The webinar convened via Video Teleconference, at 5:00 p.m. EDT, Georges Benjamin, Executive Director, APHA, presiding.

PRESENT
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DR. DZAU: So good afternoon. I'm Victor Dzau, the President of the National Academy of Medicine, and I want to welcome all of you to today's webinar. It's on the current state of monkeypox signs and research, a really timely and important topic. We have an excellent panel put together this afternoon to discuss what we know about monkeypox, what prevention and treatment options are available, and what emerging policy issues and research topics we must consider as we move forward.

First, I'd like to thank the co-sponsor, my good friend, APHA Executive Director Georges Benjamin for his efforts in organizing today's event. I'd like to thank Carlos del Rio of Emory University, the NAM International Secretary; and Nicole Lurie, the former Secretary for Preparedness and Response, for her helping us plan today's agenda.

So the topic. In May, the first
recorded cases in the current monkeypox outbreak was reported in the state of Massachusetts. Since then, there have been over 13,000, I think 13,500 recorded cases in the United States since then. The WHO declared monkeypox outbreak a public health emergency in July, and the White House followed suit earlier this month.

Well, this current outbreak is a matter of both global and, of course, U.S. public health importance. And as you'll hear from our speakers, testing for the virus remains a challenge. You know, the early testing program was slow to ramp up. Then commercial reps have rapidly increased capacity, but results can still take some time to return. And as you all know, the current tests are only capable of detecting virus in active lesions, which appear or do not appear until one to two-week incubation period. This means that we all estimate, given the way in which we've had testing, there's probably a lot more cases than we are led to believe and they're not able to fully capture impact of ongoing
community spread.

In terms of prevention, we have effective vaccines approved by FDA, but U.S. has very limited vaccine supplies, which, unless efficiently came up, at least I think, with easy spread. As you know, FDA recently issued an EUA, Emergency Use Authorization, permitting people delivering the vaccine to use fractional doses by intradermal, that is under the skin, to people 18 and older. You will hear a lot more discussion about this and the pros and cons of some of this. Suffice it to say that the data for intradermal administration has been shown to generate good immune responses.

And because we have also other questions in regards to treatment, TPOXX, the antiviral medication is an option for those in need of treatment, but it calls into question about whether there's enough doses and then providers are facing bottleneck because the drug is still investigational.

So, in short, there's a lot to learn,
and I'm really looking forward to learning from the experts.

I think that we know about knowledge gaps among providers, stigma that can prevent an individual from seeking care. I think it's such a high priority for both APHA and NAM to put this webinar together to hope to give you information for those interested in understanding more about the current state of science.

So with that introduction and without further ado, I'd like to introduce my good friend and our collaborator and moderator for today's webinar, Georges Benjamin, Executive Director of APHA. Georges, over to you.

DR. BENJAMIN: Victor, thank you very much for that very important introduction. So I'm going to cover some administrative things first. First of all, if you have questions or topics you'd like us to address today or in future webinars, please enter them in the Q&A box or email us at apha@apha.org. So either the Q&A box or email us at apha@apha.org.
If you experience technical difficulty during the webinar, please enter your questions in the Q&A box. Please pay attention to the chat for announcements about how to troubleshoot.

Now, this webinar will be recorded and a recording and transcript will be available on APHA's website. We are not offering continuing education credits for this particular webinar.

In this webinar, you will hear from experts, as you heard from Dr. Dzau, about a whole range of issues around monkeypox, and I want you to remember to use the Q&A feature to ask your questions as they arise.

With that, I'd like to introduce our panelists. We have four amazing panelists today. We've got Dr. Demetre Daskalakis who is an infectious disease physician and public health practitioner who currently serves as a Deputy Coordinator for the National Monkeypox Response. He comes to that position from a background in HIV prevention and outbreak response and local
and federal governmental public health.

We have Dr. B.K. Titanji. Dr. Titanji is a Cameroonian-born physician and scientist and the Assistant Professor of Medicine at the Emory University in Atlanta. She obtained her M.D. agree from the University of Yaoundé in Cameroon where she worked as a medical officer after graduating before pursuing post-graduate research training in the United Kingdom. She has a master's degree in tropical medicine and international health from the London School of Hygiene and Tropical Medicine, a diploma in tropical medicine and hygiene from the Royal College of Physicians in London, and a Ph.D. in virology from the University College London. She joined Emory University School of Medicine in 2016 where she completed a residency in both internal medicine and a fellowship in infectious diseases. She's really got three parallel career interests: translation of clinical research in HIV and emerging viruses, science communication, and global health equity.
Dr. David Heymann. Dr. Heymann is a medical epidemiologist and professor of infectious disease epidemiology at the London School of Hygiene and Tropical Medicine. From 2009 to 2017, he was Chairman of Public Health England and Head of the Center on Health Security at Chatham House, which is also in London. From 1989 to 2009, he held various leadership positions in infectious diseases at the World Health Organization and, in 2003, head of the WHO global response to SARS in his role as the Executive Director of Communicable Diseases. In 1976, after spending two years working in India on smallpox eradication, Dr. Heymann was a member of the CDC Atlanta team to investigate the first Ebola outbreak in DRC and stayed on in Sub-Saharan Africa for 13 years in various field research positions on Ebola, monkeypox, Lassa fever, malaria, and other tropical diseases.

As like all these folks, he's extraordinarily well published, but I need to give David a shout-out because he's also the
editor of the APHA book, Control of Communicable Diseases Manual, as well. And also just to point out that he has been named an honorary Commander of the Most Excellent Order of the British Empire for services to global health. I love to always say that about you every time I talk to you.

We have Dr. Emily Erbelding. Dr. Erbelding has served as the Director of the NIAID Division of Microbiology and Infectious Diseases since 2017. She's an expert in infectious diseases and responsible for the strategic and scientific vision for the division's complex national and international research programs. Her division has an annual budget over $2 billion and supports basic pre-clinical and clinical investigations into the causes, diagnosis, treatment, and prevention of a broad range of pathogens, including those related to biodefense and emerging infectious diseases.

So with that introduction, I'd like to now bring our first speaker, Dr. Daskalakis. Demetre.
DR. DASKALAKIS: Thank you very much for having me. So I will start off by giving a monkeypox update, and I'll start with the monkeypox situation update.

Next slide, please. All right. So this slide is from the 15th of August. I will give an updated number. I think we heard that, nationally, there are 13,517 cases of monkeypox as of August 17th at 2 p.m. The map demonstrates where cases are located. The darker blue in the United States representing higher numbers of cases, and I put in the epi curve on the bottom. And as you see, the contour of the curve, it continues to be climbing up.

In terms of the international scenario, the updated number as of the 17th is 40,399 so continuing to see a pretty steep increase in cases in the U.S., as well as globally.

Next slide, please. So I want to give a view about the epidemiology, and I'm actually presenting from a couple of different data
sources. So the first, our data from CDC that show what we're currently seeing as of August 4th from the perspective of race and ethnicity. So you can see that Hispanic represent about 35 percent, white about 33 percent, black about 28 percent, Asian 3.3, multiple races 0.2 percent, American Indian or Alaskan Native 0.1, and Native Hawaiian or other Pacific Islanders 0.1.

