
Syphilis Overview: Best Practices for Screening & Management



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Presentation Roadmap

- Updated Screening recommendations
- Natural History/Clinical Manifestations
- Diagnostic and Screening Algorithms
- Point of Care Testing
- Syphilis Staging and Treatment

Disclosures

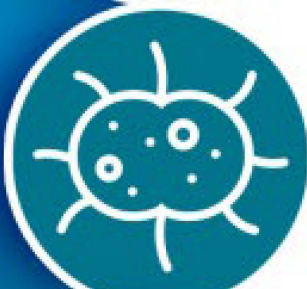
- **Sharon Adler MD, MPH has no relevant financial relationships with an entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on patients.**

THE
STATE OF STIs
IN THE
UNITED STATES,
2022

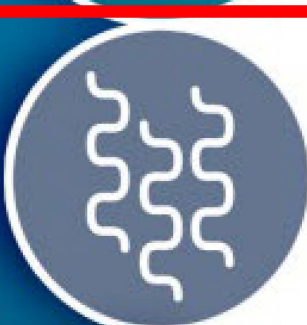
CDC's 2022 STI Surveillance
Report underscores that STIs
must be a public health
priority



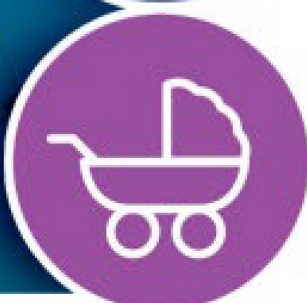
1.6 million
CASES OF CHLAMYDIA
6.2% decrease since 2018



648,056
CASES OF GONORRHEA
11% increase since 2018



207,255
CASES OF SYPHILIS
80% increase since 2018

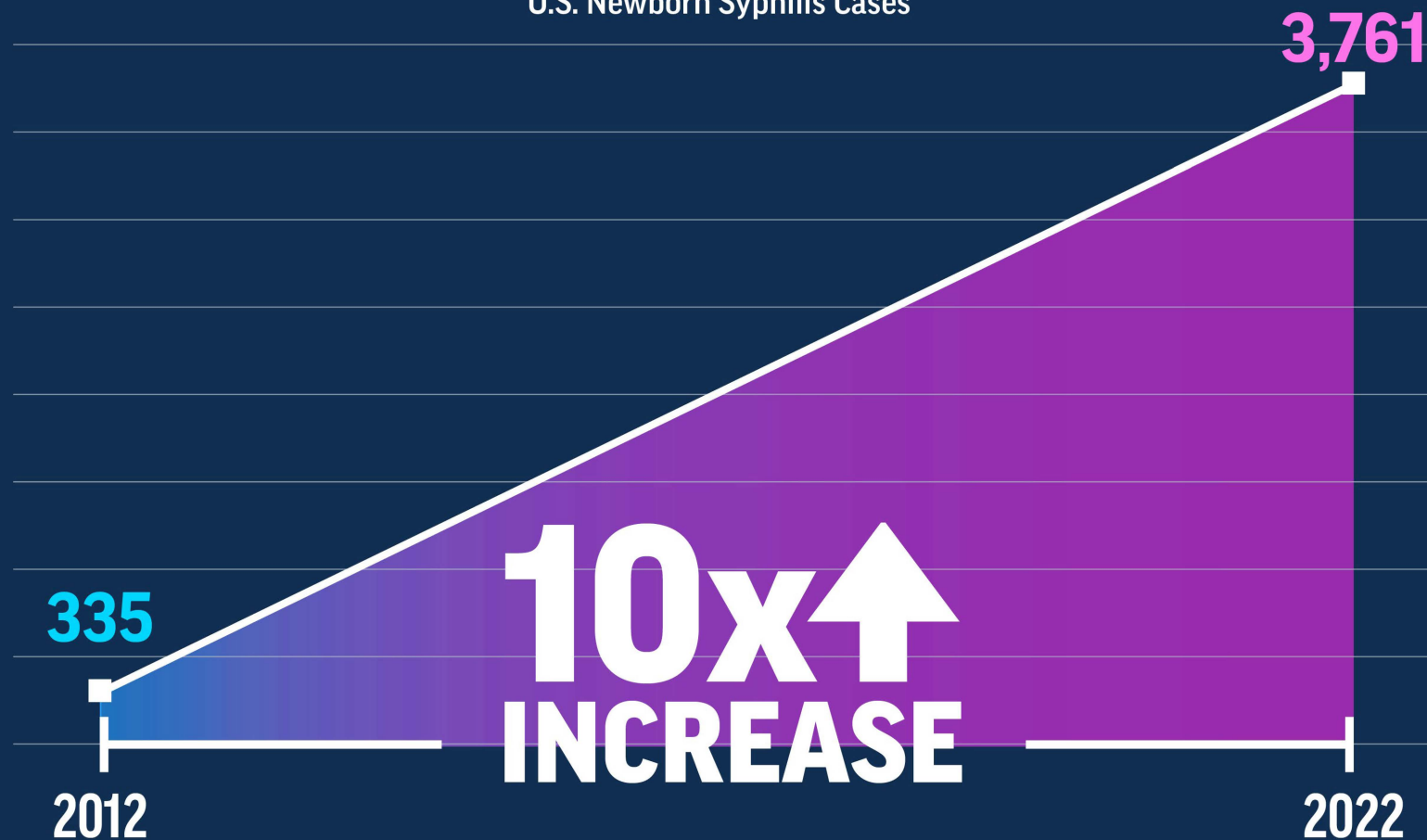


3,755
CASES OF SYPHILIS
AMONG NEWBORNS
183% increase since 2018

LEARN MORE AT: www.cdc.gov/std/

U.S. Newborn Syphilis Cases Surge Over 10 Years

U.S. Newborn Syphilis Cases



^{CDC}
Vitalsigns[™]

Source: November 2023 Vital Signs



CS341746

CDC: “Up to 40% of infants born to [persons] with untreated syphilis may be stillborn or die from the infection”



Syphilis Screening Recommendations

CDC Syphilis Screening Recommendations

Change in 2021 STI Treatment Guidelines

- **Non-pregnant women:** risk-based screening
- **MSW:** risk-based screening
- **MSM:** at least annually, every 3-6m if risk
- **HIV+ (all persons):** at first HIV eval, then at least annually
- Anyone diagnosed with chlamydia or gonorrhea
- **Correctional settings:** based on local area or institutional incidence
- **Pregnant women:** First prenatal visit and if risk retest at 3rd trimester (28 weeks) **PLUS** delivery.

CDPH Syphilis Screening in Pregnancy

Screen **1st** prenatal visit (ideally 1st trimester)

-and **3rd** trimester (28-32 weeks)

-and **Screen at delivery- unless low risk*** And a documented negative screen in 3rd trimester

- ***Syphilis risk factors in CA include:** late or limited prenatal care; new or multiple partners; unstable housing or homelessness; sub use (esp. Meth); incarceration w/n past 12 mo; partner with male or concurrent partners; new STI dx during pregnancy; sex partner dx STI; CSW ; **living in area with high CS rates (>8.4 cases per 100,000 live births in at least 1 of past 3 yrs)**

Screening for Syphilis: IHS CMO Letters 7 /23 & 2/24



JULY 19, 2023

Dear Tribal Leader and Urban Indian Organization Leader:

I am writing to provide you with information regarding the syphilis epidemic affecting American Indian and Alaska Native (AI/AN) communities. American Indian and Alaska Native people have the highest rates of syphilis and congenital syphilis of any group in the country. Some congenital syphilis cases have resulted in stillbirths or death shortly after birth. The Indian Health Service (IHS) is committed to reducing the prevalence of syphilis in AI/AN communities and I ask for your assistance in helping us achieve this goal.

To address the syphilis epidemic, IHS Chief Medical Officer, Dr. Loretta Christensen, has recommended the following guidelines and resources for all IHS, Tribal, and Urban Indian Organizations:

1. **Annual syphilis testing** for persons aged 13 to 64 to eliminate syphilis transmission by early case recognition.
2. **Turn on the annual Electronic Health Record reminder** at all sites to facilitate testing for two years or until incidence rates decrease locally to baseline.
3. **Three-point syphilis testing for all pregnant people** at the first prenatal visit, beginning of the third trimester, and delivery.

CMO IHS/Tribal/UI Leader Letter

- 3-point syphilis testing for **all Pregnant people**
 - **1st trimester & Beginning of 3rd trimester & Delivery**
- **Annual syphilis screening for all ages 13-64**
- **Enhance screening rates- ER's & Urgent Care**
- **Screen outside of hospitals & clinics.**
 - **Field testing -community centers, sporting events, health fairs, correctional settings, or on the street.**

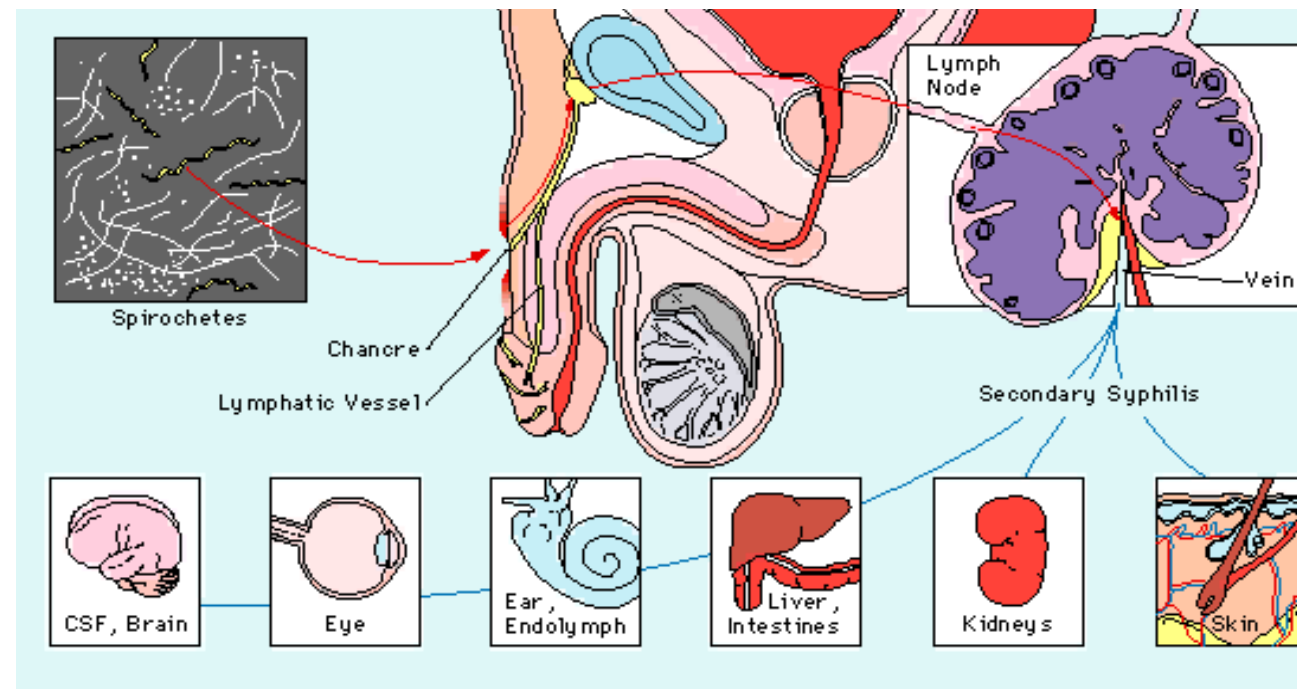
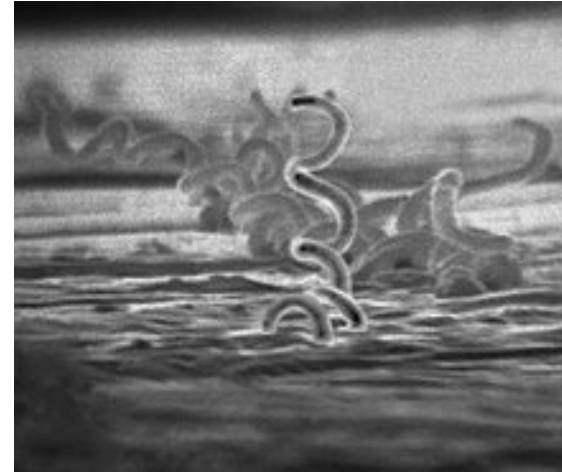
<https://www.ihs.gov/newsroom/triballeaderletters/2023-letters/>
https://www.ihs.gov/sites/newsroom/themes/responsive2017/display_objects/documents/2024_Letters/DTLL_DUIOLL_021524.pdf



