Emerging Infectious Disease Threats
Influenza A, Dengue Fever, Chikungunya Fever, and Ebola

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Disclosures
Edward A. Dominguez, MD

- Research
  - Cubist
  - Durata

- Consultancy
  - Pfizer
  - Activis
  - Astellas
  - Merck
What I hope to achieve...

- Influenza A
  - Seasonal and pandemic
  - Treatment
  - Vaccines
- Dengue and Chikungunya
  - Epidemiology
  - Diagnosis
  - Prevention
- Ebola
Influenza Viruses

- RNA virus
- *Orthomyxoviridae* family
- Types A, B or C based on antigenic differences of their nucleo- and matrix proteins
- Avian influenza viruses (AIV) belong to type A
- On the basis of the antigenicity of these glycoproteins, influenza A viruses currently cluster into *sixteen H* (H1 - H16) and *nine N* (N1 - N9) subtypes.
Circulating Influenza Viruses

- Seasonal influenza
  - A(H3N2), A(H1N1), B
- Avian influenza (‘bird flu’)
  - A(H5 and H7, e.g. HPAI H5N1)
- Swine influenza (‘swine flu’) -> variant flu
  - A(H1N1v) - 2009 pandemic strain
  - A(H3N2v) – 2011-2012 US strain
US Influenza Activity, 2013-2014

Influenza Positive Tests Reported to CDC by U.S. WHO/NREVSS Collaborating Laboratories, National Summary, 2014-15

