RECOGNITION AND MANAGEMENT OF AGENTS OF BIOTHREATS AND HIGHLY COMMUNICABLE INFECTIONS

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TERRORISM TODAY



New York, September 11, 2001



Time, Special Edition

LECTURE TOPICS

- Potential exposures to rare and exotic diseases
- Major biologic warfare agents
- For most likely BW agents (anthrax, smallpox): Preexposure prophylaxis, post-exposure prophylaxis, therapy
- Recognizing a biologic warfare attack
- Review of anthrax and smallpox

EMERGING INFECTIOUS DISEASES: DEFINITION

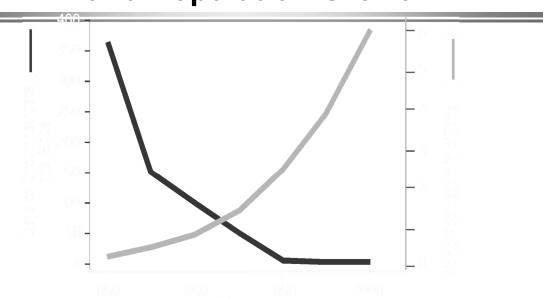
 Emerging infectious diseases can be defined as infections that have newly appeared in the population, or have existed but are rapidly increasing in incidence or geographic range



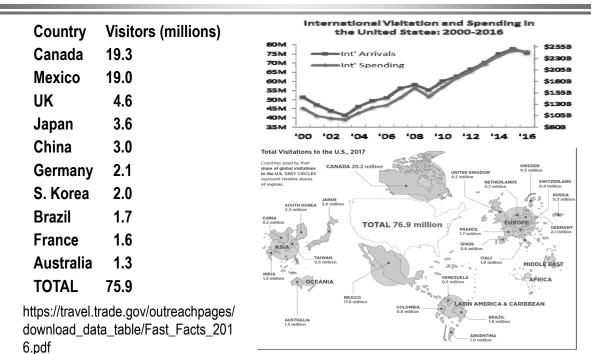
SOURCES OF EXOTIC DISEASES

- Travel
- Animal exposure (zoonotic diseases)
 - Exposure via travel, leisure pursuits (hunting, camping, fishing), occupation (farming), pets
- Bioterrorist agents
- Research
 - Exposure via laboratory work or animal care

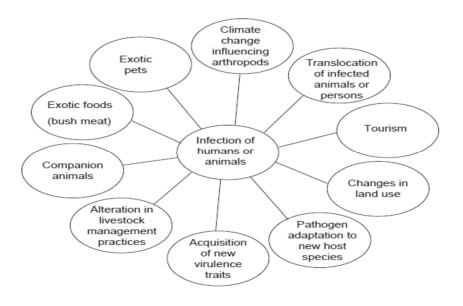
Speed of Global Travel in Relation to World Population Growth



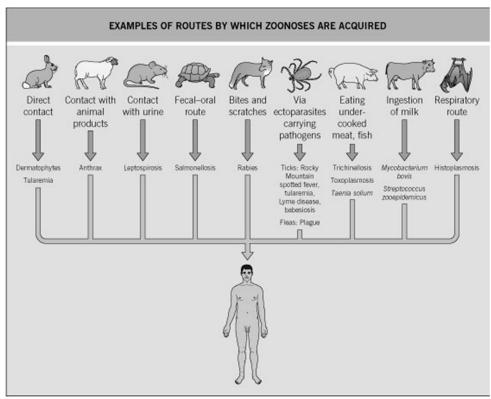
VISITORS TO THE US, 2016



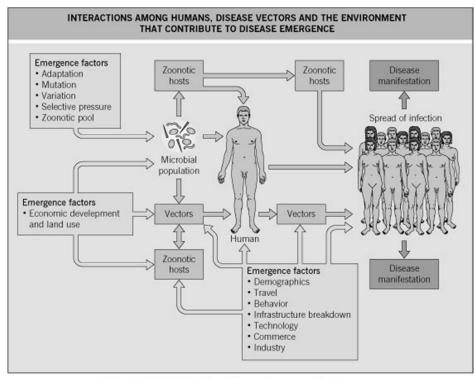
FACTORS INFLUENCING NEW AND REEMERGING ZOONOSES



