Sexually Transmitted Disease:
Three Old Friends Keep Coming Back to Visit

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Disclosure

I have no financial interests or relationships to disclose.

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Good Morning!
I'd Like to Be Screened for STIs Today

What Are You Going to Order?

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2021 CDC STI Treatment Guidelines
Highlights/Significant Changes

- Chlamydia, Gonorrhea, Trichomonas treatment
- Genital herpes serologic testing
- *M. genitalium* management
- PID outpatient treatment – addition of metronidazole
- Bacterial vaginosis – new treatment options
- Syphilis testing in pregnancy
- HPV vaccine counseling
- Hepatitis C one-time testing
- MSM sexual assault evaluation

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Since the 2021 Guideline

- Doxycycline PEP guidelines (6/24)
- Gepotidacin (8/25)
  - Triazaacenaphthylene, new class topoisomerase inhibitor
  - FDA priority review for urogenital gonorrhea

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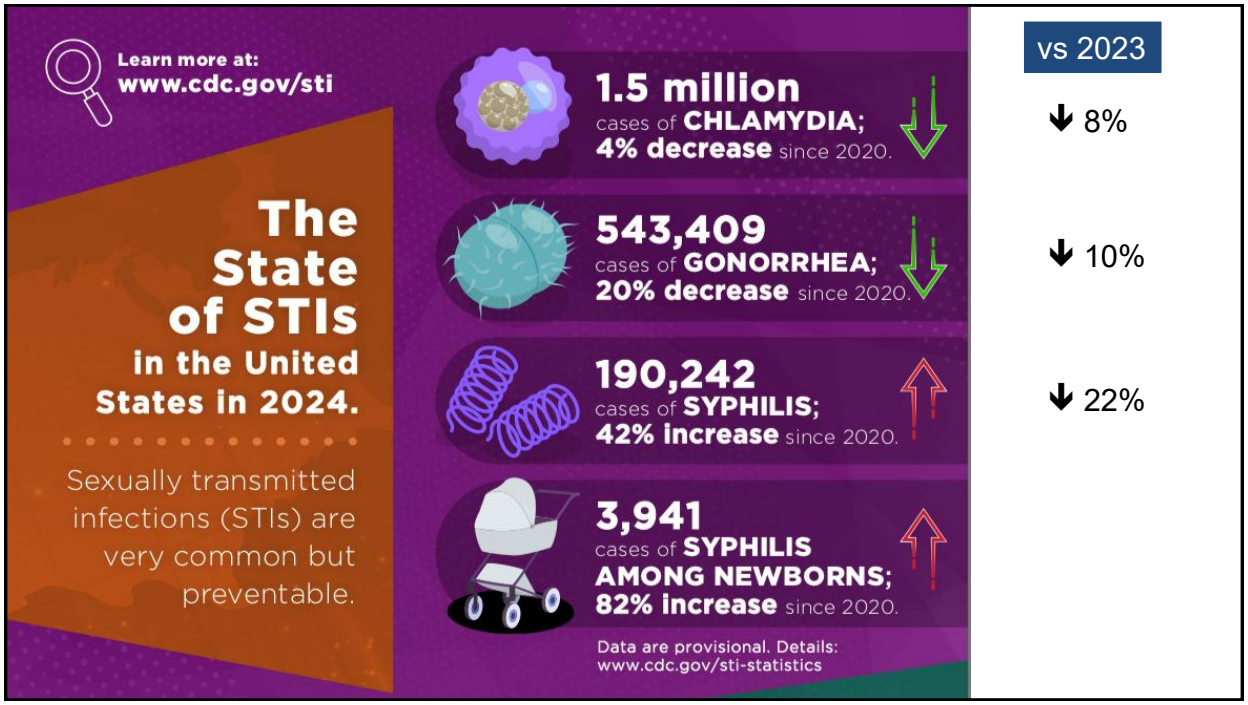

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You Have No Shortage of Great Resources

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.

Author: 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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Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources

Print

By Disease | By Population

Chlamydia

Women	• Sexually active women under 25 years of age[1] • Sexually active women 25 years of age and older if at increased risk*[1] • Retest approximately 3 months after treatment[2] • 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 age[1] • Pregnant women 25 years of age and older if at increased risk*[1] • Retest during the 3rd trimester for women under 25 years of age or at risk[2] • Pregnant women with chlamydial infection should have a test of cure 4 weeks after treatment and be retested within 3 months[2]
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/sexual 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 use[2] • 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 cisgender 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 exposure[2]
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 behavi… local epidemiology[2]