http://www.cdc.gov/flu/weekly/
Avian InfluenzaViruses

Kaye and Pringle 2005
Virologic Diagnosis

- Culture
- Antigen detection (Rapid tests, ELISA, IFA)
- RT-PCR
- Serology

- All studies more likely to be positive if collected in first 3 days of illness
## Influenza Virus Testing Methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Acceptable Specimens</th>
<th>Test Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral cell culture (conventional)</td>
<td>NP swab, throat swab, NP or bronchial wash, nasal or endotracheal aspirate, sputum</td>
<td>3-10 days</td>
</tr>
<tr>
<td>Rapid cell culture (shell vials; cell mixtures)</td>
<td>As above</td>
<td>1-3 days</td>
</tr>
<tr>
<td>Immunofluorescence, Direct (DFA) or Indirect (IFA) Antibody Staining</td>
<td>NP swab or wash, bronchial wash, nasal or endotracheal aspirate</td>
<td>1-4 hours</td>
</tr>
<tr>
<td>RT-PCR (singleplex and multiplex; real-time and other RNA-based) and other molecular assays</td>
<td>NP swab, throat swab, NP or bronchial wash, nasal or endotracheal aspirate, sputum</td>
<td>1-6 hours</td>
</tr>
<tr>
<td>Rapid Influenza Diagnostic Tests (antigen)</td>
<td>NP swab, (throat swab), nasal wash, nasal aspirate</td>
<td>&lt;30 min.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antiviral Agent</th>
<th>Activity Against</th>
<th>Use</th>
<th>FDA Approved For</th>
<th>Not Recommended for Use in</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oseltamivir (Tamiflu®)</td>
<td>Influenza A and B</td>
<td>Treatment</td>
<td>2 wks and older</td>
<td>N/A</td>
<td>Adverse events: nausea, vomiting. Sporadic, transient neuropsychiatric events (self injury or delirium) mainly reported among Japanese adolescents and adults.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chemoprophylaxis</td>
<td>1 yr and older</td>
<td>N/A</td>
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</tr>
<tr>
<td>Zanamivir (Relenza®)</td>
<td>Influenza A and B</td>
<td>Treatment</td>
<td>7 yrs and older</td>
<td>people with underlying respiratory disease (e.g., asthma, COPD)</td>
<td>Allergic reactions: oropharyngeal or facial edema. Adverse events: diarrhea, nausea, sinusitis, nasal signs and symptoms, bronchitis, cough, headache, dizziness, and ear, nose and throat infections.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chemoprophylaxis</td>
<td>5 yrs and older</td>
<td>people with underlying respiratory disease (e.g., asthma, COPD)</td>
<td></td>
</tr>
<tr>
<td>Vaccine</td>
<td>Trade name</td>
<td>Manufacturer</td>
<td>Presentation</td>
<td>Mercury content (µg Hg per 0.5 mL dose)</td>
<td>Ovalbumin content (µg per 0.5 mL dose)†</td>
</tr>
<tr>
<td>----------------</td>
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<td>----------------------------------------</td>
</tr>
<tr>
<td>TIV</td>
<td>Fluzone</td>
<td>Sanofi Pasteur</td>
<td>0.25 mL prefilled syringe</td>
<td>0.0</td>
<td>–5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.5 mL prefilled syringe</td>
<td>0.0</td>
<td>–5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.5 mL vial</td>
<td>0.0</td>
<td>–5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5.0 mL multidose vial</td>
<td>25.0</td>
<td>–5</td>
</tr>
<tr>
<td>TIV</td>
<td>Agriflu****</td>
<td>Novartis Vaccines</td>
<td>0.5 mL prefilled syringe</td>
<td>0.0</td>
<td>&lt;0.4</td>
</tr>
<tr>
<td>TIV</td>
<td>Fluvirin</td>
<td>Novartis Vaccines</td>
<td>0.5 mL prefilled syringe</td>
<td>≤1</td>
<td>≤1</td>
</tr>
<tr>
<td>TIV</td>
<td>Fluarix</td>
<td>GlaxoSmithKline</td>
<td>0.5 mL prefilled syringe</td>
<td>0.0</td>
<td>≤0.05</td>
</tr>
<tr>
<td>TIV</td>
<td>FluLaval</td>
<td>ID Biomedical Corporation of Quebec (distributed by GlaxoSmithKline)</td>
<td>5.0 mL multidose vial</td>
<td>&lt;25.0</td>
<td>≤0.3</td>
</tr>
<tr>
<td>TIV</td>
<td>Afluria</td>
<td>CSL Biotherapies (distributed by Merck)</td>
<td>0.5 mL prefilled syringe</td>
<td>0.0</td>
<td>≤1</td>
</tr>
<tr>
<td>TIV high-dose§§</td>
<td>Fluzone High-Dose</td>
<td>Sanofi Pasteur</td>
<td>0.5 mL prefilled syringe</td>
<td>0.0</td>
<td>–5</td>
</tr>
<tr>
<td>TIV intradermal§§</td>
<td>Fluzone Intradermal</td>
<td>Sanofi Pasteur</td>
<td>0.1 mL prefilled microinjection system</td>
<td>0.0 (per 0.1 mL)</td>
<td>–5</td>
</tr>
<tr>
<td>LAIV</td>
<td>FluMist****</td>
<td>MedImmune</td>
<td>0.2 mL prefilled intranasal sprayer</td>
<td>0.0 (per 0.2 mL)</td>
<td>&lt;0.24 (per 0.2 mL)†††</td>
</tr>
<tr>
<td>Quadrivalent Vaccines</td>
<td>Manufacturer</td>
<td>Format</td>
<td>Age Group</td>
<td>Route</td>
<td></td>
</tr>
<tr>
<td>-------------------------------</td>
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<td></td>
</tr>
<tr>
<td><strong>Fluarix Quadrivalent</strong></td>
<td>GlaxoSmithKline</td>
<td>0.5 mL single-dose prefilled syringe</td>
<td>≥3 yrs</td>
<td>IM</td>
<td></td>
</tr>
<tr>
<td><strong>FluLaval Quadrivalent</strong></td>
<td>ID Biomedical Corp (distributed by GSK)</td>
<td>0.5 mL single-dose prefilled syringe</td>
<td>≥3 yrs</td>
<td>IM</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL multidose vial</td>
<td>&lt;25</td>
<td>IM</td>
<td></td>
</tr>
<tr>
<td><strong>Fluzone Quadrivalent</strong></td>
<td>Sanofi Pasteur</td>
<td>0.25 mL single-dose prefilled syringe</td>
<td>6–35 mos</td>
<td>IM</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 mL single-dose prefilled syringe</td>
<td>≥36 mos</td>
<td>IM</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 mL single-dose vial</td>
<td>≥36 mos</td>
<td>IM</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.0 mL multidose vial</td>
<td>≥6 mos</td>
<td>IM</td>
<td></td>
</tr>
</tbody>
</table>
## Novel Vaccine Options

