Syphilis and Congenital Syphilis in Oregon

Tim W Menza, MD, PhD

Medical Director, HIV/STD/TB Section, OHA

Assistant Professor, Infectious Diseases, OHSU

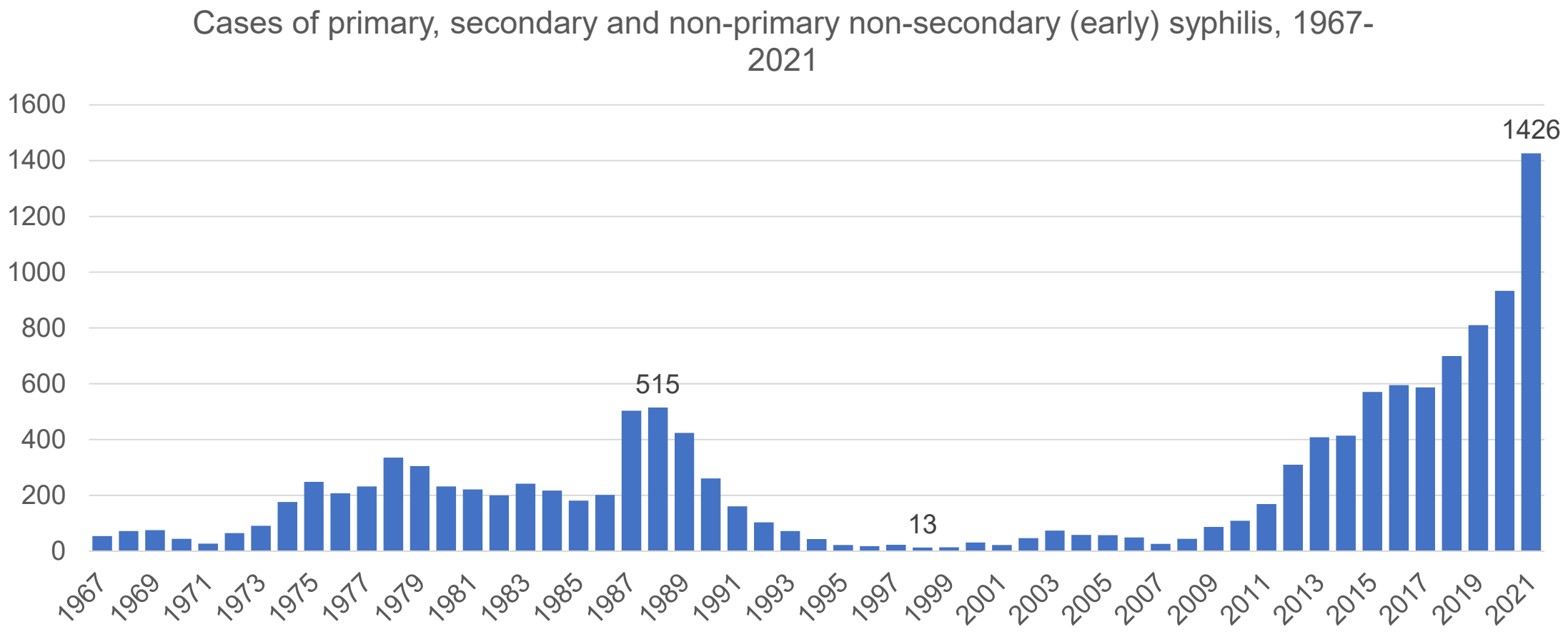
Objectives for today's case-based discussion

- Describe the epidemiology of syphilis in Oregon
- State the Oregon-specific syphilis screening recommendations
- Describe the signs and symptoms of primary and secondary syphilis
- Describe the criteria for early non-primary non-secondary and late/unknown duration syphilis
- State stage-specific treatment for syphilis
- Interpret syphilis serologies
- Assess for complicated syphilis

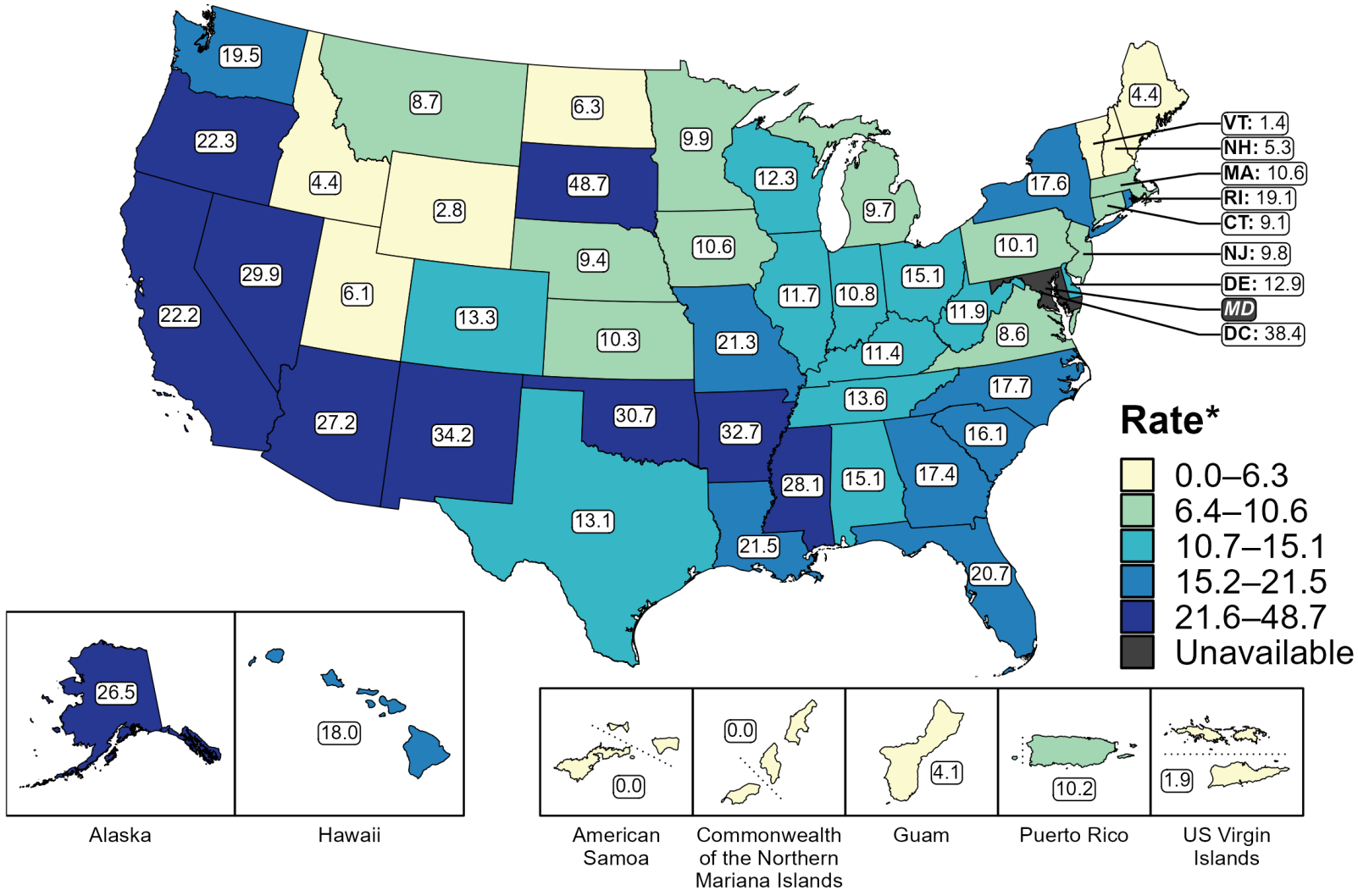
Case 1.

- A 23-year-old G0P0 cisgender woman with a positive home pregnancy test comes to clinic to confirm the pregnancy and establish prenatal care
- Her LMP was about 10 weeks ago
- She's accompanied by her mother who just read a Washington Post article on the rise of syphilis among women and infants in the U.S.
- What can you tell her about the epidemiology of syphilis in Oregon?

