WHY IS THIS IMPORTANT?

- The world is facing challenges from both new diseases and re-emerging ones
- Methods of management and prevention can be developed by understanding the dynamics of disease
- Understanding how once dormant diseases are now re-emerging is critical to controlling the damage such diseases can cause

OVERVIEW
GIROLAMO FRASCATORO
Speaking About Syphilis

“There will come yet other new and unusual ailments in the course of time. And this disease will pass away, but it later will be born again and be seen by our descendants.”

This quote was written 450 years ago.

INFECTIONOUS DISEASE

Infectious disease has played a prominent role in world history:

- The Black Death in the Middle Ages killed millions in Europe
- Measles destroyed the South American Aztec civilization
- Smallpox destroyed indigenous peoples of North and South America

More than 30 new diseases have been identified in the past 30 years, including:

- Legionnaires’ disease
- Acquired Immune Deficiency Syndrome (AIDS)
- Hepatitis C infection
- Nipah virus infection
**INFECTIOUS DISEASE**

- More than 30 new diseases have been identified in the past 30 years, including:
  - Hemorrhagic fevers
  - Severe Acute Respiratory Syndrome (SARS)
  - Creutzfeldt-Jacob disease (CJD)
  - Avian influenza

**RE-EMERGING INFECTIOUS DISEASE**

- Some diseases are re-emerging after being dormant for more than one hundred years.
  - Tuberculosis
  - Cholera

**RE-EMERGING INFECTIOUS DISEASE**

- Many of these diseases were thought to be controlled through antibiotics
  - In some cases the re-emerging disease is resistant to antibiotics
- In recent years, falling living standards and decline of infrastructure in some countries has aided the re-emergence of some infectious diseases
EMERGING INFECTIOUS DISEASES

- Emerging infectious diseases are those whose incidence has increased over the past 30 years
  - Some are diseases that have never been seen before
  - Some were previously documented but without a known etiology
EMERGING INFECTIOUS DISEASES

- 25-35% of the 60 million deaths worldwide that occur each year are due to infectious disease
- Established, emerging, and re-emerging diseases continue to affect worldwide societies
- Four patterns of transition have been identified in emerging diseases
- All four transition mechanisms contribute to rapid spread of emerging and re-emerging diseases

First transition (also referred to as crowd transition)
- Occurs when people begin to live in much closer proximity to one another
- Proximity between populations allows for easy transmission of disease

Second transition
- Neighboring civilizations made contact with each other through war or trade
- Contact allowed the exchange of pools of infectious organisms and vectors between populations
EMERGING INFECTIOUS DISEASES

- Third transition
  - Worldwide exploration and colonization led to the identification of new populations
  - Newly identified populations came into contact with pathogens never seen before within their cultures

EMERGING INFECTIOUS DISEASES

- Fourth transition – this is happening today. The ongoing causes are:
  - Global urbanization
  - Increase in population density
  - Poverty
  - Social upheaval
  - Travel
  - Long distance trade
  - Technology development
  - Land clearance
  - Climate change

ENVIRONMENT AND INFECTIOUS DISEASE

- Humans continue to encroach on uncultivated environments
- This can create an increased risk of contact with new pathogens
- Examples of diseases encountered as a result of this encroachment are:
  - Hanta virus pulmonary syndrome
  - Dengue fever
FOOD-BOURNE INFECTION VECTORS

- As populations grow, there is an increased pressure to produce more meat
- This has led to the emergence and spread of pathogens from farm animals to humans
  - *Salmonella* species
  - Variant CJD
  - *E. coli* O157:H7

GLOBALIZATION AND TRANSMISSION

- Changing patterns in human behavior and changing ecology contribute to the emergence of infectious disease in two ways:
  - Increased opportunity for animal-to-human transfer because of greater exposure
  - Increased opportunity for the transmission from one human to another once a person is infected

GLOBALIZATION AND TRANSMISSION

- Genetic changes in pathogens can occur through a process known as re-assortment
  - An example of this is influenza
- Modern air travel disperses pathogens worldwide very rapidly
- Increasing numbers of immunocompromised hosts presents an increasing number of potential targets
HURDLES TO INTERSPECIES TRANSFER

- A pathogen must overcome two major hurdles to replicate successfully in a human host
  - Must adapt in such a way that it can replicate in human cells
    - This can be a complex problem for the pathogen
  - Must be able to configure itself so that it can be easily transmitted from one human to another

