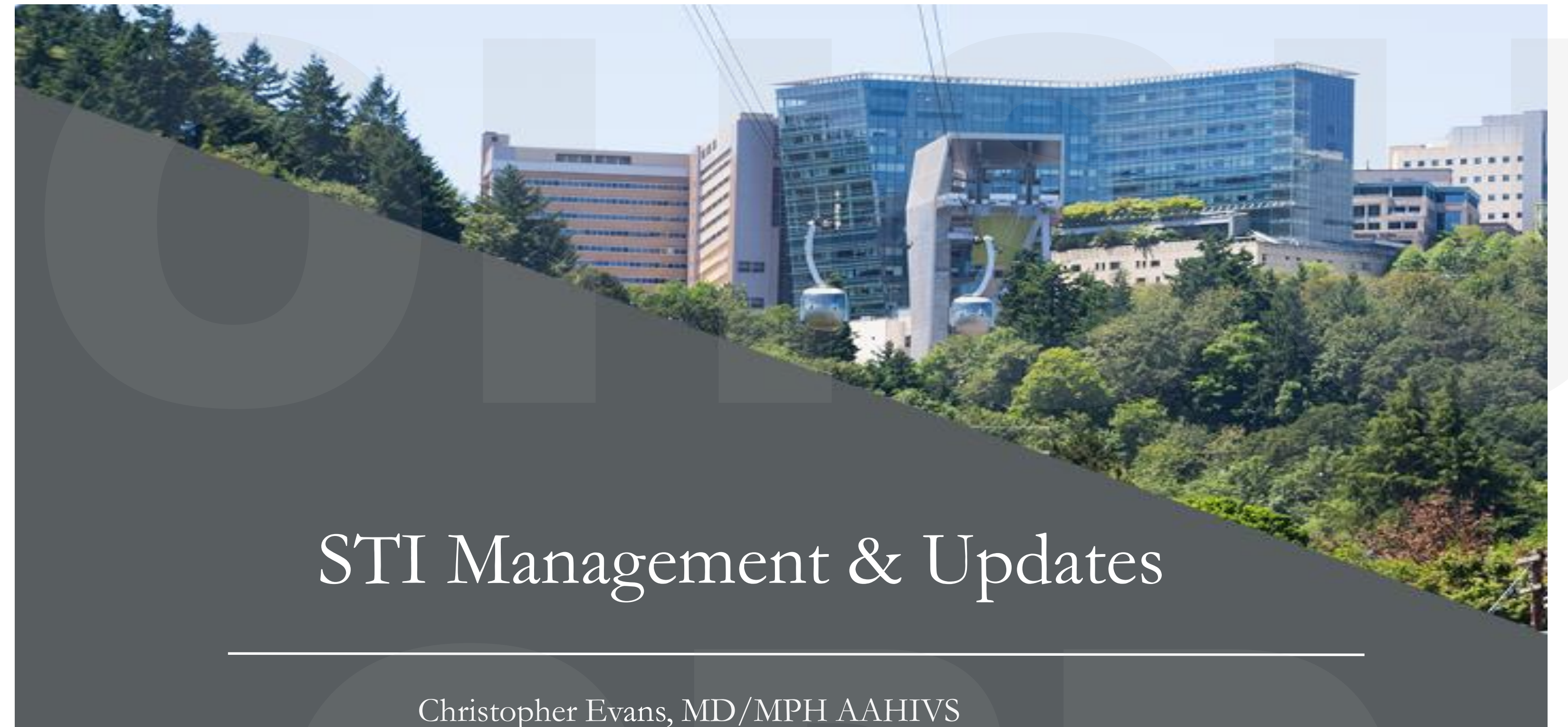
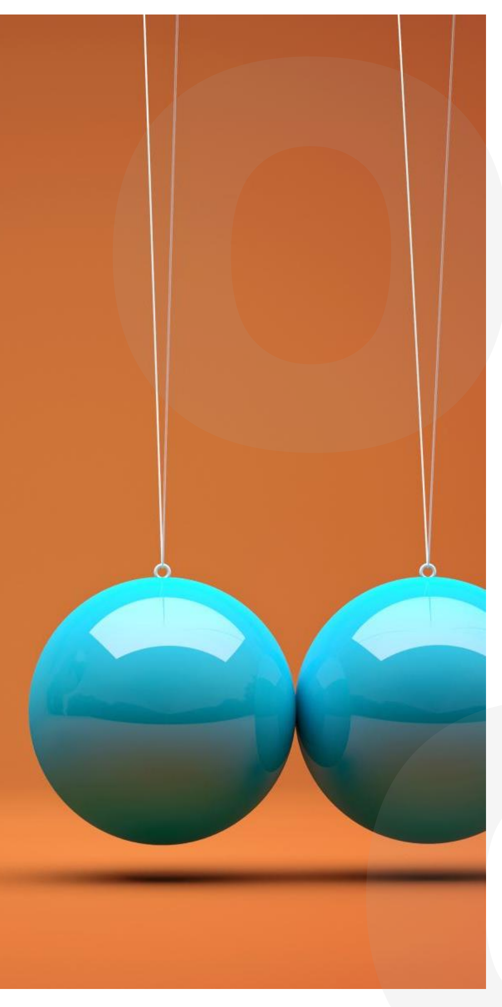


STI Management & Updates

Christopher Evans, MD/MPH AAHIVS
Associate Professor of Medicine
Oregon Health & Science University
Primary Care Conference
February 11th 2026



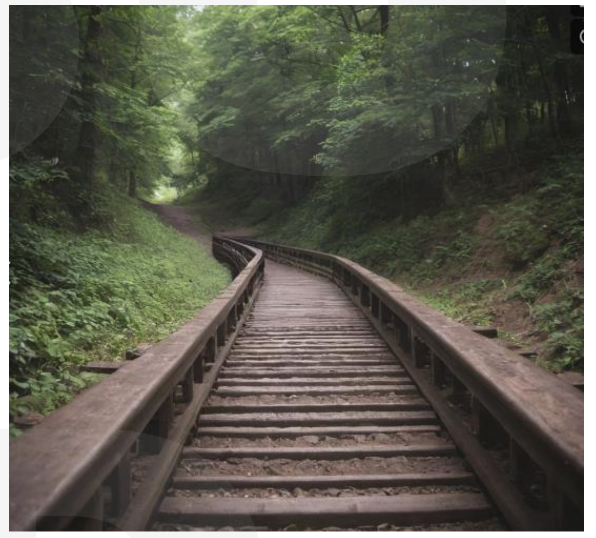
Disclosures

Research Funds:

GlaxoSmithKline

Learning Objectives

- Describe epidemiologic patterns of STIs
- Outline basic lab workup and follow-up testing for STIs
- Summarize first-line treatment options for major STIs



OREGON HEALTH & SCIENCE UNIVERSITY

STI Trends in the United States (2015–2024)

Cases

3,000,000
2,000,000
1,000,000
0

2015 2016 2017 2018 2019 2020 2021 2022 2023 2024*

Year

Total syphilis
Gonorrhea
Chlamydia

* 2024 data are provisional as of August 14, 2025.

NOTE: "Total syphilis" includes all stages of syphilis and congenital syphilis.

- **Chlamydia** is the most common STI reported
- **Gonorrhea** and **Syphilis** have both increased since 2015

OHSU CPD

Real Talk: Patient Concerns with STIs

How it's usually presented:

- *"I have a sore,"* or *"something doesn't feel right."*

How did I get this?

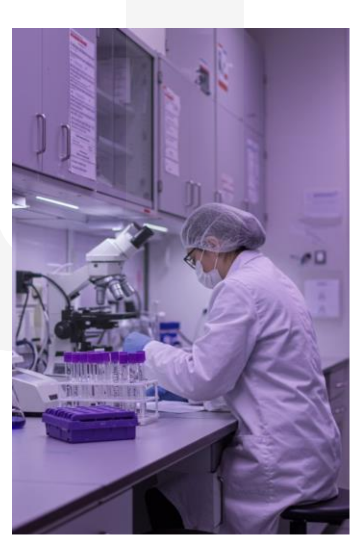
- Questions about timing
- Source…especially recent sexual encounters

🔄 **What happens next?**

- Understand treatment options
- Do the other partners need testing or treatment as well?

One Symptom, Many Possibilities: Testing

Test	Pathogen	Advantages	Limitations
NAAT (PCR)	HSV, Mpox, Chlamydia, Gonorrhea	High sensitivity	Not POC; variable availability
Darkfield Microscopy	Syphilis	Immediate results	**Requires expertise;** low sensitivity
Serology	Syphilis, HSV HIV	Widely available	Window period; **false positives**



The Type of Testing Matters

DETECTION OF COMMON SEXUALLY TRANSMITTED INFECTIONS:
SWABS VS URINE

Gonorrhea and Chlamydia Screening

- Vaginal swabs are the most sensitive method for women
- Men, first-void urine is the preferred

https://genesisreferencelabs.com/2023/06/detection-of-common-sexually-transmitted-infections-swabs-vs-urine/

What Drives STI Risk? Networks, Partners

- **Community Prevalence & Sexual Networks**
  - Connections →, exposure pathways
  - ZIP code with high STI rates may ↑ increase your individual risk

Partner Characteristics

- Partner's behaviors may matter more than partner count… does your partner
- **Taking a sexual history: The 5 Ps**
- **Asking the right Question about condoms**
  - Condom-Use Scale (0–10)
    - More nuanced discussion

Bacterial STIs can increase risk of HIV

Rectal GC or CT

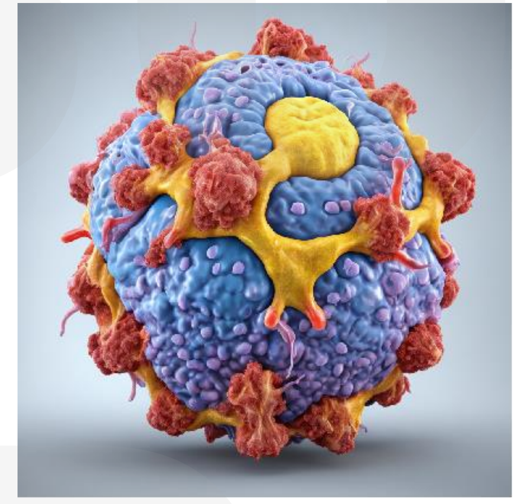
1 in 15 MSM were diagnosed with HIV within 1 year.*

Primary or Secondary Syphilis

1 in 18 MSM were diagnosed with HIV within 1 year.**

No rectal STD or syphilis infection

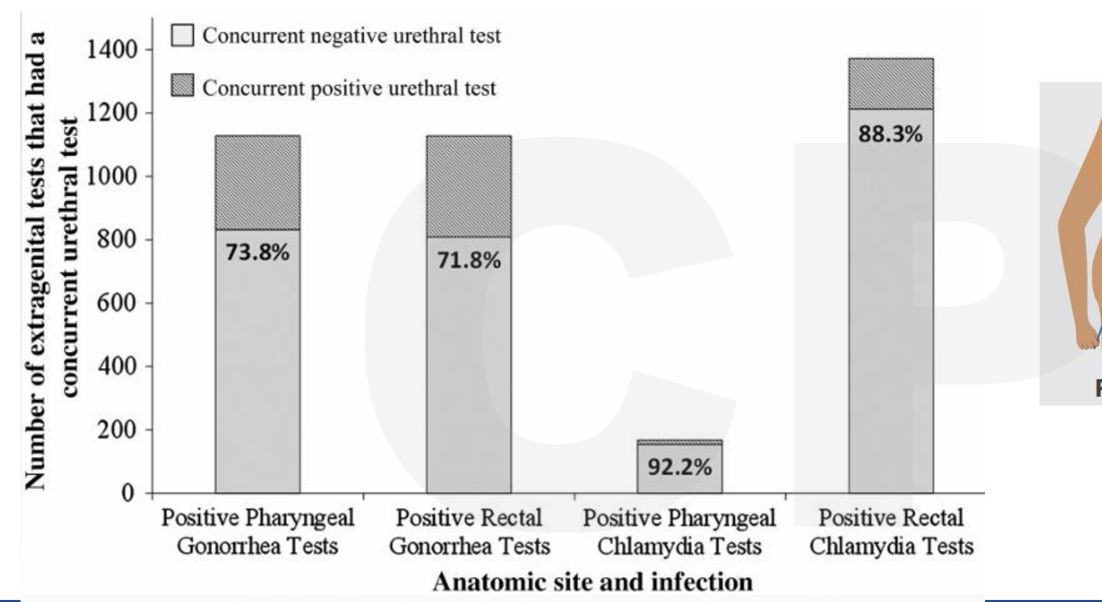
1 in 53 MSM were diagnosed with HIV within 1 year.*

