Ruth Adewuya, MD (host):

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This episode is part of our hot topics miniseries and today I'm joined by Dr. Pinsky and Dr. Jorge Salinas. Dr. Pinsky is a professor of pathology and medicine in the Division of Infectious Diseases and Geographic Medicine and has a courtesy appointment in the Department of Pediatrics' Division of Infectious Diseases of the Stanford University School of Medicine. He is the associate director of clinical pathology for COVID-19 testing and is the director of the clinical virology laboratory for Stanford Healthcare and Stanford Children's Health. Dr. Pinsky earned his M.D. and Ph.D. degrees in the medical scientist training program at the University of Washington School of Medicine in Seattle. He received residency training in clinical pathology and fellowship training in molecular genetic pathology at the Stanford University School of Medicine.

Dr. Pinsky's research interests include the design of novel diagnostics and investigation of the clinical impact of infectious disease testing, particularly in the areas of the respiratory and arthropod borne viruses. He is the U.S. editor in chief of the Journal of Clinical Virology and the president-elect of the Pan-American Society of Clinical Virology.

Dr. Jorge Salinas joined Stanford in 2021 as an associate professor of medicine, infectious diseases. He is the director of the Hospital Epidemiology or Infection Prevention and Control Fellowship at Stanford University and he is the co-medical director of the Infection and Prevention Control Program at Stanford Healthcare. Before joining Stanford, he was a hospital epidemiologist at the University of Iowa. Dr. Salinas earned his M.D. degree at the Universidad Nacional De San Marcos in Peru. He received residency training at the University of Alabama and fellowship training in infectious diseases at Emory University. Dr. Salinas also serves on the editorial of the anti-microbial stewardship and health care epidemiology journal.

Welcome and thank you both for being here.

Benjamin Pinsky, MD, PhD (guest speaker):

Thank you for having us.

Ruth Adewuya, MD (host):

Monkeypox became a trending topic in the United States this summer and in July of 2022, I had the opportunity to talk with Dr. Deresinski about what we knew at that time. But, in the past few months, there have been several more developments on this front, including monkeypox being declared a public health emergency by the Biden administration. I thought it would be fitting to continue this conversation with both of you. Dr. Salinas, could you update us on the status of the monkeypox outbreaks since June?

Jorge Salinas, MD (guest speaker):

At the global level, most regions are seeing a decrease in cases, including the United States. In America, we have gone from an average of about 400 daily cases in August to less than 100 cases per day currently. That is the result of multiple public health interventions put in place, including vaccination, access to therapeutics, but also awareness, education and behavioral modification, among others.

Ruth Adewuya, MD (host):

Can you talk more about some of those measures? Outside of vaccines, what were the new measures that we have adopted to combat the spread?

Jorge Salinas, MD (guest speaker):

People at risk of acquiring monkeypox have definitely modified their behavior. CDC has done analysis and people have been more careful and have reduced the number of sexual partners that they have. There has been also more knowledge about how this disease is transmitted and how it is not. Initially, there was some fear that this would be more easily transmissible, but now [inaudible 00:04:59] believed to require a great amount of physical contact such as during sex.

Ruth Adewuya, MD (host):

It sounds like these measures have been effective because I think I heard you say that it went from about 400 cases a day to 100. Is that correct?

Jorge Salinas, MD (guest speaker):

Definitely. Yes. There has been, especially in America but also in Europe, a steep decline in cases. How low it goes, it's still to be seen.

Ruth Adewuya, MD (host):

Dr. Pinsky, when monkeypox was declared a national public health emergency, it did cause a level of panic. We were still riding off of the COVID-19 pandemic. What does this declaration mean and what led to monkeypox being put into this category?

