Labs ramp up for Ebola patients, specimens

Karen Lusky

Amid Ebola preparation, an EV-D68 outbreak

December 2014—Clinical laboratories have made impressive headway in their Ebola preparedness, though their plans are shaping up in different ways. That's due, in part, to varying opinions about how to manage a dangerous and unpredictable virus.

"We are really learning as we go along with this," says D. Jane Hata, PhD, D(ABMM), director of microbiology and serology at Mayo Clinic in Jacksonville, Fla. For years there has been talk of the possibility of an airplane passenger bringing Ebola into the U.S., she says. "But we are on the ground now and we're all actively planning to deal with this."

Above all, says Cleveland Clinic's Gary W. Procop, MD, MS, institutions need a procedure to determine if a patient meets the Centers for Disease Control and Prevention's criteria for a person under investigation (PUI) for Ebola. Two experienced physicians, one of whom should have infectious diseases training, should make that assessment, says Dr. Procop, an infectious disease pathologist and microbiologist and chair of the CAP's Microbiology Resource Committee. (The CDC describes the PUI criteria at www.cdc.gov/vhf/ebola/hcp/case-definition.html.)

Dr. Procop

This type of approach, Dr. Procop says, weeds out the worried well, ensuring that only those truly at risk receive testing and care in a situation requiring heightened safety measures. "Once the person has been appropriately identified as a PUI, then the designated health care provider would obtain the appropriate specimens for necessary testing after, of course, they have donned their personal protective equipment."

As for how labs are handling diagnostic testing for suspected Ebola patients, Kaiser Permanente's Susan Novak, PhD, D(ABMM), says many are moving to point-of-care testing to mitigate exposure to Ebola in the laboratory setting.

"Clinical laboratories are at a disadvantage since we haven't really worked with specimens positive for this virus before," says Dr. Novak, director of microbiology at Kaiser Permanente Regional Reference Laboratories in Southern California. "So testing specimens in the open clinical laboratory environment has caused some concern within the microbiology community. Ebola isn't known to be transmitted via aerosols, but most clinical laboratories are hesitant to place specimens on analyzers within the open lab space."

Bourgeault

A survey of the laboratories that are members of the Compass Group, which includes 28 health care systems and more than 350 hospitals, found that only four of 17 respondents say they will allow suspected or confirmed Ebola virus disease specimens into their labs, says Robert Bourgeault, MS, MLS(ASCP), director of laboratory operations at Baystate Health in Springfield, Mass., and a member of the board of directors of the Compass Group.

One of those four will restrict testing to a biosafety level 3 isolation room and use handheld point-of-care analyzers, Bourgeault tells CAP TODAY. Another respondent will start with laboratory-based testing and then move to point-of-care over time. "A third respondent plans to discourage sending specimens to the laboratory but will remain open to requests from clinicians on a case-by-case basis," he says. Bourgeault presented all of the survey's findings in a recent Compass Group webinar.

Dr. Campbell

Sheldon Campbell, MD, PhD, associate professor of pathology at Yale University, is uneasy about the clinical impact of "stringent point-of-care only protocols," which he agrees are being implemented widely. The problem, he says, "is that the Emory [point-of-care] laboratory was set up to manage a patient who came in with a diagnosis of Ebola and most of us aren't going to be doing that. We are going to be managing the patient who has risk factors for Ebola and a fever, and a differential diagnosis includes a dozen things other than Ebola." Malaria, for example. "In Liberia last year, there were 1.2 to 1.6 million cases of malaria, so that's high on everybody's list," he says.

Dr. Hata

Mayo Clinic's Dr. Hata agrees it's a dilemma that's generating much discussion. "I think everyone has to come up with a solution that works for their institution and the levels of containment they can realistically achieve at the patient site and in the laboratory."

In Chicago's northern suburbs, NorthShore University HealthSystem plans to perform all laboratory testing for potential Ebola patients in its biosafety level 3 microbiology laboratory. It will do blood cultures and a malaria smear, a basic metabolic group, and a peripheral smear for a white count and platelet assessment, says Richard B. Thomson Jr., PhD, D(ABMM), division head of clinical laboratories.

Dr/ Thomson

To perform malaria testing safely, the laboratory is adding Triton X to its malaria reagents, Dr. Thomson says, noting the CDC has documented that the substance will kill Ebola. “We actually do our malaria smear in a biological safety cabinet even though we have it in a reagent that will kill the virus. Then we do the stain and coverslip it in the hood, and bring it out to read,” he explains.

