Newer and emerging sexually transmitted infections: A narrative review

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ABSTRACT

Sexually transmitted infections (STIs), including traditionally curable diseases like syphilis and gonorrhoea, have seen a recent resurgence. Concurrently, newer atypical infections presenting as STIs have emerged, driven by changes in pathogen virulence, host behaviours, and environmental factors. The spectrum of STIs is expanding due to evolving behaviours, globalisation, and pathogen adaptability. This review aims to highlight key viral, bacterial, fungal, and enteric infections that are newly identified or increasingly transmitted through sexual contact, introducing the concept of sexually transmissible infections. Though sexual transmission plays a minor role in their spread, it cannot be neglected and thus requires heightened awareness among clinicians and public health officials to ensure timely identification, management, and prevention.

Keywords: Ebola, genital tuberculosis, mPox, *Tinea genitalis*, sexually transmitted infections, Zika

Introduction

Sexually transmitted infections (STIs), including viral and curable infections like syphilis and gonorrhoea, have seen a recent increase.[1-3] Moreover, there has been a spate of newer infections presenting as STIs, summarised in the table [Table 1].

Agent factors (change of the pathogens' virulence factors and routes of transmission), host factors (including change in behavioural factors, increasing oral and anal sexual practices, behavioural alteration in high-risk population), and environmental factors (increasing globalisation and connection opportunities increasing probability of edge cases) are responsible for this increase. It is important to be aware of these infections, as they can present as an unfamiliar constellation of symptoms in high-risk populations, which may not respond to empirical syndromic treatments used for common STIs.[2]

"Sexually transmissible infections" is a broader term introduced by Jeffrey Klausner, which indicates that a disease can be transmitted through sexual contact. Sexual contact, while a possible route, may not be the primary means of transmission. However, sexually transmitted infections and sexually transmissible infections are used interchangeably in the literature.

Newer sexually transmissible viral infections

mPox

Monkeypox, or mPox, is a viral zoonosis caused by the monkeypox virus of the *Orthopoxvirus* genus. The disease was first discovered in 1958 in monkeys and in 1970 in humans in the Democratic Republic of Congo (DRC).[4] Traditionally confined to Central and West Africa, mPox has recently gained international attention due to a significant outbreak in 2022 in which cases spread to non-endemic countries. It primarily affected men who have sex with men (MSM).[5] On July 23, 2022, the World Health Organization (WHO) declared the outbreak a Public Health Emergency of International Concern (PHEIC).[6] Genetic analysis revealed the emergence of a novel lineage, B.1, later classified under Clade IIb.[7]

Transmission occurs through direct contact with lesions, body fluids, respiratory droplets, and contaminated

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materials. Factors such as deforestation increase human-animal contact. The cessation of smallpox vaccination campaigns has contributed to a rise in cases.[8] As per World Health Organisation , the current outbreak has demonstrated staggering MSM predominance (98%–99), with similar data from studies in Spain, the UK, and a multicentric study across 16 countries. In a recent Google Form-based survey of physicians from all six WHO regions, about half (54.5%) the reported cases were in MSM/bisexual males. However, heterosexual predominance was noted in African, the East-Mediterranean, and South-East Asian regions.

Traditionally, mPox's prodromal phase presents with fever, headache, and lymphadenopathy, followed by a characteristic rash that progresses through macular, papular, vesicular, and pustular stages. However, the clinical features observed in the current outbreak are atypical.[9,10] The presence of fewer lesions with localisation to anogenital and perioral regions [Figures 1a and b] and the development of complications like proctitis, and tonsillitis have been reported more frequently, making diagnosis challenging.

Conventional or real-time PCR on lesional fluid can diagnose 97% of cases,[7] and loop-mediated isothermal amplification tests may be valuable in rural health clinics or hospitals with limited access to high-precision Polymerase Chain Reaction (PCR) instruments.[11]

Treatment is primarily supportive, and smallpox antivirals such as cidofovir, brincidofovir, and tecovirimat have shown effectiveness.[12-14] Smallpox vaccines such as ACAM2000, MVA-BN, and LC-16 are available, of which, MVA-BN is the only FDA-approved vaccine.[15] US Centers for Disease Control and Prevention (CDC) recommends vaccination for post-exposure prophylaxis within 4 (up to 14) days of exposure, for high-risk individuals.[16]

Zika virus

Zika virus is a mosquito-borne flavivirus, primarily transmitted by *Aedes* mosquitoes, particularly *Aedes aegypti*. It was first identified in 1947 in monkeys and later in humans in 1952 in Uganda and the United Republic of Tanzania, respectively.