Some pathogens have overcome the first hurdle but not the second one
- Hanta virus
- Avian influenza virus

Overcoming these two hurdles requires:
- Extensive genetic mutation
- Genetic re-arrangement
- Genetic re-assortment

These changes are easier for viruses, which are prone to mutation because of the lack of fidelity in replication (especially RNA viruses)
HURDLES TO INTERSPECIES TRANSFER

SARS

- SARS became readily transmissible in the 1990s
- First documented case was identified in mainland China
- It is transmitted by droplet aerosol and fomites deposited on the respiratory mucosal epithelium
SARS: Pathogenesis

- SARS is an infection of the lower respiratory system and symptoms include fever, malaise, and lymphopenia of T cells
- 20-30% of patients infected with SARS require intensive care and approximately 10% will die
- The pathogenesis of SARS is due to a high viral load in the lower respiratory tract

SARS: Host Response & Treatment

- Patients with SARS have elevated levels of cytokines and chemokines
- There is a prolonged immunological impairment during the disease
- Therapy includes antiviral drugs but they are only effective if given during the first few days of the infection. Attempts to develop a vaccine for SARS are under way

WEST NILE VIRUS

- West Nile fever is caused by an arbovirus (RNA viruses)
- The virus is carried in the saliva of mosquitoes and is transmitted through bites
- West Nile virus is a flavivirus
- Birds are the primary hosts and the infection is spread from bird to bird by mosquitoes
WEST NILE VIRUS
- Humans and animals such as horses are incidental hosts
  - They can be infected by mosquitoes carrying the virus
  - The illness can also be transferred through blood transfusions and transplantation

WEST NILE VIRUS: Pathogenesis
- Most infected people are asymptomatic unless the infection causes an invasive neurological disease called West Nile Fever
  - Symptoms include fever, headache, myalgia, and anorexia
  - Severe infection can cause profound fatigue, myocarditis, pancreatitis, and hepatitis
  - Particularly severe cases can result in encephalitis or meningitis and death

DENGUE FEVER VIRUS
- Dengue fever is caused by dengue virus (flavivirus, RNA virus)
  - The virus is carried in the saliva of mosquitoes and is transmitted through bites
  - There is no vaccine or specific treatment
  - A severe flu-like illness is seen with high fever, severe headache, pain behind the eyes, muscle and joint pain, and a rash
  - Dengue shock syndrome and dengue hemorrhagic fever can lead to organ impairment or failure
VIRAL HEMORRHAGIC FEVER (VHF)

- Emerging infectious diseases classified as VHF's include the conditions caused by the Ebola, Marburg, and Yellow fever viruses
- VHF, in particular that caused by Ebola and Marburg, is frequently fatal
- All of the viruses are single-stranded enveloped RNA viruses

VHF: Pathogenesis

- These viruses are transmitted in diverse ways including both arthropod and rodent vectors
  - All of the hemorrhagic viruses can be transmitted directly from human to human
- Symptoms include fever, bleeding, and circulatory shock

VHF: Pathogenesis

- Fatality rates average between 5-20% for all of these viral infections
  - The Ebola death rate is between 50 to 90%
- Outbreaks of VHF are often in small remote areas
- There is currently no successful therapy for VHF infection. The 2014 Ebola outbreak caused a renewed interest in vaccine and drug development. Candidate vaccines and experimental drugs are in use by early 2015
RE-EMERGING INFECTIOUS DISEASES

- A number of diseases we once thought were no longer a threat to humans have bounced back in recent years
- All of them present important challenges to health care workers today
- Two good examples of re-emerging infectious disease are:
  - Tuberculosis
  - Influenza

TUBERCULOSIS (TB)

- An estimated 2 billion people worldwide are infected with tuberculosis
- *Mycobacterium tuberculosis* is the causative agent for TB
- Each year 8-9 million people worldwide are infected with TB
- It is estimated that up to 2 million deaths occur worldwide per year

TUBERCULOSIS (TB)

- TB is still a leading killer of young adults worldwide
- In high-income countries, minorities are affected disproportionately by TB
  - It is nine times more frequent among foreign-born individuals living in the US than in native-born people
TUBERCULOSIS (TB)

- Antibiotics developed in the 1950s slowed the spread of TB, but by the year 2000, the incidence began to rise.
- Possible causes of the increase in TB:
  - HIV/AIDS epidemic
  - Increased poverty, IV drug abuse, and homelessness
  - Increased immigration of infected individuals
  - Increased elderly population, especially those in long term care facilities
  - Failure of patients to complete antibiotic treatments

