

From Sores to Serious: The Hidden Dangers of Syphilis

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May 19th, 2025

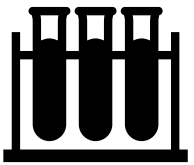
Disclosure

I have no actual or potential conflicts of interest
to disclose

Objectives



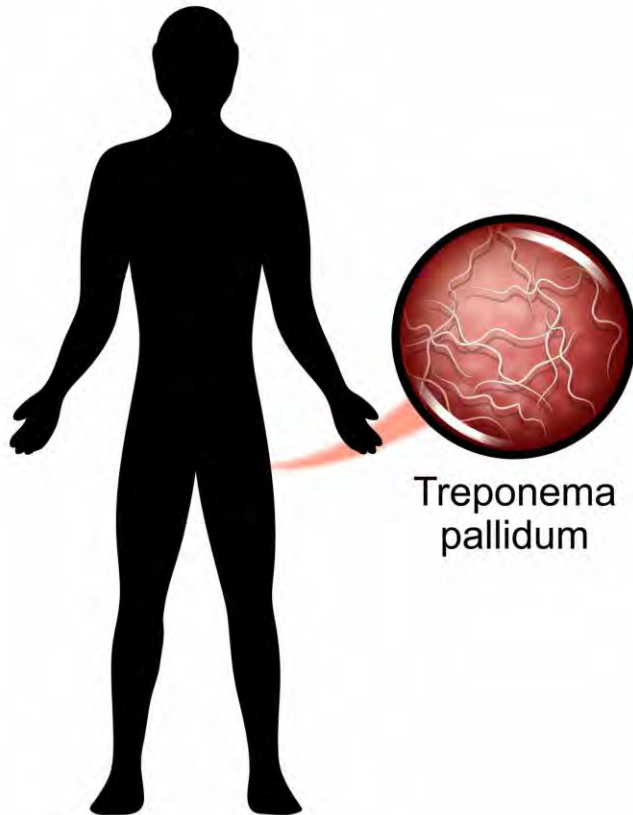
Review trends of syphilis epidemiology and highlight the societal importance of syphilis



Discuss clinical presentation and methods for laboratory diagnosis of syphilis

Treponema pallidum

SYPHILIS



- Spirochetes
- Obligate parasite
- Rapidly disseminate

Syphilis

Sexually transmitted bacteria

Direct contact or vertical

Most contagious in early stages

Disseminates via lymphatic and bloodstream

Tissue damage through induced inflammatory processes

“The Great Imitator”