The primary mode of transmission is through the bite of infected *Aedes* mosquitoes. It can also be transmitted through blood transfusions, sexual contact, and from pregnant females to their foetuses, leading to congenital Zika syndrome. Sexual transmission has been documented in both heterosexual and homosexual encounters.[17] The virus' ability to persist in semen and vaginal fluids making sexual transmission through oral, anal, and vaginal intercourse possible is a significant concern. Zika viral RNA has been detected up till 188 days in semen, 3 days in vaginal fluid, and 11 days in cervical secretions by RT-PCR, and 69 days in semen by culture, even after the virus is no longer detectable in blood or urine.[17-20] This proves that the virus poses risks of transmission long after the initial infection.

Most Zika infections are asymptomatic (80%) or mildly symptomatic, lasting for 2-7 days, presenting with fever, maculopapular rash, conjunctivitis, headache, arthralgia, and myalgia, with rare fatalities.[21] Complications include neurological complications like Guillain-Barré syndrome and congenital Zika Syndrome, characterised by severe birth defects such as microcephaly, brain damage, eye defects, including microphthalmia, coloboma, optic atrophy, sensorineural hearing loss, and impaired growth.

Figure 1a: Mpox: Multiple umblicated vesicles localised over the penis and scrotum.

Figure 1b: Mpox: Similar vesicles over the anogenital region.

Table 1: Salient features of newer and emerging sexually transmitted infections (STIs).

Disease	Pathogen	Primary mode of transmission	Incubation period	Clinical features	Fatality rate	Risk factors	Treatment	Preventive measures
Monkeypox	dsDNA virus (Orthopoxvirus)	Direct contact, respiratory droplets, sexual contact	6-13 days (mean 7 days)	Rash, fever, lymphadenopathy, genital and perianal lesions	0-11% (higher in children)	MSM, recent travel, HIV infection	Antiviral therapy (Tecovirimat), supportive care	JYNNEOS, AC AM2000 vaccine, avoiding close contact with infected individuals
Zika Virus	RNA virus (Flavivirus)	Mosquito bites, sexual transmission	3-12 days	Fever, rash, conjunctivitis, arthralgia	Generally low (<1%)	Pregnant women (risk of microcephaly in foetus)	Symptomatic treatment (rest, hydration, pain relief)	Mosquito control, safe sex practices, avoiding pregnancy during outbreaks
Ebola Virus	RNA virus (Filovirus)	Direct contact with body fluids	2-21 days	Fever, haemorrhage, vomiting, diarrhoea	25-90% depending on outbreak	Healthcare workers, burial practices, contact with bats	Supportive care, Inmazeb	Avoiding contact with infected individuals, Proper protective equipment Ervebo vaccine
Genital Tuberculosis	Bacteria (*Mycobacterium tuberculosis*)	Sexual transmission, hematogenous spread	Variable (weeks to years)	Pelvic pain, menstrual irregularities, infertility	Variable depending on treatment	Immunocompromised individuals, previous tuberculosis infection	Combination antibiotic therapy (e.g., Isoniazid, Rifampin, Ethambutol)	Early detection and treatment, avoiding close contact with infected individuals
Neisseria meningitidis	Bacteria (Gram-negative diplococcus)	Respiratory droplets, close contact, oral sex	Few weeks to months	Urethral discharge, meningitis, septicaemia	10-15%	Crowded living conditions, smoking, viral infections, oral sex	Ceftriaxone 250mg IM, Azithromycin 1g stat	Vaccination, prophylactic antibiotics for close contacts
Tinea Genitalis	Fungal infection (Dermatophyte)	Direct skin-to-skin contact	4-14 days	Erythematous annular plaque, abscess, scaling in genital area	Not typically fatal	Warm and moist environments, immunocompromised individuals	Topical or oral antifungals (e.g., terbinafine, clotrimazole)	Maintaining hygiene, keeping skin dry, avoiding sharing personal items

Diagnosis is confirmed through nucleic acid amplification tests (NAATs) and is recommended for symptomatic pregnant women and those with recent exposure in high-risk areas. Infants exposed to Zika *in utero* should undergo testing immediately after birth.

