Ebola: A Global Health Crisis

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Global Health Sciences

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Outline

• What is Ebola and where it came from?
• Current outbreak and projections
• Cases outside West Africa
• Transmission, prevention and containment
• Global epidemic, local and global response
• Preparedness at UCSF
Marburg, Germany, 1967

• Three simultaneous outbreaks of acute hemorrhagic fever in research laboratory workers and their family contacts in Marburg and Frankfurt, West Germany, and Belgrade, Yugoslavia

• Progressive symptoms include fever, rash, vomiting, massive hemorrhage and multi-organ failure

• Thirty-one cases, seven deaths (23%)

• Primary cases had been exposed to African green monkeys imported from Uganda or their tissues
Zaire, 1976

- 318 cases of a hemorrhagic fever occurred in Yambuku, near Ebola River, a northern headwater of the Congo River
- Spread nosocomially through contaminated needles and syringes and by burial practices
- Closely followed by outbreak in southern Sudan with 254 cases (1300 km away)
- Case fatality rates 88% in Zaire and 53% in Sudan
- Caused by newly recognized Ebola virus
Ebola virus is thought to persist in reservoir species in areas where it is endemic. Humans, apes, and other mammalian species develop severe disease and are therefore considered end hosts rather than reservoir species. Viral antibodies and RNA have been identified in three species of fruit bats from the Pteropodidae family (Hypsignathus monstrosus, Epomops franqueti, and Myonycteris torquata). Rodents are also potential reservoirs. Reston ebolavirus has been identified in domestic pigs in the Philippines. Other species may serve as viral reservoirs. Once humans are infected, person-to-person transmission occurs after direct contact with infected bodily fluids or tissues.
Hemorrhagic fever viruses

- Group characterized by symptom complex
- At least five different families of viruses
- All RNA viruses
- All have animal or insect hosts
- Human-to-human transmission mostly nosocomial

<table>
<thead>
<tr>
<th>Family</th>
<th>Virus (examples)</th>
<th>Distribution</th>
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<tbody>
<tr>
<td>Arenaviridae</td>
<td>Junin, Machupo, Lassa</td>
<td>Argentina, Bolivia, Nigeria</td>
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<tr>
<td>Bunyaviridae</td>
<td>Rift Valley fever, Congo-Crimean, Sin nombre</td>
<td>Africa, Africa, Ukraine, Korea, US</td>
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<td>Filoviridae</td>
<td>Ebola, Marburg</td>
<td>Africa</td>
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<td>Flaviviridae</td>
<td>Yellow fever, Dengue, West Nile</td>
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<tr>
<td>Paramyxoviridae</td>
<td>Hendra, Nipah</td>
<td>Asia, Australia</td>
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</tbody>
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Patient Zero of current outbreak: 2-year old boy in Guéckédou, a border town in Guinea
How Ebola Spread

MELIANDOU VILLAGE, GUÉCKÉDOU, GUINEA
DEC. 6, 2013
The suspected first case, a 2-year-old child living in Meliandou Village, Guéckédou, dies after being sick for four days.

DEC. 13, 2013 TO FEB. 2, 2014
The child's sister, mother and grandmother die. The village midwife is hospitalized in Guéckédou and also dies.

MACENTA, GUINEA
FEB. 10, 2014
A health care worker from Guéckédou hospital dies at Macenta hospital after being sick for five days.

FEB. 24, 2014
A doctor at Macenta hospital who treated the health care worker dies. His funeral is held in Kissidougou.

NZÉRÉKORÉ, GUINEA
FEB. 28, 2014
A relative of the Macenta hospital doctor dies in Nzérékoré.

