Syphilis

Jacob McLean, DO
Adult Infectious Diseases
Assistant Professor of Medicine at Columbia University Medical Center
NYC STD Prevention Training Center
jm5146@cumc.columbia.edu

Disclosures

- The author and their spouses/partners wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters.

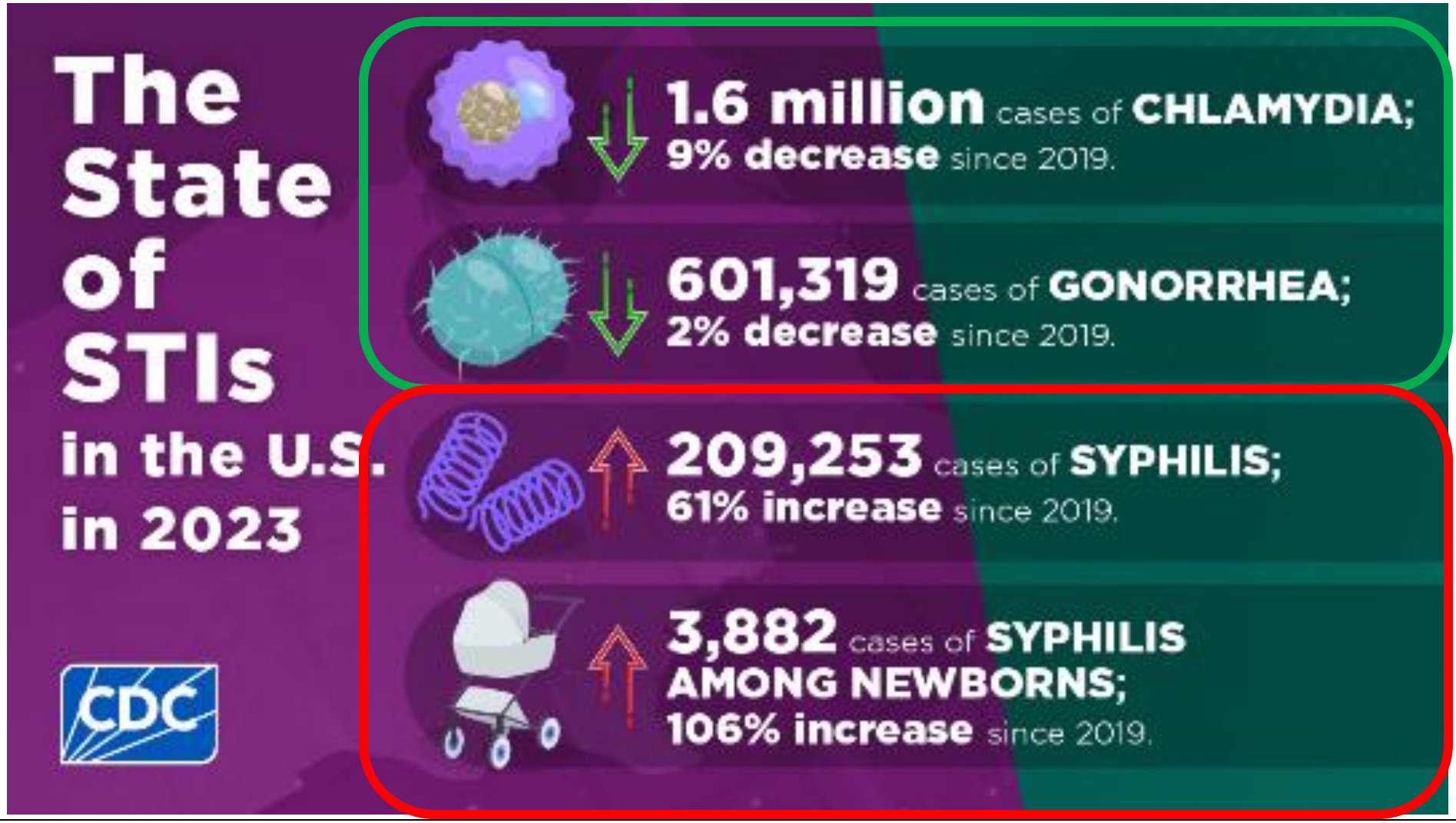
Objectives

1. Recognize the burden of syphilis
2. Identify the stages of syphilis infection
3. Interpret syphilis serologic tests
4. Determine appropriate syphilis treatments by stage
5. Summarize changes in syphilis diagnosis and treatment in special cases

Not covered

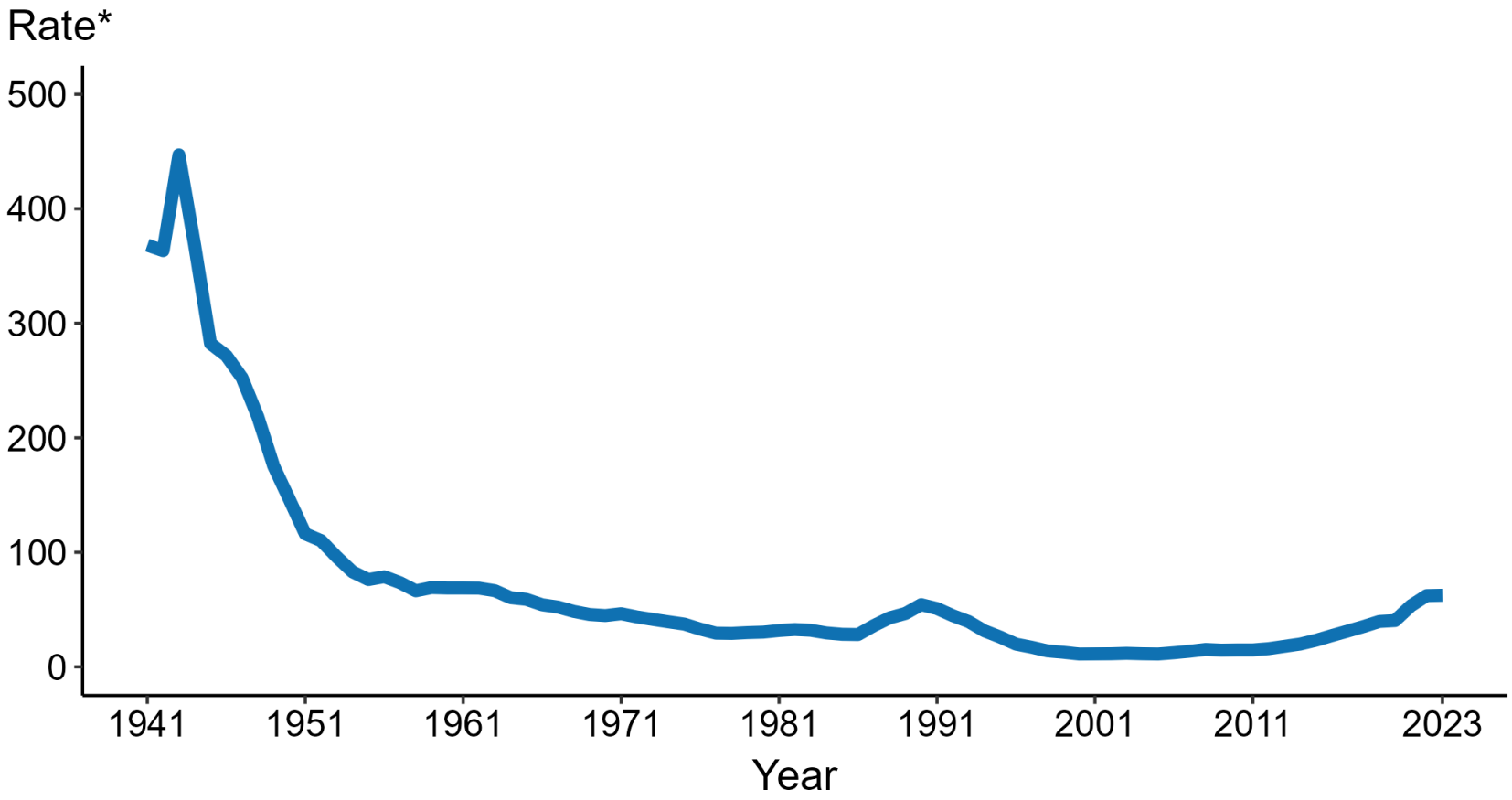
- Congenital syphilis
- Syphilis in pregnancy
- Syphilis prevention e.g. Doxy PEP

Bacterial STIs—a surging public health concern



- *Sexually Transmitted Infections Surveillance, 2023. Centers for Disease Control and Prevention*

Syphilis – bouncing back



* Per 100,000

NOTE: Includes all stages of syphilis and congenital syphilis.

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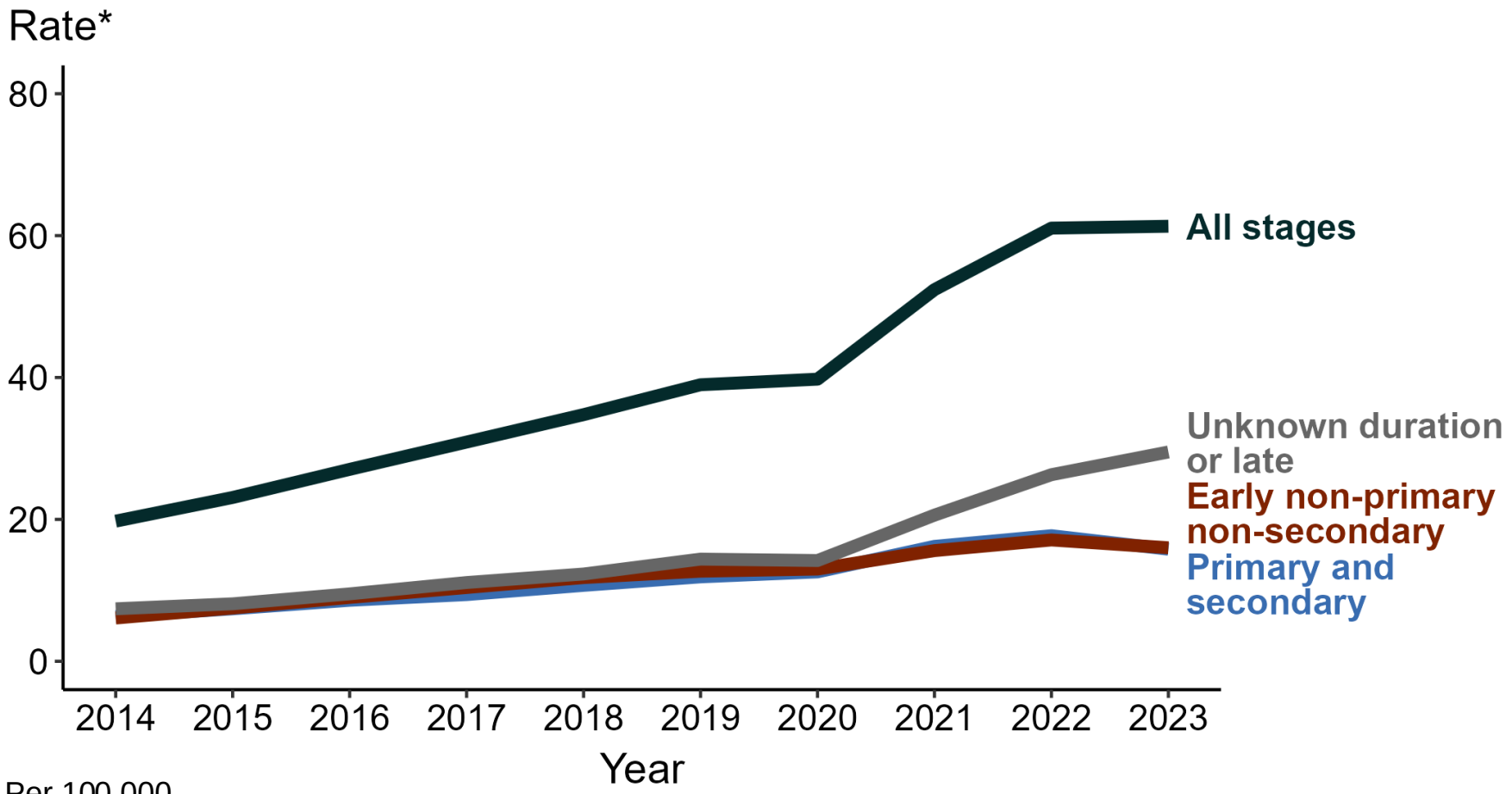
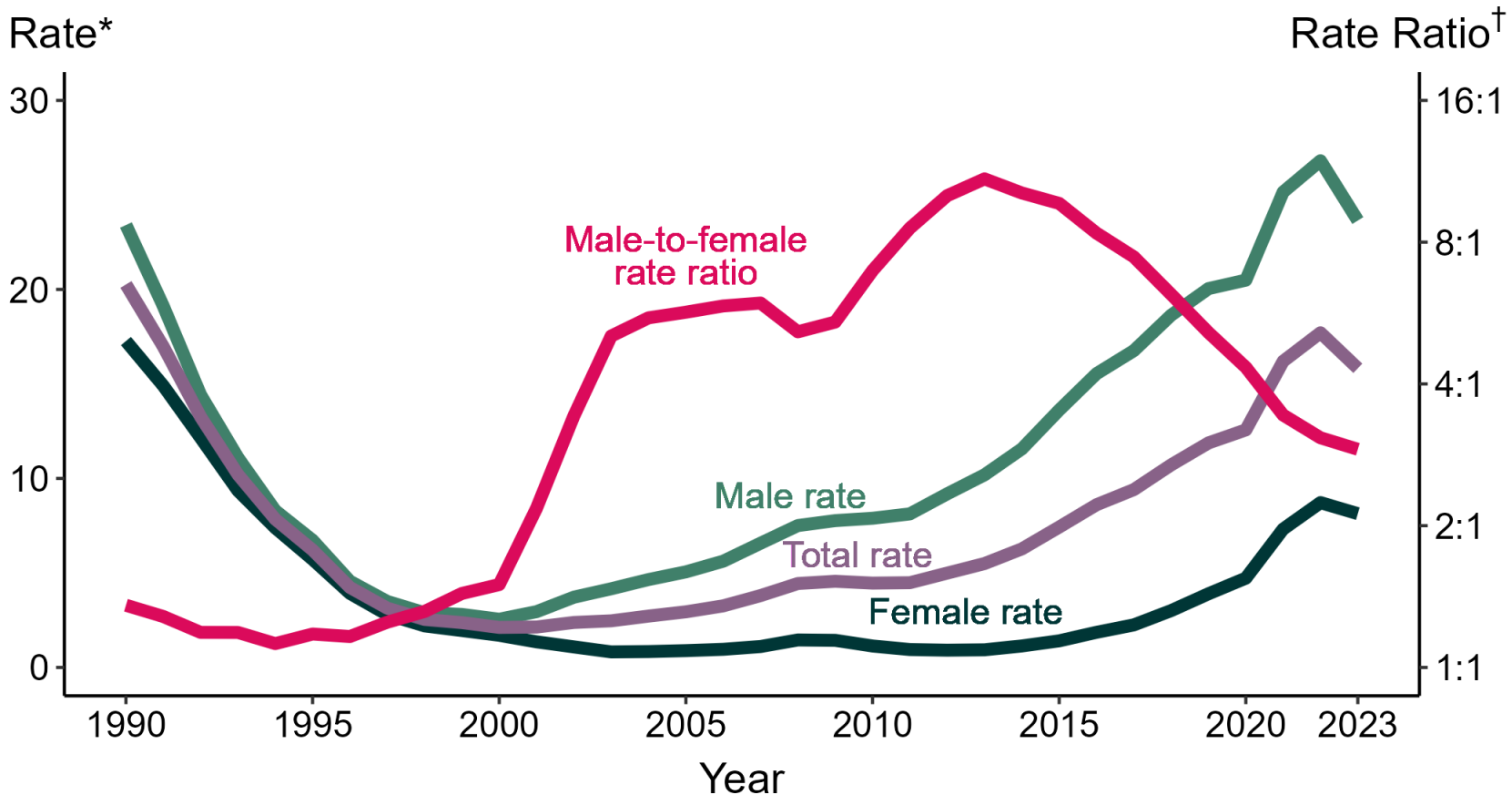
Syphilis — Rates of Reported Cases by Stage of Infection and Year, United States, 2014–2023



