

Sexually Transmitted Infections: An Update on Some Old Friends

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Disclosure

I have no financial interests or relationships to disclose.

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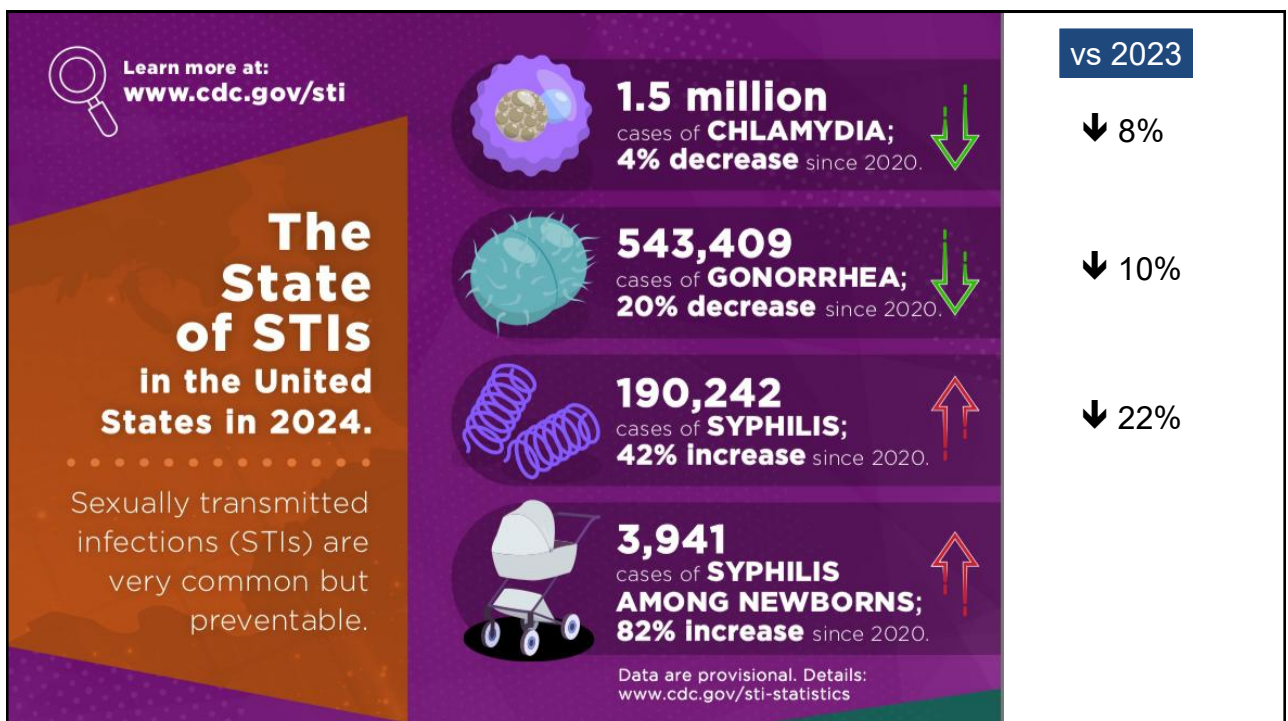
Andrew Urban, MD
Sexually Transmitted Infections

Good Morning!

I'd Like to Be Screened for STIs Today

What Are You Going to Order?

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No Shortage of Great STI Resources

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Screening for sexually transmitted infections

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Contributor Disclosures

All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: Oct 2025.
This topic last updated: Sep 10, 2025.

STI Treatment Guide Mobile App



Visit Website

The new app offers quick and easy access to streamlined STI prevention, diagnostic, and treatment recommendations. The user-friendly interface includes more clinical care guidance, sexual history resources, patient materials, and other features to assist with patient management. Download the free app for Apple and Android mobile devices.

Authen: Centers for Disease Control and Prevention

Format: Other

Publication Date: 2022

Recommended Regimen for Nongonococcal Urethritis

Doxycycline 100 mg orally 2 times/day for 7 days

Alternative Regimens

Azithromycin 1 g, orally in a single dose

OR

Azithromycin 500 mg orally in a single dose; then 250 mg orally daily for 4 days

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2021 CDC STI Treatment Guidelines Highlights/Significant Changes

- Treatment
 - Chlamydia and Gonorrhea
 - *Mycoplasma genitalium*
 - Trichomonas
 - Bacterial vaginosis
 - Outpatient PID
- Testing
 - Genital herpes serology
 - Syphilis in pregnancy
 - Hepatitis C
- HPV vaccine counseling
- MSM sexual assault eval

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Since the 2021 Guideline

- Doxycycline PEP guidelines (6/24)
 - High-risk groups, 200 mg within 72 hrs after sexual activity
- Gepotidacin (12/25)
 - FDA approved for urogenital gonorrhea in those who have limited or no alternative treatment options

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CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024

Recommendations and Reports / June 6, 2024 / 73(2):1–8

Discuss doxy PEP with patients who would benefit most

CDC recommends healthcare providers [discuss](#) doxy PEP with all gay, bisexual, and other men who have sex with men and transgender women with a history of at least one bacterial STI (gonorrhea, chlamydia, and syphilis) in the last 12 months.