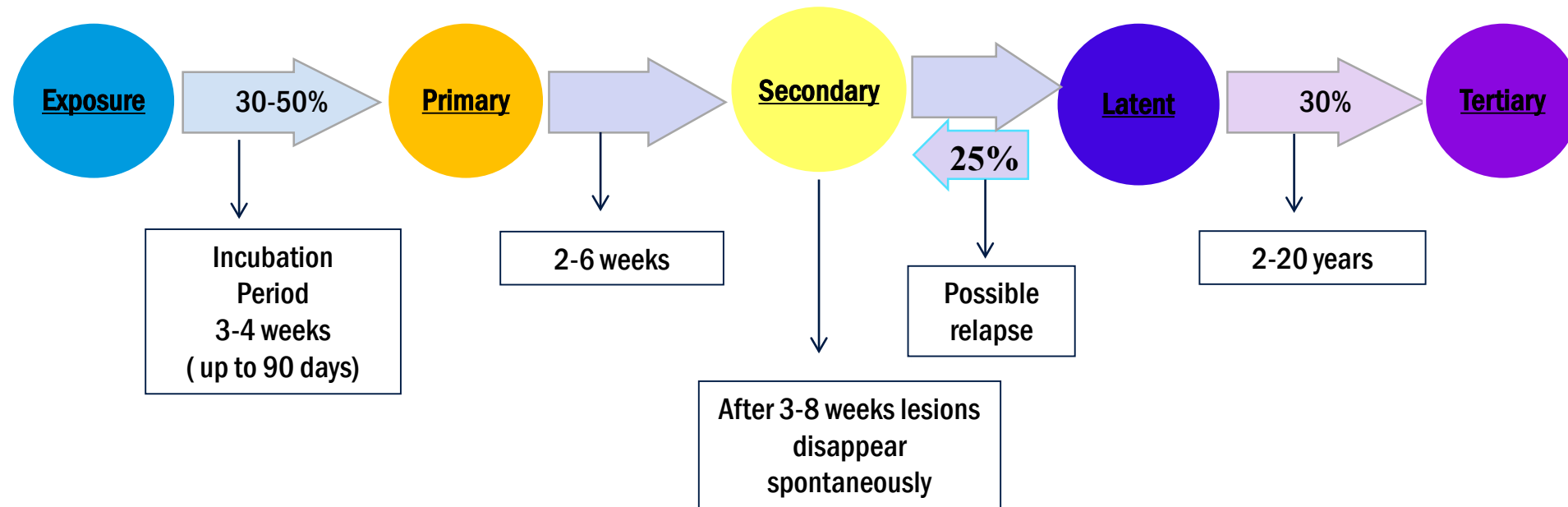
Syphilis
Natural History/
Clinical Manifestations

Syphilis Overview

- **Causative organism:** *Treponema pallidum*,
- **Incubation:** ~3-4 weeks (up to 90 day)
- Causes systemic infection, with episodes of active disease interrupted by periods of latent infection
- **Transmission:** direct contact to infectious lesion, blood-borne, in utero.

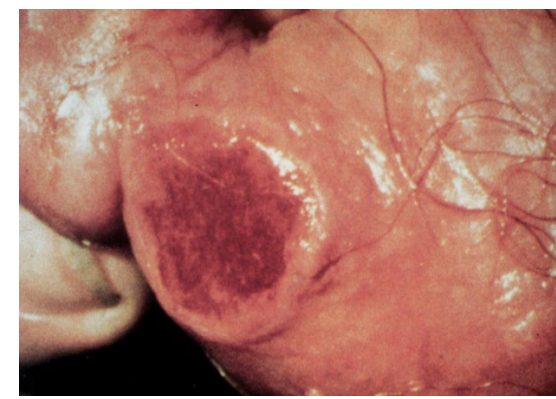


Syphilis Natural History: Stages



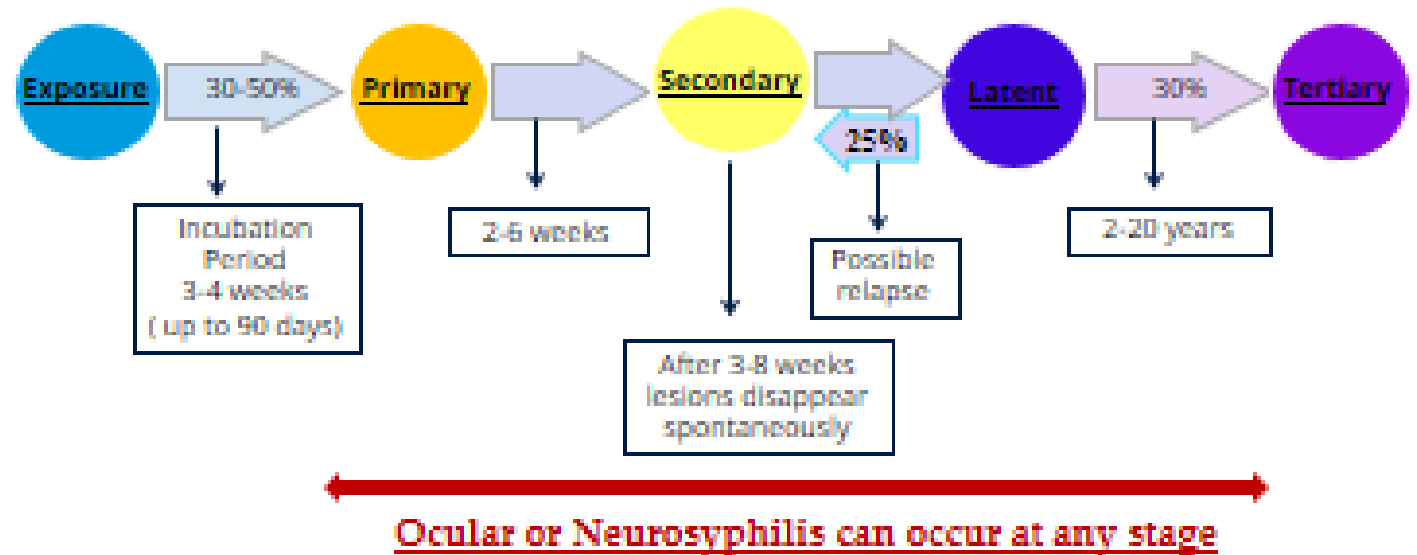
Ocular or Neurosyphilis can occur at any stage

Natural History: Primary Syphilis

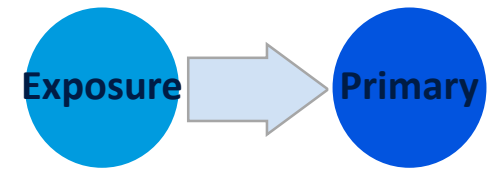


Chancre (ulcer)

- Single, painless, indurated, clean-based lesion with rolled edges.
- Can go unrecognized, esp if in the rectum or vagina
- Possible regional adenopathy (rubbery, bilateral, painless)



Primary Syphilis



DMHC



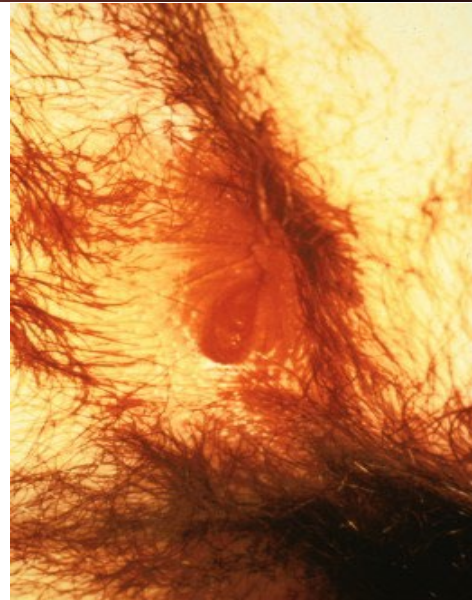
DMHC



SFCC



SFCC

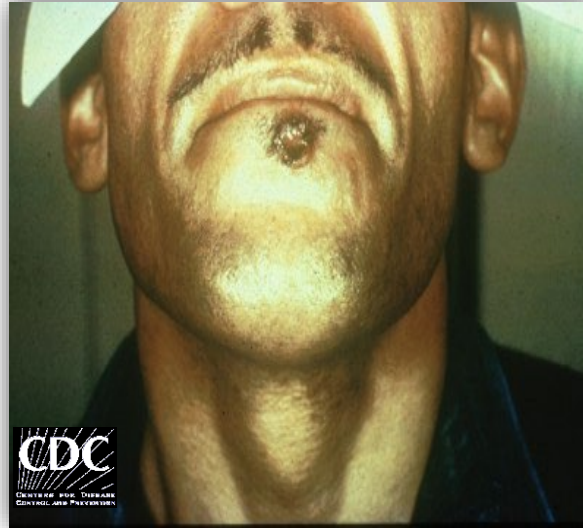
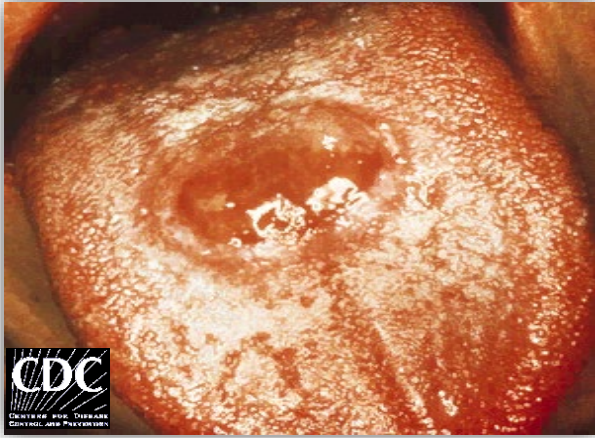


Primary Syphilis: Women

If painless, may go unrecognized



Primary Syphilis Chancres: Extragenital sites



Raguse et al. AIM 2012.



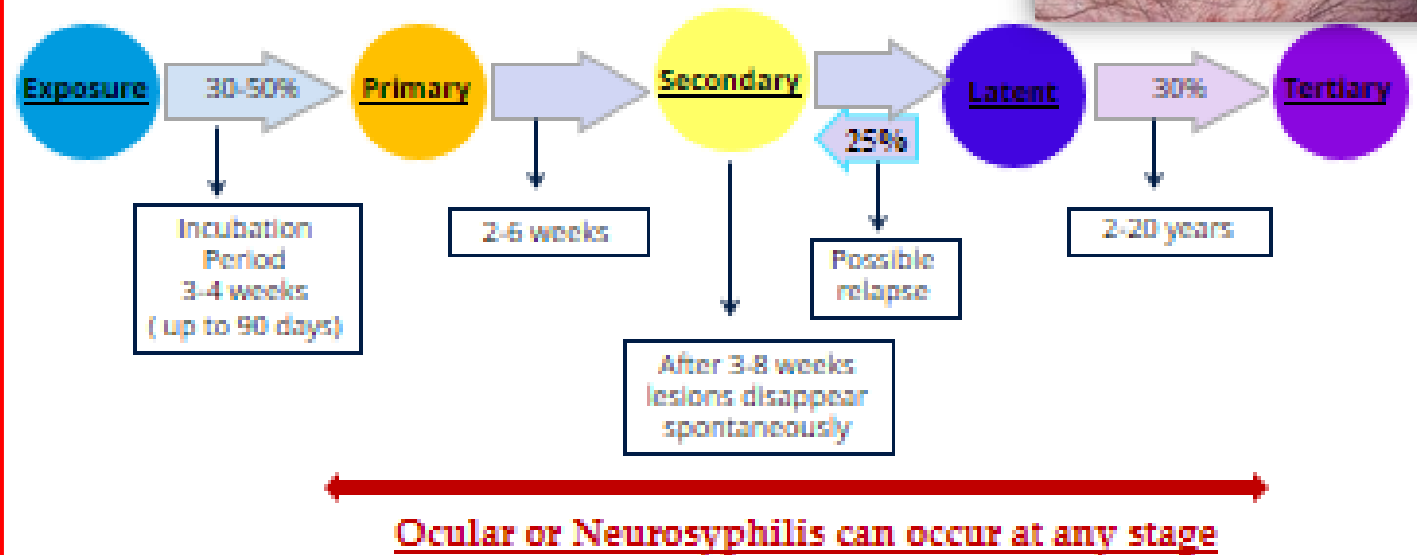
Clinics in Dermatology, 2016



Natural History: Secondary Syphilis

Secondary signs

- Rash (75-90%),
 - Involving palms/soles (60%)
- Generalized lymphadenopathy (70-90%)
- Constitutional symptoms (50-80%)
- Mucous patches (5-30%)
- Condyloma lata (5-25%)
- Patchy alopecia (10-15%)
- Symptoms of neurosyphilis (1-2%)



Secondary Syphilis



Mosby

DMHC

DMHC



Mosby

Mosby

Differential DX of Secondary Syphilis Rash

- Tinea versicolor
- Pityriasis rosea
- Drug reaction
- Erythema multiforme
- Guttate psoriasis
- Scabies
- Viral Exanthem



Condyloma Lata can Mimic Genital Warts

- Don't forget to think about syphilis (*condylomata lata*) when you see something that looks like anogenital warts!



