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VIEWPOINTS

A Position Statement on Mpox as a Sexually Transmitted Disease

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(See Viewpoints by Hazra and Cherabie on pages 1504–7.)

The global outbreak of mpox virus constituted an international public health emergency. Reports have highlighted (1) a temporal association between sexual activity and mpox, (2) an association between specific sexual practices and location of lesion development, (3) a high frequency of sexual practices conferring risk for other sexually transmitted infections among cases of mpox, (4) that mpox virus can be isolated from sexual fluids, (4) that isolated virus is infectious, and (5) 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 mpox virus. We therefore conclude that mpox is a sexually transmitted disease. Labeling it as such will help focus public health interventions, such as vaccinations, testing, and treatment, as well as facilitate focused awareness and education programs toward behavioral modifications to reduce exposures.

Keywords. mpox; sexually transmitted disease; public health.

The United States (US) and the World Health Organization (WHO) have both declared mpox a public health emergency [1, 2]. Outbreaks of mpox in the past have predominantly been short-lived, limited to already endemic regions in Africa, and transmitted predominantly via animals to humans as well as via human-to-human exposure through close physical contact [3]. Since May 2022, however, the large outbreak of mpox in the US, Europe, and now 110 countries globally [4] has consistently highlighted the role of sexual transmission [5–8].

The understanding that mpox is a sexually transmitted disease (STD) is gaining increasing recognition [9–12], but whether or not to label it as such is the subject of ongoing discussion. Sexually transmitted infections (STIs) 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) *predominantly* during oral, anal, or vaginal sex with a partner who is infected [13], as well as via direct skin-to-skin contact through macro- or microabrasions of epithelia or mucous membranes during sexual activities. Common sexually transmitted pathogens include human papillomavirus, human immunodeficiency virus (HIV), *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Treponema pallidum* (the cause of syphilis), and herpes simplex virus types 1 and 2 [11].

Other pathogens, however, that 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* [14]. Those infections are considered sexually transmissible, but not STIs because the primary mode of transmission is not sexual contact. We, therefore, aimed to synthesize the current scientific evidence, detailing the sexual transmission of mpox virus (Table 1) in the 2022 outbreak. We also highlight the reasons why identifying mpox as an STD is justified and important.

THE EVIDENCE SUPPORTING MPOX AS AN STD

The most commonly utilized framework for evaluating epidemiologic evidence to determine causality is the Bradford Hill criteria, based on 9 aspects of epidemiologic association: strength of association, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, and analogy [33]. The Bradford Hill criteria may be applied to the current body of epidemiologic literature in the large mpox outbreak in 2022 as follows.

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Table 1. Summary Justification of mpox as a Sexually Transmitted Disease

Bradford Hill Criteria	Evidence	References
Strength of association	• Between 84% and 100% of patients with mpox report recent sexual activity • Sexual practices conferring risk for other STIs are common among patients with mpox	[5–8, 15–18]
Consistency	• The association between sexual practices and mpox has been observed from 17 countries in 8 reports • Few reports note any nonsexual transmission	[5–8, 15–18]
Specificity	Needs to be established	…
Temporality	• Sexual contact has been reported preceding the majority of cases of mpox • The location of the initial rash is correlated with the type of sexual exposure	[5–8, 15–18]
Biological gradient	Needs to be established	…
Plausibility	• mpox viral DNA is consistently isolated from sexual fluids • The isolated mpox virus from semen and urethral swabs has been shown to be infectious *in vitro* • The viral load in semen is at a similar level that has been shown to be infectious from lesion swabs • The rash frequently localizes to the genitals prior to further clinical dissemination	[3–8, 15–17, 19–22]
Coherence	• Predominant sexual transmission would explain the high proportion (92%–100%) among populations at risk for other STIs and the high prevalence of concurrent STIs	[5, 6, 8, 15, 17]
Experiment	Needs to be established	…
Analogy	• Other STIs including herpes and syphilis can be transmitted via skin-to-skin contact, and more including *Neisseria gonorrhoeae*, hepatitis B virus, and HIV have other secondary transmission routes that are nonsexual	[23–32]

Abbreviations: HIV, human immunodeficiency virus; STI, sexually transmitted infection.

