

Will DoxyPEP have an impact on antimicrobial resistance for other STIs such as chlamydia, syphilis, or mycoplasma genitalium?

Chlamydia: Doxycycline is considered first line treatment. There is no tetracycline clinical resistance that has been reported.

Syphilis: Doxycycline is an alternative therapy for syphilis that has been utilized increasingly in non-pregnant individuals due to the recent bicillin shortage. There is no tetracycline clinical resistance that has been reported.

Mycoplasma genitalium: Doxycycline is part of a two-step treatment, and clinical resistance to this regimen has not been described.

Does DoxyPEP impact syphilis serologies such as delayed diagnoses or false negative results?

There is still more information needed in this area. If a patient is suspected of having syphilis while on DoxyPEP, then treat according to CDC STI treatment guidelines. If a patient has been exposed to syphilis while on DoxyPEP, presumptive treatment for syphilis is recommended since *Treponema pallidum* (bacteria responsible for syphilis) has a long incubation period and serologic testing window period.

Does DoxyPEP affect the *Staphylococcus aureus* and the microbiome?

In those that used doxycycline within the DoxyPEP trial, there was a 14% absolute reduction in *Staphylococcus aureus* colonization, and there was an 8% absolute increase in doxycycline resistant *Staphylococcus aureus* compared to baseline. We do not know yet the impact of doxycycline on the microbiome and significance of these changes.

References:

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- ANRS 174 DOXYVAC Study: Molina J. M., Bercot B., Assoumou L., et al. ANRS 174 DOXYVAC: an open-label randomized trial to prevent STIs in MSM on PrEP. Abstract 119. CROI; 2023 Feb 19-22; Seattle, WA. <https://www.croiconference.org/abstract/anrs-174-doxyvac-an-open-label-randomized-trial-to-prevent-stis-in-msm-on-prep/>
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- IAS-USA Invited Review (Vol 31, Issue 5, November/December 2023): Cannon, CA. Doxycycline Postexposure Prophylaxis for Prevention of Sexually Transmitted Infections
- Haaland, R. et al. Mucosal pharmacology of doxycycline for bacterial STI prevention in men and women. Conference on Retroviruses and Opportunistic Infections (CROI) Conference, Abstract 118, Seattle, WA. Link: <https://www.croiconference.org/abstract/mucosal-pharmacology-of-doxycycline-for-bacterial-sti-prevention-in-men-and-women/>
- CDC Considerations for DoxyPEP: <https://www.cdc.gov/std/treatment/guidelines-for-doxycycline.htm>

What is DoxyPEP?

Doxycycline is an antibiotic active against *Chlamydia trachomatis* (CT), *Treponema pallidum* (bacteria responsible for syphilis), and some strains of *Neisseria gonorrhoeae* (GC). In a randomized controlled trial published in 2023, doxycycline was shown to greatly reduce syphilis, gonorrhea, and chlamydia infections in populations with high sexually transmitted infection (STI) incidence when it was used as post-exposure prophylaxis (DoxyPEP) within 72 hours of condomless oral, anal, or vaginal sex.

What is the efficacy of DoxyPEP?

- DoxyPEP has been studied in men who have sex with men (MSM), transgender women (TGW), and cisgender women (CGW) and has not yet been studied in transgender men (TGM).
- Below are the seminal DoxyPEP trials and findings that showed an overall reduction in bacterial STI incidence in MSM and TGW. Despite a modest reduction in STI incidence in cisgender women (CGW), this finding was likely due to low adherence to the DoxyPEP regimen.

Study	Population	STI Risk Reduction Findings
IPERGAY (Paris, France, 2015-2016)	MSM on HIV PrEP	47% risk reduction for chlamydia and syphilis
DOXYPEP (Seattle, WA and San Francisco, CA, 2020-2022)	MSM and TGW on HIV PrEP or People with HIV (PWH) with: <ul style="list-style-type: none"> History of at least 1 STI in the past 12 months Condomless sex with at least 1 male partner in the past 12 months 	<p>HIV PrEP Cohort: 66% overall risk reduction STI risk reduction per quarter listed below:</p> <ul style="list-style-type: none"> Chlamydia: 88% Syphilis: 87% Gonorrhea: 55% <p>PWH Cohort: 62% overall risk reduction STI risk reduction per quarter listed below:</p> <ul style="list-style-type: none"> Chlamydia: 74% Syphilis: 77% Gonorrhea: 57%
DOXYVAC (Paris, France, 2021-2022)	MSM on HIV PrEP with a bacterial STI in prior 12 months	84% risk reduction for chlamydia and syphilis
DPEP (Kisumu, Kenya, 2020-2022)	Cisgender women on HIV PrEP	12% risk reduction for chlamydia and gonorrhea. The finding is likely due to low adherence to the DoxyPEP regimen.

