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THE 2022 MPOX OUTBREAK: WHERE ARE WE NOW?

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[video transcript]

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00:50
Good morning. And thank you so much for having me today to talk about the 2022 Mbox outbreak. Where are we now? In terms of disclosures, I have none. And the goals for today are to talk about the epidemiology of the 2022 Mbox outbreak, recognize the clinical presentation of impacts, and describe current testing and treatment recommendations for impacts in New York State. Just so everybody knows there was a terminology change. Following a series of consultations with global experts, the World Health Organization began yesterday using a new preferred term and pox as a synonym for monkey pox. And both names will be used simultaneously for a year. I'll try and use Mbox throughout today's talk, because that's going to be the new terminology moving forward, at least for now. So I want to just start from the beginning. And as with COVID, infectious disease, outbreaks can happen quickly. And that's what happened here. In early May, the first case of M pox was confirmed outside of endemic areas in England. This was quickly followed by other cases around the world, including the first US case about one month later. And what was just originally a few cases has truly turned into an A worldwide outbreak with over 80,000, almost 81,000 cases as of Monday's reporting. And this rapid increase led the World Health Organization to declare public health emergency of international concern on July 23, just 10 weeks after that first case was reported. And once again, the US is at the center of this outbreak, the US has had over 29,000 cases, and remains number one in the world. This led to on August 4, the US declaring the human monkey could or the impacts, or impacts virus, a public health emergency freeing up needed resources. And finally, within the United States, New York state remains number two with over 4000 cases. And as a sexual health practitioner in New York City. It's been my privilege to care for many of these patients, and to be able to share what I've learned with everyone today. Now, the good news is the cases are declining. But as you can see, they're not reaching zero. And so it's important that in spite of cases declining and maybe the major outbreak being over, then we continue to have a high index of suspicion and to be able to make this diagnosis when we see it in order to reduce the risk of future outbreaks. I always like to start by telling you a little bit about my first case of Mbox. The patient came in mid June, so very early on when there were few use cases. And there are a lot of features to this patient that we now recognize as being common to this outbreak. I'll also mention here that this patient, and many others you'll hear about today are real. Well I've changed their names and identifying details. These are all patients who gave me

permission to share their stories and photos and hopes that their experience can benefit others. So let's start with John. John's a mid 30 cisgender identifying now, he's living with long term well controlled HIV. He's sexually active with manages that for recent partners, all our partners he's known for a long time. And this is this all started when he noticed a mild mild eye irritation that he thought was allergies. Three days later, he started to feel warm, and found that in a temperature of 100.7 he had some worsening eye redness and drainage. And he actually thought it could have been from a recent sexual encounter, where he got some bodily fluids in his eye. It turns out that that partner had just told him that he recently tested positive for gonorrhea and chlamydia. And so John's primary concern was about having a gonorrhea or chlamydia infection in his eye. He went to the emergency department the next day, and this is what his eye look like at a time. As you can see here pretty significant conjunctival injection. In the emergency room they did the following workup. They tested his urine for gonorrhea and chlamydia which came back negative. They tested him for syphilis that returned positive at one to four consistent with a documented previously treated infection. His HIV viral load was undetectable Oh, as it had been for several years, his CD for cam was 282 down from 543, which was attributed to his acute infection. He was treated with one gram of stuff Traxion a higher dose than standard for his gonorrhea exposure in order to treat a presumed ocular infection. And he was also given doxycycline for seven days for as chlamydia exposure. ophthalmology was called and recommended antibiotic eyedrops and follow up in their outpatient clinic. Two days later, which is about day six after this all started, he was seeing an ophthalmology clinic. This is a photo from that visit. And as I hope you can see, he actually has these pustular lesions along the lower lid margin. In clinic, they actually did a gonorrhea chlamydia swab of the eye which came back negative and the bacterial culture of the eye which also returned negative. They recommended ongoing antibiotic treatment and drops. That same day, he texted me and asked if he could walk into sexual health clinic because he wanted me to look at his eye and test him for sector transmitted infections. I agreed although admittedly grateful he'd already seen ophthalmology for the eye. However, when he came to clinic, he told her triage staff that he had a weird rash with lesions on his left wrist, left forearm, left shoulder and scrotum. On my exam, this rash had lesions in several different forms, including a pustule, a manual and an ulcerated lesion. We thought about impacts at the time, however, testing was only available to those who traveled to Europe. He had not and his partners had not that he knew of. So in terms of my workup, I started by ruling out common causes. I did a herpes and Varicella Zoster swab of the pustule and center bacterial culture. They both came back negative. I completed his three site STI screening and want to highlight that his throat was positive for gonorrhea, reminding us the importance of extra genital STI testing. I also did a respiratory pathogen panel that was positive for rhinovirus and enterovirus because his gonorrhea was still positive. Although it was a few days early, I did repeat his dose of Secretary XO and because of the concern for bacterial infection, continued doxycycline monocultures were pending. I told him to stay in close touch with me. He actually didn't respond to my text over the weekend, but the following week was seen in ophthalmology clinic. At that time, he reported worsening eye symptoms with swelling, erythema and blurry vision. He also told the eye clinic that he had an increasing number of skin lesions, more on his extremities, genitals and feet. A repeat eye exam continued to show those papilla formed lesions along the lower lead. He messaged me the next day, and because of the increasing lesions we were able to arrange to bring him in for Mbox testing. These are actual pictures for that second visit. On the

