Overview of Ebola Outbreak and System for U.S. Response
Learning Objectives

➢ Know basic facts of:

- Epidemiology of Ebola virus, including human-to-human transmission
- 2014-15 Ebola outbreak in West Africa
- Clinical presentation and course of Ebola virus disease

➢ Know the definition of a confirmed case and a person under investigation (PUI)

➢ Understand U.S. system for screening and evaluating to prevent spread of Ebola
Overview

- Ebola Virus Overview

- Symptoms and Presentation
  - Case Definition/Epidemiology
  - Clinical Presentation and Course
  - Differential Diagnoses
  - Diagnosis

- Characteristics of Transmission

- Screening and Monitoring Returning Travelers

- Clinical Management
Ebola Virus

- 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)
Ebola Virus

- Zoonotic virus - bats the most likely reservoir, although species unknown
- Spillover event - infected wild animals (e.g., fruit bats, monkey, duiker) to humans, followed by human-to-human transmission
Ebola cases, per outbreak

Source: CDC, WHO
Ebola 1976-2014 cont’d

www.who.int accessed 11/1/2014
New Cases by Week* Reported in Situation Reports

* All suspect, probable and confirmed EVD cases for weeks 13-44; confirmed and probable cases weeks 45-50; confirmed cases only from week 51
Epidemiologic weeks correspond to Mar 29, 2014–May 2, 2015
# Ebola Cases and Deaths*

as of September 27, 2015

<table>
<thead>
<tr>
<th></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>3,805</td>
<td>3344</td>
<td>2533</td>
</tr>
<tr>
<td>Sierra Leone</td>
<td>13,911</td>
<td>8,704</td>
<td>3,955</td>
</tr>
<tr>
<td>Liberia**</td>
<td>10,672</td>
<td>3,157</td>
<td>4,808</td>
</tr>
<tr>
<td>Italy</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>United Kingdom**</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Nigeria**</td>
<td>20</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Spain**</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Senegal**</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>United States**</td>
<td>4</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Mali**</td>
<td>8</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>TOTAL</td>
<td>28,424</td>
<td>15,239</td>
<td>11,311</td>
</tr>
</tbody>
</table>


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

**There are currently no cases of Ebola in Senegal, Nigeria, Spain, the United States, the United Kingdom, Mali, and Liberia.
4 confirmed cases of Ebola virus disease (EVD) reported in the week to 28 June- all in Guinea

All cases in western Guinea

All cases were registered contacts
During this outbreak:

- Six persons (five healthcare workers and one journalist) infected in West Africa and transported to U.S. hospitals
- Five recovered, one healthcare worker died

Ebola has been diagnosed in the United States in four people:

- One who traveled to Dallas, Texas, from Liberia
- Two healthcare workers who cared for the patient in Dallas
- One medical aid worker who traveled to New York City from Guinea
- Three recovered, the patient infected in Liberia died

Case Definition

- **Person Under Investigation (PUI)**
  - A person who has both consistent signs or symptoms and risk factors as follows should be considered a PUI:
    - Elevated body temperature or subjective fever or symptoms, including severe headache, fatigue, muscle pain, vomiting, diarrhea, abdominal pain, or unexplained hemorrhage; AND
    - An epidemiologic risk factor within the 21 days before the onset of symptoms.

- **Confirmed Case**
  - Laboratory-confirmed diagnostic evidence of Ebola virus infection.

[http://www.cdc.gov/vhf/ebola/hcp/international/case-definitions.html](http://www.cdc.gov/vhf/ebola/hcp/international/case-definitions.html)
Early Clinical Presentation

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

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

- **Other possible infectious causes of symptoms**
  - Malaria, typhoid fever, meningococcemia, dengue, influenza, Lassa fever and other bacterial infections (e.g., pneumonia) – all very common in Africa

- Clinicians should be aware of other similar infections, such as malaria
Clinical Features

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

- Non-fatal cases
  - Typically improve 6–11 days after symptom onset if supportive care is provided promptly

