

Ebola Virus Disease



CDC Slides for U.S. Healthcare Workers*

November 21, 2014

Presentation is current through November 21, 2014 and will be updated every Friday by 5pm.

For the most up-to-date information, please visit www.cdc.gov/ebola.

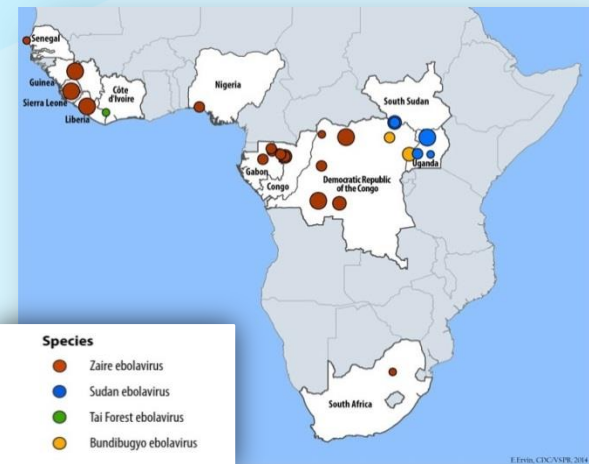
*Presentation contains materials from CDC, MSF, and WHO



Centers for Disease Control and Prevention
Office of the Director

Ebola Virus

- ❑ Prototype Viral Hemorrhagic Fever Pathogen
 - Filovirus: enveloped, non-segmented, negative-stranded RNA virus
 - Severe disease with high case fatality
 - Absence of specific treatment or vaccine
- ❑ >20 previous Ebola and Marburg virus outbreaks
- ❑ 2014 West Africa Ebola outbreak caused by *Zaire ebolavirus* species (five known Ebola virus species)



Ebola Virus

- ❑ Zoonotic virus – bats the most likely reservoir, although species unknown
- ❑ Spillover event from infected wild animals (e.g., fruit bats, monkey, duiker) to humans, followed by human-human transmission

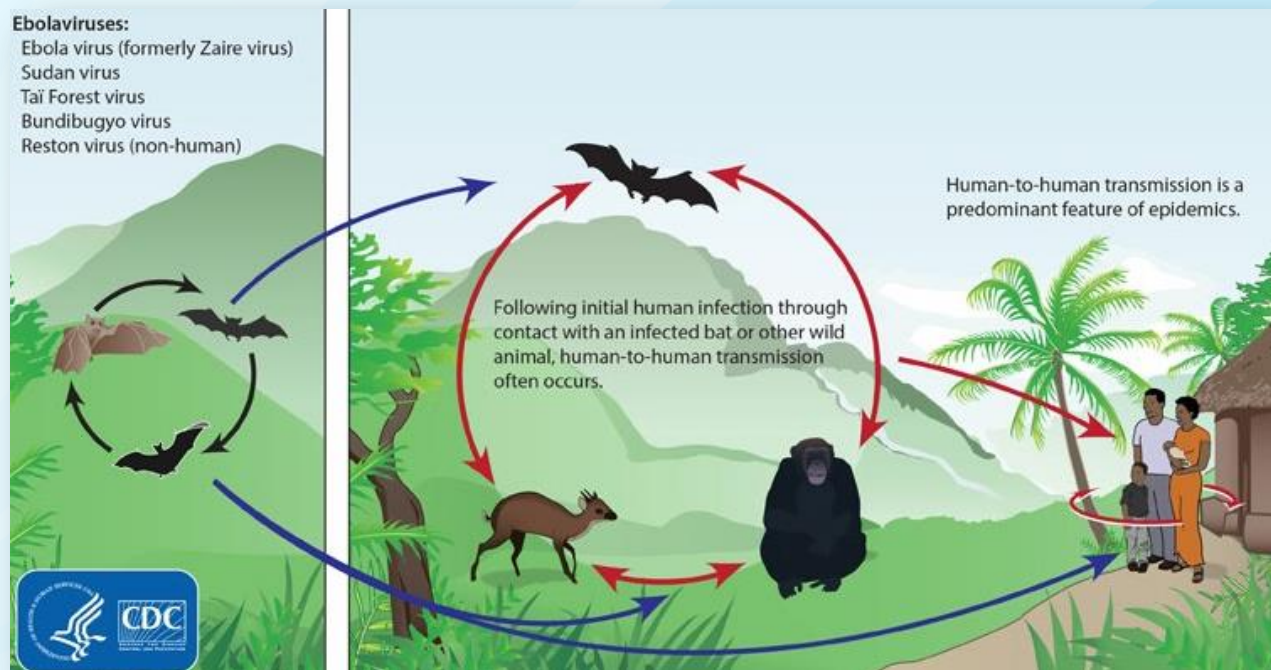
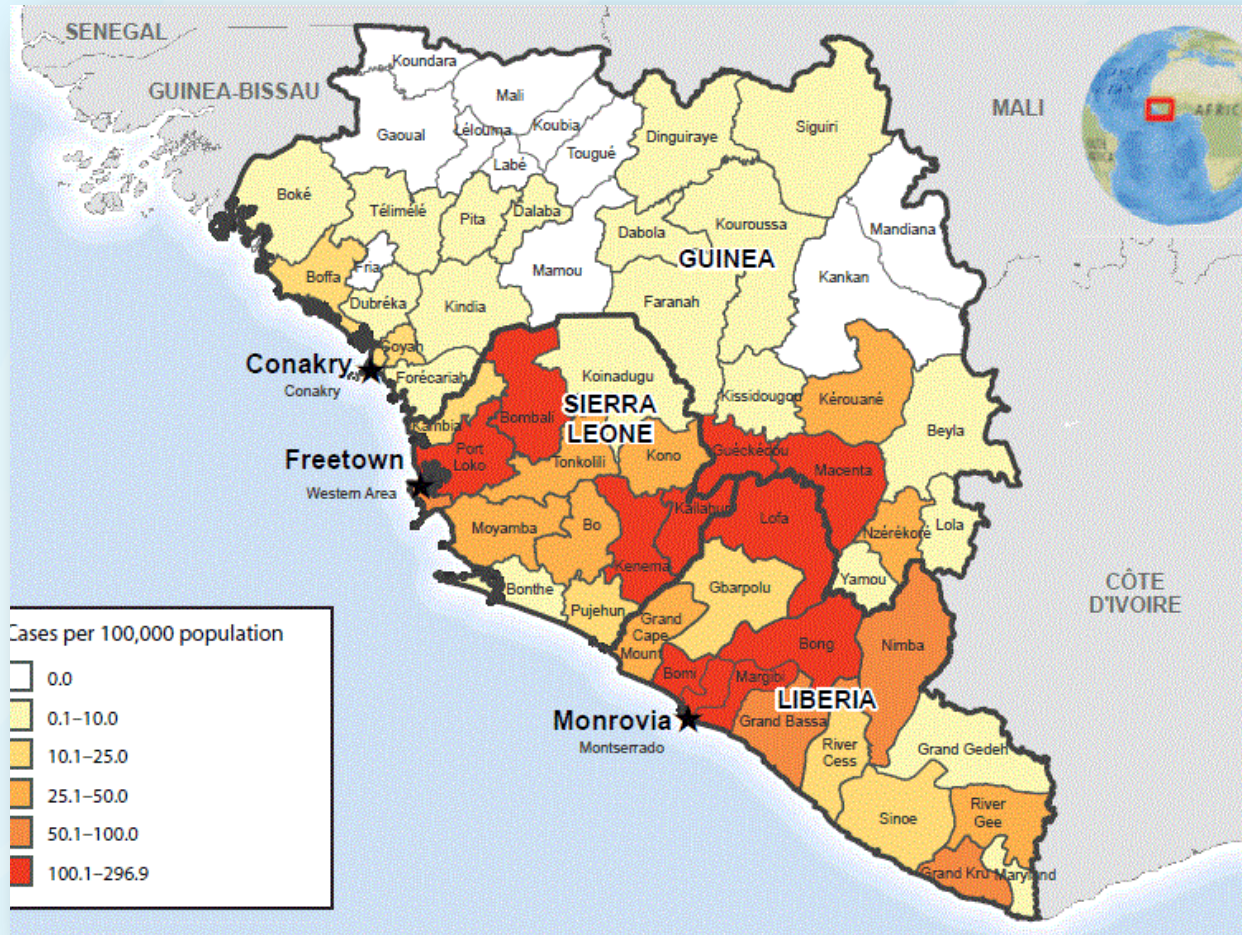


