

A Commentary on Ebola Virus Testing: *Can We Talk?*

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Laboratory testing of potential Ebola patients remains a moving target. As new information comes out, risk assessments change, personal protective equipment (PPE) is altered and media hype escalates. Nonetheless, a few things are definitive: **1) Ebola virus does not spread through the air. Nor is it transmitted through casual contact. 2) Ebola is spread by direct contact with fluids from a patient who is symptomatic with disease.** A list of potentially infectious and/or Ebola RNA-positive fluids includes blood, feces, vomit, saliva, mucus, tears, breast milk, urine, semen, vaginal secretions and sweat. If these fluids from an ill individual come in contact with a healthy person's broken skin, eyes, nose or mouth, transmission may occur. Bodily fluids from an infected corpse are extremely infectious. **3) An infected patient is not contagious unless he or she is exhibiting symptoms.** Added to this *Trinity* is one more certainty – the mere word (Ebola) strikes fear in the hearts of many, including healthcare workers (HCW).

Being new to Public Health when we received word that our lab was one of the first initially chosen to test for Ebola virus, I worried about how to allay fears when announcing this to the virology laboratory staff. My concern was unfounded. I was overwhelmed with pride as these scientists accepted the task in stride. I had misjudged them - they told me that this was their job, this is what they do and their responsibility.

Soon after that I got a call from Specimen Receiving (SR) informing us a box with "Ebola" written on it had just been delivered. This created quite a stir as we had not yet formulated a plan for how SR would handle potentially (Ebola)-infectious blood. They had not been briefed on the virus or on our testing status. Our relief in discovering it was just the reagents used to test for Ebola rather than an Ebola specimen soon turned to realization that we needed a plan in place immediately. I met with Receiving and answered their questions openly and honestly. They too took it in stride. Next we held brown-bag symposia for everyone in the building, from chemists and housekeepers to maintenance workers and laboratory information specialists. There were a lot of questions, mostly about how the virus spreads and stories reported in the news, some second-hand from friends or family. It was an enlightening experience for all of us, especially me. It reiterated once again that what we perceived to be staff concerns were unrealized once an open dialog was in place. Information may be power, but it also provides a sense of control over the situation.

Lesson Learned No. 1: *Educate everyone in your facility about the Ebola "Trinity." Engage them early in the process of planning and risk assessment. Be honest and open and they will listen to and trust the facts.*

Lesson Learned No. 2: *Like a boy scout, be prepared. Get a plan into place. Practice it and tweak it. A plan is fluid; it evolves as conditions change and new information becomes available. Keep up.*

The Ebola virus RNA detection kit, distributed by the Centers for Disease Control and Prevention (CDC) was developed by the United States Department of Defense (DoD). It requires whole blood collected in a purple-top (EDTA) tube. An extra tube is requested to send to the CDC for additional testing, including assays for other hemorrhagic disease viruses, e.g., Lassa fever virus. The procedure was put into place and our scientists were trained using test specimens. And, as we like to say, there were no problems, only unexpected challenges.

Ebola virus has an outer lipid envelope, making it easy to inactivate (“kill”) and easy to decontaminate laboratory surfaces. However it is a RNA virus, so more care is needed to protect the extract from degradation. This creates a challenge when chemically inactivating the virus to render it non-infectious prior to laboratory handling. Chemicals can destroy the RNA, reducing the viral load in the sample to undetectable. The importance of this is stressed because in early symptomatic disease, the Ebola viral load is naturally low. A specimen collected on day 1 of illness can test falsely-negative, thus requiring repeat testing on a subsequent specimen (assuming symptoms of Ebola virus-infection progress rather than resolve). Any treatment that reduces the detectability of viral RNA should be avoided if possible. Another challenge with testing is how to handle the chemical waste produced during testing. The DoD procedure uses Trizol which cannot be added to bleach, a commonly used laboratory decontaminant.

Lesson Learned No.3: *Your risk assessment plan must include the elimination of hazardous chemical waste as well as biological waste.*

Early CDC recommendations for PPE, meant to protect HCWs in immediate proximity to bodily fluids while caring for infected patients, i.e. long-term exposure to extraordinary volumes of vomitus and cholera-like quantities of liquid feces, with the late-illness potential of aggressive, demented behavior, were translated to the laboratory worker, creating havoc on risk assessment.

Lesson-Learned No.4: *Devise your plan with an “abundance of caution.” Do not try to reason with personal fear. There will always be something, real or not real, to support it. Instead, embrace it; work with it, and as long as it does no harm, give in by relinquishing control. Choose a consensus PPE acceptable to those involved, especially those performing the testing.*

An Ebola virus-infected patient could walk into an Emergency Department of any Michigan hospital at any time, so plans for transport and laboratory coverage must be addressed ahead of time. This awareness opened up a whole new set of challenges for us. Our virology lab hours are Monday-Friday, 8 am to 5 pm. That meant large blocks of off-hours time had to be covered by one of our three molecular scientists; “Ebola call” was put into place for our small “Ebola Team”. The call rotation continued until the CDC published a recommendation of paired

HCWs for donning and doffing of PPE - another new challenge for the small “Ebola Team”. We enlisted some of our non-molecular volunteer scientists to work as testing assistants until they could be cross-trained on the assay. The training is time-consuming, but will be worth it when we get a larger pool of scientists trained to respond to “Ebola call”.

