



What's New in Adult Sexually Transmitted Infections Management and Prevention for 2024

By

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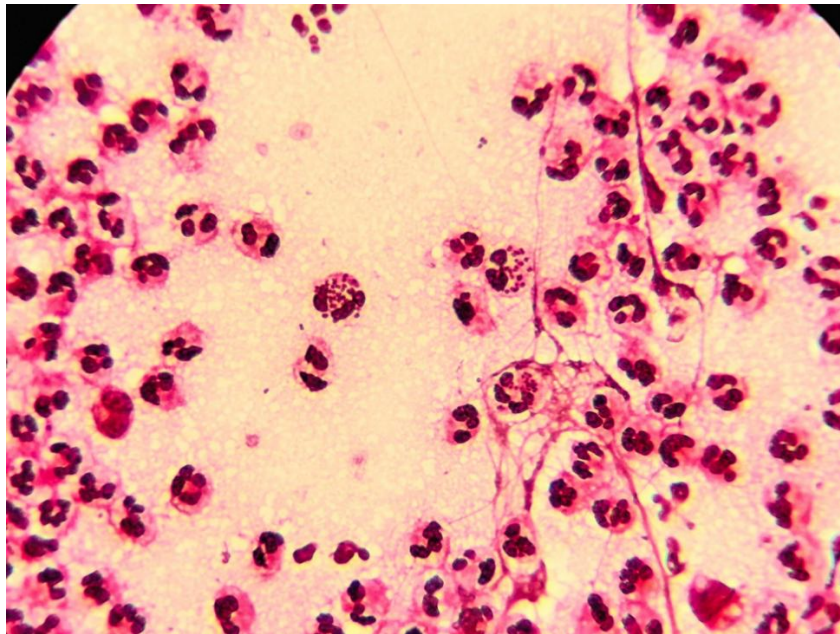
This article highlights the latest advancements in the management and prevention of adult sexually transmitted infections (STIs). We'll explore updated treatment recommendations, promising new therapies and vaccine developments for some common STIs.

Gonorrhea

According to the Centers for Disease Control (CDC), there were 601,319 reported cases of gonorrhea, caused by *Neisseria gonorrhoeae*, (a gram-negative diplococcus bacterium) in the U.S. in 2023, a decrease of 7% from 2022.[1,2] Globally, in 2022, the World Health Organization (WHO) estimated that there were 82 million gonorrhea infections.[3]

Gonorrhea typically presents with a white, yellow or greenish vaginal or urethral discharge. More serious disease such as pelvic inflammatory disease, conjunctivitis (also seen in newborns if the mother is infected), pharyngitis, and disseminated infection with the possibility of arthritis, skin lesions, meningitis or endocarditis.

There are three major updates in the treatment of gonorrhea. The first is the concerning emergence of drug-resistant *Neisseria gonorrhoeae*, unresponsive to ceftriaxone therapy. Ceftriaxone-resistant isolates increased in China from 2.9% in 2017 to 8.1% in 2022.[4] In 2020 the CDC increased the standard dosage of ceftriaxone for uncomplicated gonorrhea from 250mg to 500mg due to increasing resistance.[5]

