The 2021 CDC STI Treatment Guidelines: Highlights [02/22/2022]

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Disclosures

- None

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Objectives

At the end of this presentation, attendees should be able to:

- Recognize the latest changes in recommendations for the management of gonococcal infections
- Describe changes in the management of chlamydia infections
- Recall some important clinical manifestations of syphilis and the changes in its epidemiology

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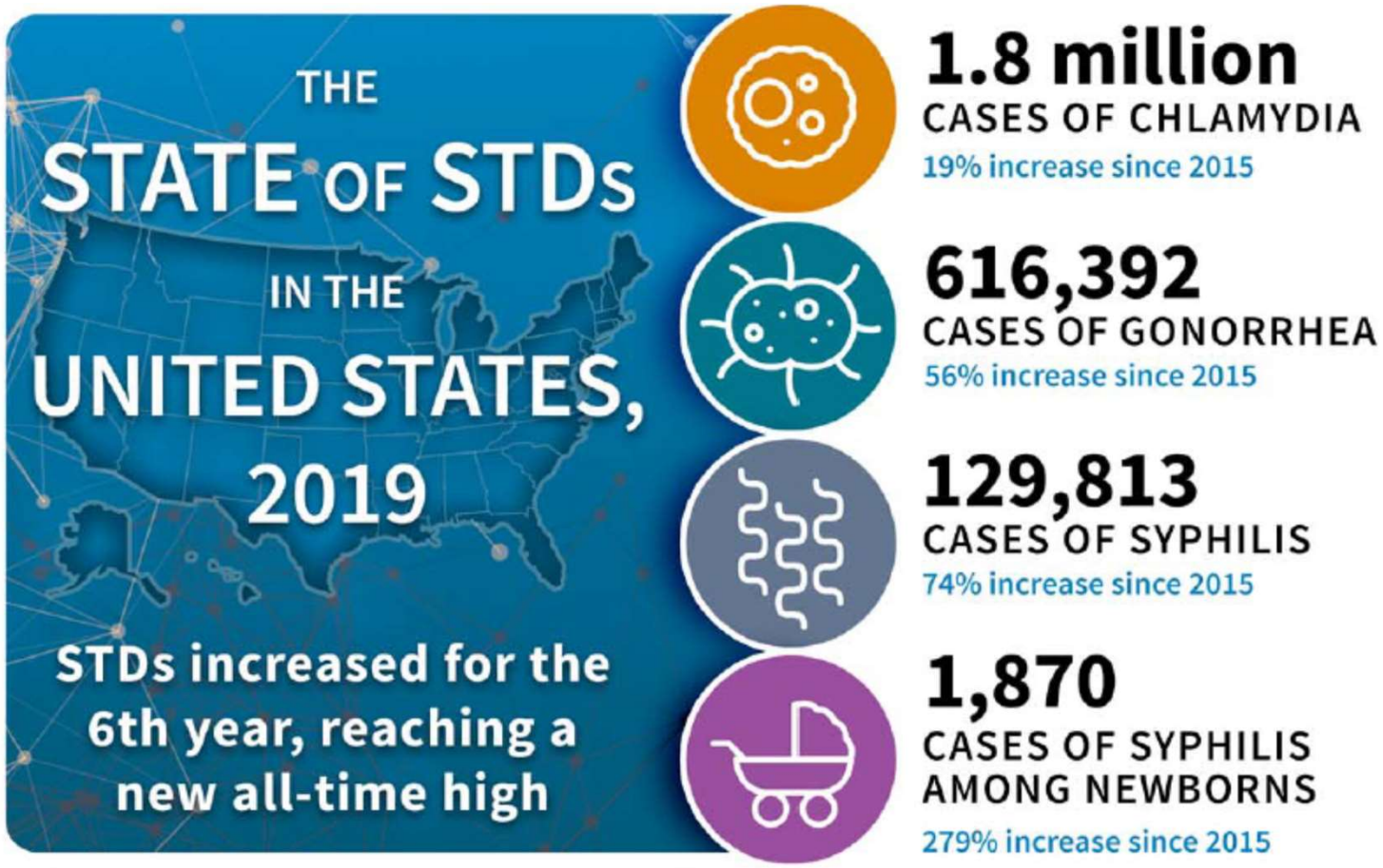

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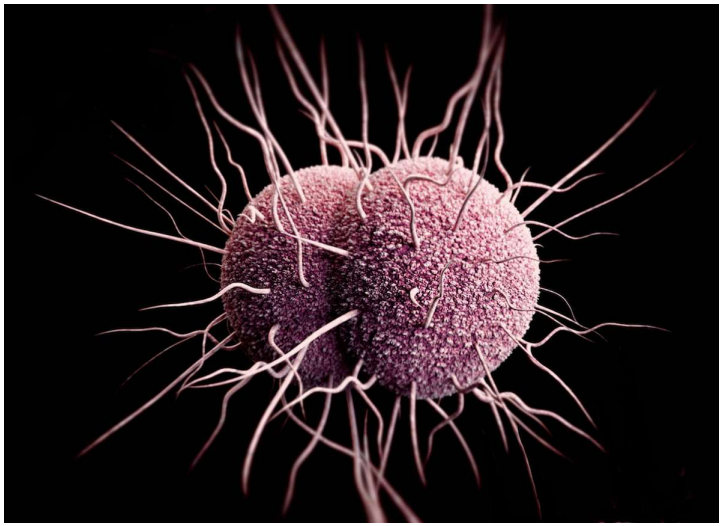
CDC *Sexually Transmitted Disease Surveillance* 2019

Gonorrhea

- Common syndromes
  - Urethritis
  - Cervicitis
  - No symptoms!
    - Don’t miss extragenital infection (rectal, pharynx!)
- Other syndromes to be vigilant for:
  - Pelvic inflammatory disease
  - Epididymitis
  - Proctitis
  - Conjunctivitis
  - Gonococcal arthritis (after dissemination)



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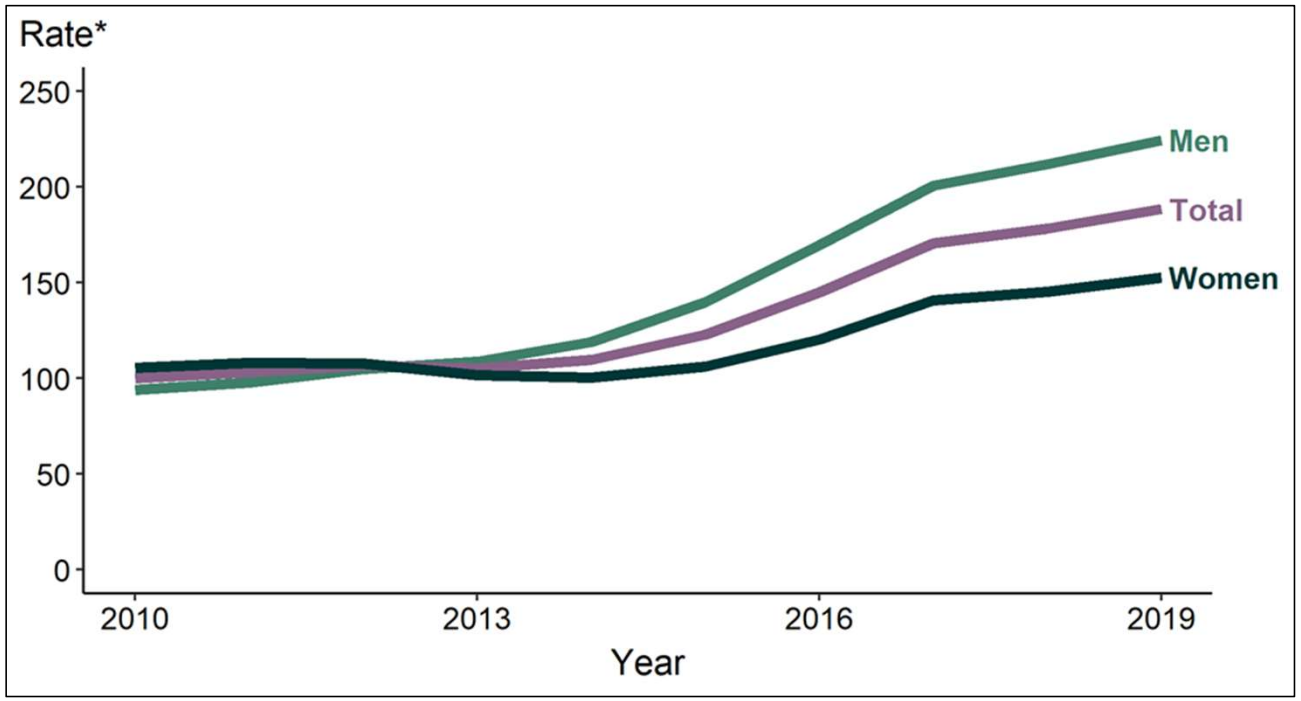
Gonorrhea
616,392 cases;
up 56% from 2015



What are some implications of these STI trends?

As an example, let's look at what's happening with gonorrhea in the US…

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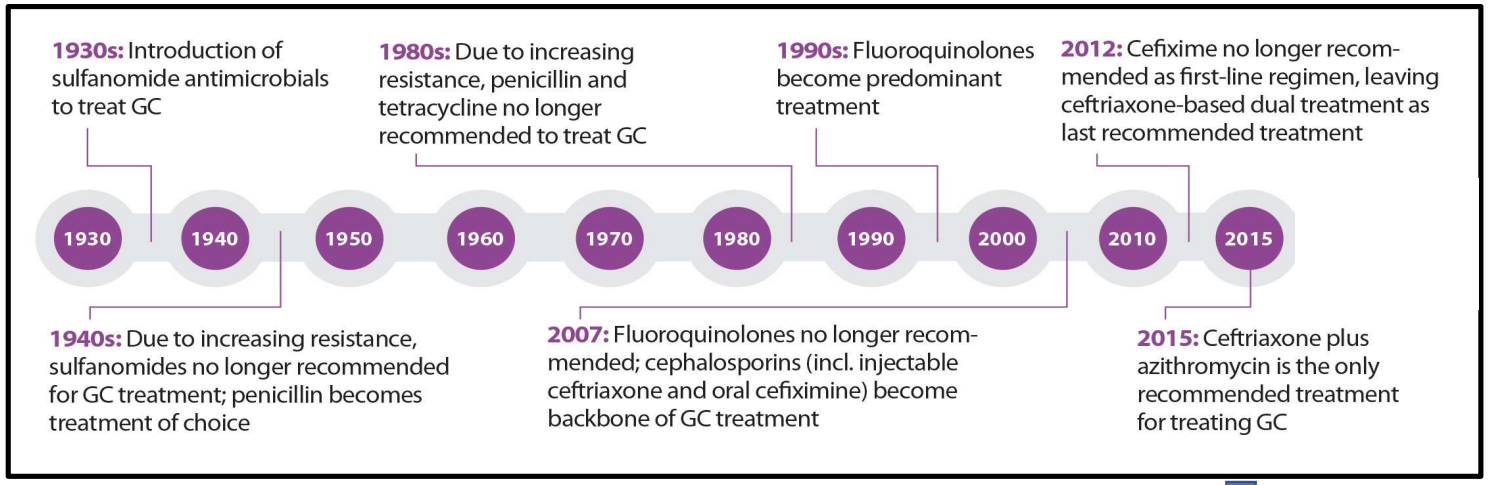
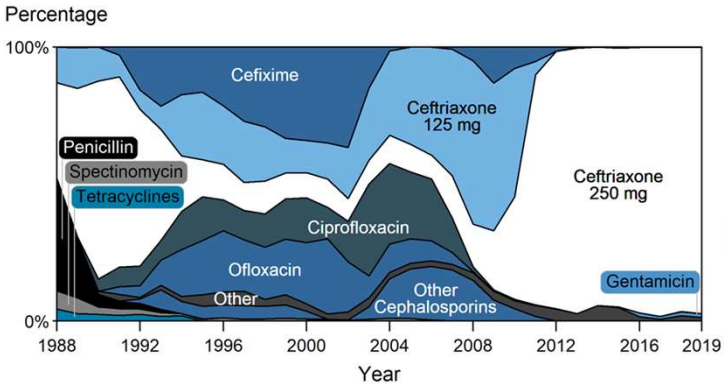
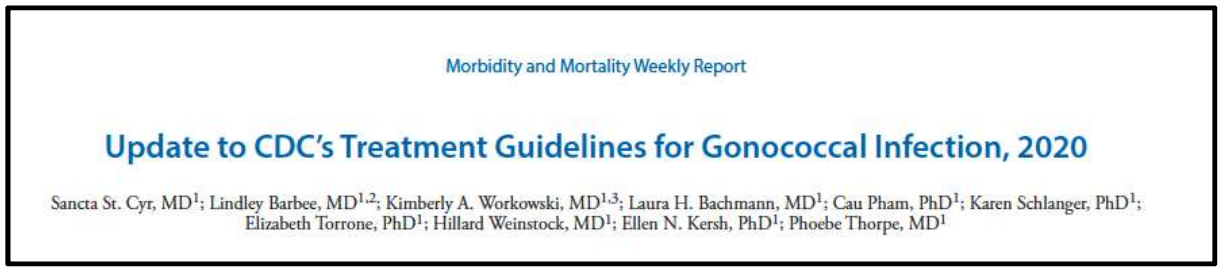
CDC *Sexually Transmitted Disease Surveillance* 2019

Gonorrhea Treatment & Resistance Timeline





CDC *Sexually Transmitted Disease Surveillance* 2019



Therapy for Urogenital and Rectal Gonorrhea Infections 2021

Regimen for uncomplicated gonococcal infections of the cervix, urethra, or rectum:

Ceftriaxone 500 mg IM as a single dose for persons weighing <150 kg (300 lb).

- For persons weighing ≥150 kg (300 lb), 1 g of IM ceftriaxone should be administered.
- If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally twice daily for 7 days. During pregnancy, azithromycin 1 g as a single dose is recommended to treat chlamydia.

Alternative regimens for uncomplicated gonococcal infections of the cervix, urethra, or rectum if ceftriaxone is not available:

Gentamicin 240 mg IM as a single dose plus azithromycin 2 g orally as a single dose OR

Cefixime 800 mg orally as a single dose. If treating with cefixime, and chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally twice daily for 7 days. During pregnancy, azithromycin 1 g as a single dose is recommended to treat chlamydia.

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St Cyr *MMWR* 2020

Why did the CDC change the dual treatment regimen recommendation and why did they increase the dose of ceftriaxone?