App St…

By Disease | By Population

Women

Chlamydia	• Sexually active women under 25 years of age[1] • Sexually active women 25 years of age and older if at increased risk*[1] • Retest approximately 3 months after treatment[2] • 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 age[1] • Sexually active women 25 years of age and older if at increased risk*[1] • Retest 3 months after treatment[2] • 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, geography, race/ethnicity) for syphilis infection[2,5]
Herpes†	• 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)[2]
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]

Syst…

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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)
- *Herpes simplex*
- Syphilis
- *Mycoplasma genitalium*
  - (Not so) new friend making trouble

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Chlamydia and Gonorrhea

Treatment and Testing Considerations

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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. gonorrheae*, the chlamydia NAAT is negative
- Pregnancy test is negative

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

STI Syndromes to Consider in a UTI DDx

- Urethritis
  - Infectious: *C. trachomatis*, *N. gonorrheae*, *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
- Proctitis
- Lymphogranuloma venereum (LGV)
  - Serotypes L1-L3

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NAAT Testing

- Urogenital chlamydia and gonorrhea[2]
  - Women: first-void urine, vaginal swab (self-collect or clinic), cervical swabs[2]
  - Men: first-void urine, urethral swab[2]
- Rectal chlamydia and gonorrhea[2]
  - Rectal swabs[1] (self-collect or clinic)
- Oropharyngeal chlamydia and gonorrhea[2]
  - Swabs (self-collect or clinic)[1]

[1] Be sure to use the correct swabs for these sites

[2]GC Culture & suscept testing can be done at all sites and should be done in suspected treatment failure

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Follow-Up

Test of cure to detect therapeutic failure (i.e., repeat testing 4 weeks after completing therapy) is not advised for nonpregnant persons treated with the recommended or alternative regimens, unless therapeutic adherence is in question, symptoms persist, or reinfection is suspected. Moreover, using chlamydial NAATs at <4 weeks after completion of therapy is not recommended because the continued presence of nonviable organisms (*553*,*818*,*819*) can lead to false-positive results.

A high prevalence of *C. trachomatis* infection has been observed among women and men who were treated for chlamydial infection during the preceding months (*753*,*755*,*820–822*). The majority of posttreatment infections do not result from treatment failure but rather from reinfection caused by failure of sex partners to receive treatment or initiation of sexual activity with a new infected partner (*823*), indicating a need for improved education and treatment of sex partners. Repeat infections confer an elevated risk for PID and other complications among women. Men and women who have been treated for chlamydia should be retested approximately 3 months after treatment, regardless of whether they believe their sex partners were treated; scheduling the follow-up visit at the time of treatment is encouraged (*753*). If retesting at 3 months is not possible, clinicians should retest whenever persons next seek medical care <12 months after initial 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 for NAAT or culture test-of cure

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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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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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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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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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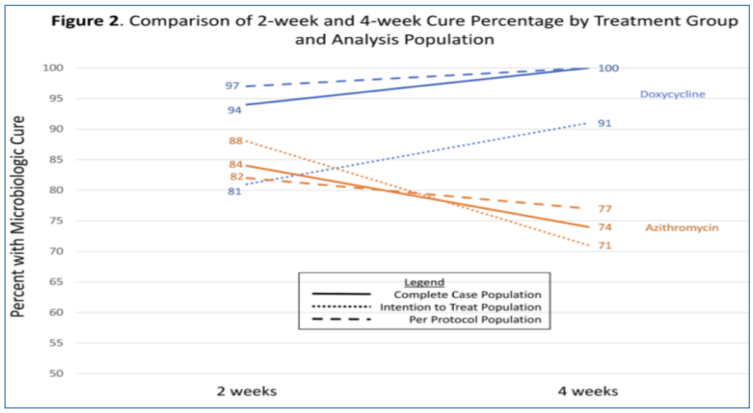

Percent with Negative NAAT at 4 Weeks (ITT)

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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PRESS RELEASE

Department of Public Health announces first cases of concerning gonorrhea strain

FOR IMMEDIATE RELEASE:
1/19/2023 Department of Public Health

BOSTON — The Department of Public Health (DPH) today announced it has detected a novel strain of gonorrhea in a Massachusetts resident that showed reduced response to multiple antibiotics and another case with genetic markers that indicate a similar drug response. This is the first time that resistance or reduced response to five classes of antibiotics has been identified in gonorrhea in the United States.

