

Ebola 2014: From Exotic Tropical Disease to International Emergency

Dr. Jill Hacker
Viral and Rickettsial Disease Laboratory
CDPH



Dr. Patrick Ayscue
Division of Communicable Disease Control



Viral Hemorrhagic Fevers

Arenaviridae

- Junin, Machupo, Sabia, Guanarito, Lassa

Bunyaviridae

- Crimean Congo HF, Hantavirus, Rift Valley Fever

Flaviviridae

- Kyasanur Forest Disease, Omsk, Yellow Fever, Dengue

Filoviridae

- Ebola, Marburg
- RNA viruses
- Enveloped in lipid coating
- Survival depends on an animal or insect host natural reservoir

Virology

Family Filoviridae, genus Ebolavirus

Species:

– **Ebola** (*formerly Zaire*)



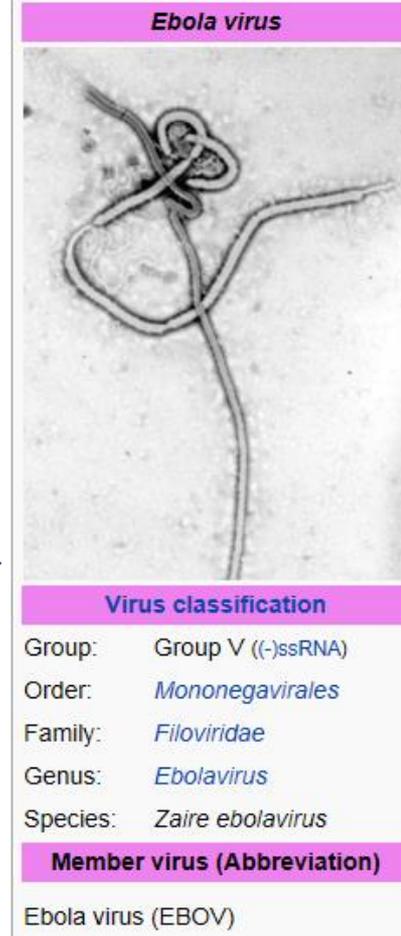
– Sudan

– Tai Forest (formerly Ivory Coast),

– Bundibugyo

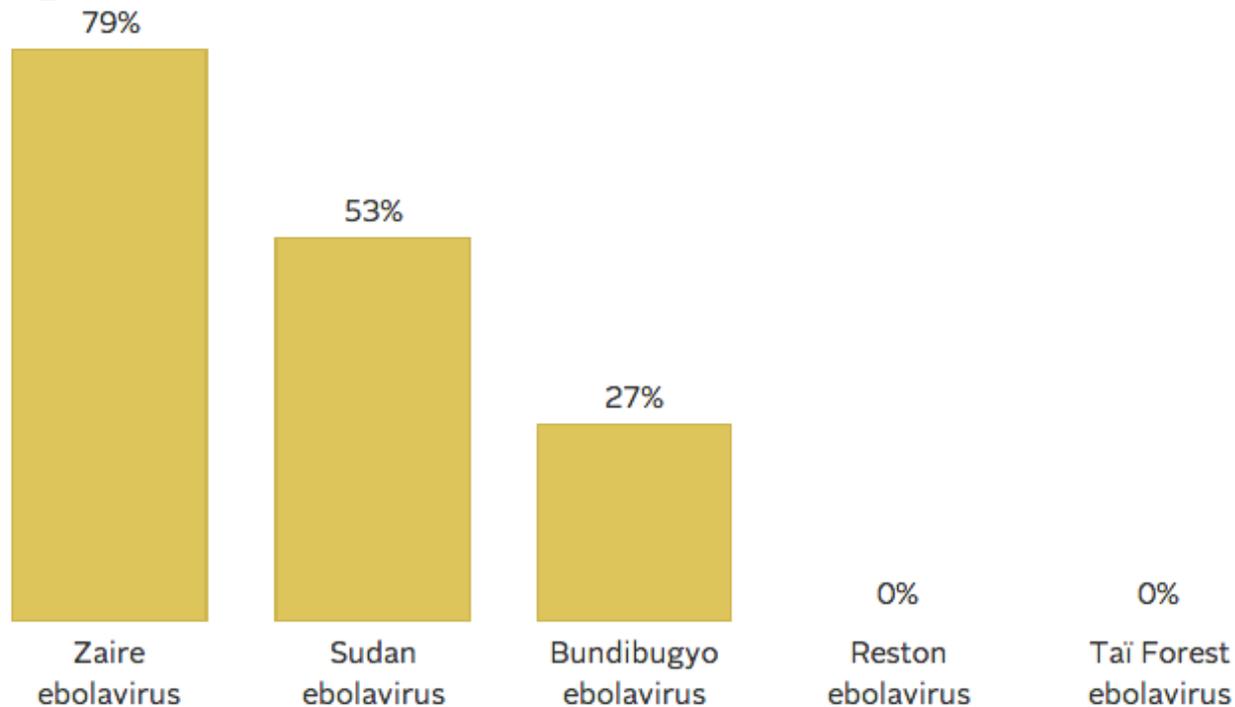
– Reston (cause monkey death and swine infection, not human)