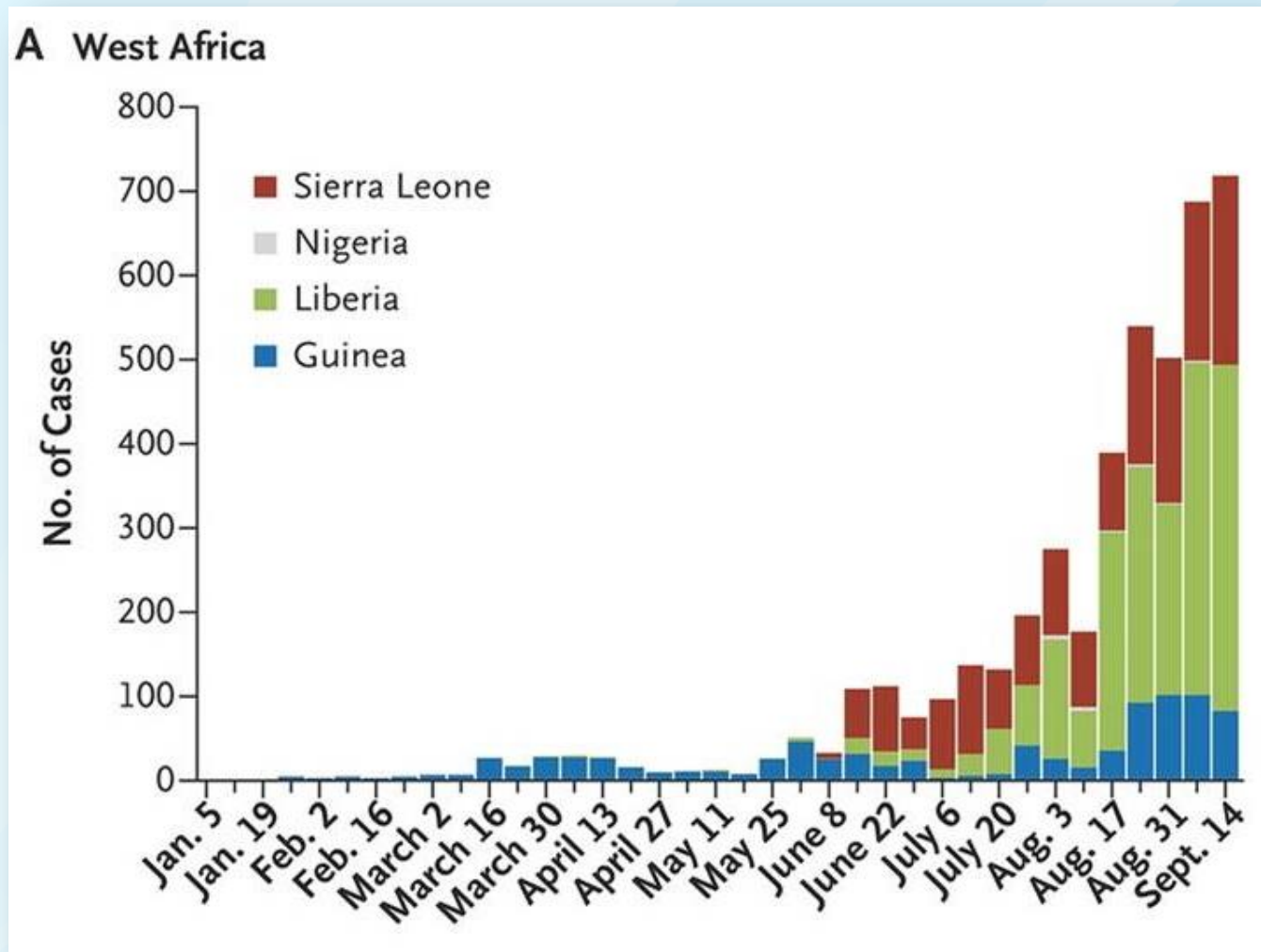
Figure. Ebola virus disease (EVD) cumulative incidence* — West Africa, October 18, 2014



