RECOGNITION AND MANAGEMENT OF AGENTS OF BIOTHREATS: OVERVIEW

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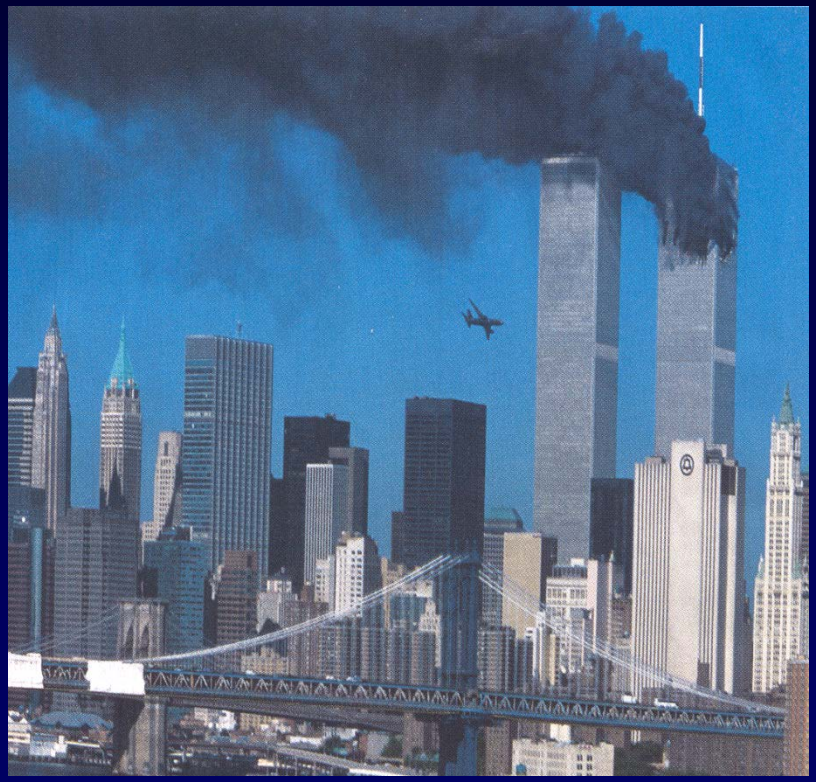
TERRORISM TODAY



New York, September 11, 2001

Time, Special Edition

LECTURE TOPICS

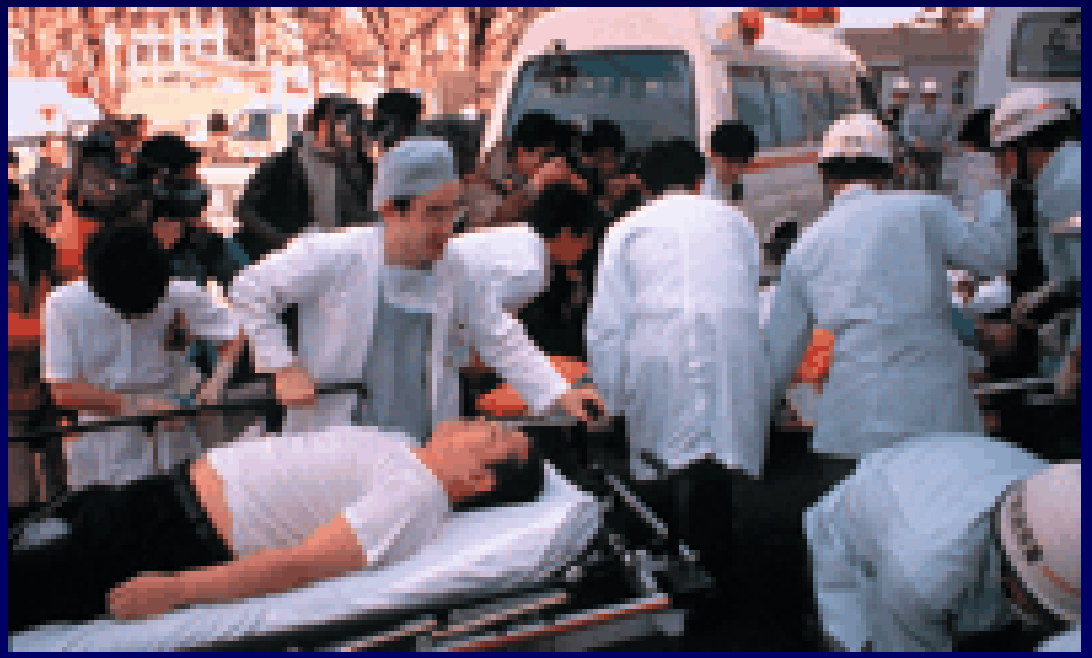
- Major biologic warfare agents
- For most likely BW agents (anthrax, smallpox): Pre-exposure prophylaxis, post-exposure prophylaxis, therapy
- Recognizing a biologic warfare attack
- Review of key agents
  - Variolla (smallpox)
  - *Yersinia pestis* (plague)
  - *Franciscella tularensis* (tularemia)

BIOLOGIC WARFARE: HISTORY

- 300 BC: Greeks pollute wells and drinking water with animal corpses
- 1346, Kaffa: Attacking Tatar force catapulted cadavers of plague victims into city – outbreak of plague led to defeat
- 1763, Fort Pitt, North America: Blankets from smallpox hospital provided to Native Americans – resulted in epidemic of smallpox among tribes in Ohio River valley
- 1932-45, Manchuria: Japanese military physicians infected 10,000 prisoners with biological agents (*B. anthracis, Y. pestis, V. cholerae, Salmonella* spp., *Shigella* spp.) – 11 Chinese cities attacked via food/water contamination, spraying via aircraft

Attack in Northern Iraq by former Government using nerve and mustard gas

Sarin gas attack in Tokyo subway

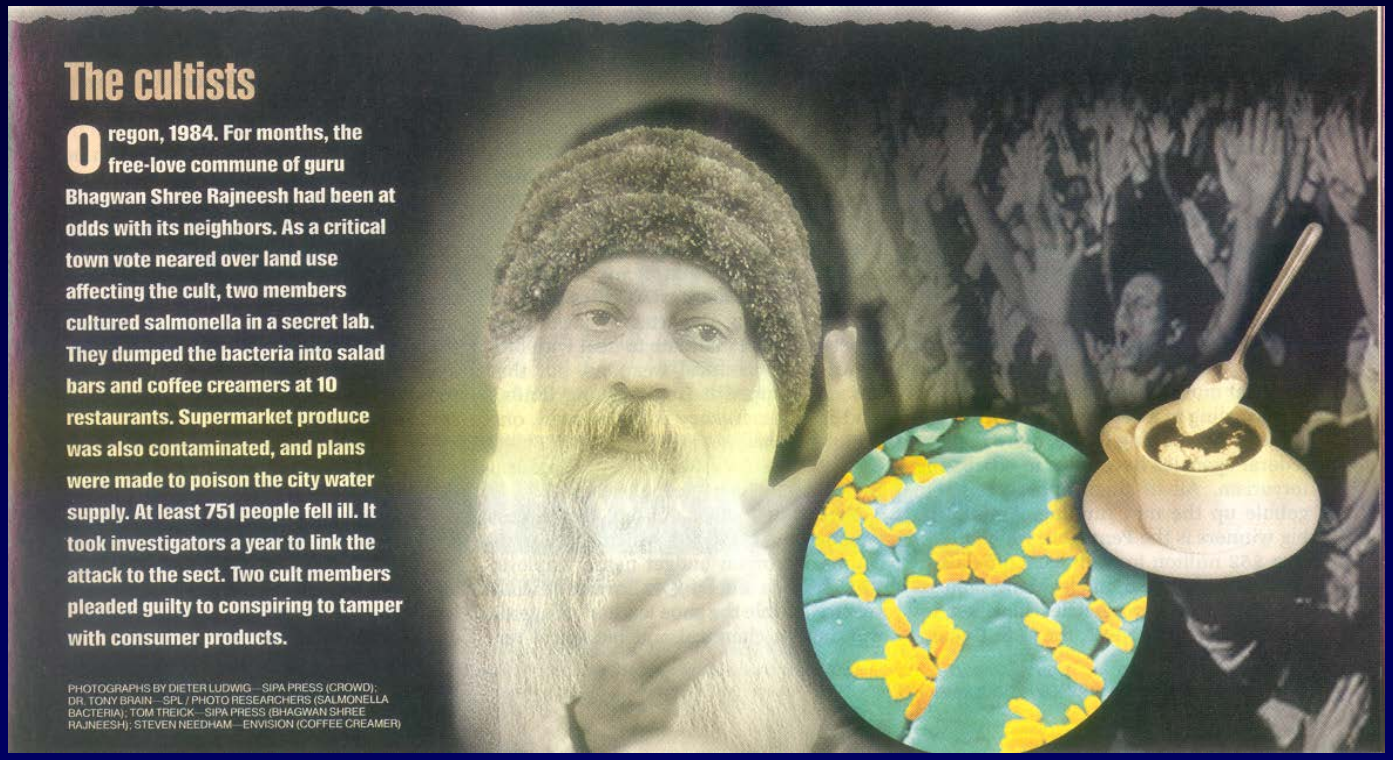


USE OF BIOLOGICAL AGENTS: US

- Site: The Dalles, Oregon, 1984
- Agent: *Salmonella typhimurium*
- Method of transmission: Restaurant salad bars
- Number ill: 751 (45 hospitalized)
- Responsible party: Members of a religious community had deliberately contaminated the salad bars on multiple occasions (goal to incapacitate voters to prevent them from voting and thus influence the outcome of the election)

Torok TJ, et al. JAMA 1997;278:389-395

GURU BHAGWAN SHREE RAJNEESH



USE OF BIOLOGICAL AGENTS: US

- Site: Large medical center, Texas, 1997
- Agent: *Shigella dysenteriae*
- Method of transmission: Ingestion of muffins/doughnuts
- Number ill: 45 (4 hospitalized)
- Responsible party: Disgruntled lab employee? *S. dysenteriae* identical by PFGE from stock culture stored in laboratory

Kolavic S, et al. JAMA 1997;278:396-398.

BIOTERRORISM: WHY NOW?