– *Often named for place of discovery*



Death rates different Ebola species

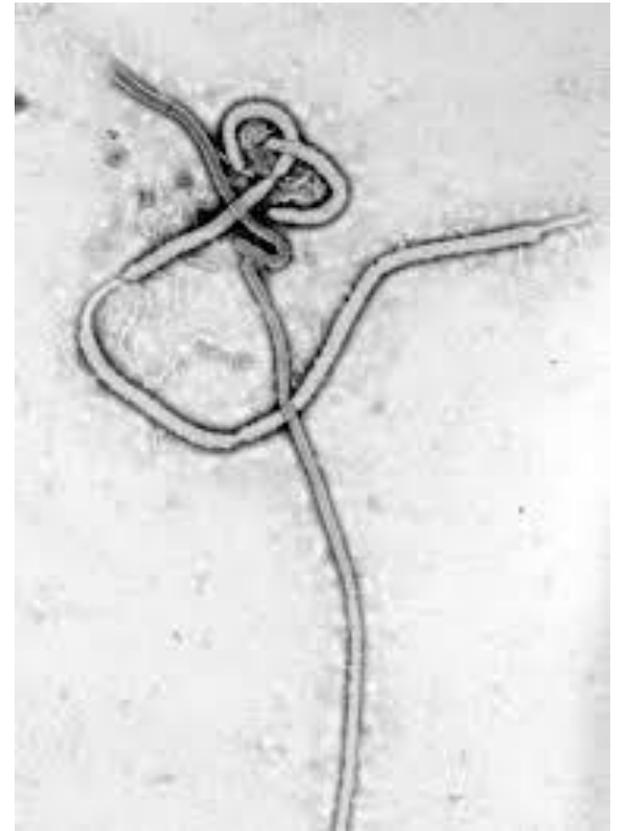
Death rates of the 5 Ebola virus species



Viral Hemorrhagic Fevers

All are characterized by:

- Severe multi-organ damage
- Damage to overall vascular system
- Symptoms often accompanied by hemorrhage (conjunctivitis, petechiae, ecchymosis)



Ebola Pathology

- Hepatocellular necrosis and associated with dysregulation of clotting factors and subsequent coagulopathy
- Adrenocortical necrosis associated with hypotension and impaired steroid synthesis
- Release of pro-inflammatory cytokines with subsequent vascular leak and impairment of clotting ultimately resulting in multi-organ failure and shock

Ebola Virus Disease

- Incubation period: 2-21 days (typically 5-10 days)
- Nonspecific prodrome: **fever** (87%), chills, myalgia (39%), malaise, **asthenia/weakness** (76%)
- Day 4: **severe watery diarrhea** (65%), nausea, **vomiting** (67%), abdominal pain (44%), chest (37%), SOB (23%), profound weakness
 - hiccups (12%), conjunctival injection (21%)
 - seizures, cerebral edema, confusion (13%)
- Day 5-7 (in some): diffuse erythematous maculopapular rash involving face, neck, trunk and arms that desquamates (6%)
- Day 6-16: multiorgan failure, septic shock, hemorrhage (18%), death

Laboratory Findings

- Leukopenia frequently with lymphopenia followed later by elevated neutrophils and a left shift
- **Platelet counts decreased (50,000 - 100,000)**
- **Elevated hepatic transaminases**
- Prothrombin (PT) and partial thromboplastin times (PTT) are prolonged and fibrin degradation products are elevated (c/w DIC)
- Proteinuria may be present

Ebola Transmission

- Contact with infectious bodily fluids
 - Increasing infectivity with course of disease
 - Low infectious dose
- Initial introduction from wildlife to humans
 - Typically from contact with bushmeat (e.g. primates, duiker, bat)
 - Carrying or preparation
- Human-human transmission
 - Caregivers to the sick
 - Good Samaritans
 - Healthcare workers
 - Funerals



Interventions

- Contact tracing
- Isolation
- Supportive care
- Education
- Travel screening

Chain 2: LIB-MONT-010

LIB-MONT-010
40 yo female
HCW (Nurse)
Onset 5/14/2014
Symptom onset: Bernard's Farm, Montserrado
Hospitalized: Redemption Hospital 6/9/2014
Death 6/14/2014

LIB-MONT-018
25 yo female
Last contact 6/24/2014
Visited in hospital
? Onset 6/10/2014
Hospitalized 6/26/2014
Bernard's Farm,
Monrovia, Montserrado
Alive as of 6/26/2014
Probable case

LIB-MONT-020
67 yo female
Last contact 6/14/2014
Visited in hospital
Onset 6/19/2014
Hospitalized 6/28/2014
Foya town, Lofa
Bernard's Farm,
Monrovia,
Montserrado
Alive
Probable case

LIB-MONT-003
39 yo female
HCW (PA)/co-worker
Last contact 6/9/2014
Onset 6/20/2014
Hospitalized
6/30/2014
Discharged 7/4/2014
Wrote Town,
Monrovia,
Montserrado

