Good afternoon, I'm Nikki Grimsley and I am representing the Clinician Outreach and Communication Activity, COCA, with the Emergency Risk Communication Branch at the Centers for Disease Control and Prevention. I'd like to welcome you to today's COCA call, Monkeypox: Updates about Clinical Diagnosis and Treatment. All participants joining us today are in listen only mode. Continuing education is not offered for this COCA call. After the presentation, there will be a Q and A session.

You may submit questions at any time during today's presentation. To ask a question using Zoom, click the Q and A button at the bottom of your screen, then type your question in the Q and A box. Please note that we receive many more questions than we can answer during our webinars. If you are a patient, please refer your question to your healthcare provider. If you are a member of the media, please contact CDC Media Relations at 404-639-3286 or send an email to media@cdc.

gov. I would now like to welcome our presenters for today's COCA call. We are pleased to have with us, Dr. Agam Rao who is a medical officer in the Poxvirus and Rabies Branch in the National Center for Emerging and Zoonotic Infectious Diseases at CDC. Dr.

Leandro Mena, who is the director of the Division of STD Prevention and CDC's National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention. And Dr. Brett Petersen, who is the deputy chief of the Poxvirus and Rabies Branch in CDC's National Center for Emerging and Zoonotic Infectious Diseases. I will now turn it over to Dr. Rao.

Dr. Rao, please proceed.

Great, thank you Nikki. Next slide. Next slide. I will present about the situational awareness for the current Monkeypox outbreak so just as some background; Monkeypox is a rare, sometimes life-threatening zoonotic infection that's endemic in west and central Africa. It's caused by Monkeypox virus which is an orthopoxvirus but the specific animal reservoir is unknown but probably small mammals that occur in some part of Africa.

It can spread from infected animals to humans and also person to person, but Monkeypox does not spread as easily as COVID-19. It spreads through respiratory secretions so droplets, saliva, through skin to skin contact with infected body fluids, for example the fluid from vehicles and pustules that make up the rash, and through fomites; example, shared towels or contaminated bedding. Next slide. Before 2022, we have had U. S.

cases of Monkeypox, in 2003 there was an outbreak linked to small mammals that were imported from Ghana so there were 47 cases at that time, it was a multistate outbreak, involving the upper Midwest United States and the cause was traced to the spread of Monkeypox virus from imported African rodents to pet prairie dogs, to people who had contact with those pet prairie dogs. And then after that, the next time we had Monkeypox cases in the U. S. was in 2021, so just last year. There were two unrelated cases in travelers from Nigeria.

So in July there was a case in Texas and in November in Maryland. So similar to imported cases, during 2018 to 2021 that, these two, sorry, these two unrelated cases in travelers are similar to the imported cases during 2018 to 2021 that were reported in travelers to the United Kingdom, there were four, Singapore, one, and Israel, one. All were in travelers from Nigeria. Next slide. So this is the appearance, the classic appearance of the lesions, it's always described as firm, deep-seated, well circumscribed, they can be painful, itchy, and sometimes umbilicated.

And hopefully you can see from the pictures that that is how they appear. So in the top row here, you can see lesions that were observed during the 2003 U. S. Monkeypox outbreak, these were mostly from bites and scratches from animals. The images on the bottom side of your screen are the lesions that are observed in endemic countries.

So they're very noticeable, they're very obvious, but again, they are these firm, deep-seated, well circumscribed lesions that are sometimes umbilicated and by umbilicated we mean there's a little pit there in the center. Next slide. Now things, everything sort of changed in May of 2022, this month or sorry, that month, May of 2022, the United Kingdom reported cases in three distinct clusters and announced each of those clusters on May 7, 14, and 16. The first was a travel associated case, the second was a family cluster of unknown etiology involving three people, and then the third were cases identified at sexual health clinics among gay, bisexual, or other men who have sex with men or MSM, and there were four individuals who were identified in that cluster. So it's really that last cluster that is what we are seeing now in the United States.

The very, the day after this cluster was reported in the United Kingdom, so on May 17, the United States recognized the first suspected case here and that was in a resident of Massachusetts who had traveled to Canada. The rash began as an anogenital rash involving vesicles and pustules and then it spread to the face and trunk. And later that day tested positive by the OPX generic test at the Massachusetts Laboratory Response Network laboratory. Next slide. So since then, we've had many cases here in the United States as of 2:00 pm Eastern time yesterday, Tuesday, June 28, there have been 305 cases diagnosed in the United States and among residents of 28 states and the District of Columbia.

It's mentioned here in the footnotes, but I just want to mention that sometimes that number is reported as 306 because there is one individual who was diagnosed in another country but who is resident of the U. S. and being monitored in the U. S. So if you see a difference by one, you'll know the reason.

The map on the left side of your screen along with the worldwide map of reported cases is posted to our CDC webpage and it's updated at 2:00 pm Eastern time on weekdays so it might already be updated for today. You can find a link to information specific to this 2022 outbreak, including these maps from our website at www. cdc. gov/monkeypox, there's information there. You can see here on this image though that the largest number of cases at this time are in California, New York State, and Illinois.

