



# Emerging Infectious Diseases: A Global Perspective

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### Disclosures

- I have no financial relationships to disclose.
- I will not discuss off-label use and/or investigational use in my presentation.
- Slides provided by various sources including CDC, WHO, and AETC

#### **Globalization and Infectious Diseases**

- Globalization is a complex and multi-faceted set of processes having diverse and widespread impacts on human societies worldwide
- Globalization is driven and constrained by a number of forces:
  - Economic processes
  - Technological developments
  - Political influences
  - Cultural and value systems, and social and natural environmental factors

### Globalization and Infectious Diseases



- Globalization has led to profound, unpredictable, changes in the ecological, biological and social conditions that shape the burden of infectious diseases
- There is accumulating evidence that changes in these conditions have led to alterations in the prevalence, spread, geographical range, and control of many infections, particularly those transmitted by vectors

#### **Globalization and Infectious Diseases**



# **Contributing Factors**



- International travel and commerce
- Changes in food processing and handling
- Evolution of pathogenic infectious agents
- Development of multi-drug resistant organisms
- Resistance of the vectors
- Immunosuppression
- Deterioration of surveillance systems
- Illiteracy
- Political changes, war, civil unrest, bio-warfare, and famine

#### Bioterrorism categories



- Bioterrorism categories, is a classification system developed by the Center of Disease Control (CDC) to better prepare for, respond to and recover from incidents involving biological agents
- These categories are based on how easily they are spread and the severity of the illness or death they cause
- Category A is considered the highest risk and Category C are those that are considered emerging threats for disease

Category	А	В	С
Definition	<ul> <li>Pose the highest risk to national security because they</li> <li>Can be easily disseminated or transmitted from person to person</li> <li>Result in high mortality rates</li> <li>Have potential to cause public panic and social disruption</li> <li>Require special preparedness actions</li> </ul>	<ul> <li>Pose the second highest risk because they</li> <li>Are moderately easy to disseminate</li> <li>Result in low mortality rates</li> <li>Require enhancement of diagnostic and surveillance capability</li> </ul>	Emerging pathogens that could be engineered for mass dissemination because they: • Are available • Are easily produced and disseminated • Have potential for high mortality rates
Examples	<ul> <li>Anthrax</li> <li>Botulism</li> <li>Plague</li> <li><u>Smallpox</u></li> <li><u>Tularemia</u></li> <li>Viral hemorrhagic fevers (e.g. <u>Ebola</u>, Marburg)</li> </ul>	<ul> <li>West Nile Virus</li> <li><u>Caliciviruses</u></li> <li>Hepatitis A</li> <li>Ricin toxin</li> <li>Salmonella</li> <li>Diarrheagenic E. coli</li> </ul>	<ul> <li>Influenza</li> <li>SARS</li> <li>Rabies</li> <li>Multi-drug resistant tuberculosis</li> <li>Yellow fever</li> <li>Tickborne hemorrhagic fever</li> </ul>

**REVIEW ARTICLE** 

Dan L. Longo, M.D., Editor

#### Clinical Management of Potential Bioterrorism-Related Conditions

Amesh A. Adalja, M.D., Eric Toner, M.D., and Thomas V. Inglesby, M.D.

Condition	Contagious	Clinical Form or Forms	Vaccine Available	Treatment
Anthrax	No	Three primary forms: cutaneous, in- halational, 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

N ENGL J MED 372;10 NEJM.ORG MARCH 5, 2015





#### Human pathogen transmission

Infection caused by airborne transmission

## Transmission?

Infection caused by contact and faeces

Infection caused by pathogens in bloodstream and tissues

# **Modes of Transmission**

- Direct Transmission
  - Direct Contact
  - Droplet
- Indirect Transmission
  - Vehicle-borne
  - Vector-borne
  - Airborne
- Vertical Transmission

# Transmission of Infections by Respiratory Aerosols

- Droplets: >5 μm in diameter and transmitted only over a limited distance. Droplets can be deposited on the nasal mucosa, conjunctivae or mouth
  - Highest exposures within 3-6 feet
- Airborne: aerosols become smaller by evaporation; small aerosols (≤ 10 microns) remain suspended for longer periods
- Contact: Aerosols/ secretions contaminate nearby surface.
   Touch surfaces → can infect self or others