<table>
<thead>
<tr>
<th>Vaccine/Type</th>
<th>Manufacturer</th>
<th>Formulation/Volume</th>
<th>Age</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flucelvax ccIIIV3 (dog cell culture)</td>
<td>Novartis</td>
<td>0.5 mL single-dose prefilled syringe</td>
<td>≥18 yrs</td>
<td>IM</td>
</tr>
<tr>
<td>Flublok RIV4 (recominant)</td>
<td>Protein Sciences</td>
<td>0.5 mL single-dose vial</td>
<td>≥18 yrs</td>
<td>IM</td>
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<tr>
<td>FluMist LAIV4</td>
<td>MedImmune</td>
<td>0.2 mL single-dose prefilled nasal sprayer</td>
<td>2-49 yrs</td>
<td>IN</td>
</tr>
<tr>
<td>FluZone High-Dose IIIV3</td>
<td>Sanofi Pasteur</td>
<td>0.5 mL single-dose prefilled syringe</td>
<td>≥65 yrs</td>
<td>IM</td>
</tr>
</tbody>
</table>
Dengue Fever

- Virology
- Epidemiology
  - Transmission
- Clinical syndromes
- Diagnosis
- Management and Prevention
Dengue Fever

- Family: *Flaviviridae*
- Genus: *Flavivirus*
- 5 Serotypes, all cause disease
  - No cross-protection between types
- An *old* disease
  - Jin Dynasty, 265-420 AD
  - Pandemic, 1779-80
  - Severe form first reported in Philippines, 1953
Dengue Fever

- Over 400 million infected annually
- Transmitted from person to person via mosquito is major route
- *Aedes aegypti* and *Aedes albopictus* species
  - Ubiquitous
  - Feed during day as well as dusk and dawn
- Other transmission routes are rare:
  - Vertical transmission
  - Blood product transfusion
- Donor-derived organ transmission
Aedes Mosquitoes

- Appearance
  - Black and white stripes
- Flies dusk till dawn
  - Short flights, e.g. house to house
- Dayfeeder
- Bite often asymptomatic
Dengue Syndromes

- Dengue fever
  - “Breakbone fever”
  - Incubation range 2-15 d
  - Bimodal fever
  - Maculopapular rash 3-4 d
- Dengue hemorrhagic fever (DHF)
- Dengue shock syndrome (DSS)
Differential Diagnosis

- Influenza
- Measles
- Rubella
- Leptospirosis
- Meningococcemia
- Rickettsial infections (e.g. RMSF)
- Bacterial sepsis
- Malaria
- Chikungunya fever
- Typhoid fever
- Other hemorrhagic fevers (e.g. Ebola)
Tourniquet Test

- Inflate BP cuff to pressure roughly halfway between SBP and DBP for 5 minutes
- **POSITIVE:**
  - > 20 petechiae per sq. in (6.25 cm²)
Dengue Fever: Diagnosis


- Laboratory diagnosis:
  - RT-PCR
  - IgM MAC-ELISA (may be positive with other flaviviruses like WNV)

- **EARLY DIAGNOSIS** can decrease case mortality from 10% to < 0.1%
Dengue Hemorrhagic Fever

Note: DHF develops 24-48 hours after defervescence
Dengue Fever: Treatment and Prevention