Next slide. So this an epi curve of those U. S. cases by date of laboratory report. It also shows the earliest date of rash onset that we know of so far, it was very late April or early May.

The first cases were due to exposures that occurred abroad, in places that were experiencing outbreaks. But since then we are seeing persistent local transmission in addition to regular importations from exposures abroad. Monkeypox again, as a reminder, does not spread as easily as COVID, during this outbreak many people who have gotten Monkeypox were exposed or in close contact, class contact includes intimate contact or in sex but is not exclusive to that. Most cases I will explain on the next slide. So next slide.

Alright, so for the 305 cases confirmed by yesterday afternoon, the median age is 36 years with a range of 20-76 years, so it is a broad age range. Most cases are among people who were male sex at birth, all men for whom gender identity was reported are cis gender men and nearly all of the patients were asked if they participate in male to male sexual contacts and 99 percent reported that they do. But I do want to caution you, there are some cases, we have five in the U. S. , among people who were female sex at

birth, some of these are cis gender women and some are transgender men, but some may have been exposed to bisexual men.

We do know that worldwide, some household contacts have gotten Monkeypox from fomites or shared materials. So it is not just affecting men. There are no cases in children in the United States, there is at least one child though in Europe who's been diagnosed with Monkeypox in the last week. No deaths have occurred in the United States but also no deaths in any country outside of countries where Monkeypox is endemic. It's important to note again that any person, regardless of gender identity or sexual orientation can get and spread Monkeypox.

Next slide. So I want to highlight some of the clinical symptoms and the features that we're hearing about. So the skin rash or enanthem is present in all the patients, the lesions seem to be in different phases of development seen side by side, which is a little different from what we historically have thought about Monkeypox. The rash is either scattered or diffused, so sometimes it's limited to just one body site and mucosal area, like the anogenital region or the lips or face. Sometimes it involves several, like there are lesions in the anogenital area but then there's a couple scattered lesions on the abdomen and a couple on the scapula.

So it's not quite as diffuse as we have always thought of it. The presenting complaint for some patients has been anal rectal pain or tenesmus but physical examination has always yielded these visible lesions and sometimes it shows proctitis as well, but the lesions do seem to be present whenever these symptoms have been related to Monkeypox. Prodromal symptoms have been mild or not occurring, so that's another feature that's different from what we've always historically thought about Monkeypox. And fever or lymphadenopathy have not always occurred which is also different. I also want to just point out that some co-infections, sexually transmitted infections or STIs, have occurs so the presence of an STI does not necessarily rule out Monkeypox as well.

Next slide. So again, lesions for May and June of 2022, they still are that firm, deep-seated, well circumscribed, painful, itchy and sometimes umbilicated lesions. They are however much smaller. So these are photographs, in panel A and panel B, are actually cases in 2022 during May and June. This panel C though, I'll just say is from a patient during the 2003 U.

S. outbreak. And the reason it is here is to show that even though the classic lesions occurred at that time, during that outbreak, there were some lesions that were unusual appearing and more consistent with what we're seeing right now. And for additional references, I guess I would recommend, I don't have them in my slide deck, but I think Dr. Mena has them in his.

Some images from anogenital lesions, you can find them in the manuscripts that are noted here on the right side of your screen. There's also an increasing number of papers coming out about this outbreak that also have photographs that would be helpful for clinicians to see how these lesions occur in the anogenital region. These lesions might actually rapidly progress through the stages from papules, vesicles, pustules, and scabs. The papulovesicular and pustular lesions are sometimes seen on the same body site, so right next to each other, side by side. Next slide.

These are some more photographs that I just wanted to show again that even though they might seem like they are not your typical classic appearance, they do have features, they are firm, well circumscribed, deep-seated, and by deep-seated I mean that the opposite of veriscella, they are not superficial lesions, you cannot unroot them with your fingertip, they are deep down in the skin and symptoms they're umbilicated as you can see from that group of six, the top right one you can see that,

and even in the bottom left, when it's in that scab form, you can see it's well circumscribed. So hopefully these are some distinctive features. Monkeypox can also affect the palms and soles so if you do see lesions in the palms and soles, although there are other things that present with lesions on the palms and soles, perhaps knowing a patient with epidemiologic risk factors and some of these other characteristics and lesions on the palms and soles might lean you in the direction of Monkeypox. Next slide. And these are still more photographs, these are from here in the United States.

And these are all from shared through permissions from the patients. The ones on the left side of the screen, hopefully you can see some of these images again, firm, deep-seated, round, sometimes umbilicated, you can see the top in panel B in the far left, that these are very small lesions so sometimes they are really small and can be easy to miss some of these characteristic features but they are there in at least many of the cases that we have heard about. And in the right side of the screen are some more images, so we have a palm here on the bottom left, on the right side of your screen and then two fingers and hopefully you can see that round, well circumscribed, firm appearance, umbilicated appearance there. Next slide. So what we in health alert messaged to clinicians and health departments was to first perform a thorough skin and mucosal exam for the rash, so that includes the anal, vaginal, and oral, parts of the patient's body.