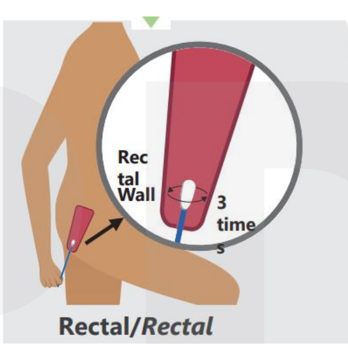


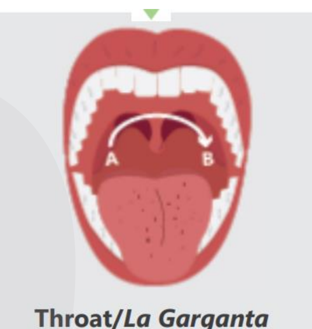
*STD Clinic Patients, New York City. Pathela, CID 2013:57;
**Matched STD/HIV Surveillance Data, New York City. Pathela, CID 2015:61

Extragenital Gonorrhea & Chlamydia

- **Surveillance Network**: 42 STI clinics
- 21,994 Men with male partners (July 2011–June 2012)
- GC/CT testing at last visit or past 12 months
  - **70% of extragenital GC infections,** urethral-negative (urine only)
  - **85% of extragenital Chlamydia** urethral-negative (urine only)
  - Screen at ALL sites of sexual exposure



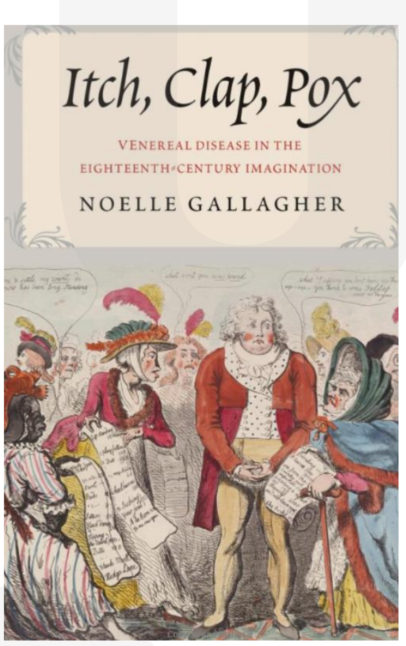




https://californiaptc.com/resources/extragenital-screening Patton et al Clin Infect Dis. 2014 Mar 18;58(11):1564–1570

Gonorrhea

Gerrit van Honthorst — *Merry Company* (c. 1620–1622)



Clapier = medieval French term for a **rabbit hutch**, which later became slang for a **brothel**.
Gonorrhea was commonly acquired in brothels, so people said someone "got it from the *clapier*," later shortened to **"the clap."**

Case

- 25-year-old man routine clinic visit
- HIV Prevention (PrEP) on **Tenofovir DF / emtricitabine**
  Sexual Hx: Two male partners
- **STI screening tests : (Asymptomatic)**
  - 4th generation HIV ag/ab screening
  - RPR (Syphilis)
  - Gonorrhea/chlamydia NAAT (urine, rectal, pharyngeal)
- **Lab result:**
  - **Pharyngeal NAAT + for *Neisseria gonorrhoeae***
  - *RPR . Non-reactive*
  - *HIV ab/ag negative.*

Gonorrhea Dx in OR have decreased since 2021

Year	number of diagnoses
2014	2,291
2015	3,240
2016	4,358
2017	5,024
2018	5,928
2019	6,130
2020	6,414
2021	6,223
2022	5,494
2023	4,960
2024	4,469

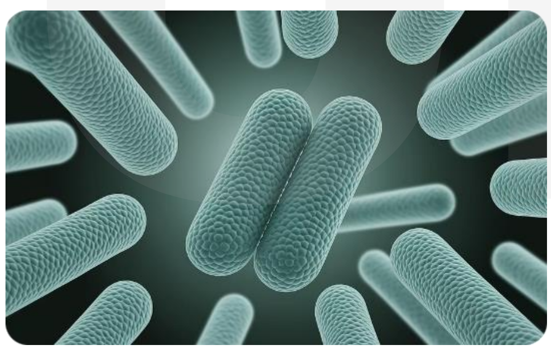
104.60

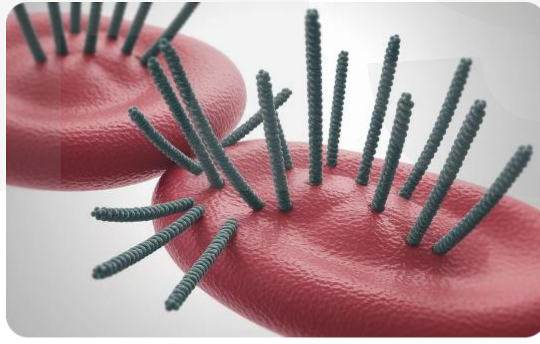
number of diagnoses

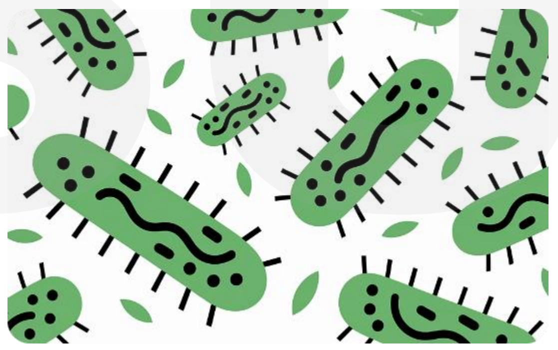
number of diagnoses per 100,000 people

In 2023, there were **601,319 cases of GC** reported in the United States.
Rates have consistently been **higher among males** than female patients

Gonorrhea Pathogenesis







Gram-Negative Diplococci

Characteristic "coffee bean" appearance under microscope

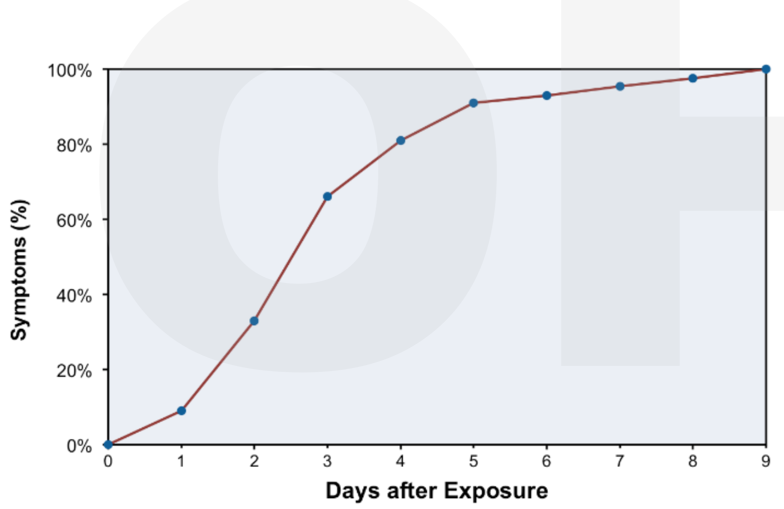
Pili for Attachment

help bacteria adhere to mucosal surfaces

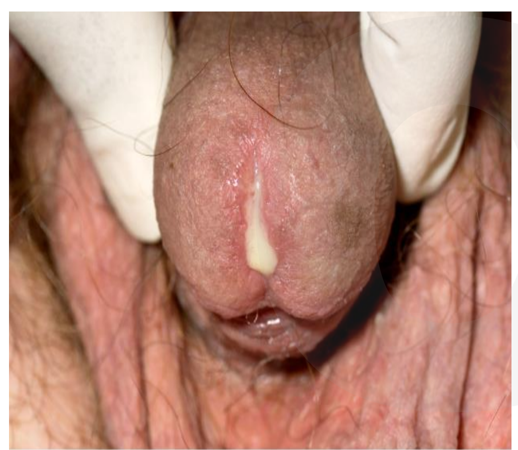
Antigenic Variation

Rapidly changes surface proteins to evade immune detection

Gonorrhea in Male Patients



Penile discharge



Incubation: 1 to 14 days

Clinical Presentation

Symptomatic (2 to 5 days)

- Urethritis
- Dysuria
- Urethral discharge: mucopurulent
- Epididymitis (unilateral)

Anogenital Infections

- Anal pruritus
- mucopurulent discharge
- Proctitis & Painful defecation
- Pruritus

https://www.msdmanuals.com/professional/infectious-diseases/sexually-transmitted-infections-stis/gonorrhea
UW STD Curriculum

Gonorrhea in Female Patients

Incubation. ≈2-7 days

Clinical Presentation

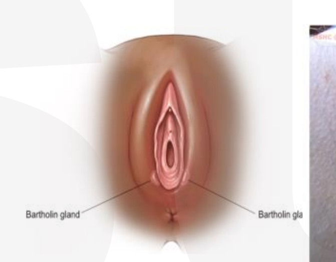
- Asymptomatic: **Common**
- Symptomatic (10 days)
- Discharge: Yellow/green, dysuria
- Bartholin's gland infection
- **Nonspecific symptoms**: cervicitis, intermenstrual or postcoital bleeding

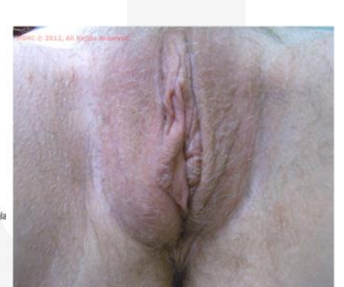
Complications:

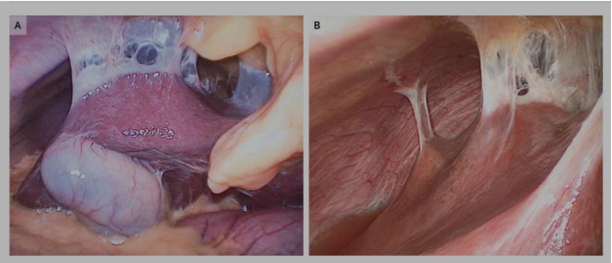
- PID, Perihepatitis (Fitz-Hugh–Curtis Syndrome -Liver capsule inflammation)

Pregnancy complications

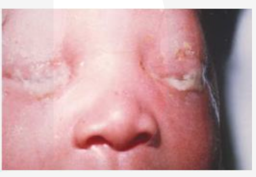
- Prematurity, conjunctivitis, meningitis







Fitz-Hugh–Curtis Syndrome (FHC)



Conjunctivitis Ophthalmia neonatorum

Gonorrhea Screening

- **Women: Screen <25 yrs**
  - Pregnancy: retest 3rd trimester if <25 or ongoing risk.
- **Screen ≥25 yrs if "increased risk"**
- **Men who have sex only with women**
  - No routine screening.
- **Men who have sex with male partners**
- Screen annually (all exposure sites)
  - Every 3–6 months if High risk
  - PrEP, multiple partners

Disseminated Gonococcal Infection (DGI)

Clinical Presentation

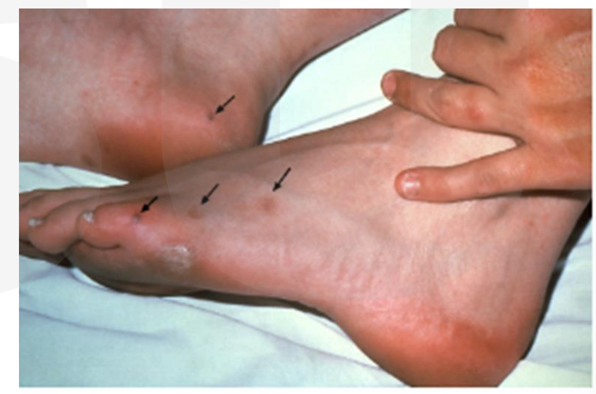
- Polyarthralgia (small or large joints)
- Tenosynovitis
- Dermatitis: **Painless skin lesions**

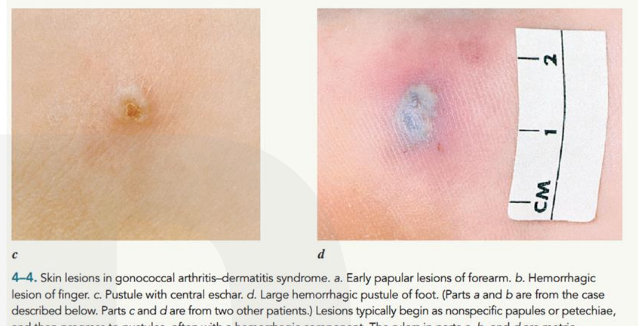
⚠️ **Risk Factors for DGI**

- Post-menses
- **Pregnancy is a risk**
- Complement deficiencies (C5, C6, C7, C8)

Testing for DGI

- NAAT testing of urogenital, rectal, pharyngeal, and urine sites
- Blood Cx (many times negative)



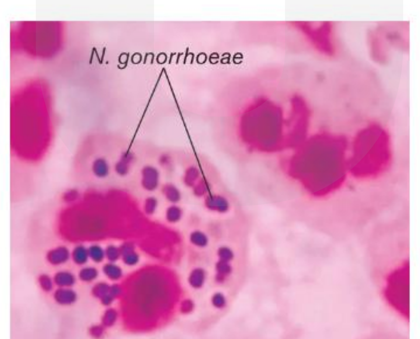


4–4. Skin lesions in gonococcal arthritis–dermatitis syndrome. *a.* Early papular lesions of forearm. *b.* Hemorrhagic lesion of finger. *c.* Pustule with central eschar. *d.* Large hemorrhagic pustule of foot. (Parts *a* and *b* are from the case described below. Parts *c* and *d* are from two other patients.) Lesions typically begin as nonspecific papules or petechiae, and then progress to pustules, often with a hemorrhagic component. The rulers in parts *a*, *b*, and *d* are metric.