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ANTIBIOTIC RESISTANCE THREATS IN THE UNITED STATES

2019

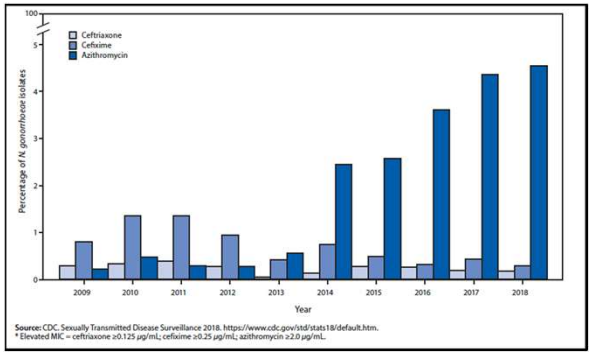
Urgent Threats

- Carbapenem-resistant *Acinetobacter*
- *Candida auris (C. auris)*
- *Clostridioides difficile (C. difficile)*
- Carbapenem-resistant Enterobacteriaceae (CRE)
- Drug-resistant *Neisseria gonorrhoeae (N. gonorrhoeae)*

Commit to Antibiotic Stewardship

Implement practice-level stewardship activities, including documenting antibiotic use data, examining use practices, and serving as an educational resource for clients. Engage veterinary diagnostic labs to provide antibiograms to help determine which antibiotics will effectively treat infections. Become familiar with and use the American Veterinary Medical Association established antibiotic use principles to build an antibiotic stewardship plan for your practice settings.

For the sake of **antimicrobial stewardship**



Source: CDC, Sexually Transmitted Disease Surveillance 2018. https://www.cdc.gov/std/stats18/default.htm.
* Elevated MIC – ceftriaxone ≥0.125 µg/mL; cefixime ≥0.25 µg/mL; azithromycin ≥2.0 µg/mL.

Because of **increasing macrolide resistance**

Antimicrobial Agents and Chemotherapy

PHARMACOLOGY

Pharmacokinetic Data Are Predictive of *In Vivo* Efficacy for Cefixime and Ceftriaxone against Susceptible and Resistant *Neisseria gonorrhoeae* Strains in the Gonorrhea Mouse Model

Kristie L. Connolly,[a] Ann E. Eakin,[b] Carolina Gomez,[a] Blaire L. Osborn,[b] Magnus Unemo,[c] Ann E. Jerse[a]

To **optimize ceftriaxone dosing**: In a murine model, the lowest ceftriaxone dose that was 100% effective at eradicating the susceptible organism 48 hours after treatment was 5 mg/kg body weight. Translating into human doses, a 500-mg dose corresponds to 5 mg/kg body weight, whereas 250 mg only corresponds to 3 mg/kg body weight for an average person

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Therapy for Pharyngeal Gonorrhea 2020

Recommended regimen for uncomplicated gonococcal infections of the pharynx:

Ceftriaxone 500 mg IM as a single dose for persons weighing <150 kg (300 lb).

- For persons weighing ≥150 kg (300 lb), 1 g of IM ceftriaxone should be administered.
- If chlamydia coinfection is identified when pharyngeal gonorrhea testing is performed, providers should treat for chlamydia with doxycycline 100 mg orally twice a day for 7 days. During pregnancy, azithromycin 1 g as a single dose is recommended to treat chlamydia.
- No reliable alternative treatments are available for pharyngeal gonorrhea. For persons with a history of a beta-lactam allergy, a thorough assessment of the reaction is recommended.*
- 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.

St Cyr *MMWR* 2020

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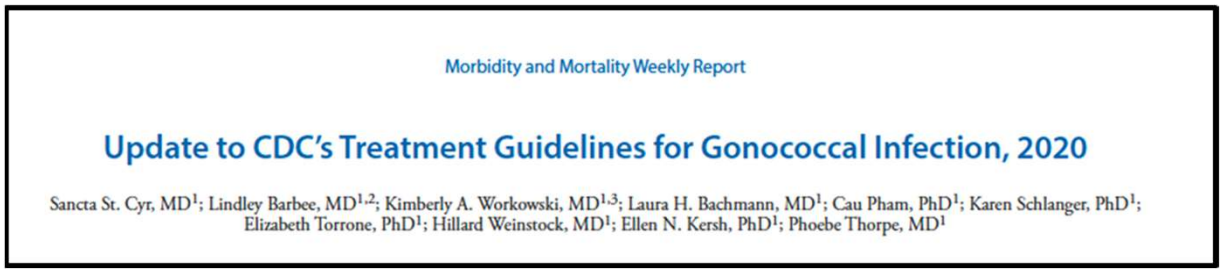

Morbidity and Mortality Weekly Report

Update to CDC's Treatment Guidelines for Gonococcal Infection, 2020

Sancta St. Cyr, MD[1]; Lindley Barbee, MD[1,2]; Kimberly A. Workowski, MD[1,3]; Laura H. Bachmann, MD[1]; Cau Pham, PhD[1]; Karen Schlanger, PhD[1]; Elizabeth Torrone, PhD[1]; Hillard Weinstock, MD[1]; Ellen N. Kersh, PhD[1]; Phoebe Thorpe, MD[1]

- For persons with pharyngeal gonorrhea, a **test-of-cure** is recommended, using culture or nucleic acid amplification tests 7–14 days after initial treatment, regardless of the treatment regimen
- **For EPT**: the partner may be treated with a single 800 mg oral dose of cefixime, provided that concurrent chlamydial infection in the patient has been excluded. Otherwise, the partner may be treated with a single oral 800 mg cefixime dose plus oral doxycycline 100 mg twice daily for 7 days
- Persons should be **retested 3 months after treatment** regardless of whether they believe their sex partners were treated.

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Why does the CDC only recommend ceftriaxone for pharyngeal gonorrhea infections and why recommend the test of cure for all pharyngeal infections?

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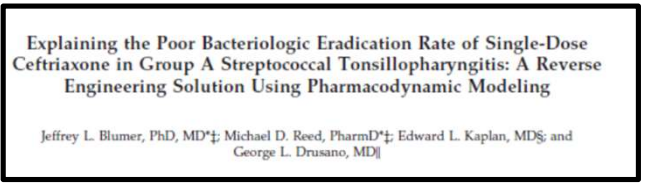


Explaining the Poor Bacteriologic Eradication Rate of Single-Dose Ceftriaxone in Group A Streptococcal Tonsillopharyngitis: A Reverse Engineering Solution Using Pharmacodynamic Modeling

Jeffrey L. Blumer, PhD, MD*‡; Michael D. Reed, PharmD*‡; Edward L. Kaplan, MD§; and George L. Drusano, MD‖

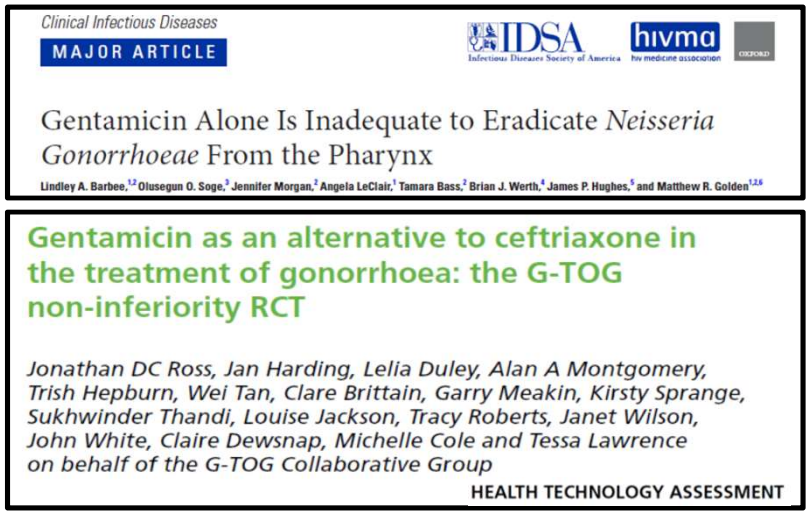
- Ceftriaxone concentrations tend to be more variable in the pharynx
- Treatment of gonorrhea likely requires longer times above the strain's MIC
- Continued uncertainty regarding ceftriaxone PK/PD

ORIGINAL STUDY

A Phase 1 Pharmacokinetic and Safety Study of Extended-Duration, High-dose Cefixime for Cephalosporin-resistant *Neisseria gonorrhoeae* in the Pharynx

Lindley A. Barbee, MD, MPH,† Seema U. Nayak, MD,‡ Jeffrey L. Blumer, MD, MPH,§ Mary Ann O'Riordan,¶ Wesley Gray, MSc,§ Jonathan M. Zenilman, MD,‡ Matthew R. Golden, MD, MPH,*† and J. McLeod Griffiss, MD‖*

- Absence of cefixime in oropharyngeal fluid after the 400-, 800-, and 800-mg doses every 8 hours;
- While the 800-mg single dose regimen would effectively treat anogenital infections, only the 800 mg every 8 hours for 3 doses <u>may</u> cure pharyngeal infection if the MIC is 0.5 µg/mL or less



Clinical Infectious Diseases

MAJOR ARTICLE

Gentamicin Alone Is Inadequate to Eradicate *Neisseria Gonorrhoeae* From the Pharynx

Lindley A. Barbee,[1,2] Olusegun O. Soge,[3] Jennifer Morgan,[2] Angela LeClair,[1] Tamara Bass,[2] Brian J. Werth,[4] James P. Hughes,[5] and Matthew R. Golden[1,2,6]

Gentamicin as an alternative to ceftriaxone in the treatment of gonorrhoea: the G-TOG non-inferiority RCT

Jonathan DC Ross, Jan Harding, Lelia Duley, Alan A Montgomery, Trish Hepburn, Wei Tan, Clare Brittain, Garry Meakin, Kirsty Sprange, Sukhwinder Thandi, Louise Jackson, Tracy Roberts, Janet Wilson, John White, Claire Dewsnap, Michelle Cole and Tessa Lawrence on behalf of the G-TOG Collaborative Group

HEALTH TECHNOLOGY ASSESSMENT

- While effective for anogenital infections, gentamicin does <u>not</u> effectively eradicate pharyngeal gonorrhea infections

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What's to be done if a patient reports an allergy to penicillin?

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STOP!

DON'T ABANDON CEFTRIAXONE JUST YET

GET MORE INFORMATION ABOUT THE NATURE OF THE PATIENT'S PENICILLIN ALLERGY

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The Nature of the Penicillin Allergy

- Is the presentation consistent with drug hypersensitivity?
- If so, is this an immune-mediated reaction?
  - Is it immediate in onset (likely to be IgE-mediated)?
    - Urticarial rash; pruritus; flushing; angioedema of the face, extremities, or laryngeal tissues (leading to throat tightness with stridor, or rarely asphyxiation); wheezing; gastrointestinal symptoms; and/or hypotension
    - Keep in mind: ~80 percent of patients with IgE-mediated penicillin allergy have lost the sensitivity after 10 years
  - Is it delayed in onset (most often a T-cell-mediated reaction)
    - Contact dermatitis, maculopapular eruptions; SJS; DRESS; drug fevers

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Pichler W. UptoDate: Drug hypersensitivity: Classification and clinical features

Cross-reactivity and tolerability of aztreonam and cephalosporins in subjects with a T cell–mediated hypersensitivity to penicillins

Antonino Romano, MD,[a,b] Francesco Gaeta, MD,[a] Rocco Luigi Valluzzi, MD,[a] Michela Maggioletti, MD,[a] Cristiano Caruso, MD,[a] and Donato Quaratino, MD[c] *Rome, Troina, and Capranica, Italy*

Conclusions: These data demonstrate a rate of cross-reactivity between aminopenicillins and aminocephalosporins (ie, cephalexin, cefaclor, and cefadroxil) of around 20%, as well as the absence of cross-reactivity between penicillins and cefuroxime, ceftriaxone, and aztreonam in all subjects with T cell–mediated hypersensitivity to penicillins, almost exclusively aminopenicillins. Therefore these subjects could be

Original Article

Cross-Reactivity and Tolerability of Cephalosporins in Patients with IgE-Mediated Hypersensitivity to Penicillins

Antonino Romano, MD[a,b], Rocco Luigi Valluzzi, MD[a,c], Cristiano Caruso, MD[a], Michela Maggioletti, MD[a], Donato Quaratino, MD[d], and Francesco Gaeta, MD, PhD[a] *Rome, Troina, and Capranica, Italy*

CONCLUSIONS: Cross-reactivity between penicillins and cephalosporins seems to be mainly related to side chain similarity or identity. Subjects with an IgE-mediated hypersensitivity to penicillins could be treated with cephalosporins such as cefuroxime and ceftriaxone that have side-chain determinants different from those of penicillins and are negative in pretreatment skin testing. (J Allergy Clin Immunol Pract 2018;6:1662-72)

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Gonorrhea: Take-Home Points

- The treatment of uncomplicated gonorrhea is now **500 mg of intramuscular ceftriaxone**; if chlamydia is present or is not ruled out, add one week of 100 mg of oral doxycycline taken twice daily
  - Alternate regimens for **urogenital or rectal infections** include oral cefixime 800 mg; intramuscular gentamicin 5mg/kg plus 2 g oral azithromycin
- Patients with pharyngeal gonorrhea should be treated with ceftriaxone- **no alternate regimens are recommended**; a test-of-cure should be performed one to two weeks later
- A reported history of penicillin allergy should prompt clinicians to obtain more information about the nature of that allergy; a majority of these patients may be safely treated with ceftriaxone
- Re-screen all persons diagnosed with gonorrhea in 3 months
- Treat all sex partners in the preceding 60 days of index patients diagnosed with gonorrhea

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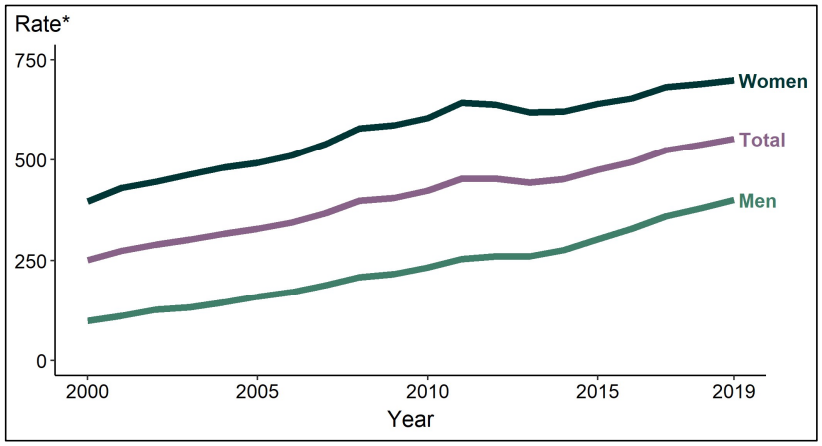
Chlamydia

- Common syndromes
  - Urethritis
  - Cervicitis
    - Vaginal discharge, dysuria
  - No symptoms!
- Other syndromes to be vigilant for:
  - Pelvic inflammatory disease
  - Epididymitis
  - Proctitis
  - Conjunctivitis
  - Reactive arthritis

Chlamydia trachomatis



- During 2018–2019, rates of reported chlamydia increased among both males and females, in all regions of the United States, and among all racial/Hispanic ethnicity groups.
- In 2019, almost two-thirds (61.0%) of all reported chlamydia cases were among persons aged 15–24 years.
- Although rates of reported cases among men are generally lower than rates among women, reflecting the larger number of women screened for this infection, rates among men increased 32.1% during 2015–2019

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CDC *Sexually Transmitted Disease Surveillance* 2019

Chlamydia Treatment Take-home Points

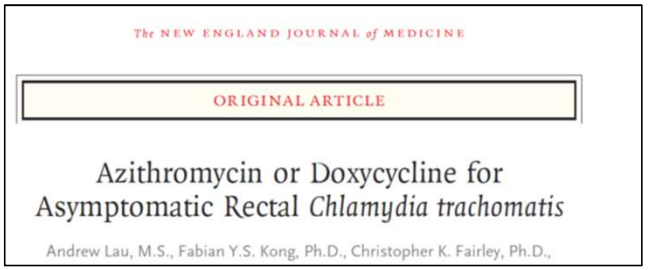
- Doxycycline 100mg orally twice daily will be the **preferred option** to treat *Chlamydia trachomatis* infections
  - Azithromycin 1g orally is a second-line regimen
- Azithromycin was 3% less effective when treating urogenital infections compared with doxycycline NEJM 2015; 373;26:2513-2521
- **Two recent RCTs demonstrated that azithromycin was 20% less effective when treating rectal chlamydia infections compared with doxycycline**

Clinical Infectious Diseases

Doxycycline Versus Azithromycin for the Treatment of Rectal Chlamydia in Men Who Have Sex With Men: A Randomized Controlled Trial

Julia C. Dombrowski,[1,2] Michael R. Wierzbicki,[3] Lori M. Newman,[4] Jonathan A. Powell,[3] Ashley Miller,[5] Dwyn Dithmer,[2] Olusegun O. Soge,[6] and Kenneth H. Mayer[7,8]

- Microbiologic cure was higher with doxycycline than azithromycin (91% [80 of 88] vs 71% [63 of 89]; absolute difference, 20%; 95% CI, 9–31%; P < .001)
- The mechanism of azithromycin treatment failure in rectal CT is not known but is **not** likely due to antibiotic resistance, inadequate tissue penetration of the drug, or the prevalence of LGV biovars.