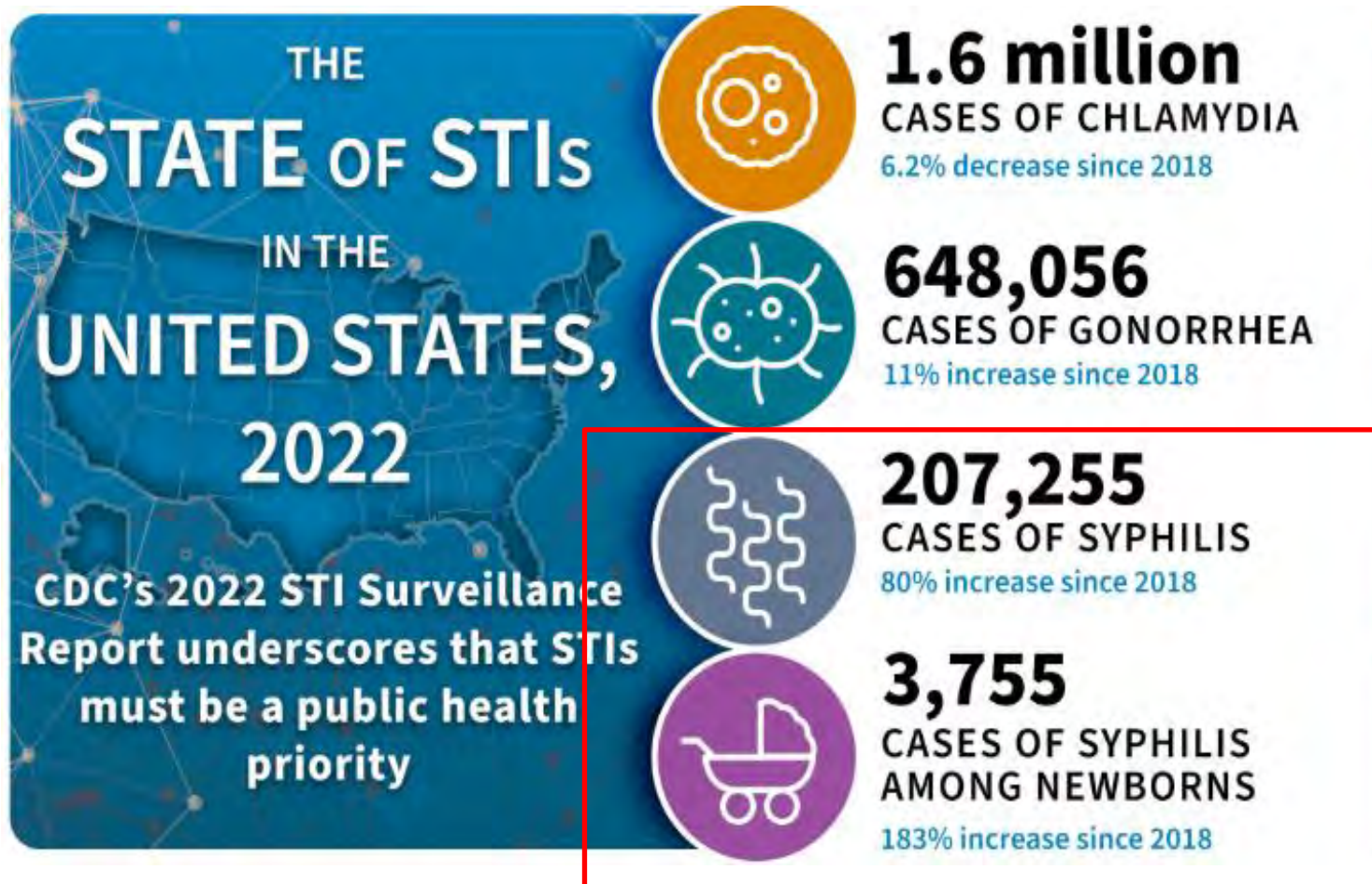
Mimics a variety of different disorders

- Complicates diagnosis, especially in later stages

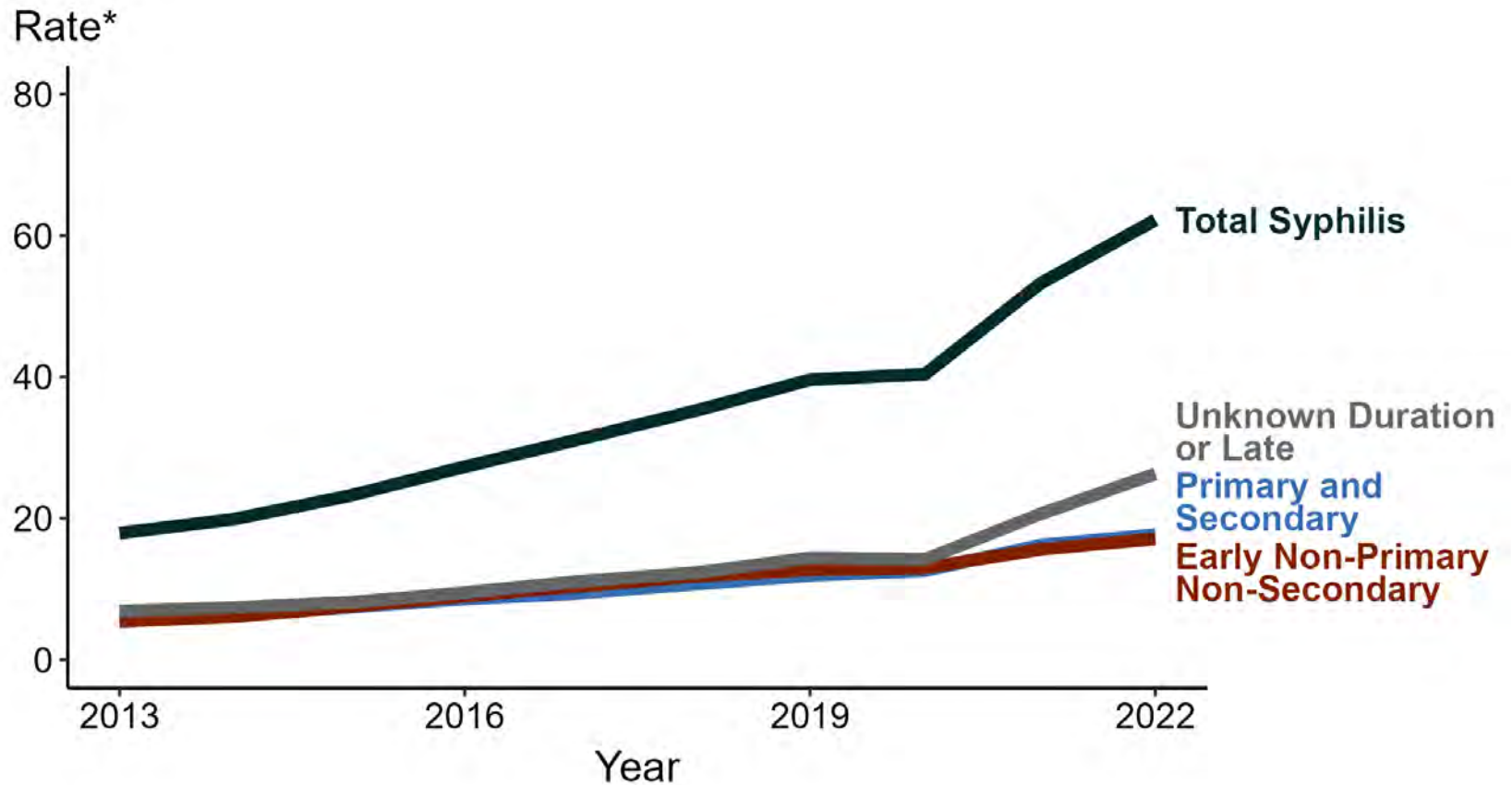
Differential diagnosis

- Primary: HSV, chancroid, lymphogranuloma venereum, neoplasm, fixed drug eruption
- Secondary: Acute HIV infection, drug eruption, psoriasis, erythema multiforme, RMSF

Epidemiology



Rates of Reported Cases from 2013-2022



* Per 100,000

Clinical Presentation

Primary

- Painless chancre
- Regional lymphadenopathy

Secondary

- Maculopapular rash
- Fever
- Lymphadenopathy
- Malaise

Latent

- No visible signs and symptoms



Clinical Presentation



Tertiary Syphilis

- Varies widely depending on organ systems affected
- Cardiovascular syphilis
- Gummatous syphilis

Neurosyphilis

- Severe headache
- Seizures
- Tabes dorsalis
- Altered mental status

Ocular Syphilis

- Eye pain
- Changes to vision
- Light sensitivity
- Posterior uveitis
- Panuveitis

Otosyphilis

- Sensorineural hearing loss
- Tinnitus
- Vertigo

Clinical Presentation

Primary

- Chancre
- Regional

Secondary

- Maculop
- Fever
- Lymphac
- Malaise

Latent

- No visible signs and symptoms

Neurosyphilis

Many cases are asymptomatic

Otosyphilis

- Sensorineural hearing loss
- Tinnitus
- Vertigo



Societal Importance

Study	Design	Population	Purpose	Outcomes
Oslo Study (1891-1910)	Retrospective	Patients with primary and secondary syphilis (n= 2000)	Investigate progression of the course of illness	28% developed one or more manifestations of tertiary syphilis
Tuskegee Study (1932-1972)	Prospective, controlled	Male, black (n=431)	Investigate if syphilis manifests differently in black host compared with white hosts	Death rate in the syphilis group was 17% higher than uninfected subjects