INFLUENZA

- Influenza is caused by an RNA virus that:
  - Contains eight separate segments of nucleic acid
  - Has high mutation rates that continuously change its characteristics
  - Has two surface glycoproteins, hemagglutinin and neuraminidase, both of which occur in several subtypes
  - The virus has a stable reservoir in aquatic birds

INFLUENZA

- Several influenza pandemics have occurred throughout history:
  - 1918 - Spanish flu
  - 1957 - Asian flu
  - 1968 - Hong Kong flu
  - 2009 - Swine flu
- Spanish flu in 1918 was the most devastating, causing an estimated 30-50 million deaths worldwide
AVIAN INFLUENZA

- Avian influenza is potentially the most devastating re-emerging disease in the world today
  - It can be transmitted from animal hosts to humans
  - The pathogen mutates very rapidly
  - It is capable of spreading at an alarming rate
  - Fortunately, it is not yet easily transmitted between humans

- Avian influenza is more deadly than any other form of influenza
  - It could be 10 times more dangerous than the Spanish flu
  - It could have a 50% mortality rate
  - Avian influenza is resistant to amantadine and rimantadine
  - It can be easily transmitted to pigs and can use the pig as an “incubator.”
PRIONS AND PRION DISEASES

- These infectious diseases are not caused by microorganisms
- They are caused by infectious proteins called prions
- Diseases are called transmissible spongiform encephalopathies (TSE)

PRION HYPOTHESIS

- Prions are proteins normally found on nerve cells and are known as PrP<sup>c</sup> (prion protein cellular)
- Infectious prions are folded improperly and are known as PrP<sup>sc</sup> (prion protein scrapie)
  - They are routinely found in scrapie (a neurological disease of sheep)

PRION HYPOTHESIS

- Abnormally folded PrP<sup>sc</sup> prions:
  - Aggregate into fibrous structures in the brain, referred to as a plaque, due to increased hydrophobicity
  - Disrupt the cell membrane, causing cell death
  - Convert normal prions into abnormal prions
**PRION HYPOTHESIS**

- Prions are practically indestructible
  - They can withstand cooking
  - They can withstand autoclaving
  - They are resistant to strong alkali treatment
  - They are resistant to disinfectants
  - They can survive in soil for years
- Inactivation requires autoclaving in an alkali solution (bleach containing 2% chlorine) for one hour

**TSE**

- Infective prions can be ingested with prion-containing material
- These prions can move through the intestinal wall rapidly and enter lymph nodes where they incubate
  - They are picked up by peripheral nerves and moved to the spinal cord and brain
- Infectious prions can be transmitted between species
  - Incubation time is significantly longer when they cross between species
- Prions produce transmissible spongiform encephalitis (TSE)
  - It is a neurodegenerative disease
  - It can affect cattle, humans and other species
  - There is no test for it in live organisms
  - There is no treatment
  - There is no cure
**TSE**

- Symptoms include:
  - Lack of coordination
  - Staggering
  - Slurred speech
  - Dramatic mood swings
  - Paralysis
  - Death within one year of symptom onset

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**TSE**

- Mad cow disease was first seen in Britain in 1986
- The infection in cattle has been attributed to sheep brain supplement included in cattle feed
- First human case documented in Britain was in 1996
  - To date, there have been more than 175 cases documented in humans
- Cases have declined since 2000

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**BIOLOGY OF TSE**

- Biological characteristics of the illness include:
  - Long incubation time
  - Plaque deposits in the brain
  - No antibody response
  - No inflammatory response
There are five forms of this infection seen in humans:

- Kuru
- Creutzfeldt-Jacob disease (CJD)
- Variant CJD (vCJD)
- Gerstmann-Sträussler-Scheinker syndrome (GSS)
- Fatal familial insomnia (FFI)

The different forms affect different areas of the brain.

In the US and other countries there are bans on blood donors who resided in the United Kingdom for three or more months between 1980 and 1996.

- These bans also apply to anyone residing in Europe for five or more years.
- These bans also apply to anyone receiving a blood transfusion in the United Kingdom between 1980 and the present.
WHAT IS BIOTERRORISM?