Gonorrhea Diagnostics: Swab, Stain, or Amplify?

NAAT: Nucleic Acid Amplification Test

- **Gold standard.** Highest sensitivity for dx
- **Culture**
  - Chocolate or Thayer–Martin agar
  - Incubate in **a CO_2-enriched environment**
  - **Antibiotic Resistance Testing**



Gram Stain

- Gram-negative diplococci
- Rapid but less sensitive
- Best in symptomatic males with urethritis

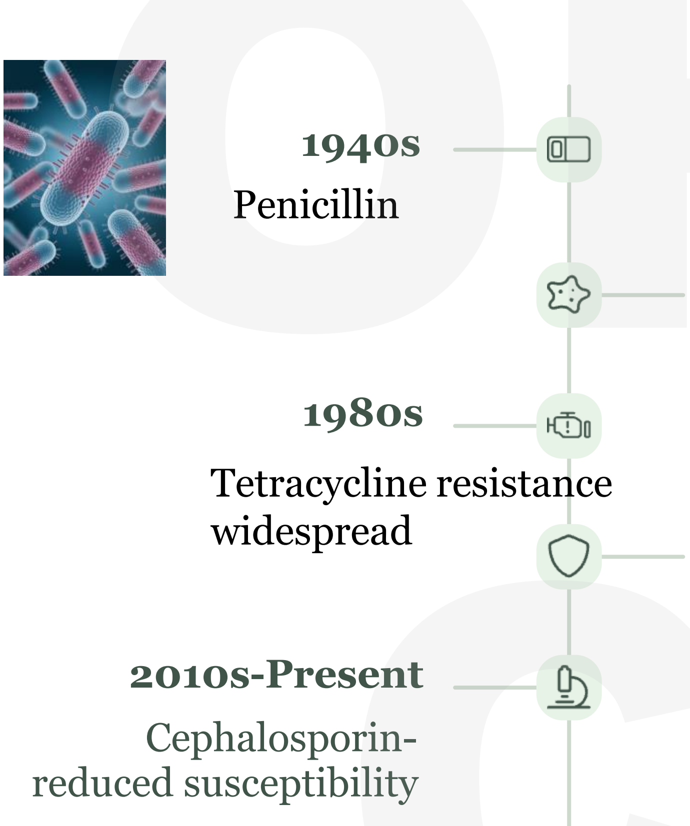
/

Uncomplicated Gonorrhea Treatment

First-Line Therapy	**Ceftriaxone 500 mg IM ×1 (<150 kg)** **Ceftriaxone 1 g IM ×1 (≥150 kg)**
If Chlamydia Not Excluded	• Doxycycline 100 mg PO × 7 days • Avoid Doxycycline in pregnancy
Alternative (Nonpregnant)	• Cefixime 800 mg PO × 1 • Lower efficacy for pharyngeal infection
Alternative * Allergy to cephalosporins	• Gentamycin 240 mg + • Azithromycin 2 gram x 1 dose.

- Sexual partners w/in prior 60 days , tested & presumptively treated.
- Retest at 3 months (reinfection is common)

Gonorrhea Antibiotic Resistance



1940s
Penicillin

1970s
Penicillin resistance emerges

1980s
Tetracycline resistance widespread

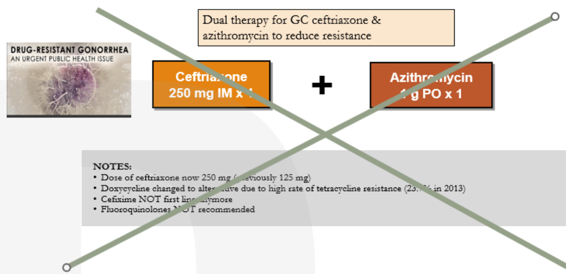
2000s
Fluoroquinolone resistance leads to removal from guidelines

2010s-Present
Cephalosporin-reduced susceptibility

The New York Times

More than 2.4 million cases of syphilis, gonorrhea and chlamydia infections were reported in the United States last year, the Centers for Disease Control and Prevention said in its annual report. Richard Levine/Alamy

Previous Recommendations: Gonorrhea Treatment



Oropharynx harbors multiple **commensal *Neisseria* species**
These non-pathogenic species often carry **intrinsic and acquired resistance genes**

When to Suspect Treatment Failure

Test of Cure

- **All pharyngeal infections.** Retest **7–14 days** after treatment

When to Suspect Treatment Failure

- Persistent symptoms **without sexual re-exposure**
- Positive **NAAT 7–10 days** post-treatment
- Most failures occur at the **pharyngeal site**

Recommended Actions

- **NAAT + culture with antibiotic susceptibility**
- **Repeat treatment with ceftriaxone** if an alternative regimen was previously used
  - Consider **gentamicin 240 mg IM + azithromycin 2 g PO**
- **Report suspected treatment failure** to Health Dept/ CDC

Novel Oral Agents for Gonorrhea

Mechanism: Bacterial Topoisomerase inhibitors

Gepotidacin

- FDA approved Dec 2025
- **3 g PO twice**, 10–12 hours apart

Zoliflodacin

- FDA approval Dec 2025
- **3 g PO single dose**

Non-gonococcal Urethritis

Infectious Causes

- ***Chlamydia trachomatis***
- ***Mycoplasma genitalium***
- *Trichomonas vaginalis*
- Herpes simplex virus (HSV)

Non-Infectious Causes

- Local irritation (e.g., soaps, Detergents, hygiene products)
- Contraceptives (e.g., spermicides, condoms, topical products)

Rate of Chlamydia in OR 2014-2024

Year	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
number of diagnoses	15,339	16,334	17,410	18,627	19,110	19,253	15,844	15,601	15,506	15,354	13,991
number of diagnoses per 100,000 people											327.5

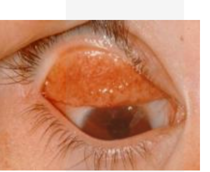
In 2023, **1,648,568 cases** of chlamydia were reported in the US
Reported rates are consistently **higher among females than males**.

OHA Data. UW STI Curriculum

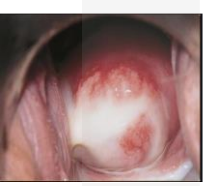
Chlamydia Clinical Infections

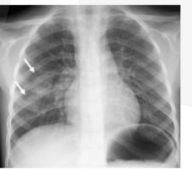
C. trachomatis	• **Serovars A–C** Trachoma • **Serovars D–K** Urogenital • **Serovars L1–L3 –**LGV
C. pneumoniae	• Respiratory infections • Pneumonia in young populations
C. psittaci	• Psittacosis (from birds)

Trachoma



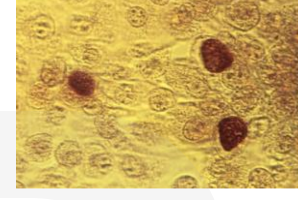
Urogenital





C. Pnemoniae

C. Psittaci



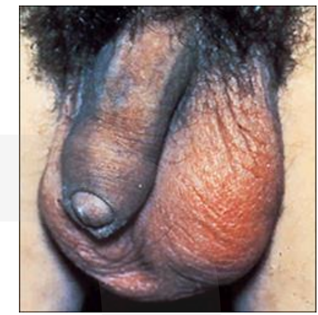
"Chlamydia" derives from the Greek *chlamys*, meaning "cloak." The name reflects the organism's cloak-like intracellular inclusions.

CDC/ Dr. E. Arum; Dr. N. Jacobs.

Chlamydia: Male patients

Incubation Period	**5–14 days post-exposure Serovars- D-K**
Urethritis	Dysuria; clear → mucoid urethral discharge
Epididymitis	Scrotal pain, swelling
Prostatitis	Pelvic/perineal discomfort
Proctitis	Rectal pain, discharge; ~50% asymptomatic
Complications	Reactive arthritis; circinate balanitis; conjunctivitis

Penile discharge



Epididymitis

Uni of Washington. STI curriculum.
https://www.ecdc.europa.eu/en/chlamydia/facts#:~:text=At%20least%2070%25%20of%20genital,asymptomatic%20infections%20is%20not%

Chlamydia : Female patients.

Incubation	**~ 5–14 days after infection** **Serovars D-K**
Asymptomatic Infection	Up to 80% have no symptoms
Cervicitis	Mucopurulent discharge, postcoital bleeding, friable cervix
Urethritis	Dysuria, frequency, sterile pyuria
Upper Tract Infection	PID, salpingitis, perihepatitis (Fitz-Hugh–Curtis syndrome)
Reproductive Complications	Tubal scarring → infertility, ectopic pregnancy; preterm labor
Neonatal Infection	Neonatal conjunctivitis and pneumonia

Lymphogranuloma Venereum:L1–L3 serovars

1 Primary Stage

- Painless papule/ulcer (Often not noticed)
- 3–12 days post-exposure

2 Secondary Stage

- Inguinal lymphadenopathy (buboes)
- Develops 2–6 weeks after infection

3 Anorectal Infection

- *Severe proctocolitis with mucopurulent,*
- *bloody discharge*
- Mimics inflammatory bowel disease

- **Treatment:** Doxycycline × 21 days

Chlamydia Screening

Women: Screen <25 yrs

- Pregnancy: retest 3rd trimester if <25 or ongoing risk
- **Screen ≥25 yrs if increased risk**

Pregnant Women (if positive)

- Test-of-cure at 4 weeks. Retest in 3 months

Men who have sex only with women

- No routine screening

Men who have sex with male partners

- Screen annually (all exposure sites)
- Every 3–6 months if high risk
- PrEP, HIV, multiple partners

Chlamydia Diagnosis

NAAT (Nucleic Acid Amplification Test)

- Gold standard 95% sensitivity and specificity

- **Penile Specimen**
  - First-void urine sample
  - Urethral swab if discharge is present
- **Vaginal Specimens**
  - Self-collected vaginal swab (**highest sensitivity**)
  - Endocervical swab during pelvic exam

Extragenital Testing

- Rectal swab for receptive anal exposure
- Pharyngeal swab for orogenital contact

LGV

- **NAAT for *Chlamydia trachomatis***
- Labs do not differentiate serovars
- Based on clinical symptoms

Chlamydia Treatment

First-Line

- **Doxycycline 100 mg PO BID × 7 days**
    - Preferred for rectal infection

Alternatives

- Azithromycin 1 g PO × 1 dose
- Levofloxacin 500 mg PO BID × 7 days

Follow-Up

- Retest at 3 months to assess for reinfection

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., David J. Templeton, Ph.D., Janaki Amin, Ph.D., Samuel Phillips, Ph.D., Matthew Law, Ph.D., Marcus Y. Chen, Ph.D., Catriona S. Bradshaw, Ph.D., Basil Donovan, M.D., Anna McNulty, M.D., Mark A. Boyd, M.D., Peter Timms, Ph.D., Eric P.F. Chow, Ph.D., David G. Regan, Ph.D., Carole Khaw, M.D., David A. Lewis, Ph.D., John Kaldor, Ph.D., Mahesh Ratnayake, M.D., Natalie Carvalho, Ph.D., and Jane S. Hocking, Ph.D.

Mycoplasma genitalium (Mgen):

Male Patients

- Symptomatic urethritis
- 15–20% of NGU
- ~40% of persistent/recurrent urethritis
- Rectal infection -1–26% of MSM (depending on study)
- **Consider for <u>male pts with recurrent NGU</u>**

Female Patients

- Linked to cervicitis, PID
- Preterm delivery, and infertility
- 10–30% of women with cervicitis
- **Frequently asymptomatic**
- **Consider for <u>female pts with recurrent cervicitis</u>**

Screening & Testing

- Culture impractical (growth may take up to 6 months)
- NAAT for urine, urethral, penile, endocervical, vaginal swabs.

Diagnosis & Treatment M. genitalium

Screening & Testing

- Preferred test: N**AAT** on urine or urethral, penile, endocervical, or vaginal swab.