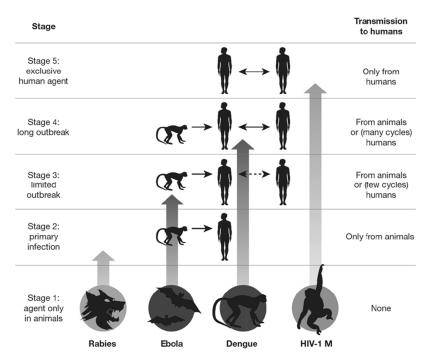
Cutler SJ et al. Emerg Infect Dis 2010;16:1-7



© Elsevier 2004. Infectious Diseases 2e - www.idreference.com



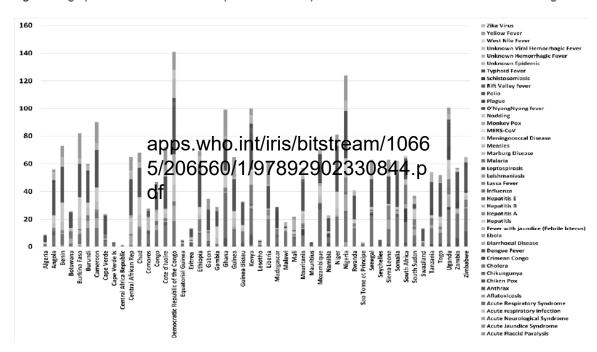
© Elsevier 2004. Infectious Diseases 2e - www.idreference.com

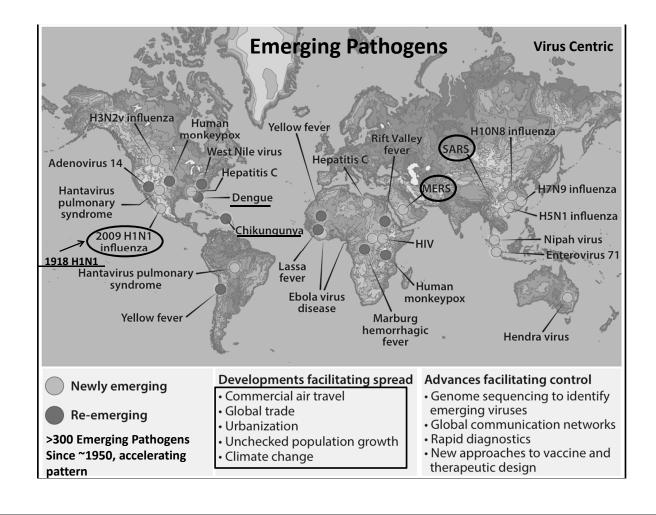


http://web.stanford.edu/group/parasites/ParaSites2012/Lassa%20Libby%20Burch/LassaEbolaMarburg_LibbyBurch_3-8-2012.htm

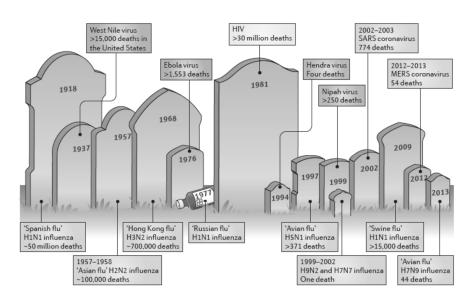
OUTBREAKS AND EPIDEMICS IN AFRICA, WHO, 1970-2016

Figure 1 A graph of all the outbreak and epidemic events by disease in the countries of the WHO African region





EMERGING ZOONOSES



Bean A, et al. Nature Rev 2013;13:851-61

SARS

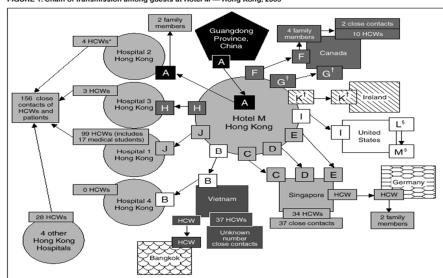


FIGURE 1. Chain of transmission among guests at Hotel M — Hong Kong, 2003

EMERGING DISEASES IN THE US

DISEASE (source)	CASES	OUTCOME	YEAR
West Nile virus (Israel)	Thousands	Endemic (US)	1999
SARS (China)	8096 (8 US, 1 UNC)	Controlled	2003
Monkeypox (Africa)	71	Controlled	2003
Novel flu, H1N1 (Mexico)	Thousands	Endemic (Worldwide)	2009
MERS-CoV (Arabian Peninsula)	Hundreds	Epidemic (Arabian area)	2014
Enterovirus D68	Hundreds (13 UNC)	Epidemic (US)	2014
Ebola	Thousands (1 US)	Epidemic (West Africa)	2014-15

Health-care workers.