- The Centers for Disease Control (CDC) in Atlanta defines bioterrorism as:
  - The intentional release of bacteria, viruses, or toxins for the purpose of harming or killing civilians
- The agents of bioterrorism can be found in nature, but may be altered:
  - More effective in causing disease, spreading disease, or resisting treatment

WHAT IS BIOTERRORISM?

- Biological agents appeal to terrorists:
  - They are difficult to detect
  - May not cause disease for hours or days
    - Difficult to trace the illness back to the source
  - Can be spread in a variety of ways, including person-to-person

HISTORY OF BIOTERRORISM

- The use of biological weapons has been around for centuries
  - Intentional contamination of drinking water has occurred throughout history
  - In the Middle Ages, Tartar forces catapulted plague victims into besieged villages
  - Wars of the twentieth century also used biological weapons. Strategies were informed and more directed
BIOLOGICAL WEAPONS

- Bioterrorist attacks aim to cause public panic and social disruption
- A good biological weapon has certain requirements:
  - Can be easily disseminated over a large population
  - Highly contagious so that it will spread quickly
  - Causes high mortality rates
  - Some survivors are necessary so as to transmit the disease
  - Causes disease that will have a significant impact on the resources of the health care system

BIOLOGICAL WEAPONS

- CDC separates bioterrorism agents into three categories based on how easily they can be spread and severity of illness they cause
- Category A agents have the highest priority:
  - Pose greatest risk to national security
  - Easily disseminated with high mortality rates
  - Cause public panic
  - Require special preparations by public health authorities

BIOLOGICAL WEAPONS

- Category B agents:
  - Moderately easy to disseminate
  - Low mortality rates
  - Require increased disease surveillance
- Category C agents:
  - Emerging infectious diseases that could be engineered in future as bioweapons due to
    - Availability
    - Ease of dissemination
    - High mortality rates
ANTHRAX

- Three routes by which anthrax can infect the body:
  - Skin – cutaneous anthrax
  - Digestive tract – gastrointestinal anthrax
  - Inhalation – inhalation anthrax

ANTHRAX

- Cutaneous anthrax is the most common form
  - Requires direct contact with *Bacillus anthracis*
  - Infected individual develops localized itching
    - Incubation period of 1 day
  - Papular lesions form and turn into a black eschar
    - 7 - 10 days later
  - Cutaneous anthrax is not considered lethal
    - Easily treated with antibiotics

ANTHRAX

- Gastrointestinal anthrax
  - Contracted after eating undercooked meat or dairy products from infected animals
  - Initial symptoms nausea, vomiting, anorexia, fever, bloody diarrhea, bloody vomit, abdominal pain
    - Incubation period 1-7 days
  - Shock and death occur 2-5 days after symptoms appear
ANTHRAX

- Difficult to infect a large number of individuals through the cutaneous or digestive routes
  - Probably not used by terrorists
- Terrorists would most probably release anthrax by aerosol
  - Cause inhalational anthrax – the rarest and most deadly form

ANTHRAX

- Inhalation anthrax:
  - Incubation period usually 7 days, can be as long as 2 months
  - First develop nonspecific signs and symptoms
  - Mimic much milder infections – fever, nonproductive cough, malaise, fatigue, muscle aches, and chest discomfort
    - Diagnosis of inhalation anthrax could easily be delayed

ANTHRAX

- Inhalation anthrax:
  - Frequently short respite – person seems to be getting better
  - Couple of days later, there is high fever and respiratory distress
  - Without antibiotic or supportive treatment, shock and death ensue in 24-36 hours. Mortality rate can be up to 90%
**ANTHRAX**

- Mass casualties with inhalational anthrax would place enormous strain on the health care system
  - Especially in areas where intensive care beds are in short supply
- Vaccine for all forms of anthrax available to US military personnel
- Even vaccinated patients require antibiotic therapy after exposure

**BOTULISM**

- Five ways botulism can be acquired:
  - Food borne botulism – ingestion of food contaminated by the toxin
  - Infant botulism – spores are ingested and colonize an infant’s gastrointestinal tract
    - Germinate into organisms that produce and release toxin
  - Adult infectious botulism – similar to infant botulism
  - Wound botulism – wound contaminated with *Clostridium botulinum* which then produces toxin
  - Inhalational botulism – if the toxin has been aerosolized and released

**BOTULISM**

- Botulism toxins distributed by bloodstream
  - Blocks the release of acetylcholine at cholinergic receptors
  - Results in a descending paralysis:
    - Begins with the face
    - Progresses to upper and lower extremities
    - Eventually reaches the respiratory muscles
BOTULISM