left you'll see two lesions on the forearm. The one closer to the wrist was there at our first visit. That's the one I swapped for HSV VCV and culture. The one further up the arm was new at the second visit. He also had two lesions on his face that were not there the first time I saw him these are a Papillon ulcerated lesion both on his back. The papular can be very easily confused with acne or any other inflammatory skin condition. I ended up swapping the risk Legion and the pappy on his back for Mbox. Finally, on day 17 of his illness, his testing came back positive for Mbox for both swabs. By this time, when I called him to tell him his results, he reported that his eye was almost entirely better, and the skin lesions were healing. He went on to have no ongoing vision issues and healed completely and was able to return to his normal life. So as you can see, this case, this first case really highlights a lot of important points about the virus. So now that you've heard about this case, let's take a step back and talk about what is impacts and pox is an ortho pox virus. This means that it's similar to smallpox but not smallpox. However, the fact that it's similar is important, because it means that many treatments and vaccines for smallpox have the potential to work against Mbox as well. There are many ortho pox viruses that we know about, including Variola, which is a smallpox vaccine, Nia, which is what the smallpox vaccine is based on cow pox, rabbit pox, camel pox, Alaska Potts, and many other ortho poxviruses. There are two virus clades or type clade one which was formerly referred to as the Central African clade which has a mortality rate as high as 10% and clade two formerly referred to as the West African clade with a much lower mortality rate of around 1%. This outbreak has been primarily played to virus and claimed to be specific virus and because of a recent experience with SARS, cov, two and COVID-19 it's also important to highlight This virus is not. And pox is not a novel virus. It was first discovered in Africa in 1958, and research monkeys, which is where the name comes from. However, that name is more of a misnomer as the natural web reservoirs unknown, and it's known to infect both non human primates and African rodents. The first human case was described back in 1970, in the Democratic Republic of the Congo. And before this outbreak, nearly all cases were able to be linked to travel to Central and Western Africa. It's also important to highlight that this is not the first US outbreak. The first major US outbreak was in 2003, and included 47 cases traced back to pet prairie dogs. What this all means is that in spite of this outbreak being novel, we're not starting from scratch. We just haven't just six months, I can talk to you today about testing, treatment and vaccination for impacts.

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In terms of transmission, the biggest thing I want to highlight is it's not easily transmissible. It can be transmitted from animals to humans, like the prairie dogs I mentioned earlier. And animal to human transmission can be from direct contact with infected lesions or body fluids, contaminated fomites bites or scratches or animal products. While animal to human transmission does occur. In this outbreak, what we're really talking about is human to human transmission, which occurs primarily through three ways. direct contact with infected lesions or body fluids, contaminated fomites and exposure to respiratory secretions. So whenever I list these three routes of transmission, I get all sorts of questions about can I get, can I get Mbox in the bus or subway, the grocery store, clothing store, gym, salon, classroom, or any other place that I go frequently? And the answer is probably not. Well, I listed out three ways for human to human transmission to occur. The epidemiology of this outbreak has really highlighted one. And that's direct contact with infected lesions or body fluids through close personal skin the skin

contacts that like that occurs during sex is by far the most common way to acquire impacts. While contaminated fomites particularly soft, porous items, and respiratory secretions are all reported. That's not what we're seeing in this outbreak. For example, I like to use New York City here because we all know that New York City is very crowded, people are next to each other on the subway, they're crowded into stores, it's Christmas time and people will be gathering around the tree and other things. However, even in a crowded city like New York City, the vast majority of infections remain in men. There are a few children and individuals born female infected, which is not what you would expect to see in a crowded city if this was transmitted other than through close physical contact. If fomites and respiratory secretions were significant drivers of spread, we would expect a much more varied epidemiology. And I want to be clear that yes, anyone can get impacts. But in general, that's not what we're seeing. As overall numbers increase, we're seeing a slow expansion of the epidemiology with few women and children infected. Currently, the over 29,000 use cases, there have been less than 800 and women and less than 60 cases and children less than 16 years of age. So now that we've covered how it's spread, let's take a second talk about how it impacts presents. So this is the classic presentation, or what you would have expected to see if you read a book on Mbox. The vz starts with a viral program similar to many viral illnesses. This includes fevers, chills, headaches, malaise, myalgias and lymphadenopathy. After the prodrome, the patients usually develop a rash and the rash occurs before day five, usually days one to three. These rashes are traditionally firm, deep seated, well circumscribed, and sometimes I'm dedicated and I promise you'll see plenty of rash pictures coming up today. They classically start on the face and spread to the extremities, including the palms and soles, and they classically progressed through several synchronized stages, they can be painful, and lasts up to four weeks. So this is the timeline, it starts with an incubation period of five to 21 days. That means that after a significant exposure, it can be up to 21 days before you have any symptoms, although usually occurs around day six to seven. That's followed by the prodrome we described earlier, followed by an anatomy, which are lesions that start in the mouth. During this period, you can have infectious virus in your mouth that can spread through kissing and oral contact before you may even realize you're infected. That's followed by macules which are flat lesions on the skin. And because they're small and flat, they can be easy to miss. These are followed by papules which are solid and superficial, not yet fluid filled. They're less than one centimeter in size and look a little bit like acne These two progressive vesicles which are less than one centimeter filled with a clear fluid before further progressing to pustules, which are filled with a darker fluid. It's also during the stage when they can become a medicated developing a hole in the center, which is extremely classic for this disease. After that they start to scab. And it's important to note that the scabs are still infectious. Patients are not considered fully resolved and no longer infectious until the scabs have fallen off and there's new fresh skin underneath. Because of that the infectious period is long. The infectious period lasts from when the prodromal symptoms start until the scabs fall off. Patients can be infectious for as long as 28 days or longer, which makes this disease very challenging comanage. should understand how Mbox is presenting during this outbreak, we can look at a few of the early case series that were published. I did my best to put some of these findings into a table to help us see some of the trends. One of the first things that obvious is that the majority of cases in this outbreak are male, greater than 95% In most cases, compared to about 1/3 in the African case series. This is likely related to how the disease is transmitted across networks, more than anything about the virus itself. Another important thing

