Safety Considerations in the Laboratory Testing of Specimens Suspected or Known to Contain Ebola Virus

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Reference to the Ebola virus causes concern among all individuals, whether from the public or within the medical community. Realization that patients with Ebola virus disease (EVD) have now been recognized in the United States in response to the major outbreak occurring in West Africa has heightened this fear. Recently, the World Health Organization declared the Ebola epidemic to be a Public Health Emergency of International Concern to provide containment of this major international health threat. In response to this threat to public health, the United States has stepped up efforts to provide care for infected patients, which include bringing individuals with EVD into the United States for treatment. These activities, along with the increased possibility of having more individuals recognized with EVD in the United States, have caused hospitals to evaluate how to contain and care for patients suspecting of having EVD. As a part of this response, laboratorians have been asked to be prepared to test specimens from persons under investigation (PUIs) for EVD or patients known to have EVD.

Recently, the Centers for Disease Control and Prevention (CDC) provided an interim guideline followed by a supplemental document for how US laboratories could safely manage specimens from PUIs for EVD.[1,2] In these documents, the CDC recommended that risk assessments be conducted by each laboratory to determine the potential for sprays, splashes, or aerosols generated from laboratory procedures when handling these specimens and to adjust work practices, safety equipment controls, and personal protective equipment (PPE) requirements as needed to provide a safe environment in the laboratory. Recently, we described an integrated approach on how laboratory tests could be conducted on specimens from Ebola-infected patients.[3] In our risk assessment, we determined that the core laboratories where chemistry and hematologic testing takes place do not have facilities that can safely handle specimens suspected of containing or known to contain Ebola virus. For example, the processing of open tubes without the availability of a biosafety cabinet and the centrifugation of specimens without safety cups or sealed rotors are common practices within the core laboratory. In addition, clinical laboratories that do have the facilities to perform biosafety level 3 (BSL-3) practices (to include processing within a biosafety cabinet, centrifugation using safety cups or sealed rotors, and enhanced PPE to include respiratory protection) are generally available only to the clinical microbiology laboratory and specific to the testing of specimens potentially containing the causative agents for tuberculosis or for endemic fungi such as *Coccidioides immitis* and *Histoplasma capsulatum*.

Subsequently, a risk assessment within our laboratories was done that focused on the potential for microdroplet or aerosol generation. Although Ebola virus is not thought to be spread through human-generated aerosols, automated instruments that include centrifuges are capable of generating microdroplets of blood. Ebola virus has an infectious dose of fewer than 10 organisms and a blood virus concentration in excess of 10E8 viral particles per milliliter, and a blood droplet theoretically would be sufficient to cause infection. The primary risk was considered the mucous membranes and eyes of laboratorians. As a result of this assessment, we determined that only closed manual or automated chemistry and hematology analyzers were considered safe for the testing of blood containing specimens with potential Ebola virus present outside the BSL-3 containment laboratory. We

Table 1
Essential and Supplemental Tests Used for the Support of a Patient Infected With Ebola Virus[a]

Test	Laboratory Location[b]	Centrifugation Required[c]
Essential		
CBC count with automated differential	Core	No
Basic metabolic panel	Core	Yes[d]
Magnesium	Core	Yes
Comprehensive metabolic panel	Core	Yes[d]
Ionized calcium[e]	BCU	No
Standard calcium	Core	Yes[d]
Phosphorus	Core	Yes
Cortisol	Core	Yes
Troponin	Core	Yes
Blood gases[e]	BCU	No
Lactate	Core	Yes[d]
Prothrombin time[e]	BCU	No
Partial thromboplastin time[e]	BCU	No
Platelet count	Core	No
Blood typing[f,g]	BCU	No
Culture procedures[h]	NPHL[i]	No
Molecular assay[j]	NPHL[i]	No
Supplemental		
Manual differential	Core	No
Lipase	Core	Yes
Amylase	Core	Yes
Creatine kinase total	Core	Yes
Malaria smear[k]	Core	No
HIV screen	Core	No

BCU, biocontainment unit; HIV, human immunodeficiency virus; NPHL, Nebraska Public Health Laboratory.
[a] All open-tube testing and centrifugation were performed within the biosafety level 3 (BSL-3) laboratory environment. The lists of tests were determined from a risk assessment for safety in consultation with infectious diseases and critical care physicians. This list will not necessarily represent capabilities and needs for all clinical laboratory applications.
[b] Laboratory locations were determined following a risk assessment.
[c] Centrifugation was performed in the BCU laboratory and transferred to the core laboratory as noted.
[d] Testing also available on point-of-care testing instrument.
[e] Utilization of point-of-care testing instrument.
[f] Using slide agglutination method.
[g] Type O, Rh- and Kell-negative blood were recommended where appropriate.
[h] All cultures were performed in the BSL-3 laboratory using culture media contained in plastic containers.
[i] Provides for a BSL-3 containment facility.
[j] Using an emergency use authorization kit assay approved by the Food and Drug Administration.
[k] Smear prepared and fixed in the BCU laboratory.

subsequently met with the clinical team, including infectious diseases and critical care physicians, to define an expanded list of assays that could be done safely to help provide optimal patient care. The goal was to determine which assays could be performed in the patient care biocontainment unit using point-of-care (POC) instruments, the Nebraska Public Health Laboratory BSL-3 laboratory, or the core laboratory. **Table 1** lists both the essential and supplemental tests that we identified could be done safely to manage our patients infected with Ebola virus along with the laboratory locations where the tests were performed. As expected, other tests could be anticipated following an evaluation of the safety to perform the test as needed. In some cases in the evaluation, testing was considered not safe (ie, fibrinogen levels, procalcitonin levels, and cross-matching of blood), requiring consultation between the requesting physicians and the laboratory personnel to determine what alternative tests might be considered.

Since the clinical management of patients with EVD is heavily focused on cardiopulmonary function and electrolyte balance, we found that this expanded menu of laboratory tests was necessary to support optimal patient management. In addition, although the original plan was to use our standard policy for transfusion of type O, Rh-negative blood, it became necessary to perform reverse typing when consideration was given for use of apheresis plasma from a patient who had been infected with and recovered from the Ebola virus. Kell-negative units were held in reserve in case a hemolytic episode was encountered under this circumstance.

A general understanding among our laboratory staff was that no room existed for error when handling specimens that contained Ebola virus. A laboratory-based transmission would not only cause human distress but also have detrimental consequences for the laboratory operation with a subsequent limit to the ability of the entire hospital to function optimally. Our described plan may have general applicability to tertiary medical centers where closed-system automated instruments are commonly used and where a BSL-3 facility (such as a mycobacteria testing laboratory) is available where appropriate BSL-3 practices are done. Using this combination of capabilities, laboratories could provide for the initial processing of specimens (eg, centrifugation and subsequent testing in locations that are appropriate for either POC assays or closed automated platforms). The approach described here is offered to provide a baseline for further discussion of the processing and testing of specimens with the potential to contain the Ebola virus or other high-consequence pathogens.

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