- SecDef William Cohen, March 1998, Heritage Foundation
  - Our American military superiority presents a paradox…because our potential adversaries know they can't win in a conventional challenge to the U.S. forces, they're much more likely to try unconventional or asymmetrical methods, such as biologic or chemical weapons
- Richard Betts, Council on Foreign Relations
  - Nuclear arms have great killing capacity but are hard to get; chemical weapons are easy to get but lack such killing capacity; biological agents have both qualities.

TRENDS FAVORING BIOLOGICAL WEAPONS

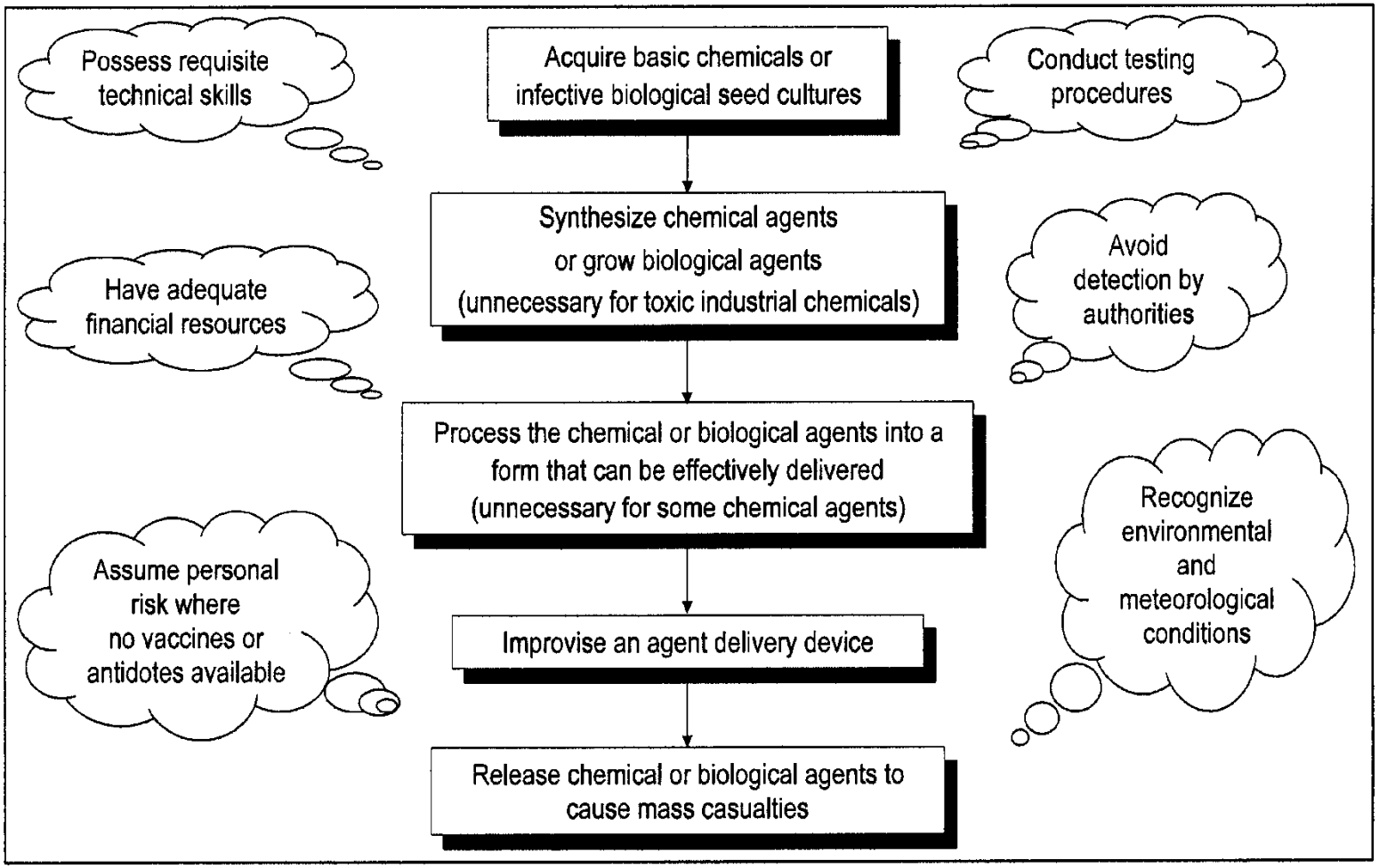
- Biological weapons have an unmatched destructive potential
- Technology for dispersing biologic agents is becoming more sophisticated
- The lag time between infection and appearance of symptoms generally is longer for biological agents than with chemical exposures
- Lethal biological agents can be produced easily and cheaply
- Biological agents are easier to produce clandestinely than are either chemical or nuclear weapons

Heritage Foundation

TRENDS FAVORING BIOLOGICAL WEAPONS

- Global transportation links facilitate the potential for biological terrorist strikes to inflict mass casualties
- Urbanization provides terrorists with a wide array of lucrative targets
- The Diaspora of Russian scientists has increased the danger that rogue states or terrorist groups will accrue the biological expertise needed to mount catastrophic terrorist attacks
- The emergence of global, real-time media coverage increases the likelihood that a major biological incident will induce panic

Figure 1: Stages and Obstacles for Chemical and Biological Terrorism



Source: GAO, on the basis of analysis of technical data and discussions with chemical and biological warfare experts.

CENTERS FOR DISEASE CONTROL BIOTERRORIST AGENTS: CATEGORY A

- Easily disseminated or transmitted person-to-person
- High mortality, with potential for major public health impact
- Might cause public panic and social disruption
- Require special action for public health preparedness .
- Viruses: Variola major (smallpox), filoviruses (e.g., Ebola, Marburg), arenaviruses (e.g., Lassa, Machupo)
- Bacteria: *Bacillus anthracis* (anthrax), *Yersinia pestis* (plague), *Francisella tularensis* (tularemia)
- Toxins: *Clostridium botulinum* toxin (botulism)

http://emergency.cdc.gov/agent/agentlist-category.asp

CLASS A AGENTS OF BIOTERRORISM

Disease	Agent	Incubation period	Transmission	Clinical symptoms and signs	Treatment
Anthrax	*Bacillus anthracis*	2–4 d	Direct contact, inhalation, or ingestion	Cutaneous eschar, fever, mediastinitis with widened mediastinum on chest radiograph	Doxycycline or ciprofloxacin plus one or two other agents (see text)
Smallpox	Smallpox virus	10–12 d	Airborne droplets and direct contact	Fever followed by vesicular rash in centrifugal distribution	Supportive treatment, consider early vaccination
Hemorrhagic fever viruses	Four families of viruses (see text)	2–21 d	Airborne droplets, bite of infected carrier, or direct contact	Virus dependent (see Table 2); fever, petechiae, bleeding, disseminated intravascular coagulation	Consider ribavirin
Plague	*Yersinia pestis*	2–4 d	Flea bite (most common), airborne droplet, and direct contact	Buboes, fever, pneumonia, acute respiratory distress syndrome, sepsis	Streptomycin or gentamicin
Botulism	*Clostridium botulinum*	12–36 h	Airborne droplet, ingestion, or contaminated wound	Descending paralysis with diplopia, dysphagia, dysarthria, and dysphonia	Supportive treatment and botulinum antitoxin
Tularemia	*Francisella tularensis*	3–5 d	Arthropod bite, airborne droplets, or ingestion	Fever, dry cough, pneumonia, pulse-temperature dissociation	Streptomycin, gentamicin, ciprofloxacin, doxycycline

Kman NE, Nelson RN. Emerg Med Clin NA 2008;26:517-547

HEMORRHAGIC FEVER VIRUSES

Virus	Family	Key clinical features	Vector	Person-to-person transmission	Incubation period (d)	Mortality (%)	Treatment
Ebola	Filoviridae	Sudden onset fever, weakness, muscle pain, headache, sore throat and maculopapular rash by day 5 Bleeding and disseminated intravascular coagulation common	Unknown (possibly bat)	Yes	2–21	50–90	Supportive
Marburg	Filoviridae	High fever, myalgia Nonpruritic maculopapular rash may develop Bleeding and disseminated intravascular coagulation common	Unknown (probably bat)	Yes	2–14	23–70	Supportive
Lassa fever	Arenaviridae	Early gradual fever, nausea, abdominal pain, pharyngitis, cough, conjunctivitis, cervical lymphadenopathy Late pleural and pericardial effusions Hemorrhage less common	Rodent	Yes	5–16	15–20	Ribavirin, supportive
New World arenaviruses	Arenaviridae	Gradual fever, myalgia, nausea, abdominal pain, conjunctivitis, facial flushing and generalized lymphadenopathy Possible petechiae, bleeding, and central nervous system dysfunction	Rodent	Yes	7–14	15–30	Ribavirin, supportive
Rift Valley fever	Bunyaviridae	Fever, retro-orbital headache, photophobia, jaundice, and retinitis (up to 10%) Hemorrhagic fever or encephalitis rare (>1%)	Mosquito	No	2–6	<1	Ribavirin, supportive
Yellow fever	Flaviviridae	Fever, myalgia, facial flushing, and conjunctival injection Patients either recover or experience fever, bradycardia, jaundice, renal failure, and hemorrhagic complications after short remission	Mosquito	No	3–6	20	Supportive

CENTERS FOR DISEASE CONTROL BIOTERRORIST AGENTS: CATEGORY B

- Moderately easy to disseminate
- Moderate morbidity and low mortality
- Require improved diagnostic capacity & enhanced surveillance .
- Viruses: Alphaviruses (VEE, EEE, WEE)
- Bacteria: *Coxiella burnetii* (Q fever), *Brucella spp*. (brucellosis), *Burkholderia mallei* (glanders) , *B. pseudomallei* (melioidosis), *Rickettsia prowazekii* (typhus fever), Chlamydia psittaci (psittacosis)
- Toxins: *Rinus communis* (caster beans) ricin toxin, *Clostridium perfringens* episolon toxin, *Staphylococcus* enterotoxin B
- Food/waterborne pathogens: *Salmonella spp*., *Vibrio cholerae*, *Shigella dyseneriae*, *E. coli* O157:H7, *Cryptosporidium parvum*, etc.

