Updates in STI Detection and Treatment

L. Beth Gadkowski MD, MPH, MS
University of Florida
Division of Infectious Diseases and Global Medicine
Faculty, North Florida AETC

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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.

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Objectives

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

1. 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

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

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

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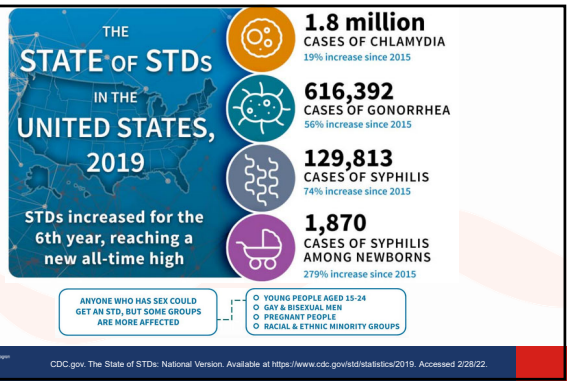

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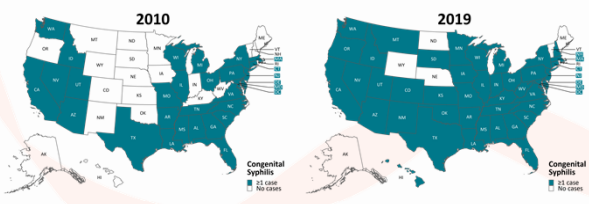
Over the last decade, congenital syphilis has diffused across the nation. By 2019, 43 states and D.C. reported at least one case.



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

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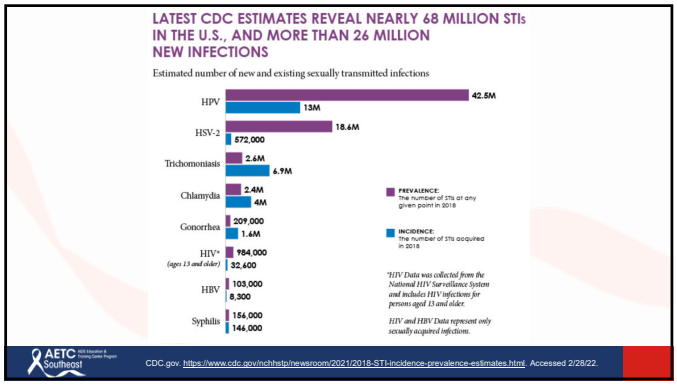
LATEST CDC ESTIMATES REVEAL NEARLY 68 MILLION STIs IN THE U.S., AND MORE THAN 26 MILLION NEW INFECTIONS
Estimated number of new and existing sexually transmitted infections
HPV
42.5M
13M
HSV-2
18.6M
572,000
Trichomoniasis
2.6M
6.9M
Chlamydia
2.4M
4M
Gonorrhea
209,000
1.4M
HIV*
(ages 13 and older)
984,000
32,600
HBV
103,000
8,300
Syphilis
156,000
146,000
PREVALENCE: The number of STIs at any given point in 2018
INCIDENCE: The number of STIs acquired in 2018
*HIV Data was collected from the National HIV Surveillance System and includes HIV infections for persons aged 13 and older.
HIV and HBV Data represent only sexually acquired infections.
CDC.gov. https://www.cdc.gov/nchhstp/newsroom/2021/2018-STI-incidence-prevalence-estimates.html Accessed 2/28/22.

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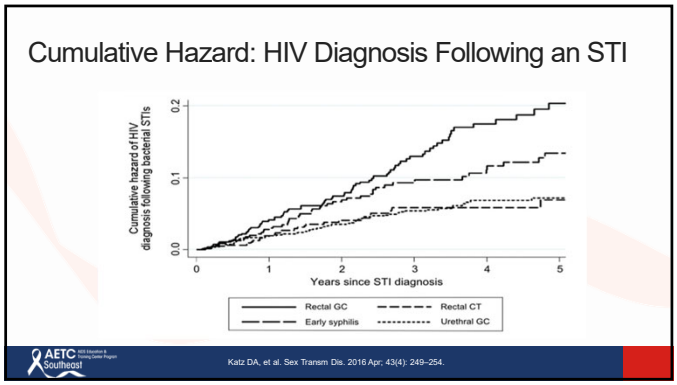
Cumulative Hazard: HIV Diagnosis Following an STI
Cumulative hazard of HIV diagnosis following bacterial STIs
0.0
0.1
0.2
0
1
2
3
4
5
Years since STI diagnosis
Rectal GC
Rectal CT
Early syphilis
Urethral GC
Katz DA, et al. Sex Transm Dis. 2016 Apr; 43(4): 249–254.