* Per 100,000

NOTE: "All stages" includes cases of syphilis reported as primary, secondary, early non-primary non-secondary, or unknown duration or late.

Primary and Secondary Syphilis — Rates of Reported Cases by Sex and Male-to-Female Rate Ratios, by Year, United States, 1990–2023



* Per 100,000

† Log scale

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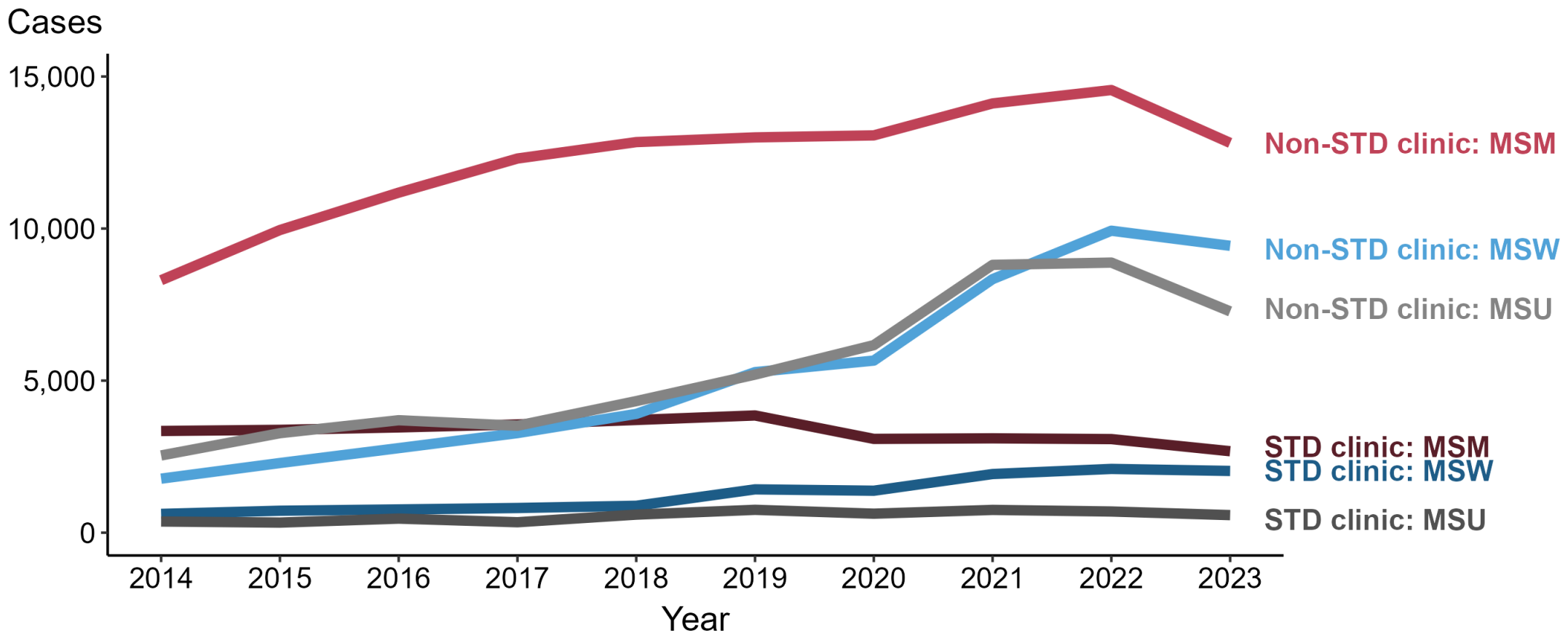
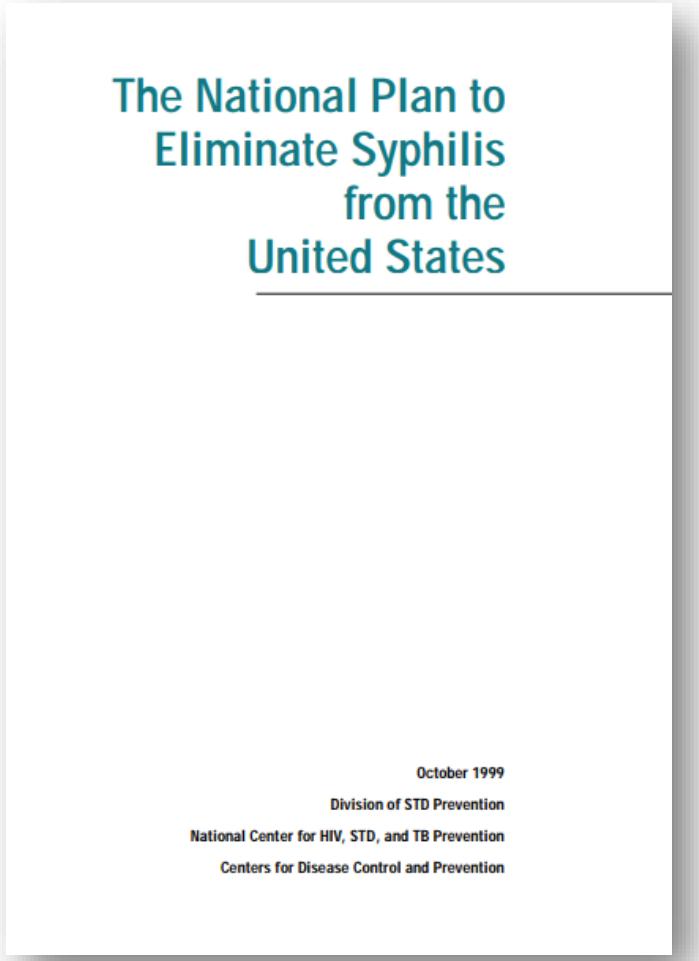
Primary and Secondary Syphilis — Reported Cases among Men by Reporting Source and Sex of Sex Partners and Year, United States, 2014–2023



ACRONYMS: MSM = Men who have sex with men; MSW = Men who have sex with women only; MSU = Men with unknown sex of sex partners

NOTE: During 2014 to 2023, the percentage of all male cases with unknown reporting source was 10.4%, from a low of 6.6% (n = 1,201) in 2014 to a high of 12.6% (n = 3,777) in 2018.

The National Plan to Eliminate Syphilis


The National Plan to Eliminate Syphilis from the United States

October 1999

Division of STD Prevention

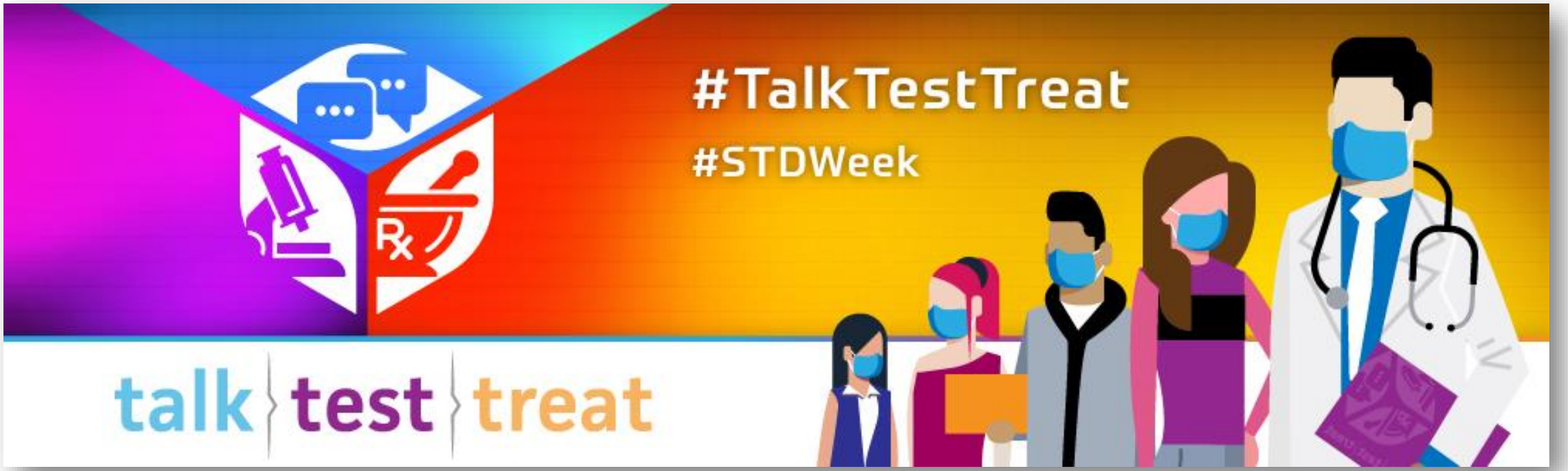
National Center for HIV, STD, and TB Prevention

Centers for Disease Control and Prevention

As we approach the end of the 20th century, the United States is faced with a unique opportunity to eliminate syphilis within its borders. Syphilis is easy to detect and cure, given adequate access to and utilization of care. Nationally, it is at the lowest rate ever recorded and it is confined to a very limited number of geographic areas, primarily in the southern United States. Where syphilis does persist in the U.S., it disproportionately burdens African Americans living in poverty. Syphilis elimination is not only feasible, but also can have far-reaching public health implications by removing its devastating consequences—increased likelihood of HIV transmission and spontaneous abortions, stillbirths, and multi-system disorders caused by congenital syphilis acquired from mothers with syphilis.

- https://www.cdc.gov/stopsyphilis/exec.htm

What can we do?