CENTERS FOR DISEASE CONTROL BIOTERRORIST AGENTS: CATEGORY C

- Availability
- Ease of production and dissemination
- Potential for high morbidity and mortality and major public health impact
- Emerging agents such as Nipah virus and hantavirus

CDC FACT SHEETS AVAILABILITY

- Anthrax
- Botulism
- Brucellosis
- Plague
- Smallpox
- Tularemia
- Viral hemorrhagic fevers

http://emergency.cdc.gov/bioterrorism/factsheets.asp

CHARACTERISTICS* OF PRIORITY AGENTS

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

* Priority agents may exhibit all or some of the above characteristics

Sample Biological Agent Ratings

	Public Health Impact		Dissemination Potential		Special	Pubic
Disease	Morbidity	Mortality	Stable/Produce/Distribute	Transmissable	Preparedness	Perception
Smallpox	+	++	++	+++	+++	+++
Inhalational anthrax	++	+++	+++	-	+++	+++
Pneumonic plague	++	+++	++	++	+++	+++
Tularemia	++	++	++	-	+++	++
Botulism	++	+++	++	-	+++	++
VHF	++	+++	+	+	+++	+++
Glanders	++	+++	++	-	++	+
VE	++	+	++	-	++	+
Q fever	+	+	++	-	++	+
Brucellosis	+	+	++	-	++	+
Toxins	++	++	+	-	++	+
HPS	++	++	+	++	-	+
Nipah encephalitis	++	++	-	-	+	+

CHEMICAL AGENTS

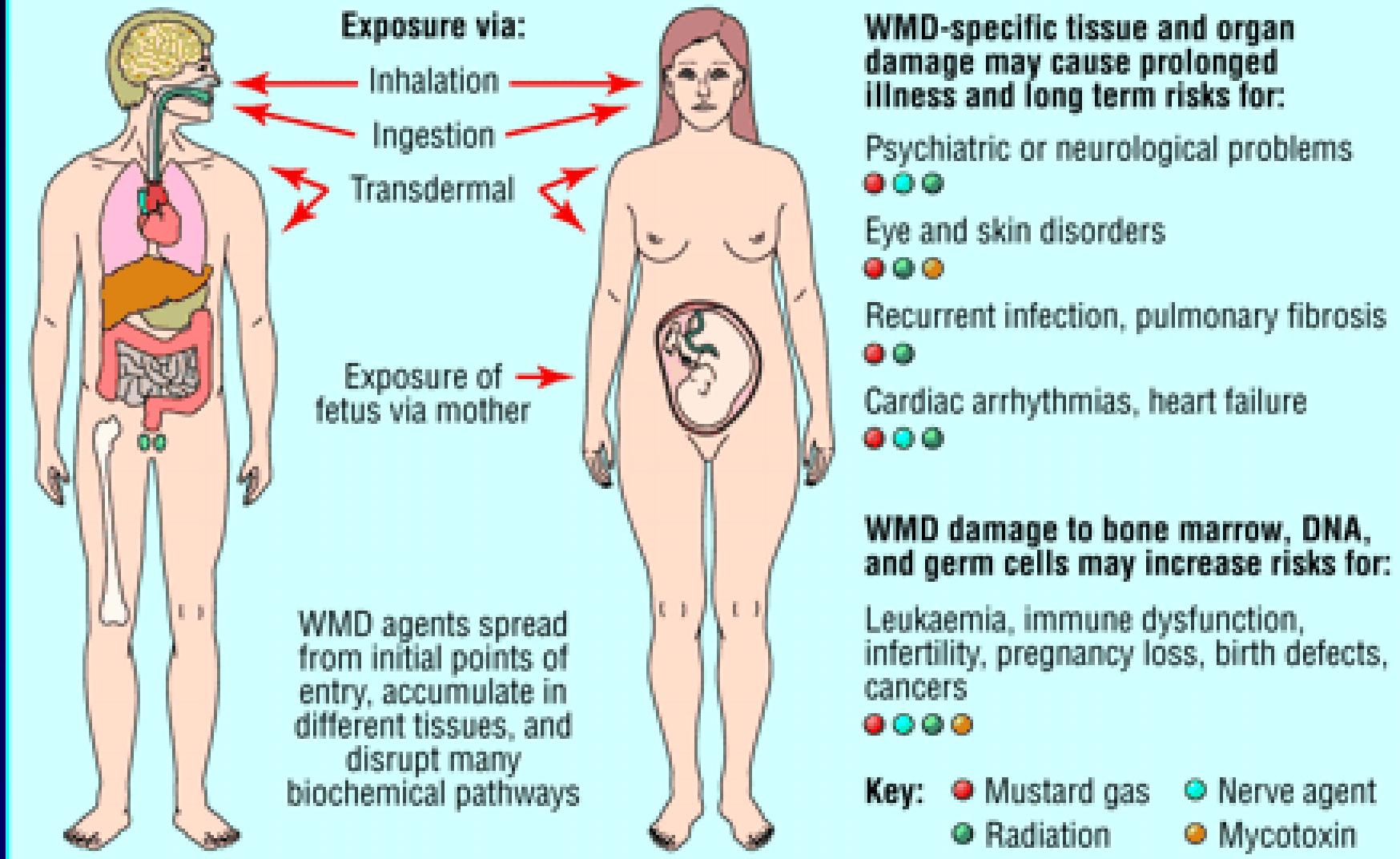
- Biotoxins
  - Abrin
  - Brevetoxin
  - Colchicine
  - Digitalis
  - Nicotine
  - Ricin
  - Saxitoxin
  - Tetrodotoxin
  - Trichotecene
- Blood agents
  - Arsine (SA)
  - Carbon monoxide
  - Cyanogen chloride (CK)
  - Hydrogen cyanide (AC)
  - Potassium cyanide (KCN)
  - Sodium cyanide (NaCN)
  - Sodium monfluoracetate

CHEMICAL AGENTS

- Blister agents/vesicants
  - Mustards
  - Phosgene (CX)
- Caustics (acids)
  - Hydrofluoric acid
- Incapacitating agents
  - BZ
  - Fentalyls & other opioids
- Choking/lung agents
  - Ammonia
  - Bromine, Chlorine
  - Hydrogen chloride
  - Methyl bromide
  - Methyl isocynante
  - Osmium tetroxide
  - Phosgene, Disphosgene
  - Phosphine, Phosphorus
  - Sulfuryl fluoride

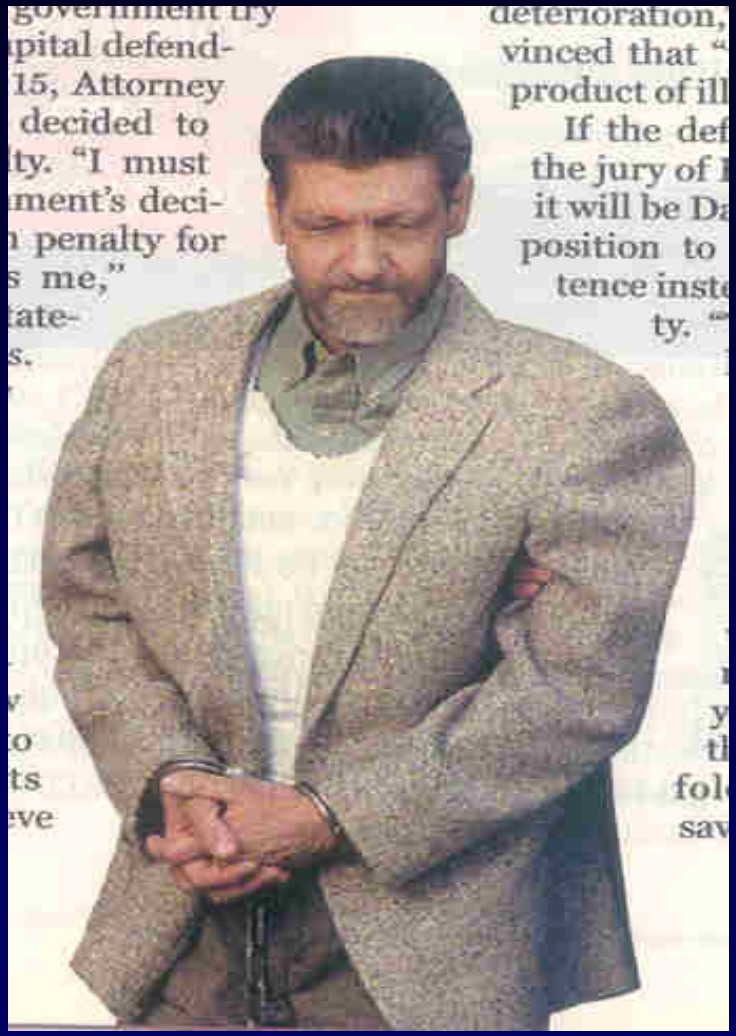
CHEMICAL AGENTS

- Riot control agents
  - Bromobenzylcyanide
  - Chloracetophenone
  - Chlorobenzyl-idenemalononitrile
  - Debenzoxazepine
- Nerve agents
  - G agents
  - Sarin (GB)
  - Soman (GD)
  - Tabun (GA)
  - VX
- Metals
  - Arsenic
  - Barium
  - Mercury
  - Thallium


Exposure via:
Inhalation
Ingestion
Transdermal
Exposure of fetus via mother
WMD agents spread from initial points of entry, accumulate in different tissues, and disrupt many biochemical pathways
WMD-specific tissue and organ damage may cause prolonged illness and long term risks for:
Psychiatric or neurological problems
Eye and skin disorders
Recurrent infection, pulmonary fibrosis
Cardiac arrhythmias, heart failure
WMD damage to bone marrow, DNA, and germ cells may increase risks for:
Leukaemia, immune dysfunction, infertility, pregnancy loss, birth defects, cancers
Key:
Mustard gas
Nerve agent
Radiation
Mycotoxin

SOURCES OF BIOTERRORISM

- Biological warfare
- State sponsored terrorism
- International terrorist groups
- National cults
- The deranged “loner”