So that's a quick overview of the race ethnicity of cases in the United States. But I want you to take a look at the graph, and you don't have to really look deeply to understand the front of the graph, which is the blue bars represent individuals who are white, and then you can see at the beginning it was a pretty monolithic group, but then, subsequently, a disparity begins to be seen with black and Hispanic individuals now representing the majority. So you can see as those blue bars go down, the lighter blue and the orange bars and the lighter orange bars also go up.

Next slide, please. The second data
source I want to use is from our recent publication of our Morbidity and Mortality Report Weekly that talks about the cases that were reported on for May 17th to July 22nd, so that represents cases after which we got case reports from. So there are a total of 1,195 cases that were included in this group, and it's important to note that the lion's share, 1,178, 98.7 percent of the cases, were among men. You can also see numbers for transgender men, women, transgender women, and others who preferred not to answer. And so looking at the international epidemiology, which I'm not presenting here, again, men continue to be overrepresented in this outbreak.

Next slide, please. So in terms of exposure history, looking at the first cases from May 17th to July 22nd, 358 out of 1,178, or 30 percent of men, whether cis or trans, provided information on recent sexual behaviors and the gender of their sexual partners in the three weeks prior to presentation.
percent reported sex or close intimate contact with a man, so, most frequently, cases describe close intimate contact with a man. Among the 291 men who reported information about their male sexual partners, about 27 percent reported one partner and then the rest reported more than one partner. So really talking about multiple partners in the time period of three weeks prior to diagnosis.

Additionally, among the 86 men in the cohort with more detailed sexual histories, 38 percent reported group sex, and that was defined as sex with more than two people in a venue or a private party.

Next slide, please. Other features of those cases for May 17th to July 22nd, 2022, 41 percent with known HIV status or reported living with HIV, hospitalization was not very common, 954 persons had a hospitalization status and 8 percent of them were reported hospitalized. And we also had some data on vaccination status in 339 of those initial 11,079 cases. Fourteen
percent reported previous smallpox vaccine before they had their infection diagnosed. Twenty-three percent was with JYNNEOS or the FDA vaccine and all of them had one of two doses. Twenty-three percent actually had gotten pre-exposure prophylaxis before the outbreak, and we did not really know the date of when that was specified. And 54 percent said that they had a smallpox vaccine but didn't specify other details.

To date, in the United States, no deaths were reported.

Next slide. So we talk about clinical presentation. First, classic monkeypox, the incubation period is 5 to 13 days, on average. It ranges 4 to 17 days. It usually starts with a prodrome that's often described as flu-like: fever, malaise, headache, weakness, and also lymphadenopathy. And that lymphadenopathy, or swollen lymph nodes, can be generalized all over the body or localized to several areas, like the neck or armpit.

Generally, the rash appears shortly
after the prodrome in the classic presentation of monkeypox. So usually the lesions develop simultaneously and evolve together on any given part of the body. They have four stages. They start with macular, move on to papular, they look vesicular, and then they become pustular, before they scab over and resolve. They tend to be well-circumscribed, really deep-seated, and have a little divot on top or umbilication and are painful.

When they disseminate, they tend to be centrifugal, so more on arms, legs, hands, and feet, but could also involve palms and folds. The illness typically lasts two to four weeks.

Next slide, please. Here are a couple of photos of the classic rash presentation so you can see the pustular lesions in various different distributions.

Next slide, please. So the monkeypox outbreak in 2022 is a bit different. The pattern of the rash is often scattered or it could also be localized to a body site area, rather than
diffuse. It often starts in mucosal areas, so it's seen in genital, perianal, and oral mucosa, and it may not develop simultaneously in all body areas. A couple of important clinical findings that are also seen are proctitis, which is anal rectal pain, often feeling of having to defecate but not being able to, rectal bleeding, and it's often associated with visible perianal vascular, pustular, or ulcerative skin lesions and frank proctitis.

Additionally, oropharyngitis can also occur, and that is often complicated by tonsillar swelling, abscesses, and descriptions of dysphagia. Interestingly, in this outbreak, prodromal symptoms are often absent or sometimes actually follow with rash onset.

Next slide, please. So here's some photos of rashes presenting in 2022.

Next slide, please. I'd like to just, for one moment, focus on multi-domain strategies for prevention. So really there's not one single way to prevent monkeypox, so a lot of the domestic
work has been on creating clear guidance about ways to alter behavior, especially most recently with the clear data from our MMWR that demonstrates the role of sexual interactions in the transmission of monkeypox. This information had been posted on the CDC website initially June 6th, but the data, as the data has evolved, so has the guidance. So current guidance really focuses on temporarily changing behavior as we ramp up vaccination to be able to curtail the outbreak.

This harm-reduction document also focuses on social gatherings. The vast majority of cases are associated with sexual activity. There are some cases that are not so really clear guidance around ways to avoid monkeypox outside of sexual interactions, although, again, sexual interactions are the primary mechanism of transmission that we've seen in the domestic outbreak in the U.S.

Next slide, please. And I wanted to briefly just talk about the new FDA Emergency Use
Authorization that came out on August 9th. I think we heard about it briefly during the introduction. And it actually had two elements: one, it introduced the idea of intradermal dosing strategy that could potentially increase one vial from one dose to five doses and also the ability to administer subcutaneous dosing to individuals less than 18 years old. So, again, this dosing strategy demonstrated on lab-based assays similar immune response to the subcutaneous with a similar side effect profile. So in this emergency response, the EUA was moved quickly to really spare doses in the field so that we could actually use more doses to get more vaccines in arms.

Next slide, please. And I just wanted to briefly go over the logic. Next is an animation. So the JYNNEOS vaccine given at the subcutaneous dose generates immune responses measured in the lab, including in those in immunocompromising conditions that are thought to prevent monkeypox. So the next step in the
decision is that data shows that this vaccine given at the intradermal dose generates immune responses on the same types of lab-based tests that are nearly identical to subcutaneous dosing and also, as I said, have a similar side effect profile.

It's also important to note that there are other intradermal vaccines that have similar immune responses when compared to other dosing routes, including in immunocompromised. Some examples are research in flu and in hepatitis B.

So the next step in the logic is that, based on these data that support equivalence in effect and similar safety profile, intradermal dosing means up to five-fold more doses are available to safely vaccinate people who could benefit from the immune protection provided by the vaccine without sacrificing effectiveness as measured by lab-based assays.

Next slide. And so regardless of dose or route, what's important to remember is that vaccine surveillance and study will measure the
real world effectiveness and safety of the vaccine in the setting of an unprecedented domestic monkeypox outbreak. So I think, as we sort of go through the next few months, we'll learn more about how this vaccine actually functions in a real world exposure.

Next slide, please. I wanted to thank you very much, and I'll pass it back to the moderator.

DR. BENJAMIN: Thank you very much. I'd now like to ask Dr. B.K. Titanji to speak next.

DR. TITANJI: Thank you. Could you please pull up my slides? Thank you.

Over the next couple of slides, I will go over the prevention and treatment modalities that are currently available for monkeypox and being used in the ongoing outbreaks.