Benjamin Pinsky, MD, PhD (guest speaker):

Yeah. I think the most important part of that is just how it allowed the government to respond by providing a mechanism to offer testing, to get out vaccines more and make them more available. On the testing side, which is my area of expertise, that declaration really opened up additional testing. Early on in this particular outbreak, there was limited availability of testing and there was a concern that testing would not be available for those folks that needed it. Once this emergency declaration occurred and testing was opened up to large reference labs like Quest as well as some of the large academic reference labs like ARUP and Mayo, that sort of bottleneck at the public health laboratories was eased and I think it became relatively straightforward for folks outside of academic medical centers like ours to get testing.

Ruth Adewuya, MD (host):

Great segue way to our conversation about testing. Let's start with how is testing for monkeypox done.

Benjamin Pinsky, MD, PhD (guest speaker):

Testing for monkeypox is done by detection of the viral nucleic acids, typically in a swab from the lesion, and that swab can be submitted to the laboratory as is or in something called viral transport media, which sort of protects the sample, if you will. And, then the testing, like folks are familiar with from COVID, is nucleic acid amplification testing or... And, a version of that is PCR or polymerase chain reaction. Most tests that are available are PCR-based testing for the viral nucleic acid.

Ruth Adewuya, MD (host):

And, how available are these tests and have we experienced any shortages with testing similar to what we did for COVID?

Benjamin Pinsky, MD, PhD (guest speaker):

The scale of this outbreak was much, much lower than of course what we've seen with COVID-19, so we didn't really run into the supply chain issues and re-agent availability that we did early on in the course of the COVID-19 pandemic. But, I think that there has been some difficulty, particularly early on in getting testing. But, as I said, now that the reference labs have opened up, that testing is much more available. We offered testing at Stanford very early on because we have this capability to do laboratory developed tests, so we were able to take the published information from the CDC and develop our own tests. We took those sequences and we utilized re-agents at hand to optimize those targets and offer testing for our patient population.

Ruth Adewuya, MD (host):

Am I correct that there is a monkeypox rapid test in development? And, if so, where are we with that and how effective are we finding it to be?

Benjamin Pinsky, MD, PhD (guest speaker):

Yeah. In preparation for this discussion, I did a little bit of research to try and find out what was available. So, as far as I can tell, there are no rapid antigen tests for monkeypox available in the United States. There may be these sorts of tests for sale outside of the U.S. The regulatory pathway in our country goes through the FDA of course and at the moment, there's only two tests that are available through the FDA. One is FDA approved. This is the non-vary orthopox virus QPCR test that was developed by the CDC and distributed to what's called the Laboratory Response Network. And, this has been FDA cleared for several years and it detects monkeypox but also cross-reacts with some other pox viruses like cowpox, for example, or vaccinia virus.

The other FDA authorized test, so the other pathway I think that everyone's familiar with from COVID, is emergency use authorization. There's almost 300 emergency use authorized, maybe more, COVID tests. But, for monkeypox, there's just one and that's through Quest Diagnostics and they use this same non-variola orthopox target which is the viral DNA polymerase and a second target which is called the viral tumor necrosis factor receptor gene. So, that's specific for monkeypox and in particular is more specific for the clade of monkeypox that is currently causing this outbreak. So, that's the clade two virus, which was previously called the West African virus.

Ruth Adewuya, MD (host):

Was that name change a direct result of conversation about naming viruses and the stigma that comes with naming it based on the location?

Benjamin Pinsky, MD, PhD (guest speaker):

That's the case. You know, we've learned that and seen that from SARS-COV-2 that the variants were named after the countries from which they were first identified and that practice is now in the past. So, that's what's occurred with monkeypox. The two clades now are just named Clade One and Clade Two, both to their geographic areas where they were identified originally.

Ruth Adewuya, MD (host):

That's fantastic.

Benjamin Pinsky, MD, PhD (guest speaker):

Yeah. I totally agree. We don't need to put the stigma on the place of origin. It's not even known if it's the place of origin. It's the place where it was first identified. Folks shouldn't be penalized for doing important surveillance work. They should actually be applauded and we should name it just with these number and letter designations.

