

A Position Statement on Monkeypox as a Sexually Transmitted Disease

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Executive Summary

The rapidly developing outbreak of monkeypox constitutes a national and international public health emergency. Our current public health strategies are predicated on transmission dynamics from historical outbreak. Numerous reports from the current outbreak have highlighted 1) a temporal association between sexual activity and monkeypox disease, 2) an association between specific sexual practices and location of lesion development, 3) that specific sexual practices conferring risk for other sexually transmitted infections occur with notable frequency among cases of monkeypox, 4) that *Monkeypox virus* can be detected and isolated from sexual fluids, and 4) a high frequency of anogenital lesions prior to disease dissemination suggesting direct inoculation during sexual activities. Finally, a growing body of evidence suggests that sexual transmission is the *predominant* mode of transmission for *Monkeypox virus*.

We therefore conclude that monkeypox is a sexually transmitted disease. Labeling it as such will help focus our public health interventions, such as vaccinations, testing, and treatment. Moreover, understanding the primary mode of transmission can help facilitate focused awareness and education programs, as well as allow for behavioral modifications to reduce exposures, which in turn may augment outbreak control efforts and prove to be cost effective. We recommend that governments and other policy-making bodies define monkeypox as a sexually transmitted infection for monkeypox.

Introduction

The United States and the World Health Organization have declared monkeypox a public health emergency (1, 2). Outbreaks of monkeypox in the past have predominantly been short-lived, limited to already-endemic regions in Africa, with transmission described as occurring via animal-to-human and human-to-human through close physical contact (3). Since May 2022, however, the large outbreak of monkeypox in the United States, Europe, and now 109 countries (4) have near-universally highlighted the role of sexual transmission (5-8).

The understanding that monkeypox is a sexually transmitted disease is gaining increasing recognition (9-12). Sexually transmitted diseases are caused by organisms which are predominantly, though not exclusively, spread through sex. Those include common pathogens such as human papillomavirus, human immunodeficiency virus, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Treponema pallidum* (the cause of syphilis), and *Herpes Simplex Virus Types 1 and 2* (11). Other pathogens, however, which are predominantly transmitted through close contact, insect or animal vectors or contaminated food or water may also be occasionally transmitted via sex, including *Ebola virus*, *Zika virus*, and *Shigella* (13). Those infections are considered sexually transmissible, but not sexually transmitted because the primary mode of transmission is not sexual contact.

We synthesized the current scientific literature detailing the evidence for the predominance of sexual transmission for *Monkeypox virus* (Table) in the 2022 outbreak. We highlight the reasons why identifying monkeypox as a sexually transmitted disease is justified and important.

Monkeypox is a Sexually Transmitted Disease

The most commonly utilized framework for evaluating epidemiologic evidence to determine causality is the Bradford Hill Criteria, based on nine aspects of epidemiologic association: strength of association, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, and analogy (14). Sexually transmitted diseases are typically defined as being caused by an infectious microorganism transmitted from one person to another through bodily fluids (blood, semen, saliva, or vaginal, rectal or urethral fluids) during oral, anal, or vaginal sex with an infected partner (15) or direct skin-to-skin contact through macro or micro abrasions of epithelia or mucous membranes during sexual activities. Thus, to classify as a sexually transmitted disease, monkeypox must be predominantly transmitted via sex either through bodily fluids or direct contact with infectious lesions in the genital area, rectum, or oropharyngeal cavity. The Bradford Hill Criteria may be applied to the current body of epidemiologic literature in the large monkeypox outbreak of 2022 as follows.

Monkeypox is Strongly Linked to Sexual Activity

There is a strong association between sex and monkeypox. Thirteen different published series from 17 countries report that between 84% to 100% the 2,483 cases reported sexual activity, most with a new sex partner, prior to the onset of symptoms (5-8, 16-19). Furthermore, among cases of monkeypox, sexual practices conferring elevated risk for other sexually transmitted infections occur at a high frequency among cases as well as with a temporal association between the sexual activities and the disease. Such practices have included attending sex-on-site venues, multiple recent sex

partners, group sex, substance use during sex, and condomless receptive anal intercourse (5, 6, 8, 17, 18). One series, for example, reported that the risk of proctitis due to monkeypox was 5.5 times higher among those who recently engaged in receptive anal intercourse, and that 95% of patients who presented with tonsillitis reported receptive oral sex in the preceding days (8).

Another case series concluded that all 21 secondary cases – patients with monkeypox for whom the index case could be identified – were likely due to sexual transmission – based on anogenital and perineal localization of the rash in 72% of cases, associated inguinal lymphadenopathy in 72% of cases, and frequent report of sexual activity including condomless anal sex and sex with multiple partners within the preceding three weeks among 84% of cases (17). Another report of more than 500 cases similarly noted that the clinicians seeing patients with monkeypox suspected sexual transmission in 95% of cases (6), although the specifics on how that determination was made were unavailable in the report. Finally, among the published studies during the current outbreak in the United States and Europe, the proportion of cases in which non-sexual household transmission was suspected ranged from 1% to 3% (6, 8), further supporting the nearly exclusive sexual spread of monkeypox, at least within the United States and Europe.

