

Updates in STI Detection and Treatment

Jennifer Janelle, MD
University of Florida, Gainesville
Principal Investigator, North
Florida AETC

L. Beth Gadkowski MD MPH MS University of Florida, Gainesville Faculty, North Florida AETC

Continuing Education Disclosure

 The speakers do not have any financial relationships with commercial entities to disclose.

This slide set has been peer-reviewed to ensure that there are no conflicts of interest represented in the presentation.



Objectives

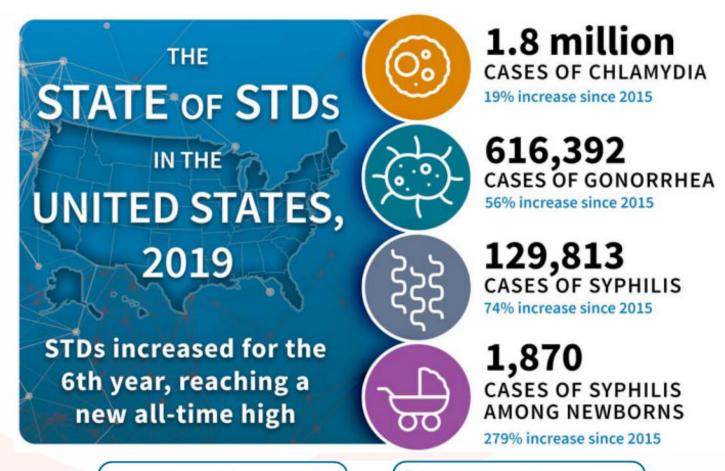
At the end of this session, participants will be able to:

- Recognize and diagnose common bacterial sexually transmitted infections (STIs)
- 2. Choose appropriate treatment for common bacterial STIs
- 3. Share barriers to, facilitators of, and lessons learned from the field regarding improvements in STI screening, testing and treatment.



Which is the most common reportable STI in the U.S.?

- A. Syphilis
- B. Gonorrhea
- C. Human papilloma virus
- D. Chlamydia

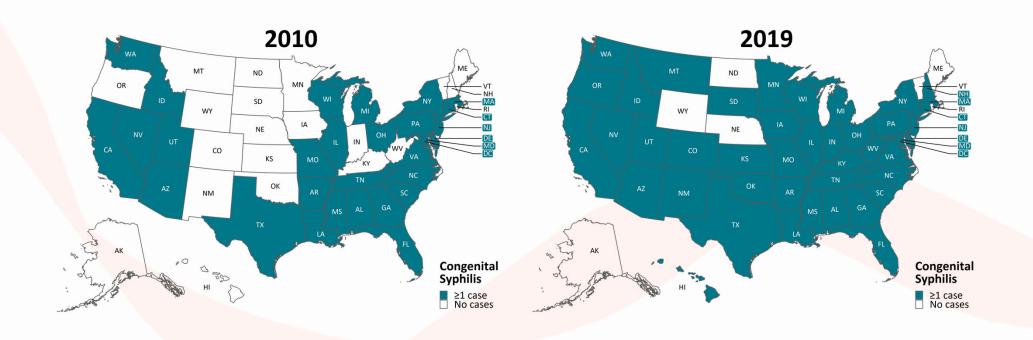


ANYONE WHO HAS SEX COULD GET AN STD, BUT SOME GROUPS ARE MORE AFFECTED

- O YOUNG PEOPLE AGED 15-24
 O GAY & BISEXUAL MEN
 - O PREGNANT PEOPLE
 - O RACIAL & ETHNIC MINORITY GROUPS



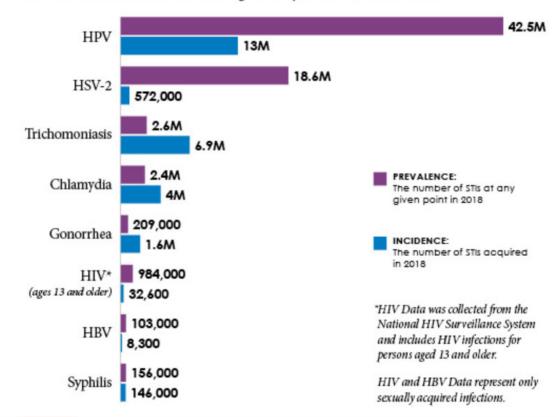
Over the last decade, congenital syphilis has diffused across the nation. By 2019, 43 states and D.C. reported at least one case.



Congenital Syphilis — Reported Cases by State, United States, 2010 and 2019, CDC.gov

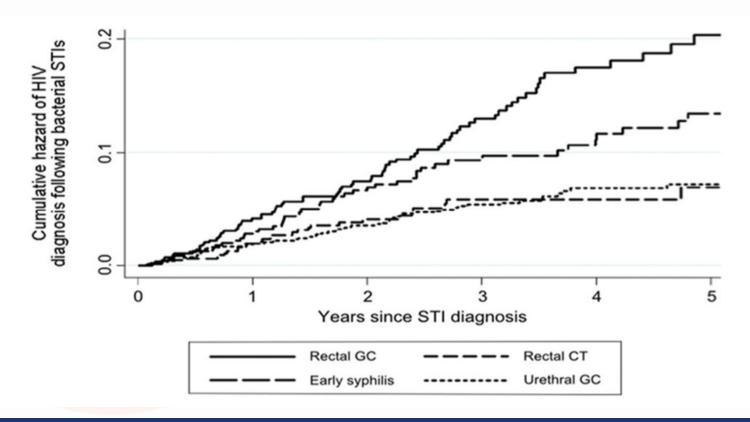
LATEST CDC ESTIMATES REVEAL NEARLY 68 MILLION STIS IN THE U.S., AND MORE THAN 26 MILLION NEW INFECTIONS