Neurosypphilis: Can Occur at Any Stage of Syphilis

Early (months to yrs after infection)

- Cranial nerve dysfunction (II,VI,VIII), meningitis, stroke, AMS
- Ootosyphilis- hearing loss w/wo tinnitus
- Ocular- range of visual symptoms, vision changes

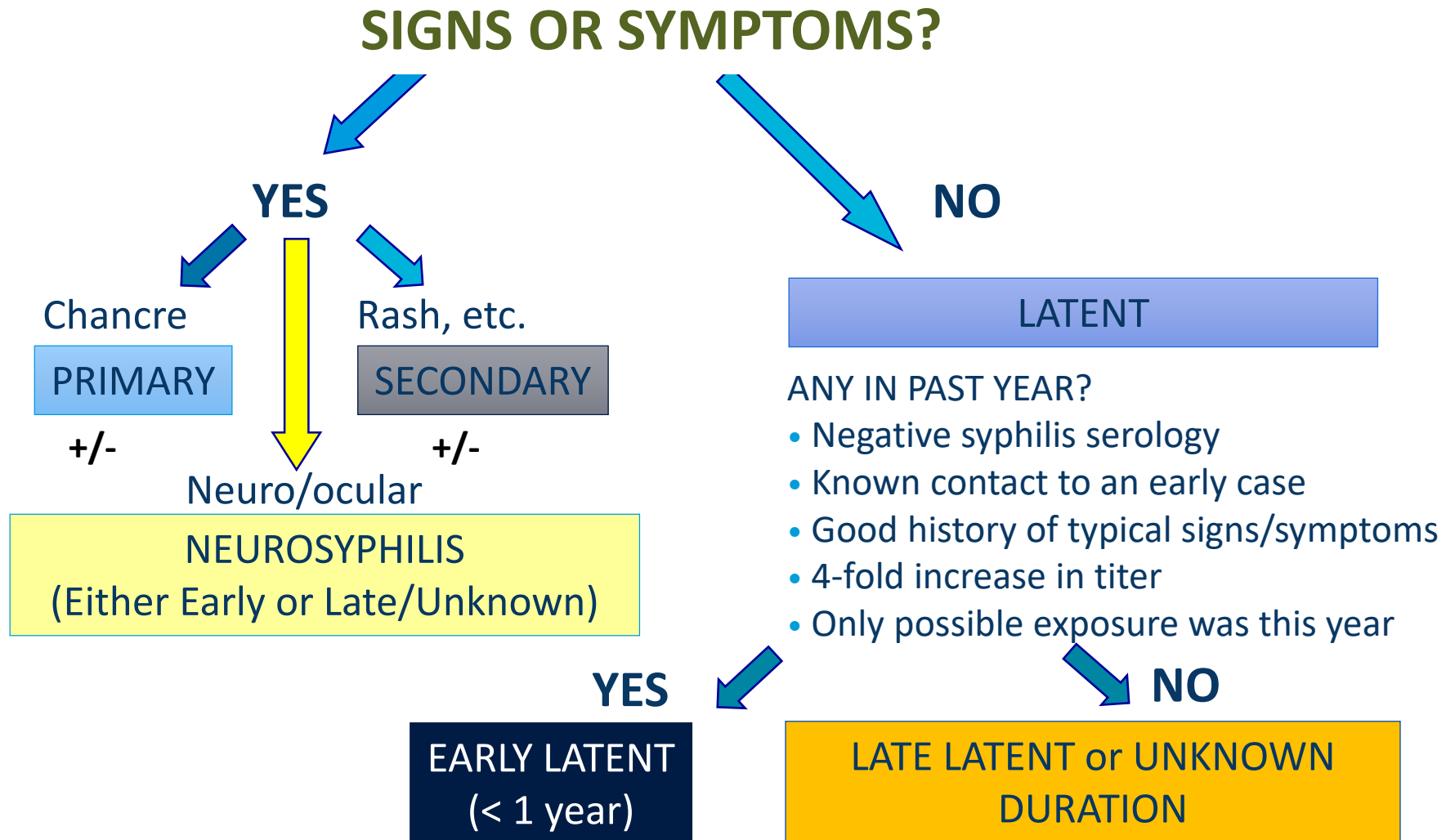
Late (10-30 yrs after infection)

- Tabes dorsalis , general paresis (progressive dementia ¶lysis)

ALL with syphilis need neuro exam including ophtho/auditory symptoms

- **LP** needed if clinical evidence of neuro involvement

Syphilis Staging Flowchart



Case 1 Stephanie

*28 y/o female with painless
"sore" on vulva*


- No history of genital herpes, no syphilis history
- H/o GC and CT
- 3 Male partners in past 6 months, no travel



Stat RPR Negative, HSV testing pending

Audience Poll: Management painless/indurated ulcer and negative RPR



- A. Wait for tests result to determine treatment
- B. Presumptively treat for syphilis now
- C. Order TP-PA
-  D. B and C
- E. A and C

Management Issues in Primary Syphilis

Serology may be negative ~ 25% primary syphilis

- Non treponemal tests may have slightly lower sensitivity than treponemal tests in early primary syphilis
 - *Consider ordering TP-PA along with non-treponemal test*
- If serology negative and *suspicion is low* and F/U likely, repeat 2-4 weeks after onset of lesion
- **If serology negative and *suspicion is high*, empirically treat and repeat serology 1 week after treatment**



Syphilis Diagnostics

Syphilis Diagnostics

Direct detection methods

- **Darkfield microscopy**

- Not widely available
- Sensitivity declines with age of lesion & use of topical agents

- **Polymerase chain reaction (PCR)**

- None FDA approved for commercial
- Best for primary syphilis- usefulness for secondary lesions unclear
- Not useful in TP identification in blood, serum, plasma or CSF

- **Serology**

- Non-treponemal test
- Treponemal tests



Treponema pallidum cannot be cultured

Syphilis Serology: Need both Types of Tests to Confirm Diagnosis

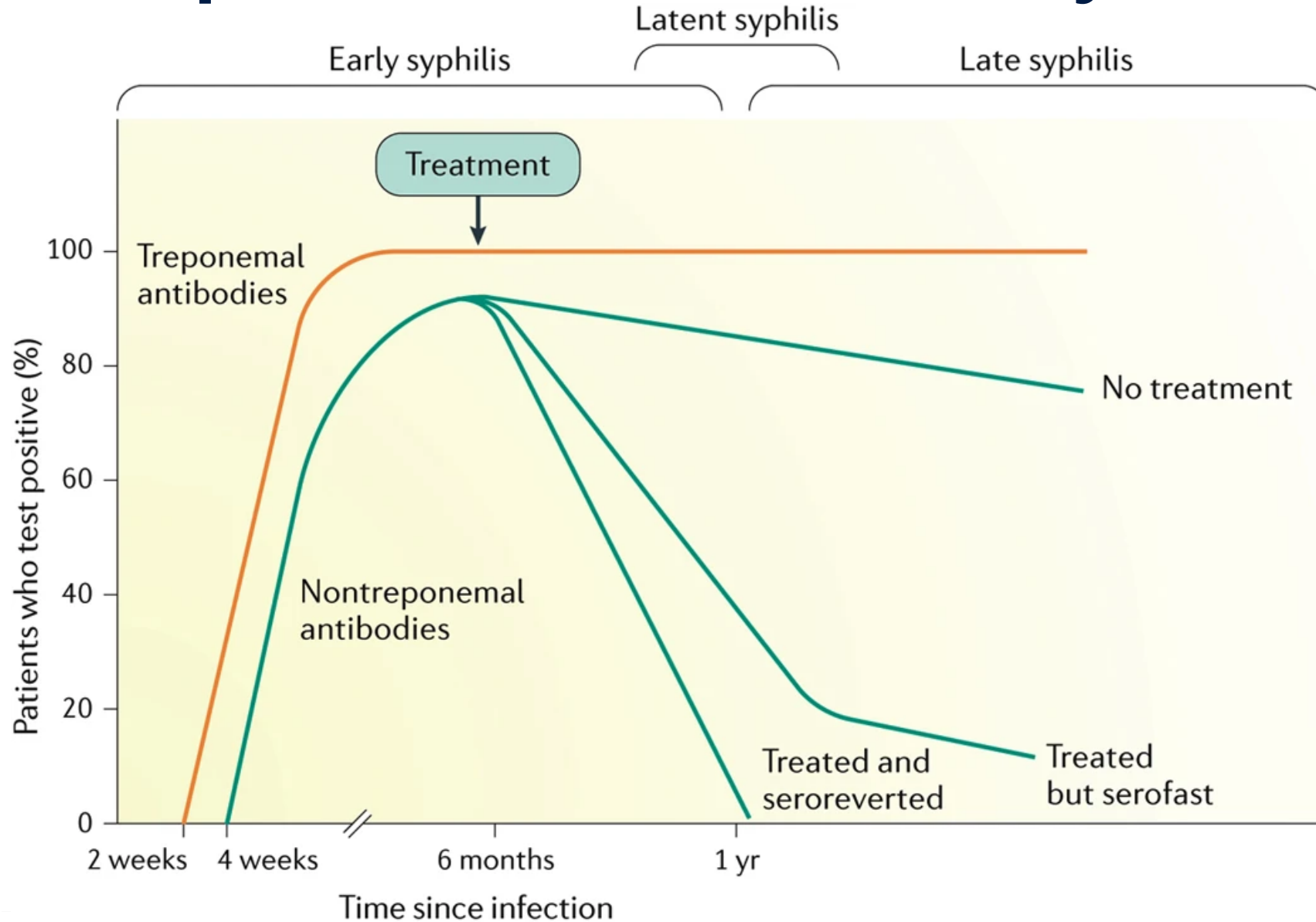
Non-treponemal tests

- Examples: **RPR and VDRL**
- Quantitative tests, allowing for assessment of disease burden, treatment adequacy, and re-infection
 - Give you a TITER
- Non-specific (can be positive in patients with other conditions)

Treponemal tests

- Examples: **TPPA, TPHA, FTA-ABS, EIA, CIA**
- Detect antibodies specific to *T. pallidum*
- Antibodies usually stay positive for life after initial infection
- Not quantitative; cannot be used to assess for reinfection or response to treatment

Treponemal tests (TPPA) may turn reactive 1st



RPR/VDRL Measure disease *burden*

- May stay positive even after adequate treatment (“serofast reaction”)
- Treponemal tests (FTA, TP-PA, EIA/CIA) remain positive for life
- Increasingly used as initial test for screening (reverse screening algorithm)
- May turn reactive earlier than non-trep

Titers: What Do They Mean?

