Division of Laboratory Systems

Thank you for joining! We will begin at 12pm ET.



Division of Laboratory Systems



When Receiving Samples from Patients Suspected to be Infected with Ebola: What's the Plan?

Nancy Cornish, M.D., PhD Sheldon Campbell, M.D., PhD Michael Pentella, PhD



Agenda

- Introduction
 - New and relevant OneLab™ Resources
 - Today's Presenters
- When Receiving Samples from Patients Suspected to be Infected with Ebola: What's the Plan?
- Q&A
- Upcoming Events

Laboratory Outreach Communication System (LOCS) Guidance

10/19/2022: Lab Advisory: Guidance for Transport and Shipment of Specimens for Ebola Virus Testing

Print



Audience: Clinical Laboratories

Level: Laboratory Advisory

Although the risk of a travel-associated Ebola case in the United States is low, CDC recommends that clinical laboratories review information on <u>specimen collection and transport</u> and <u>transporting infectious substances safely</u> for specimens suspected to contain Ebola virus.

CDC recommends that Ebola testing should only be ordered and performed for patients who meet the criteria for <u>Persons</u> <u>Under Investigation for Ebola virus disease</u>. Before collecting specimens for Ebola testing, clinical laboratories must first contact their state health department. State health departments must consult CDC to determine if testing for Ebola virus is

<u>Lab Advisory: Guidance for Transport and Shipment of Specimens for Ebola Virus Testing (cdc.gov)</u>

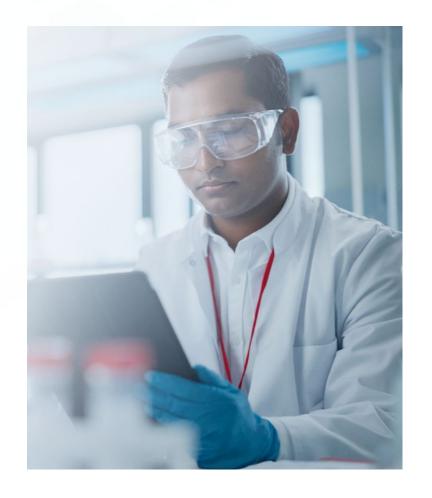
Resources

Emergency Preparedness Response Guide

This <u>guide</u> covers available resources for biological, chemical, and radiological emergencies for laboratories to reference during an emergency. It can also help train new laboratory professionals hired to support emergency responses.

Ebola Specific Job Aid

This <u>job aid</u> provides important guidance for collection, transport, and submission of specimens for Ebola virus testing in the United States.





INTRODUCING OneLab

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OneLab REACH™ is part of the CDC OneLab initiative. OneLab's mission is to strengthen interconnections between clinical, public health, and CDC laboratory education and training professionals to collectively support rapid, large-scale responses to public health emergencies.

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Slide decks may contain presentation material from panelists who are not affiliated with CDC. Presentation content from external panelists may not necessarily reflect CDC's official position on the topic(s) covered.



Moderator



Nancy Cornish, M.D., PhD

Medical Officer, Senior Advisor for Quality and Safety
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Presenter



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Professor of Laboratory Medicine

Yale School of Medicine

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Presenter



Michael Pentella, PhD

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When receiving specimens from patients suspected to be infected with Ebola, what's the plan?

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Situation Update

- On September 20, 2022, the Ministry of Health of Uganda officially declared an outbreak of Ebola virus disease (EVD) due to the *Sudan ebolavirus*. As of October 28, 2022, there have been 109 cases and 30 deaths.
- No suspected, probable, or confirmed EVD cases have been reported to date outside of Uganda and the risk
 of importation into the U.S. is currently assessed as low.
- Uganda is screening departing travelers.
- CDC is routing all travelers from Uganda to the U.S. through 5 airports (JFK New York, Newark New Jersey, Dulles Virginia, Atlanta– GA, and O'Hare Chicago) for screening purposes.
- Travelers without high-risk exposure who are asymptomatic do not need to be quarantined and may travel onward.
- State and Local Health Departments will follow up with travelers for an initial risk assessment and postarrival symptom monitoring for 21 days post Uganda departure date.

Objectives

- Recognize the factors associated with risk in laboratory handling of specimens from patients under investigation (PUI) for Ebola virus disease (EVD).
- Review the potential tests for specimens from PUI for EVD.
- Recognize the risk assessment approach for testing in PUI.
- Discuss the steps to take to be prepared to receive specimens from PUI for EVD



'The Seventh Plague of Egypt', by John Martin (England, 1823) From the collection of the Museum of Fine Arts, Boston



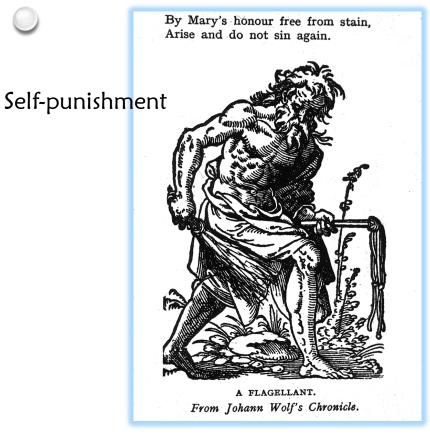
Emerging infections in Context

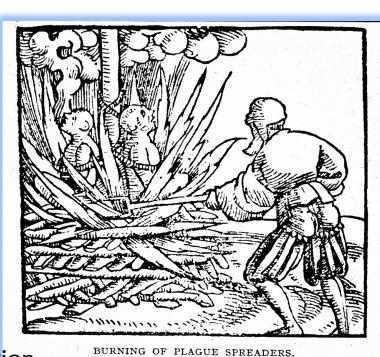
Plagues have been a part of human existence During recorded history; and have had a deep impact on societies.

