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# Ebola virus disease: What clinicians in the United States need to know

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## Abstract

In March 2014 the World Health Organization was notified of an outbreak of Ebola virus disease (EVD) in the forest region of Guinea. Over the subsequent 8 months, this outbreak has become the most devastating Ebola epidemic in history with 21,296 infections and 8,429 deaths. The recent introduction of Ebola into noncontiguous countries including the United States from infected travelers highlights the importance of preparedness of all healthcare providers. Early identification and rapid isolation of patients suspected of being infected with Ebola virus is critical to limiting the spread of this virus. Additionally, enhanced understanding of Ebola case definitions, clinical presentation, treatment and infection control strategies will improve the ability of healthcare providers to safe care for patients with Ebola virus disease.

### Keywords

Ebola; Personal Protection Equipment; Person Under Investigation; Viral Hemorrhagic Fever

The Ebola epidemic currently spreading in West Africa has evolved into a full-scale humanitarian crisis. As of January 14, 2015, 21,296 cases of Ebola Virus Disease (EVD) with 8,429 deaths have been reported to the World Health Organization (WHO) from Guinea, Liberia, and Sierra Leone (1). This includes 825 cases and 493 deaths of healthcare

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personnel (1). An additional 32 cases and 15 deaths linked to this outbreak have been reported from Nigeria, Senegal, Mali, Spain and the United States (1). It is likely that cases reported to WHO are substantial underestimates (2). Despite heroic efforts by public health and healthcare providers on the front lines, the numbers of EVD cases continue to rise, and estimates of the number of infections and deaths that could occur in coming months, unless transmission is slowed, are enormous (3, 4).

The long incubation period (typically 8–10 days, but up to 21 days) and an increasingly interconnected global community increases the likelihood that other individuals from West Africa with EVD infection will travel to the United States and other countries. Indeed, the first imported case of EVD in the U.S. was recently identified in a traveler from West Africa resulting in the infection of two healthcare providers (5). Early recognition of suspect cases of EVD is critical to prevention of secondary Ebola virus transmission. In addition to vigilance, healthcare providers can benefit from increased preparedness including a working knowledge of Ebola case definitions, clinical presentation, treatment, and strategies to protect themselves and others while caring for patients with suspected or confirmed EVD. The CDC website regularly posts updated information and guidance related to the care of patients with Ebola virus disease (www.cdc.gov/vhf/ebola/).

The genus *Ebolavirus*, first discovered in 1976 during simultaneous outbreaks in Yambuku, Zaire and Nzara, Sudan causes a severe acute viral illness with a case fatality rate of 45–88% (6). In nearly forty years since, there have been 25 outbreaks with over 2,600 cases and more than 1,500 deaths prior to the current outbreak. The current West African EVD outbreak has now infected and killed more people than all previous outbreaks combined. There are five known species that comprise the genus *Ebolavirus*. The etiologic species of the current outbreak is *Zaire ebolavirus* (Ebola virus [EBOV]). Ebola virus is non-segmented negative sense, single-stranded RNA enveloped virus that is detected in a number of body fluids of infected patients, including blood, diarrhea, vomit, sweat, breast milk, vaginal secretions and semen (7, 8). Transmission occurs through direct contact between infectious body fluids of a symptomatic EVD patient and breaks in the skin and/or mucous membranes of an un-infected person, and thus can be interrupted with barrier precautions and disinfection. Despite this knowledge, Ebola virus transmission continues unabated in some countries in West Africa.

EVD patients initially present with non-specific symptoms including fever, chills, fatigue, malaise, anorexia, asthenia, weakness, maculo-papular rash and myalgia (Table 1) (4, 7). After several days, abdominal pain and pronounced gastrointestinal symptoms occur. Vomiting, and especially, profuse watery diarrhea, can result in intravascular volume depletion and electrolyte abnormalities including hypo- and hyper-natremia, hypokalemia, hypomagnesaemia and hypocalcemia (9–12). In most cases the profound volume loss from diarrhea leads to a decrease in effective circulating volume, poor organ perfusion and eventually multi-organ failure and shock. Conjunctival injection, chest pain, headache, and joint pain have also been noted. Respiratory symptoms including shortness of breath, and a nonproductive cough occur in a minority of patients but may be more frequently observed in resource-rich countries where the possibility of more aggressive volume resuscitation may lead to a comprise in oxygenation (4). Neurological signs may occur including seizures,

confusion, delirium, and coma. Hiccups may also occur later in the clinical course. Hemorrhagic manifestations including petechiae, ecchymosis, oozing from venipuncture sites, mucosal hemorrhage, hematemesis, melena, or frank hemorrhage occur in 30–50% of cases but blood loss is rarely sufficient to be the cause of death (7, 13, 14). Pregnant women however often experience spontaneous miscarriages and significant bleeding (15). There are no approved antiviral therapeutics or vaccines.