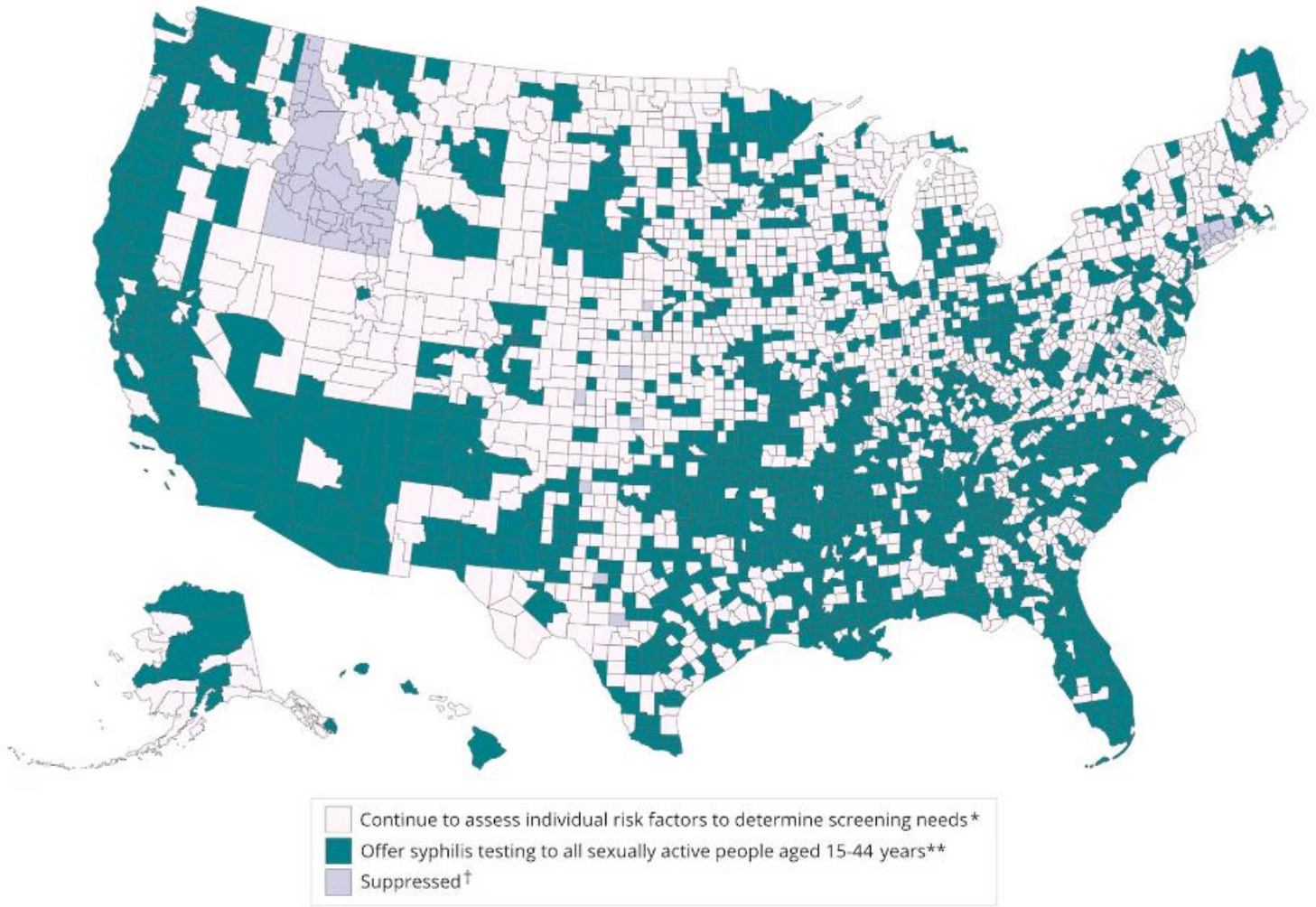


General Screening for Syphilis

Population	Recommendations
Men who have sex with men	• At least annually if sexually active • Every 3-6 months based if increased risk*
Transgender and Gender Diverse People	• Consider screening at least annually based on reported sexual behaviors and exposure
Patients taking PrEP	• At initiation and every 3-6 months if increased risk*
Persons living with HIV	• At diagnosis and at least annually if sexually active, and more frequently depending on individual risk and local epidemiology*
Non-pregnant Women (Cis-gender) and Non-MSM Men	• No national recommendation for **routine** screening • Screen asymptomatic adults at increased risk*
Pregnant Women	• First prenatal encounter plus third trimester (28 weeks) and at delivery if increased risk or in a community with increased prevalence***

• Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1-187. Published 2021 Jul 23. doi:10.15585/mmwr.rr7004a1

Syphilis rates are high (almost) everywhere

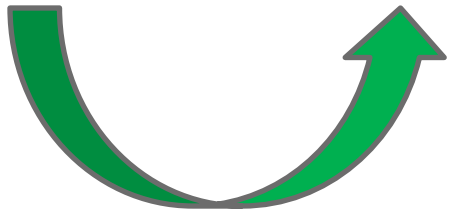


- Counties with syphilis rates >4.6 per 100,000 among females 15-44
- **72%** of the US population

McDonald R et al. *Vital Signs*: Missed Opportunities for Preventing Congenital Syphilis — United States, 2022. MMWR Morb Mortal Wkly Rep 2023;72:1269–1274

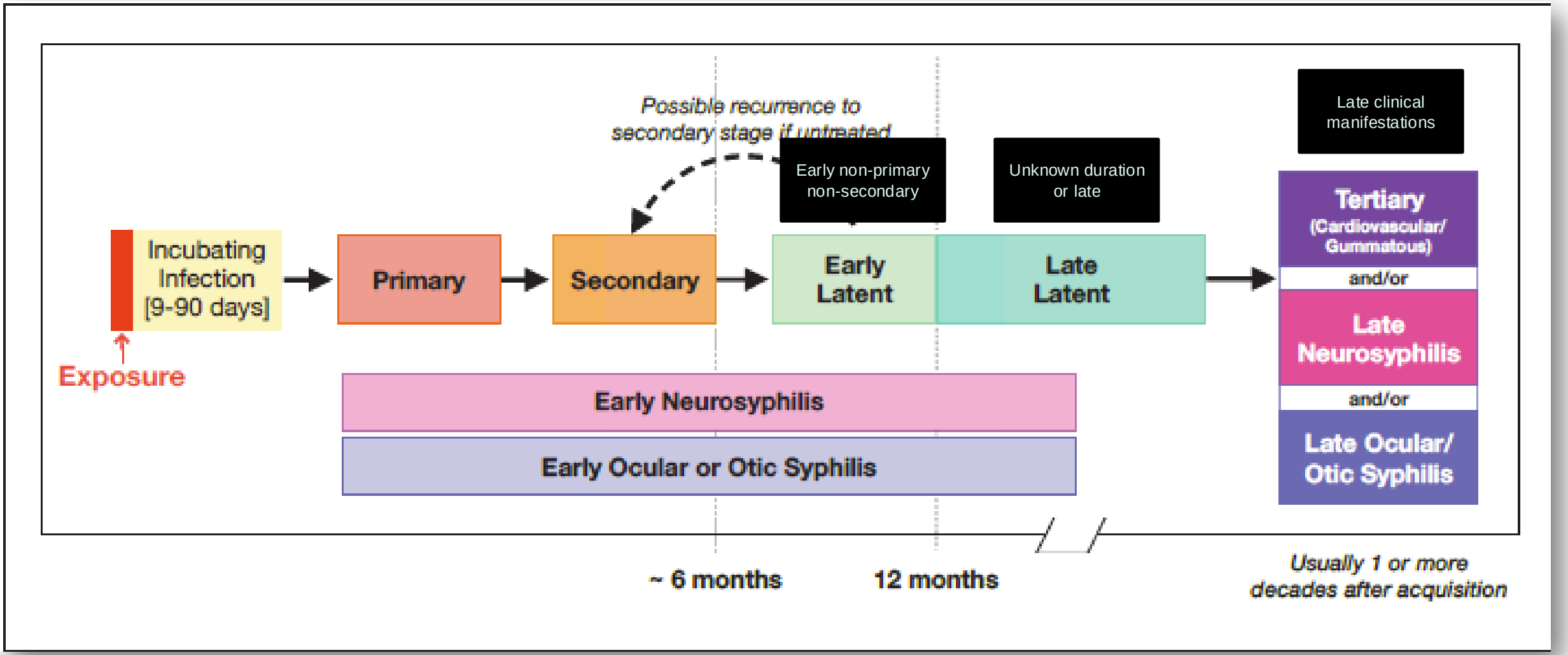
A missing step

talk | test | treat



stage

Syphilis – Natural History



- New York City Department of Health and Mental Hygiene, and the New York City STD Prevention Training Center. The Diagnosis and Management of Syphilis: An Update and Review. March 2019. A PDF version is available at www.nycptc.org.

Meet Jack

- 24-year-old bisexual male
- Presents for “an ulcer on my penis”
- “It has been there for a few days but doesn’t hurt”
- On exam had some inguinal lymphadenopathy

- **Where to stage Jack?**

Syphilis – Primary

A stage of infection with *Treponema pallidum* characterized by one or more ulcerative lesions (e.g. chancre), which might differ considerably in clinical appearance

- CTSE Definition Available at: https://cdn.ymaws.com/www.cste.org/resource/resmgr/2017PS/2017PSFinal/17-ID-11.pdf
- Image: https://www.cdc.gov/std/training/picturecards.htm

Syphilis – Primary

- Primary Syphilis
  - **Local**
  - **One or more ulcers (chancres) at inoculation site**
  - Occur 10 – 90 days after infection
  - Painless
    - May go unnoticed
    - Often associated with regional or bilateral lymphadenopathy
  - Highly infectious
  - Resolves in 1-6 weeks

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Primary Syphilis

Possible recurrence to secondary stage if untreated

Incubating Infection [9-90 days]

Exposure

Primary

Secondary

Early Latent

Late Latent

Tertiary (Cardiovascular/ Gummatous)

and/or

Late Neurosyphilis

and/or

Late Ocular/ Otic Syphilis

Early Neurosyphilis

Early Ocular or Otic Syphilis

~ 6 months

12 months

Usually 1 or more decades after acquisition

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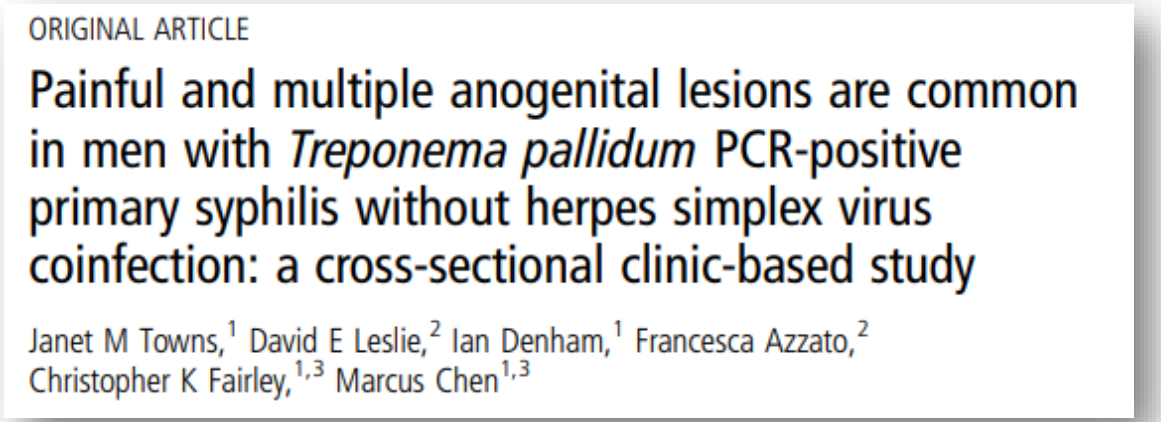
2021 STI Guideline Updates to Primary Syphilis

2021 Update

- Classic Presentation
  - Single painless ulcer or chancre at the site of infection

- **Atypical presentations**
  - Multiple, atypical, or painful lesions at the site of infection



ORIGINAL ARTICLE

Painful and multiple anogenital lesions are common in men with *Treponema pallidum* PCR-positive primary syphilis without herpes simplex virus coinfection: a cross-sectional clinic-based study

Janet M Towns,[1] David E Leslie,[2] Ian Denham,[1] Francesca Azzato,[2] Christopher K Fairley,[1,3] Marcus Chen[1,3]

- Towns JM, Leslie DE, Denham I, Azzato F, Fairley CK, Chen M. Painful and multiple anogenital lesions are common in men with Treponema pallidum PCR-positive primary syphilis without herpes simplex virus coinfection: a cross-sectional clinic-based study. Sex Transm Infect. 2016 Mar;92(2):110-5. doi: 10.1136/sextrans-2015-052219. Epub 2015 Sep 16. PMID: 26378262.

Meet Jill

- 26-year-old female
- Presents for “routine STI testing”
- In a new (last 3 weeks) relationship with a bisexual male who was recently diagnosed with syphilis (Jack)
- She reports no lesions, no rash, and her exam is benign

Does she even go on the diagram?