Early (Infectious) Syphilis Diagnoses Are Higher Than Ever

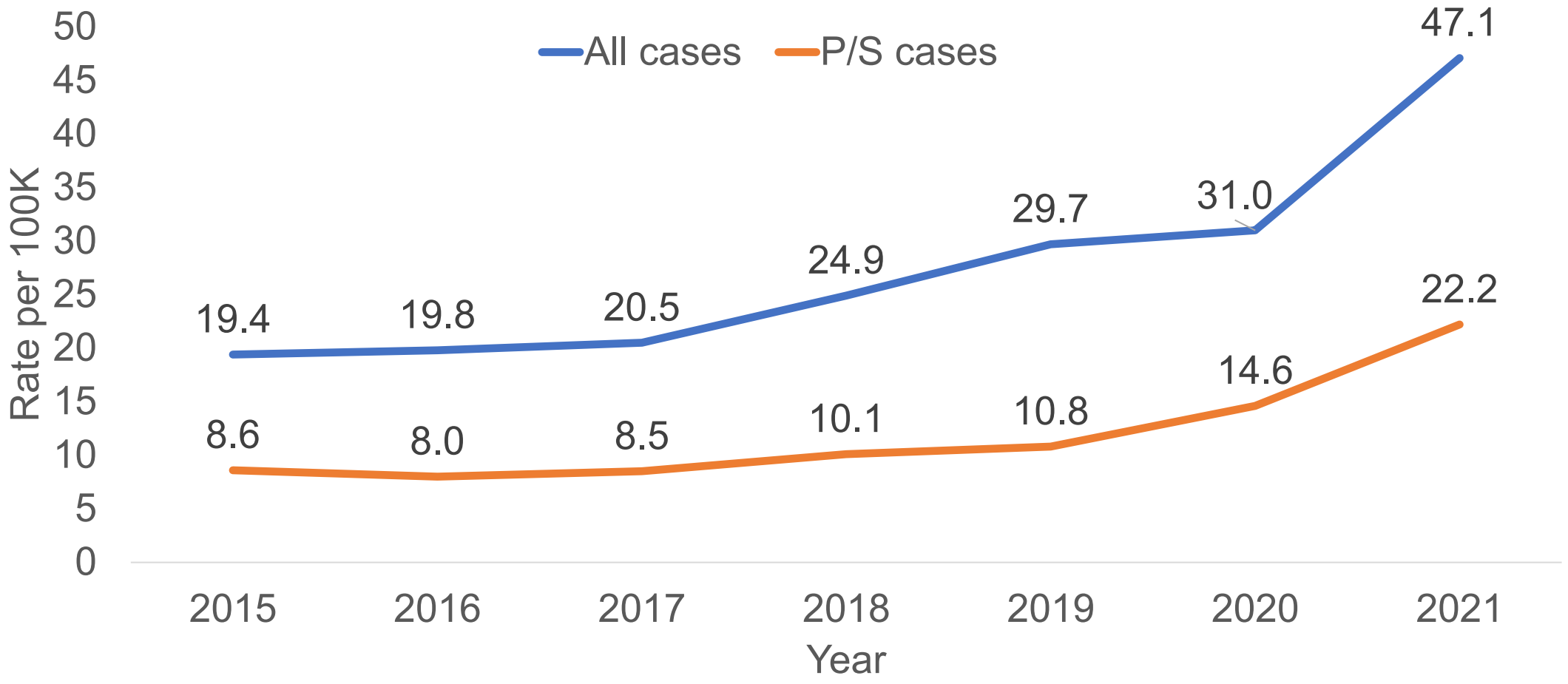


Oregon was 9th in the nation for primary and secondary syphilis in 2021

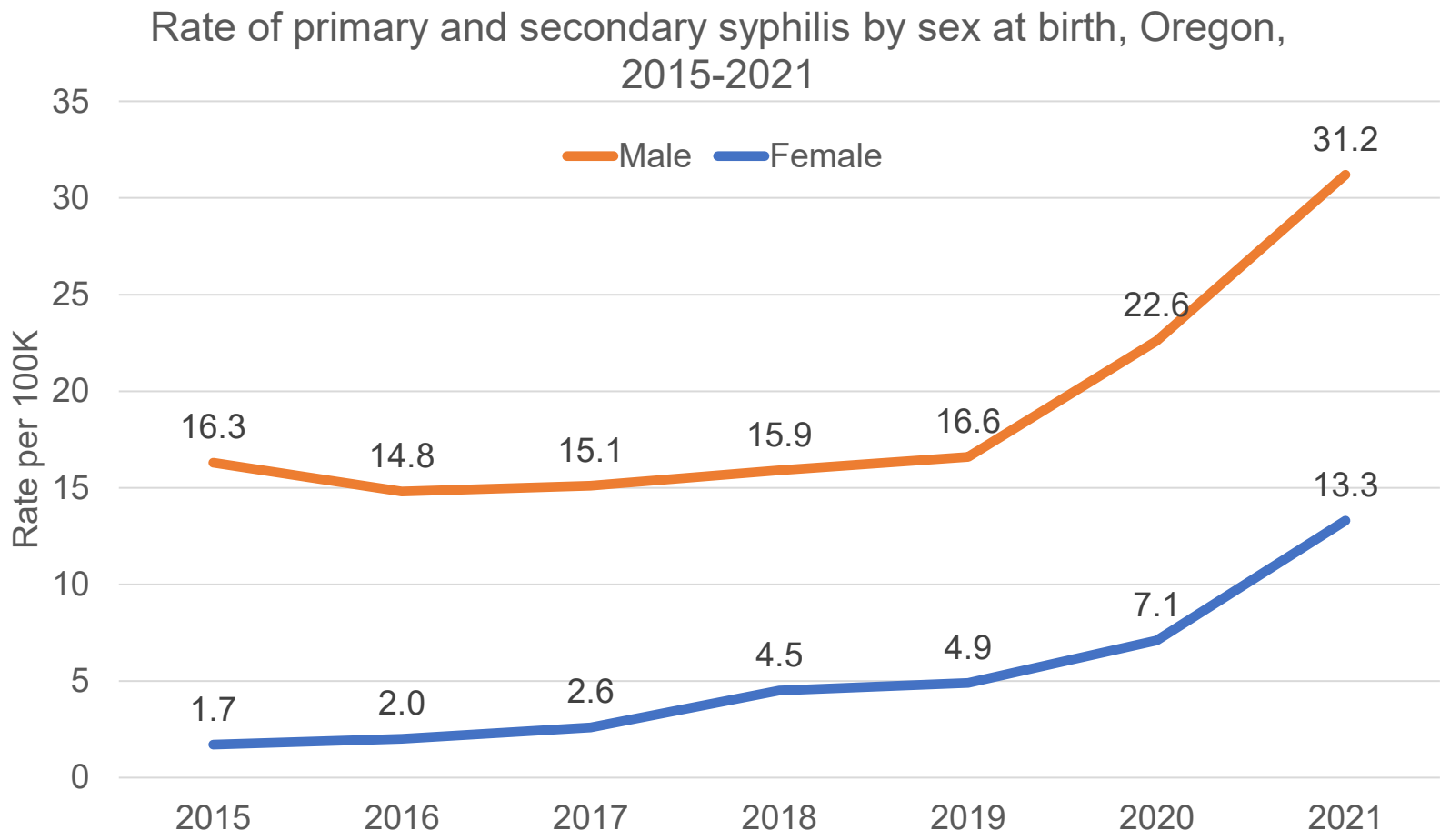


* Per 100,000

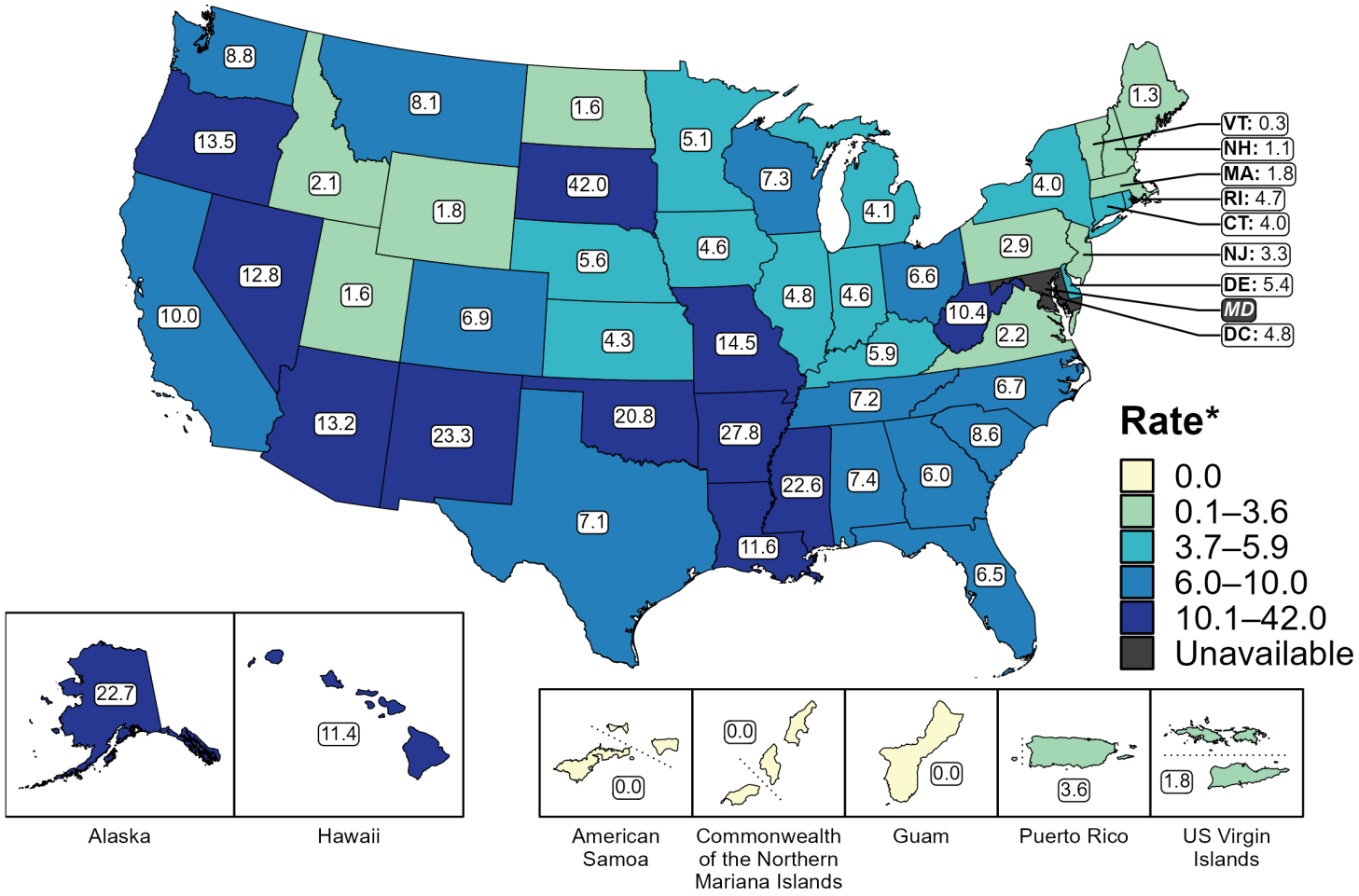
Since 2019, the Rate of Syphilis Diagnoses Has Been Increasing Rapidly



Primary and Secondary (P/S) Syphilis Diagnoses Almost Tripled among People Assigned Female at Birth between 2019 and 2021



Oregon was 8th in the nation for primary and secondary syphilis among people assigned female at birth in 2021



Syphilis Cases among Women Interviewed for Partner Services by Stage and Risk, Oregon, 2021				
	N	%	N	%
Total cases (% interviewed)	388	68%	225	52%
		Stage		
	Early		Late	
	N	%	N	%
Total interviewed cases	265	100%	116	100%
Individual-level risk				
Methamphetamine	75	28%	46	40%
PWID	53	20%	26	22%
Houseless or unstably housed	39	15%	24	21%
Transactional sex	16	6%	8	7%
Criminal justice involvement	11	4%	4	3%
Prior STI (prior 2 years) and HIV/HCV (ever)				
Prior chlamydia	39	15%	15	13%
Prior gonorrhea	37	14%	21	18%
Prior syphilis	16	6%	4	3%
Prior HCV case	4	2%	4	4%
Prior HIV case	1	<1%	0	0%
Partner-level risk				
Partner: PWID	75	28%	42	36%
Partner: Houseless	4/81	5%	3/27	11%
Partner: criminal justice involvement	3/81	4%	0	0%
Risk Identified (any of above)	143	54%	65	56%
No Risk Identified	122	46%	51	44%

Updates to Oregon-specific Syphilis Screening Recommendations

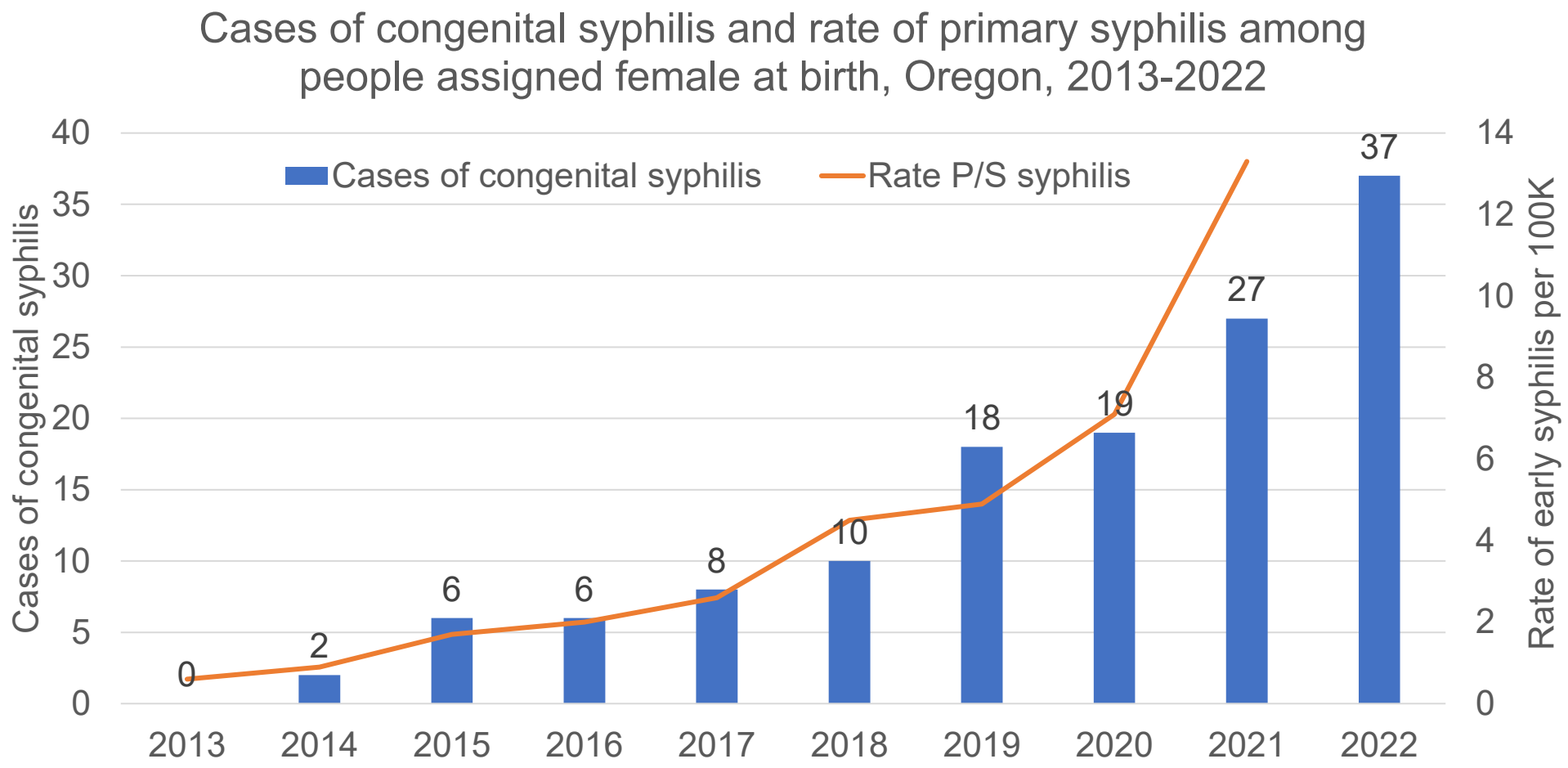
- Screen all people under 45 years of age at least once starting 1/1/2021 (in addition to screening during pregnancy)

- Screen those with indications for more frequent screening at least yearly

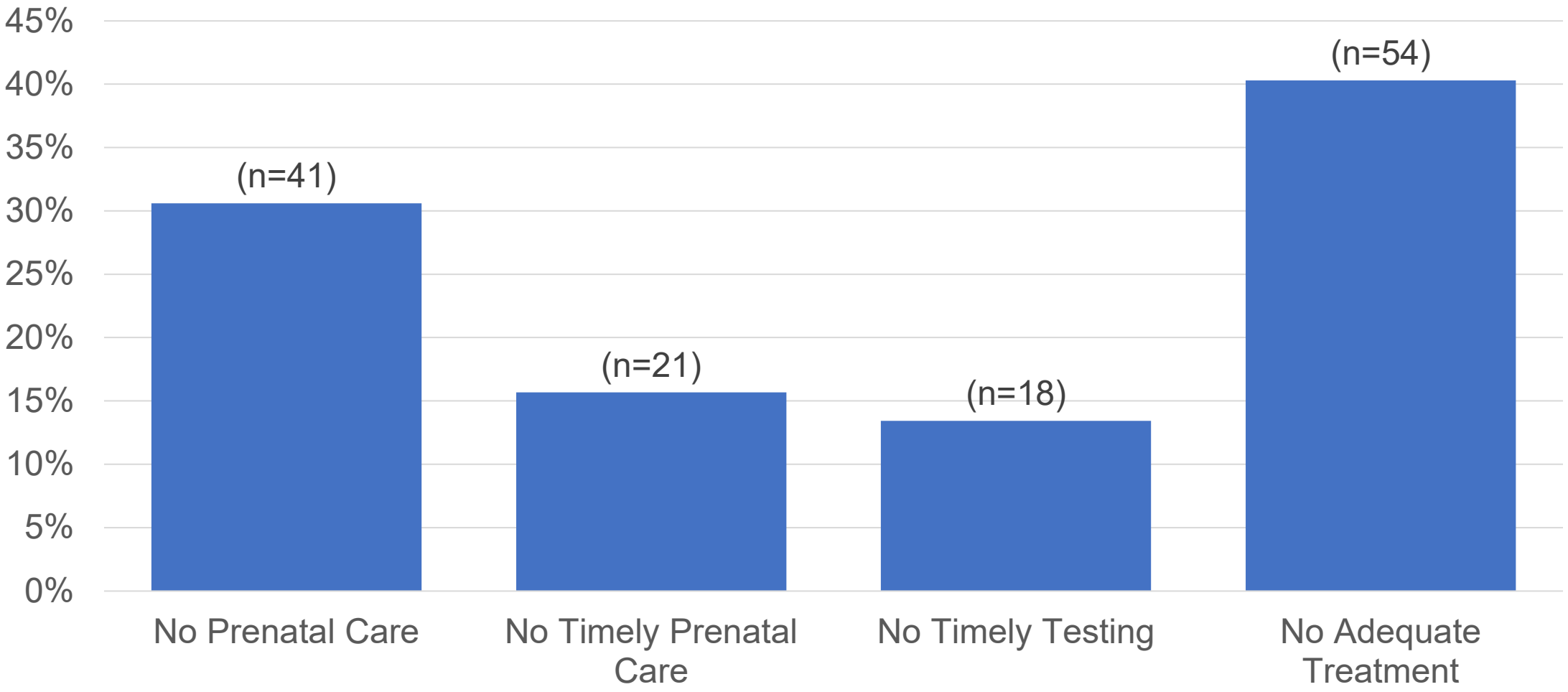
Indications for more frequent screening (HIV, syphilis)

Individual-level	Partner-level	Community/clinic-level
Multiple sex partners (>1) in the prior year	Multiple sex partners	High prevalence geography
New sex partner since last test	MSM/MSMW	School-based health centers
GC, CT, syphilis diagnosis in the prior 2 years	Methamphetamine use	Sexual health clinics
History of HCV infection	Injection drug use	Correctional facilities
Methamphetamine use	Criminal justice involvement	Substance disorder treatment
Injection drug use		
Transactional sex		
Criminal justice involvement		
Houselessness		
Taking PrEP		
Not on PrEP and condomless anal sex with a person who is either living with HIV (and not undetectable) or of unknown HIV status		

There Were 0 Cases of CS in 2013 and 37 Cases of CS in 2022 (n = 134 cases from 2014-2022)



Missed opportunities to prevent congenital syphilis, Oregon 2014-2022 (n = 134)



Case 1 continued.