Four Horsemen of Apocalypse, by Viktor Vasnetsov. Painted in 1887. From left to right, they are Death/Plague on the pale horse, Famine on the black, War on the red, and a rider whose identity is unclear in the Revelation text on the white.



Reactions to Infectious Diseases





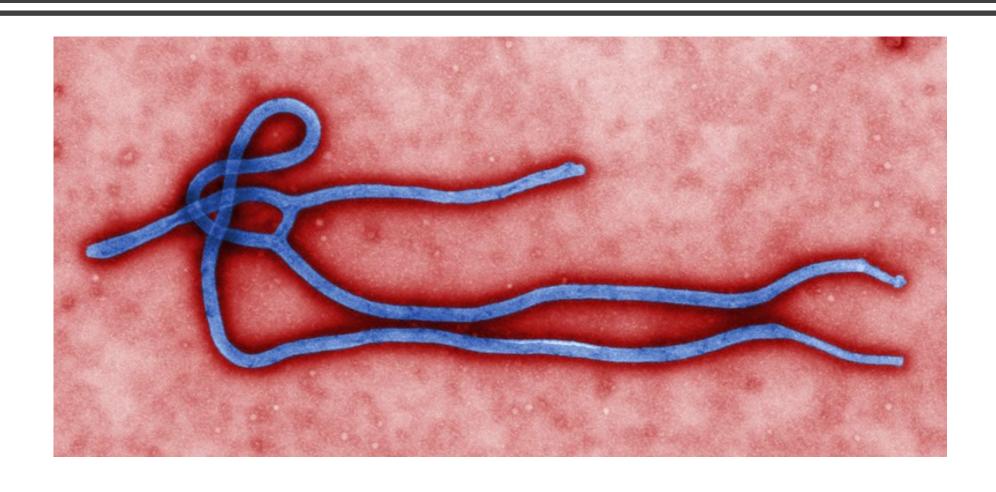


Persecution

BURNING OF PLAGUE SPREADERS

From Sebastian Muenster's "Cosmographie."

Ebola virus background Epidemiology, clinical manifestations, outbreaks



Ebola virus Overview

- A rare but severe, often fatal illness in humans.
- Average case fatality rate is around 50%.
 - Case fatality rates have varied from 25% to 90% in past outbreaks.
- Community engagement is key to successfully controlling outbreaks.
- Good outbreak control relies on applying a package of interventions, namely case management, infection prevention and control practices, surveillance and contact tracing, a good laboratory service, safe and dignified burials and social mobilization.
- Early supportive care with rehydration, symptomatic treatment improves survival.

Ebolavirus Ecology

Enzootic Cycle

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

Ebolaviruses:

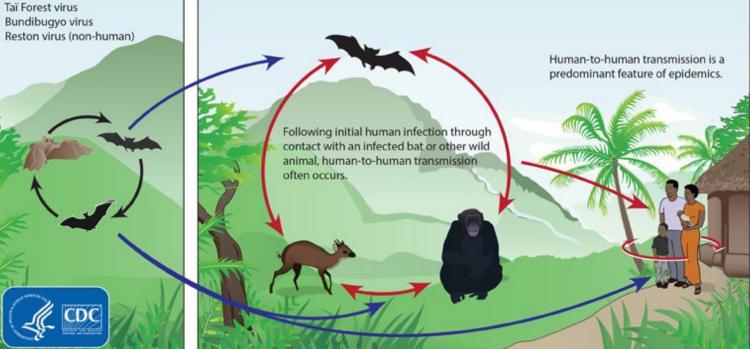
Ebola virus (formerly Zaire virus) Sudan virus Taï Forest virus

Bundibugyo virus

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.



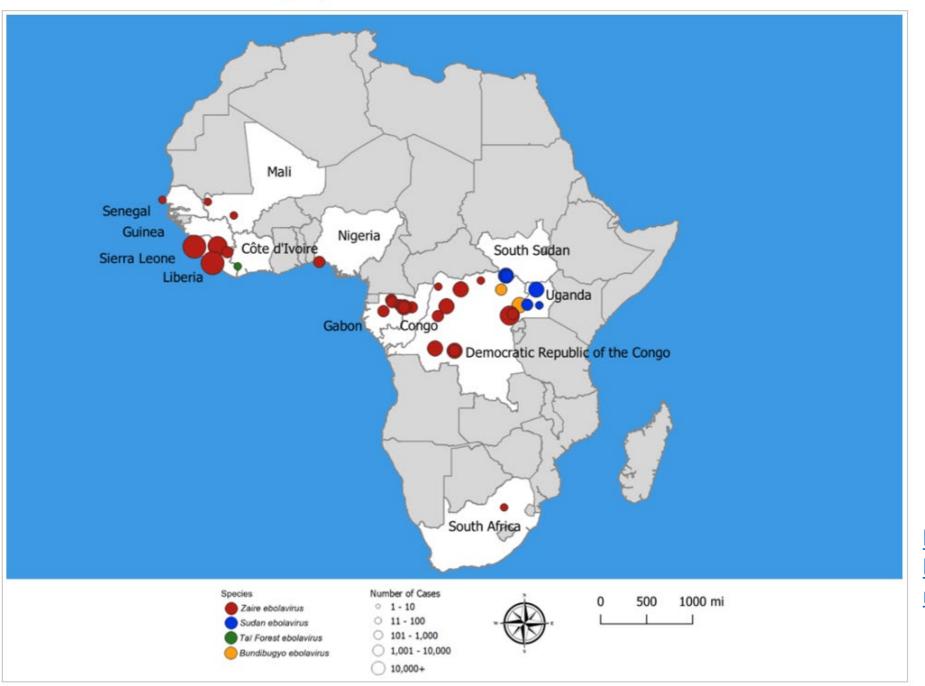
Clinical Disease

- The incubation period for EVD can range from 2-21 days following exposure (typically 8-12 days).
- A person with EVD is **not contagious** (through the usual routes) **until symptoms develop**.
- Initial signs and symptoms are non-specific: fever, headache, muscle and joint pain, fatigue, nausea, vomiting, diarrhea, abdominal pain. Unexplained bleeding occurs later, and is *not* invariably present.
- During the early phase of illness, it is not possible to distinguish clinically between EVD, other viral hemorrhagic fevers such as Marburg virus, or other febrile illnesses such as malaria or influenza.
- Relapses have occurred in privileged sites (eye, CNS) post recovery.

