Syphilis Update

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Outline

Syphilis Epidemiology in the USA

Diagnostic testing and screening for syphilis

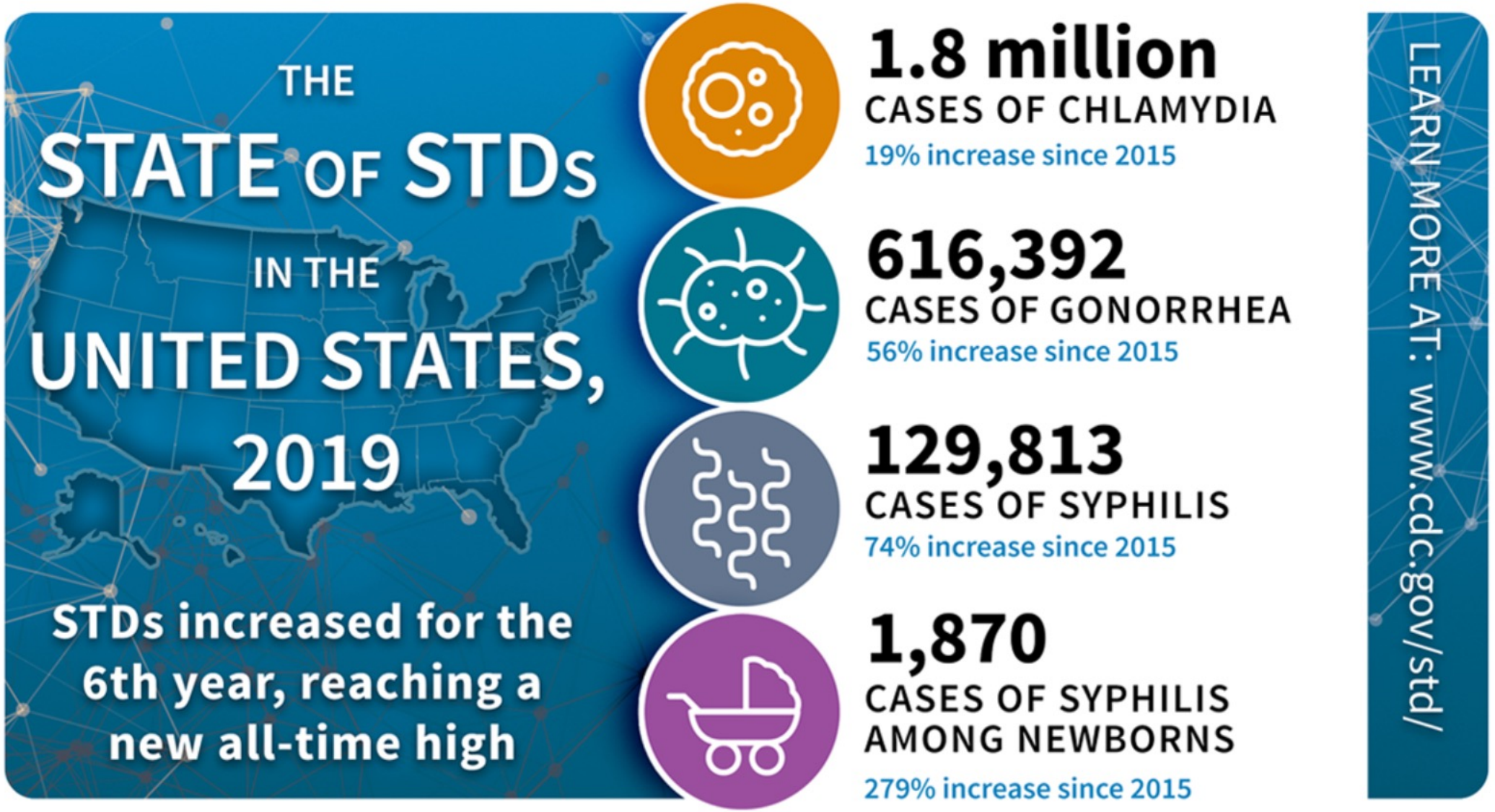
- Who and how often?

Staging syphilis

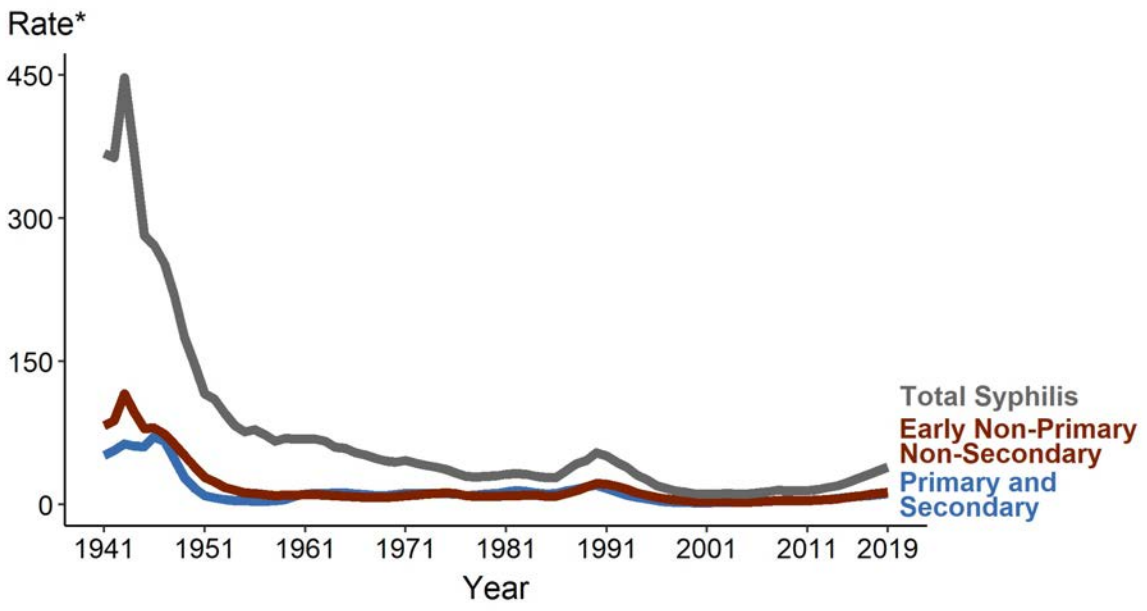
- How and why

Interpreting laboratory tests for syphilis

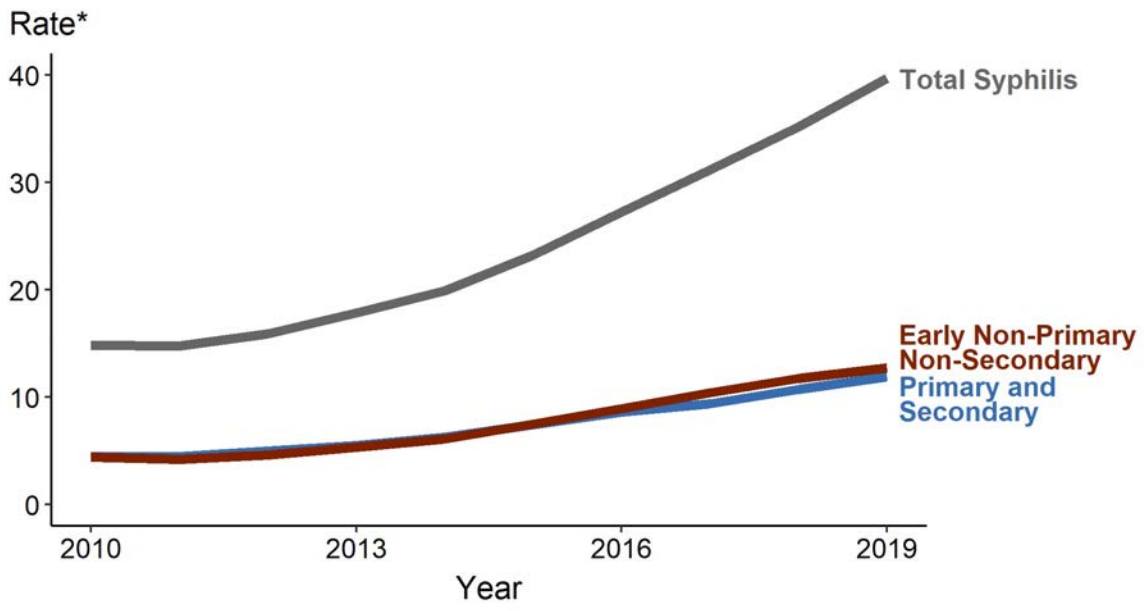
Treatment


THE
STATE OF STDs
IN THE
UNITED STATES,
2019
STDs increased for the 6th year, reaching a new all-time high
1.8 million
CASES OF CHLAMYDIA
19% increase since 2015
616,392
CASES OF GONORRHEA
56% increase since 2015
129,813
CASES OF SYPHILIS
74% increase since 2015
1,870
CASES OF SYPHILIS AMONG NEWBORNS
279% increase since 2015
LEARN MORE AT: www.cdc.gov/std/

Syphilis — Rates of Reported Cases by Stage of Infection, United States, 1941–2019

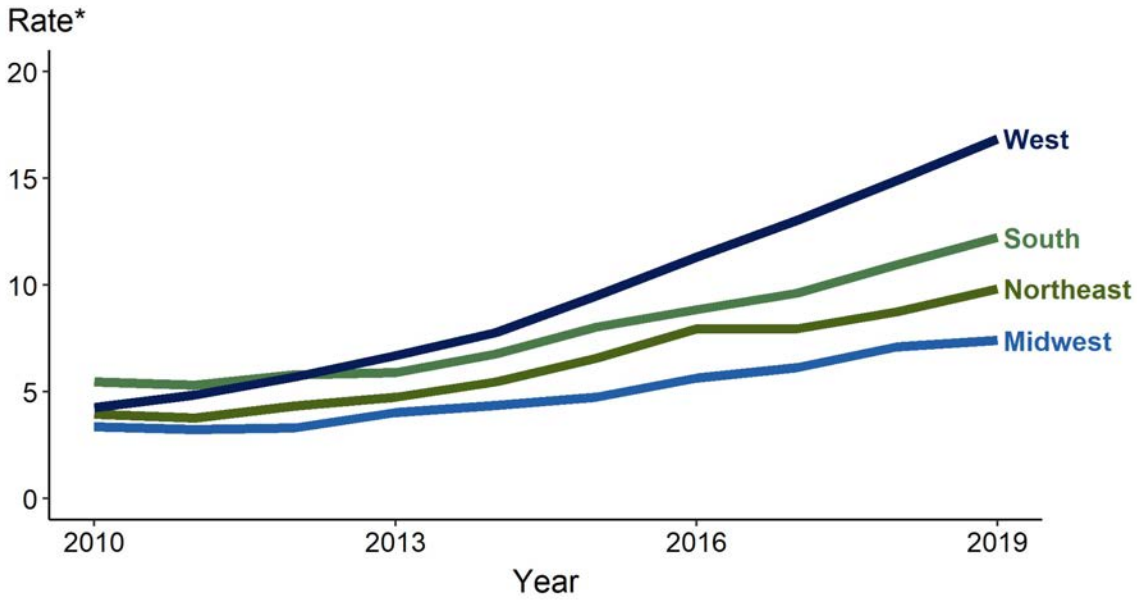


Syphilis — Rates of Reported Cases by Stage of Infection, United States, 2010–2019

