Case Study 3: Viral Hemorrhagic Fevers

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Learning Objectives

- Recognize when to be concerned about potential emerging infections
- Outline universal actions that can and should be taken to care for patients, staff, and public
- Describe diagnostics for Ebola virus disease
Inadequate Basic Healthcare Infrastructure

Courtesy of Dr. Tom Fletcher
HCWs and Ebola

- 1995 outbreak (Kikwit¹)
  - 80 (25%) occurred in HCWs
- 2013-2016 outbreak (West Africa²,³)
  - 881 HCWs infected
  - 513 deaths
  - 21- to 32-fold higher risk

Source of HCW Infection

- Difficult to identify the precise risk factor and setting
  - Community vs nosocomial transmission?
- Serious gaps in IPC
  - Deficiencies in administrative and environmental control
  - Inappropriate use or lack of PPE
  - Defective IPC practice and behavior
  - Poor employment conditions and social determinants


Infection in HCWs Can and Must Be Prevented

- HCW protection is **PARAMOUNT** to maintain healthcare capacity
  - 38%-111% increase in maternal mortality
  - 45%-140% increase in untreated malaria
- HCW infection decreased with training
  - 12% in July 2014 to 1% in February 2015


Ebola Virus Ecology

Human-to-Human Transmission

- Ebola is spread through direct contact (through broken skin or unprotected mucous membranes) with:
  - An infected person’s blood or body fluids, including but not limited to urine, saliva, diarrhea, vomit, semen, vaginal fluid, and breast milk
  - Contaminated objects (e.g., needles, syringes)
- Human-to-human transmission via aerosols has not been demonstrated
- Asymptomatic individuals are generally not infectious (vs sexual activity)
- Infectivity increases with illness severity

Viral Load Correlates With Illness

How Contagious Is Ebola?

The number of people that one sick person will infect (on average) is called $R_0$. Here are the maximum $R_0$ values for a few viruses.

- Hepatitis C (2)
- Ebola (2)
- HIV (4)
- SARS (4)
- Mumps (10)
- Measles (18)

Ebola Transmission in the US

- **Sep 20, 2014**: Liberia to Texas
- **Sep 25, 2014**: ED $\rightarrow$ Sinus infection
- **Sep 28, 2014**: Admitted to hospital
- **Oct 8, 2014**: Died
- **Oct 10, 2014 and Oct 15, 2014**: 2 HCWs infected

Contact with 48 individuals

Contact with 120 individuals

**Ebola Diagnosed Outside of Africa and Secondary Transmission**

- **Ohio**: 164 contacts traced, 0 transmissions
- **New York**: 117 contacts traced, 0 transmissions
- **Texas**: 177 contacts traced, 0 prehospital transmissions
- **Spain**: 83 contacts traced, 0 transmissions
- **United Kingdom**: 55 contacts traced, 0 transmissions

**Persistence of Ebola Virus in Body Fluids**

<table>
<thead>
<tr>
<th>Body Fluid</th>
<th>Symptom Onset Mean Death Day</th>
<th>Last Virus Isolation</th>
<th>Last Detectable IgG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viremia/Blood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saliva/Swab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tears/Conj.</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Semen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin/Sweat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectal/Feces</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Breast Milk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSF</td>
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</tbody>
</table>

*CDC. www.cdc.gov/vhf/ebola/transmission/human-transmission.html.*
Infection Prevention and Control

- **Goal**—to decrease exposure
  - Environmental controls
    - Construction/maintenance of an appropriate facility
    - Establishment of clean water and sanitation
    - Waste management
  - Administrative controls
    - Triage
    - Training of HCW (including donning/doffing processes)
  - Personal controls
    - Standard precautions (including hand hygiene and PPE use)

IPC: Environmental Considerations

- Dedicate a zone for screening and organize areas into:
  - A low-risk zone for HCW
  - A high-risk zone for suspected and confirmed cases
  - A triage area accessible to both high- and low-risk zones
- Ensure unidirectional flow
- Restrict all nonessential staff and visitors from screening/isolation areas
- Ensure proper waste management
  - Sharps disposal

Personal communications with Dr. Fischer.
Institutional and Environmental Controls

Personal communications with Dr. Fischer.