Lesson Learned No.5: *A trained molecular scientist plus an assistant knowledgeable in donning and doffing of PPE must be available 24 hours a day to support testing of potential Ebola virus-infected patients.*

Solving the problem of competent testing staff availability was a huge relief, but we still had to deal with transport, both facilitating movement of specimens to our Lansing Bureau of Laboratories (BOL) and forwarding one of the submitted tubes to the CDC. Clearly packaging should be Category A – less due to the risk of the virus than the resulting panic created should an accident damage the shipping container of blood specimens from a patient under investigation (PUI) for Ebola virus disease. This leaves few transport options – FedEx (which now refuses to pick-up clinical samples from a suspected Ebola-infected patient), a private courier (found in an ideal world), *me* (don’t hitch a ride if there is snow on the ground) or some other State of Michigan salaried employee. (For legal reasons this must be in a state vehicle, increasing the turn-around time since no one is permitted to routinely keep these at their homes overnight.), and World Courier (at a cost of \$800-900/shipment). For this purpose, some states have engaged their state police for transport assistance.

Lesson Learned No. 6: *Solve transport problems now. Make sure your facility has Category A shippers, as well as personnel certified in packaging and shipping.*

The likelihood that one of the specimens sent for testing is positive for Ebola virus is extremely low. Even with positive travel and/or risk history, a patient presenting with fever plus fatigue and flank or muscle pain (and even with more striking symptoms, e.g., vomiting/diarrhea/hemorrhage) cannot be diagnosed clinically given a zero prevalence of Ebola in Michigan. Other etiologies causing infections with similar symptoms are much more likely in a traveler from West Africa, e.g., malaria, *Salmonella*, influenza, HIV and hepatitis, of which malaria is the most dangerous. Any delay in a malaria diagnosis can result in death. Thus clinical laboratories are asked to perform tests to rule out non-Ebola agents prior to calling in a state epidemiologist. See newly published CDC recommendations, “Guidance for U.S. Laboratories for Managing and Testing Routine Clinical Specimens When There is a Concern About Ebola Virus Disease” found at <http://www.cdc.gov/vhf/ebola/healthcare-us/laboratories/safe-specimen-management.html>. After recommending a minimum of at least malaria smears and influenza PCR, we discovered our greatest challenge thus far, one anticipated neither by us nor the CDC. Some laboratories could not perform any tests on an Ebola virus potentially-infected patient presenting at their facility.

Lesson-Learned No.7: *Standard precautions are not used universally in laboratories.*

Lesson Learned No.8: Plan ahead as to how you will care for and support a patient with symptoms that place Ebola on the differential diagnosis. This is essential for those hospitals designated as Tier 1 (one that will treat and accept transferred Ebola-infected patients) or Tier 2 (a hospital that will not accept a transferred Ebola patient, but will treat such a patient presenting to them). Lower Tier facilities still need to be prepared for a suspicious walk-in.

Some hospitals spent huge sums of money establishing separate, Ebola-designated laboratories. Many invested in point-of-care (POC) instruments. Important to remember if traveling down this path is the capability to perform specific tests, e.g., platelet count, complete blood count (hemoglobin, hematocrit, red and white blood cell counts) with white cell differential, liver enzymes, kidney function tests, prothrombin time, blood culture and malaria smears, in addition to limited “STAT” assays usually reserved for intensive care units, e.g., glucose and electrolytes. In any event, dialog needs to continue and expand to include intra-laboratory (all disciplines, i.e. Hematology and Chemistry) and inter-laboratory (between institutions) communication with infection preventionists and State Public Health.

Another more recent possibility is the adding the BioThreat-E test (BioFire Defense LLC) performed on the Film Array for Ebola virus RNA. Laboratories may choose to use this as a pre-screen and, if negative, treat the specimens as one would treat any laboratory specimen – no special precautions, no funneling to a special out-of-the-core lab. It should be noted that the Public Health DoD test is at least a 10-fold more sensitive than the commercially available Film Array assay. Lower sensitivity becomes important early in symptomatic disease when the viral load is low. Also, whether the result is negative or positive with the Film Array, the specimen must still be tested by the Public Health DoD assay. If a negative result is found with the DoD assay, it does not need to be confirmed and is considered final. On the other hand, positive results are considered and reported presumptive until further testing is completed at the CDC.

In closing, I believe now is the time to get everyone involved in patient care and laboratory testing to discuss how we can better plan for infection control issues resulting when any patient presents to a facility with a suspected emerging infectious disease. This interaction should include public health and other hospitals with the same Tier designation.

Future planning needs to be both inclusive and cooperative with all parties involved.

Let's talk.

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Suggested Web References

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CDC Healthcare Infection Control Practices Advisory Committee (HICPAC).
(http://www.cdc.gov/hicpac/2007IP/2007ip_part2.html#e)

Packaging and Shipping Clinical Specimens Diagram.
(<http://www.cdc.gov/vhf/ebola/healthcare-us/laboratories/shipping-specimens.html>)

Revised NYS/NYC Laboratory Guidelines for Handling Specimens from Patients with Suspected or Confirmed Ebola Virus Disease.
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BioFire Defense LLC. FilmArray™ BioThreat-E Instructions for Use. 2015.
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