Epidemiology and Forecast of the Current West African Ebola Outbreak

Jeffrey Shaman
16 October 2014
Bats Believed to be Natural Reservoir

Enzootic Cycle

New evidence strongly implicates bats as the reservoir hosts for ebolaviruses, though the means of local enzootic maintenance and transmission of the virus within bat populations remain unknown.

Ebolaviruses:
- Ebola virus (formerly Zaire virus)
- Sudan virus
- Tai Forest virus
- Bundibugyo virus
- Reston virus (non-human)
Range of putative EBOV reservoir species, the little collared fruit bat (yellow), hammer-headed fruit bat (blue), and straw-colored fruit bat (green) -- thought to be associated with previous Central African EBOV outbreaks

Alexander et al., in review
Pathogen spillover to humans is typically associated with the use of bush meat and direct contact with tissues or bodily fluids through handling and eating of infected animals (e.g. duiker, primates, or fruit bats).

Predation and consumption of a red colobus monkey by chimpanzees has also been linked to an outbreak of Ebola among chimpanzees and one researcher in Côte d'Ivoire.
Ingestion of fruit contaminated with Ebola infected bat saliva or feces may be another mechanism by which bats infect other species (e.g., duiker, non-human primates), including humans.

- Human-to-human transmission associated with traditional burial practices, caregiving, or other forms of direct physical contact with infected individuals or bodily fluids.
• Transmission dynamics in high-density urban centers (C) will differ importantly from rural villages (B) influencing outbreak progression and control efforts.
• Transmission in the hospital setting is largely associated with failures in infection control procedures and standard barrier precautions (D).
Ebola in Humans is Novel to West Africa

Ng et al., 2014
Emergence of the West African Epidemic

Suspected first case a 2-year old infected in early December 2013 in Guéckédou, Guinea

The Guinean Ministry of Health was alerted in early March 2014 by local hospitals and public health officials of the appearance of a new disease with high case fatality

Baize et al., 2014
Prior Outbreaks in Isolated Rural Communities

Monrovia
West Africa an Area of High Connectivity

Based on travel time to nearest settlement of 500,000+

Flow of 500,000 mobile phone users in Côte d’Ivoire

No previous recorded outbreak in an area of such population density or connectivity

Model estimated flow built using mobile phone data

Wesolowski et al., 2014
International Travel

Gomes et al., 2014
Traditional Intervention in Remote Settings

1. ISOLATION FACILITY/CASE MANAGEMENT/LAB
2. CONTACT TRACING
3. EPIDEMIOLOGICAL SURVEILLANCE
4. ALERT SYSTEM/REFERRALS
5. EPI INVESTIGATION & RUMOR CHECKING
6. HEALTH PROMOTION
7. INFECTION CONTROL
8. BURIAL TEAMS
9. PSYCHOSOCIAL SUPPORT
10. TRAINING

Courtesy: Estrella Lasry, MSF
Weeks, very few confirmed cases were reported from Monrovia between 6 and 11 October (figure 2), reflecting ongoing delays in matching laboratory results with clinical surveillance data. By contrast, 138 suspected and probable cases were reported from Monrovia during the same period, many of which are likely to be genuine cases of EVD.

Outside Monrovia, most newly reported cases have come from the districts of Bong (75 cases) and Margibi (28 cases). The recent fall in the number of new cases reported from Lofa, which borders Gueckedou in Guinea, appears to have continued, with reports from observers in the area suggesting that there is evidence of a genuine decline.

It should be noted, however, that the 13 new cases that were reported in Lofa between 6 and 11 October represents a high number in the context of an EVD outbreak, and a concerted effort will be required to halt all transmission in the area.

**Figure 2:** Ebola virus disease cases reported each week from Liberia and Monrovia

Data are based on official information reported by Ministries of Health up to the end of 12 October for Guinea and Sierra Leone, and 11 October Liberia. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results.

### Table 1: Probable, confirmed, and suspected cases in Guinea, Liberia, and Sierra Leone

<table>
<thead>
<tr>
<th>Country</th>
<th>Case definition</th>
<th>Cases</th>
<th>Cases in past 21 days</th>
<th>Cases in past 21 days/total cases (%)</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Guinea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Confirmed</td>
<td>1184</td>
<td>289</td>
<td>24%</td>
<td>653</td>
</tr>
<tr>
<td></td>
<td>Probable</td>
<td>190</td>
<td>19</td>
<td>10%</td>
<td>190</td>
</tr>
<tr>
<td></td>
<td>Suspected</td>
<td>98</td>
<td>89</td>
<td>91%</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>1472</td>
<td>397</td>
<td>27%</td>
<td>843</td>
</tr>
<tr>
<td><strong>Liberia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Confirmed</td>
<td>950</td>
<td>66</td>
<td>7%</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td>Probable</td>
<td>1923</td>
<td>468</td>
<td>24%</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td>Suspected</td>
<td>1376</td>
<td>555</td>
<td>40%</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>4249</td>
<td>1089</td>
<td>26%</td>
<td>2458</td>
</tr>
<tr>
<td><strong>Sierra Leone</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Confirmed</td>
<td>2849</td>
<td>1110</td>
<td>39%</td>
<td>926</td>
</tr>
<tr>
<td></td>
<td>Probable</td>
<td>37**</td>
<td>0</td>
<td>0%</td>
<td>157**</td>
</tr>
<tr>
<td></td>
<td>Suspected</td>
<td>366</td>
<td>220</td>
<td>60%</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>3252</td>
<td>1330</td>
<td>41%</td>
<td>1183</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>8973</td>
<td>2816</td>
<td>31%</td>
<td>4484</td>
</tr>
</tbody>
</table>

*No available data. **For Sierra Leone, 120 more probable deaths have been reported than have probable cases. Data are based on official information reported by Ministries of Health. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results.
Based on detailed records from 4010 cases.