Higher numbers correspond to higher level of antibodies in patient's serum

Number determined by progressive dilution of serum until it becomes non-reactive

Two-fold change

- Generally considered within margin of test error

Sustained four-fold change

- Considered to be significant

Compare titer using same serologic test

- RPR often higher than VDRL

1:1024

1:512

1:256

1:128

1:64

1:32

1:16

1:8

1:4

1:2

1:1



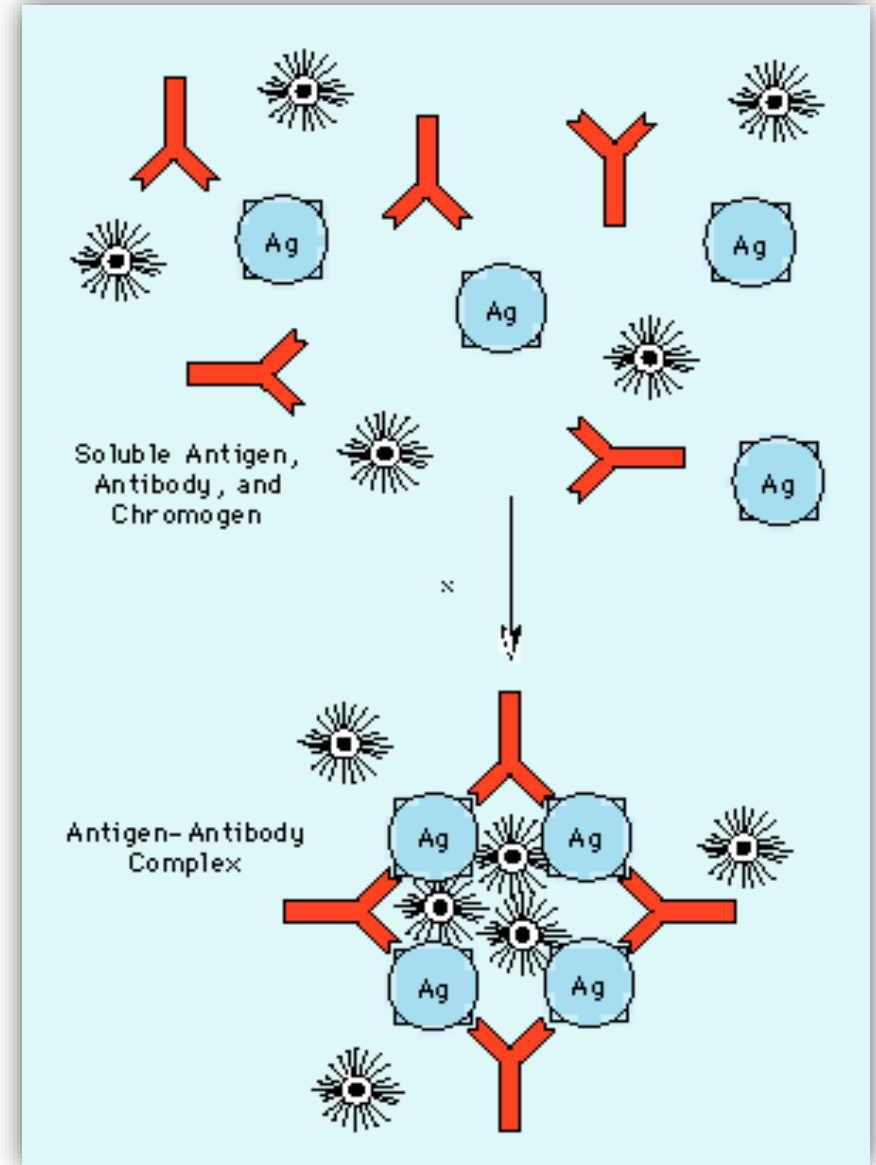
**2-fold
change**



**4-fold
change**

Prozone Phenomenon

- **False Negative RPR**
 - High Ab titers prevent antibody/antigen lattice formation
- **Rare**
 - Occurs ~0.3-2% (early syphilis/ secondary)
 - May be more common in HIV+ and neurosyphilis



Audience Poll: Management of Discordant serologic test results



Case 2: Jackie - Asymptomatic 30 y/o Female screening results .

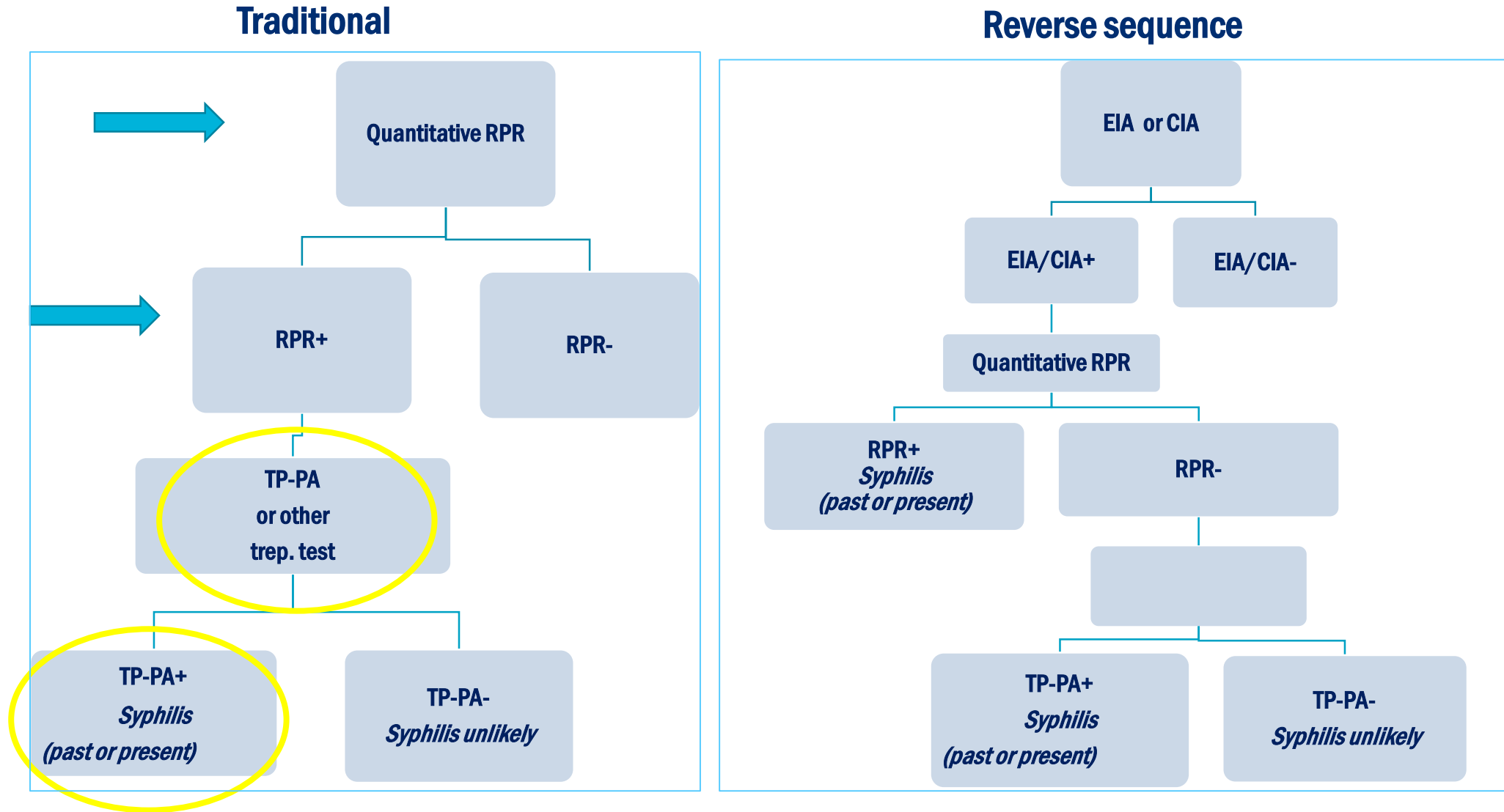
NO history of syphilis diagnosis/treatment.

- *Trep IgM/IgG Antibody Positive , RPR Non-Reactive, TP-PA Positive*

How would you manage?

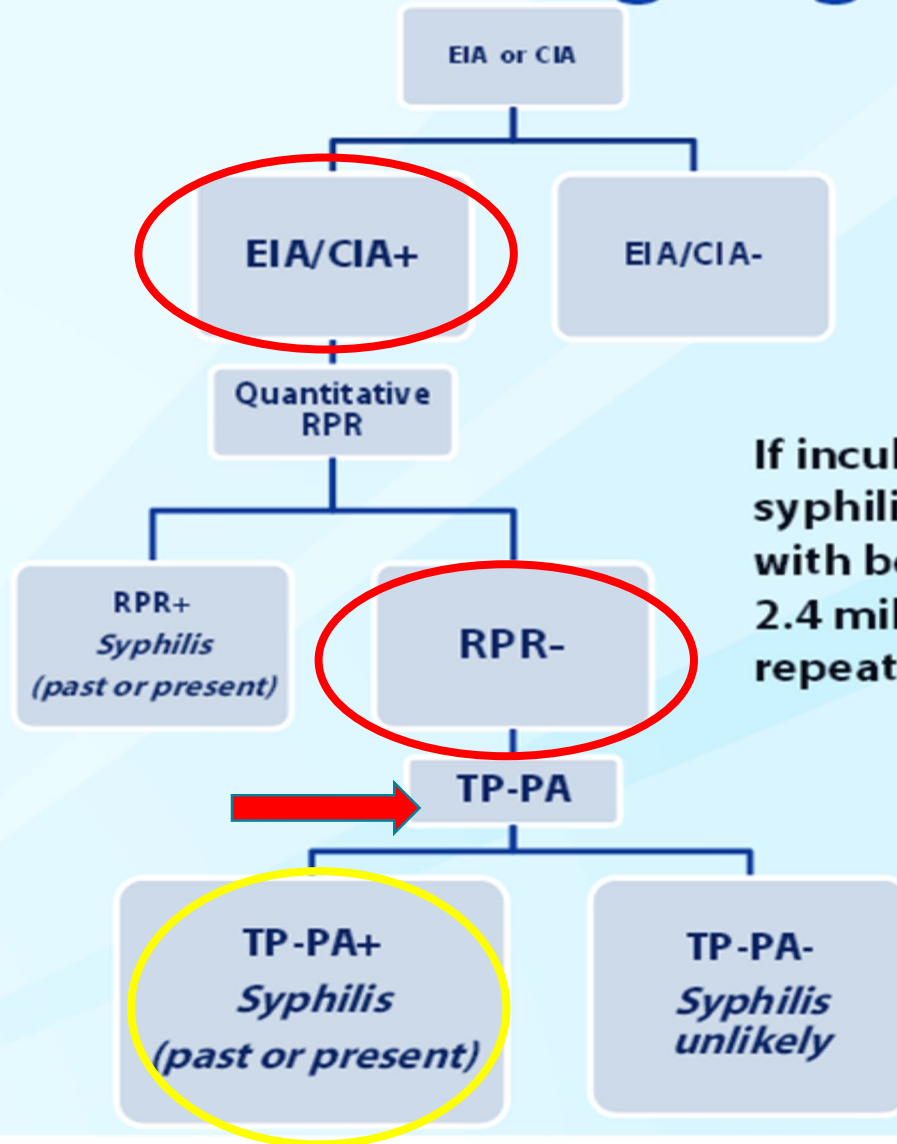
- A. Repeat labs in 2-3 months**
- B. RPR is non-reactive so no treatment needed**
- ✓ C. Since no prior syphilis treatment, needs treatment**
- D. None of the above**

Syphilis serologic screening algorithms



Reverse Screening Algorithm

Evaluate clinically, determine if treated for syphilis in the past, assess risk of infection, and administer therapy according to guidelines if not previously treated.



If incubating or primary syphilis is suspected, treat with benzathine penicillin G 2.4 million units IM x 1 and/or repeat in 2-4 weeks.

If at risk for syphilis, repeat RPR in 2 to 4 weeks.