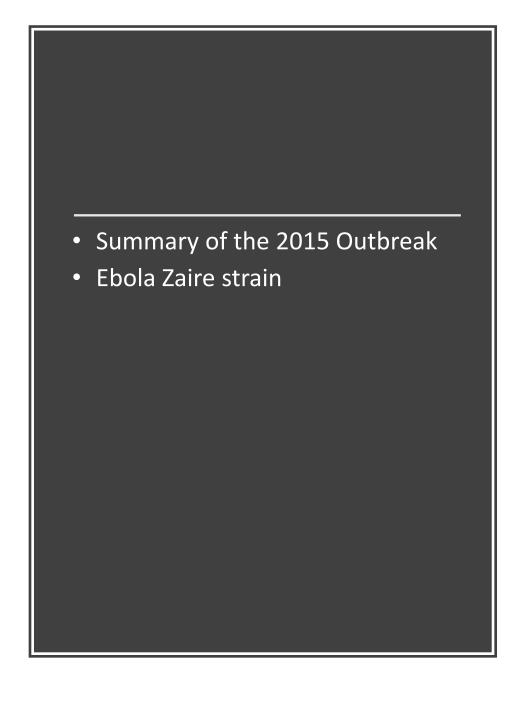
Ebola Vaccine and Treamtent

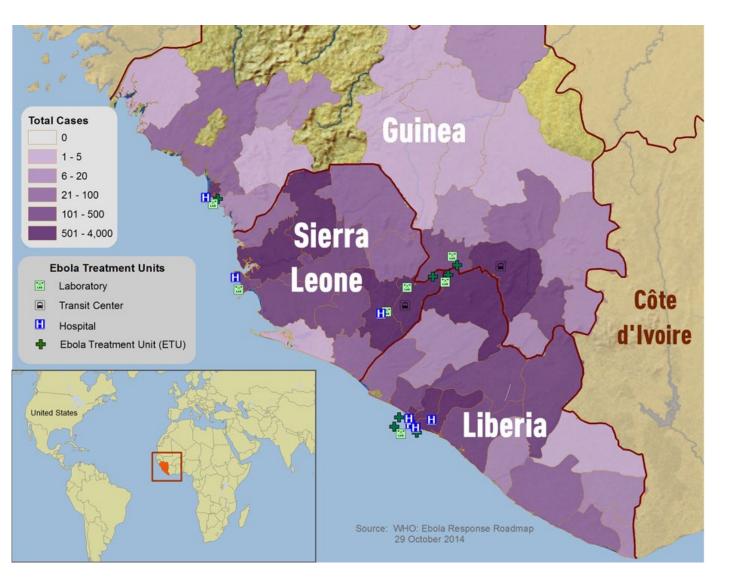
- The U.S. Food and Drug Administration (FDA) approved the Ebola vaccine rVSV-ZEBOV (called Ervebo®) on December 19, 2019, given as a single dose vaccine. has been found to be safe and protective against Zaire ebolavirus, which has caused the largest and most deadly Ebola outbreaks to date.
 - Unfortunately, it is not tested against the Sudan ebolavirus.
- A Sudan ebolavirus vaccine is expected to go into trials in the near future.
- There are currently two treatments approved by the U.S.
 Food and Drug Administration (FDA) to treat EVD caused by
 the Zaire ebolavirus. These mAbs bind to a portion of the
 Ebola virus's surface called the glycoprotein, which
 prevents the virus from entering a person's cells.
 - Inmazeb™ is a combination of three monoclonal antibodies.
 - Ebanga[™] is a single monoclonal antibody
 - Neither has been evaluated for efficacy against species other than Zaire ebolavirus.

Ebola Virus Outbreaks by Species and Size, Since 1976



https://www.cdc.gov/vhf/ebo la/history/distributionmap.html

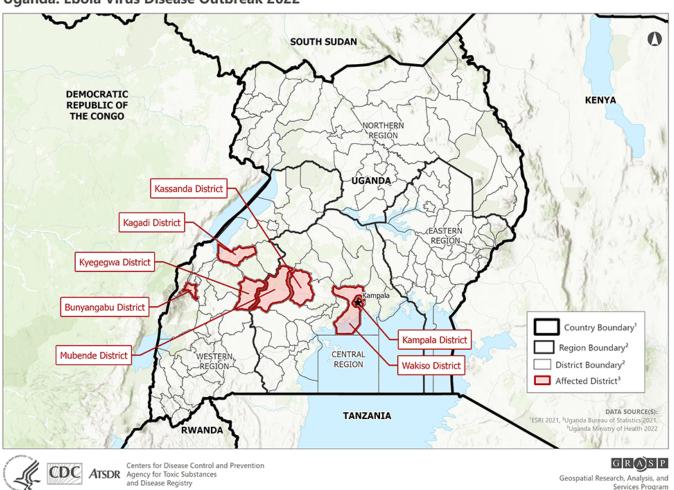




Ebola Epidemic Uganda 2022

- As of 10/28/22
 - Sudan ebolavirus
 - 109 cases, 30 deaths
- Médecins Sans Frontières, (Doctors Without Borders) treatment centers in place and deploying; were heavily engaged and gained experience in the 2014-15 outbreak.