Syphilis – Incubation

Possible recurrence to secondary stage if untreated

Incubating Infection [9-90 days]

Exposure

Primary

Secondary

Early Latent

Late Latent

Tertiary (Cardiovascular/ Gummatous)

and/or

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Meet Jordan

- 17-year-old man who has sex with men who started PrEP 6 months ago
- Presents to clinic today for a routine PrEP visit and notes a diffuse skin rash that has largely faded
- 6 weeks ago he presented to an urgent care when the rash appeared, and was sent home with a topical steroid cream

Jordan's Urgent Care Visit

- Diffuse, non-pruritic, non-painful, rash
- Erythematous macules and patches on his chest, axilla, abdomen, and bilateral upper and lower extremities

Jordan's Urgent Care Visit

Secondary Syphilis

- Secondary Syphilis
  - Bacterial dissemination
  - **Dermatologic manifestations**
  - Systemic symptoms
    - Painless generalized adenopathy
    - Low-grade fever
    - Fatigue
  - Usually, 4-8 weeks after infection
    - Resolves in 6 weeks
    - Highly infectious

- Photos from CDC Public Health Image Library (PHIL). Available: https://phil.cdc.gov/Default.aspx Stock photo. Posed by model

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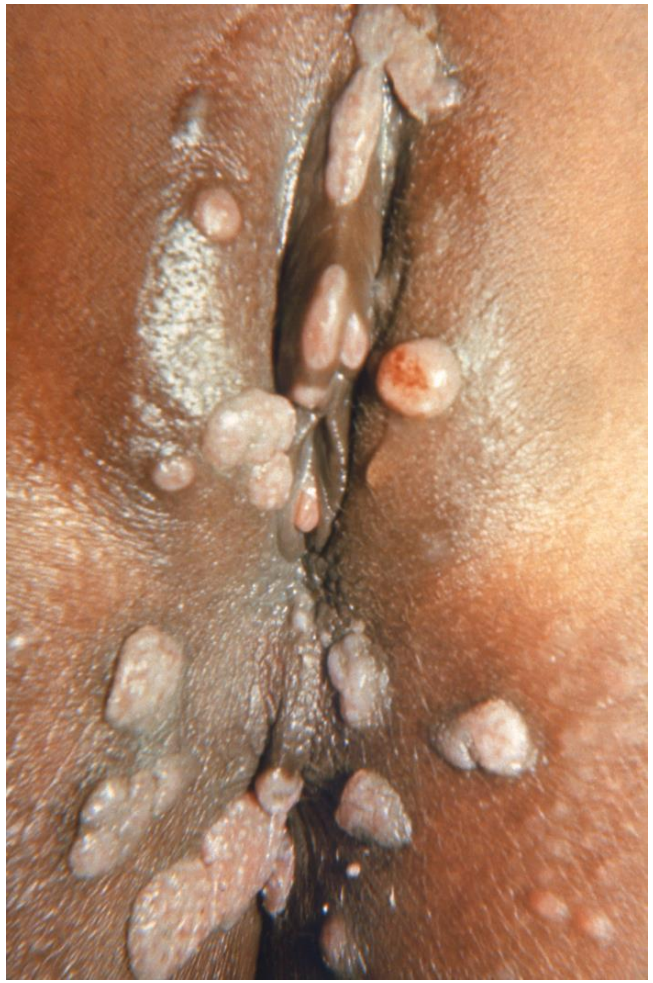

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Syphilis - Secondary

Organ System	Clinical Findings
Skin and Mucous Membranes	• Rash or other skin lesions with varied appearance frequently on palms/soles – Macular/papular/maculopapular – Annular – Psoriasiform – Necrotic (rare) • Condyloma lata: moist, gray-white, wart-like growths appearing in warm moist areas such as the perineum and the anus • Patchy alopecia, often with a moth-eaten appearance • Mucous patches: flat, silver-gray discrete macules, plaques or erosions involving the mouth, tongue, or ano-genital mucosa • Split- or fissured-papules at the angles of the mouth and nasolabial folds (rare)
Systemic	• Lymphadenopathy • Systemic symptoms including: malaise, fever, and other nonspecific constitutional symptoms
Gastrointestinal	• Gastric syphilis • Hepatitis (usually subclinical)
Renal	• Glomerulonephritis • Nephrotic syndrome
Musculoskeletal	• Arthritis • Periostitis

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Secondary Syphilis

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Incubating Infection [9-90 days]

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Tertiary (Cardiovascular/ Gummatous)

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Today's Visit with Jordan

- 1 week ago Jordan felt like he was having a hard time hearing the TV
- Went to the urgent care where he was seen by ENT
  - "Asymmetric hearing loss, please get MRI"
  - MRI unremarkable
  - Told to follow-up outpatient

Today's Visit with Jordan

- At today's visit, Jordan notes that he's also having a hard time reading his homework
- A thorough neurologic exam reveals decreased visual and auditory acuity, but no other CN abnormalities
- You send him urgently to the ophthalmology clinic
- On the note from his fundoscopic exam:
  - "Panuveitis"

Enhanced Clinical Descriptions of Ocular and Otic Manifestations

NEW Symptoms

Ocular Syphilis

- Often presents as panuveitis
- Can involve any structure in the anterior and posterior segment of the eye including:
  - Conjunctivitis
    - Red eye/Pain
  - Anterior uveitis
  - Posterior interstitial keratitis
  - Optic neuropathy
  - Retinal vasculitis
- Can lead to **permanent** vision loss

Otosyphilis

- Typically presents with cochleo-vestibular symptoms including
  - Tinnitus
  - Vertigo
  - Sensorineural hearing loss
    - Unilateral/Bilateral
    - Have a sudden onset
    - Progress Rapidly
- Can result in **permanent** hearing loss

Other neurosyphilis manifestations

Neurologic	• Signs/symptoms of meningitis (eg, subtle headache) • Cranial nerve (CN) dysfunction (especially 6th, 7th, 8th CN) • Meningovascular syphilis with stuttering stroke symptoms

Screening for Neuro, Ocular, and Otic Syphilis

Screening Questions for Neurosyphilis (Including Ocular and Otosyphilis)

Questions		
Symptoms of Otosyphilis		
1) Have you recently had new trouble hearing?	☐ Yes – refer to ENT	☐ No
2) Do you have ringing in your ears?	☐ Yes – refer to ENT	☐ No
Symptoms of Ocular syphilis		
3) Have you recently had a change in vision?	☐ Yes – refer to ophthalmology	☐ No
4) Do you see flashing lights?	☐ Yes – refer to ophthalmology	☐ No
5) Do you see spots that move or float by in your vision?	☐ Yes – refer to ophthalmology	☐ No
6) Have you had any blurring of your vision?	☐ Yes – refer to ophthalmology	☐ No
Symptoms of neurosyphilis		
7) Are you having headaches?	☐ Yes	☐ No
8) Have you recently been confused?	☐ Yes	☐ No
9) Has your memory recently gotten worse?	☐ Yes	☐ No
10) Do you have trouble concentrating?	☐ Yes	☐ No
11) Do you feel that your personality has recently changed?	☐ Yes	☐ No
12) Are you having a new problem walking?	☐ Yes	☐ No
13) Do you have weakness or numbness in your legs?	☐ Yes	☐ No

- https://kingcounty.gov/depts/health/communicable-diseases/hiv-std/~/media/depts/health/communicable-diseases/documents/hivstd/Screening-Tool-Neurosyphilis.ashx

Syphilis – Early Complications

recurrence to
tage if untreated

Incubating Infection [9-90 days]

Primary

Secondary

Early Latent

Late Latent

Tertiary (Cardiovascular/ Gummatous)

and/or

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Exposure

Early Neurosyphilis

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Meet Jackie

- 27 year old female presents for a follow up visit
- At a recent OB-gyn visit she noted during a family planning visit that she was considering becoming pregnant
- Comprehensive STI testing was performed at that time at the discretion of the treating clinician, and included syphilis testing
- She has been referred to you for a positive result
- A pregnancy test from that visit was negative
- Prior syphilis testing just under a year ago was negative
- She notes no symptoms today, and has a normal exam

Syphilis – Latent

Latent Phase	Definition
Syphilis, early non-primary non-secondary	Duration of infection <= 1 year
Syphilis, unknown duration or late	Duration of infection >1 year
	Unknown duration of infection

*****Latent syphilis requires no exam findings of primary, secondary or tertiary syphilis**

- Early latent disease is differentiated due to the risk of relapsed or intermittent bacteremia
  - This can occur in up to 24% of patients
  - Manifests as symptoms of secondary syphilis including CNS disease
- Risk for infecting partners remains
- Risk of relapsed symptoms and infectiousness decreases after 1 year

Syphilis – Latent




Incubating Infection [9-90 days]

Exposure

Primary

Secondary

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Late Latent

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How Do We Test for Syphilis?

- Multiple options exist to test directly for the presence of treponemes in primary syphilis lesions
  - Dark-field microscopy
  - Direct fluorescent antibody testing
  - T palladium NAAT
    - No FDA-approved tests are commercially available

- Unfortunately, these are not available in most clinical settings

Serologic testing

Non-treponemal (lipoidal antigen) tests	Treponemal tests
Test reactivity of serum to cardiolipin-cholesterol-lecithin	Test serum reactivity against T. pallidum-specfic antigens
Antigen response is due both directly to bacteria and host tissue damage	More specific than non-treponemal tests
Up to 11% of positive tests in one series not due to T pallidum	Often remain positive for life
Degree of reactivity changes over disease course/after treatment	Generally automated
Generally manual	

Papp JR, Park IU, Fakile Y, Pereira L, Pillay A, Bolan GA. CDC Laboratory Recommendations for Syphilis Testing, United States, 2024. MMWR Recomm Rep 2024;73(No. RR-1):1–32.

Serologic Testing

Non-treponemal (lipoidal antigen) tests	Treponemal tests
Rapid plasma reagin (RPR)	Enzyme Immunoassay (EIA)
Venereal disease research laboratory (VDRL)	Fluorescent treponemal antibody (FTA-ABS)
	Treponema pallidum particle agglutination (TP-PA)
	Chemiluminescence assay (CIA)

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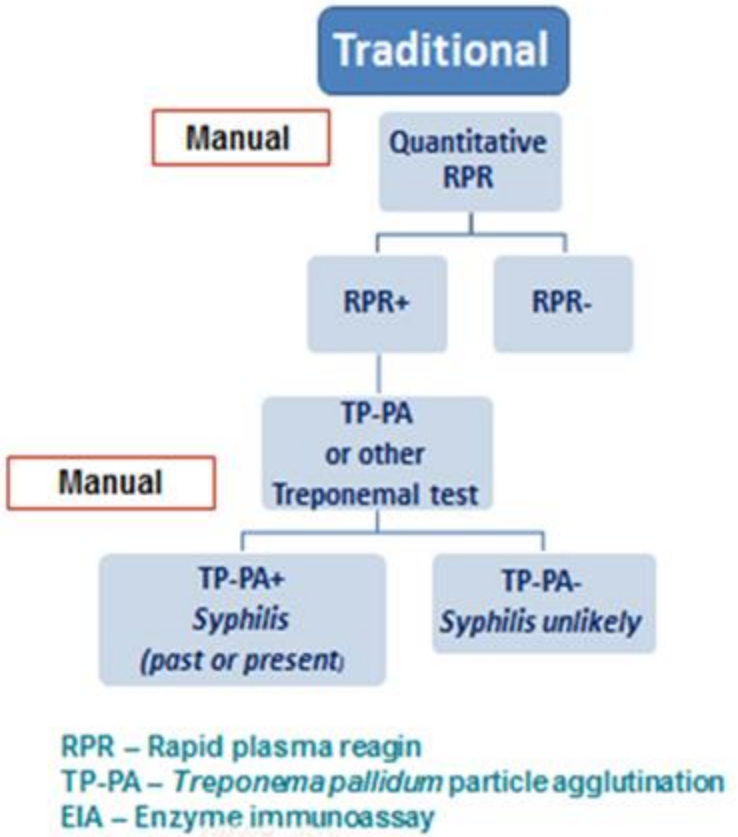
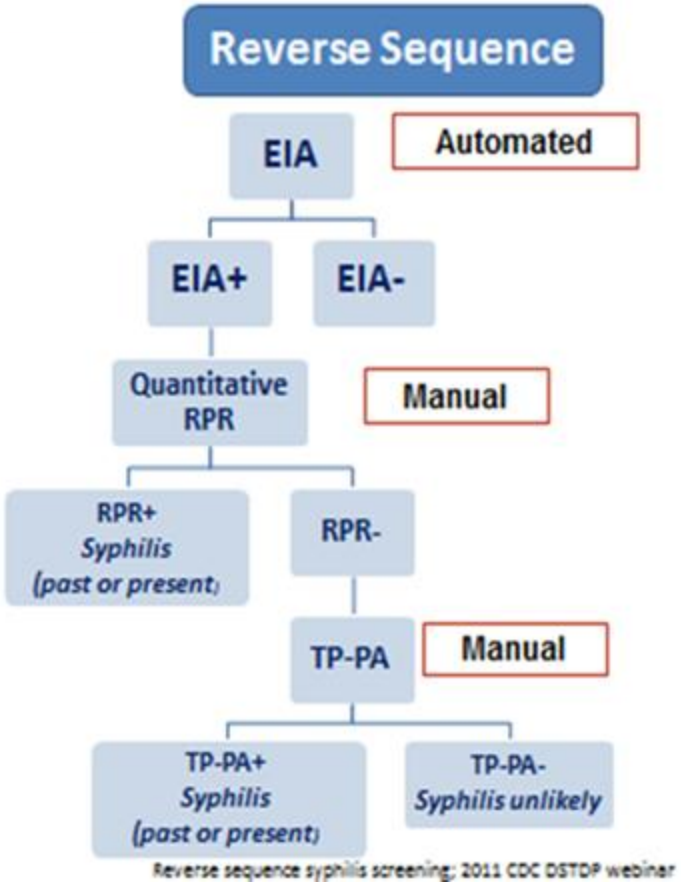
Serologic Testing





RPR – Rapid plasma reagin
TP-PA – *Treponema pallidum* particle agglutination
EIA – Enzyme immunoassay

- Thanks to Hilary Reno and Joseph Cherabie from the St. Louis PTC for this slide

Syphilis – Traditional Algorithm

Nontreponemal Test
(Quantitative RPR)

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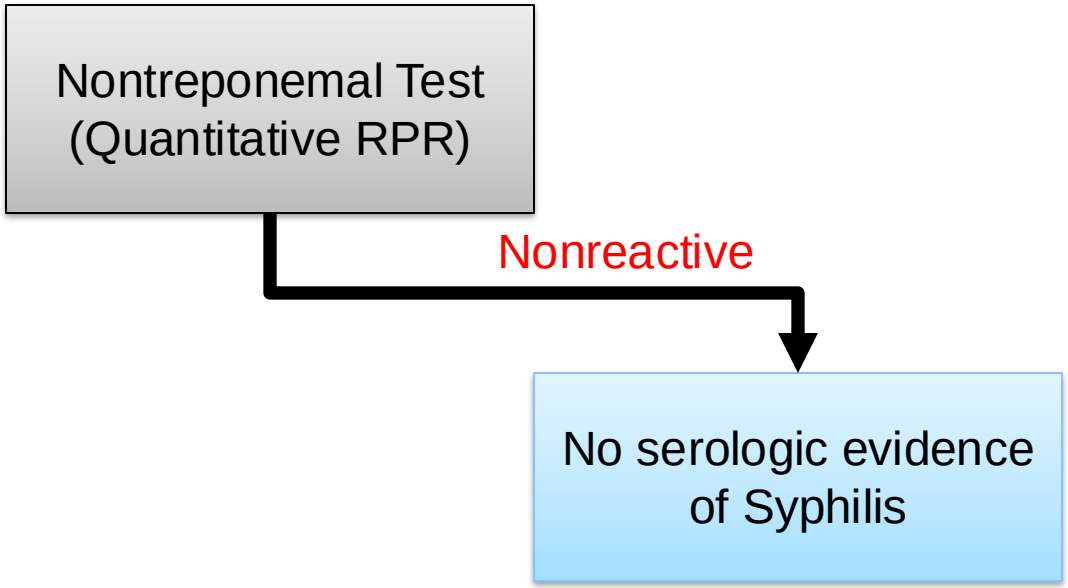