I know that's the standard of care and maybe it's obvious to say that, but we just wanted to point it out because this is not necessarily appearing as a diffuse rash and sometimes even if the lesions look one way on one part of the body, you'll see the more characteristic lesions on another part of the body. And especially if a patient is co-infected with a STI, if the patient has both an STI and Monkeypox, some of the lesions might not look terribly characteristic and so a full body exam, a full body skin and mucosal exam may help. Swabs should then be obtained if you observe the classic Monkeypox rash or if you think that the rash could be consistent with Monkeypox in persons with epidemiologic risk factors and those epidemiologic risk factors are listed here, they are contact with a person or people with a similar appearing rash or with diagnosis of Monkeypox, close or intimate in-person contact with people in a social network experiencing Monkeypox activity, for example men what over sex with men, who meet partners through an online website, digital app, or social event. And a history of recent international travel to a country currently with many cases, and I guess going to that country and having those sorts of interactions with other people. The diagnosis of an STI does not rule our co-infection with Monkeypox, and again, reminder again, any person irrespective of gender identity or sexual identity, sexual orientation, can acquire and spread Monkeypox.

I will just say that close contacts includes intimate contact during sex, and most cases have occurred in MSM but we know that this is not a heterogeneous group of people. At this time what we know about the patients is that some visited bath houses or participated in group sex surrounding large Pride events or had a single anonymous sex with a single partner or partners that they met on social networking apps. But we are still trying to understand further and as I mentioned earlier, we are aware of household contacts and other people who worldwide who have acquired Monkeypox through this outbreak and also before. So what we know about it it at it can spread to household contacts and other close, very close contacts, intimate contacts. Next slide.

So this is a selected listing of current CDC priorities, so we are working really hard to try to understand the situation that is ongoing, we're trying to understand clusters and cases including risk factors to inform guidance. Sequencing genomes of Monkeypox virus isolated from patients to monitor the spread variance and track virus evolution. Launching retrospective and prospective serosurveys to determine the prevalence and how long Monkeypox might have been in the United States. We're refining our case definitions based on the data collected from clinics where cases are being detected so we have

partnerships with certain clinics around the countries where we're trying to obtain specimens from a wider variety of rashes to try to understand whether anything needs to be modified about our case definitions. We are understanding the natural history of current clinical presentation, expanding testing capacity at LRN laboratories and commercial laboratories.

And then we're providing case by case consultations for clinicians considering treatment and post exposure prophylaxis for patients. And then I just want to also say that at this time we're not aware of presymptomatic or asymptomatic spread of Monkeypox, we're remaining open and want to understand everything that is occurring in the current situation and not limiting ourselves to what we know about Monkeypox from the many decades that we've been investigating it. We do recommend that people who are at risk for getting Monkeypox self-isolate if they have a skin rash or oral lesions that could indicate Monkeypox and contact their healthcare provider so that they can be evaluated. Next slide. And then finally, I'll just say that we are trying to keep all of this guidance as we're learning more and more information, updated on our website for healthcare providers, for public health authorities, and also for the public.

So you can find various links to information that we're doing our best to keep up to date at www. cdc. gov/monkeypox. This includes case definitions, clinical recognition, which is the topic of the next presentation, prevention strategies, Monkeypox can be prevented through harm reduction strategies to reduce the risk of sexual exposure to Monkeypox or exposures related to close skin to skin contact, we have information about that on the website. Exposure risk assessment, guidance for monitoring exposed persons, infection control in home and healthcare settings, specimen collection, so CDC does provide testing guidance to local jurisdictions and health departments.

It's a partnership, so those jurisdictions develop the local logistics and guidance for ordering tests. And at this time a testing request in many jurisdictions are managed by health departments so if anything changes on that front we hope to update our website. And then the last issue here, considerations for medical countermeasures is the topic that Dr. Petersen will be presenting. So just as an intro to that, the vaccines and biologics to prevent and treat Monkeypox are not commercially available.

The U. S. government stockpiles these as they do other biologics that are not commercially available and CDC fills that gap, providing those stockpile vaccines to patients. So this is not unusual, it's done for other vaccines and biologics as well. And with that, I will turn it over to the next speaker, Dr.

Mena. Thank you.

Thank you, Dr. Rao. And good afternoon everyone. As mentioned earlier, we have a lot to learn about the clinical signs and symptoms that patients may experience due to current Monkeypox outbreak. Today I'll be presenting a case study in order to familiarize these clinicians with the varied manifestations of this infection and potential diagnostic challenges that clinicians may face.

I would like to thank the patients, the patients who generously agreed to share their pictures that I will show today. As the pictures are absolutely critical to educating healthcare providers today about the diagnosis and management of this infection. I will warn you that the images that I will present are graphic. Next slide. On Thursday, June 2, the patient, who is a 26-year-old Hispanic man who has sex with men and established client at a publicly funded STI clinic, presented for a routine 3-month HIV PrEP clinic visit via telehealth.

