Ebola –The Hard Facts and Lessons Learned

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Treatment of a Laboratory-Acquired Sabiá Virus Infection

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Ebola-Filovirus

RNA-single stranded virus
Ebola

- Disease
- Global Statistics and Response
- Surgical Risks
- Why this epidemic is out of control
- Future Proposals
Ebola-Filovirus

Five Subspecies:

- Zaire
- Sudan
- Bundibugyo (Uganda)
- Tai Forest (Cote d’ivoire)
- Reston (monkeys and pigs)
Ebola virus Ecology

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)

Epizootic Cycle

Epizootics caused by ebolaviruses appear sporadically, producing high mortality among non-human primates and duikers and may precede human outbreaks. Epidemics caused by ebolaviruses produce acute disease among humans, with the exception of Reston virus which does not produce detectable disease in humans. Little is known about how the virus first passes to humans, triggering waves of human-to-human transmission, and an epidemic.

Following initial human infection through contact with an infected bat or other wild animal, human-to-human transmission often occurs.

Human-to-human transmission is a predominant feature of epidemics.
Transmission --- Ebola-Zaire

- Contact with body fluids—blood, saliva, feces, vomit, sweat, skin—or by eating or handling infected meat
- Virus is viable--24 hours to 6 days on surfaces (rare fomite transmission)
- This outbreak-Ebola-Zaire-/300 mutations since May 2014
- Airborne transmission, -no lung tropism, rare for a virus to mutate mode of transmission

Ebola-Reston - Philippines


Ebola-Reston

Outbreaks in Macaque monkeys and pig clusters
asx antibody conversion in handlers-aerosol transmission
Pathogenesis of Disease

- Macrophages and dendritic cells-first to be infected
- Pro-inflammatory cytokines-SIRS
- Tropism to hepatocytes and endothelial cells
- Activation of extrinsic coagulation pathway via TF
- Nitric oxide generation
- Host response/ vascular permeability, hypotension and shock
Ebola---Clinical Disease in the News/Web
Disease – Current Epidemic/4010 cases

- Incubation 2-21 days – (11.4 days-mean) Demographics: Equal gender/ 60% age 15-44
- Abrupt onset of fever – 87%
- Fatigue- 76%
- Nausea, vomiting, diarrhea 65 %
- Headache-53%
- Abdominal pain-44%
- Sore throat-21%
- Hiccups-11%
- Rash 5.8%
- Unexplained bleeding- 18% Melena 5%, gums 2%, epistaxis 1.9%, venipunctures 2.4%, skin 0.6% hemoptysis 2.4 %
- Poor prognosis- older age, diarrhea, hemorrhagic conjunctivitis, SOB, confusion/coma, hemorrhage
- Recovered patients: Semen for up to 3 months post recovery/Breast milk 15 days

Secrets of an effective pathogen

R₀ (basic reproduction number) needs to be >1

- Infectiousness (probability of infection given exposure)
- Rate of contact between infectious and susceptible people
- Duration of infectiousness

Ebola:

- Requires close contact to be infectious; probability increases in absence of protective clothing
- Rate of contact is low because sick people do not circulate
- Duration of Infectiousness is relatively short
### REPRODUCTIVE NUMBERS OF COMMON VIRUSES

Values of $R_0$ of well-known infectious diseases[^1]

<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[^2]</td>
</tr>
<tr>
<td>SARS</td>
<td>Airborne droplet</td>
<td>2–5[^2]</td>
</tr>
</tbody>
</table>
- **$R_0$ basic reproduction number**
  - Guinea: 1.71
  - Liberia: 1.83
  - Nigeria: 1.20
  - Sierra Leone: 2.02

- **Case Fatality Rate**
  - Guinea/Liberia/Sierra Leone: 70%
  - Nigeria: 45%
  - US: 1/9 -- 11%

- **Health Care Workers**
  - WAfrica: 318 cases/151 deaths
  - MSF: 24 cases/13 deaths/3000 staff
5. How deadly is Ebola?