LIB-MONT-012
45 yo male
**HCW (MD
Redemption)**
Last contact not
specified (patient)
Onset 6/20/2014
Tarr Town,
Monrovia,
Montserrado
Death 7/1/2014

LIB-MONT-026
55 yo female
HCW (Nurse's aide)
Last contact 6/14/2014
At Redemption Hosp
Onset 6/20/2014
Hospitalized 6/29/2014
Old Road, Monrovia,
Montserrado
Death 6/30/2014
Probable case

LIB-MONT-035
26 yo male
HCW (PA Redemption)
Last contact 6/23/2014
Visited in hospital
Onset 6/25/2014
Hospitalized 6/28/2014
Monrovia, Montserrado
Alive as of x/x/2014

LIB-MONT-025
54 yo female
Last contact 6/15/2014
Attended funeral in Zay
Zay
Onset 6/25/2014
Hospitalized 6/26/2014
Zay Zay, Monrovia,
Montserrado
Alive as of 6/26/2014
Death 6/30/2014

LIB-LOFA-013
45 yo female
Onset ?
Zhango Town,
Voinjama, Lofa
Death 6/18/2014

LIB-MONT-029
39 yo male
Last contact 6/14/2014
Visited in hospital
Onset 6/26/2014
Hospitalized 6/26/2014
Chicken Soup Factory,
Monrovia, Montserrado
**Death: date not
recorded**

Same person ?

LIB-MONT-019
26 yo male
HCW (PA; Redemption
Hosp)
? Last contact 6/23/2014
Onset 6/23/2014
Monrovia, Montserrado
Alive as of 6/28/2014
Probable case

Ebola background

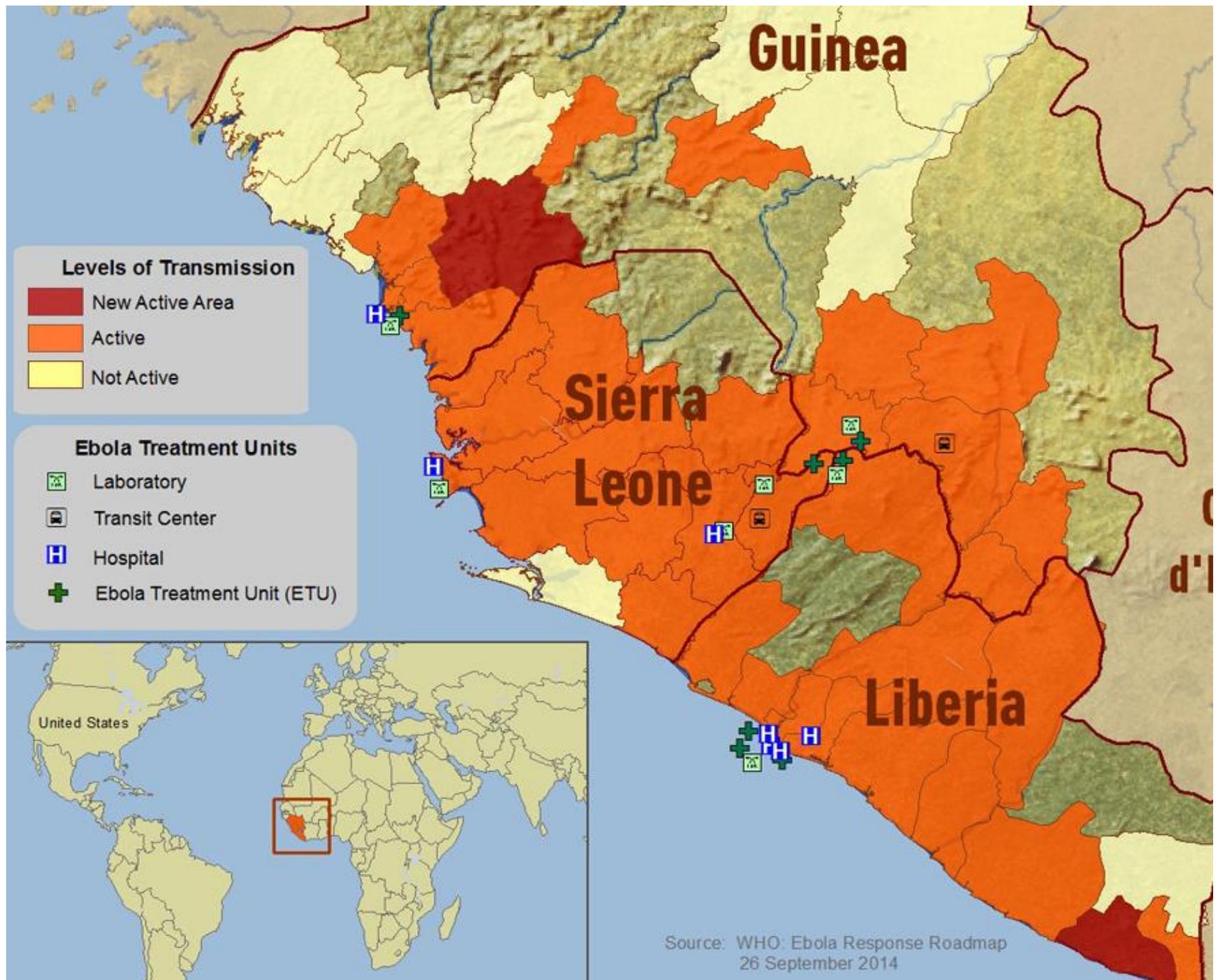
1976-2013:

- ~50 “outbreaks” recognized
 - 10 were 1-5 cases
 - 25 were >5-100 cases
 - 14 > 100 cases
 - Largest OB=425
- Most due to
 - Zaire-Ebola (30)
 - Sudan (14)
 - Bundibogyo (4)
- Countries (# OB reported)
 - Democratic Rep Congo (formerly Zaire) – 12
 - Congo – 10
 - Uganda – 10
 - Sudan – 5
 - Gabon – 8
 - Often rural settings



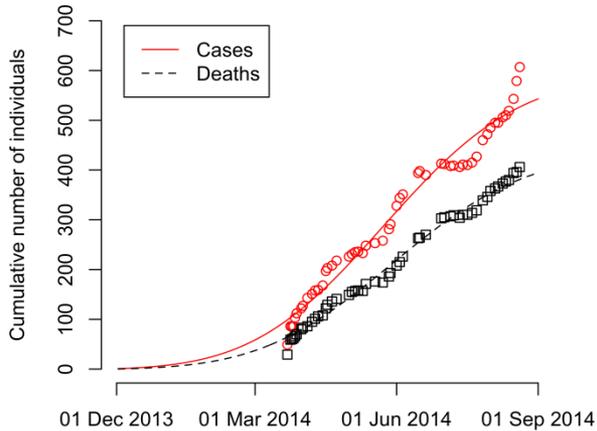
Current Outbreak Overview

- Ebola outbreak identified in Guinea in mid-March, 2014
 - Likely had been ongoing since Dec 2013
 - Subsequently spread to Liberia, Sierra Leone, and Nigeria
 - US and Senegal have each identified an imported case
 - Spain has identified local transmission to one individual
- Largest EVD outbreak ever; more cases than all other outbreaks combined
 - Transmission in capitals, across borders, via plane