* Cumulative number of reported EVD cases per 100,000 persons since December 22, 2013.

[MMWR 2014;63\(43\):978-981](#)

2014 Ebola Outbreak, West Africa



WHO Ebola Response Team. *N Engl J Med* 2014. DOI: 10.1056/NEJMoa1411100
<http://www.nejm.org/doi/full/10.1056/NEJMoa1411100?query=featured Ebola#t=articleResults>

EVD Cases and Deaths*

	Reporting Date	Total Cases	Confirmed Cases	Total Deaths
Guinea	16 Nov 14	1,971	1,698	1,192
Liberia	15 Nov 14	7,069	2,643	2,964
Sierra Leone	16 Nov 14	6,073	5,056	1,250
Nigeria**	15 Oct 14	20	19	8
Spain	27 Oct 14	1	1	0
Senegal**	15 Oct 14	1	1	0
United States	24 Oct 14	4	4	1
Mali	16 Nov 14	6	5	5
TOTAL		15,145	9,427	5,420

Updated case counts available at <http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/case-counts.html>.

*Reported by WHO using data from Ministries of Health

**The outbreaks of EVD in Senegal and Nigeria were declared over on October 17 and 19, respectively.

EVD Cases (United States)

- ❑ EVD has been diagnosed in the United States in four people, one (the index patient) who traveled to Dallas, Texas from Liberia, two healthcare workers who cared for the index patient, and one medical aid worker who traveled to New York City from Guinea
 - **Index patient** – Symptoms developed on September 24, 2014 approximately four days after arrival, sought medical care at Texas Health Presbyterian Hospital of Dallas on September 26, was admitted to hospital on September 28, testing confirmed EVD on September 30, patient died October 8.
 - **TX Healthcare Worker, Case 2** – Cared for index patient, was self-monitoring and presented to hospital reporting low-grade fever, diagnosed with EVD on October 10, recovered and released from NIH Clinical Center October 24.
 - **TX Healthcare Worker, Case 3** – Cared for index patient, was self-monitoring and reported low-grade fever, diagnosed with EVD on October 15, recovered and released from Emory University Hospital in Atlanta October 28.
 - **NY Medical Aid Worker, Case 4** – Worked with Ebola patients in Guinea, was self-monitoring and reported fever, diagnosed with EVD on October 24, recovered and released from Bellevue Hospital in New York City November 11.

