Interventions for Bioterrorism

Civilian Perspective

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Iraq Produced Biologic Weapons

- 19,000 tons of botulinum toxin
- 8,500 liters of concentrated anthrax
- 2,200 liters of aflatoxin

- And weaponized each

Why not a terrorist?

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Goals

- Give you a broad, participative overview of a possible bioterrorism attack
- Show an epidemiologic approach that you can use in many situations requiring epidemiology

Preparation for a Civilian Bioterrorism Attack

- Pre-attack
  - Examples of measures
    - Education of population or health care system
    - Vaccination
- Post-attack
  - Examples of measures
    - Emergency plan
    - Stockpiles of antibiotics, antitoxin, vaccine

There Are Many Steps in an Epidemic Investigation

- For simplicity, I'll list major ones and in general order
- In reality, many things are going on at once

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Steps in an Epidemiologic Investigation

1. Is there a problem?
2. Characterize the illness
3. Construct a case definition
4. Identify and count cases
5. Time, person, place
6. Identify the cause of disease
7. Begin interventions

Night Falls Over a City

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At a Large Hospital, on a Saturday Evening in Late November, Several People Enter the Emergency Department Over a Several Hour Time Period with Vague Feelings of Being Ill

- Fever
- Mild headache
- Mild difficulty breathing
- Not feeling good

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Is There a Problem?

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1. Is There a Problem?

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Over the Next Several Hours, More People Become Ill

- The Emergency Department is crowded, and other health care facilities begin to see patients
- People are calling for emergency help, e.g., ambulances and taxis, to take them to health care facilities
- The police and news agencies sense something is wrong and begin queries
- Someone notifies the city health department

IF You a Received a Nonspecific Terrorist Threat, What Illness Is This?

- Anthrax
- Plague
- Tularemia
- Brucellosis
- Smallpox
- Venezuelan Equine Encephalitis (VEE)
- Staphylococcal Enterotoxin B (SEB)
- Ricin
- Etc.

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Illness and Mortality Varies Considerably Among Possible Agents

Disease	Death Rate (%)	Cost to society per 100,000 perso attacked without prophylaxis (mi
Anthrax	85	$26,204
Plague	80	
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Brucellosis	1	579
Smallpox	35	
VEE	70	
SEB	3?	
Ricin	20?	

[1] Kaufmann A, Meltzer M, Schmid G. Emerg Infect Dis 1997;3:88-94

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2. Characterize the Illness

- Who is going to do this?
  - Physically, who?
  - Do they have general epidemiology training, or, training in bioterrorism and its possible agents?
  - Is there a sense of urgency?
- How are they going to do this?
  - Communications?
  - Level of skill of health care facilities?

3. Construct a Case Definition

- Case definition=clinical, and often laboratory, features of cases that characterize the unusual illness
- Often somewhat vague and *sensitive* early in the epidemic, and become more *specific* over time as more information occurs
- May use categories, depending upon the likelihood of cases of illness being the illness you are concerned about:
  - Definite
  - Probable
  - Possible

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You Case Definition(s)?

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Possible Case Definitions

- Definite Case
  - An illness in a person with fever, rapid breathing, and an x-ray with features of pneumonia
- Probable Case
  - An illness in a person with fever and rapid breathing, but without an abnormal x-ray (either not taken or negative)

Possible Pneumonic Plague Case Definitions

- Definite Case
  - An illness in a person with fever, rapid breathing, an x-ray with features of pneumonia, and a positive culture for *Yersinia pestis*
- Probable Case
  - An illness in a person with fever, rapid breathing, an x-ray with features of pneumonia
- Possible Case
  - An illness in a person with fever and rapid breathing, but without an abnormal x-ray (either not taken or negative) and no culture for *Y. pestis* (either not taken or negative)

It Is Sunday, 10:00 a.m.

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4. Identify and Count Cases

- Where do we count the cases?
  - Everywhere in the city, or environs?
  - At what locations?
- What else do we know about the cases, e.g., x-ray findings, general laboratory findings, clinical course of the earliest cases or cases coming in now?
- Who else do you alert?
- What do you tell health care facilities about isolation, or management of exposed persons, or suggested treatment?

