disorders
  - Stroke syndrome
  - Myasthenia gravis
  - Guillain-Barre syndrome (Miller-Fisher variant)
  - Tick paralysis
  - Atropine poisoning
  - Paralytic shellfish/puffer fish poisoning
- Diagnosis based on clinical presentation and laboratory confirmation

Botulism: Treatment/Prophylaxis

- Ventilatory assistance and supportive care
- Botulinum antitoxin
  - Trivalent equine product against types A,B, and E currently available from CDC
  - Most effective if given early
- Antibiotics for infant/wound botulism
  - Penicillin
- Recovery may be prolonged with supportive care necessary
- Vaccine investigational, not available

Laboratory Capacity for Botulinum Toxin Testing



Hemorrhagic Fever Viruses

Dengue

Ebola

Rift Valley Fever

Yellow Fever

Lassa

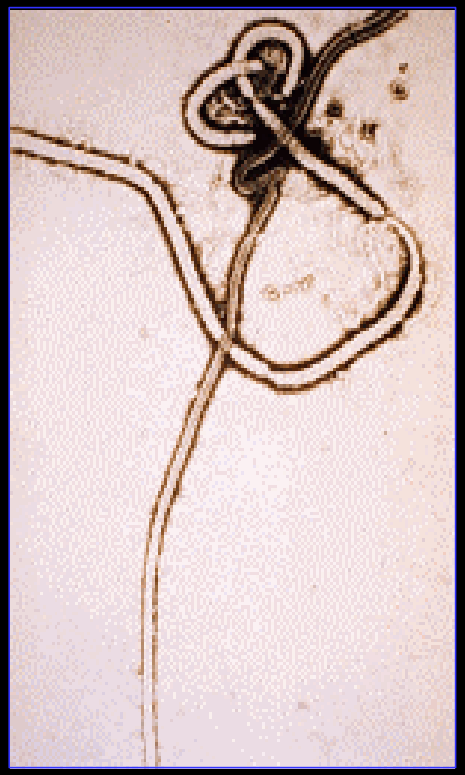
Marburg

Hantaan

Congo/Crimean

Junin/Machupo

Hemorrhagic Fever Viruses



Ebola

Marburg

Viral Hemorrhagic Fevers

- Contagious --- Moderate
- Infective dose --- 1-10 particles
- Incubation period --- 4-21 days
- Duration of illness --- 7-16 days
- Mortality ---variable
- Persistence of organism --- unstable
- Non-endemic in U.S.
- Vaccine efficacy --- no vaccine

VHF: Clinical Presentation

- Usual patient history
  - Foreign travel to endemic or epidemic area
  - Rural environments
  - Nosocomial exposure
  - Contact with arthropod or rodent reservoir
  - Domestic animal blood exposure
- Incubation
  - Typical 5 to 10 days
  - Range 2 to 16 days

VHF: Clinical Presentation

- Symptoms
  - Fever, headache, malaise, dizziness
  - Myalgias
  - Nausea/vomiting
- Initial signs
  - Flushing, conjunctival injection
  - Periorbital edema
  - Positive tourniquet test
  - Hypotension

VHF: Clinical Presentation

- Other signs/symptoms
  - Prostration
  - Pharyngeal, chest, or abdominal pain
  - Mucous membrane bleeding, ecchymosis
  - Shock
- Usually improving or moribund within a week
- Bleeding, CNS involvement, marked SGOT elevation indicate poor prognosis
- Mortality: agent dependent (10 to 90%)