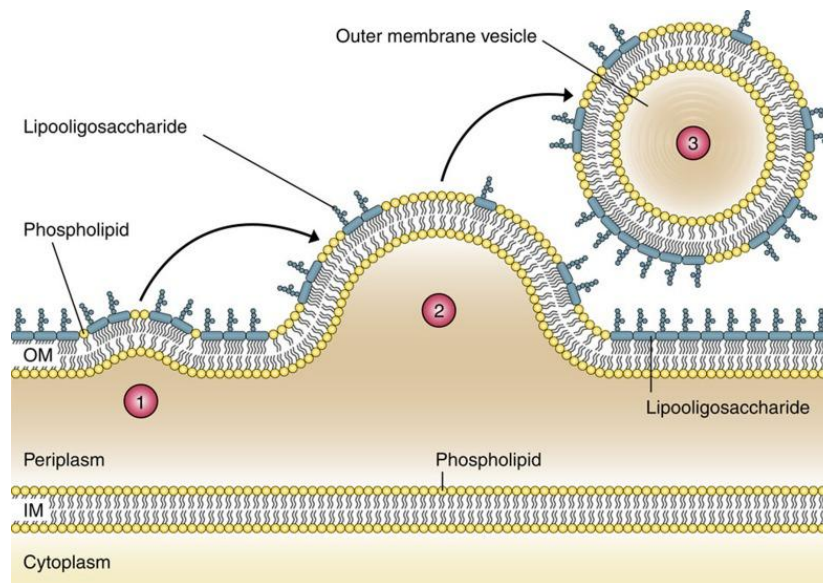


Gram-negative intracellular diplococci of *Neisseria gonorrhoeae*

Zoliflodacin, a new oral antibiotic to treat gonorrhea is in phase 3 clinical testing and in vitro has shown effectiveness in strains resistant to ceftriaxone and azithromycin. Zoliflodacin inhibits the bacterial enzyme type II topoisomerase, which is needed for bacterial function and reproduction.[6,7]

Two types of vaccines are currently being tested to prevent gonorrhea. One is the meningococcal B vaccine (already in use to prevent *Neisseria meningitidis* meningitis), to see if there is cross reactivity with *Neisseria gonorrhoeae*, as both organisms are *Neisseria* species.[8]

The second potential vaccine is in pre-clinical testing and creates an immunogenic response against small polysaccharide–protein outer membrane vesicles (OMVs). OMVs are naturally created by many gram-negative bacteria using their bacterial cell membrane as the outer sphere of the OMV which is then extruded from the bacteria. OMVs, after being released from the bacteria, then carry proteins to host cells which can result in biochemical changes in the host that allow the bacteria to better survive and multiply. OMVs have antigens on their surfaces from the bacterial cell membrane that can be used in a vaccine to induce immunity.[9]



OMV formation in gram-negative bacteria[10]

Recommended Regimen for Uncomplicated Gonococcal Infection of the Cervix, Urethra, or Rectum Among Adults and Adolescents

Ceftriaxone 500 mg* IM in a single dose for persons weighing <150 kg

If chlamydial infection has not been excluded, treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days.

* For persons weighing ≥ 150 kg, 1 g ceftriaxone should be administered.

Alternative Regimens

If cephalosporin allergy:

Gentamicin 240 mg IM in a single dose

PLUS

Azithromycin 2 g orally in a single dose

If ceftriaxone administration is not available or not feasible:

Cefixime 800 mg* orally in a single dose

* If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days.

[11]

[Click here for current recommended gonorrhea therapy and for information on complicated infections.](#)

Syphilis

Syphilis is a systemic bacterial infection caused by the spirochete *Treponema pallidum*. In 2023, the CDC reported there were 209,253 cases of syphilis in the U.S., an increase of 84% from 2018, and the highest number of cases reported since 1950.[1,2] The WHO estimated that in 2022 there were eight million infections world-wide.[12]



Two *Treponema pallidum* spirochetal bacteria magnified 950 times under darkfield illumination microscopy

A syphilis vaccine has so far eluded scientists.[13]

The treatment for uncomplicated primary and secondary syphilis in non-pregnant adults remains a single dose of benzathine penicillin G. For penicillin-allergic non-pregnant patients, doxycycline is recommended. Although azithromycin has in the past been effective in treating syphilis, due increasing resistance, it is no longer recommended.[14]

Pregnant women who are allergic to penicillin should undergo desensitization for penicillin G prior to treatment.[14,15,16] The treatment of pregnant women with syphilis differs from non-pregnant women and clinicians are advised to use the link below to get more information.