However, I have to say... Just a brief aside with COVID. It's getting a little out of control with the alphabet and numerical soup that we're seeing now.

Ruth Adewuya, MD (host):

[inaudible 00:11:28]

Benjamin Pinsky, MD, PhD (guest speaker):

There's so many different variants. It's getting a little bit hard to keep track of, even for the aficionado like myself.

Ruth Adewuya, MD (host):

The CDC released a report stating that monkeypox eradication is unlikely in the U.S. and that it will continue to spread indefinitely at a low level, particularly in men. What are your thoughts on this statement, Dr. Salinas?

Jorge Salinas, MD (guest speaker):

The CDC and others have always said that it's difficult to make long term predictions. However, because this infection is being transmitted as a sexually transmitted infection, it is possible for it to become endemic in certain groups such as men who have sex with men. We have had serious difficulties controlling or eradicating other sexually transmitted infections in the United States. Even syphilis cases are in the rise in America. I don't think it would surprise me to know that some low level of transmission continued occurring in a concentrated fashion, in a high risk population, men who have sex with men and who have multiple sexual partners. But, I don't think that it will impact all men or the entire population.

Benjamin Pinsky, MD, PhD (guest speaker):

I agree with Dr. Salinas' statements. I think that we're perhaps likely to see low level transmission for some time, but again, throughout all of this now, laboratorians and infectious disease physicians and basically everyone is asked to break out their crystal ball and tell us what's going to happen next week, next month, next year, and [inaudible 00:13:01].

Ruth Adewuya, MD (host):

Wait. That is a question that's coming up for you guys.

Benjamin Pinsky, MD, PhD (guest speaker):

I know. It's [inaudible 00:13:05]. It's difficult to predict these things with infectious diseases. They're, by nature, unpredictable and we'll have to see and we always say that we'll have to closely monitor, which at times seems self-serving. But, it's true. We'll have to monitor the high risk at risk populations and determine whether this is going to continue to be a problem or if it's something that through the behavior modifications and vaccination and availability of testing that's something that we've been able to get completely under control.

Ruth Adewuya, MD (host):

Let's talk about vaccines. Dr. Salinas, with the monkeypox vaccine, should people get it preventatively or once they are experiencing symptoms?

Jorge Salinas, MD (guest speaker):

Vaccines work primarily as prevention. They should be given or received before exposure. That being said, not every American is eligible for vaccinations. Vaccines are currently recommended for people at the highest risk and that involves people that have multiple sexual partners, preferentially men. Vaccines can also be given as post-exposure prophylaxis if you have been exposed to somebody known to have monkeypox or in very infrequent instances in which a health care worker, for example, has an unprotected clinical encounter with somebody that later was found to have monkeypox. So, yes. Vaccines can be used, but preferentially should be used as prevention.

Glass half empty or half full. Only 30% of the eligible population in the United States have been vaccinated with a first dose. So, there is still a lot of room for increased uptake and on a bigger scale, another problem is that most countries in the world do not have access to these vaccines. So, that is still a big problem for the long term global eradication of this infection.

Ruth Adewuya, MD (host):

You talked about the people are more at risk. Are front line workers also in that category or it's usually post-exposure?

Jorge Salinas, MD (guest speaker):

Some health care workers are eligible for vaccinations, especially those that have a greater probability of encountering either the virus or somebody with the virus. So, at the top are laboratory workers that process samples for monkeypox or that do research with monkeypox. It could also include other health care workers, perhaps in sexually transmitted infection clinics, STI clinics. They may be eligible as well.

Ruth Adewuya, MD (host):

How soon does the vaccine take to become effective?

Jorge Salinas, MD (guest speaker):

Classically, people recommend obviously to receive both doses of the vaccine and to wait a couple of weeks after the last dose. However, some recent analysis has shown effectiveness 14 days after the first

dose. So, vaccines do start working after the first dose, but the full effect is expected after having completed the full series.

