When the Rubber Meets the Road
Dealing With a Returning Traveler From West Africa During the Ebola Outbreak of 2014

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Ebola virus is a single-stranded RNA-enveloped virus that has caused more than 20 outbreaks of hemorrhagic fever in Africa. This virus and Marburg virus (both filoviruses), as well as Lassa and Machupo viruses (both arenaviruses), are considered category A bioterrorism agents under the label of hemorrhagic fever viruses. Even though Ebola virus was discovered in 1976, it was not until August 2014 that American media started paying attention because two Ebola-infected health care professionals were brought for treatment to the United States. The attention given to the patients who came to the United States and the extensive spread of the current outbreak bring to the forefront the fact that a patient with Ebola is a flight away from being anywhere in the world. The diagnosis was known for the Americans who came to the United States, the Spanish priest who succumbed to the disease in Spain, and a health care worker who traveled for care in the United Kingdom. However, the question arises on how to determine whether someone has been infected with Ebola when he or she has traveled to countries where the outbreak is occurring and develops a fever upon returning to the United States—in other words, those for whom a diagnosis will need to be done in the United States.

The Centers for Disease Control and Prevention (CDC) provides guidelines regarding who is at high risk for the infection from the epidemiologic and clinical perspective, infection control for viral hemorrhagic fevers, and how to send specimens for Ebola virus testing, which is available within the United States only at state health departments and the CDC. However, anxiety has increased with the media attention, so there may be different expectations from patients who have traveled to the epidemic area and clinicians taking care of them. In addition, these patients will need to be tested for other more frequent causes of symptoms that overlap with Ebola infection, such as malaria, typhoid fever, and respiratory and gastrointestinal infections, which may present as medical emergencies. A group from Australia has published the laboratory features of returning travelers with fever. They found that dengue had much higher increases in C-reactive protein with low white blood cell counts compared with malaria and enteric fevers, while platelets were frequently low in patients with dengue and malaria. Although few patients infected with Ebola and Marburg viruses have been studied regarding laboratory parameters, features include leukopenia, thrombocytopenia, elevated aminotransferases, and increased prothrombin time and activated partial thromboplastin time.

Similar to laboratory features, clinical presentation, particularly early in the infection, is nonspecific. During early Ebola infection, patients have fever, myalgias, weakness, and headaches. Sometimes a maculopapular rash can be observed. As the disease progresses, patients have nausea, vomiting, diarrhea, and respiratory symptoms. It is not until the final stages of the disease that there is multiorgan failure, with hemorrhages from mucosal surfaces or puncture sites. It should be noted that there is serologic evidence that some of the infections are asymptomatic. As opposed to other viral diseases such as viral hepatitis, Ebola is not transmissible when the patient is asymptomatic. Thus, an asymptomatic person who has been exposed, and thereby considered at high risk, will not be able to transmit the disease during this period. The CDC classifies the following persons at high risk for infection: those who have used inappropriate personal protective equipment (PPE) and performed laboratory testing on body fluids, treated patients, or have had direct exposure to human remains of those suspected of having or known to have Ebola infection. As an infected patient becomes symptomatic, contact and droplet precautions need to be taken.
A lack of health care infrastructure is evident from the images the media are showing regarding how Ebola-infected patients are handled in Africa. Photographs show that patients are treated in premises that have dirt floors, do not have running water, and have no climate control or supplies such as intravenous (IV) hydration to give supportive treatment to patients. Because of these conditions, health care workers are wearing PPE that allows them to handle all situations (droplet, contact, and airborne). As many health care workers have been deployed to help contain the current outbreak, we are bound to see some returning home with fever. For their treatment and the safety of our health care workers, it is imperative to define their risk exposure. Thus, if they have used appropriate PPE, they will be in the low-risk category, but if there has been a break in their PPE, they will be in the high-risk exposure category. The risk assessment likely will be performed by infectious disease physicians, who will also define other tests needed to provide care to the patient.

Our health care infrastructure is very different from what occurs in the African regions where the outbreak is occurring. We have hospitals with private rooms with bathrooms, supplies for contact and droplet precautions are frequently used in hospitals for a variety of infections, supportive treatment with IV fluids is the norm, and diagnostic tests are performed on a routine basis on infectious samples, such as human immunodeficiency virus, hepatitis B, and hepatitis C, with automated instruments where laboratorians are minimally exposed. The CDC recommends isolation and use of adequate PPE, restriction of visitors, avoidance of procedures that generate aerosols, and appropriate environmental infection control measures if a patient has Ebola infection or in symptomatic patients who have high-risk exposure while Ebola is being ruled out.