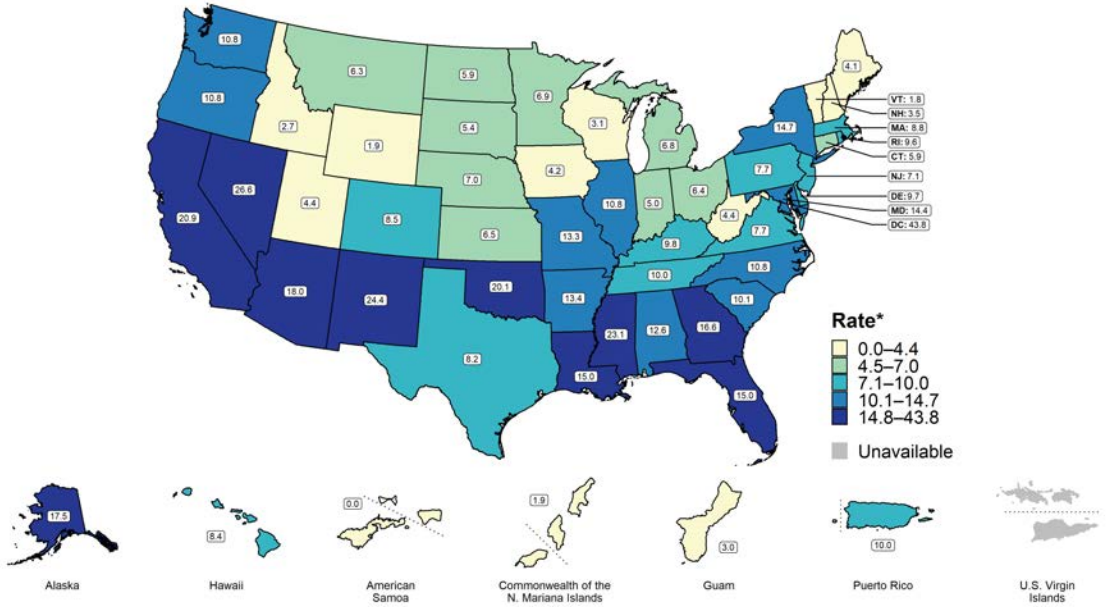


* Per 100,000

Primary and Secondary Syphilis — Rates of Reported Cases by Region, United States, 2010–2019

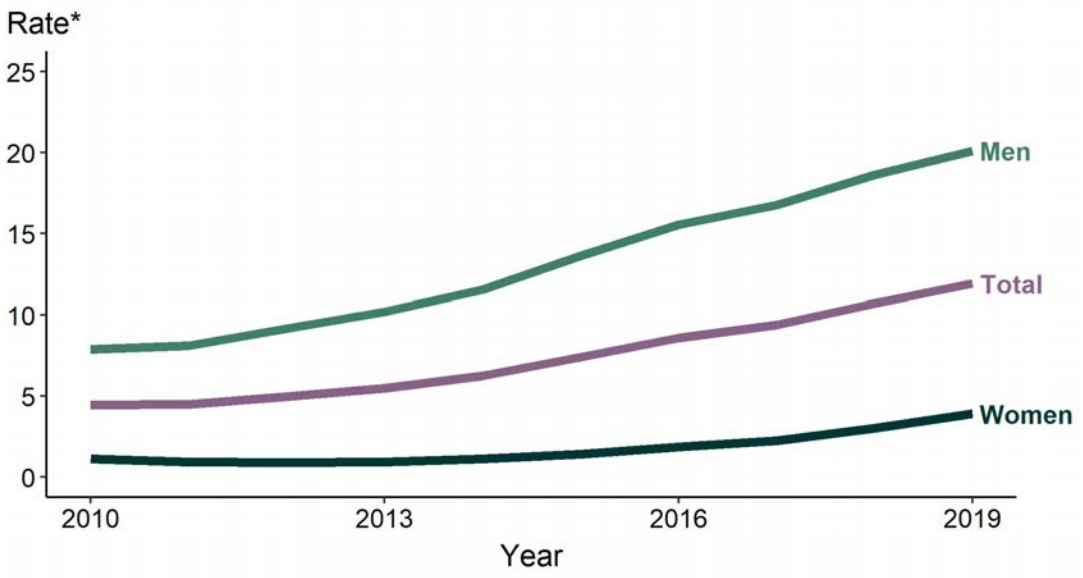


Primary and Secondary Syphilis — Rates of Reported Cases by State, United States and Territories, 2019



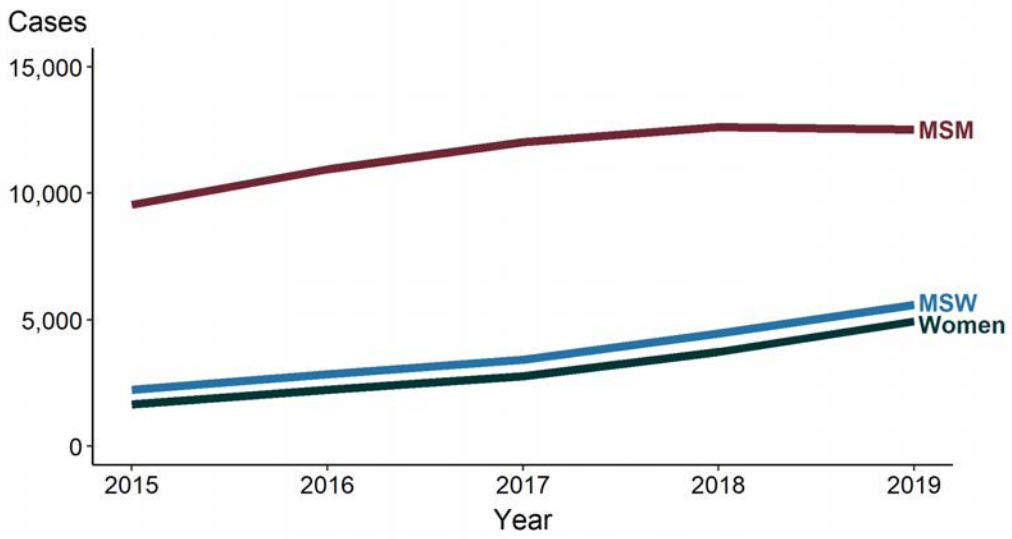
* Per 100,000

Primary and Secondary Syphilis — Rates of Reported Cases by Sex, United States, 2010–2019



* Per 100,000

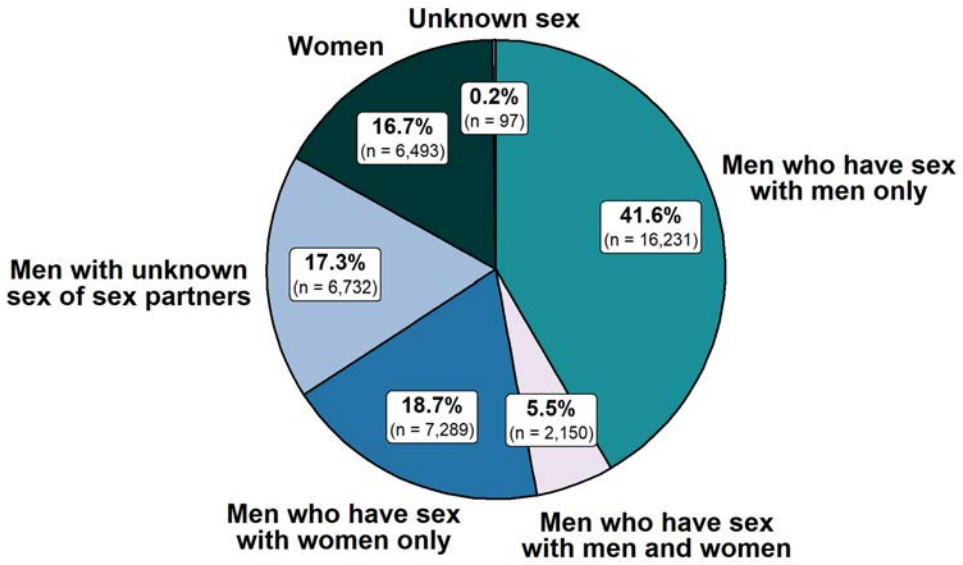
Primary and Secondary Syphilis — Reported Cases by Sex and Sex of Sex Partners, 31 States*, 2015–2019



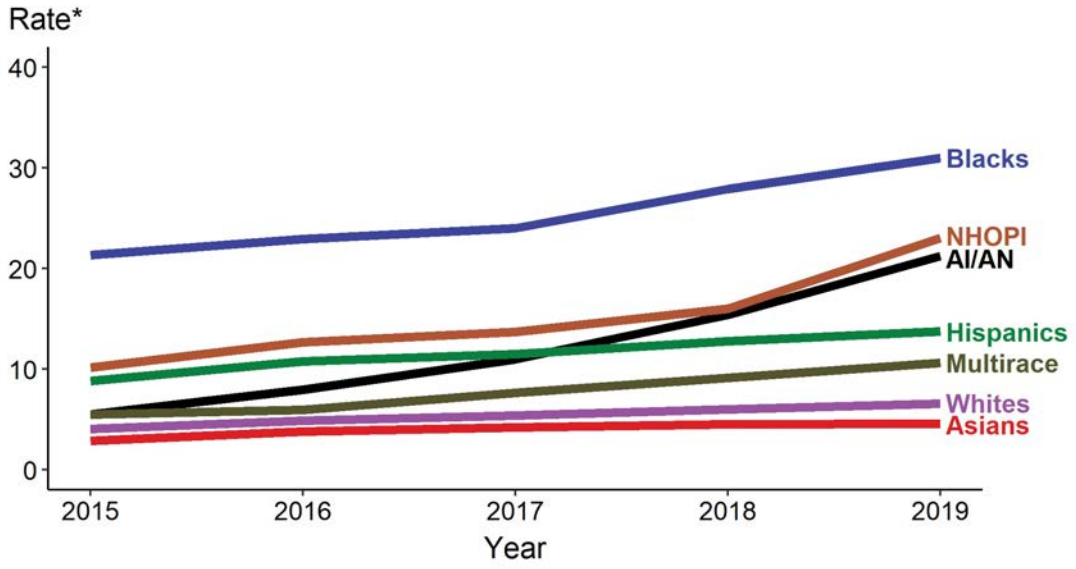
*31 states were able to classify ≥70% of reported cases of primary and secondary syphilis among males as either MSM or MSW for each year during 2015–2019.

ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men; MSW = Men who have sex with women only

Primary and Secondary Syphilis — Distribution of Cases by Sex and Sex of Sex Partners, United States, 2019



Primary and Secondary Syphilis — Rates of Reported Cases by Race/Hispanic Ethnicity, United States, 2015–2019

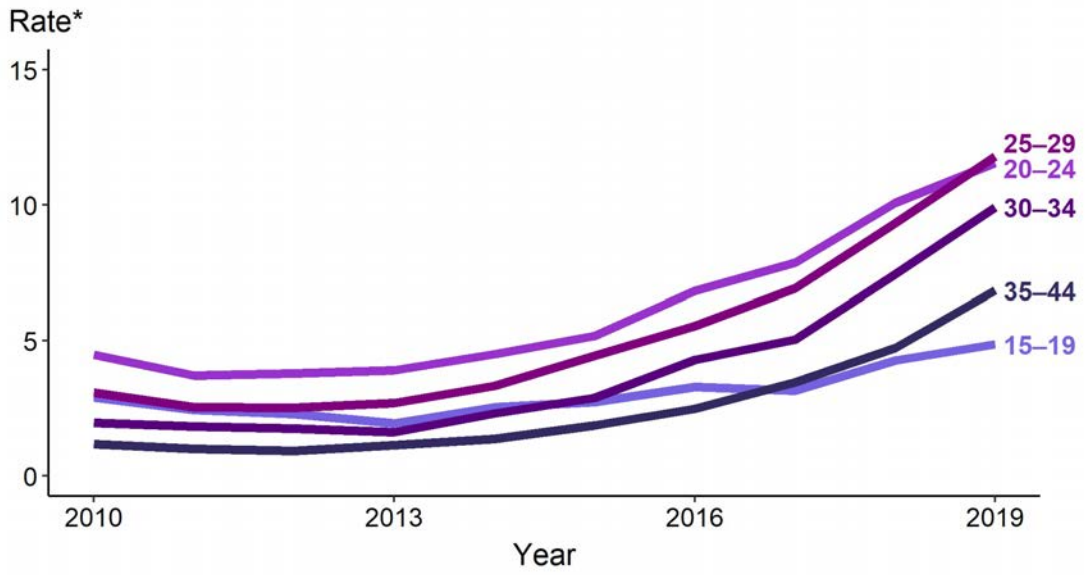


* Per 100,000

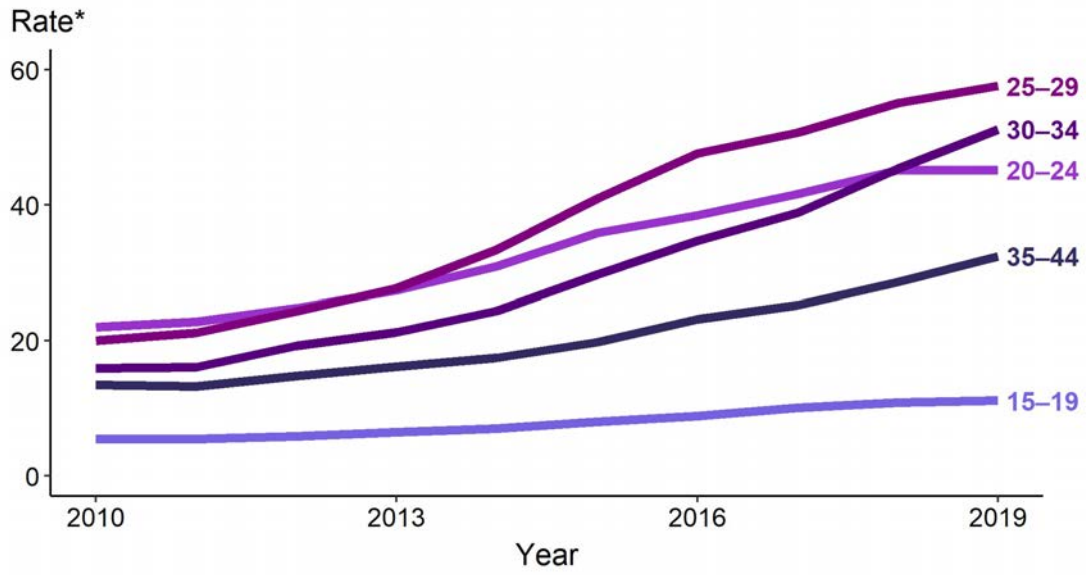
ACRONYMS: AI/AN = American Indians/Alaska Natives; NHOPI = Native Hawaiians/Other Pacific Islanders

Primary and Secondary Syphilis — Rates of Reported Cases Aged 15–44 Years by Age Group, United States, 2010–2019

Females

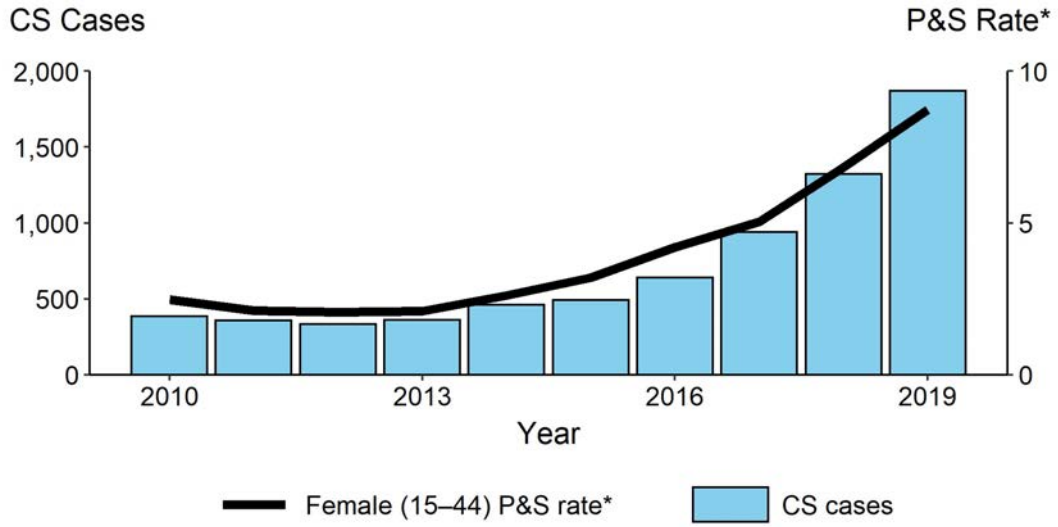


Males

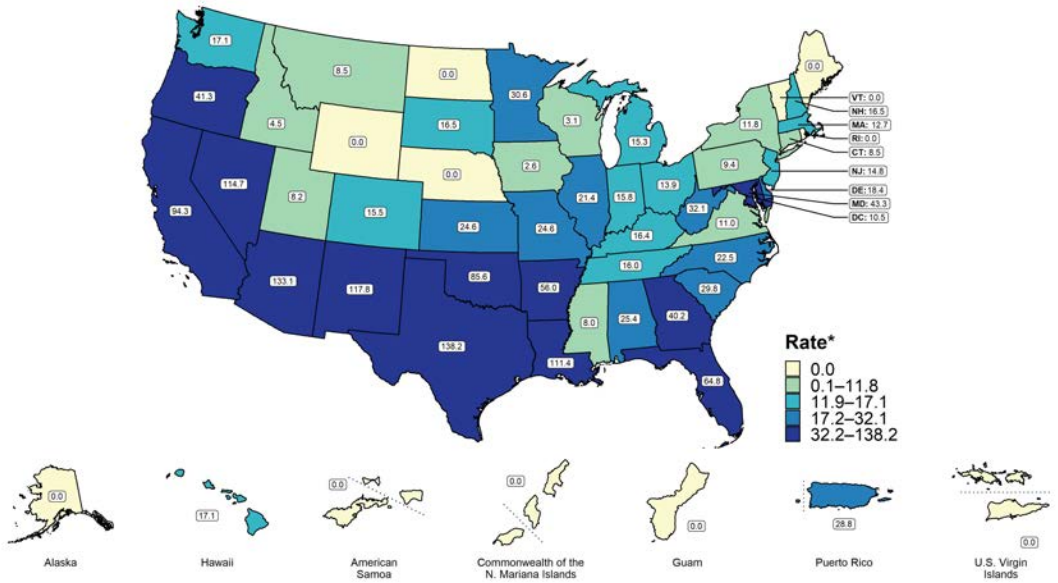


* Per 100,000

Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Females Aged 15–44 Years, United States, 2010–2019



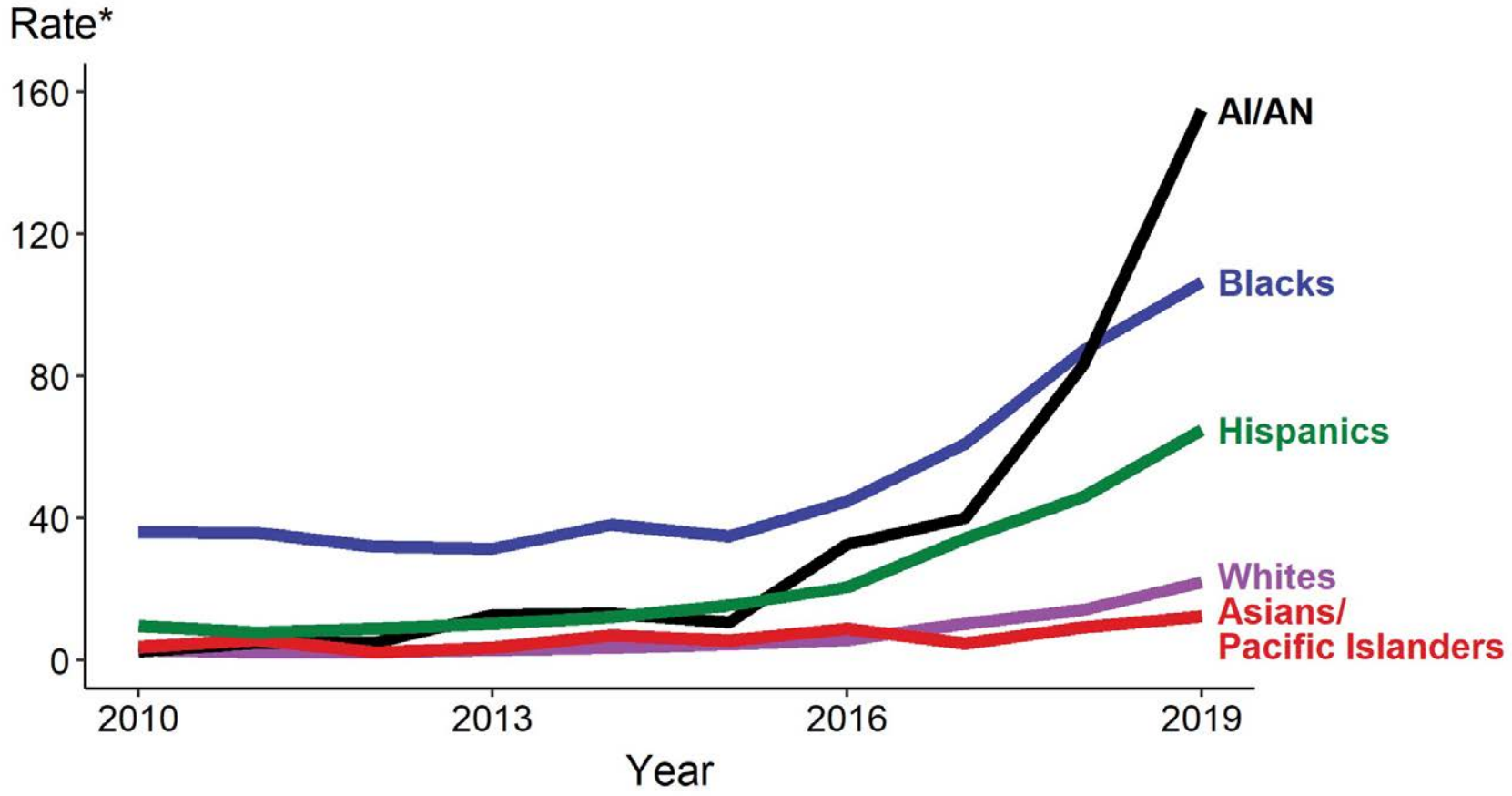
Congenital Syphilis — Rates of Reported Cases by Year of Birth and State, United States and Territories, 2019