Ruth Adewuya, MD (host):

I understand that there are two vaccination options. Can you elaborate and talk about the difference between those two and what are the metrics that clinicians should consider when deciding which one is right for a patient?

Jorge Salinas, MD (guest speaker):

It's true that there are at least these two types, the JYNNEOS vaccine, [inaudible 00:16:18] activated [inaudible 00:16:20] vaccine and the ACAM2000 vaccine that is less activated. But, preferentially, in the United States we are using the JYNNEOS vaccine. So, that's the one we are administering to people and the main advantage of it is that it has less side effects. The virus is non-competent in its replication, and Ben can further correct me on this. So, that leads to better tolerance of the vaccine, less side effects, and in general, the studies and now our experience shows that again it's well-taken. People may have a mild local reaction or some. They may feel a bit tired or have headache a little bit after vaccine, but not to the same level as some other vaccines, for example. So, it seems to be well-tolerated.

Ruth Adewuya, MD (host):

You mentioned that we're generally using the JYNNEOS here in the United States. Is that just because of availability and what you mentioned in terms of tolerability and less side effects? Or, is the other one not available in the United States?

Jorge Salinas, MD (guest speaker):

Both are available in the United States, but the JYNNEOS one... Again, because it's more tolerable and probably equally effective, is preferred.

Ruth Adewuya, MD (host):

Switch gears to talking about therapy and treatment. One method of treatment is TPOXX for someone who has contracted monkeypox and is experiencing symptoms. Can you talk about what this treatment is and how does it work even compared to vaccination?

Jorge Salinas, MD (guest speaker):

Absolutely. So, TPOXX is an antiviral that is FDA approved against smallpox. Interestingly enough, it was studied in animals using monkeypox. But, it is approved for treatment against the smallpox and currently is being used under an expanded access investigation of a new drug protocol, EAIND. And, as part of that, there are some regulatory steps and paperwork that needs to be taken before prescribing it and that's one of the quickest systems to the response.

And, this antiviral works by targeting orthopox virus protein that works helping the virus exit a cell and infecting other cells. So, by giving this antiviral, we prevent the virus from infecting other cells and therefore the number of viruses in general decrease in the body. There is not enough clinical data. There has not been the randomized control trial completed in humans for Tecovirimat. We have observational data now for hundreds of patients that have been treated under these expanded access IND from CDC. But, we need the clinical trials and the NIH is leading those efforts in America preferentially so we will be able to know more about the true effectiveness of this antiviral.

Ruth Adewuya, MD (host):

Other than this antiviral, TPOXX, are there other medications that are given to treat monkeypox?

Jorge Salinas, MD (guest speaker):

Anyone with monkeypox, especially if they have multiple lesions, can have pain, and CDC has launched a campaign to address the pain associated. So, symptomatic management of the lesions. But, there are some other antivirals that can be used. None of them have an FDA approval against monkeypox but Cidofovir, [inaudible 00:19:26] Cidofovir could be used against the monkeypox or even [inaudible 00:19:30] globulin. But, for all of these antivirals, we don't have a lot of clinical data proving their effectiveness against this infection.

But, for many of them, you also need to go through the expanded access investigation of new drug, EAIND, protocol through CDC. So, by large in the United States, the treatment against monkeypox is TPOXX.

Ruth Adewuya, MD (host):

For a patient who's contracted monkeypox, how long are they contagious for and how long should they isolate for?

Jorge Salinas, MD (guest speaker):

Yeah. This is a difficult issue and Ben can probably also give us his ideas about the virology of this. But, classically, it is believed that people are infectious until all the lesions are not only crusted but the crust has fallen off. That can be a long time. Can be a couple of weeks. Can be three weeks. Now, because that ends up being somewhat impractical to ask somebody to not go to work and to stay at home for such long periods, CDC has given a tiered isolation approach, has said, "Hey, you can go out if you can cover your lesions, if you wear a mask. You can do certain things. Run errands, buy groceries. You're not going to infect people that way."