Treatment

- Resistant to PCN & Ceph (lacks a cell wall).
- High rates of macrolide resistance.
- **Empiric regimen**: Doxycycline 100 mg twice daily × 7 days→ then moxifloxacin 400 mg daily × 7 days.

Partner Management

- Test and treat recent sexual partners to prevent reinfection and ongoing transmission.

“Syphilis sive morbus gallicus: Syphilis

The name “Syphilis”

- **Girolamo Fracastoro’s Poem (c. 1521)**
  - Story of a shepherd named **Sifilo**, cursed by the sun god

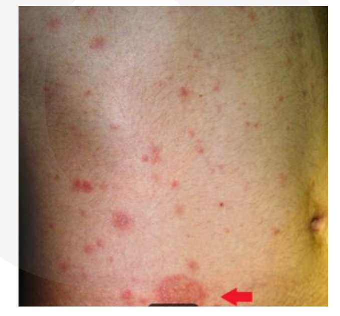
Historical Name

- **“The Great Pox”**
  - **Disfiguring lesions** and **social stigma**

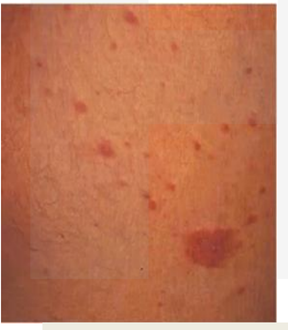
🌍 **National Labels & Stigmas**

- “Polish disease” — used by Russians
- “Spanish disease” — used by Dutch

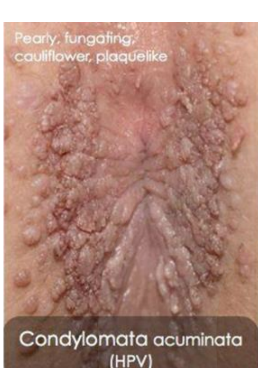
Syphilis: Master of Disguise



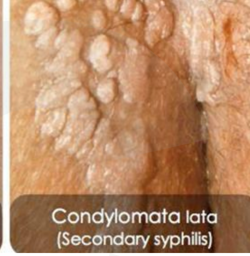
Secondary Syphilis



Pityriasis Rosea



Warts



Syphilis

Patients rarely say, *"I have syphilis."*

- Syphilis may look like other conditions

Secondary Syphilis

- Rash may appear maculopapular and resemble **Pityriasis Rosea**
- **Condyloma lata** can look like genital warts

Courtesy. https://www.chegg.com/flashcards/skin-and-eye-pictures-21375f0d-0188-481f-b926-d9a625546a49/deck

Repeat Syphilis infections may different symptoms

Kenyon *et al. BMC Infectious Diseases* (2018) 18:479
https://doi.org/10.1186/s12879-018-3399-8

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

CrossMark

Syphilis reinfection is associated with an attenuated immune profile in the same individual: a prospective observational cohort study

Chris Kenyon[1,2*], Kara Krista Osbak[1], Tania Crucitti[3] and Luc Kestens[4,5]

- Syphilis reinfection often shows **attenuated immune responses** compared to **the first infection**
- **Symptoms may be milder or atypical**, making diagnosis harder

Early syphilis Dx in OR highest in recent history

Cases of primary, secondary and non-primary non-secondary syphilis (early syphilis), 2000-2023

Number of early syphilis

1800
1600
1400
1200
1000
800
600
400
200
0

31 22 46 74 58 58 49 27 44 86 109 169 312 408 415 571 595 588 699 810 933 1,424 1,640 1225

2000 2002 2004 2006 2008 2010 2012 2014 2016 2018 2020 2022

■ Early syphilis

SYPHILIS

Stages of Syphilis

Treponema pallidum Infection

Primary Syphilis

Secondary Syphilis

Latent Syphilis

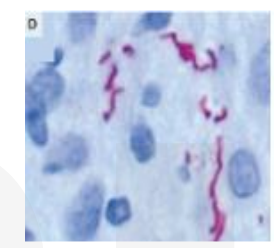
Resolved

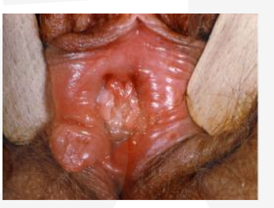
Tertiary Syphilis

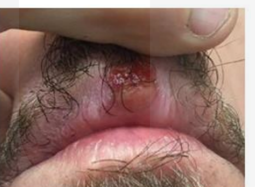
Neurosyphilis
Ocular Syphilis
Otosyphilis

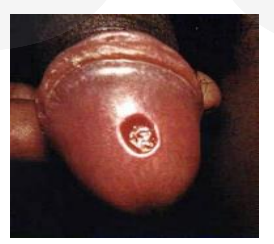
can occur at any stage

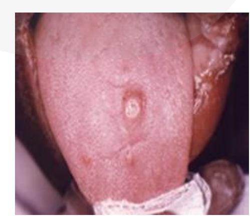
Primary Syphilis











Incubation Period

- 10–90 days post-exposure (avg. 3 wks)

Chancre – Key Features

- Solitary, painless ulcer
- **Clean base** (0.5–2 cm)
- Round or oval shape

⚠ Highly infectious

- Heals in 3–6 weeks

Common Sites

- Genital area
- Rectum
- Oral cavity (oral sex)

Hunter, H. Color Atlas & Synopsis of Sexually Transmitted Diseases, Third Edition. Asai et al. Journal of Medical Case Reports (2020) 14:211. Indian J Sex Transm Dis AIDS. 2014 Jan-Jun; 35(1): 71–73. Ghanem et a Feb 2020. Indian J Sex Transm Dis AIDS. 2014 Jan-Jun; 35(1): 71–73. Ghanem et al . NEJM Feb 2020. https://www.jlgh.org/Past-Issues/Volume-17-Issue-2/Carr_Reese_Syphilis.aspx

Secondary Syphilis

Timing

- Occurs **2–6 weeks** after initial lesion
- ✋ **Rash** involving **palms and soles**

Constitutional Symptoms

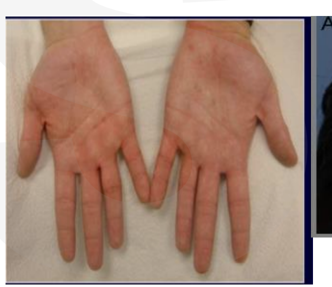
- Lymphadenopathy, fever
- **Condyloma Lata** (wart-like lesions)
- **Mucous patches**
- **Patchy alopecia**
  - ("moth-eaten" hair loss)

Organ Involvement

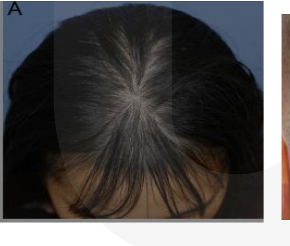
- Nephrotic syndrome or nephritis
- Hepatitis (↑ alkaline phosphatase)

Course

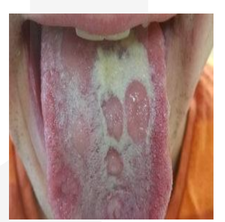
- Resolve **spontaneously in 2–5 weeks**



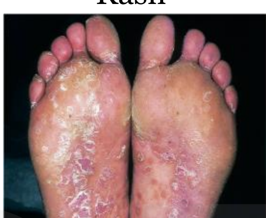
Rash



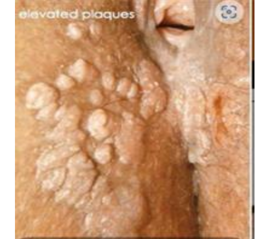
Patchy alopecia



Mucus patches

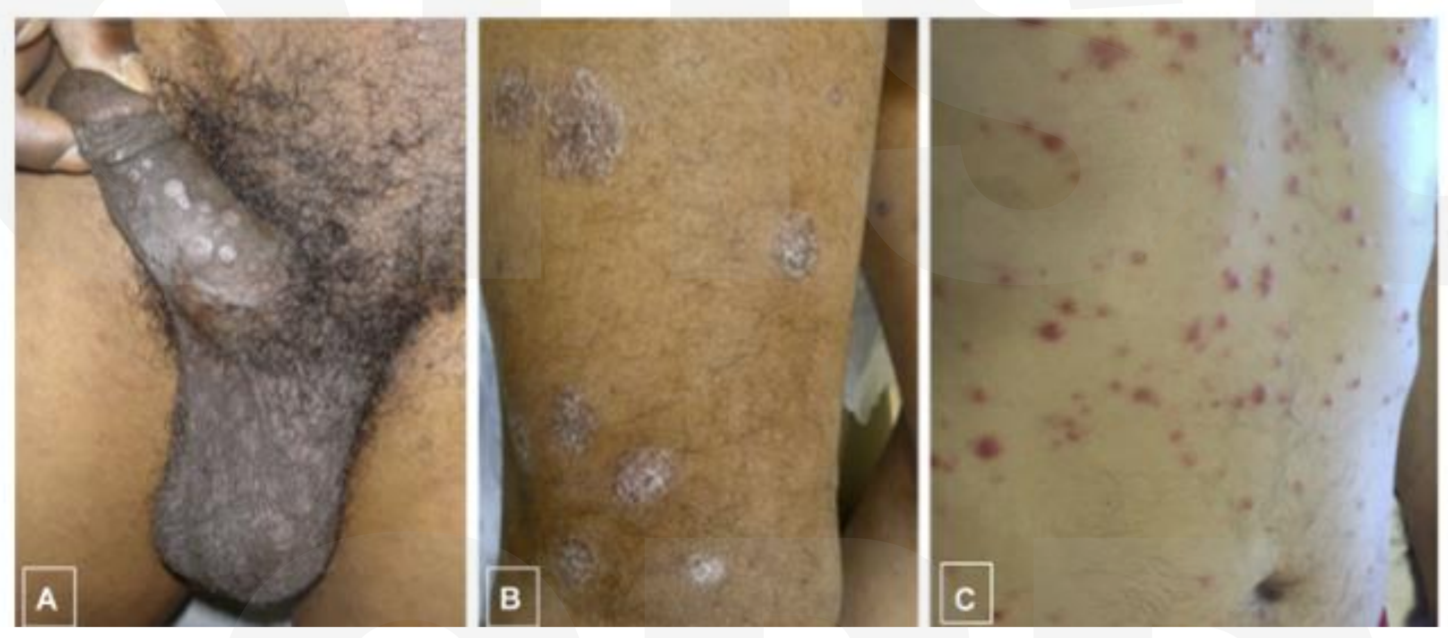


Rash



Condyloma lata

Atypical Secondary Syphilis in People Living with HIV



Morphologies of secondary syphilis: (A) annular, (B) psoriasiform, and (C) nodular.

CNS Invasion Occurs Early in Syphilis—Up to 40%, Often Asymptomatic

Infection

40%

CNS Invasion

10%

Primary
2–6 Wk
after infection

- Chancre
- Regional lymphadenopathy

Concurrent chancre and rash (9%)

Early Latent
- Asymptomatic
- ≤1 Yr after infection

Early Neurosyphilis

Asymptomatic

≤30%

Symptomatic
- Meningeal syphilis
- Meningovascular syphilis

Ocular Syphilis
Otic Syphilis

Secondary
1–2 Mo after
primary syphilis

- Rash
- Fever
- Generalized lymphadenopathy
- Mucosal lesions
- Alopecia
- Hepatitis
- Nephritis

Recurrent secondary syphilis (24%)

Late Latent
- Asymptomatic
- >1 Yr after infection

70%

30%

Late Neurosyphilis

Lifetime Latency
Asymptomatic

Tertiary
2–50 Yr after infection

Gummatous disease (15%)

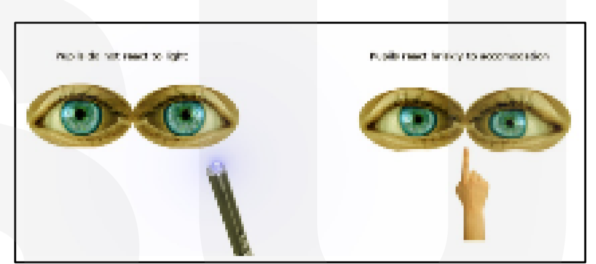
Cardiovascular syphilis (10%)

Ocular syphilis

Otic syphilis

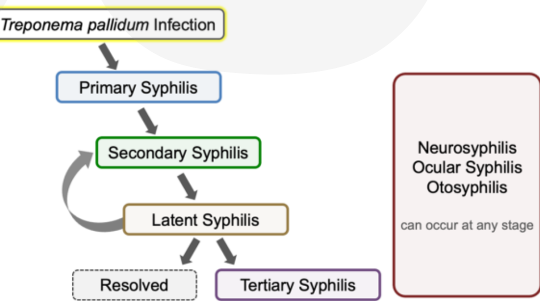
Meningovascular disease, meningomyelitis, general paresis, tabes dorsalis (5%)

Neurosyphilis – CNS Involvement



Neurosyphilis – CNS Involvement

- **Early Neurosyphilis**
- **Meningitis** or stroke
- **Cranial nerve abnormalities** (III, VI, VII, VIII)
- Crosses **blood–brain barrier** → CNS involvement within days



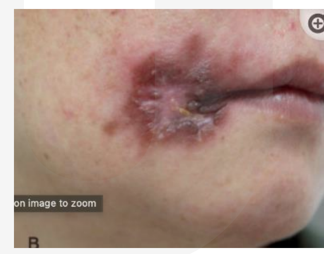
Late Neurosyphilis

- **Tabes dorsalis** (progressive sensory ataxia)
- **Argyll Robertson pupil**: no light response, contracts to accommodation
- **Paresis of the insane**
- Personality changes

Tertiary (Late) Syphilis

Timing

- Appears **10–20 years after initial infection**
- Rare today due to antibiotic treatment



Clinical Manifestations

- **Gummas**:
  - Destructive lesions in skin, bones, or any organ

- **Cardiovascular involvement**
  - Ascending **aortic aneurysm**
  - Aortic valve insufficiency
- **Late neurosyphilis**
  - Lumbar puncture required for all tertiary cases

Adam Inc. Moon et Ann Dermatol. 2018 Dec; 30(6): 749–751.