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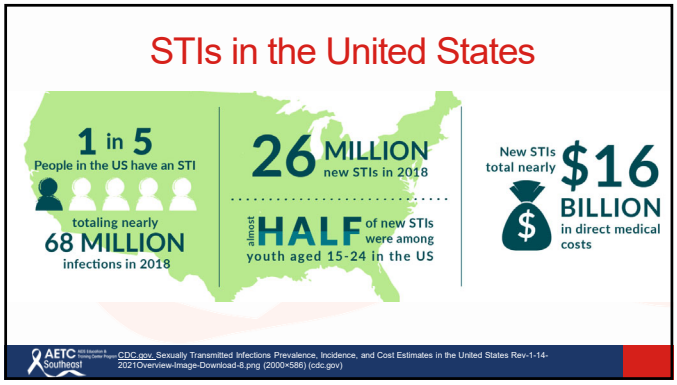
STIs in the United States
1 in 5
People in the US have an STI
totaling nearly
68 MILLION
infections in 2018
26 MILLION
new STIs in 2018
almost HALF of new STIs were among youth aged 15-24 in the US
New STIs total nearly $16 BILLION in direct medical costs
CDC.gov Sexually Transmitted Infections Prevalence, Incidence, and Cost Estimates in the United States Rev-1-14-2021Overview-Image-Download-8.png (2000×586) (cdc.gov)

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5 Major Strategies to Prevent STIs

1. Accurate risk assessment and education and counseling of persons at risk
2. Pre-exposure vaccination for vaccine-preventable STIs
3. Identification of 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

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Question

- What strategies do you use to make patients feel safe when discussing their sexual health?

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LGBTQ Welcoming Indicators

1. Gender-neutral bathroom(s)
2. Visible gender and sexual minority inclusiveness in waiting room materials
3. Gender and sexual minority inclusive educational materials
4. 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
6. Clinic registration/intake form has a question for client preferred name and pronoun (in addition to legal name)
7. 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

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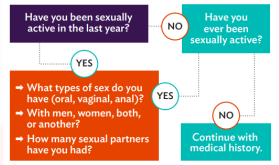
Sexual Health History "5 Ps"

- 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

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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

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Fairley CK et al. (2010). *Sexually Transmitted Diseases, 37(11),* 665-668
Jones J et al. (2014). *SpringerPlus, 3.* doi:10.1186/2193-1801-3-708
Kurth AE et al. (2004). *Sexually Transmitted Diseases, 31(12),* 719-726
Vodstrcil LA et al. (2011). *PLoS One, 6(3).*

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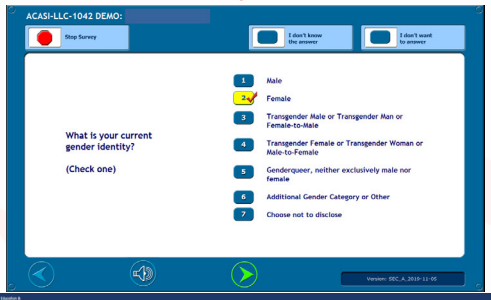
ACASI Sample Question 1



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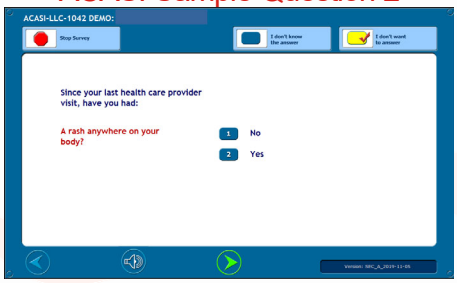
ACASI Sample Question 2



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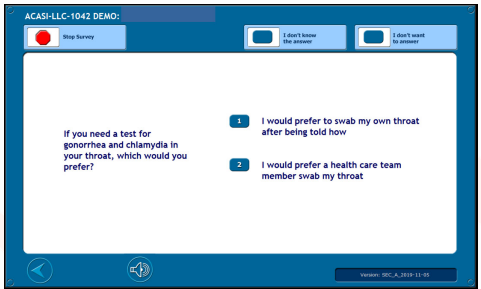
ACASI Sample Question 3