Although not directly assessed in the research studies, providers may also wish to discuss doxy PEP with other gay, bisexual, and other men who have sex with men and transgender women who have not had a bacterial STI in the past year but who will be participating in sexual activities known to pose an increased risk of infection.

Prescribe doxy PEP, as appropriate

1. Write a prescription for self-administration of doxycycline 200 mg (any formulation) as soon as possible, within 72 hours after oral, vaginal, or anal sex. Patients should not take more than 200 mg every 24 hours. Provide enough doses until next follow up visit.
3. Set up routine follow-up visits at intervals that align with the patient's existing HIV and STI screening recommendations based on their chosen HIV prevention strategy, as recommended intervals differ for individuals on HIV PrEP. Patients on doxy PEP should test for STI and HIV every 3 - 6 months as appropriate. During these visits, reassess whether there is an ongoing need for doxy PEP.

Recommended target population limited at present based on how the studies were performed

Doxycycline 200 mg ASAP within 72 hours

Set up routine STI screening every 3-6 months, reassess the need for PEP

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Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

Authors: Anne F. Luetkemeyer, M.D., Deborah Donnell, Ph.D., Julia C. Dombrowski, M.D., M.P.H., Stephanie Cohen, M.D., M.P.H., Cole Grabow, M.P.H., Clare E. Brown, Ph.D., Cheryl Malinski, B.S., ¹⁰ for the DoxyPEP Study Team^{*} [Author Info & Affiliations](#)

Published April 5, 2023 | N Engl J Med 2023;388:1296-1306 | DOI: 10.1056/NEJMoa2211934 | VOL. 388 NO. 14

- Open label, randomized, 501 MSM and TGW (327 on HIV PrEP, 174 PLWH) who had GC, chlamydia, or syphilis in the past year
- 200 mg doxycycline within 72h after condomless sex vs SOC
- RR reductions GC (43-45%), Ct (12-26%), early Syph (13-23%)
- Quarterly visits STI dx 10.7-11.8% doxy arm vs 30.5-31.9% SOC arm
- Tetracycline-R GC in 5/13 doxy arm vs 2/16 SOC arm

Clinical Infectious Diseases

REVIEW ARTICLE



Filling in the Gaps: Updates on Doxycycline Prophylaxis for Bacterial Sexually Transmitted Infections

Aniruddha Hazra,^{1,2,8} Meira C. McNulty,¹ Maria Pyra,³ Jade Pagkas-Baether,¹ Jose I. Gutierrez,⁴ Jim Pickett, Jenell Stewart,⁵ Robert K. Bolan,⁶ Jean-Michel Molina,^{7,8} Connie Celum,^{1,8} Anne F. Luetkemeyer,⁹ and Jeffrey D. Klausner²

NEJM 2023;388(14):1296-1306
Clin Infect Dis 2026;82(2):312-20

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By Disease	By Population
Chlamydia	
Women	- Sexually active women under 25 years of age¹ - Sexually active women 25 years of age and older if at increased risk¹ - Retest approximately 3 months after treatment² - Rectal chlamydial testing can be considered in females based on reported sexual behaviors and exposure, through shared clinical decision between the patient and the provider^{2,3,4}
Pregnant Women	- All pregnant women under 25 years of age¹ - Pregnant women 25 years of age and older if at increased risk¹ - Retest during the 3rd trimester for women under 25 years of age or at risk² - Pregnant women with chlamydial infection should have a test of cure 4 weeks after treatment and be retested within 3 months²
Men Who Have Sex with Women	There is insufficient evidence for screening among heterosexual men who are at low risk for infection, however, screening young men can be considered in high prevalence clinical settings (adolescent clinics, correctional facilities, STI/biomedical health clinic)^{1,5}
Men Who Have Sex With Men	- At least annually for sexually active MSM at sites of contact (urethra, rectum) regardless of condom use² - Every 3 to 6 months if at increased risk (i.e., MSM on PrEP, with HIV infection, or if they or their sex partners have multiple partners)²
Transgender and Gender Diverse Persons	- Screening recommendations should be adapted based on anatomy, (i.e., annual, routine screening for chlamydia in transgender women < 25 years old should be extended to all transgender men and gender diverse people with a cervix, if over 25 years old, persons with a cervix should be screened if at increased risk)² - Consider screening at the rectal site based on reported sexual behaviors and exposure²
Persons with HIV	- For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter^{2,6} - More frequent screening might be appropriate depending on individual risk behavior and local epidemiology⁷