- All forms of botulism give almost identical neurological symptoms
- Incubation period for botulism from 2 hours to 8 days
  - Most commonly 12 - 36 hours
- Initial symptoms are dry mouth, double vision, difficulty in speaking and swallowing
  - Commonly proceeds to shortness of breath and loss of muscle tone
  - Eventually complete paralysis

- Mortality rate for botulism is 5-10%
- Clinical manifestations vary widely, and botulism is frequently misdiagnosed
- Paralysis can last for weeks or months and requires extensive medical support
- Only treatment is supportive care and administration of antitoxin

- Inhalational botulism most likely form to be used in a bioterrorist attack
  - Not easily detected initially
  - First patients who were maximally affected would not present to a medical facility until a few days after exposure
  - Significant number of patients will require ventilator support
  - Immobilize intensive care units for months
- Botulism toxin makes a good biological agent.
  - Significant morbidity and toll on the health care system
PLAGUE

- Plague is rapidly fatal, highly contagious, and not easily contained
  - *Yersinia pestis* is an excellent bioweapon candidate
- Reservoirs usually rodents
- Vector for transmission is a flea
- Humans become infected by:
  - Being bitten by an infected flea
  - Inhaling respiratory secretions from infected animals
  - Handling infected animal tissues

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PLAGUE

- Three main types of clinical syndrome are associated with plague:
  - Bubonic – most common
  - Septicemic – bacteremia without a bubo
  - Pneumonic – from inhaling microorganisms in an aerosolized form
    - Can also develop secondarily to the hematogenous spread of bubonic plague

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PLAGUE

- Bubonic plague:
  - Incubation period is 2-8 days
  - Sudden onset of fever, chills, weakness, and headache
  - Tender lymphadenopathy in groin, axilla, and neck
  - Buboes develop after hours to days, with rapid deterioration 2-4 days after that (high fever, tachycardia, malaise, headache, vomiting, chills, altered mental status)
  - Estimated mortality rate is 50% without treatment
  - Treatment consists of antibiotics and supportive treatment
PLAGUE

- Septicemic plague:
  - Difficult to diagnose
  - May be no detectable lymph node involvement, no buboes
  - Fever without localized signs or symptoms
  - High concentration of bacteria in blood overwhelms patients
  - Standard treatment includes antibiotics, supportive treatment, often intensive care
  - Without treatment, hypotension and multiorgan failure lead to death

- Pneumonic plague:
  - Incubation period of 1-3 days, rapidly fatal
  - Fever, chills, headache, body pains, weakness, and chest discomfort, sputum production, chest pain, hemoptysis and respiratory. No buboes
  - 100% fatal in 18-24 hours after onset of symptoms without antibiotic treatment
  - Patients are highly contagious (cough!) from the onset
  - Strict respiratory isolation is critical
  - In a bioterrorist attack:
    - Antibiotics for anyone with temperature above 38.5°C or new cough
    - Precautions should be taken to prevent droplet transmission

- World Health Organization studied potential consequences of using plague as a biological weapon
  - Most probably be disseminated in an aerosolized form
  - An outbreak of pneumonic plague
  - Symptoms would initially resemble those of other respiratory illnesses:
    - Crowded emergency departments have the potential to infect dozens of individuals
  - Health care professionals would not initially think of pneumonic plague as natural occurrence is so rare
  - Patients would most probably be treated for simple respiratory infection and continue to infect others until properly treated
SMALLPOX

- Virus migrates from respiratory tract to nearby lymph nodes
  - Asymptomatic viremia develops
- Virions move to the spleen, bone marrow, and other lymph nodes
  - Virions replicate
- Secondary viremia develops
  - Signs and symptoms appear

SMALLPOX

- Incubation period typically 12-14 days
- Initial signs and symptoms are fever, malaise, and headache and a maculopapular rash begins
- Oral lesions form vesicles and break down
  - Large numbers of virions are released
  - Infectivity is at its greatest
- 2 or 3 days later, rash becomes vesicular and pustular
- 6-9 days later, crusts form over pustules, followed by scabs and scarring
- Death is caused by hypotension and multiorgan failure usually during the second week