Uganda: Ebola Virus Disease Outbreak 2022





Ebola Virus Trasmission

- Asymptomatic people, incubating infection, non-infectious through typical routes.
- Virus in blood and body fluids, including stool, vomitus, urine, saliva, semen, vaginal fluid and sweat
 - Virus may be present in fluid, but not necessarily infectious
 - Some fluids contain virus after recovery
- Infectiousness least early in disease, with increased risk after day 5 as complications become more severe.
- Not airborne
- Contaminated PPE a problem, but other fomites and inanimate surfaces not documented to play a role in transmission.

Facts about Ebola in the U.S.

You CAN'T get Ebola through WATER



You CAN'T get Ebola through AIR



You CAN'T get Ebola through FOOD grown or legally purchased in the U.S.



Precautions Work!

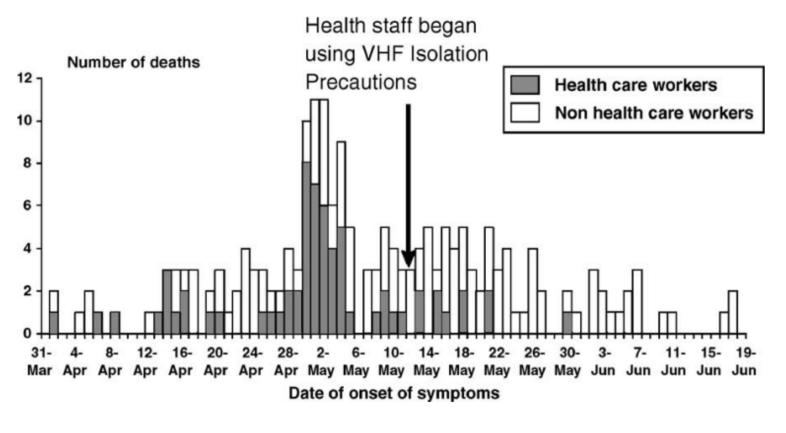


Fig. 2. The number of infected health care workers declined after barrier nursing practices were begun during the Ebola hemorrhagic fever outbreak at Kikwit, Democratic Republic of Congo, 1995. (*From* Centers for Disease Control and Prevention and World Health Organization. Infection control for viral haemorrhagic fevers in the African health care setting. Atlanta (GA): Centers for Disease Control and Prevention; 1998. Figs. 1, 3; with permission.)

Ebola and the Lab

• https://www.cdc.gov/vhf/ebola/laboratory-personnel/specimens.html

Guidance for Collection, Transpo Specimens for Ebola Virus Testin

NOTIFICA

Hospitals should follow their state and procedures for notification and consultar

WHEN SPECIMENS SHOULD BE COLLECTED FOR EBOLA TE



Ebola virus is detected in blood only af usually fever. It may take up to 3 days aft the virus to reach detectable levels. Virus by real-time RT-PCR from 3-10 days afte

Ideally, specimens should be taken wh reports to a healthcare facility and is susp exposure. However, if the onset of sympt specimen may be needed to completely if the first specimen tests negative.

PREFERRED SPECIMENS FOR I

A minimum volume of 4 milliliters of whole blood preserved with



Specimens should be shipped frozen on dry ice.



Do not submit specimens in glass containers to CDC.

DIAGNOSTIC TESTING FOR EBOLA VIRUS

Real-time PCR testing for Ebola virus is available at over 50 Laboratory Response Network (LRN) laboratories located throughout the United States. LRN laboratories are currently using an FDA-approved Emergency Use Authorization (EUA) assay to detect the Ebola (Zaire spp positive using the presumptive posreal time RT-PCF to CDC for addit

Every clinical laboratory has a role to play in preparing to care for a PUI.

(Ebola Virus Disease) > For Public Health Planners

Interim Guidance for U.S. Hospital Preparedness for Patients Under Investigation (PUIs) or with Confirmed Ebola Virus Disease (EVD): A Framework for a Tiered Approach

Print

Page Summary

Who this is for: State and local health departments, acute care hospitals, and other emergency care settings, including urgent care clinics.

What this is for: Guidance to assist state and local health departments, acute care hospitals, and other emergency care

https://www.cdc.gov/vhf/ebola/healthcare-us/preparing/hospitals.html

CDC Domestic Preparedness Activities

- CDC has activated its emergency response structure
- Standing up multidisciplinary CDC Ebola Response Teams (CERT)
- Updating guidance on the management of patients with suspected SUDV
- Outlining a process to access experimental Sudan virus therapeutics