Women	
Chlamydia	- Sexually active women under 25 years of age¹ - Sexually active women 25 years of age and older if at increased risk¹ - Retest approximately 3 months after treatment² - Rectal chlamydial testing can be considered in females based on reported sexual behaviors and exposure, through shared clinical decision between the patient and the provider^{2,3,4}
Gonorrhea	- Sexually active women under 25 years of age¹ - Sexually active women 25 years of age and older if at increased risk¹ - Retest 3 months after treatment² - Pharyngeal and rectal gonorrhea screening can be considered in females based on reported sexual behaviors and exposure, through shared clinical decision between the patient and the provider^{2,3,4}
Syphilis	Screen asymptomatic adults at increased risk (history of incarceration or transactional sex work, sex work, race/ethnicity) for syphilis infection^{2,5}
Herpes ¹	Type-specific HSV serologic testing can be considered for women presenting for an STI evaluation (especially for women with multiple sex partners)²
Trichomonas	Consider screening for women receiving care in high-prevalence settings (e.g., STI clinics and correctional facilities) and for asymptomatic women at increased risk for infection (e.g., women with multiple sex partners, transactional sex, drug misuse, or a history of STI or incarceration)⁴
HIV	- All women aged 13-64 years (opt-out)^{6,7} - All women who seek evaluation and treatment for STIs^{2,7}
HPV, Cervical Cancer	- Women 21-29 years of age every 3 years with cytology^{8,9,10} - Women 30-65 years of age every 3 years with cytology, or every 5 years with a combination of cytology and HPV testing^{8,9,10}
Hepatitis B Screening	Women at increased risk (having had more than one sex partner in the previous 6 months, evaluation or treatment for an STI, past or current injection-drug use, and an HBsAg-positive sex partner)¹¹
Hepatitis C Screening	All adults over age 18 years should be screened for hepatitis C except in settings where hepatitis C infection (HCV) positivity is < 0.1%¹²

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Screening Recommendations

- CDC STI guidelines by disease and population
- Up to Date
- State and local public health
- Make an order set and use delegation protocols

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Old Friends

- Chlamydia and Gonorrhea
- Genital herpes
- Syphilis
- *Mycoplasma genitalium*

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Chlamydia and Gonorrhea

Treatment Update

Testing Considerations

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23-year-old Woman

- New onset dysuria
- UA with pyuria, urine culture no growth
- Urine NAAT is positive for Chlamydia
- Pregnancy test is negative



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ARS Question #1**What Would You Use ?**

- A. Doxycycline 100 mg BID x 7 days
- B. Azithromycin 1 gram single-dose (SD)
- C. Ceftriaxone 250 mg IM + Azithromycin 1 gm SD
- D. Ceftriaxone 500 mg IM



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ARS Question #2**After Treatment, Should She Be Retested?**

- A. Yes at 4 weeks
- B. Yes at 3 months
- C. Not needed when using CDC recommended therapy



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23-year-old Woman

- New onset dysuria
- UA with pyuria, urine culture no growth
- Urine NAAT is positive for *N. gonorrhoeae*, the chlamydia NAAT is negative
- Pregnancy test is negative



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ARS Question #3

What Would You Use ?

- A. Doxycycline 100 mg BID x 7 days
- B. Azithromycin 1 gram single-dose (SD)
- C. Ceftriaxone 250 mg IM + Azithromycin 1 gm SD
- D. Ceftriaxone 500 mg IM



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STI Syndromes in a Culture-Negative UTI DDx

- Urethritis
 - Infectious: *C. trachomatis*, *N. gonorrhoeae*, *M. genitalium*, Ureaplasma, *T. vaginalis*, HSV, adenovirus, etc
 - Noninfectious
- Recurrent/persistent urethritis
 - *M. genitalium*
- Recurrent/periodic GU symptoms
 - Herpes simplex

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Chlamydia trachomatis

Clinical Syndromes Serotypes D-K

- Asymptomatic infection
- Conjunctivitis
- Pharyngitis
- Reactive arthritis
- Urethritis, epididymitis, cervicitis, Bartholinitis, PID
- Proctocolitis
- Lymphogranuloma venereum (LGV)
 - Serotypes L1-L3

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Rectal Chlamydia

- Asymptomatic infection = most common
 - 8-fold increased risk HIV with 2 prior rectal infections
- Proctocolitis
 - Rectal pain, discharge, bleeding
- Lymphogranuloma venereum (LGV)
 - Short lived painless ulcer + painful inguinal adenopathy
 - Proctocolitis can be severe and mimics IBD
 - L1-L3 serovars = specific LGV testing is needed
 - 21 day treatment duration of doxycycline

JAIDS 2010;53(4):537

2021 STI Treatment Guidelines

MMWR 2016;65:920

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NAAT Testing for Chlamydia and GC

- Urogenital chlamydia and gonorrhea²
 - Women: first-void urine, vaginal swab (self-collect or clinic), cervical swabs²
 - Men: first-void urine, urethral swab²
- Rectal chlamydia and gonorrhea²
 - Rectal swabs¹ (self-collect or clinic)
- Oropharyngeal chlamydia and gonorrhea²
 - Swabs (self-collect or clinic)¹

¹ Be sure to use the correct swabs for these sites²GC Culture & suscept testing can be done at all sites and should be done in suspected treatment failure

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Extragenital Testing for Chlamydia and Gonorrhea

- Testing rectal and pharyngeal sites when exposure at those sites has occurred
 - Important to ask about exposure and offer screening
- What proportion of chlamydia and gonorrhea cases are missed by only performing urogenital screening?