Clinical Interpretation of Syphilis Screening Algorithms: A Resource for Local Health Jurisdictions

Clinical Interpretation of Syphilis Screening Algorithms A Resource for Local Health Jurisdictions

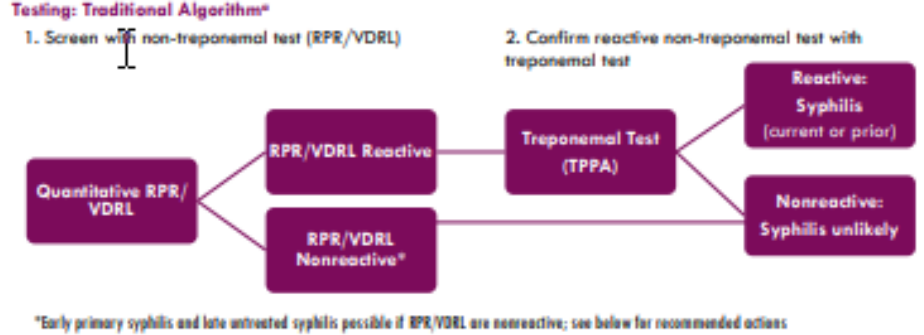


Table 1: Interpretation of Syphilis Serologies, Traditional Algorithm

Non-Treponemal (RPR/VDRL)	Treponemal (TPPA)	Possible Interpretations	Recommended Actions
Nonreactive	Nonreactive or not done	<ol style="list-style-type: none"> 1. No syphilis 2. Early/incubating syphilis (too early to be detected by serology) 	<ul style="list-style-type: none"> • If syphilis unlikely, no further action needed. • If early syphilis suspected, consider ordering a treponemal test (if not done initially) and repeating an RPR/VDRL in 1-2 weeks; if either test is reactive, treat for syphilis. • If concerned for early syphilis (e.g., chancere present or known exposure) treat presumptively. If treating presumptively, repeat RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion.
	Reactive	<ol style="list-style-type: none"> 1. Prior treated syphilis 2. Untreated syphilis 	<ul style="list-style-type: none"> • Treponemal tests (e.g., TPPA) often stay reactive for life; if patient has a history of adequate treatment for syphilis & no new exposures/symptoms, no further action needed. • If early syphilis suspected (e.g., chancere present or known exposure), treat presumptively according to stage. If treating presumptively, repeat RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion. • If no signs or symptoms, order a second treponemal test (e.g., EIA or CIA); see table 2 for recommendations based on results.
Reactive	Nonreactive	1. False positive RPR or VDRL	<ul style="list-style-type: none"> • Likely false positive (not syphilis).^b • In pregnancy or in patients at high risk for syphilis, consider rescreening with serologic testing in 2-4 weeks – if unchanged, no action needed.^c
	Reactive	<ol style="list-style-type: none"> 1. Current syphilis 2. Treated syphilis with residual/persistent RPR/VDRL titer 	<ul style="list-style-type: none"> • If RPR/VDRL is newly reactive, stage and treat. • If previously treated and sustained (≥ 2 weeks) 4-fold rise in RPR/VDRL titer, manage as treatment failure versus re-infection.^d • Note that RPR/VDRL may still be reactive after treatment; if there is a fourfold decline within 12-24 months, treatment is considered to have been adequate even if RPR/VDRL remains reactive. • Some treated patients may have a persistent low level RPR/VDRL titer for a prolonged period; re-treatment is not necessary in the absence of new exposures or symptoms.

Clinical Interpretation of Syphilis Screening Algorithms A Resource for Local Health Jurisdictions

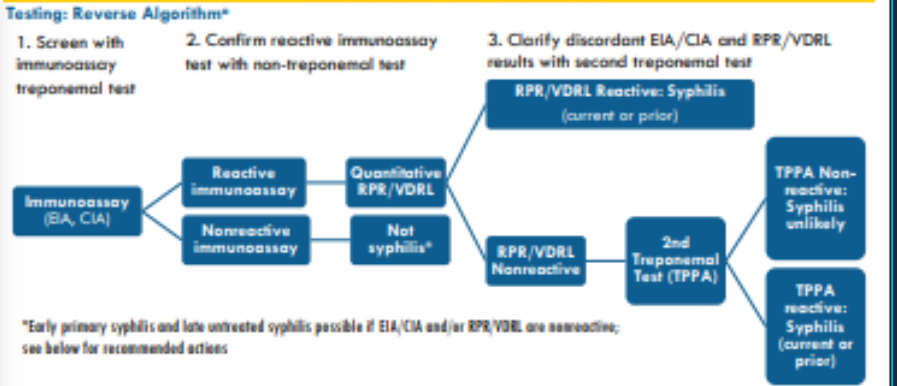
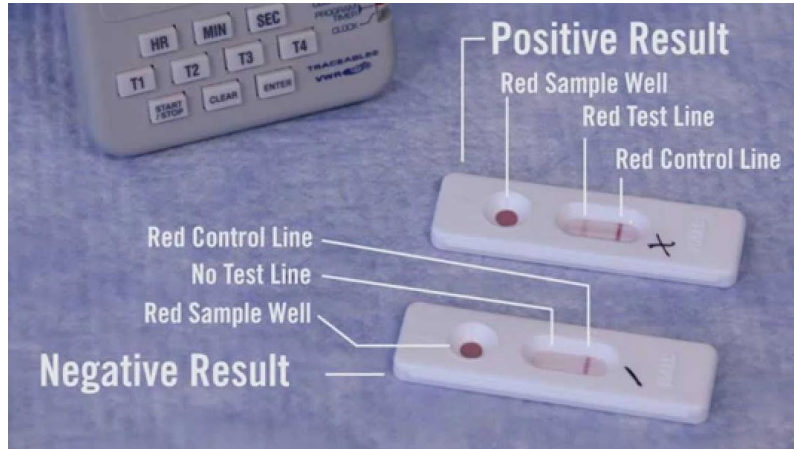


Table 2: Interpretation of Syphilis Serologies, Reverse Screening Algorithm

Immunoassay (CIA or EIA)	RPR/VDRL	TPPA	Possible Interpretations	Recommended Actions
Non-reactive	Non-reactive or not done	Non-reactive or not done	<ol style="list-style-type: none"> 1. Syphilis unlikely 2. Early/incubating syphilis (too early to be detected by serology) 	<ul style="list-style-type: none"> • If syphilis unlikely, no further action needed. • If immunoassay nonreactive but high clinical suspicion (such as a chancere or known exposure), treat presumptively for early syphilis. If treating presumptively, obtain RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion.
		Reactive	<ol style="list-style-type: none"> 1. False positive immunoassay 2. Early/incubating syphilis 3. Latent or prior syphilis (treated or untreated) 	<ul style="list-style-type: none"> • If no signs/symptoms and low risk for syphilis, most likely a false positive immunoassay.^b No further action needed. • If concerned for early infection or in pregnant patients, re-screen in 2-4 weeks.^c • If signs/symptoms or contact to syphilis, treat presumptively. Repeat RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion.
Reactive	Reactive	Non-reactive or not done	<ol style="list-style-type: none"> 1. Latent or prior syphilis (treated or untreated) 2. Early syphilis (prior to RPR/VDRL seroconversion) 	<ul style="list-style-type: none"> • No further action needed if patient treated appropriately for syphilis in past, assuming no new exposures/symptoms and a negative clinical exam. • If no symptoms and no known prior adequate treatment, treat presumptively for latent syphilis. • If early syphilis suspected (symptoms or known exposure), treat presumptively. Obtain RPR/VDRL on day of treatment. If nonreactive, repeat in 2-4 weeks to assess for seroconversion.
		Reactive	<ol style="list-style-type: none"> 1. Current syphilis 2. Prior syphilis (treated or untreated) 	<ul style="list-style-type: none"> • If RPR/VDRL is newly reactive, stage and treat. • If previously treated and sustained (≥ 2 weeks) 4-fold rise in RPR/VDRL titer, manage as treatment failure versus re-infection.^d • If known prior adequate treatment for stage of infection and RPR/VDRL declining appropriately (i.e., a fourfold decline within 12-24 months), no further action needed. • Some treated patients may have a persistent low level RPR/VDRL titer for a prolonged period; re-treatment is not necessary in the absence of new exposures or symptoms.

Point of Care(POC) Syphilis Tests: Syphilis Health Check



Treponemal only- EIA detects IgG& IgM

Results in 10 min

FDA approved, CLIA waived (2014)

Fingerstick(whole blood), serum or plasma

- Use for screening asymptomatic persons
- Use along with RPR for diagnosis of symptomatic
- **Not useful in someone with prior history of syphilis (TP test can remain positive for life)**
- Details on who can perform test on CDPH/CAPTC fact sheet*

*<http://californiapctc.com/resources/syphilis-health-check/>

More: Point of Care Syphilis Tests: DPP HIV & Syphilis

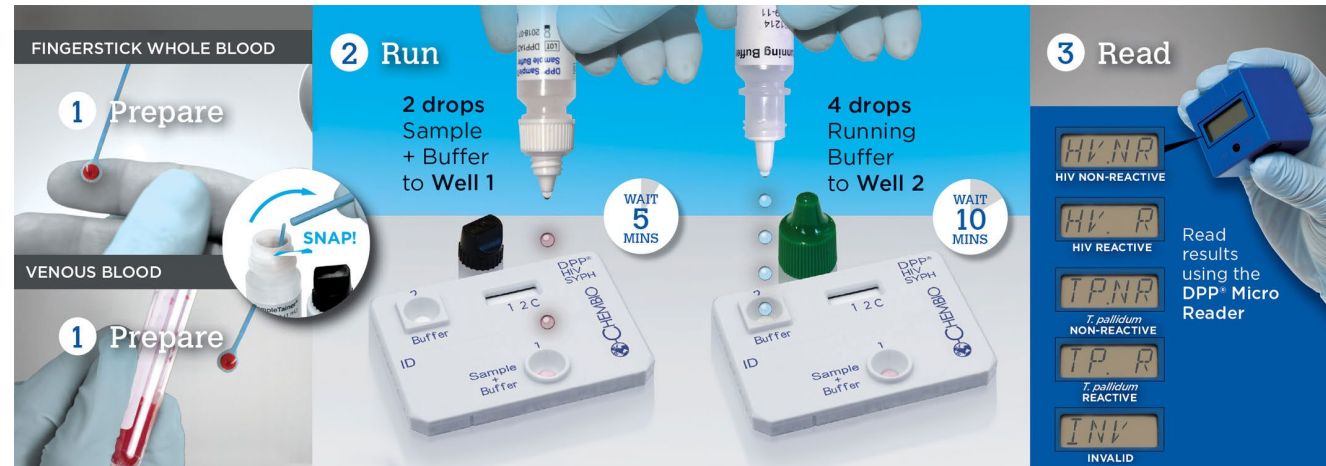
DPP HIV and Syphilis

Treponemal only

Results in 15 min

FDA Approved 10/20

CLIA Waived 2/23(finger stick whole blood)



Rapid Immunochromatographic Assays: lateral flow

POC Testing for Syphilis: IHS CMO Letters 2/24



February 15, 2024

Dear Tribal Leader and Urban Indian Organization Leader:

As syphilis rates continue to rise among our service population, I am writing to provide you with an update to my July 19, 2023, letter regarding the syphilis epidemic in Indian Country. In October 2023, the Indian Health Service (IHS) announced our [National STI Initiative](#) to address the syndemic. If you have not yet accessed those resources, I encourage you to [click this link](#) for an [STI Toolkit](#) and [Community & Patient Resources](#) from our IHS National Pharmacy & Therapeutics Committee, developed in collaboration with the IHS Chief Clinical Consultant in Infectious Disease and the IHS HIV/HCV/STI Branch.

Recent IHS data shows that syphilis screening in IHS facilities has increased by 98 percent from 2022 to 2023, representing a syphilis screening coverage rate of 9.4 percent of the eligible IHS user population. Implementing these recommendations can help further increase the levels of syphilis screening, treatment, and follow up care in IHS Tribal and Urban Indian (T/U) facilities.