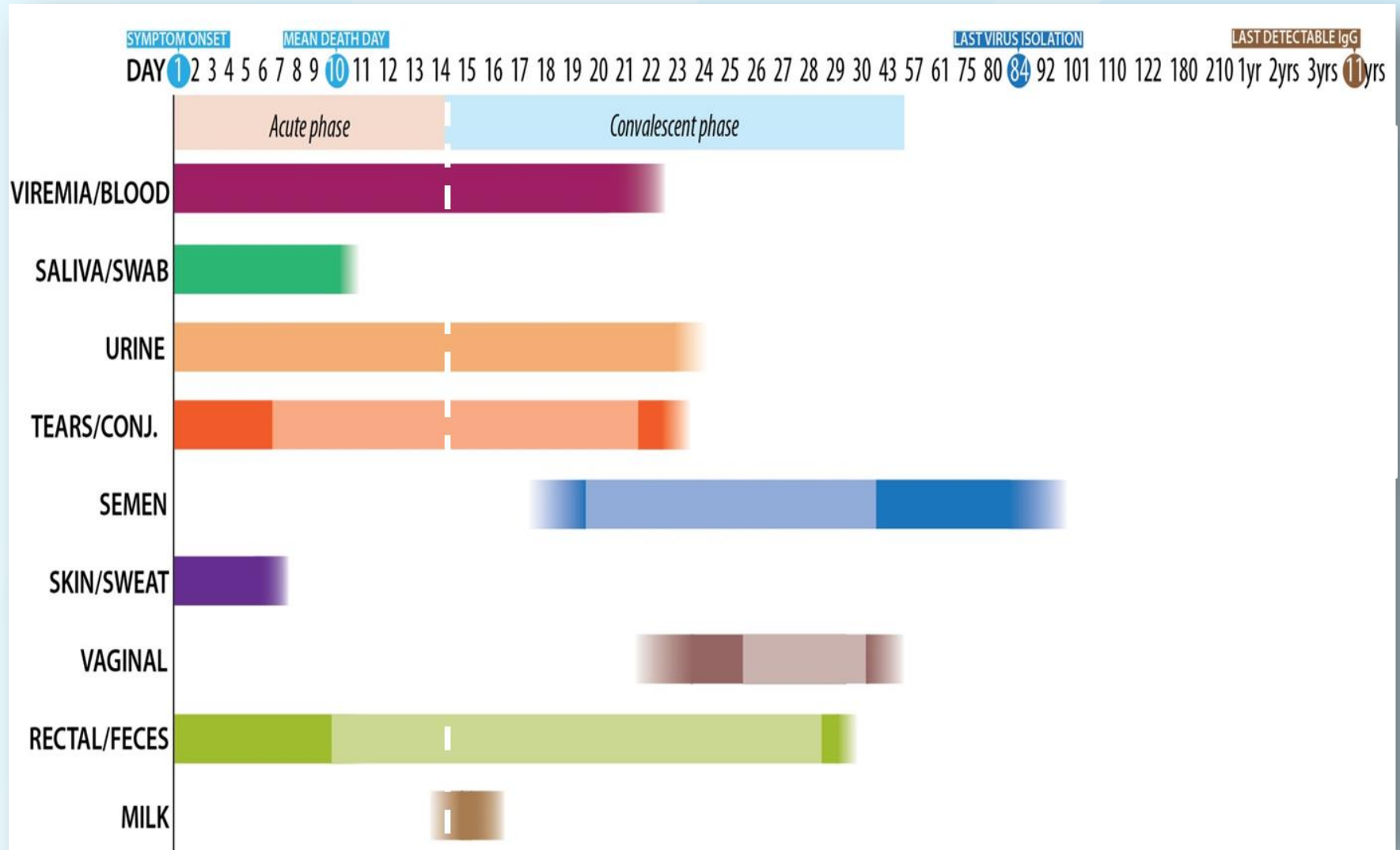
EVD Cases (United States)

- During this outbreak, five health workers and one journalist have been infected with Ebola virus while in West Africa and transported to hospitals in the United States. Five of these patients have recovered.
 - One of the health workers died on November 17 after being transported from Sierra Leone to Nebraska Medical Center.

Ebola Virus Transmission

- ❑ Virus present in high quantity in blood, body fluids, and excreta of *symptomatic* EVD-infected patients
- ❑ Opportunities for human-to-human transmission
 - Direct contact (through broken skin or unprotected mucous membranes) with an EVD-infected patient's blood or body fluids
 - Sharps injury (with EVD-contaminated needle or other sharp)
 - Direct contact with the corpse of a person who died of EVD
 - Indirect contact with an EVD-infected patient's blood or body fluids via a contaminated object (soiled linens or used utensils)
- ❑ Ebola can also be transmitted via contact with blood, fluids, or meat of an infected animal
 - Limited evidence that dogs become infected with Ebola virus
 - No reports of dogs or cats becoming sick with or transmitting Ebola

Detection of Ebola Virus in Different Human Body Fluids over Time



Human-to-Human Transmission

- ❑ Infected persons are not contagious until onset of symptoms
- ❑ Infectiousness of body fluids (e.g., viral load) increases as patient becomes more ill
 - Remains from deceased infected persons are highly infectious
- ❑ Human-to-human transmission of Ebola virus via inhalation (aerosols) has not been demonstrated

EVD Risk Assessment

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 a country with wide-spread Ebola transmission** 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 a country with wide-spread Ebola transmission** without HIGH- or LOW-risk exposure

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

Ebola Virus Pathogenesis

- ❑ Direct infection of tissues
- ❑ Immune dysregulation
- ❑ Hypovolemia and vascular collapse
 - Electrolyte abnormalities
 - Multi-organ failure, septic shock
- ❑ Disseminated intravascular coagulation (DIC) and coagulopathy

Early Clinical Presentation

- ❑ Acute onset; typically 8–10 days after exposure (range 2–21 days)
- ❑ Signs and symptoms
 - Initial: Fever, chills, myalgias, malaise, anorexia
 - After 5 days: GI symptoms, such as nausea, vomiting, watery diarrhea, abdominal pain
 - Other: Headache, conjunctivitis, hiccups, rash, chest pain, shortness of breath, confusion, seizures
 - Hemorrhagic symptoms in 18% of cases
- ❑ Other possible infectious causes of symptoms
 - Malaria, typhoid fever, meningococemia, Lassa fever and other bacterial infections (e.g., pneumonia) – all very common in Africa

Clinical Features

- ❑ Nonspecific early symptoms progress to:
 - Hypovolemic shock and multi-organ failure
 - Hemorrhagic disease
 - Death
- ❑ Non-fatal cases typically improve 6–11 days after symptoms onset
- ❑ Fatal disease associated with more severe early symptoms
 - Fatality rates of 70% have been reported in rural Africa
 - Intensive care, especially early intravenous and electrolyte management, may increase the survival rate