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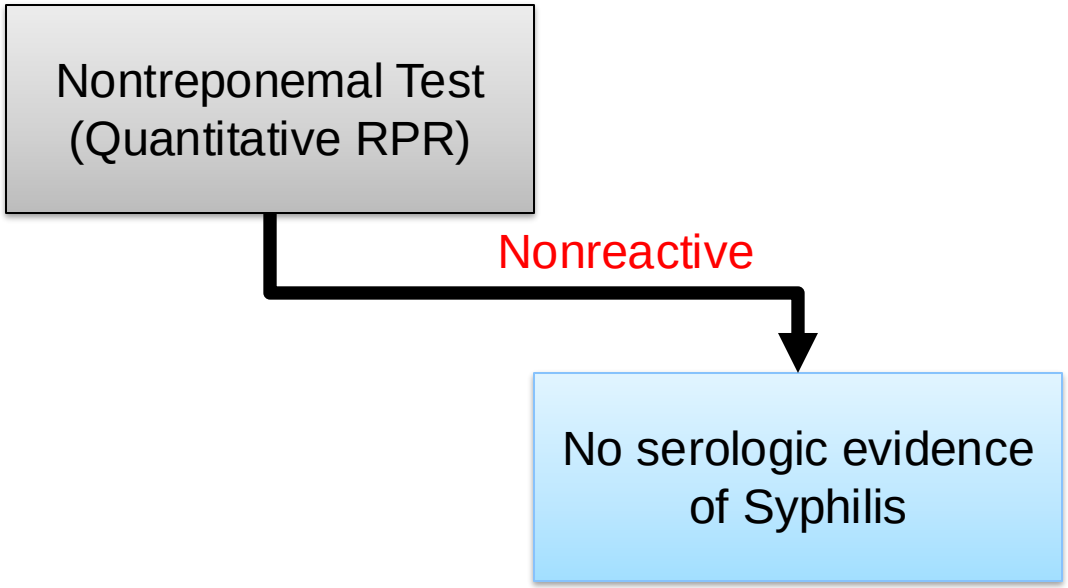

Limitations:

- Incubation period
- Early primary infection

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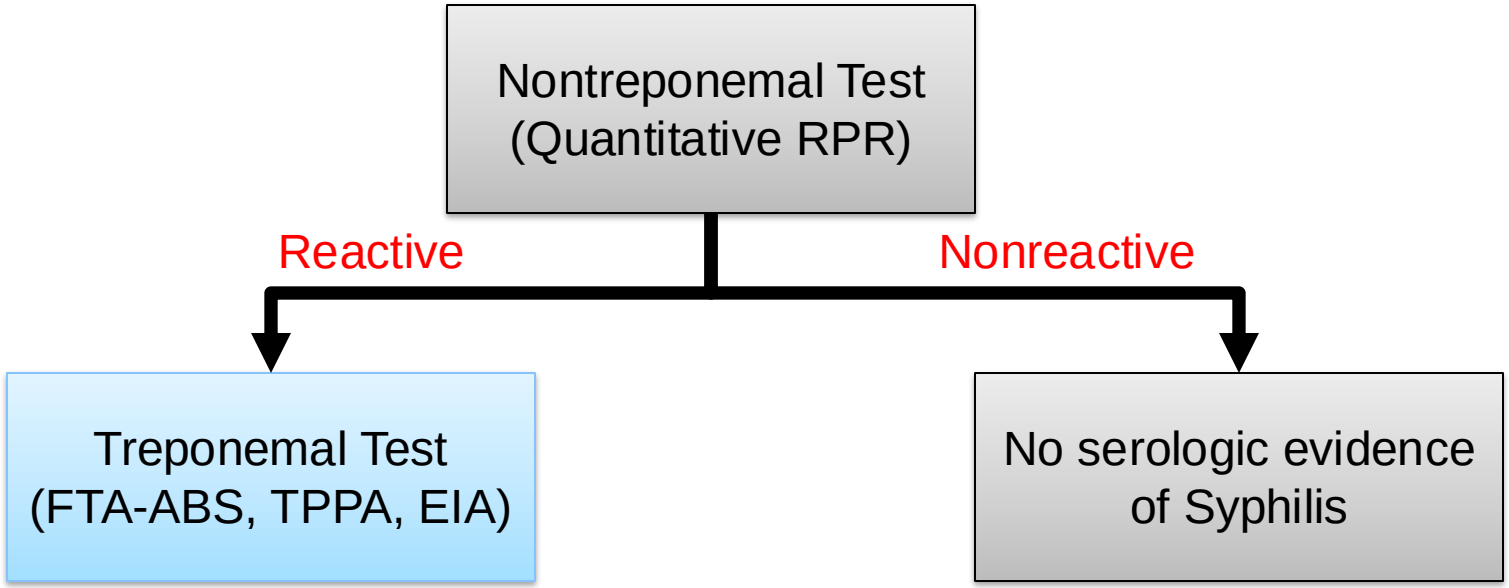

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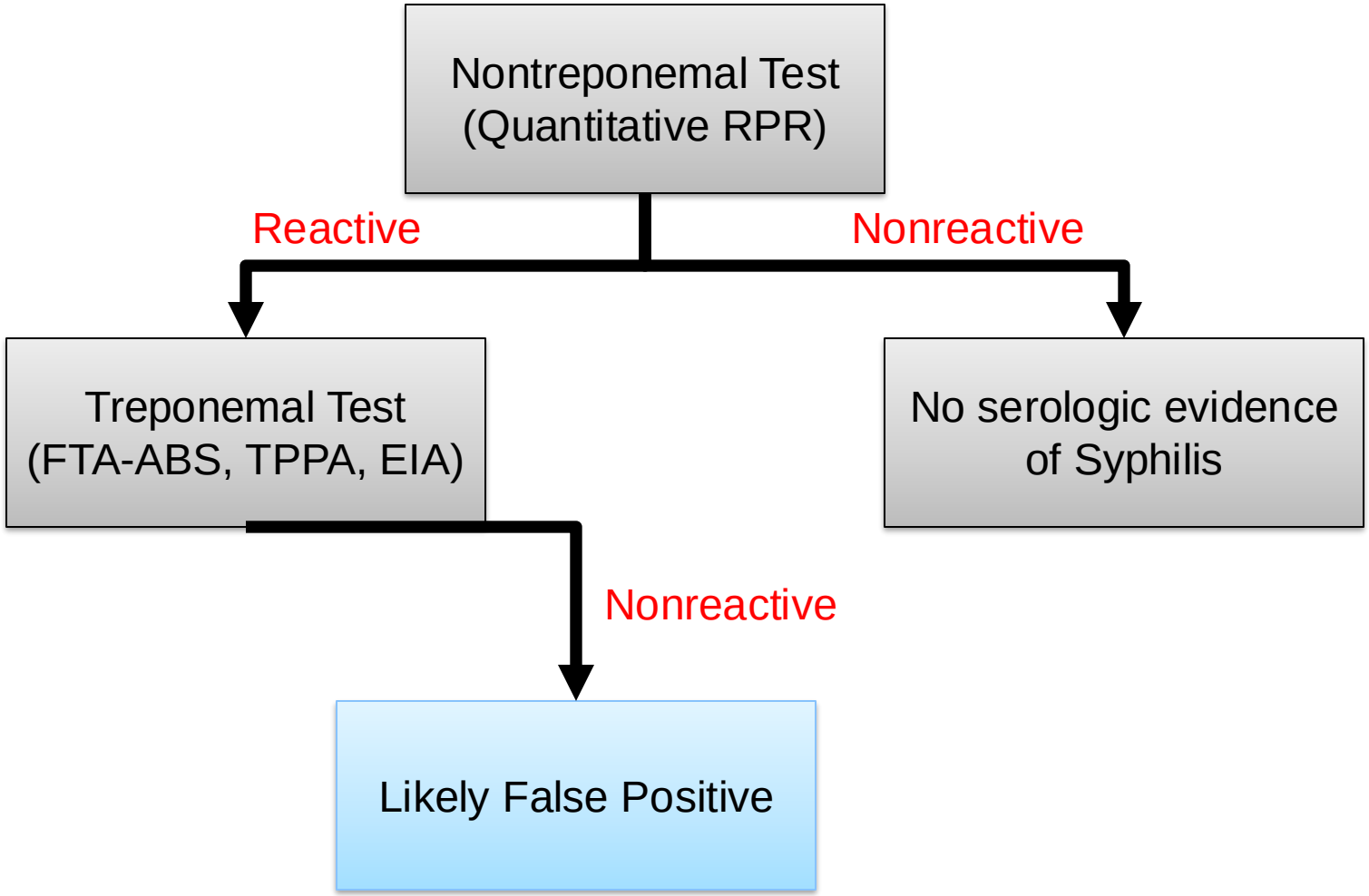

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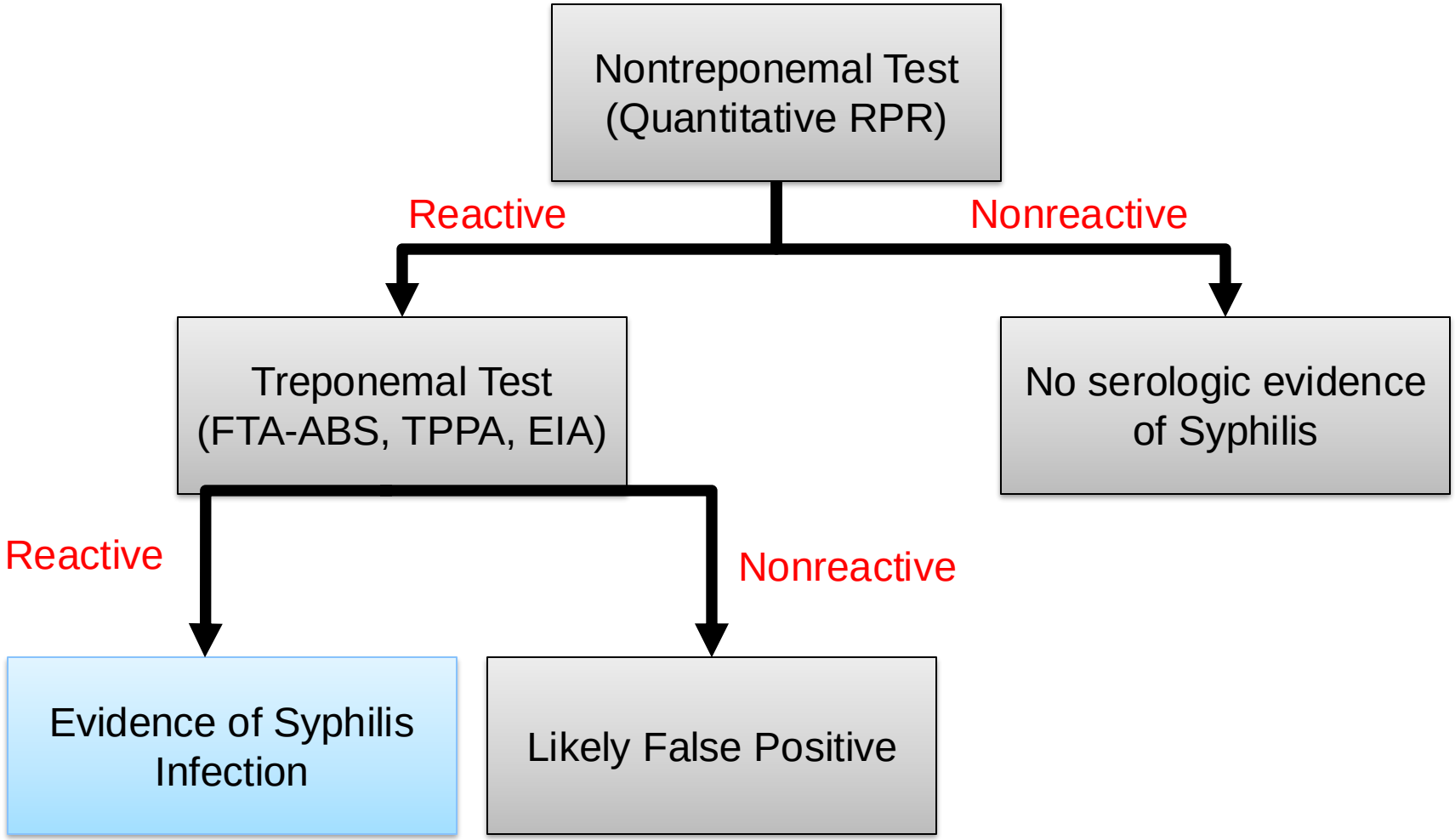