Learned Complications

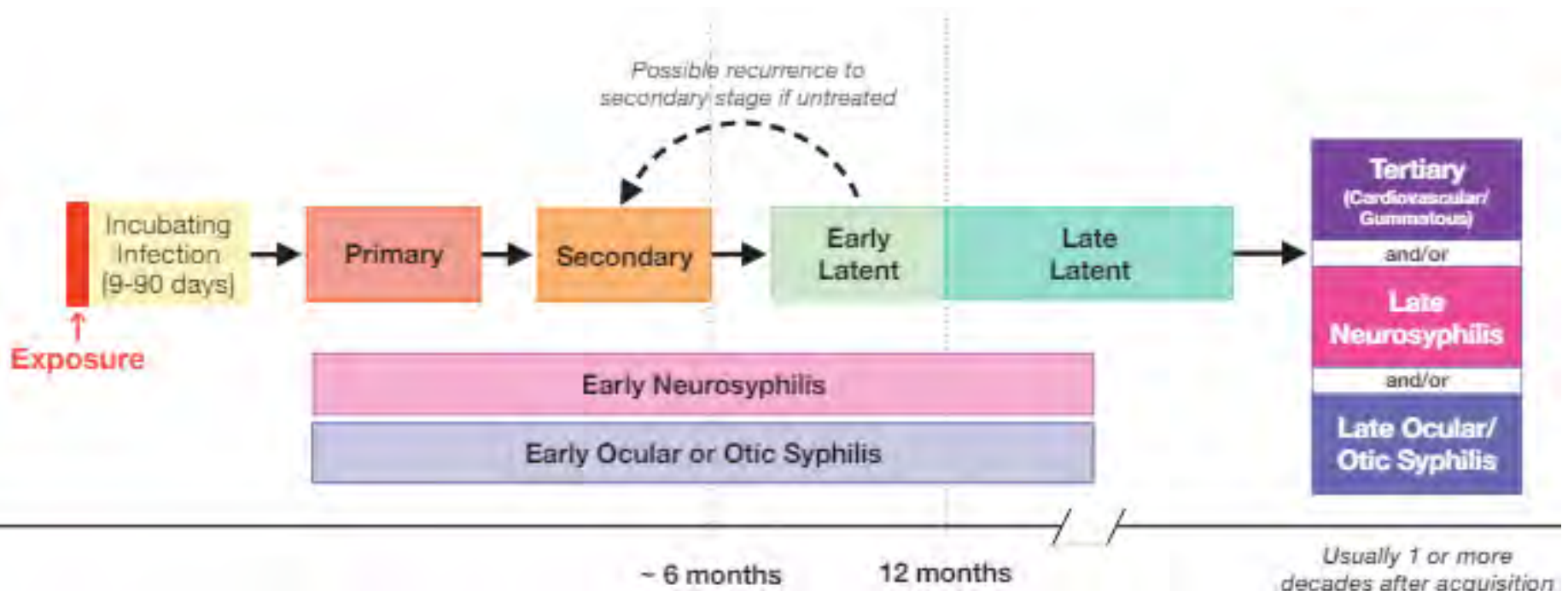
1/3 patients with untreated syphilis develop tertiary