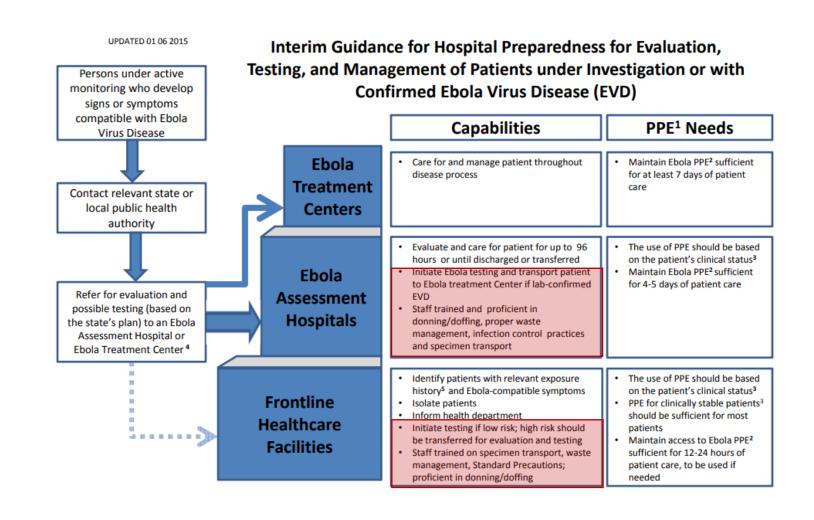
CDC Domestic Preparedness Activities

- Expanding testing capabilities to 10 Regional Emerging Special Pathogens
 Treatment Centers and to 28 Laboratory Response Network (LRN)
 laboratories
- Preparing specialized high-level isolation units equipped with infrastructure, laboratory capabilities, and staff to care for patients with highly hazardous communicable diseases

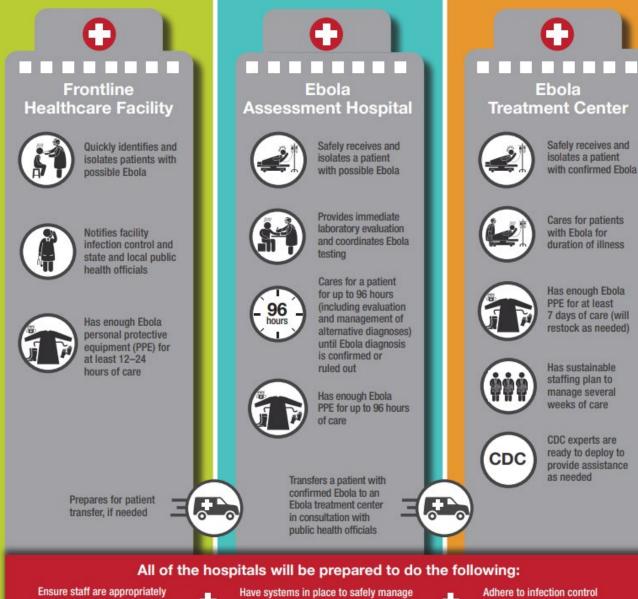
Hospitals in US Fall Into Three Groups

- Note that laboratories in each group must at least be able to pack and ship specimens for Ebola testing.
- For the current guidance, visit:

https://www.cdc.gov/vhf/ebola/healthcareus/preparing/hospitals.html



CDC has developed a strategy to help healthcare facilities and state health officials prepare for patients with possible or confirmed Ebola. This strategy identifies which hospitals will provide different levels of care for patients being assessed and treated for Ebola.



Every clinical laboratory has a role to play in preparing for caring a PUI

trained and have documented competency in safe PPE practices



waste disposal, cleaning and disinfection



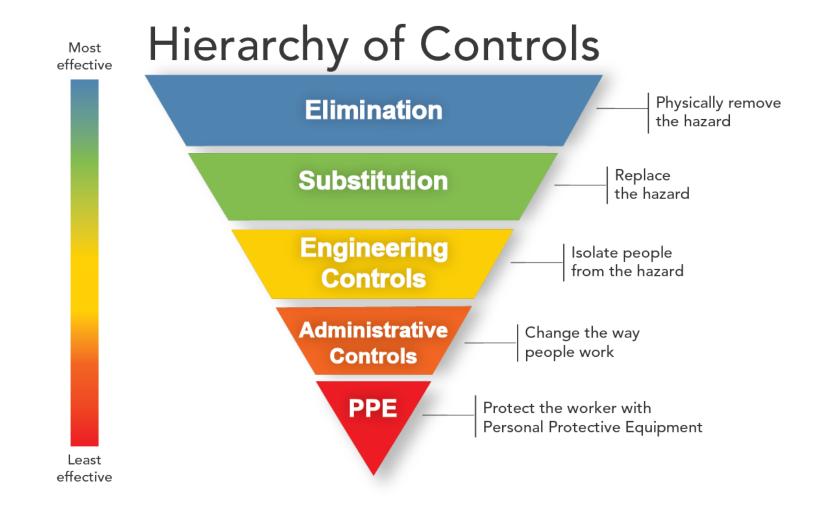
protocols

Preparation is essential!

- Laboratories, in collaboration with other facility leadership, must:
 - Plan what care / testing can safely be provided for PUI.
 - Insure that providers are aware of how to collect and transport specimens.
 - Have a plan for routine testing to support care of PUI.
 - Have public health collaboration in place to monitor personnel involved in care for patients if a diagnosis is established.
 - Have a plan for diagnostic testing for the pathogen.
 - Have resources to package and ship presumed category A specimens.
 - Adapted from NETEC Health Care Facility Special Pathogen Preparedness Checklist