* Per 100,000

ACRONYMS: CS = Congenital syphilis; P&S = Primary and secondary syphilis

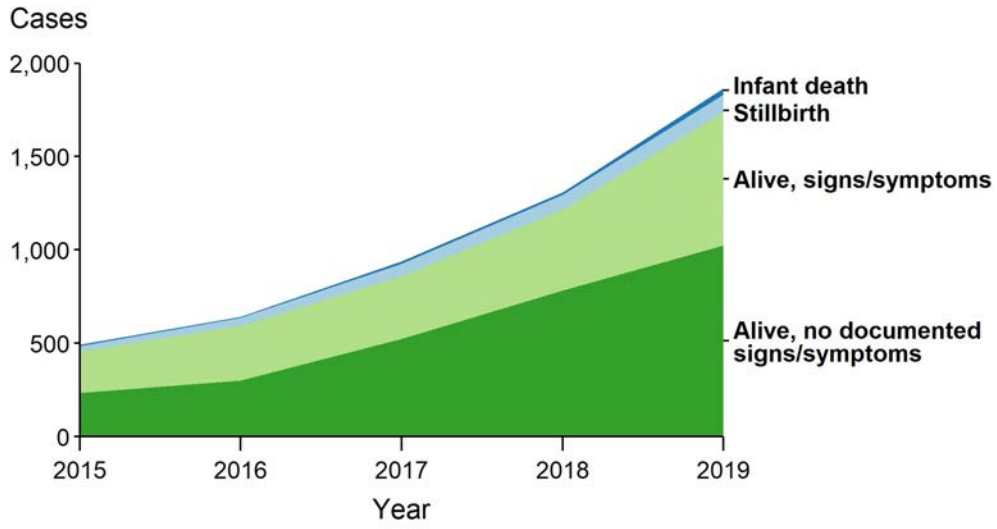
Congenital Syphilis — Rates of Reported Cases by Year of Birth, Race, and Hispanic Ethnicity of Mother, United States, 2010–2019



* Per 100,000 live births

ACRONYMS: AI/AN = American Indians/Alaska Natives

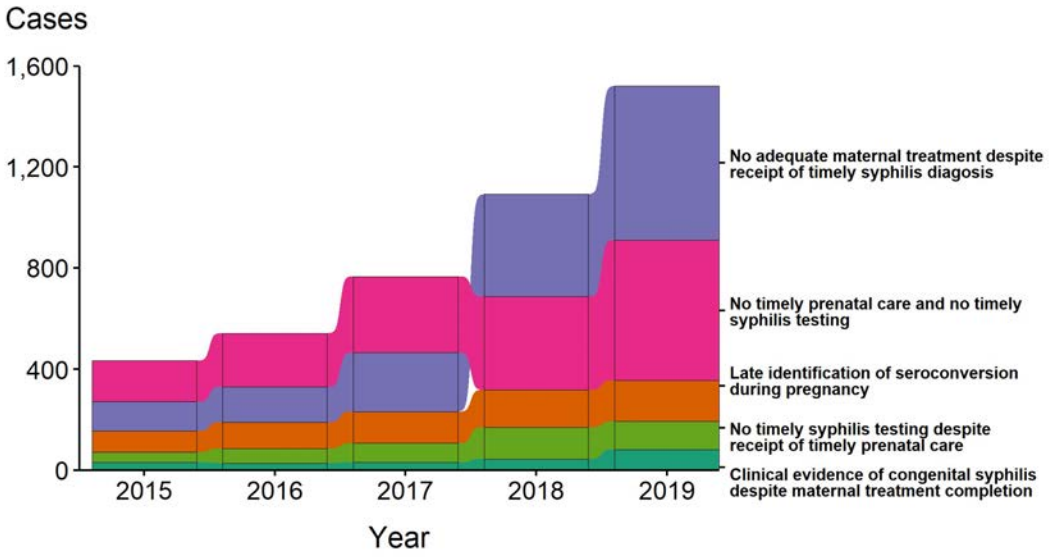
Congenital Syphilis — Number of Reported Cases by Vital Status and Clinical Signs and Symptoms* of Infections, United States, 2015–2019



* Signs/symptoms include long bone changes, snuffles, condyloma lata, syphilitic skin rash, pseudoparalysis, hepatosplenomegaly, edema, jaundice, hepatitis, reactive CSF-VDRL, elevated CSF WBC or protein, or evidence of direct detection of *T. Pallidum*.

NOTE: Of the 5,269 congenital syphilis cases reported during 2015–2019, 22 (0.4%) did not have sufficient information to be categorized

Congenital Syphilis — Missed Prevention Opportunities among Mothers of Infants with Congenital Syphilis, United States, 2015–2019



NOTE: Of the 5,268 congenital syphilis cases reported during 2015–2019, 912 (17.3%) were not able to have the primary missed prevention opportunity identified due to insufficient information submitted to CDC related to maternal prenatal care, testing, or treatment.

Outline

Syphilis Epidemiology in the USA

Diagnostic testing and screening for syphilis

- Who and how often?

Staging syphilis

- How and why

Interpreting laboratory tests for syphilis

Treatment

Who to Test/Screen for Syphilis?

Patients with classic symptoms

Patients with symptoms without an alternative explanation

Patients at risk

13

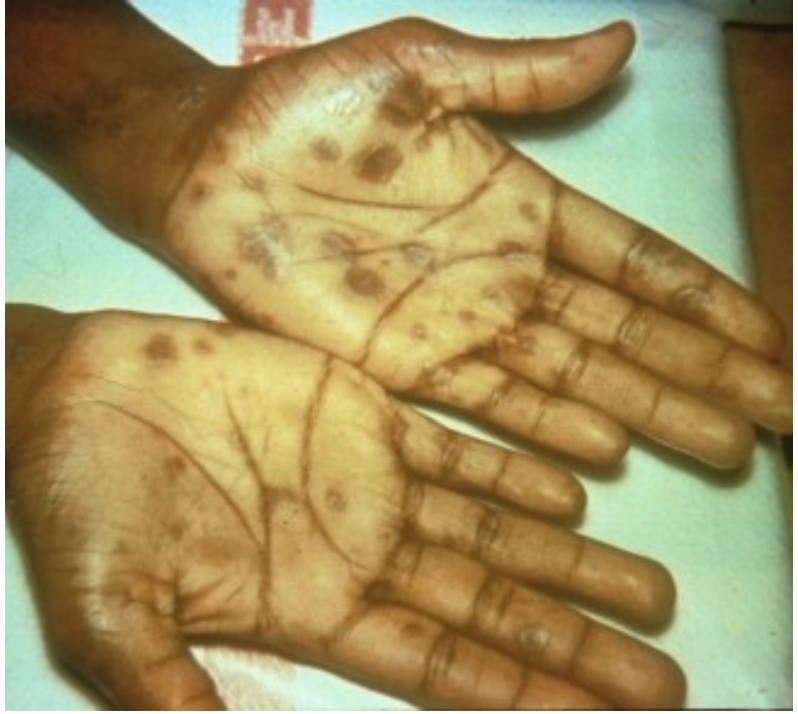
Who to Test?
Classic Symptoms

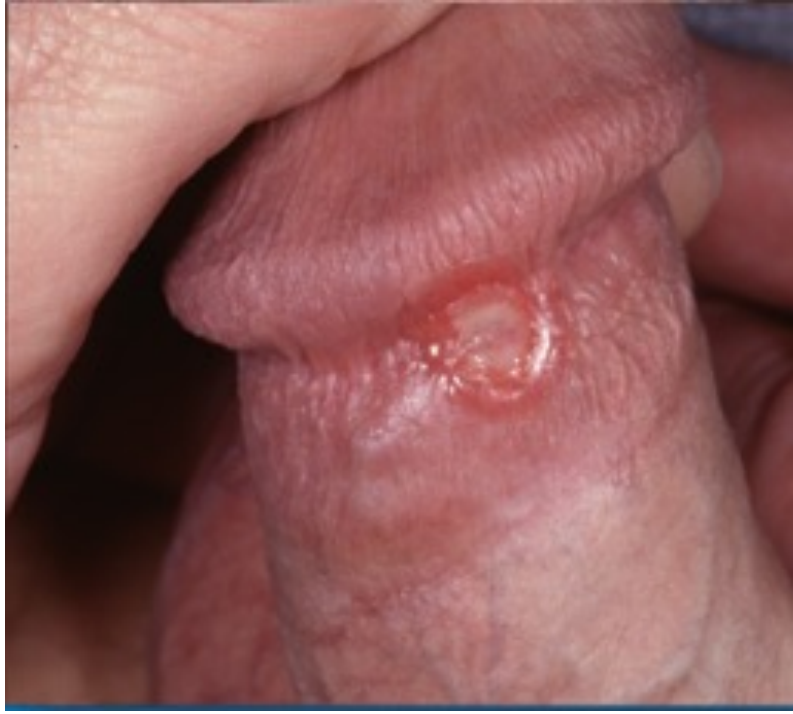
- **Painless genital ulcer (**Primary Syphilis)

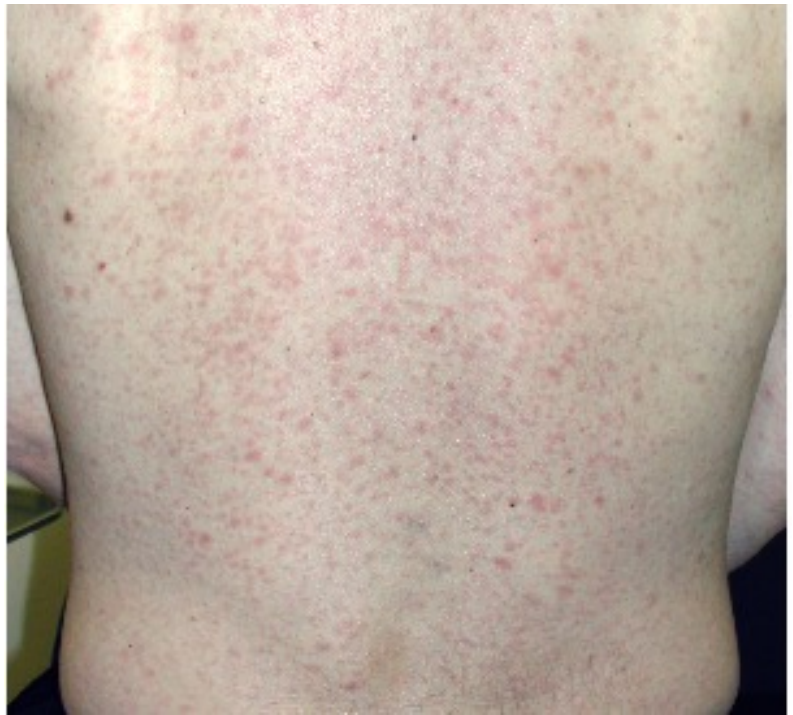
- **Rash (**Secondary Syphilis)
  - Diffuse, symmetric maculopapular
  - involving trunk and extremities
  - Involvement of palms and soles

- **General paresis or tabes dorsalis**

  (Tertiary Syphilis)







Who to Test? Symptoms without an alternative explanation

- Cranial nerve dysfunction/Chronic headache
- Meningitis, meningovascular disease or stroke
- Acute hepatitis
- Renal abnormalities
  - Albuminuria, nephrotic syndrome, acute nephritis or renal failure
- Ocular findings
  - Uveitis, retinal necrosis or optic neuritis
- Aortic insufficiency

Who to Screen? Asymptomatic Individuals

Pregnant women

Patients with a sexual partner who has early syphilis

Sexually active men who have sex with men (MSM)

HIV positive individuals

https://www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm. Accessed October 8,,2021

Who to Screen? Asymptomatic Individuals

Patients currently engaging in high-risk sexual behaviors

- Individuals with an STI
- Individuals who exchange sex for drugs or money
- Individuals having condom less sex with multiple partners
- Individuals with a history of incarceration or commercial sex work.