Estimated number of new and existing sexually transmitted infections





Cumulative Hazard: HIV Diagnosis Following an STI





Mentimeter

Age ranges



STIs in the United States

1 in 5 People in the US have an STI totaling nearly 68 MILLION infections in 2018

To f new STIs were among youth aged 15-24 in the US



STI Treatment Guidelines

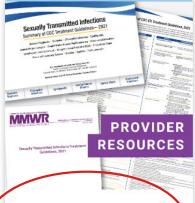
2021 RECOMMENDATIONS NOW AVAILABLE

STI Treatment Guidelines Update

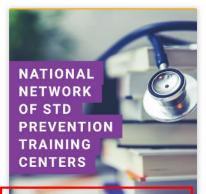
CDC's Sexually Transmitted Infections (STI) Treatment Guidelines, 2021 provides current evidence-based prevention, diagnostic and treatment recommendations that replace the 2015 guidance. The recommendations are intended to be a source for clinical guidance. Healthcare providers should always assess patients based on their clinical circumstances and local burden.



View the full STI Treatment Guidelines.



Access print-friendly versions of the wall chart, pocket guide, and guidelines.



Explore STD trainings, technical assistance, clinical consultation services, and more.

2021 Mobile App in Development Learn how to use the interim, mobile-friendly solution



Learn about recommendations and tools to help healthcare settings improve STD care services.



5 Major Strategies to Prevent STIs

- Accurate risk assessment and education and counseling of persons at risk
- 2. Pre-exposure vaccination for vaccine-preventable STIs
- 3. Identification asymptomatic and symptomatic STIs
- 4. Effective diagnosis, treatment, counseling, and follow-up of persons who are infected with an STI
- 5. Evaluation, treatment, and counseling of sex partners of persons who are infected with an STI



LGBTQ Welcoming Indicators

- Gender-neutral bathroom(s)
- Visible gender and sexual minority inclusiveness in waiting room materials
- 3. Gender and sexual minority inclusive educational materials
- A gender identity, gender expression, and sexual orientation nondiscrimination policy clearly displayed
- 5. History taking that includes current gender identity and sex at birth inclusive of non-binary identities
- Clinic registration/intake form has a question for client preferred name and pronoun (in addition to legal name)

- Display materials for community-based affiliations with sexual/gender minority supportive organizations
- 8. Community advisory board sexual and gender minority members
- 9. All staff training on gender identity diversity and sexual orientation
- 10. LGBTQ flag in waiting room
- 11. Transgender flag or symbol in waiting room
- 12. Acknowledgement of LGBTQ awareness and recognition days/events

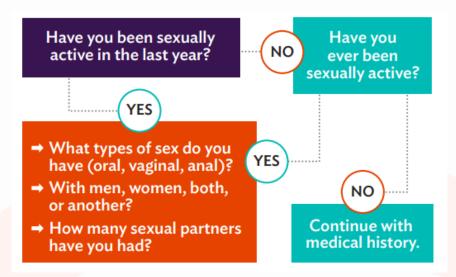




Sexual Health History

- Partners
- Practices
- Prevention of pregnancy
- Protection from STDs
- Past history of STDs

Essential Questions to Ask at Least Annually



https://nationalcoalitionforsexualhealth.org/tools/for-healthcare-providers/asset/Sexual-Health-Questions-to-Ask-All-Patients.pdf



Audio Computer-Assisted Self-Interview (ACASI): 1

Use of ACASI for STI risk assessment has been associated with:

- Identifying high-risk behaviors
- Less time spent by provider taking a sexual health history (SHH)
- High acceptability when used by patients

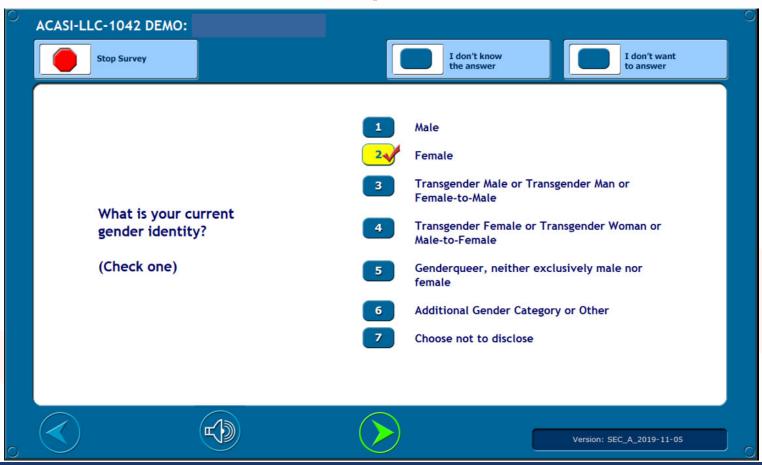
Potential barriers include:

- Computer literacy
- Implementation expense
- Export of data to EMR when used for clinical care
- Https:targethiv.org/library/sexual-history-taking-toolkit