Clinical Manifestations by Organ System in West African Ebola Outbreak

Organ System	Clinical Manifestation
General	Fever (87%), fatigue (76%), arthralgia (39%), myalgia (39%)
Neurological	Headache (53%), confusion (13%), eye pain (8%), coma (6%)
Cardiovascular	Chest pain (37%),
Pulmonary	Cough (30%), dyspnea (23%), sore throat (22%), hiccups (11%)
Gastrointestinal	Vomiting (68%), diarrhea (66%), anorexia (65%), abdominal pain (44%), dysphagia (33%), jaundice (10%)
Hematological	Any unexplained bleeding (18%), melena/hematochezia (6%), hematemesis (4%), vaginal bleeding (3%), gingival bleeding (2%), hemoptysis (2%), epistaxis (2%), bleeding at injection site (2%), hematuria (1%), petechiae/ecchymoses (1%)
Integumentary	Conjunctivitis (21%), rash (6%)

Examples of Hemorrhagic Signs

Hematemesis



Gingival bleeding



Bleeding at IV Site

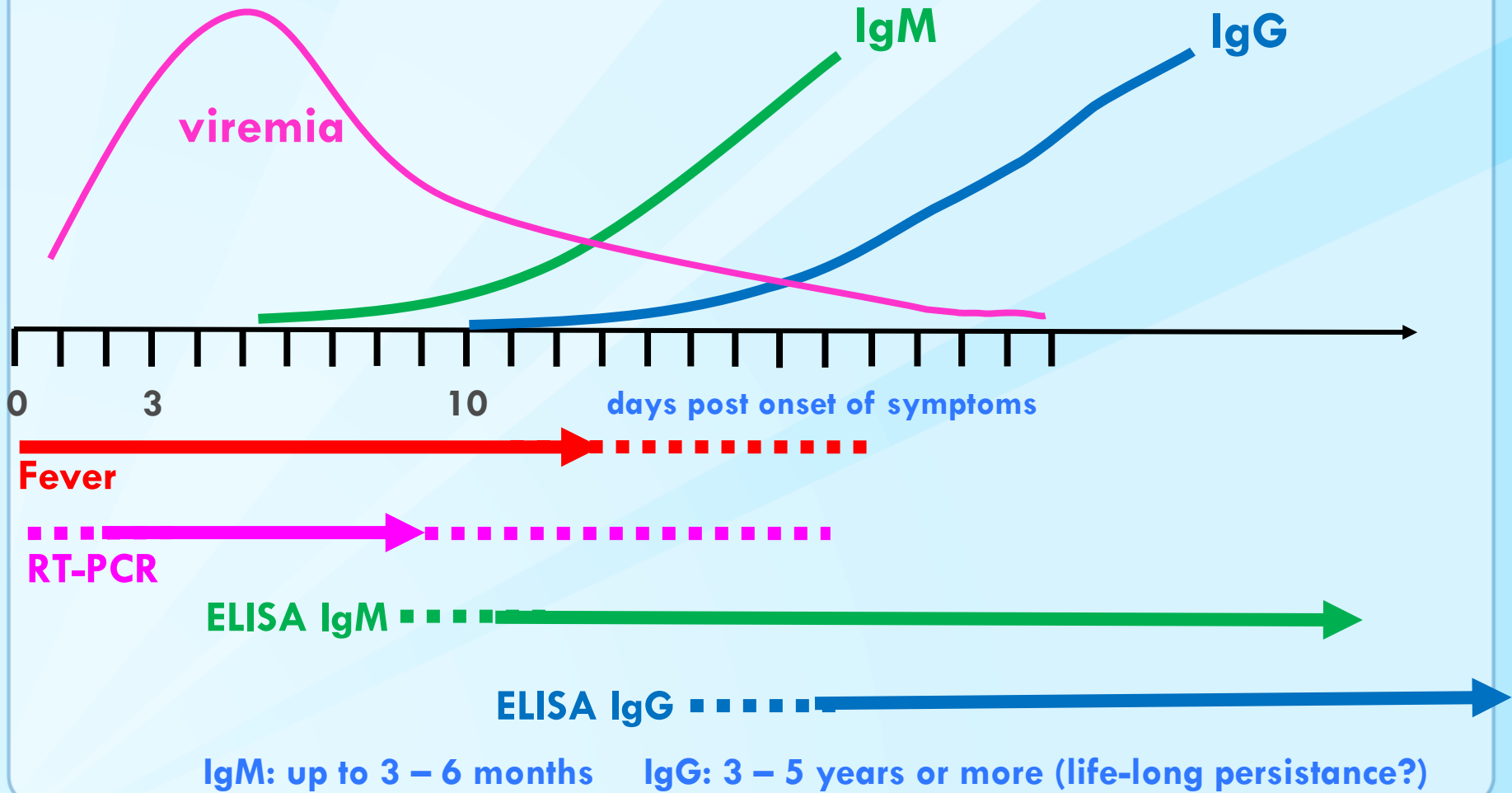


Laboratory Findings

- ❑ Thrombocytopenia (50,000–100,000/ μ L range)
- ❑ Leukopenia followed by neutrophilia
- ❑ Transaminase elevation: elevation serum aspartate aminotransferase (AST) > alanine transferase (ALT)
- ❑ Electrolyte abnormalities from fluid shifts
- ❑ Coagulation: PT and PTT prolonged
- ❑ Renal: proteinuria, increased creatinine

EVD: Expected diagnostic test results over time

Critical information: Date of onset of fever/symptoms



Ebola Virus Diagnosis

❑ Real Time PCR (RT-PCR)

- Used to diagnose acute infection
- More sensitive than antigen detection ELISA
- Identification of specific viral genetic fragments
- Performed in select CLIA-certified laboratories

❑ RT-PCR sample collection

- Volume: minimum volume of 4mL whole blood
- Plastic collection tubes (not glass or heparinized tubes)
- Whole blood preserved with EDTA is preferred
 - Whole blood preserved with sodium polyanethol sulfonate (SPS), citrate, or with clot activator is acceptable