There was a benzathine penicillin G shortage in early 2024 at which time the CDC recommended treating only pregnant women and neonates with congenital syphilis with benzathine penicillin. The recommendation was to treat everyone else with doxycycline, but as of September 2024 the shortage had ended and benzathine penicillin G is again the recommended antibiotic for all.[14,17]

Recommended Regimen for Primary and Secondary Syphilis* Among Adults

Benzathine penicillin G 2.4 million units IM in a single dose

[14]

[Click here for further information on syphilis, syphilis and pregnancy, tertiary and neurosyphilis and HIV patients with syphilis.](#)

Chlamydia

Chlamydial infection, caused by *Chlamydia trachomatis* is the most frequently reported bacterial infectious disease in the U.S. In 2023 there were 1,648,568 reported cases of chlamydia, a decrease of 6% from 2018.[1,2] In 2020, the WHO estimated there were 129 million chlamydial infections worldwide.[18]

Doxycycline is first line treatment in adults, with azithromycin and levofloxacin as alternatives, although levofloxacin should not be used routinely due to potential adverse quinolone side effects.[19] In pregnant women, azithromycin is first line therapy with amoxicillin as an alternative.

Recommended Regimens for Chlamydial Infection Among Adolescents and Adults

Doxycycline 100 mg orally 2 times/day for 7 days

Alternative Regimens

Azithromycin 1 g orally in a single dose

OR

Levofloxacin 500 mg orally once daily for 7 days

[19]

Expedited partner therapy for chlamydial infections is permissible in 47 states and potentially allowable in three, although not specifically legislated for in those three states. This allows patients to be given prescriptions for their partners, to try to reduce disease transmission and complications.[20]

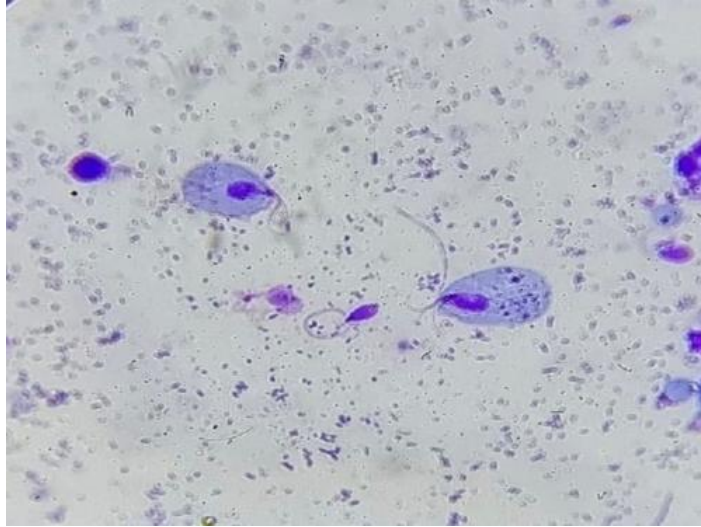
There is an experimental chlamydia vaccine currently called CTH522 which has completed a phase 1 trial. In that trial, there were 3 intramuscular injections at 0, 1 and 4 months followed by intranasal administration at 4.5 and 5 months. The vaccine induced anti-CTH522 IgG seroconversion in 100% of the fifteen subjects.[21]

[Click here for further information on chlamydial infections and treatment during pregnancy.](#)

Trichomoniasis

An estimated 2.6 million people in the U.S. are infected with trichomonas, caused by the flagellated protozoan parasite *Trichomonas vaginalis*. [22] According to the WHO, in 2020 there were approximately 156 million new cases worldwide of *T. vaginalis* infections among people aged 15–49 years old.[23]

Trichomoniasis is typically asymptomatic in men but may occasionally cause urethritis or prostatitis symptoms. Women may be asymptomatic or present with a yellow-green vaginal discharge.