5. Time, Place, Person

Why are these important?

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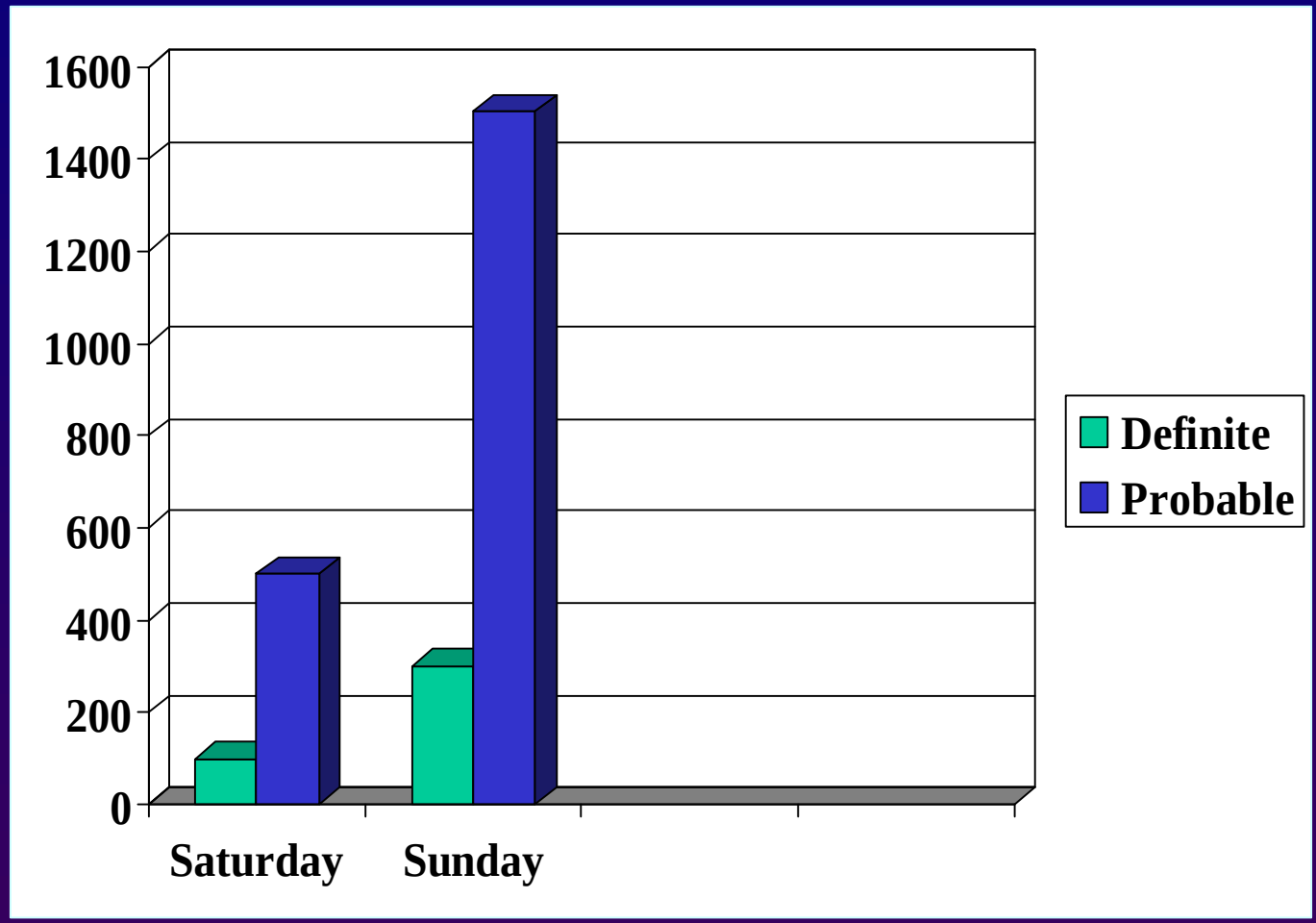
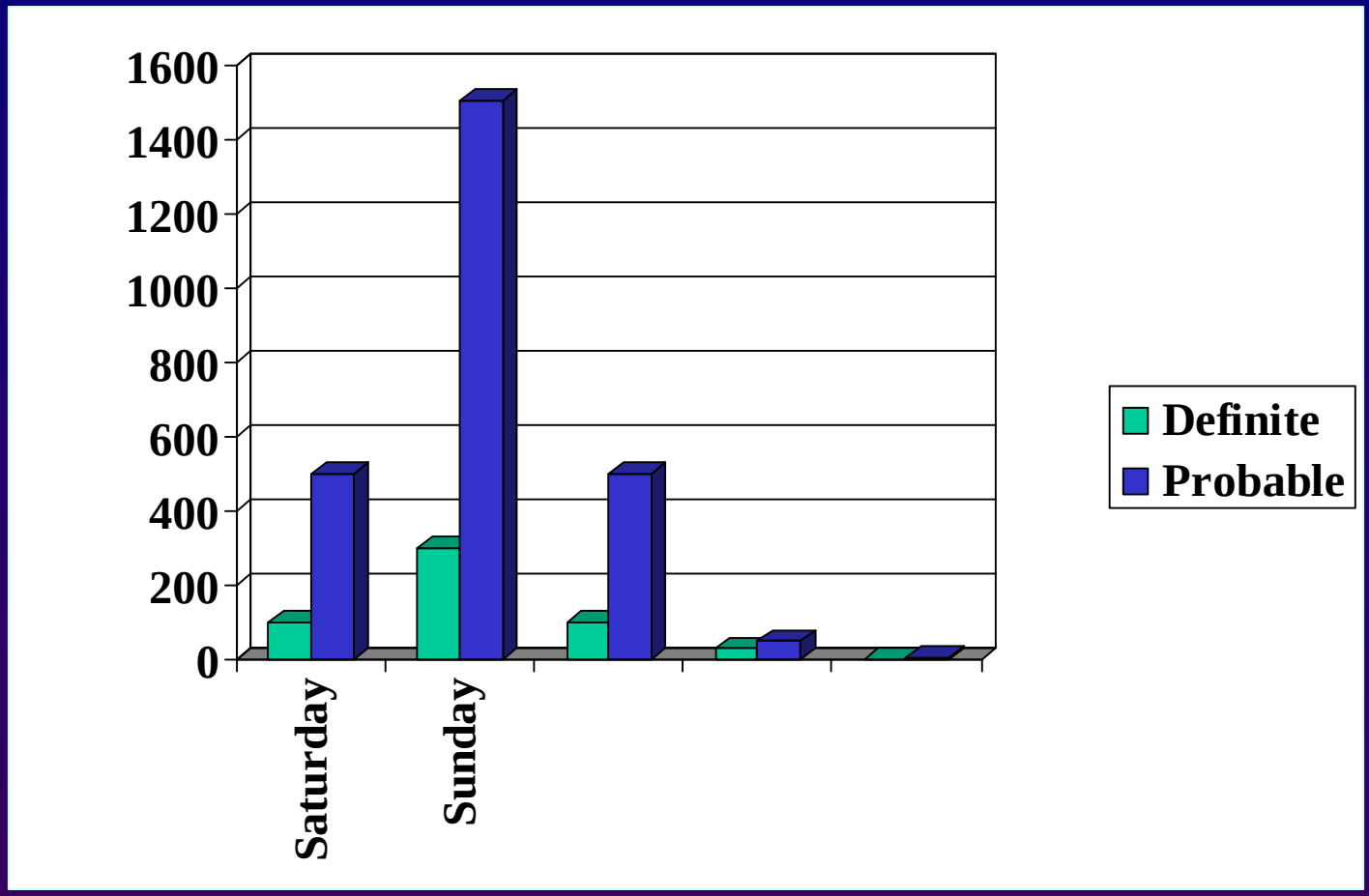
5. Time, Place, Person