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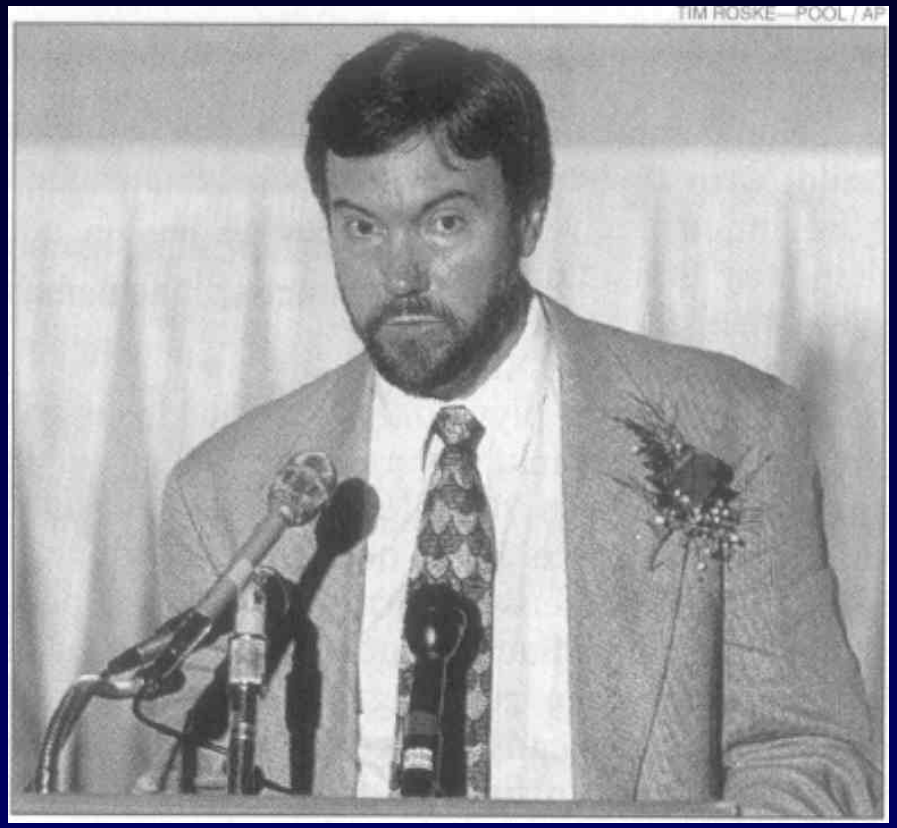

Kaczynski's mailbox near Lincoln, Mont. Says one trial expert: "He was never able to have any social interaction except through the mail."

ELAINE THOMPSON—AP

SADDAM'S GAME PLAN
AFFIRMATIVE ACTION'S FATE

U.S. News & WORLD REPORT

NOVEMBER 17, 1997/$2.95

The Next Unabomber

As accused murderer Theodore Kaczynski goes on trial, the FBI is investigating more than 50 cases of terrorists suspected of plotting attacks here. Their tools are easy-to-make chemical and biological weapons

EXCLUSIVE
DAVID KACZYNSKI'S PLEA FOR HIS BROTHER'S LIFE

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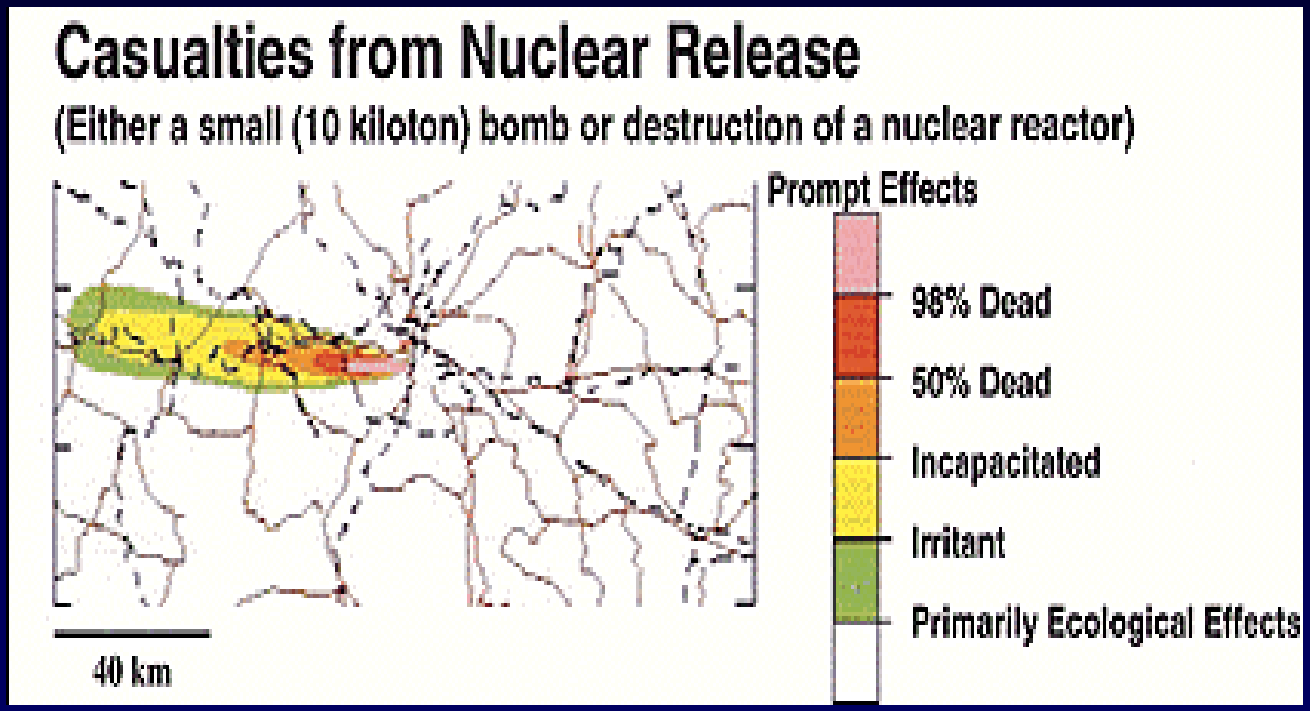
BIOTERRORISM: IMPACT

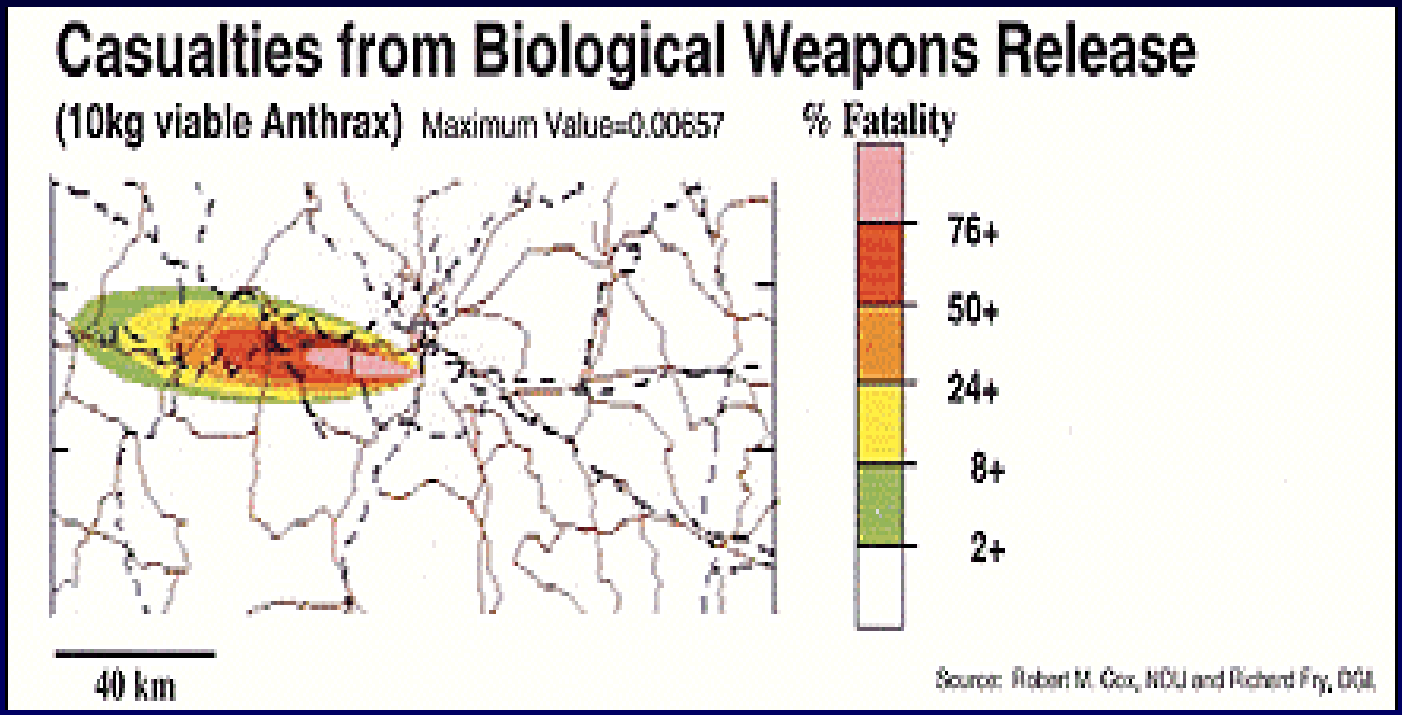
- Direct infection: Mortality, morbidity
- Indirect infection: Person-to-person transmission, fomite transmission
- Environmental impact: Environmental survival, animal infection
- Other: Social, political, economic

EFFECTS OF A NUCLEAR WEAPONS RELEASE



Siegrist, Emerging Infectious Diseases 1999

EFFECTS OF A BIOLOGICAL WEAPONS RELEASE



Siegrist, Emerging Infectious Diseases 1999

BIOLOGICAL WARFARE: IMPACT

[release of 50 kg agent by aircraft along a 2 km line upwind of a population center of 500,000 – Christopher et al., JAMA 278;1997:412]

Agent	Downwind reach, km	No. dead	No. incapacitated
Rift Valley fever	1	400	35,000
Tick-borne encephalitis	1	9,500	35,000
Typhus	5	19,000	85,000
Brucellosis	10	500	125,000
Q fever	>20	150	125,000
Tularemia	>20	30,000	125,000
Anthrax	>20	95,000	125,000

CHARACTERISTICS OF BIOWARFARE

- Potential for massive numbers of casualties
- Ability to produce lengthy illnesses requiring prolonged and intensive care
- Ability of certain agents to spread via contagion
- Paucity of adequate detection systems
- Presence of an incubation period, enabling victims to disperse widely
- Ability to produce non-specific symptoms, complicating diagnosis
- Ability to mimic endemic infectious diseases, further complicating diagnosis

US Army, Biologic Casualties Handbook, 2001

STEPS IN MANAGEMENT

1. Maintain an index of suspicion
2. Protect thyself
3. Assess the patient
4. Decontaminate as appropriate
5. Establish a diagnosis
6. Render prompt therapy
7. Practice good infection control
8. Alert the proper authorities
9. Assist in the epidemiologic investigation
10. Maintain proficiency and spread the gospel