VHF: Clinical Presentation

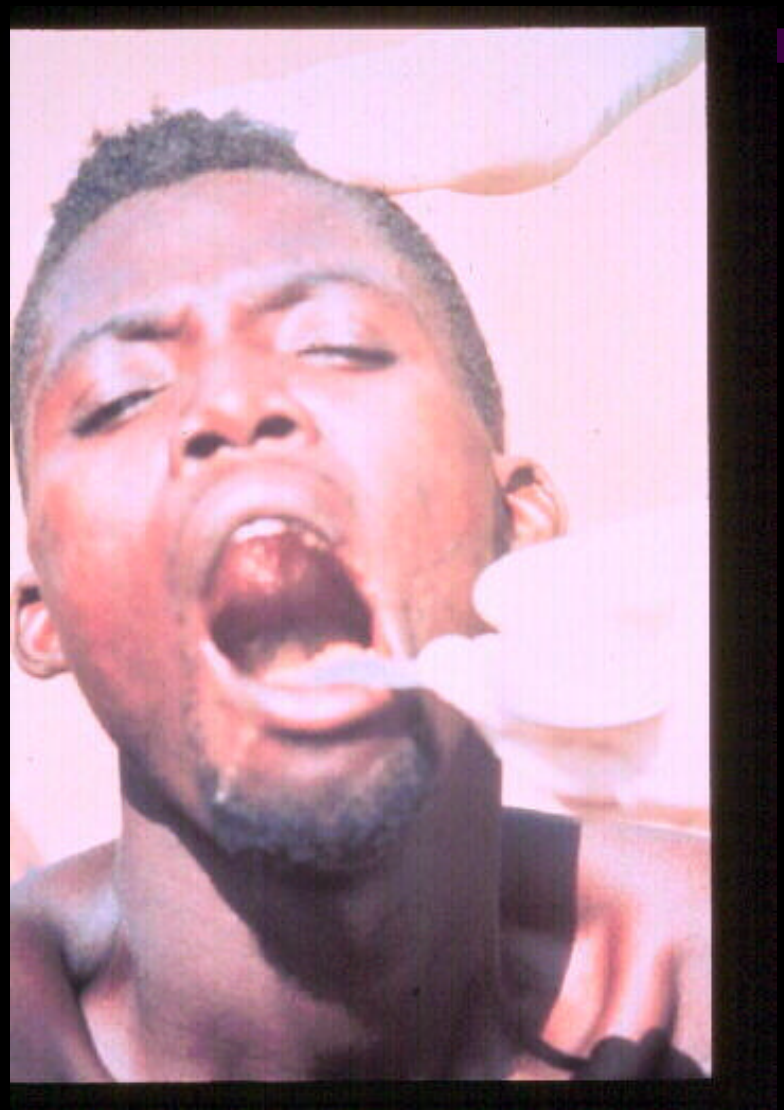
Conjunctival hemorrhage: Argentine HF (Junin virus)

VHF: Clinical Presentation

Oral hemorrhage:
Bolivian HF
(Machupo virus)

VHF: Clinical Presentation

VHF: Clinical Presentation



Palatal hemorrhage: Ebola

VHF: Clinical Presentation

Conjunctival hemorrhage: Lassa fever

VHF: Differential Diagnosis

- Bacterial
  - Typhoid fever, meningococcemia, rickettsioses, leptospirosis
- Protozoa
  - Falciparum malaria
- Other
  - Vasculitis, TTP, Hemolytic Uremic Syndrome (HUS), heat stroke

VHF: Treatment

- Supportive care
- Cautious sedation and analgesia
- Correct coagulopathies as needed
- No antiplatelet drugs or IM injections
- Ribavirin effective for:
  - Arenaviruses
  - Bunyaviridae (CCHF, Hantaan, RVF)

VHF: Patient Isolation

- Single room w/ adjoining anteroom (if available)
  - Handwashing facility with decontamination solution
- Negative air pressure
- Strict barrier precautions including protective eye wear or face shield
- Disposable equipment /sharps in rigid containers with disinfectant then autoclave or incinerate
- All body fluids disinfected

VHF: Contact Management

- Casual contacts - No known risk

VHF: Contact Management

- Close contacts
  - Household, physical, nursing, handle lab specimens
  - Record temp b.i.d. for 3 weeks post-exposure
  - Consider prophylaxis (Ribavirin) if temp > 101ºF or other systemic symptoms within 3 weeks