The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

Azithromycin or Doxycycline for Asymptomatic Rectal *Chlamydia trachomatis*

Andrew Lau, M.S., Fabian Y.S. Kong, Ph.D., Christopher K. Fairley, Ph.D.,

- Microbiologic cure occurred in 281 of 290 men (96.9%; 95% CI: 94.9 to 98.9) in the doxycycline group and in 227 of 297 (76.4%; 95% CI, 73.8 to 79.1) in the azithromycin group, for an adjusted risk difference of 19.9 percentage points (95%CI, 14.6 to 25.3; P<0.001)

Chlamydia Proctitis Take-Home Points

- There are currently no commercial tests that distinguish between LGV (lymphogranuloma venereum) and non-LGV strains of *Chlamydia trachomatis*
- The treatment duration for chlamydia **proctitis** depends on symptoms:
  - **Asymptomatic and mildly symptomatic** persons should be treated with **one week** of doxycycline
  - **Moderately to severely symptomatic persons** should be treated with **3 weeks** of doxycycline

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Take-Home Points: Managing Urethritis

- **When there is clinical concern:**
  - test for both gonorrhea and chlamydia
  - treat for both empirically with ceftriaxone and doxycycline [if you are able to do a Gram's stain, or have access to another POC diagnostic, and it does not show evidence of gonorrhea, just treat for chlamydia with doxycycline]
- If the patient has persistent symptoms:
  - **Confirm objective signs of** urethritis (≥2 WBCs/HPF in high-prevalence settings [STI clinics] or ≥5 WBCs/HPF in lower-prevalence settings OR positive leukocyte esterase test on first-void urine OR microscopic examination of sediment from a spun first-void urine demonstrating ≥10 WBCs/HPF):
  - Test MSW for both trichomonas and *M genitalium*
  - Test MSM for *M genitalium*
- Treat the patient with persistent symptoms based on testing results

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Mycoplasma genitalium: Testing and Treatment

- NAATs now FDA-cleared
- Test men with persistent urethritis and women with persistent cervicitis
- CONSIDER testing women with PID (don't do it)
- Do NOT routinely test extragenital sites
- Do NOT screen asymptomatic men or women
- Partners: If you can test partners, treat those who are positive; if you cannot, consider treating the partner with the same regimen used to treat the patient

Two-stage therapy approaches, (ideally using resistance-guided therapy) are recommended for treatment:

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 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 Regimen if *M. genitalium* Resistance Testing Is Not Available
If *M. genitalium* is detected by an FDA-cleared NAAT: Doxycycline 100 mg orally 2 times/day for 7 days, followed by **moxifloxacin** 400 mg orally once daily for 7 days

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Pelvic Inflammatory Disease Take-Home Points

- Test all women for gonorrhea and chlamydia. The value of testing women with PID for *M. genitalium* is unknown
- The risk for PID associated with IUD use is primarily confined to the first 3 weeks after insertion. If an IUD user receives a diagnosis of PID, the IUD does not need to be removed
- **2021: All outpatient regimens now include metronidazole (no longer optional)**

All outpatient regimens to treat PID are cephalosporin-based

Recommended Intramuscular or Oral Regimens for Pelvic Inflammatory Disease

Ceftriaxone 500 mg IM in a single dose*

PLUS

Doxycycline 100 mg orally 2 times/day for 14 days

WITH

Metronidazole 500 mg orally 2 times/day for 14 days

OR

Cefoxitin 2 gm IM in a single dose and Probenecid 1 gm orally administered concurrently in a single dose

PLUS

Doxycycline 100 mg orally 2 times/day for 14 days

WITH

Metronidazole 500 mg orally 2 times/day for 14 days

OR

Other parenteral third-generation **cephalosporin** (e.g., ceftizoxime or cefotaxime)

PLUS

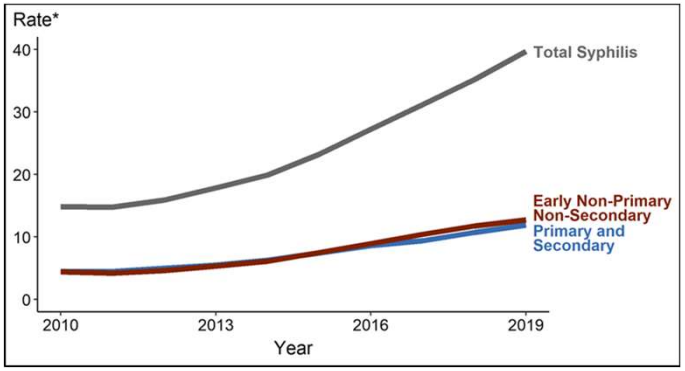
Doxycycline 100 mg orally 2 times/day for 14 days

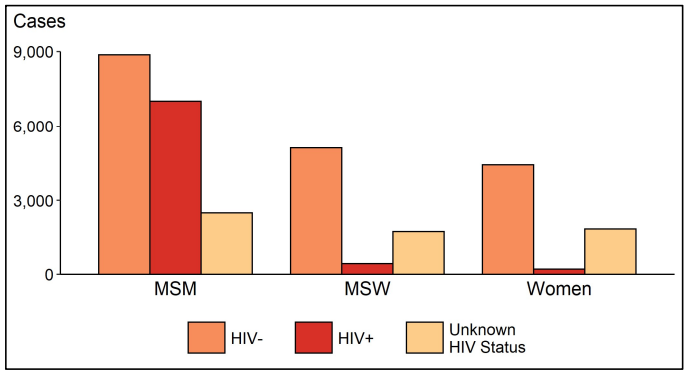
WITH

Metronidazole 500 mg orally 2 times/day for 14 days

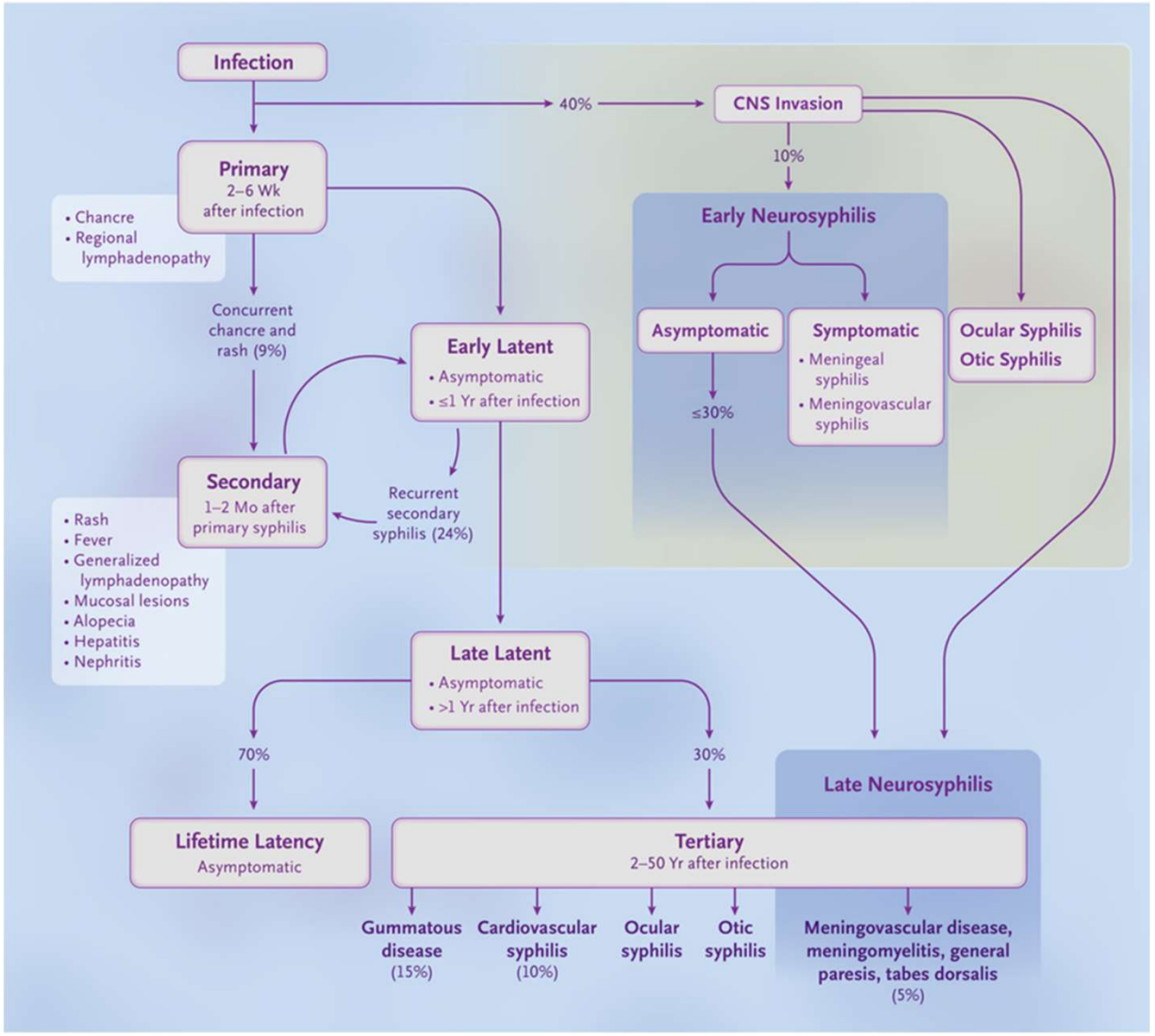
*For persons weighing >150 kg (~300 lbs.) with documented gonococcal infection, 1 gm of ceftriaxone should be administered.

Syphilis

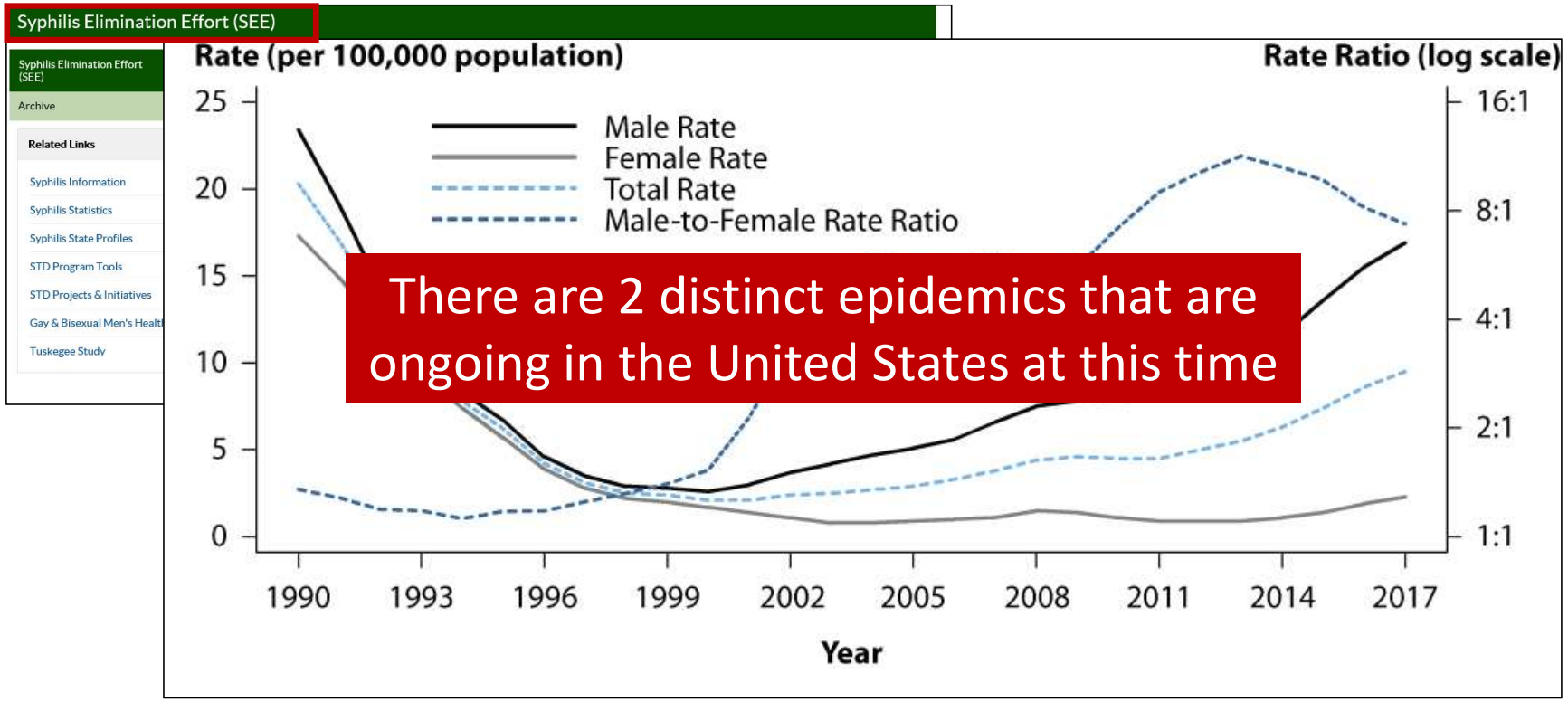




CDC *Sexually Transmitted Disease Surveillance* 2019
Ghanem NEJM 2020



Where we are now…



There are 2 distinct epidemics that are ongoing in the United States at this time