Characterizing the Rise of Disseminated Gonococcal Infections in California, July 2020–July 2021

Get access >

Eric C Tang ✉, Kelly A Johnson, Lizzete Alvarado, Nicole O Burghardt, Cindy Hernandez, Edwin Lopez, Tazima Jenkins-Barnes, Bryan Hughes, Krysta L Salas, Kathleen R Jacobson

Clinical Infectious Diseases, Volume 76, Issue 2, 15 January 2023, Pages 194–200,

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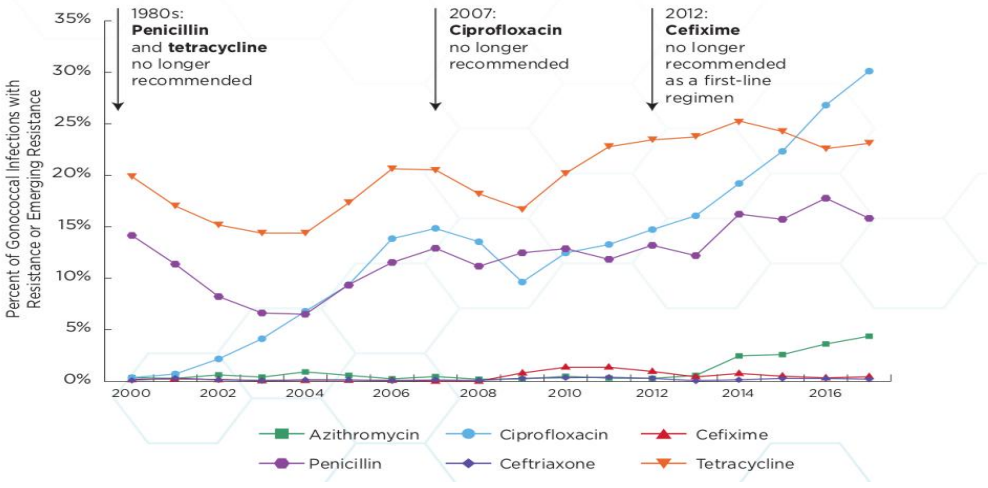
Gonorrhea rapidly develops resistance to antibiotics—ceftriaxone is the last recommended treatment.



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

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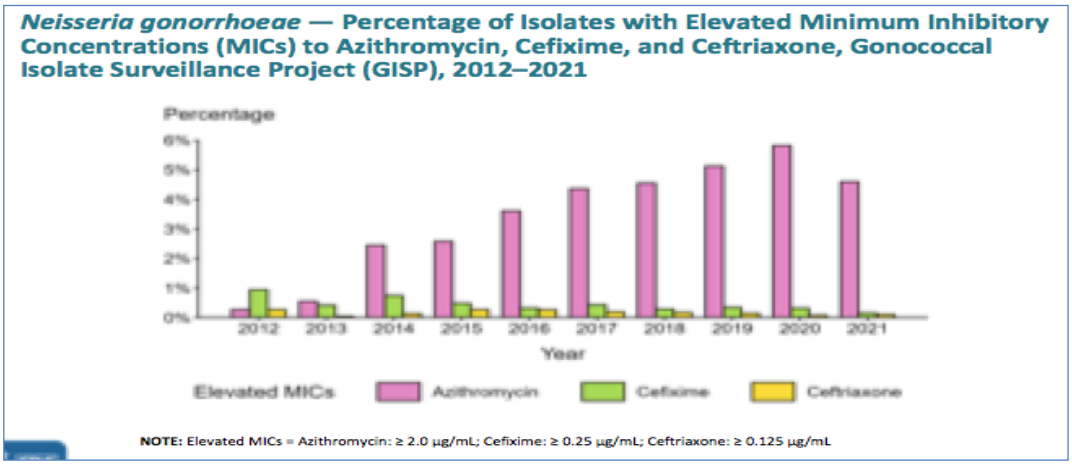

CDC STD Surveillance 2021

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Gonorrhea Treatment

2021 CDC STI Treatment Guidelines

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.

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Gonorrhea Treatment – Pharyngeal

2021 CDC STI Treatment Guidelines

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

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Gonorrhea Management

- **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**, refer to Allergy for testing or graded challenge
- **Treatment failure**
  - Most treatment failure is **reinfection**
  - **Partner treatment** is critical, but poorly done
  - Suspect **drug failure**? Contact local health department, send culture and susceptibility testing

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Genital Herpes

Recognition, Testing, Advice

2023 USPSTF Statement on Screening

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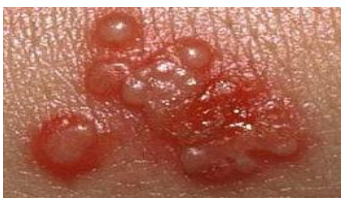
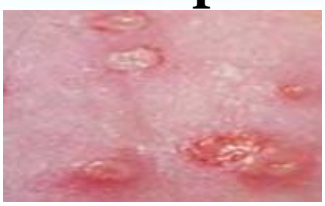
What Is the Most Common Appearance of Recurrent Genital Herpes?



