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Laboratory Preparedness for the Current Monkeypox Outbreak

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Kyle G Rodino, N Esther Babady, Gonzalo Bearman, Matthew J Binnicker, Stuart N Isaacs, Benjamin A Pinsky, and David J Weber.
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Guest: Dr. Kyle Rodino is an Assistant Professor of Pathology and Laboratory Medicine in the Perelman School of Medicine at the University of Pennsylvania, as well as Assistant Director of the Clinical Microbiology Laboratory and Director of the Rittenhouse Molecular Laboratory at the Hospital of the University of Pennsylvania.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the American Association for Clinical Chemistry. I'm Bob Barrett. Following closely on the heels of the SARS-CoV-2 pandemic, a cluster of infections from another virus, monkeypox, was reported in London in May 2022. Unlike prior monkeypox outbreaks, this one was unique in that transmission occurred primarily person-to-person, typically through direct skin-to-skin contact. Why was this monkeypox outbreak different from those experienced previously? With monkeypox declared a public health emergency, would access to testing be sufficient to help prevent further spread? And could lessons learned from the SARS-CoV-2 pandemic be applied to monkeypox, or would a completely new approach be required?

A Q&A feature appearing in the February 2023 issue of *Clinical Chemistry* examines these questions in detail. Clinicians specializing in public health and infectious diseases, as well as clinical laboratorians with expertise in microbiology and molecular diagnostics weigh in, with particular focus given to the lessons learned during these two viral outbreaks, whether strategies appropriate for one can be translated to the other, and our collective level of preparedness for the next viral outbreak.

In this podcast, we are excited to talk with the moderator of the Q&A feature. Dr. Kyle Rodino is an Assistant Professor of Pathology and Laboratory Medicine in the Perelman School of Medicine at the University of Pennsylvania. He is also the Assistant Director of the Clinical Microbiology Laboratory and Director of the Rittenhouse Molecular Laboratory at the Hospital of the University of Pennsylvania. Doctor, since the Q&A feature was written, how has the monkeypox pandemic evolved? Specifically, what is the current trend with infections and how has the diagnostic landscape changed?

Kyle Rodino: We started writing the Q&A back in July or August, so we were really still in the peak area of there epidemic and there were lots of questions about how things would trend, how quickly.

At least our hope was that infections would drop off. So, as we fast forward five or so months now, there are really very few documented infections per day, like less than ten or so is the current trend on the CDC available data. And it's been that way for quite a number of weeks. It was a very clear downtrend.

The pandemic itself does not appear to be expanding in any fashion. In fact, the trajectory looks like it will continue to drop. But I guess still interesting in the documenting of cases, is that the positivity rate of testing in the country has still maintained above 10, in between 10 and 20% for some period of time. So what that says to me is a couple things: that clinicians are quite good at identifying patients that may have monkeypox virus and sending testing on those individuals because they're right quite regularly. But on the other side of that, I think we need to recognize that it indicates that there's still a considerable amount of the virus circulating in the population. And if monkeypox become sort of an afterthought, we have the -- or maybe changes sort of the classic presentation or looks different or people start to forget--we should recognize that there are still a number of individuals that could have monkey pox and there's plenty still circulating and it's not in fact gone.

Bob Barrett: From the testing perspective, what went well with the monkeypox response?

Kyle Rodino: I think there are actually quite a few things that went really well and I speak mostly from local experience being in Philadelphia, which did see quite a lot of infections, particularly during the peak of the pandemic. We never really approached a range where we were exceeding testing capacity. So different from say, the beginnings of the COVID-19 pandemic, was testing was available, the testing capacity was always available. We were never reaching the limit of what we could test. What was, however, challenging is that sometimes utilizing that testing from the actual providers and patients in clinic was challenging.

So just staying with what was good is that we always had capacity. The turnaround time of that capacity was predictable, so in my situation mostly using testing available to Pennsylvania Department of Health. The turnaround time was really fantastic and some days we were getting results the same day if the sample was delivered and coordinated with a run that was ongoing, or next day really at the worst. So the speed at which we were receiving testing was really fantastic as well.

Bob Barrett: It sounds like testing efforts then were successful but is there anything that could have improved access to testing?

Kyle Rodino: Yeah, from the lab side, sort of seeing the ability to test, getting this test back really quite easily, it really looked great, but the feedback from the user, the provider in the clinics, seeing patients in real time, is that some of the components that went along with the initial testing were tough to overcome.

And what those were really was the need for prior approval before sending a sample. So reaching out to public health, having a consultation, getting approval to send the testing in a rapid-fire sort of modern clinic environment, those patients are coming in quickly. Sometimes it's very unclear what they're going to present with, things change in the appointment, that testing is needed and there's not like a couple hours to work through the consultation and talk to individuals, fill out paperwork. So, some of those like administrative details to actually utilize the testing were problematic in like the patient-provider environment.