During this telehealth visit, the patient had no concerns and he was instructed to come to the clinic for his routine testing the next day. Next slide. On the same day, after his morning telehealth visit, the patient noted new penile lesions as shown here. Next slide. In the clinic on Friday, June 3, while self-collecting specimens for STI testing, the patient mentioned to staff that he had this new rash on his penis that started late the day before but had worsened since that time.

Additional patient history was listed on his visit during, including that the patient had sex with three men at a sex party in New York City on May 29. The patient did not know whether any of these partners had recently traveled. He denied recent international travel and he reported no fever, swollen glands or fatigue. Next slide. On physical examination, the patient was uncircumcised, with multiple discrete small papules and macules on the penis glands, coronal sulcus, and distal penile shift.

Some of the lesions were flesh colored and some were pale. There were no pustules. At first glance, the lesions appear to be consistent with genital herpes, however, the lesions were firm and slightly rubbery which is not consistent with HSV. The lesions also could not be unroofed or denuded. The lesions were painful and there was no inguinal lymphadenopathy.

It is difficult to see but if you look closely, you will see that there are pinpoint umbilications in many of the lesions which is an important clue. Next slide. During this visit for PrEP clinic HIV STI testing was performed, including an RPR. An HSV culture was also collected. The patient was empirically started on treatment for his first clinical episode of genital herpes and anticipatory guidance and counseling was provided for other possible diagnoses, including molluscum contagiosum, and Monkeypox.

Monkeypox swabbing was discussed but not performed at this time because there was no prominent symptoms and only four days had passed between the sex party and the onset of symptoms. The patient agreed to return to clinic the following week to discuss the testing results and reassess his symptoms. He also agreed to sexual abstinence pending results and a definitive diagnosis. Next slide. Over the weekend his sometimes evolved.

As shown in this photo from Sunday, June 5, as you can see the lesions became more prominent, developing a more pustular appearance. Next slide. On Monday, June 6, the patient called the clinic to discuss his lab results and provide updates of his sometimes. His lab results included a non-reactive RPR, a negative HSV culture. His pharyngeal and rectal NAATS were negative for both chlamydia and gonorrhea, and his urine NAAT was positive for chlamydia and negative for gonorrhea.

He reported that his genital lesions had increased in size and number over the weekend and had become more painful. In addition, his penis and foreskin had become more edematous. He also now had a couple of additional lesions elsewhere on his body and reported a subjective fever for the past two nights that was associated with fatigue and decreased appetite. In the interim, he had learned that one of his partners at the New York City sex party lives in Toronto, was symptomatic and was diagnosed with Monkeypox. The patient was scheduled to be seen again the next morning.

Next slide. The patient returned to clinic with his most recent sexual partner on Tuesday, June 7, for follow-up. At that time provided additional history. The patient history included the following; he reported 10 male sex partners in the past 90 days and 40 in the past year. He reported using the substances ecstasy and ketamine in the past 30 days.

He reported sex with anonymous or pseudo-anonymous partners, meaning that he only knew some partners by their app profile name. And he engaged in receptive and insertive oral and anal intercourse

and reported never using condoms. His past medical history included a prior history of chlamydia, gonorrhea, and syphilis infection. Next slide. For the examination of the patient was significant for a lesion in the mouth.

Specifically a small ulcerated area in the upper right rear oral cavity and on the hard palate that was painful when swabbed. Next slide. There was one skin lesion on the person's chin which had a white rim with a dark center and erythematous base as shown here. Note that this lesion is very characteristic of Monkeypox. Demonstrating the value of performing a complete skin and mucosal examination, individuals presented with genital lesions.

Next slide. On the genital exam, there were multiple white lesions with umbilicated center. The foreskin and distal end of the penis were edematous and the patient was unable to retract the foreskin. The area was generally painful and a possible white urethral discharge was noted. Next slide.

At this visit, all three of the patient's anatomic sites with lesions were swabbed for Monkeypox testing. The patient was started on doxycycline 100 milligrams by mouth, twice a day for 7 days for urogenital chlamydia treatment. And the patient was instructed to call the clinic in the next day or two to discuss results and reassess symptoms. Next slide. The patient's partner, a 23-year-old white MSM also presented for evaluation on June 6 and reported onset of a new rash at this time.

The partner reported that he was last together, that he was last together with the index case patient on Wednesday, June 1, one day before the index patient's symptoms started. The partner reported three male sex partners in the last 90 days, and 10 partners in the past year. He reported sex with anonymous and pseudo-anonymous partners. He engaged in receptive and insertive oral sex and receptive anal intercourse and reported never using condoms. His past medical history included a prior history of chlamydia and gonorrhea in the previous year.

Next slide. On the partners physical exam he had one nodular firm papule, approximately 0. 5 centimeters in size, in the right axillae as shown here. Next slide. And he had five popular, mildly erythematous lesions across his chest in varying size, largest was approximately 0.

5 centimeters, including one lesion with white rim, dark center, and erythematous base. Next slide. He also had one very small papular lesion on his left lower buttock. Next slide. On lymph node examination he had no axillary, supraclavicular, or inguinal adenopathy.

