Clinical Chemistry

Deadly Pathogens, Transformative Technologies, and Protracted Pandemics: Challenges and Opportunities in Laboratory Medicine

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Guest: Dr. Bobbi Pritt is a Professor of Laboratory Medicine and Pathology at the Mayo Clinic in Rochester, Minnesota, where she serves as the Chair of the Division of Clinical Microbiology and Medical Director of the Clinical Parasitology Laboratory.

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.

These are unprecedented times in medicine, and laboratory medicine is at the forefront. While advances in genomics and proteomics have dramatically improved our ability to diagnose and characterize infectious diseases, the world faces momentous challenges from increasing antimicrobial resistance, resurgence of ancient scourges, and outbreaks of emerging pathogens. Most notable is the COVID-19 outbreak, which continues to upend daily lives around the planet and raise many medical, social, economic, and political issues. But there have been more than a dozen other viral disease outbreaks in the past two decades alone, and the emergence of the novel viral pathogens is predicted to accelerate in the coming years.

A Special Issue of *Clinical Chemistry* appearing in January 2022 covers emerging applications to diagnose and manage infectious diseases and highlights the major challenges faced by the global laboratory medicine community, as well as the opportunities provided by the development and implementation of transformative technologies.

We are fortunate to have with us today one of the guest editors of this special issue. Dr. Bobbi Pritt, is a Professor of Laboratory Medicine and Pathology at the Mayo Clinic in Rochester, Minnesota, where she serves as the Chair of the Division of Clinical Microbiology and Medical Director of the Clinical Parasitology Laboratory.

Dr. Pritt, welcome back. Can you tell us a little bit about what prompted this special edition of *Clinical Chemistry*?

Bobbi Pritt: Well, that's a great question. These are definitely extraordinary times as I think we all recognize in medicine and laboratory medicine is really at the forefront. Not only do we have a lot of exciting advances in the fields of genomics and proteomics, which has drastically improved our ability to diagnose infectious diseases.

Of course, we also have the ongoing pandemic, so there's certainly a lot of things to talk about. And in just reflecting back you can think of the laboratory as it was a hundred years ago and it was significantly different. We didn't even know what viruses were back then, which is amazing, much less how to detect them. But now we can detect viruses like the SARS-CoV-2 virus, the SARS coronavirus and many, many other organisms.

Of course, with our current outbreak, we are now facing something that we haven't faced in recent years, really more than a century. Even though there's been a dozen viral outbreaks in the past two decades alone: we've had Ebola, H1N1, influenza, the original SARS outbreak.

This current outbreak is really a global pandemic that we have not seen since probably 1918 with the Spanish influenza. And this is so serious that this in addition to all the other things going on, we thought it was time to have a Special Edition in *Clinical Chemistry*, to highlight the major challenges that we're facing but also to discuss the positive opportunities. Not just focusing on SARS coronavirus, but all of the other things going on, the recent outbreaks, antimicrobial resistance, all of these new exciting technologies that we have, many transformative technologies.

Bob Barrett: So there's an awful lot going on and I'm sure you didn't have a problem coming up with topics for this special edition, but let's talk about the elephant in the room first: what research, what research did you include on the COVID-19 pandemic?

Bobbi Pritt: Yeah, that's a great place to start Bob, because yeah, it is the elephant in the room for sure. So we knew that a significant portion of the special edition would be dedicated to the ongoing pandemic, given its momentous impact on the field.

So in reflecting on this when all of the editors got together and I was one of the special guest editors, we started thinking about all of the different things that we would want to include and in thinking of SARS-CoV-2, I think that a lot of the innovations that came out of this really came out of necessity.

You can reflect back on that old proverb: "necessity is the mother of invention." That really struck a chord with me, and I don't know if you know this, but it actually came from a phrase that Plato wrote, which is actually "our need will be the great creator."

Well, we had a really great need and that just really encapsulates the spirit of the pandemic and laboratories had to respond. We had to come up with many, many improvisations, we had global supply shortages, so we had to do things like make our own media. We ran out of swabs, so

we had to come up with different specimens to test like saliva, and we didn't have enough tests. So we had to come up with things like pulling samples.

So given all of these innovations, there were so many possible topics we could have covered in our special edition and I think we really encompassed all of the major things that labs did, all of these innovations.

Laboratories explored novel collection devices in addition to saliva, some labs use 3d printing devices to create their own swabs. We pulled specimens together for testing, thus saving on valuable reagents. And so, all of these topics are covered. We even touched on collecting specimens at home and even testing specimens at home.

So, that's COVID right there. But then, of course, we didn't stop with COVID. They are many other topics as I mentioned that we wanted to include. So other topics that are covered in our special edition include preparation for the next pandemic because unfortunately, we're all pretty sure that there will be more pandemics in our future. The estimate is every three to five years now about, we've been seeing new outbreaks. At the very least, there will be new outbreaks of emerging infectious diseases.