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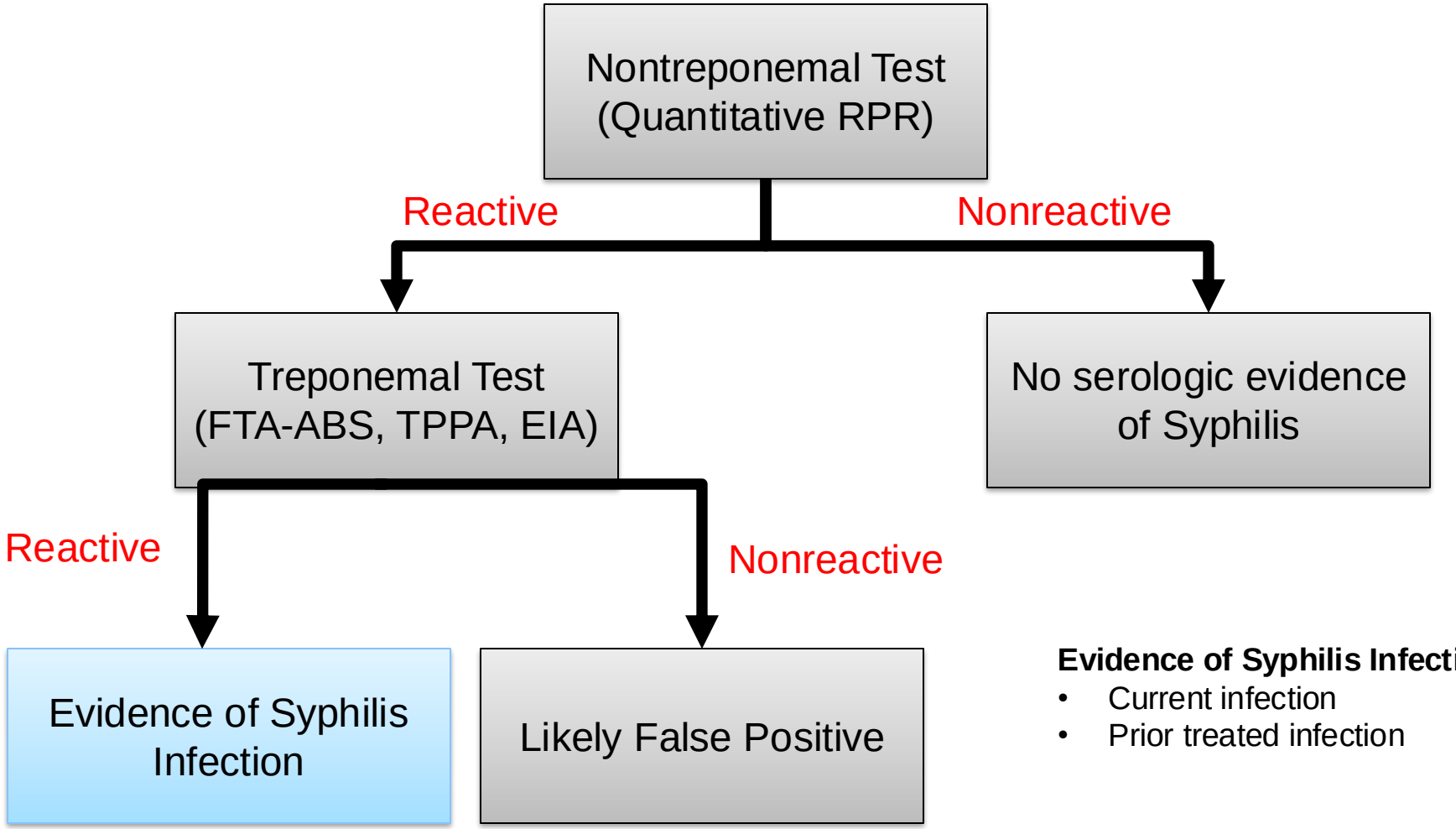

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Syphilis – Reverse Algorithm

Screening Treponemal Test (EIA)
Automated

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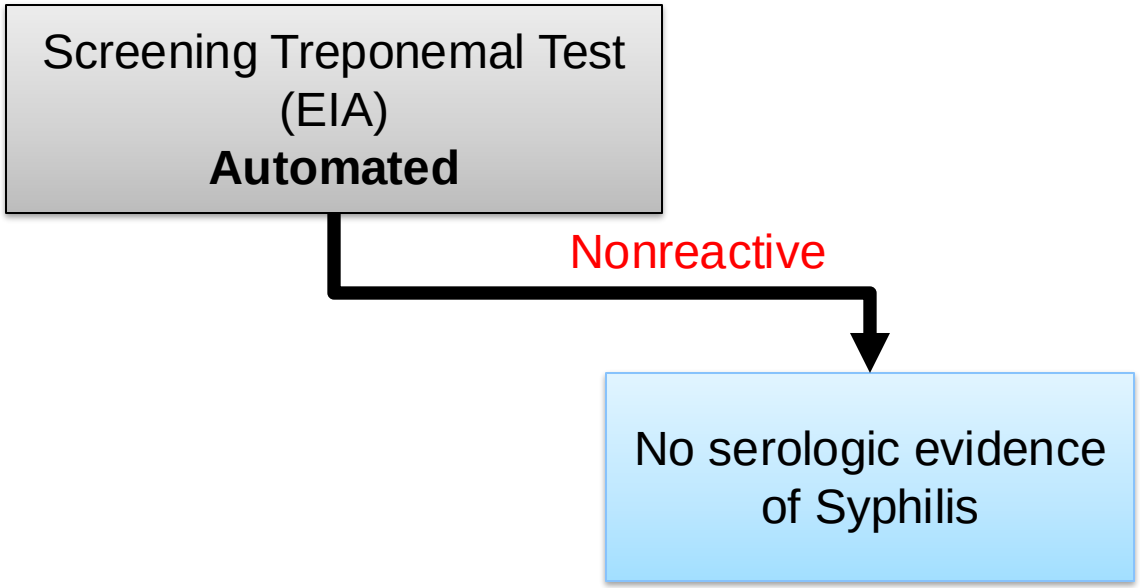

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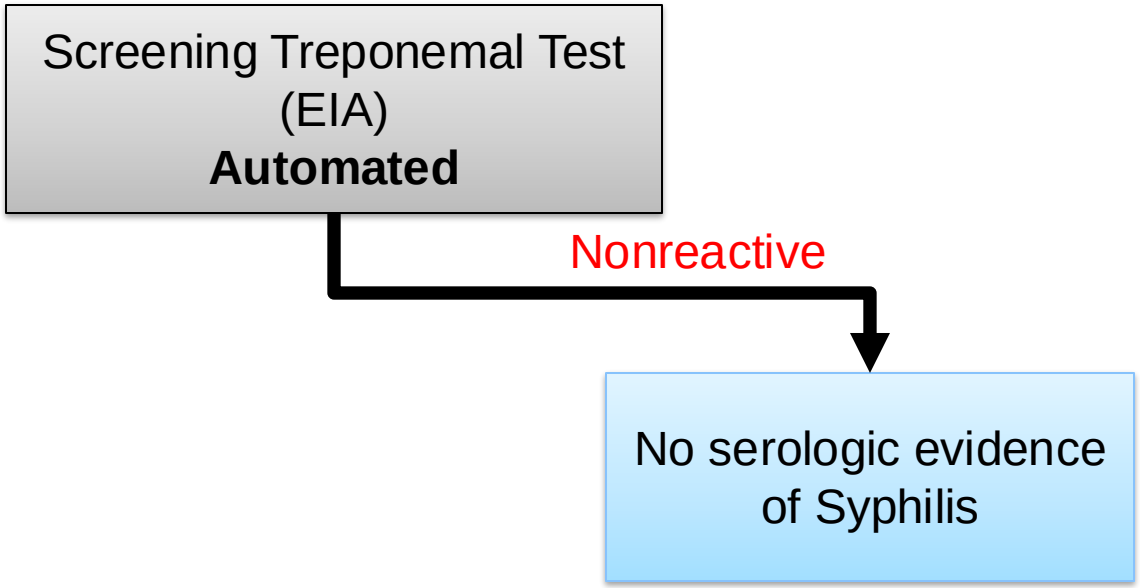

Limitations:

- Incubation period
- Early primary infection

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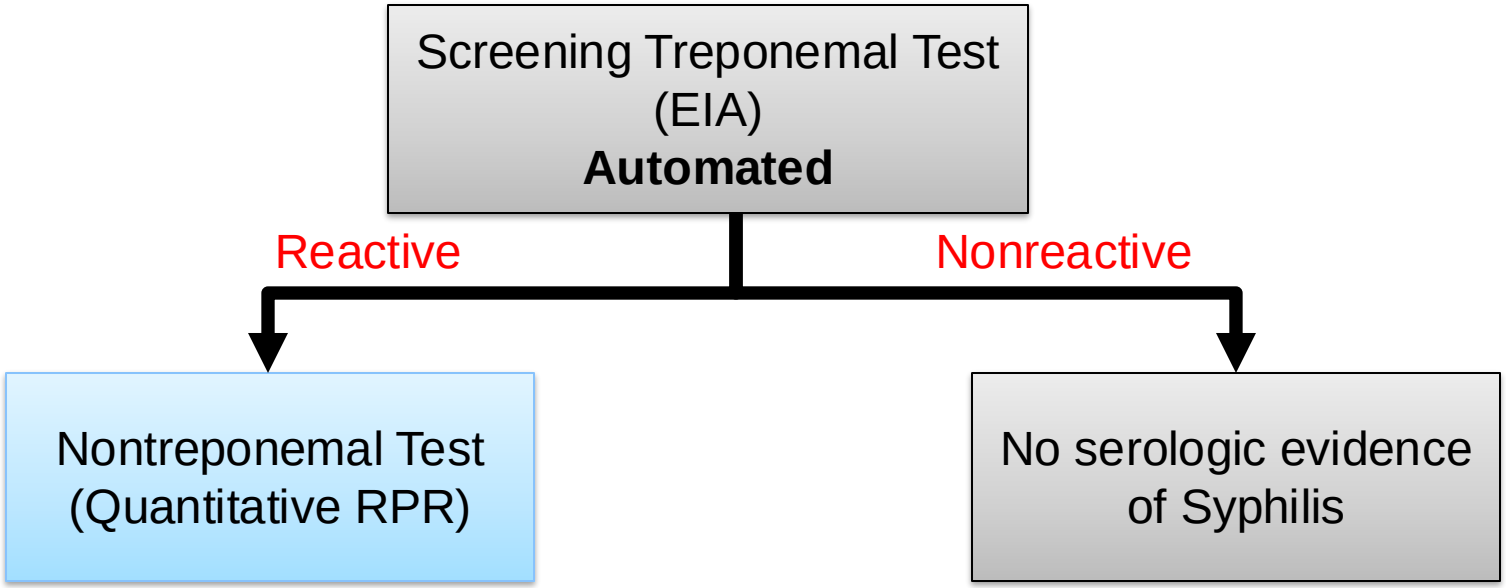

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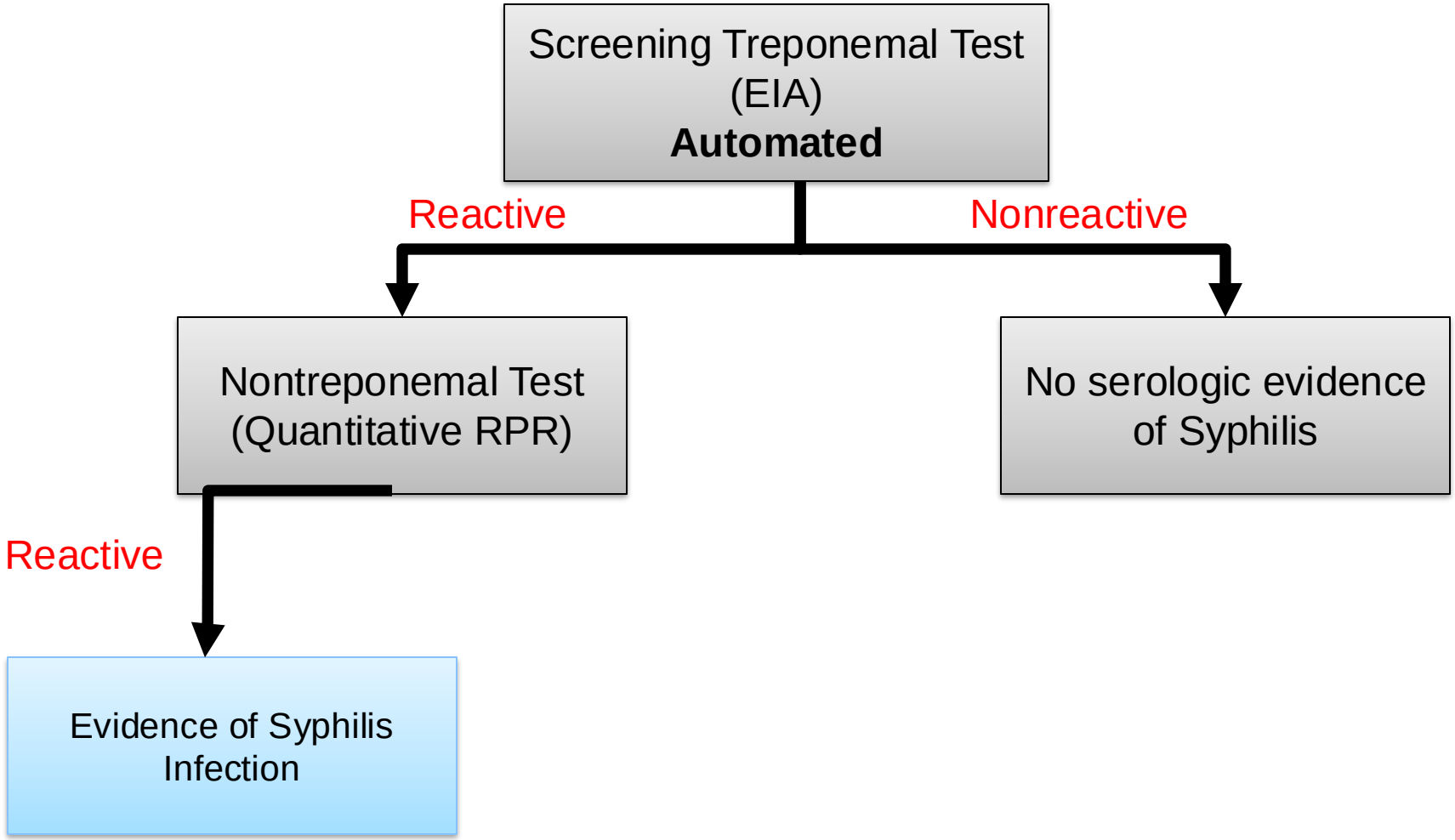