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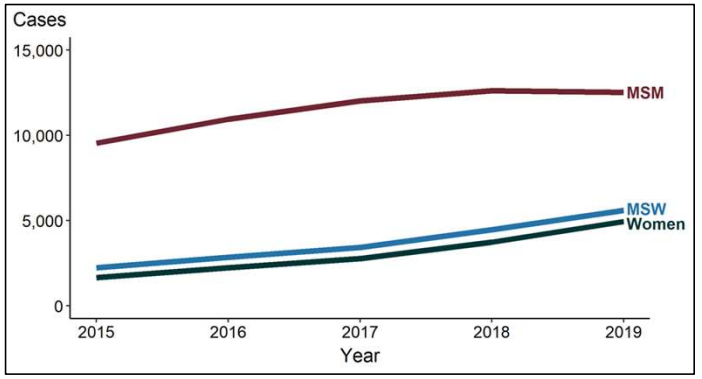
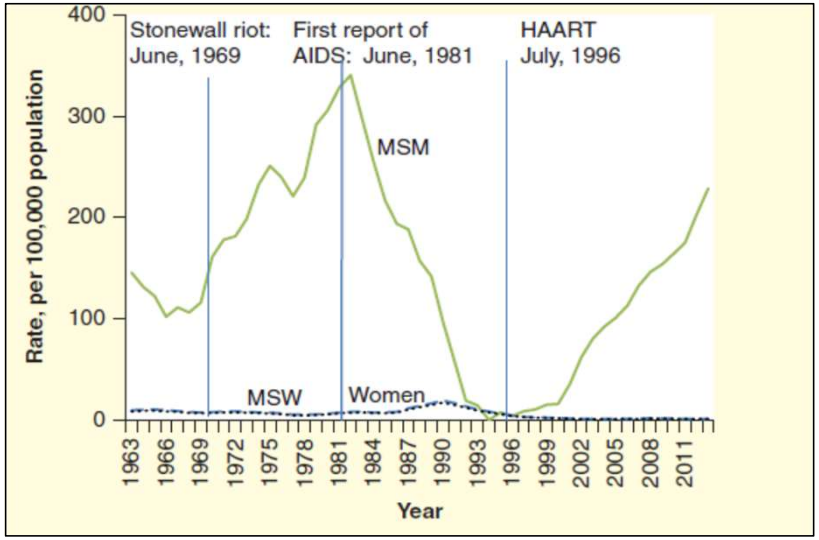
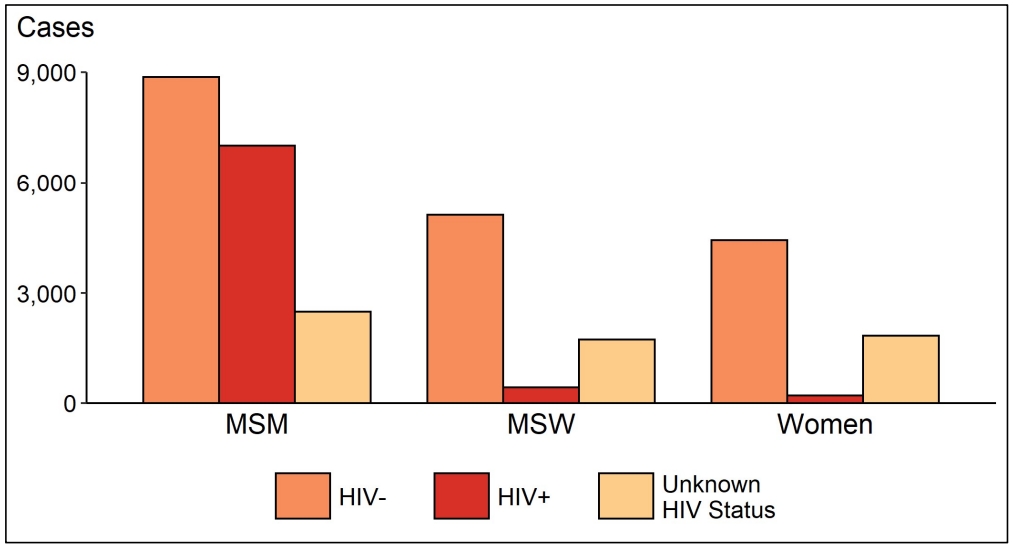
CDC. Sexually Transmitted Disease Surveillance 2017. Atlanta: U.S. Department of Health and Human Services; 2018

Syphilis: Men who have sex with men



- Increasing rates since 2001
  - >75% increase since 2013
  - **42% are HIV-infected**
  - **Nearly 30% are re-infected 3-6 months after treatment**



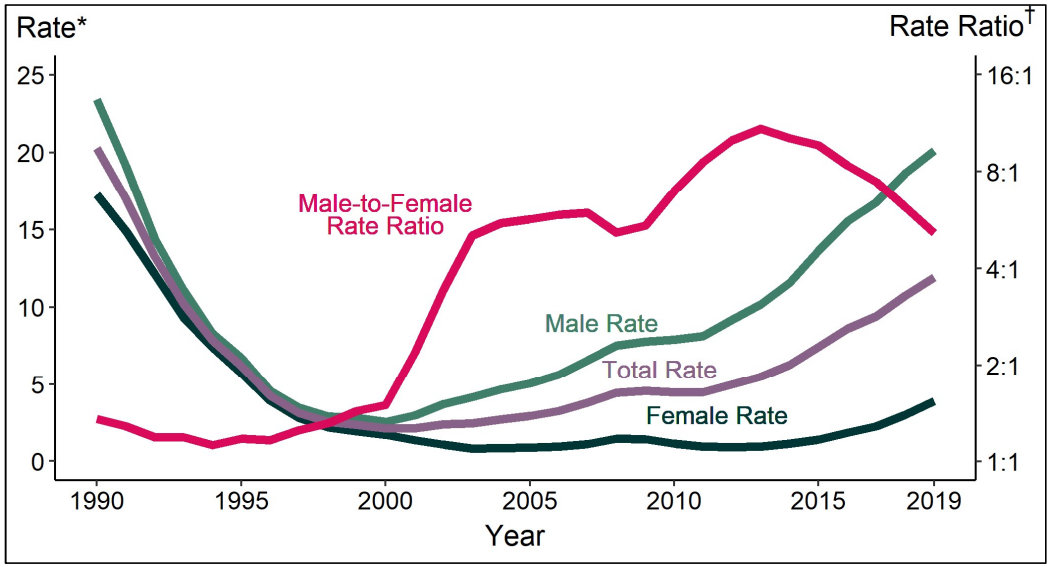


CDC. Sexually Transmitted Disease Surveillance 2019. Atlanta: U.S. Department of Health and Human Services; 2021

Expert Rev Anti Infect Ther 2015; 13(2):161–168

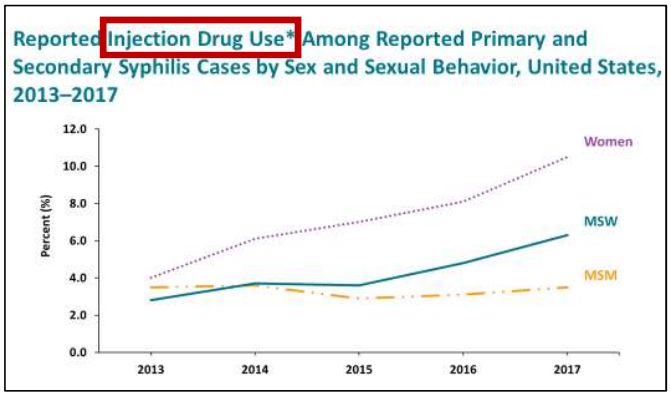
Syphilis: The heterosexual epidemic

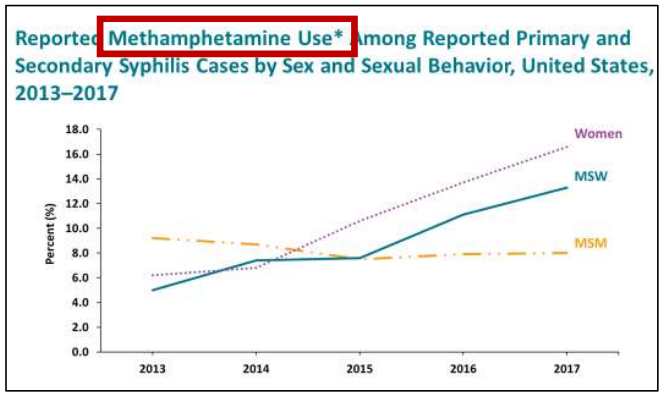
- During 2015–2019, the primary & secondary syphilis rate among women more than doubled (179% increase).
- During 2018–2019, the primary & secondary syphilis rate among women increased 30%.

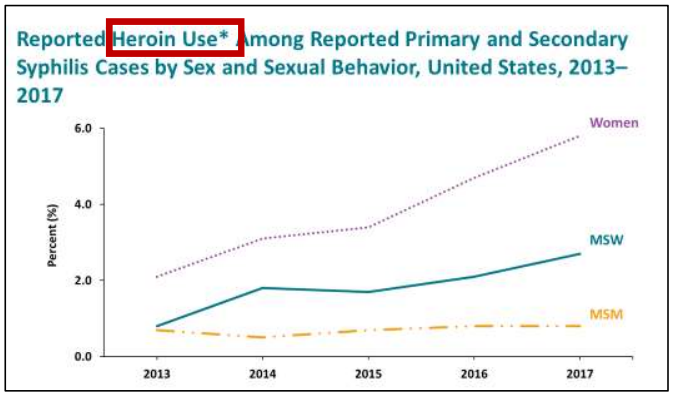


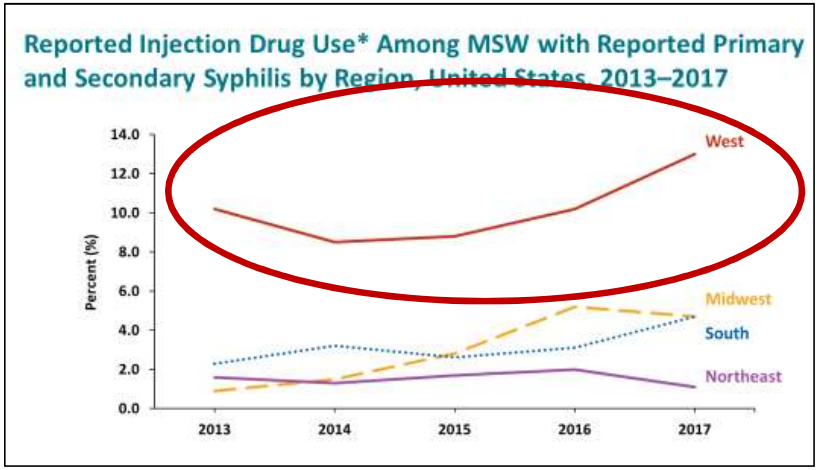
CDC. Sexually Transmitted Disease Surveillance 2019. Atlanta: U.S. Department of Health and Human Services; 2021

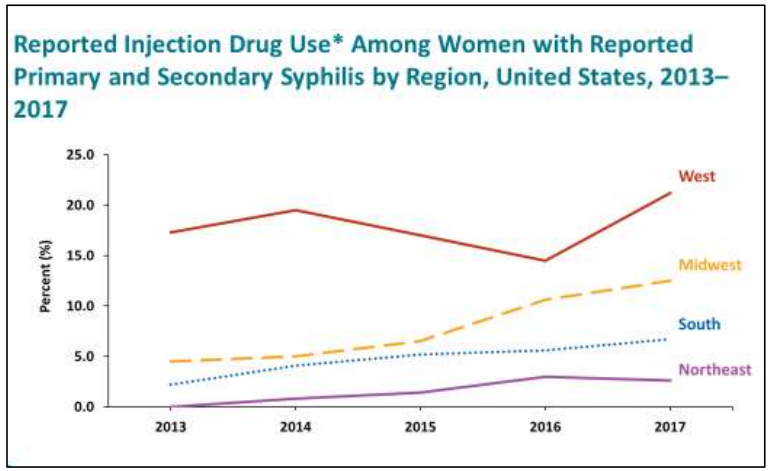
The intersection of epidemics: Drug use and heterosexual syphilis transmission