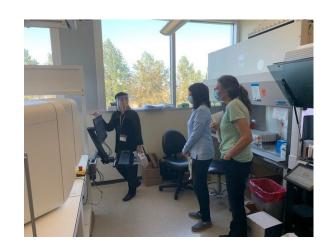
Biosafety Mitigation

NIOSH

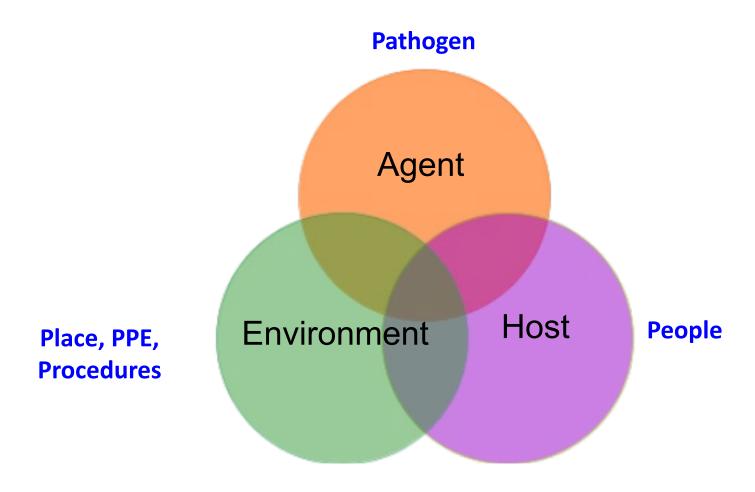


Considerations to handle PUI specimens

- Consultation with clinician, health department, & CDC
- Collection of specimens at the bedside
- Package receipt and transfer of packages to testing area
- Internal transport of specimens between testing areas
- Packaging and shipping of specimens to refer to public health lab
- Preparation of specimens for testing
- Centrifuging specimens
- Testing
- Medical waste handling



Risk of a Lab Acquired Infection is a combination of Factors



Source: B. Johnson, Anthology of Biosafety, IV, 2001

Follow the specimen path and examine risks

 Risk is the likelihood of an undesirable event happening, that involves a specific hazard or threat and has consequences

1. Define the situation:

What work is occurring?

2. Define the risks within the situation:

What can go wrong?

3. Characterize the risks:

How likely is it to happen?

What are the consequences?

Ebola Risk to Laboratorians

- Virus in blood and body fluids, including stool, vomitus, urine, saliva, semen, vaginal fluid and sweat
- High viral loads in symptomatic patient
 - >100,000,000 pfu/ml
- Infectious dose
 - <10 viable viral particles
- Blood micro-droplets
 - Easily contain enough virus to cause infection





Occupational Safety and Health Administration

OSHA ✓ STANDARDS ✓ ENFORCEMENT TOPICS ✓ HELP AND RES

By Standard Number / 1910.1030 - Bloodborne pathogens.

Part Number: 1910

Part Number Title: Occupational Safety and Health Standards

Standard Number: 1910.1030

Title: Bloodborne pathogens.

Appendix: AGPO Source: e-CFR

https://www.osha.gov/laws-regs/regulations/standardnumber/1910/1910.1030

OSHA Bloodborne pathogens standard is a starting point in the consideration of preventing a laboratory acquired infection from working on specimens for PUI.

Perform a risk assessment for collection, receiving, and handling specimens from patients expected to be infected with the emerging agent

- Before a PUI is seen at your facility, do a provisional risk assessment
 - pre, analytic and post analytic
 - Facility specific that reviews the procedures performed, identifies the hazards involved in test performance, determine personnel competency level, and evaluates the equipment and facility design
 - Identify mitigation strategies
 - Implement mitigation strategies



Mitigation Control Measures

- ★ Engineering Controls: HVAC system, biosafety cabinets, sealed rotors etc. used to prevent exposure
- ★ Administrative Controls: Policies, standards and guidelines used to control risks
- Practices and Procedures: Processes and activities that have been shown in practice to be effective in reducing risks
- Personal Protective Equipment: Devices worn by the worker to protect against hazards in the laboratory

Advantages/Disadvantages

Control Measure	Advantages	Disadvantages
Engineering	Efficient, eliminates hazard	Cost, complexity
Administrative	Authority approach	Indirect approach, primarily addresses the human factor
Practices & Procedures	SOP based (standardized approach)	Training and supervision requirements
PPE	Ease of use, relative cost	Does not eliminate hazard, PPE fails exposure happens, uncomfortable, limits ability

Example Mitigation used in combination

Engineering Controls	Administrative Controls	Practices and Procedures	Personal Protective Equipment (PPE)
BSC	Policy on when to use the BSC	Training and competency on BSC use	Gloves, gowns, face shields, eye protection, respirator
Centrifuge with a sealed rotor	Policy on using only centrifuges with sealed rotor, open sealed rotor in the BSC	Training and competency on centrifuge use	Gloves, gowns, face shields, eye protection, respirator

Risk Assessment Matrix for Ebola*

Risk factors	Degree of Laboratory Risk		
Agent Hazards	Low to Moderate	Moderate to High	High
Pathogenicity	Mild to moderate disease	Moderate to serious disease	Severe disease
Virulence	Mild to moderate disease or low infectivity	Severe disease or moderate infectivity	Lethal disease/ high infectivity
Infective dose	>106	10 ⁶ – 100	<10
Transmission	Indirect contact (contact with contaminated surfaces)	Direct contact (droplet, tissue)	Percutaneous inoculation (needle stick)

^{*}adapted from D.O. Fleming ,personal communication

What tests may be ordered for a PUI?

- A complete blood count (CBC), including differential, and platelet count (For information on automated CBCs
- Sodium, potassium, bicarbonate, blood urea nitrogen, creatinine, and glucose concentrations
- Liver function tests
- Coagulation testing, specifically prothrombin time (PT), expressed as an international normalized ratio (INR)
- Urinalysis (dipstick)
- Blood culture for bacterial pathogens
- Malaria testing (smear or rapid testing or PCR)
- Influenza virus testing during periods when influenza, COVID-19, and RSV prevalence is high

Guidance for U.S. Laboratories for Managing and Testing Routine Clinical Specimens When There is a Concern about Ebola Virus Disease | For Laboratory Personnel | Ebola (Ebola Virus Disease) | CDC