Provide field testing outside hospitals
and clinics to increase screening rates

-Use **POC rapid syphilis, or dual HIV/syphilis antibody tests**

- **Field treatment for syphilis for adults diagnosed with syphilis & their partners if there is uncertainty about f/u.**



Syphilis Treatment

Syphilis Treatment: Primary, Secondary, and Early Latent

Benzathine penicillin G* 2.4 million units IM in a single dose

*** Bicillin L-A is the trade name. DO NOT USE Bicillin C-R!**

**** No enhanced efficacy of additional doses of BPG, amoxicillin or other antibiotics even if HIV infected**

Alternatives (non-pregnant penicillin-allergic adults):

- ❖ **Doxycycline 100 mg po bid x 2 weeks**
- ❖ **Tetracycline 500 mg po qid x 2 weeks**
- ❖ **Ceftriaxone 1 g IV or IM qd x 10 d (limited evidence)**

Syphilis Treatment: Late Latent or Latent of Unknown Duration

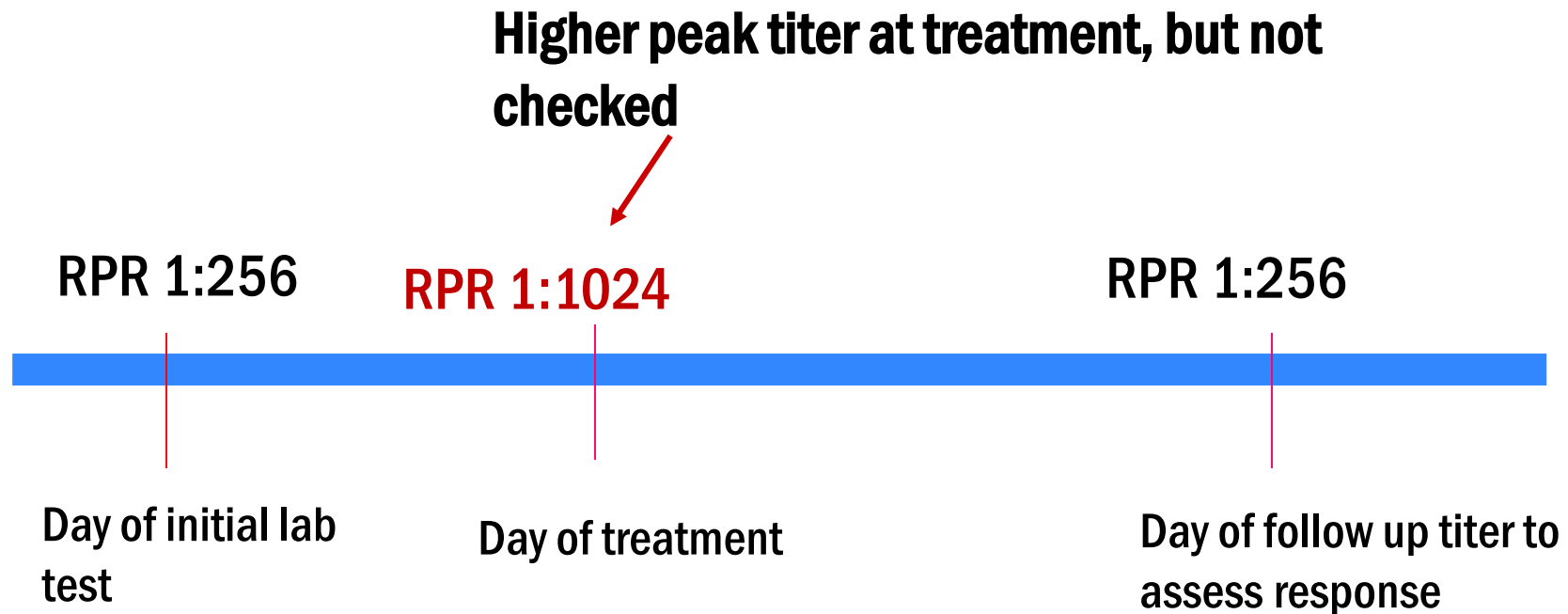
**Benzathine penicillin G* 7.2 million units IM total in
3 doses of 2.4 MU each at one week* intervals**

- **Maximum 10-14 day interval (7-9 day ideal)**
- **7 day interval in Pregnancy optimal** restart entire series if interval >9 days (**Note:CDPH- 6-8 days ok- restart >8days**)

Alternatives (non-pregnant penicillin-allergic adults):

- ❖ **Doxycycline 100 mg po bid x 4 weeks**
- ❖ **Tetracycline 500 mg po qid x 4 weeks**

Importance of Day of Treatment Titer



- Establishes baseline to compare response post treatment
- Frequently forgotten and without baseline makes assessment of titer response difficult

Syphilis Treatment Issues

▪ Jarisch-Herxheimer Reaction

- Acute febrile reaction that may occur within 24 hours (usually 2-8 hours) of syphilis treatment
- Headache, myalgias and exacerbation of cutaneous lesions (rash)
- Most common in primary, secondary
- Uncommon in latent
- Does not indicate drug hypersensitivity

Bicillin Availability: IHS CMO 2/24

- Prescribe & administer **Penicillin G Benzathine** for every age and every stage of syphilis infection in the absence of contraindications
- The IHS National Supply Service Center (NSSC) & IHS Pharmaceutical Prime Vendor report all reasonable orders for Bicillin are being fulfilled

For ordering/ questions contact at NSSC: Weston.Thompson@ihs.gov

Follow-up and Serologic Response

Change in 2021 STI
Treatment Guidelines

- **Primary and Secondary Syphilis**

- Examine at ~1 week assess symptom resolving
- Repeat titers at 6 and 12 months (3, 6, 9, 12, and 24 for HIV+)
- Expect fourfold decrease in serology in 12 months (24 months for HIV+)

- **Latent Syphilis**

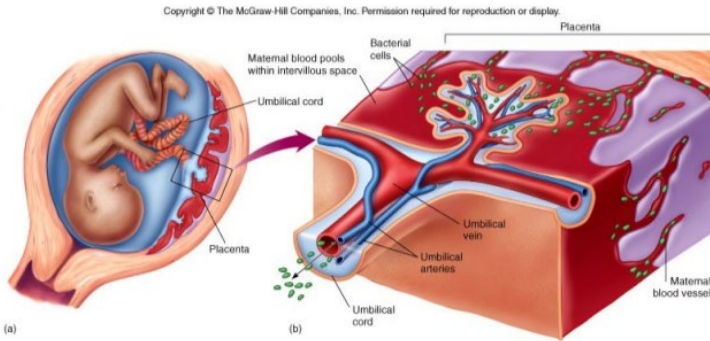
- Re-examine at 6, 12, and 24 months (6, 12, 18 and 24 for HIV+)
- Expect fourfold decrease in serology in 24 months (if titer initially >1:16)



Congenital Syphilis

Congenital Syphilis: Transmission

A fetus can acquire an infection from the mother via transplacental infections.



Transplacental infection of the fetus.

23

- **Transplacental transmission is Primary mode**
- **Rarely via contact of infectious lesions at birth**
- **Transmission Risk**
 - **50-70% early stage syphilis**
 - **15% late latent**

Congenital Syphilis: Early (Birth- 2 yrs)

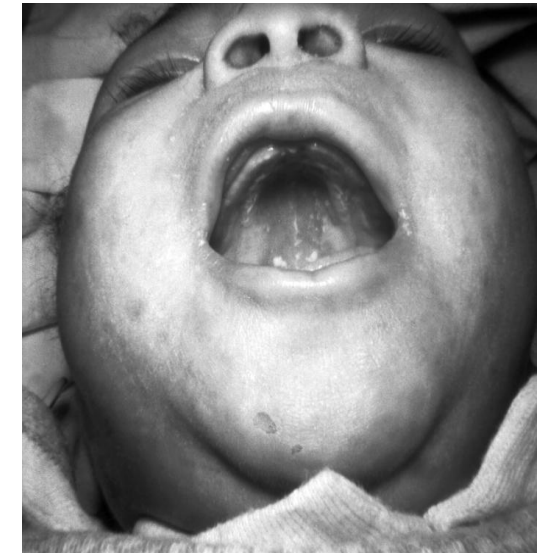
- **Hepatomegaly**
- **Splenomegaly**
- **Lymphadenopathy**
- **Edema**
- **Rash**
- **Snuffles** (copious nasal secretions – infectious!)
- **Mucoc**
- **Pneum**
- **Osteo**
- **Pseud**



Plantar Rash



Cutaneous lesion



Important: Most infants (60-90%) are ASYMPTOMATIC at birth
IF untreated will progress to symptoms

Congenital Syphilis: Late (2+ yrs)

Ophthalmic and Neurologic

- **Interstitial keratitis** (5–20 years; corneal scarring)
- **Eighth cranial nerve deafness** (10+ years)

Dental

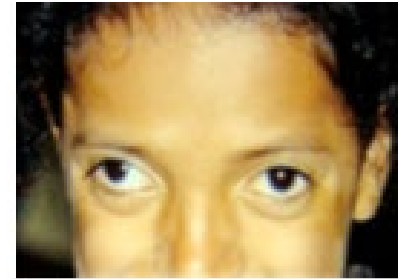
- **Hutchinson teeth** (peg-shaped, notched central incisors) & **Mulberry molars**

Skeletal

- **Anterior bowing of the shins**
- **Frontal bossing**
- **Clutton joints** (painless swelling of knees)

Facial

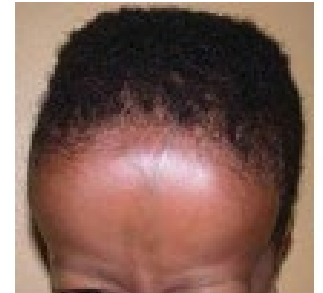
- **Saddle nose & Rhagades** (perioral fissures)



Interstitial keratitis



Hutchinson's teeth

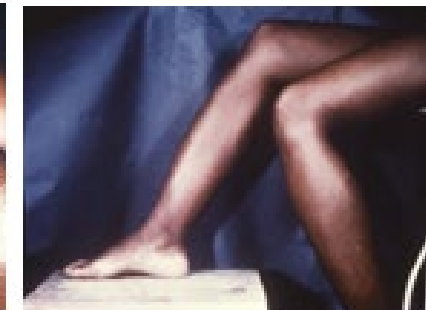


Frontal bossing



Clutton's joints

Courtesy CDC Public Health Image Library



"Saber shins"



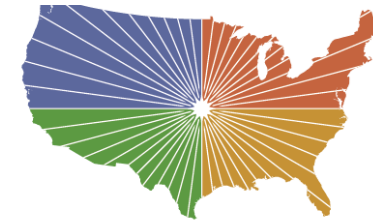
Rhagades

Syphilis: Take Home Points

- **Syphilis mimics other disease, keep in differential Dx**
 - Empiric treatment if high suspicion
- **Need Trep and Non-Trep serology for diagnosis**
 - Remember day of treatment titer
- **Syphilis Stage guides treatment**
 - Follow RPR to assess treatment response
- **Congenital Syphilis is preventable with early screening & treatment**
 - 3 x screening for all pregnant persons
- **Report Cases to Local Health Department**

STD Clinical Consultation Network (STDCCN)

- Provides STD clinical consultation services within 1-5 business days, depending on urgency, to healthcare providers nationally
- Your consultation request is linked to your regional PTC faculty
- We are just a click away!
- www.STDCCN.org



National Network of
STD Clinical Prevention
Training Centers

STD Clinical Consultation Network

Important for Requestors to Consider

The Clinical Consultation Service is intended for licensed healthcare professionals and STD program staff. We do not provide direct medical care, treatment planning, or medical treatment services to individuals.

The information provided through the Clinical Consultation Service is not a replacement for local expertise or your state STD program protocols. Information is offered as clinical decision support, is advisory in nature and is not intended to replace local healthcare decision-making or provision. Requestors are free to disregard any advice offered. Final clinical decisions are the sole responsibility of the healthcare provider.