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Infections Missed by Urethral-Only Screening for Chlamydia or Gonorrhea Detection Among Men Who Have Sex With Men

Julia

The Case for Extragenital Screening of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in the College Health Setting

Neisseria gonorrhoeae and *Chlamydia trachomatis* Among Women Reporting Extragenital Exposures

Extragenital Gonorrhea and Chlamydia Among Men and Women According to Type of Sexual Exposure

David M. Bamberger, MD,*†‡ Georgia Graham, MD,*§
Lesha Dennis, BA,† and Mary M. Gerkovich, PhD,‡

Percent Cases MISSED by Only Doing Urethral Screening

Study	Chlamydia	Gonorrhea
3398 MSM, San Fran City Clinic	77	95
4093 college men	26	63
4400 women	14	30
4093 MSW/WSM	33/33	36/28

STD 2011;38(10):922

Sex Trans Dis 2017;44(5):274

STD 2015;42(5):233

Sex Trans Dis 2019;46(5):329

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Follow-up Testing After Treatment

- Chlamydia = 3-month follow-up testing
 - Pregnancy + Chlamydia = 4 weeks NAAT test-of-cure
- Gonorrhea = 3-month follow-up testing
 - Pharyngeal Gonorrhea = 7-14 days NAAT or culture test-of cure

The “Follow Up” section of the CDC STI guidelines for each pathogen and syndrome is a must read and has tremendous practical guidance

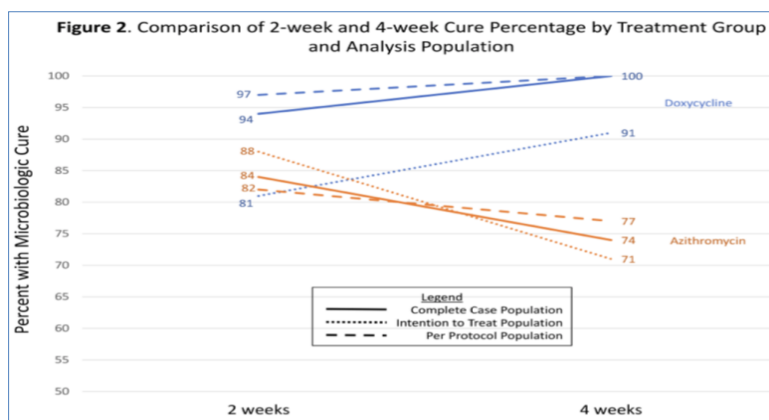
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Randomized Trial Azithromycin vs Doxycycline for Treatment of Rectal Chlamydia in MSM

- MSM diagnosed with rectal chlamydia (goal n=274)
 - Randomized, placebo
 - Single dose azithromycin vs 7 days doxycycline
 - 2 week and 4-week test of cure with rectal NAAT
 - Trial stopped early by DMSB based on efficacy

Clin Inf Dis 2021;73(5):824

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Percent with negative NAAT at 4 weeks (ITT)

Doxycycline 91% (80/88)

Azithromycin 71% (63/89)

Absolute Δ 20%
95% CI: 9-31% $p < 0.001$

Clin Inf Dis 2021;73(5):824

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Chlamydia Treatment

2021 CDC STI Treatment Guidelines

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

Recommended Regimen for Chlamydial Infection During Pregnancy

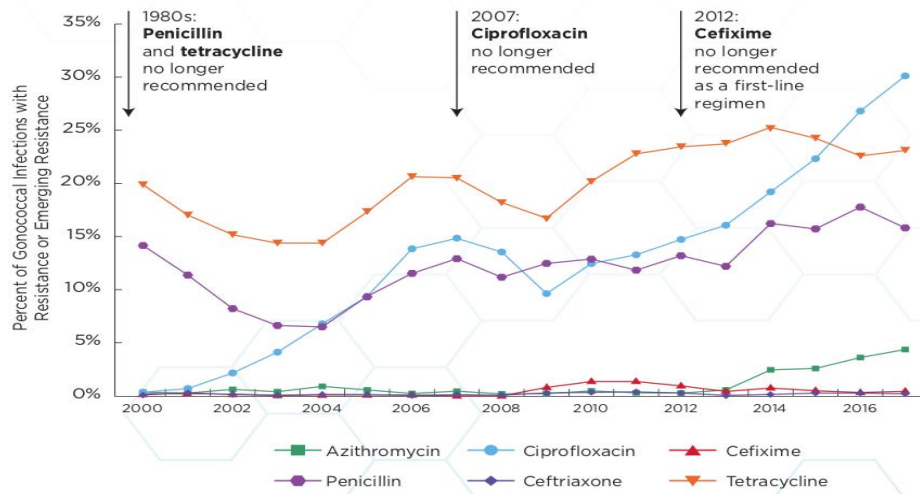
Azithromycin 1 g orally in a single dose