Flagellated *Trichomonas vaginalis*

The medication of choice is oral metronidazole, with tinidazole as an alternate drug. Men can be treated with a single dose of metronidazole while women are generally treated for 7 days.[22] Treatment recommendations are different when breast feeding or during pregnancy and providers are advised to review current recommendations.

Recommended Regimen for Trichomoniasis Among Women

Metronidazole 500 mg 2 times/day for 7 days

Recommended Regimen for Trichomoniasis Among Men

Metronidazole 2 g orally in a single dose

Alternative Regimen for Women and Men

Tinidazole 2 g orally in a single dose

[22]

There is no current human vaccine for trichomoniasis but there is basic science research underway to try to develop one.[24]

[Click here for further information on *Trichomonas* infections including during pregnancy and while breast feeding.](#)

HIV

There are two new developments with respect to HIV (human immunodeficiency virus) treatment and prevention.

A phase 1/2 trial was completed with five patients using the drug EBT-101, a CRISPR derived gene editing therapy designed to cure HIV. It was well tolerated by the subjects. However, three of the patients developed a rebound serum HIV viral load, indicative of a return of their HIV disease. While EBT-101 at this dose did not succeed, further research into this type of therapy will continue, possibly at higher doses of EBT-101.[25]

In 2022, the antiviral lenacapavir was approved by the FDA for treatment for patients with multiple drug-resistant HIV. One of the advantages of lenacapavir is that it only needs to be administered subcutaneously once every 6 months.[26]

In July 2024, a phase 3 study for pre-exposure prophylaxis (PrEP) of HIV compared every 6-month subcutaneous lenacapavir versus daily oral HIV PrEP. It was reported that no cases of HIV developed in 2,134 women who received subcutaneous lenacapavir. Lenacapavir's zero HIV conversion rate compared to 1.5%-1.8% new cases of HIV in the oral PrEP groups. Lenacapavir's 100% effectiveness in the phase 3 study is felt to be a major step forward in drug compliance and effective prevention of HIV.[27] However, the cost of lenacapavir may be an issue as it currently costs tens of thousands of dollars more per year than oral HIV PrEP medications. FDA approval is now being sought to allow use of subcutaneous lenacapavir for HIV PrEP.[26]

Genital Herpes Simplex

An estimated 491 million people worldwide ages 15-49 (13% of the total population) have had a herpes simplex virus type 2 (HSV-2) infection, the main cause of genital herpes.[28] In 2018, among people aged 14-49 the CDC estimated that there were 572,000 new genital herpes infections in the U.S.[29] Although much less common, herpes simplex virus type 1 (HSV-1), typically seen in the mouth or on the lips, can also cause genital herpes.

The medications recommended in the treatment of genital herpes simplex are acyclovir, famciclovir, or valacyclovir. Recommended therapies for an initial infection are below.

Recommended Regimens*

Acyclovir† 400 mg orally 3 times/day for 7–10 days

OR

Famciclovir 250 mg orally 3 times/day for 7–10 days

OR

Valacyclovir 1 gm orally 2 times/day for 7–10 days

* Treatment can be extended if healing is incomplete after 10 days of therapy.

†Acyclovir 200 mg orally five times/day is also effective but is not recommended because of the frequency of dosing.

Recommended therapy for recurrent infections:

Recommended Regimens for Episodic Therapy for Recurrent HSV-2 Genital Herpes*

Acyclovir 800 mg orally 2 times/day for 5 days

OR

Acyclovir 800 mg orally 3 times/day for 2 days

OR

Famciclovir 1 gm orally 2 times/day for 1 day

OR

Famciclovir 500 mg once, followed by 250 mg 2 times/day for 2 days

OR

Famciclovir 125 mg 2 times/day for 5 days

OR

Valacyclovir 500 mg orally 2 times/day for 3 days

OR

Valacyclovir 1 gm orally once daily for 5 days

*Acyclovir 400 mg orally 3 times/day is also effective, but are not recommended because of frequency of dosing.