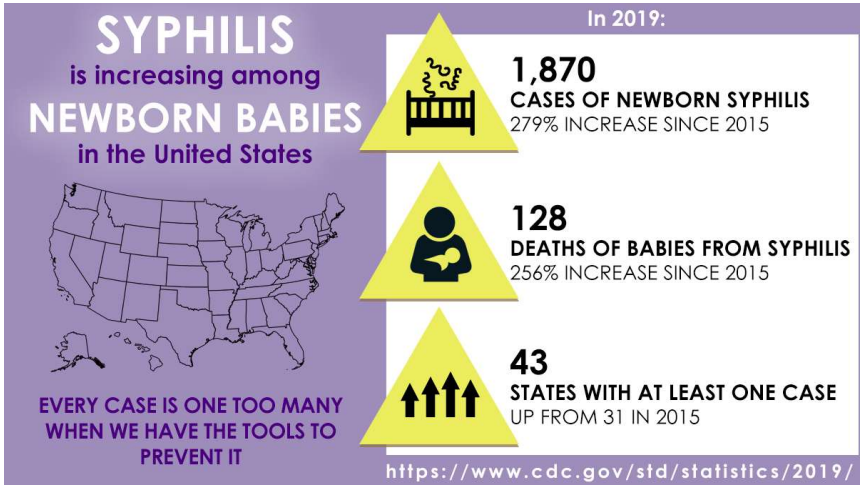


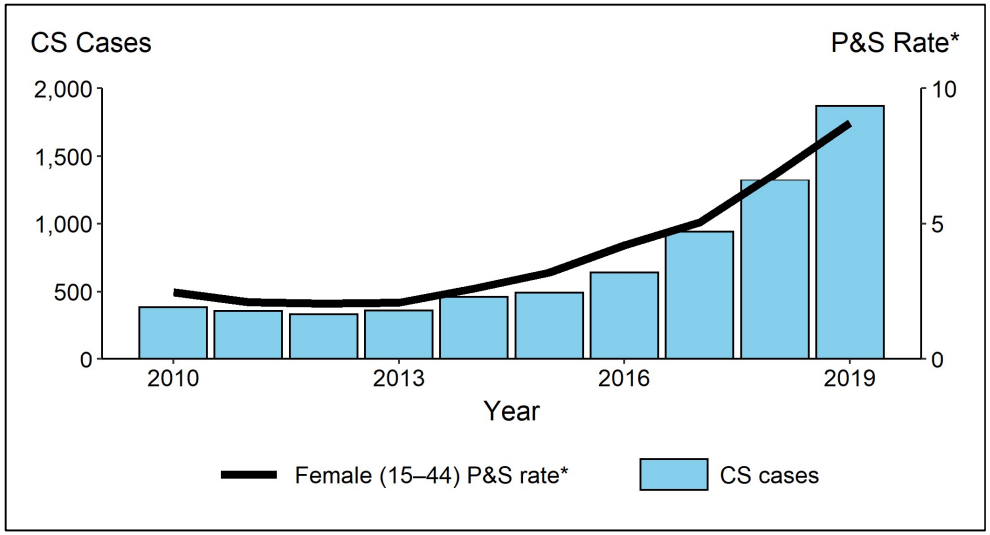


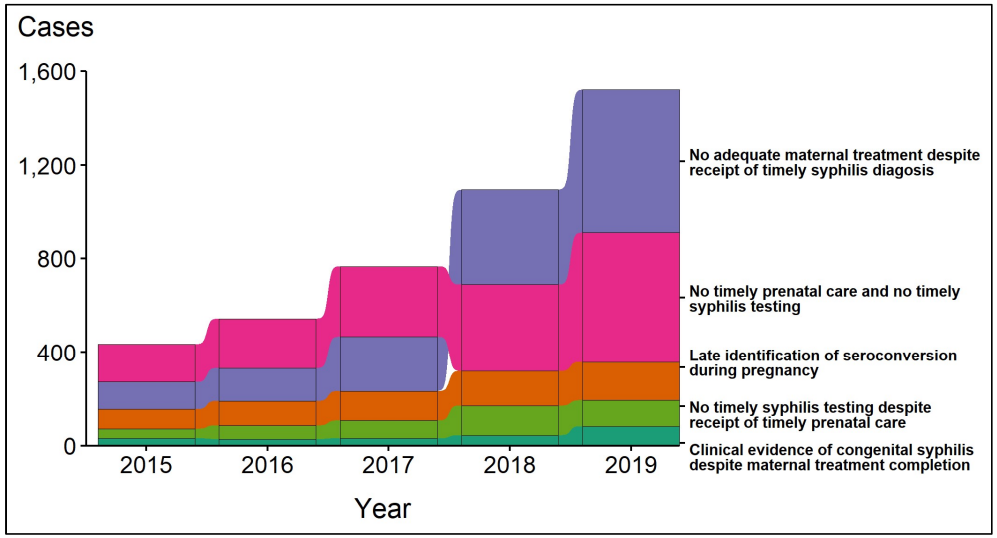




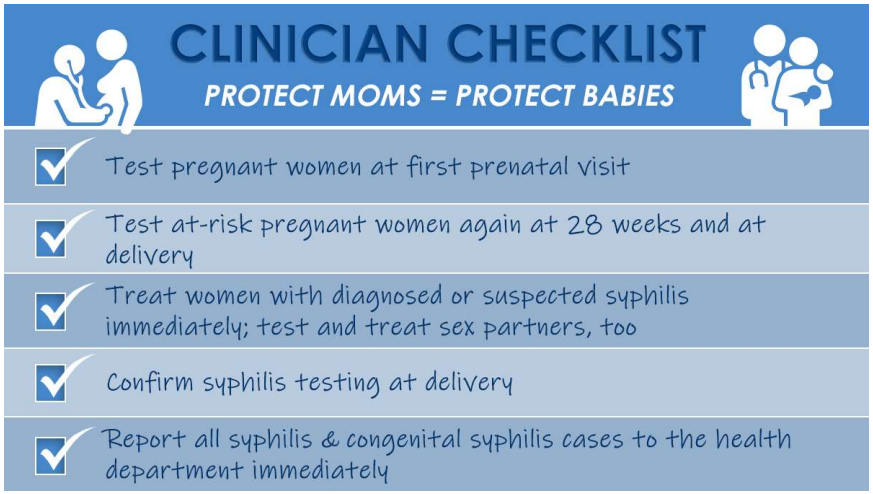
CDC. Sexually Transmitted Disease Surveillance 2017. Atlanta: U.S. Department of Health and Human Services; 2018







CDC *Sexually Transmitted Disease Surveillance* 2019



Symptoms of syphilis

- Any and all!
- Absolutely none……

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Syphilis: Transmission

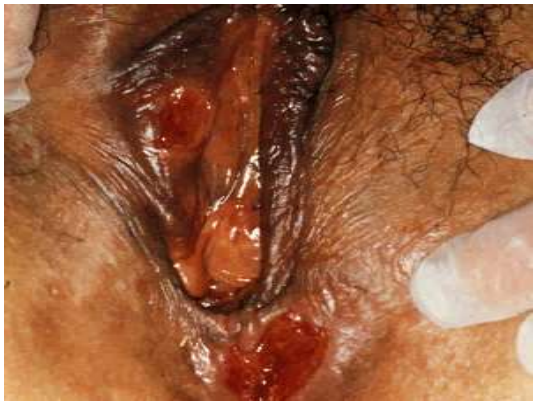
- Major routes:
  - Mucous membranes & skin
  - in utero from infected pregnant women to her fetus (vertical)
- Risk of infection after 1 exposure: 40%
- Index patient is most contagious to sexual partners during primary and secondary stage, less so in early latent stage

Syphilis: Pathogenesis

- Eventually, the host suppresses the secondary infection enough so that no lesions are clinically apparent
- This is latency; 60-85% of patients remain asymptomatic
- Some progress to tertiary stage in 1-20 years
- Immunity is present with chronic infection but lost after treatment

Primary syphilis

- Chancre: appears 2-3 wks after exposure (range 3-90 days)
  - local lesion at site of inoculation
  - typically painless, indurated, clean base
  - 25% have multiple lesions
  - Regional adenopathy: classically rubbery, painless, bilateral
  - Resolves without scar within 3-8 weeks



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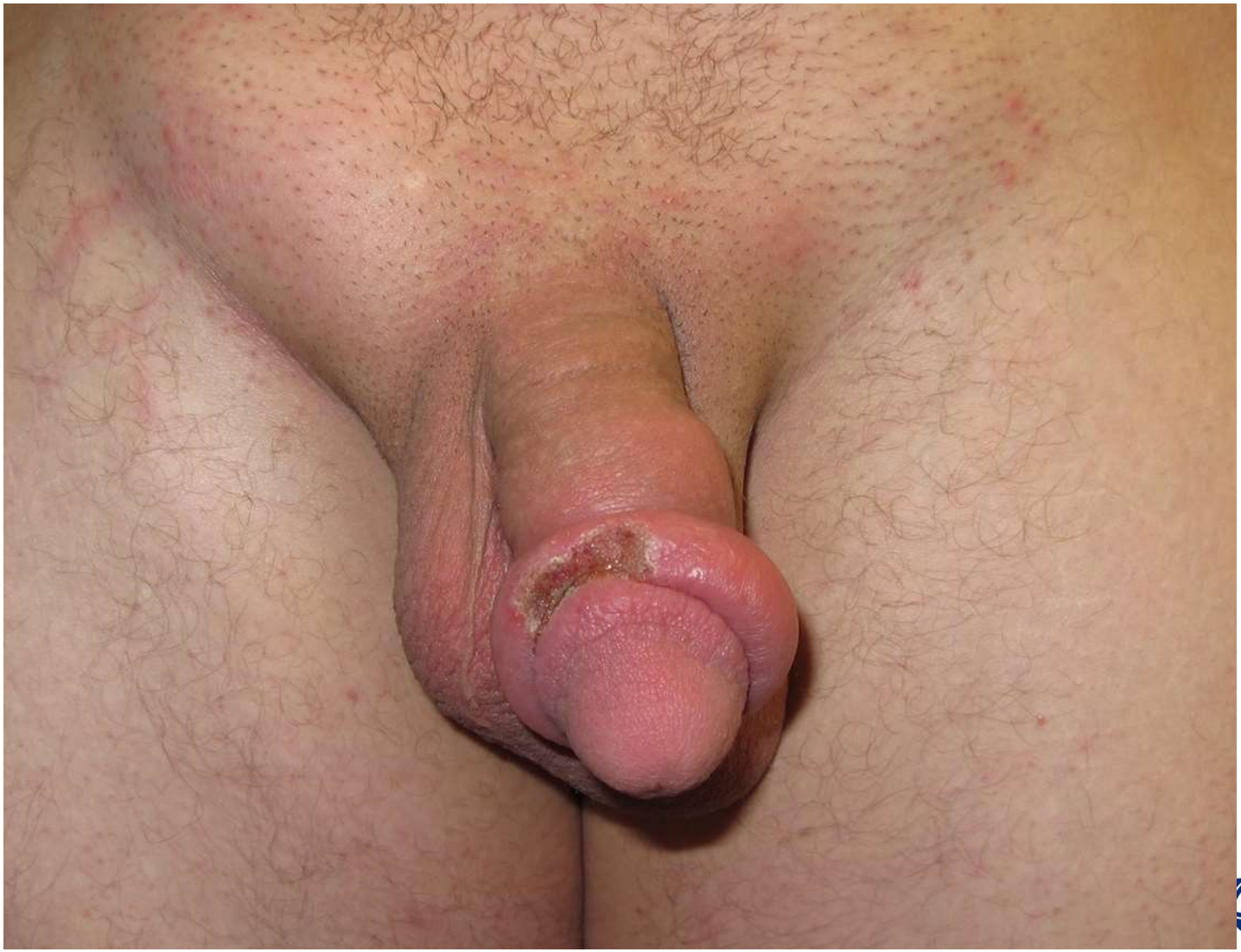

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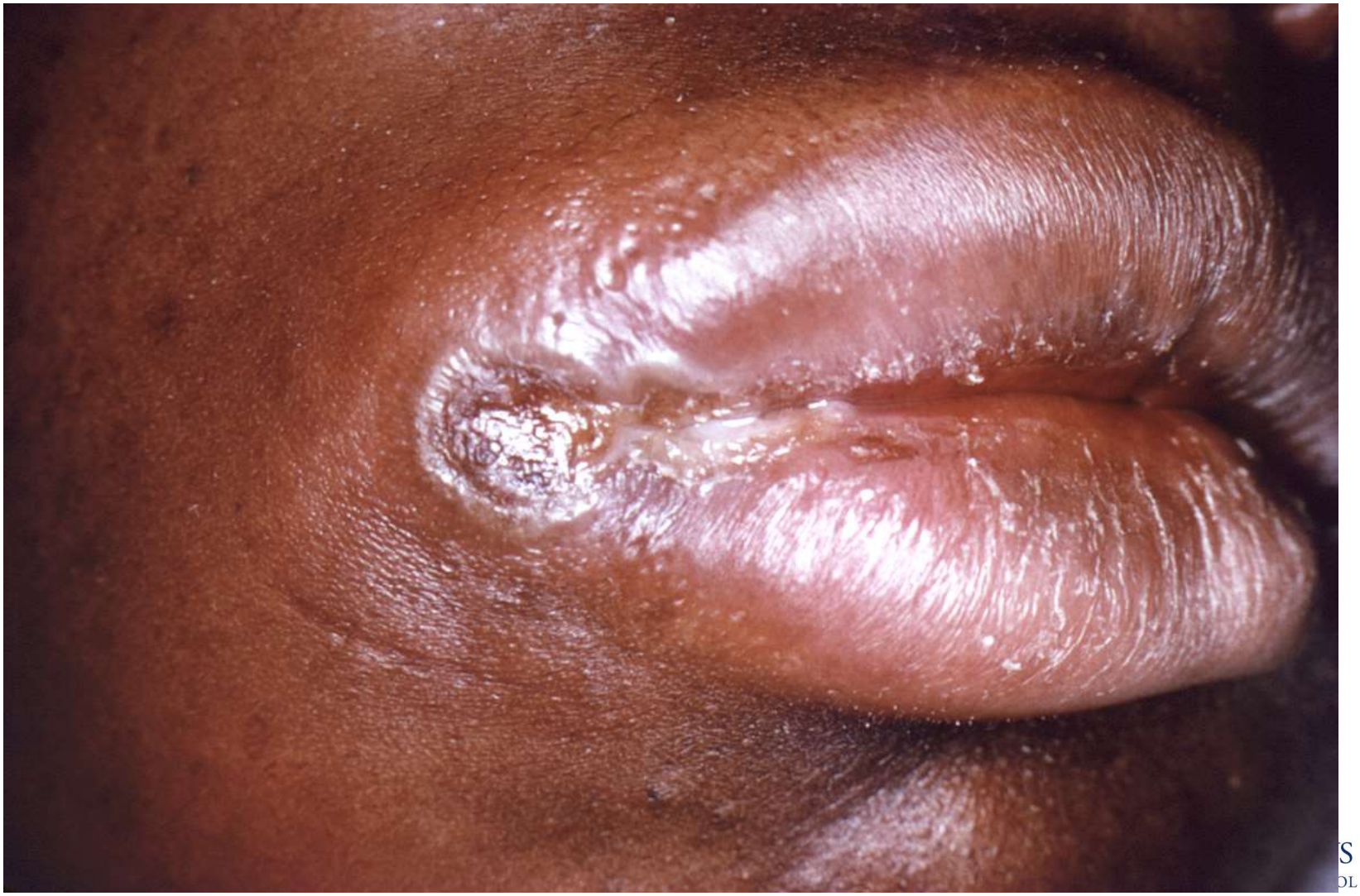
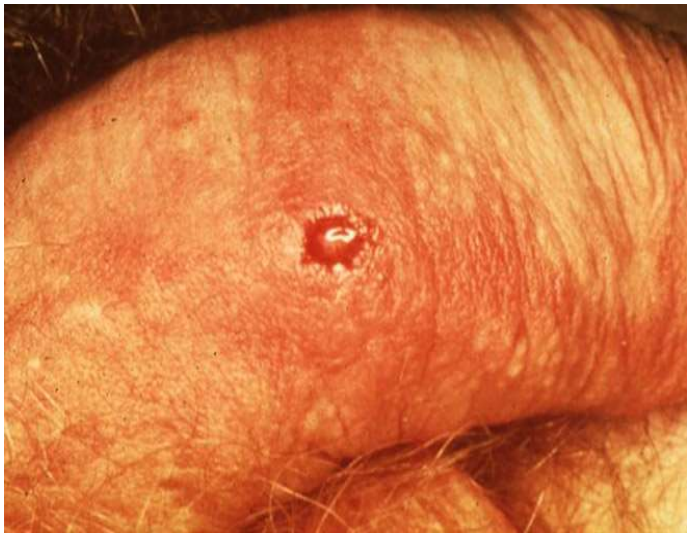
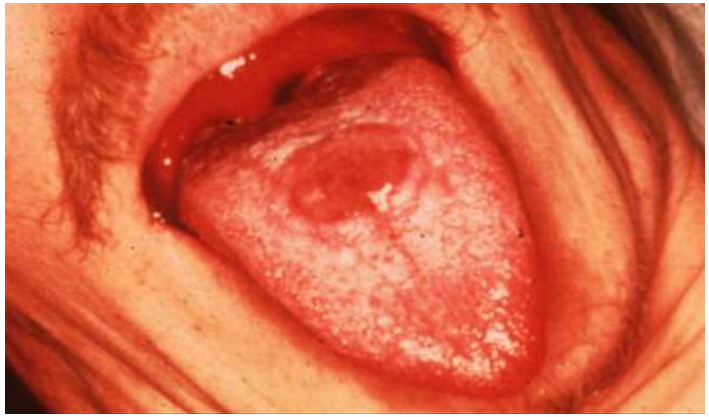