Treatment is supportive with no specific antivirals. CDC recommends abstinence from sex for at least 3 months after symptom onset (if symptomatic) or their last possible Zika virus exposure (if asymptomatic) to minimise their risk for sexual transmission of the Zika virus.[22] Women trying to conceive should also consider waiting for at least 8 weeks after possible exposure before attempting to become pregnant to reduce the risk of congenital Zika syndrome.[23]

Ebola virus

Ebola virus, a member of the Filoviridae family, has five distinct species: Zaire, Sudan, Tai Forest, Bundibugyo, and Reston. Known for causing severe haemorrhagic fever, Ebola has caused several significant outbreaks in Africa, with the 2014–2016 West Africa outbreak being the largest and deadliest that led to more than 28,000 confirmed cases and 11,310 deaths.[24]

Natural hosts of the Ebola virus are fruit bats. Transmission occurs by contact with excrement or human consumption of bats or through antelopes and great apes consumed as bushmeat. Human-to-human transmission occurs through direct contact with blood, body fluids, or tissues of infected individuals and vertical transmission from mother to foetus, resulting in stillbirths or miscarriages (80%) and live births (20%) with death within 19 days of life.[25]

Sexual transmission through semen has also been identified. Viral RNA is detected for up to 19 months post-infection in semen. Viral RNA has also been detected by RT-PCR in

vaginal fluid; however, a live virus has never been isolated and thus the prospect of transmission has not been established. This long-term persistence provides an opportunity for the transmission of the Ebola virus from survivors even after the official end of an outbreak.[26]

The incubation period is 2-21 days, followed by symptoms including fever, vomiting, diarrhoea, headache, abdominal pain, and unexplained bleeding.[25] The high case fatality rate and the potential for rapid spread make Ebola a significant public health concern.

RT-PCR on blood samples can diagnose the disease, with the ability to detect it from 3 days to 17 days of symptom onset, and culture requires BSL-4 laboratories. Supportive management, including fluid-electrolyte balance, oxygen support, and treatment of concomitant infections, remains essential.[27,28]

Inmazeb, the first FDA-approved monoclonal antibody treatment, has shown efficacy in trials compared to controls.[29] Ervebo, the first FDA-approved vaccine, has also shown efficacy in preventing Ebola virus infection.[30] WHO recommends male Ebola survivors should be offered semen testing at 3 months after the onset of the disease, and then, for those who test positive, every month thereafter until their semen tests negative for the virus twice by RT-PCR, with at least an interval of 1 week between tests.[31]

Newer sexually transmissible bacterial infections

Neisseria meningitidis

Approximately 5%–10% of healthy adults are nasopharyngeal carriers of *Neisseria meningitidis* and have it as a commensal organism, compared to *Neisseria gonorrhoeae,* which is always pathogenic whenever present. A pathogenic mechanism involving the loss of capsule, enables nasopharyngeal *Neisseria meningitidis* to infect the urogenital tract, making the species untypable by common diagnostic techniques.

A unique aspect of its transmission is that it occurs exclusively during oral sex, where the bacteria transfer from the normal microbiota of the sexual partner's upper respiratory tract to the individual who develops urethritis and can be both through homosexual and heterosexual contact.Most men with meningococcal urethritis are symptomatic, displaying signs like urethral discharge and dysuria. According to a study, the incidence of *Neisseria meningitidis* urethritis escalated from 2.78% in 2011 to 8.93% in 2015, particularly among male patients.[32] Specifically, the "*Neisseria meningitidis* urethritis clade" (US NmUC) or "*Neisseria meningitidis*, non-groupable" (NmNG) predominantly affects heterosexual men, with a high percentage reporting oral sex as the likely route of transmission. MSM were unaffected by these strains, but they were infected by a highly virulent serogroup C (ST-11 clonal complex) responsible for multiple outbreaks of invasive meningococcal disease (IMD), especially among those infected with HIV (four times higher), which further increases their susceptibility.[33,34]

Neisseria meningitidis is assigned as the causative agent in a case of genital discharge when gram-negative diplococci are seen, but the specimen tests negative for nucleic acid amplification test for *N. gonorrhoeae*.

Genital tuberculosis

Sexual transmission of tuberculosis, while rare, has been documented. Primary genital TB can develop through sexual intercourse with a male partner who has penile or epididymal TB.[35] The first reported case of asymptomatic female genital TB from spousal epididymal TB was identified through active screening and whole genome sequencing.[36] Active screening of the female partner is recommended soon after the diagnosis of male genital TB, even if she is asymptomatic.[37]

Interestingly, papulonecrotic tuberculid (PNT) presenting over the glans penis in isolation [Figure 2] has been postulated to be sexually transmitted, as partners of some of these patients have shown features of genital tuberculosis.[38] Active screening of sexual partners, especially when one is diagnosed with genital TB, is crucial. However, genital tuberculosis, similar to that of other organs, spreads through prolonged contact, and thus, primarily affects couples and is less likely to occur in casual encounters.