Sexually active people from a demographic group with high prevalence rates of syphilis

- Living in areas where there is a high prevalence
- Men aged 20 to 29 years
- Racial/ethnic minority groups
  - Blacks, Latinos, American Indian/Alaska Native, and Native Hawaiian/Pacific Islanders

https://www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm. Accessed October 8,,2021

How often to Screen for Syphilis?

Women and Men Who Have Sex with Women	Pregnant Women	Men who have sex with men (MSM)	HIV+ Persons
*	• First prenatal visit • If high risk, retest at 28-32 weeks and at delivery	• At least annually • Every 3-6 months if increased risk*	• At initial visit thereafter at least annually • Every 3-6 months if increased risk

* Patients diagnosed with a sexually transmitted disease, people who exchange sex for drugs or money, individuals having condomless sex with multiple partners sex partners, and those who engage in unprotected intercourse, sex in conjunction with illicit drug use, and methamphetamine use

2021 CDC STD Treatment Guidelines

When am I supposed to do this? Opportunities for Syphilis Screening

- After Positive STI Diagnosis
- New Patient Visits
- Annual Visits
- Pre-natal & Post-partum Visits
- Family Planning Consultations
- After Negative HIV test

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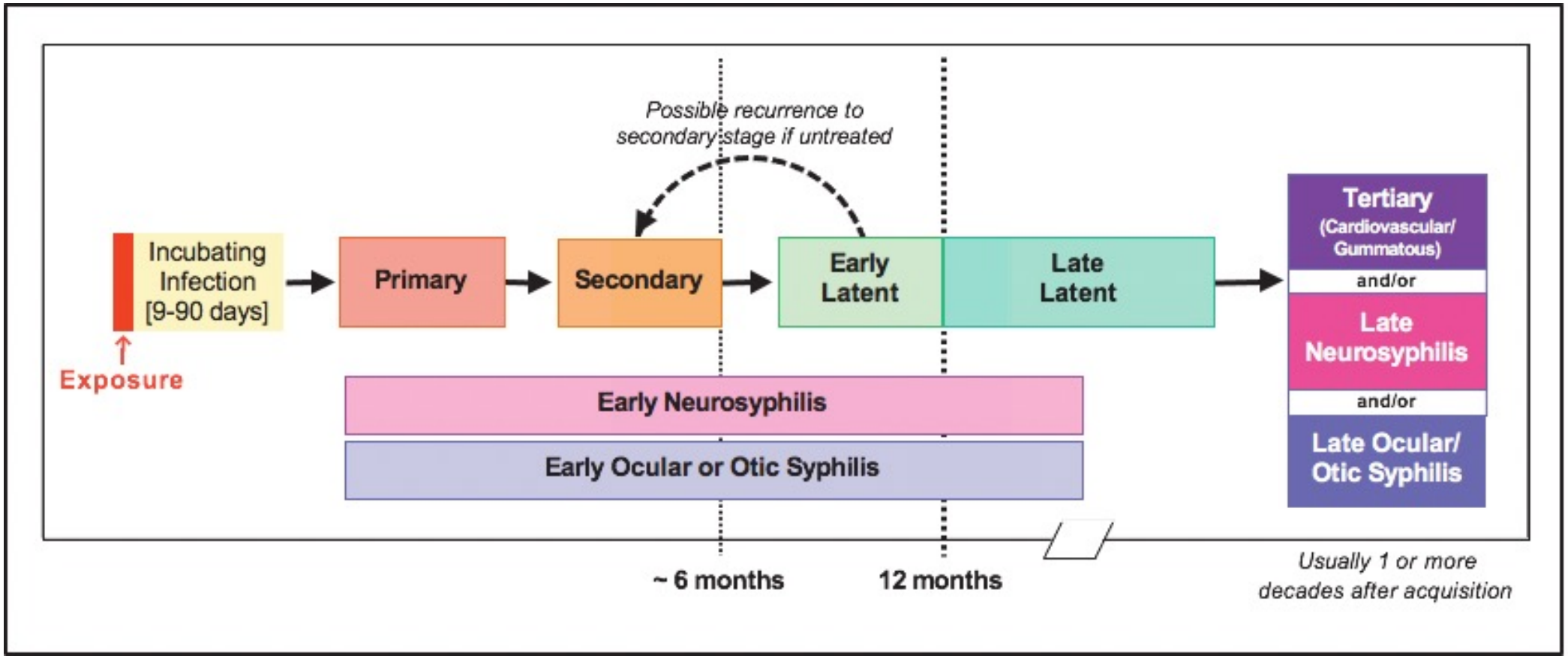
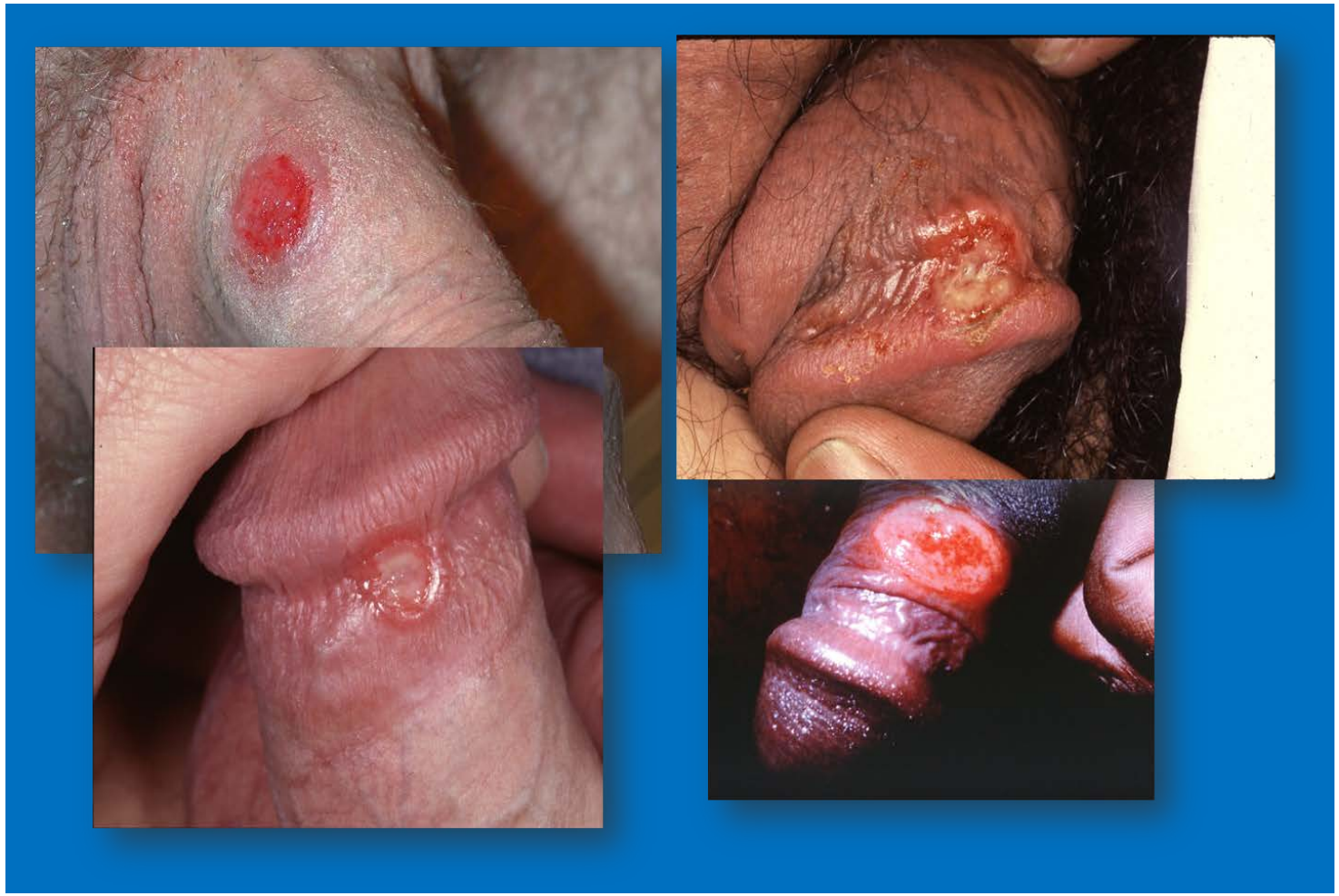
Syphilis Stages of infection

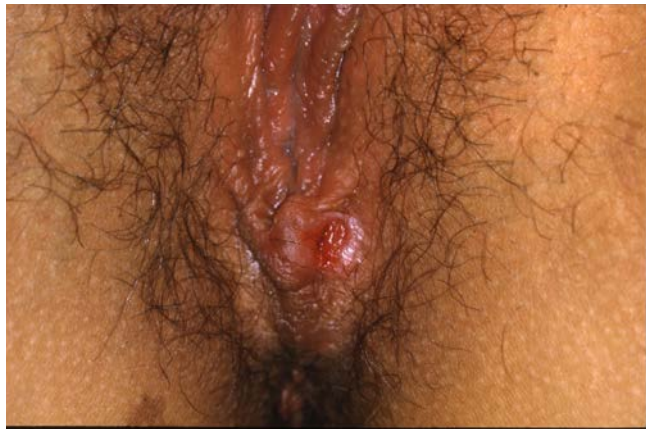


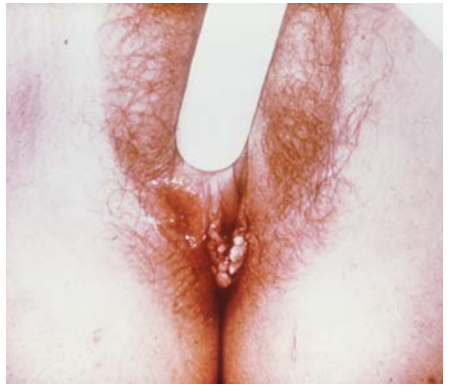
Infection

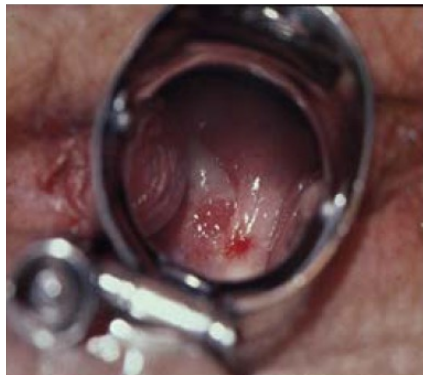
Incubation
10-90 days
Avg: 21

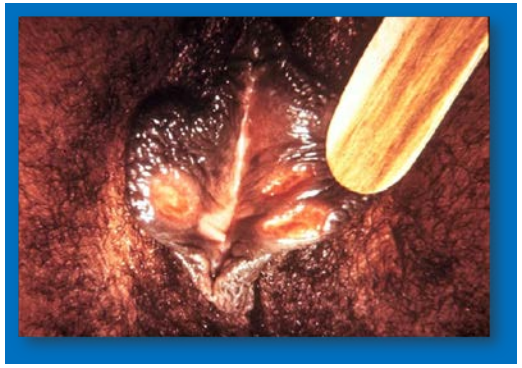
Primary – Chancre, regional lymphadenopathy











Primary Syphilis: Chancre in Women

- In women, chancres are more subtle, and clinicians need to do a closer examination.
- Chancres can occur in places that patient may not be able to detect.
  - Internal chancre will be painless and difficult to detect.
  - The patient will likely not be complaining of symptoms.