VIRUS AND BACTERIAL TRANSMISSION

Ian M Mackay, PhD v6 15-Aug-2014 virologydownunder.blogspot.com.au

# Modes of Transmission via Infectious Respiratory Secretions

- Airborne: Tuberculosis, measles, varicella, SARS, MERS-CoV
- Droplet:
  - Respiratory viruses (Influenza, adenovirus, respiratory syncytial virus, human metapneumovirus)
  - Bordetella pertusis
  - For first 24 hours of therapy: Neisseria meningitides, group
     A streptococcus

# Preparing Public health Agencies for Biological Attacks

**Steps in Preparing for Biological Attacks:** 

- Enhance epidemiologic capacity to detect and respond to biological attacks
- Supply diagnostic reagents to state and local public health agencies
- Establish communication programs to ensure delivery of accurate information
- Enhance bioterrorism-related education and training for health-care professionals

# Preparing Public Health Agencies for Biological Attacks

- Prepare educational materials to inform and reassure the public during and after a biological attack
- Stockpile appropriate vaccines and drugs
- Establish molecular surveillance for microbial strains, including unusual or drug- resistant strains
- Support the development of diagnostic tests
- Encourage research on antiviral drugs and vaccines





Arizona Health Sciences Center

#### UAHN Named Ebola Treatment Center by CDC

Ebola drill at UAMC on Nov. 21.



The U.S. Centers for Disease Control and Prevention has named the <u>University</u> of Arizona Health Network one of 55 Ebola Treatment Centers in the United States. The Maricopa Integrated Health System in Phoenix also was named.





# Epidemiology

- Ebola viruses are found in several Sub-Saharan African countries
- Ebola was first discovered in 1976 near the Ebola River in what is now the Democratic Republic of the Congo (DRC)
- 1976 2013, the WHO reported 1,716 cases









- 1976 DRC, 318 cases and 280 (88%) deaths
- First recognition of the disease





As of 29 October 2014, 13,676 suspected cases and 4,910 deaths had been reported



**Total Cases** 

1

United States

21 - 100

Hospital

# **Ebola Cases (United States)**

- Four U.S. health workers and one journalist who were infected with Ebola virus in West Africa were transported to hospitals in the United States for care
  - All the patients recovered and were released from the hospital after laboratory testing confirmed that they no longer had Ebola virus in their blood





# **Ebola Virus Transmission**



- Ebola has been detected in blood, saliva, mucus, vomit, feces, sweat, tears, breast milk, urine, and semen
- Human-to-human transmission of Ebola virus via inhalation (aerosols) has not been demonstrated

# **Ebola Virus Transmission**

- Direct contact (through broken skin or unprotected mucous membranes) with an EVD-infected patient's blood or body fluids
- Sharps injury
- Direct contact with the corpse of an infected person
- Indirect contact with an EVD-infected patient's blood or body fluids via a contaminated object (soiled linens or used utensils)
- Sexual intercourse

### Treatment



- Nucleotide Prodrug GS-5734 is a Filovirus inhibitor that provides therapeutic protection against the development of EVD in Infected Non-human Primates
- GS-5734 inhibits Ebola virus, Sudan, and Marburg virus, and exhibits low cytotoxicity in multiple human cells
- Treatment of infected monkeys after systemic viremia (Day 2 to 4) resulted in 50% survival compared to no survival in placebo-treated arm (P < 0.003)</li>

#### Treatment



- Administration of GS-5734 10 mg/kg IV initiated on Day 3 was associated with 100% survival, and a profound suppression of EVD signs including thrombocytopenia, coagulopathy and serum chemistry alterations
- Neither brincidofovir nor favipiravir have been approved to treat Ebola
- In January 2015, the manufacturer of brincidofovir decided to withdraw support for the trial and end discussion of future trials

## Vaccines

- Numerous Ebola virus vaccine candidates are in preclinical development, and some have proceeded to human trials
- An Ebola virus vaccine candidate based on an attenuated, replication-competent, recombinant vesicular stomatitis virus (rVSV) has shown great promise in preclinical studies



- Marburg virus Disease (MVD) formerly known as Marburg Hemorrhagic Fever is a genetically unique zoonotic RNA virus of the filovirus that causes a severe hemorrhagic infection
- It was first identified in 1967 during epidemics in Marburg and Frankfurt
- The five species of Ebola virus are the only other known members of the filovirus family