to note is that a disproportionate percentage of patients around 40% across studies are persons living with HIV. Second, is that while we're going to hear about a lot of other symptoms today, the rash remains common and appears in most patients. However, what you won't get from this table is that some in some cases the rash appears after other symptoms, instead of being the initial symptom. One of these major symptoms is rectal pain, presenting his proctitis within without 10 Asmus. This occurs between 14 and 36% of patients in these case series and is one of the major unique symptoms of this outbreak. And this symptom also fits with lesion location. The majority of patients have lesions on their genitals or anal and periodontal regions. These are frequently the locations the rash starts as well as differentiating it from the classic presentation. What's also interesting is that we're not seeing a huge number of lesions like those reported in the African case series. In many of these cases, the median number of legions is around or less than 10. So to briefly summarize the way Mbox is presenting during this outbreak, it's occurred primarily among gay, bisexual and other men who have sex with men. Among smaller numbers is transmitted to women and adolescents via close contact during sexual activity and young children via household spread. The prodrome may or may not be present, and may also occur after the rash or other symptoms. The rash remains common but it's presenting a typically, the rash is often starting in the general periodontal areas, and mucous membrane involvement is common. Scattered diffuse lesions, or localized with specific bodies that are both reported. And lesions in different stages of progression can be seen side by side. I want to highlight some of the more clinical presentations that we've seen, in particular because my impacts can be a severe disease. I want to take a second just to thank our patients again for providing us permission to share their stories and images. And as a reminder, some of the images in the next few slides may be graphic. The first manifestation I want to highlight is less severe, but not less important, and it's as viral like exact them. We're seeing this in numerous patients, and it was not reported prior to this outbreak, but tends to improve as the patients improve. It's important to think about this because you can look like many other viral or other infectious exam items. The next year, genital lesions and pox which we've mentioned numerous times, are very common during this outbreak. Here you can see these umbilical cord lesions on the penis, these umbilical cord lesions in the peri anal area, and vaginal umbilical lesions as well. In terms of significant presentations, ones that we're seeing both commonly and they can cause a lot of pain and discomfort to patients. There's this list here. The first one I want to talk about is proctitis, which has been incredibly common during this outbreak. proctitis can present with or without Peri Anaa lesions and can present with extreme pain. You know, we had one of our early patients presented without any periodontal lesions, but extreme proctitis. And the pain did not improve after greater than a week of supportive care. So this patient actually underwent a sigmoidoscopy to try to better understand what's going on. And you can see a picture of that here, but he actually had friable mucosa and ulcerative lesions up to 15 centimeters from the anal verge that tested negative for all of our traditional viral pathogens make it most likely consistent with an Hawkes proctitis. And so you can see these really painful lesions in patients. And this has been a very big reason for patients to present. The second thing I want to highlight is urethritis. So this was a patient who presented with dysuria, who initially tested negative for traditional STI pathogens. And actually, when he looked into his urethral urethral meatus, you can actually see he has lesions here, that were likely getting irritated every time he urinated. And so urethritis can actually be the presenting symptom. In this case, he presented with urethritis, but then develop skin lesions later on in his course. pharyngitis has probably been the

number one reason we've had to admit patients to the hospital. This is a lesion on the hard palate. However, we've not done any laryngoscopy to look at lesions down the throat, but patients are presenting with severe pharyngitis and an inability to swallow.

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And these are patients who are getting into the hospital for supportive care IV fluids and IV pain medication because they're unable to swallow or take anything by mouth. This was a unique case of presenting with periodontitis. This patient presented with European after a nonconsensual bite on his ear that then had progressive disease. He also developed prodromal symptoms and rash several days after developing this STR at the site of the bite. Ocular disease has been well reported and pox both in the United States and in Africa. This recent CDC report describes five cases with ocular Mbox, who also experienced delays in treatment initiation, prolonged illness, hospitalization and and vision impairment. You know, it's a good reminder that ocular monkey box can be a sight threatening, in fact condition. Were very lucky in that initial patient that I described because it took us a long time to make the diagnosis that didn't have any long term complication, but other ones can. And so it's important that patients with ocular impacts be considered for urgent ophthalmologic evaluation and treatment. lymphadenopathy is a another frequent presentation, patients can present with significant lymphadenopathy usually in the region of the initial infection. So for example, in patients with pharyngitis they're often presenting with cervical lymphadenopathy. And there are actually case reports of patients with such significant cervical lymphadenopathy that they required intubation. For patients with genital lesions they often present with inguinal lymphadenopathy. In this particular case, this patient presented with super pubic lymphadenopathy and came in describing it as like walking with a fanny pack. And you could see that he was actually struggling to walk due to the pain lymphadenopathy is one of the classic presentations of Mbox it's one of the things that separated from smallpox when that was still around, and it can be quite severe and quite painful for patients. The next thing is bacterial superinfection. And I put these four pictures here because I want to tell you that we've had a lot of patients with genital infections that look very impressive. These are patients who are presenting with general infections that become super infected. It's not uncommon when you have skin breakdown in the groin for bacterial superinfection to occur. And these patients were actually all managed with outpatient oral antibiotics and wound debridement in consultation with our urological services. And so the teamwork aspect is really important working with your colleagues in other services to help manage these more complex presentations. In this case, I can actually show you the same four patients later, all of whom healed I apologize, I don't have later pictures for some of them, but all of them who healed well, all of them that have no loss of sexual function, and all of them were able to be managed as an outpatient. And you can manage pretty complicated bacterial superinfection as an outpatient for these patients. One of the other the most significant presentation has been these patients with persistent progressive disease. The CDC recently put out an mm WR covering a large number of these patients and over 70% of them had HIV with low CD four counts or AIDS. Patients with age level trouble clearing this virus and can present with extremely severe disease lasting for weeks to months if they don't receive any supportive care and treatment. This was a patient that we recently had in the CDC MWR 12 of their patients or 21% of the total patients in their cohort actually passed away thought to be related to Mbox disease, and this is a patient's facial lesions. And he also had a pretty significant and