CONTINUE

Clinician Resources

- CDC 2021 STD Treatment Guidelines

<https://www.cdc.gov/std/treatment-guidelines/>

- 2021 CDC Guidelines App

- National STD Curriculum

<https://www.std.uw.edu/>

 National **STD** Curriculum

- National Network of STD/HIV Prevention Training Centers

— <http://nnptc.org/>

- California Prevention Training Center

— <https://californiaprtc.com/>

STI Treatment Guidelines

2021 RECOMMENDATIONS NOW AVAILABLE



National Network of
STD Clinical Prevention
Training Centers

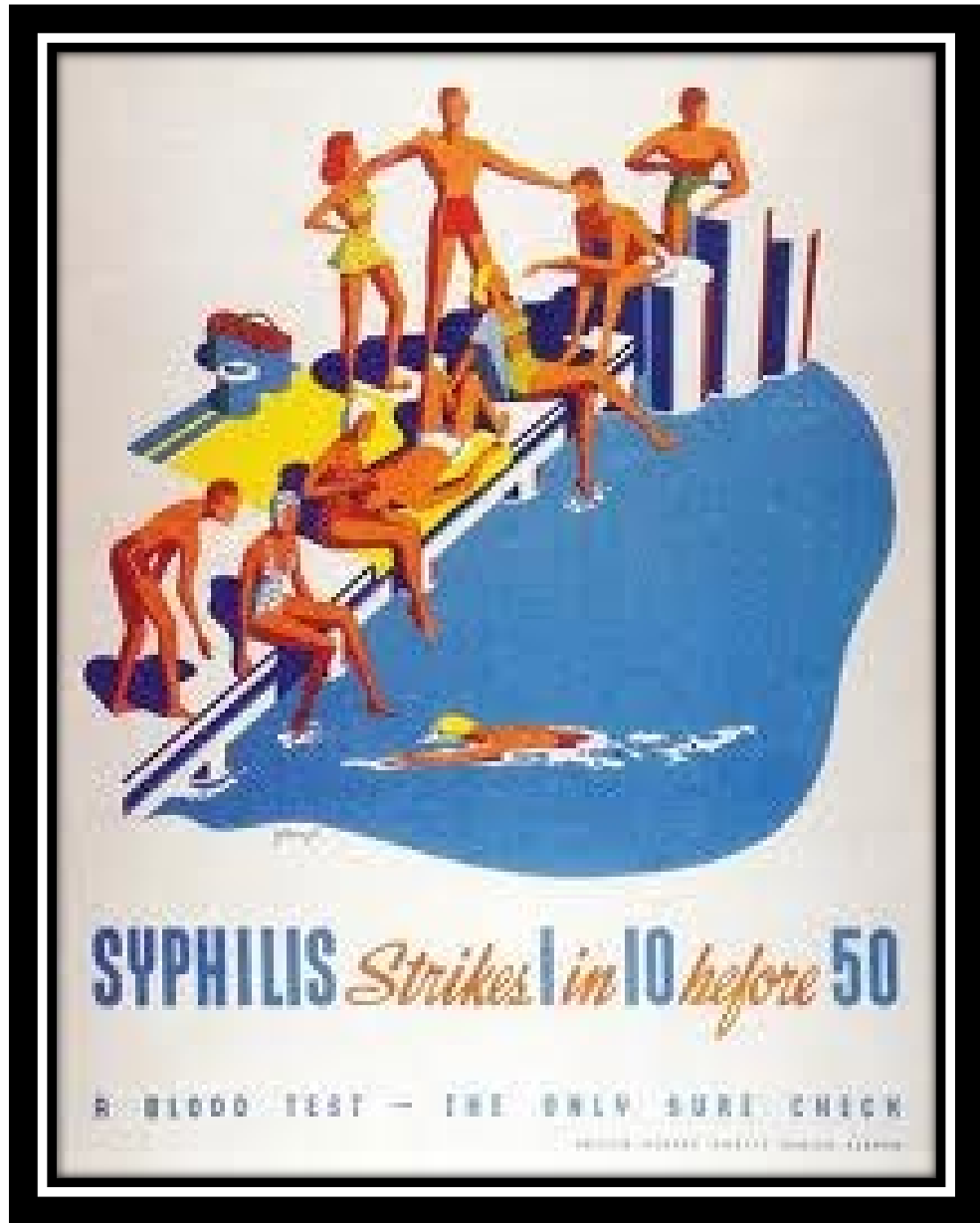


Acknowledgements

- Dr. Ina Park (CAPTC)
- Dr. Kelly Johnson (CAPTC)
- Dr. Joe Engelman (SFCC)

Thank you!!

Questions?



Extra Slides for Q & A

Primary Syphilis Algorithm

Evaluating Patients For Primary Syphilis

SEXUAL HISTORY, RISK ASSESSMENT, & PHYSICAL EXAM

Sexual History, Risk Assessment (past year)

- Gender of partners, number of partners
- Drugs, anonymous, serodiscordant HIV status, exchange of sex for drugs or money
- Types of sexual exposure
- Recent STDs; HIV serostatus
- Substance abuse
- Condom use
- History of Syphilis
- Prior syphilis (last serologic test & last treatment)

Physical Exam

- Oral cavity
- Lymph nodes
- Skin
- Palms & soles
- Neurologic
- Eyes
- Genitalia/pelvic
- Perianal

DIAGNOSTIC ISSUES IN PRIMARY SYPHILIS

- Darkfield – Not sensitive, varies with skill of examiner; decreased sensitivity at lesion edges
- A negative RPR/VDRL does not exclude syphilis diagnosis; ~75-85% sensitive in primary syphilis
- Use same test (RPR or VDRL) in sequential testing; titers are not interchangeable
- Need both non-treponemal (RPR or VDRL) and treponemal test (TP-PA, FTA-ABS, EIA, CIA) to make syphilis diagnosis
- Treponemal tests can remain positive for life; utility limited in patients with history of prior syphilis, comparison of non-treponemal titers needed

For more details on Treponemal Immunoassays: www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Documents%20Library/UseofTreponemalImmunoassays_Syphilis.pdf

Note: Evaluate for neurosyphilis (assess if neurologic, ophthalmic or otic symptoms present, as neurosyphilis can occur at any stage of syphilis)

TREATMENT & FOLLOW-UP

Treatment of Primary Syphilis

Recommended Regimen

- Benzathine Penicillin G 2.4 million units IM x 1

Alternative Regimens for Penicillin Allergic Non-Pregnant Patients: Efficacy not well established & not studied in HIV+ patients; close follow-up essential:

- Doxycycline 100 mg po bid x 3 weeks or
- Tetracycline 500 mg po qid x 3 weeks

*Pregnant patients with penicillin allergy should be desensitized and treated with penicillin

See CDC STD Treatment Guidelines: www.cdc.gov/std/treatment

California STD Treatment Guidelines Gold: www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Documents%20Library/STD-Treatment-Guidelines-Gold.pdf

****Additional Testing and Follow-up**

Note: Also test for HIV, GC/CT, and pregnancy (if female of reproductive age)

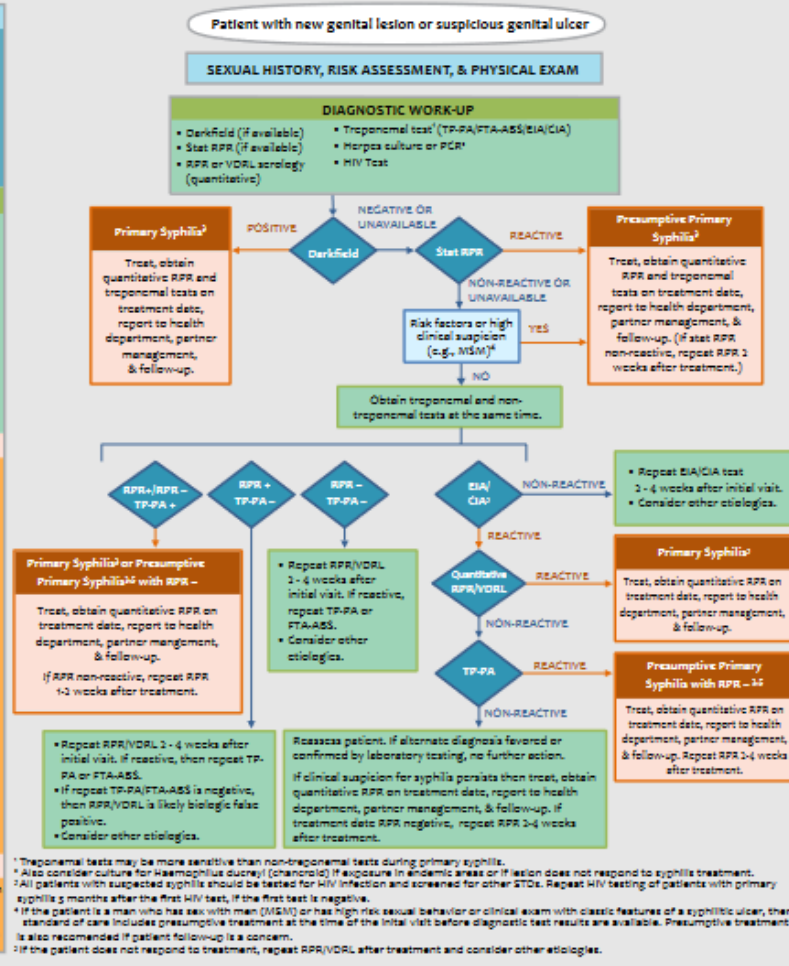
- 10 weeks: clinical follow-up
- 3, 6, 9, 12, 24 months: serologic follow-up for HIV+ patients
- 6, 12 months: serologic follow-up for HIV- patients

Failure of titer to decline fourfold (e.g. 1:64 to <1:16) within 6-12 months from start at time of treatment may indicate treatment failure. Titer decline may be slower in HIV+ patients.

- Consider retreatment and CSF evaluation if titer fails to decline appropriately

REPORTING & PARTNER MANAGEMENT

- All syphilis cases and presumptive cases must be reported to the local health department within one working day of diagnosis
- Local health departments will assist in partner notification & management
- Contact Number at Local Health Department: _____



CLINICAL PRESENTATIONS OF PRIMARY SYPHILIS

- Lesion appears 10-90 days after contact at site of exposure; may persist for >5 weeks then resolves
- Usually genital but may be extragenital, depending on exposure site
- Clinical presentation, typical or atypical
- Typical: single painless, indurated, clean-based ulcer with rolled edges & bilateral painless adenopathy
- Atypical: can mimic herpes & other genital ulcers
- ~5% present with multiple lesions
- Lesions of primary and secondary syphilis can be present at the same time, especially in HIV positive individuals

Differential Diagnosis

- Herpes (most common), primary HIV ulcers, chancroid, granuloma inguinale, trauma, and many non-STD infectious and non-infectious causes of genital ulcers
- More than one etiology can be present at the same time

Photo Credits

- D - Centers for Disease Control and Prevention; E - With permission from the Denver Metro Health Clinic; F - With permission from San Francisco City Clinic; G - With permission from University of Washington STD Prevention Training Center Washington (photos from UW HSCER Slide Bank)

To Order Additional Copies

See the online version of the Primary Syphilis Algorithm on the clinical resources page of the CA PTC website: www.californiaptc.com

Acknowledgments

Medical Directors from the National Network of STD Clinical Prevention Training Centers, California STD Controllers Association, Division of STD Prevention of the Centers for Disease Control and Prevention

Revised 1/2018

California PTC

Secondary Syphilis Algorithm

Evaluating Patients For Secondary Syphilis

SEXUAL HISTORY, RISK ASSESSMENT & PHYSICAL EXAM

Sexual History, Risk Assessment (past year)

- Gender of partners
- Number of partners (new, anonymous, serodiscordant HIV status, exchange of sex for drugs or money)
- Types of sexual exposure
- Recent STDs/HIV serostatus
- Substance abuse
- Condom use
- History of syphilis
- Prior syphilis (last serologic test & last treatment)

Physical Exam

- Oral cavity
- Lymph nodes
- Skin
- Palms & soles
- Neurologic
- Eyes
- Genitalia/rectal
- Paranasal

DIAGNOSTIC ISSUES IN SECONDARY SYPHILIS

- RPR/VDRL - not sensitive in secondary syphilis
 - Rare caveat: prozone reaction, false negative RPR/VDRL from excess antibody interfering with antibody/antigen reaction
 - Prozone occurs <1% of secondary syphilis cases; if suspected ask lab to dilute serum to at least 1:16
- Use same test (RPR or VDRL) in sequential testing; there are not interchangeable
 - Lead both non-treponemal (RPR or VDRL) and treponemal test to make syphilis diagnosis
 - Treponemal tests (TP-PA, FTA-ABS, CIA, CIA) can remain positive for life; utility limited in patients with history of prior syphilis, comparison of non-treponemal tests needed

