

Doxy-PEP: doxycycline post-exposure prophylaxis for STI prevention

The good, the bad, and the unknowns

Chase Cannon, MD, MPH 25 October 2023



Are you currently discussing or prescribing doxy-PEP for any of your patients or clients?

- A. Yes, definitely!
- B. Sometimes, it depends on the person
- C. Never and don't plan to
- D. No, but I'm considering it



What are your concerns about doxy-PEP, if any? (Select all that apply)

- A. We don't have enough evidence to support its use
- B. Doesn't work in all populations
- c. Risk for antimicrobial resistance
- D. Risk for inducing resistance in STI pathogens
- E. Side effects of doxycycline
- F. Changes to microbiome
- G. Giving out doxy-PEP will lead to changes in sexual behavior
- H. The risks aren't worth the benefits at this time

The US STI epidemic disproportionately impacts MSM





Rates of STI soar while new HIV diagnoses continue to decline



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STD Prevention Training Center

The unspoken burden of STI



ERASE THE STIGMA Except for rare cases of complicated syphilis, most STIs in MSM and transgender women **do not** have long-term or serious physical health effects

Risk for transmission to women and other pregnancy capable people?

Being diagnosed with and disclosing STIs to partners can be annoying, stressful and stigmatizing

CDC's effort to "Talk, Test, Treat" has been the STI control strategy to date - is this enough?



Doxycycline post-exposure prophylaxis (doxy-PEP) is the strategy of taking 200 mg of doxycycline within 24-72 hours after condomless sex to prevent bacterial sexually transmitted infections (STI) like gonorrhea, chlamydia and syphilis.

IPERGAY: doxy PEP



Substudy of doxy PEP in 232 MSM on HIV PrEP as part of larger PrEP trial Open-label doxycycline PEP 200 mg with 24 hrs (and no more than 72 hrs) vs. no PEP 1:1 randomization Doxy PEP up to 3x weekly Median of 660 mg doxy taken per month Significant reduction in chlamydia & syphilis and but not effective for gonorrhea (GC)



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DOXYPEP

Study was done to understand if taking intermittent doxy-PEP after sex would:

Decrease the 3 most common bacterial STIs, and

Lead to antibiotic resistance in STIs and other bacteria.

Why doxycycline?

Generally safe, well tolerated and inexpensive Active against chlamydia & syphilis without evidence of resistance Some gonorrhea have resistance; unknown how much activity is needed for PEP



Intervention: <u>Open label</u> doxycycline 200mg taken as PEP within 72 hours after condomless sexual contact *Maximum of 200 mg every 24 hours*

Inclusion criteria:

- Male sex at birth
- Living with HIV or on PrEP
- ≥ 1 STI in past 12 months
- Condomless sex with ≥ 1 male partner in past 12 months

STI Testing: Quarterly 3 site GC/CT testing + RPR, GC culture before treatment

Sites: San Francisco & Seattle HIV & STI clinics



DOXYPEP

DoxyPEP: baseline characteristics



	PrEP	Living with HIV	Total
Participants* (ITT population)	327	174	501
Age	36 (31 - 42)	43 (36 - 54)	38 (32 - 47)
Race			
White	210 (67%)	111 (66%)	321 (67%)
Black	14 (5%)	22 (13%)	36 (8%)
Asian/Pacific Islander	45 (14%)	8 (5%)	53 (11%)
Multiple races/other	44 (14%)	28 (17%)	72 (15%)
Ethnicity: Hispanic/Latino	96 (29%)	55 (32%)	151 (30%)
Gender identity			
Man	319 (98%)	163 (94%)	482 (96%)
Trans woman/gender diverse	8(2%)	11 (6%)	19 (4%)
Gender of sexual partners: Male only	281 (86%)	153 (88%)	434 (87%)
STI in past 12 months**			
Gonorrhea	233 (71%)	110 (63%)	343 (69%)
Chlamydia	207 (63%)	85 (49%)	292 (58%)
Syphilis†	48 (15%)	52 (30%)	100 (20%)
Sexual partners in past 3 months	9 (4 - 17)	8.5 (3 - 20)	9 (4 - 17)
Substance use in past 3 months	178 (55%)	115 (68%)	293 (59%)
Stimulants (methamphetamine, cocaine,	73 (23%)	73 (43%)	146 (30%)
crack)			
Ecstasy, GHB, ketamine	97 (30%)	60 (35%)	157 (32%)
Amyl Nitrates (poppers)	140 (43%)	84 (49%)	224 (45%)