KISSIDOGOU, GUINEA
MARCH 7 AND 8, 2014
Two of the Macenta doctor's brothers die in Kissidougou.
Where is the Ebola outbreak?
Comparison of past and current Ebola outbreaks

Ebola cases and deaths by year, and countries affected

- **2nd-worst year**
  - Sudan, Democratic Republic of Congo
  - 602 cases
  - 431 deaths
  - Source: World Health Organization

- **5th**
  - Democratic Republic of Congo
  - 315 cases
  - 254 deaths

- **3rd**
  - Uganda
  - 425 cases
  - 224 deaths

- **4th**
  - Uganda, Democratic Republic of Congo
  - 413 cases
  - 224 deaths

- **1st**
  - Guinea, Liberia, Nigeria, Senegal, and Sierra Leone
  - 6,553 cases
  - 3,083 deaths
  - As of Sept. 26
Current outbreak

• Increasingly Draconian control measures
  – Community wide quarantines in Liberia and Sierra Leone (~1 million people)
  – South Africa bans travelers from Guinea, Liberia and Sierra Leone
  – Chad closes border with Nigeria
  – Saudi Arabia stopped issuing hajj visas to Guineans

• WHO declares epidemic to be public health emergency of international concern on 8 August
Ebola cases by country and date as of October 8th

- **Guinea**: 1,298 cases, 768 deaths
- **Liberia**: 3,924 cases, 2,210 deaths
- **Sierra Leone**: 2,789 cases, 879 deaths
- **Nigeria**: 20 cases, 8 deaths
Ebola cases in health care workers in West Africa as of October 8th

Source: World Health Organization
How many people can become infected?

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
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Thomas Duncan: First case of Ebola in the U.S.

From Monrovia to Dallas
Thomas Duncan: First case on Ebola in the U.S.

- SEPT. 19: Foreign Airport Check-in
- SEPT. 20: Going Through U.S. Customs
- SEPT. 25: First Hospital Visit
- SEPT. 28: Second Hospital Visit
- SEPT. 29-30: Testing and Contact Tracing

- OCT. 1: Isolating the Closest Contacts
- OCT. 2: Sanitizing the Apartment
- OCT. 4: Trying an Experimental Drug
- OCT. 8: Handling the Body
Cases of Ebola Outside of West Africa

Sunday: A hospital worker involved in the treatment of an Ebola patient from Liberia has tested positive for the disease.

A Spanish nurse contracted Ebola while treating a missionary who died in a Madrid Hospital.

Countries with Ebola outbreaks
## Ebola cases outside of west Africa

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<thead>
<tr>
<th>United States</th>
<th>Arrival date</th>
<th>Status</th>
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<tbody>
<tr>
<td>Aid worker</td>
<td>Aug. 2</td>
<td>Recovered</td>
</tr>
<tr>
<td>Missionary</td>
<td>Aug. 2</td>
<td>Recovered</td>
</tr>
<tr>
<td>Doctor</td>
<td>Sept. 5</td>
<td>Recovered</td>
</tr>
<tr>
<td>Doctor</td>
<td>Sept. 9</td>
<td>In treatment</td>
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<tr>
<td>Visitor</td>
<td>Sept. 30*</td>
<td>Died</td>
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<td>NBC cameraman</td>
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<td>In treatment</td>
</tr>
<tr>
<td>Hospital worker</td>
<td>Oct. 11*</td>
<td>In treatment</td>
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<tr>
<th>France</th>
<th></th>
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<tbody>
<tr>
<td>Nurse</td>
<td>Sept. 19</td>
<td>Recovered</td>
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<tbody>
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<td>Nurse</td>
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<thead>
<tr>
<th>Spain</th>
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<td>Missionary</td>
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<tr>
<td>Priest</td>
<td>Sept. 22</td>
<td>Died</td>
</tr>
<tr>
<td>Nurse</td>
<td>Oct. 6*</td>
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<tr>
<th>Germany</th>
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<tr>
<td>Doctor</td>
<td>Aug. 27</td>
<td>Recovered</td>
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<tr>
<td>Doctor</td>
<td>Oct. 3</td>
<td>In treatment</td>
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<tr>
<td>U.N. medical worker</td>
<td>Oct. 9</td>
<td>Died</td>
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<th>Norway</th>
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</thead>
<tbody>
<tr>
<td>Aid worker</td>
<td>Oct. 6</td>
<td>In treatment</td>
</tr>
</tbody>
</table>

*Date of Ebola diagnosis.
Teresa Romero: First case of Ebola outside Africa

Spanish missionary Manuel Garcia contracted Ebola in Sierra Leone. He died on Sept 25th in Madrid.