We also included topics such as groundbreaking technologies like CRISPR. And for those of you who haven't heard of CRISPR before, that stands for Clustered Regularly Interspaced Short Palindromic Repeats, bit of a mouthful, but that could be used for detecting the SARS coronavirus.

And then we also in the special edition talked about, well we included manuscripts that examined the controversial role of using quantitative PCR and the cycle threshold values for predicting COVID prognosis and virus infectivity. So a lot of great material on the pandemic that we included.

Bob Barrett: A quick aside, 12 years of podcasting, you're the first person who quoted Plato, so congratulations.

Bobbi Pritt: Well, thank you.

Bob Barrett: Now CRISPR sounds like a really interesting technology that we hear a lot about within the lay press and scientific journals. So, let's talk about it some more. Can you tell us more and how it's used to detect pathogens such as the SARS coronavirus that causes COVID-19?

Bobbi Pritt: Sure, I'd be happy to. I'll give you just a brief overview. It's this fascinating technology that's derived from nature. So it's not man-made. It came from an ancient system used by microbes to defend themselves and they do that by cutting

up foreign DNA that they encounter, and they do this in conjunction with a type of proteins called Cas proteins. So the system is often referred to as CRISPR-Cas systems.

So scientists have harnessed this CRISPR-Cas system to use it as like a molecular scissors to identify genes that they want to cut, go in and cut that gene in a very specific way and then even insert a gene that they want to replace in that area.

So, let's being done in terms of genetic and inheritable diseases. Lots of opportunities there. This will definitely change science and is already changing and impacting science.

Now, in the cases of infectious diseases, the CRISPR based systems have also been harnessed, but it's really more their ability to detect specific sequences for bacteria, viruses etc., in human specimens. So if you pair that this with an amplification method, you amplify the sequence of interest viral or bacterial and then you apply the CRISPR-Cas system that will cleave the specific area of interest. And then if you couple it with a reporting mechanism, you can get a fluorescent result.

So it's similar to PCR in that you're amplifying and detecting but it uses an amplification system that doesn't require cycling, and it's relatively cheap and relatively fast. So, these tests in general are sensitive, rapid, and unlike PCR don't require expensive thermal cyclers. They've been used to detect SARS-CoV-2 and I'm sure we're going to be hearing about them for detecting all sorts of other infectious agents.

Bob Barrett: Well, thanks for that. Even I can understand that. So you did a great job explaining it. So what else is in this special issue? Tell us about some of the other topics included in this special *Clinical Chemistry* edition.

Bobbi Pritt: Yeah, of course. We had a lot more than COVID to talk about. Other articles in the special edition cover the remarkable range of transformational technologies that drove major changes in the fields in recent years. I would say, a must-read is the reflections piece by my colleague Dr. Robin Patel, which described her experience of developing and implementing novel genomic and proteomic essays over her esteemed 25-year career in microbiology and those, among those major innovations included things like CRISPR. Also just general nucleic acid amplification, matrix-assisted laser desorption ionization which we call MALDI-TOF for short, massively parallel sequencing, which we call next-generation sequencing, artificial intelligence, so called laboratory automation, total laboratory is not really "total" laboratory but we call it that. And then there is breath analyte analysis, and rapid antimicrobial susceptibility testing.

So lots of exciting things there. We also do acknowledge, though, that none of these tests are perfect. Of course, none of our laboratory tests are completely perfect. Many are excellent and very sensitive and specific. But with all tests, they have several strengths and limitations. So also in the Special Edition, we included an insightful piece by Dr. Kaede Sullivan explains the importance of diagnostic tests stewardship and the role of the laboratory in partnering with the ordering providers to make sure that the patients are getting the right test at the right time, and so really ensuring appropriate patient testing.

We know that the laboratory has an important role in the diagnosis and prevention of infection, informing public health response, but we also know we can't do it alone as the laboratory. We need to partner with the people who are ordering our tests.

So there's a continued need for that to ensure our tests are used correctly.

Bob Barrett: Well, thanks so much Dr. Pritt. Do you have any last messages that you would like to share with our listeners?

Bobbi Pritt: Just that we are really excited to share the special edition with you, we think it's forward-looking and thought-provoking and we just want to thank laboratorians around the world for their tireless efforts battling the COVID-19 pandemic, and hope that our readers enjoy the special issue.

Bob Barrett: That was Dr. Bobbi Pritt from the Mayo Clinic in Rochester, Minnesota, where she serves as the Chair of the Division of Clinical Microbiology and Medical Director of the Clinical Parasitology Laboratory. She is one of the guest editors of the January 2022 special issue of *Clinical Chemistry*, "Deadly Pathogens, Transformative Technologies, and Protracted Pandemics: Challenges and Opportunities in Laboratory Medicine."

I am Bob Barrett. Thanks for listening.