Thus, according to the Bradford Hill Criteria, the association between monkeypox and sexual transmission thus far fulfills three important requisites: strong association, consistency across time and geographic location, and temporality (see Table).

Monkeypox is Transmitted Through Sexual Fluids

Monkeypox is an orthopoxvirus in the *Poxviridae* family and its genetic material is double stranded DNA. In addition to skin lesions, monkeypox viral DNA has been consistently detected in seminal fluid (6, 18, 20), rectal swab specimens (18, 21), saliva and respiratory secretions (3, 18, 22), as well in from the blood (22). Further, a recent study identified protracted detection over 19 days of monkeypox DNA in the semen of an infected individual (20). Those investigators additionally isolated *Monkeypox virus* from semen of that individual and subsequently demonstrated infectivity of that cultured virus *in vitro* after six days (20). Another study reported high monkeypox viral loads in semen samples (18). Similarly elevated viral loads from samples in animal studies have been correlated with infectivity (23). Thus, it is biologically plausible that the sexual fluids transmit the infection.

Furthermore, during the current outbreak across the United States and Europe the characteristic rash of monkeypox frequently localizes to the genitalia and within the rectum (5-8, 16-18, 24). *Thornhill et al.* reported that 383 (72.5%) of 528 cases of monkeypox had anogenital lesions (6), while *Iñigo Martínez et al.* reported that 359 (72.1%) of 498 cases had anogenital lesions (17). Notably, anogenital lesions often develop prior to further dissemination of the rash to other parts of the body (6-8, 16, 24). Those findings suggest direct inoculation of the infection during sex either through exposure to infected fluids or through direct skin-to-skin or mucosal-to-mucosal contact. Notably, while reports have indicated high monkeypox viral loads from swabs collected from saliva and the rectum (18, 25), one study demonstrated significantly higher viral loads from lesion swabs compared to pharyngeal swabs, further suggesting direct

inoculation from contact with a lesion during sex may be a principal mode of transmission (25).

Such transmission dynamics would explain the vastly disproportionate burden of monkeypox disease among gay, bisexual, and other men who have sex with men, who constitute 92%-100% of reported cases (5, 6, 8, 16), as well as the high prevalence of concurrent sexually transmitted infections (17-29%) among patients with monkeypox in the 2022 outbreak (6, 8, 18). Thus, two more Bradford Hill criteria, plausibility and coherence, can be added to the justification (see Table).

Monkeypox is Not Exclusively Sexually Transmitted

Globally, the World Health Organization recognizes more than 30 sexually transmitted infections including monkeypox (11). Yet sometimes distinguishing between those infections which are *transmitted* (i.e., the 'primary' mode of transmission is through sex) and those which are *transmissible* (i.e., transmission may be sexual but the 'primary' mode of transmission is not sexual but through other modes) is challenging. Quantifying the risk of sexual transmission when other modes of transmission exist is difficult and additional data beyond information obtained from a sexual history can be helpful. Prior work has suggested utilizing genetic concordance between strains, models of the probability of transmission per coital act, and the proportion of cases attributable to sex, among other factors, as means of distinguishing sexually transmitted infections from sexually transmissible infections (13). Such factors may be necessary to satisfy Bradford Hill's specificity criterion.

Yet, while monkeypox is not *exclusively* transmitted through sexual activity (3, 6, 8, 26), such does not preclude it from being considered sexually transmitted. In fact, many infections recognized as sexually transmitted infections by the World Health Organization similarly have secondary modes of transmission (11). A related poxvirus, *molluscum contagiosum*, can be transmitted via both skin-to-skin contact and sex (27). *Herpes simplex virus type 2* - while predominantly transmitted sexually - can also be transmitted via close skin-to-skin contact (28). Similarly, *Treponema pallidum*, the cause of syphilis, is predominantly transmitted through sex (29). However historical reports prior to routine use of latex gloves in the healthcare setting frequently noted syphilitic lesions on the fingers of physicians acquired via non-sexual skin-to-skin contact (30, 31). Human bites can also rarely spread syphilis (32). Herpes simplex virus, human papillomavirus, *Treponema pallidum*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and *Monkeypox virus* can all be further transmitted perinatally (33, 34). However, the proportion of cases of monkeypox that are transmitted via sexual contact appears to be far greater than the proportion transmitted via other means. Therefore, by analogy to other classic sexually transmitted diseases (adding another Bradford Hill criterion in the Table), and in contrast to sexually *transmissible* infections (13), monkeypox may be considered a sexually transmitted disease despite a minority of cases transmitted via other means.

Why Categorizing Monkeypox as a Sexually Transmitted Disease Matters

The ramifications of classifying monkeypox as a sexually transmitted disease is important for several reasons. Identifying populations at increased risk of infection, in

this case gay, bisexual or other men who have sex with men, who have multiple partners, or who participate in group sex can help focus our public health interventions, such as vaccinations, testing, and treatment. For example, public health departments can be mobilized to prioritize funding sexually transmitted diseases clinics and HIV care clinics to receive resources necessary to screen, treat and prevent monkeypox (35). Similarly, sexually transmitted diseases treatment guidelines should be updated to formally include guidance on monkeypox.