- **Treatment**
  - Symptomatic treatment alone
  - No antiviral available
  - **Fluid management critical to survival**

- **Prevention**
  - Use mosquito repellent
  - Wear long-loose clothing
  - Drain standing water
  - Vaccine in development for years…
Chikungunya Fever

- Virology
- Epidemiology
  - Transmission
- Clinical syndrome
- Treatment and Prevention
Chikungunya Virus

- Family: *Alphavirus*
- Genus: *Togaviridae*
- Related viruses:
  - O’nyong-nyong (ONN) virus
  - Semliki Forest antigenic complex
- Transmitted from person to person via mosquito
  - Blood-borne transmission not yet reported
  - Vertical transmission reported but very rare
- *Aedes aegypti* and *Aedes albopictus* species
  - Ubiquitous
  - Feed during day as well as dusk and dawn
Chikungunya Virus

- “That which bends up" or "to be contorted" in the Kimakonde language
- First case detected in Tanzania, 1953
- Since 1953, > million cases in Africa and SE Asia
- 2013-14: 1.2 million cases in 44 countries in Western hemisphere
- In US as of March, 2015
  - >2,500 cases, all acquired in travelers (prior average: 28/yr)
  - Local transmission in southern Florida, Puerto Rico, and USVI
Chikungunya Virus in US, 2014

2,492 cases

11 cases

4,467 cases

http://www.cdc.gov/chikungunya/geo/united-states-2014.html
Chikungunya Virus in US, 2015

Chikungunya Fever: Disease

- Incubation time: 3-7 days
- Most exposed people will become symptomatic
- Common:
  - Fever
  - Arthralgias/arthritis
- Less common:
  - Headache
  - Myalgias
  - Rash
- Self-limiting infection, most recover within 7-10 d; rarely fatal
- Severe or chronic disease in elderly, immunosuppressed, chronic medical illnesses including arthritis
- Immunity likely life-long
Chikungunya Fever: Diagnosis, Treatment, and Prevention

- **Diagnosis**
  - Serum or blood serology, sent to State Dept of Health
    - RT-PCR
    - IgM EIA
  - Contact local health department for instructions

- **Treatment**
  - Symptomatic treatment alone
  - No antiviral available

- **Prevention**
  - Use mosquito repellent
  - Wear long-loose clothing
  - Drain standing water
If Lightening Strikes Twice

During the first 5 days of illness
- Serum RT-PCR for CHIKV or DENV nucleic acid

After 5 days of illness
- Serum for anti-CHIKV and anti-DENV IgM antibodies by immunoassay
- If initial results are negative and dengue or chikungunya is still suspected, collect convalescent serum seven days or more after illness onset and retest for anti-CHIKV and anti-DENV IgM antibodies
Ebola Virus Disease CDC Slides for U.S. Healthcare Workers

Current through April 3, 2015; updated every Friday by 5pm. www.cdc.gov/ebola
Prototype Viral Hemorrhagic Fever Pathogen
- *Filovirus*: enveloped, non-segmented, negative-stranded RNA virus
- Severe disease with high case fatality
- Absence of specific treatment or vaccine

>20 previous Ebola and Marburg virus outbreaks

2014 West Africa Ebola outbreak caused by *Zaire ebolavirus* species (five known Ebola virus species)
Proposed Ebola Virus Disease Epidemiology