#### 7 deaths reported

The first people infected had been exposed to imported African green monkeys while conducting research

- Early infection is virtually indistinguishable from other systemic infections with an incubation period of 3-10 days
- Clinical presentation includes fever, headaches, and myalgia in 5-7 days; later, hemorrhagic signs appear with a case fatality of 25- 80%
- Early physical examination is often not revealing because findings are related to underlying organ dysfunction and are not pathognomonic of Ebola or MHF





- Appearance of a rash between days 5 and 7 can be a helpful differentiating factor
- It has been described as an initially pinpoint rash in central intertriginous areas that spreads outward and evolves into a maculopapular rash

- Diagnosis: Polymerase chain reaction (PCR), IgG BY enzyme-linked immunosorbent assay (ELISA), IgM ELISA, antigen detection by ELISA
- Electron microscopy is useful in diagnosing filovirus infections in general
- There are not yet any approved treatments for Ebola or MVD
- Recommend supportive therapy

# Anthrax

- A total of 22 anthrax cases and 5 deaths occurred where anthrax spores were sent through the U.S. mail in 2001
- *Bacillus anthracis* the agent of Anthrax is a spore-forming, exotoxin-producing, gram positive bacillus
- The four human forms of anthrax include:
  - Cutaneous
  - Gastrointestinal
  - Inhalational
  - Injectional



# Anthrax

The four human forms of anthrax include:

- Cutaneous
- Gastrointestinal
- Inhalational
- Injectional








- Incubation period: 24 hours to 6 weeks
- Clinical Manifestations:
  - Early: Influenza-like symptoms
  - Late: Fever, Shock, Respiratory failure (ARDS),
    Hemorrhagic mediastinitis, toxin-laden pleural and pericardial effusions, hemorrhagic meningitis
- Diagnosis: Routine Blood cultures, cultures from affected sites, and PCR

- Treatment: In the setting of bioterrorism, duration of therapy is 60 days (full incubation period)
- Meningitis: A fluoroquinolone, a drug that inhibits protein synthesis, such as linezolid; and drugs that penetrate the CNS such as carbapenems
- Two-drug regimen: A fluoroquinolone plus linezolid or clindamycin

- Raxibacumab: FDA-approved monoclonal antibody targeted at the protective antigen component of the toxins (single dose)
- Anthrax immune globulin
- Drainage of are toxin-laden pleural effusions, ascites, and pericardial effusions
- Infection Control: Standard Precautions

- Anthrax vaccine adsorbed (AVA) is the FDA-licensed vaccine used for the prevention of anthrax (includes post exposure prophylaxis)
- Vaccination for post exposure prophylaxis: (ciprofloxacin and doxycycline)



#### Smallpox



- Infectious Route: Droplet or aerosol exposure
- Incubation Period: 10- 14 days
- Clinical Manifestations:
  - Prodrome of fever and constitutional symptoms
  - Rash (1 to 4 days) after the onset of fever
- Rash is centrifugal, with lesions progressing synchronously from macules to papules to umbilicated vesicles to pustules to scabs over 2 weeks



## Smallpox

- Diagnosis: Serologic testing, cell culture, PCR, or electron microscopy
- A single case is a public health emergency, requiring immediate notification of the CDC
- Treatment: There are currently no FDA-licensed treatments
- Tecovirimat and liposomal cidofovir in development

## Smallpox

- ACAM2000 vaccine (Sanofi Pasteur Biologics), Jenner vaccine (vaccinia), administered in a single percutaneous dose
- Post exposure vaccination after exposure but before the rash





#### Middle East Respiratory Syndrome Coronavirus (MERS-CoV)



- Middle East respiratory syndrome (MERS) is a viral respiratory disease caused by a novel coronavirus (MERS-CoV), first identified in Saudi Arabia in 2012
- The virus has circulated throughout the Arabian Peninsula, primarily in Saudi Arabia, where the majority of cases (>85%) have been reported

#### Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

- Most infections are believed to have been acquired in the Middle East, and then exported outside the region
- The outbreak in the Republic of Korea was the largest outbreak outside of the Middle East with no evidence of sustained human to human transmission in the Republic of Korea