Courtesy of Dr. Tom Fletcher
Identification of Suspected Cases

1. Epidemiologic risk factor
   - High risk
     - Percutaneous or mucous membrane exposure to blood or body fluids from an infected patient
     - Direct contact with a symptomatic patient without appropriate PPE
     - Direct contact with a dead body without appropriate PPE
   - Some risk (in countries with widespread transmission)
     - Direct contact while using appropriate PPE
     - Any direct patient care in non-Ebola healthcare settings

2. Clinical signs/symptoms of Ebola

<table>
<thead>
<tr>
<th>Presenting Signs/Sx</th>
<th>All Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>84-89</td>
</tr>
<tr>
<td>Fatigue</td>
<td>65-76</td>
</tr>
<tr>
<td>Headache</td>
<td>53-80</td>
</tr>
<tr>
<td>Weakness</td>
<td>79</td>
</tr>
<tr>
<td>Vomiting</td>
<td>43-68</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>61-67</td>
</tr>
<tr>
<td>Unexplained hemorrhage</td>
<td>18-19</td>
</tr>
</tbody>
</table>

Identification of Suspected Cases (cont.)

1. Epidemiologic risk factor (cont.)
   - Low risk
     - Having been in a country with widespread transmission
     - Brief contact (e.g., shaking hands) with an infected patient in the early stages of disease (without appropriate PPE)
     - Direct contact with an infected patient (while using appropriate PPE) in countries without widespread transmission
     - Having traveled on an airplane with an infected person


Rapid Identification and Isolation

- **ASK**
  - Ask every patient with fever or symptoms of Ebola **if he/she recently traveled to Ebola epidemic country**
    - Headache, weakness, nausea/vomiting, diarrhea, muscle/joint/abdominal pain, hiccups, unexplained hemorrhage

  **Travel history is the 6th vital sign**

- **ISOLATE**
- **CALL** (hospital epidemiology, state health department, and CDC)

Confirmation of Ebola Virus Infection

- **Ebola diagnostics**
  - Serology
  - Antigen detection
  - Molecular-based diagnostics (EZ1 rRT-PCR)
    - Approximate run time: 1 hour (results in 4-6 hours)
    - LOD: 100-1,000 PFU/mL for molecular-based diagnostics
    - High specificity (no cross-reactivity detected)
  - Presumptive testing is available at 52 LRN laboratories
  - Must be confirmed at the CDC
  - Call CDC for authorization (770 488 7100)


State Coverage for Ebola Testing

- LRN Labs
- LRN Labs Testing for Ebola
- Hospitals Accepting Ebola Patients

CDC. www.cdc.gov/vhf/ebola/healthcare-us/laboratories/specimens.html
CDC. www.cdc.gov/vhf/ebola/healthcare-us/laboratories/safe-specimen-management.html

SHEA/CDC OUTBREAK RESPONSE TRAINING PROGRAM
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**Ebola: Expected Diagnostic Test Results Over Time**

Critical Information: Date of Onset of Fever/Symptoms

- **Viremia**
- **IgM**
- **IgG**

Days post onset of symptoms:

- **Fever**
- **RT-PCR**
- **ELISA IgM**
  - IgM: up to 3-6 months
- **ELISA IgG**
  - IgG: 3-5 years or more (life-long persistence?)


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**Interpreting Negative Test Results**

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


Personal Protection Equipment

- PPE
  - Scrubs
  - Rubber boots
  - 2 pairs of gloves
  - Tychem suit
  - Hood
  - N-95
  - Goggles
  - Apron

PPE Works, but Its NOT Enough

Photo courtesy of Tom Fletcher.

Courtesy of Dr. Andres Kurtha.
This Will Happen Again
ABBREVIATIONS/ACRONYMS

Case Study 3: Viral Hemorrhagic Fevers

CDC = Centers for Disease Control and Prevention
CSF = cerebrospinal fluid
ED = emergency department
ELISA = enzyme-linked immunosorbent assay
HCW = healthcare worker
Ig = immunoglobulin
IPC = infection prevention and control
LOD = limit of detection
LRN = Laboratory Response Network
PFU = plaque-forming units
PPE = personal protective equipment
R₀ = basic reproduction number
RT-PCR = reverse transcription polymerase chain reaction
S = suspected case
SARS = severe acute respiratory syndrome