Infection

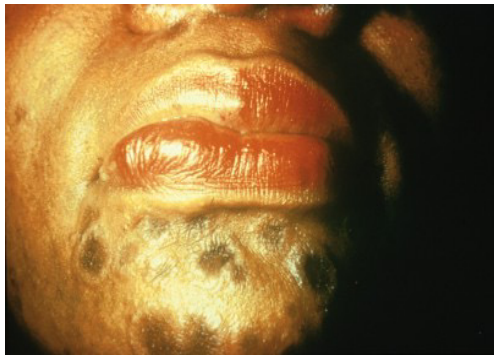
Incubation
10-90 days
Avg: 21

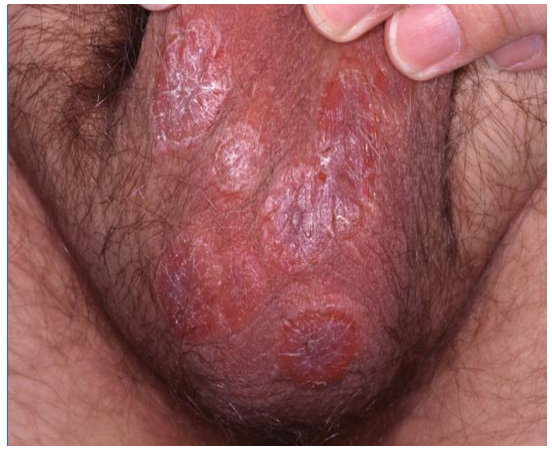
Primary - Chancre, regional lymphadenopathy