- Zoonotic virus – bats the most likely reservoir
- Spillover event from infected wild animals (e.g., fruit bats, monkey, duiker) to humans, followed by human-human transmission
<table>
<thead>
<tr>
<th>Country</th>
<th>Reporting Date</th>
<th>Total Cases (Suspected, Probable, and Confirmed)</th>
<th>Confirmed Cases</th>
<th>Total Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guinea</td>
<td>31 Mar 15</td>
<td>3,494</td>
<td>3,073</td>
<td>2,320</td>
</tr>
<tr>
<td>Liberia</td>
<td>29 Mar 15</td>
<td>9,712</td>
<td>3,151</td>
<td>4,332</td>
</tr>
<tr>
<td>Sierra Leone</td>
<td>31 Mar 15</td>
<td>12,022</td>
<td>8,547</td>
<td>3,810</td>
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<tr>
<td>United Kingdom**</td>
<td>29 Dec 14</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Nigeria**</td>
<td>15 Oct 14</td>
<td>20</td>
<td>19</td>
<td>8</td>
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<tr>
<td>Spain**</td>
<td>27 Oct 14</td>
<td>1</td>
<td>1</td>
<td>0</td>
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<tr>
<td>Senegal**</td>
<td>15 Oct 14</td>
<td>1</td>
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<tr>
<td>United States**</td>
<td>24 Oct 14</td>
<td>4</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Mali**</td>
<td>23 Nov 14</td>
<td>8</td>
<td>7</td>
<td>6</td>
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<tr>
<td>TOTAL</td>
<td></td>
<td>25,228</td>
<td>14,804</td>
<td>10,462</td>
</tr>
</tbody>
</table>

*Total cases include probable, suspected, and confirmed cases. Reported by WHO using data from ministries of health.

**There is currently no Ebola virus transmission in Senegal, Nigeria, Spain, the United States, the United Kingdom, and Mali.
EBV Cases in the US

- EVD has been diagnosed in the United States in four people: one (the index patient) who traveled to Dallas, Texas from Liberia, two healthcare workers who cared for the index patient, and one medical aid worker who traveled to New York City from Guinea

  - **Index patient** – Symptoms developed on September 24, 2014 approximately four days after arrival, sought medical care at Texas Health Presbyterian Hospital of Dallas on September 26, was admitted to hospital on September 28, testing confirmed EVD on September 30, patient died October 8.

  - **TX Healthcare Worker, Case 2** – Cared for index patient, was self-monitoring and presented to hospital reporting low-grade fever, diagnosed with EVD on October 10, recovered and released from NIH Clinical Center October 24.

  - **TX Healthcare Worker, Case 3** – Cared for index patient, was self-monitoring and reported low-grade fever, diagnosed with EVD on October 15, recovered and released from Emory University Hospital in Atlanta October 28.

  - **NY Medical Aid Worker, Case 4** – Worked with Ebola patients in Guinea, was self-monitoring and reported fever, diagnosed with EVD on October 24, recovered and released from Bellevue Hospital in New York City November 11.

EBV Cases in the US

- During this outbreak, 6 health workers and one journalist have been infected with Ebola virus while in West Africa and transported to hospitals in the United States.
  - One of the health workers died on November 17 after being transported from Sierra Leone to Nebraska Medical Center.
- On March 13, an American health worker volunteering in Sierra Leone was evacuated to the United States for treatment after testing positive for Ebola.
EBV Transmission

- Virus present in high quantity in blood, body fluids, and excreta of symptomatic EVD-infected patients

- Opportunities for human-to-human transmission
  - Direct contact (through broken skin or unprotected mucous membranes) with an EVD-infected patient’s blood or body fluids
  - Sharps injury (with EVD-contaminated needle or other sharp)
  - Direct contact with the corpse of a person who died of EVD
  - Indirect contact with an EVD-infected patient’s blood or body fluids via a contaminated object (soiled linens or used utensils)

- Also be transmitted via contact with blood, fluids, or meat of an infected animal
  - No reports of dogs or cats becoming sick with or transmitting Ebola
EBV Human-to-Human Transmission

- Infected persons are not contagious until onset of symptoms
- Infectiousness of body fluids (e.g., viral load) increases as patient becomes more ill
  - Remains from deceased infected persons are highly infectious
- Human-to-human transmission of Ebola virus via inhalation (aerosols) has not been demonstrated
**EBV Risk Assessment**

**HIGH-RISK EXPOSURE**

Percutaneous (e.g., needle stick) or mucous membrane exposure to blood or body fluids of a person with Ebola while the person was symptomatic