Alternative Regimen

Amoxicillin 500 mg orally 3 times/day for 7 days

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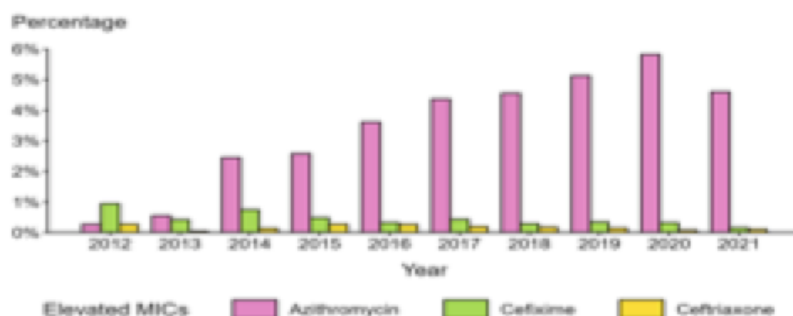
Gonorrhea rapidly develops resistance to antibiotics—ceftriaxone is the last recommended treatment.



Antibiotic Resistance Threats in the United States, November 2019 cdc.gov

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***Neisseria gonorrhoeae* — Percentage of Isolates with Elevated Minimum Inhibitory Concentrations (MICs) to Azithromycin, Cefixime, and Ceftriaxone, Gonococcal Isolate Surveillance Project (GISP), 2012–2021**



CDC STD Surveillance 2021

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Gonorrhea Treatment

Uncomplicated Infection of the Cervix, Urethra, Rectum

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.

2021 CDC STI Guidelines

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Gonorrhea Treatment

Uncomplicated Infection of the Pharynx

Recommended Regimen for Uncomplicated Gonococcal Infection of the Pharynx Among Adolescents and Adults

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

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

If chlamydial infection is identified when pharyngeal gonorrhea testing is performed, treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days. No reliable alternative treatments are available for pharyngeal gonorrhea. For persons with an anaphylactic or other severe reaction (e.g., Stevens Johnson syndrome) to ceftriaxone, consult an infectious disease specialist for an alternative treatment recommendation.

- Most pharyngeal infections are asymptomatic and serve as a major source of GC transmission and antibiotic resistance
- This site is much harder to eradicate than urogenital or anorectal GC, very few therapeutics can achieve good enough (>90%) eradication of pharyngeal GC
- Note the absence of alternatives to ceftriaxone

2021 CDC STI Guidelines

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Gepotidacin

- Triazaacenaphthylene
 - New class of topoisomerase inhibitor
- Uncomplicated urogenital GC in adult/peds $\geq$ age 12 and > 45 kg who have limited or no alternative treatment options
 - EAGLE 3 study, urogenital, non-inferior to ceftriaxone/azithromycin
 - 3gm oral dose followed by 3gm oral dose 12 hours later
- Warnings/Precautions (read before using)
 - Qtc prolongation, CYP3A4 interactions, acetylcholinesterase inhibition
 - Avoid use severe renal (eGFR <30 or dialysis) and hepatic impairment
- Adverse reactions EAGLE 3: 49% diarrhea, 24% nausea

Gepotidacin prescribing information 12/25

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Important GC Management Considerations

- Penicillin or cephalosporin allergy is a **huge deal**
 - Ceftriaxone is critical and alternatives are either not available, poorly tolerated or non-existent (pharyngeal)
 - Take a **good history of their allergy**, and refer to Allergy for testing or graded challenge
- Treatment failure
 - Most treatment failure is **reinfection, but if you**
 - **Suspect drug failure** = Contact state or local health department, send culture and susceptibility testing

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Genital Herpes

Recurrent Genital Herpes Recognition

2023 USPSTF Statement on Screening

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ARS Question #4

A patient asks you about daily long-term suppression antiviral therapy for their recurrent genital herpes.

They read about it in a New York Times article.

What Is the Minimum Number of Recurrences Needed before Prescribing Daily Suppression for Genital Herpes?

- A. Any
- B. 3 per year
- C. 6 per year
- D. 10 per year
- E. 12 per year



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45 Million People Have Genital Herpes Most Do Not Know They Have It

70% of Transmission Occurs via Asymptomatic
Shedding from Infected Individuals

15-20% Report Vesicles & Ulcers with Recurrences

Recurrent Genital Herpes Has Symptom Periodicity
and Is Usually Attributed to Something Else

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TABLE 1. Patient-reported etiology of genital lesions from which
HSV was isolated

Women	Men
Yeast infection	Folliculitis
Vaginitis	Jock itch
Urinary tract infection	“Normal” itch
Urethral syndrome	Zipper burns
Menstrual complaint	Hemorrhoids
Hemorrhoids	Allergy to condoms
Allergy to:	Irritation from:
Condoms	Tight jeans
Sperm	Sexual intercourse
Spermicide	Bike seat
Elastic/pantyhose	Insect or spider bites
Irritation or rash from:	
Sexual intercourse	
Bike seat	
Shaving	