(A) Classic Vesicles



(B) Classic Ulcers

A. (A) Classic Vesicles
B. (B) Classic Ulcers
C. Nothing

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45 Million People Have It

Most Do Not Know They Have It

Only 15-20% Report Classic Vesicles & Ulcers

Recurrent Herpes 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 Symptoms and Signs Are the Clue

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

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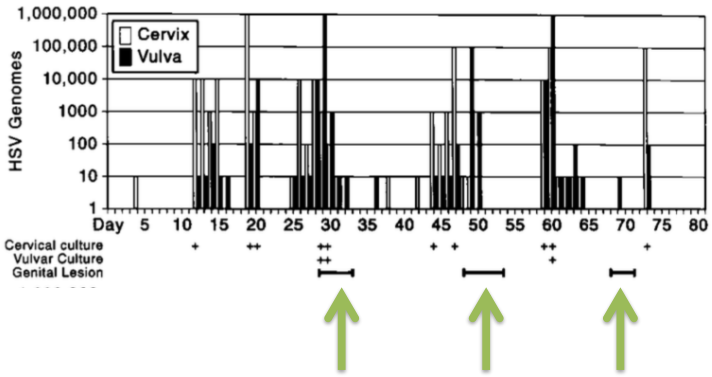
Asymptomatic Viral Shedding: Presence of HSV on the Skin or Mucosa in the Absence of Signs of Symptoms. Landmark Studies Using PCR Have Taught Us a Lot.



Shedding Occurred an Average of **28% of Days**

J Clin Invest 1997;99:1092

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70% of Transmission Occurs from Asymptomatic Shedding

- 144 couples serodiscordant for genital herpes
  - Followed for a mean of 334 days
  - Kept journal of sexual activity, herpes in the + partner
- 9.7% of partners became infected
  - 30% of transmissions during symptomatic outbreaks
  - 70% of transmissions during asymptomatic periods

Mertz GJ et al. Ann Intern Med. 1992;116:197-202

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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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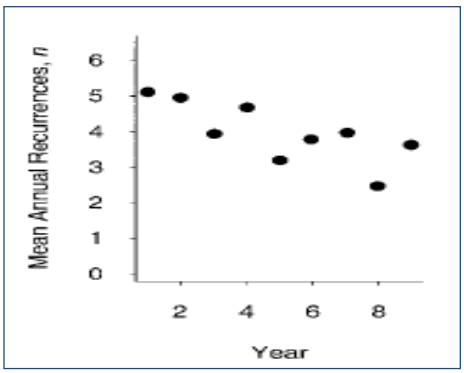
HSV-2 vs HSV-1: Genital Recurrence Rates

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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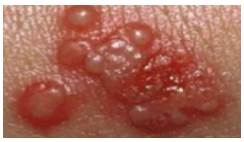
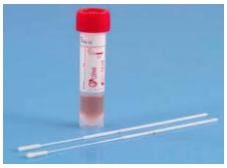
Herpes Diagnostics

Presents with Lesions





HSV-2
- Expect more recurrences
- Counsel
- Suppression important

HSV-1
- Expect few recurrences
- Counsel
- Suppression less studied

Herpes Diagnostics	Comments
Swab for PCR (Direct detection)	Fresh vesicle, pustule, ulcer Swab the base with "vigor" Types the virus – important for prognosis **BEST** test

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Presents with Recurrent GU Symptoms, No Visible Lesions

Type Specific Glycoprotein G HSV-2 Ab

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 Diagnostics	Comments
Type-specific HSV-2 IgG (IgG to glycoprotein G2)	Can distinguish HSV-2 from HSV-1 Caution when Index values are low **GOOD** test with important **LIMITATIONS**
Western Blot (Univ Washington Clinical Virology Lab)	Can determine if low-positive type-specific HSV-2 IgG is true positive. Gold standard **CONFIRMATORY**, not screening, test
Non type-specific antibodies	**WORTHLESS** but still orderable Older tests that cannot distinguish HSV-1/2
Herpes IgM tests	**WORTHLESS** but still orderable IgM gets made with recurrences

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USPSTF: Serologic Screening for Genital Herpes

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?

- HSV-2 serologic testing
  - Low specificity
  - High false-positive rate
  - Confirmatory test 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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So ... When Should I Order Herpes Serology?
(Meaning HSV-2 Type-Specific Ab)

Situation	Meaningful result
Genital lesion might be herpes but the PCR comes back negative	Positive HSV-2 type-specific Ab would confirm the diagnosis of genital herpes
Recurrent genital symptoms but no lesion to swab for PCR	Positive HSV-2 type-specific Ab would confirm the diagnosis of genital herpes
Somebody wants to know their serostatus for herpes	Positive HSV-2 type-specific Ab would confirm the diagnosis of genital herpes

Be mindful that low-positive index values could be false-positive, and should be confirmed with a different type-specific test or the Univ of Washington Western blot

