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Can't Touch This! Contamination of Laboratory Equipment with Bloodborne Pathogens

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Guests: Dr. Carey-Ann Burnham is an Associate Professor of Pathology and Immunology at Washington University School of Medicine in St. Louis. Dr. Susan Butler-Wu is the Director of Clinical Microbiology at LAC+USC Medical Center in Los Angeles.

Bob Barrett: This is a podcast from *Clinical Chemistry*, sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I'm Bob Barrett.

The Ebola outbreak in the fall of 2015 led to emergent responses by hospitals to prepare for potential patients. This included preparedness efforts by laboratories, which was challenging as they was evolving and at times contradicting information about how samples from patients under investigation for Ebola should be handled.

One important question was whether or not total laboratory automation or other instrumentation commonly employed in clinical laboratories could be used for these specimens. There was little evidence and large differences in opinion on this topic.

In the July 2016 issue of *Clinical Chemistry*, Dr. Andrew Bryan and colleagues report on their investigation into the levels of blood-borne viral pathogen contamination of a total laboratory automation system. This article was accompanied by an editorial by Dr. Carey-Ann Burnham and Dr. Susan Butler-Wu. They joined us for this podcast. Carey-Ann Burnham is an Associate Professor of Pathology and Immunology at Washington University School of Medicine in St. Louis and the Medical Director of Clinical Microbiology for Barnes-Jewish Hospital. Susan Butler-Wu is the Director of Clinical Microbiology at LAC+USC Medical Center in Los Angeles and an Associate Professor of Pathology and Laboratory Medicine at the University of Southern California.

Dr. Butler-Wu, can you tell us a bit about the events that prompted your recent study published in *Clinical Chemistry*.

Susan Butler-Wu: So basically, during the recent Ebola outbreak, labs in the US were kind of faced with this evolving guidance from the CDC, and so that evolving guidance coupled with really what had been much more stringent lab guidance that had been previously published by overseas authorities, basically led to a lot of questions about how samples from patients who

were categorized as being under investigation for Ebola should be handled.

So really, honestly, it was a very challenging time for lab directors, because in one hand you turned on the TV and you saw healthcare workers in space suites, and then on the other hand you had guidance that told labs to just go ahead and select the level of personal protective equipment for your own lab based on the risk assessment that you performed.

So for those of us in the clinical microbiology community, the recommendations prior to this outbreak had been that specimens from person who's suspected of having Ebola should be handled in a BSL level four containment facility. So there are really only a handful of those in the country. So basically, as a result of all this, some hospitals made the decision to go exclusively with point of care testing, so basically, to bring that lab testing to the bedside of patients who were under investigation for Ebola.

But the issue was that many hospitals didn't have the right point of care instruments that one would need to provide sufficient clinical monitoring of a patient while they were being ruled out for Ebola, or even to adequately rule out other potential infectious causes of these patient symptoms using point of care systems.

So, some of these instruments are actually quite expensive and in many cases because there were such a panic at the time, they were even back-ordered. So even if you actually manage to purchase one of these instruments, you still had to validate it to use on patient specimens, you need to train personnel and your staff and then to ensure that they were competent and maintained that competency to run the test on these instruments.

So really, because of all these issues, the question came up as to whether samples from persons under investigation for Ebola could really just be run safely on a facility's--it's called the total lab automation system or TLA, particularly because patients with Ebola virus disease can have really large quantities of virus present in their blood, so up to 10 to the 10th or basically over a billion copies of virus per milliliter.

So, these TLA systems that are used by many labs to automate, they basically automate all the steps that are required to perform many of the lab tests that are done in clinical labs such as centrifuging the specimen, taking the cap off, and even performing the test itself.

So on one hand, you can make an argument that maybe the TLA system could potentially be safer for lab staff because

you could reduce the amounts of manual manipulation of the specimen that was required.

So at the University of Washington Medical Center, which is in Seattle which is where I was at the time, we were really lucky to have just this brilliant lab medicine resident called Dr. Andrew Bryan. Andrew was really interested in the Ebola planning process for our institution.

If I'm being honest, there really was a diversity of opinion among our faculty in the department at that time as to whether we should be using this TLA system for specimens from these patients. So Andrew, our Director of Labs Dr. Mark Wener, and myself decided to go to the chemistry lab and look at the TLA in action.