1/4 dies as a direct result of tertiary

Additional excess mortality not directly attributable to tertiary

Transmission to sexual partners and children

Staging Syphilis



Societal Importance

Study	Design	Population	Purpose	Outcomes
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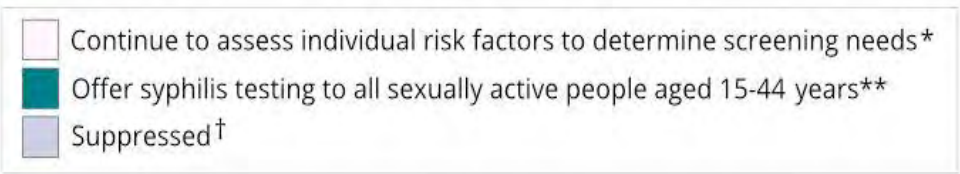
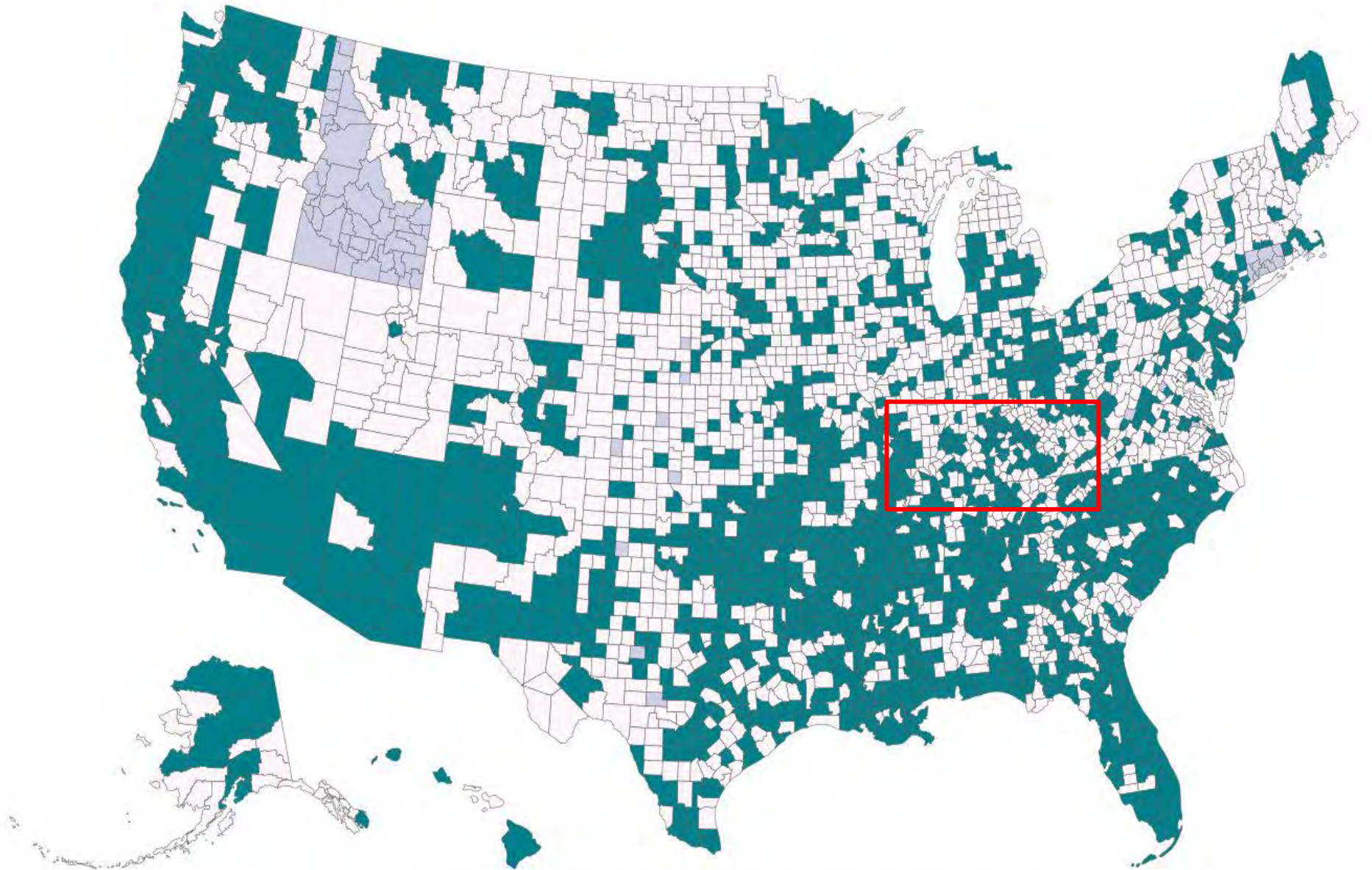
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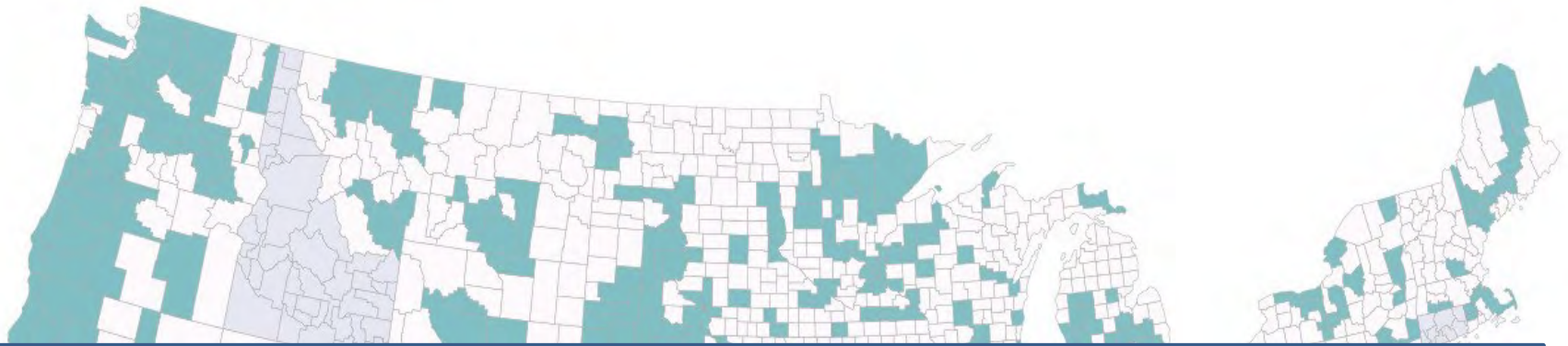
Proven cure (penicillin) became available in the 1940s

What was done?