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Management

- First episode genital herpes
  - Everyone should be treated
- Recurrent genital herpes
  - Individualize your care over the life of the patient

  3 options
  - Suppression (reduces recurrences 70-80%, safe)
  - Self-directed therapy (start at prodrome)
  - Nothing

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The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JANUARY 1, 2004 VOL. 350 NO. 1

Once-Daily Valacyclovir to Reduce the Risk of Transmission of Genital Herpes

Table 2. Acquisition of HSV Infection among the Susceptible Partners, According to the Source Partner's Treatment Assignment.*

Variable	Valacyclovir (N=743)	Placebo (N=741)	Total No.	Hazard Ratio (95% CI)	P Value
	no. (%)				
Acquisition of symptomatic HSV-2 infection	4 (0.5)	16 (2.2)	20	0.25 (0.08–0.75)	0.008
Overall acquisition of HSV-2 infection	14 (1.9)	27 (3.6)	41	0.52 (0.27–0.99)	0.04
Acquisition of HSV-1 or HSV-2 infection	14 (1.9)	31 (4.2)	45	0.45 (0.24–0.84)	0.01

- 1484 monogamous couples serodiscordant for HSV-2
  - Source partner randomized to valacyclovir 500 mg daily vs placebo x 8 mos
  - Susceptible partner monitored for acquisition of HSV

48% reduction in the risk of the seronegative partner acquiring HSV-2

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Antivirals for HSV

- 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)

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

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Syphilis

You Pick 'Em

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For Your Syphilis CME Today, How Can I Help You the Most ?

A. Review syphilis screening recommendations
B. Review syphilis recognition, clinical stuff
C. Review syphilis serology testing
D. Review syphilis treatment
E. Move on to Mgen, if I diagnosed a case of syphilis, I would refer them to ID anyway

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Syphilis

Women	• Screen asymptomatic women at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity) for syphilis infection[2,7]
Pregnant Women	• All pregnant women at the first prenatal visit[8] • Retest at 28 weeks gestation and at delivery if at increased risk due to geography or personal risk (substance use, STIs during pregnancy, multiple partners, a new partner, partner with STIs)[2]
Men Who Have Sex With Women	• Screen asymptomatic adults at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity, and being a male younger than 29 years) for syphilis infection[2,7]
Men Who Have Sex With Men	• At least annually for sexually active MSM[2] • Every 3 to 6 months if at increased risk[2] • Screen asymptomatic adults at increased risk (history of incarceration or transactional sex work, geography, race/ethnicity, and being a male younger than 29 years) for syphilis infection[2,7]
Transgender and Gender Diverse People	• Consider screening at least annually based on reported sexual behaviors and exposure[2]
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 behaviors and the local epidemiology[2]

Syphilis Screening Recommendations
2021 CDC STI Guidelines

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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
  - Neurosyphillis
  - Ocular syphilis
  - Otosyphilis

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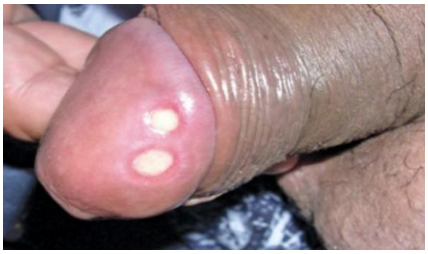
Primary Syphilis