Officials are investigating whether the Spanish nurse may have inadvertently touched her face while taking her suit off.
Nina Pham: First case of Ebola Transmission in the U.S.

Thomas Duncan, a Liberian citizen, is the first person to die from EVD in the United States.

Nina Pham, a nurse at Texas Health Presbyterian Hospital, contracted EVD after caring for Thomas Duncan.
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Ebola virus
Transmission

• Primary transmission likely from bats
• Secondary transmission is from percutaneous or mucous membrane contact with blood or body fluids (e.g., vomitus) and unsterilized medical instruments
• Burial preparation
• At highest risk are health care workers and close contacts (family members)
• Transmission only from symptomatic people
FIGURE 4. Distribution of Ebola virus incubation period, by days of incubation

*Frequency relates to number of patients out of a total of 5,000 patients.

Preventing transmission

• No vaccine available although some substantial portion of people may be immune from earlier asymptomatic infection

• Focus is on preventing transmission in health care facilities
  – Make diagnosis
  – Barrier precautions (mask, gloves, impermeable gowns, goggles or eye shields)
  – Isolation

• Safe burial practices
Ebola hemorrhagic fever
Signs and symptoms

- Fever ≥38.6°C
- Severe headache
- Hiccups in 50%
- Myalgias and weakness
- Vomiting and diarrhea
- Abdominal pain
- Half will develop bleeding or unexplained bruising
- Symptoms appear 2-21 days post exposure (usually 4-6)
Are there drugs to treat or prevent ebola?

**The Ebola virus** infects cells by punching into the cell and injecting a small piece of viral RNA. The RNA hijacks the machinery of the cell and uses it to create more copies of the Ebola virus, which in turn infect other cells.

**Ebola survivors** have antibodies against the Ebola virus in their blood. Antibodies are Y-shaped proteins that can latch on to a specific virus and prevent it from infecting cells. Plasma extracted from the blood of Ebola survivors might be transfused into infected people, possibly helping them fight the virus.

**The drug ZMapp** is a mixture of three different antibodies that were developed in mice and modified to work in humans. The drug was first tested in humans during the current outbreak, but it is unclear if the drug is effective. ZMapp is made in tobacco plants and there is only limited manufacturing capacity.
What to do locally and globally?

• LOCAL
  – Training of health workers
  – Specialized care in major cities
  – Information to public
  – Awareness of interconnectness and interdependence

• GLOBAL
  – Resource mobilization
  – Sending specialized personnel
  – Global surveillance and control
  – Health system strengthening
Basic infection control

- Standard precautions
- Identify suspected cases of VHF
- Isolate patients
- Protective clothing
- Disinfection on non-disposable supplies
- Safe waste disposal
- Cremating bodies and not washing them
Health Care Facility Preparedness Checklist for Ebola Virus Disease (EVD)

All U.S. health care facilities need to be prepared for managing patients with infectious diseases such as Ebola virus disease (EVD). Facilities should review infection control policies and procedures and incorporate plans for administrative, environmental, and communication measures. Facilities should also define the individual work practices that will be required to detect the introduction of a patient with EVD or other emerging infectious disease, prevent spread, and manage the impact on patients, the facility, and staff.

- Monitor the situation
- Assess and ensure availability of PPE and other infection control supplies
- Review your infection control policies for consistency with CDC
- Review environmental cleaning procedures
- Educate HCW on signs and symptoms of EVD
- Review triage procedures and be sure travel questions are asked
- Review lab procedures for collection, transport and testing of suspect specimens
- Review policies and procedures for screening HCW
- Designate points of contact for communications with PH officials
- Confirm local health department contacts for reporting suspect cases
Back-up slides
Ebola Virus Disease (Ebola)
Algorithm for Evaluation of the Returned Traveler