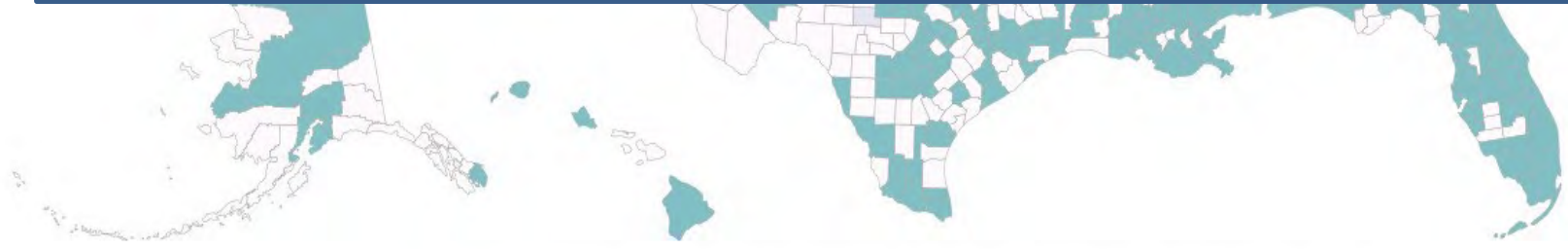
Establishment of
the Office for
Human Research
Protections

Requirement of
institutional review
boards





- CDC recommendations: syphilis rate > 4.6 per 100,000
- Fayette county: 29.1 cases per 100,000 people



Recommended Screening

Women	<ul style="list-style-type: none">• History of incarceration or transactional sex work, geography, race/ethnicity
Pregnant women	<ul style="list-style-type: none">• First prenatal visit• 28 weeks gestation if geography, substance use, STIs during pregnancy, multiple partners or new partners
MSW	<ul style="list-style-type: none">• History of incarceration or transactional sex work, geography, race/ethnicity, < 29 years old
MSM	<ul style="list-style-type: none">• At least annually• Every 3-6 months if at increased risk
Transgender and Gender Diverse	<ul style="list-style-type: none">• Consider annually
Persons with HIV	<ul style="list-style-type: none">• First HIV evaluation and at least annually

Gaps in Screening

- Failure to ask questions needed to identify high-risk groups
- Considerable less data available to describe risk for cisgender women
- Interventions primarily aimed at MSM and persons living with HIV
- Lack of clinician awareness for proactive screening

Treponemal vs. Nontreponemal testing

Treponemal

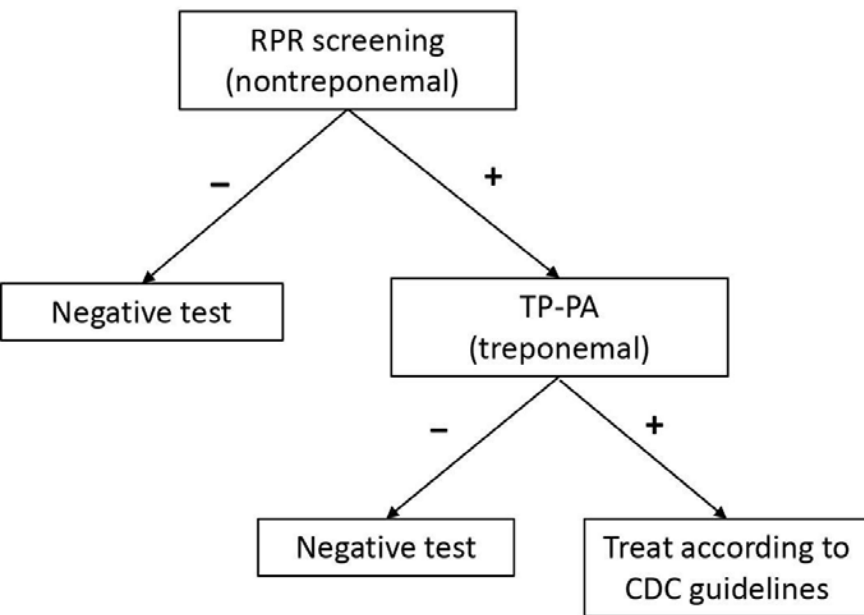
- Immunoglobulin G or total antibody (EIA, TP-PA, CIA)
- Specific to *T. pallidum*
- Appear earlier after acute infections
- Detectable for life