## I. Identification of Patients Suspected of Having Ebola: Persons Under Investigation (PUI)

Early identification and isolation of patients suspected of having Ebola is critical to controlling the spread of Ebola (17). A patient who has both signs and symptoms consistent with EVD and an epidemiologic risk factor, including a history of travel in a country with widespread Ebola virus transmission or contact with a symptomatic Ebola-infected patient within the preceding 21 days, is referred to as a Person Under Investigation (PUI) (Table 2) (18). The epidemiology link is further stratified into high, some, low (but not zero), and no identifiable risk (Table 2). While travelers returning from affected West African countries may have fever from a number of different infectious diseases, EVD should be considered immediately to protect healthcare workers, and interventions should be implemented to prevent ongoing transmission. Once identified as a PUI case of EVD, patients must be quickly triaged into the categories of confirmed cases or those without Ebola virus disease (17).

Evaluation of Persons Under Investigation is dependent on three components:

1. Epidemiologic risk factors (Table 2)
2. Clinical findings (Table 1)
3. Laboratory confirmation

### Laboratory Confirmation

As soon as a PUI is identified, the patient should be isolated, and recommended infection control precautions should be implemented immediately (see below). The local and state health departments should be notified, and arrangements made to collect blood for plasma to be tested by RT-PCR assay at a qualified laboratory. On August 6, 2014 the Food and Drug Administration (FDA) issued an Emergency Use Authorization to allow use of a RT-PCR assay in the diagnosis of Ebola virus disease(19). This specimen should be obtained following recommended precautions because of the potential for Ebola virus transmission associated with percutaneous exposure (see below) (20). Blood can be tested by the Laboratory Response Network (LRN; http://www.bt.cdc.gov/lrn/) as directed by the state public health department. If the sample is obtained at least 72 hours after the onset of symptoms and is negative this can be considered a final result (21). However, a positive test for Ebola virus disease must be confirmed at CDC, Atlanta, Georgia.

Patients with confirmed Ebola virus infection will need to remain isolated in a single room (with a private bathroom) with rigorous adherence to recommended infection control

precautions (18). This should be at a facility with dedicated isolation rooms and appropriately trained staff. Additionally local and state health departments can also provide guidance on which hospital(s) in the area are equipped and trained to care for patients with Ebola. All persons who have had close or direct contact with an EVD patient during their illness (either suspect or confirmed) must be actively monitored by public health authorities for 21 days after that contact to ensure that they do not develop Ebola virus disease throughout the duration of the incubation period. A confirmed case may be discharged once clinical recovery and clearance of virus has been documented with a negative result from a validated RT-PCR test, in consultation with CDC.

### Exclusion of Ebola Virus Disease

In a PUI, Ebola virus disease is excluded when a patient with fever and symptoms for greater than 3 days has a plasma specimen that is negative for Ebola virus by a validated RT-PCR assay at an approved laboratory in consultation with the CDC. These patients may be safely discharged if clinically stable, but still must be followed as part of contact tracing for 21 days if their history includes contact with a PUI or confirmed EVD case in collaboration with State public health departments and the CDC. If testing is done on plasma collected earlier than three days after symptom onset, a negative result does not exclude Ebola virus infection; therefore, if symptoms persist, repeat testing should be performed on a specimen collected after the 3$^{rd}$ day of illness.

## II. Protecting Healthcare Workers While Caring for Patients with EVD

Protection of healthcare workers is critical and requires the knowledge and understanding of Ebola virus transmission, proper use of personal protective equipment (PPE), and strict adherence to guidelines for donning and doffing. Interruption of Ebola virus transmission through the institution of barrier precautions, including the use of PPE, is a cornerstone of healthcare worker protection. All healthcare workers must be trained in Ebola-specific infection control practices and procedures especially donning and doffing proper PPE prior to providing care to a patient with suspected or confirmed Ebola virus disease. Donning and Doffing protocols are dependent on the personal equipment used and may need to be modified accordingly. Two options are presented.