Next slide. All the pox viruses have a distinct property in the sense that infection with an Orthopox virus or immunization with an Orthopox virus vaccine confers immunologic cross
protection, basically meaning that, if you have an infection with one Orthopox virus, then the immunity that you develop from that infection or from a vaccine directed towards that particular virus would confer some degree of protection to other Orthopox viruses. And it is that property that is being exploited to allow us to use vaccines that were originally designed for smallpox protection in the ongoing monkeypox outbreaks.

Now, when it comes to vaccines that are available for monkeypox, there are two vaccination modalities that are currently available. The first of these are live inactivated virus vaccines which are vaccines that are based on a replication-deficient Orthopox virus known as vaccinia virus. Now, this vaccinia virus has been modified so that it doesn't cause disease because it's not able to replicate when it is administered in the form of a vaccine.

The JYNNEOS vaccine, which is the
inactivated vaccine that is currently being used in the U.S., was licensed in 2019 both for the prevention of smallpox and monkeypox. Now, the licensing of this vaccine was largely based on effectiveness studies that were based on animal models, and, in these studies, animals that are susceptible to Orthopox viruses were exposed to monkeypox, and then it was observed that animals who had been immunized had protection against this infection. Especially in monkeys who are challenged with a lethal dose of monkeypox, two doses of the JYNNEOS vaccine led to full protection against fatality from this infection.

The vaccine is currently licensed to be administered subcutaneously, and it requires two doses, which are spaced 28 days apart. And the maximal immune response following a complete course of the vaccine peaks at about two weeks after the second dose.

Next slide, please. The correlates of protection from these vaccines are incompletely characterized because the vaccines
have not been used or studied in Phase III studies in humans because they were licensed initially for smallpox and it's not ethical to conduct vaccine effectiveness studies on smallpox, which is a, by far, more fatal Orthopox virus. However, we do know that, from the data in animal studies, that they do confer meaningful immune responses that are thought to be protective or at least mitigate the severity of monkeypox infections.

Other modes of administration of the vaccine have been considered, as Dr. Daskalakis detailed in his previous presentation. And, currently, there has been a recent EUA that now has authorized the use of one-fifth of the dose administered between the layers of the skin called intradermal administration. And I put on this slide just to show you the difference between the subcutaneous administration of the vaccine which goes into the subcutaneous tissue just underneath the more superficial layers of the skin compared to the intradermal vaccination
administration that is between the more superficial layers of the skin. And the thinking behind why you get similar immune responses between one-fifth of the dose compared to the subcutaneous full dose of the vaccine is that the superficial layers of the skin are packed with immune cells that help amplify the response, leading to comparable antibody responses by either route of administration.

Given the limited supply of vaccination, exploring alternative modes of administration that can be dose-bearing is essential to really broaden the availability of these vaccines to individuals that need them. And I would like to also highlight the fact that the limitation of doses is not only a problem that is being seen in the United States. There are very limited doses of vaccine worldwide, and, currently, vaccines are only available in North America and in European countries.

Next slide, please. The second modality of vaccines that is available is the
replication-competent virus vaccine, which also contains the vaccinia virus. Now, these vaccines are much older and the second-generation vaccines that were used towards the end of the smallpox eradication program, not only in the U.S. but in other parts of the world.

Now, these vaccines are different in the sense that they contain a virus that is replication-competent. It is an Orthopox virus that itself can also cause an infection, albeit a milder form of infection than the most severe Orthopox viruses, like monkeypox and smallpox. Because of its replication-competent properties, it is, therefore, associated with a higher risk of more severe adverse reactions, such as significant skin infections in individuals who have atopic dermatitis, as well as inflammation of the heart and progressive or disseminated vaccinia infections.

It is contraindicated in individuals who are immunocompromised. Compared to JYNNEOS, it requires just one single dose of vaccine and
has been utilized in the U.S. after the smallpox eradication, primarily in individuals who have occupational exposures that may put them in risk of coming in contact with Orthopox viruses.

Next slide, please. Now, I just wanted to highlight some of the special considerations that I would like the audience to be aware of when we think about the vaccination modalities that are available for monkeypox. Besides pre-exposure vaccination, that is vaccinating people to protect them from developing monkeypox, JYNNEOS has also been utilized for post-exposure prophylaxis, meaning that it has been utilized as a strategy to be administered to individuals who might have had a high-risk exposure to someone who has tested positive for monkeypox and has monkeypox infection.

When it is used as post-exposure prophylaxis, ideally, the recommendation is that it should be given within four days of that high-risk exposure. However, the current guidelines
do allow for post-exposure prophylaxis to be administered up to 14 days after the exposure because, remember, monkeypox does tend to have quite a long incubation period. So the thinking is that, even if you administer the post-exposure prophylaxis several days after the exposure, you may still catch the tail end of the incubation period and, by so doing, mitigate the chances of that individual either developing infection or, if they go on to develop infection, that infection would potentially be one with a milder course.

Now, the effectiveness of post-exposure prophylaxis is still being evaluated, but there is emerging data from cohorts in Europe indicating that there is some benefit of post-exposure prophylaxis that prevents individuals from going on to develop monkeypox or at least mitigating the severity of their symptoms if they do progress to having a full infection.

Inactivated vaccines are safe to use in immunocompromised individuals. Remember,
they do not contain replication-competent virus so, as a result of that, are not feared to cause an infection in immunocompromised folks. However, there is insufficient data of the safety of either modality of vaccines in pregnant persons. In some of the animal studies that looked at the safety in setting of the pregnancy, there have been studies in pregnant mice that did not show any teratogenic effects associated with these vaccines.

The currently-licensed vaccines are authorized for individuals above the age of 18. And JYNNEOS can be considered for use in pediatric populations on the emergency authorization and I&D protocols. Now, it's important to note that the inactivated form of the virus, of the vaccinia virus that is present in the JYNNEOS vaccine has also been used as a vector for other vaccines that have been trialed in pediatric populations. So based on this data, the safety in pediatric populations is inferred.
And if there is a need for using pediatric populations, that should be a shared discussion with the provider based on these considerations. Replication-competent vaccines are contraindicated in all immunocompromised persons due to the risk associated with them leading to a more disseminated infection.

Next slide, please. Now, there are lots of questions and things that we do not know when these vaccines are concerned. I think that there's still a need for us to gain a better understanding of how much protection they actually confer in terms of their ability to prevent monkeypox infection but also in terms of their ability to mitigate the clinical severity of infection when infection happens even in individuals who have been immunized.

Now, the efficacy data that we have is really based from inferences on population studies that were done in the setting of surveillance in the DRC in the late '80s, which suggest that previous immunization with smallpox
vaccination may confer up to an 85-percent protection against monkeypox. We don't know how durable the immunity of these vaccines confer will be. And when you think about the durability of the immunity, then comes the question of whether individuals who are getting vaccinated now may need boosters in the future and, if they do, how soon would these boosters be required.

We are yet to fully characterize the correlates of protection, and we also need to better understand if there are any differences in terms of efficacy and effectiveness depending on the route by which these vaccines are administered, specifically thinking about intradermal versus subcutaneous modes of administration.

And it's also important for us to gain more understanding of the impact of vaccination when it's used as post-exposure prophylaxis and to think about special groups, such as pediatric populations, pregnant people, and immunocompromised individuals to better
characterize their immune responses to these vaccines so that we know which of these vaccines are suitable for special populations.