- You confirm that your patient is pregnant.
- She's had condomless vaginal and oral sex with two male partners in the prior year. She is now in a committed relationship with the most recent partner and they have been trying to get pregnant.
- She has good familial support, stable housing, does not report alcohol or drug use. Works in construction management.
- She was diagnosed with chlamydia at age 18
- Received the HPV vaccine at age 13

Case 1 continued.

- What do you recommend regarding syphilis screening in pregnancy?

Recommendations for Syphilis Screening in Pregnancy in Oregon

Boodman et al. CJPH, 2023: triple screening is highly cost-avoidant

- Screen at first presentation to care
- Screen again at 24-28 weeks (early third trimester)
  - We recommend pairing with an oral glucose tolerance test
    - Allows enough time to arrange for treatment
    - Detects seroconversion and re-infection
- Screen at delivery
- Any pregnant person with a fetal demise after 20 weeks

At presentation to ER/urgent care, carceral settings, and substance use disorder treatment when syphilis status is unknown

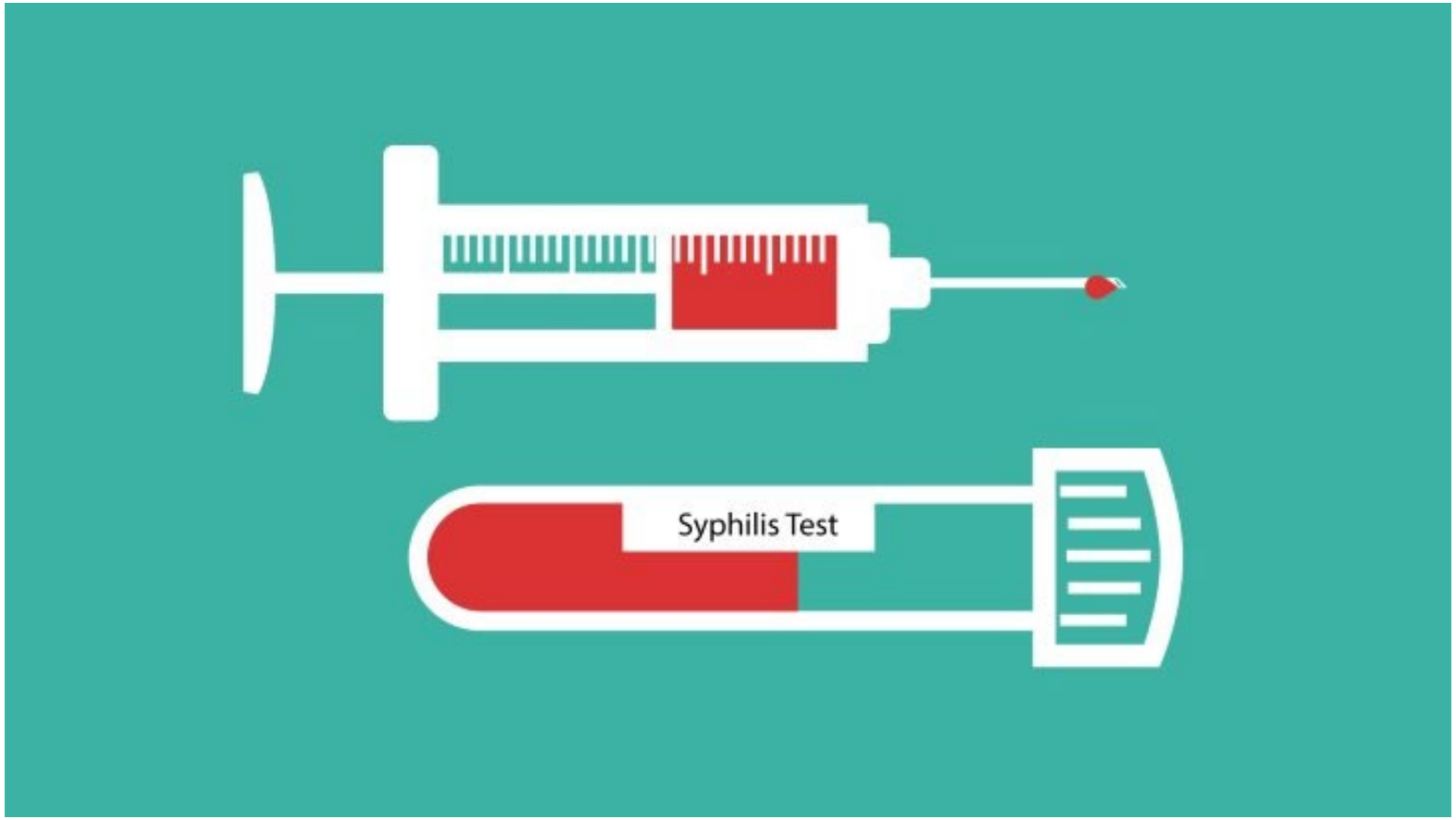
CS Is A Serious Infection

- Congenital syphilis results from transplacental infection of the fetus
- In primary (chancre) and secondary syphilis (rash), 80% of infants are affected
  - 25% stillbirth, 14% neonatal death, 41% alive but affected
- In late syphilis (asymptomatic), 23% of infants are affected
  - 12% stillbirth, 9% neonatal death, 2% alive but affected
- The clinical manifestations are varied:
  - Reticuloendothelial
  - Mucocutaneous
  - Skeletal
  - Neurologic, ocular, otic
  - Other (renal, hepatic, pulmonary, GI)

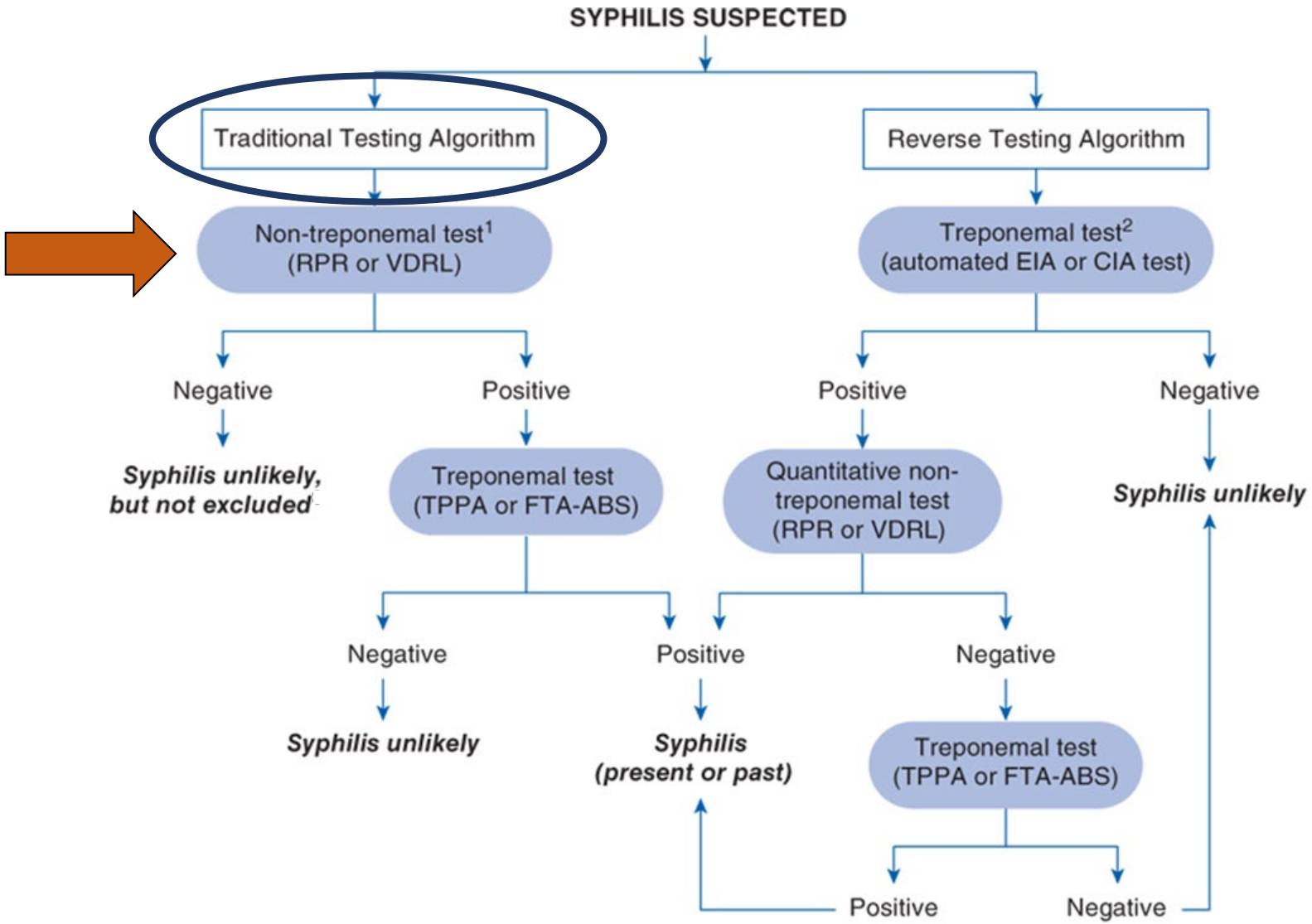
Case 1 continued.

- What testing do you send for syphilis?