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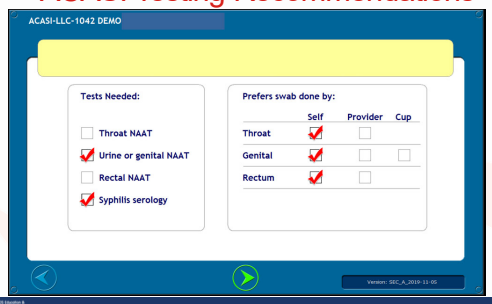
ACASI Testing Recommendations



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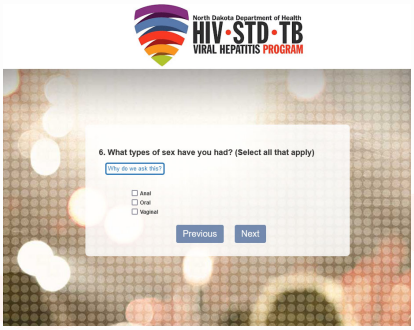

North Dakota Department of Health. Know Your Risk. Available at http://www.ndhealth.gov/hiv/knowyourrisk/. Accessed 10.21.2021.

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Case

- Mr. J is a 22 yo man who comes for his annual visit
- You obtain a sexual health history
  - **P**artners: 4 male partners since his last visit with an associated urogenital STI screen
  - **P**ractices: oral sex and anal receptive and insertive sex
  - **P**rotection from STIs: not on PrEP, inconsistently uses condoms for anal sex, no condom use for oral sex
  - **P**rior STI: He has had one episode of urogenital gonorrhea at age 20
- He is feeling well

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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

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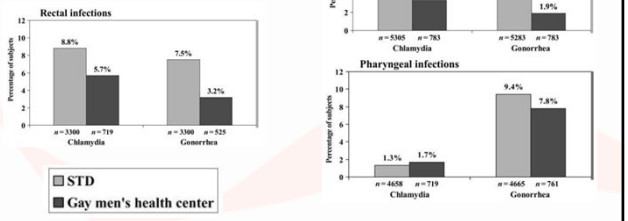
Prevalence of GC and Chlamydia by Site of Infection



Kent, CK, et al. Clin Infect Dis **2005;41:67–74.**

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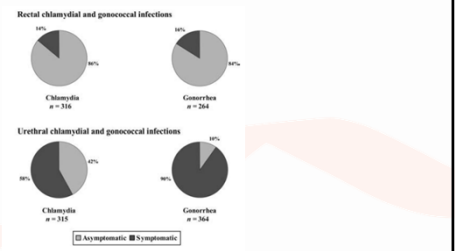
Proportion of Asymptomatic Rectal and Urethral Gonococcal and Chlamydial Infections in MSM, San Francisco



Kent, CK, et al. Clin Infect Dis **2005;41:67–74.**

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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

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https://www.fda.gov/news-events/press-announcements/fda-clears-first-diagnostic-tests-extragenital-testing-chlamydia-and-gonorrhea, 36(8), 493-497

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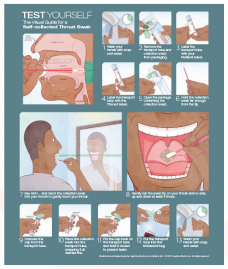
Patient Education: Self Collection of NAAT Swabs



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Poster courtesy of the University of Washington Prevention Training Center (http://uwptc.org/)

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UFHealth UNIVERSITY OF FLORIDA HEALTH 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
Total	94	53	147

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

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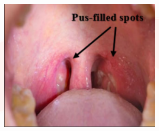
Pharyngeal Gonorrhea

- < 10% diagnosed are symptomatic
- More common in men who have sex in men (MSM)
- Most ceftriaxone treatment failures have involved pharyngeal gonorrhea



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

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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**

CDC.gov. 2021 STI Guidelines Available at https://www.cdc.gov/mmwr/volumes/69/wr/mm6950a6.htm?s_cid=mm6950a6_w