More primary syphilis…





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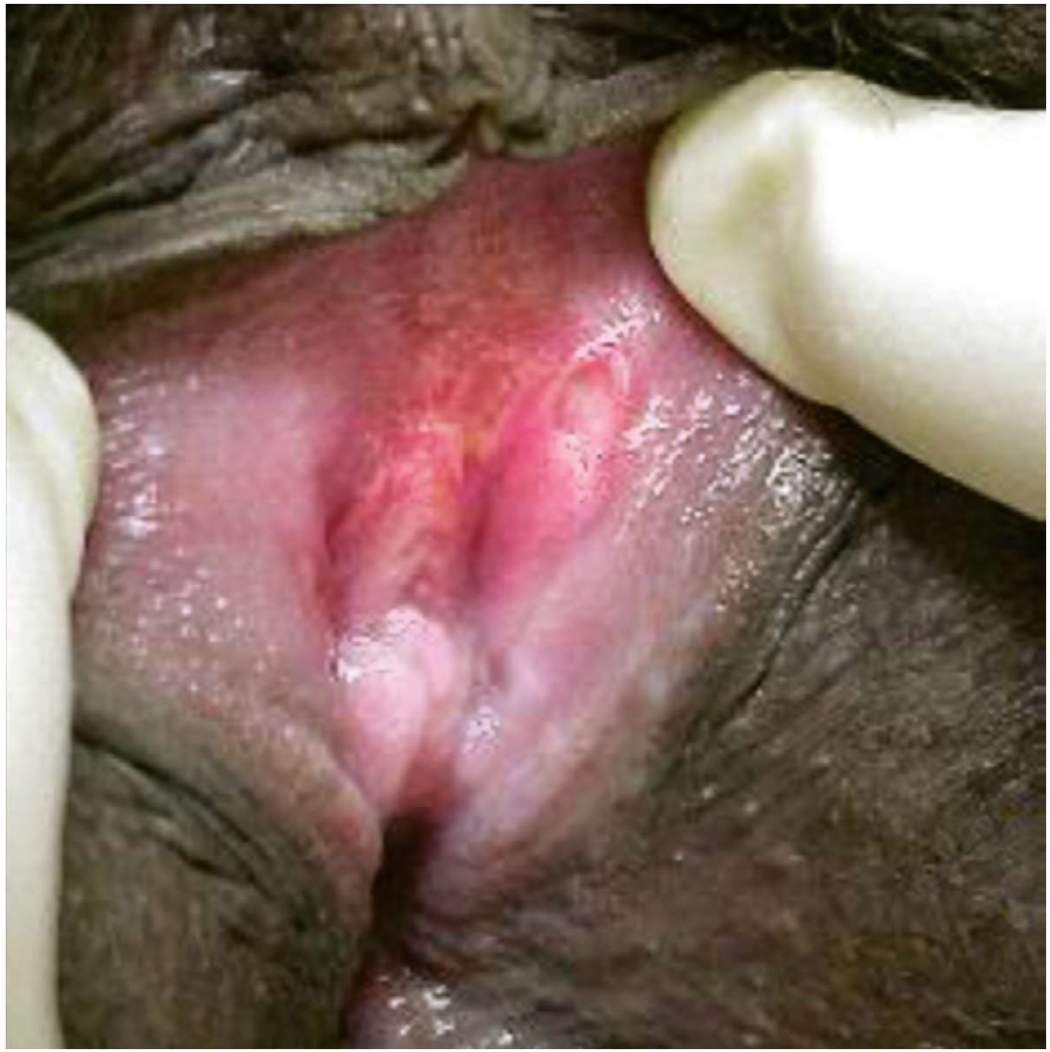

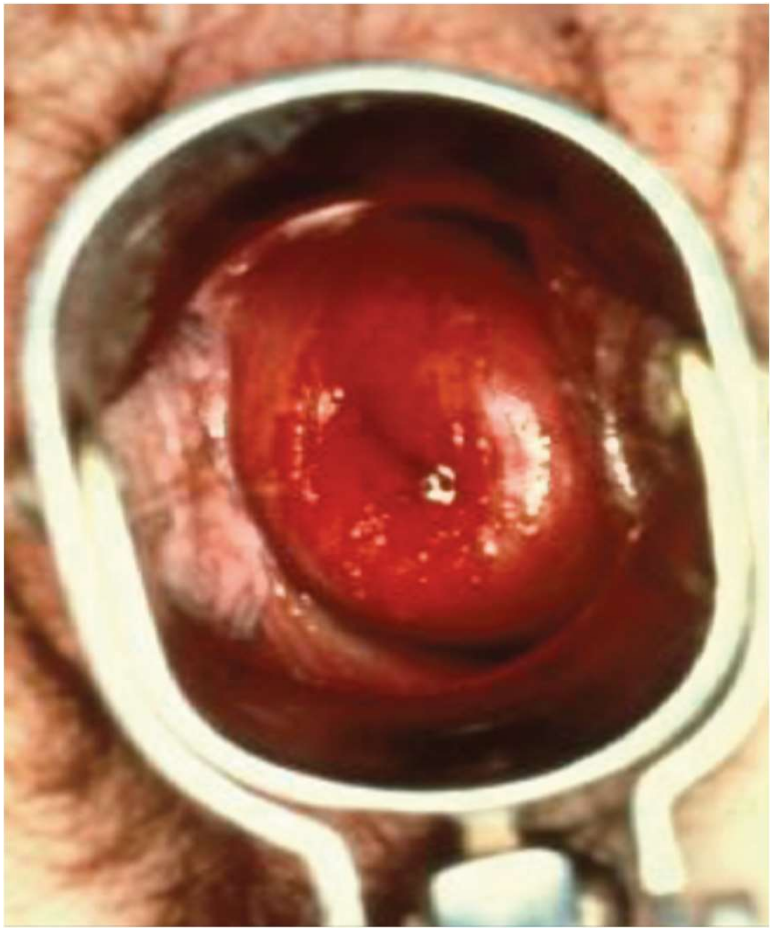

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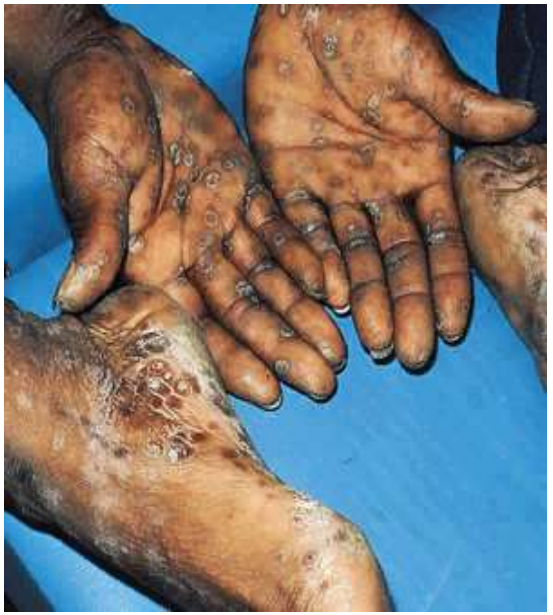
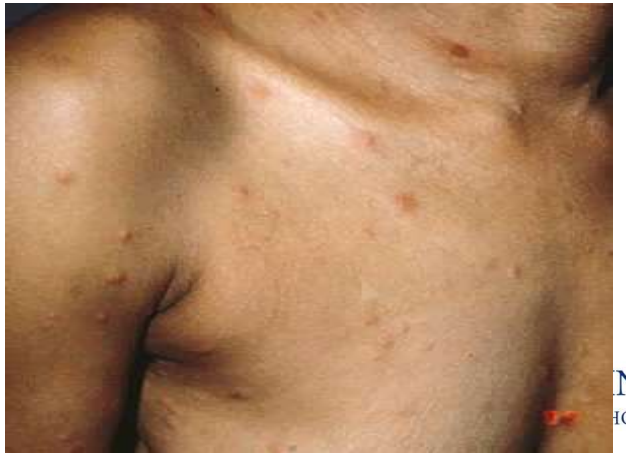
Secondary Syphilis

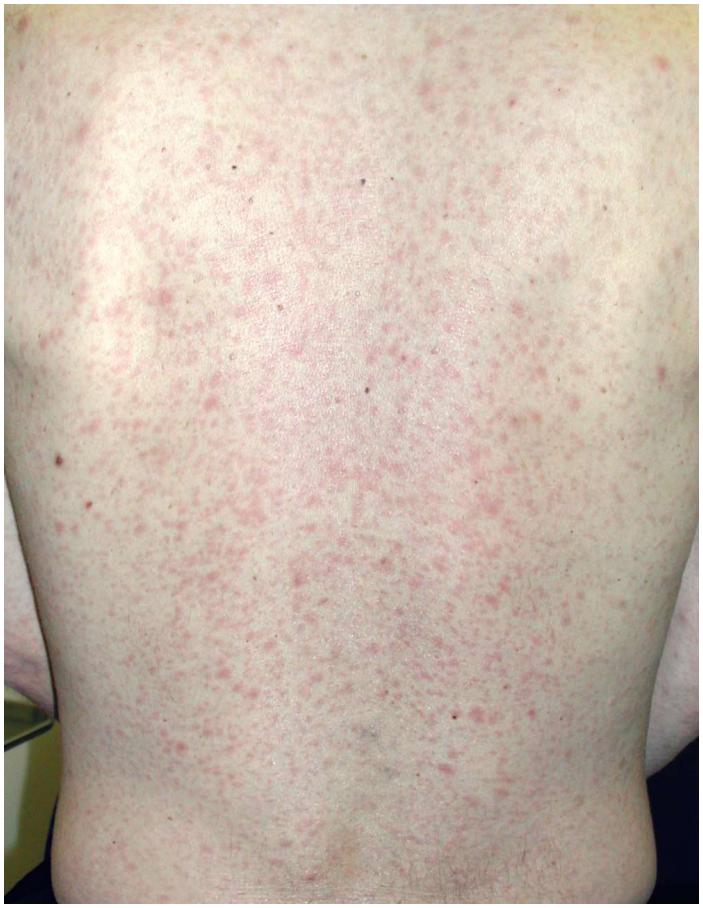
- Onset 4-10 weeks following primary and may overlap with it
- Rash:
  - macular, papular, pustular, combination;
  - usually not itchy
  - 60%-85% or more involve palms and soles
- Mucus patches (5-30%)
  - flat patches in mouth, pharynx, genitals





Secondary syphilis symptoms

- Rash (75-100%): macular, papular, squamous, pustular…
- Lymphadenopathy (50-80%)
- Malaise, fever, nonspecific constitutional symptoms
- Mucous patches (6-30%)
- Condylomata lata (10-20%)
- Alopecia (5%)
- Visceral organ involvement
- Neurologic symptoms



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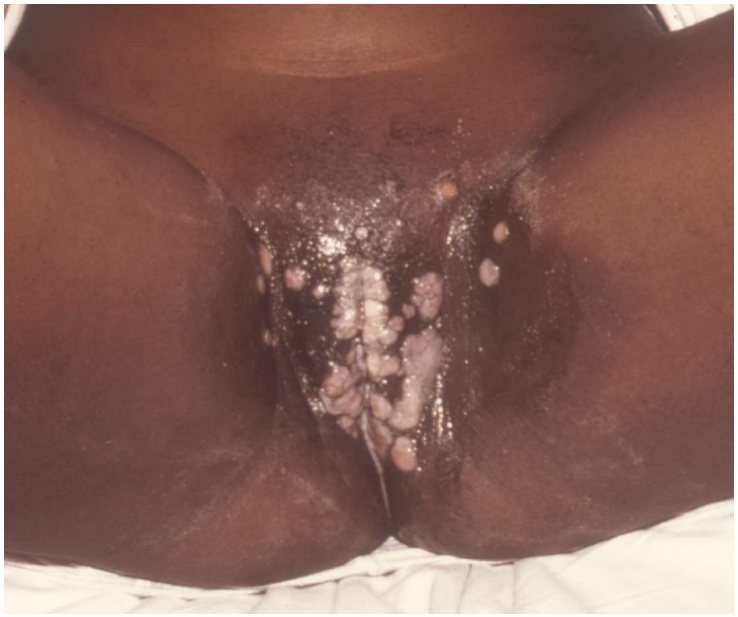
More secondary syphilis…

- Condylomata lata (5-25%)
  - heaped, moist wart-like papules
  - in warm intertriginous areas
  - teeming with spirochetes
- Constitutional symptoms:
  - malaise, headache, slight fever, myalgia
  - liver/kidney involvement
  - patchy alopecia