US Army, Biologic Casualties Handbook, 2001

INFECTION CONTROL ISSUES FOR SELECTED AGENTS OF BIOTERRORISM

Disease	Incubation period (days)	Person-to-person transmission	Infection control precautions
Inhalational anthrax (see Chapter 185)	2–43*	No	Standard
Botulism (see Chapter 25)	12–72 hours	No	Standard
Primary pneumonic plague (see Chapter 176)	1–6	Yes	Droplet
Smallpox (see Chapter 151)	7–17	Yes	Contact and airborne
Tularemia (see Chapter 177)	1–14	No	Standard
Viral hemorrhagic fevers (see Chapter 183)	2–21	Yes	Contact and airborne
Viral encephalitides (see Chapter 23)	2–14	No	Standard
Q fever (see Chapter 235)	2–14	No	Standard
Brucellosis (see Chapter 180)	5–60	No	Standard
Glanders	10–14	No	Standard

* Based on limited data from human outbreaks; experimental animal data support clinical latency periods of up to 100 days

BW AGENT PROPHYLAXIS AND TREATMENT

Disease	Vaccine Efficacy*	PEP	Treatment
Anthrax**^	Effective, 1,000 LD_{50} monkeys	Antibiotics	Antibiotics
Smallpox	Effective, high dose primates	Vaccine, VIG	Cidofovir?
Plague**^	Ineffective, 118 LD_{50} monkeys	Antibiotics	Antibiotics
Q fever#	94%, 3500 LD_{50} guinea	Antibiotics	Antibiotics
Tularemia#	80%,1-10 LD_{50}	Antibiotics	Antibiotics
VHF+	No vaccine	None	Ribavirin@

VHF-viral hemorrhagic fevers, PEP-postexposure prophylaxis

*Aerosol exposure; **Pneumonic form; ^FDA approved vaccine (not available); #IND

+ IND BHF, RVF; @ CCHF, Lassa

US Army, Biological Casualties Handbook, 2001

FOMITE ACQUISITION

- Agents acquired from contaminated clothes
  - Variola major (smallpox)
  - *Bacillus anthracis* (anthrax)
  - *Coxiella burnetii* (Q fever)
  - *Yersinia pestis* (plague)
- Management
  - Remove clothing, have patient shower
  - Place contaminated clothes in impervious bag, wear PPE
  - Decontaminate environmental surfaces with EPA approved germicidal agent or 0.5% bleach (1:10 dilution)

Bioterrorism Agents: Laboratory Risk

Agent	BSL	Laboratory Risk
B. anthracis	2	low
Y. pestis	2	medium
F. tularensis	2/3	high
Brucella spp.	2/3	high
Botulinum toxin	2	medium
Chlaymdia pittaci	2/3	medium
Smallpox	4	high
Viral Hemorrhagic fever	4	high

http://www.cdc.gov/od/biosfty/bmbl/BMBL_5th_Edition.pdf

DETECTION OF OUTBREAKS

- Epidemiologic clues
- Medical clues
- Syndromic surveillance
- Other
  - Intelligence reports
  - Claims of release
  - Discovery of munitions or tampering
  - Increased numbers of pharmacy orders for antibiotics
  - Increased number of 911 calls

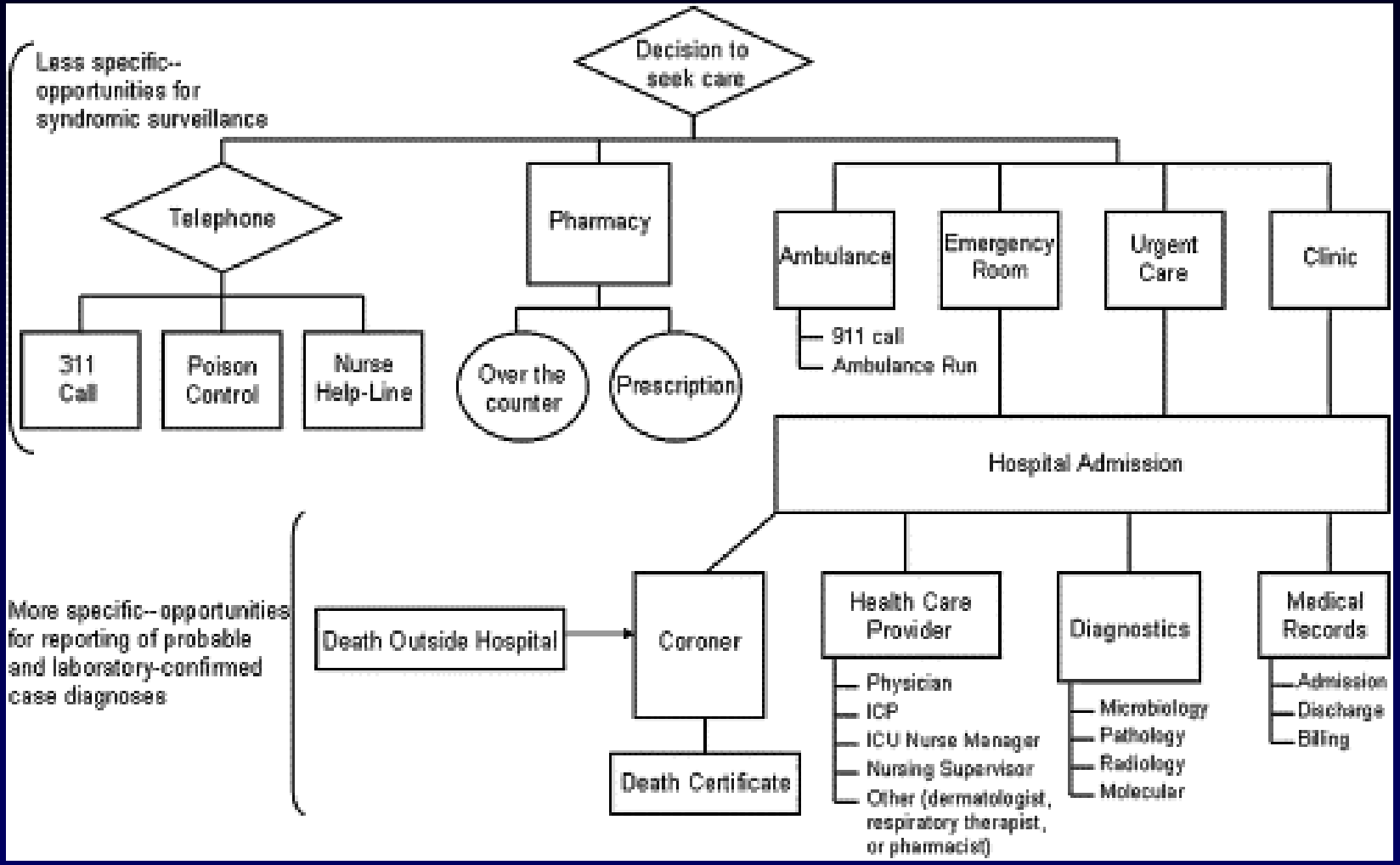
ID Clinics NA 2006;20:179-211

DETECTION OF BT OUTBREAKS: EPIDEMIOLOGIC CLUES

- A rapidly increasing disease incidence
- Unusual clustering of disease for the geographic area
- Disease occurrence outside of the normal transmission season
- Simultaneous outbreaks of different infectious diseases
- Disease outbreak in humans after recognition of disease in animals
- Unexplained number dead animals or birds
- Disease requiring for transmission a vector previously not seen in the area
- Rapid emergence of genetically identical pathogens from different geographic areas

DETECTION OF BT OUTBREAKS: MEDICAL CLUES

- Unusual route of infection
- Unusual age distribution or clinical presentation of common disease
- More severe disease and higher fatality rate than expected
- Unusual variants of organisms
- Unusual antimicrobial susceptibility patterns
- Any patient presenting with a disease that is relatively uncommon and has bioterrorism potential



An unusual increase in the number of people seeking care, esp. with fever, respiratory, or gastrointestinal symptoms

DEVELOPING A BT PLAN

- Recognition of infection
- Incident command system
- Communication with public health
- Triage of patients
- Decontamination of patients
- Maintaining clean and contaminated areas
- Proper patient isolation
- Post-exposure prophylaxis
- Treatment
- Control/screening of visitors
- Immunization of HCWs
- Internal communications
- Availability of diagnostic tests
- Availability of PPE

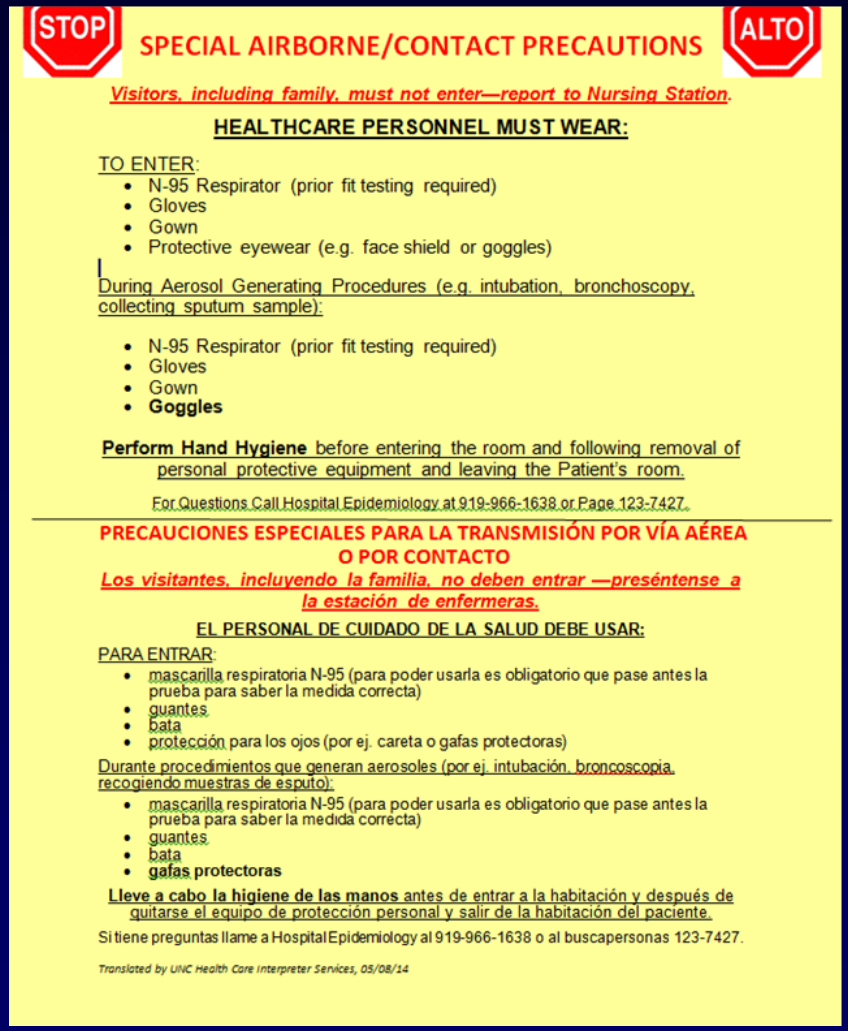
DEVELOPING A BT PLAN

- Have a written BT preparedness plan
- Assess the feasibility and viability of the plan
- Disseminate the plan and ensure familiarity by all key stakeholders
- Use elements of daily practice as the backbone of the plan
- Incorporate internal mechanisms for intensified surveillance
- Ensure appropriate internal and external mechanisms of communication
- Test the plan periodically through drills
- Incorporate flexibility and build redundancy for key components
- Address logistics involving surge capacity
- Emphasize community preparedness