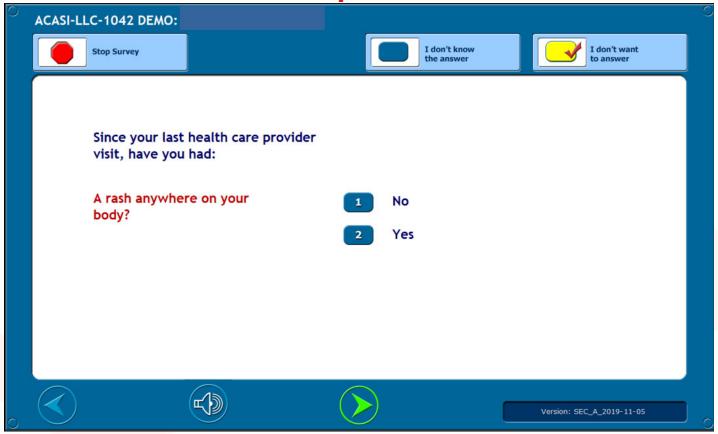


ACASI Sample Question 1



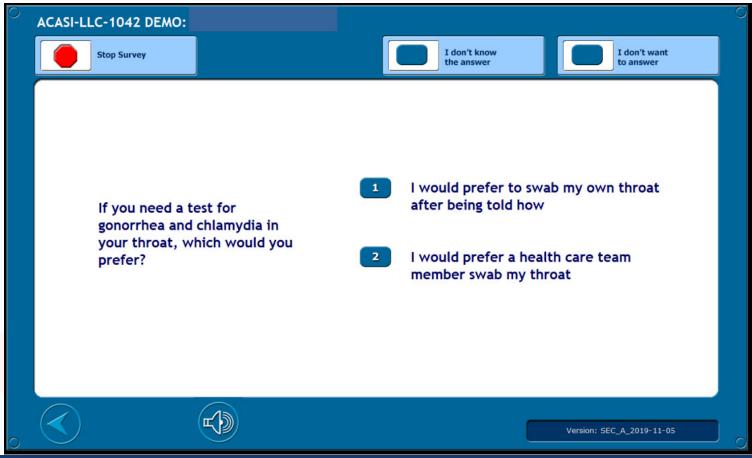


ACASI Sample Question 2



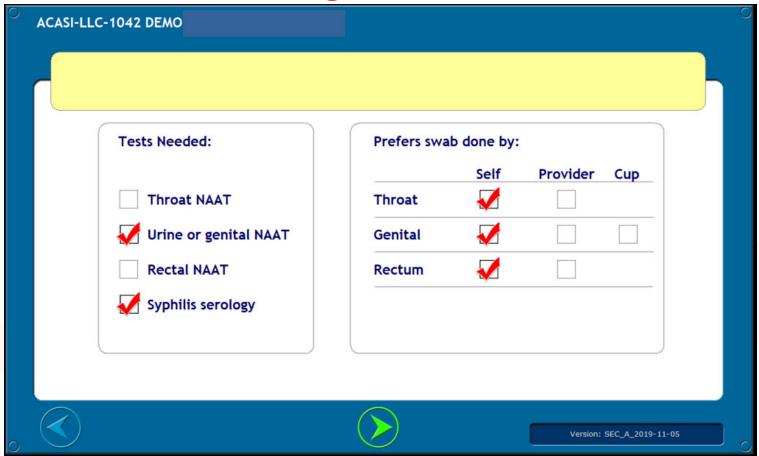


ACASI Sample Question 3



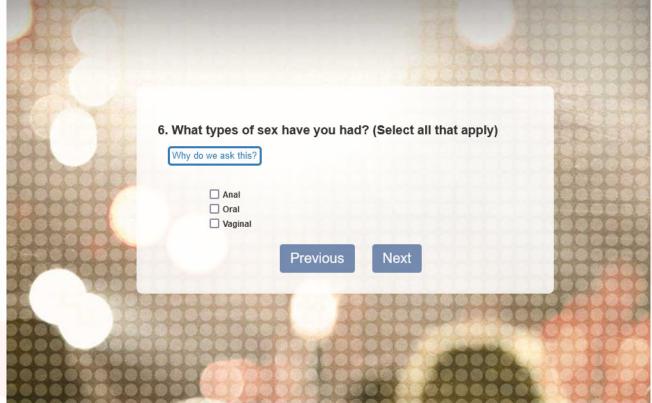


ACASI Testing Recommendations











MMWR MSM* & STDs: TEST MORE THAN GENITALS

STDs IN THE THROAT **AND RECTUM**

- MSM AT HIGH RISK
- OFTEN NO SYMPTOMS
- DETECT BY SCREENING
- INCREASES HIV RISK



OF MSM SCREENED FOR **CHLAMYDIA & GONORRHEA**:**





SCREEN SEXUALLY ACTIVE MSM FOR STDs!

- AT LEAST 1X/YEAR
- HIGHER RISK? EVERY **3-6 MONTHS**
- IF INDICATED, TEST **THROAT & RECTUM**



Data from National HIV Behavioral Surveillance (NHBS) as published in Johnson Jones et. al. MMWR 2019.