So how fast should you act on malaria clinically? One type of malaria, Plasmodium falciparum, found in West Africa, can be fatal within 24 hours, Dr. Thomson cautions.

Decatur (Ill.) Memorial Hospital has obtained a small, mobile point-of-care lab with a class II biologic safety hood that the laboratory plans to deploy wherever a potential Ebola patient is in the hospital, says laboratory director Michael Sass, MD. The hospital laboratory won’t perform malaria testing with peripheral blood films until it receives a negative Ebola test result from the Illinois Department of Public Health, which may take 24 to 48 hours from the time of specimen collection. “If our infectious disease physician on staff felt that the patient’s problem was more likely due to malaria, he would probably institute treatment for that while waiting for [Ebola] results” from the health department, Dr. Sass says.

Dr. Burd

Some laboratories are using point-of-care malaria testing. Among them is Emory University, which tests for malaria using the Alere BinaxNow Malaria test in its lab in the serious communicable diseases unit, says Eileen Burd, PhD, D(ABMM), director of clinical microbiology at Emory University Hospital. “If a patient was found to concurrently have Ebola virus, we would not confirm a negative test with smears,” she says. Once Ebola infection is ruled out, however, “we would proceed with thin and thick smears in the main laboratory to confirm a negative malaria test.”

Some laboratory professionals think that doing presumptive Ebola testing with the BioFire Defense FilmArray BioThreat-E test, approved by the FDA in October for emergency use, could be useful during the rule-out phase for possible Ebola. Others aren’t sure or foresee challenges.

Drs. Campbell and Procop are in the latter camp. Dr. Campbell says it’s unclear at this point how valuable the test would be for hospitals doing rule-outs. For one, “The performance characteristics of the test are still poorly understood,” he says. And a state public health laboratory or the CDC would still have to confirm a negative or positive result for diagnostic purposes.

The Cleveland Clinic is considering using the test, but Dr. Procop says he thinks validating it will be complicated. “The challenge with using any on-site assay for Ebola virus is the validation of the assay,” he says, noting that “naturally occurring specimens are not readily available in North America. And the virus is a [federal] Select Agent and cannot be handled without special license.”

NorthShore’s Dr. Thomson thinks the assay may be useful as a “second opinion test.” By that he’s referring to situations in which the hospital would like to test a patient for Ebola but the public health department, the CDC, or

both refuse to do so because they don't think the person meets the CDC criteria. "That's sort of a crack that some patients may fall through where a second opinion test would be good to have," Dr. Thomson says.

Dr. Woods

Gail Woods, MD, chief of pediatric pathology at Arkansas Children's Hospital in Little Rock, says she doesn't yet know what the assay's false-positive rate is but surmises that you would treat a patient differently if he or she tested positive. "If the result was negative, depending on the sensitivity, I doubt one would feel totally safe saying the person does not have Ebola" until the result is confirmed. "However, you could, for example, test for respiratory pathogens, such as influenza, on [the same instrument]. If you got a positive result for influenza and a negative for Ebola, you might conclude they may have the flu and not Ebola," says Dr. Woods, who is also a professor of pathology at the University of Arkansas for Medical Sciences.

Emory University is using the BioThreat-E assay to presumptively test patients at risk for Ebola who come to its emergency department and clinics. "The ability to generate rapid results is helpful for the subsequent management of the patient by the clinical teams," Dr. Burd says. "A medical technologist and laboratory director are on call around the clock, and even with transport time, testing can be completed within several hours."

The laboratory has a protocol for packaging the specimens, which are transported by couriers, Dr. Burd says. "All testing is done in the satellite lab in our serious communicable diseases unit. The pouches are inoculated in a biological safety hood and placed in the FilmArray instrument, which is located on a bench outside the hood."

A large part of Ebola readiness, of course, involves figuring out the optimal way to keep staff from becoming infected.

In that regard, laboratory professionals aren't disputing use of the CDC-recommended enhanced standard precautions for handling suspected Ebola specimens, though some labs are taking additional protective steps.

Dr. Campbell says as far as he can tell, the CDC guidelines do not differentiate between handling suspected and confirmed Ebola specimens, "which is appropriate." (The CDC spells out the enhanced precautions at www.cdc.gov/vhf/ebola/hcp/safe-specimen-management.html.)

As an extra precaution, the Cleveland Clinic has implemented the buddy system for laboratory testing, one that nurses and physicians also use for patient care. "One of the big challenges in using all of this personal protective equipment, particularly if it is above and beyond what one uses every day, is that people can make mistakes," Dr. Procop says. "Testing specimens from a PUI, therefore, becomes a two-person job, with one technologist performing the testing and another to observe and assist."