**OR**

Exposure to the blood or body fluids (including but not limited to feces, saliva, sweat, urine, vomit, and semen) of a person with Ebola while the person was symptomatic without appropriate personal protective equipment (PPE)

**OR**

Processing blood or body fluids from an Ebola patient without appropriate PPE or standard biosafety precautions

**OR**

Direct contact with a dead body without appropriate PPE in a country with widespread transmission or cases in urban areas with uncertain control measures*

**OR**

Having lived in the immediate household and provided direct care to a person with Ebola while the person was symptomatic

**SOME RISK EXPOSURE**

In countries with widespread transmission or cases in urban areas with uncertain control measures*:

- Direct contact while using appropriate PPE with a person with Ebola while the person was symptomatic or with the person's body fluids
- Any direct patient care in other healthcare settings

**OR**

Close contact in households, healthcare facilities, or community settings with a person with Ebola while the person was symptomatic

- Close contact is defined as being for a prolonged period of time while not wearing appropriate PPE within approximately 3 feet (1 meter) of a person with Ebola while the person was symptomatic

EBV Risk Assessment

**LOW (but not zero) RISK EXPOSURE**

Having been in a country with widespread transmission or cases in urban areas with uncertain control measures* within the past 21 days and having no known exposures

**OR**

Having brief direct contact (e.g. shaking hands) while not wearing appropriate PPE, with a person with Ebola while the person was in the stage of disease

**OR**

Brief proximity, such as being in the same room for a brief period of time, with a person with Ebola while the person was symptomatic

**OR**

In countries without widespread transmission or cases in urban settings with uncertain control measures*: direct contact while using appropriate PPE with a person with Ebola while the person was symptomatic or with the person’s body fluids

**OR**

Traveled on an aircraft with a person with Ebola while the person was symptomatic

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**NO IDENTIFIABLE RISK EXPOSURE**

Contact with an asymptomatic person who had contact with person with Ebola

**OR**

Contact with a person with Ebola before the person developed symptoms

**OR**

Having been more than 21 days previously in a country with widespread transmission or cases in urban areas with uncertain control measures*

**OR**

Having been in a country with Ebola cases, but without widespread transmission or cases in urban settings with uncertain control measures*, and not having any other exposures as defined above

**OR**

Having remained on or in the immediate vicinity of an aircraft or ship during the entire time that the conveyance was present in a country with widespread transmission or cases in urban areas with uncertain control measures* and having had no direct contact with anyone from the community

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EBV Pathogenesis

- Direct infection of tissues
- Immune dysregulation
- Hypovolemia and vascular collapse
  - Electrolyte abnormalities
  - Multi-organ failure, septic shock
- Disseminated intravascular coagulation (DIC) and coagulopathy

EBV Early Clinical Features

- Acute onset; typically 8–10 days after exposure (range 2–21 days)

- Signs and symptoms
  - Initial: Fever, chills, myalgias, malaise, anorexia
  - After 5 days: GI symptoms, such as nausea, vomiting, watery diarrhea, abdominal pain
  - Other: Headache, conjunctivitis, hiccups, rash, chest pain, shortness of breath, confusion, seizures
  - Hemorrhagic symptoms in 18% of cases

- Differential diagnosis
  - Malaria, typhoid fever, meningococcemia, Lassa fever and other bacterial infections (e.g., pneumonia) – all very common in Africa
EBV Clinical Features

- Nonspecific early symptoms progress to:
  - Hypovolemic shock and multi-organ failure
  - Hemorrhagic disease
  - Death

- Non-fatal cases typically improve 6–11 days after symptoms onset

- Fatal disease associated with more severe early symptoms
  - Fatality rates of 70% have been historically reported in rural Africa
  - Intensive care, especially early intravenous and electrolyte management, may increase the survival rate
# EBV Clinical Features by Organ System