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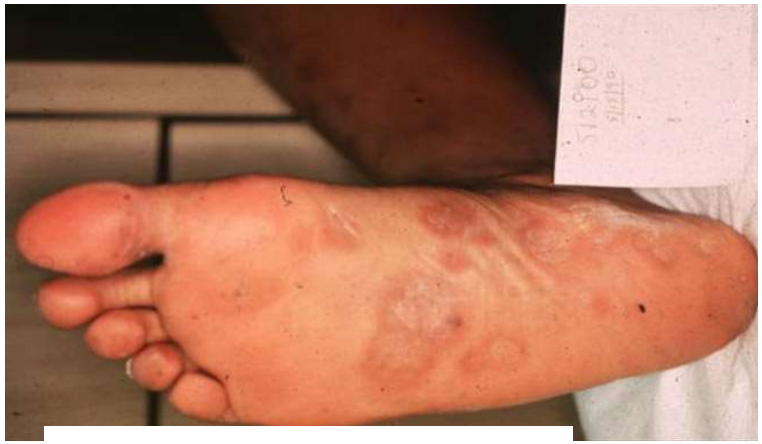
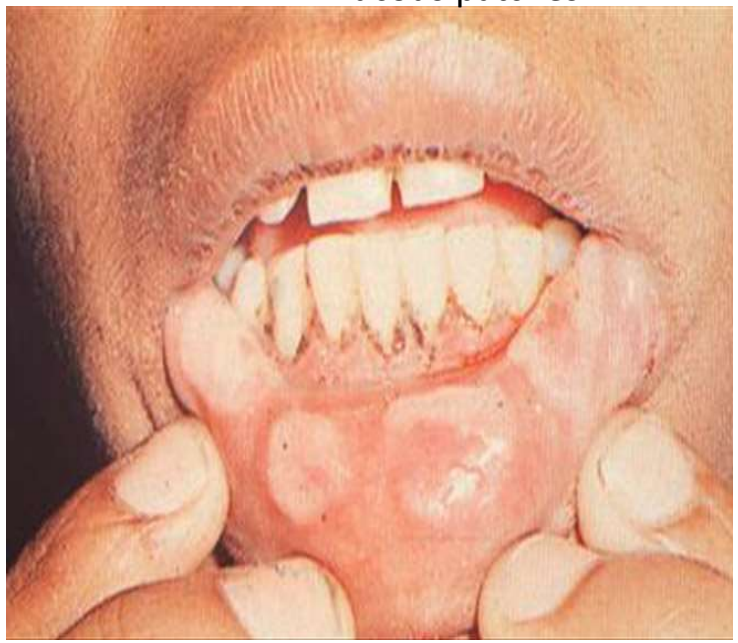
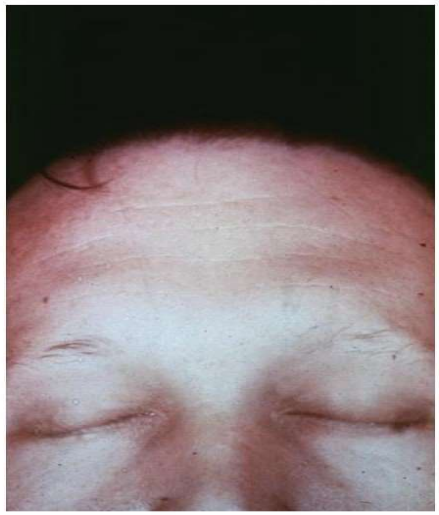
More Secondary Syphilis…



Mucous patches



Lateral eyebrow loss



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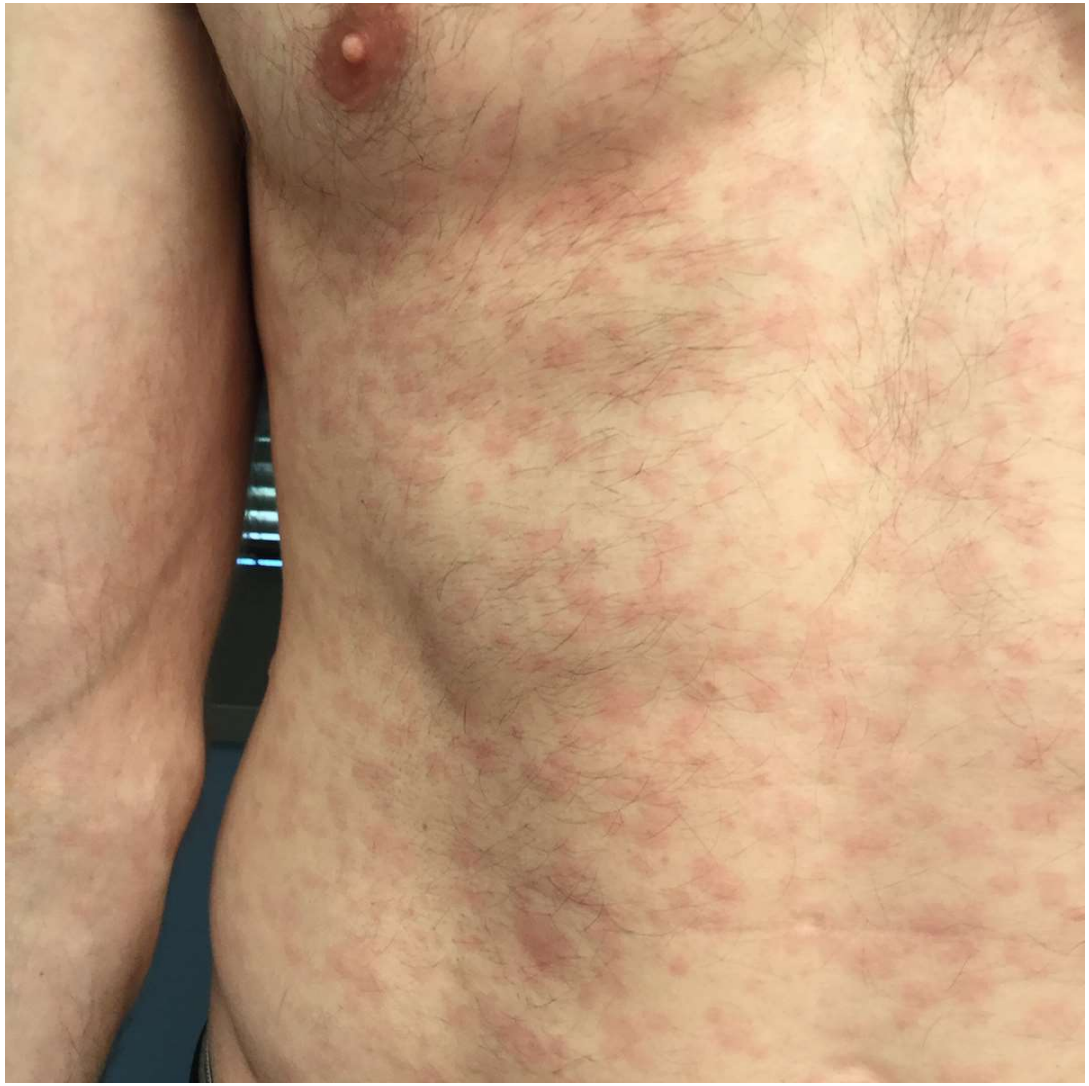

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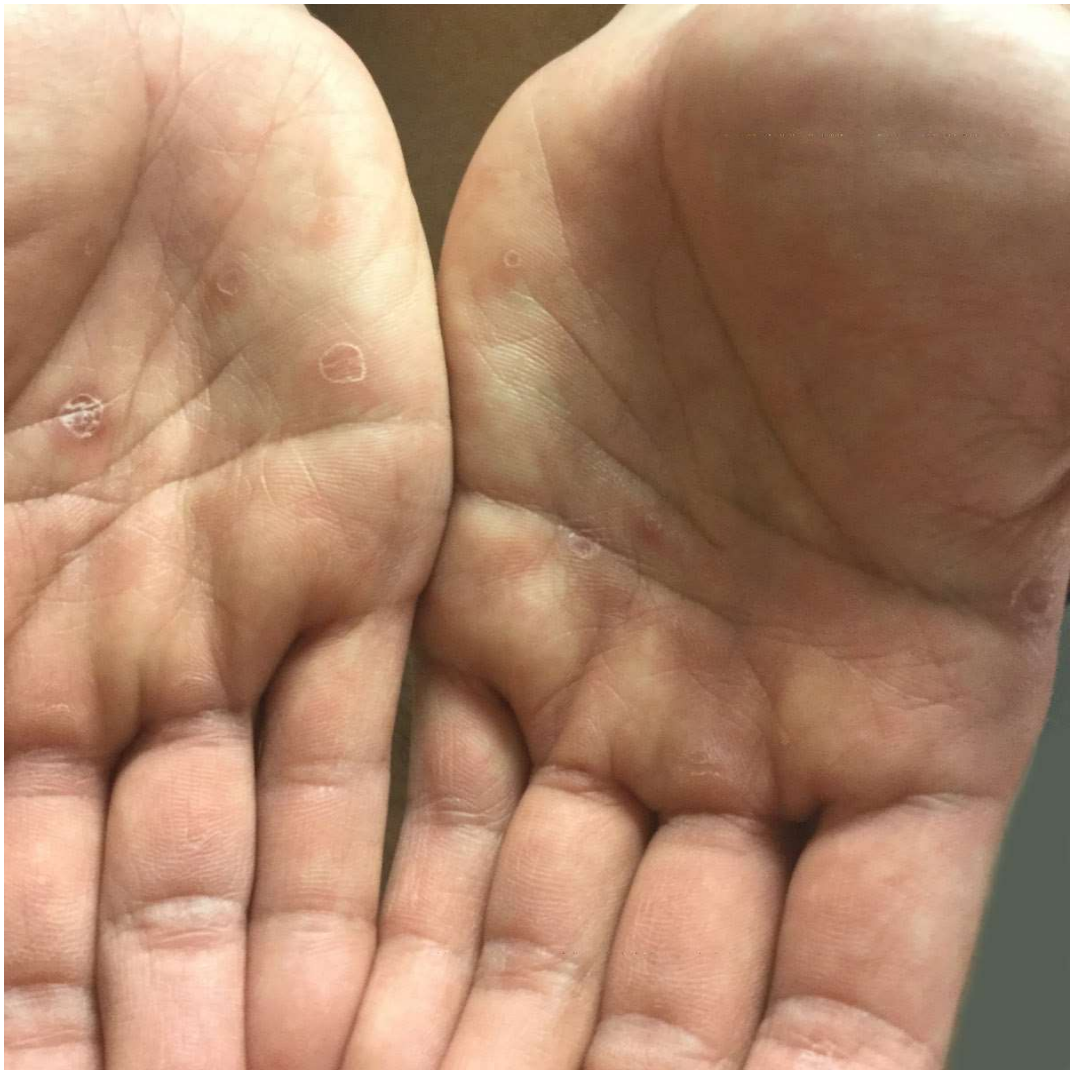

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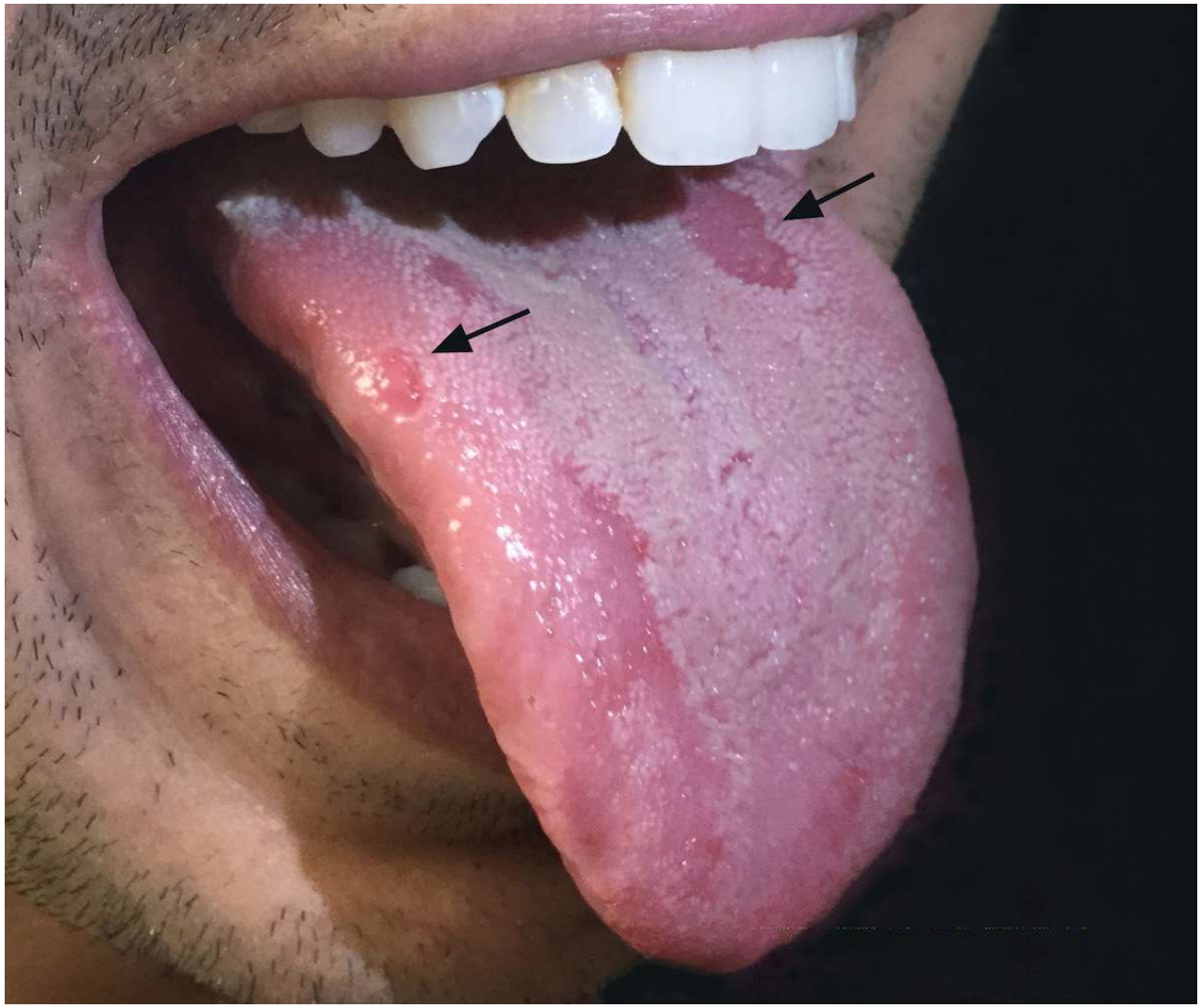
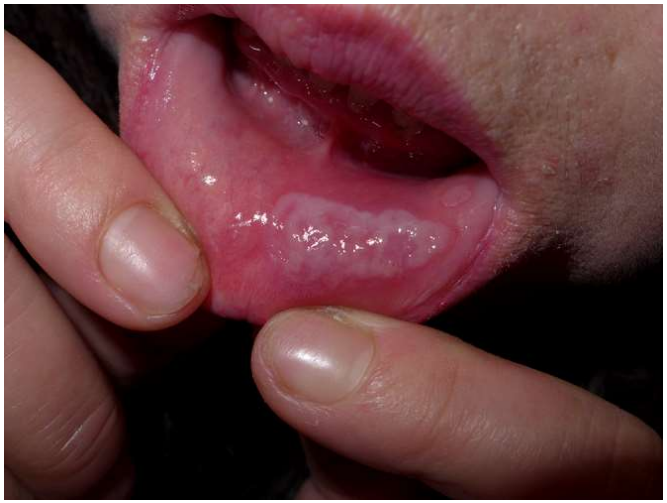
Mucous Patches





www.std.uw.edu; Liu and Li, IDCases. 2017; 9

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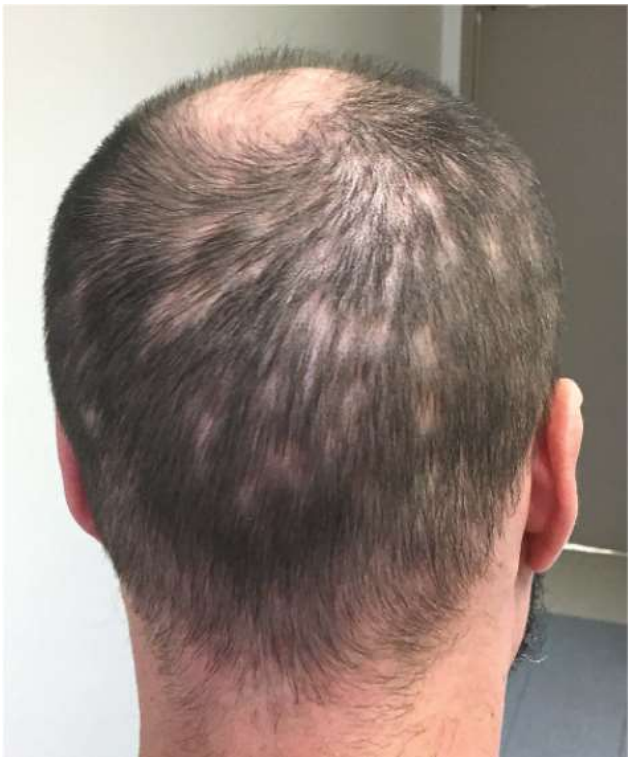