Other Ebola Virus Diagnostics

- ❑ Virus isolation
 - Requires Biosafety Level 4 laboratory;
 - Can take several days
- ❑ Immunohistochemical staining and histopathology
 - On collected tissue or dead wild animals; localizes viral antigen
- ❑ Serologic testing for IgM and IgG antibodies (ELISA)
 - Detection of viral antibodies in specimens, such as blood, serum, or tissue suspensions
 - Monitor the immune response in confirmed EVD patients



Laboratories

- ❑ CDC has developed interim guidance for U.S. laboratory workers and other healthcare personnel who collect or handle specimens
- ❑ This guidance includes information about the appropriate steps for collecting, transporting, and testing specimens from patients who are suspected to be infected with Ebola
- ❑ Specimens should NOT be shipped to CDC without consultation with CDC and local/state health departments

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 CONSULTATION, CALL THE EMERGENCY OPERATIONS 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 3 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.

PREFERRED SPECIMENS FOR EBOLA TESTING

A minimum volume of 4 milliliters of whole blood preserved with EDTA, clot activator, sodium polyanethanol sulfonate (SPS), 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 applied for each specimen. The requested test needs to be identified only on the requisition and CDC specimen submission forms.

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 directory 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-10310 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 1910.1030, 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.

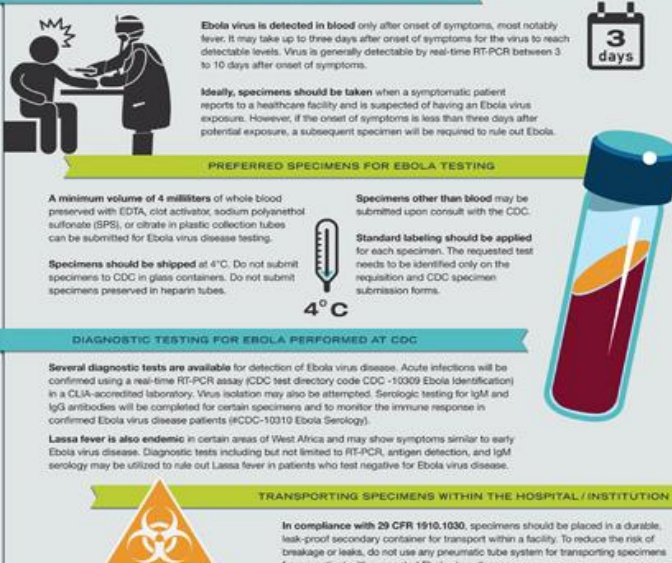
PACKAGING & SHIPPING CLINICAL SPECIMENS TO CDC

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 (a sealable specimen bag) wrapped with absorbent material, secondary receptacle (leak-proof, leak-proof), and an outer shipping package.