OR Congenital Syphilis: Highest Case Counts in Recent History

Counts and rates of congenital syphilis infections by year, Oregon 2018-2023

Year	Cases of congenital syphilis	Rate of congenital syphilis
2018	10	23.7
2019	18	43
2020	19	45.4
2021	27	65.7
2022	37	93.7
2023	30	

Left axis: Congenital syphilis cases (0–40)
Right axis: Congenital syphilis cases per 100K live births (0–100)

Oregon in 2024 (a 2,150% increase) and ranked #24 nationally in 2023 based on rates per live births.

OHSU CPD

Congenital Syphilis

Screen at 3 time points

TEST
Test all pregnant women for syphilis at their first prenatal visit

RE-TEST
Re-test women at risk or living in high-burden areas at 28 weeks & again at delivery

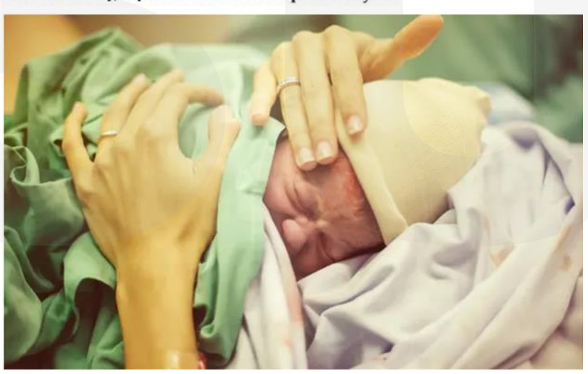
TREAT
Treat* all women with diagnosed or suspected syphilis **immediately** using long-acting benzathine penicillin G; test & treat sex partner(s)

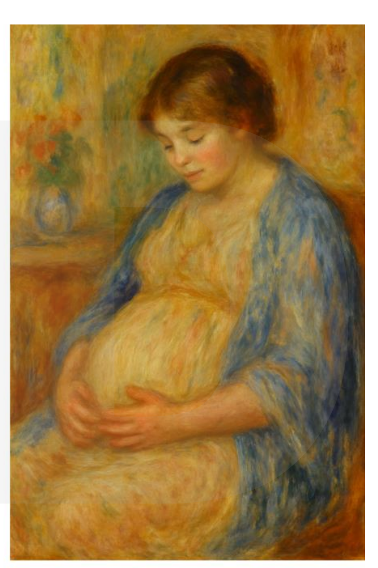
High-Risk Indicators:

- New STI
- New sexual partner
- Multiple sex partners
- **Early Fetal Loss:**
  - **Deaths ≥20 weeks of gestation**

Number of babies born with syphilis in US hits 20-year high, report finds

Centers for Disease Control recorded 918 cases of syphilis in infants in 2017, a 46% increase on the previous year





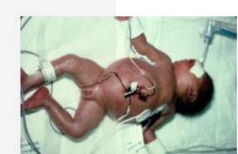
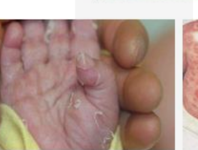
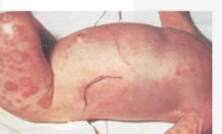
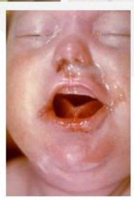
Physical Findings in Congenital Syphilis

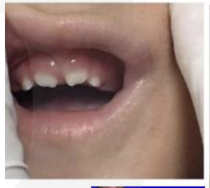
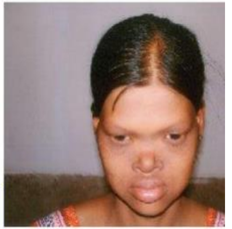
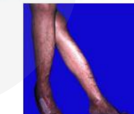
Birth to 2 years

- Hepatomegaly
- Splenomegaly
- Mucocutaneous lesions
- Pneumonia Alba
- Rash
- Edema
- Hemolytic anemia
- Lymphadenopathy
- Snuffles

2 years +

- Interstitial Keratitis
- 8th cranial nerve deficits
- Hutchinson's Teeth [Notched incisors]
- Anterior bowing of shins
- Frontal bossing
- Saddle nose

Rembrandt portrait of fellow Dutch painter Gerard de Lairesse, at age 25 with the **'saddle nose**

Latent Syphilis (No symptoms of syphilis)

Latent Syphilis

- **Host suppresses infection** → asymptomatic
  Occurs **between primary and secondary** stages
- Can also occur **after secondary stage**
- **Need two dates** to confirm duration

Classification

- **Early latent:** < 1 year duration
- **Late latent:** ≥ 1 year duration (not infectious)

Syphilis

Exposure → Primary → Secondary → Latent → 30% → Tertiary

Incubation Period 2-4 weeks

2-6 weeks

Possible relapse

2-20 years

Traditional Testing Algorithm

Non-treponemal test (e.g., RPR)

- Reactive → Treponemal test (e.g., FTA)
  - Reactive → Syphilis
  - Non-reactive → Negative for syphilis
- Non-reactive → Negative for syphilis

Timing of Syphilis Tests

Treponemal antibodies
Nontreponomal (lipoidal antigen)

Early syphilis
Laten syphilis
Late syphilis

No treatment
Treated and seroreverted
Treated but serfast

Patients who test positive (%)
100
80
60
40
20
0

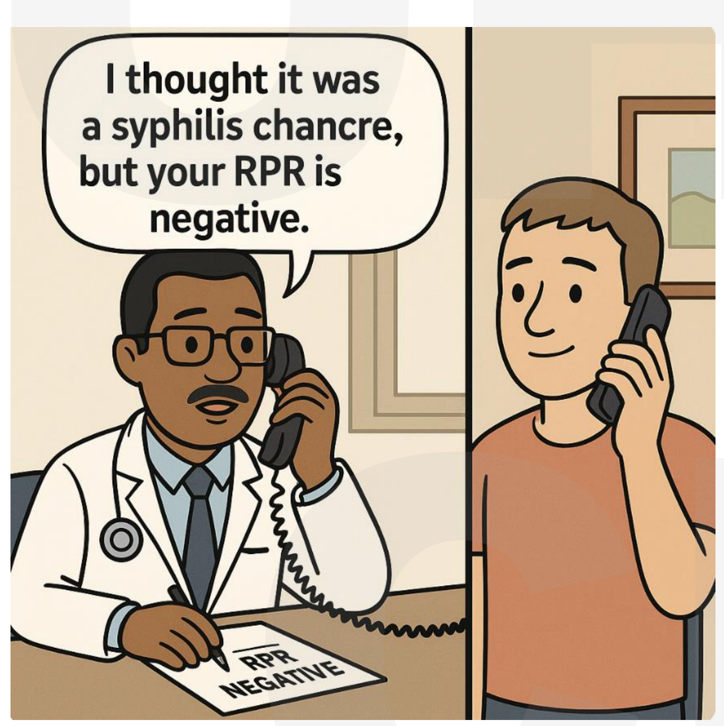
2 weeks
4 weeks
6 months
6 monts
1 year

Time

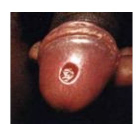
Treponemal antibodies appear earlier than nontreponemal [RPR]

Seña AC, White BL, Sparling PF. Novel *Treponema pallidum* serologic tests: a paradigm shift in syphilis screening for the 21st century. Clin Infect Dis. 2010;51:700-8.

Sensitivity & Specificity of Tests in Untreated Syphilis Stages

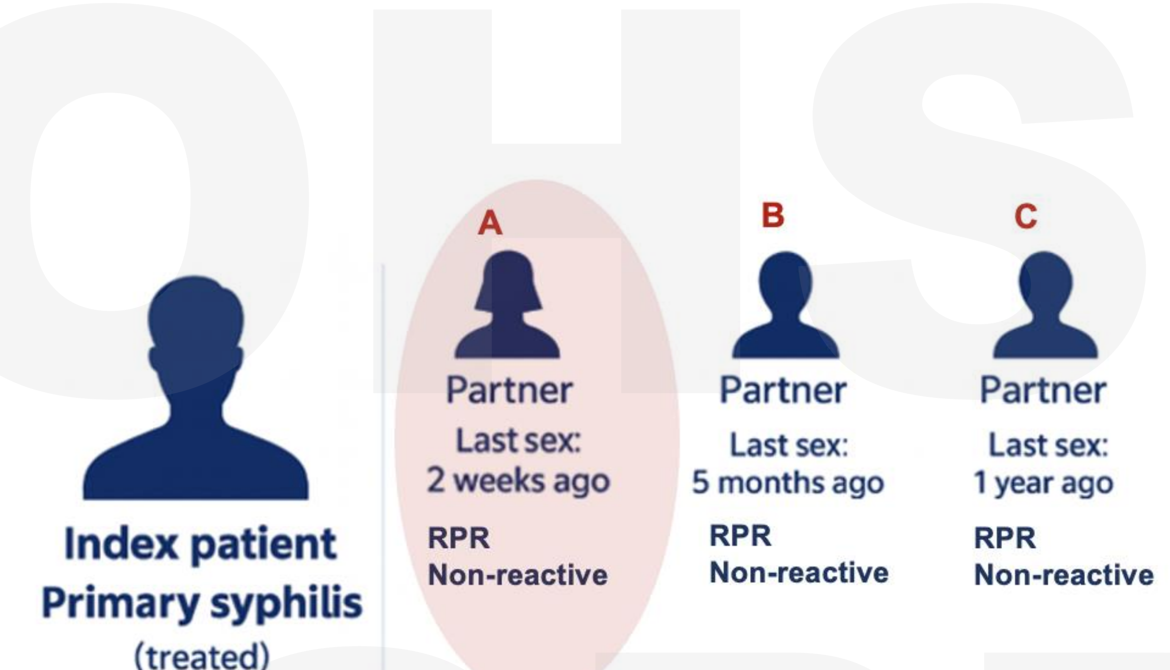


Test	Primary	Secondary	Latent	Late	Specificity (% range)
VDRL	78 (74–87)	100	96 (88–100)	71 (37–94)	98 (96–99)
RPR	86 (77–99)	100	98 (95–100)	73	98 (93–99)
FTA-ABS	84 (70–100)	100	100	96	97 (94–100)
TP-PA	88 (86–100)	100	100	NA	96 (95–100)
ELISA (IgG)	100	100	100	NA	100



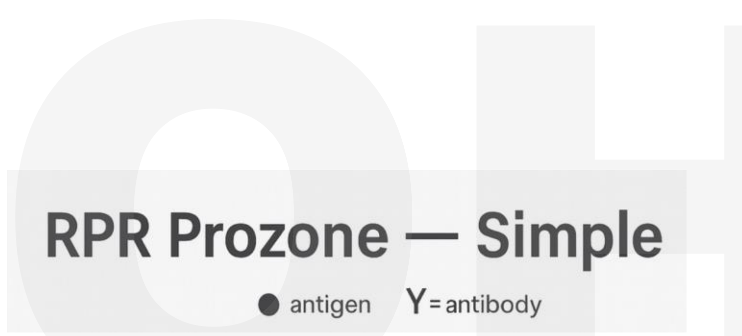
Seña AC, White BL, Sparling PF. Novel *Treponema pallidum* serologic tests: a paradigm shift in syphilis screening for the 21st century. Clin Infect Dis. 2010;51:700-8.