#### **CONFIRMED CASES OF MIDDLE EAST RESPIRATORY SYNDROME - CORONAVIRUS 2012 - 2015**

MAP DATE: 09 October



Number of cases reported in previous years



Map Scale (A3): 1:73,252,234 1 cm = 733 km Coordinate System: GCS WGS 1984 Detum: WGS 1984 Lhits: Degree

2 - 5 6 - 20 21 - 136

137 - 679



2012

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

#### Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

- Clinical Presentation: Asymptomatic or mild respiratory symptoms to severe acute respiratory disease and death
- Common Symptoms: Fever, cough and shortness of breath
- Pneumonia is a common and gastrointestinal symptoms, including diarrhea, have been reported
- Approximately 36% of reported patients with MERS-CoV have died



## Middle East respiratory syndrome coronavirus (MERS-CoV)

- Source: Zoonotic virus, transmitted from animals to humans
- The origins of the virus are not fully elucidated, however; it likely originated in bats and later transmitted to camels
- Transmission: Camels are likely a major reservoir host for MERS-CoV and an animal source of infection in humans
- The virus does not appear to pass easily from person to person unless there is close contact



Lindsay Lohan @lindsaylohan · Dec 29

In good faith with good people. I refuse to let a virus effect my peaceful vacation 🙏



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51 % 🔳

#### Lindsay Lohan Battling Untreata... m.usmagazine.com





#### 4 FREE ISSUES!



#### **CELEBRITY NEWS**

Lindsay Lohan Suffering From Rare, Untreatable Virus During Holiday Vacation, Urges Fans to Use Bug Spray --Details

CELEBRITY NEWS DEC 30, 2014 AT 7:30PM BY SIERRA MARQUINA





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Morbidity and Mortality Weekly Report

December 5, 2014

Transmission of Chikungunya Virus in the Continental United States — Florida, 2014

Katherine Kendrick, MPH<sup>1</sup>, Danielle Stanek, DVM<sup>1</sup>, Carina Blackmore, DVM, PhD<sup>1</sup> (Author affiliations at end of text)

 Since the first case of locally acquired chikungunya virus infection in the Americas was reported on the Caribbean island of St. Martin in December 2013, the United States has seen an increase in chikungunya cases among travelers returning from new endemic regions, particularly the Caribbean and South America

## Chikungunya

- Following its discovery in 1952, following an outbreak on the Makonde Plateau (border area between Mozambique and Tanzania) the first documented CHIKV emergence spread to generate urban outbreaks in India and Southeast Asia
- The mosquito-borne chikungunya virus (CHIKV; *Togaviridae*: *Alphavirus*) causes a febrile illness typically accompanied by rash and severe, debilitating arthralgias
- The name chikungunya is derived from the Makonde word meaning "that which bends up" in reference to the stooped posture developed as a result of the arthritic symptoms of the disease

Figure 1. Map showing the distribution of chikungunya virus enzootic strains in Africa and the emergence and spread of the Asian lineage (red arrows and dots) and the Indian Ocean lineage (yellow arrows and dots) from Africa.



Weaver SC (2014) Arrival of Chikungunya Virus in the New World: Prospects for Spread and Impact on Public Health. PLoS Negl Trop Dis 8(6): e2921. doi:10.1371/journal.pntd.0002921 http://127.0.0.1:8081/plosntds/article?id=info:doi/10.1371/journal.pntd.0002921



## **Epidemiology and Transmission**

Chikungunya is spread through bites from
 Aedes aegypti mosquitos

 The strain associated with the Reunion Island outbreak (2005 - 2006) carried a muation that led to its facilitated transmission by *Aedes albopticus* (Tiger mosquito)

#### Approximate distribution of Aedes aegypti in the United States\*



\*This map was developed using currently available information. Aedes aegypti mosquito populations (a known vector of chikungunya) may be detected in areas not shaded on this map, and may not be consistently found in all shaded areas. The shaded areas are NOT locations of chikungunya transmission.

#### Approximate distribution of Aedes albopictus in the United States\*



\*This map was developed using currently available information. Aedes albopictus mosquito populations (a known vector of chikungunya) may be detected in areas not shaded on this map, and may not be consistently found in all shaded areas. The shaded areas are NOT locations of chikungunya transmission.