The care of an Ebola patient requires a team effort to mitigate risks to healthcare workers. Protection of healthcare workers is guided by infection control trained donning and doffing observers who are responsible for ensuring that PPE is both worn correctly and removed safely. Prior to entry into an Ebola-patient care area, the donning observer will guide each healthcare provider through each step of donning to ensure complete adherence with donning protocols. Similarly, upon exiting, a doffing observer will instruct the healthcare provider how to remove each article of contaminated PPE in a systematic fashion to reduce risk of direct exposure with infectious bodily fluids.

### Donning PPE Option 1-N95 Respirator (22)

Donning of appropriate PPE should be monitored by an infection-controlled trained donning observer:

1. Engage donning observer
2. Change into scrubs and boots or washable footwear and remove personal clothing and items (jewelry, cell phones, pagers, pens etc.)
3. Inspect PPE prior to donning to ensure it is in optimal condition
4. Perform hand hygiene with Alcohol Based Hand Rub (ABHR)
5. Put on first “inner” pair of gloves
6. Put on boot or shoe covers
7. Place impermeable gown or coveralls on over scrubs and over first pair of gloves (ideally this gown will have thumb loops which will keep cuffs over the first pair of gloves)
8. Place N-95 respirator over nose and mouth and complete a user seal check
9. Put on surgical hood over N-95 respirator ensuring that the hood covers all of the hair, ears, and extends past the neck to the shoulders
10. Put on outer impermeable apron if used
11. Put on a second pair of “outer” gloves with extended cuffs ensuring that they cover the sleeves of the gown or coverall
12. Cover face with face shield
13. Verify the integrity of the ensemble and test range of motion
14. Disinfect outer gloves using ABHR

### Donning Option 2 (Use of powered air-purifying respiratory – PAPR)

Donning of appropriate PPE should be monitored by an infection-controlled trained donning observer:

1. Engage donning observer
2. Change into scrubs and boots or washable footwear and remove personal clothing and items (jewelry, cell phones, pagers, pens etc)
3. Inspect PPE prior to donning to ensure it is in optimal condition
4. Perform hand hygiene with ABHR
5. Put on first pair of “inner” gloves
6. Put on boot or shoe covers
7. Place impermeable gown or coveralls on over scrubs and over first pair of gloves (ideally this gown will have thumb loops which will keep cuffs over the first pair of gloves)
    a. If a PAPR with a self-contained filter and blower unit that is integrated inside a helmet is used then this must be placed on before the gown or coverall

   b. If a PAPR with external belt-mounted blower is used, the blower/tubing must be on the outside of the gown or coverall

8. Put on a second pair of “outer” gloves with extended cuffs ensuring that they cover the sleeves of the gown or coverall
9. Put on PAPR with disposable hood that covers face, hair, ears, and extends past the neck to the shoulders
10. Put on impermeable apron
11. Verify the integrity of the ensemble and test range of motion
12. Disinfect outer gloves with AHBR

After completing the donning process have the donning observer verify PPE is on correctly and is intact.

Although barrier precautions protect exposed skin and mucous membranes, wearing PPE by itself is not enough. In addition to clinical care, healthcare workers are also at risk of coming into contact with infected body fluids while removing (doffing) contaminated PPE. A structured and supervised process of instructed doffing is critical and will help mitigate these risks (22, 23). The process required to safely remove PPE however is dependent on the equipment used and will need to be optimized when using a different type of PPE. Doffing should occur in a dedicated exit site outside of the patient isolation area with a clearly defined contaminated zone (where the person who is doffing stands and a clearly defined clean zone, where the doffing observer stands). A trained doffing observer guides the healthcare worker through each step of doffing to ensure strict adherence with a safe method of contaminated clothing removal.