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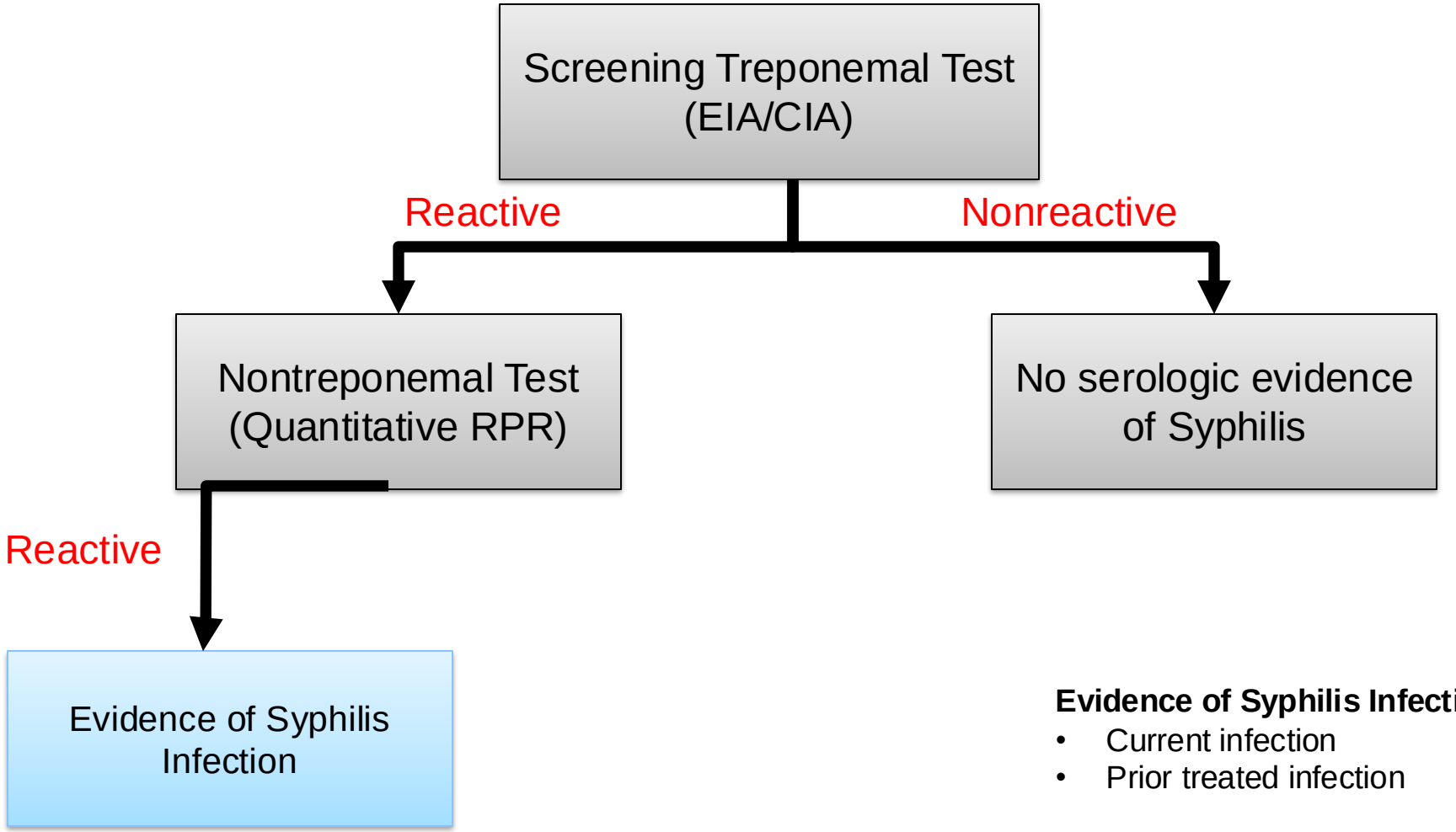

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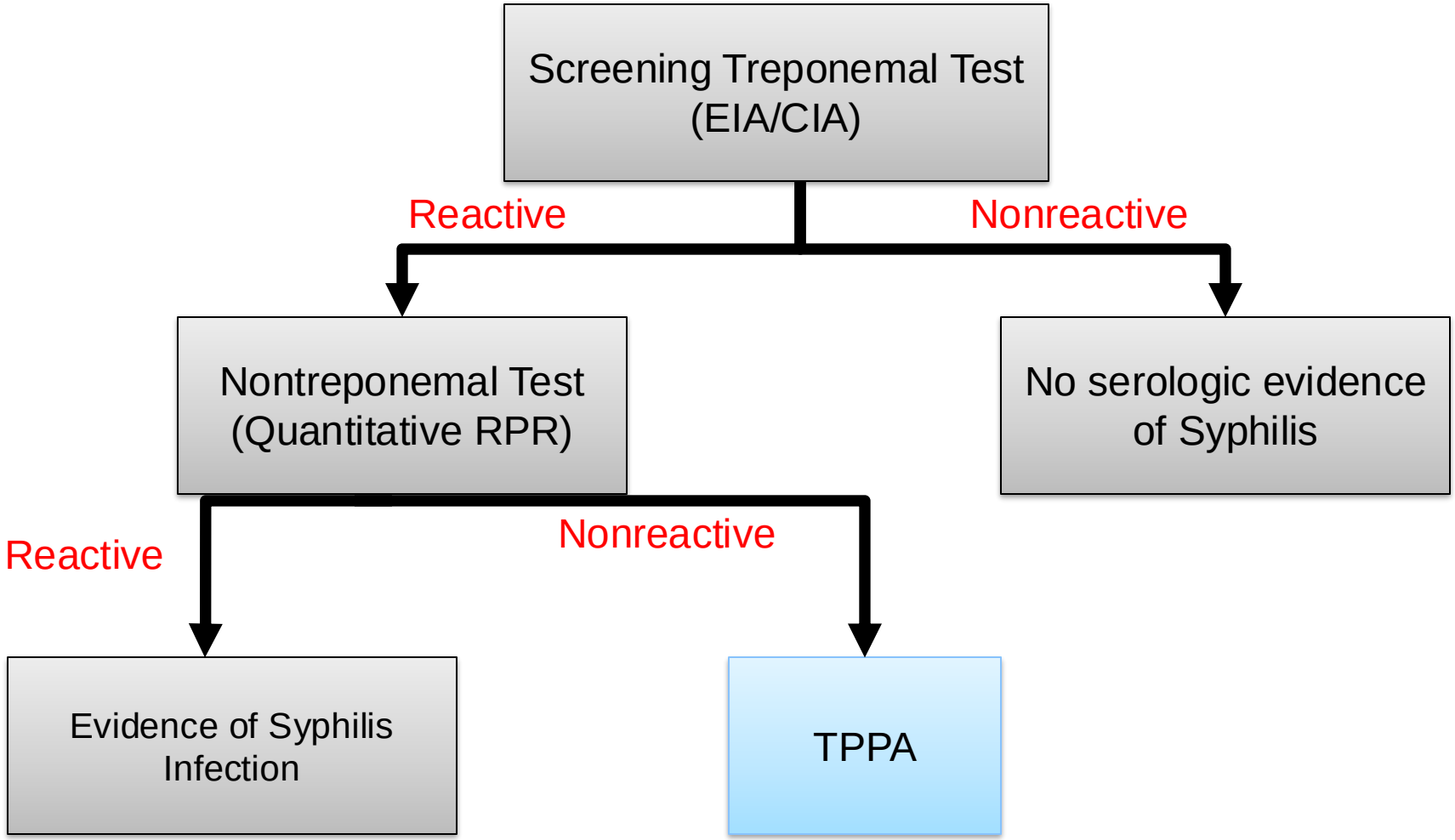

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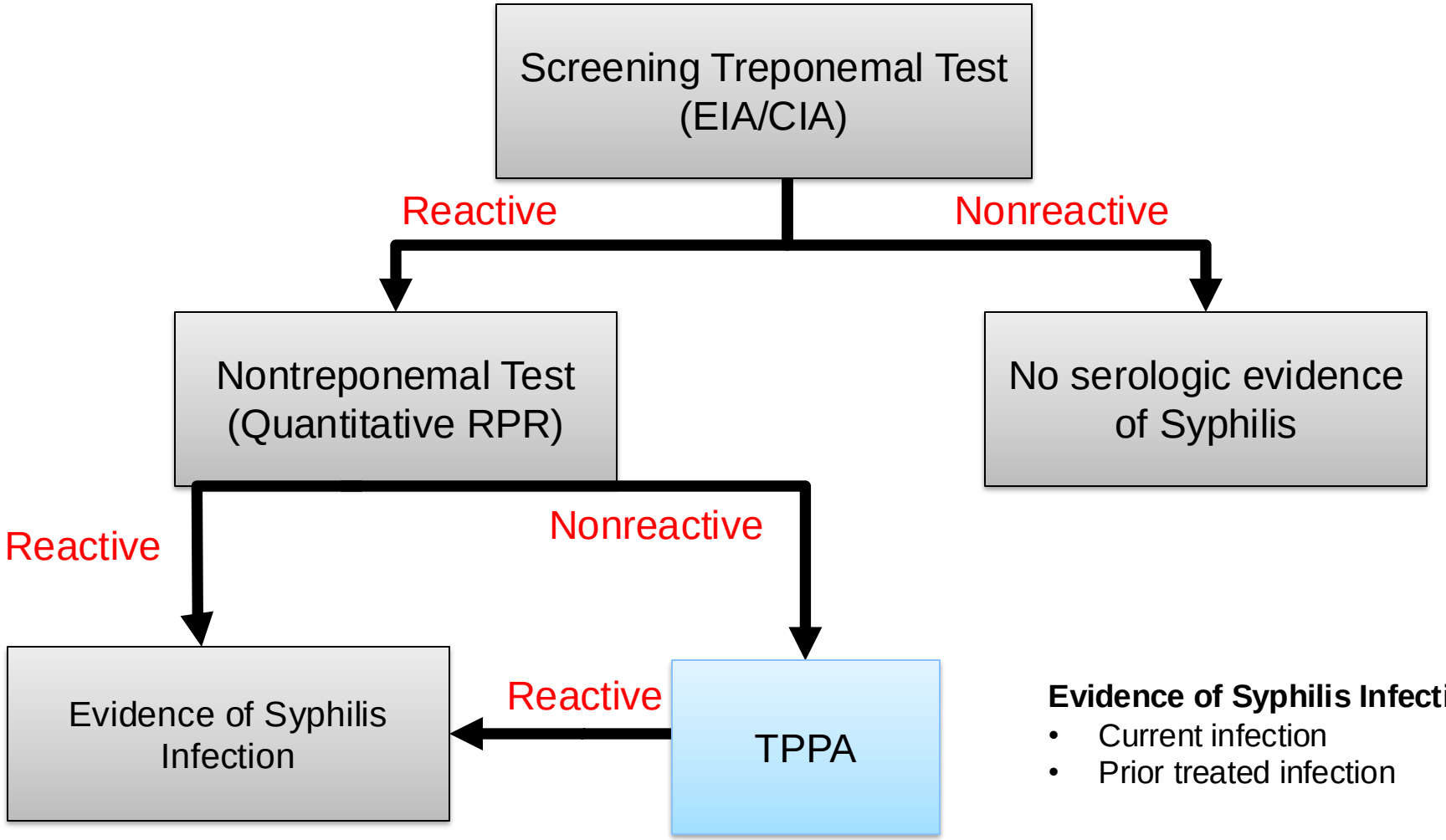