All guests except G and K stayed on the 9th floor of the hotel. Guest G stayed on the 14th floor, and Guest K stayed on the 11th floor.

Guests L and M (spouses) were not at Hotel M during the same time as index Guest A but were at the hotel during the same times as Guests G, H, and I, who were ill during this period.

WHO LIST OF PRIORITY DISEASES, 2015

- Arenaviral hemorrhagic fevers (including Lassa Fever)
- Crimean Congo Haemorrhagic Fever (CCHF)
- Filoviral diseases (including Ebola and Marburg)
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
- Other highly pathogenic coronaviral diseases (such as Severe Acute Respiratory Syndrome, (SARS))
- Nipah and related henipaviral diseases
- Rift Valley Fever (RVF)
- Severe Fever with Thrombocytopenia Syndrome (SFTS)
- Zika

UNC HOSPITAL PREPAREDNESS: HIGHLY COMMUNICABLE DISEASES

- Critical issues
 - Surge capacity
 - Maintaining adequate staffing
 - Provision of essential services/supplies
- Additional issues
 - Surveillance
 - Diagnosis
 - Protecting personnel
 - Occupational health
 - Stockpiling PPE
 - Triage of limited supplies/beds
 - Security

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



Visitors, including family, must not enter-report to Nursing Station HEALTHCARE PERSONNEL MUST WEAR:

- TO ENTER:

 N-95 Respirator (prior fit testing required)
- 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 ENTRAS:

 mascanila respiratoria N-95 (para poder usaria es obligatorio que pase antes la prueba para saber la medida correcta)

 pasca.

 p

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

• mascapilla respiratoria N-95 (para poder usarla es obligatorio que pase antes la prueba para saber la medida correcta)

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.

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

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Major article

Emerging infectious diseases: Focus on infection control issues for novel coronaviruses (Severe Acute Respiratory Syndrome-CoV and Middle East Respiratory Syndrome-CoV), hemorrhagic fever viruses (Lassa and Ebola), and highly pathogenic avian influenza viruses, A(H5N1) and A(H7N9)

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Selected emerging diseases of infection control importance

Disease (initial location)	Cases (United States)	Outcome	Person-to-person transmission	Patient-to-HCP transmission	Infection control risk	Year
Legionnaires' disease	Unknown (thousands)	Endemic and epidemic	No	No	High	1976-present
HIV (Africa)	Millions (thousands)	Ongoing epidemic	Yes (blood exposure, organ transplantation, vertical, sexual)	Yes (blood exposure)	Moderate	1978-present
vCJD	Hundreds	Controlled	Yes (blood, theoretically via contaminated medical instruments)	No	Low	1996
West Nile fever	(Thousands)	Endemic	Yes (blood transfusions, vertical, organ transplantation)	No*	Low	1999
SARS (China)	~8,000 (8)	Controlled	Yes (droplet, contact, airborne?)	Yes	High	2003-2004
Monkeypox (Africa)	(37 confirmed, 10 probable)	Eliminated in United States	Yes (droplet, contact)	Yes [†]	High	2003
MERS (Middle East)	Thousands (2)	Controlled	Yes (droplet, contact)	Yes	High	2014-present
Ebola (West Africa)	Thousands (4)	Controlled United States, reduced Africa	Yes (contact, sexual)	Yes	High	2014-present

HCP, health care personnel; MERS, Middle East respiratory syndrome; SARS, severe acute respiratory syndrome; vGD, variant Creutzfeldt-Jakob disease. *Infection via a needlestick theoretically possible.