Luetkemeyer, AIDS 2022

* As of 5/13/22 with at least one follow-up visit ** Total may exceed 100% as more than 1 STI possible, † Syphilis: Limited to 1°, 2°, early Latent

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Primary Endpoint: STI incidence per quarter







Impact on symptomatic STIs by anatomic site



	Doxy-PEP	Standard of care	RR (95% CI)	Р
	n/1,201 quarters	n/533 quarters		
Gonorrhea	79 (6.6%)	78 (14.6%)	0.45 (0.33-0.60)	<.0001
Symptomatic rectal GC	6 (0.5%)	8 (1.5%)	0.33 (0.11-0.99)	0.0478
Symptomatic urethral GC	3 (0.2%)	15 (2.8%)	0.09 (0.03-0.31)	0.0002
Chlamydia	20 (1.7%)	50 (9.4%)	0.18 (0.10-0.31)	<.0001
Symptomatic rectal CT	0 (0.0%)	6 (1.1%)	-	-
Symptomatic urethral CT	0 (0.0%)	6 (1.1%)	-	-
Site specific GC + CT				
Pharyngeal (GC or CT)	55 (4.6%)	52 (9.8%)	0.47 (0.33-0.67)	<.0001
Rectal (GC or CT)	54 (4.5%)	77 (14.4%)	0.31 (0.21-0.46)	<.0001
Urethral (GC or CT)	11 (0.9%)	23 (4.3%)	0.21 (0.09-0.49)	0.0003
Syphilis	4 (0.3%)	10 (1.9%)	0.18 (0.06-0.56)	0.0031

- Doxy-PEP \downarrow the incidence of STIs associated with greater morbidity: syphilis and symptomatic rectal & urethral GC/CT
- More than 80% of rectal GC & CT infections were asymptomatic in both arms. Doxy-PEP also significantly reduced incidence of asymptomatic infections.



44 participants from doxy-PEP arm interviewed

Structured 1:1 interviews, oversampled racial and ethnic minorities

17% Black, 30% Hispanic; 45% LWH

Overarching themes about doxy-PEP

Lived experience of doxy-PEP generally expressed as giving more sexual pleasure and "peace of mind."

Did not believe it changed their sexual behavior (just their mindset about it).

Viewed as being proactive, responsible about one's health & health of community. "It just means that I'm taking care of myself, I'm staying healthy, that I care, that I don't want to be transmitting STDs."

Aware of risk of AMR, but not a barrier to use.



Doxy-PEP AMR Data

GC: resistance testing through CDC SURRG & ARLN

Chlamydia: culture w/ phenotypic susceptibility

Syphilis- molecular testing (exploratory)

M. gen: asymptomatic prevalence & symptomatic incidence, urine/rectal, & TCN-R

S. aureus & commensal Neisseria: tetracycline class resistance

Gut microbiome: change in flora, diversity & tetracycline resistance genes

DOXYVAC Study Design

Combined Prevention of STIs in MSM using oral PrEP with TDF/FTC



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4CMenB Vaccine for GC prevention

Bexsero data being reanalyzed - stay tuned

Current ACIP Recommendations:

Quadrivalent (ACWY) recommended for:

- Adolescents aged 11 or 12, booster at 16
- ▶ People at increased risk for severe disease, including people living with HIV
- ▶ People at increased risk because of an outbreak caused by A, C, W or Y

MenB recommended for:

- >Adolescents and young adults aged 16-23 years based on shared clinical decision-making
- People at increased risk for severe disease

New pentavalent combination meningococcal vaccines in pipeline (ABCWY)- GSK (has GC OMV homology) and Pfizer (does NOT have OMV)