Next slide. All three of the partner's anatomic sites with lesions, right axilla, chest, left buttock, were also swabbed for Monkeypox testing. The partner was started on doxycycline 100 milligrams by mouth twice a day for seven days as a contact chlamydia infection. Next slide. All three sites of the index patient's lesions tested orthopoxvirus positive.

All three sites of the partner's lesions tests orthopoxvirus negative. Of note, orthopoxvirus results are reported as positive, negative, or quantity not sufficient. Meaning that there was not enough DNA material to run this test. The partner's specimen was adequate enough to report a negative result. Next slide.

The next day, June 9, the index patient called the clinic with an update that the number and size of the penile lesions had continued to increase and that he was no longer able to urinate due to the pain and swelling. The clinic staff communicated with a local emergency department by the attending physician and the manager, to have the patient evaluated. The patient was seen in the emergency department and

treated with oxycodone and with phenazopyridine. He was successfully able to void spontaneously after the pain was controlled. He was discharged home with pain management medication and an additional week of doxycycline for possible cellulitis by the patient's report.

Next slide. The patient's final results at return to clinic for JYNNEOS post-exposure prophylaxis on June 10, nine days after his last contact with a now confirmed case of Monkeypox. By this time the partner's lesions has almost resolved and there was nothing present to re-swab for orthopoxvirus. Given the adequacy of the specimen collection, the negative orthopoxvirus results and the rapid resolution, the partner was given a diagnosis of folliculitis. Next slide.

This Monkeypox case highlighted multiple lessons learned, including the reminder that complete sexual histories need to be taken, especially when patients present with symptoms that suggest sexually transmitted infections. Clinicians should familiarize themselves with the Monkeypox clinical presentations that have been reported in the 2022 Monkeypox outbreak. Notably, similar to this case, the rash has often begun in mucosal areas, such as the genital, perianal and oral mucosa. And in some patients, the lesions have been scattered or localized to a specific body site. In this case, the rash began in mucosal areas, including the genitals and oral mucosa.

The clinicians could not see the classic Monkeypox lesions umbilications in clinic on Day 2 but noticed it in photos the patient subsequently shared with the staff. In addition, prodromal syndrome, including fever, malaise, headache, and lymphadenopathy have not always occurred before the rash. If they have occurred at all. In this case, the prodromal syndrome begin three days after the onset of penile lesions and the patient did not have lymphadenopathy which has historically been a hallmark of Monkeypox infection. Clinicians should evaluate any individual presenting with perineal and genital ulcers, diffused rash and symptoms for STIs per the 2021 CDC STI treatment guidelines.

Testing for STIs should be performed. The diagnosis of an STI does not exclude Monkeypox as a concurring infection may present such as in this case where the patient was co-infected with genital chlamydia. This case also highlights the importance of conducting a thorough examination of all skin and mucosal surfaces using good lighting, as lesions appear on other areas of the body may appear more characteristic for Monkeypox. Additionally, the patient had a sex partner one day before his Monkeypox symptoms began, who does not appear to have been affected. Thank you.

I'll pass it now to Dr. Brett Petersen.

Thank you very much. So I will now provide an overview of the medical countermeasures for Monkeypox. Next slide, please. Currently this slide lists the available countermeasures stockpiled for orthopoxviruses, including Monkeypox, with respect to vaccine we have two available, JYNNEOS and ACAM2000, and for treatment; Tecovirimat, Vaccinia Immune Globulin, and Cidofovir are available. Next slide, please.

Starting with vaccines, JYNNEOS is a live various vaccine produced from the strain Modified Vaccinia Ankara-Bavarian Nordic, which is an attenuated, non-replicating orthopoxvirus. This vaccine is also known as IMVAMUNE, IMVANEX, or MVA. JYNNEOS was licensed by FDA in September of 2019 and is indicated for the prevention of smallpox and Monkeypox disease in adults 18 years of age and older. CDC is developing an expanded access investigational new drug protocol for IND to allow the use of JYNNEOS for Monkeypox in pediatric populations. Next slide.

The other vaccine current available is ACAM2000. ACAM2000 is a live, replicating vaccinia virus vaccine. ACAM2000 was licensed by FDA in August of 2007 and replaced the previously licensed vaccine, Dryvax. ACAM2000 is indicated for active immunization against smallpox disease for persons determined to be at high risk for smallpox infection. CDC holds an expanded access IND, which allows the use of ACAM2000 for non-Variola orthopoxvirus infections, including Monkeypox, during an outbreak.

Next slide. There are significant differences between ACAM2000 and JYNNEOS as described on this slide. The first is that the vaccine virus contained in ACAM2000 is replication competent vaccinia virus whereas JYNNEOS is a replication deficient modified vaccinia Ankara virus. As such, ACAM2000 produces a take, or a vaccine site lesion at the site of inoculation which can be used as a marker of successful vaccination. JYNNEOS on the other hand, does not, however this take or vaccine site lesion does contain infectious virus and as such, ACAM2000 does carry a risk of inadvertent inoculation and auto inoculation.