Next slide, please. Now, I'll switch over to the available antiviral treatments. The first medication that I wanted to highlight was tecovirimat, which is an antiviral medication that is licensed for the treatment of smallpox. It is currently being used in the ongoing outbreak under EA I&D protocols. It is an antiviral that works or exerts its antiviral effects by targeting a protein, a viral protein that is important for the formation of new viral particles. The efficacy data on tecovirimat, again, is based on animal challenge studies in which it has been shown to reduce severity of illness in monkeys that have been exposed to monkeypox virus.

There are very limited clinical data of its efficacy in humans. However, it does have a very good safety profile from Phase I and Phase II studies and is generally very well tolerated.
In the ongoing outbreak, there have been anecdotal reports of patients reporting improvement in their symptoms and fewer lesions developing following the start of treatment with tecovirimat. But we need studies that better characterize how best to utilize this antiviral medication, when to give it to patients, and for how long, and to better understand their real impact on the course of the disease.

Next slide. The other two antiviral medications that I wanted to highlight are brincidofovir and cidofovir. Cidofovir, they're basically the same medication with the small difference that brincidofovir is a prodrug of cidofovir and is available orally, whereas cidofovir can only be administered or is only available in IV formulations and topical formulations.

They have an impact on the virus replication by inhibiting viral DNA synthesis, and both of them have been shown to have in vitro antiviral activity against Orthopox viruses.
There is also animal data that indicates that they have efficacy in mitigating or reducing the severity of symptoms in animals that have been challenged or infected with monkeypox.

The data in humans remains quite limited, and we also need studies to fully understand how best to utilize these medications in the setting of the ongoing monkeypox outbreaks. It's important to highlight that they are associated with unfavorable adverse effect profiles, especially when you compare them to the previous medication that I showed you, tecovirimat, especially pertaining to impacts on the liver and on the GI tract with many patients complaining of nausea and vomiting associated with the administration of these medications.

Next slide. Like with the vaccines, there are several outstanding questions when it comes to antiviral therapies for monkeypox. How effective are these antiviral medications for the treatment of monkeypox in humans is an aspect that we need to better understand and
characterize? Is there a role for combination therapy in severe disease? A lot of these medications that I have shown you we do not fully understand whether they have good CNS penetration, specifically thinking about infections that may progress to involve the central nervous system. So is there a role for using them in combination in more severe forms of the disease?

It there a risk that, as we use these medications more, we will start to see antiviral drug resistance emerge? And if yes, what impact would those have on their utility in the treatment of monkeypox in the current outbreak? And I think also it is a real opportunity for us to better understand whether there might be a role for using antiviral medications as pre-exposure prophylaxis or even post-exposure prophylaxis to prevent individuals from either developing monkeypox symptoms or progressing in the course of their disease if we start these treatments earlier or if we give them
preemptively before the exposure actually happens.

Next slide, please. Next slide. And I just wanted to conclude with a word on the importance of adjunctive therapies outside of antivirals. As Dr. Daskalakis very clearly highlighted in his presentation, the ongoing outbreak has really been characterized by a preponderance of patients presenting with mucosal lesions and also patients presenting with lesions in the genital area, which can be quite severe. And monkeypox lesions have been associated with very painful symptoms for these patients, so it's very important that we also factor in the importance of treating these painful lesions and ensuring that the skin lesions heal appropriately so that we minimize scarring once the patients have fully recovered. So thinking about things like skin protectants when we are addressing these lesions. In patients who have proctitis that is associated with significant pain, we have seen the use of lidocaine-based preparations or
topical anti-inflammatory agents or perineal treatment such as sitz baths to sort of alleviate some of these associated symptoms, as well as the use of systemic opioids.

And I think I really wanted to stress the fact that it is important to engage the assistance of our dermatology colleagues in assisting us with managing this condition when the patients first present and not wait until it's too late before we engage their expertise.

And with that, I will stop here and pass on to the next speaker. Thank you.

DR. BENJAMIN: Dr. Titanji, thank you very, very much. That was an amazing presentation.

Dr. David Heymann.

DR. HEYMANN: Thanks very much, Georges. Let me get my screen on. It's a real pleasure to be with you today, and I'd just like to pick up where others have left off and go to the first slide, which is just to remind you that there are actually 13 different pox viruses in
the Orthopox family. Of course, the Variola virus, the smallpox virus, was the most important, and that's at the top, as you can see. And that was a human infection, and the reservoir of the natural host was, in fact, a human.

And then if you look down, you'll see others that can infect humans, including the monkeypox virus, which is down in the middle of this slide. And you can also see below that camelpox, which also has recently infected humans.

So these are zoonotic infections that occasionally infect humans. They have a reservoir in nature. Humans and, in the case of monkeypox, monkeys or non-human primates become infected, as well, from some type of reservoir in nature.

Next slide. This is just to show you a picture of smallpox before it was eradicated in the 1980s and just to talk a little bit about its epidemiology. The transmission was droplet transmission face-to-face by very close contact
in a cough or a sneeze and direct contact with the lesions or with scabs from those lesions. Very much the same as for monkeypox.

Every infection was clinically expressed in the same manner. In other words, a clear pattern of infection, including lesions on the palms and soles, as you see in monkeypox today. The case fatality rate, however, was 20 to 40 percent, and 100 percent of patients had permanent facial scarring, which is many times quite disfiguring. And this was a very serious infection as recently as 1967 when there were 2.7 million deaths.

So this is a disease which shows the inequalities that occurred in the world because the Northern Hemisphere really didn't have any smallpox and the death was occurring in Africa, in Asia, and in some parts of Latin America.

Next. This is, again, to remind you about smallpox and the vaccine, which was a replicating vaccine, as we heard earlier and which we know now cannot be used in HIV-infected
persons because of a military recruit in 2004 who was vaccinated with this replicating smallpox vaccine, HIV infected but didn't know he was HIV infected, and in six months he had unfortunately passed away from AIDS. Generalized vaccinia was an AIDS-defining event.

At the same time, there was permanent protective immunity against future infection after recovery from disease, which we don't know yet about monkeypox. The vaccine was very stable. In fact, it could be carried in the back pocket for up to a month at 39 degrees or more centigrade, and it could then be diluted and used rapidly. And there was no animal reservoir.

So smallpox was quite an easy infection to eradicate. And as you can see, there was the bifurcated needle that we talked about earlier, which was a very important tool in making sure that you could do that ring vaccination with contacts in persons living around a person with smallpox.

Next. In 1970, in DRC, when smallpox
had already been pretty well eliminated from Africa, there was this child who developed what looked like smallpox and what was thought to be smallpox. In fact, however, this was human monkeypox, and this was the first patient identified with human monkeypox.

Next. Now, it was first identified, the monkeypox virus, actually in 1958, as most of you know, in Copenhagen in a laboratory where there were monkeys being used in some experiments. These monkeys had been brought in to Copenhagen and stored in a central storage of live animals with other animals, including animals from Africa. And they were likely infected from African primates or non-human primates in that laboratory setting.

Next. Now, there was a series of investigations. Between 1970 and 1979, every case that was identified in West and Central Africa, and there were a total of 48 identified, was investigated. I participated in many of those investigations with African colleagues.
using a standardized questionnaire and form that could help identify the epidemiology.

