

Study finds doxycycline reduces sexually transmitted infections by two-thirds

April 7 2023



Scanned electron micrograph image of *Neisseria gonorrhoeae* bacteria, which can cause gonorrhea. Credit: NIAID

The oral antibiotic doxycycline prevented the acquisition of sexually transmitted infections (STIs) when tested among men who have sex with

men (MSM) and transgender women who took the medication within 72 hours of having condomless sex, according to findings published today in the *New England Journal of Medicine*. Specifically, the post-exposure approach, termed doxy-PEP, resulted in a two-thirds reduction in the incidence of syphilis, gonorrhea, and chlamydia among the study participants, all of whom reported having an STI within the previous year. However, the research also revealed a slight increase in antibacterial resistance that requires further exploration, the authors found.

"Effective methods for preventing sexually transmitted infections are badly needed," said Hugh Auchincloss, M.D., NIAID acting director. "This is an encouraging finding that could help reduce the number of sexually transmitted infections in populations most at-risk."

STI incidence has been increasing in the United States over the past few years with a disproportionate impact among MSM and [transgender women](#). An estimated 2.5 million cases of syphilis, gonorrhea, and chlamydia occurred in 2021 up from 2.4 million cases in 2020, according to the Centers for Disease Control and Prevention. If left untreated, STIs can lead to serious health consequences, including brain and nerve problems, blindness, infertility and increased risk of HIV acquisition. Antimicrobial resistance among STIs is an emerging public health threat, particularly with *Neisseria gonorrhoeae*, and threatens available treatment options.

The study was led by researchers at the University of California at San Francisco (UCSF) and the University of Washington, Seattle. It enrolled 501 adults at four clinic sites in San Francisco and Seattle who were at least 18 years of age; assigned male sex at birth; reported sexual activity with a man in the previous year; diagnosed with HIV or taking or planning to take pre-exposure prophylaxis (PrEP) medication to prevent HIV acquisition; and diagnosed with gonorrhea, chlamydia or early

syphilis in the prior year. Of those enrolled, 327 participants were taking HIV PrEP medications, and 174 participants were people living with HIV.

Participants were randomly assigned to receive either doxy-PEP or standard of care. Those in the doxy-PEP arm were instructed to take one 200 milligram (mg) doxycycline-delayed release tablet, ideally within 24 hours but no later than 72 hours after condomless sex. Doxycycline is a broad-spectrum antibiotic in a family called tetracyclines. Participants were assessed by study staff every three months for adherence and side effects to the medication regimen and tested for STIs. Participant acceptability of the medication was assessed at six-and-12-month clinic visits. An independent data and safety monitoring board reviewed study progress and safety and effectiveness data every six months.

Among participants on HIV PrEP, at least one or more STIs were diagnosed in 10.7% of quarterly clinic visits in the doxy-PEP study arm compared to 31.9% of visits in the standard of care arm. Among study participants living with HIV, one or more STIs were diagnosed in 11.8% of quarterly visits in the doxy-PEP arm versus 30.5% in the standard of care arm. Gonorrhea was the most frequently diagnosed STI in the study. Participants reported good adherence to the medication regimen with 86.2% reporting taking doxy-PEP consistently within 72 hours of condomless sex, and 71.3% reported never missing a dose. No safety or acceptability issues were identified in the study.

"Given its demonstrated efficacy in several trials, doxy-PEP should be considered as part of a sexual health package for men who have sex with men and transwomen if they have an increased risk of STIs," according to Annie Luetkemeyer, M.D., professor of infectious diseases at Zuckerberg San Francisco General Hospital at UCSF, and co-principal investigator of the study. "It will be important to monitor the impact of doxy-PEP on antimicrobial resistance patterns over time and weigh this

against the demonstrated benefit of reduced STIs and associated decreased antibiotic use for STI treatment in men at elevated risk for recurrent STIs."

In examining the potential for antimicrobial resistance during doxy-PEP use, the researchers discovered tetracycline resistance in a greater number of incident gonorrhea strains among those in the doxy-PEP arm than among those in the standard of care group (38.5% versus 12.5%, respectively). This suggests that doxy-PEP may offer less protection against gonorrhea strains that are already tetracycline-resistant and that wider population-based surveillance for this type of resistance is important. Additionally, the researchers found that doxy-PEP reduced *Staphylococcus aureus*—a bacteria commonly found on the skin "colonization"—by 50% after a year. However, in those who still had *Staphylococcus aureus* colonization at month 12, a modestly higher proportion of those in the doxy-PEP group had doxycycline resistance (16% vs. 8%). This is important because doxycycline may be used to treat methicillin-resistant *Staphylococcus aureus* skin and soft tissue infections. Additional research and longer follow-up periods are needed to examine the potential [antimicrobial resistance](#) effect of intermittent doxy-PEP use. Doxy-PEP use in other populations disproportionately impacted by STIs, including women with HIV and those taking HIV PrEP, deserves further exploration as well.

"We need new, effective STI prevention methods and three studies have now demonstrated that doxy-PEP significantly reduces gonorrhea, chlamydia and syphilis. In the next several years during the implementation of doxy-PEP, we need to learn about maximizing equitable access and impact," said Dr. Connie Celum, Professor of Global Health and Medicine at the University of Washington and co-principal investigator of the DoxyPEP Study.

More information: Anne F. Luetkemeyer et al, Postexposure

Doxycycline to Prevent Bacterial Sexually Transmitted Infections, *New England Journal of Medicine* (2023). [DOI: 10.1056/NEJMoa2211934](https://doi.org/10.1056/NEJMoa2211934)

Provided by NIH/National Institute of Allergy and Infectious Diseases

Citation: Study finds doxycycline reduces sexually transmitted infections by two-thirds (2023, April 7) retrieved 2 May 2024 from <https://medicalxpress.com/news/2023-04-doxycycline-sexually-transmitted-infections-two-thirds.html>

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