Serological Tests for Syphilis

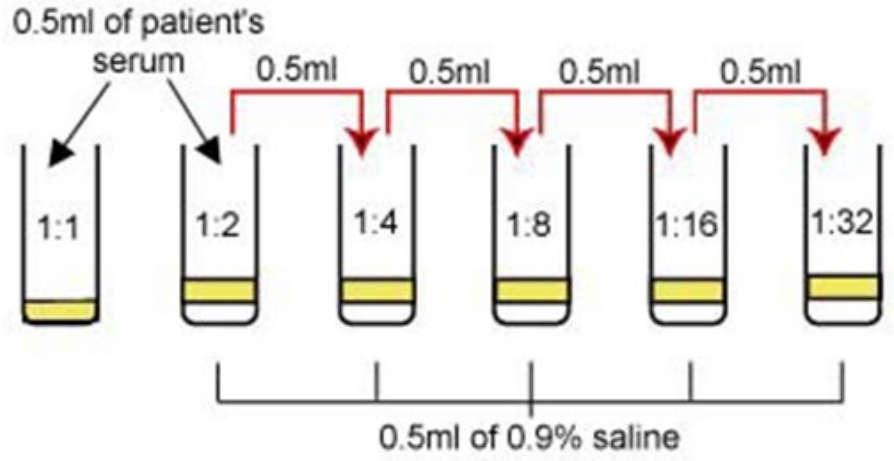


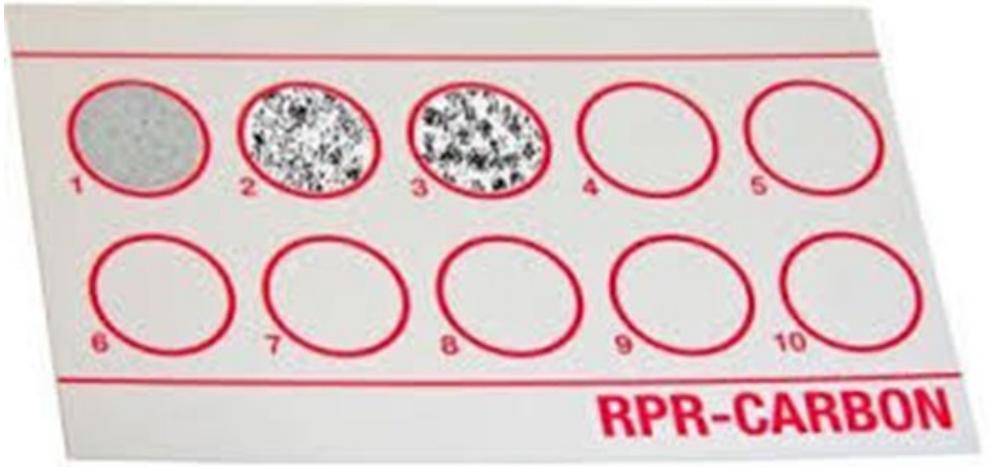
Syphilis Screening Algorithms



Non-treponemal tests: RPR and VDRL

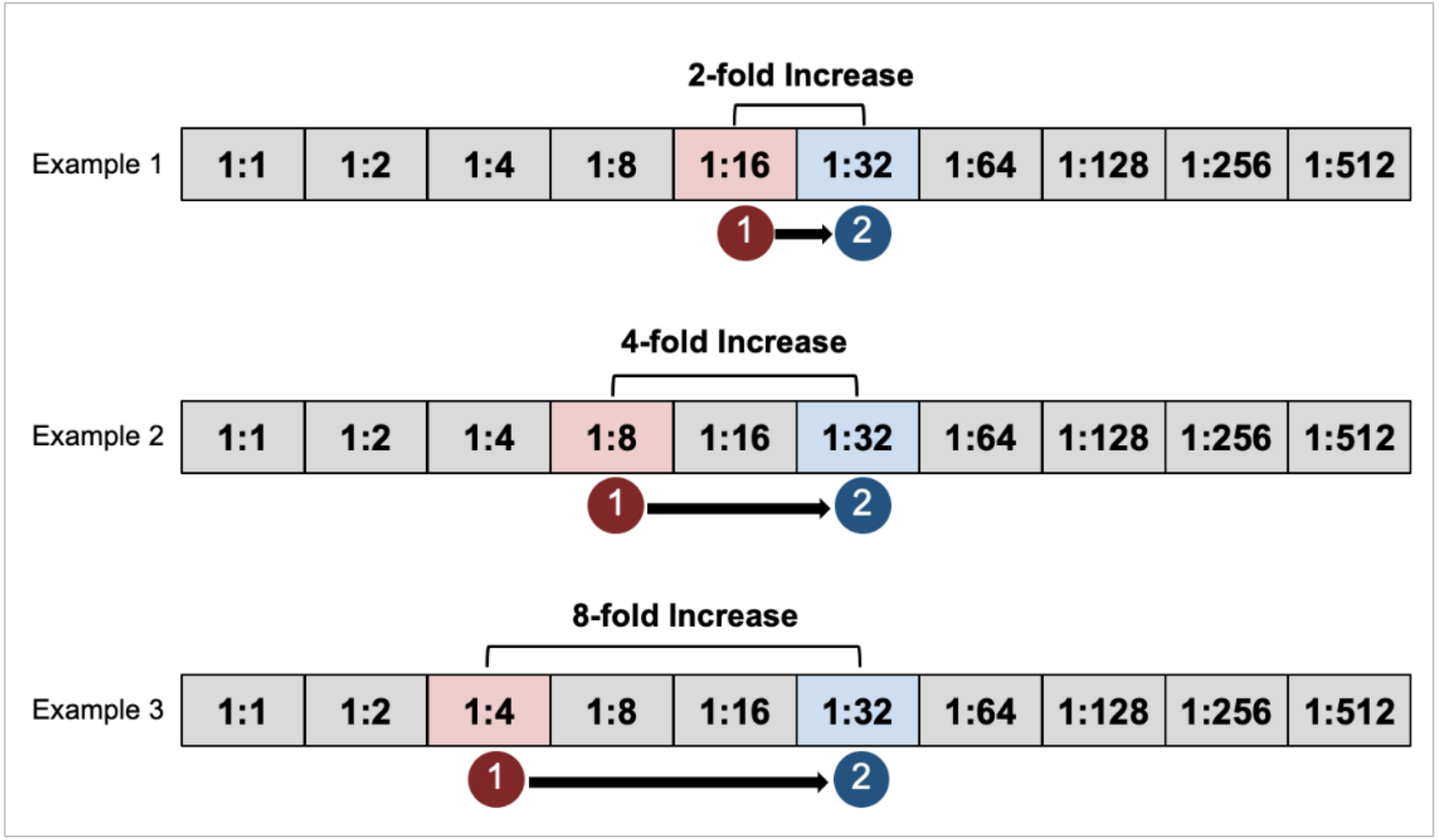
- RPR: most common
- VDRL: mostly used to test CSF in congenital syphilis or neurosyphilis cases
- Qualitative
- Quantitative titer (e.g.1:4, 1:32, 1:512)



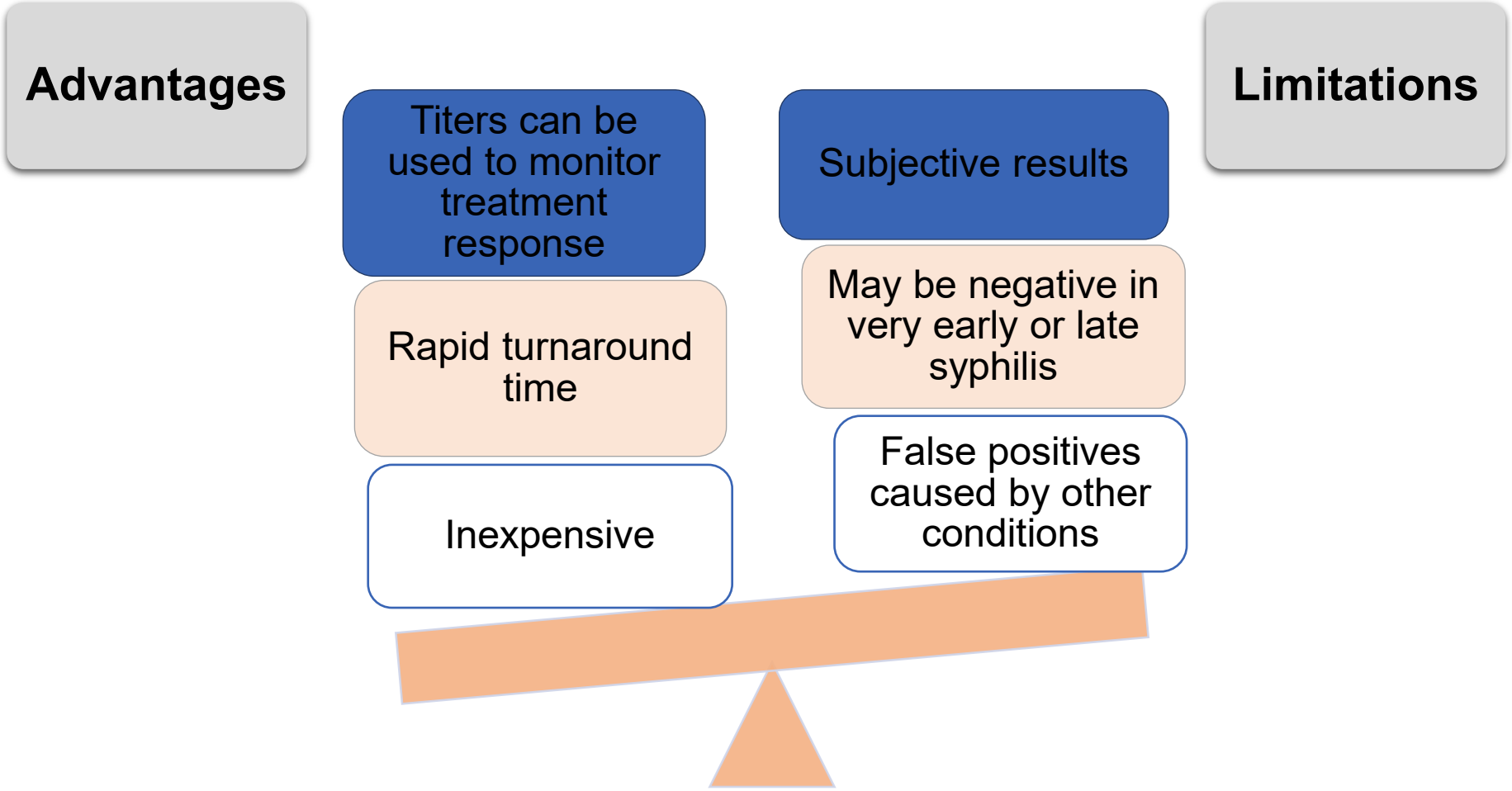


Examples of increases in RPR titers

From the National STD Curriculum



Non-treponemal test: RPR



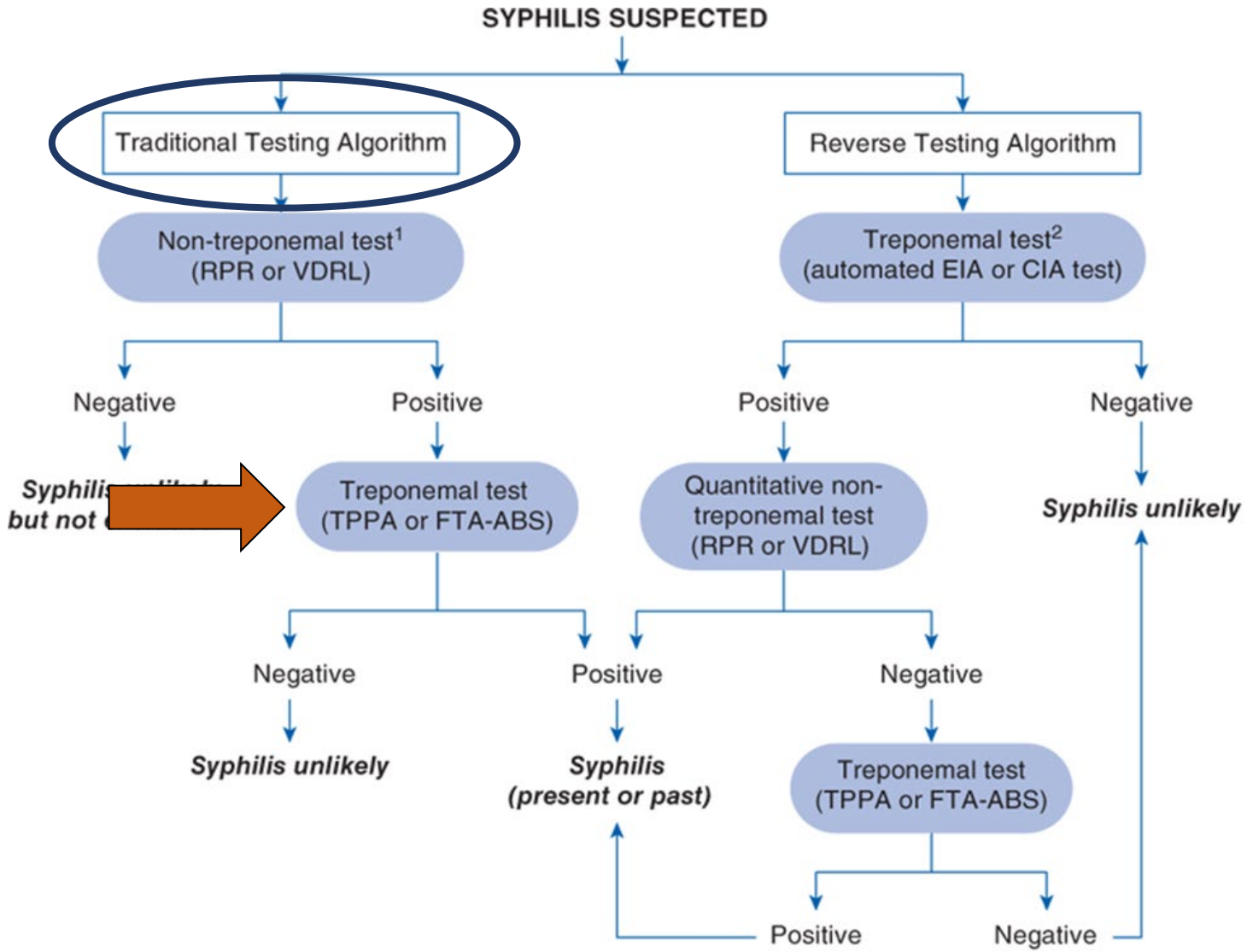
RPR: biologic false positives

- A reactive RPR alone does not confirm syphilis infection

- Measures antibody response to damage caused by syphilis, other treponemal diseases, and nontreponemal diseases

Acute or Chronic Infections	Autoimmune Diseases	Other Conditions
• TB • Malaria • Early HIV infection	• Systemic lupus • Rheumatoid arthritis	• Pregnancy • Older age • Following vaccination • Injection drug use