severe genital lesion as well. And so patients with who are immunocompromised whether it's for with AIDS with sed for low CD four counts, or patients are immunocompromised for transplant or other reasons, definitely need to be prioritized for vaccination if their risk and for treatment, which we'll talk about later, if they have an infection. Finally, the last one is encephalitis. There have been cases of patients presenting with in several encephalitis, who had pretty bad outcomes as well including death And just this is the CDC MWR that I mentioned recently talking about looking at severe monkey pox in hospitalized patients during the start of this outbreak. So just some lessons learned from the significant presentations. You know, the significant presentation may be the presenting symptom, many patients actually present with proctitis urethritis. Ocular symptoms that occurs pre rash or pre prodrome we definitely need a high index of suspicion, especially if we have a reasonable pretest probability. And most patients can be matched in the outpatient setting in consultation with sub specialists. The differential diagnosis for empaths really overlapped with a lot of what we do in sexual health. The Diffuse rash can look a lot like syphilis, varicella, HSV, molluscum, other poxviruses, disseminated fungal infections, disseminated gonorrhea, and a few months ago, enter a virus infection, hand Foot Mouth Disease, which was extremely prevalent before our current outbreak of flu and RSV everywhere. For patients with genital lesions, it can look a lot like HSV, syphilis, shank, right and LGV. And for patients with proctitis, gonorrhea, chlamydia, HIV and syphilis are on the differential. You'll notice they made syphilis red because it shows up in all the categories. But also because it's the thing that I've been fooled by the most in patients that I thought might have impacts who actually ended up having syphilis. It's important to know that just because they have impacts doesn't mean they can't have another sexually transmitted infection. In this CDC report of the first 2000 patients 38% of patients diagnosed with Mbox were living with HIV and 41% had an STI in the past year. So hopefully, I've established that Mbox is presenting a typically can be a devastating and painful disease. And so how can we help patients prevent disease. So one way in our best way to or one way to prevent infection is through changing behaviors. The CDC has put together several great resources, including this one on safer sex and Mbox. And Dr. Daskalakis, from the CDC has made several videos and community engagement efforts to talk about how individuals can reduce their personal risk of Mbox especially while awaiting things like vaccination. This was an early report from the CDC that demonstrated that very early on in this outbreak 50% of patient about 50% of patients reported a decrease in the number of partners, a decrease in one time sexual encounters, decreased sex with partners meant on apps or sex venues, and decreased group sex 42% reported decreased going to sex vet and using events and 35% reported decrease going to social events with close contact like dance parties and raves. So the one thing I always say about behavioral interventions is that it's not long term change. behavioral interventions are very effective as a bridge to something else. But we can't expect people to change their behavior forever. So what in this case behavioral change led to was vaccination, and the best way to prevent disease is through vaccination. For impacts there are two main vaccines. The first a cam 2000 is a second generation smallpox vaccine that is live vaccinated virus. Just like with first generation smallpox vaccines, you get a lesion or a take inoculation site, and it only requires one injection with a booster every three years. This is approved for individuals aged 12 months and up. The second is the genius vaccine. This is a third generation smallpox vaccine. It's a live non replicating virus, meaning it does not cause human disease. This requires doses four weeks apart, with maximum unity occurring 14 days after the second dose. It requires a booster every two to 10

years and is approved for those age greater than 18. Although a recent emergency use authorization allows for its use in pediatric patients as well. The vaccine can be used for both post exposure prophylaxis and pre exposure prophylaxis. For PEP, it should be given as soon as possible after an exposure. While there's no human efficacy data for PEP, non human primate and other animal models suggest that giving the vaccine within four days may prevent disease, while giving it up to 14 days after an exposure may reduce symptoms. I'll also highlight here that for those that can't receive vaccination for PEP, or whom vaccination would not be expected to elicit a response. Vaccine immune globulin is also available for PEP through an IND. For PrEP, the longstanding recommendation has been to vaccinate clinical research lab workers, as well as public health response team members. However, during this outbreak, we've started to vaccinate epidemiological risk groups as well. So how effective is vaccination does vaccination prevent and pox the truth As it currently we don't really know the best data we have. And when you hear that 85% Number talked about, know that it's from patients from 1980 to 1984, and Africa vaccinated with the first generation smallpox vaccine. The hope is that observational studies have and will continue to give us a sense of the effectiveness of vaccination. When we talk about vaccination, we really don't have a lot of human efficacy data. When we're talking about assessing the effectiveness of a cam 2000. The FDA approved it by comparing the immunologic response or immuno bridging compared to the first generation smallpox vaccine, which is Dr. Max. Virginia knows, the FDA assessed and approved it by comparing immunologic response or immuno Bridgen to a camp 2000 and animal studies. So as you can see, we don't actually have human efficacy data for either of these two vaccinations.