WWW.CDC.GOV

^{**} MSM recruited from social venues in 5 cities provided data and self-collected swabs bit.ly/CDCVA24

Case

- Mr. J is a 22 yo man who comes for his annual visit
- You obtain a sexual health history
 - Partners: male
 - Practices: oral sex and anal receptive and insertive sex
 - Partners: 4 since his last visit with an associated urogenital STI screen
 - HIV/STI Prevention: not on PrEP, inconsistently uses condoms for anal sex, no condom use for oral sex
 - Prior STI: He has had one episode of urogenital gonorrhea at age 20
- He is feeling well

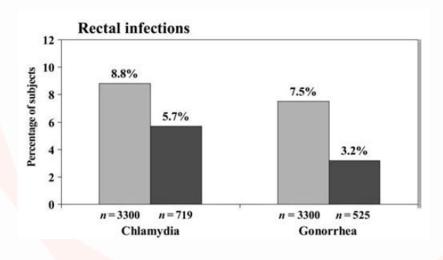


Mr. J:

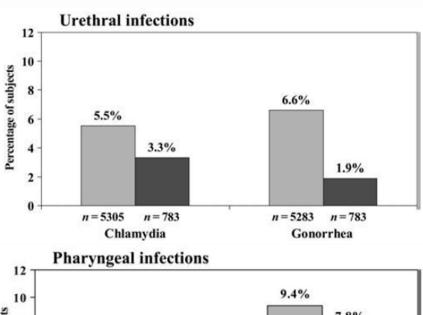
- Sexual health history suggests risks for syphilis, gonorrhea and chlamydia
- Recommended mucosal sites to be tested for gonorrhea and chlamydia: throat, rectum and urogenital
- Samples collected
- Client-centered STI prevention counselling performed, condoms offered, discussed HIV pre-exposure prophylaxis (PrEP)
- Test results returned: pharyngeal swab positive for gonorrhea

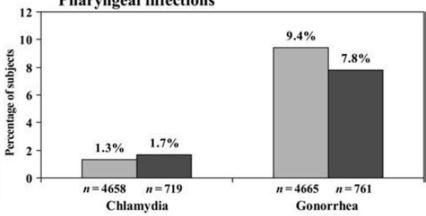


Prevalence of GC and Chlamydia by Site of Infection



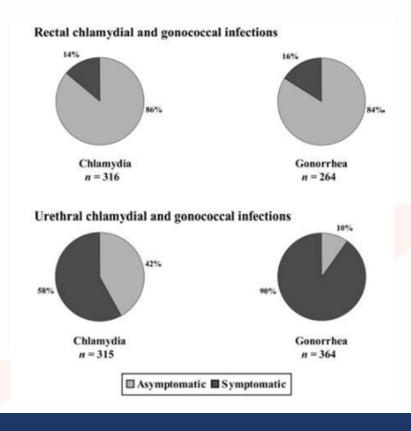








Proportion of Asymptomatic Rectal and Urethral Gonococcal and Chlamydial Infections in MSM, San Francisco





Patient Self-Collected Nucleic Acid Amplification Test (NAAT)

Patient self-collection has been shown to be equally effective to provider-collection in clinical and non-clinical settings for the following specimens:

- Vaginal swabs
- Rectal swabs
- Pharyngeal swabs
- Urine samples

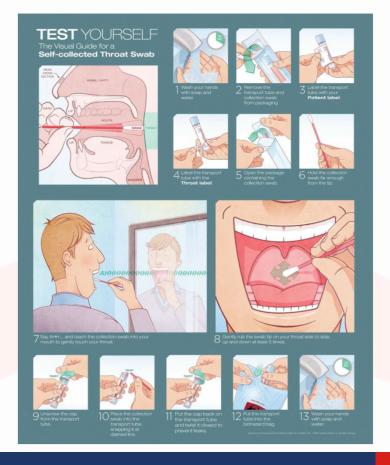


Acceptability by patients, especially those at high-risk for STIs is high



Patient Self-Collected Nucleic Acid Amplification Test (NAAT): Patient Education









UFHealth Specimen Collection: Alachua County

- The majority of patients preferred to self-collect rectal/vaginal swabs
- More reluctant to self-collect throat swabs

ACASI Ordered Extragenital STI Labs by Specimen Collection Type

	Self-collected	Provider- collected	Total
Throat	46	47	93
Rectal	43	6	49
Vaginal	5	0	5
Vaginal Total	94	53	147

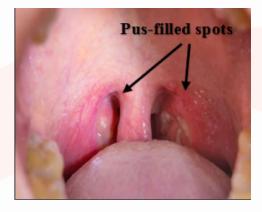
DOH Alachua County. 8/5/20-8/23/2021

Pharyngeal Gonorrhea

- < 10% diagnosed are symptomatic</p>
- More common in men who have sex in men (MSM)

Most ceftriaxone treatment failures have involved pharyngeal

gonorrhea



https://stdcenterny.com/gonorrhea-signs.html



Uncomplicated Gonorrhea: Treatment

- Ceftriaxone (weight based)
 - < 300 pounds give 500 mg IM x 1
 - >300 pounds give 1 g IM x 1
- Treat for chlamydia if infection has not been excluded
- Alternative regimens for urogenital or rectal gonorrhea
 - Gentamicin 240 mg IM + 2g azithromycin orally
 - Cefixime 800 mg PO x 1
- There are no reliable treatment alternatives for pharyngeal gonorrhea

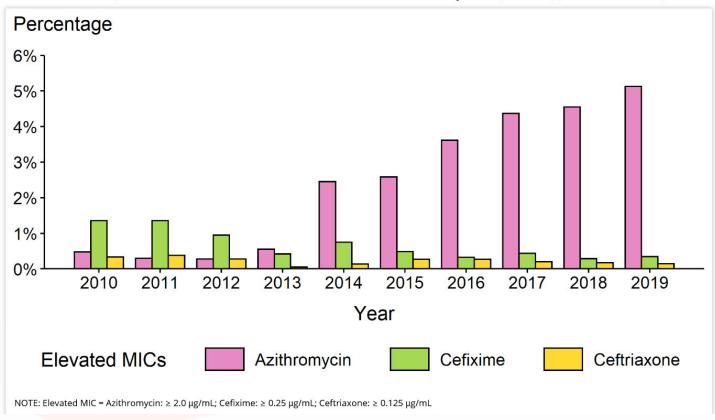


Follow-up testing:

- Test-of-cure is recommended for pharyngeal gonorrhea
 - Culture or NAAT 7-14 days after initial treatment
 - If NAAT is positive, perform confirmatory culture
 - All positive cultures for test of cure should undergo antimicrobial susceptibility
- Due to high reinfection rates (7-12%) among persons with previously treated gonorrhea, persons treated for gonorrhea should be retested 3 months after treatment



Neisseria gonorrhoeae — Percentage of Isolates with Elevated Minimum Inhibitory Concentrations (MICs) to Azithromycin, Cefixime, and Ceftriaxone, Gonococcal Isolate Surveillance Project (GISP), 2010–2019





Drug Resistant Gonorrhoeae

- Commercial lab testing
 - Quest Diagnostics Neisseria gonorrhoeae culture with reflex to Susceptibility
 - Preferred Specimen(s):
 - Urethral, cervical, anorectal, throat or conjunctiva swab collected in Amies gel (blue-cap) or ESwab (white-cap) transport medium
 - Test Code 38404
 - Labcorp GC (Neisseria gonorrhoeae) culture
 - Test code 008128
- DOH testing: Contact local health department to help arrange collection of sample to be sent to state lab



Case

- Ms. M is a 23 yo woman presenting for her 6-month follow-up of well controlled HIV. She is taking bictegravir/emtricitabine/tenofovir alafenamide every day with no medication related side effects.
- She tested negative for STIs 6 months ago. Today, she states she would like to be tested for STIs "to be on the safe side."



Mentimeter

What will you do?

- A. Tell her she doesn't have any STIs as if she did, she would have symptoms
- B. Perform a sexual health history and offer STI testing based on this



Ms. M:

- Sexual Health History
 - Partners: two male, their sexual health unknown to her
 - Practices: Vaginal receptive sex only
 - Prevention of STIs: Not consistently using condoms
 - Past history of STIs: None
 - Prevention of Pregnancy: Nexplanon implant placed last year
- Testing done: self-collected vaginal swab for GC/CL NAAT, syphilis cascade
- NAAT is positive for Chlamydia



Treatment

Preferred regimen:

Doxycycline 100 mg by mouth twice daily for 7 days

Alternative regimens:

Azithromycin 1 g by mouth in a single dose (preferred in pregnancy) or

Levofloxacin 500 mg by mouth daily for 7 days

Follow-up: Retest approximately three months after treatment; schedule this follow-up appointment at the time of initial treatment



Follow-up After Treatment

- Non-pregnant people should be rescreened 3 months after treatment
- Pregnant people should undergo test of cure to document chlamydia eradication by NAAT 4 weeks after treatment



Chlamydia & Gonorrhea: Partner Management

- Sex partners should be evaluated, tested and treated if they had sexual contact with the patient during the 60 days preceding the patient's onset of symptoms or diagnosis of chlamydia
- The most recent sex partner should be evaluated and treated even if last sexual contact was > 60 days before symptom onset or diagnosis

Expedited Partner Therapy (EPT)

- Clinical practice of treating sex partners of persons with diagnosed chlamydia or gonorrhea who are unable or unlikely to seek timely treatment
- Medical providers should offer EPT when the provider cannot ensure that all of a patient's sex partners from prior 60 days will seek treatment

If you've been diagnosed with an STD, you may be able to get treatment for your partner, too.



If you've been diagnosed with chlamydia or gonorrhea, the first step is to get treatment.

But did you know that you may be able to get treatment for your

Talk to your doctor. They may be able to give you medicine or a prescription for your partner even without seeing them. This is called expedited partner therapy (EPT) or patient-delievered partner therapy (PDPT), and it's available in most states.

With EPT:





- ✓ Your partner can get treated quickly without having to go to the doctor first
- You'll be protected from your partner passing the infection back to you
- Neither of you will pass the infection on in the future



Why does my partner need treatment?

Without treatment, your partner could pass the STD back to you. Keep in mind that many people with chlamydia and gonorrhea have no signs or symptoms, so your partner may have the STD and not know it. Left untreated, chlamydia and gonorrhea can cause serious health problems.

If you've been diagnosed with chlamydia or gonorrhea, talk to your doctor to find out if EPT is an option for you and your partner.

To learn more about how you can prevent STDs, visit cdc.gov/std/prevention.





Doxycycline vs. Azithromycin: Rectal Chlamydia in Men

Dombrowski et al., CID 2021

- Randomized double-blind, placebo-controlled trial in MSM in Seattle and Boston
- Microbiologic cure in rectal infections across analysis groups
 - Azithromycin 71-77%
 - Doxycycline 91-100%
- Trial stopped early due to interim analysis

Lau et al., *NEJM* 2021

- Randomized double-blind, placebo-controlled trial in Australian men with asymptomatic rectal chlamydia
- Microbiologic cure in rectal infections
 - Azithromycin 76.4%
 - Doxycycline 96.9 %

RESEARCH SUMMARY

Azithromycin or Doxycycline for Asymptomatic Rectal Chlamydia trachomatis

Lau A et al. DOI: 10.1056/NEJMoa2031631

CLINICAL PROBLEM

Chlamydia trachomatis is a common STI globally among men who have sex with men and is most often asymptomatic. Although guidelines have recommended treatment with either doxycycline or azithromycin, data from randomized trials are lacking.