Moreover, understanding the primary mode of transmission can help facilitate focused awareness and education programs, as well as allow for behavioral modifications to reduce exposures, which in turn may augment outbreak control efforts and prove to be cost effective. As with other sexually transmitted disease, community and provider awareness is fundamental to disease control; lack of provider awareness regarding syphilis likely directly contributed to numerous missed cases and delays in diagnosis during the resurgence of the disease in the early 2000s (36). By labeling monkeypox as a sexually transmitted diseases, public health messaging can shift to ensure that the community and the providers are aware of the disease, its manifestations, and its correct risk-factors. It is further essential that our public health messaging be clear, a lesson learned during the SARS-CoV-2 pandemic. By classifying monkeypox as a sexually transmitted disease rather than a sexually *transmissible* disease, the public health messaging can be focused and more easily disseminated.

Furthermore, given that more than half of all sexually transmitted disease in 2020 were among adolescents and young adults (37), it is likely some adolescents may be impacted by monkeypox. While many states have some form of minor consent laws,

and in states like California minors age 12-17 years of age may self-consent for testing, treatment and vaccination for sexually transmitted diseases (38), such services are limited to only those infections labeled as sexually *transmitted*. Treatment without the need for parental consent has the potential to greatly improve healthcare seeking behavior and linkage to care among minors. Confidential access to healthcare may also help reduce stigma about sexual health among minors who are often embarrassed to reveal personal information to anyone including their parents (39). Without labeling monkeypox a sexually transmitted disease, teenagers who are at risk would not be able to seek treatment and prevention services without parental consent, thereby limiting provision of such services and thus exacerbating the transmission risk among an already vulnerable population.

It is further important to consider, however, the role of non-sexual transmission. Among other sexually transmitted diseases, when a child is infected, an appropriate concern is raised for child abuse. Similar concerns might be considered for children infected with *Monkeypox virus*. However, as discussed above, non-sexual transmission does occur. As of August 26, 2022, the World Health Organization reported 46,869 laboratory confirmed cases and 302 probable monkeypox cases in the 2022 outbreak, including 151 (0.6%) cases in individuals 0-17 years, out of which 39 (0.1%) were aged 0-4 years (40). The 2003 outbreak of monkeypox in the United States (which originated from pet prairie dogs infected with monkeypox from exposure to infected rodents from Ghana) traced 11 cases among children in contact with infected animals (41). The presentation in those children consisted of painful lymphadenopathy associated with diffuse pox lesions. While remote in time, the different localization of the rash and mode

of acquisition may suggest that cases occurring among children are acquired via non-sexually. Therefore, caution must be exercised to discern the route of transmission among rare cases of monkeypox occurring in children.

Conclusion

The current transmission dynamics of monkeypox are highly consistent with a sexually transmitted disease. Recognizing monkeypox as a sexually transmitted disease should facilitate important public health interventions, access to testing, treatment and vaccination, and other prevention interventions for affected communities. It is further important to remember that some diseases are not mere medical conditions but indicators of structural deficiencies and societal dysfunction. Sexually transmitted diseases are glaring examples of such dysfunction, driven by poverty, exclusion, and other social determinants of health and health inequities. Lessons learned from HIV and syphilis prevention should not be forgotten when addressing the rising tide of monkeypox in the United States and Europe. Individuals, communities, health care providers, public health programs, and decision makers all need to be involved.

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Table: Summary Justification of Monkeypox as a Sexually Transmitted Disease

Bradford Hill Criteria	Evidence	Reference
Strength of Association	<ol style="list-style-type: none"> Between 84% to 100% of patients with monkeypox report recent sexual activity Sexual practices conferring risk for other sexually transmitted infections are common among patients with monkeypox 	5-8, 16-19
Consistency	<ol style="list-style-type: none"> The association between sexual activity and sexual practices and monkeypox has been observed from 17 countries in 13 reports Few reports note any non-sexual household transmission 	5-8, 16-19
Specificity	Needs to be established	-
Temporality	<ol style="list-style-type: none"> Sexual contact has been reported preceding the majority of cases of monkeypox The location of the initial rash is correlated with the type of sexual practice 	5-8, 16-19
Biological Gradient	Needs to be established	-
Plausibility	<ol style="list-style-type: none"> Monkeypox viral DNA is consistently isolated from sexual fluids The isolated <i>Monkeypox virus</i> from semen has been shown to be infectious <i>in vitro</i> The viral load in semen is at a similar level that has been shown to be infectious in animal studies The rash frequently localizes to the genitals prior to further clinical dissemination 	3-8, 16-24
Coherence	1. Predominant sexual transmission would explain the high proportion (92%-100%) among populations at risk for other sexually transmitted infections and the high prevalence of concurrent sexually transmitted infections	5, 6, 8 16, 18
Experiment	Needs to be established	-
Analogy	1. Other sexually transmitted infections including herpes and syphilis, are predominantly transmitted through sexual contact but have secondary transmission routes that are non-sexual	27-34