- **EBOLA**: 50–90%
- **Influenza-H1N1 Pandemic**: 0.01–0.3%
- **Marburg**: 23–90%
- **Measles**: 1–30%
- **Influenza Seasonal**: <1%
- **Polio**: 15–30%
- **Pertussis**: ≤4%
- **Lassa Fever**: 50%
- **Malaria**: ≤20%
- **SARS**: 13–43%
## Diagnostic Testing

- **US –PCR and ELISA**
  - Send specimens to CDC or USAMRID

- **Viral antigen and nucleic acid detection in blood**
  - Positive around day 3 to 7 days

- **IgM antibodies**
  - Detected early as Day 2 and disappear between day 30-168

- **IgG antibodies**
  - Develop between day 6-18 and persist for many years

### Timeline of Infection

<table>
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<tr>
<th>Timeline of Infection</th>
<th>Diagnostic tests available</th>
</tr>
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</table>
| Within a few days after symptoms begin | • Antigen-capture ELISA  
• IgM ELISA  
• PCR  
• Virus isolation |
| Later in disease course or after recovery | • IgM and IgG antibodies |
| Retrospectively in deceased patients   | • Immunohistochemistry testing  
• PCR  
• Virus isolation |

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**Stanford Medicine**  
**Hospital & Clinics**  

**BioFire Diagnostics**  
@BioFireDX  

@BioFireDX provides diagnostic solutions which determine the source of disease & contamination to help make the world a healthier and safer place.  

Salt Lake City, Utah, USA · http://www.BioFireDX.com
Treatment of Ebola

- Supportive therapy- Rehydration
- Blood from convalescent or immune patients
- Monoclonal antibodies to glycoproteins (tobacco!)/Zmapp?
- Vaccines
  - Vesicular stomatitis vaccine-Canada (New Link/Genetics)
  - Adenovirus vaccine-NIH/Glaxo-fast tracked for humans
  - Rabies-based vaccine-NIAID
- Si-Rna-small interfering RNAs to Ebola RNA polymerase-TekMira
- Antivirals for RNA viruses- eg brincidofovir
- Repurposed Drugs- statins, erlotinib
Ebola-Prevention
Ebola-Prevention

Disinfection and Proper Removal of PPE
RISKS FOR SURGEONS

BLOOD

Ebola---untreated viral load-- BILLION per cc/blood

HIV---untreated viral load---100,000’s/cc blood

Hepatitis C---untreated viral load- 5-20 million/cc blood

Ebola-2014

How does this compare to past outbreaks?

It is the deadliest, eclipsing an outbreak in 1976, the year the virus was discovered.

Total Cases: 10,141/5,692-conf
Total Deaths: 4,922

CDC - as of 10/24/14
Why this Outbreak is out of Control

- Globalization-porous borders/air travel
- Urban spread-denser population
- Weak health infrastructure—-but not non-existent
- Cultural practices – distrust/traditional healers
- Lack of coordination and inattention-WHO cutbacks
- Weak governance-post/conflict states with legacy of distrust of govts
- Poor preparedness of US hospitals can possibly amplify risk in US
JFK Hospital - Monrovia
Cumulative cases in Liberia and Sierra Leone

**Best-case scenario**
11,000-27,000 cases through Jan. 20

Assumes 70 percent of patients are treated in settings that confine the illness and that the dead are buried safely. About 18 percent of patients in Liberia and 40 percent in Sierra Leone are being treated in appropriate settings.

**Worst-case scenario**
537,000-1.4 million cases through Jan. 20

If the disease continues spreading without effective intervention. Dr. Thomas R. Frieden, the C.D.C. director, said, “My gut feeling is, the actions we’re taking now are going to make that worst-case scenario not come to pass. But it’s important to understand that it could happen.”

Source: Centers for Disease Control and Prevention
Lessons Learned?

- Strong governance is important – at WHO level and Nation level for Rapid Epidemiologic Response with Quarantine and Contact Tracing

- A process for ethical allocation of drugs, vaccines and rollout of research trials

- Health-work forces need to be strengthened in low resourced settings
  Global Health Reserve Corps---for rapid scale-up

- Better Biosurveillance---One Health Movement
Multiple Ebola Virus Transmission Events and Rapid Decline of Central African Wildlife


Ebola

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