What we learned from these 48 patients was that 72 percent had animal contact, and this was usually a young child, unvaccinated, who either found or picked up some type of a sick animal and became sick, went home, and became sick with human monkeypox. Occasionally, hunters who were unvaccinated also developed monkeypox.

Next. At that time, during this period of '70 to '79, three generations was the maximum amount of transmission, and this occurred in 8 percent of outbreaks. And all those people who were infected in those three generations of transmission were unvaccinated against smallpox.

Next. The case fatality rate was 10 percent, and there was some facial scarring, not quite so much as from smallpox. Next. And primary cases over 15 years of age were rare, except in those unvaccinated hunters who came in with an animal. And, finally, most secondary and
tertiary infections, as I said, occurred in unvaccinated parents or siblings. So this was an infection, a new infection, and 48 cases gave us a good idea of the epidemiology in Africa.

Next. Now, in 1980, as smallpox eradication, vaccination was discontinued and smallpox eradication had been certified, there was great concern that human monkeypox might fill the epidemiological niche left by smallpox. The presumed reservoir of the virus in nature was monkeys or rodents was probably the reservoir, monkeys carried it and transferred it to humans in West and Central Africa.

Next. There were sporadic breaches in the species barrier between rodents and humans, and we knew this was going on at least 48 times during that period before 1980. Next. Secondary and tertiary cases appeared to occur in unvaccinated persons. Next. And the concern was that, as residual herd immunity for the smallpox vaccination decreased, would human monkeypox fill the epidemiological niche by
smallpox and itself become endemic?

And so in 1980, there were a series of serological surveys throughout West and Central Africa looking at children under 15 who had no vaccination scar to see whether or not they had antibody to Orthopox viruses. And among them, there were about 50 out of this 15,000 children who did have some type of Orthopox antibody, and later on it was determined that possibly four of those Orthopox infections were actually monkeypox. So monkeypox was circulating, at least infecting people, possibly sporadically, at a low level.

But the concern was there, and, in 1996, from an outbreak that occurred in DRC in Katako-Kombe, it was found that this disease was actually changing in epidemiology. This was an outbreak in 1996 through 1999 that was quite continuous, and it infected over 500 people. In that outbreak, between 1996 and 1995, the percent of infections greater than 15 years of age were 85 percent, reflecting, again, the decrease in
people who were vaccinated.

The index cases with animal contact went from 72 percent to 23 percent. In fact, this was an outbreak that was being sustained by periodic emergence from nature but was transmitting quite easily, as you can see. Nine generations from 16 percent of the index cases. And the case fatality rate remained the same at 10 percent, the virus on genetic sequencing had remained stable since those first viruses back in the 1970s.

Next. The conclusion at that time was that intensified surveillance needed to continue.

Next. This is the picture between 2000 and 2009, and you can see that this was a time when monkeypox occurred in the U.S. because it was exported to the United States. And at the same time, there were over 10,000 cases reported in DRC, and the Congo had several, and South Sudan had 19.

Next. Then all of a sudden, in 2009, Anne Rimoin's study in DRC showed that there was
Next. The vaccinated persons had a 5.2-fold lower risk of monkeypox. And, again, improved surveillance and epidemiological analysis was the conclusion. It needed to continue.

But at this point, I'd just stop to say that we've neglected this disease in Africa for many, many years. Research has been piecemeal. It's been to study antivirals in DRC from USAMRIID. It's been to study occasionally the epidemiology. But now you can see that it's clearly in West Africa and it's throughout Africa, and it's been exported, as you know, to their countries. It was being exported in the late 2000s.

Next. So what we know today about this is it's not just one clade. It's two different clades of human monkeypox, as you know. And between 1970 and 1979, in the Central African clade 39, West African clade 9, a total of 47 - 48 cases actually. And then you can see that these clades have increased, especially in
Central Africa where there have been over 18,000 suspected cases between 2009 and 2019. Again, an infection which has been neglected in study in Sub-Saharan Africa when there are researchers in Sub-Saharan Africa who are doing the work that they can do to hold things together, but they need partnerships and they need support from the north.

Next. And at the same time, the case fatality rate, as you know, varies between the clades. In the Central African clade, about 10 percent, as we'd shown previously. West Africa clade less, about 3 percent, and you can see the confidence limits on that.

And the next and final slide. What you can see here is that both the West African clade and the Central African clade have been increasing dramatically recently. And I would just say an aside here that we're very fortunate that it's not the Central Africa clade that has spread into Europe and North America. People with this disease are very sick. They have a
smallpox-like illness. They have a high risk of mortality. And what you can see is that the Central African clade has increased dramatically, as has the West African clade.

And so next slide. The question remains will human monkeypox replace smallpox? Will it fill that epidemiological niche left by smallpox? We still don't know whether the West African or the Central African clade will, in fact, continue to spread within Sub-Saharan Africa and out.

So there is some research priorities, and we've heard many of those. But these are priorities, especially for colleagues in Africa, where the disease needs to be dealt with, as well. What we're seeing in monkeypox in the north is an amplification of transmission because of a chance occurrence of genital lesions, but in Sub-Saharan Africa this is a daily event and we need to pay more attention to this. We need to understand whether every infection is symptomatic and clinically expressed in the same manner. We need
to understand whether there's permanent protective immunity against future infection after recovery. We need to know whether the infection causes more severe illness in those who are immunocompromised. We know from patients in Nigeria and we know from patients in DRC that this is the case that some persons who are immunocompromised and not on antiretrovirals, in fact, do have more serious illness. We need to know whether the vaccine, as we heard earlier, modifies disease if provided within four days of infection, as did smallpox vaccine, the vaccinia. We need to know whether the current vaccine produces lifelong immunity against infection, and we really need to understand what strategies to use for the new vaccines in dealing with monkeypox. And, finally, we need to better understand what the animal reservoir is in nature and how we can best deal with this.

So thanks very much, and I just turn over to the next speaker. Back to you, Georges.

DR. BENJAMIN: Dr. Heymann, thank you
very, very much. Dr. Erbelding.

DR. ERBELDING: So thank you. And I've been asked to discuss the monkeypox research agenda. I don't have slides. So many studies are in the late planning stages and changing on a daily basis that I didn't want to give misinformation.

So my colleagues have highlighted some of the critical gaps in knowledge, and I'm going to describe clinical trials that are currently being designed to address some of those major gaps that I think will launch fairly soon in the United States and worldwide.

At NIAID, we are currently in the late stages of planning a trial that will generate more robust data on dose-sparing options for the JYNNEOS vaccine. As you heard earlier in this webinar, the vaccine was licensed for protection against monkeypox and smallpox based upon immunogenicity trials that showed that the two subcutaneous doses given four weeks apart, the licensed doses, were not inferior to ACAM2000, an
earlier vaccine. And then ACAM2000 was not inferior to the take rate at the same immunogenicity levels, was not inferior to the take rate in smallpox vaccine of several decades ago. So the licensure of the JYNNEOS vaccine was also supported through the Animal Rule by monkeypox challenge studies in animals.

So at NIAID, we're planning to launch a clinical trial soon, probably within the next month, that will compare the standard and the standard licensed subcutaneous doses, two doses given four weeks apart subcutaneously, to the authorized intradermal dose, the dose that the FDA authorized about two weeks ago and is now being rolled out in the United States. So two doses, subcutaneous two doses, one-fifth dose given intradermally, and then a single intradermal dose in a third arm.