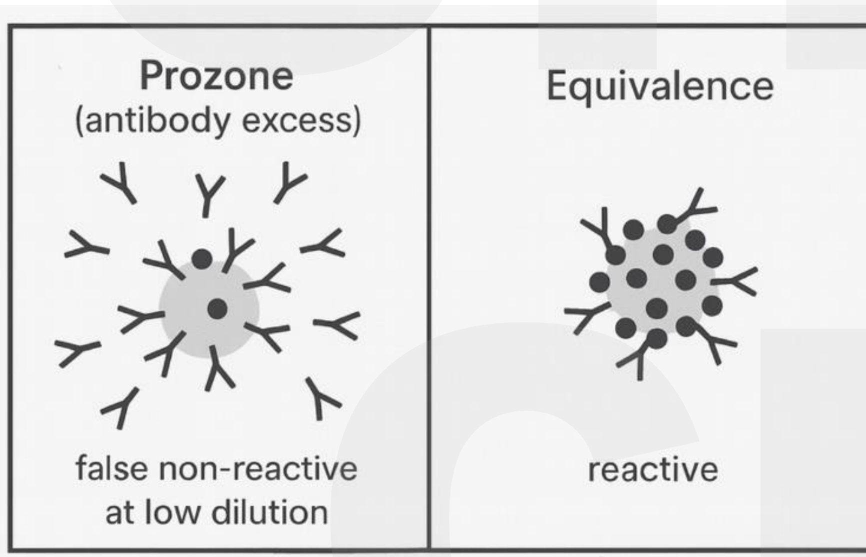
Syphilis Exposures



- Treat partners within **90 days** of exposure to someone with **primary, secondary, or early latent syphilis**
- **RPR may be falsely negative** during early infection
- **Get RPR w/in 7 days of Treatment**

False Negative RPR





Prozone phenomenon in secondary syphilis with HIV co-infection: Two cases

Praneet Awake [1], Kalpana Angadi [2], Sourav Sen [2], Prasad Bhadange [1]

Affiliations + expand

PMID: 36743087 PMCID: PMC9891016 DOI: 10.4103/ijstd.ijstd_43_22

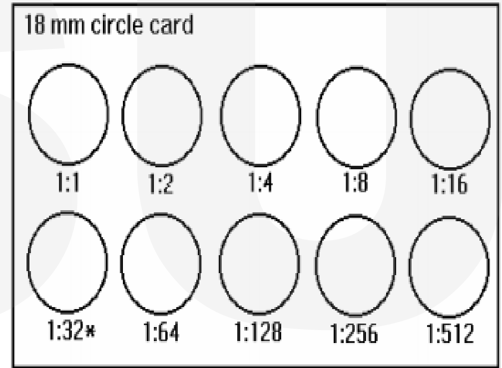
Free PMC article

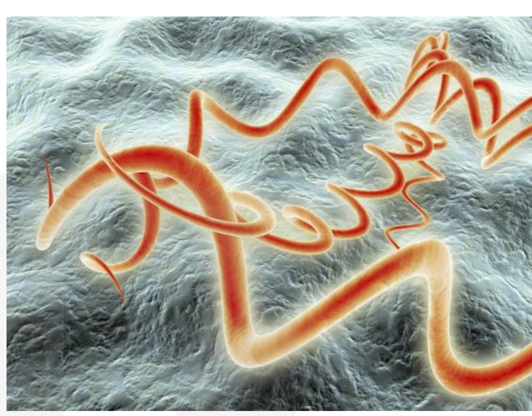
- **Prozone = antibody excess**
  - **→ false NR or /low RPR.**
- **Mechanism:** antibodies saturate antigen → **no lattice formation**, no visible charcoal flocculation.
- **Fix:** ask lab for **serial dilutions (≥1:16–1:64)** to reveal true reactivity.

Non-Treponemal Tests (Screening)

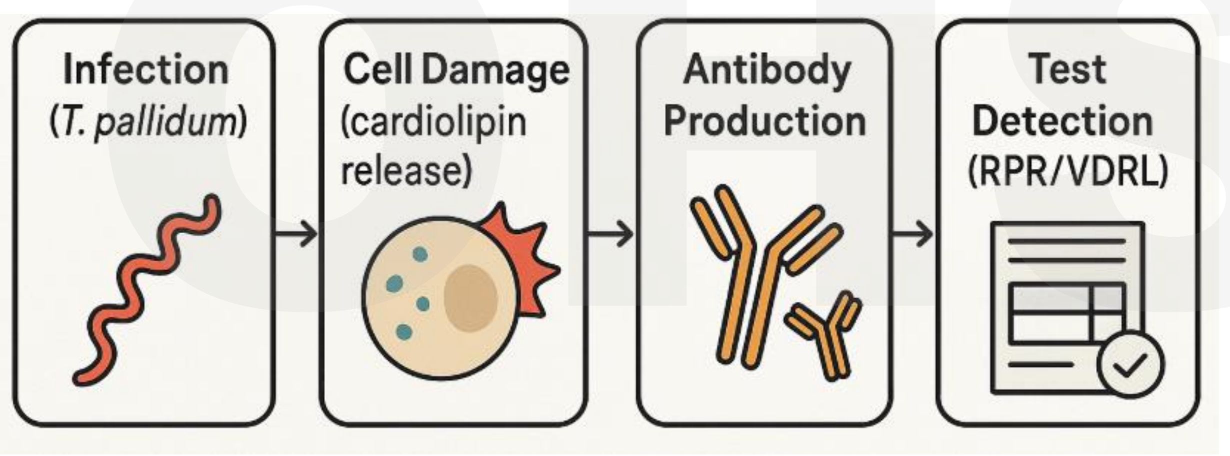
🧪 **Nontreponemal Tests:**

- **VDRL & RPR**
- **Rapid & Cost-Effective**
- Low-cost, fast turnaround
- **Screening** and **treatment monitoring**
- **Non-Specific**
  - False Positives:
    - Autoimmune conditions
    - Pregnancy
- **Quantitative Titers**
  - Ratios (e.g., **1:8**)
  - **Titer declines** after treatment
    - (e.g., **1:8** → **1:2** after therapy)
  - Non-reactive test may take **years**





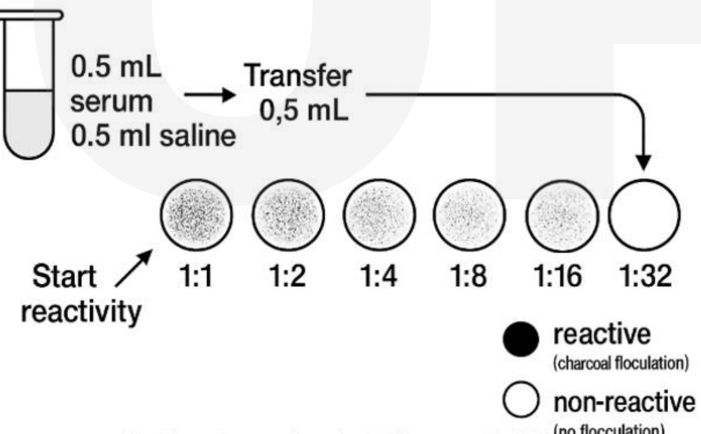
What is an RPR? (Nonspecific)



Disease	RPR/VDRL
Autoimmune Diseases	Yes
Dermatologic Diseases	Yes
Drug Abuse	Yes
Febrile Illness	Yes

- Antibodies to **cardiolipin are released by cell damage**
- **Not specific** → false positives
  - Used for **screening** and **treatment monitoring**
  - False +: **autoimmune, pregnancy**
  - Confirm with a **Treponemal test (TP-PA or FTA)**

RPR testing



- Blood sample collected
- Patient serum mixed with cardiolipin antigen on test card
  - **Reactive:** clumping
  - **Non-reactive:** smooth background
- Reactive → perform serial dilutions (1:2, 1:4, 1:8, etc.) to determine titer

Treponemal Tests: Confirmatory

Treponemal Tests

- **EIA, FTA-ABS, TP-PA**
  - Detects **T. pallidum antibodies**
  - **3–4 weeks post-infection (+)**

Peak Sensitivity

- Positive for life
- **Remains reactive after treatment**
- ⚠️ **Not used** for monitoring treatment response
- ❌ Titers do **not** decline over time

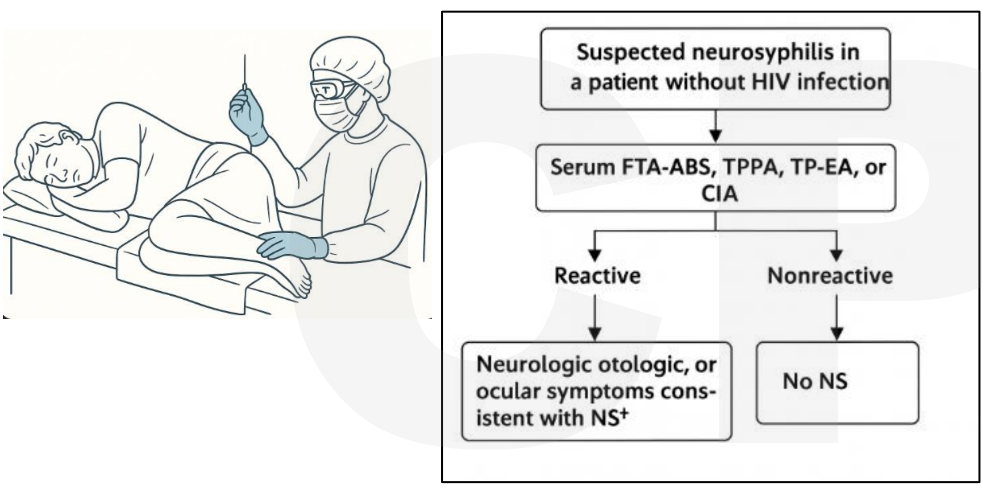
Clinical Snapshot

- *Jan 2022:* RPR 1:16 → **TP-PA** + → treated
- *Nov 2023:* RPR non-reactive → **TP-PA+**

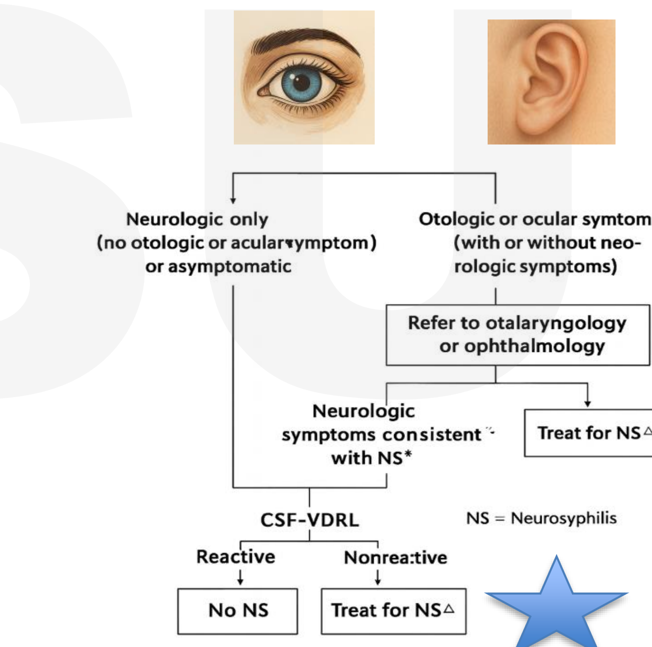
Treponemal Test

Neurosyphilis: Diagnosis

- **VDRL-CSF**: very insensitive
- **Non-treponemal tests**: often negative
- **CSF WBC count**
  - 5 WBCs/mm³ → HIV–
  - 20 WBCs/mm³ → HIV+
- **Repeat LP**: not needed if serologic response adequate
- *Exception*: HIV+ and off treatment



Hearing & Vision

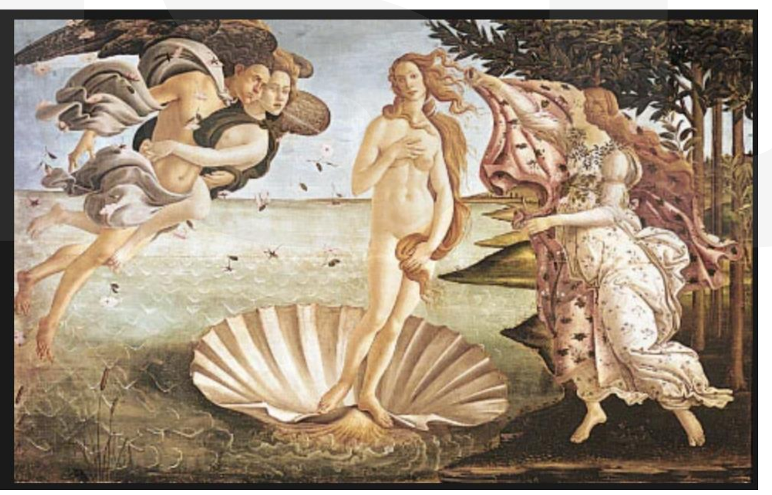


- **Otosyphilis & Isolated ocular symptoms.**
- **LP is *not required*** (if CN *normal)*
- Treat with IV PCN