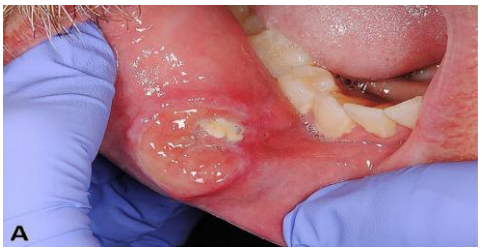
Painless chancre, single > multiple

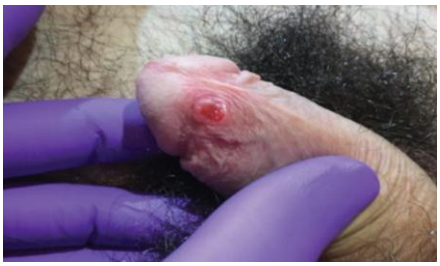
Lymphadenopathy

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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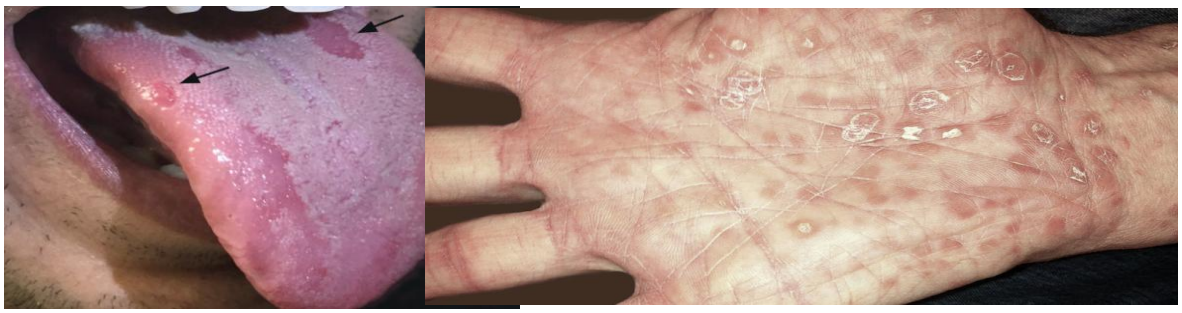
Secondary Syphilis "All of Medicine"

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

Beware Prozone (false neg RPR); BUT all treponemal specific tests are POS



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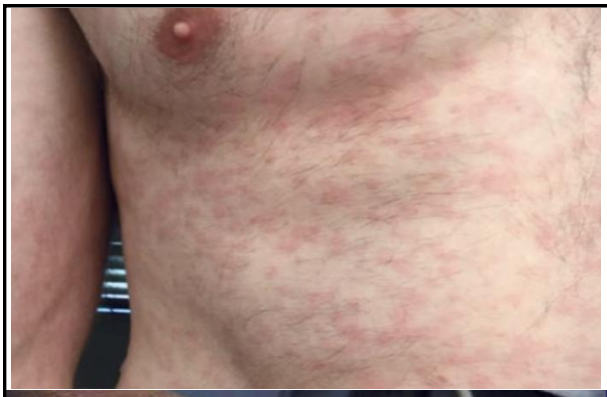
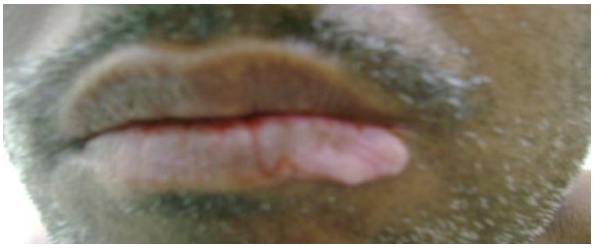
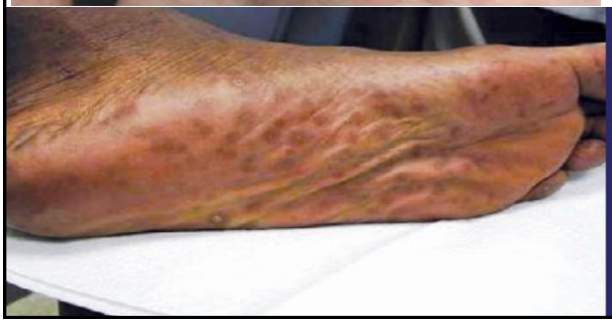
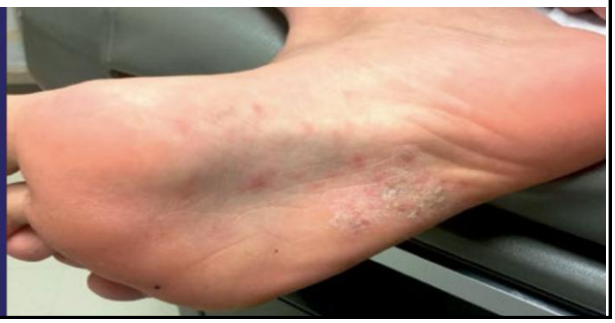




NYCPTC March 2019 Syphilis Update





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A Systematic Literature Review of Syphilitic Hepatitis in Adults

Jiaofeng Huang[1], Su Lin[1], Bo Wan[2] and Yueyong Zhu*[1]

[1]*Liver Research Center of the First Affiliated Hospital of Fujian Medical University, Fuzhou, Fujian, China;*
[2]*Institute of Neurology, University College London, London, UK*

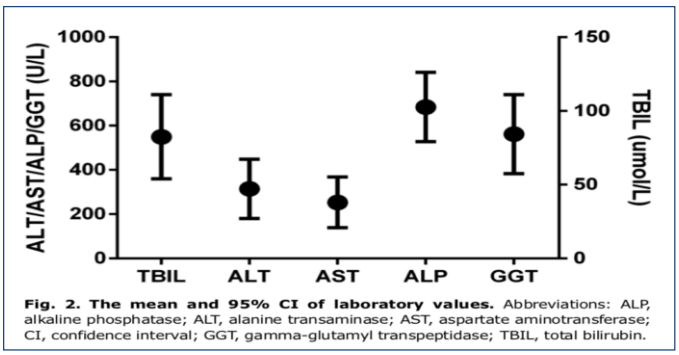

Fig. 2. The mean and 95% CI of laboratory values. Abbreviations: ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase; CI, confidence interval; GGT, gamma-glutamyl transpeptidase; TBIL, total bilirubin.