[29]

EBT-104 is an investigational CRISPR-editing therapy for herpes simplex, still in pre-clinical investigation. It has been reported that a single dose reduced herpes virus DNA by over 99.99% in laboratory cells[25] and significantly decreased viral shedding in a rabbit keratitis (corneal infection) model.[30]

[Click here for further information on genital herpes simplex infections including chronic suppressive therapy, treatment during pregnancy, severe infections and patient counseling.](#)

Human Papilloma Virus (HPV)

There are about 200 viruses that can cause an HPV infection. Some cause genital or oropharyngeal warts and some high-risk types can cause cancer, typically of the cancers of the vulva, vagina, mouth/throat, penis and rectum.[31] About 90% of HPV infections are effectively eliminated by the immune system within two years, but some continue on to become cancerous. It is estimated by the CDC that about 13 million Americans become infected each year and about 36,500 people per year are diagnosed with a cancer caused by HPV infection.[32,33] In 2019, it was estimated by the WHO that HPV caused approximately 620,000 cancer cases in women and 70,000 cancer cases in men worldwide.[31]

The CDC recommends two doses of HPV vaccine for all adolescents at age 11 or 12 years, that has been found to be over 90% effective at preventing HPV warts and induced cancers.[34]

[Click here for more information about the HPV vaccine.](#)

[Click here for further information on the treatment of anogenital warts.](#)

Mycoplasma genitalium [35]

Mycoplasma genitalium has been found to be the cause in 15% to 40% of cases of urethritis in men. In women with cervicitis, *M. genitalium* has been found in 10% to 30% of cases and found in 4% to 22% of women who have pelvic inflammatory disease.

M. genitalium is an extremely slow-growing organism and culture can take up to six months. The nucleic acid amplification test (NAAT) is considered the test of choice.

There is increasing macrolide resistance to *M. genitalium* and azithromycin is only recommended as first line therapy if macrolide sensitivity testing is available. Otherwise, the recommended treatment is doxycycline followed by moxifloxacin, each for 7 days. There appears to be a lack of consensus regarding the dosing schedule of azithromycin in pregnancy or when breast feeding. Moxifloxacin and doxycycline are contraindicated during pregnancy. In some areas of the world, pristinamycin is a second line drug for pregnant patients, but it is not available in the U.S. and data is limited as to safety. Clinicians are advised to review the latest information before treating pregnant women.[36,37]

Recommended Regimens if *M. genitalium* Resistance Testing is Available

If **macrolide sensitive**: **Doxycycline** 100 mg orally 2 times/day for 7 days, followed by **azithromycin** 1 g orally initial dose, followed by 500 mg orally once daily for 3 additional days (2.5 g total)

If **macrolide resistant**: **Doxycycline** 100 mg orally 2 times/day for 7 days followed by **moxifloxacin** 400 mg orally once daily for 7 days

Recommended Regimens if *M. genitalium* Resistance Testing is Not Available

If *M. genitalium* is detected by an FDA-cleared NAAT: **Doxycycline** 100 mg orally 2 times/day for 7 days, followed by **moxifloxacin** 400 mg orally once daily for 7 days

[34]

[Click here for more information on *Mycoplasma genitalium* diagnosis and treatment.](#)

Summary

Sexually transmitted infections affect millions of people each year. Increasing antibiotic resistance, especially for gonorrhea, may present therapeutic challenges. A new antibiotic to treat gonorrhea, zoliflodacin, is currently in clinical trials. The incidence of syphilis is rising, but benzathine penicillin G is still the drug of choice.

For HIV pre-exposure prophylaxis, an every 6-month injection of lenacapavir has been found to be very effective. It is still waiting FDA approval in the U.S. for that indication and is more expensive than oral prophylaxis, which may be an issue limiting use.

Vaccines, such as the HPV vaccine and ones being developed and tested for gonorrhea and chlamydia may be crucial in the future to help control global STI incidence.

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