But, if, for example, you're a health care worker, you work in a hospital, they are going to ask you to isolate for that full duration. So, there is some leeway but in general that's the principle. I don't know what Ben can say, whether he thinks there is new knowledge that hopefully shorter duration infectiousness or isolation.

Benjamin Pinsky, MD, PhD (guest speaker):

I haven't seen any published data on that. I can't shed any more light on that area. I think it's an important area for future studies.

Ruth Adewuya, MD (host):

Obviously, coming off of the pandemic, where we know that a lot of people have been impacted in terms of their jobs and then you layer this and the potential of not being able to do basic things or go to work for several weeks, just one thing after the other that I think that's a topic for another podcast, education on mental health, perhaps.

But, Dr. Pinsky, I think you alluded to variants with the COVID-19 pandemic. For monkeypox, are there any monkeypox variants or are we still seeing the same strain circulating?

Benjamin Pinsky, MD, PhD (guest speaker):

Yeah. That's an excellent question. I think folks have variant on the mind because of COVID. Monkeypox viruses that are causing this outbreak are very closely related. There is evidence of some evolution going on in the virus, but this is a very slow changing virus and so we're not seeing the same sort of major shifts in variants that we've seen with SARS-COV-2. And, of course, monkeypox is a DNA virus and typically, although not always, DNA viruses have much more stable genomes than RNA viruses, which is what SARS-COV-2 is

Ruth Adewuya, MD (host):

As we wrap up our conversation, I wanted to ask both of you your reflection on the past couple months. What were some of the strides or missteps and learnings from monkeypox in terms of containing the spread of disease? And, even if you had to compare and contrast it with the COVID-19 pandemic. I'll start with you, Dr. Pinsky, and then go to Dr. Salinas.

Benjamin Pinsky, MD, PhD (guest speaker):

I'll focus here on the testing part. Initially, I think that there was not enough testing available for monkeypox very early on in the outbreak in the United States. And, again, perhaps we could have seen this coming based on the number of cases that were being reported in Europe prior to the peak in the United States. However, I think that one lesson learned from the COVID-19 pandemic was this importance of diagnostics and I think CDC and FDA moved much more quickly for monkeypox than they did for COVID-19 and that the emergency declaration that you mentioned earlier and this opening up testing to reference laboratories and making the EUA process actually... I didn't mention this before, but making it easier for academic laboratories to offer testing I think is really of critical importance for getting this under control relatively rapidly.

Jorge Salinas, MD (guest speaker):

I think that for treatment, there were some delays and the regulatory steps required prevented more people from being treated and the CDC pivoted and modified the requirements, made it easier and easier to give treatment. But, yes. I wish that we had a pathway for faster approvals of testing, of treatments. So, that's regarding treatment for the past. And, for the future epidemics or pandemics, we have to deal side by side with this problem of misinformation. There's always an epidemic of misinformation in parallel to any problem and it just makes things worse from the fears that some people may have about the virus being more transmissible than it really is, from fears against the vaccine. For example, there are people that are very against any vaccine without even knowing what the vaccine is or what it does or... They're really against it.

So, that is something that we have to continue working and preparing for because this issue will come up again. But, at the same time, I see some positive to the CDC response to this pandemic. They appointed experts on the prevention of sexually transmitted infections, people that know how to work with their affected communities, using behavioral health, and having a positive message asking for risk reduction, behavioral modification. So, I think that there are some lessons learned and I think that overall I am on the positive side in my rating of the American response against this virus.

Ruth Adewuya, MD (host):

Thank you both again for stopping by and sharing your insights with us on this topic. If there are any future updates, we'd love to hear back from both of you as well.

Benjamin Pinsky, MD, PhD (guest speaker):

Great. Thanks for having us on.

Ruth Adewuya, MD (host):

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