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

J Clin and Trans Hepatol 2018;6:306

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Early Latent Syphilis

Latent = Asymptomatic, the only indicator is a positive serology

Early = Acquired in the preceding 12 months

Contrast this with the other forms of latent syphilis:

Late Latent = duration > 1 year

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 is most common, but pathology is diverse

Also conjunctivitis, anterior uveitis, posterior interstitial keratitis, optic neuropathy, retinal vasculitis

Vision blurred, loss, painful, red eye

Bilateral in 56%

Neurosyphilis and CSF findings are variable

Invest Ophthalmol Vis Sci 2014;55:5394; 20121 CDc STD Guidelines

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Excellent Screening Tool for Neuro, Ocular, Oto

Screening Questions for Neurosyphilis (Including Ocular and Otosyphilis)

Questions	
Symptoms of Otosyphilis	
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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Syphilis[24]

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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Syphilis Serology

- Non-treponemal tests = RPR, VDRL
  - Initial tests in traditional testing algorithms
  - Quantitative, helps determine disease activity
  - Titer decreases with treatment and time
- Treponemal tests = MHA-TP, FTA-ABS, TPPA, CIA, EIA
  - Initial tests in reverse testing algorithms
  - Qualitative
  - Lifelong persistence

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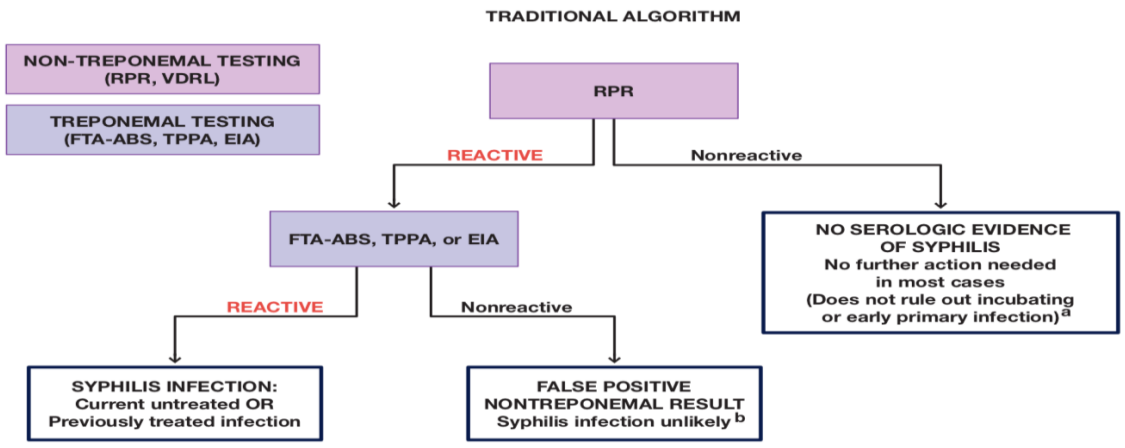

https://www.nycptc.org/x/Syphilis_Monograph_2019_NYC_PTC_NYC_DOHMH.pdf

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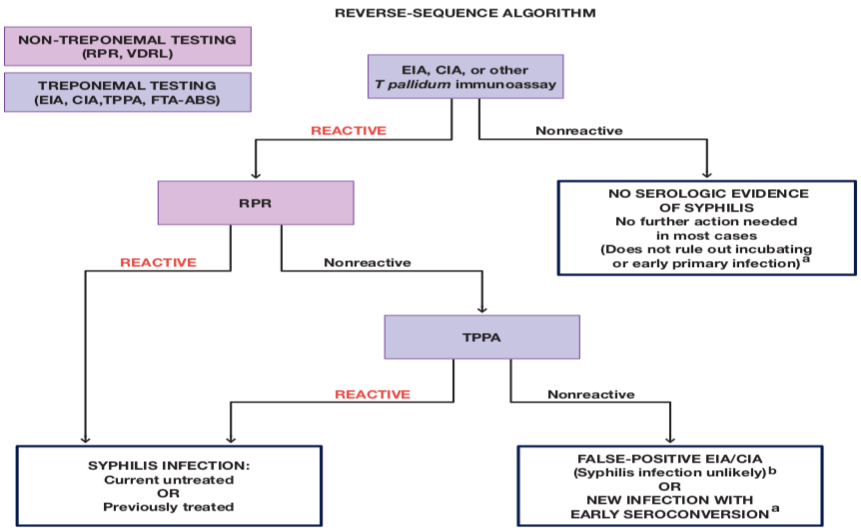

https://www.nycptc.org/x/Syphilis_Monograph_2019_NYC_PTC_NYC_DOHMH.pdf

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Syphilis Serology Is Positive, What Next?