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One of the questions I always get about this is does long term or prior vaccination protect against Mbox? And the truth is, again, we don't really know the CDC does recommend repeat vaccination if your vaccine was greater than three years ago. I will say that we do have one case report of this. It was a 34 year old MSM who percentage STI clinic. He'd been vaccinated about eight years prior while in the military with the smallpox vaccine. He had four days of fatigue, headache, malaise, and for painless penile lesions. He was diagnosed with Mbox and his lesions healed without scarring. What's impossible to say from the single case report is what's his was vaccination. The reason is infection was mild, it contained primarily to his genitals, or was vaccination worn off by that time and really had no impact. And the truth is, without bigger and larger studies, we just won't know. In terms of observational data, we do have this one study from the CDC. It certainly has its flaws, but it definitely implies the vaccination is helping, we just don't know by how much. In this case, they looked at people eligible for the impact vaccine. And they found that there was one infection among people receiving one dose of vaccination compared to 14 infections among people receiving no doses. Again, this is certainly just an observational study with lots of limitations, but it does suggest that vaccination has a benefit and protecting individuals against NParks. One of the other big questions we often get is about intradermal dosing. So an EUA came out back in August, that allowed individuals under age 18 to receive the vaccine subcutaneously as per its license. However, it also allowed for individuals age greater than 18, to be given the vaccine intradermally intradermal vaccination is 1/5 the dose of the subcutaneous dose, and the hope was an intradermal dosing could increase the supply by five times. This was based on a study that was done for smallpox to look at if we were in a situation with decreased vaccination about

availability, could we extend the amount of doses we had through intradermal dosing. That study did find the lower intradermal dose was immunologically non inferior to the standard subcutaneous dose. The intradermal route did result in more erythema and in duration than the subcutaneous route. So you're getting more redness and swelling than subcutaneous injection, but that the intradermal route may increase the number of available doses in an emergency situation. And as, as many of us remember, a few months back, we really did have a significant shortage of N pox vaccination, particularly with a third generation vaccine. And so this was a strategy that was used in many jurisdictions to extend the availability of vaccination to more patients. We don't know a lot about it. And so the NIH did put together a rapidly developed vaccine trial to better understand the immunogenicity of the dose reduction strategy of genomes for impacts. It was a phase two trial so not a phase three efficacy traveled a phase two trial, with 210 participants getting three in three arms, each getting two doses. And the primary outcome was again, not efficacy, but antibody changes, and to hopefully that will give us more immunologic data about this dose reduction strategy. I always get asked what I tell my patients about preventing Mbox. And the truth is, it's similar to what I tell them for anything. First, it's get vaccinated if you're eligible. Know that it may not be 100% effective, but it likely provides some protection against disease and especially severe disease. before engaging in sexual activity. Talk with and check out your partner. have open conversations about symptoms or exposures. Examine yourself regularly. See your healthcare provider if you find anything suspicious. If you're having prodromal symptoms and think you're at risk, please self quarantine, and boxes unlike unlikely if a rash does not appear within five days. As important as anything else and pox is not something to be embarrassed about. It's transmitting just like many other sexually transmitted infections. So if you're unsure, come in and get tested

35:11
so now that we know what to look for and how to prevent it, if a patient comes in how do we diagnose them pox. The most common way is to do a swab of the lesion and send it to either your local lab, a commercial lab or the public health lab. Lesions tend to have extremely high viral loads, and so you don't need to improve them, but just swab them vigorously and follow local procedures for the medium and sending it to the lab. I also please avoid unroofing if possible, there are numerous case reports now of individuals acquiring and POCs through a needle stick after unrefined ripping a lesion. Again, these lesions have extremely high viral loads. And so it's not surprising that if you were to stick yourself with a lesion that you just unroofed after just unroofing, a lesion that you could acquire it that way. It is good practice to swab at least two lesions as we have had somewhere one of the two lesions tested negative. People always ask the metrology and it does exist to the Orthodox virus. In general, the IgM will turn positive about five days post rash onset, while the IgG turns positive at eight days post rash onset. It's unclear during this outbreak if it's truly from rash onset, or could be from other symptoms that they start first. One of the major challenges is that this asset cross reacts with like sending a virus. So people will test positive after receiving vaccination, which many patients at risk are now receiving. And finally, it's not easily commercially available. Although it is available through the CDC if needed for special cases. I always get asked if current testing is enough. There are a lot of studies like this one, where there were 70 men who presented with Mbox 26 or 37%, with proctitis 42% of those with proctitis. The practise preceded the skin rash. So the first symptom they had was proctitis. Again, going back to the people are presenting with