### Doffing PPE Option 1 (N95 respirator option)(22)

At the exit site doffing should be supervised and guided by a designated infection control trained doffing observer

1. Engage trained doffing observer
2. Inspect the PPE including boots to assess for cuts, tears, or visible contamination, then disinfect using EPA-registered disinfectant wipe.
3. Disinfect outer gloves with ABHR
4. Remove impermeable apron by grabbing the neck loop from the back of the neck and dispose of in a designated waste container
5. Inspect PPE to assess for visible contamination, cuts or tears before further removal
   a. If visible decontamination is discovered disinfect using EPA-registered disinfectant wipe
6. Disinfect outer gloves with AHBR
7. Remove boot or shoe covers
8. Disinfect outer gloves with AHBR and remove outer gloves

9. Inspect inner gloves and disinfect inner gloves with ABHR
10. Remove face shield
11. Disinfect inner gloves with AHBR
12. Remove surgical hood
13. Disinfect inner gloves with AHBR
14. Remove coverall by tilting head back and unzip/unfasten completely
    a. Remove the coverall suit by pulling away from body, rolling inside out and pushing down past waist and then stomping out of the suit and discard in a designated waste container.
15. Disinfect inner gloves with AHBR and change inner gloves
16. Remove N95 Respirator
17. Disinfect inner gloves with ABHR
18. Disinfect washable shoes/boots using an EPA-registered disinfectant wipe
19. Disinfect inner gloves with ABHR and Remove inner gloves
20. Perform Hand Hygiene with ABHR
21. A final inspection of the healthcare worker by the doffing observer will be performed to evaluate for contamination of surgical scrubs
22. Healthcare worker can leave PPE removal area wearing dedicated washable footwear and surgical scrubs
23. Showers are recommended at each shift's end for healthcare workers performing high risk patient care
24. Protocol evaluation – Either the infection control officer or occupational health safety and health coordinator should meet with each healthcare worker to review the patient care activities to identify any concerns about care protocols

### Doffing PPE Option 2 (PAPR option) (22)

At the exit site doffing should be supervised and guided by a designated infection control trained doffing observer

1. Engage trained doffing observer
2. Inspect the PPE including boots to assess for cuts, tears, or visible contamination, then disinfect using EPA-registered disinfectant wipe.
3. Disinfect outer gloves with ABHR
4. Remove apron, if used, by grabbing the neck loop from the back of the neck and dispose of it in a designated waste container
5. Inspect PPE to assess for visible contamination, cuts or tears before further removal

   a. If visible decontamination is discovered disinfect using EPA-registered disinfectant wipe

6. Disinfect outer gloves with ABHR
7. Remove boot/shoe covers
8. Disinfect outer gloves with AHBR and remove outer gloves
9. Inspect and disinfect inner gloves with ABHR
10. Remove PAPR and set aside for decontamination
    a. If using a PAPR with a self contained integrated filter and motor unit then wait until step 16 for removal and instead proceed with step 12
    b. If using a PAPR with an external belt-mounted blower then all components must be removed now
        i. Remove and discard outer hood
        ii. Disinfect inner gloves
        iii. Remove headpiece, blower, tubing, battery, and belt
        iv. Disinfect inner gloves
        v. Place all reusable PAPR components in a designated area for the collection and disinfection of all PAPR components
11. Remove coverall by tilting head back and unzip/unfasten completely
    a. Remove the coverall suit by pulling away from body, rolling inside out and pushing down past waist and then stomping out of the suit and discard in a designated waste container.
12. Disinfect inner gloves with AHBR
13. Disinfect boots or washable shoes
14. Disinfect inner gloves with ABHR
15. Remove respirator if not already removed
    a. Remove and discard disposable hood
    b. Disinfect inner gloves with ABHR
    c. Remove and discard inner gloves taking care not to contaminate bare hands
    d. Perform hand hygiene with ABHR
    e. Don a new pair of inner gloves
    f. Remove helmet and the belt and battery unit. This step may require assistance from the trained observer
16. Disinfect inner gloves with ABHR and remove inner pair of gloves and discard in a designated waste container

17. Perform Hand Hygiene with ABHR
18. A final inspection of the healthcare worker by the doffing observer will be performed to evaluate for contamination of surgical scrubs
19. Healthcare worker can leave PPE removal area wearing dedicated washable footwear and surgical scrubs
20. Showers are recommended at each shift's end for healthcare workers performing high risk patient care
21. Protocol evaluation – Either the infection control officer or occupational health safety and health coordinator should meet with each healthcare worker to review the patient care activities to identify any concerns about care protocols

## III. Medical Management of Ebola Virus Disease

EVD patients with gastrointestinal symptoms often progress to intravascular depletion, complicated by electrolyte abnormalities (hypokalemia, hypocalcemia, and hypomagnesemia,), organ hypoperfusion, shock and finally, death (9–12). Hemorrhagic complications including melena and hematemesis are often late manifestations and occur in less than 50% of patients (7, 13, 14, 24). The volume of blood loss is rarely sufficient to cause death (25). Similar to bacterial sepsis, the pathophysiology of EVD has been linked to cytokine dysregulation and the generation of a systemic inflammatory response. In contrast to bacterial sepsis however, oxygenation and ventilatory complications are rarely seen in Ebola virus disease in West Africa, which may reflect differences in pathophysiology or more likely a consequence of the difficulty providing sufficient volume resuscitation in austere environments typical of most Ebola virus outbreaks (9).