So this trial is going to add to the data package that could support licensure of intradermal delivery. And it could also provide data of the durability of the immune response to
the single intradermal dose.

Those living with HIV will not be excluded from this eligibility for this trial. We realize that we also need to generate data in younger age groups, in the pediatric age groups, and in pregnant and breastfeeding persons, and so those trials or expansion of the trial that will launch within the next month may, expansion and amendments may generate data for those special groups, as well.

We also need to evaluate the efficacy and safety of tecovirimat in clinical illness. And you heard this, again, earlier in this webinar. As you know, the drug was licensed for smallpox based upon data generated in animal models and a small amount of safety data in humans.

So to address the unknown of whether it's clinically efficacious in clinical illness in humans, there's several trials that have been launched worldwide, and I'll describe to you two randomized control trials that will be supported
by NIAID and probably be implemented, the protocols will probably be implemented within the next month.

So one trial will occur in Africa. This was planned even before the current outbreak outside of Africa was described, and it will enroll patients diagnosed with, hospitalized patients diagnosed with monkeypox. It will be in the Democratic Republic of the Congo where monkeypox has been endemic for decades now, and there's also a very high mortality rate, as was noted by Dr. Heymann in the earlier presentation. In some regions of the DRC, as high as 15 percent.

So the trial will randomize hospitalized patients to tecovirimat or placebo, in addition to standard of care. And the main outcome measure will be clinical resolution and lesion healing.

A second trial supported by NIAID will be conducted by the AIDS Clinical Trial Group and will enroll participants in U.S. sites. It's designed to generate data that could support
authorization or licensure of the drug in the United States.

So this trial will have three arms. Patients who are heavily symptomatic who have ocular disease or who are pregnant or younger than the age of 18, so the pediatric population, will be offered open enrollment in an open label arm. Others who have mild to moderate disease being treated as an outpatient will be randomized to either receive tecovirimat or placebo. And, again, the main outcome measure is time to lesion healing, as with the DRC trial.

So another major gap in our knowledge base that we recognize is just an understanding of the natural history of monkeypox infection and factors that might modify the disease course and the duration of infectiousness. So even though case series are being reported and they can provide some information, it really would be much better to conduct well-designed prospective trials which would enroll cases, monkeypox cases, as well as exposed contacts and follow their
natural history longitudinally.

So important descriptive measures would include the duration of viral shedding from lesions as a surrogate marker perhaps for infectiousness. Also, the time to generation of neutralizing antibodies and the relationship of that to symptom resolution. And in exposed contacts, it would be very important to investigate whether there's an asymptomatic phase of virus shedding.

So data generated from prospective natural history studies would provide much better information than we have now on activities that might lead to a high exposure risk, a high risk of acquiring disease, and also measures that might be protective against developing disease if a person has been exposed.

So other studies that are being discussed right now but, to my knowledge, aren't in the planning stages yet are studies that would test the efficacy of combination therapy, particularly for individuals who are heavily
symptomatic or who might progress on tecovirimat alone. Also, it's important, as noted earlier, to know how we can use antivirals and vaccines for post-exposure prophylaxis. I think, in order to get proof of efficacy in that and the exact interval where those post-exposure prophylaxis might provide benefit, we would have to conduct randomized trials and not necessarily rely upon reports from real world effectiveness studies.

At NIAID, we realized that we still need new antiviral drugs. Even though this is a DNA virus and the mutation rate is not expected to be as rapid as the RNA viruses, we realize that we need more tools in our toolbox and we need to continue to identify new antivirals that might be promising clinically, preferably with mechanisms of action that are different than the antivirals that we currently have available.

So I've tried to hit the highlights of our research agenda, and I'm happy to turn over the microphone to our moderators.

DR. BENJAMIN: Listen, thank you very
much, Dr. Erbelding. I'm going to ask all of our
panelists to cut on their videos, and then we can
certainly have a conversation about some of the
stuff we've heard. So if everybody would cut on
their videos. Let's see. There we go.

So let me start and let me start with
Dr. Daskalakis. You know, one of the questions
that someone posed was that the reports of -- can
you hear me -- reports of asymptomatic
infections. What do we know about that? You
know, everyone is always afraid that the person
next to them who seems to be asymptomatic might
be someone who is infectious. What do we know
about that at least to date?

DR. DASKALAKIS: Well, certainly
saying the person next to you is less of a concern
than the person you may be having sex with. So
I'll start with that really important range of
potential exposures.

I think we're still learning about
folks and their level of symptomatology. I think
there are individuals who may have one lesion or
very, very few manifestations of the disease. So I think we're learning more as we go along about the potential for is there an asymptomatic phase or really, potentially, is there a paucisymptomatic phase and then also the potential for transmission during the prodromal phase. And I think a lot of interest in sort of understanding virus on mucosal surfaces even in the absence of rashes. I'm sure others will likely want to chime in on that one, as well.

DR. BENJAMIN: Any other thoughts?

DR. TITANJI: Yes, I could add to that. A lot of the data that has been reported on the asymptomatic transmissions are emerging from cohorts in Europe where they have gone back retrospectively and looked at clinical samples collected to test for other sexually-transmissible infections and are finding some of those samples positive for monkeypox in individuals who did not have any symptoms. Some of those cohorts have been reported out of Belgium and also out of, I believe, France, and
those are two published studies that are out.

What we don't know is when people start shedding virus from different compartments and whether they do that even before they actually manifest symptoms of the infection. And this is one of those areas where we really need studies that further characterize the natural course of the infection.

Secondly, we also now know that virus is detectable in certain body compartments, like semen, even in individuals 19 days outside of the first presentation of symptoms. We need to characterize further for how long virus shedding may persist for and whether there are implications for transmission if you're still shedding virus even when your skin lesions are fully healed.

So lots of unanswered questions around asymptomatic transmission. I put that in quotes because we don't really know whether it is truly asymptomatic or whether it's a reflection of virus shedding before symptoms begin or continued
virus shedding after the resolution of symptoms.

DR. BENJAMIN: Great thought, great thought. Dr. Heymann, sure.

DR. HEYMANN: It's also important to remember that scabs can be infectious, as well. And it's thought in the United Kingdom, in fact, that one of the persons who was cleaning the bed of a person who had had monkeypox actually became infected from scabs that might have been within the bed linens when she cleaned the bed.

So the scabs are highly infectious after they leave the body, at least for a certain amount of time.

DR. BENJAMIN: Okay. David, you talked certainly about the two claims of this virus. Is there anything that differentiates them in terms of how infectious they are? And then that's one question, and the second question is do we understand why there's a higher mortality with one clade versus the other?

DR. HEYMANN: Yes, those are two good questions, Georges, and I'm not sure I can answer
either one of them. What I can say is that, in Africa, this is a disease which is occurring regularly, and we've neglected it for many, many years as a research project, a coordinated research activity, although, as I said, there's been piecemeal research going on and we understand quite a bit.

The difference in clades is not clear to me. I can only say that, in West Africa, it's a self-limited infection. It doesn't cause serious illness, unless there's comorbidities. One patient who was on renal dialysis developed serious illness. Another was immunocompromised and developed serious illness. Both of them died. And it's also a disease in children.