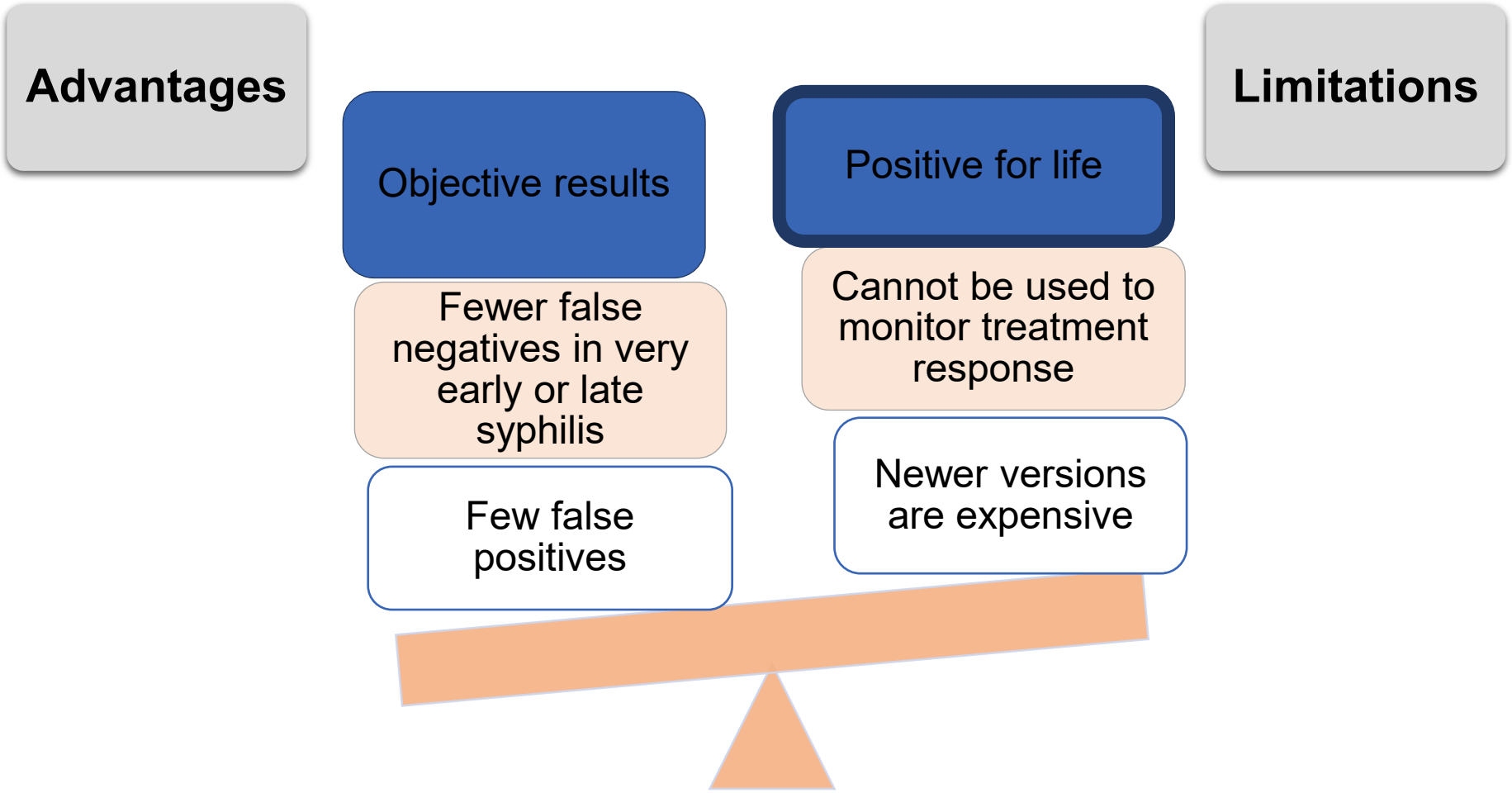
Syphilis Screening Algorithms



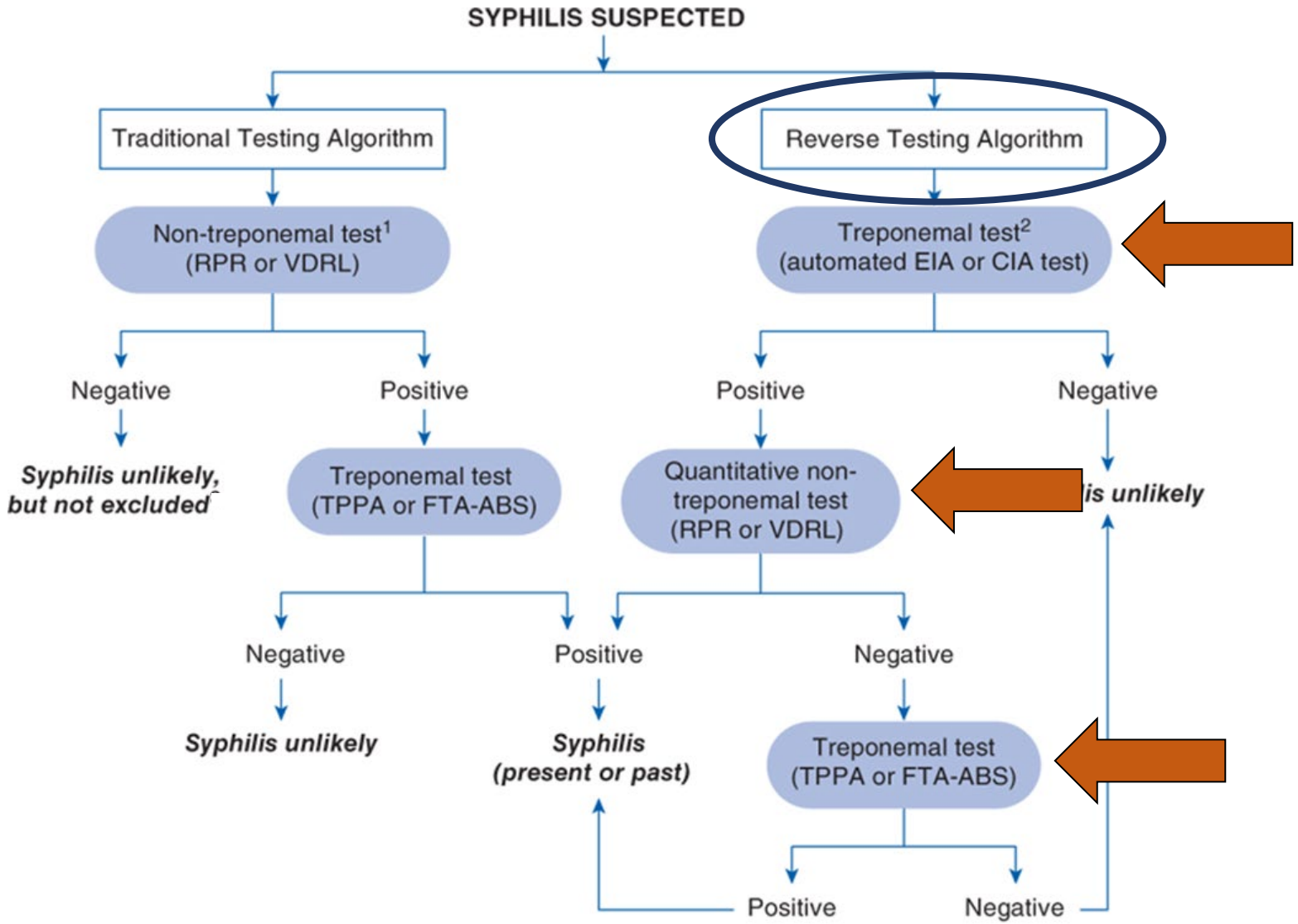
Treponemal tests

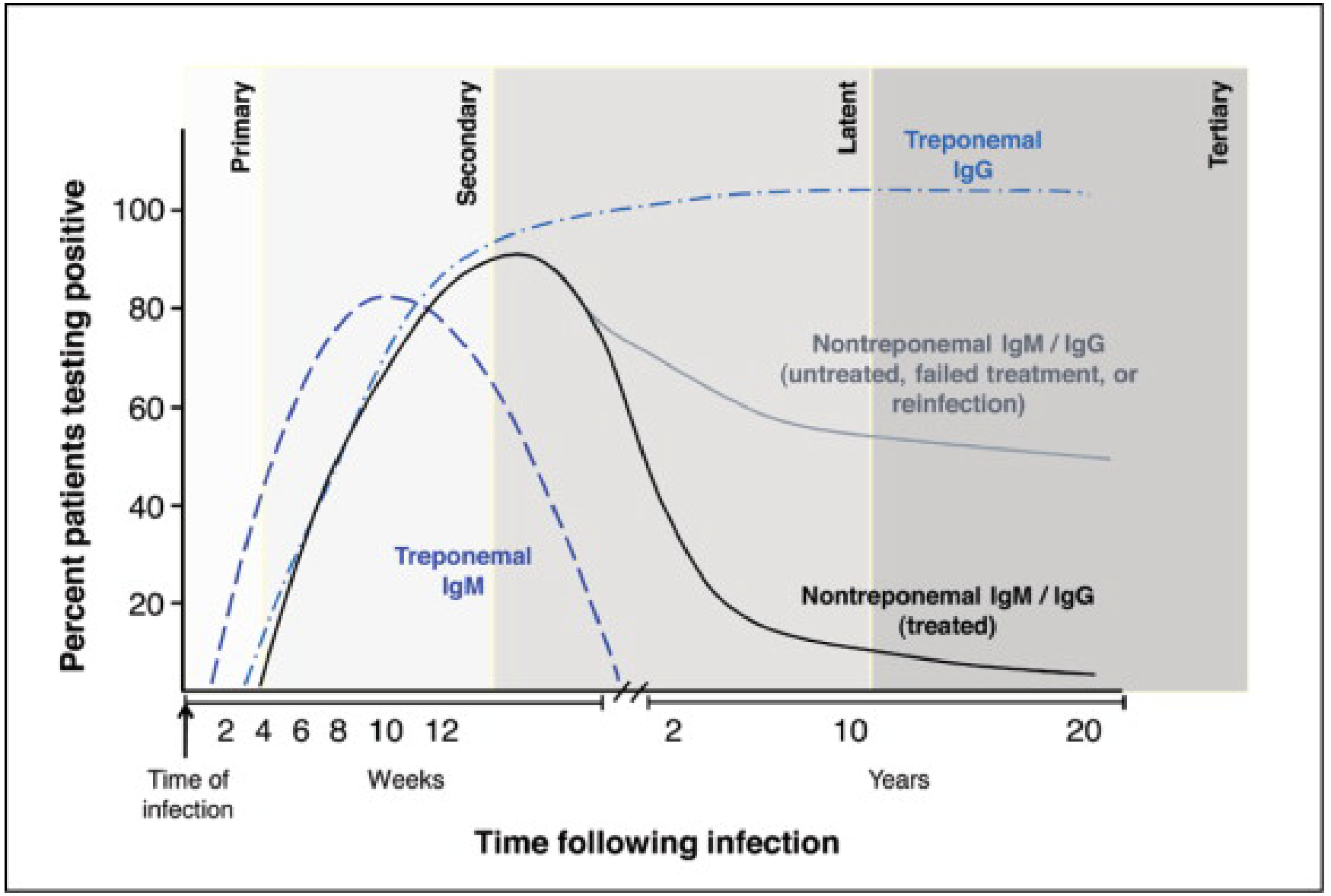
- Detect antibodies to *T. pallidum*
- Test types: Syph-TP, FTA, TPPA, EIA, CLIA, and more!
- Qualitative
- Quantitative (1+ to 4+)

Treponemal tests



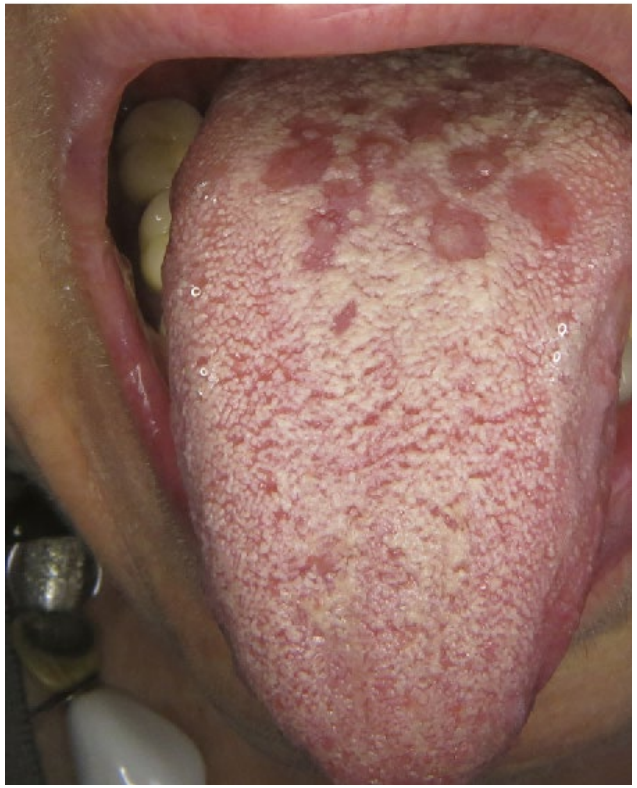
Syphilis Screening Algorithms

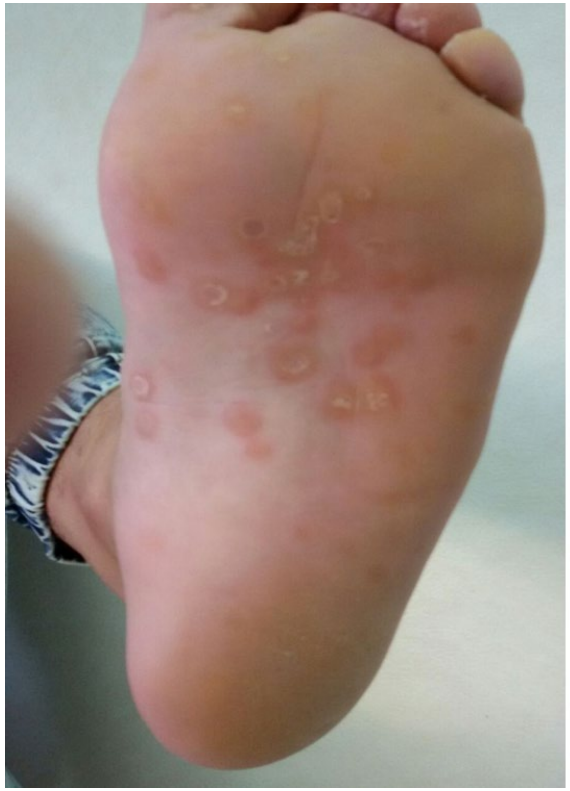



Primary
Secondary
Latent
Tertiary
Treponemal IgG
Nontreponemal IgM / IgG (untreated, failed treatment, or reinfection)
Treponemal IgM
Nontreponemal IgM / IgG (treated)
Percent patients testing positive
100
80
60
40
20
2 4 6 8 10 12
2 10 20
Time of infection
Weeks
Years
Time following infection

Case 2.

- A 31-year-old G1P0 cisgender woman at 26 weeks EGA comes to urgent care for a chief complaint of a “tongue problem”





Case 2 continued.