Shaikh Z. ID Clinics NA 2006;20:433-453

SPECIAL AIRBORNE/CONTACT PRECAUTIONS

- New outpatient clinic constructed to see patients with highly contagious diseases
  - Direct entry from outside
  - All rooms have airborne isolation
- Representative pathogens
  - Monkeypox
  - SARS Co-V
  - Smallpox
  - Ebola



STOP

SPECIAL AIRBORNE/CONTACT PRECAUTIONS

ALTO

Visitors, including family, must not enter—report to Nursing Station.

HEALTHCARE PERSONNEL MUST WEAR:

TO ENTER:

- N-95 Respirator (prior fit testing required)
- Gloves
- Gown
- Protective eyewear (e.g. face shield or goggles)

During Aerosol Generating Procedures (e.g. intubation, bronchoscopy, collecting sputum sample):

- N-95 Respirator (prior fit testing required)
- Gloves
- Gown
- **Goggles**

Perform Hand Hygiene before entering the room and following removal of personal protective equipment and leaving the Patient's room.

For Questions Call Hospital Epidemiology at 919-966-1638 or Page 123-7427.

PRECAUCIONES ESPECIALES PARA LA TRANSMISIÓN POR VÍA AÉREA O POR CONTACTO

Los visitantes, incluyendo la familia, no deben entrar —preséntense a la estación de enfermeras.

EL PERSONAL DE CUIDADO DE LA SALUD DEBE USAR:

PARA ENTRAR:

- mascarilla respiratoria N-95 (para poder usarla es obligatorio que pase antes la prueba para saber la medida correcta)
- guantes
- bata
- protección para los ojos (por ej. careta o gafas protectoras)

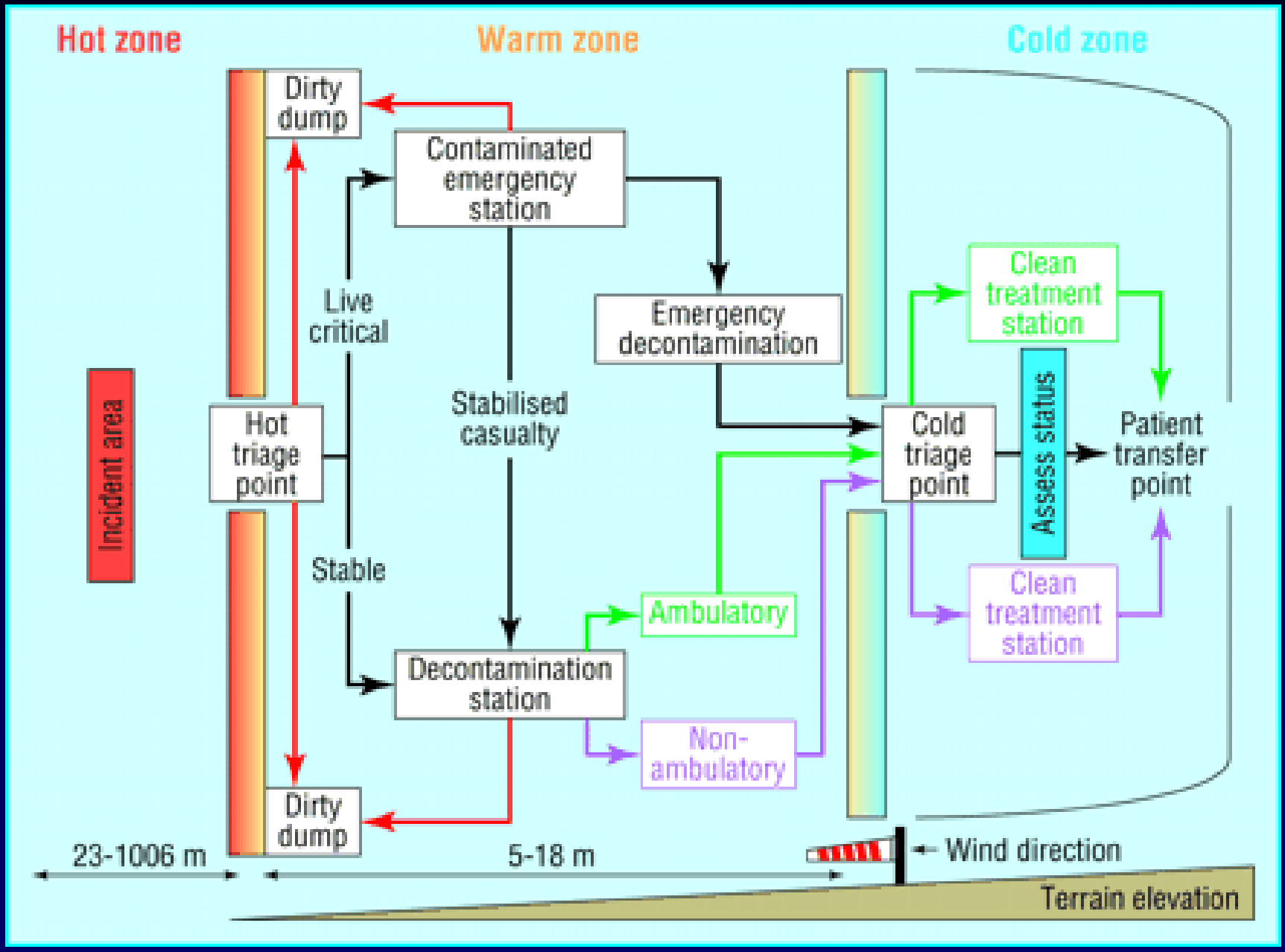
Durante procedimientos que generan aerosoles (por ej. intubación, broncoscopia, recogiendo muestras de esputo):

- mascarilla respiratoria N-95 (para poder usarla es obligatorio que pase antes la prueba para saber la medida correcta)
- guantes
- bata
- **gafas protectoras**

Lleve a cabo la higiene de las manos antes de entrar a la habitación y después de quitarse el equipo de protección personal y salir de la habitación del paciente.

Si tiene preguntas llame a Hospital Epidemiology al 919-966-1638 o al buscapersonas 123-7427.

Translated by UNC Health Care Interpreter Services, 05/08/14



Gosden C, Gardner D. BMJ 2005;331:397

Figure 16-6 A high-efficiency particulate air (HEPA)–filtered mobile isolation device designed for transport of patients with contagious diseases.

(Demistifier, Peace Medical Inc., Orange, NJ.)

WE HAVE A DUTY TO BE PREPARED

2011, NYC, Attack by hijacked planes

1995, Tokyo, Attack subways with Sarin
by Aum Shinriko cult

SUPPLEMENTAL SLIDES

Anthrax, Smallpox, Plague, Tularemia

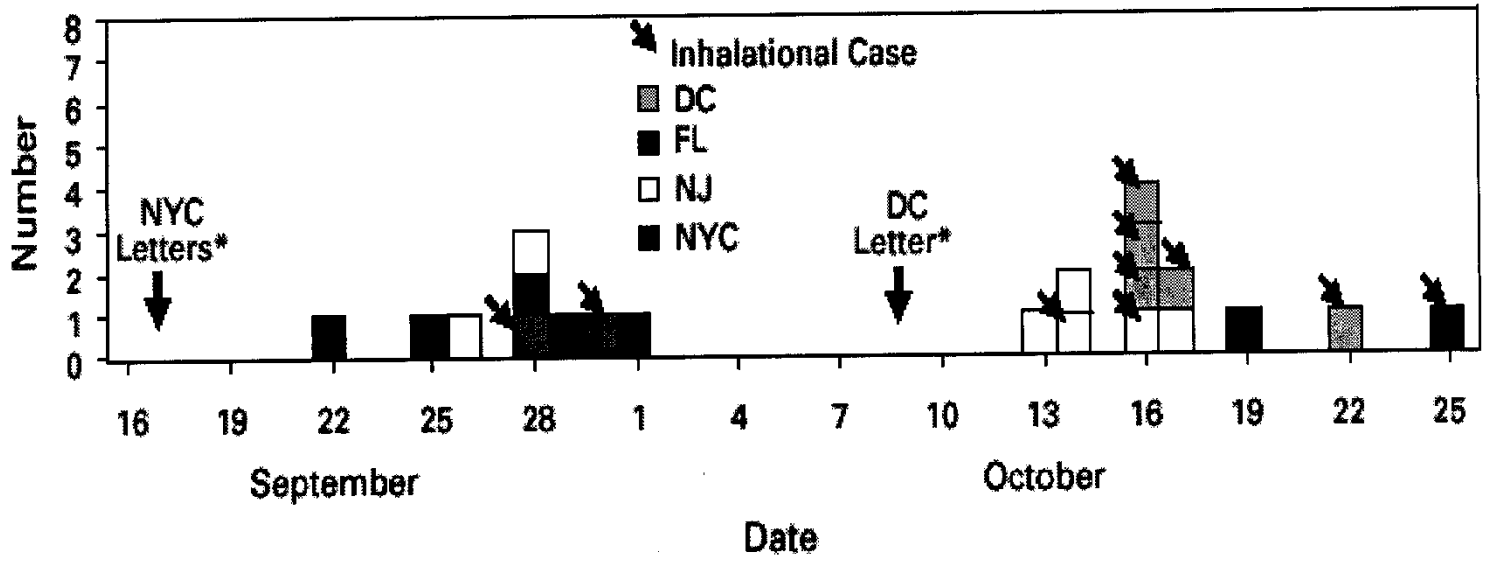
ANTHRAX IN THE US, 2001

- Locations: FL, NY, DC, NJ, CT, VA
- Mechanism: Via the mail (4 letters positive)
- Infections: 22 cases
  - Cutaneous anthrax: 11 (fatality rate = 0)
  - Inhalation anthrax: 11 (fatality rate = 45%)
- Prophylaxis
  - Initiated: ~32,000
  - 60 day course recommended: ~5,000