Perform a Risk Assessment Considering the Testing Continuum

Pre-analytic

Specimen collection

Transport

Reception and Unpacking

Centrifugation

Uncapping

Aliquoting

Transport within the Lab

Transport to Reference Labs

<u>Analytic</u>

Chemistries

Blood Gases

Hematology

Bacteriology

Molecular

Parasitology

Transfusion Medicine

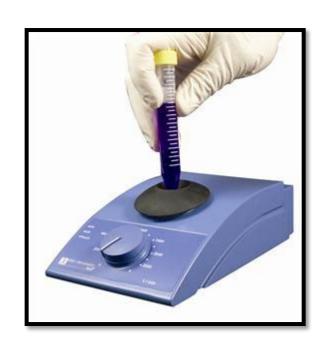
Post-Analytic

Waste Management

Specimen Storage - Retrieval

46

Protocol Driven Risk Assessment: Consider every step in the process



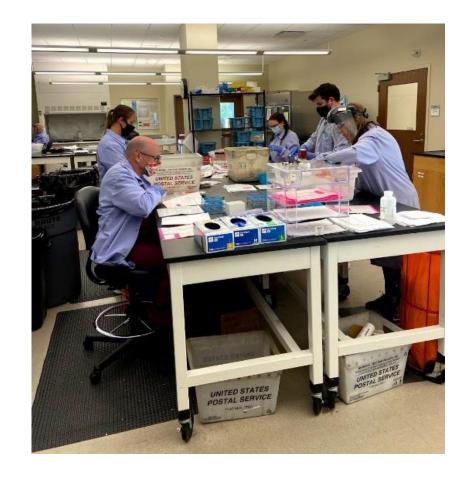
- The procedures performed
- •The hazards involved in the processes and procedures
- •The competency level of the personnel who perform the procedures
- The laboratory equipment and facility

Ex. Risk Assessment Matrix for Protocol Hazards

Protocol Hazards	Low Risk	Moderate Risk	High Risk
Suspension Volume	<25 ul	50-100 ul	>100 ul
Generate droplets & droplet nuclei		Pipetting	
Protocol Complexity	Standard repetitive procedures	Periodic change in procedures	Frequent change and complex procedures
Use of Sharps		With protective devices - safety sharps	Without protective devices

Risk assessment for pre-analytical phase

- What can go wrong during specimen receiving?
- How likely is it? What factors did you consider in assessing the likelihood?
- What are the consequences? What factors did you consider in assessing the consequences?
- What mitigation measures should you put in place to make the risks of specimen receiving acceptable?



Example: Specimen receiving

Identify Potential Hazards

- Leaking Package
- Breakage of the specimen container
- Aerosolization, Splash, Splatter
- Contamination of surfaces
- External contamination of waste containers



Mitigation of Risks

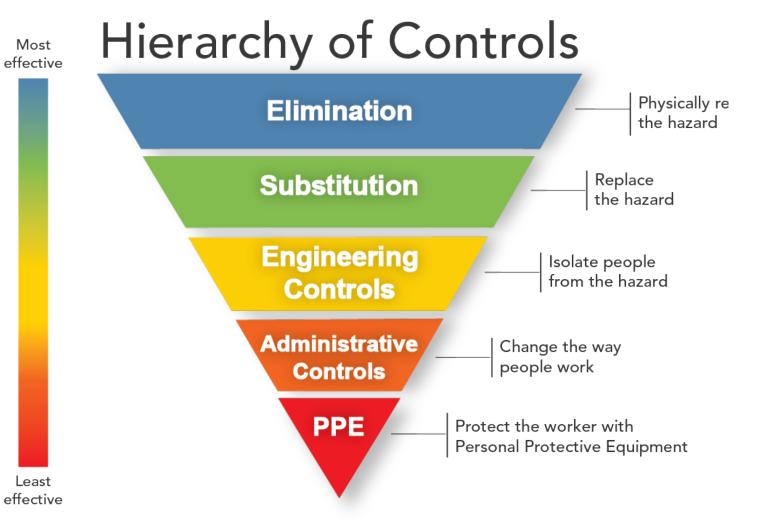


- Potential Hazards
 - Leaking Package use secondary containers to prevent leakage
 - Breakage of the specimen container use secondary container
 - Aerosolization, Splash, Splatter use Biological Safety Cabinet OR splash guards and additional personal protective equipment
 - Contamination of surfaces Disinfect immediately following handling the specimen
 - External contamination of containers disinfect containers immediately after use

Based on the risk assessment, mitigate the risk

Fill the biosafety gaps before first case

- Equipment and instrument safety
- Laboratory waste management
- Disinfectant practices
- Handwashing reminders
- PPE selection, use, and enforcement











- Select appropriate PPE based on a protocol driven risk assessment
- Train staff on donning and doffing procedures
- Monitor use

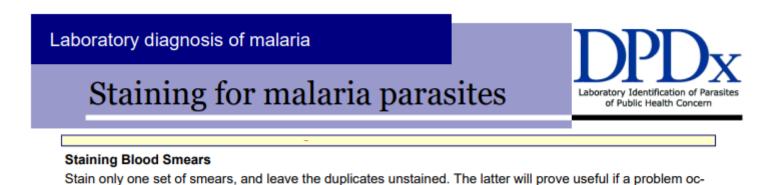
University of Nebraska PPE Instructions

Risk Assessment for Analytical Phase

- Chemistry automated analyzer
 - Is the initial centrifugation performed in a sealed rotor?
- Coagulation automated analyzer
 - Does the analyzer perform an open tube testing?
- Blood Bank
 - Does cross match require open tube centrifugation?
- Microbiology Blood Cultures
 - Are positive blood cultures handled in a biosafety cabinet?



Staining for malaria using Triton X-100



curs during the staining process and/or if you wish later to send the smears to a reference laboratory.