- **11.4 day mean incubation period** (time from infection to symptom onset)
- **15.3 (+/- 9.3) day serial interval**
- **5.0 (+/- 4.7) day time from symptom onset to hospitalization**
- **4.2 (+/- 6.4) day time from admission to death**
- **11.8 (+/- 6.1) day time to discharge**
- **70.8% case fatality rate**
- Doubling time (as of September 14) ~ 16, 24 and 30 days in Guinea, Liberia and Sierra Leone, respectively.

WHO Ebola Response Team, 2014
Figure 1: Ebola virus disease cases reported each week from Guinea and Conakry

Data are based on official information reported by Ministries of Health up to the end of 12 October for Guinea and Sierra Leone, and 11 October for Liberia. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results.
Figure 2: Ebola virus disease cases reported each week from Liberia and Monrovia

Data are based on official information reported by Ministries of Health up to the end of 12 October for Guinea and Sierra Leone, and 11 October Liberia. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results.

Growing number of Suspected Cases may be indicative of overwhelmed medical infrastructure
EVD transmission is rampant in Sierra Leone, with 425 new confirmed cases reported between October 6 and 12 (figure 3). The areas hardest hit are the capital, Freetown, with 172 new cases, along with the neighboring western districts of Bombali (94 cases) and Port Loko (67 cases). The central districts of Bo (22 new cases) and Tonkolili (27 new cases) are also areas of intense transmission. Transmission appeared to have been slowing in recent weeks in Kailahun and Kenema. However, this week has seen an increase in new cases, with eight new cases in Kailahun and 16 in Kenema.

Figure 3: Ebola virus disease cases reported each week from Sierra Leone and Freetown

Data are based on official information reported by Ministries of Health up to the end of 12 October for Guinea and Sierra Leone, and 11 October for Liberia. These numbers are subject to change due to ongoing reclassification, retrospective investigation and availability of laboratory results.
Data Quality in an Unfolding Crisis

‘We knew the ~350 confirmed cases last week were an undercount….we now think there are 7-900 in reality.’ Les Roberts, Blog: Day 7 (Oct. 11), Sierra Leone.

Under-reporting, particularly as systems are overwhelmed, is a huge concern.

The large spatial extent of the outbreak within country may mean that areas of activity go unreported

Few cases in Liberia are confirmed
The outbreak is unprecedented.
The data are poor
The transmission dynamics are under-resolved
How will it progress? How does this all end?
Ebola Modeling and Forecast

Forecasting approach based on our work with influenza

To predict Ebola, we mimic strategies used in numerical weather prediction

Requires 3 ingredients:

1) Real-time estimates of Ebola incidence and mortality (i.e. observations)

2) Model of Ebola transmission dynamics

3) Data assimilation method to rigorously combine #1 and #2.
We use basic compartmental models run at the country level

We impose some features, including a stochastic component in the force of transmission, that enable simulation of time series (by the model alone) similar to observed incidence time series.
Model Emulation of Observed Characteristics at the Country Level

Guinea through End of July

SEIRX Free Simulation
Prior to Forecast: Training the Model

- Errors in the model structure, model parameters and initial model state amplify through time.
- Left to its own devices the model forecast will deviate from reality.

![Graph showing true outcome and model simulated outcomes](image)
Guinea Forecast, October 12, 2014
Liberia Forecast: October 11, 2014
Sierra Leone Forecast: October 12, 2014
Why are the Liberia forecasts consistently high?

1) Model is mis-specified or not well optimized; hence the ‘no change’ predictions consistently over-predict new case levels;

2) Data are biased low—under-reporting; delays in reporting such that some of those new cases and deaths belong to earlier weeks;

3) Virus has changed, against evolutionary theory, and is less transmissible;
Why are the forecasts consistently high?

4) Virus is in areas where the effects of localized herd immunity are evident and transmission is slowing;

5) There has been an improvement in intervention and control.
Asymptomatic Infection

Is asymptomatic infection common?

Will herd immunity become a factor in the current outbreak?

Need different levels of vaccine coverage

Bellan et al., 2014 The Lancet
Asymptomatic Infection in NE Gabon

Within general population in area with multiple Ebola outbreaks, 1% positive, suggesting low general levels of asymptomatic infection

Heffernan et al., 1997, JID

Asymptomatic Infection in Northern Gabon

Found IgG and IgM response to Ebola antigens in 11 of 24 close asymptomatic contacts of symptomatic patients.

Leroy et al., 2000, The Lancet
Cameroon
Evidence of antibodies to Ebola found in 9.7% of the 1517 tested. Highest in Pygmies, young adults and rain forest farmers

Bouree and Bergmann, 1983, AJTMH

Central African Republic
Evidence of antibodies to Ebola found in 5.3% of the 240 tested. Higher in Pygmies than Bantu

Gonzalez et al., 2000, Microbes and Infection
Evidence of antibodies to Ebola found in 17.6% of the 427 tested. Higher in Pygmies

Johnson et al., 1993, TRSTMH
Selection of a More Transmissible Virus?

Humans are not the natural host for Ebola

Evolutionary theory indicates that with repeated serial passage in the human host less virulent but more transmissible virus phenotypes will be selected.
Collaborators

Wan Yang, Columbia University
Sasi Kandula, Columbia University

Funders

NIH (NIGMS)/NSF (DMS) joint initiative to support research at the interface of the biological and mathematical sciences