The Central Africa clade is the one that looks like smallpox. You know, I started my work in Africa for CDC after two years seeing smallpox in India. And when I saw that first case of monkeypox, it was hard for me to believe that that wasn't smallpox. It's a very, very serious illness. It hasn't, as far as known,
left Sub-Saharan Africa yet, and that may be because people are so ill at the time when they get infected that they just don't travel. I think maybe Dr. Titanji would have a good idea on that, as well, because I know she comes from Cameroon.

But the fact remains that the two clades are different. I can't say why they're different, but they are. And this was not understood early on in the infection.

DR. BENJAMIN: Great. Dr. Titanji, do you have any thoughts on that?

DR. TITANJI: Yes. Just coming back to sort of my thoughts around why the two clades might be different in terms of their presentation, I'd just like to highlight the fact that there's a lot about the biology of monkeypox virus that we don't fully understand. A lot of the virology is extrapolated from our understanding of smallpox, as well as vaccinia, which is a more mild Orthopox virus that lends itself more readily to being studied in a lab.
environment.

So it is quite possible that, between the two clades, there might be unique virulence factors that are yet to be characterized, again highlighting the importance of basic science research to really understand the biology of this virus and the pathogenesis factors that may drive the differences in presentation.

And in addition to that, to what Dr. Heymann just mentioned, it's also important to remember that when monkeypox happens in a lot of countries that have historically been affected, including Cameroon where both clades actually circulate, both the West African clade and the Central African clade, they're happening, the outbreaks are happening in very remote parts of the country where access to sophisticated healthcare is also severely limited, and people are really relying on supportive care to manage these cases. Even when you think about complications, be it bacterial superinfection, you may not necessarily always have the right
antibiotics to treat those complications.

So a certain portion of that excess mortality is a reflection of that sort of resource-constrained healthcare system. And, yes, it is a very serious infection, as well.

DR. BENJAMIN: You know, one of the challenges we have, I think, just from a population perspective, you know, we stopped vaccinating in what, about 1972, routinely. Is that about right? So that means that I'm, you know, theoretically, I have some protection against monkeypox, but my grandkids don't. Any sense of what this means as we begin to think forward about, you know, vaccination policy with smallpox?

DR. HEYMANN: You know, I would just say that I think we're very fortunate to have a non-replicating vaccine, which is safe to use in all populations. And, you know, just like with polio eradication, polio hopefully will soon be eradicated, I think that people will not stop vaccinating against polio and I think that
there's a feeling, as you know, in the U.S. that it was a mistake to stop vaccinating against smallpox. In fact, the risk-benefit was such that it was necessary to stop because the original vaccine had a mortality rate of 1 per million doses.

But, you know, now, I think that there will be thought about whether or not populations need to be more vaccinated moving forward, especially in Sub-Saharan Africa where it may be that there are some strategies that could be developed which would prevent this from continuing to spread and cause illness in Sub-Saharan Africa and a risk of exportation.

DR. BENJAMIN: Let me ask Dr. Erbelding, do we have any studies that we're contemplating to try to answer the question about how we're protected, you know, from those who were vaccinated and then, of course, in an environment where we have a lot of immune compromise both from underlying diseases, like HIV/AIDS, as well as the things that we purposely
do to people, you know, high-dose steroids, cancer chemotherapy, et cetera.

DR. ERBELDING: Certainly, people living with HIV are not excluded from the trials that I outlined. But other immune-compromised groups we would probably need to design studies that would specifically target them for vaccination and test the immune response.

I'm sorry. Your earlier question was about are we looking at whether, like a surveillance study of whether or not early vaccination for smallpox or prior vaccination for smallpox was protective.

DR. BENJAMIN: How protective prior vaccination is.

DR. ERBELDING: How protective. I think that Dr. Daskalakis sort of alluded to -- well, you did your questionnaire, and some people said, yes, I got smallpox vaccination, but they didn't describe it. If they maybe were in the military up until a certain point or if they were above a certain age or if they worked with
vaccinia in a laboratory, that would be the other group that would have specifically gotten vaccinia vaccination, and I don't know if you want to comment on whether or not you think that those results were meaningful for suggesting protection based upon prior vaccination.

I think it would have to be a surveillance study, though, if we were going to look at that. And I don't know that we have plans to do that, but it would be interesting.

DR. DASKALAKIS: I'll just add -- so thank you. I'm just going to add that, in terms of the work that's currently going in surveillance studies, there's a package of studies that are looking at the current vaccination efforts. I think we'll learn more about the sort of, this vaccine in sort of this domestic real-world experience. There are no current plans at CDC or that I've heard about elsewhere to do a more longitudinal study in folks with more remote vaccination.

We will, through some future reports,
learn if people have had prior vaccine. I think the issue is going to be is the number going to be big enough to be able to say something definitive.

In terms of guidance, the guidance that we are giving is that prior vaccination could be partially protected. But in individuals who currently have indications for vaccine, the recommendation is to get vaccinated again.

DR. BENJAMIN: Okay. Go ahead.

DR. ERBELDING: I'll just add that there are people working on assays that might, serologic assays that might discriminate between prior vaccinia vaccinations, prior types of vaccination and actually history of monkeypox, you know, the serologic response to that. So that might also, if they successfully develop those assays, that might provide an opportunity to examine this issue more closely. That's not, those tools are not in our hands yet.

DR. BENJAMIN: You know, since the highest risk group right now seems to be men who
have sex with men and I think every one of us on this panel has had enormous experience with HIV/AIDS, what are the lessons learned? I mean, let's start with the lessons around the fact that do we need the stigma for the at-risk population? You know, how do we message it? Do we need to change the name of monkeypox?

So let's start with the stigma question around communicating effectively. Maybe if I could have Doctor --

DR. DASKALAKIS: I think that's me.

DR. BENJAMIN: Yes, I'm sorry.

DR. DASKALAKIS: No, that's okay. Daskalakis. Call me Demetre; it's easier. That's what everyone calls me anyway.

So I think that it's really been inspired a lot by the experience in HIV in terms of a strategy for communicating monkeypox. So I think one of the things that I say often is that it's the responsibility of government and governmental public health to model the best behavior in terms of how to communicate about
disease, and so I think this is an example where we've learned, I'm sure, from the past to making sure that we don't associate a virus with an identity but rather talk about the behaviors and activities that could potentially lead to exposures to the virus while also being diligent about trying to get that information to trusted messengers and to trusted sources of the population that's overrepresented in the outbreak. So really making sure that we communicate to gay, bisexual, and other men who have sex with men in really frank terms that they understand.

So I think we, as early as June 6th, the CDC posted guidance on safer sex and safer gatherings, even in the absence of a lot of data and sort of experience in this outbreak. So I think that's an important lesson. That one actually doesn't come from public health, it comes from the community where a group of individuals put out guidance for how to have sex during an epidemic. And so really taking that
cue from community, I think sort of having public health and governmental public health lead on this to make sure that good information is available, while also towing that line. We have to make sure that we talk to the population and inform them without stigmatizing, but it's really important to be frank and engaged. So I think that that's sort of the line that we tow all the time. It's the HIV line that we towed for a long time, and I think also learning the lessons from the first 41 years of HIV are really important in terms of creating a strategy for communicating about monkeypox. Always, we could do better, but I think the lessons from HIV really put us in a place where at least, from the perspective of governmental public health, we were able to at least avoid some stigma.