• Malaria signs and symptoms may be mistaken for Ebola. Being able to perform a test for malaria will remove the need to test for Ebola in some low-risk patients.

Risk assessment for the Post-Analytical Phase

- Medical waste stream
 - Autoclave
 - Incineration
 - Off-site transport
- Long term storage of specimen



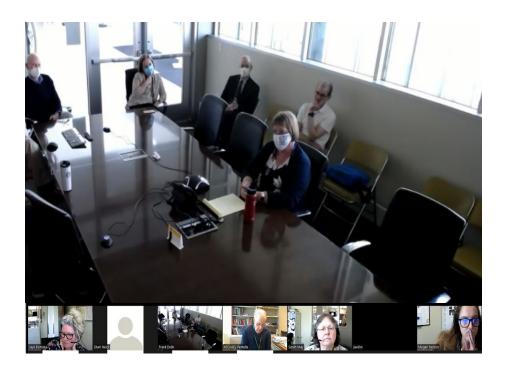
Communicate - staff, administration and public health

- Front-line laboratorians concerns:
 - How infectious are the specimens?
 - Are the controls sufficient?
 - Will handling infectious specimens impact the workflow?
 - Should I agree to handle the specimens?
- Administration concerns:
 - Should we accept specimens?
 - How will accepting these specimens impact other tests?
 - What is the risk of environmental contamination?

- Contact Public Health
 - Verify connections for information
 - Determine how, where, and when testing will be performed
 - Review specimen collection
 - Identify packaging and shipping needs for 24/7/365 response

Plan, Train, and Communicate

- Remember planning is important but it is what you do everyday to build the culture of biosafety that will predict the success of your plan
- Provide necessary training
- Consider performing a drill or exercise



BIOSAFETY ROAD MAP A 7-step guide to creating a culture of safety in the laboratory STOP 7 STOP 6 Creating a Culture of Safety Occupational 4 STOP 4 Health **Program** STOP 5 Safety Orientation Audits. and Training Monitoring, Safety STOP 3 Committee Select and Incorporate STOP 2 **Biosafety** Competencies Selection **Selection of Safety** of Safety Practices to **Practices to Prevent Portal Prevent** of Entry **Transmission** STOP 1 **Biosafety** Risk Assessment

- Risk Assessment and mitigation of risk are the first two steps to take.
- Also consider the:
 - Competency of the staff
 - Training
 - Audits, monitoring, safety committee
 - Occupational health
 - Culture of safety that exists in your laboratory

Clinical Laboratory Medicine, 2020 (4) 473-482.

Checklist to prepare your lab for testing a suspect patient for Ebola

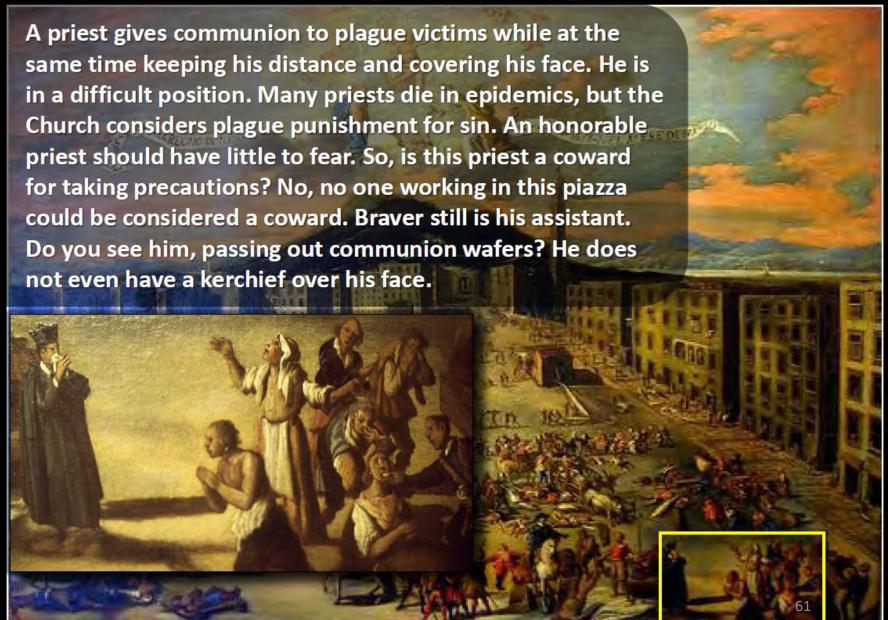
- ☐ Risk assessment ■Mitigation steps □Update the biosafety plan if needed ☐ Training of staff ☐ Packaging and shipping supplies □Sufficient trained staff on packaging and shipping for 24/7/365 □PPE supplies ☐ Donning and doffing training ☐ Training on the use of the biosafety cabinet
- https://www.cdc.gov/vhf/ebola/healthcare-us/preparing/hospitals.html#:~:text=Ebola%20assessment%20hospitals%20are%20facilities,discharge%20or%20transfer%20is%20completed

Reactions to Infectious Diseases

...and occasional heroism

From Carlo Coppola's painting of Naples's Piazza Mercato as it appears in 1657 during an epidemic that kills 150 thousand people, half the population of Naples.

Two 17th Century Italian Plague Paintings



Questions





Thank you for preparing to handle specimens from a PUI!

Important Reminders

- There are no documented EVD laboratory-acquired infection(LAI) cases in the U.S.
- OSHA Bloodborne Pathogens Standard

Check CDC's guidance regularly for guidance updates

Perform a site-specific and activity-specific risk assessment

Upcoming OneLab Network Events

A Unified Response to Training Needs

Third Ebola-related event in November

November 17, 2022, 12 – 1PM ET

Register Now!

Webinar Registration - Zoom (zoomgov.com)