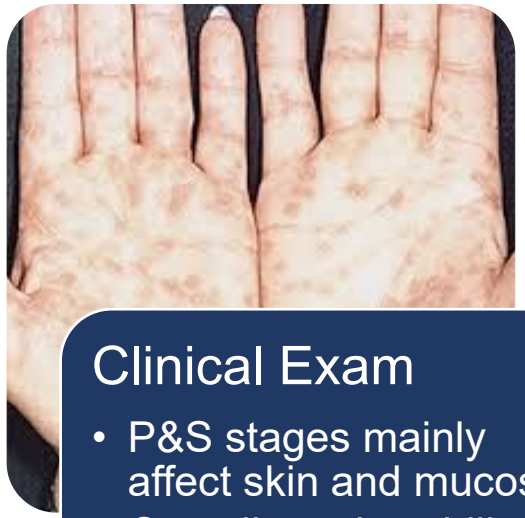
- What is the diagnosis?

  - Geographic tongue
  - Primary syphilis
  - Secondary syphilis
  - Hand foot and mouth disease
  - Palmar pustular psoriasis of pregnancy

Diagnostic Approach

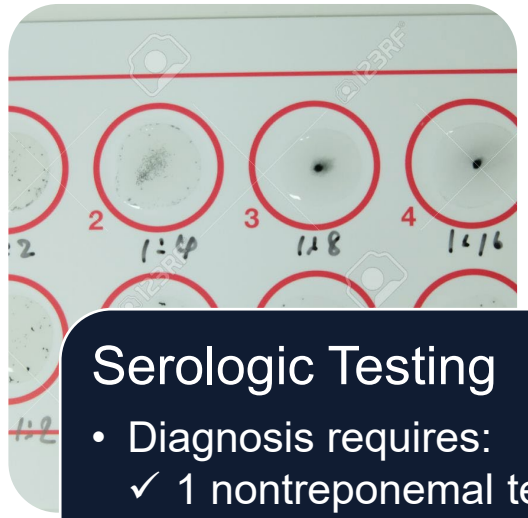
Medical History (including sexual hx)

- Partners
- Practices
- Pleasure
- Protection from STIs
- Past history of STIs
- Pregnancy plans



Clinical Exam

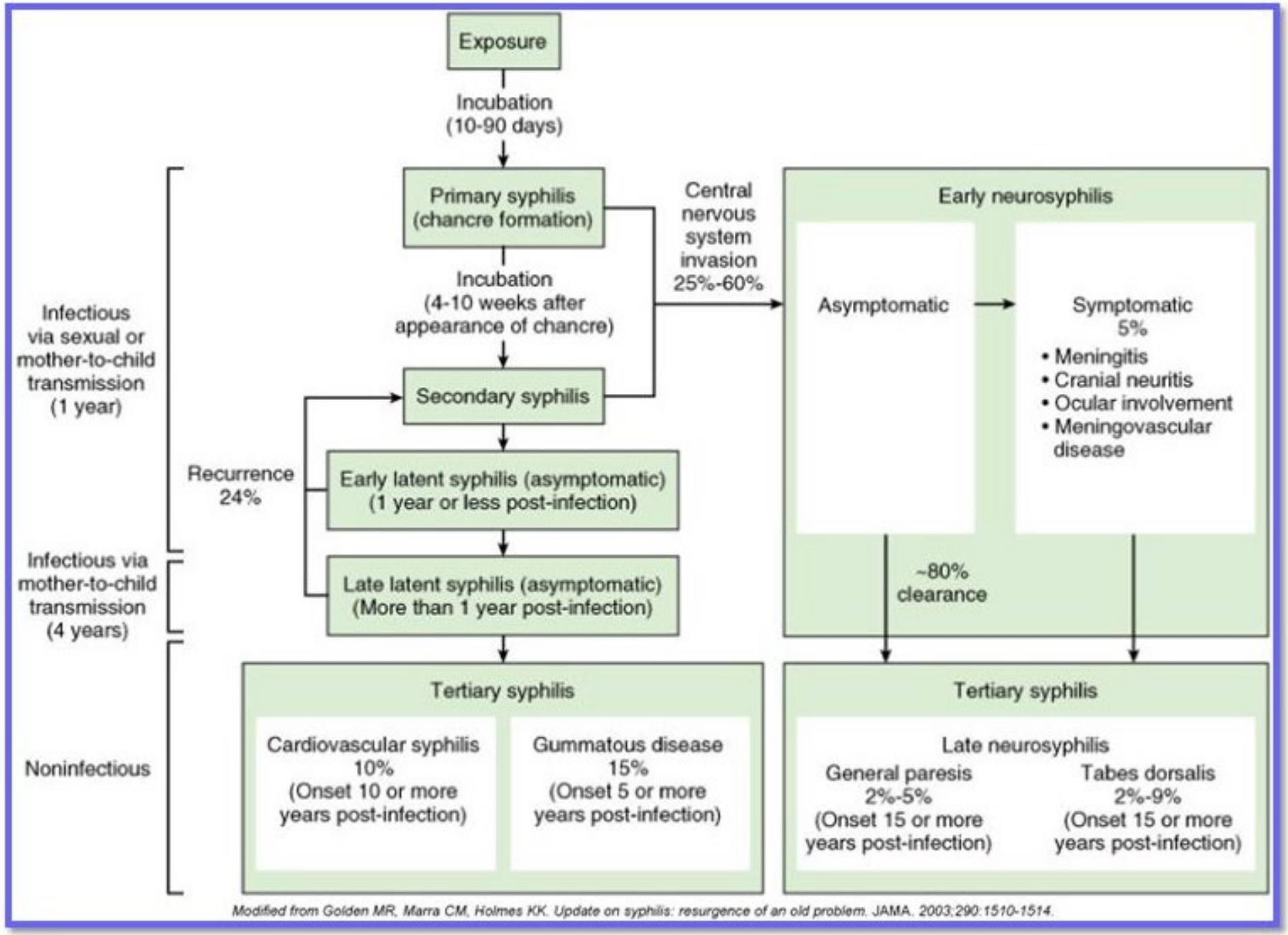
- P&S stages mainly affect skin and mucosa
- Complicated syphilis (neuro, otic, ocular) can occur at any stage



Serologic Testing

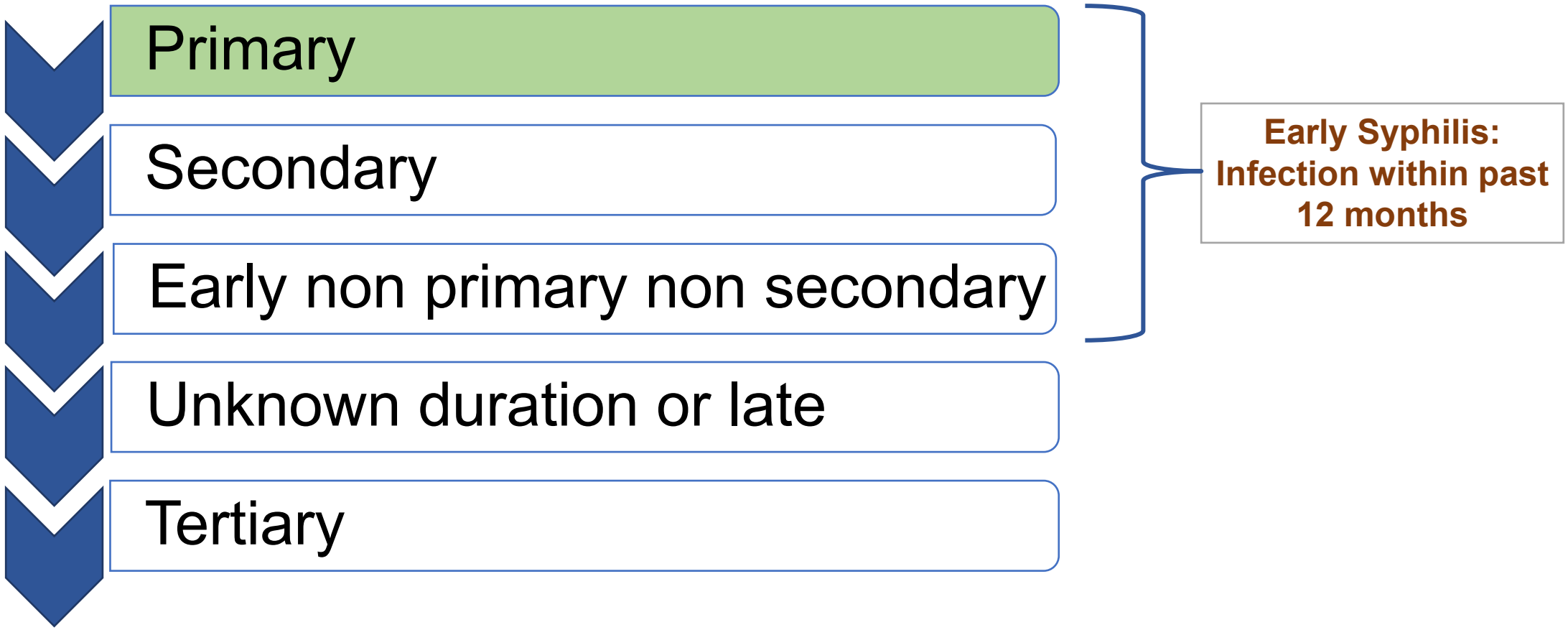
- Diagnosis requires:
  - ✓ 1 nontreponemal test
  - ✓ 1 treponemal test

Source: Centers for Disease Control and Prevention, National Center for HIV Viral Hepatitis STD and TB Prevention. Atlanta: U.S. Department of Health and Human Services; Updated March 2014.



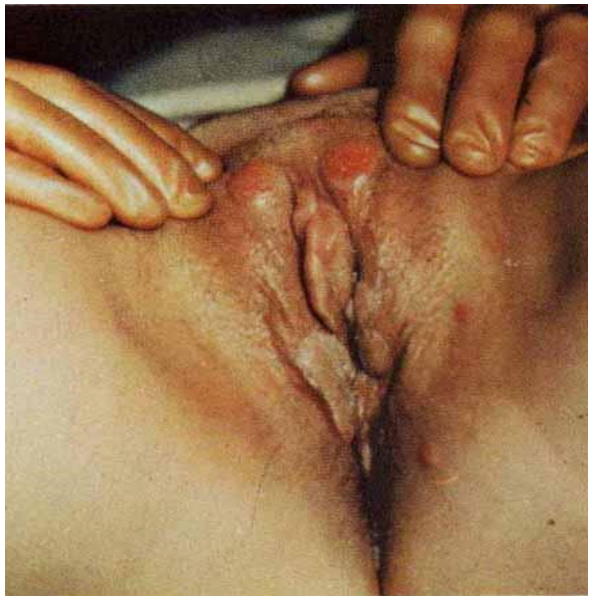
Modified from Golden MR, Marra CM, Holmes KK. Update on syphilis: resurgence of an old problem. JAMA. 2003;290:1510-1514.

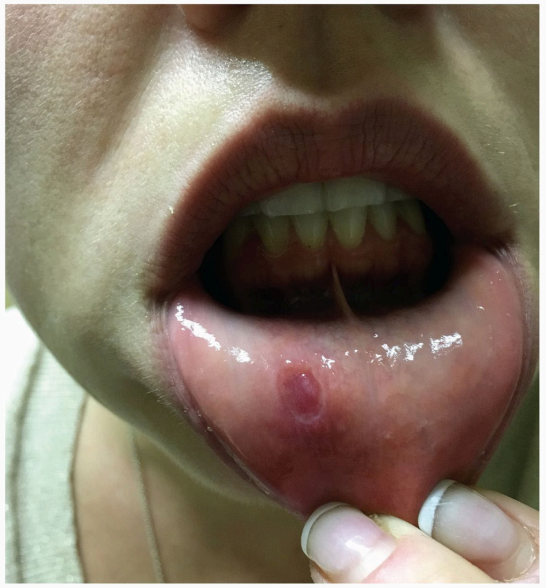
Stages of Disease Progression

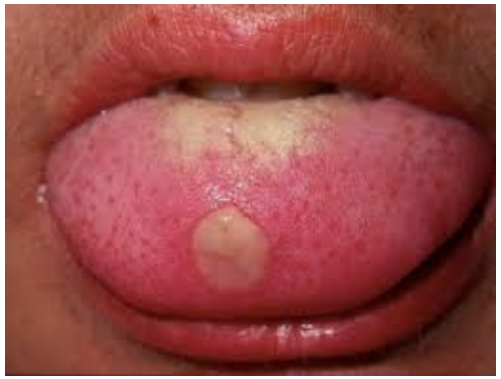


Primary Syphilis

- Test results are positive ~21 days after exposure
  - In 12-15% of cases, treponemal test will be positive before an RPR
- Painless chancre at site of inoculation (e.g., genitals, rectum, mouth)
  - Most patients will not notice or remember a sore
  - Occurs 10-90 days after infection is acquired
- Highly contagious