Who can take DoxyPEP?

- Based on efficacy data, LAC **recommends** DoxyPEP for gay, bisexual, and other men who have sex with men (MSM) and transgender women (TGW) who had 1 bacterial STI in the past 12 months or patients that have frequent condomless sex with multiple partners that are at elevated risk of a STI.
- LAC recommends providers to **consider prescribing** DoxyPEP utilizing shared-decision making to patients where efficacy has not been demonstrated yet (cisgender women, transgender men, and cisgender men who have sex with women with history of condomless sexual intercourse) or those who are interested in DoxyPEP based on current evidence.
- Doxycycline is contraindicated in pregnancy, so DoxyPEP should not be prescribed to pregnant persons.

What formulations of doxycycline can be used for DoxyPEP?

While the DoxyPEP randomized controlled trial utilized delayed-release 200mg doxycycline *hyclate* tablets, this option might not be easily available. It is recommended to use 2 doxycycline *hyclate* or *monohydrate* immediate release 100mg tablets or capsules taken together. The monohydrate formulation may have less gastrointestinal symptoms.

Is the concentration of doxycycline the same in all tissues?

Based on pharmacokinetic studies, the concentration of doxycycline is not the same in all tissues. Vaginal secretions have the highest maximum doxycycline concentration after a dose is taken followed by plasma and rectal secretions. With all patients, adherence counseling and STI testing is important.

Is DoxyPEP safe and well tolerated?

Doxycycline is safe and well tolerated. The most common side effects are gastrointestinal in nature such as nausea, vomiting, and diarrhea. Additional safety considerations include not lying down 30 minutes before or after taking doxycycline, pill esophagitis, esophageal ulceration, and benign intracranial hypertension. The potential for side effects is generally low and would be more likely with more frequent DoxyPEP use.



What are some drug interactions to consider with DoxyPEP?

Providers should take a complete medication history including prescribed and over-the-counter supplements. Doxycycline interacts with antacids, Pepto-Bismol, warfarin, certain anti-epileptic medications, and any supplements that contain calcium, zinc, magnesium, or iron. If there is a concern for a potential drug interaction, then recommend to the patient to take doxycycline 2 hours before or after antacids or medications that contain calcium, zinc, magnesium, or iron.

What type of monitoring is needed for DoxyPEP?

No baseline labs are required, but labs should be checked annually at a minimum. The doxycycline FDA package insert notes that liver function tests (LFTs), renal function, and complete blood count (CBC) should be checked periodically.

Screen for STIs at all anatomic exposure sites every 3-6 months. If a patient is diagnosed with a STI on DoxyPEP, then treat according to CDC STI treatment guidelines. Since *Treponema pallidum* (bacteria responsible for syphilis) has a long incubation period and serologic testing window period, presumptive treatment for syphilis is recommended if infection is suspected regardless of DoxyPEP use.

Will DoxyPEP drive antimicrobial resistance?

Studies have not been conducted looking at whether DoxyPEP would drive antimicrobial resistance. There is a potential drive for resistance, but the data is limited. In addition to treating STIs, doxycycline is utilized to treat many medical conditions such as acne and malaria. As a result of this and the short time frame surrounding DoxyPEP use, it would be difficult to isolate the resistance to the use of just DoxyPEP for STIs.

Will existing tetracycline-resistance affect DoxyPEP efficacy against gonorrhea?

About 20% of gonococcal isolates in the USA are resistant to doxycycline. Also, doxycycline has not been the first line treatment for gonorrhea in decades. This makes it all the more impressive that DoxyPEP still had a profound impact on subsequent gonococcal infections in both the USA and France, where rates of gonorrhea resistance are even higher.