symptoms other than rash and developing the rash later. However, in this case, 23% of those patients proctitis was the only clinical manifestation and they never developed a skin rash. So they never developed the rash. How could we make the diagnosis This is another example of that. They actually went back in Belgium and retrospectively screen 224 samples that were originally collected for gonorrhea and chlamydia testing, and random Mbox PCR essay on them. They found four positives, three of the four never developed any symptoms. All three had positive serology, and two of the three had culturable virus, suggesting that asymptomatic infection as well as asymptomatic spread as possible. So is current testing enough? I think the answer is probably not. You know, future of diagnosis probably includes PCR from other compartments that's available currently in other countries, but not commercially available in the United States. In the future, I do suspect that we'll see multiplex assays with things like HSV VCV, as well as gonorrhea, chlamydia, making the diagnosis easier in the future and making it available to more people. So now that you've made the diagnosis, how do we treat and pox? What can we offer them? The first and most important thing is that most patients fully recover with or without treatment. As we as I mentioned earlier, there's been over 85,000 worldwide infections, with only a handful of deaths, something like 32 or so deaths at the last time I looked. However, while not many patients have died, there is considerable morbidity and supportive care can help patients when they're recovering. Most of the symptomatic treatment recommendations are not strictly evidence based, but they make sense, and the CDC collate the experience from a variety of providers to put together a Dear Colleague letter. In terms of what they put in this letter supportive care recommendations include for proctitis things like stool softeners, to decrease pain and going to the bathroom, and especially for patients who may require opioids for pain control. Topical agents like sitz baths and lidocaine gels, but be careful with immunosuppressive that have the potential to worsen disease. pain control with over the counter pain relievers like NSAIDs or Tylenol, and finally prescription analgesics like Gabapentin and or opioids if needed. I always recommend carrying consideration with opioids due to the risk of constipation making things worse, but there are patients whose pain we were not able to control in any other way. For pharyngeal disease. We have topical agents like viscous lidocaine and saltwater gargles as well as over the counter and prescription pain relief. Finally, well not in the Dear Colleague letter, we found that the biggest complication with genital lesions is bacterial superinfection. So we recommend trying to keep that area clean as best you can. And if infected, consider topical or systemic antibiotics as well as what to dry dressings for patients who may He needs a mild to bereavement. supportive care works for most patients, but some patients do require an antiviral medication. At one point in New York City estimated that about 25% of patients required antiviral treatment. In terms of indication for treatment, there are three categories severe disease presenting with sepsis or requiring hospitalization. Evidence of viremia or lesions is concerning locations like the eye pharynx, rectum urethra and vagina. There's also patients with illness complications like secondary infections proctitis Whitson Asmus, uncontrolled pain, rectal bleeding, gastroenteritis, pneumonia and encephalitis. Finally of groups of people at risk of severe disease, which includes persons living with HIV with a low CV for count or high viral load, individuals who are severely immunocompromised, it used to be children less than eight but they've recently actually edited that to be children less than one year of age, pregnant women, individuals with significant exfoliating conditions and those at increased risk of complications like those living with inflammatory bowel disease. First one therapy that we have to talk about is antibody therapy with vaccine immune globulin. Vaccine

immune globulin is available through the CDC through an IND. And it's primarily been used for individuals with severe disease who are immunocompromised, so it is available for those patients, particularly those with severe and persistent disease are unlikely to mount an immune response on their own. They've been using this pretty aggressively and patients with HIV and who are immunocompromised. After vaccine immune globulin there's antiviral medications, and there are three systemic and one topical that I'll review. Remember that orthoplex Viruses are not herpes viruses, and Acyclovir which requires phosphorylation is not going to be active. However, both cidofovir and brincidofovir are potential agents against orthoplex viruses. cidofovir acts as a competitive inhibitor incorporated into the growing DNA strand blocking DNA synthesis. However cidofovir Its use is limited due to significant renal toxicity. Given the low overall mortality of this disease, and the significant risk of renal injury with cidofovir. This drug has rarely been used except in the most severe cases. brincidofovir is similar but to pro drug. It has a side chain that gets cleaved releasing cidofovir and is thought to have less renal toxicity. brincidofovir is now available through the CDC through an IND. However, in England, the first three patients were treated with oral brincidofovir. That's seven days after rash. All three patients developed develop elevated liver enzymes, and none were able to complete the course of treatment. In some ways dampening enthusiasm for this agent. It is available through an IV D through the National Stockpile. However, one of the other major side effects of it is gi including diarrhea. And so there is some concern that you're using it with something like Tyco VR mat that you actually may get decreased absorption of TECHO VR mat due to the side effect of brincidofovir. So again, it's being reserved for only the cases that are not responding to firstline therapy and patients that are extremely severe. Next, I'll mention this one only briefly, but try Florida and drops. These eyedrops are FDA approved for herpes infection of the eye and are thought to have activity against orthodox viruses. They've been recommended by the CDC in most cases of severe ocular disease. Echo Vera Matt is the drug has been used as first line during this outbreak. It's an antiviral drug initially developed against Variola to treat smallpox infection, and works by inhibiting viral protein ki 37. This protein is highly conserved in Orthodox viruses, allowing takeover you're meant to have in vitro activity against many or most orthodox viruses. It was approved in 2018, but it was approved via the FDA animal efficacy rule or animal rule, which allows a pathway for approval of drugs for severe or life threatening conditions when it's not ethical or feasible to conduct efficacy and human trials. And so it can't be used off label the same way we can use other drugs off label. Because it was approved for smallpox through this animal rule, we had extremely limited human data on this medication prior to this outbreak. efficacy data was done entirely through animal studies. And the human safety data that led to its approval included only 359 patients with only one serious adverse event not attributed to the drug.