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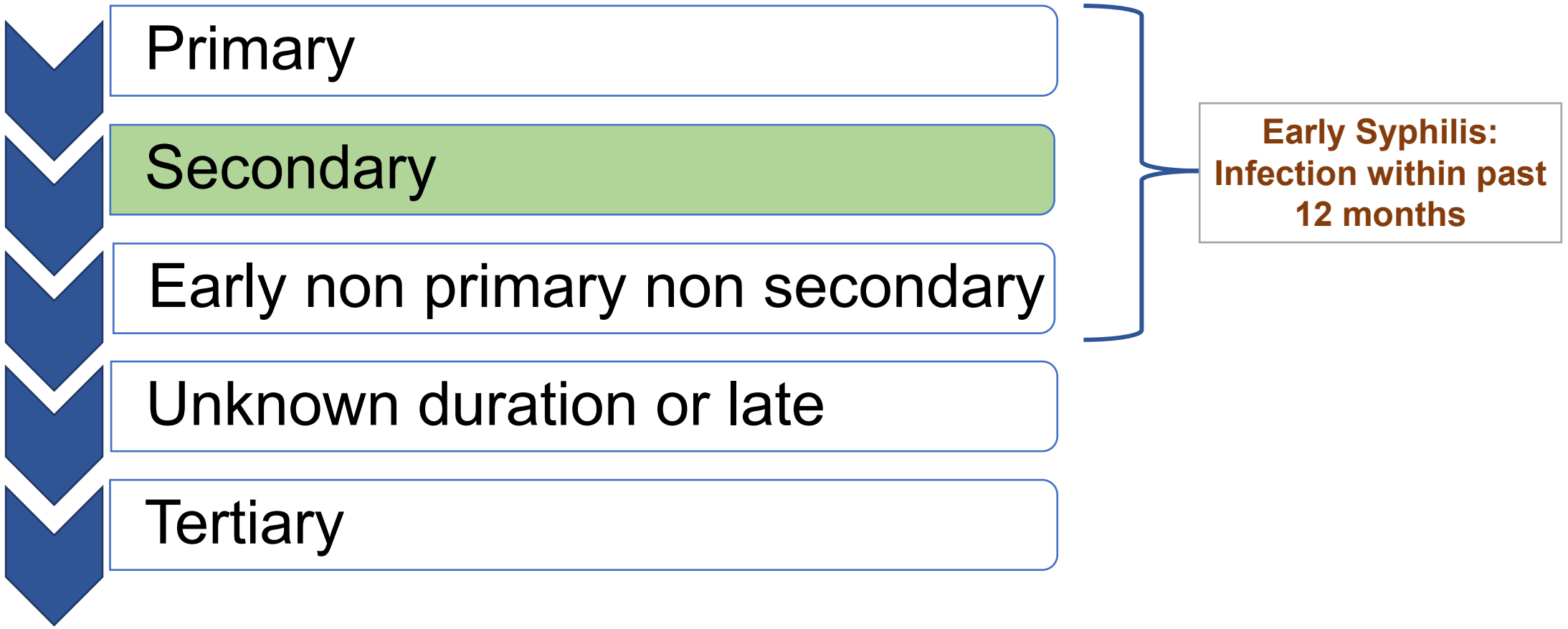


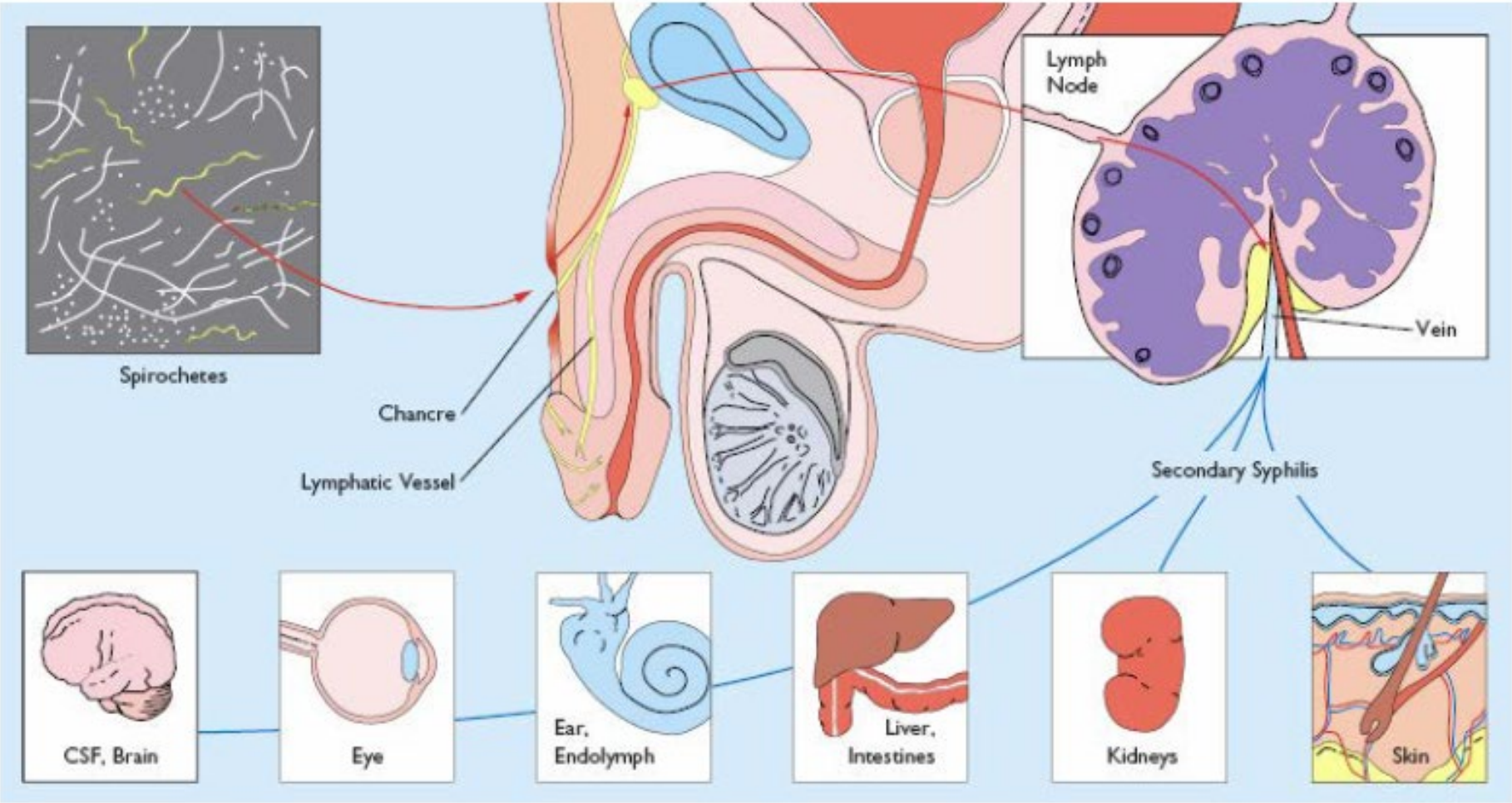
Secondary Syphilis

- Begins 4-8 weeks after primary chancre appears

- Common symptoms include:
  - Generalized body rash - classically palmar or plantar rash, but often on the trunk, arms, and legs
  - Lymphadenopathy
  - Mucous patches
  - Condyloma lata – flat topped lesions around the genitals, rectum, umbilicus
  - Alopecia – patchy, moth-eaten appearance

- Highly contagious

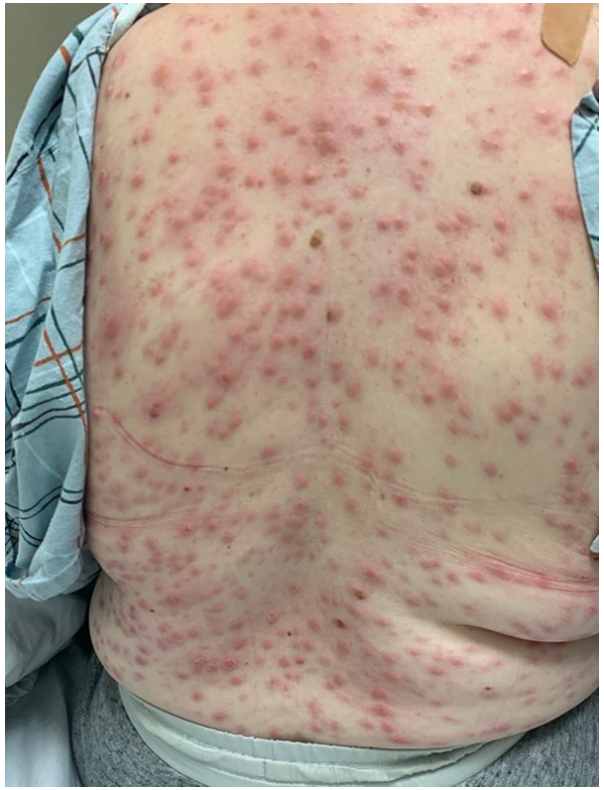
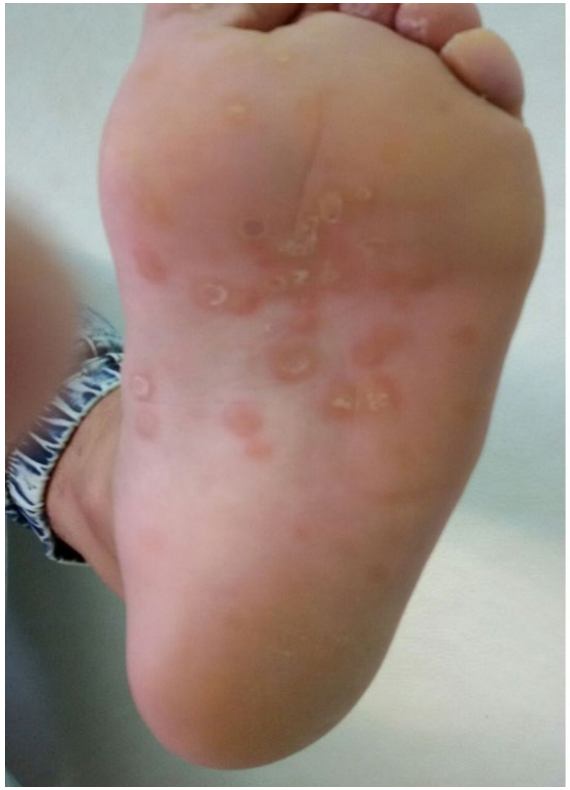
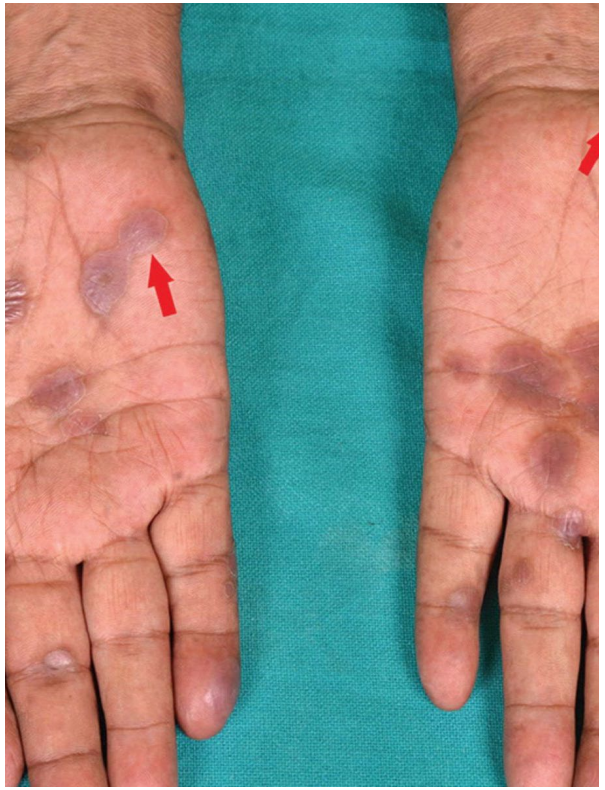
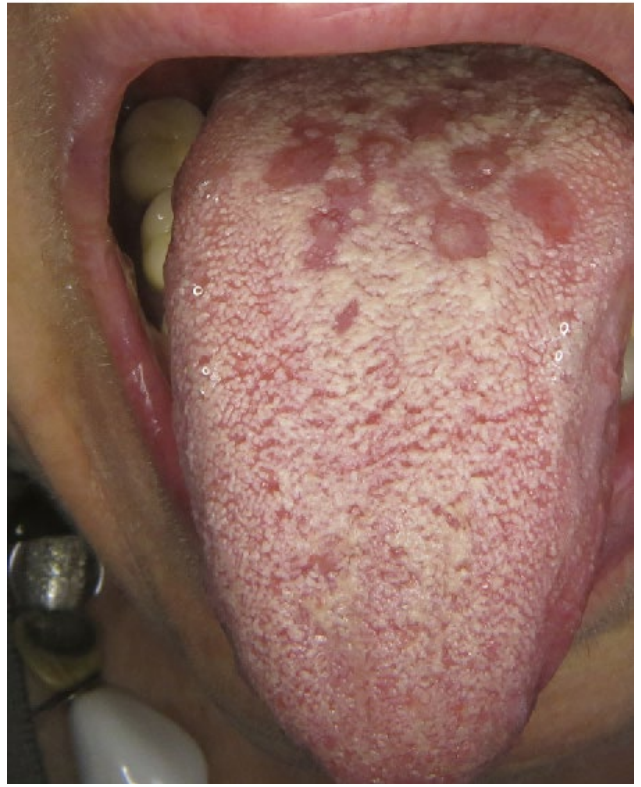
“Secondary is systemic”