JYNNEOS does not carry this risk. Seriously, similarly with respect to serious adverse events, ACAM2000 does have a risk for severe adverse events associated with uncontrolled replication of the virus. With JYNNEOS there are not expected and fewer serious adverse events are expected. For cardiac adverse events, ACAM2000 does have reports of myopericarditis occurring in an estimated 5. 7 per 1000 primary vaccinees.

Myopericarditis has not been reported in association with JYNNEOS in the limited numbers of individuals that have received the vaccine in clinical trials so the risk is believed to be lower than that for ACAM2000. With respect to effectiveness, ACAM2000 was assessed by FDA by comparing the immunologic response, take rates, ACAM2000 to Dryvax. And similarly, JYNNEOS was assessed by comparing the immunologic response of JYNNEOS to ACAM2000 in combination with other animal study done. ACAM2000 is administered per cutaneously by multiple puncture technique in a single dose. JYNNEOS is administered subcutaneously in two doses, 28 days apart.

Next slide. With respect to Monkeypox vaccine preexposure prophylaxis the Advisory Committee on Immunization Practices, ACIP, did vote to recommend vaccination for select persons at risk for occupational exposure to orthopoxviruses in November of 2021 and a policy note fully describing these recommendations was published in the MMWR on June 3 of this year. Next slide. In these recommendations, people who should get preexposure prophylaxis include the clinical laboratory personnel who perform diagnostic testing for orthopoxviruses, research laboratory workers who are directly handling cultures or animals contaminated or infected with orthopoxviruses and also for certain healthcare and public health response team members that are designated by public health authorities to be vaccinated for preparedness purposes. Next slide.

ACIP also recommended vaccination under shared clinical decision making for some healthcare workers but at this time, most clinicians in the United States and laboratories not performing orthopoxvirus generic test to diagnose orthopoxviruses are not advised to receive orthopoxvirus preexposure prophylaxis. Laboratorians should consult with their laboratory biosafety officers and supervisors to identify risks and precautions depending on the type of work they are doing and clinicians and laboratorians should use recommended infection control practices. Next slide. ACIP did also include a list of contraindications for ACAM2000 and JYNNEOS for this population of persons at risk for occupational exposure to orthopoxviruses. As you can see, there are a number of contraindications for ACAM2000 among vaccinees as well as household contacts given the risk of severe adverse events in these individuals.

Of note, JYNNEOS also does carry a contraindication for serious vaccine component allergies. Next slide. The current outbreak response in the United States has focused on surveillance through case identification and laboratory testing to confirm cases, containment through isolation of cases and contact tracing, and postexposure prophylaxis vaccination of close contacts based on a risk exposure assessment which is available on CDC's website. In brief, people with a high degree of exposure are recommended to receive close exposure prophylaxis, and people with an intermediate degree of exposure is recommended to undergo informed clinical decision making on an individual basis to determine whether benefits of PEP outweigh the risks. It is important to note that brief interactions and those conducted using appropriate PPE in accordance with standard precautions are not high risk and generally do not warrant close exposure prophylaxis.

Next slide. As the outbreak has evolved, our vaccine strategy considerations have evolved as well. Jurisdictions with larger number of cases are reporting that high percentages of contacts cannot be identified and there has been a desire to plan and implement expanded vaccination programs using similar approaches and strategies being used in Montreal, the UK, and other locations. These strategies are broadly known as Monkeypox vaccine close exposure prophylaxis PEP plus plus or expanded vaccination. This strategy means to vaccinate people with certain risk factors that might make them more likely to have been recently exposed to Monkeypox with the aim of reaching these individuals for postexposure prophylaxis vaccination even if they have not had a confirmed exposure to Monkeypox.

Next slide. We currently have limited supplies of JYNNEOS although more expected in July of this year. Currently the goal is to focus the allocation of currently available JYNNEOS doses to those areas with highest transmission and they're working to distribute JYNNEOS to states for immediate use for expanded Monkeypox vaccine postexposure prophylaxis. These allocations are based on areas of highest transmission based on current and projected population adjusted incident cases and is also weighted by population of men who have sex with men with HIV or eligible for HIV preexposure prophylaxis. So in short, this strategy is aiming to mitigate spread of the virus in communities where transmission has been the highest and with the populations most at risk.

Next slide. Shifting now to treatment considerations for Monkeypox, it's important to note that many individuals infected with Monkeypox in this outbreak have had a mild, self-limiting disease course even in the absence of specific therapy. However, the prognosis for Monkeypox does depend on multiple factors such as previous vaccination status, initial health status, and concurrent illnesses or comorbidities. Next slide. CDC has produced treatment considerations for Monkeypox and recommends considering treatment following consultation with CDC for the individuals listed here.