mpox Is Strongly Linked to Sexual Activity

There is a strong association between sexual activity and mpox. Eight different published series from 17 countries during the 2022 outbreak noted that between 84% and 100% of the 3235 cases reported sexual activity, most with a new sex partner, prior to the onset of symptoms [5–8, 15–18]. Furthermore, during the 2022 outbreak sex practices associated with other STDs such as multiple recent sex partners, attending sex-on-site venues, group sex, substance use during sex, and condomless receptive anal intercourse have been reported at a high frequency among cases of mpox [5, 6, 8, 16, 17]. There also appears to be a temporal and anatomic association between sexual activities reported and the manifestations of the disease; recent receptive anal intercourse was associated with a >5-fold increased risk of proctitis due to mpox, and receptive oral intercourse was reported in the days preceding the diagnosis of 95% of patients who presented with tonsilitis due to mpox [8].

Another case series concluded that all 21 secondary cases—patients with mpox for whom the index case could be identified—were likely due to sexual transmission from 20 primary cases [16], while another report noted that 95% of >500 cases of mpox from the 2022 outbreak were thought by the clinicians seeing patients to be sexually transmitted [6]. Finally, among the published studies during the current outbreak in the US and Europe, the proportion of cases in which nonsexual transmission was suspected ranged from 1% to 3% [6, 8], further supporting the nearly exclusive sexual spread of mpox, at least within the US and Europe.

Therefore, according to the Bradford Hill criteria, the association between mpox and sexual transmission thus far fulfills 3 important requisites: strong association, consistency across time and geographic location, and temporality (Table 1).

mpox Is Transmitted Through Sexual Fluids

mpox is an orthopoxvirus in the Poxviridae family and its genetic material is double-stranded DNA. In addition to skin lesions, mpox viral DNA has been consistently detected in seminal fluid [6, 17, 19], rectal swab specimens [17, 34], and respiratory secretions [3, 17, 35], as well as from the blood of patients during the 2022 outbreak [35]. Furthermore, a recent study identified persistent detection of mpox DNA over 19 days in the semen of an individual with the infection [19]. Those investigators additionally isolated mpox virus from semen of that individual and subsequently demonstrated infectivity of that cultured virus in vitro after 6 days [19]. Another report demonstrated that viral loads among polymerase chain reaction (PCR) tests from lesion swabs correlated with infectivity as measured by plaque assay [20]. Those viral loads from lesions were of the same magnitude as the viral loads from semen samples [17]. Finally, a recent study was able to culture mpox virus from urethral swabs in 11 of 15 PCR-positive cases, and from 13 rectal swabs among 18 PCR-positive cases [21], indicating infectivity. Thus, it is biologically plausible that the sexual fluids transmit the infection.

Furthermore, during the 2022 outbreak across the US and Europe, researchers described that the characteristic rash of mpox frequently localized to the genitalia and within the rectum [5–8, 15–17, 22]. Thornhill et al reported that 383 of 528 (72.5%) cases of mpox had anogenital lesions [6], while Iñigo Martínez et al reported that 359 of 498 (72.1%) cases had anogenital lesions [16]. Notably, anogenital lesions often develop prior to further dissemination of the rash across other parts of the body [6–8, 15, 22]. Those findings suggest direct inoculation of the mpox virus during sex either through exposure to infected fluids or through direct skin-to-skin contact with anogenital lesions.

Such transmission dynamics would further explain the vastly disproportionate burden of mpox disease among gay, bisexual,

and other men who have sex with men, who constitute 92%–100% of reported cases [5, 6, 8, 15], as well as the high prevalence of concurrent STDs (17%–29%) among patients with mpox in the 2022 outbreak [6, 8, 17]. Thus, 2 more Bradford Hill criteria, plausibility and coherence, can be added to the justification (Table 1).

mpox Is Not Exclusively Sexually Transmitted

Globally, the WHO recognizes >30 STIs including mpox [11]. Yet sometimes distinguishing between those infections which are *transmitted* (ie, the "primary" mode of transmission is through sex) and those which are *transmissible* (ie, the "primary" mode of transmission is through other modes; sexual transmission is possible but not the major mode of transmission) 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 among infected sex partners, 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 from sexually transmissible infections [14]. Such factors may be necessary to satisfy Bradford Hill's specificity criterion.