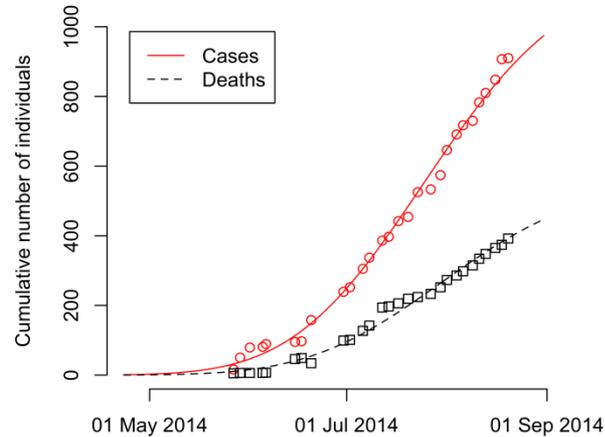


Case Counts

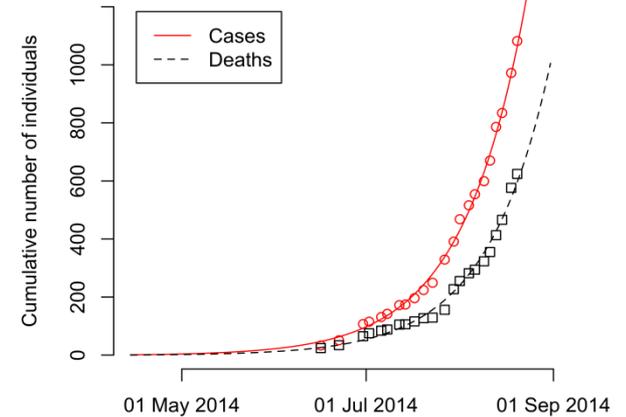
Guinea



Sierra Leone



Liberia



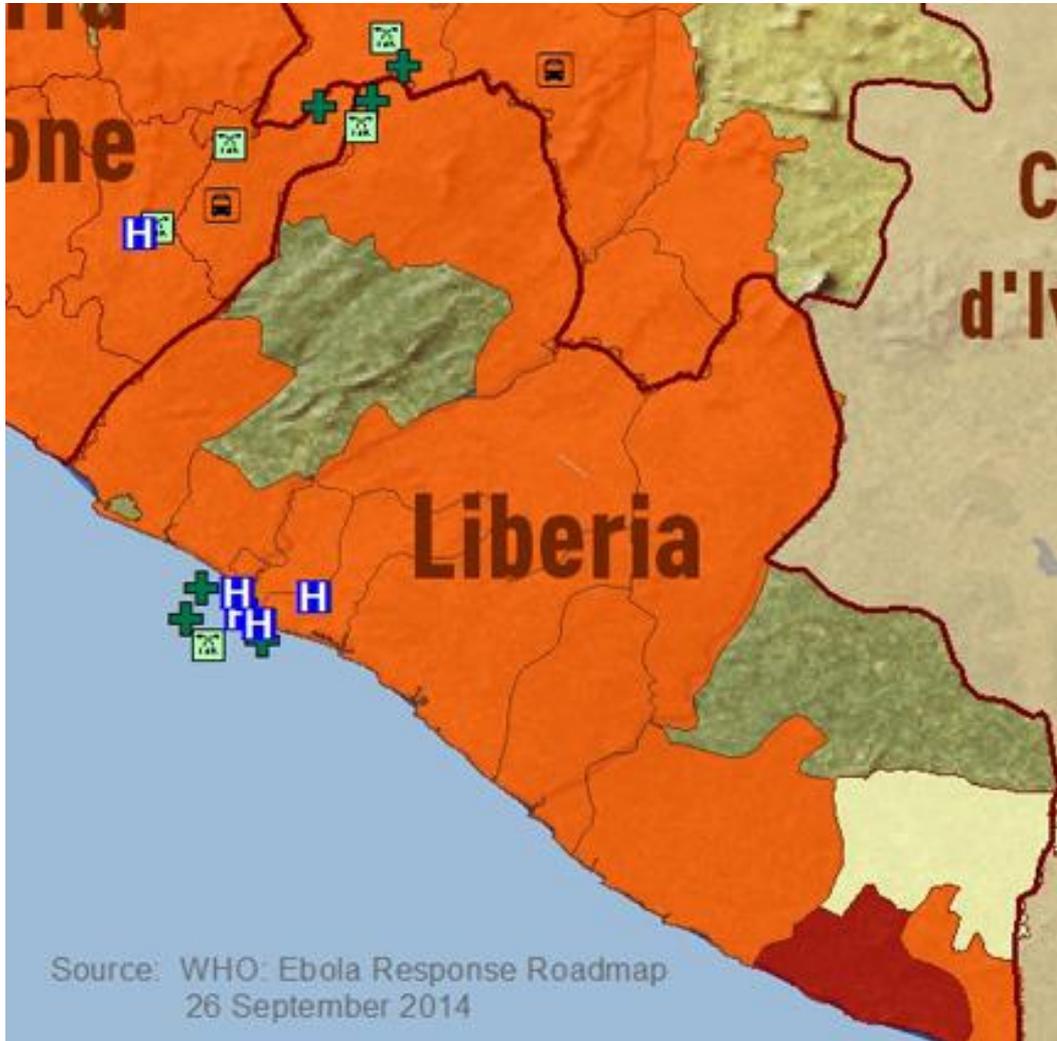
- CDC estimates true number of cases is 2.5x what is being captured by surveillance

What is different in this outbreak?

- Urban areas affected
- Months of transmission before identified
- Unprepared health and public health systems
 - Lack of familiarity with illness
- Mobile populations
 - Fluid national borders in region
- Distrust of government/authority
- Profoundly resource-poor settings

Liberia

- 175th of 187 countries in Human Development
- 184 of 189 in GDP per capita
- One of lowest literacy rates in the world
- Brutal civil war from 1989-2003





A white SUV, possibly a Toyota Land Cruiser, is parked on the road surface to the left of the landslide.

A yellow truck is partially buried under the landslide, with its front end and wheels visible.

A large white shipping container with the Maersk logo and name printed on its side. The container is tilted and partially buried under the landslide.

MAERSK





LIBERIA GOVERNMENT HOSPITAL - TUBMANBU

EMERGENCY PARKING



Infection Control in the US

Effective isolation of patients and appropriate infection control measures applied to any suspect EVD patient would contain any potential spread

Infection Control for Hospitalized Suspect Cases

Patient Placement	Single patient room (containing a private bathroom) with the door closed
Personal Protective Equipment (PPE)	<ul style="list-style-type: none">• Gloves• Gown (fluid resistant or impermeable)• Eye protection (goggles or face shield)• Facemask Additional PPE might be required in certain situations including but not limited to: <ul style="list-style-type: none">• Double gloving• Disposable shoe covers• Leg coverings
Patient Care Considerations	Phlebotomy, procedures, and laboratory testing should be limited to the minimum necessary for essential diagnostic evaluation and medical care
Aerosol Generating Procedures (AGPs)	<ul style="list-style-type: none">• Avoid Aerosol Generating Procedures• If performing AGP, wear gloves, a gown, disposable shoe covers, and either a full face shield or goggles, and respiratory protection at least as protective as a NIOSH certified fit-tested N95 filtering facepiece respirator or higher (e.g., powered air purifying respiratory or elastomeric respirator)

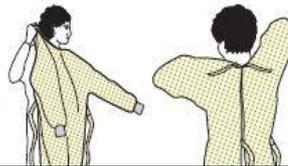
Isolation and Personal Protective Equipment

SEQUENCE FOR PUTTING ON PERSONAL PROTECTIVE EQUIPMENT (PPE)

The type of PPE used will vary based on the level of precautions required, such as standard and contact, droplet or airborne infection isolation precautions. The procedure for putting on and removing PPE should be tailored to the specific type of PPE.