Dr. Campbell reports that his laboratory may adopt enhanced standard precautions for every specimen. "We are worried that it will be the one we don't know about that will get us. We haven't yet implemented that. We haven't tested it to see how practical it is, but one thing we may need to do is make our standard precautions more stringent."

There are data to suggest that enhanced standard precautions are sufficient when testing Ebola specimens, Dr. Campbell continues. "People have been doing lab testing in the Ebola zone on people with the disease since March, and none of the lab workers there have gotten sick. But we haven't run things in our own environment here, doing the full range of tests on a variety of complex instruments. I think it's clear that Ebola is more infectious than HIV,

hepatitis B, and hepatitis C, which are the sorts of things our standard precautions are designed to deal with."

At Arkansas Children's Hospital, the issue of using enhanced precautions for all testing came up in a recent quality improvement meeting, Dr. Woods says. "People who present to our ED or a clinic may not be honest when they are asked if they traveled outside the country. If that happened, we could get an [Ebola] specimen." Some laboratory staff want to be extra cautious and wear N95 respirator masks even when laboratory protocols don't require it, she says. "I've told them if they want to wear one, they can. I'm certainly not going to tell them not to."

Dr. Romero

That people will hide their illness is always a possibility, says Jose Romero, MD, section chief of pediatric infectious diseases at Arkansas Children's and professor of pediatrics at the University of Arkansas for Medical Sciences. "Ebola may be a little different because of the fatality rate, but they may wait until they are pretty sick until they come in."

The laboratory may also fail to receive warning that a specimen is from a suspected Ebola patient, which Dr. Campbell says happened at his facility. A couple of minutes after the laboratory received the specimen, "someone rushed down and said it might be from somebody with Ebola," he says. The patient didn't "have any meaningful risks, but we got the specimen before we got the word, so that was very disturbing."

Baystate's Bourgeault says that everyone who responded to the Compass Group survey has a notification plan that depends on either infection control, the direct care provider, or the command center. "But we want to do everything possible, by active communication, to prevent a physician office [from] blindly submitting specimens to the laboratory or sending a patient to a laboratory patient service center for phlebotomy," when they suspect Ebola infection, he says.

Clinical laboratories also have plans for springing into action if a patient's Ebola test is confirmed as positive.

NorthShore University HealthSystem would transfer a confirmed Ebola patient to a specialized center. But until the transfer took place, the laboratory would continue to offer the limited list of tests performed before the Ebola diagnosis was confirmed, Dr. Thomson says. "We have discussed ordering and testing at certain times each day, rather than testing on demand all day, to limit laboratory exposure."

Arkansas Children's will care for a known Ebola patient in a private, negative-pressure room in the hospital. Point-of-care testing will be performed in an area adjacent to the patient's room, and no specimens will go to the lab, Dr. Woods says. "We have an i-Stat, which gives you most of the chemistry tests you need plus a hemoglobin and hematocrit, but our intensivists want additional tests, so we have to purchase additional point-of-care instruments."

"Very fluid" is how Dr. Hata describes Mayo Clinic's plans for testing a confirmed Ebola patient. The plans have been constantly changing, she says, "based on guidance from the CDC, the Florida Department of Health, what we have learned about the virus in the current outbreak, and the experience in other institutions." Point-of-care testing, she says, will be limited to what can be performed inside the patient's room, which will have negative airflow. The infectious disease and laboratory management groups would have to approve additional testing.

At Baystate Health, patients suspected of having Ebola will be admitted to a negative-pressure isolation room in the emergency department. There, nurses will perform testing using point-of-care analyzers, and a blood sample

will be sent to the Massachusetts Department of Public Health for Ebola virus PCR. “This will not change should EVD be confirmed,” Bourgeault says. The Massachusetts Department of Public Health has designated Baystate as one of seven hospital systems that can provide care to Ebola patients. “We believe we are prepared, from the biosafety [and] PPE, testing, and clinical care aspects. This planning and preparation process is ongoing,” he says, “and we have begun drills to test all processes and techniques.”

What might become of the extensive preparedness if no more Ebola cases occur in the U.S. for a while? In that case, the plans would go into a “maintenance mode,” Dr. Woods says.

“Right now, it’s in the ramping up mode, and once you are convinced you are ready to do everything you need to do, then it will go into maintenance mode. But will it ever go away? At least not in the near future.”

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