#### Chikungunya

• Incubation period: 2-6 days

#### Acute phase

- Typically lasts from a few days to 2 weeks
- Fever 40 °C (104 °F), vomiting, headache, arthralgia, and in some cases, maculopapular rash
- Severe joint and myalgia is the main and most problematic symptom
- Clinical laboratory findings include lymphopenia, thrombocytopenia, elevated creatinine, and elevated hepatic transaminases





#### Artritis aguda por CHIKV



Figure 1 Acute arthritis involving wrist and interphalangeal joints in a patient with Chikungunya infection. (Color version

## Chikungunya

#### Chronic phase

- characterized by polyarthralgias lasting from weeks to years
- 95% of infected adults are symptomatic after infection, and most become disabled for weeks to months due to decreased dexterity and loss of mobility
- Recurrent joint pain is experienced by 30–40%
- Rare but serious complications include myocarditis, meningoencephalitis, myelitis, Guillain-Barré syndrome, and cranial nerve palsies, nephritis, hepatitis, uveitis, and retinitis
- Death appears to be rare



- Joints affected include hands (50 -76%), wrists (29 81%), and ankles (41 - 68%)
- Arthralgia is symmetrical in 64 73% and involves distal joints more often. Involvement of the axial skeleton was noted in 34 -52% of cases
- Chronic inflammatory, erosive and rarely deforming polyarthritis does occur in 5.6% of cases
- It is seronegative and Anti-CCP positive in majority

## Diagnosis of Chikungunya

- Confirmed by the detection of the virus, viral RNA, or specific antibodies in patient samples
- Reverse transcriptase-polymerase chain reaction (RT-PCR) from patients during the acute phase of infection
- ELISA detects both anti-CHIKV immunoglobulin IgM and IgG from either acute- or convalescent-phase samples.
- Serological diagnosis requires a larger amount of blood than the other methods

## Treatment of Chikungunya

- There are no specific treatments nor vaccines for chikungunya
- Chikungunya is treated symptomatically with bed rest, fluids, and non-steroidal anti-inflammatory drugs (NSAIDs) to relieve acute pain and fever
- Persistent joint pain may benefit from use of NSAIDs, corticosteroids, or physiotherapy

#### Prevention

## GOING TO THE CARIBBEAN?

MOSQUITOES

spread diseases such as CHIKUNGUNYA and DENGUE.

Mosquitoes bite during the day and night.



Protect yourself by preventing mosquito bites.

#### DON'T LET MOSQUITOES RUIN YOUR TRIP.

For more information: call 800-CDC-INFO (232-4636) or visit www.cdc.gov/travel.



5. Department of saith and Human Servis inters for Disease ontrol and Prevention



# Infection Control Policies and Procedures. Should be supported by an authoritative source



#### CENTERS FOR DISEASE" CONTROL AND PREVENTION







U.S. Food and Drug Administration



## **The Chain of Infection**



#### Preventing and Treating human Infections

To prevent infection, *interrupt transmission of an infectious agent by*:

- Eliminating sites where pathogens, vectors, or intermediate hosts proliferate
- Reducing human exposure to pathogens or vectors through:
  - Regulating the natural and built environment and/or trade
  - Using protective equipment
  - Using chemoprophylaxis and vaccine development
  - Modifying behavior (e.g. not engaging in unprotected sex to prevent HIV/AIDS)
- Isolating and treating infected cases (human or animal) to prevent them from spreading the infection to others (e.g. identifying and treating TB cases as soon as possible to

#### Preventing and Treating human Infections

- Increasing human immunity to pathogens through vaccination programs
- To treat established infections, control multiplication of a pathogen in an infected person by:
  - Administering chemotherapy to kill pathogens
  - Using surgery or medical treatment to remove any continued source of infection, such as an abscess
  - Providing supportive treatment to enhance a person's ability to destroy the pathogen
  - Using his/her natural immunity to infectious agents
  - New drug development

#### Preventing and Treating human Infections

- Decrease inappropriate drug use
- Improved and widespread health eduction
- Development of low cost health technology
- Increased research
- Elimination of poverty

SO HERE WE GO VIRUSES. AND DON'T FORGET: SPREAD IMMEDIATELY AFTER LANDING, MULTIPLY AND CAUSE INFECTIONS.

do?

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LAST

MINUTE

BAGS

FRANKFURT