- Fatal disease associated with more severe early symptoms
  - Fatality rates of 70% have been reported in rural Africa
  - Intensive care, especially early intravenous and electrolyte management, may increase the survival rate
Early symptoms of Ebola are non-specific
- Seen in many diseases that are common in Africa (malaria, typhoid fever, etc)

Available diagnostic tests include:
- Polymerase chain reaction (PCR)
- Enzyme-linked immunosorbent assay (ELISA)
- IgM/IgG antibodies
- Virus isolation
- Immunohistochemistry testing (post-mortem exam: liver, spleen)

It can take up to 3 days after onset of initial symptoms (usually fever) to detect the virus
Ebola Virus Pathogenesis

- Direct infection of tissues and blood vessels
- Vascular leak / cytokine effect
- Hypovolemia and vascular collapse with third spacing of fluids
  - Electrolyte abnormalities
  - Multi-organ failure, septic shock
- Disseminated intravascular coagulation and coagulopathy
- Immune dysregulation
Opportunities for human-to-human transmission:

- Direct contact (through broken skin or unprotected mucous membranes) with an Ebola-infected patient’s blood or body fluids
- Sharps injury with Ebola virus-contaminated needle or other sharp
- Direct contact with the remains of a person who died of Ebola
- Indirect contact with an infected patient’s blood or body fluids via a contaminated object (soiled linens or used utensils)
- Possibly from contact with semen from a man who has recovered from Ebola (for example, by having oral, vaginal, or anal sex)
- Probably from contact with amniotic fluid in a woman who is currently infected or who has recently recovered
Human-to-Human Transmission

- Infectiousness of Ebola Virus Disease
  - Infected persons are not contagious until onset of symptoms
  - Infectiousness of body fluids increases due to increased viral load as patients become more ill
  - Infection can occur from indirect contact with blood or body fluids via a contaminated object (soiled linens or used utensils)
  - Remains from deceased infected persons are highly infectious

- Human-to-human transmission of Ebola virus via inhalation has not been demonstrated
  - However, respiratory protection (e.g. N-95, PAPR) is recommended in case there is an unexpected need to perform an aerosol-generating procedure (e.g. emergency intubation)
Key points: Identify, Isolate, Inform

CDC encourages all U.S. healthcare providers to
- Ask patients about travel or contact with individuals within previous 21 days
- Know signs and symptoms of Ebola
- Know initial steps to take if a diagnosis of Ebola is suspected

CDC has developed documents to facilitate these evaluations
Screening and Monitoring Travelers to Prevent the Spread of Ebola

- Exit screening of travelers departing from areas where there is transmission

- Entry screening in the United States
  - Education
  - Contact information
  - Connection with health department for 21 days of monitoring

- Ebola patient in the U.S.
  - If a person with possible Ebola presents to a facility in the U.S., it is likely that person is already known to public health authorities and is being monitored

Screening and Monitoring Travelers to Prevent the Spread of Ebola

➢ High risk:

• Percutaneous (e.g., needle stick) or mucous membrane exposure to blood or body fluids (including but not limited to feces, saliva, sweat, urine, vomit, and semen) from a person with Ebola while the person was symptomatic.

• Direct contact without appropriate personal protective equipment (PPE) with a person with Ebola while the person was symptomatic or the person’s body fluids.

• Laboratory processing of blood or body fluids from a person with Ebola while the person was symptomatic without appropriate PPE or standard biosafety precautions.

• Direct contact with a dead body without appropriate PPE in a country with widespread transmission or a country with cases in urban settings with uncertain control measures.

• Having provided direct care in a household setting to a person with Ebola while the person was symptomatic.
Some risk:

- In countries with widespread transmission
  Direct contact *while using appropriate PPE* with a person with Ebola while the person was symptomatic or the person's body fluids or being in the patient-care area of an Ebola treatment unit
  Any direct patient care in non-Ebola healthcare settings

- Close contact (< 3 feet) in households, healthcare facilities, or community settings with a person with Ebola while the person was symptomatic
Screening and Monitoring Travelers to Prevent the Spread of Ebola

Low risk:

- Having been in a country with widespread transmission, a country with cases in urban settings with uncertain control measures, or a country with former widespread transmission and now established control measures and having had no known exposures.
- Brief direct contact (e.g., shaking hands), while not using appropriate PPE, with a person with Ebola while the person was in the early stage of disease.
- Brief proximity with a person with Ebola while the person was symptomatic, such as being in the same room (not the patient-care area of an Ebola treatment unit) for a brief period of time.
- In countries other than those with widespread transmission: direct contact while using appropriate PPE with a person with Ebola while the person was symptomatic or the person's body fluids or being in the patient-care area of an Ebola treatment unit.
- Laboratory processing of blood or body fluids from a person with Ebola while the person was symptomatic while using appropriate PPE and standard biosafety precautions.
- Having traveled on an airplane with a person with Ebola while the person was symptomatic and having had no identified some or high risk exposures.
Interim Guidance for Monitoring and Movement of Persons with Ebola Exposure

CDC has created guidance for monitoring people exposed to Ebola virus but without symptoms

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Public Health Action</th>
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<tbody>
<tr>
<td></td>
<td>Monitoring</td>
</tr>
<tr>
<td>HIGH risk</td>
<td>Direct Active Monitoring</td>
</tr>
<tr>
<td>SOME risk</td>
<td>Direct Active Monitoring</td>
</tr>
<tr>
<td>LOW risk</td>
<td>Active Monitoring for some; Direct Active Monitoring for others</td>
</tr>
<tr>
<td>NO risk</td>
<td>No</td>
</tr>
</tbody>
</table>

Active monitoring - State or local public health authority establishes regular communication, including daily check for presence of symptoms and fever.

Direct active monitoring - Public health authority conducts active monitoring through direct observation.

Purpose - Ensure that if individuals with epidemiologic risk factors become ill, they are identified as soon as possible after symptom onset so they can be rapidly isolated and evaluated.

Cross jurisdictions - Active (or direct active) monitoring and prompt follow-up should continue uninterrupted if the person travels out of the jurisdiction.

Clinical Management of Ebola: Supportive but Aggressive

- Hypovolemia and sepsis pathophysiology
  - Aggressive intravenous fluid resuscitation
  - Hemodynamic support and critical care management if necessary
- Electrolyte and acid-base abnormalities
  - Aggressive electrolyte repletion
  - Correction of acid-base derangements

Clinical Management of Ebola: Supportive but Aggressive (cont’d)

- Symptomatic management of fever and gastrointestinal symptoms
  - Avoid NSAIDs, aspirin
  - Anti-emetics and antidiarrheal agents may be needed

- Multisystem organ failure can develop and may require
  - Oxygenation and mechanical ventilation
  - Correction of severe coagulopathy
  - Continuous renal replacement therapy

Investigational Therapies for Ebola Patients

- 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
      – Brincidofovir – oral nucleotide analogue with antiviral activity
      – Favipiravir – oral RNA-dependent RNA polymerase inhibitor

Investigational Therapies for Ebola Patients

- Vaccines – in clinical trials
  - Chimpanzee-derived adenovirus with an Ebola virus gene inserted
  - Attenuated vesicular stomatitis virus with an Ebola virus gene inserted
  - Study published in Lancet (August 3, 2015) - ring vaccination cluster-randomized trial performed in Guinea demonstrated a vaccine efficacy of 100%

**Patient Recovery**

- Case-fatality rate between 50%-70% in the 2014 Ebola outbreak
  - Case-fatality rate is likely much lower with access to intensive care

- Patients who survive often have signs of clinical improvement by the second week of illness
  - Associated with the development of virus-specific antibodies
  - Antibody with neutralizing activity against Ebola persists greater than 12 years after infection

**References:**

Prolonged convalescence

- Includes arthralgia, myalgia, uveitis, abdominal pain, extreme fatigue, and anorexia; many symptoms resolve by 21 months
- Significant arthralgia and myalgia may persist for >21 months
- Depression, headache, skin sloughing, and hair, vision, and hearing loss have also been reported

? EBV sanctuaries (anterior chamber of eye, sperm, amniotic fluid)

Questions?