Phase II study of Bexsero in US men & women for GC prevention underway (MAGI, NCT04350138)

https://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-positive-top-line-results-phase-3-trial-0 https://www.gsk.com/en-gb/media/press-releases/gsk-announces-positive-pivotal-phase-iii-data-for-5-in-1-meningococcal-abcwy-vaccine-candidate/ Slide courtesy of Stephanie Cohen



dPEP Kenya results in 449 cisgender women



Analysis	Endpoint	Total	PEP (N=224)	SOC (N=225)	RR	95% CI	P-value
Intention to	All STIs	109	50	59	0.88	0.60-1.29	0.51
Treat	Chlamydia	85	35	50	0.73	0.47-1.13	0.16
	Gonorrhea	31	19	12	1.64	0.78-3.47	0.19
Censoring	All STIs	105	48	57	0.91	0.62-1.35	0.65
Pregnancy Time	Chlamydia	82	33	49	0.73	0.46-1.15	0.18



Stewart CROI 2023, abstract 121

Adherence likely explains low efficacy in Kenyan cis women

High Self-reported adherence

- Quarterly surveys
- 77% (579/755) coverage of last sexual exposure

Timeline follow-back calendar

 In 72.8% of the quarterly surveys, >80% of sexual acts were covered

Weekly SMS

- 64% (134/211) participants reported full coverage in at least 80% of weeks
- 78% of weekly SMS reported full coverage

Doxy Hair testing: 44% without doxy detected

Results: Hair drug testing

- In a randomly selected subset of 50 participants assigned to doxycycline PEP
 - 56.0% (28/50) of participants had doxycycline detected at least once
 - 29.0% (58/200) of all quarterly visits had doxycycline detected,
 - 32.6% (58/178) when medication holds excluded
- 6.7% (3/45) of enrollment visits had doxycycline detected
- 5.1% (2/39) of follow up visits among SOC group had doxycycline detected

Mucosal Doxycycline Concentrations



Minimum Inhibitory Concentrations (MIC):

*Fold above MIC

N gonorrhoeae (NG) MIC = 250 ng/mL CDC Antimicrob Resist Susc Test

T pallidum (TP) MIC₉₀ = 100 ng/mL Edmondson *Antimicrob Agents Chemother* 2020

C trachomatis (CT) MIC₉₀ = 64 ng/mL Zheng *Sex Transm Dis* 2015

Haaland CROI 2023, abstract 118



Evidence for doxy-PEP in 2023

Study	Participating population		Participating STI rate or outcome population		Relative risk reduction	Absolute risk reduction
			Doxy-PEP	No doxy-PEP		
IPERGAY* (France, 2015- 2016)	232 MSM on	HIV PrEP	37.7 per 100 person- years	69.7 per 100 person- years	47%* (15-67%)	32 per 100 person-years
DoxyPEP 501 MSM &	501 MSM & TGW with	PWH (n=174)	11.8% per quarter	30.5% per quarter	52% (17-72%)	18.7% per quarter
(Seattle & SF, 2020-2022)	recent bact. STI	PrEP (n=327)	10.7% per quarter	31.9% per quarter	66% (49-77%)	21.2% per quarter
DOXYVAC* (France, 2021- 2022)	502 MSM on with recent	HIV PrEP bact. STI	5.6 per 100 person- years	35.4 per 100 person- years	84%* (70-92%)	30 per 100 person-years
dPEP (Kenya, 2020- 2022)	449 cis wom PrE	en on HIV P	50 CT/GC infections total	59 CT/GC infections total	12% (P=0.51)	9 total infections at 12 months

*Point estimates are for CT & syphilis only

Molina JM et al, Lancet Infect Dis 2018; Luetkemeyer A et al, NEJM 2023; Molina JM CROI 2023, Stewart J CROI 2023



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In Seattle & SF, taking doxy-PEP reduced risk of STI by 65% in MSM and transgender women

Over 70% of prevented STIs were asymptomatic

Participants took median of 4 doses of doxy PEP per month



Of the STIs prevented: 50% were gonorrhea 43% were chlamydia 7% were syphilis

43 extra days of antibiotics per year

1.4 fewer STIs per year

Reintroducing doxycycline





Tetracycline class antibiotic in use since 1967

Side effects: sun sensitivity, nausea and stomach upset, pill esophagitis Broad spectrum of activity against bacteria and parasites Used to treat many conditions: acne, rosacea, cholera, Lyme disease, Staph infections, walking pneumonia In STI world: syphilis, chlamydia, *Mycoplasma genitalium*, donovanosis, chancroid, etc.



If used broadly for PEP, what undesired effects will it have on the population at large?