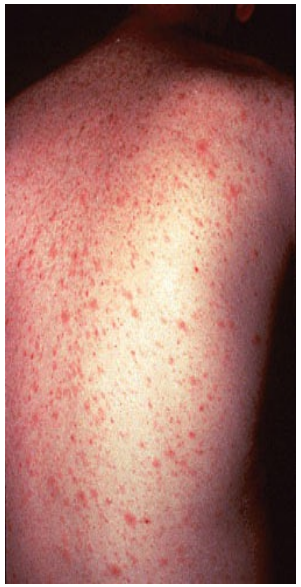
1-3 months

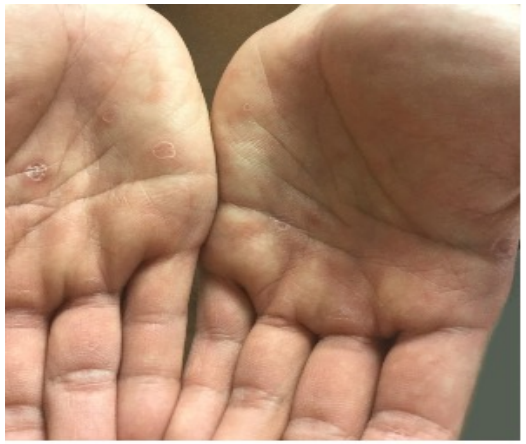
Secondary

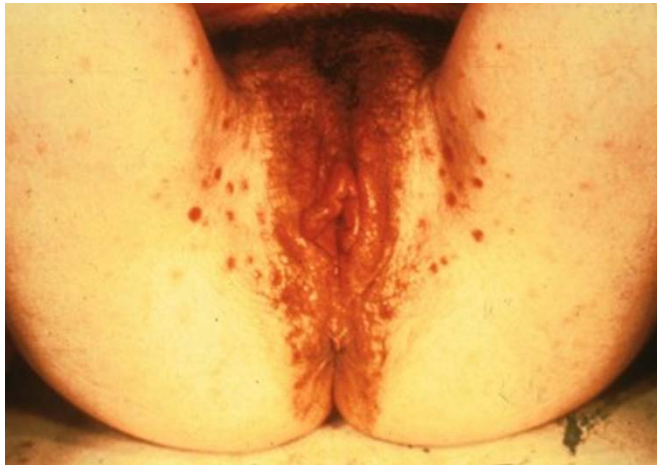
Rash, generalized lymphadenopathy



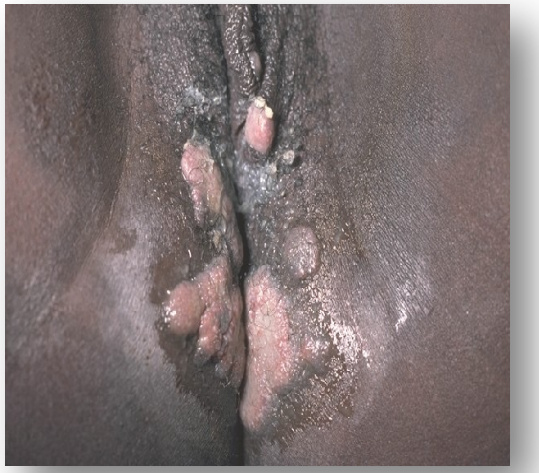


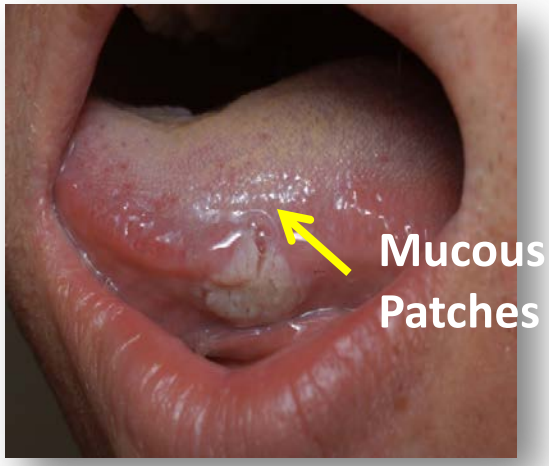


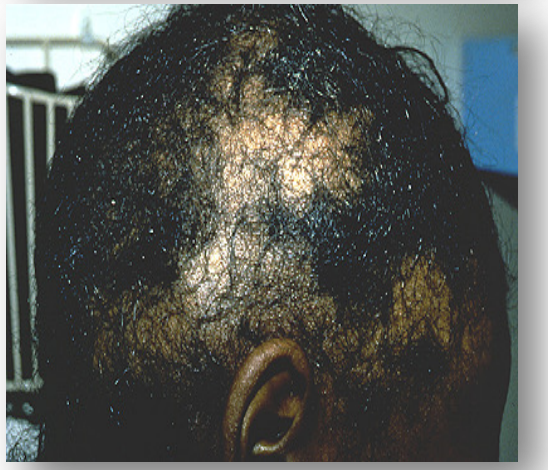


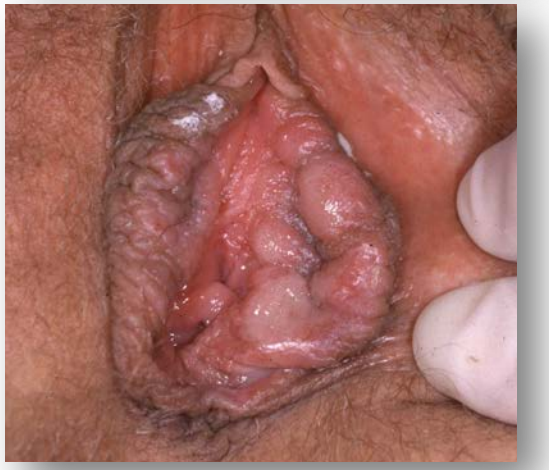


Secondary Syphilis









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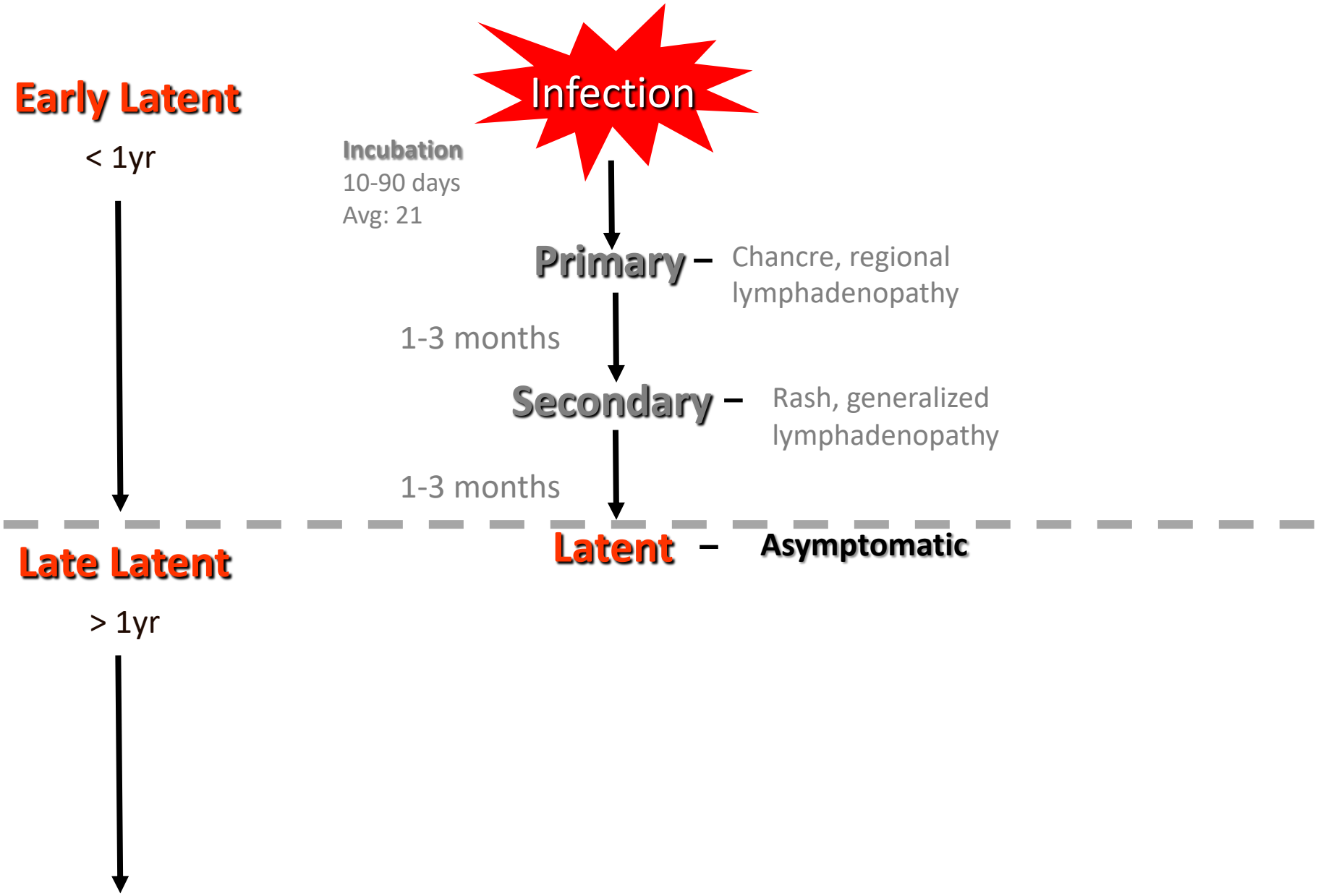
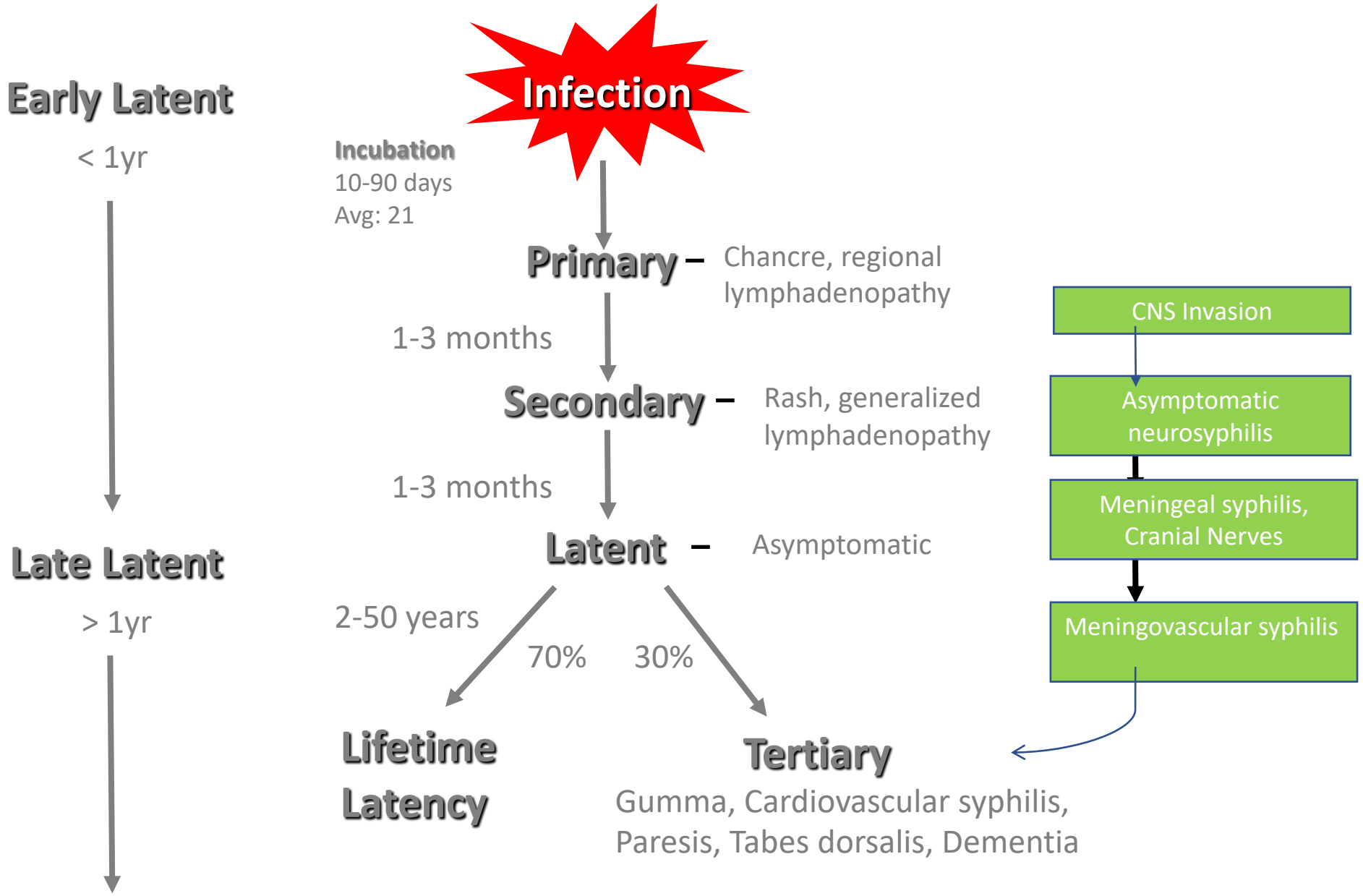
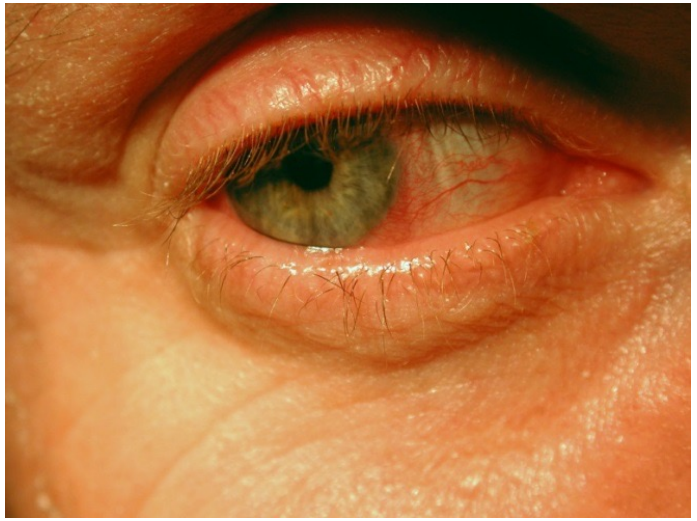

Infection
Incubation
10-90 days
Avg: 21
Primary – Chancre, regional lymphadenopathy
1-3 months
Secondary – Rash, generalized lymphadenopathy
1-3 months
Latent – Asymptomatic
Early Latent
< 1yr
Late Latent
> 1yr


Early Latent
< 1yr
Late Latent
> 1yr
Infection
Incubation
10-90 days
Avg: 21
Primary – Chancre, regional lymphadenopathy
1-3 months
Secondary – Rash, generalized lymphadenopathy
1-3 months
Latent – Asymptomatic
2-50 years
70%
30%
Lifetime Latency
Tertiary
Gumma, Cardiovascular syphilis, Paresis, Tabes dorsalis, Dementia
CNS Invasion
Asymptomatic neurosyphilis
Meningeal syphilis, Cranial Nerves
Meningovascular syphilis

Neuro-Syphilis

- Screen for ocular and/or neuro syphilis in all patients being treated for syphilis
- Treatment is different (IV Penicillin)



Note: “ciliary flush” around the edge of the cornea

Symptoms present?

- Change in or blurring of vision?
- Recent eye pain or redness?
- Spots or distortion in vision?
- Double vision?
- Light hurting eyes?
- New weakness in arms, legs, or face?
- New headache unlike usual headaches?
- Stiff neck?
- New/recent hearing loss?
- New/recent ringing of ears?

Signs present?

- Ocular infection
- Photophobia
- Nuchal rigidity
- Facial palsy

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- How and why

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Treatment

Syphilis: Serologic Tests

Non-treponemal

- Detects non-specific antibodies caused by damage to cell membrane
- Reflects activity of disease
- Screening or confirmatory
- RPR, VDRL

Treponemal

- Detects specific antibodies against *T. pallidum*
- Remains positive after 1st infection
- Screening or confirmatory
- TPPA, EIA, CIA, FTA-ABS,

RPR: Rapid Plasma Reagin; VDRL: Venereal Disease Research Laboratory; FTA-AB: Fluorescent Treponemal Antibody Absorption;
TPPA: *T. pallidum* particle agglutination; EIA: Enzyme immunoassay; CIA: Chemiluminescence immunoassay

Table 1.
Sensitivity and Specificity of Common Serological Tests in Untreated Syphilis

	Sensitivity During Stage of Infection, % (range)				Specificity, % range
Test	**Primary**	**Secondary**	**Latent**	**Late**	
VDRL	78 (74-87)	100	95 (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

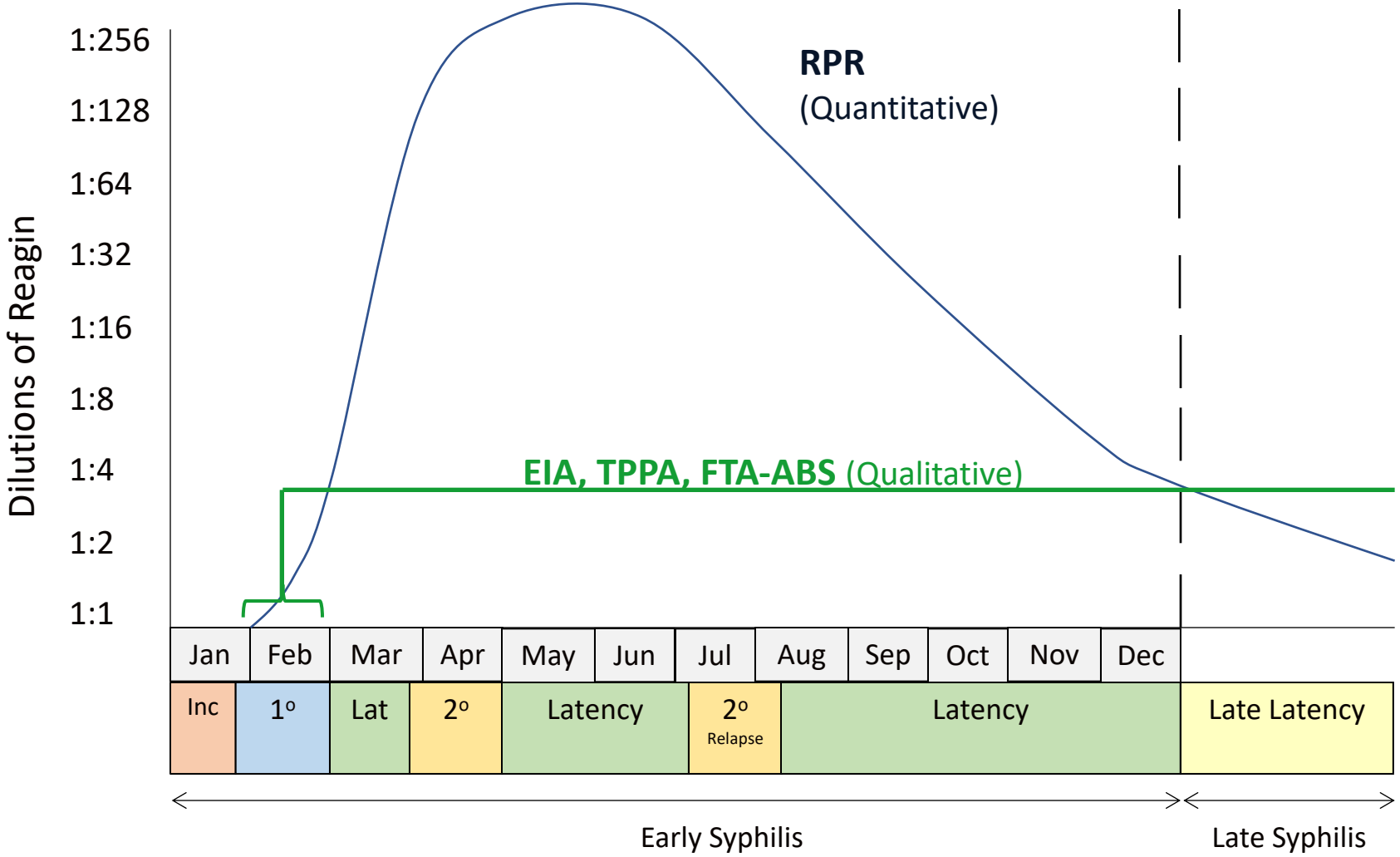
*FTA-ABS and TP-PA are generally considered equally sensitive in the primary stage of disease.