CLINICAL TRIAL

Design: A double-blind, randomized trial in Australia involving men with asymptomatic rectal chlamydia to compare the efficacy of doxycycline with that of azithromycin.

Intervention: 625 men were assigned to receive either doxycycline or azithromycin. The primary outcome was a negative nucleic acid amplification test for rectal chlamwdia (microbiologic cure) at 4 weeks.

RESULTS

Efficacy: The doxycycline regimen was significantly more efficacious than the azithromycin regimen for the treatment of asymptomatic rectal chlamydia.

Safety: Adverse events including nausea, diarrhea, and vomiting were less common in the doxycycline group than in the azithromycin group.

LIMITATIONS AND REMAINING QUESTIONS

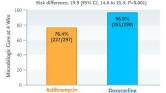
Further study is required to understand the following:

- Why azithromycin is less efficacious for rectal chlamydia, since other trials have shown it to be only slightly less effective than doxycycline for urogenital infection.
- Whether larger azithromycin doses may be more effective for higher-load infections
- Whether azithromycin will cure rectal chlamydia in women

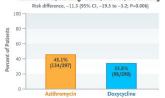
Links: Full article | NEJM Quick Take



Microbiologic Cure in Modified Intention-to-Treat Population



Adverse Events, including Nausea, Diarrhea, and Vomiting



CONCLUSIONS

A 7-day course of doxycycline was superior to single-dose azithromycin in the treatment of rectal chlamydia infection among men who have sex with men.



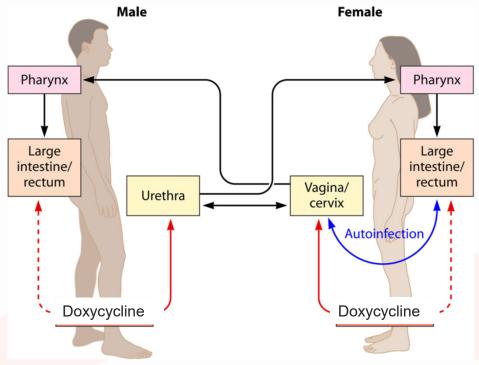
Doxycycline vs. Azithromycin: Rectal Chlamydia in Women

- Prospective multicenter cohort study of azithromycin and doxycycline in uncomplicated rectal and vaginal chlamydia
- Microbiologic cure in vaginal infections (n=394)
 - Azithromycin: 93.5 %
 - Doxycycline: 95.4 %
- Microbiologic cure in rectal infections (n=341)
 - Azithromycin 78.5%
 - Doxycycline 95.5 %



Rectal Chlamydia in Women

- Can occur concomitantly with urogenital chlamydia
- Cannot be predicted by reported sexual activity
- Inadequately treated rectal chlamydia among women with concomitant urogenital chlamydia can increase risk for transmission
 - women at risk for repeat urogenital chlamydia infection through autoinoculation from anorectal site



Rank RG, Laxmi Y. Infection and Immunity. April 2014; 82(4). 1362-1371



Why is doxycycline better?

- Mechanism of azithromycin failure is unknown:
 - Mechanism of action of doxycycline and azithromycin both target bacterial protein synthesis
 - Antibiotic resistance has not been conclusively demonstrated in vivo
 - Rectal tissue penetration of azithromycin has been shown to be above MIC for chlamydia
 - Presence of LGV biovars
- Temporary suppression with single-dose azithromycin (chlamydia persistence)
- Different host-microbe interactions in rectal environment vs. genital trach



Case

Ms. T is 24 yo woman, currently 32 weeks pregnant, presenting for OB follow-up. She has a history of previously treated syphilis. At entry to care this pregnancy, she had a negative HIV test and a nonreactive RPR. Ms. T's third trimester syphilis test shows an RPR of 1:8. Her HIV test remains negative.



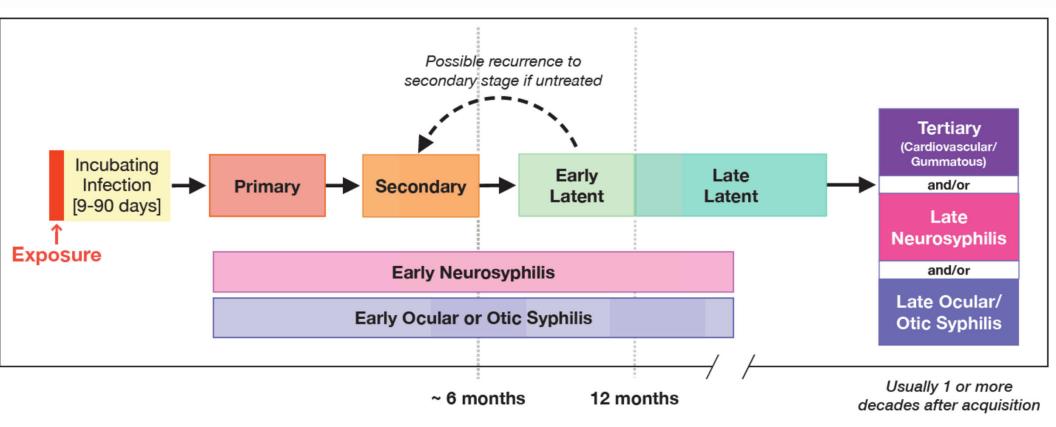
Mentimeter

What will you do?