EID 2002;8:1019

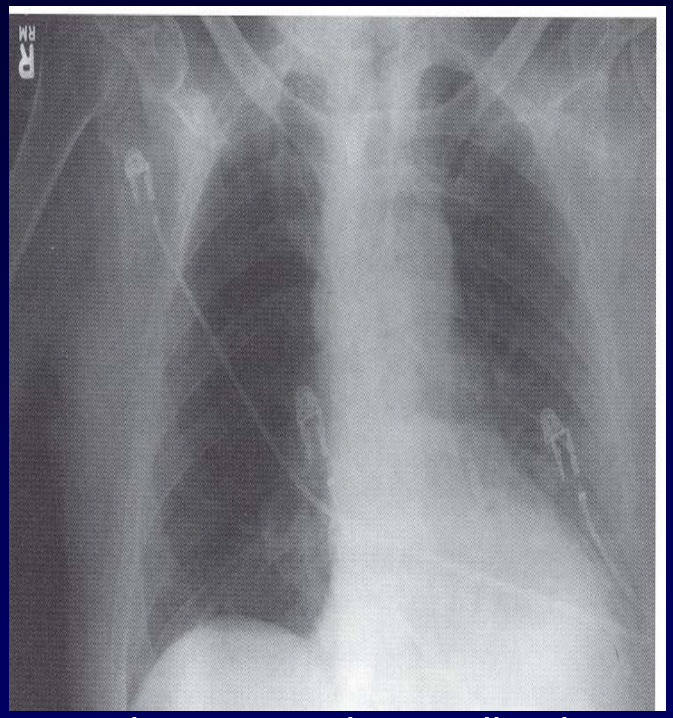
ANTHRAX CASES, US

FIGURE 1. Number of bioterrorism-related anthrax cases, by date of onset and work location — District of Columbia (DC), Florida (FL), New Jersey (NJ), and New York City (NYC), September 16–October 25, 2001

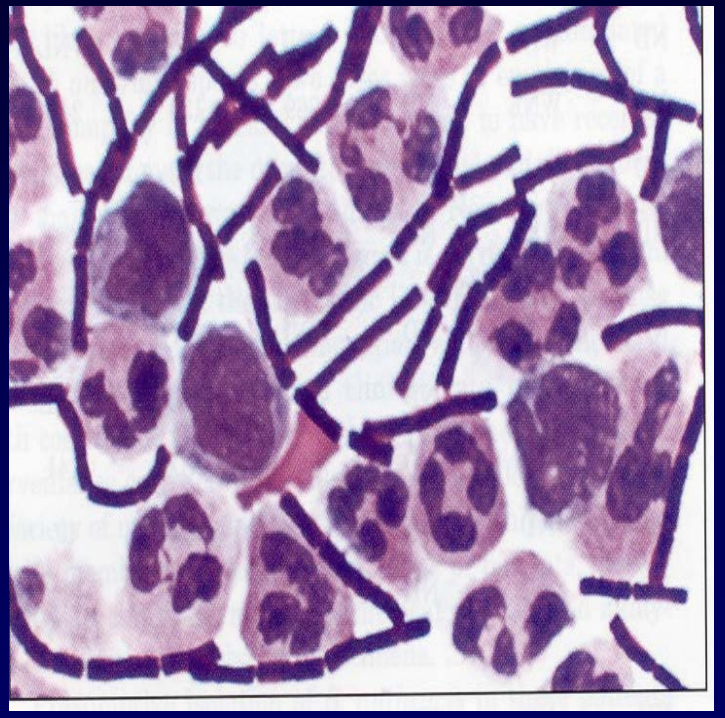


CDC. MMWR 2001;50:941

INHALATION ANTHRAX, US: CASE 1



Prominent superior mediastinum,
?small left pleural effusion

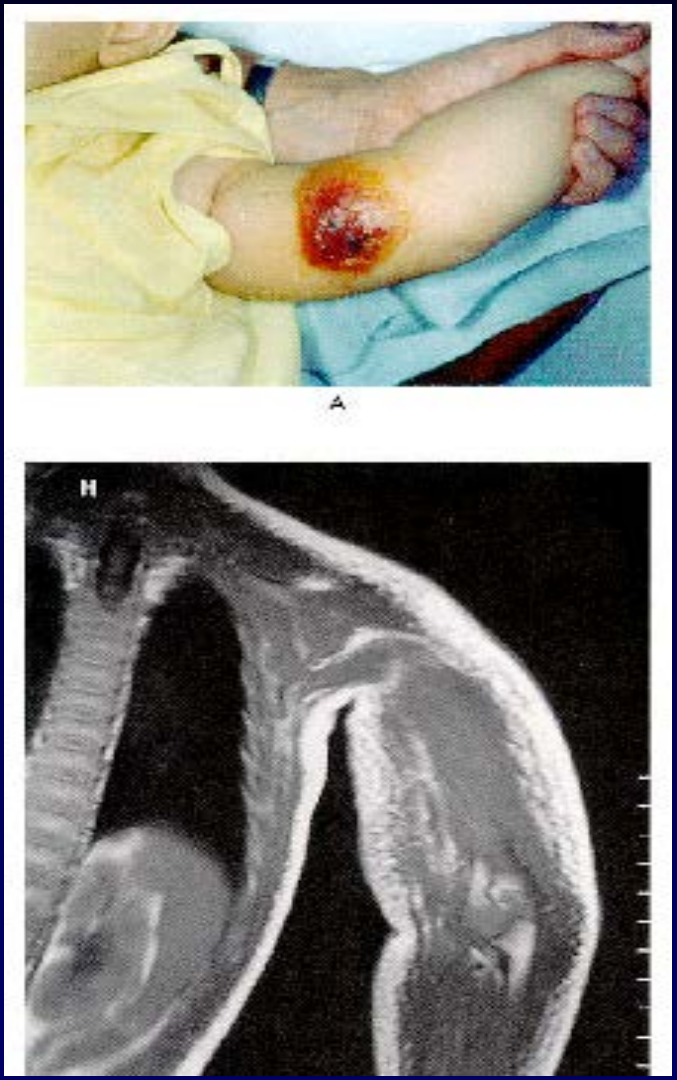


CSF Gram stain

Cutaneous Anthrax, US

7 mo male infant hospitalized with 2 day history of swelling left arm and weeping lesion at left elbow. Patient had been at his mother's office at a TV network. Biopsies yielded *B. anthracis.*

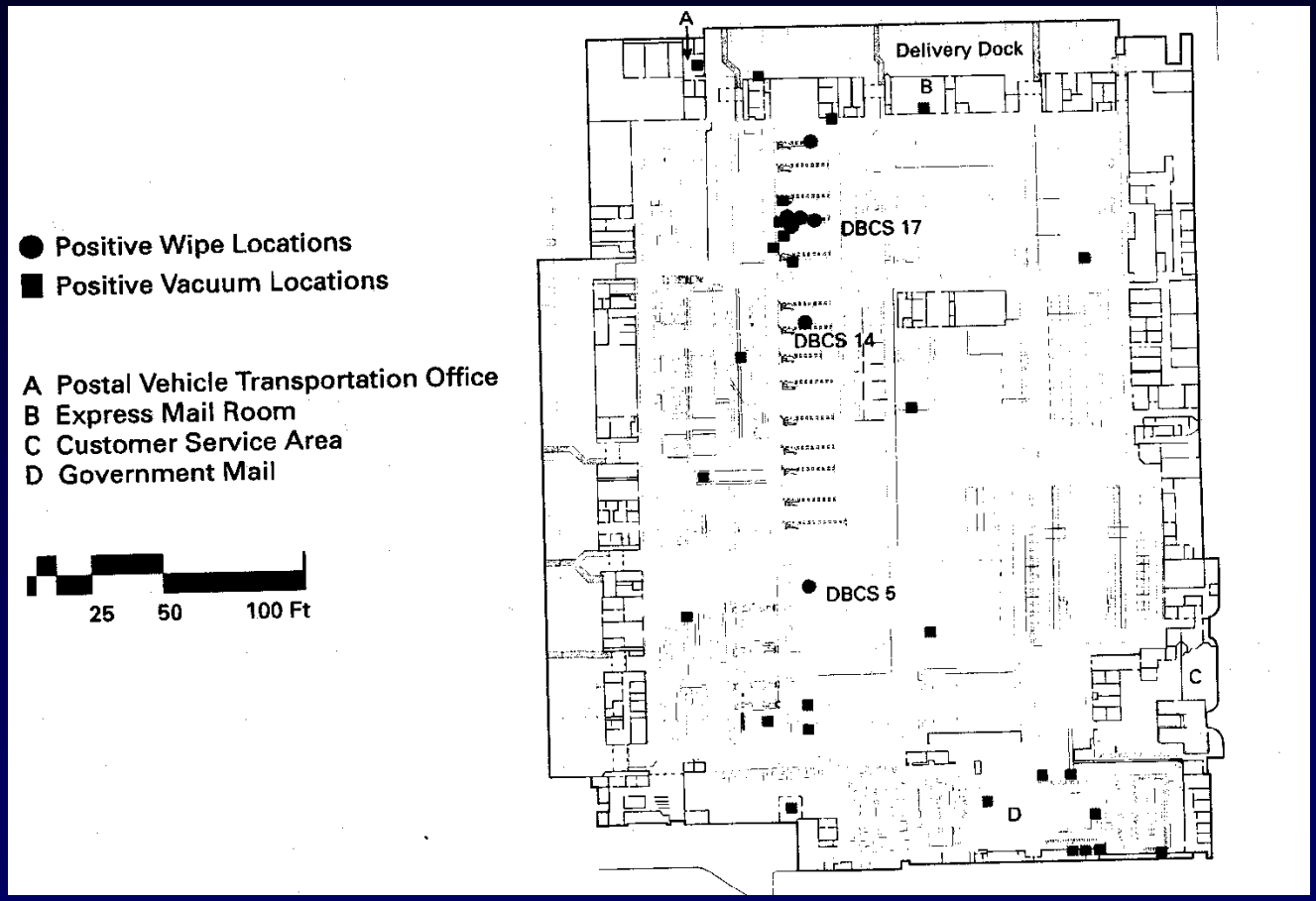
Roche KJ, et al.
NEJM 2001;345:1611



UNEXPECTED FEATURES OF ATTACK

- Targets (news media)
- Vehicle (US mail)
- Source of strain (US, probably weaponized)
- Translocation of spore through envelope
- Airborne acquisition in mail facilities
- Wide spread contamination in mail facilities
- Transmission via mail-to-mail contamination
- No person or group has claimed responsibility