Abbreviations
NA = not available
VDRL = Venereal Disease Research Laboratory
RPR = Rapid Plasma Reagin
FTA-ABS = Fluorescent Treponemal Antibody Absorbed
TP-PA =*Treponema pallidum*-Particle agglutination
ELISA= Enzyme Linked Immunoassay

National STD Curriculum University of Washington

•Source: 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

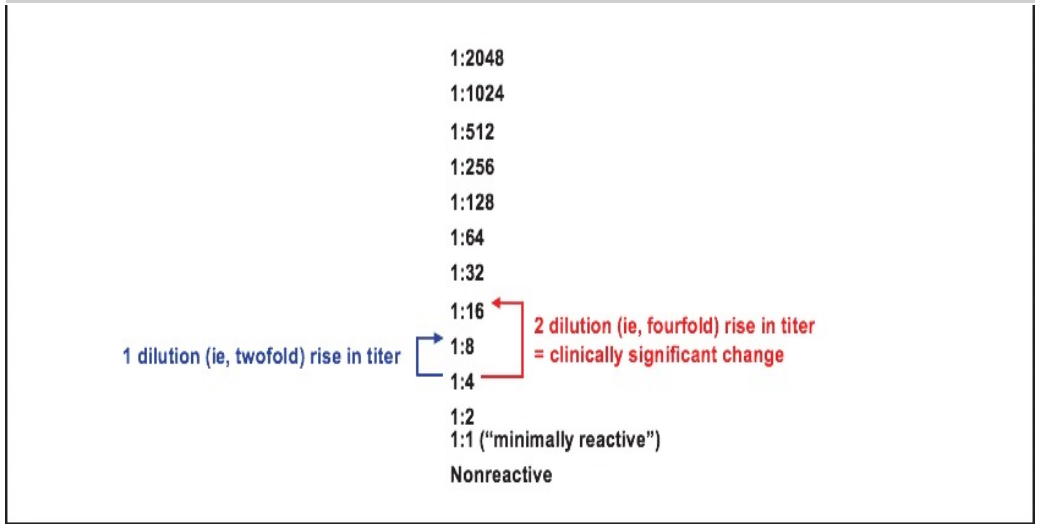
Serology of Untreated Syphilis



Serologic Tests

False-positive RPR

Example of Quantitative Nontreponemal Titers That Indicate a Clinically-significant Change



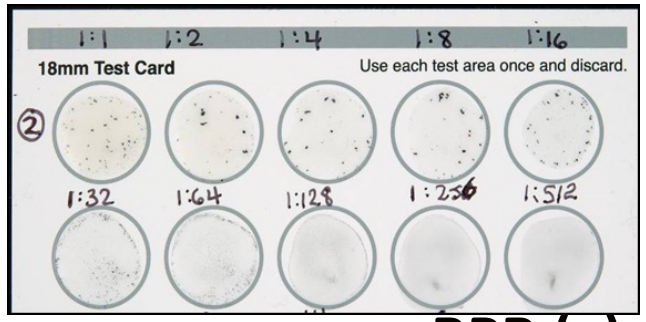
General Population
1-2%

Causes of False Positives on RPR				
IV drug use (10%)	Pregnancy	Major febrile illnesses	Autoimmune disorders	Aging

33

Testing Algorithms

- Traditional Algorithm



RPR (+)

TPPA/FTA

- Reverse Algorithm

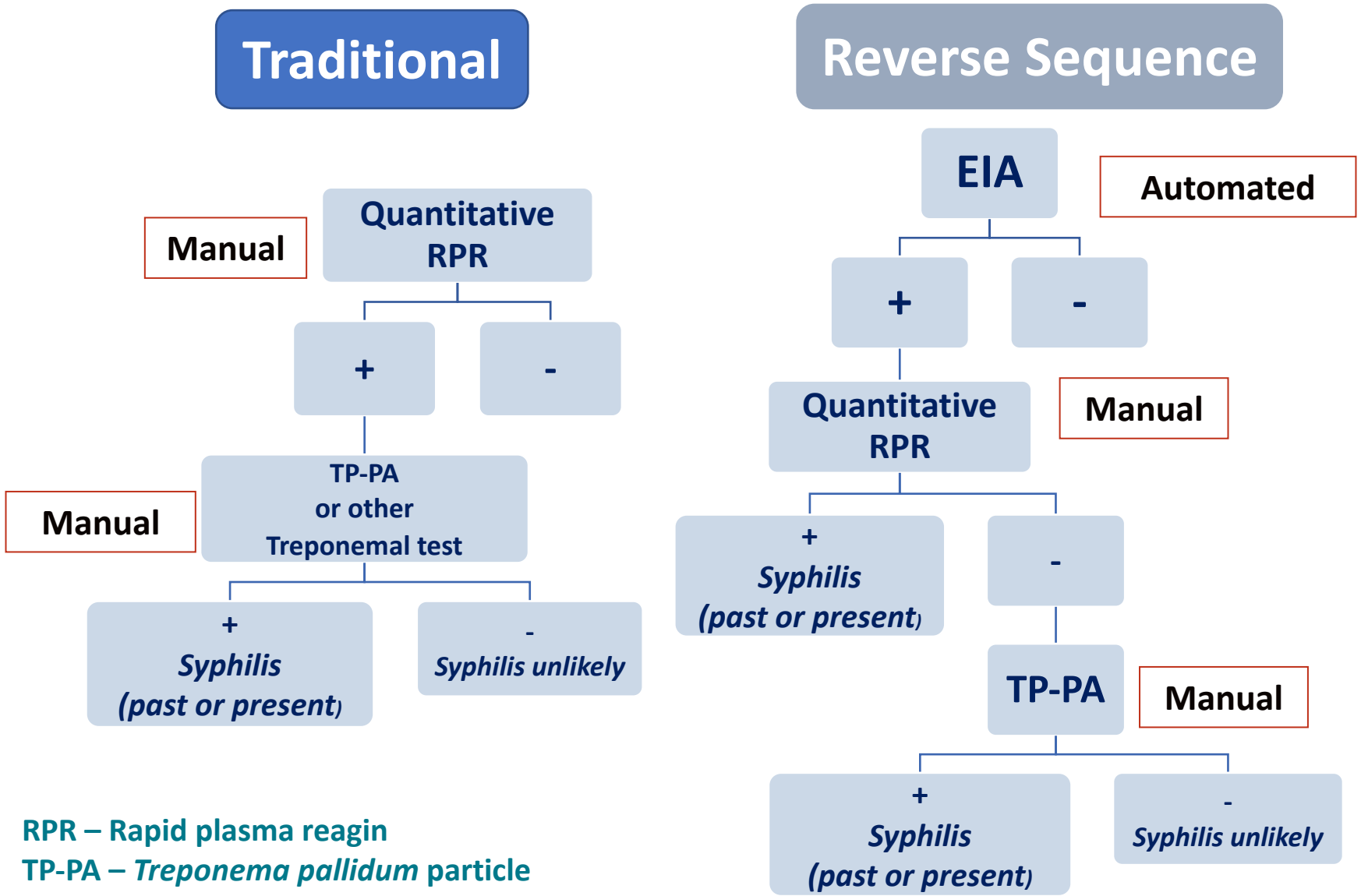
EIA/CIA (+)

RPR

Discordant Results: (+) EIA/CIA with (-) RPR

TPPA/FTA

Syphilis Serologic Screening Algorithms



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

Reverse sequence syphilis screening; 2011 CDC DSTDP webinar

Outline

Syphilis Epidemiology in the USA

Diagnostic testing and screening for syphilis

- Who and how often?

Staging syphilis

- How and why

Interpreting laboratory tests for syphilis

Treatment

Syphilis Treatment

Recommended Regimens – Primary, Secondary, Early Latent
Benzathine Penicillin G, 2.4 million units IM x 1
Recommended Regimens – Late or Unknown Latent
Benzathine Penicillin G, 2.4 million units IM at one week intervals x 3 doses

*Benzathine Penicillin G = Long-Acting Bicillin (LAB)

Recommended Regimens: Penicillin allergy* - Primary, Secondary, Early Latent
Doxycycline 100 mg po bid x 14 days OR
Ceftriaxone 1 gm IM/IV daily x 8-10 days (limited studies) OR
Azithromycin 2 gm po single oral dose (try to avoid)
Recommended Regimens: Penicillin allergy - Late or Unknown Latent**
Doxycycline 100 mg po bid x 28 days

*Other alternatives see STD Treatment Guidelines
**Close clinical and serologic follow-up; data to support alternatives to PCN are limited

Syphilis in Pregnancy

Screen at 1st prenatal visit
Repeat screen in 3rd trimester and at delivery for high risk or high prevalence areas
If PCN allergic, desensitize and treat with PCN
Treat with PCN for appropriate stage; you don't need extra PCN in order to reach the fetus

Treatment Follow-up*

Early (Primary and Secondary)	Latent (Early, Late, or Unknown)
• If lesions present, clinical exam in 1 week • Clinically evaluate and repeat RPR at 6 and 12 months • Suggest HIV test with repeat HIV test at 6 months • If known HIV+, repeat RPR at 3, 6, 9, 12 and 24 months	• Repeat RPR at 6, 12 and 24 months • If known HIV+, repeat RPR at 6, 12, 18 and 24 months

Following RPR Titers

January 2013

Test & Treat:
RPR = 1:32

July 2013

RPR: 1:8
(4-fold decrease)

RPR: 1:128
(4-fold increase)

January 2014

Early disease:
Seronegative within 1 year
Latent disease:
Low titer may persist for life

Management of Sex Partners

Treat presumptively if:

- Exposure to primary, secondary, early latent ≤ 90 days
- Exposure to primary, secondary, early latent > 90 days and no serology is available
- Exposure to unknown latent syphilis*

Treatment for Syphilis Contact

Benzathine Penicillin G, 2.4 million units IM x 1

* If exposed to unknown latent syphilis > 90d , treat according to serologic evaluation

Thank You

QUESTIONS?