Nontreponemal

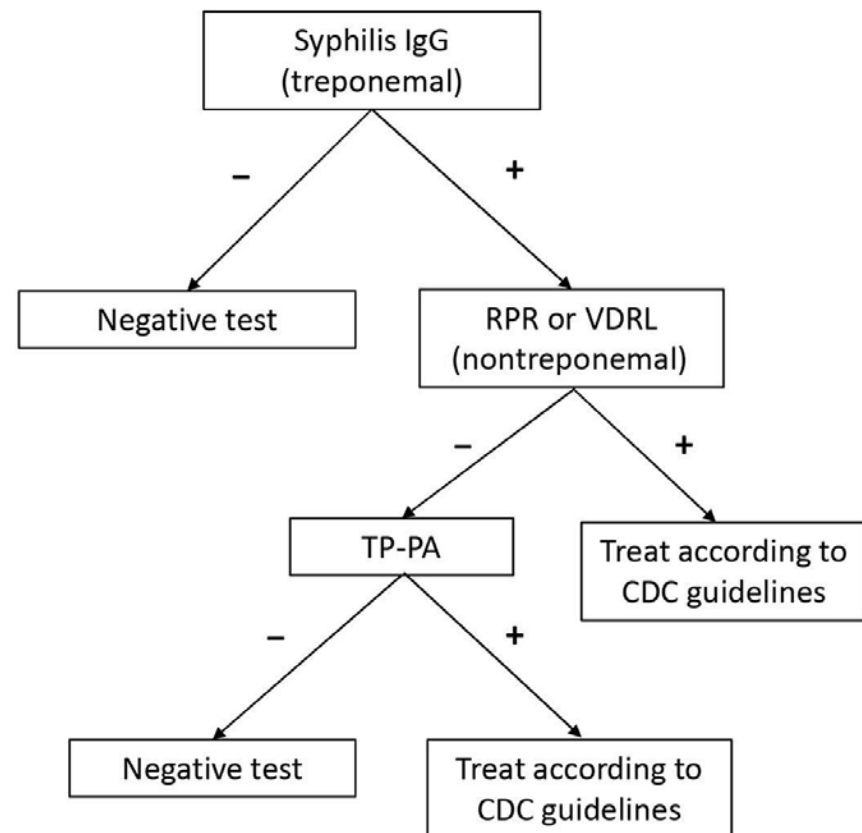
- Rapid plasma reagin (RPR) or Venereal Disease Research Laboratory (VDRL)
- Lipoidal antigens, damaged host cells, possibly treponemes
- Non-specific