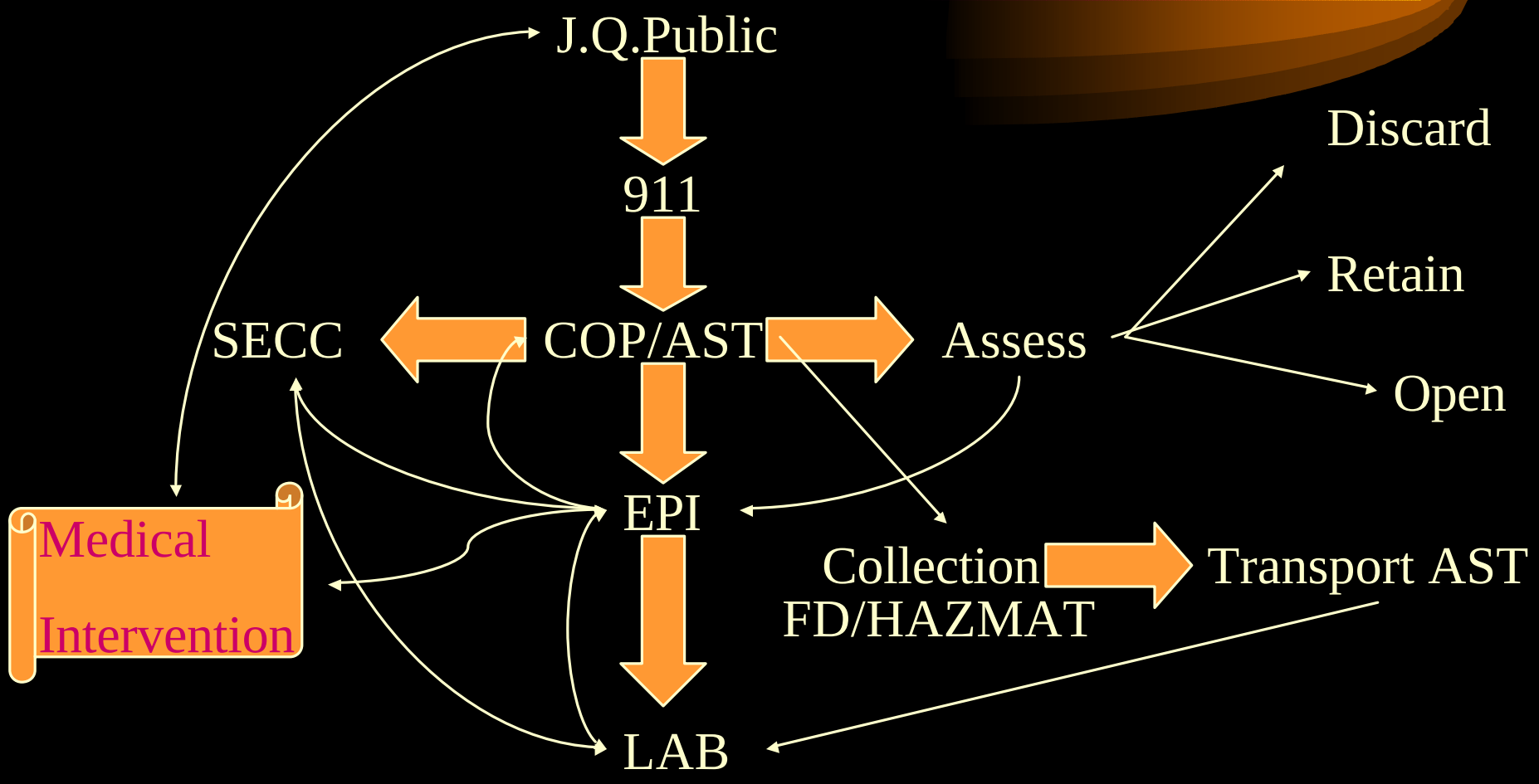
VHF: Contact Management

- High-Risk contacts
  - Mucous membrane, penetrating injury with exposure to body fluids or tissue
  - Consider post-exposure prophylaxis

Biological Terrorism:
What Can Be Done?

Biological Terrorism:

What Should Be Done?



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