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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

https://www.cdc.gov/mmwr/volumes/69/wr/mm6950a6.htm?s_cid=mm6950a6_w

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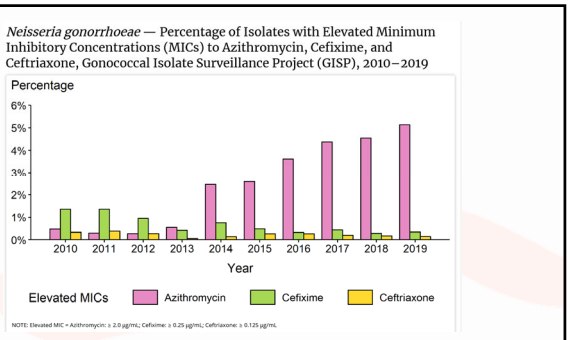

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Drug Resistant Gonorrhoeae

- 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

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https://testdirectory.questdiagnostics.com/test/test-detail/38404/neisseria-gonorrhoeae-culture-with-reflex-to-susceptibility?p=r&q=gonorrhea&cc=TMP
https://www.labcorp.com/tests/008128/gc-i-neisseria-gonorrhoeae-i-culture-only

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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.”

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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

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Ms. M:

- Sexual Health History
  - **P**artners: two male, their sexual health unknown to her
  - **P**ractices: Vaginal receptive sex only
  - **P**revention of STIs: Not consistently using condoms
  - **P**ast history of STIs: None
  - **P**revention of Pregnancy: Nexplanon implant placed last year
- Testing done: self-collected vaginal swab for GC/CL NAAT, syphilis cascade
- NAAT is positive for chlamydia

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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

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Chlamydia & Gonorrhea: Partner Management

- Sexual contacts during the 60 days preceding patient's onset of symptoms or diagnosis of chlamydia should be evaluated, tested and treated
- The most recent sex partner should be evaluated and treated
  - Even if last sexual contact was > 60 days before symptom onset or diagnosis

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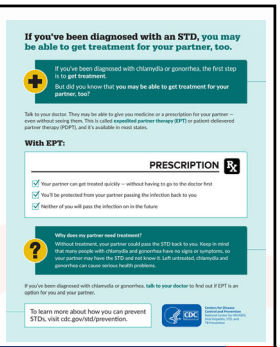
Expedited Partner Therapy (EPT)

- 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



https://www.cdc.gov/std/ept

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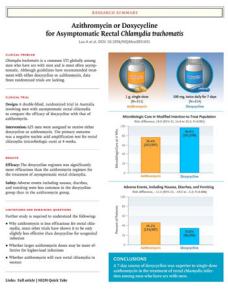
Doxycycline vs. Azithromycin: Rectal Chlamydia in Men

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 %



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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 %

Dukers-Muijrers N, et al. Clin Infect Dis. 2019;69(11):1946-1954.

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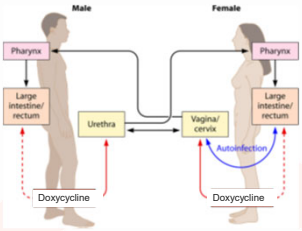
Rectal Chlamydia in Women

- Can occur concomitantly with urogenital chlamydia
- Cannot be predicted by reported sexual activity
- Risk for autoinfection
  - Inadequately treated rectal chlamydia



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

https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf

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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 tract

USF Internal Medicine Grand Rounds, Dr. Katherine HSU, February 3, 2022
https://usfondemand.hosted.panopto.com/Panopto/Pages/Viewer.aspx?id=02d941ee-48d0-41f0-9370-ae3101315f71

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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.

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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

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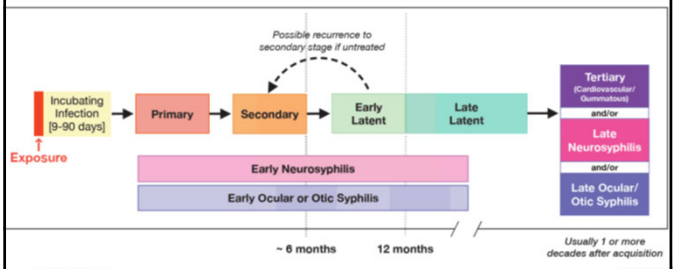
Syphilis Staging:



01_08-20_syphilis_poster_14x8.pdf (targethiv.org)