1. GOWN

- Fully cover torso from neck to knees, arms to end of wrists, and wrap around the back
- Fasten in back of neck and waist



2. MASK OR RESPIRATOR

- Secure ties or elastic bands at middle of head and neck
- Fit flexible band to nose bridge
- Fit snug to face and below chin
- Fit-check respirator



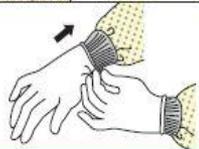
3. GOGGLES OR FACE SHIELD

- Place over face and eyes and adjust to fit



4. GLOVES

- Extend to cover wrist of isolation gown



USE SAFE WORK PRACTICES TO PROTECT YOURSELF AND LIMIT THE SPREAD OF CONTAMINATION

- Keep hands away from face
- Limit surfaces touched
- Change gloves when torn or heavily contaminated
- Perform hand hygiene



SEQUENCE FOR REMOVING PERSONAL PROTECTIVE EQUIPMENT (PPE)

Except for respirator, remove PPE at doorway or in anteroom. Remove respirator after leaving patient room and closing door.

1. GLOVES

- Outside of gloves is contaminated!
- Grasp outside of glove with opposite gloved hand; peel off
- Hold removed glove in gloved hand
- Slide fingers of ungloved hand under remaining glove at wrist
- Peel glove off over first glove
- Discard gloves in waste container



2. GOGGLES OR FACE SHIELD

- Outside of goggles or face shield is contaminated!
- To remove, handle by head band or ear pieces
- Place in designated receptacle for reprocessing or in waste container



3. GOWN

- Gown front and sleeves are contaminated!
- Unfasten ties
- Pull away from neck and shoulders, touching inside of gown only
- Turn gown inside out
- Fold or roll into a bundle and discard



4. MASK OR RESPIRATOR

- Front of mask/respirator is contaminated – DO NOT TOUCH!
- Grasp bottom, then top ties or elastics and remove
- Discard in waste container



PERFORM HAND HYGIENE BETWEEN STEPS IF HANDS BECOME CONTAMINATED AND IMMEDIATELY AFTER REMOVING ALL PPE



Phlebotomy

Any person collecting specimens from a patient with suspected Ebola virus disease should **wear gloves, water-resistant gowns, full face shield or goggles, and masks** to cover all of nose and mouth. Additional PPE may be required in certain situations.



Source: <http://www.>

nl

Laboratory Testing

- Possibly one of the more challenging areas for hospital and their staff
- Routine diagnostic testing
- Testing & shipping for Ebola

Routine Diagnostics

- Results from routine lab tests (e.g., CBC, U/A, LFT, PT/PTT) could be very helpful in assessing likelihood of Ebola as well as for care of patient
- Other testing could be helpful, particularly because the differential includes:
 - Malaria, typhoid, shigella, cholera, leptospirosis, plague and rickettsia
- “Routine” testing may not be so “routine”

Laboratory Risk Assessment

- Risk assessments should be performed to determine the potential for sprays, splashes, or aerosols generated from laboratory procedures
 - Conducted by each laboratory director, biosafety officer, or other responsible personnel
 - Adjust, as needed, PPE requirements, practices, and safety equipment controls to protect the laboratorian's skin, eyes, and mucous membranes

Routine Testing

- Traditional chemistry, hematology, and other supportive clinical testing
- ASM has drafted *Interim Laboratory Guidelines for Handling/Testing Specimens from Cases or Suspected Cases of Hemorrhagic Fever Virus* to assist lab personnel in following guidelines currently recommended by CDC
 - Guidelines for testing should be thoroughly discussed with the appropriate medical personnel and a site-specific and procedure-specific risk assessment should be conducted prior to implementation and may include significant changes of protocols recommended in this document

Specimen Collection

- Specimen containers should be disinfected after specimen collection
- Follow recommended procedures for transport through healthcare facility, clean-up of spills, storing, packaging and shipping

INTERIM GUIDANCE FOR Specimen Collection, Transport, Testing, and Submission for Patients with Suspected Infection with Ebola Virus Disease

NOTIFICATION & CONSULTATION

Hospitals should follow their state and/or local health department procedures for notification and consultation for Ebola testing requests before contacting CDC. CDC cannot accept any specimens without prior consultation.

For Clinical Centers, call the Laboratory Support Center at 770-488-7100

WHEN SPECIMENS SHOULD BE COLLECTED FOR EBOLA TESTING

Ebola virus is detected in blood only after onset of symptoms, most notably fever. It may take up to three days after onset of symptoms for the virus to reach detectable levels. Virus is generally detectable by real-time RT-PCR between 2 to 10 days after onset of symptoms.

Ideally, specimens should be taken when a symptomatic patient reports to a healthcare facility and is suspected of having an Ebola virus exposure. However, if the onset of symptoms is less than three days after potential exposure, a subsequent specimen will be required to rule out Ebola.

3 days

PREFERRED SPECIMENS FOR EBOLA TESTING

A minimum volume of 4 milliliters of whole blood preserved with EDTA, citric acid/oxalate, sodium polyanthracene citrate (SPC), or citrate in plastic collection tubes can be submitted for Ebola virus disease testing.

Specimens should be shipped at 4°C. Do not submit specimens to CDC in glass containers. Do not submit specimens preserved in heparin tubes.