Moth eaten alopecia

https://www.nejm.org/doi/full/10.1056/NEJMicm1804118
https://cmr.asm.org/content/18/1/205/figures-only

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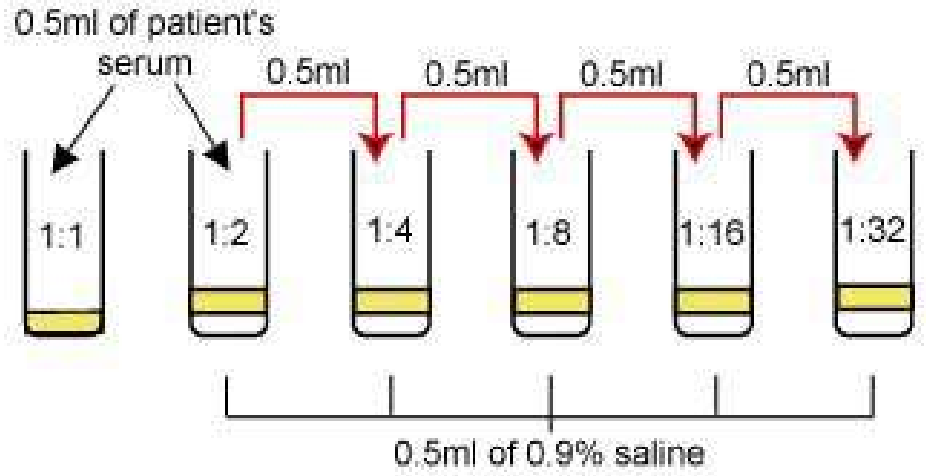
Diagnosis of syphilis: Testing

- Requires BOTH:
  - A treponemal specific test (TP-PA, FTA, Syphilis IgG, EIA, CIA, etc)
  - A nonspecific treponemal test (RPR with titer)
  - Be sure you are ordering a screening test that will reflex when positive to a confirmatory test
- Success of treatment hinges on fall of RPR titer by 2-dilutions, AKA 4-fold drop
  - Such as 1:16 to 1:4 or less, or 1:256 to 1:64 or less
  - Treponemal test may remain reactive forever

SEROLOGIC TITERS OF RPR

1 : 1024
1 : 512
1 : 256
1 : 128
1 : 64
1 : 32
1 : 16
1 : 8
1 : 4
1 : 2
1 : 1



2-fold decline/ 1 dilution

2-fold decline/ 1 dilution

Appropriate treatment response after treatment: 4-fold/2 dilution drop measured at:

- 12 months after primary/secondary/ early latent

OR

- 24 months after late latent

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Primary and Secondary Syphilis: Therapy

Benzathine penicillin G

2.4 million units IM ONCE

- No benefit for additional therapy (IM+ oral)
- Same for HIV+

2021 CDC STD Treatment Guidelines

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Primary and Secondary Syphilis
Penicillin Allergic
Nonpregnant Patients

Doxycycline 100 mg PO BID for 2 weeks

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Latent Syphilis Treatment

Early

Benzathine penicillin G 2.4 million units IM ONCE

Late or Unknown Duration

Benzathine penicillin G 7.2 million units TOTAL

=Three doses of 2.4 million units IM each at 1-week intervals

Latent Syphilis Treatment: Penicillin allergic

Early

Doxycycline 100 mg PO BID for 2 weeks

Late or Unknown Duration

Doxycycline 100 mg PO BID for 28 days

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Take-Home Points: What to do with RPR Titers that Don't Respond Appropriately

- **Lack of a fourfold decline in titers** after waiting a **full 12m** following therapy for early syphilis and a **full 24m** following therapy for late syphilis:
  - Any neurological signs/symptoms? **If yes, perform immediate LP**
  - Could the patient have been reinfected? **If yes, treat**
  - If both of the above are negative, you can either follow the patient carefully or you can give additional antibiotics. Several observational studies suggest that there are **NO short/intermediate-term benefits to additional antibiotics**
- A **four-fold increase in titers** after appropriate therapy:
  - Any neurological signs/symptoms? **If yes, perform immediate LP**
  - Could the patient have been reinfected? **If yes, treat**
  - If the patient denies the possibility of reinfection, and the titer continues to be elevated when repeated two weeks later, **consider performing a LP**

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Syphilis: CSF Examination

- Perform a lumbar puncture (LP) in persons who:
  - **Have neurological signs and symptoms**
  - Are diagnosed with tertiary syphilis (cardiovascular, gummas)
  - Consider in those who are asymptomatic but whose serological titers increase four-fold after stage-appropriate therapy and in whom the likelihood of reinfection is low
- No data to support routine LP in asymptomatic people with HIV
- No need for follow-up LP 6 months after the diagnosis and treatment of neurosyphilis in HIV uninfected or PWH who are on ART if they improve clinically, and their serological titers are responding appropriately

Otic and Ocular Syphilis Take-Home Points

Otosyphilis

- **Clinical manifestations**: cochleovestibular dysfunction and syphilis infection without an alternate diagnosis; ~50% bilateral
  - Symptoms: **Hearing loss, vertigo, and/or tinnitus** (ringing in the ears)
  - Diagnosis is presumptive; **CSF examination is normal in 90% of cases and is NOT recommended if patient only has otic signs and symptoms**
- **Therapy**: IV penicillin (+ corticosteroids)
- **Prognosis**: 23% experience improvement in hearing; up to 80% experience improvement in tinnitus and vertigo

Ocular Syphilis

- Clinical manifestations: any portion of the eye; any ocular manifestation; **immediate ophthalmological examination**
  - Symptoms: Redness, pain, floaters, flashing lights, visual acuity loss
  - Diagnosis is presumptive; **CSF examination is normal in 40% of cases and is NOT recommended if patient only has ocular signs and symptoms**
- **Therapy**: IV penicillin (+ corticosteroids)

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Trichomonas vaginalis

- Majority of infections asymptomatic in both men and women; causes vaginitis and non-gonococcal urethritis (especially among heterosexual men)
- Older women and MSW are at higher risk
- Diagnosis: culture and **PCR**; wet mount is not sensitive
- Vaginal pH usually >4.0
- Therapy: **Metronidazole 500mg PO BID X 7 days for all women** [never use topical gel formulations]; Metronidazole 2g PO X1 is ok for men; **Tinidazole 2g orally X1 ok for both men and women**
- Partners in the preceding 60 days must be treated
- **Screen HIV+ women annually**

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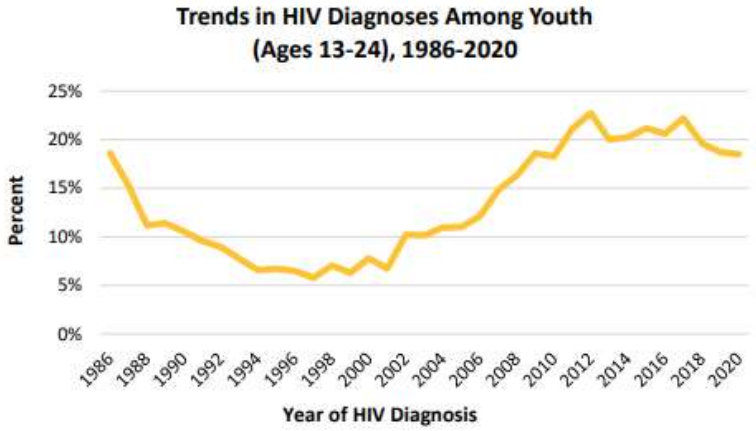
HIV Pre-exposure Prophylaxis (PrEP)

- 2020: youth made up 18.5% of new HIV diagnoses in MD
- 2021 CDC PrEP guidelines:
  - "PrEP is recommended for adolescents (weighing at least 35 kg or 77 lb) who report sexual or injection behaviors that indicate a risk of HIV acquisition"
  - Daily dosing safe & effective
    - TAF/FTC: Descovy- OK if exposure risk not injection use, receptive vaginal sex
    - TDF/FTC: Truvada- OK for all exposure types; generic version!
  - Injectable q2 mo's now FDA approved- cabotegravir



PrEP in Maryland:
www.prepmaryland.org

Email BCHD clinics to refer!
prep@baltimorecity.gov

https://health.maryland.gov/phpa/OIDEOR/CHSE/SiteAssets/Pages/statistics/Youth--Fact-Sheet.pdf
https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

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Screening recommendations: Women

Chlamydia and Gonorrhea	• Annually sexually active women <25 • Annually sexually active women 25+ if at increased risk (those who have a new sex partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner who has an STI)
Syphilis	• Pregnancy • Screen if increased risk • Personal recommendation: If seeking STI care
Trichomonas	• "Consider screening" in high prevalence settings (multiple sex partners, STI clinic pop, drug misuse, transactional sex)
HIV	• Ages 13-64 (once) • All women seeking care for STIs • Rescreening: new sex partners, partner with new partners
Hepatitis C	• All adults over 18 once, rescreen if at ongoing exposure risk
HPV/ Pap	• Begin age 21; new combinations of HPV PCR +/- cytology

*Herpes: Consider ONLY- provide counseling/discussion. Not recommended for M. genitalium!

Screening recommendations: Men who have sex with women only

Chlamydia and Gonorrhea	• Not recommended • Strong consideration: adolescent clinic, STI clinic
Syphilis	• Once if male <29 • Screen if increased risk: incarceration, transactional sex • Personal recommendation: If seeking STI care
Trichomonas	• Not recommended
HIV	• Ages 13-64 (once) • All men seeking care for STIs • Rescreening: new sex partners, partner with new partners
Hepatitis C	• All adults over 18 once • Rescreen if at ongoing exposure risk

*Herpes: Consider ONLY- provide counseling/discussion
Not recommended for mycoplasma genitalium!

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Screening recommendations: Men who have sex with men

Chlamydia and Gonorrhea	• Annually at all sites of sexual contact (genital, rectal, pharyngeal) regardless of condom use • Every 3-6 months if at high risk (on PrEP)
Syphilis	• Annually at all sites of sexual contact (genital, rectal, pharyngeal) regardless of condom use • Every 3-6 months if at high risk (on PrEP)
HIV	• At least annually for sexually active MSM if HIV status is unknown or negative and the patient or their sex partner(s) have had more than one sex partner since most recent HIV test • Increased risk: every 3-6 months
Hepatitis C	• All adults over 18 once, Rescreen if at ongoing exposure risk
HPV	• Digital rectal exam • Not enough evidence for routine anal cancer screening

*Herpes: Consider ONLY-infection status is unknown in MSM with previously undiagnosed genital tract infection

*Trichomonas and M. genitalium- not recommended for screening

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Screening: other important populations

- Transgender and gender diverse persons
  - Screening recommendations should be adapted based on anatomy (i.e., annual, routine screening in cis-gender women < 25 years old should be extended to all transgender men and gender diverse people with a cervix)
  - Consider choices based on reported sexual behaviors and exposure
- More info at 2021 CDC STD Treatment guidelines!!
  - Pregnancy
  - People living with HIV

https://www.cdc.gov/std/treatment-guidelines/screening-recommendations.htm

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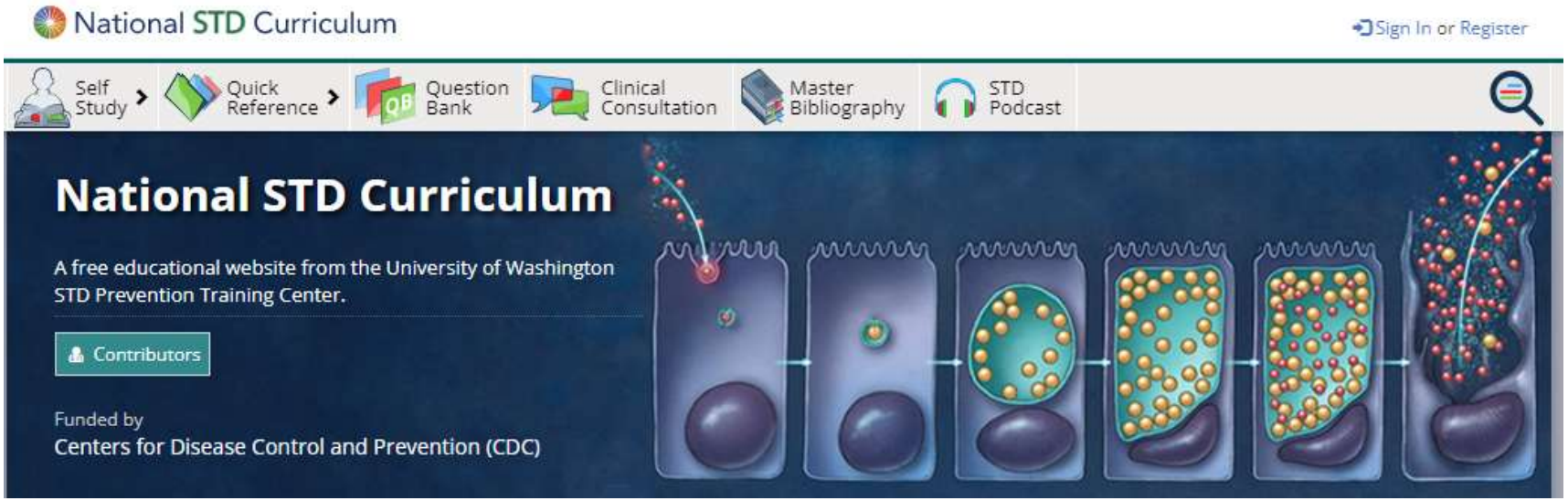
National STD Curriculum

www.std.uw.edu



FREE CE/ CNE/ CME credits!

Quick reference sections to refer back to!

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National HIV Curriculum

FREE CE/ CNE/ CME credits!

Great info on PEP and PrEP too

JOHNS HOPKINS
SCHOOL of MEDICINE

The NNPTC provides:

- Clinical training
- STD clinical consultations
- Resources and tools for STD treatment

Visit: www.nnptc.org

National Network of STD Clinical Prevention Training Centers

CDC
Centers for Disease Control and Prevention

Thank you!

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