- Good history and exam to stage
  - Past testing and treatment (call), risks for syphilis
  - Do they have neuro-, ocular-, or otosyphilis?
- Check HIV and other STIs
  - Report it (public health)
- Treat and follow
  - Penicillin
  - Clinical and RPR followup (STI guidelines excellent section)
  - Risk modification (HIV PrEP, vaccines, etc)

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Mycoplasma genitalium Mgen

Updated Treatment Guidance

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Mycoplasma genitalium

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

2021 STI Treatment Guidelines

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Mgen - Major Treatment Challenge

- Doxycycline poor response (31% cure)
- Azithromycin decreasing response (80% → 40% cure) including emergence of resistance in 10-20% of cases after single dose
- Moxifloxacin 95% effective but resistance can emerge
- Resistance testing not readily available

2021 STI Treatment Guidelines

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M. genitalium Treatment Update

- Sequential treatment to reduce bacterial burden

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

2021 STI Treatment Guidelines

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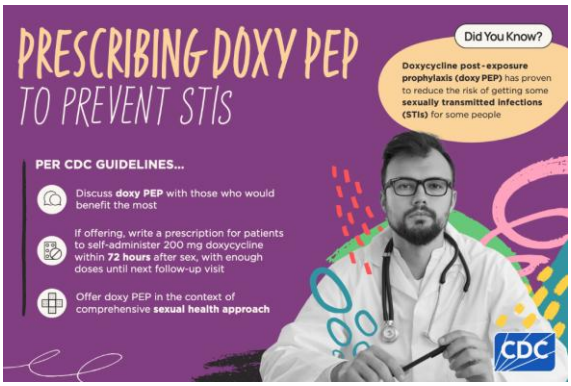
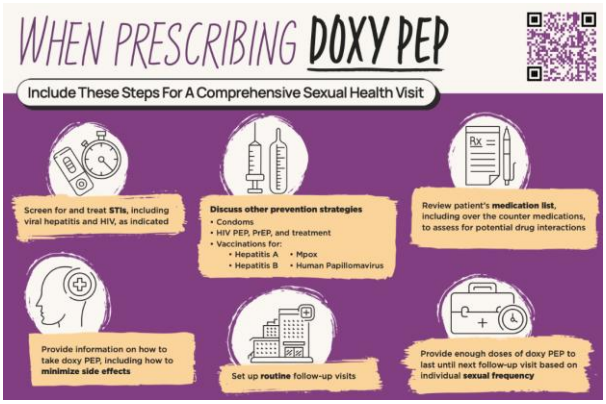
Doxycycline as STI PEP

2024 CDC Guidelines





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Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial

- Open label study (n=232)
  - HIV-negative high risk MSM enrolled in IPERGAY On Demand PrEP study
- On demand PEP doxycycline 200 mg vs no PEP
  - Take ~24 hours after condemless anal or oral sex, up to 72 hours
  - Syphilis serology, PCR for gonorrhea/chlamydia (3 sites)
- PEP reduced overall incidence of bacterial STD by 47% over 8.7 mos of follow-up
  - 70% relative reduction in chlamydia
  - 70% relative reduction in syphilis
  - NO effect on gonorrhea

Lancet ID 2018;18:308

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Doxycycline PEP Studies

- DoxyPEP (2022, San Francisco, Seattle)
  - 501 MSM and TGW w/ HIV or on HIV PrEP
  - RR reductions GC (43-45%), Ct (12-26%), early Syph (13-23%)
- DOXYVAC (2022, France)
  - MSM on HIV PrEP, 1 or more STI last 12 months, stopped early
  - Doxycycline and 4CMenB arm
  - Reductions in GC, chlamydia, syhphilis
- Kenya, 449 cisgender women
  - No significant reduction on bacterial STI, chlamydia or gonorrhea, and syphilis could not be evaluated as only 2 cases

2024 CDC Doxycycline PEP Guidelines

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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.

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Trichomonas: Single-dose Metronidazole No Longer Recommended for Women

- Metronidazole
  - 7 day regimen 500 mg BID for women
    - Single-dose therapy for women no longer recommended; Higher rates of persistent infection (19% vs 11%) at 4-week test of cure with single-dose
  - Single-dose 2 gm still OK for male partner treatment or male urethritis (no data)
- Tinidazole for suspected MTZ resistance
  - 2 gm single dose

2021 STI Treatment Guidelines Lancet 2018;18(11):1251 MTZ = metronidazole

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Considerations for Screening

STD Pathogen	Testing 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	4th 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. 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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