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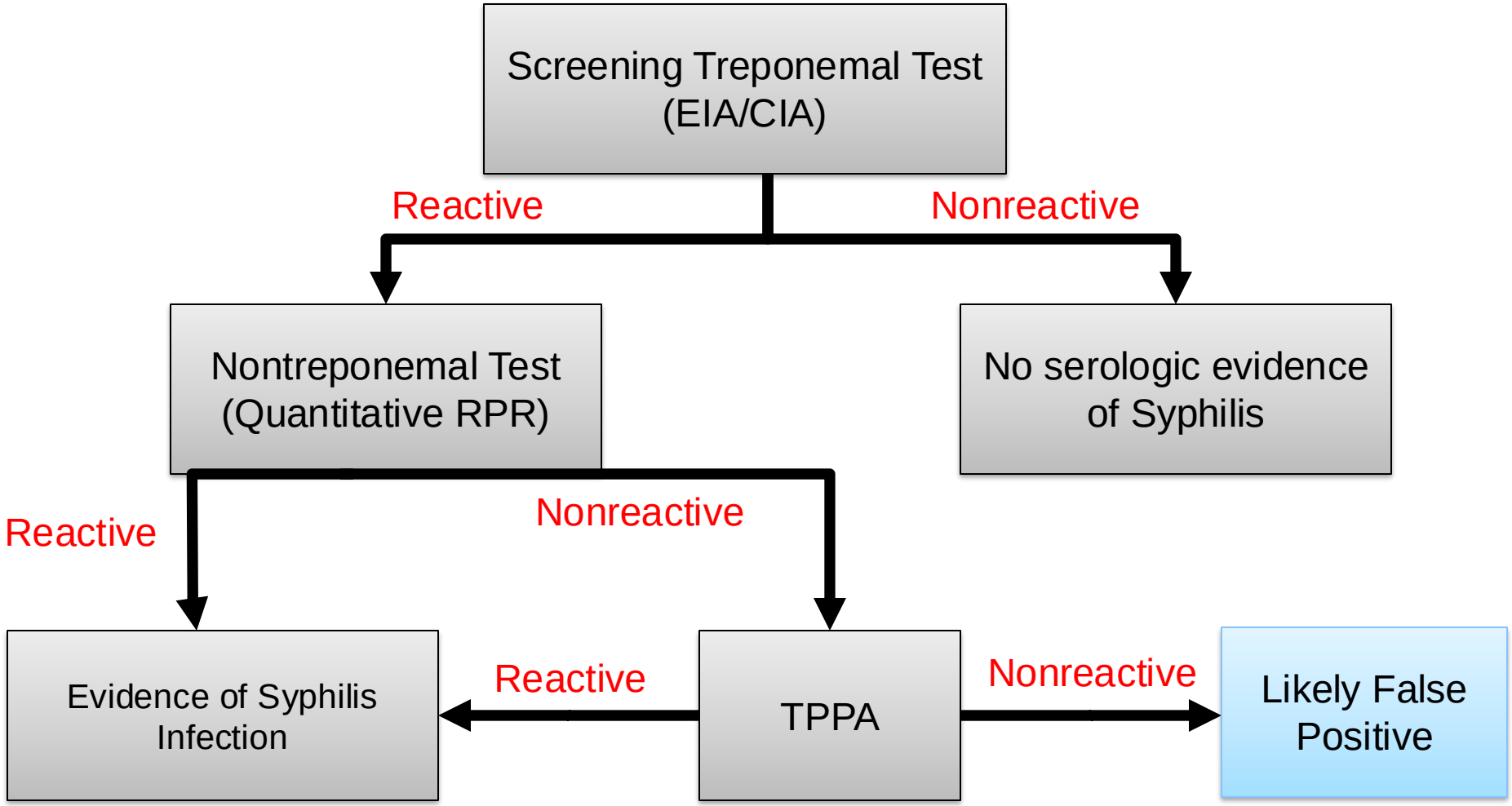

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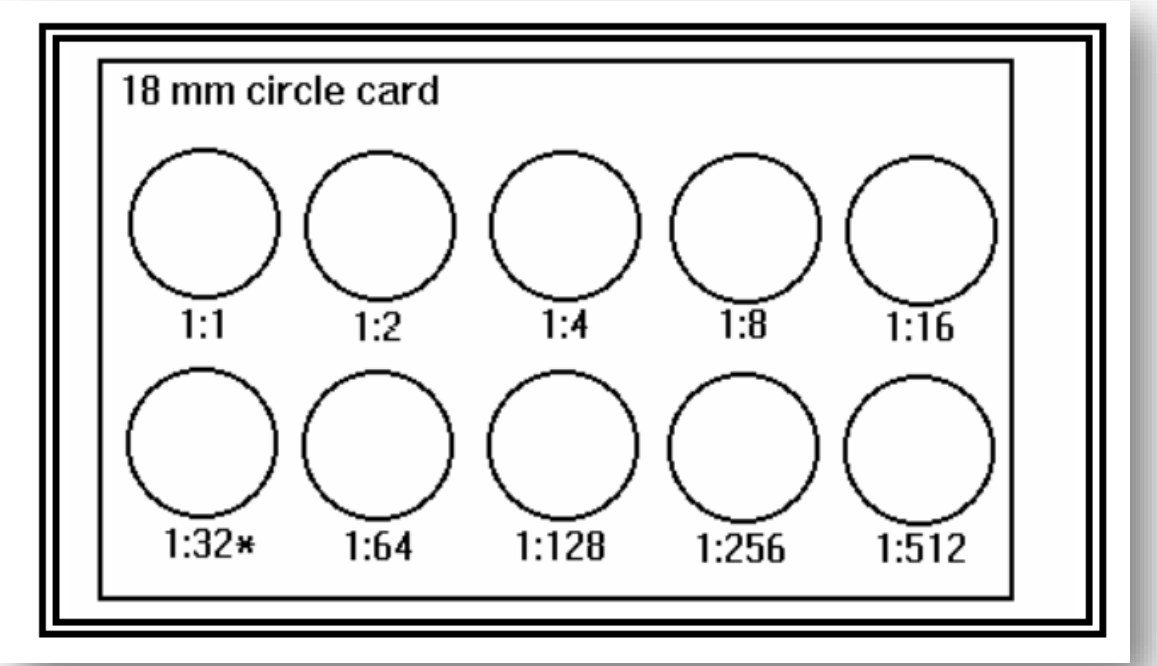
Syphilis – Interpreting RPR Titers

1:2048
1: 1024
1:512
1: 256
1:128
1: 64
1:32
1: 16
1:8
1: 4
1:2
1: 1
Nonreactive

What Do Titers Mean?



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- https://www.cdc.gov/nchs/data/nhanes/nhanes_01_02/l36_b_met_syphillis_rapid_plasma_reagin.pdf

Syphilis – Interpreting RPR Titers

2 dilution change = 4 x increase or decrease in titers

1:2048

1: 1024

1:512

1: 256

1:128

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1 dilution change = 2 x increase or decrease in titers

Syphilis – Interpreting RPR Titers

1:2048

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Nonreactive

Syphilis – Interpreting RPR Titers

1:2048

1: 1024

1:512

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1:128

1: 64

1:32

1: 16

1:8

1: 4

1:2

1: 1

Nonreactive

FAQ: What about CNS disease?

NEW Testing

- Neurological disease previously always required diagnosis with CSF studies
- Hallmark CSF abnormalities include
  - Pleocytosis
    - >5 cells/mL in most patients
    - >20 cells/mL in people with HIV
  - Elevated protein
    - Limited sensitivity and specificity
  - Reactive CSF CDRL
    - Less than 80% sensitive

2021 Updates

NEW Testing

Fewer Lumbar Punctures

- Isolated ocular symptoms and no cranial nerve dysfunction
  - CSF exam is not necessary

- Otic syphilis
  - CSF exam is not necessary

- Neuro syphilis
  - No repeat CSF exam at 6 months with adequate RPR response (HIV - and HIV+/ART)

FAQ: When Do I Need to Report This?

- Syphilis cases must be reported to the Department of Health within 72 hours of diagnosis.
- For this outbreak, reporting time for syphilis cases in this area was sped up to within 48 hours due to the outbreak
- **Always check with your local Department of Health regarding reporting requirements and processes**

Finally, treatment!

- Treatment continues to rely on penicillin, to which resistance has not been observed
- Long-acting benzathine penicillin-G sustains treponemocidal drug levels for 7-10 days
- Due to long generation times (33 hours), sustained drug levels are felt to be necessary for bacterial elimination
- Due to a recent shortage of this drug, doxycycline has been introduced as an alternative, supported primarily by retrospective studies
- On 1/16 the FDA announced that it would allow importation of Extencilline (an equivalent penicillin manufactured in Italy)

Syphilis Treatment – Early (uncomplicated)

Stage	Treatment	Alternative
Incubation	Benzathine penicillin G 2.4 million units intramuscular injection once	Doxycycline 100mg twice daily for 14 days
Primary		
Secondary		
Syphilis, early non-primary non-secondary		

Syphilis Treatment – CNS disease

Neurosyphilis, Ocular, or Otic Syphilis	Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units intravenously every 4 hours, or by continuous infusion, for 10–14 days	Procaine penicillin G 2.4 million units IM once daily *PLUS* Probenecid 500mg 4 times daily for 10–14 days
Tertiary		

• Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1-187. Published 2021 Jul 23. doi:10.15585/mmwr.rr7004a1

Syphilis Treatment

Stage	Treatment	Alternative
Incubation (<90d)	Benzathine penicillin G 2.4 million units intramuscular injection once	Doxycycline 100mg twice daily for 14 days
Primary		
Secondary		
Syphilis, early non-primary non-secondary		
Syphilis, unknown duration or late	**Benzathine penicillin G 2.4 million units intramuscular injection 3 times at one week intervals**	**Doxycycline 100mg twice daily for 28 days*** **
Neurosyphilis, Ocular, or Otic Syphilis	Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units intravenously every 4 hours, or by continuous infusion, for 10–14 days	Procaine penicillin G 2.4 million units IM once daily *PLUS* Probenecid 500mg 4 times daily for 10–14 days
Tertiary		

FAQ

- How many days between injections is acceptable for latent syphilis?
  - **General Population**
    - "If a person receives a delayed dose of penicillin in a course of weekly therapy for late latent syphilis or syphilis of unknown duration, the course of action that should be recommended is unclear"
    - Interval of 7–9 days **preferred**
    - An interval of 10–14 days between doses of benzathine penicillin for latent syphilis "**might**" be acceptable before restarting the sequence of injections
      - **Check with local health departments for their policies**
  - **Pregnant women**
    - Optimal Interval is 7 days
    - Missed doses >9 days between doses are **not acceptable**
    - Missed doses = repeat the full course of therapy

Follow up and treatment failure

- Quantitative nontreponemal serologic tests should be repeated at least at:
  - 6 months
  - 12 months
  - 24 months

- An inadequate serologic response after treatment is failure for titers to decrease by 4x:
  - 12 months after treatment for primary, secondary, and early latent
  - 24 months after treatment for late latent or unknown duration, HIV

FAQ: Am I Infectious During Early Latent Syphilis?

- Transmission
  - "Microscopically abraded" **skin**
  - **Mucous membrane** lesions
- Skin and mucous membrane lesions occur during the first year after infection and can be easily missed

Table 14. Infectiousness and Duration of Infectivity by Syphilis Stage

STAGE OF INFECTION	MAXIMUM PERIOD OF INFECTIOUSNESS * (Prior to symptom onset or first serologic evidence of infection/reinfection)	MANAGEMENT OF CONTACTS AT RISK FOR EXPOSURE
Incubating Infection	Persons being treated presumptively for incubating infection following a known exposure, who lack any exam or serologic evidence of syphilis, are **not** considered infectious—but will become infectious if left untreated. Therefore, contacts of persons treated for incubating infection are not at risk of exposure but may benefit from syphilis/STI screening.	N/A
Primary Syphilis	**3 months**	**Evaluation and presumptive treatment** of contacts exposed *within 3 months* prior to the onset of symptoms or signs in the case patient.
Secondary Syphilis	**6 months**	**Evaluation and presumptive treatment** of contacts exposed *within 6 months* prior to the onset of symptoms or signs in the case patient.
Early Latent Syphilis	**12 months** Since skin and mucous membrane lesions, which often go unrecognized by patients, occur predominately during the first year of infection, persons diagnosed with early latent syphilis are potentially infectious to contacts despite their lack of symptoms or exam findings at the time of treatment.[23]	**Evaluation and presumptive treatment** of contacts exposed *within 12 months* of first serologic evidence of infection or re-infection, in the case-patient.
Late Latent Syphilis	Persons diagnosed with late latent infection (ie, acquired > 1 year prior to treatment) are not considered to be infectious to current/recent sexual or needle-sharing contacts.	Long-term ongoing partners exposed to the case-patient more than 1 year ago may benefit from syphilis screening.
Latent Syphilis of Unknown Duration	If there is insufficient information to determine the duration of latent infection, the case-patient may have been infectious over the past year. Patients with latent syphilis of unknown duration who have high nontreponemal serologic titers (ie, > 1:32) have an increased likelihood of recent acquisition and of being infectious.[23]	**Evaluation and presumptive treatment** of contacts exposed *within 12 months* of first serologic evidence of infection, or re-infection in the case-patient.
Ocular, Otic, or Neurosyphilis	Central nervous system, ocular and otic infection are not sexually transmissible.	If the case-patient also meets the diagnostic criteria for primary, secondary, early latent, or latent of unknown duration, contacts should be managed as noted above.
Tertiary Syphilis	Not considered infectious.	

- New York City Department of Health and Mental Hygiene, and the New York City STD Prevention Training Center. The Diagnosis and Management of Syphilis: An Update and Review. March 2019. A PDF version is available at www.nycptc.org.
- Bolan G, Workowski. Sexually Transmitted Diseases Treatment Guidelines, 2015 MMWR Recomm Rep 2015;64. Available at https://www.cdc.gov/std/tg2015/default.htm

FAQ: When is it safe to have sex again?

- If you have been treated for syphilis, you should not have sex until 7 days after your treatment is over
  - And if present, sores have completely healed

- https://www.health.ny.gov/publications/3807/#:~:text=If%20you%20have%20been%20treated.he%20or%20she%20finishes%20treatment.
- https://www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm#:~:text=Persons%20who%20receive%20syphilis%20treatment,and%20receive%20treatment%20if%20necessary.

Summary

- Syphilis cases are rising
- Think about testing your patients
  - If at risk (take a good history)
  - When screening for other sexually transmitted infections
- Knowing which syphilis testing algorithm is in use at your institution is important for diagnosis and staging
- Treatment is based on the stage of disease
  - Remember to screen for neurologic, ocular, and otic manifestations
- Identifying syphilis cases requires a high index of suspicion