Persons who can be considered for treatment include people with a severe disease, for example, hemorrhagic disease, persons who may be at high risk for severe disease, such as people with immunocompromised conditions like HIV or AIDS, pediatric populations, pregnant or breastfeeding women, people with a history of atopic dermatitis or people with one or more complications. It's also reasonable to consider treatment for persons who have aberrant infections involving anatomical areas that may present a special hazard, including the eyes, mouth, or anogenital areas. Next slide. Tecovirimat is the principle antiviral medication that is currently being used during this outbreak. It was developed to treat smallpox and is also known as TPOXX or ST-246.

Tecovirimat was approved my FDA as both an oral capsule and IV formulation in July of 2018 and May of 2022, respectively. It is indicated for the treatment of humans smallpox disease in adults and pediatric patients, weighing at least 3 kilograms. And CDC does hold an expanded access IND that allows for the use of Tecovirimat for non-variola orthopoxvirus infections including Monkeypox. Tecovirimat is

currently available from the strategic national stockpile as an oral capsule formulation and an intravenous vial. Next slide.

Other treatment options are also available in the stockpile and can be considered. VIGIV is listened by the FDA for treatment of complications due to vaccinia virus vaccination. Cidofovir, also known as Vistide, is an antiviral medication that is approved by the FDA for treatment of cytomegalovirus retinitis in patients with AIDS. Both of these products are available from the strategic national stockpile and can be considered as alternatives to Tecovirimat or adjuncts to Tecovirimat in severe cases or other unique circumstances. CDC does hold expanded access INDs for both of these products that would allow them to be used for Monkeypox.

Next slide. One other treatment option is brincidofovir which is also known as CMX001 or Tembexa and this is an antiviral medication that was approved by the FDA for the treatment of human smallpox disease in adult and pediatric patients, including neonates. Brincidofovir is not currently available from the SNS, nonetheless, CDC is currently developing an expanded access IND protocol to help facilitate the use of brincidofovir as a treatment for Monkeypox if and when this product becomes available. Next slide. For ocular infections, trifluridine is an antiviral medication licensed for the treatment of herpes keratoconjunctivitis or keratitis.

There is in vitro evidence of trifluridine activity against orthopoxvirus and there are case reports of use of trifluridine for treatment of ocular orthopoxvirus infections like vaccinia virus. This is an option that can be considered if Monkeypox virus infections involve the eyes. Next slide. CDC is available for consultations to assist with medical countermeasure utilization including appropriate vaccine and antiviral use. Clinicians should work with their state or territorial health authorities to request vaccines, Tecovirimat, VIGIV or Cidofovir.

And the health departments can reach out to CDC consultants through the CDC emergency operations center. Next slide. Thank you, and with that I will return to the moderator.

Presenters, thank you for providing our audience with this very timely information. We will now go into our Q and A session. Joining us for the Q and A session are Dr. Laura Bachmann, who is the chief medical officer in the division of STD prevention at CDC. Dr.

Bryce Furness, and Miss Rachel Kachur, also from the division of STD prevention at CDC. Please remember that to ask a question using Zoom, click the Q and A button at the bottom of your screen, then type your question. Please remember that we receive many more questions than we can answer during our Q and A session. Our first questions; to collect a sample for Monkeypox testing do you need to unroof the lesion?

Yes, I can answer that question. So in general, what we recommend is that we vigorously swab the lesion and in some instances, it will not be possible to unroof the lesion so swabbing vigorously the lesion is all that is needed.

Okay, thank you. Our next question; do prodromal symptoms always precede the appearance of Monkeypox lesions?

Prodromal symptoms, the emergent of lesion was the classical presentation and this is actually one of the initial things that we are seeing in the current 2022 outbreak where very often individuals who

develop lesions, develop lesions without any prodromal symptoms or sometimes these symptoms develop after developing of the rash.

Thank you. Our next question; for those who receive the smallpox vaccination or a chickenpox vaccination, do either of those vaccines provide any protection against Monkeypox?

Hi, this is Brett Petersen, so with respect to previous vaccination with smallpox vaccine, that is expected to provide some protection against Monkeypox as these, as Monkeypox is a related virus to the smallpox virus. We don't know exactly how long the protection lasts after vaccine, what we saw in the 2003 Monkeypox outbreak is that there were six individuals who were previously vaccinated as children who did acquire Monkeypox infection. However, an analysis of all of the cases did suggest that among those who were previously vaccinated, there was a protective affect even after many decades of receiving the smallpox vaccine. So that's something that we're interested in learning more about and learning more precisely how long vaccine protection lasts. With respect to chickenpox vaccination, chickenpox is actually a herpes virus and is unrelated, it's a different virus, different virus family from Monkeypox and smallpox and so the vaccination against chickenpox would not be expected to provide any protection from Monkeypox.

Thank you. Our next question; is there any indication or evidence that someone can be infected more than once with Monkeypox?

This is Agam Rao, we don't have any, we don't have enough experience in this. We have not seen that happen but that does not mean that it could not happen. Dr. Petersen, do you want to provide any additional information about that?

Yeah, so what was typically seen with a related virus, smallpox, was that generally infection with smallpox virus did provide lifelong protection. However, it's not clear if that will apply also to Monkeypox virus infections. We are aware of one single case report of a possible reinfection with Monkeypox virus but we would expect that to be rare. What we don't know is with this new outbreak and the new epidemiology and route of transmission, whether that may impact some of what was previously seen with Monkeypox and other related viruses like smallpox. So I think there's still more to learn there.