RECURRENT genitourinary or anorectal symptoms and signs are the clue

Clin Micro Rev 1999;12(1):1-8

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Genital Herpes Is both HSV-1 and HSV-2

- HSV-1
 - 70% of genital herpes in young adults
 - Seropositivity means cold sores or genital herpes
- HSV-2
 - Decreasing prevalence 18% to 12.1% age 14-49
 - Seropositivity means genital herpes

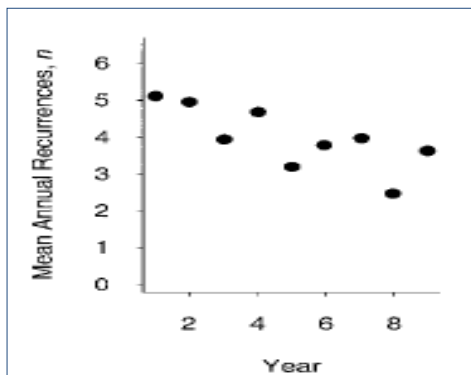
NCHS Data Brief No. 304 Feb 2018

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HSV-2 vs HSV-1: Genital Herpes Recurrence Rates

Determining Which Virus Is Important for Counseling and Treatment

HSV-2 (5 per year)



HSV-1 (1 per year)

TABLE 2. Time to First Recurrence of HSV-1 and Recurrence Rates Stratified by Gender

Gender	Days to First Recurrence, Median	Recurrence Rate Post-Primary (Range)		
		Year 1	Year 2	Years 3–5
Male	567	0.76 (0–4)	0.33 (0–2)	0.31 (0–2)
Female	195	1.63 (0–8)	0.94 (0–5)	0.87 (0–4)
All	280	1.30 (0–8)	0.70 (0–5)	0.69 (0–4)

43%=0

67%=0

Ann Intern Med 1999;131:14
Sex Trans Dis 2002;30(2):174

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Final Recommendation Statement

Genital Herpes Infection: Serologic Screening

February 14, 2023

Recommendation Summary

Population	Recommendation	Grade
Asymptomatic adolescents and adults, including pregnant persons	The USPSTF recommends against routine serologic screening for genital herpes simplex virus infection in asymptomatic adolescents and adults, including pregnant persons.	D

Routine serologic screening for genital herpes
in asymptomatic adolescents, adults, or pregnant
women is **NOT RECOMMENDED** by CDC or USPSTF

JAMA 2023;329(6):510 2021 CDC STI Treatment Guidelines

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Why Not?

The problem lies in the operating characteristics of the tests. This does not mean they are bad tests, the type-specific tests are quite good, just not good for asymptomatic screening

- HSV-2 serologic testing
 - Specificity is low
 - High false-positive rate
 - Confirmatory test is not widely available
- HSV-1 serologic testing
 - Cannot tell if the site of infection is oral or genital

JAMA 2023;329(6):510 2021 CDC STI Treatment Guidelines

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Clinical Situation

Lesions suspicious for herpes



HSV-2

Expect more recurrences
Counsel



HSV-1

Expect few recurrences
Counsel

1. Lesion is PCR –
2. Recurrent GU Sx
3. Serostatus



Positive, high index value – Dx is genital herpes



Positive, low index value – repeat using a different Type-specific assay or send WB to U Wash



Negative – repeat in 3 months if recent acquisition suspected

Herpes Diagnostic Test	Comments
Swab for PCR (direct detection)	Fresh vesicle, pustule, ulcer. BEST test, types the virus
Type-specific HSV-2 antibody	Can distinguish HSV-2 from -1. GOOD test w/ LIMITATIONS
Western Blot (University of Washington)	CONFIRMATORY test for low index value type-specific tests
Herpes IgM tests	WORTHLESS but still orderable. IgM gets made with recurrences

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Management

- First episode genital herpes
 - Everyone should be treated
- Recurrent genital herpes – 3 options
 - Suppression (daily antiviral reduces recurrences 70-80%, reduces transmission, long-term use is safe)
 - Episodic self-directed therapy (start at prodrome, always have a supply on hand)
 - Nothing

Individualize your care of recurrent HSV over the lifetime of the patient

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Antivirals for Genital Herpes

Indication	Acyclovir	Valacyclovir	Famciclovir
First Episode ¹	400 mg TID x 7-10 d	1gm BID x 7-10 d	250 mg TID x 7-10 d
Suppression ²	400 mg BID	500-1000 mg once/d	250 mg BID
Episodic ³	2 regimens	2 regimens	3 regimens