Currently there are no approved specific antiviral therapies for patients with EVD. Clinical management of EVD patients is thus largely supportive. Given the substantial volume loss and subsequent hypotension experienced by patients, volume resuscitation is a key aspect of this supportive care. During past EVD outbreaks, oral rehydration was encouraged without intravenous fluid resuscitation to reduce the risk of percutaneous exposures to healthcare personnel. However, emerging data suggest that aggressive supportive care including the early use of intravenous resuscitation and electrolyte replacement reduces mortality in EVD patients and can be performed safely (9, 14, 26–28).

In addition to aggressive critical care support, consideration should be given to the empiric use of antimalarial medications given the high prevalence of malaria in the affected region. The use of empiric antibiotics is also often undertaken due to the critical nature of this illness and the theoretical risk of translocation of intestinal bacteria. Acetaminophen and other analgesics are used for the severe abdominal pain that is often experienced by EVD patients, however NSAIDS and aspirin should be avoided because they can inhibit platelet function and aggravate the thrombocytopenia which is a prominent feature of EVD.

## IV. Investigational treatments

There are a number of promising novel antiviral therapeutics and vaccines that are currently being developed. Recently, the immunotherapeutic ZMapp, a cocktail of three monoclonal antibodies directed against the Zaire ebolavirus glycoprotein has received considerable attention due to its efficacy in Non-human primates infected with Ebola.. A recent trial demonstrated 100% (18/18) protection of rhesus macaques up to five days following lethal Ebola virus challenge, suggesting possible benefit of initiating treatment of infected patients after signs and symptoms of EVD have occurred (29). This immunotherapy has been administered through compassionate use in an uncontrolled manner to 7 medically evacuated EVD patients to date who also received advanced medical care with 71% survival (30). Three other agents with unknown efficacy, brincidofovir, favipiravir, and TKM-Ebola, have been used in repatriated patients. TKM-Ebola is a small interfering RNA formulated in a lipid nanoparticle that has been shown to have antiviral activity in Guinea Pigs and protecting 2 of 3 non-human primates following Ebola virus challenge (12, 31). Favipiravir is a nucleotide analogue that has demonstrated both in vitro and murine in vivo efficacy against Ebola and is currently undergoing a clinical trial in Guinea (32). CBrincidofovir, a novel prodrug of cidofovir, has been developed to treat DNA viruses including cytomegalovirus (CMV) has also demonstrated some *in vitro* activity against Ebola and have been used in a small number of patients with uncertain efficacy. A number of other investigational antiviral therapies are under development, including an RNA polymerase inhibitor, siRNA product, phosphoro diamidate oligonucleotide, and others (33). However, controlled clinical trials are required to establish the safety and efficacy of any investigational immunotherapeutics or antivirals for treatment of EVD in humans.

Convalescent blood products from surviving EVD patients are also being evaluated as a potential therapy (34, 35). Although early use of convalescent whole blood or convalescent plasma treatment in mice and guinea pig models appeared successful, the benefit in EVD patients has not been well-studied (36, 37). Moreover, interpretation of uncontrolled use has been confounded by the timing of treatment as many of the survivors who received the blood products were far along in their clinical course and likely already had a good chance of recovering or had received higher level of supportive care than the comparison group (28, 38, 39). Recent studies in non-human primates recapitulating the conditions in which human patients received convalescent blood products unfortunately were unsuccessful (40). Further evaluation of passive immunotherapy in controlled clinical settings is needed to delineate whether convalescent blood products or hyper-immune serum have roles in the treatment of patients with EVD.