Thank you. Can you review what type of transmission based precautions should be taken when caring for a patient with Monkeypox?

I think we might not have the experts who are working on that in the call.

Okay, thank you. We'll move on to the next question then. Okay, our next question, do you think that this could spread easily, meaning Monkeypox could be spread easily from person to person like COVID-19.

Sure, this is Agam Rao, I can take that. So COVID-19 spreads a lot easier. Monkeypox is certainly no COVID-19. Monkeypox transmission from what we know before this 2022 outbreak, but also during this outbreak, seems to be spreading through direct close contact. So intimate contact that might happen during sex but also any other close contact that might occur, for example, if you live with someone who has Monkeypox and you are sleeping on the same bedding and using the same towels.

That sort of thing. So it really is not something that you will just pass on to someone walking down the street or anything like that. We don't, we're obviously keeping an open mind in this outbreak to make sure that we consider whether or not it can spread more easily, but at this time, there's no indication that would spread the way that COVID spread and spread to as many people. At this time the risks for the worldwide population, if you consider everyone in the world, is low.

Thank you. Can you review how to correctly swab a specimen of suspected lesions if they are deep-seated and without drainage?

Yeah, I can start and maybe Dr. Furness who is a clinician in the emergency prevention division can expand on that. Really, you take a sterile swab and vigorously swab on the lesion. Right, very often what's going to happen is that because of the characteristics of the lesion, it will not unroof but let me allow Dr. Furness to expand since he has done this multiple times in his clinic.

Thank you, Dr. Mena. Yeah, this is Dr. Furness and I've swabbed at least more than ten lesions so far on several different patients and not one of them has unroofed. These are truly small, rubbery, deep-seated lesions and unlike HSV lesions, you don't really, you can't really tell whether you've gotten a good specimen or not based on whether or not there's fluid present or whether or not there happens to be some bleeding.

This is just, you have to rub the swab aggressively over the lesions and so far almost every one that we, every case that we swabbed and suspected as Monkeypox has come back as orthopox positive. So I just want to say in the cases that I've taken care of, we haven't been able to unroof the lesion. There hasn't really been fluid you can see or witness. You just have to scrub the swab over the surface of these umbilicated, rubbery, deep-seated lesions as hard and aggressively as the patient can tolerate because most of these are quite tender.

So this is Brett Petersen, I'll just add that with Monkeypox lesions, they do contain infectious virus so it is important to keep those lesions covered to prevent any transmission of infectious virus that is present on those lesions or any lesion materials. And with that in mind, the assay that is being used to diagnose Monkeypox is a very sensitive PCR assay, so with vigorous swabbing of these infectious lesions, that should be sufficient to detect virus and to make the diagnosis.

Thank you. And related to specimen collection, can samples be collected before they become pustule?

So I guess I'll take this. This is Agam Rao. Yeah, they can be taken during the vesicular phase, I mean there's no lesions often, sometimes, at least before 2022 there would be lesions in the mouth before the lesions on the skin presented and we do have one patient in the United States who we know had those lesions were swabbed before anything else developed on the skin of his body, so you can swab the vesicles, pustules, the scabs can also be collected and tested, scabs are a common source of transmission to others, like if there's a lot of scabs from these lesions that are collected on bedding. So, any of those can be infectious, any of those can be swabbed. Dr.Petersen, did you want to add anything at all?

No, I concur, lesions at any stage of development can be swabbed and as they progress and start to develop crusts or scabs, those, that lesion material can be collected for diagnostic testing as well.

Thank you. We have time for one last question, and there were quite a few questions on this topic, can you differentiate between the Monkeypox and other umbilicated lesions like molluscum contagiosum?

This is Leandro Mena, I can start. I think that the key point is that many of these lesions can really mimic other infections, especially because of their location, other sexually transmitted infections. So that's why it's so important in evaluating the patients we do photo, history and physical examination, we in the sexual history illicit in sexual behavior, recent sites of exposure, you examine as I mentioned earlier, with good light, mucosal areas, areas that have been exposed, and then do screen for some of the sexually transmitted that we know including Monkeypox if the person has the right epidemiologic history as we have mentioned. If people have multiple sex partners, people who may have had anonymous partners, men with anonymous partners, where Monkeypox should be considered.

Thank you. Thank you again to our presenters and to our other subject matter experts for answering these questions and for sharing their expertise with us today. Today's COCA call will be available to view on demand a few hours after this live call ends at emergency.cdc.gov/COCA.

A transcript and closed caption video will also be available on demand on the COCA call webpage shortly after that. Continue to visit emergency.cdc.gov/COCA, to get more details about upcoming COCA calls. We invite you to subscribe to receive announcements for future COCA calls by visiting emergency.cdc.gov/COCA/subscribe.asp. You will also reference values other COCA products to help keep you informed about emerging and existing public health topics.

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