- A. Retest in 2 weeks in case this is a false positive result
- B. Obtain a sexual health history to see if she has had any new exposures, signs or symptoms of syphilis or other STIs
- C. Treat for syphilis with 2.4 MU IM benzathine penicillin
- D. B and C



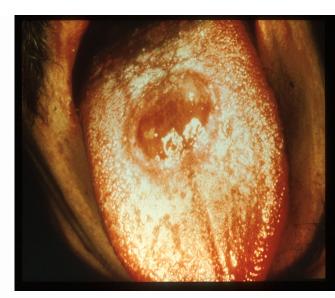
Syphilis Staging:





Primary Syphilis

- Primary lesion or "chancre" develops at the site of inoculation.
- Chancre
 - Progresses from macule to papule to ulcer
 - Typically painless, indurated, and has a clean base
 - Highly infectious
 - Heals spontaneously within 3 to 6 weeks
 - Multiple lesions can occur
- Regional lymphadenopathy: classically rubbery, painless, bilateral
- Both treponemal and non treponemal tests may be negative in primary syphilis





Secondary Syphilis

- Secondary lesions occur several weeks after the primary chancre appears
 - Primary and secondary stages may overlap
- Clinical Manifestations:
 - Rash (75%–100%)
 - Lymphadenopathy (50%–86%)
 - Malaise
 - Mucous patches (6%–30%)
 - Condyloma lata (10%–20%)
- RPR is usually highest during this stage









Per 2021 CDC Guidelines, LP no longer recommended for purely ocular and otic syphilis

Screening Questions for Neurosyphilis (Including Ocular and Otosyphilis)

Questions	
Symptoms of Otosyphilis	
Have you recently had new trouble	□ Yes – refer to ENT □ No
hearing?	
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	□ Yes – refer to ophthalmology □ No
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	□ Yes – refer to ophthalmology □ No
your vision?	
6) Have you had any blurring of your vision?	
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	□ Yes □ No
recently changed?	
12)Are you having a new problem walking?	□ Yes □ No
13)Do you have weakness or numbness in	□ Yes □ No
your legs?	

Medical providers should consider evaluation and treatment for neurosyphilis in persons with new persistent headaches rated as moderate or greater; new change in vision, including loss, blurring, seeing spots or flashing lights; new change in hearing, including loss, muffling or tinnitus; new and persistent change in personality, memory or judgment; new numbness in both legs; or new gait incoordination.

HIV / STD Program

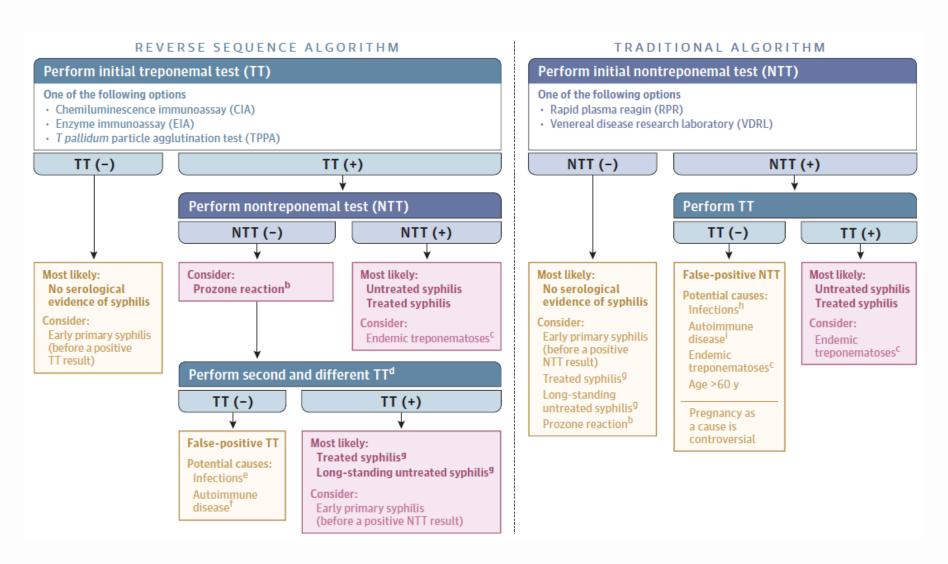
January 21, 2015



Diseases That Mimic Early Syphilis

	Differential diagnosis			
Genital ulceration	Genital herpes (very common), chancroid, Bechet's syndrome, trauma			
Palmar or plantar skin rash	Contact dermatitis, eczema, atopic dermatitis, erythema multiforme, Rocky Mountain spotted fever			
Generalised skin rash	Systemic allergy, pityriasis rosea			
Generalised lymphadenopathy	Mononucleosis syndrome, Hodgkin's lymphoma			
Aseptic meningitis	Viral exanthem			
Table 1: Differential diagnosis of diseases that can mimic early syphilis, by manifestation				





Tuddenham S, Hamill M, Ghanem K. *JAMA*. 2022;327(2):161-172.