Specimens other than blood may be submitted upon consult with the CDC.

Standard labeling should be required for each specimen. The requested test needs to be identified on the requisition and CDC specimen-submission forms.

4°C

DIAGNOSTIC TESTING FOR EBOLA PERFORMED AT CDC

Several diagnostic tests are available for detection of Ebola virus disease. Acute infections will be confirmed using a real-time RT-PCR assay (CDC test identifier code CDC-10309 Ebola Identification) in a CLIA-accredited laboratory. Virus isolation may also be attempted. Serologic testing for IgM and IgG antibodies will be completed for certain specimens and to monitor the immune response in confirmed Ebola virus disease patients (CDC-10313 Ebola Serology).

Lassa fever is also endemic in certain areas of West Africa and may show symptoms similar to early Ebola virus disease. Diagnostic tests including but not limited to RT-PCR, antigen detection, and IgM serology may be utilized to rule out Lassa fever in patients who test negative for Ebola virus disease.

TRANSPORTING SPECIMENS WITHIN THE HOSPITAL/INSTITUTION

In compliance with 29 CFR 1910.1032, specimens should be placed in a durable, leak-proof secondary container for transport within a facility. To reduce the risk of breakage or leaks, do not use any pneumatic tube system for transporting specimens from a patient with suspected Ebola virus disease.

PACKAGING & SHIPPING CLINICAL SPECIMENS TO CDC

Specimens collected for Ebola virus disease testing should be packaged and shipped without attempting to open collection tubes or aliquot specimens.

Specimens for shipment should be packaged following the basic triple packaging system, which consists of a primary receptacle in a leak-proof specimen bag wrapped with absorbent material, secondary receptacle (leak-tight, leak-proof), and an outer shipping package.

THE SUBMISSION PROCESS

Contact your state and/or local health department and CDC (770-488-7100) to determine the proper category for shipment based on clinical history and their assessment by CDC and to obtain detailed shipping guidance and required CDC submission documents. State guidelines may differ and state or local health departments should be consulted before shipping.

Specimen Handling

- All specimens should be labeled “Suspected HFV”
- Testing that requires specimen removal from patient’s room and transport to lab should be kept to a minimum
- Do not use pneumatic tube system
- All specimen manipulation should be performed in patient’s room, or biologic safety cabinet in AFB suite or isolated area of lab while wearing PPE
- In compliance with 29 CFR 1910.1030, specimens should be placed in a durable, leak-proof secondary container for transport within a facility

Disinfection

- Disinfect outside of sample containers before transport and/or packaging
- There are no disinfection products with specific label claims against Ebola virus
- Enveloped viruses such as Ebola are susceptible to a broad range of hospital disinfectants used to disinfect hard, non-porous surfaces
- EPA-registered hospital disinfectants with label claims against non-enveloped viruses (e.g., norovirus, rotavirus, poliovirus) are broadly antiviral and capable of inactivating both enveloped and non-enveloped viruses
- Possible disinfectants for use in the lab include 10% bleach or a quaternary disinfectant

Select Agent?

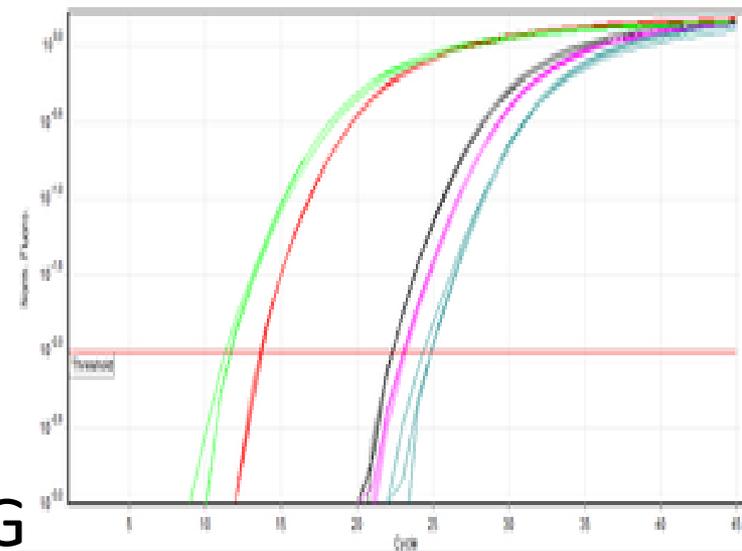
- Specimens from a suspected Ebola patient are not covered by the Select Agent regulations, **unless** the CDC has isolated live Ebola virus from that patient
 - A positive PCR result alone is not cause for select agent classification
 - As soon as a patient has had a positive Ebola culture, all specimens fall under Select Agent rules

Preferred specimens for Ebola testing

- Whole blood in plastic vial x2
 - 4 ml minimum volume; No processing is necessary
 - EDTA-preserved is preferred
 - SPS, citrate, or with clot activator is acceptable
 - Do not submit in glass tubes or in heparinized tubes
- Store or transport at 4C or frozen on cold packs to the CDC
- NO specimens will be accepted for testing without prior consultation with CDC EOC