SMALLPOX

- Last documented case in Somalia in 1977
- Vaccinations ceased in 1980
- Virus stocks are kept in Moscow and at the CDC in Atlanta
- Before 1972 every US child received a smallpox vaccination.
  - Vaccine does not confer lifelong immunity
  - Adults who were vaccinated as children are probably no longer protected
  - Characteristic vaccination scar (skin is broken with a bifurcated needle)
  - Vaccination within 4 days of exposure may prevent or decrease effects of disease
  - Only other treatment is supportive care
**SMALLPOX**

- If used as a bioterrorist agent, smallpox virus would most probably be aerosolized
- Long incubation period makes smallpox an attractive bioweapon
  - Many humans could be infected before detection of the virus
- Very few individuals have immunity against smallpox
  - Attack would require administering the limited amount of vaccine to thousands of exposed individuals
  - Task would prove difficult after an attack
- Initial diagnosis is critical

**TULAREMIA**

- Humans infected by:
  - Bite of an infected animal or through vectors such as ticks and deerflies carrying *Francisella tularensis*
  - Ingestion or inhalation of the pathogen
- Tularemia gives several clinical syndromes
  - 60-80% of cases are ulceroglandular
    - Incubation period is 2-5 days
    - Abrupt onset of fever, chills, malaise, sore throat, and headache
- If route of infection is through the skin or mucous membranes, primary ulcer develops
- Ulcer begins as a solitary papule that changes to a pustule with surrounding inflammation
- In 30-40% of cases lymph node enlargement occurs with suppuration without antibiotics treatment within 7-10 days
- If pathogen is inhaled, signs and symptoms are variable and resemble those of less threatening infections
- Severity of symptoms depends on the subspecies of the infecting *F. tularensis*
TULAREMIA

- *Francisella tularensis* subspecies *tularensis* is the most likely subspecies to be used as a bioweapon through aerosolization
  - Causes fever, lymph node enlargement, dry cough, and retrosternal pain
  - Carries a 30% mortality rate if left untreated
  - Takes just 10-50 bacteria to cause disease
- Spread of tularemia would quickly overwhelm health care communities

VIRAL HEMORRHAGIC FEVERS

- Principal sign of a hemorrhagic fever is hemorrhaging of capillaries of the patient’s circulatory system
- At least 18 viruses cause human hemorrhagic fevers
- Several of these listed as Category A agents
  - Ebola and Marburg – filoviruses
  - Lassa and Machupo – arenaviruses
- Aerosolizing produces a high infectivity rate in nonhuman primates
- No known incident in which these viruses have been used in a biological attack

VIRAL HEMORRHAGIC FEVERS

- Treatment of viral hemorrhagic fevers is mainly supportive
  - Patients should be handled with great care to prevent bleeding
  - Only one specific antiviral therapy has potential for a few viruses – ribavirin
  - Only vaccine for viral hemorrhagic fevers is for yellow fever. There are candidate Ebola vaccines
VIRAL HEMORRHAGIC FEVERS

- Infected individuals should be isolated
  - Virus is transmissible through close contact
- Respiratory isolation is ideal
  - May not be possible in large outbreak
- Contact barrier precautions are essential to prevent spread of the disease

PROBABILITY & EFFECTS OF A BIOLOGICAL ATTACK

- Bioweapons are cheaper to produce than chemical weapons.
- They can cause mass destruction
- Several countries have established bioweapons programs
- Individuals who possess knowledge of genetic engineering could alter simple biological agents to make them more virulent and resistant to antibiotics

PROBABILITY & EFFECTS OF A BIOLOGICAL ATTACK

- Biggest consequence of a bioterrorist attack may be not the physical causalities but the psychological impact
- Just a few causalities could cause mass panic and alarm
- This would disrupt communities, health care systems, and government
PROBABILITY & EFFECTS OF A BIOLOGICAL ATTACK
- Initial symptoms may not lead health care providers to suspect bioterrorism
  - Proper precautions may not be used at first
  - Potentially increases number of people exposed and infected
- Majority of any population is susceptible to infection with a Category A agent
  - A few initial exposures could quickly turn into mass casualties
  - Especially when infection is one that can be transferred through human contact

WARNING SIGNS
- In any location hit by a bioterrorism act, the public health system will probably be first to detect and respond
- May not be realistic to wait for confirmation of diagnosis
- Emergency response may need to be activated on basis of patterns and timing of patient presentation
- Preparation is the key to controlling the effects of a bioterrorist attack
- Bioterrorism is a matter of national and international security