Ordering Syphilis Tests at UF Health

¹ Procedures ≈						
	Px Code	Name				
☆	LAB2107249	DONOR Syphilis(T pallidum IgG)				
☆	LAB5395	Lyme Syphilis AB Diff Profile				
☆	LAB550	Obstetric Panel (aka SYPHILIS)				
☆	LAB21049401	Syphilis Follow-up testing(RPR w/ titer)				
☆	LAB51010	Syphilis Screen (T pallidum Ab) w/ reflex conf.				
☆	LAB338	Treponema Pallidum Confirmatory (aka SYPHILIS)				
☆	LAB859	VDRL (aka SYPHILIS)				



Syphilis Treatment:

		Recommended Rx	Dose/Route	Alternatives
	rimary, secondary, early latent <1 year	benzathine penicillin G	2.4 million units IM in a single dose	doxycline 100mg 2x/day for 14 days OR tetracycline 500mg orally 4x/day for 14 days
	atent >1 year, latent unknown duration	benzathine penicillin G	2.4 million units IM in 3 doses each at 1 week intervals (7.2 million units total)	doxycline 100mg 2x/day for 28 days OR tetracycline 500mg orally 4x/day for 28 days
• Pr	regnancy	IV Penicillin only option		
• Ne	eurosyphilis	aqueous crystalline penicillin G	18-24 million units per day, administered as 3-4 million units IV every 4 hours or continuous infusion, for 10-14 days	procaine penicillin G 2.4 MU IM 1x daily PLUS probenecid 500 mg orally 4x/day, both for 10-14 days
• Cc	ongenital syphilis	See complete CDC guidelines.		
se	hildren: Primary, econdary, or early tent <1year	benzathine penicillin G	50,000 units/kg IM in a single dose (maximum 2.4 million units)	
ye	hildren: Latent >1 ear, or unknown uration Latent	benzathine penicillin G	50,000 units/kg IM for 3 doses at 1 week intervals (maximum total 7.2 million units)	



Syphilis Follow-up

HIV Negative

- Primary and secondary syphilis
 - Clinical and serologic evaluation at 6 & 12 months after treatment
- Latent Syphilis
 - Clinical and serologic evaluation at 6, 12, and 24 months

HIV Positive

- Primary and secondary syphilis
 - Clinical and serologic evaluation at 3, 6, 9, 12 and 24 months after treatment
- Latent syphilis
 - Clinical and serologic evaluation at 6, 12, 18, and 24 months

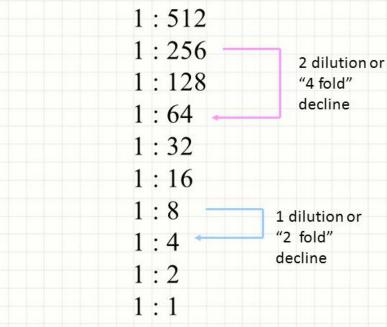


Follow-up:

If persistent symptoms, or persistent titer elevation (less than 4 fold decline)

- Retest for HIV if HIV negative initially
- Consider lumbar puncture
- Re-treat with benzathine penicillin G 2.4 million units IM once weekly for 3 weeks

Dilutions of Non-specific Tests (RPR/VDRL) 1:1024 1:512 1:256





Treating Sexual Partners

>90 days Within 90 days

Treat for primary syphilis if no serology or f/u uncertain

If serology negative, no treatment

If serology positive, treat as appropriate for stage of infection

Empiric treatment for primary syphilis Even if serology negative

Day of diagnosis of infectious syphilis



Other Important Guideline Change Metronidazole

- Trichomonas
 - Metronidazole 500 mg BID x 7 days preferred over single dose
 - Alcohol + metronidazole?



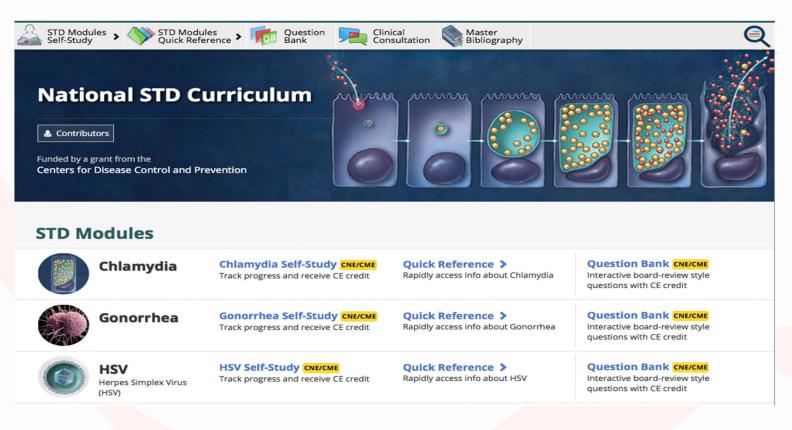
 Metronidazole does not inhibit acetaldehyde dehydrogenase so no disulfiram reaction based on evidence review

2021 CDC STI Treatment Guidelines Fjeld H, Raknes F. Tidssr Nor Laegeforen. 2014;134(17):1661-3.









Pharmacology CE now Available

Pharmacology CE for advanced practice nurses is now available for some activities (as designated in the self-study module and question bank topic overview). CNE

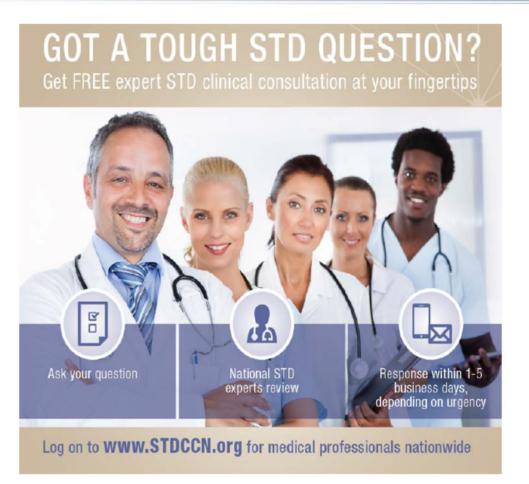
Free CE Available! CNE/CME

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