So, really, it was from going and observing the tubes working their way along the system that the idea to do this study was kind of collectively hatched to look more closely, really, at the possibility of blood-borne pathogen contaminations of the TLA system. So then, Dr. Bryan took that ball around with it and so here we are.

Bob Barrett: Dr. Burnham, let's talk about how Ebola has spread. Have there been instances of infection acquired by lab workers who've handled specimens containing the Ebola virus?

Carey-Ann Burnham: Well, Bob, that's a very common question. But from years of experience with this virus, it is known that Ebola is spread by direct contact with blood or body fluids of infected patients.

As Dr. Butler-Wu mentioned already, the virus can be present in really high quantities in the blood, but it is also found in other body fluids. We now increasingly recognize that the virus can even persist for a long time in certain body fluids such as semen, and the virus can even be found in sweat. This is why the traditional burial practices in some parts of Africa where the body is washed and prepared by the deceased person's family members can dramatically contribute to the spread of the virus.

Although there has been some debate previously as to whether or not Ebola virus can be spread by the airborne route, we now know that this is not the case. With regards to your second question, we recall the situation in Dallas where there was Ebola transmission to healthcare workers that cared for the Ebola patient there.

Of note, there were no cases of Ebola acquired by any of the laboratory workers in that hospital, even though there were specimens tested by the laboratory before they were aware that the patient had Ebola, and they were not taking any

specific safety precautions beyond the standard precautions that laboratories use.

Similarly, there had been previously published cases of Ebola patients in hospitals overseas where neither the clinicians nor the laboratory were aware that the patient had Ebola, and ultimately no transmission to staff occurred.

So in terms of transmission on the Ebola to laboratory staff, all signs would point to the need for strict adherence to standard precautions. What they need for addition precautions really being considered on a case by case basis and being dependent on the nature of the laboratory testing that is specifically being performed.

Bob Barrett: So Dr. Butler-Wu, given all of this, what were the major findings of this study?

Susan Butler-Wu: So really, there were two main questions that Dr. Bryan answered in our study. At the time, there was really very little known about contamination of TLA systems by blood-borne pathogens. So the first goal of the study was to see if we could detect nucleic acid from two commonly encountered blood-borne pathogens, and the ones that we chose to look at were hepatitis B and hepatitis C virus and we looked at the TLA system itself to see whether certain components of the system were more prone to contamination than other components of the system.

Then the second goal of the study was to assess what contamination occurs right after a specimen that has large quantity of virus runs through that system. So, obviously, we didn't have a specimen with Ebola virus and even if we had, we wouldn't have been running on it to see how it performed. So instead, we chose a specimen that was known to contain hepatitis C virus.

So, we chose hepatitis C virus because like Ebola virus, it's an enveloped RNA virus and patients who have hepatitis C can have very high quantities of virus present in their blood samples. Although, it should be said that the quantity of virus that was present in the specimens that we use in the study was in the order of 10 to the 7th copies per milliliter, which is lower than the quantities that can be seen with Ebola patients.

So when we started the study, the first thing that had to be done was to check to see whether we were able to recover the nucleic acid of these viruses from non-porous surfaces such as those surfaces that are found on the TLA system.

So we did indeed established that this was the case, but interestingly we were only able to recover about 50% of the

hepatitis C RNA that was originally put on to the surface. So this is important because it tells us that any nucleic acid that we might have actually detected from the system would likely actually be an underestimate.

So now, when we looked at the baseline background contamination of our TLA system with these two blood-borne pathogens, we found that we were able to detect viruses from 22% of the 79 swabs that we had sampled. Also, we weren't able to detect any baseline contamination with these viruses away from the TLA system itself and that was important because it meant that the contamination seemed to be confined to the TLA system.

So, when we looked at the specific sites where we detect the contamination, we consistently detected the contamination from the decapper chute. This is where the caps go after they're removed from the patient's blood tube, but we were also able to detect background contamination and other portions of the TLA as well.

In fact, some of the swabs that we sampled even have dried flakes of blood on them. But to be honest, what gave us the most pause was the fact that we could detect contamination on exposed areas where there were no protective barriers between the samples and the lab personnel themselves.