"Pros" and documented benefits



- Doxy PEP substantially reduced bacterial STIs in certain MSM & TGW, regardless of HIV status, and could decrease STI rates at the population level
- Doxy PEP was safe, well tolerated, highly acceptable and adherence was high
- People want it! High uptake in San Francisco, Detroit, other parts of California
- Low "number needed to treat" (5 people) for large effect size
- Qualitative data: improved peace of mind and sexual pleasure, decreased stigma associated with being diagnosed with and disclosing STI
- Reduced exposure to ceftriaxone by 50% but increased doxy use
- Doxycycline is very cheap (5-6¢ per pill)
- PEP involves less use of antibiotics than PrEP (~50 days vs 365 days per year)

"Cons" and potential risks



- Most prevented STIs are asymptomatic. It's not clear if doxy PEP prevents STI-related morbidity
 - On average, doxy PEP will prevent <1 symptomatic STI per year in people who use it
 - We don't know if this will include complicated syphilis
- High chance that widespread use of doxy PEP will result in gonorrhea resistance. This would decrease the possible benefit of doxy PEP by 50%
- Doxy PEP could increase risk of resistance in bystander bacteria like *Staph aureus*, which can cause severe infections
- Doxy PEP could negatively impact the individual and population-level microbiome and increase risk for chronic illnesses (diabetes, autoimmune disease or some cancers)
- Goes against trend to use fewer antibiotics (antimicrobial stewardship)
- Doxy supply may run low and limit availability for treating other infections

Remaining unknowns and what we're still learning



How well does one need to take doxy-PEP to be protected?



Sexual behavior at enrollment: Median of 9 sexual partners (IQR 4,17) with 5 sexual acts per month (IQR 1.7, 10.7) and 90.1% of sex as condomless.

No significant change in sexual behavior during follow-up in doxy-PEP arm Adherence to doxy-PEP:

86% reported doxy-PEP always/often after anal/vaginal sex

Median doxy-PEP doses: 4.0 per month (IQR 1.0- 10.0)

25% with \geq 10 doses/month, based on quarterly interview

Ceftriaxone use: 50% less in doxy-PEP arm

Doxy-PEP: 48.4 person-years vs SOC: 103.6 person years

Luetkemeyer, AIDS 2022



DOXYVAC: Changes in Sexual Behavior



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Remaining unknowns and what we're still learning



- How well does one need to take doxy-PEP to be protected?
- What level of tetracycline resistance in *Neisseria gonorrhoeae* will render doxy-PEP ineffective when used for prevention vs treatment?
- What will be the impact on bystander bacteria like *Staph aureus*, commensal *Neisseria* spp, gut microbiome?
- Could resistance develop in *T. pallidum* and *C. trachomatis*? Some evidence of resistance in pigs with *C. suis* (human transfer)?



 Doxy-PEP associated with 14% absolute reduction in colonization and an 8% absolute increase in doxycycline resistance compared to baseline.



 MRSA prevalence was low (6%) & doxy-R MRSA was unchanged with doxy-PEP use.





S. aureus

N.

• Doxy-PEP associated with 14% absolute reduction in colonization and an 8% absolute increase in doxycycline resistance compared to baseline.



- MRSA prevalence was low (6%) & doxy-R MRSA was unchanged with doxy-PEP use.
- DoxyPEP: TCN-R was present in 4 baseline GC isolates, 6 incident GC isolates in doxy-PEP arm, and 2 incident GC isolates in SOC arm.
- *gonorrhoeae* DOXYVAC: High-level TCN-R in 33% of isolates in doxy-PEP arm vs. 19% in SOC arm

Suggests doxy-PEP may be less protective against existing TCN-R strains; however, limited by small numbers

Limitations:

- Small number of GC isolates available from incident cases
- ≤12 months of follow-up
- SOC participants also received doxycycline for incident STIs





Luetkemeyer et al DoxyPEP CROI 2023 Molina et al DOXYVAC CROI 2023 What are the implications if doxy-PEP use increases *N. gonorrhoeae* TCN resistance?

TREATMENT: Will not impact gonorrhea therapy: doxycycline/tetracycline not used for treatment

OVERALL RESISTANCE: Could potentially drive resistance to other classes- data are mixed

 \downarrow DOXY-PEP EFFICACY? ANRS DOXYVAC study found doxy-PEP effective despite current TCN resistance of in France of 65-85%. Threshold to impact doxy-PEP is not known. Impact of high-level vs lower level TCN resistance in GC?