Treatments for syphilis

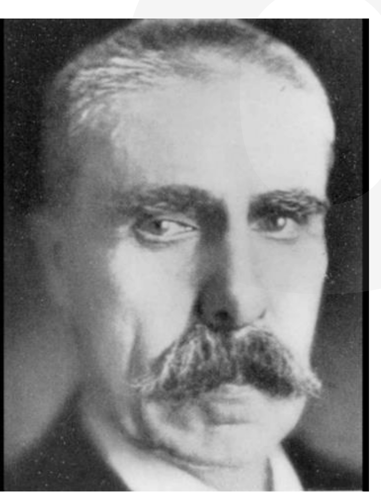
"A night with Venus, a year with mercury "

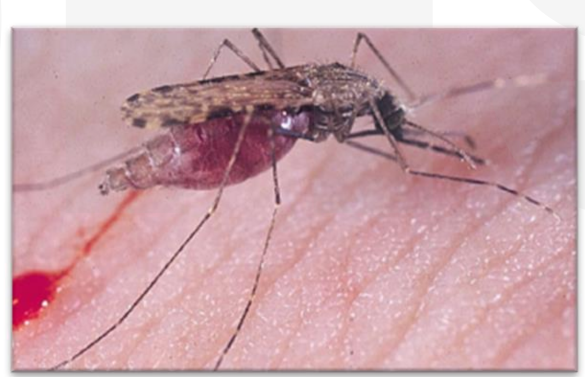
SOURCE: MUSEUM OF THE ROYAL PHARMACEUTICAL SOCIETY

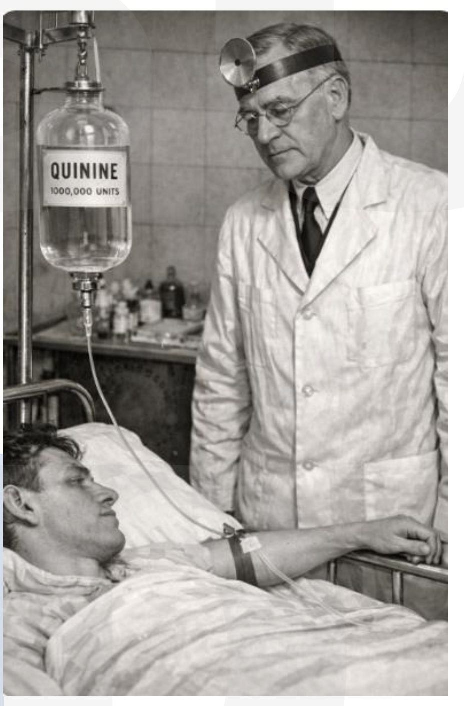


Sandro Botticelli: Birth of Venus Birth of Venus, tempera on canvas by Sandro Botticelli, c. 1485; in the Uffizi Galle

Fun Syphilis Fact. What is Malariotherapy?







Plasmodium Vivax malariotherapy

- 1927: Nobel Prize to Julius Wagner-Jauregg
- Treated neurosyphilis with **Plasmodium vivax** malaria
- Fevers sometimes improved symptoms
- Stopped after 1940s: **penicillin safer, effective**

Syphilis Treatment

Early Syphilis

- *Primary, Secondary, Early Latent*
  - **Benzathine Penicillin G**:
    - 2.4 million units IM × 1
    - **Non-pregnant**: . Doxycycline 100 mg × 14 days

Late Latent Syphilis

- **Benzathine Penicillin G**:
  - 2.4 million units IM weekly × 3 doses
  - **Non-pregnant**: Doxycycline 100 mg × 28 days
- **Pregnancy**: Desensitize → treat with Penicillin

Tertiary Syphilis

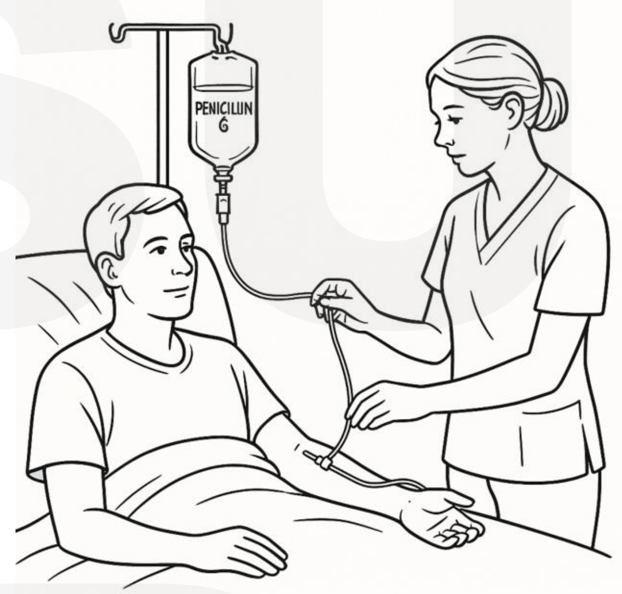
- **Benzathine Penicillin G**:
  - 2.4 million units IM weekly × 3 doses
  - R/o Neurosyphilis in ALL cases.

Neurosyphilis Treatment

Preferred:
- Aqueous PCN G 3–4 million units IV every 4 hrs
- (or continuous infusion 18–24 million units/day
    - Duration -10–14 days

Penicillin Allergy
- If allergic to PCN: desensitize and treat with IV penicillin when possible

Alternative: ‡
- Ceftriaxone 2 g IV daily for 10–14 days
    - Limited data in People living with HIV



Syphilis Follow-Up: RPR Testing

Primary & Secondary

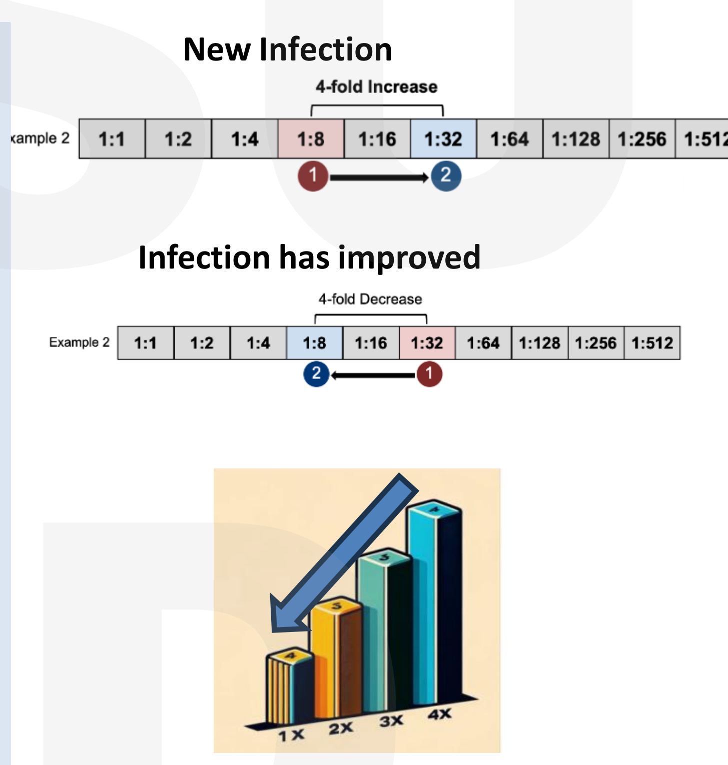
- PLWH: 3, 6, 12, 24 months
- HIV-negative: 6, 12 months

Early Latent

- PLWH: 3, 6, 12, 24 months
- HIV-negative: 6, 12 months

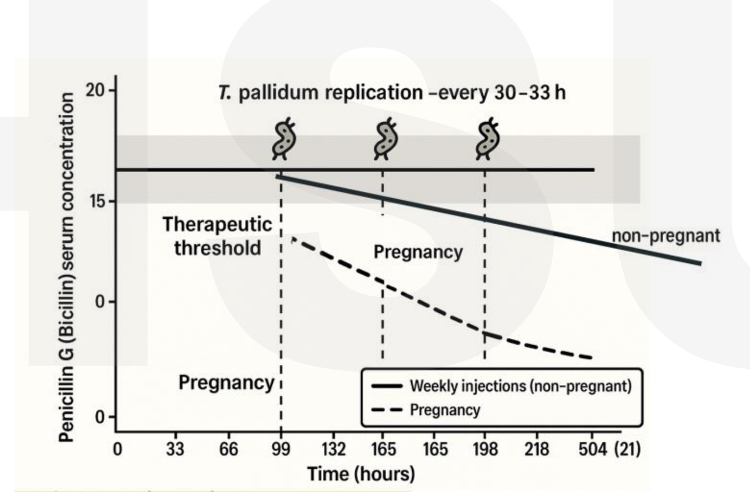
Late Latent / Unknown

- PLWH: 6, 12, 18, 24 months
- HIV-negative: 6, 12, 24 months



PLWH – People living with HIV

Missed Doses: Timing Limits for Late Latent Treatment



Late Latent Syphilis (3 Weekly Doses)

Pregnant

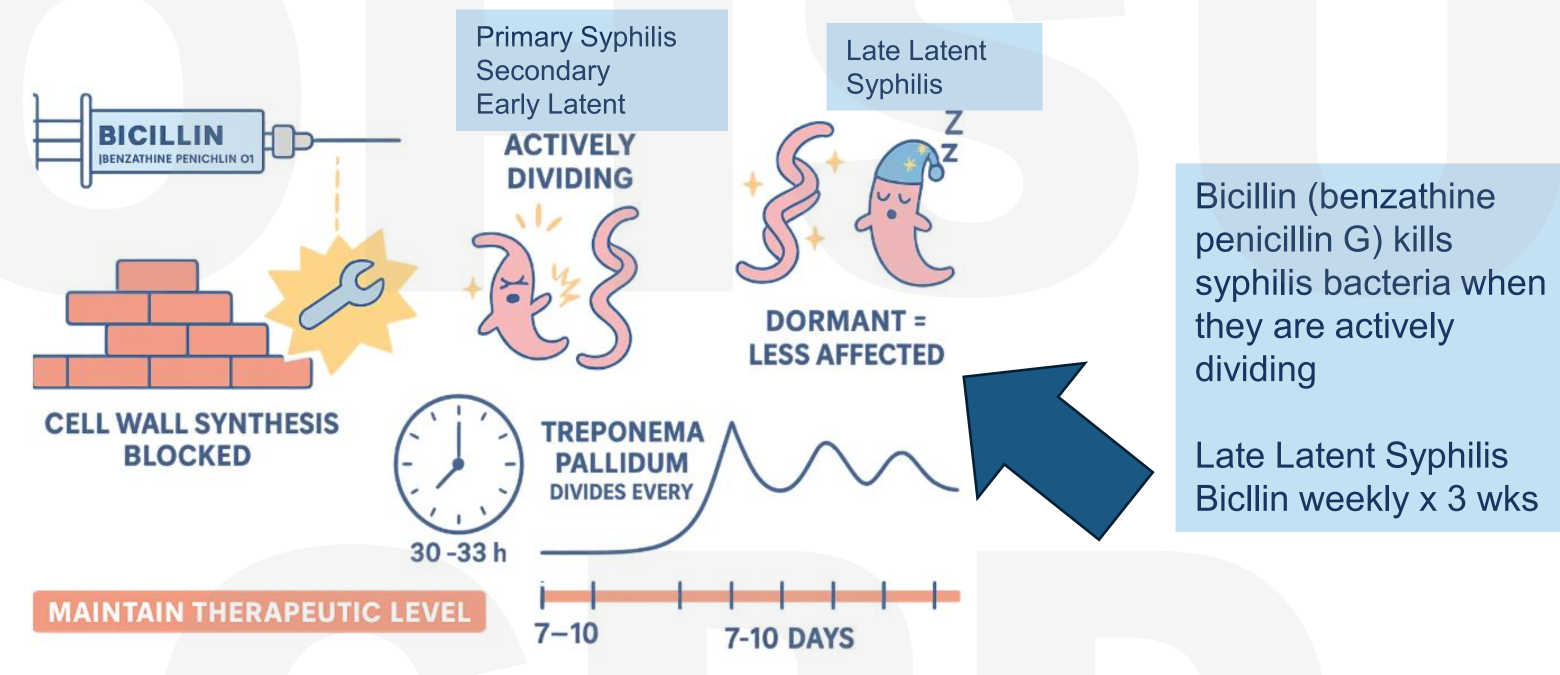
- **Bicillin L-A** every **7–9 days** (due to increased volume distribution)
- **Do not exceed >9 days** between doses in pregnancy — drug levels fall too low
- **Restart treatment** if a pregnant pt misses a dose >9 days