Traditional vs. Reverse Algorithm Testing

Traditional testing

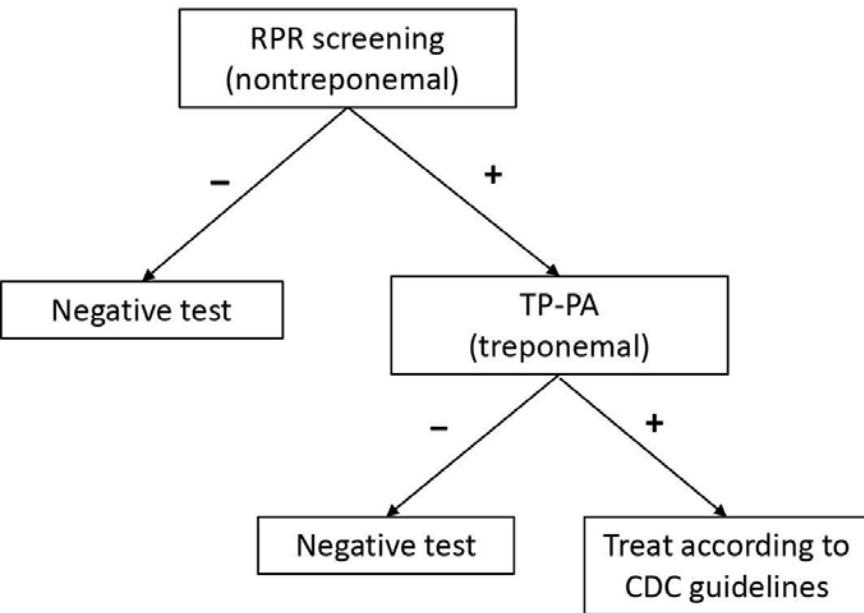


Reverse algorithm testing



Traditional vs. Reverse Algorithm Testing

Traditional testing

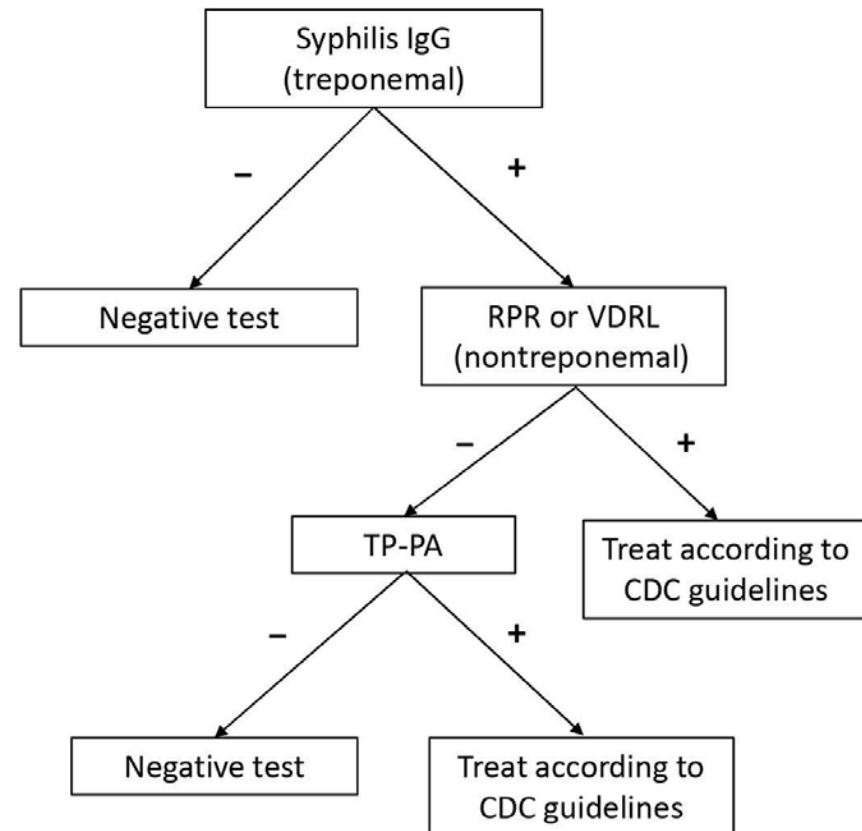


- Positive RPR interpretation necessary
- Requires both nontreponemal and treponemal tests to be positive

Traditional vs. Reverse Algorithm Testing

- Treponemal results may be positive for life
- Detection of early primary and treated infection, lower cost, reduced time

Reverse algorithm testing



Titers and Their Role

- Positive non-treponemal test results are then reported as a quantitative titer
 - Described as quantitative fold increase or decrease
- Typically correlates with disease activity
- Important for evaluation of possible treatment failure or reinfection

Titers and Their Role

4-fold

Serologic cure: 4-fold or greater decline in titer

Serologic non-response: failure to achieve a 4-fold or greater decline

Possible reinfection or treatment failure: 4-fold or greater increase

Titers and Their Role

4-fold Decrease



Management

- Penicillin remains treatment of choice
- Resistance to penicillin has never been reported in *T. pallidum*
- Syphilis is easily curable with the use of proper antibiotics

Treatment Summary

Stage	Preferred Treatment	Alternative (penicillin allergic)	Exceptional circumstances
Primary, secondary, early latent	Benzathine penicillin G 2.4 million units IM once	Doxycycline 100 mg PO BID for 14 days, tetracycline 500 mg PO QID for 14 days	Ceftriaxone 1 g IV/IM daily for 10 days
Late latent, latent syphilis of unknown duration	Benzathine penicillin G 2.4 million units IM weekly for 3 doses	Doxycycline 100 mg PO BID for 28 days, tetracycline 500 mg PO QID for 28 days	Ceftriaxone 1 g IV/IM daily for 10 days
Neurosyphilis, ocular/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	Ceftriaxone 1-2g IV daily for 10-14 days	

Urgent Need for Innovation and Collaboration

Screening

STI bundle testing

Outreach strategies

FDA approved syphilis POC

Improved testing modalities

Vaccinations

Conclusion

Midst of an epidemic that demands better screening and identification of at-risk populations

Appropriate laboratory testing prevents risk of inadequate identification of active infection

Easily curable and preventable

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