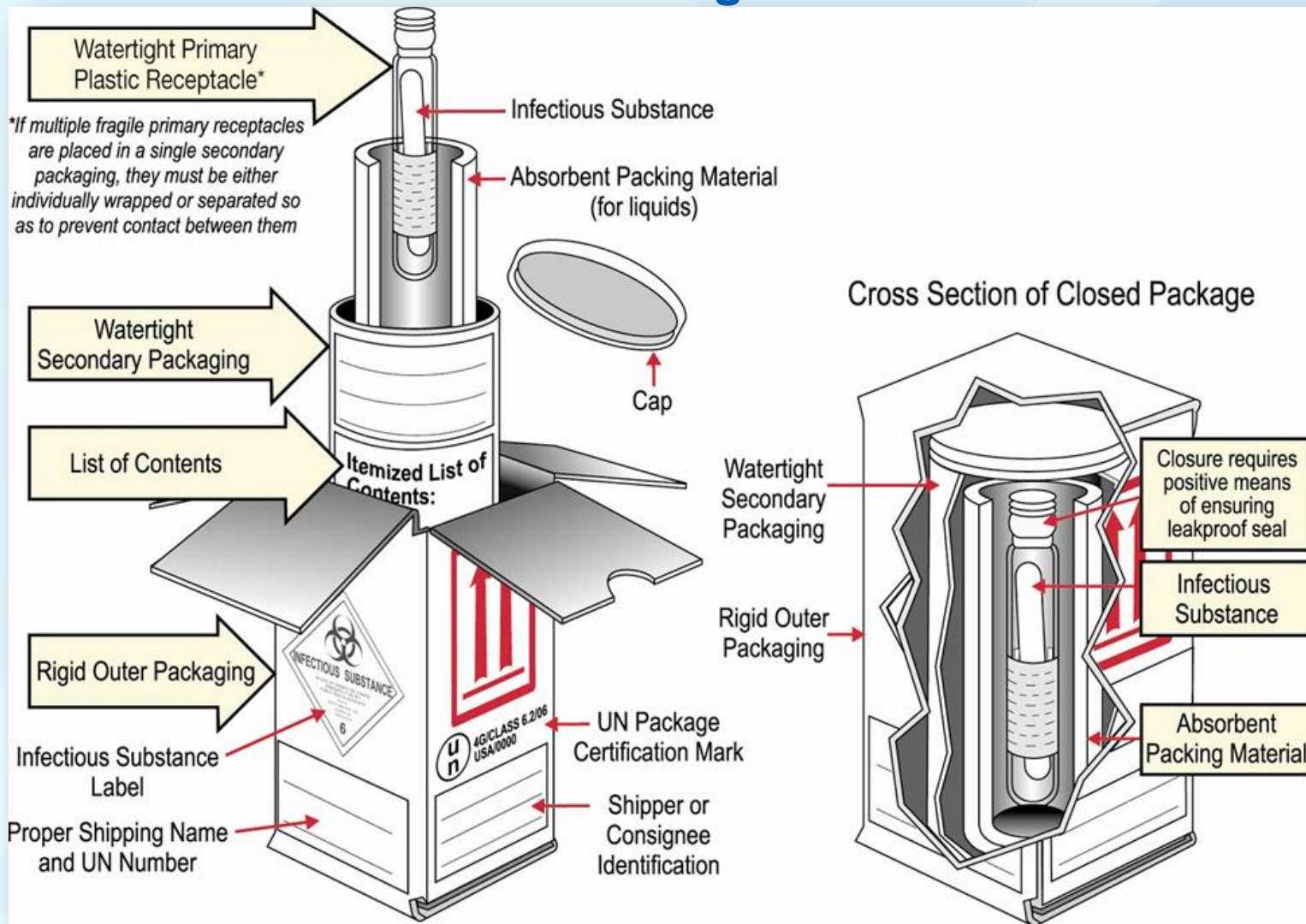
THE SUBMISSION PROCESS

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.



Information available at: <http://www.cdc.gov/vhf/ebola/hcp/interim-guidance-specimen-collection-submission-patients-suspected-infection-ebola.html>

Packaging & Shipping Clinical Specimens to CDC for Ebola Testing



Interpreting Negative Ebola RT-PCR Result

- ❑ If symptoms started ≥ 3 days before the negative result
 - EVD is unlikely \rightarrow consider other diagnoses
 - Infection control precautions for EVD can be discontinued unless clinical suspicion for EVD persists

- ❑ If symptoms started < 3 days before the negative RT-PCR result
 - Interpret result with caution
 - Repeat the test at ≥ 72 hours after onset of symptoms
 - Keep in isolation as a suspected case until a repeat RT-PCR ≥ 72 hours after onset of symptoms is negative

Clinical Management of EVD: Supportive, but Aggressive

- ❑ Hypovolemia and sepsis physiology
 - Aggressive intravenous fluid resuscitation
 - Hemodynamic support and critical care management if necessary
- ❑ Electrolyte and acid-base abnormalities
 - Aggressive electrolyte repletion
 - Correction of acid-base derangements
- ❑ Symptomatic management of fever and gastrointestinal symptoms
 - Avoid NSAIDS
- ❑ Multisystem organ failure can develop and may require
 - Oxygenation and mechanical ventilation
 - Correction of severe coagulopathy
 - Renal replacement therapy

Reference: Fowler RA et al. *Am J Respir Crit Care Med.* 2014

Investigational Therapies for EVD Patients

- ❑ No approved Ebola-specific prophylaxis or treatment
 - Ribavirin has no in-vitro or in-vivo effect on Ebola virus
 - Therapeutics in development with limited human clinical trial data
 - Convalescent serum
 - Therapeutic medications
 - Zmapp – chimeric human-mouse monoclonal antibodies
 - Tekmira – lipid nanoparticle small interfering RNA
 - Brincidofovir – oral nucleotide analogue with antiviral activity
 - Vaccines – in clinical trials
 - Chimpanzee-derived adenovirus with an Ebola virus gene inserted
 - Attenuated vesicular stomatitis virus with an Ebola virus gene inserted

References: ¹Huggins, JW et al. *Rev Infect Dis* 1989; ²Ignatyev, G et al. *J Biotechnol* 2000; ³Jarhling, P et al. *JID* 2007 S400; ⁴Mupapa, K et al. *JID* 1999 S18; ⁵Olinger, GG et al. *PNAS* 2012; ⁶Dye, JM et al. *PNAS* 2012; ⁷Qiu, X et al. *Sci Transl Med* 2013; ⁸Qiu, X et al. *Nature* 2014; ⁹Geisbert, TW et al. *JID* 2007; ¹⁰Geisbert, TW et al. *Lancet* 2010; ¹¹Kobinger, GP et al. *Virology* 2006; ¹²Wang, D JV 2006; ¹³Geisbert, TW et al. *JID* 2011; and ¹⁴Gunther et al. *JID* 2011.

Patient Recovery

- ❑ Case-fatality rate 57% in the 2014 Ebola outbreak
 - Case-fatality rate is likely much lower with access to intensive care
- ❑ Patients who survive often have signs of clinical improvement by the second week of illness
 - Associated with the development of virus-specific antibodies
 - Antibody with neutralizing activity against Ebola persists greater than 12 years after infection
- ❑ Prolonged convalescence
 - Includes arthralgia, myalgia, abdominal pain, extreme fatigue, and anorexia; many symptoms resolve by 21 months
 - Significant arthralgia and myalgia may persist for >21 months
 - Skin sloughing and hair loss has also been reported

References: ¹WHO Ebola Response Team. *NEJM* 2014; ²Feldman H & Geisbert TW. *Lancet* 2011; ³Ksiazek TG et al. *JID* 1999; ⁴Sanchez A et al. *J Virol* 2004; ⁵Sobarzo A et al. *NEJM* 2013; and ⁶Rowe AK et al. *JID* 1999.