- Time
  - Draw an epidemic curve (if you have time)
- Place
  - Where are cases being reported from?
- Person
  - What persons are becoming ill?
    - Any particular age or gender distribution?

Epidemic Curve, Sunday, 10:00 a.m.



Possible Subsequent Epidemic Curve



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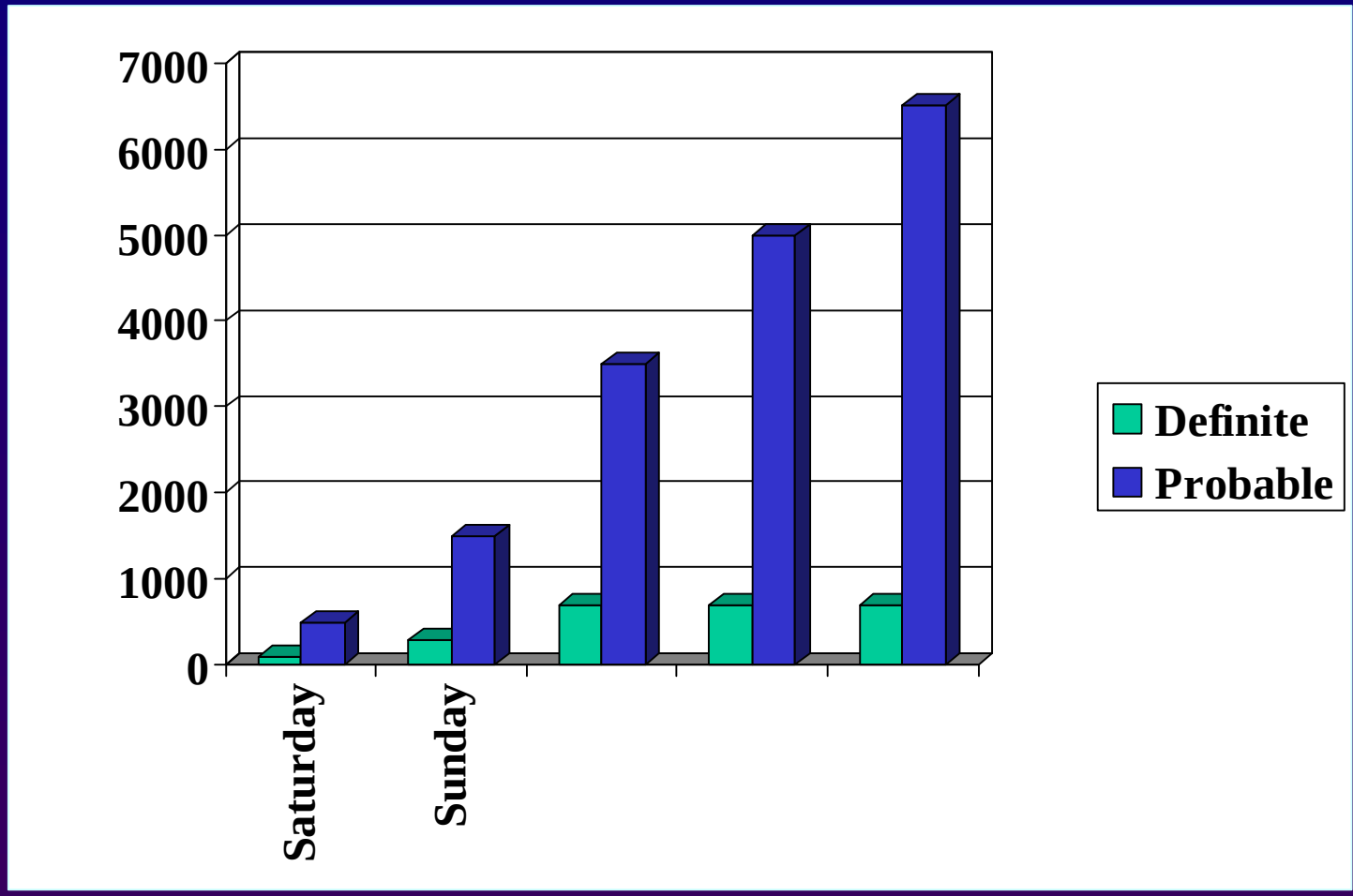

It Is Sunday, 10:00 p.m.