**FEVER** (subjective or ≥101.5°F or 38.6°C) or compatible Ebola symptoms* in patient who has traveled to an Ebola-affected area** in the 21 days before illness onset

* headache, weakness, muscle pain, vomiting, diarrhea, abdominal pain, or hemorrhage

NO

Report asymptomatic patients with high- or low-risk exposures (see below) in the past 21 days to the health department

YES

1. Isolate patient in single room with a private bathroom and with the door to hallway closed
2. Implement standard, contact, and droplet precautions (gown, facemask, eye protection, and gloves)
3. Notify the hospital Infection Control Program and other appropriate staff
4. Evaluate for any risk exposures for Ebola
5. IMMEDIATELY report to the health department

**HIGH-RISK EXPOSURE**
Percutaneous (e.g., needle stick) or mucous membrane contact with blood or body fluids from an Ebola patient
OR
Direct skin contact with, or exposure to blood or body fluids of, an Ebola patient
OR
Processing blood or body fluids from an Ebola patient without appropriate personal protective equipment (PPE) or biosafety precautions
OR
Direct contact with a dead body (including during funeral rites) in an Ebola affected area** without appropriate PPE

**LOW-RISK EXPOSURE**
Household members of an Ebola patient and others who had brief direct contact (e.g., shaking hands) with an Ebola patient without appropriate PPE
OR
Healthcare personnel in facilities with confirmed or probable Ebola patients who have been in the care area for a prolonged period of time while not wearing recommended PPE

**NO KNOWN EXPOSURE**
Residence in or travel to affected areas** without HIGH- or LOW-risk exposure

Review Case with Health Department Including:
- Severity of illness
- Laboratory findings (e.g., platelet counts)
- Alternative diagnoses

Ebola suspected ↔ Ebola not suspected
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- Severity of illness
- Laboratory findings (e.g., platelet counts)
- Alternative diagnoses

Ebola suspected

TESTING IS INDICATED

The health department will arrange specimen transport and testing at a Public Health Laboratory and CDC

The health department, in consultation with CDC, will provide guidance to the hospital on all aspects of patient care and management

Ebola not suspected

TESTING IS NOT INDICATED

If patient requires in-hospital management:
- Decisions regarding infection control precautions should be based on the patient’s clinical situation and in consultation with hospital infection control and the health department
- If patient’s symptoms progress or change, re-assess need for testing with the health department

If patient does not require in-hospital management:
- Alert the health department before discharge to arrange appropriate discharge instructions and to determine if the patient should self-monitor for illness
- Self-monitoring includes taking their temperature twice a day for 21 days after their last exposure to an Ebola patient

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

** CDC Website to check current affected areas: www.cdc.gov/ebola

This algorithm is a tool to assist healthcare providers identify and triage patients who may have Ebola. The clinical criteria used in this algorithm (a single symptom consistent with Ebola) differ from the CDC case definition of a Person Under Investigation (PUI) for Ebola which is more specific. Public health consultation alone does not imply that Ebola testing is necessary. More information on the PUI case definition: www.cdc.gov/vhf/ebola/hcp/case-definition.html
What’s happening in the US?

• 3 health care workers evacuated from West Africa treated successfully; 2 still in care
• 1 traveler from Liberia who was asymptomatic on entry into the US admitted to a Dallas hospital and died
• 1 healthcare worker at Dallas hospital has tested positive
• US now screening returning travelers in five airports
• Massive CDC, USAID, DoD response
• Preparedness in US hospitals
Treatment

• No specific antiviral drug available and approved
• Focus in on supportive care
  – IV fluids and electrolytes
• Oxygenation and perfusion
• Immunomodulators
• Treating endothelial dysfunction
  – Statins
  – ACE inhibitors
  – Angiotensin receptor blockers

• Experimental antiviral drugs
  – May be accessible under emergency IND from FDA
  – ZMapp (monoclonal Ab to 3 glycoprotein epitopes) provides protection in non-human primates
  – TkM-Ebola – RNA polymerase blocker
  – AVI-7535 – target EV protein VP24
  – ECX-4430 – adenosine analogue