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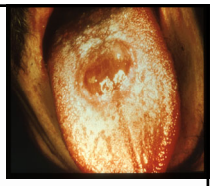
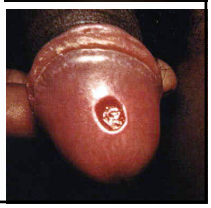
Primary Syphilis

- 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





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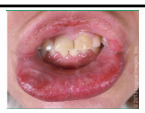
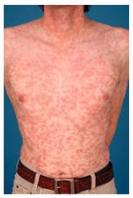
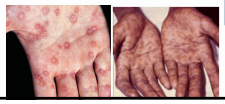
Secondary Syphilis

- 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







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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		
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 ☐ Yes – refer to ophthalmology	☐ No ☐ 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?		
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

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

Public Health
Seattle & King County

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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**

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Hook EW. Lancet 2017; 389: 1550–57.

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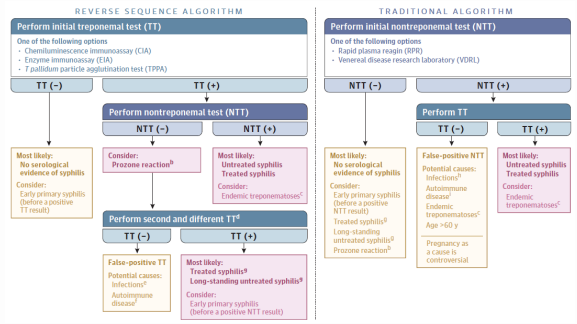

Tuddenham S, Hamill M, Ghanem K. *JAMA*. 2022;327(2):161-172.

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Syphilis Treatment:

	Recommended Rx	Dose/Route	Alternatives
• Primary, secondary, or 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
• Latent >1 year, latent of 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
• Pregnancy	IV Penicillin only option		
• Neurosyphilis	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
• Congenital syphilis	See complete CDC guidelines.		
• Children: Primary, secondary, or early latent <1year	benzathine penicillin G	50,000 units/kg IM in a single dose (maximum 2.4 million units)	
• Children: Latent >1 year, or unknown duration Latent	benzathine penicillin G	50,000 units/kg IM for 3 doses at 1 week intervals (maximum total 7.2 million units)	

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01_08-20_syphilis_poster_14x8.pdf (targethiv.org)

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Syphilis Follow-up

HIV Negative	HIV Positive
▪ 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	▪ 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

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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
1 : 128
1 : 64
1 : 32
1 : 16
1 : 8
1 : 4
1 : 2
1 : 1

2 dilution or "4 fold" decline

1 dilution or "2 fold" decline

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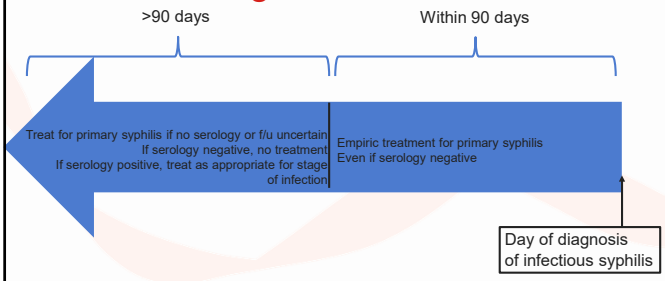
Treating Sexual Partners



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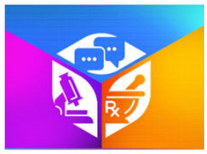
One Last Point…

- 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. Tidsr Nor Laegeforen. 2014;134(17):1661-3.

55



Talk. Test. Treat.
Encourages individuals and health care providers to take 3 simple actions: talk, test, treat

https://www.cdc.gov/std/saw/talktesttreat/providers.htm

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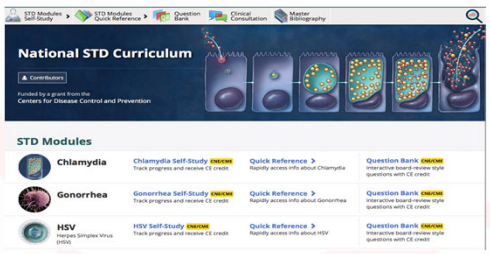

https://www.std.uw.edu

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www.STDCCN.org

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