- You have 2, 403 cases reported
  - 403 are definite, and 2,000 are probable
  - You know there are many more cases
  - The cases are being reported from everywhere, but seem mostly from the large metropolitan hospital and the eastern part of the city
- Health care facilities are overwhelmed and some personnel are refusing to work with patients
- Early cases are becoming sicker, with increasing respiratory difficulty and pneumonia

It Is Sunday, 10:00 p.m. (continued)

- What do you tell the mass media? How do you use the mass media?
- What do you tell contacts of cases (medical care/family)?
- What do you do about transportation into and out of the city?
- How do you judge the need for additional resources?

There is panic

It Is Monday, 4:00 a.m.

- A few cases have died with sepsis, and no particular antibiotics seem effective
- New cases continue to appear, and resemble the old cases, although pneumonia on x-ray seems to be more prominent in these
- Sputum exams show just white cells and no particular organism; laboratory studies, and culture of the sputum and blood from some patients, do not show anything specific

It Is Monday, 4:00 a.m. (continued)

- Back to Time, Person, Place

It Is Monday, 4:00 a.m. (continued)

- Cases are concentrated in the eastern neighborhoods of the city
  - You know that a large celebration was held there several days ago, attended by people from throughout the city
  - These are religious neighborhoods that recently rebelled against considerable illegal drug activity (cocaine and Mandrax), helping the police against drug networks
- You are tired

And…?

- Your diagnosis?
- Your intervention?

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It Is Monday, 10:00 a.m.

- You have reports of 156 deaths, with many more people close to dying
  - 7,333 cases (1,080 definite)
- Hospitals are turning away patients, whose fate is largely unknown despite early efforts to set up temporary facilities in large, public buildings and “cohort” patients
- A private hospital with excellent, modern laboratory facilities has just reported organisms growing in the blood culture bottles from several patients
  - The organisms are small, gram-negative bacilli
  - Are they real or contaminants?

You Conclude That This Is An Event That Is Not Naturally-occurring Disease

- You narrow your list of possible causes to several diseases, including:

You Conclude That This Is An Event That Is Not Naturally-occurring Disease

- You narrow your list of possible causes to several diseases, including:
  - Plague (*Yersinia pestis*)
  - Tularemia (*Francisella tularensis*)
  - (maybe) *Haemophilus influenzae*, influenza, *Mycoplasma pneumoniae* or *Chlamydia pneumoniae*
- Awaiting identification of the organism, you bet on plague or tularemia

Points 6 And 7

- 6. Possible causes
- 7. Possible interventions

How rapidly you must determine, and implement, these is guided by the urgency of the epidemic

Steps in an Epidemiologic Investigation

1. Is there a problem?
2. Characterize the illness
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Challenges

- Confirming the disease
- Confirming the mode of transmission
- Selecting the medical intervention(s) (if any)
- Defining the population at risk
- Obtaining the medical intervention(s)
- Obtaining other medical supplies
- Containing the epidemic
- Using the mass media
- Obtaining relief workers
- Protecting relief workers
- Body disposal
- Safe food/drinking supplies (if needed)
- Decontamination

Challenges--Confirming the Cause of Disease

Many bioterrorist diseases are difficult to confirm

- Two “ways” to confirm
  - The putative source
  - Patients

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Diagnostic Methods

	Culture (1-4 days)	Serology (7-14 days)	Nucleic acid, antigen, toxin (1 day)
Plague	Yes	Yes	Yes
Anthrax	Yes	Yes	Yes
Tularemia	Yes	Yes	Yes
Brucellosis	Yes	Yes	Probably
Smallpox	No	Yes	Yes
VEE	Yes	Yes	No
SEB	No	No	Maybe
Ricin	No	No	Yes

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Medical Prophylaxis and Treatment After Attack

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Challenges--Selecting the Medical Intervention(s)

Medical Interventions

	Antimicrobial	Vaccine[1]	Antitoxin
Anthrax	Yes	+/+	No
Plague	Yes[2]	+/+	No
Tularemia	Yes[2]	+/-	No
Brucellosis	Yes[2]	-/-	No
Smallpox	No	+/+	No
VEE	No	+/-	No
SEB	No	No	No
Ricin	No	No	No