44:36

In terms of efficacy prior to this outbreak, there was really this one paper published, which was the seven patient cases included three got brincidofovir and this series one patient was treated with that Govier Matt experienced no adverse effects and had a shorter duration of viral shedding illness. Hopefully we all recognize though that one patient is more anecdote than data. And I'm sure we'll see more during the course of this outbreak. But we've already started to see case series, a case series of two patients whose practice improves and takeover format and a series of 26 cases as well. There's also this case series from the CDC that had 549 patients,

although 100 Only 174 had intake and outtake forms. What I take from this CDC study that the most important though, is that TECHO Vir Mehta appears relatively safe. Under the 549 patients, there are only 12 adverse events, none of which were labeled as serious. So just to review them at work for impacts, and the answer is we just don't know. These case reports don't remove the need for clinical trial, they can help us know definitively whether this drug works and is safe. We need to know this because it's important to gain support for local and worldwide distribution, and to not have to use it under solely an IND, we need to learn if the virus developed resistance to the drug. We need to understand if there are markers that tell us the drug is working so we can identify future promising drugs. If it doesn't work, we're spending time and money that could be used to find drugs that do so the NIH funded a rapidly developed treatment trial as well. The study of tegova mat for human monkeypox virus stomp it's a two to one randomized blinded placebo controlled trial with an open label arm available for certain populations, including pediatric patients, individuals with severe disease as defined by the study and pregnant or breastfeeding women. So our patients are diagnosed, what do I tell them? Well, I told them that we have supportive care options and a clinical trial available to all patients. We have E ind treatment options for patients with severe disease, stay home and separate from others in your household. If you can't fully separate, wear a mask, avoid physical contact and cover your lesions within shared spaces. If you must leave home, cover your rational agent with clothing and wear a face mask. Patients always want to know when they can have sex again after Mbox. And the truth is there's very little data, the CDC suggests considering condoms for a minimum of eight weeks after infection, the WHA who is suggested considering condoms for a minimum of 12 weeks after recovery. But the truth is at this point, we just don't know the right answer. To wrap up today, the 2022 impacts outbreak spread rapidly and can be serious. It is not presented classically, but is presenting commonly with genital urinary, rectal and pharyngeal complaints. It commonly looks like other sexually transmitted infections. So don't forget a detailed sexual history of exposure history. It can present concurrently with other STIs. So make sure to get complete STI testing. We have supportive care in a clinical trial option for all patients. We have E ind treatment options for patients with severe disease. What we really need are more studies to better understand the transmission dynamics, prevention and treatment options and long term outcome of this disease have a low threshold to think about impacts in patients with a rash. And this disease can be severe. Patients are grateful for our support. This is just some information about the clinical trial stomp. You can get more information at stomped epochs.org. Or you can refer patients to call center to connect to local sites. This was a huge presentation. I just want to make sure I thank everybody who helped contribute to this over the past six months, including Columbia, New York Presbyterian, the CVC, New York City doh and everybody else is the CI slide. And I will take any questions now. Thank you guys very much.

48:27
Wonderful, thank you Dr. Zucker. I see one question in our q&a box that says has the CDC recommended yet of health care workers should get vaccinated for chickenpox.

48:37
The CDC has not necessarily recommended the health care workers get vaccinated if they're not at risk outside of work.

48:45
Dr. Zucker, that was really a terrific presentation. I have a couple of questions that I'll hold unless there's another one. If there's others that come in, but while we're waiting, do you have any? I don't know if I missed this. Are there any data about its natural infection providing durable immunity? So we don't

49:10
know yet? You know, the current suspicion is that yes, it provides some level of immunity. The question is exactly how durable that is? I don't think we know.

49:20
And has there been any talk about boosting people who, who get the primal series? I guess, sort of similar questions.

49:29
We've talked about that a lot. You know, the initial thought was that yes, we can offer them a vaccination in the future only because in some ways we suspect that combined vaccine plus natural immunity may be superior, but there's not a formal recommendation on that, or timecourse. Currently, what we're telling people is that we should readdress this when vaccination becomes more widely available, because we're we're pretty confident that they're at least immune for the immediate period of time after infection, and then we can re address it when vaccine becomes more available. I know many of my patients do want vaccination, and I'll likely vaccinate them once vaccination is more widely available.

50:07
One thing we've seen far less than you have in upstate New York, but I've really been struck by the patients that have come to our clinic have sort of how unpredictable it is of those who will develop severe disease. Like we've seen some people, you know, you see them on Monday, and they seem great and think, Oh, this isn't somebody who needs treatment, they're going to do fine. And then, you know, three days later, they're really quite ill. And vice versa. Yes. So do you have any thoughts on that? Is it sort of mechanism of inoculation? Are you more likely to have severe disease if you had, for instance, receptive anal intercourse? Or? Yeah,

50:46
I mean, you know, one of the challenges around this is like, what is severe disease? Right? Like, I think it's pretty clear that the patients who have a low CD four count, who developed this persistent progressive disease for months on end and end up intubated, or in the ICU, have severe disease, you know, we have a lot of patients who present with mild proctitis, and then come back with more severe proctitis, some of whom, though, declined to go beyond that, and improve on their own. And so sort of the sort of definition of this one is tricky, because as I said earlier, you know, hospitalization or mortality is extremely rare. Most patients will get better with or without treatment. And the trick is figuring out which ones will really a benefit from treatment, if it works, and which ones really need it. And so I think it's a really tricky question, you know, we are still offering it to our immunocompromised patients, for sure. And we're offering to patients who meet criteria, but we're also trying to encourage them to enroll in the study so we could get

a better understanding of whether or not this treatment works, but also the natural history of disease. You know, one of the big challenges is the natural history of disease is still not fully known. And so they're doing natural history studies as well to better understand, you know, virologic outcomes, how what the viral logic course looks like, and things like that. I think that all plays into your question about severity, because I just don't think we understand well enough yet, who's going to go on to more severe disease or even what more severe disease is?