Male genital tuberculosis often presents with symptoms such as swelling of the epididymis and systemic signs like fever and weight loss. However, shedding of bacteria from epididymal TB is extremely rare. In India, tuberculosis most commonly affects the female reproductive organs in the following order: fallopian tubes (95–100%), uterine endometrium (50–60%), ovaries (20–30%), cervix (5–15%), uterine myometrium (2.5%), and the vagina and/or vulva (1%).[39] Most patients are asymptomatic, and the primary presentation is usually infertility. While one study reported a 16% prevalence of genital TB in infertile women, a more recent systematic review and meta-analysis found the prevalence to be 34.86%.[40]

Fungal infections that spread through sexual contact

Tinea genitalis

Tinea genitalis (syn. genital tinea, pubogenital tinea, genital dermatophytosis) is a relatively new entity, defined by its location on the mons pubis and labia in women, and on the penile shaft in men, with the possibility of spreading into the groin and scrotum[41] [Figure 3]. As it does not spread through bodily fluids but through close contact during sexual activity, it is not truly a sexually transmitted infection. However, as tinea conventionally spares the genitals, it is worthwhile to discuss the genital involvement, especially in the context of the recent epidemic of tinea in the Indian subcontinent.

Figure 2: Penile papulonecrotic tuberculid: Irregular shaped punched out ulcer with overlying necrotic slough, present over the glans penis.

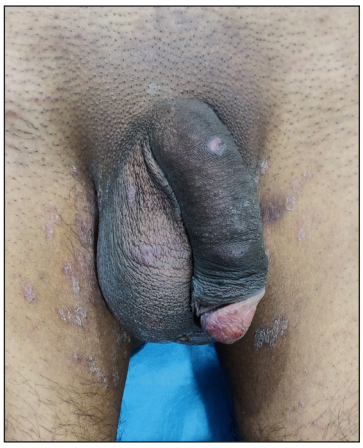

Figure 3: Tinea genitalis in a male patient, showing erythematous scaly annular papules and plaques over the groins, scrotum, shaft of the penis, and the glans as well.

Dermatophytosis of the genitals can spread through sexual contact, autoinoculation, and overuse of potent corticosteroids, especially in hot, humid regions. In India, an outbreak of tinea cruris and *Tinea genitalis* due to *Trichophyton mentagrophytes* genotype VIII was first reported by Thakur *et al*., with human-to-human transmission being more common.[42] While traditionally linked to anthropophilic dermatophytes, recent cases involve zoophilic dermatophytes like *T. mentagrophytes, Microsporum canis*, and *T. benhamiae*.[41,43] *T. mentagrophytes* genotype VII causes severe, persistent infections often linked to sexual contact in Thailand, whereas genotype VIII (*T. indotineae*) is associated with milder symptoms in rural India.

Clues to diagnosis include lesions which may be inflammatory or abscess-forming. Routine culture cannot distinguish *T. mentagrophytes* from the closely related *T. interdigitale*. Sequencing of the Internal Transcribed Spacer (ITS) region identifies species and genotypes, yet may not be widely available. Prolonged treatment duration may be necessary. When *Tinea genitalis* is suspected or diagnosed, sexual partners should be evaluated, and the patient can be further screened for other STIs.[44]

Sexually transmitted enteric and anorectal infections

Sexually transmitted enteric infections in homosexuals have been described since the 1970s, but there has been a recent increase in the number of outbreaks. These infections are more likely in the high-risk groups with multiple sexual partners, HIV-positive MSM, substance abuse, concomitant STIs, and indulging in diverse sexual practices.

Traditionally transmitted through food and waterborne routes, sexual transmission of enteric pathogens in MSM through direct (anilingus/rimming) or indirect oral–anal sexual contact have been reported. Sexual transmission of bacterial infections like *Campylobacter sp*., *Shigella sp.* (particularly antibiotic-resistant strains), protozoal infections like *Giardia lamblia*, *Entameoba histolytica* and viral infections such as Hepatitis A have been described. Chronic cases may lead to reactive arthritis or irritable bowel syndrome.

In 2024, the National AIDS Control Organisation (NACO) has come out with national technical guidelines on syndromic management of anorectal discharge and recommends doxycycline 100 mg twice daily for seven days (extended to 21 days to cover lymphogranuloma venereum if nucleic acid amplification test (NAAT) is positive for *C. trachomatis*) plus ceftriaxone 500 mg intramuscularly or cefixime 800 mg orally as single doses.