[1]Available/licensed

[2]Oral or intramuscular administration, or both, may be needed

Examples of Medical Interventions

Disease and prophylaxis	Effectiveness (%)
Anthrax	
28 day course of ciprofloxacin or doxycycline	90
Above, plus three doses of intramuscular vaccine	95
Tularemia	
14 day course of doxycycline	80
Above, plus 7 days of intramuscular gentamicin	95
Brucellosis	
42 day course of doxycycline and rifampin	80
42 day course of either antimicrobial plus 7 days of intramuscular gentamicin	95

Kaufmann AF et al. Emerg Infect Dis 1997;3:83-94

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Post-Exposure Prophylaxis Must Be Started Early

Disease	Incubation Period (days)[1]
Anthrax	1-5
Plague	2-3
Tularemia	2-10
Brucellosis	5-60
Smallpox	7-17
VEE	2-6
SEB	hours
Ricin	hours

[1] Franz DR et al. JAMA 1997;278:399-411

Within 72 hours for short incubation diseases

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Challenges--Defining the Population at Risk

- Determines who gets the medical intervention
- May not know
- Many people may want the intervention, even if they are unlikely to have been exposed

Challenges--Obtaining the Medical Intervention(s)

- Where is the item?
- Is there enough?
- How do we get it to the city?
- How do we distribute it?

Challenges--Obtaining Other Medical Supplies

- Personal protection, e.g., masks
- Respiratory support
- Other drugs, e.g., oxygen, heparin for hemorrhagic diseases
- Dressings
- Etc.

Challenges--Containing the Epidemic

- Where have *afflicted* persons gone?
  - Here, the emphasis is on helping those afflicted
- Is there secondary transmission of *infection*?
  - Here, the emphasis is on preventing others from being infected
    - Outside the medical care facilities
    - Inside the medical care facilities

Challenges--Using the Mass Media

- What are the messages?
  - What has happened?
  - What should I do?
  - What should I not do?
  - Where should I go?
- How do we get them out?

"The communication of the risk to individuals following a bacteriologic attack will critically affect how communities and individuals respond." (Holloway HC et al. JAMA 1997;278:425-7.

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Challenges--Obtaining Relief Workers

- What kind of workers do you need?
- Where are they?
- What fears do they have?

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Challenges--Protecting Relief Workers

- Is protection needed?
- How do we get it?

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Challenges--Body Disposal

- What preparation will morticians have?
- Where do the bodies go?

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Challenges--Safe Food/Drinking Water

- If you do not know mode of spread, what do you do?
- If you do know and it is a continuing threat, e.g., botulinum toxin in food or *F. tularensis* in drinking water, what do you do?

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Challenges--Decontamination

- Agent-dependent
  - Some agents are very stable and persist, e.g., anthrax spores or botulinum toxin
  - Some agents are very labile, e.g., *F. tularensis* or VEE
- What to decontaminate
  - Clothing must be disposed of
  - The environment/vehicle

Illness and Mortality Varies Considerably Among Possible Agents

Disease	Death Rate (%)	Cost to society per 100,000 persons attacked without prophylaxis (mil)[1]
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It is Tuesday, 1:50

- Large numbers of cases are being reported
  - The case count is 14,666, with 2,160 being definite
  - But, it appears that there is no increased numbers of cases in the past 12 hours compared to the preceding 12 hours
- Reports of cases in health care workers are being received
- Many people have left the city
- There is panic
- And your diagnosis of the cause of the attack?

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  - But, it appears that there is no increased numbers of cases in the past 12 hours compared to the preceding 12 hours
- Reports of cases in health care workers are being received
  - But, airborne transmission from patients to health care workers or other contacts is said not to occur
- Many people have left the city
- There is panic
- And your diagnosis of the cause of the attack?

Francisella tularensis!

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Summary

- The prospect of a bioterrorist attack is very real
- A variety of agents could be used, the choice depending upon the desires of the terrorists
  - An attack could be disabling
  - An attack could be a catastrophe
- Existing worldwide preparation for such an attack is poor
- Determining if an attack has occurred and, then, the cause of an attack is far easier in hindsight than as it is occurring

Summary (continued)

- Having plans and resources, e.g., diagnostics, antimicrobials and vaccines, prior to a bioterrorist attack is essential to the management of the attack
- There is little experience with these agents and the ways to manage them in attack scenarios; best guesses must be made but expect surprises