Yet, while mpox is not *exclusively* transmitted through sexual activity [3, 6, 8, 36], this does not preclude it from being considered an STI. In fact, many infections recognized as STIs by the WHO similarly have secondary modes of transmission [11]. *Molluscum contagiosum*, a related poxvirus, also causes cutaneous lesions and can be transmitted via both skin-to-skin contact and sex [23]. Herpes simplex virus type 2—while predominantly transmitted sexually—can also be transmitted via close skin-to-skin contact [24]. Similarly, *Treponema pallidum*, the cause of syphilis, is predominantly transmitted through sex [25]. Historical reports prior to the routine use of latex gloves in the physical examination, however, noted syphilitic lesions on the fingers of physicians acquired via skin-to-skin contact [26, 27]. Human bites can also rarely spread syphilis [28]. Herpes simplex virus, human papillomavirus, *Treponema pallidum*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, HIV, hepatitis B virus, and mpox virus can all be further transmitted perinatally [29–32]. However, the proportion of cases of mpox that are transmitted via sexual contact appears to be far greater than the proportion transmitted via other means. Therefore, by analogy to other classified STIs (adding another Bradford Hill criterion in Table 1), and in contrast to sexually *transmissible* infections [14], mpox may be considered an STI despite a minority of cases transmitted via other means.

WHY CATEGORIZING MPOX AS AN STD MATTERS

The ramifications of classifying mpox as an STD are important for several reasons. Concerns have been raised that such a classification would heighten the stigma surrounding an already stigmatized disease, particularly among the communities already affected by both stigma and mpox. Stigmatization may, in turn, lead to reduced healthcare seeking and partner notification [37, 38], thus increasing disease transmission. Importantly, however, public health messaging has the capacity to overcome stigma, analogous to the effective messaging and public health strategies used during the latter part of the HIV pandemic [39].

By identifying populations at increased risk of infection, in this case gay, bisexual, or other men who have sex with men, specifically those who have multiple partners or who participate in group sex, public health interventions such as vaccinations, testing, and treatment can be tailored. For example, public health departments can support clinics specializing in STIs and HIV to receive resources necessary to screen, treat, and prevent mpox [40]. Similarly, treatment guidelines and clinical education for STIs should be updated to formally include guidance on mpox.

Moreover, understanding the primary mode of transmission can help facilitate focused community 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 STDs, 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 mid 2000s [41]. By labeling mpox as an STD, public health messaging can shift to ensure that the community and the providers know about the disease, its manifestations, and its risk factors. It is further essential that our public health messaging be clear. By classifying mpox as a sexually transmitted 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 STIs in 2020 were among adolescents and young adults [42], it is likely some adolescents may be impacted by mpox. Importantly, while in states such as California, minors 12–17 years of age may self-consent for testing, treatment, and vaccination for STDs [43], such services are limited to only those diseases 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 [44]. Without labeling mpox an STD, 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 nonsexual transmission. Among other STDs, when a child is

infected, an appropriate concern is raised for child abuse. Similar concerns might be considered for children infected with mpox virus. However, as discussed above, nonsexual transmission does occur. As of 9 November 2022, the WHO reported 78 924 laboratory-confirmed cases in the 2022 outbreak, including 542 (1.2%) among individuals 0–17 years of age, of which 141 (0.3%) were aged 0–4 years [4]. The 2003 outbreak of mpox in the US (which originated from pet prairie dogs infected with mpox virus) traced 11 cases among children in contact with an infected animal [45]. The presentation in those children consisted of painful lymphadenopathy associated with diffuse pox lesions requiring hospitalization. While remote in time, the difference in localization of the rash and the mode of acquisition may suggest that cases occurring among children are most likely acquired via nonsexual routes. Therefore, caution must be exercised to discern the route of transmission among rare cases of mpox occurring in children.

Similarly, while the evidence of predominantly sexual transmission is apparent for the recent outbreak in the US and Europe, historical outbreaks, even recent ones, within Africa have not consistently demonstrated that pattern of transmission [3]. There remains mixed evidence of sexual transmission of mpox virus within Africa [18, 46], and thus this classification presently applies predominantly to the 2022 outbreak in US and Europe but may inform the study of mpox virus transmission dynamics in other settings. Labeling of mpox as sexually transmitted may also have negative repercussions in settings with punitive policies for same-sex partners [47].

CONCLUSIONS

The current transmission dynamics of mpox are highly consistent with an STD. Recognizing mpox as an STD should facilitate important public health interventions, including 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. STIs 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 mpox in the US and Europe. Individuals, communities, healthcare providers, public health programs, and decision makers all need to be involved.

Notes

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