Ebola: the Basics and the Background
A disaster!

“Our people are dying, children are being orphaned, most of the dead are women and over two-thirds of those infected belong to the most economically active age category of 15 to 50. Children are not going to school; doctors and nurses are dying, and non-Ebola illnesses are adding to the toll of death and suffering due to further strains and weakening of the healthcare delivery system in the country.”

DR ERNEST BAI KOROMA, PRESIDENT OF SIERRA LEONE
Filovirus Cycle of Transmission

Reservoir hosts

Spillover
Objectives

- To describe Ebola virus and its natural history in the human host and in the environment
- To explain some communicable disease terminology and concepts useful for controlling Ebola
- To give an overview of the West African outbreak
- To highlight the importance of detecting cases rapidly and responding rapidly
Ebolavirus

• Filovirus family (Filoviridae)
• Five species
  – Zaire Ebolavirus (EBOV)
  – Sudan Ebolavirus (SUDV)
  – Bundibugyo Ebolavirus (BDBV)
  – Tai Forest Ebolavirus (TAFV)
  – Reston Ebolavirus (RESTV)
**Reston Ebolavirus (REBOV)**  
*The Good Cousin*

- Found in Philippines and China
- Causes respiratory disease in pigs
- Infects humans, but no disease
- Pig farmers, abattoir workers, others have antibodies
- Some cross-reaction with Zaire EBOV
- Are people with REBOV antibodies immune?
- Can REBOV antibodies be used for therapy?
- Will REBOV antibodies from natural infections confuse diagnosis of Ebola virus disease?

*Miranda & Miranda 2011; Pan et al 2014*
EbolaVirus

- Long narrow virus, length 1400 nm & width 80 nm
- Filamentous
- RNA with protein as inner core; matrix layer next; then membrane from host cell outside
- RNA codes for 8 proteins
- Virus takes over the cell
Natural history

- Virus enters the cell – any cell, but particularly uses macrophages, dendritic cells and monocytes
- Spreads to lymph nodes via lymphatics and then to liver and spleen via blood
- Secondary spread to all organs
- Exits the body in faeces, saliva, sweat, tears, sputum, skin cells, breast milk, semen, urine, vomitus
Virus in blood

Figure 1. Ebola virus RNA copy levels in sera over time from 45 Ebola Virus Disease (EVD) patients (27 fatal, 18 non-fatal)\(^{14}\)

>100 million viruses per ml

No virus before symptoms
Detection of Ebola Virus in Different Human Body Fluids over Time
Pathogenesis of Ebolavirus

- Destroys cells – focal necrosis in many organs
- Suppresses inflammation
- Causes cytokine storm
- Induces clotting
- Multi-organ focal necrosis and disseminated intravascular coagulation with focal haemorrhage and minimal inflammation
Survival outside host

- Dried – 24 hr at 25°C; 14 days at 4°C
- In fluids – up to 46 days at 25°C
- Ebolavirus is killed by:
  - Heat 60°C for 1 hr
  - Hypochlorite (Chlorine solution)
  - Alcohols
  - 3% acetic acid
  - 1% glutaraldehyde

Environmental contamination in isolation ward

- Sudan Ebolavirus outbreak – Uganda 2000
- 2 positives from 33 environmental specimens
- Ebolavirus was detected on a bloody glove and a bloody IV insertion site
- Not isolated on bedframes, chairs, stethoscopes, clean gloves, food bowl, spit bowl, body bag cleaned with bleach, body louse
- **Suggests** that environmental contamination and fomites are possible modes of transmission in an ETC

Bausch et al. J Inf Dis 2007
Infectious disease terminology

• **Inoculating dose** = the number of viral particles that enter the host; minimum inoculating dose of Ebolavirus is very low (1-10 viruses)

• **Incubation period** = days from when the person was exposed and symptoms first develop; aver. EBOV = 11 days (2 – 21 days)
The Importance of Maximum Incubation Period