Now we just have to make sure that others, including media, follow our lead because I think sometimes that's confounded pretty seriously. And I think all of us will agree that when stigma becomes a part of an outbreak
response, there are rabbit holes that people go down that mislead you and you end up missing very important pieces of outbreaks or potential strategies to mitigate those outbreaks.

DR. BENJAMIN: David, you know, we changed the name of COVID pretty early on. You know, we went from the novel coronavirus to something else to COVID-19. We kind of skipped over the fact that it's really SARS-CoV-2. But if we changed the name of monkeypox, what does that, you know, is that going to really change anything?

DR. HEYMANN: I think it will be very hard to change the name now. You know, you've got to get in early and do that. But if it does change in name, it would certainly -- I think I'll come back to what Demetre said: it should come from the community. The community should decide what they want to call this infection, what they want to call this disease.

But I think what's really important not to forget is that this disease can be
controlled without a vaccine. This disease can be controlled by behavior change, and that has to come from within the community. It can't come from the top down. But behavior change, paying attention to who you have sexual contact with, and making sure that you are, that your colleagues are aware of this infection can do a lot to control it. And, in fact, we're already seeing in some countries, in the UK, I mean, it was very surprising after Gay Pride about four weeks ago when there were a million people in London parading that there wasn't a rapid increase in infections because the message had already penetrated to a certain extent. And now in the UK there is thought that it might be plateauing because behavior change is occurring.

So let's not always look for the medical solutions. Let's look also to the behavioral solutions.

DR. BENJAMIN: You mean public health works?

DR. HEYMANN: Public health works.
DR. BENJAMIN: Prevention at least, to the extent we can do that.

Let me ask another question. You know, I was around when the 2003 outbreak in the United States where it was clearly a zoonotic infection and almost every case was related to the handling of a prairie dog, Gambian rat, et cetera. There's concern, of course, about this disease getting into the animal population, and any thoughts about that?

DR. TITANJI: I could comment on this. I think that there is certainly a risk that we might see monkeypox maybe establish itself in animal reservoirs, but, you know, one thing that sort of gets missing in this conversation around the virus establishing itself in an endemic fashion in newly-affected countries is the fact that we don't even know what its true natural reservoir is. Although it has been detected in animal species in West and Central Africa, these animals have typically presented with pox lesions on themselves. So the animals are actually
infected. They're not the reservoir.

So it's still a big question mark what is the natural reservoir of monkeypox virus? And if we haven't fully characterized the reservoir, it is difficult to know what is the true potential zoonotic species in newly-affected countries that could then become a reservoir of the virus that would perpetrate the infection in an endemic fashion.

Going back to Dr. Heymann's point on the fact that this is an infection that we neglected for 50 years in Africa and really missed the opportunity to learn some of these finer points about the virus, its reservoir, its biology, that would have been very useful to us as we think about the current outbreak. That being said, we do know that it's not a very picky virus in terms of what it's able to infect, and there have now been reports about infections in domestic animals, notably a case report of a pet dog that got infected through contact with its owners in France and more recently another animal
exposure in the Netherlands resulting in infection in a domestic pet.

So very important for individuals who test positive to really be mindful of the fact that, if they have pets, they should be talking to their health department to make sure that they isolate properly from their pets, as well.

DR. BENJAMIN: What's the guidance that we should have for employers and for, you know, schools? We've lost your sound.

DR. DASKALAKIS: Sorry. It's my technical limitation with having the phone as my source here.

So I think the guidance for most venues, like schools as an example, it's really sort of a weaving together of guidance that already exists. I think CDC has great guidance posted for congregate setting and, depending on the level, also the guidance around safer sex. I think it's really, again, about engaging schools and also universities to make sure they're aware of the guidance and have a plan in
place.

So I think the guidance really is, like, the reality of this outbreak is that the majority, the vast majority is happening in men who have sex with men and it's related with sexual exposures. So I think we have to sort of level set and make sure that we're sort of creating guidance that is right sized to what the risk is in the environment, realizing that people may have sex in congregate settings and then they have sex at university. So that's why I think we're really focusing on giving good information about what it's like if you're in a congregate setting and what to do and also how to mitigate risk based on behavior.

DR. BENJAMIN: What about this whole issue of aerosolization? You know, there's always this question, it certainly is one way, I guess, that the virus does spread. What do we know about that? Dr. Erbelding, is there research going on in that area?

DR. ERBELDING: There are animal
studies and studies to look at, you know, the duration of infectiousness in environmental samples, different, you know, different environmental conditions. I'm not aware of any aerosolization studies right now.

DR. BENJAMIN: Does anybody know of anything else that's going on in the aerosolization area?

DR. TITANJI: Well, not in studies that are ongoing now, but in some of the vaccination studies that were used, the animal challenge studies, one of the ways in which non-human primate macaques were infected with monkeypox in some of these animal studies was really exposing them to aerosolized high concentrations of the virus as a mechanism of infecting them to assess the efficacy of either medications or vaccinations.

But I would like to stress that the amount of virus that is used in these animal models is really a very, very high inoculant and not reflective of what you would see if you were
thinking about droplets or aerosols that are generated when we speak.

And now we do know that, in terms of looking at the data that's emerging on the viral loads that patients with monkeypox have from different body compartments, the recent cohort study coming out of Spain did show that the highest compartment in terms of virus shedding is still very much the skin lesions. When they checked the viral load in the oral and pharyngeal secretions, the viremia was actually quite low compared to other compartments. And that, to me, kind of, as a virologist, doesn't really speak to aerosols being the predominant mechanism of transmission. This is really a virus that is transmitting through prolonged contact skin to skin with the skin lesions that have a very high burden of virus.

DR. BENJAMIN: Thank you very much. You know, we could obviously talk about this for another hour, and I wish we had another hour to talk about it. I want to thank our panelists for
being here today. This was absolutely an amazing conversation. You know, we've got a lot of tools in our toolshed. We do have behavior change, for one. But we do have effective vaccines, we do have effective antiviral agents, but I think, like anything else, the most effective thing we have is education, good, clear communication in a way that doesn't stigmatize people, in a way that really engages people as part of the process, engaging the at-risk community. Hearing and listening more than talking I think is going to be very important. Those are lessons that we learned from HIV/AIDS. Many of these lessons we also learned from COVID or should have learned from COVID, as well.

So as we close out, I want to let everybody know that, if you registered for today's webinar, you'll receive an invitation to any of the next webinars that the Academy does. This webinar has been recorded. The recording, the transcript, and the slide presentation will be available on the APHA website. And if you
have any ideas or suggestions for future topics, you can send it to apha@apha.org.

And I wanted to see if Dr. Dzau has any final comments before we close out.

DR. DZAU: My only comment would be thank you, first, Georges, for your moderating, you know, effective moderating and, of course, all the panelists for really a robust discussion, lots of information. I look forward to seeing all of you in person one day, and thank you again and thank the attendees.

DR. BENJAMIN: Thank you, everybody. Everyone have a good evening.

(Whereupon, the above-entitled matter went off the record at 6:30 p.m.)