## V. Disinfection and Waste Management

Waste management is an important aspect of infection control and caring for patients with EVD, especially given the characteristic voluminous diarrhea and occasional hemorrhage. Chlorine, soap, and alcohol solutions of at least 80% are all capable of destroying Ebola virus (41). As a precaution the use of disinfectants with label claims for the inactivation of non-enveloped viruses should be used (42). Laboratory studies indicate that Ebola virus can remain viable on solid surfaces for up to 50 days (43). However Ebola virus may be able to

survive even longer on solid surfaces when protected in body fluids such as vomit, blood, or stool (44). Incineration, or disinfection by autoclave, of contaminated materials onsite or after transport to a medical waste incinerator is the preferred method of disposal. Guidelines for disinfection and waste management can be found at http://www.cdc.gov/vhf/ebola/hcp/environmental-infection-control-inhospitals.html

## V. Public health response – Active Monitoring (45)

Contact tracing is integral to arresting the transmission of Ebola virus. Although the incubation period is typically 8–10 days, it may range from 2–21 days. EVD patients are not considered contagious until fever and/or symptom onset. State health departments with the assistance and technical support of CDC will perform contact tracing to identify and actively monitor contacts of PUI or confirmed cases of Ebola for any symptoms within 21 days of the last contact they had with a symptomatic patient if EVD is confirmed. This includes any healthcare personnel who have had direct interaction with a patient since presentation to medical care. Active monitoring involves an initial risk stratification of exposure (Table 2) and subsequent daily assessment (either by patient report or direct observations if direct active monitoring is performed) for the presence of symptoms and/or fever to ensure the rapid identification, isolation and evaluation of an individual (45). A coordinated public health response by the CDC and the state and local health departments is critical to limiting viral transmission in the US.

## VI. Summary

The epidemic of Ebola virus disease in West Africa represents an unprecedented humanitarian crisis of global importance. Given the increasingly interconnected global community, the arrival of patients infected with Ebola virus into the United States and other countries outside of West Africa (both of which have already recently occurred) is likely but vigilance and preparedness can help prevent ongoing transmission. Healthcare personnel and public health systems worldwide must remain vigilant for potential cases of Ebola virus disease in symptomatic travelers from affected countries and immediately isolate the patient and institute barrier precautions to stop the chain of transmission while providing life-saving supportive care.

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## Table 1

Signs and symptoms associated with Ebola virus disease (4, 12, 16)

| Presenting Signs and Symptoms | All Patients (%) |
|---|---|
| Fever (measured)* | 84–89 |
| Fatigue | 65–76 |
| Headache | 53–80 |
| Aching muscles or joints | 39 |
| Vomiting | 43–68 |
| Diarrhea | 61–67 |
| Abdominal pain | 44–46 |
| Unexplained hemorrhage (including miscarriage) | 18–19 |
| Weakness | 79 |

* Fever was reported in 84%–89% of patients; thus fever is NOT always present (4).

**Table 2**

Epidemiologic Risk Factors (17)

| | |
|---|---|
| **High Risk** | Percutaneous or mucous membrane exposure to body fluids of a person with EVD |
| | Exposure to body fluids of a person with EVD without appropriate PPE |
| | Processing body fluids of a person with Ebola without PPE or standard biosafety precautions |
| | Direct contact with a dead body in a country with widespread EVD transmission without appropriate PPE |
| | Having lived in the same house and provided care to a person with Ebola who is symptomatic |
| **Some Risk** | Direct contact with a symptomatic Ebola-infected person while using appropriate PPE in a country with widespread Ebola virus transmission |
| | Close contact with a person with Ebola in households, healthcare facilities, or community settings while the person is symptomatic |
| **Low (but not zero) Risk** | Having been in a country with widespread Ebola virus transmission within the past 21 days without a known exposure |
| | Having brief direct contact (e.g. shaking hands) while not wearing PPE with a person with Ebola while they are in the early stages of disease |
| | Being in close proximity with a symptomatic Ebola-infected patient for a brief period of time |
| | Direct contact with a person with Ebola while using appropriate PPE in an country without widespread Ebola virus transmission |
| | Having traveled on an aircraft with a person with Ebola while the person is symptomatic |
| **No Identifiable Risk** | Contact with an asymptomatic person who had contact with a person with Ebola |
| | Contact with a person with Ebola before the person develops symptoms |
| | Having been in a country with widespread Ebola virus transmission more than 21 days ago |
| | Having been in a country without widespread Ebola virus transmission but without any exposures defined above |