• Quarantine/ Monitoring of Asymptomatic individuals = 1 maximum incubation period since exposure; EBOV = 21 days

• Declaring an outbreak over = 2 maximum incubation periods since last negative test; EBOV = 42 days

Ebola outbreak in Nigeria officially over:
‘spectacular success story’
The World Health Organization has declared that Nigeria is now free of Ebola.
Infectious disease terminology

- **Attack rate** = Percent of people in an exposed group who develop the disease; EBOV = 16-40%
- **Case fatality rate** = Percent of infected people who die; EBOV West Africa = 45% (817/1804)
- **Reproduction number** = Average number of new cases that occur from a single case;

Other diseases: e.g., measles $R_0 = 20$; influenza $R_0 = 1.4$
### Values of $R_0$ of well-known infectious diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Transmission</th>
<th>$R_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>Airborne</td>
<td>12–18</td>
</tr>
<tr>
<td>Pertussis</td>
<td>Airborne droplet</td>
<td>12–17</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Saliva</td>
<td>6–7</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Airborne droplet</td>
<td>5–7</td>
</tr>
<tr>
<td>Polio</td>
<td>Fecal-oral route</td>
<td>5–7</td>
</tr>
<tr>
<td>Rubella</td>
<td>Airborne droplet</td>
<td>5–7</td>
</tr>
<tr>
<td>Mumps</td>
<td>Airborne droplet</td>
<td>4–7</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Sexual contact</td>
<td>2–5</td>
</tr>
<tr>
<td>SARS</td>
<td>Airborne droplet</td>
<td>2–5</td>
</tr>
<tr>
<td>Influenza (1918 Pandemic Strain)</td>
<td>Airborne droplet</td>
<td>2–3</td>
</tr>
<tr>
<td>2014 Ebola Outbreak</td>
<td>Bodily fluid</td>
<td>1-2</td>
</tr>
</tbody>
</table>

Unless noted $R_0$ values are from: History and Epidemiology of Global Smallpox Eradication From the training course titled "Smallpox: Disease, Prevention, and Intervention". The CDC and the World Health Organization. Slide 16-17.
The importance of Effective Reproduction Number ($R_t$)

- If one case of EVD (on average) infects greater than one other person, $R_t$ is $>1$ and the epidemic grows; e.g., as in West Africa where $R_t$ was initially 3 decreasing to 1.3.

- If one case of EVD (on average) infects less than one other person, $R_t$ is $<1$ and the epidemic slows and stops; e.g., as in DRC where $R_t$ is 0.84.

The aim of outbreak control is to reduce $R_t$ to less than 1.
Case definition

- A set of clinical, epidemiological and laboratory criteria used to identify a person as a case of a particular disease
- **Suspect**
- **Probable**
- **Confirmed**

Suspect Ebola: A person who has been in an Ebola affected area in the last 21 days and has symptoms consistent with EVD

Person Under Investigation (PUI): In Ebola infected countries <21 days before
Ebola in West Africa

- Three countries with widespread transmission
- Guinea, Sierra Leone, Liberia
Country Classifications (current)

- Countries with Widespread Transmission
  - Guinea, Liberia, Sierra Leone
- Countries with Travel Associated Cases
  - Mali
- Countries with Travel Associated Cases and Localized Transmission
  - USA, Spain
- Countries with Localized Transmission
  - Democratic Republic of Congo (separate outbreak)


<table>
<thead>
<tr>
<th>Current Country Classifications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Countries with Widespread Transmission</strong>¹</td>
</tr>
<tr>
<td>Guinea</td>
</tr>
<tr>
<td>Liberia</td>
</tr>
<tr>
<td>Sierra Leone</td>
</tr>
<tr>
<td><strong>Affected Areas</strong></td>
</tr>
<tr>
<td><strong>Countries without Widespread Transmission</strong>²</td>
</tr>
<tr>
<td>Mali</td>
</tr>
<tr>
<td>Spain</td>
</tr>
<tr>
<td>United States of America³</td>
</tr>
<tr>
<td><strong>Affected Areas</strong></td>
</tr>
<tr>
<td><strong>Countries with No current transmission</strong>⁶</td>
</tr>
<tr>
<td>Nigeria</td>
</tr>
<tr>
<td>Senegal</td>
</tr>
</tbody>
</table>