¹ Sometimes need 14-21 days if healing incomplete at 10 days

² Valacyclovir 500mg once daily not as effective when > 10 recurrences/yr

³ Acyclovir 400 mg TID x 5 days is what I recommend

Acyclovir = Valacyclovir = Famciclovir

- Choose on cost, dosing, preference
- Clinical trials used HSV-2, guidelines do not distinguish HSV-1 or -2
- Dose and duration vary by indication (table from CDC STI)

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Beyond the outbreaks

The enduring psychological burden of recurrent symptomatic genital herpes – A prospective cohort study

Sharang Gupta, Dimple Chopra

[Authors and Affiliations >](#)

International Journal of STD & AIDS 37(2):p 96-103, February 2026. | DOI: 10.1177/09564624251376077

2 year prospective study of clinical and psychological outcomes

100 adults with recurrent (≥ 2 outbreaks/yr) genital HSV-2 vs matched controls

Cases: Higher baseline depression (29%/8%), anxiety, 12 mos stigma and sexual distress

Predictors of worse psychological outcomes: frequent outbreaks (≥ 5 /yr), low antiviral adherence, female gender, serodiscordant relationship, lacking social support

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To Patients, Herpes Can Be Devastating. To Many Doctors, It's Not a Priority.

Billions of people live with the infection, but there has been scant progress for treatments and tests.

New York Times
February 18, 2023

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Syphilis

The Most Likely Presentations to Your Clinic
Screening Tool for the 3 Wild Cards

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I've Diagnosed Syphilis! What Now?

- History and exam in order to accurately stage
 - Past testing and treatment details; risk factors for syphilis
 - Is this primary, secondary or latent?
 - Concern for neuro-, oto-, or ocular syphilis means immediate action steps such as same day consults, lumbar puncture, IV penicillin
- Check HIV and other STIs, report it to public health
- Treat and follow
 - Penicillin
 - Clinical and RPR follow up for success, failure, or reinfection
 - Risk modification (HIV PrEP, scheduled STI screening, etc)

The "Follow Up" section of the CDC STI guidelines for each pathogen and syndrome is a must read and has tremendous practical guidance

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Syphilis Serology Testing

use the algorithm your lab offers, use local resources for questions

Non-treponemal tests = RPR, VDRL

- Initial tests in traditional testing algorithms
 - Confirmatory tests in reverse algorithms
- Quantitative (e.g. titer value RPR 1:128)
 - Titer decreases with treatment or the passage of time, and will increase in treatment failure or reinfection

Treponemal specific tests = MHA-TP, FTA-ABS, TPPA, CIA, EIA

- Initial tests in reverse testing algorithms
 - Confirmatory tests in traditional algorithms
- Qualitative (reactive or nonreactive)
 - Lifelong persistence

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Syphilis

- Early Syphilis
 - Primary, Secondary, Early Latent
- Late Syphilis
 - Tertiary, Late Latent, Latent of Unknown Duration

Tertiary includes cardiovascular, gummatous, and late neurosyphilis
- The 3 wild cards that occur at any stage of syphilis
 - Neurosyphilis
 - Ocular syphilis
 - Ootosyphilis

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Primary Syphilis

3 Weeks (10-90 Days) After Exposure

Painless chancre, single > multiple

Lymphadenopathy

Resolves spontaneously in 3-6 weeks

30% have nonreactive RPR

Head and Neck Pathology 2021;15:787

https://www.nycptc.org/x/Syphilis_Monograph_2019_NYC_PTC_NYC_DOHMH.pdf

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Genital, Anal, Perianal Ulcer DDX

- Herpes simplex
- Syphilis
- Chancroid
- LGV
- Donovanosis
- Noninfectious (Behcet's, fixed drug, etc)

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Secondary Syphilis Is “All of Medicine”

3 Weeks to 3 Months After Infection

Systemic low-grade fever, malaise, sore throat, adenopathy

Rash (evanescent, copper color, dry macular→red papular, palms/soles),
mucosa (ulcers or gray plaques), condyloma lata (wart-like, moist area)

Hepatitis, renal, alopecia, periostitis, gastritis, etc

All treponemal specific tests positive; RPR positive except prozone false neg

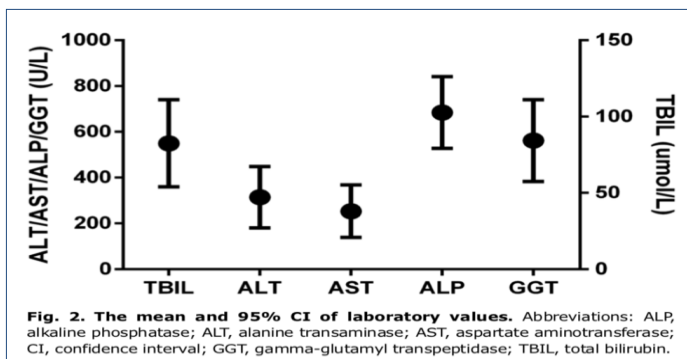
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A Systematic Literature Review of Syphilitic Hepatitis in Adults

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Clue: marked increase in ALP/GGT and mild increases in AST/ALT