Doxy-PEP reduced incident GC, thus reducing exposure to ceftriaxone by ≈50%

DRUG-RESISTANT GONORRHEA

AN URGENT PUBLIC HEALTH ISSUE



Chlamydia

- Doxy is now 1st line treatment for CT
- No clinical resistance to TCN class reported
- TCN resistance has
 been seen in *C.suis* (pig
 chlamydia) could this
 be transferred to
 humans or acquired de
 novo?

Syphilis

- Doxy is an alternative tx, used more now with Bicillin shortage
- No clinical resistance to TCN class reported
- TCN resistance is with single point mutation
- Potential impact on syphilis serologiesdelayed diagnosis or false negative?

M. genitalium

- Doxy not very effective poor cure rate as monotherapy, but part of two-step therapy for *M. genitalium*
- Substantial resistance to macrolides & fluoroquinolones
- Clinical *M. genitalium* resistance not yet described - clinical impact?



Dugan 2004 AAC, Stamm AAC 20107

Remaining unknowns and what we're still learning



- How well does one need to take doxy-PEP to be protected?
- What level of tetracycline resistance in *Neisseria gonorrhoeae* will render doxy-PEP ineffective when used for prevention vs treatment?
- What will be the impact on bystander bacteria like *Staph aureus*, commensal *Neisseria* spp, gut microbiome?
- Could resistance develop in *T. pallidum* and *C. trachomatis*? Some evidence of resistance in pigs with *C. suis* (human transfer)?
- Will intermittent doxycycline use affect our ability to diagnose syphilis?
- Efficacy & risk/benefit of using doxy-PEP in MSW, gender diverse persons?
- Would another study of doxy-PEP in cis women be useful?

Should asymptomatic STI contacts be empirically treated if taking doxy-PEP?



 Overtreatment of contacts represents an estimated 2-4% of the 47 million doses of overused antibiotics in the US

STI	Pos. test rate among MSM contacts	RRR from doxy-PEP	Estimated pos. test rate in contacts on doxy PEP
GC	34%	56%	15%
СТ	34%	81%	6.5%

Syphilis: test + empiric treatment due to transmission risk

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Doxy-PEP Guidelines and Implementation

Public health guidance for doxy-PEP



- Multiple US sites with guidance: San Francisco, Alameda County, California DPH, Santa Clara County, Seattle - King County
- CDC provisional guidelines for public comment
- IAS-USA: consider on case-by-case basis
- Public Health England/BASHH: not endorsed due to AMR concerns
- ASHM: use primarily for syphilis; consider clustering doses



POPULATION HEALTH DIVISION SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH



Health Update

Doxycycline Post-Exposure Prophylaxis Reduces Incidence of Sexually Transmitted Infections

October 20, 2022

HIV/STI/HCV Program Sexual Health Clinic Ninth and Jefferson Building 908 Jefferson St, 11th Floor Seattle, WA 98104 206-744-3590 www.kingcounty.gov/health

Public Health Seattle & King County

Guidelines, June 2023

Doxycycline Post-Exposure Prophylaxis (Doxy-PEP) to Prevent Bacterial STIs in Men who Have Sex with Men (MSM) and Transgender

Persons who Have Sex with Men



Box. Population recommended for consideration for use of doxycycline as PEP for bacterial STI prevention

Recommendation	Strength of recommendation
	and quality of evidence
 Doxycycline 200mg taken once orally within 72 hours of oral, vaginal or anal sex should be considered for gay, bisexual, and other men who have sex with men, and for transgender women, with a history of at least one bacterial STI (i.e. gonorrhea, chlamydia or syphilis) in the last 12 months. 	AI
 No recommendation can be given at this time on the use of doxycycline PEP for cisgender women, cisgender heterosexual men, transgender men, other queer and nonbinary individuals. If this intervention is offered, it should be implemented with considerations for ancillary services detailed below. 	There is insufficient evidence to assess the balance of benefits and harms of the use of doxycycline PEP