For more details on Treponemal Immunossays: www.cdph.ca.gov/Programs/CID/DCDC/DCPIDtoDocumenttoLibrary/UseofTreponemalImmunossays_syphilis.pdf

Note: Evaluate for neurosyphilis (assess if neurologic, ophthalmic, or otic symptoms present, as neurosyphilis can occur at any stage of syphilis)

TREATMENT & FOLLOW-UP

Treatment of Secondary Syphilis

Recommended Regimen

- Benzathine Penicillin G 2.4 million units IM x 1

Alternative Regimens for Penicillin Allergic Non-Pregnant Patients:

Effacy not well established & not studied in HIV+ patients; close follow-up essential:

- Doxycycline 100 mg po bid x 2 weeks or
- Tetracycline 500 mg po qid x 2 weeks

*Pregnant patients with penicillin allergy should be desensitized and treated with penicillin

See CDC STD Treatment Guidelines: www.cdc.gov/std/treatment

California STD Treatment Guidelines Grid: <https://www.cdph.ca.gov/Programs/CID/DCDC/DCPIDtoDocumenttoLibrary/STD-Treatment-Guidelines-Color.pdf>

**Additional Testing and Follow-up

Note: Also test for HIV, GC/CT, and pregnancy (if female of reproductive age)

- > 2 weeks clinical follow-up
- 2, 6, 9, 12, 24 months serologic follow-up for HIV+ patients
- 6, 12 months serologic follow-up for HIV- patients

- Failure of titer to decline fourfold (e.g. 1:16 to <1:16) within 6-12 months from titer at time of treatment may indicate treatment failure. Titer decline may be slower in HIV+ patients.
- Consider retreatment and CSF evaluation if titer fails to decline appropriately

Refer to CDC Treatment Guidelines for management of treatment failure & consult the STD Clinical Consultation Network at www.STDCON.org

REPORTING & PARTNER MANAGEMENT

- All syphilis cases and presumptive cases must be reported to the local health department within one working day of diagnosis
- Local health departments will assist in partner notification & management
- Contact Number at Local Health Department: _____

Patient with new onset rash, atypical warty lesion, or other signs & symptoms of secondary syphilis

SEXUAL HISTORY, RISK ASSESSMENT, & PHYSICAL EXAM

DIAGNOSTIC WORK-UP

- Stat RPR (if available)
- RPR or VDRL serology (quantitative)
- Treponemal test (TP-PA/FTA-ABS/EIA/CIA)
- HIV Test

Stat RPR

- REACTIVE:** Presumptive Secondary Syphilis¹
Treat, obtain quantitative RPR and treponemal tests on treatment date, report to health department, partner management, & follow-up.
- NON-REACTIVE OR UNAVAILABLE:** Possible Secondary Syphilis^{1,2}
Consider presumptive treatment if high clinical suspicion.

Obtain serologic tests.

Treponemal Test

- REACTIVE:** Secondary Syphilis³
Treat, obtain quantitative RPR on treatment date, report to health department, partner management, & follow-up.
- NON-REACTIVE & NO PROZONE:** Not Syphilis. Consider other etiologies.

Quantitative RPR/VDRL

- REACTIVE:** Secondary Syphilis³
Treat, obtain quantitative RPR on treatment date, report to health department, partner management, & follow-up.
- NON-REACTIVE:** Possible Secondary Syphilis¹
Could be prior syphilis (treated or untreated). Rule out prozone. Treat if high risk or high clinical suspicion. Repeat RPR 2-4 weeks.

EIA/CIA

- REACTIVE:** Secondary Syphilis³
Treat, obtain quantitative RPR on treatment date, report to health department, partner management, & follow-up.
- NON-REACTIVE:** Syphilis unlikely. Consider other etiologies.

TP-PA*

- REACTIVE:** Secondary Syphilis³
Treat, obtain quantitative RPR on treatment date, report to health department, partner management, & follow-up.
- NON-REACTIVE:** Interpretation: possible syphilis, prior syphilis or false positive EIA. Rule out prozone. Reassess patient. If alternate diagnosis favored or confirmed by laboratory testing, no further action. If at risk for syphilis repeat RPR testing 2-4 weeks.

CLINICAL PRESENTATIONS OF SECONDARY SYPHILIS

- Symptoms typically occur 2-6 weeks after primary stage (can overlap with primary); resolve in 2-6 weeks
- 25% may have relapse of signs & symptoms in first year

Signs & Symptoms of Secondary Syphilis

- Rash: most common feature (75-90%); can be macular, papular, equimous (scaly), pustular (rare), vesicular (very rare) or combination; usually nonpruritic; may involve palms & soles (50%)
- Lymphadenopathy: (70-90%); inguinal, epitrochlear, axillary & cervical sites most commonly affected
- Constitutional Symptoms: (50-80%); malaise, fever
- Mucous Patches: (5-50%); flat gray-white patches in oral cavity & genital area
- Condyloma Lata: (5-50%); moist, heaped, wart-like lesions in genital, peri-rectal & rectal areas, & oral cavity
- Alopecia: (10-15%); patchy hair loss, loss of lateral eyebrows
- Neurosyphilis: (<10%); visual loss, hearing loss, cranial nerve palsies among other

Differential Diagnosis of the rash of secondary syphilis includes: pityriasis rosea, psoriasis, erythema multiforme, timeo vesicular, scabies, drug reaction, primary HIV infection

Photo Credits:
 1-3 With permission from University of Washington STD Prevention Training Center Washington (photos from UNIV/IGCC Slide Bank); 4-6 With permission from San Francisco City/County Centers for Disease Control and Prevention
 7-9 To Order Additional Copies: See the online version of the Secondary Syphilis Algorithm on the clinical resources page of the CAPTC website: www.cdc.gov/ncidod/dzdx/secondary-syphilis/
 Acknowledgements: Medical Directors from the National Network of STD Clinical Prevention Training Centers, California STD Controllers Association, Division of STD Prevention of the Centers for Disease Control and Prevention
 Revised 1/2012

¹ If the patient is a man who has sex with men (MSM) or clinical exam with classic features of secondary syphilis, consider presumptive treatment at the time of initial visit before the diagnostic tests results are available. Presumptive treatment is also recommended if patient follow-up is a concern.

² All patients with secondary syphilis should be tested for HIV infection and screened for other STDs. Repeat HIV testing of patients with secondary syphilis 3 months after the first HIV test, if the first test is negative.

³ Prozone reaction is a false negative RPR or VDRL from excess antibody interfering with the antigen-antibody reaction.

⁴ FTA-ABS is no longer considered the gold standard treponemal test given concerns regarding specificity. TP-PA should be used for a second treponemal test when EIA/CIA is reactive and RPR is non-reactive.

Management of Contacts to Infectious Syphilis

- **Report all syphilis cases to Local Health Department within 1 working day (Fax, Phone, Letter)**
- **Contacts to primary, secondary or early latent**
 - Exposed \leq 90 days before diagnosis
 - Might be infected even if seronegative (can take up to 90 days for serology to convert); treat presumptively
 - Exposed $>$ 90 days before diagnosis
 - Serologic tests are negative, no treatment is needed
 - If follow-up uncertain or serology unavailable then treat presumptively

Syphilis: Management of Contacts

Late Syphilis

- Long term sex partners of patients who have late syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of findings

Neurosyphilis



Neurosyphilis

» Neurosyphilis can be characterized as early/acute or late disease. Early neurosyphilis can be symptomatic or asymptomatic and can occur at any stage of syphilis, including concurrently with primary or secondary disease. Early symptomatic neurosyphilis consists of syphilitic meningitis, ocular syphilis and/or otosyphilis. Rarely, vascular complications can result from syphilitic meningitis and lead to an ischemic stroke; vascular complications are more commonly associated with late disease.

Early Neurosyphilis: Review of Systems *(pertinent positive symptoms)*

GENERAL/CONSTITUTIONAL: headache, fever, fatigue, weakness, dizziness

HEAD, EYES, EARS, NOSE AND THROAT:

- Eyes- pain, redness, loss of vision, double or blurred vision, photophobia, flashing lights or spots
- Ears- ringing in the ears, loss of hearing

GASTROINTESTINAL: nausea, vomiting

MUSCULOSKELETAL: neck pain/stiffness, muscle weakness

NEUROLOGIC: headache, dizziness, muscle weakness, confusion, loss of consciousness, seizures, difficulty speaking

PSYCHIATRIC: confusion

Early Neurosyphilis: Focused Neurologic Exam

- **Cranial Nerve Exam:** assess for cranial nerve palsies (key maneuvers in **bold**)

Available at: <http://www.cdph.ca.gov/programs/std/Documents/NeurosyphilisGuide.pdf>

Ocular Syphilis

Manifestations:

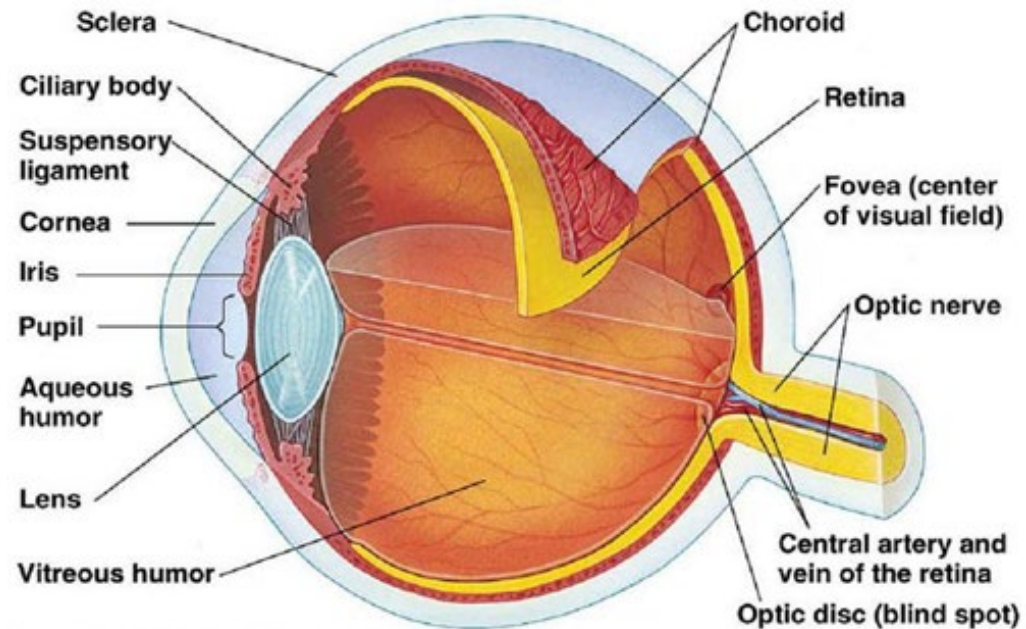
- Conjunctivitis, scleritis, and episcleritis
- **Uveitis**: anterior and/or posterior
- Elevated intraocular pressure
- **Chorioretinitis**, retinitis
- Vasculitis

Symptoms:

- Redness
- Eye pain
- Floaters
- Flashing lights
- Visual acuity loss
- Blindness

Diagnosis:

- Ophthalmologic exam
- Serologies: RPR, VDRL, treponemal tests
- Lumbar puncture not needed if isolated ophtho sx and CN/Neuro exam wnl (CDC 2021 STI Guidelines)



Treatment of Syphilis in Pregnancy

- **Penicillin is only treatment for syphilis in pregnancy**
- **Treat with the penicillin regimen appropriate for stage of infection**
 - “Certain evidence that additional BPG is beneficial” a 2nd dose of BPG 2.4 mu IM (7 days after 1st dose in early syphilis)*
- **Pregnant women with history of penicillin allergy should be desensitized and treated with penicillin.**
- **All patients with syphilis should be tested for HIV**

Syphilis Health Check



Systematic review & Meta-analysis of 15 studies

- Lower Sens/Spec in 4 prospective studies from literature (not in FDA/CLIA eval)
 - Sensitivity 68.6% (95% CI, 35.0–90.9%)
 - Specificity 95.2% (95% CI, 84.4–99.2%)
- FDA trials had rigorous training and oversight so different than studies in literature
- FDA prospective studies used sera for testing other studies used whole-blood specimens.
- Encourage implementation of ongoing quality control and quality assurance when using Syphilis Health Check POC