Key infection control information for selected highly communicable emerging infectious diseases

Characteristic	Lassa fever	Ebola virus disease	MERS	SARS	Novel influenza A
Virus					
Year identified	1969	1976	2012	2003	
Family	Arenaviridae	Filoviridae	Coronaviridae	Coronaviridae	Orthomyxoviridae
Genome	RNA	RNA	RNA	RNA	RNA
Coat	Enveloped	Enveloped	Enveloped	Enveloped	Enveloped
Epidemiology	-	-	-	-	-
Endemic location	West Africa	West and Central Africa	Middle East	China	Worldwide (location varies with strain)
Prevalence	100,000-300,000 cases per			No recent human cases	Varies by strain
	year				
Reservoir	Rodent (rat)	Bats (fruit)	Bats, camels (intermediate host)	Bats, palm civet	Migratory birds, pig
Transmission	Inhalation, ingestion, contact (nonintact skin)	Contact (nonintact skin, mucous membranes, sexual)		Droplet, contact, airborne	Inhalation, contact
Incubation period (d)	10 (range, 6-21)	6-12 (range, 2-21)	2-15	2-14 (range, 2-21)	Varies by strain
Infectivity, Rho	Not determined	1.5-2.0	0.3-1.3	2.2-3.7 (range, 0.3-4.1)	Varies by strain
Duration, maximum (d)	28	21		,	•
Case fatality rate	15%-20%, hospitalized patients	~50% (range, 25%-90%)	>35%	~10%	
Biologic safety	•				
Biothreat level	A	A	Not specified	C	C (some strains)
Biosafety level	4	4	3	3	2-3
Clinical					
Therapy	Ribavirin	Supportive	Supportive	Supportive	Neuraminidase inhibitors
Infection control					
Isolation	Contact, droplet, airborne for aerosol-generating procedures	Contact, droplet, airborne for aerosol-generating procedures	Contact, airborne	Contact, airborne	Droplet, airborne fo aerosol-generatin procedures
Pre-exposure prophylaxis, vaccine	No	No	No	No	Yes (some strains)
Postexposure prophylaxis	No	No	No	No	Yes (antivirals)

[†]No HCP developed infection during the U.S. outbreak but patient-to-HCP transmission described in Africa.

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

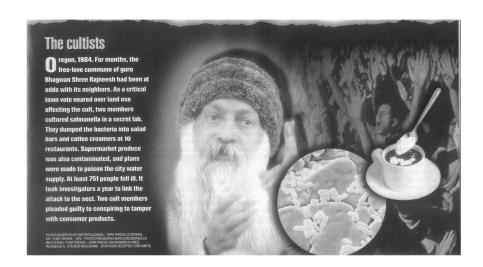


USE OF BIOLOGICAL AGENTS: US

- 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 Possess requisite Acquire basic chemicals or Conduct testing infective biological seed cultures technical skills procedures Synthesize chemical agents Avoid or grow biological agents detection by Have adequate (unnecessary for toxic industrial chemicals) authorities financial resources Process the chemical or biological agents into a form that can be effectively delivered Recognize (unnecessary for some chemical agents) environmental and Assume personal meteorological risk where conditions no vaccines or Improvise an agent delivery device antidotes available Release chemical or biological agents to cause mass casualties

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)

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

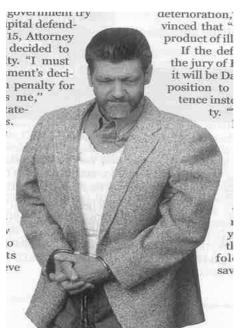
^{*} Priority agents may exhibit all or some of the above characteristics

Sample Biological Agent Ratings

	Public He	alth Impact	Dissemination Po	otential	Special	Pubic
<u>Disease</u>	Morbidity	<u>Mortality</u>	Stable/Produce/Distribute	$\underline{\textbf{Transmissable}}$	Preparedness	<u>Perception</u>
Smallpox	+	++	++	+++	+++	+++
Inhalational anthrax	++	+++	+++		+++	+++
Pneumonic plague	++	+++	++	++	+++	+++
Tularemia	++	++	++	-	+++	++
Botulism	++	+++	++		+++	++
VHF	++	+++	+	+	+++	+++
Glanders	++	+++	++	-	++	+
VE	++	+	++	-	++	+
Q fever	+	+	++	-	++	+
Brucellosis	+	+	++	-	++	+
Toxins	++	++	+	-	++	+
HPS	++	++	+	++	-	+
Nipah encephalitis	++	++			+	+

SOURCES OF BIOTERRORISM

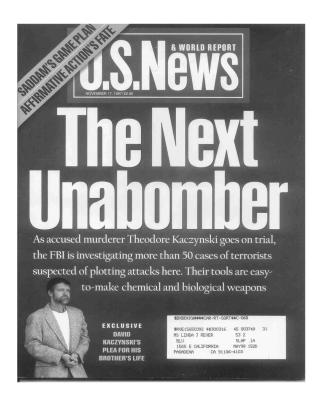
- Biological warfare
- State sponsored terrorism
- International terrorist groups
- National cults
- The deranged "loner"