Initial Visit	Follow Up Visits
GC/CT (all sites), syphilis	Same
HIV (per CDC HIV PrEP guidelines), or q 3-6 mos	Same
Risk reduction counseling: condoms, reducing partners, HIV PEP, PrEP or HIV treatment	Same
Counsel re: side effects: Photosensitivity, esophagitis, GI intolerance , potential for antibiotic resistance in other pathogen	Assess side effects
Counsel no antacids or supplements with Ca, Fe, Mg, or Na Bicarb within 2 hrs of dose	
Doxy may reduce efficacy of oral contraceptives, use backup method	
Provide enough doses until next follow up visit	Reassess need for DPEP , otherwise same as initial visit

Preliminary CDC Doxy PEP Guidelines: Please comment by Nov 16

Proposed Guidelines



https://www.regulations.g ov/document/CDC-2023-0080-0002 Submit a comment



Watch the Video



https://www.federalregister.gov/documents/2023/10/02/202 3-21725/guidelines-for-the-use-of-doxycycline-post-exposureprophylaxis-for-bacterial-sexually-transmitted https://www.youtube.com/wat ch?v=2hYvrrK_W58

Slide courtesy of Ina Park

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PHSKC Doxy PEP Guidelines

Available publicly 9 Jun 2023 at https://kingcounty.gov/depts/health/communicable-diseases/hiv-std.aspx





- (*insert your verb of choice*) doxy-PEP for MSM and trans women with h/o bacterial STI in the prior year
- Not recommended for cis women, MSW, persons of other genders at this time (lack of efficacy data) - case by case basis through shared decision making?
- It's not 100% and doesn't protect against viruses (HIV, mpox, HSV...)
 - Should HIV PrEP be "required" if prescribed doxy-PEP?
- Chronic doxy use appears to be safe, but a lot we don't know...
- Review potential side effects



- 200 mg of doxycycline should be taken ideally within 24 hours but no later than 72 hours after condomless oral, anal or vaginal sex.
- Doxycycline can be taken as often as every day, depending on frequency of sexual activity, but individuals should not take more than 200 mg within a 24-hour period.
- Immediate release 100 mg is fine; hyclate or monohydrate*
- Take with fluids and remain upright for 30 minutes after the dose. Taking with food may increase tolerability.
- Suggested: #30 tabs with 1 refill; may vary depending on frequency of sex and mutual agreement about need for monitoring
- Use ICD-10 code: Z20 (Contact with and [suspected] exposure to infections with a predominantly sexual mode of transmission)



including oral sex

Two 100mg pills of doxycycline ideally <u>within 24 hours</u> but no later than 72 hours after condomless sex

Example: Sex on Sat; take dose of doxy by Tues

Example: Sex on Thursday; take dose of doxy by Sunday



Example 2: Daily (or more) sex Sat-Tues; take daily dose of doxy and last dose within 24 hours but not later than 72 hours after last sex



No more than 200 mg every 24 hours

https://www.sfcityclinic.org/providers/guidelines/hiv-and-sti-prevention



Reference Links: Product:	Lexi-Comp DOXYCYCLINE HYCLATE 100 MG CAPSULE View Available Strengths	STD Prevention Training Center
Sig Method:	Specify Dose, Route, Frequency Taper/Ramp Combination Dosage Use Free Text	
Dose:	200 mg 100 mg	
	Calculated dose: 2 capsule PRN is important as can	
Route:	oral Oral distinguish doxy-PEP use from	
Frequency:	Daily PRN Daily BID Other doxycycline use	
	PRN Comment: Take within 24 hours after condomless sexual contact, and no later than 72 hours after sex.	
Duration:	Doses Days 30 days 3 months 1 year	
	Starting: 10/17/2022 👗 Ending: 👗 First fill: 👗	
Dispense:	Days/Fill: Full (0 Days) 30 Days 90 Days	
	Quantity: 60 capsule Refill: 0 Consider 30 days with no refill fo	r initial
	Dispense As Written dispensing, then assess usage & t	olerability
Mark Jama Annas		
Mark long-term:		Doxy-PEP
🚹 Patient Sig:	Take 2 capsules (200 mg total) by mouth 1 time each day if needed (Take within 24 hours after condomless sexual contact, and no later than 72 hours after sex.). Not to exceed 200 mg in a 24 hour period. Take large glass of water, do not lie down for 30 minutes after.	specific
	Edit the additional information appended to the patient sig	
	The sig contains both discrete and free text elements. Review the final sig above.	
Class:	Normal \wp Normal Print Phone In No Print Sample	
	(i) This medication will not be e-prescribed. Invalid items: Pharmacy	