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Clinical Manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Fever (87%), fatigue (76%), arthralgia (39%), myalgia (39%)</td>
</tr>
<tr>
<td>Neurological</td>
<td>Headache (53%), confusion (13%), eye pain (8%), coma (6%)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Chest pain (37%),</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Cough (30%), dyspnea (23%), sore throat (22%), hiccups (11%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Vomiting (68%), diarrhea (66%), anorexia (65%), abdominal pain (44%), dysphagia (33%), jaundice (10%)</td>
</tr>
<tr>
<td>Hematological</td>
<td>Any unexplained bleeding (18%), melena/hematochezia (6%), hematemesis (4%), vaginal bleeding (3%), gingival bleeding (2%), hemoptysis (2%), epistaxis (2%), bleeding at injection site (2%), hematuria (1%), petechiae/ecchymoses (1%)</td>
</tr>
<tr>
<td>Integumentary</td>
<td>Conjunctivitis (21%), rash (6%)</td>
</tr>
</tbody>
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EBV Laboratory Diagnosis

- Real Time PCR (RT-PCR)
  - For acute infection
  - More sensitive than antigen ELISA
  - Performed in select CLIA-certified laboratories

- RT-PCR sample collection
  - Volume: minimum volume of 4mL whole blood
  - Plastic collection tubes (not glass or heparinized tubes)
Interpreting Negative Ebola RT-PCR Result

- If symptoms started ≥3 days before the negative result
  - EVD is unlikely → consider other diagnoses
  - Infection control precautions for EVD can be discontinued unless clinical suspicion for EVD persists

- If symptoms started <3 days before the negative RT-PCR result
  - Interpret result with caution
  - Repeat the test at ≥72 hours after onset of symptoms
  - Keep in isolation as a suspected case until a repeat RT-PCR ≥72 hours after onset of symptoms is negative
Investigational Therapies for EVD

- No approved Ebola-specific prophylaxis or treatment
  - Ribavirin has no in-vitro or in-vivo effect on Ebola virus
  - Therapeutics in development with limited human clinical trial data
    - Convalescent serum
    - Therapeutic medications
      - ZMapp – three chimeric human-mouse monoclonal antibodies
      - Tekmira – lipid nanoparticle small interfering RNA
      - Favipiravir – oral RNA-dependent RNA polymerase inhibitor
  - Vaccines – in clinical trials
    - Chimpanzee-derived adenovirus with an Ebola virus gene inserted
    - Attenuated vesicular stomatitis virus with an Ebola virus gene inserted

Practical Considerations for Evaluating Patients for EVD in the United States

- CDC encourages all U.S. healthcare providers to
  - Ask patients with Ebola-like symptoms about travel to West Africa or contact with individuals with confirmed EVD in the 21 days before illness onset
  - Know the signs and symptoms of EVD
  - Know the initial steps to take if a diagnosis of EVD is suspected

- CDC has developed documents to facilitate these evaluations
  - Evaluating International Travelers for Level of Risk
  - Think Ebola: Early recognition is critical for infection control
EVD Summary

- The 2014 Ebola outbreak is the largest in history and has affected multiple countries.

- **Think Ebola**: U.S. healthcare providers should be aware of clinical presentation and risk factors for EVD.

- Human-to-human transmission by direct contact:
  - No human-to-human transmission via inhalation (aerosols)
  - No transmission before symptom onset

- Early case identification, isolation, treatment and effective infection control are essential to prevent Ebola transmission.
Re-Emerging Infectious Diseases

- Measles
- Enterovirus D68
- Pertussis – ongoing epidemic in US NOW!
- Syphilis – increasing rates in Bay Area
- Invasive Group A streptococci
- Tuberculosis, drug resistant
- MERS-CoV
- Cholera
- Diphtheria
- Malaria
Resources for Emerging Infectious Diseases

- Public Health Laboratories of the Ohio Department of Health, www.odh.state.oh.us/Resources/MultiMedia/EI_Slide/EIMAIN.HTM
Only One Flight Away from a Global Microbial Threat
Behind Mask
Thank You!