J Clin and Trans Hepatol 2018;6:306

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Latent Syphilis

- Latent is defined as a positive syphilis serology without other evidence of primary, secondary, or tertiary disease
 - Neurosyphilis, ocular syphilis, otosyphilis can be present
- Early Latent = acquired in the preceding 12 months
- Late Latent = acquired > 1 year ago
- Latent Syphilis of Unknown Duration = not enough information to make a determination as to when they acquired it

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Ocular Syphilis

- Happens at any stage of syphilis
 - Always screen for ocular complaints and get same day ophthalmology evaluation if positive
- Panuveitis most common but pathology is diverse
 - Also conjunctivitis, anterior uveitis, posterior interstitial keratitis, optic neuropathy, retinal vasculitis
- Vision blurred, loss, painful, red eye, bilateral 56%

Invest Ophthalmol Vis Sci 2014;55:5394; 2021 CDC STD Guidelines

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Excellent Screening Tool for Neurosyphilis, Ocular syphilis and Ootosyphilis

Screening Questions for Neurosyphilis (Including Ocular and Ootosyphilis)

Questions		
Symptoms of Ootosyphilis		
1) Have you recently had new trouble hearing?	☐ Yes – refer to ENT	☐ No
2) Do you have ringing in your ears?	☐ Yes – refer to ENT	☐ No
Symptoms of Ocular syphilis		
3) Have you recently had a change in vision?	☐ Yes – refer to ophthalmology	☐ No
4) Do you see flashing lights?	☐ Yes – refer to ophthalmology	☐ No
5) Do you see spots that move or float by in your vision?	☐ Yes – refer to ophthalmology	☐ No
6) Have you had any blurring of your vision?	☐ Yes – refer to ophthalmology	☐ No
Symptoms of neurosyphilis		
7) Are you having headaches?	☐ Yes	☐ No
8) Have you recently been confused?	☐ Yes	☐ No
9) Has your memory recently gotten worse?	☐ Yes	☐ No
10) Do you have trouble concentrating?	☐ Yes	☐ No
11) Do you feel that your personality has recently changed?	☐ Yes	☐ No
12) Are you having a new problem walking?	☐ Yes	☐ No
13) Do you have weakness or numbness in your legs?	☐ Yes	☐ No

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Syphilis²⁴

Risk Category	Recommended Regimen	Alternatives
Primary, secondary, and early latent: adults (including pregnant women and people with HIV infection)	benzathine penicillin G 2.4 million units IM in a single dose	
Late latent adults (including pregnant women and people with HIV infection)	benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals	
Neurosyphilis, ocular syphilis, and otosyphilis	aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units by IV every 4 hours or continuous infusion, for 10–14 days	procaine penicillin G 2.4 million units IM 1x/day PLUS probenecid 500 mg orally 4x/day, both for 10–14 days

Alternative for Penicillin Allergic, Primary and Secondary Syphilis
Doxycycline 100 mg BID x 14 days

Alternative for Penicillin Allergic in Late Latent and Unknown Duration
Doxycycline 100 mg BID x 28 days

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Mycoplasma genitalium (Mgen)

When to Consider Treatment

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Mycoplasma genitalium

- Urethritis in men
 - 15-20% of NGU and 20-25% of nonchlamydial NGU
 - 40% of persistent or recurrent urethritis
- Multiple associations in women
 - Cervicitis, PID, preterm delivery, spon Ab, infertility
- Testing
 - NAAT - Urine, swab (vaginal, cervical, urethral) - FDA approved 2019
- When to think of it?
 - **Persistent or recurrent urethritis**
 - Consider in persistent or recurrent cervicitis or PID

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Major Treatment Challenge

- Doxycycline poor response (31% cure)
- Azithromycin decreasing response (80% → 40% cure)
 - Emergence of resistance after single dose (10-20% of cases)
- Moxifloxacin 95% effective but resistance can emerge
- Resistance testing is not readily available
- Sequential treatment is recommended
 - 1st drug reduces bacterial burden for the 2nd drug

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M. genitalium Treatment Update

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

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STD Pathogen	Screening Considerations
Chlamydia	NAAT Urogenital, Extragenital (if risks, have to ask)
Gonorrhea	NAAT Urogenital, Extragenital (if risks, have to ask)
Syphilis	Traditional or Reverse Sequence
HIV	4 th generation Ag/Ab test
Hepatitis B	sAb (see if protected), sAg (see if chronically infected)
Hepatitis C	Very reasonable, and might be other reasons to screen (age)
Herpes	Not routine for asymptomatic. HSV-2 type specific Ab use in specific circumstances
Trichomonas	NAAT
Exam	Rash, warts, lesions, adenopathy

Clinician To Do List

- Take a good history
- Ask about sites of exposure
- Individualize the approach
- If you diagnose one STD, always look for the others
- Discuss the explosion of STD cases, how to prevent
- Can I vaccinate against one or more (HPV, HAV, HBV, MPox)?
- Are they a candidate for PrEP?
- **Thank them for asking for STD testing**

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