Although US recommendations and guides are available, gaps are noted in defining what and how to implement them. In a patient who has had a high-risk Ebola exposure, what tests will be necessary, and where will these be performed? Such a patient will likely have a fever, and thus cultures will be needed (to rule out typhoid, meningococccemia, and other bacterial agents), as well as malaria and Ebola testing. Clinicians will also want to have, at a minimum, a CBC and a metabolic panel with liver enzymes as well as basic coagulation studies, but we will need to remind clinicians that testing should be kept to the minimum necessary. The American Society for Microbiology (ASM) recommends that a rapid malaria test and any other test except for the culture be done at the patient’s bedside. Although some medical offices and emergency departments have Clinical Laboratory Improvement Amendments licenses to perform some of these tests, it is likely that malaria is not on their list. Some point-of-care devices can be taken to the room, although in many practices, testing capabilities are located away from the bedside. In addition, many practices may not have or be interested in having the capability of performing the tests. In short, for high-risk suspect Ebola cases, we will be sending samples to the state health laboratory to be tested for Ebola, and if there is no bedside point of care, another set of samples will go to either a small laboratory in the emergency room or office or the main laboratory of the hospital for the rest of the testing. The following questions arise: do you have to package the samples the same way (category A bioterrorism agents)? Can you use different packaging for the testing sent to the laboratory next door? It is obvious that these packages have to be hand-carried to the areas for testing or shipping. No specimen should be sent in the pneumatic tube system.

When one thinks about phlebotomy for high-risk patients, it is clear that this has to be done in the patient’s isolation room. Now, what should phlebotomists bring? They should pack the specimens as close as possible to where the patient is. The phlebotomists will need to have PPE, as will all other personnel taking care of the patient, and bring into the room what is necessary for obtaining the specimen. They will not bring a tray, although a bag or container that can be wiped clean and in which the specimens fit will be necessary. They will obtain the samples, wipe clean the tubes and bottles, change gloves, label the specimens once the surfaces are dry, place them in the bag or container, clean the outer surface of the bag or container, change gloves again, and exit the room with specimens. Outside, as close as possible to the patient’s room and likely on a tray, they should then place the specimens that are already inside the bag or container in another set of containers that will be closed, which they will hand-carry to the laboratory. Next question: are phlebotomists trained in packaging category A and B infectious agents? Most are not. Do we need to train them? Should those trained in packaging help phlebotomists and take over once the specimen is out of the patient’s room? Or do we let them carry the packaged samples through the hospital to the laboratory where the package will be opened to separate samples?

Once the specimens from patients suspected of having Ebola get to the laboratory, a trained packaging person will need to work on repackaging the specimen that will be sent out for Ebola testing to the state health laboratory. How do you treat the rest of the specimens? Here the UK guidelines seem more useful than those provided in the United States. They state that when using automated instrumentation the systems are closed, a small sample size is used, and dilutions...
are automatic, thereby posing minimal risk to medical technologists and creating minimal infectious waste for disposal. They comment that malaria testing (smears or rapid tests) can be performed in containment level 2 facilities. However, countering the low risk presented previously, they state that the laboratory needs to be informed that the specimen (including the malaria smear) is from a suspect Ebola case, so that it is separate from the rest and disposed of as a category A agent by incineration. Regarding cultures, similar to what the ASM suggests, they recommend placing these in automated instruments, although subculturing should be performed in a microbiology safety cabinet by experienced staff. Disinfection of surfaces can be done with hypochlorite, and cultures should be inactivated before disposal.

If a high-risk patient dies without a definitive diagnosis, it will be important to take steps to define the cause of death. However, undertaking a full autopsy poses many risks to those performing it. If the body should be placed in a leakproof body bag, with a second body bag with absorbent material and chlorine in between. Biopsy specimens can be obtained and placed in formalin. Immunohistochemistry for Ebola has been used in postmortem skin biopsy specimens, providing diagnoses and minimizing the risk to the medical personnel who obtained the specimens. Fine-needle aspirates could be used for polymerase chain reaction testing. Specimens obtained postmortem should be handled as category A agents and packaged appropriately so they can be tested by the state health department or CDC. Last, for disposal of remains, cremation is recommended while embalming is not.

For those patients known to have Ebola or any other viral hemorrhagic fever, testing specimens at the patient bedside using point-of-care devices for follow-up of different parameters may be necessary. Containment and disposal of material used for testing must be done using category A agents (autoclaving/incineration). Decontamination of the point-of-care devices will be necessary. The only two patients with Ebola who were treated in the United States were in a special pathogen containment unit that exceeded the above precautions. Units such as the one available at Emory University Hospital are few and have limited capacity. Thus, the question is where to treat patients who are infected when special containment units are at their limit of occupancy.

In summary, although there are recommendations and guides from different countries, gaps are noted when it comes to implementing laboratory work to be performed in symptomatic persons who have been exposed to Ebola. It needs to be remembered that a symptomatic high-risk exposure patient may need to stay in isolation until the Ebola testing results are available. Thus, in many ways, knowing what you are dealing with is easier than waiting to have a diagnosis in a patient who has had high-risk exposure.

References