Ebola tests used in diagnosis

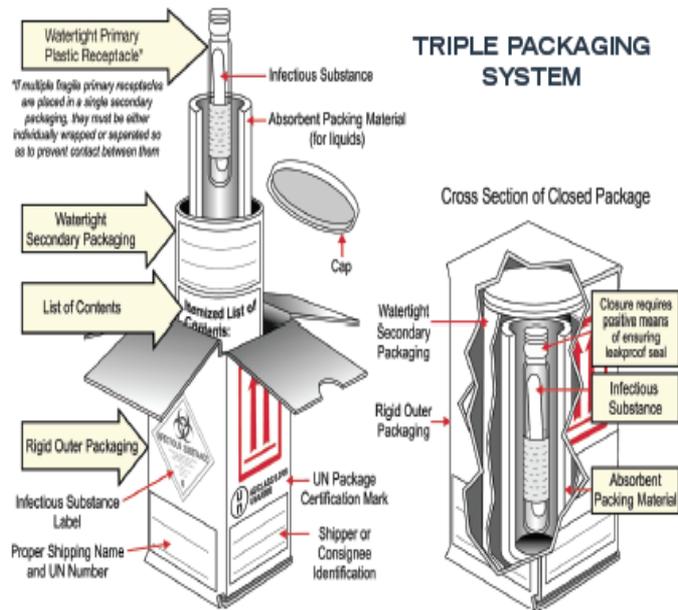
- Acute infections: real-time RT-PCR (CDC & LACPHL)
 - RNA ~detectable 3-10 days after symptom onset
- CDC only:
 - Virus isolation
 - Serologic testing for IgM & IgG
 - Lassa fever diagnostics (PCR, antigen detection, IgM serology)



(Source: CDC)

Packing and Shipping

PACKAGING & SHIPPING CLINICAL SPECIMENS TO CDC



Specimens collected for Ebola virus disease testing should be packaged and shipped without attempting to open collection tubes or aliquot specimens.

Specimens for shipment should be packaged following the basic triple packaging system, which consists of a primary receptacle (a sealable specimen bag) wrapped with absorbent material, secondary receptacle (water-tight, leak-proof), and an outer shipping package.

THE SUBMISSION PROCESS

Contact your state and/or local health department and CDC (770-488-7100) to determine the proper category for shipment based on clinical history and risk assessment by CDC and to obtain detailed shipping guidance and required CDC submission documents. State guidelines may differ and state or local health departments should be consulted before shipping.



Packaging & Shipping

- World Courier is the only available courier in California for shipping Category A and risk group 4 agents (require Biosafety Level 4 handling) such as Ebola virus
- The person doing the shipping must be certified by the employer to package and ship in accordance with International Air Transport Association (IATA) and Federal Department of Transportation (DOT) regulations.
- Local public health laboratories provide packaging and shipping guidance for hospitals

Packaging & Shipping

- Before sending specimens, the case MUST be reported to the local health department and CDPH
- Two forms must be submitted with the specimen for CDC to proceed with testing:
 - CDC Viral Special Pathogens Branch Specimen Submittal Form

**** NO SPECIMENS ACCEPTED WITHOUT PRIOR CONSULTATION ****
Call (404) 639-1510 or (404) 639-1115 for authorization to ship specimens.
for submitting Diagnostic Specimens to CDC's Viral Special Pathogens Branch

- CDC DASH form 50-34

Select the Specimen Origin to Begin the Form

CDC SPECIMEN SUBMISSION FORM: SPECIMENS OF HUMAN ORIGIN

LABORATORY EXAMINATION REQUESTED	STATE PHL / NEW YORK CITY DEPARTMENT OF HEALTH & MENTAL HYGIENE / FEDERAL AGENCY / INTERNATIONAL INSTITUTION / PEACE CORPS
Test order code: <input type="text"/>	Name: (Laboratory Director or designee)
Test order name: <input type="text"/>	Prefix <input type="text"/> Last <input type="text"/> First <input type="text"/> MI <input type="text"/>
Suspected agent: <input type="text"/>	Institution name: <input type="text"/>
Date sent to CDC: <input type="text"/> <small>MMDDYYYY</small>	Street address: <input type="text"/>
At CDC, bring to the attention of: <input type="text"/>	Line 1 <input type="text"/>

Useful Links

- <http://www.cdc.gov/vhf/ebola/hcp/index.html>
- <https://www.asm.org/images/PSAB/Ebola9-10-14.pdf>
- <http://www.cdc.gov/vhf/ebola/pdf/ppe-poster.pdf>
- <http://www.cdc.gov/vhf/ebola/pdf/ebola-lab-guidance.pdf>
- <http://www.cdc.gov/ncezid/dhcpp/vspb/pdf/specimen-submission.pdf>
- <http://www.cdc.gov/laboratory/specimen-submission/pdf/form-50-34.pdf>
- <http://www.cdc.gov/vhf/ebola/hcp/select-agent-regulations.html>

Acknowledgements

- Carol Glaser
- Janice Louie
- Kathleen Harriman
- CDC/EIS Liberia Team
- CDC and WHO