Practical Considerations for Evaluating Patients for EVD in the United States

- ❑ CDC encourages all U.S. healthcare providers to
 - Ask patients with Ebola-like symptoms about travel to West Africa or contact with individuals with confirmed EVD in the 21 days before illness onset
 - Know the signs and symptoms of EVD
 - Know the initial steps to take if a diagnosis of EVD is suspected
- ❑ CDC has developed documents to facilitate these evaluations
 - The EVD algorithm for the evaluation of a returned traveler
 - Available at <http://www.cdc.gov/vhf/ebola/pdf/ebola-algorithm.pdf>
 - The checklist for evaluation of a patient being evaluated for EVD
 - Available at <http://www.cdc.gov/vhf/ebola/pdf/checklist-patients-evaluated-us-evd.pdf>

EVD Algorithm for Evaluation of the Returned Traveler

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

Checklist for Patients Being Evaluated for Ebola Virus Disease (EVD) in the United States

Upon arrival to clinical setting/triage

- Does patient have fever (subjective or $\geq 100.4^{\circ}\text{F}$ or 38.0°C)?
- Does patient have compatible EVD symptoms such as headache, weakness, muscle pain, vomiting, diarrhea, abdominal pain, or hemorrhage?
- Has the patient traveled to an Ebola-affected area in the 21 days before onset?

Upon initial assessment

- Isolate patient in single room with a private bathroom and with the door to hallway closed
- Implement standard, contact, & droplet precautions
- Notify the hospital Infection Control Program as soon as possible
- Report to the health department as soon as possible

Conduct a risk assessment for:

High-risk exposures

- Involvement (e.g., needle stick) or mucous membrane exposure to blood or body fluids from an EVD patient
- Direct skin contact with skin, blood or body fluids from an EVD patient
- Increase in blood or body fluids from an EVD patient without appropriate PPE
- Direct contact with a dead body in an Ebola-affected area without appropriate PPE

Low-risk exposures

- Household members of an EVD patient or others who had brief direct contact (e.g., shaking hands) with an EVD patient without appropriate PPE
- Health-care personnel in facilities with EVD patients who have been in one area of EVD patients without recommended PPE

Use of personal protective equipment (PPE)

- Use a buddy system to ensure that PPE is put on and removed safely

Before entering patient room, wear:

- Gown (fluid resistant or impervious)
- Face mask
- Eye protection (goggles or face shield)
- Gloves

If likely to be exposed to blood or body fluids, additional PPE may include but isn't limited to:

- Double gloves
- Disposable shoe covers
- Gag coverings

Upon exiting patient room

- PPE should be carefully removed without contaminating neck, eyes, mucous membranes, or clothing with potentially infectious materials
- Discard disposable PPE
- In reusable PPE should be cleaned and disinfected per the manufacturer's cleaning instructions
- Hand hygiene should be performed immediately after removal of PPE

During aerosol-generating procedures

- Limit number of personnel present
- Conduct in an airborne infection isolation room
- Don PPE as described above (single use, NIOSH-certified or tested N95 filtering facepiece respirator for respiratory protection or alternative type, PPE) instead of a facemask

Initial patient management

- Consult with health department about diagnostic EVD RT-PCR testing*
- Consider, test for, and treat (when appropriate) other possible infectious causes of symptoms (e.g., malaria, bacterial infections)
- Provide appropriate supportive care including aggressive fluid resuscitation if warranted
- Assess for electrolyte abnormalities and replace
- Evaluate for evidence of bleeding and assess hematologic and coagulator parameters
- Symptomatic management of fever, nausea, vomiting, diarrhea, and abdominal pain
- Consult health department regarding other treatment options

Key checks that are essential to be comprehensive. Additions and modifications to fit local practice are encouraged.

* See <http://www.cdc.gov/ebola/diagnostic/ebola-diagnostic-testing.html> for more information.
** See <http://www.cdc.gov/ebola/diagnostic/ebola-diagnostic-testing.html> for more information.

Ebola Virus Disease (EVD)
Algorithm for Evaluation of the Returned Traveler

FEVER (subjective or $\geq 100.4^{\circ}\text{F}$ or 38.0°C) or compatible Ebola symptoms* in a patient who has resided in or traveled to a country with wide-spread Ebola transmission** in the 21 days before illness onset

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 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

Low-Risk Exposure

Unknown Exposure

Testing is Indicated

Testing is Not Indicated

FEVER (subjective or $\geq 100.4^{\circ}\text{F}$ or 38.0°C) or compatible Ebola symptoms* in a patient who has resided in or traveled to a country with wide-spread Ebola transmission** 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

**CDC Website to check current affected areas: www.cdc.gov/vhf/ebola
Algorithm available at <http://www.cdc.gov/vhf/ebola/pdf/ebola-algorithm.pdf>
Checklist available at <http://www.cdc.gov/vhf/ebola/pdf/checklist-patients-evaluated-us-evd.pdf>

Interim Guidance for Monitoring and Movement of Persons with EVD Exposure

- ❑ CDC has created guidance for monitoring people exposed to Ebola virus but without symptoms

RISK LEVEL	PUBLIC HEALTH ACTION		
	Monitoring	Restricted Public Activities	Restricted Travel
HIGH risk	Direct Active Monitoring	Yes	Yes
SOME risk	Direct Active Monitoring	Case-by-case assessment	Case-by-case assessment
LOW risk	Active Monitoring for some; Direct Active Monitoring for others	No	No
NO risk	No	No	No

EVD Summary

- ❑ The 2014 Ebola outbreak in West Africa is the largest in history and has affected multiple countries
- ❑ Think Ebola: U.S. healthcare providers should be aware of clinical presentation and risk factors for EVD
- ❑ Human-to-human transmission by direct contact
 - No human-to-human transmission via inhalation (aerosols)
 - No transmission before symptom onset
- ❑ Early case identification, isolation, treatment and effective infection control are essential to prevent Ebola transmission

For more information, please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333

Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

Visit: www.atsdr.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