Campylobacter

The majority of cases of campylobacteriosis are caused by *Campylobacter jejuni*. They are associated with symptomatic and asymptomatic anorectal or intestinal disease-causing proctocolitis presenting as watery or bloody diarrhoea, fever, abdominal cramps, and variable weight loss. Infrequently, they can cause bacteraemia and severe extra-intestinal infections in individuals with HIV. Quinn *et al*. found that a higher proportion of MSM with Campylobacter infection (74.2%) reported engaging in anilingus in the past month compared to those without enteric infections (54.9%; $P < .05$), suggesting a greater risk of enteric infection associated with this behaviour.[45]

Diagnosis is based on stool culture and PCR. Macrolides and fluoroquinolones have been the conventional agents for treating enteritis.[46] Fosfomycin has been tried as an alternative agent in case of macrolide and fluoroquinolone resistance.[47]

Shigella

Sexual mode of transmission was first identified in 1974 among MSM in the USA, after which cases have been detected globally. Shigellosis is primarily transmitted by *Shigella*

sonnei, S. flexneri, S. boydii, and *S. dysenteriae* species. Symptoms typically appear after 1-4 days post-exposure, including bloody diarrhoea, fever, and abdominal pain, and if left untreated, it can lead to chronic colorectal fistulas and strictures.[48] Shigella transmission particularly among MSM, has been linked to those with multiple sexual partners, substance use, co-infection with other STIs, and specific types of anal contact, such as fingering, instrumentation, peno anal, and oro anal contact.[49,50] Diagnosis is based on stool culture or PCR. There has been a recent increase in antimicrobial resistance in shigella isolates from MSM, often showing multidrug resistance. Strains resistant to both cephalosporins and fluoroquinolones have emerged, limiting treatment options to last-resort intravenous antibiotics like carbapenems for severe cases.[51]

Entamoeba histolytica

Since the 1980s, amoebiasis (EHI) has been increasingly reported among MSM, especially those with HIV.[52] Serological studies from this decade found a seroprevalence of 1% to 21% in MSM across developed countries, significantly higher than the 0–7% seen in heterosexual individuals.[53] They are acquired via oral-anal sex or fellatio. Most MSM affected with amoebiasis are colonised with *E. dispar*, but *E. histolytic*a-associated disease can also occur. EHI can present as asymptomatic or develop into invasive disease, with amoebic colitis and liver abscess being the most common forms. The identification of *E. histolytica*-specific nucleic acids by PCR assays is highly sensitive and has become the gold standard in diagnosing EHI. Treatment is advised for both symptomatic and asymptomatic infections to reduce transmission and prevent disease progression. For clinical cases, both a tissue-active amebicide and a luminal cysticidal agent are needed. Recommended therapies include metronidazole or tinidazole, along with iodoquinol or paromomycin.[54]

Giardia lamblia

Giardia lamblia is the most common intestinal parasite in the USA., causing around 1.2 million cases of giardiasis annually. Studies suggest sexual transmission of giardiasis among MSM, with specific behaviours like anal–penile and oral–anal contact being associated with infection.[55,56] Polymicrobial infections and a history of gonorrhoea have also been linked to protozoal infections. While most infections are asymptomatic, symptoms like diarrhoea, malabsorption, and abdominal cramps can develop 1–2 weeks post-infection. Diagnosis is via visualisation, EIA, or PCR, with treatments including tinidazole, nitazoxanide, or metronidazole.

Hepatitis A

Sexual transmission of Hepatitis A among MSM has been reported since the early 2000s. Transmission via oro-anal, digito-anal, and genito-oral contact and in casual sex venues like gay saunas have been linked to significant outbreaks, further spreading to the general population through contact with infected individuals.[57] Infection with the Hepatitis A virus is typically acute and self-limiting. Recently, an outbreak was reported between June 2016 and mid-May 2017 in low endemicity countries in the European region and in the Americas affecting MSM.[58] Hepatitis A vaccination was then recommended by WHO in high-risk populations such as travellers to endemic areas, MSM, drug users, and chronic liver disease patients. Despite this, Hepatitis A vaccination coverage remains low, with estimated coverage between 25-45% overall.[59]

Conclusion

Apart from a recent increase in the curable STIs, newer and emerging STIs pose a significant challenge to healthcare services and infrastructure. Newer infections include viruses that persist for long in the bodily fluids, requiring prolonged testing and abstention, and resulting in congenital infections. MPox has the potential to be the next global epidemic. Tropical developing nations have to deal with the unique challenges of sexually transmitted tuberculosis and *Tinea genitalis*. Changing behavioural practices imply that enteral infections spreading through sexual means have not seen a decrease either. Epidemiologists and STI specialists should keep themselves updated about these diseases to identify them early and reduce resultant morbidity and spread.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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