MAIL PROCESSING CENTER, DC, OCT. 2001



CDC. MMWR 2001;50:1130

PRE-EVENT SMALLPOX PLANNING

- Each state should establish and maintain ≥1 smallpox response team
- Each acute-care hospital should identify HCP who can be vaccinated and trained to provide direct medical care for the first smallpox patients requiring hospital admission
- Optimal infection-control practices and appropriate site care should prevent transmission of vaccinia virus from vaccinated HCP to patients
- When feasible, HCP responsible for dressing changes for smallpox vaccine recipients should be vaccinated

CDC. MMWR 2003;52(RR07):1-16

SMALLPOX RESEARCH: CURRENT NEEDS

- Developing better antiviral drugs to treat smallpox disease
  - There is currently no FDA licensed drug treatment for smallpox disease.
- Making safer vaccines
- Improving tests to detect variola virus

VACCINIA VIRUS SMALLPOX VACCINE: INDICATIONS

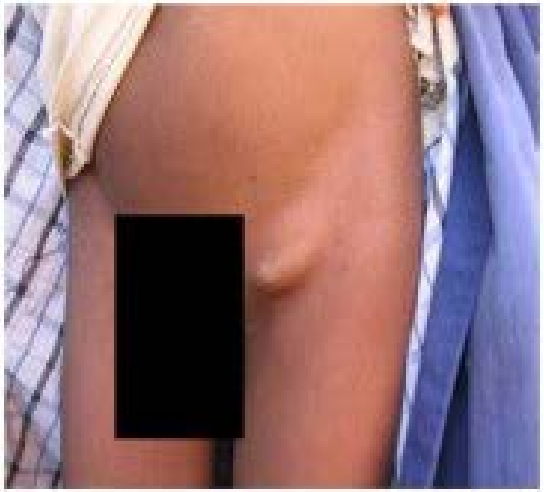
- ACIP (25 June 2015) – vaccine = ACAM2000
- Laboratory personnel who directly handle (1) cultures or (2) animals contaminated or infected with replication-competent vaccinia virus, recombinant vaccinia viruses derived from replication-competent vaccinia strains (i.e., those that are capable of causing clinical infection and producing infectious virus in humans), or other ortho-poxviruses that infect humans (e.g., monkeypox, cowpox, and variola) recommendation category: A, evidence type 2)
- Health care personnel (e.g., physicians and nurses) who currently treat or anticipate treating patients with vaccinia virus infections and whose contact with replication-competent vaccinia viruses is limited to contaminated materials (e.g., dressings) and persons administering ACAM2000 smallpox vaccine who adhere to appropriate infection prevention measures can be offered vaccination with ACAM2000 (recommendation category: B, evidence type 2)

CDC. MMWR 2016;65:757

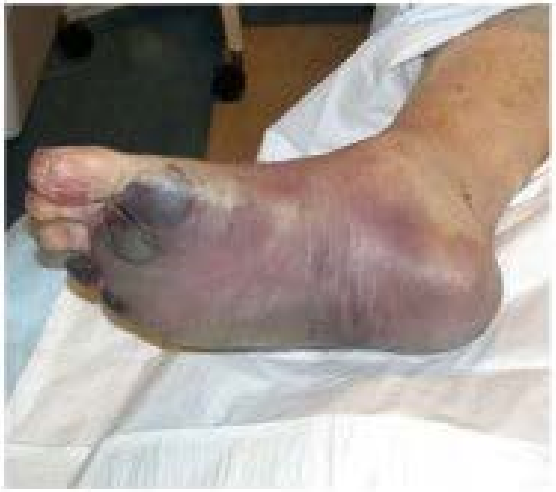
PLAGUE: CLINICAL FEATURES

- Incubation period: 1-4 days (pneumonia), 1-7 days (bubonic or septicemic)
- Clinical syndrome(s)
  - Bubonic, septicemic, pneumonic, cutaneous, meningitis
- Epidemiology and symptoms
  - Sudden onset fever, shortness of breath, hemoptysis, chest pain
  - Gastrointestinal symptoms common (N, V, diarrhea)
  - Fulminant course and high mortality

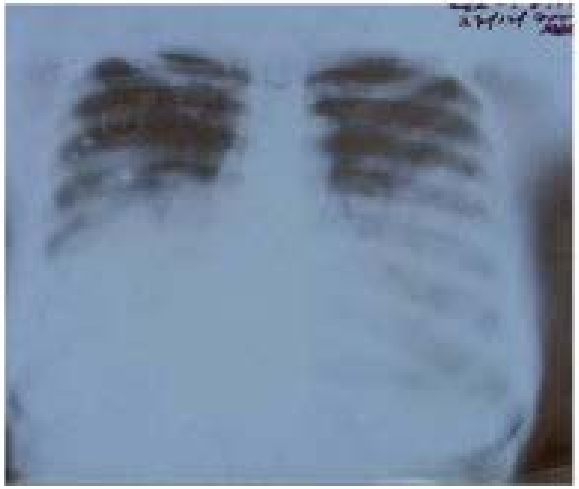
FORMS OF PLAGUE



Bubonic plague



Septicemic plague



Pneumonic plague

POST-EXPOSURE PROPHYLAXIS

	Preferred Agent	Dose	Route
Adults	Doxycycline	100 mg twice daily	PO
	Ciprofloxacin	500 mg twice daily	PO
Children	Doxycycline (for children ≥ 8 years)	Weight < 45 kg: 2.2 mg/kg twice daily (maximum daily dose, 200 mg) Weight ≥ 45 kg: same as adult dose	PO
	Ciprofloxacin	20 mg/kg twice daily (max dose, 1 g)	PO
Pregnant women	Doxycycline*	100 mg twice daily	PO
	Ciprofloxacin*	100 mg twice daily	PO

*Doxycycline and ciprofloxacin are pregnancy categories D and C, respectively. PEP should be given only when the benefits outweigh the risks.

TULAREMIA: CLINICAL FEATURES

- Incubation period: 3-5d (2-10d)
- Clinical syndromes
  - Pneumonia, typhoidal (sepsis without cutaneous or mucus membrane lesions),ulceroglandular, glandular, oculoglandular, orophayngeal
- Clues to diagnosis
  - Pulse-temperature dissociation
  - Abrupt onset, high fever, headache, chills/rigors, generalize body aches (prominent in lower back), coryza, sore throat
  - Dry or slightly productive cough, substernal chest pain with or without objective signs of pneumonia
- Duration of illness: ~2 weeks
- Mortality: Untreated, moderate; Treated, low

THERAPY, CONTAINED CASUALTIES AND FOR POST-EXPOSURE PROPHYLAXIS*

Patients	Preferred Therapy	Alternative Choices
Adults	Doxycycline, 100 mg orally twice daily Ciprofloxacin, 500 mg orally twice daily†	---
Children	Doxycycline, and If >=45kg give 100 mg orally twice daily If <45 kg then give 2.2 mg/kg orally twice daily Ciprofloxacin, 15 mg/kg orally twice daily‡	---
Pregnant women	Ciprofloxacin, 500 mg orally twice daily† Doxycycline, 100 mg orally twice daily	---

*One antibiotic, appropriate for treatment for patient age, should be chosen from among the alternatives. Treatment with streptomycin, gentamicin, or ciprofloxacin should be continued for 10 days; treatment with doxycycline or chloramphenicol should be continued for 14-21 days. Persons beginning treatment with intramuscular (IM) or intravenous (IV) doxycycline, ciprofloxacin, or chloramphenicol can switch to oral antibiotic administration when clinically indicated.

†Not a U.S. Food and Drug Administration-approved use. ‡Ciprofloxacin dosage should not exceed 1 g/d in children.

THERAPY, MASS CASUALTIES AND FOR POST-EXPOSURE PROPHYLAXIS*

Patients	Preferred Therapy	Alternative Choices
Adults	Streptomycin, 1g IM twice daily Gentamicin, 5 mg/kg IM or IV once daily†	Doxycycline, 100 mg IV twice daily Chloramphenicol, 15 mg/kg IV 4 times daily Ciprofloxacin, 400 mg IV twice daily†
Children	Streptomycin, 15 mg/kg IM twice daily (should not exceed 2 gm/d) Gentamicin, 2.5 mg/kg IM or IV 3 times daily†	Doxycycline, If weight >= 45 kg, 100 mg IV If weight < 45 kg, give 2.2 mg/kg IV twice daily Chloramphenicol, 15 mg/kg IV 4 times daily† Ciprofloxacin, 15 mg/kg IV twice daily‡
Pregnant women	Gentamicin, 5 mg/kg IM or IV once daily† Streptomycin, 1 g IM twice daily	Doxycycline, 100 mg IV twice daily Ciprofloxacin, 400 mg IV twice daily†

*One antibiotic, appropriate for treatment for patient age, should be chosen from among the alternatives. Treatment with streptomycin, gentamicin, or ciprofloxacin should be continued for 10 days; treatment with doxycycline or chloramphenicol should be continued for 14-21 days. Persons beginning treatment with intramuscular (IM) or intravenous (IV) doxycycline, ciprofloxacin, or chloramphenicol can switch to oral antibiotic administration when clinically indicated.

†Not a U.S. Food and Drug Administration-approved use. ‡Ciprofloxacin dosage should not exceed 1 g/d in children.

THANK YOU!!