52:04
And how are how are you dealing with? I think sort of the positive predictive value has gone down as the outbreak has waned. So now you have you know, syphilis hasn't really waned. But monkey pox can look like syphilis. So are you testing everyone or you know, how we

52:26
were continuing to test anyone who has either you know, who has a rash and either an epidemiological risk factor, or a rash that looks classic. And those are the two things we're trying to talk to our IDI about, you know, children who have no risk factors, and no epidemiological risk factor, who are five years old are unlikely to have Mbox. And so we should only really be testing people who have a rash and an epidemiological risk factor, or don't have a known risk factor, but have a very classic looking rash. And I think that's how we're getting there, especially as you said, the, you know, our pretest probability has gone down to our percent positives have gone down a lot.

53:03
Okay, Dr. Zagreb, we have a few for more questions in the chat. So I just wanted to launch into a couple of those. First is what are your thoughts on the future of impacts in the US?

53:17
I think it depends a little bit on how effective and long term vaccination is, you know, a vaccine vaccination is actually protective against disease entirely, then there's a chance to mostly eliminate it during this outbreak, although it's still a zoonotic disease, and so we'll never be able to fully eliminate it. But this outbreak could get to zero. If vaccination is protected against more severe disease, but shishi patients can still get it and still become infected, kind of like we see with flu or SARS, cov, two or other things that I expect we'll see more endemicity, and we'll see more ongoing transmission with scattered outbreaks occurring.

53:51
Thank you. Next one, if a patient does not receive treatment and symptoms resolve, would it lead to harsher outcomes similar to syphilis?

54:04
We don't believe so. You know, the vast majority of patients are not treated. So remember that treatment is only available for those with with severe or at risk of severe disease, because we don't have an FDA approved treatment. So most patients do not get treated, and most patients do very well. We've actually not seen so far in our cohort, any of those long term concerns that were sort of at the beginning of the outbreak, like scarring and strictures. And those are

primarily only been reported in the most severe severe cases and Towbin extremely rare outcomes.

54:34
Thank you Next one. Apologies came in late. Do we have updated recommendations for boosters after receiving the initial two doses? Of

54:45
not at this time? You know, there are some recommendations they initially said two years and they said two to 10 years after? I think probably ongoing immunologic studies will help answer that question a little bit better. But right now we have at least a minimum of two years if not longer before boosters would be needed.

55:02
So here's another one. Thank you for this great updated information. I work with a largely older LGBTQ plus population. Are there any observations you've made with the older population that have not been reported with the younger population? With an older population? Are they seeing diagnosis and treatment later in the disease process? Many of the older population are to seek treatment sooner.

55:30
Yeah, I mean, I think it's like anything, you know, it's just like HIV testing. It's just like STIs. You know, older patients are more likely to be diagnosed later, people are hesitant, you know, people are hesitant to take a sexual history, particularly younger people hasn't taken sexual history from people who look like their parents. And we just need to do a better job overall, providing better sexual health to our older patients. That's not just related to Mbox, related to HIV testing, and STI testing as well. These are the groups that are often overlooked in these care settings. And so we need to do a better job of them. They're also the group that's more likely to have a primary care doctor, and maybe a little bit less likely to show up to a sexual health clinic, because they have ongoing primary care. And so it's really important that we work with our primary care doctors to make sure that these people are receiving good sexual health care, in addition to their other primary care needs, like hypertension, diabetes, cholesterol, and everything else.

56:18
Great. Thank you. Next one, and this is something I think you alluded to earlier, the New York City Department Health Department now says that people are eligible for M pox vaccine if they consider themselves at risk through sexual exposure. So should we now be encouraging vaccination for all sexually active men who have sex with men?

56:43
I'm thinking about how to answer that question. I don't know if encouraging is the right way. I think shared decision making is the right way. Right. So I think it's talking to your patients about what their individual risk level is, you know, there are patients who see me for primary care who are men who have sex with men who are married and monogamous, and their partners are also

monogamous. And they don't have any outside partners. And so their risk is extremely low. And so the question is really for them? Do they want to get an additional vaccination or not? On the other hand, for patients who are, you know, attending, you know, on site sex venues, I think encouraging them to get vaccinated is very important. And so I think just like any other prevention method, talking to your patients about their personal risk level, and taking a shared decision making approach is best. But certainly the vaccine is safe, and we should be encouraging for anybody who is potentially at risk for this virus.

57:30
Right. Thank you. I think it's 959. We'll do this one last question. Are there any studies being done for the immunity time for those who are vaccinated and those patients who recover without medication or and vaccine,

57:47
there is not a large na child study in a trial type for that, but I know there's a lot of local sites looking at that information for their individual cohorts. Great.

57:58
Thank you so much, Dr. Zucker.

[End Transcript]