CDPH
Health and Human Services Agency
California Department of Public Health

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Doxycycline Post-Exposure Prophylaxis (doxy PEP) for the Prevention of Bacterial Sexually Transmitted Infections (STIs)

Dear Colleague,

The California Department of Public Health (CDPH) would like to inform all health care providers of a compelling new biomedical intervention to prevent bacterial STIs. Evidence from a study among men who have sex with men (MSM) and transgender women (TGW) suggests **doxycycline, when taken as doxy PEP after condomless oral, anal, or vaginal sex, significantly reduces acquisition of chlamydia (CT), gonorrhea (GC), and syphilis.**[1] Given the high rates of these STIs in California[2], **CDPH recommends the following:**

1. **Recommend doxy PEP** to men who have sex with men (MSM) or transgender women (TGW) who have had ≥1 bacterial STI in the past 12 months.
2. **Offer doxy PEP using shared decision-making** to all non-pregnant individuals (e.g., cisgender women/men, transgender women/men, and non-binary persons) at increased risk for bacterial STIs and to those requesting doxy PEP, even if these individuals have not been previously diagnosed with an STI or have not disclosed their risk status.[i]
3. **Provide comprehensive preventative sexual health counseling and education** to all sexually-active individuals to include HIV/STI screening, doxy PEP, HIV pre-exposure prophylaxis (PrEP)/HIV post-exposure prophylaxis (PEP), vaccinations (e.g., Hepatitis A/B, Human Papilloma Virus, Mpox, Meningococcal/MenACWY), expedited partner therapy, and/or contraception where warranted.

[i] Doxy PEP can be offered to all non-pregnant individuals at increased risk of STIs, including cisgender women and men, transgender women and men, and non-binary persons, but data is limited. In a randomized trial of 449 cisgender Kenyan women, doxy PEP was not shown to be protective against STIs, but hair analyses suggest that nonadherence may have been the reason for lack of efficacy.[3] Pharmacologic studies suggest that doxycycline levels in vaginal fluid should be sufficient to provide such protection.[4] Doxy PEP has not been studied in transgender men or non-binary persons.

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Evidence:
A randomized controlled trial (RCT) using **a single, oral dose of doxycycline 200mg within 72 hours after condomless oral, anal, or vaginal sex** in MSM and TGW, who were either persons living with HIV (PLWH) or taking HIV PrEP, showed **significant reductions in CT, GC, and syphilis** per quarter of study follow up. In persons on HIV PrEP, taking doxy PEP reduced syphilis by 87 percent, CT by 88 percent, and GC by 55 percent while in PLWH doxy PEP reduced syphilis by 77 percent, CT by 74 percent, and GC by 57 percent.[1]

Safety:
Taking doxycycline is safe and well tolerated, with no reported doxycycline associated Grade 2 or higher adverse events (AEs) and no documented laboratory-related severe AEs in the DoxyPEP RCT. Long-term use of doxycycline has been prescribed safely for other medical indications (e.g., acne treatment or malaria prophylaxis).

Unknowns:
Data continue to be collected and reviewed for possible antimicrobial resistance among bacterial STIs, commensal *Neisseria* (as a potential reservoir for tetracycline resistant plasmids), and *Staphylococcus aureus*. The effects of doxy PEP on the gut microbiome are also being studied.

Prescribing doxy PEP:
Doxycycline is not FDA approved for STI PEP and there is no national organizational guidance for its use as STI prevention. However, Centers for Disease Control and Prevention (CDC) has released considerations for doxy PEP as an STI preventative strategy[5] and San Francisco Department of Public Health has released their own guidance, including counseling messages.[6]

i. **Prescribe 200 mg of doxycycline taken within 72 hours** (ideally within 24 hours or as soon as possible) **after condomless oral, anal, or vaginal sex.** Doxycycline can be taken daily depending on sexual activity, but no more than 200 mg every 24 hours.
ii. **Screen for GC and CT at all anatomic sites of exposure** (urogenital, pharyngeal, and/or rectal), as well as test for **syphilis and HIV** (if not known PLWH) **at initiation of doxy PEP and every three months**. If diagnosed with an STI, treat according to standard CDPH and CDC STI treatment guidelines.
iii. Doxycycline should not be taken during pregnancy – counsel persons who can become pregnant.[7]
iv. Consider hematopoietic, renal, and hepatic laboratory monitoring as clinically indicated in addition to counseling patients on standard precautions and warnings while taking doxy PEP, as outlined in the drug package insert (e.g., sun sensitivity, pill esophagitis, and rarely intracranial hypertension).[8]

Please reach out to stdcb@cdph.ca.gov if you have any questions about this guidance.

Sincerely,

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Chief, STD Control Branch
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References:

1. Luetkemeyer et al. Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections. N Engl J Med. 2023;388(14):1296-1306. doi:10.1056/NEJMoa2211934
2. CDPH 2020 STI Surveillance Report
3. Stewart et al. "Doxycycline prophylaxis to prevent sexually transmitted infections in women." New England Journal of Medicine 389.25 (2023): 2331-2340. PMID: 38118022
4. Haaland et al. "Pharmacokinetics of single dose doxycycline in the rectum, vagina, and urethra: implications for prevention of bacterial sexually transmitted infections." EBioMedicine 101 (2024). PMCID: PMC10910237
5. CDC Considerations for Doxycycline as STI PEP: Primary Prevention Methods (cdc.gov)
6. San Francisco Department of Public Health, Health Update: Doxycycline Post-Exposure Prophylaxis Reduces Incidence of STIs
7. Doxycycline use by pregnant and lactating people: Doxycycline Use by Pregnant and Lactating Women | FDA
8. FDA. Package Insert for Doryx® (doxycycline hyclate) and Doryx® MPC Delayed-Release Tablets. February 2018. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/050795s026lbl.pdf

Additional Resources:

- CDPH STD Control Branch Homepage
  - California STI Screening Recommendations
  - California STI Treatment Guidelines
- CDC
  - STI Screening Recommendations
  - 2021 STI Treatment Guidelines
  - HIV Screening Guidelines
  - PrEP & non-occupational PEP guidelines
- Expedited Partner Therapy: CDC & CDPH recommendations and California SB306 regulations
- California Prevention Training Center – Educational opportunities and training materials for STDs
- STD Clinical Consultation Network – Online consultation for questions about evaluation and management of STDs

Addendum:
This letter was revised on 1/15/2025 to define “all non-pregnant individuals” (see pg. 1 footnote) and include updates from relevant research. Changes related to this guidance were made throughout the document. Since the initial publication of this letter, CDC released Clinical Guidelines for the Use of Doxy PEP.