Secondly, when we run through a hepatitis C containing specimen, having already previously strategically placed glass slides throughout the system so that we could look at fresh contamination rather than background contamination, we did detect hepatitis C on one of the 54 slides that we placed on the system.

Bob Barrett: And what are the implications of this study for clinical laboratories?

Susan Butler-Wu: So when we started thinking about for some, initially, I think the most surprising part for me was that certain safety features were not present and standard in these TLA systems. I should say that this isn't an issue that's unique to the particular TLA system that we used in the study, it's really a wider issue, generally speaking.

Our results also show that the process of moving specimens through a representative TLA system, it actually leads to contamination of that equipment with blood-borne pathogens, well, at least with viral nucleic acid anyway. In our study, we didn't look for the presence of live virus so we are making the assumption that live virus would be detected for some time after the contamination occurs. We don't know the duration for which it remains viable because obviously, that depends on the virus itself.

But as a clinical microbiologist, I have to be honest, I was kind of floored when I saw tubes moving through the system on a completely open track without any kind of Plexiglass cover. Because in microbiology labs, we generally don't open patient samples outside of a biosafety cabinet at all. So I've even heard from some colleagues that biosafety cabinets are sometimes removed from chemistry labs to make space for the installation of these TLA systems.

Carey-Ann Burnham: To follow on from that, I think that the study also speaks to the need for manufacturers of these systems to have clear guidance of cleaning and decontamination. We need studies to demonstrate how to adequately decontaminate this equipment, determine the frequency with which they should be deployed, and evaluate the risk that this might pose to laboratory workers.

The really challenging thing is that in the United States at least, these systems are the workhorses for a very large number of blood test that are routinely performed on patients. The thought of having to shut these systems down for any period of time is not very appealing. I think this study also really speaks to the critical roles that standard precautions play in keeping the laboratory staff safe. With regards to laboratory plans for how to handle the specimens from a patient under investigation for Ebola, or perhaps other hemorrhagic viruses, one could make the argument that the presence of sufficient safety controls on the total lab automation systems could make them an option for testing of these patients.

However, it's really worth noting that if a spill were to occur, this could basically shut down the entire laboratory, thereby putting the care of all of the other patients in the hospital at risk, so it's complicated.

Bob Barrett: Well, Dr. Burnham, let's look ahead. What additional studies might be helpful for clinical labs?

Carey-Ann Burnham: Following on from the need to have guidance on appropriate disinfection practices, I think there's an opportunity here for understanding how long blood-borne pathogens remain viable on the surfaces of TLA systems. The authors were only able to recover about 50% of the hepatitis C RNA they started with in their experimental design. So what would these results look like of the sampling or detection method had been more sensitive?

In addition, I wonder what we would observe with other blood-borne pathogens such as HIV. I think all of these begs other questions such as whether future versions of total lab automation systems could have surfaces that

themselves can inactivate the virus or have cleaning and disinfection functions built right in to the instruments himself.

Susan Butler-Wu: So Dr. Burnham is right. I think focusing on the ways to further enhance safety is really key here. We also have to remember that we need to be able to accurately diagnose infection in patients under investigation for viruses like Ebola while maintaining the upmost safety for our staff.

So for example in MMWR earlier this year, the CDC reported details of three cases of patients who returned from Africa who in fact didn't have Ebola, but who experience significant delays in receiving a diagnosis of what was actually causing their symptoms. These include diseases like malaria, which can be rapidly fatal if they're not quickly and timely diagnosed and treated.

So this actually even included one patient who had been in East Africa where there were no Ebola cases at all. So there was and really is a lot of fear out there among labs about how to protect themselves from handling specimens from patients under investigation for Ebola.

So hopefully, our study can in some way serve as a call to manufacturers themselves to really put an emphasis on safety and containment for lab staff moving forward.

Bob Barrett: Dr. Carey-Ann Burnham is an Associate Professor of Pathology and Immunology at Washington University School of Medicine in St. Louis. Dr. Susan Butler-Wu is the Director of Clinical Microbiology at LAC+USC Medical Center in Los Angeles.

They've been our guests in this podcast from *Clinical Chemistry*. I'm Bob Barrett. Thanks for listening!