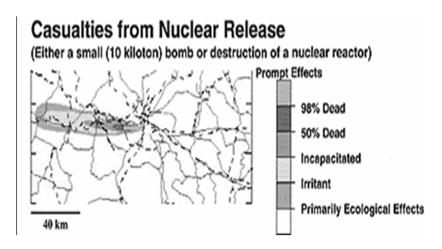




BIOTERRORISM: IMPACT

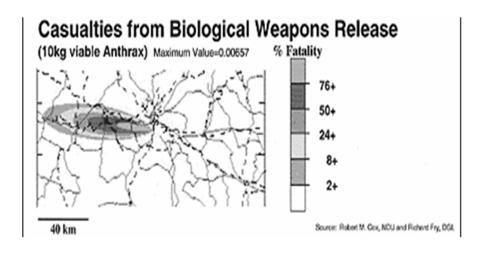
- Direct infection: Mortality, morbidity
- Indirect infection: Person-to-person transmission, fomite transmission
- Environmental impact: Environmental survival, animal infection
- Other: Social, political, economic

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

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

[©] Elsevier 2004. Infectious Diseases 2e - www.idreference.com

STAYING ALERT AND EDUCATED

Table 2. Selected Features of the Conditions Discussed.				
Condition	Contagious	Clinical Form or Forms	Vaccine Available	Treatment
Anthrax	No	Three primary forms: cutaneous, inhalational, and gastrointestinal	Yes	Combination antimicrobials, effusion drainage, monoclonal antibody
Smallpox	Yes	Centrifugal rash with same-stage lesions	Yes	Supportive treatment
Plague	Yes	Pneumonic or bubonic	No	Antimicrobials
Botulism	No	Inhalational or gastrointestinal	No	Antitoxin
Tularemia	No	Inhalational or ulceroglandular	No	Antimicrobials

Adalji AA, et al. NEJM 2015;372:954-62

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)

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

THE PROBLEM OF NEEDLES IN HAYSTACKS

- Outbreak severe acute respiratory infections
 - MERS, SARS, H5N1, H7N9, HxNy...
- Viral hemorrhagic fevers (VHF)
 - Ebola, Marburg, Lassa fever, Rift Valley, CCHF, bunyavirus
- Intentional release
 - Anthrax, smallpox, ricin
- Naturally occurring severe infections
 - Bacterial: Plague, tularemia, melioidosis
 - Viral: Adenovirus, parainfluenza, RSV

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

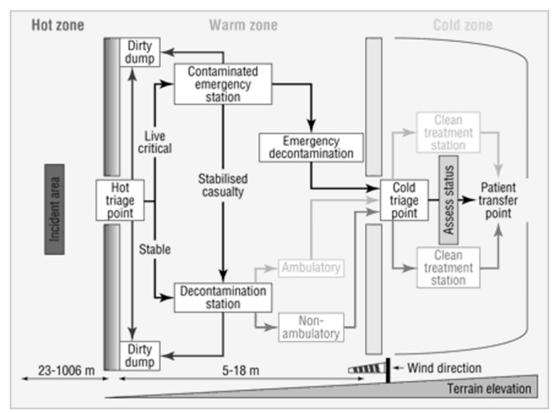
Shaikh Z. ID Clinics NA 2006;20:433-453

AN APPROACH TO BT PREPAREDNESS

- What is the external threat landscape? (Who/When)
 - State/non-state/lone wolves; covert vs overt; new biotech (gene editing)
- What is possible? What is feasible or likely? (What)
 - Bacteria, viruses, toxins
 - Combined attack all hazards (chem/bio/rad/nuclear/cyber)
- What are routes of transmission & spread? (How/Where)
 - Respiratory, food/water, mail, bomb, what else?
 - Public places, transit hubs, restaurants, what else?
- What is the intended impact & gain? (Why)
 - Mass impact vs mass casualties

THE MISSION: 4 EYES FOR BIOTHREATS

- IDENTIFY
 - Clinicians & microbiologists
- ISOLATE
 - Clinicians, infection control, hospital admin
- INFORM
 - Clinicians/labs to public health authorities, government, media
- INVESTIGATE
 - Police, internal security, governments, international agencies



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

WE HAVE A DUTY TO BE PREPARED



2011, NYC, Attack by hijacked planes



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

THANK YOU!!