¹Travelers arriving from all areas of Guinea, Liberia, and Sierra Leone are at risk for exposure to Ebola.  
²Travelers to these countries are NOT at risk for exposure to Ebola, unless they report direct contact with an Ebola case.  
³There has been a single case diagnosed in Mali on October 23, 2014, that was imported from Guinea.  
⁴A single case occurred in a healthcare worker caring for an Ebola patient who had been transported to Spain from Liberia for care. There has been no further transmission. Travelers to Spain are NOT at risk for exposure to Ebola.  
⁵One travel-associated case was imported to Dallas from Liberia, and resulted in transmission to two healthcare workers. One travel-associated case from Sierra Leone was imported to New York City. Travelers to Dallas or New York City are not at risk for exposure to Ebola.  
⁶These countries are currently Ebola-free. One international importation from Liberia into Nigeria resulted in localized transmission (20 cases and 8 deaths), which has ceased. A single case in Senegal was imported from Guinea. Travelers to Nigeria and Senegal are not at risk for exposure to Ebola, unless they report direct contact with an Ebola case.
### Countries with Widespread Transmission

<table>
<thead>
<tr>
<th>Country</th>
<th>Total Cases</th>
<th>Laboratory-Confirmed Cases</th>
<th>Total Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guinea</td>
<td>1760</td>
<td>1479</td>
<td>1054</td>
</tr>
<tr>
<td>Liberia</td>
<td>6919</td>
<td>2514</td>
<td>2766</td>
</tr>
<tr>
<td>Sierra Leone</td>
<td>4862</td>
<td>4149</td>
<td>1130</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>13241</strong></td>
<td><strong>8142</strong></td>
<td><strong>4950</strong></td>
</tr>
</tbody>
</table>

Is EVD close to Philippines?

Monrovia to Manila: 14,204 km

- Green: Country with no ongoing EVD transmission
- Orange: Country with ongoing EVD transmission
How did it start?

- Ebola virus disease had not occurred before in West Africa
- EVD not considered as a diagnosis
- First case (index case) 2 year old child in village of Meliandou in Guinea died on 6 December 2013
- Transmitted locally and new outbreaks started when people moved the virus across Guinea
Effective Reproduction number >1

- Spread to Liberia (Apr 2014), then Sierra Leone
- $R_t$ fell below 1 in June, but then rose above 1

Nishiura & Chowell Euro Surveill 2014
Priorities for the response

• Dr David Heyman emphasised two priorities
• Hear his interview with the Lancet at http://download.thelancet.com/flatcontentassets/audio/lancet/2014/lancet_141030.mp3

• **Priority 1:** Stop the outbreak; particularly involve African experts and teams with experience in managing Ebola outbreaks

• **Priority 2:** Do clinical trials of treatments (eg, blood or serum from survivors) and vaccines
The importance of acting quickly

• If HCWs act fast and reduce the number of initial cases, epidemics can be prevented
• Even one infected person (index case) that is not isolated is a danger
  – 40% chance of a major outbreak
• Very serious if >5 people are in the initial cluster of infected people
  – 90% chance of a major outbreak

Chowell et al. BMC Med 2014

Screening for that first Ebola case is vitally important!
Quick action stops outbreaks

• Detect cases early
  – Screen and triage
• Respond rapidly
  – Isolate cases
  – Implement Ebola strategies
  – Do contact tracing
• Probability of a major outbreak decreases the faster intervention occurs

Quick action can save thousands of lives!

For clinicians:
Identify
Isolate
Inform