Slide courtesy of Stephanie Cohen



Doxycycline hyclate 100 mg tabs are <u>very</u> inexpensive Nonetheless: need to identify source of funds for uninsured patients

Source	Cost/100 mg pill	Cost/month (taking 2 tabs daily)
340b	6¢	\$3.60
GoodRx Coupon*	8¢	\$5.00
Discount online pharmacy	23¢	\$13.80

*Requires redemption at specific pharmacy chain in your area

Monitoring on doxy-PEP



Laboratory

No serious lab abnormalities in DoxyPEP Package insert: LFTs, renal function & CBC checked "periodically" when taking doxycycline for a prolonged period

Take home:

- No baseline labs needed
- Consider checking annually



STIs

Screen for STIs every 3-4 months

 Can we screen less frequently? May depend on patient factors

If diagnosed with an STI on doxy-PEP, treat according to the CDC STI treatment guidelines

Consider no "epi-treatment" for GC & CT exposures







Doxy-PEP should be a part of comprehensive sexual health services









Will you plan to discuss or prescribe doxy-PEP for any of your patients or clients after today's talk?

- A. Yes, definitely!
- B. Maybe, I'm still on the fence
- C. No, I will not be recommending this for my clients or patients
- D. No, but I'm considering it



After this talk, what are your concerns about doxy-PEP, if any? (Select all that apply)

- A. We need more data or evidence to support use
- B. Doxy-PEP is ineffective or not recommended for populations I work with
- c. Risk for antimicrobial resistance
- D. Risk for inducing resistance in STI pathogens
- E. Side effects of doxycycline
- F. Changes to microbiome or other long-term effects
- G. Giving out doxy-PEP will lead to changes in sexual behavior
- H. Something else

Thanks!





National Network of STD Clinical Prevention Training Centers



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Additional slides





Participants were evaluated for STI endpoints every 3 months at study visits and were asked to report STI testing conducted outside of study clinic visits.

Luetkemeyer, CROI 2023

N. gonorrhoeae resistance data limited by rates of sample collection (~50%) before treatment and culture growth (~40%)



Gonococcal Tetracycline (TCN) culture-based susceptibility

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- Conducted through CDC SURRG & ARLN programs
- ~ 17% of baseline GC diagnoses and on-study GC endpoints have culture-based resistance data available
- Tetracycline susceptibility by ARLN agar dilution method (resistance defined as MIC ≥ 2)¹
- Baseline: $\approx 25\%$ with TCN resistance, consistent with US GISP GC TCN resistance $\approx 20\%^{2}$

¹https://www.cdc.gov/std/gonorrhea/arg/carb.htm https://www.cdc.gov/std/gonorrhea/lab/agar.htm ²CDC STD Surveillance Report 2020



AMR in Staph aureus and commensal Neisseria

- Decrease in Staph aureus colonization and slight increase in doxy R in Staph aureus at month 12 in doxy-PEP arm
- No significant change in rate of commensal Neisseria colonization in oropharynx or TCN resistance





- TCN-R similar in incident GC at baseline and on doxy-PEP
- Increased TCN-R in doxy-PEP vs. standard of care suggests doxy-PEP may be less protective against GC strains with existing TCN-R
- Limited by low number of GC samples with MIC results (56/320)

■ MIC < 2 (not resistant) ■ MIC ≥ 2 (resistant) ■ MIC ≥ 16 (high-level resistance)</p>







- S. aureus colonization is associated with subsequent clinical Staph infections, such as surgical infections and bacteremia.²
- DoxyPEP use associated with 14% absolute decrease in *S. aureus* colonization.

Oestergard AIM 2016; Jacobsson Scand JID 2008; Septimus CID 2016; Bode NEJM 2010

S. aureus: 8% absolute increase in doxycycline resistance (doxy-R) in doxy-PEP arm



MRSA: Low rate of doxycycline resistance & no change with doxy-PEP



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Commensal Neisseria: >60% with baseline doxycycline resistance





- Non-pathogenic *Neisseria* colonizing the pharynx may serve as a reservoir for drugresistant genes that can transmit to pathogenic bacteria including N. gonorrhoeae.
- No change in resistance in doxy-PEP arm.