Not Pregnant

- **10–14 days** between doses may be ok before restarting
- **Do not mix regimens:** between **penicillin** and **doxycycline** – no data

Fretz G, et al.Penicillin Concentrations in Blood and Spinal Fluid After a Single Intramuscular Injection of Penicillin G Benzathine. Eur J Clin Microbiol 1984; 3:147-149

Bicillin: Kills Syphilis Only When It's Dividing



Primary Syphilis
Secondary
Early Latent

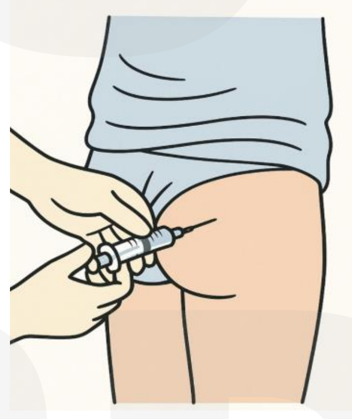
Late Latent
Syphilis

Bicillin (benzathine penicillin G) kills syphilis bacteria when they are actively dividing

Late Latent Syphilis
Bicllin weekly x 3 wks

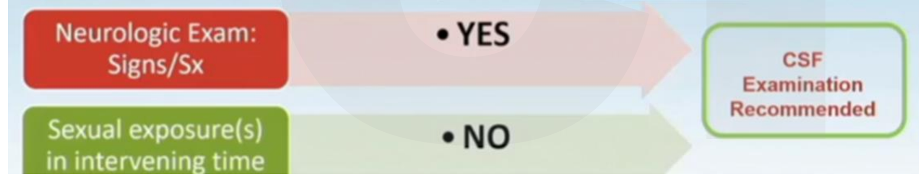
Jarisch-Herxheimer Reaction

- Self-limited inflammatory response
- Endotoxins from dying treponemes
- Fever, chills, malaise, HA, myalgias
- Usually ~ 24 hrs. of the 1st dose
- **Treat :** antipyretics (e.g., acetaminophen or NSAIDS)
- Pregnancy: → may precipitate early labor

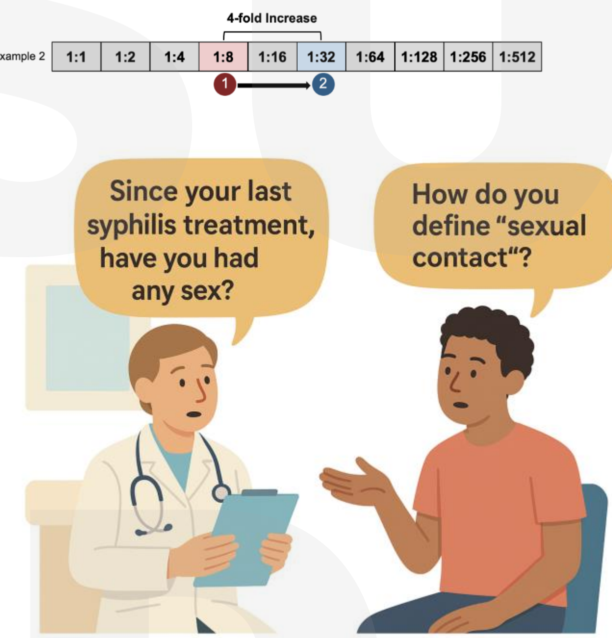


Getting an LP: Treatment Failure in Syphilis

Definition	Recurrence or persistence of clinical signs & symptoms after treatment
Causes	Inadequate treatment, **re-infection**, neurosyphilis
Evaluation	LP for neurosyphilis Retreat if new infections



New Infection



Pitfalls Interpreting RPR Results
“ Titers not going down”

Reasons RPR May Not Fall

⏳ **Too Soon**

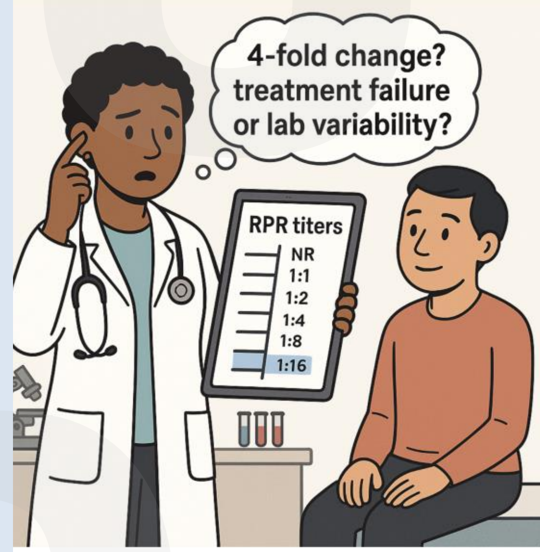
- Don’t check response until **6,12 months (…early syphilis ,)**

🔁 **Over-Testing**

- Checking too often after treatment → confusing results.
  Wait for the right follow-up time.

🧪 **Lab Variability**

- Titers can vary slightly between labs.



Syphilis and Missing information are confusing

Date	RPR Titer
1/2022	NR
6/2022	1:128
1/2023	1:64
1/2024	1:4

Date	RPR Titer
1/2022	NR
6/2022	1:128
1/2023	1:64
6/2023	1:1
1/2024	1:4

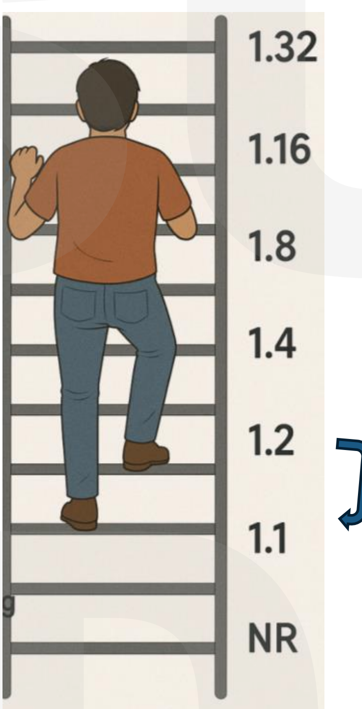
Missing info

4X increase
New infection

Serologic Failure in Syphilis

	Serologic Failure
Definition	• No 4-fold RPR drop by • 12 mo (early) or • 24 mo (late); • no symptoms. • 1:2→ 1:1
Causes	Low starting titer (late latent), older age, HIV, lab variability.
Evaluation	Consider LP if titer ≥1:32 persists >2 years.

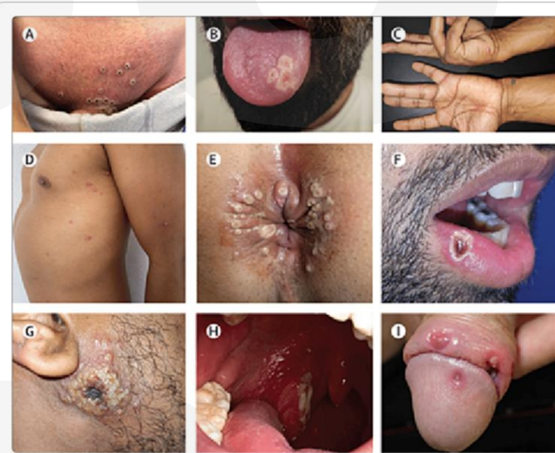
1:1	1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512



OHSU
CPD

Mpox (not an STI) but may look like STI

Category	Details
Mpox Symptoms	Anorectal pain, tenesmus, rectal discharge, bleeding w/peri-anal lesions



Who should be offered the Vaccine ?

- History of STI
- People taking PrEP
- People living with HIV
- People doing sex work
- Anyone who asks

Mpox Vaccine: JYNNEOS

Dosing Schedule

- 2-dose series, 28 days apart
- Live attenuated vaccinia virus (non-replicating)

Dorkin. CROI 2023. Patel A, Bilinska J, Tam JC, et al.: . BMJ. 2022, 378:e072410. 10.1136/bmj-2022-072410

STI Prevention –DoxyPEP

Timing & Dosage

- Take 200 mg doxycycline within 72 hours (ideally <24h) after condomless sex
- Max 200 mg every 24 hours

Eligibility Criteria

- Assigned male at birth
- Living with HIV or on PrEP
- ≥1 STI in past 12 months
- Condomless sex w ≥1 male partner in past year

Prescription Instructions

- Take 2 tablets after sex (within 24–72 hrs)
- Rx. Limit to 1 dose/24 hrs; # 60
- Discuss side effects

Infection	Risk Reduction (PrEP)	Risk Reduction (PLWH)
Gonorrhea	55% (CI: 35–68%), p<0.0001	57% (CI: 29–74%), p=0.001
Chlamydia	88% (CI: 75–95%), p<0.0001	74% (CI: 43–88%), p=0.0007
Syphilis	87% (CI: 41–97%), p=0.0084	77% (CI: 71–96%), p=0.095

Leutkemyer et al. N Engl J Med. 2023 Apr 6; 388(14): 1296–1306, Stewart et al. **December 20, 2023 N Engl J Med 2023;389:2331-2340**

PrEP OPTIONS

TDF/FTC
daily
oral pill

TAF/FTC
daily
oral pill

cabotegravir
injection
every 2 months

lenacapavir
injection
every 6 months

Which
is right
for me?

PrEP Candidates

Anal or vaginal sex in past 6 months?

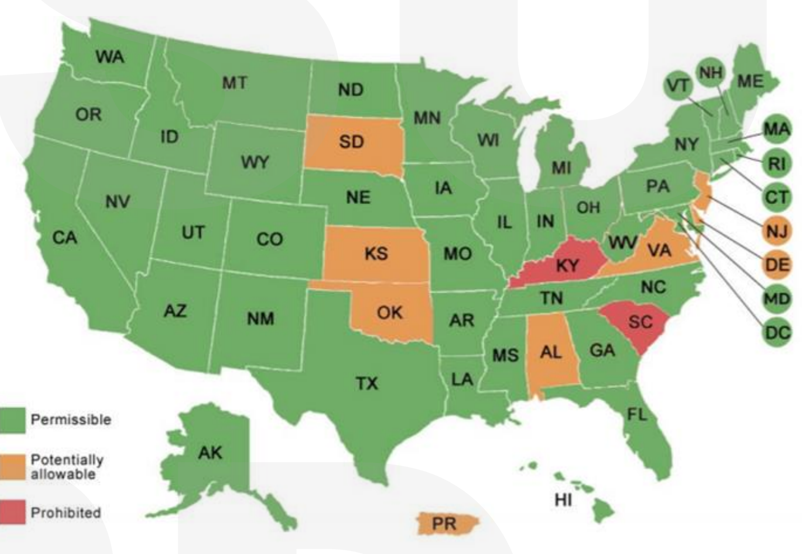
- Yes →
  - HIV+ Partner?
    - Yes → Unknown or detectable viral load?
      - Yes → Prescribe PrEP
      - No → Discuss PrEP Prescribe if requested
    - No → Discuss PrEP Prescribe if requested
  - 1 or more sex partners of unknown HIV status?
    - Yes → Always used condoms?
      - No → Prescribe PrEP
      - Yes → Discuss PrEP Prescribe if requested
    - No → Discuss PrEP Prescribe if requested
  - Had bacterial STI in past 6 months?
    - Yes →
      - MSM: GC, chlamydia, or syphilis?
        - Yes → Prescribe PrEP
        - No → Discuss PrEP Prescribe if requested
      - MSW and WSM: GC or syphilis?
        - Yes → Prescribe PrEP
        - No → Discuss PrEP Prescribe if requested
    - No → Discuss PrEP Prescribe if requested
- No → Discuss PrEP Prescribe if requested

Risk Factor	Population
HIV+ partner with unknown or detectable viral load*	All
Multiple partners of unknown status	All
Inconsistent condom use	All
Recent STI (GC, chlamydia, syphilis)	All

Risk Factor	Population
GC, chlamydia, or syphilis in past 6 months	MSM
GC or syphilis in past 6 months	MSW / WSM
Injection drug use	People who inject drugs

https://www.hivprep.uw.edu/ * U= U

Expedited Partner Therapy



Summary

1. Screen all patients for STIs without judgment and prejudice
2. Diagnosis of STIs can be challenging as may present similarly
3. Remember updated guidelines for GC TOC pharyngeal infections
4. Syphilis: take a thorough neurological assessment and treat immediate for ocular and Otic syphilis if no other CN deficits
5. Treat for Neurosyphilis if isolated otic/ocular syphilis
6. Prevention: PrEP discussion for HIV negative patients & also Mpox Vaccine and HPV (based on age) for those at risk for STIs
7. Consider DoxyPEP in high risks individuals (MSM, TGW) increased risk for STIs

Thanks for Listening
Questions?

Contact: evanch@ohsu.edu