And then the next thing that made it challenging is that even though the testing was available, the collection was a little non-traditional in the initial requirements. So initially, the requirement was like a dry swab in a sterile container, multiple swabs from different lesions and duplicates of the swabbing, with the idea being that the first swab would be tested by the public health lab, the second swab be forwarded to CDC for confirmatory testing and potential sequencing. And that's just not really a specimen collection practice that most laboratories, most academic medical centers, most clinics go through in their standard rash type testing. So educating everyone that could see a person with a potential monkeypox rule-out on this non-standard collection strategy, and of course something that could happen 24 hours a day, 7 days a week, with patients presenting to the emergency department et cetera. Getting all of that information and making sure it was done correctly, on that sometimes singular opportunity to do so, was really challenging. It would of course be better if the collection was the standard at your institution or hospital, but making that the same for everyone is really a challenge.

Bob Barrett: So Doctor, did communication between people on the ground and the labs and all the government agencies, did this help with the assay development and the total clinical response to the pandemic?

Kyle Rodino: You know, I really want to highlight that the communication that occurs between laboratories, laboratory directors, hospitals, the CDC, and the FDA and then ultimately, in some cases, coordinated through the White House was really fantastic during the beginnings of this outbreak. I never received so much help and expertise in trying to develop assays and put assays in place. And I really would say that

the function of the CDC and the FDA in this capacity was really fantastic. I think what they did well this time is that they engaged hospitals and laboratory directors with the capacity and the ability to develop assays right at the beginning. They were really helpful in providing some expertise as to assays that were available in the sense of recipes to sort of start to put together.

What we could still do better is if we could have some additional resources supplied. So one of the things that's mentioned in the articles from some of the experts is, we don't always have access to really good clinical material to validate our assays. So, and the ability to share materials that are really important to assay development and implementation would be great. And then on the FDA side with the EUA approval, I think what's really evidenced here is that they did a great job in being flexible and accepting the expertise of high-complexity CLIA-certified laboratories in being able to put together laboratory-developed tests.

At this point, I think as of this morning, I counted 87 EUA-approved LDTs. So the ability for labs that had the capability to do their own development and implement the test was, one, help serve those region's best but also expanded that national capacity for testing should we have needed that. One thing they did really well was expanding field laboratory response network into these high-capacity commercial and reference laboratories. And I would say that I think that we can however still continue to do better, is look for ways to put that sort of surge capacity in place ahead of time. Finding a way to put together a list of laboratories that are sort of pre-approved to be LRN safety nets, and rapidly expand the capacity into these automated platforms would be something we can work again in the future.

Bob Barrett: The Q&A in *Clinical Chemistry* identifies a number of areas for continued improvement when it comes to pandemic response. Can you expand on some of the key areas?

Kyle Rodino: Yeah, absolutely. So I think access was one that was really identified by lots of the experts. And what that means, is really getting all the necessary components of a response to the patients where they're being seen. So from my perspective as a laboratory director, we've just talked about sort of the challenges in making testing simple to access, available, and the results to be returned quickly.

So we can always continue to improve on our ability to get every patient the testing which they need. Some of the other things that I heard, and are mentioned in the article from our infectious diseases and infection prevention colleagues, were really the strategies around getting people vaccination and post-exposure prophylaxis.

I think there were some surprises with the availability and the number of doses of the vaccines that were EUA-approved, originally approved for smallpox but usable for monkeypox. Getting, again a lot of paperwork, a lot of pre-work, a lot of the administrative details to get individuals those sorts of EUA-approved vaccines and then EUA-approved treatments, is really challenging in the sort of real-world landscape of how that works. So, I think that we can continue to improve basically the ease in which there's the delivery of treatments, vaccination, and testing in a real emergency.

Bob Barrett: Well finally, Dr. Rodino, viral genomic surveillance has been in the spotlight with SARS-CoV-2, but this has been a lesser consideration with the monkeypox virus. Are there any general lessons we can learn about the role of sequencing in a viral pandemic response?

Kyle Rodino: Yeah, absolutely. So there's been obviously a ton, millions and millions of sequences for SARS-CoV-2 deposited in public databases. And of course, we've had three years with a very large focus and time spent on it, so not surprising so much. I would say that the need for genomic surveillance of viral pathogens in a pandemic is still really important. And even though there's been a far less sequencing in the monkeypox outbreak, the sequencing that has been done has actually been really beneficial in a few situations. So there--highlighted in the article is the fact that some sequencing confirmed the mutation that impacted the ability of some tests to perform as expected.

So I think that's the really most obvious use and need in a response, is that if we're dealing with a new pathogen or a new version of a pathogen and we're uncertain how wide replication and transmission will affect the mutation of the genome, having that safety net sequencing set up and functioning is really important. We are all, of course, investing lots of time, effort, and money in these diagnostic assays and we expect them to perform in a particular fashion. So the ability to sort of look into the genome, predict if somehow a mutation is impacting our ability to diagnose people is really important in an emergency response.

There has also been some sequencing that has gone on related to mutations that could say impact the efficacy of treatments that are available. And again, as we learn new things during an emergency response to a new pathogen, I just think having all of that information is incredibly important to be informed, to be able to pivot when needed, and to be able to make the best decisions we can related to new pathogens.

Bob Barrett: That was Dr. Kyle Rodino from the Department of Pathology and Laboratory Medicine at the University of Pennsylvania. He served as moderator for the Q&A feature on laboratory preparedness for the monkeypox outbreak in the February 2023 issue of *Clinical Chemistry*. I'm Bob Barrett. Thanks for listening.