Treponemic

Mucous membranes (mucous patches), lymph nodes

Skin and oral manifestations of secondary syphilis

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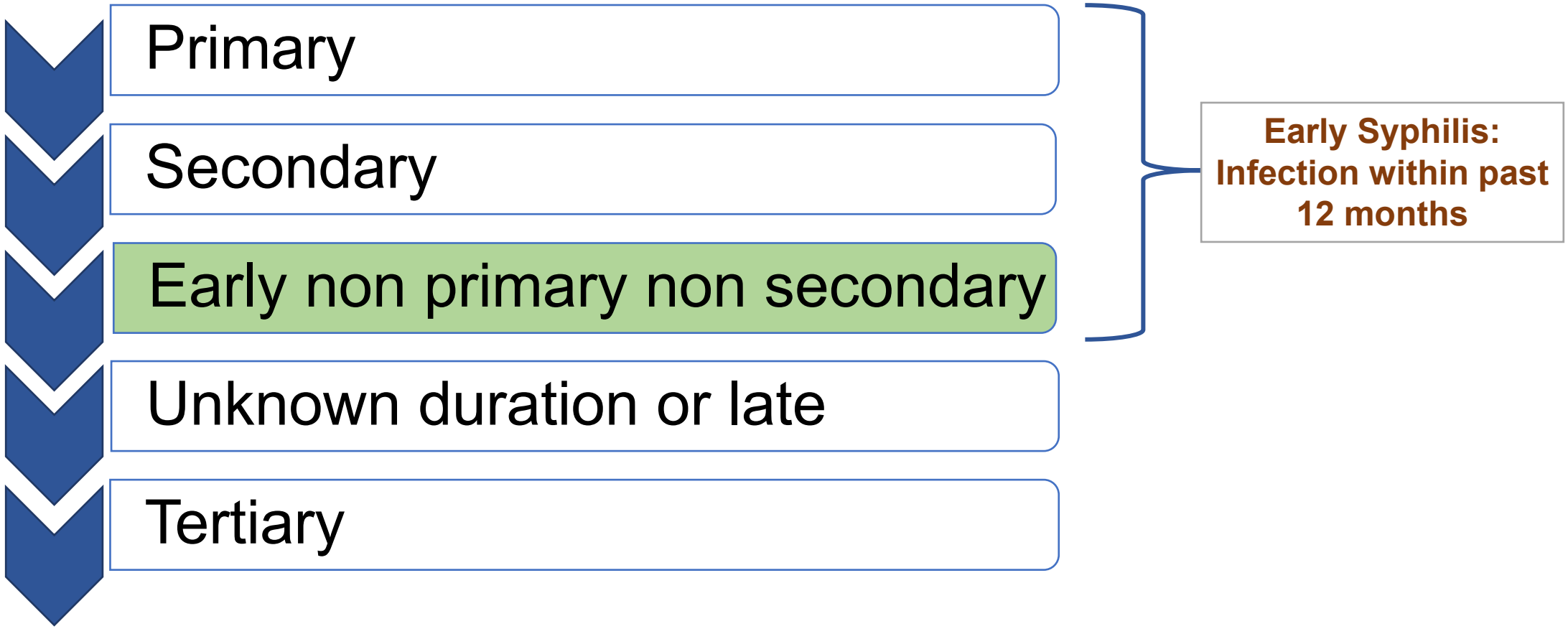
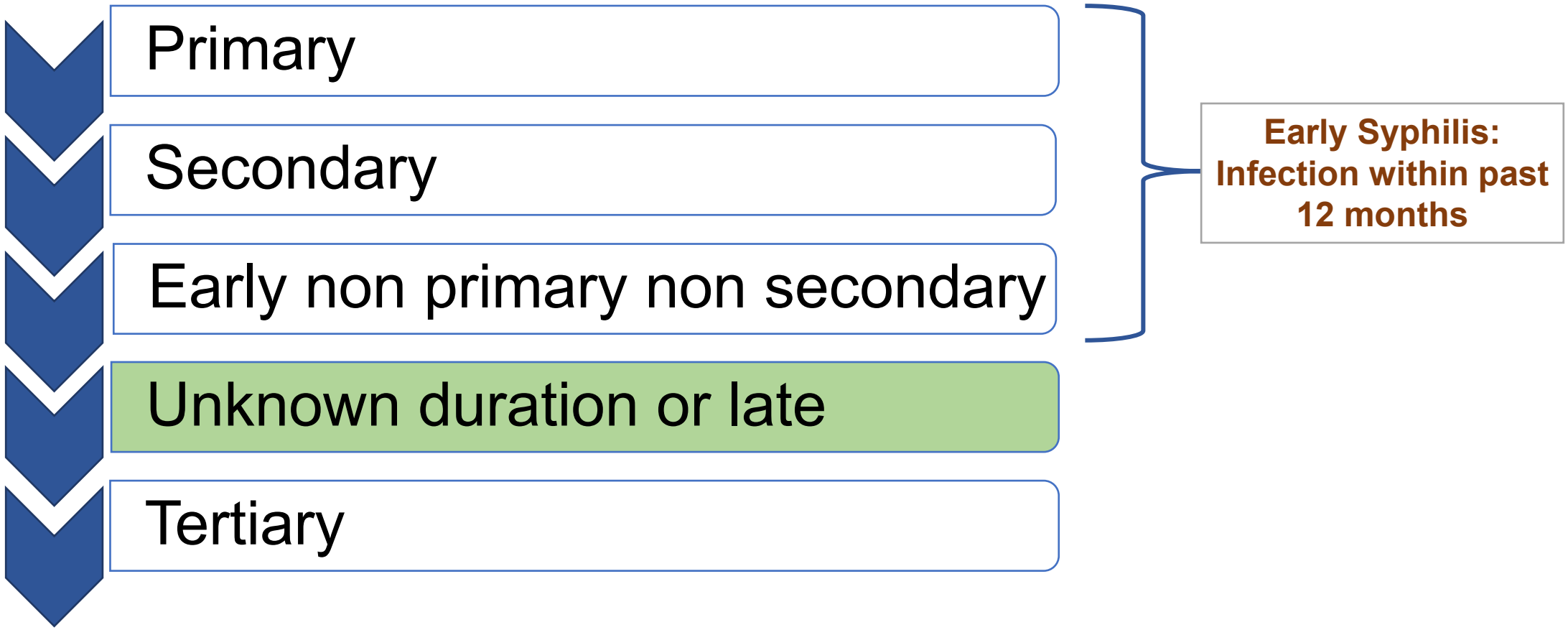


Early Non Primary Non Secondary Syphilis

- No signs/symptoms of primary or secondary syphilis at the time of initial examination/testing
- Evidence that infection with *Treponema pallidum* occurred within the previous 12 months
  - Documented seroconversion of nontreponemal or treponemal test
  - ≥ 4-fold increase in titer
  - History of symptoms of primary or secondary syphilis
  - Sex partners with and early (infectious) syphilis diagnosis
  - Sexual debut within last 12 months

Stages of Disease Progression



Unknown Duration or Late Syphilis: infection occurred >1 year ago or at unknown time

- No signs or symptoms of primary or secondary syphilis at time of initial exam/testing
- Evidence of current infection
  - No prior history of syphilis AND current reactive treponemal AND non-treponemal tests; **OR**
  - Prior history of syphilis with a current nontreponemal titer demonstrating a ≥4-fold increase from last titer; **OR**
  - Signs/symptoms/labs demonstrating neurologic, ocular, otic, or late clinical manifestations
- No evidence of acquiring infection within previous 12 months

Case 2 continued.

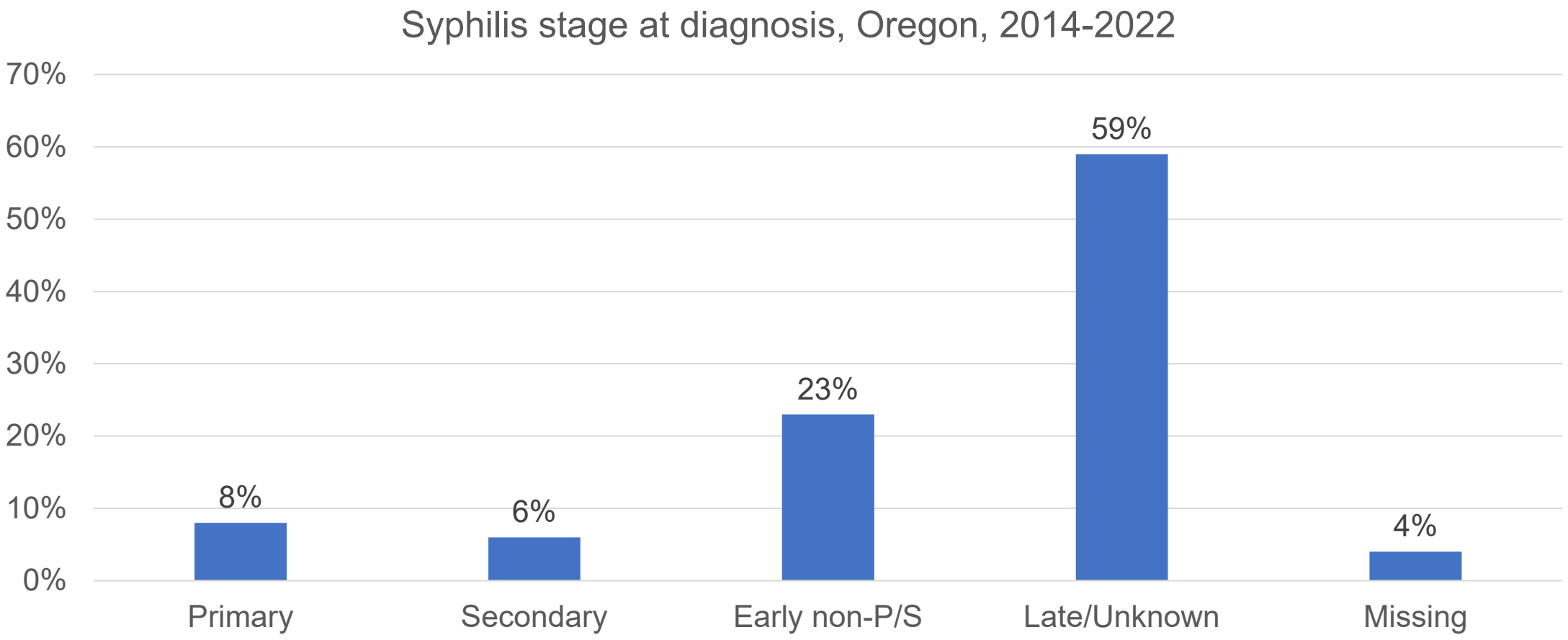
- What is your immediate next step in management?

  - Treat with long-acting benzathine penicillin G (Bicillin LA) 2.4 million units IM once now
  - Send syphilis serologies and treat if reactive
  - Refer to dermatology for a skin biopsy
  - Treat with doxycycline 100 mg PO BID for 28 days

Overall, treatment is 98% effective in preventing CS Alexander et al., Obstetrics & Gynecology, 1999

	Recommended Treatment	Notes
Primary/Secondary/ Early non-primary non-secondary	BPG 2.4 million units in a single dose	Some experts recommend a second dose (success in secondary syphilis was 95%). May consider a second dose in pregnant people with HIV.
Unknown duration or late	BPG 7.2 million units as three doses of 2.4 million units each at 7-day intervals	Max interval between doses = 9 days before re-starting treatment

Most Pregnant People Are Diagnosed with Late/Unknown Duration Syphilis Requiring a Longer Treatment Regimen



Prenatal Syphilis Screening, Staging, and Management for Congenital Syphilis Prevention

Screen

Screen all patients at three points in pregnancy:

❶ First prenatal visit or time of pregnancy testing **❷ 28 weeks' gestation** **❸ Delivery**

Initial diagnosis requires both a non-treponemal test (RPR) and confirmatory treponemal test (TP-PA, FTA-ABS, EIA/CIA)

SYPHILIS DIAGNOSIS

Stage

Primary	+ Chancre
Secondary	+ Rash and/or other signs[1]
Early Latent	NO symptoms, and infection occurred within the past year[2]

Late Latent or Unknown Duration

NO symptoms, and infection does not meet criteria for early latent[2]

Neurosyphilis/ Ocular/ Otosyphilis[3]

+ CNS signs or symptoms

+ CSF findings on lumbar puncture (LP)

Treat

Benzathine penicillin G
2.4 Million Units Intramuscularly (IM) Once

Certain evidence indicates that additional therapy is beneficial for early syphilis in pregnancy. A second dose of benzathine penicillin G 2.4 million units IM can be given 7 days after the initial dose.

Benzathine penicillin G
2.4 Million Units IM every 7 days, for 3 doses (7.2 Million Units total)

A 6-9 day interval between doses is acceptable. If any doses are late or missed, re-start the entire 3-dose series.

Aqueous penicillin G
18-24 Million Units per day, administered as 3-4 Million Units IV every 4 hours or continuous infusion for 10-14 days. See 2021 CDC STI Treatment Guidelines for non-intravenous alternative regimen.

Monitor

If syphilis treated at/before 24 weeks' gestation, wait at least 8 weeks to repeat titer and repeat again at delivery. Repeat sooner if reinfection or treatment failure is suspected. If treated after 24 weeks' gestation, repeat titer at delivery. Consider more frequent monitoring if at high risk for reinfection in pregnancy (see risks at right).

If syphilis diagnosed after 20 weeks' gestation, management should include a fetal ultrasound to look for congenital syphilis.

Post-treatment serologic response during pregnancy varies widely. Many women do not experience a fourfold decline by delivery. If sustained (>2 weeks) fourfold increase occurs after treatment completion, evaluate for reinfection and neurosyphilis.

RISK FACTORS FOR SYPHILIS IN PREGNANCY

If there is no record of syphilis screening in pregnancy or screening history is unknown, screen patients with any of these risks (particularly those who attend ED, urgent care, detention/correctional, and/or substance use treatment settings):

- Limited or no prenatal care
- Injection drug use (or partner who uses injection drugs)
- Methamphetamine or heroin use (any method)
- Houselessness or unstably housed
- Criminal justice involvement within previous 12 months (or partner with criminal justice involvement)
- Living with HIV or hepatitis C
- Other STI diagnosed within previous 12 months
- Multiple sex partners, a new partner, or partner with other partners

1. Signs of secondary syphilis also include condyloma lata, patchy alopecia, and mucous patches.
2. Persons can receive a diagnosis of early latent if, during the prior 12 months, they had a) seroconversion or sustained fourfold titer rise (RPR); b) unequivocal symptoms of primary or secondary syphilis; or c) a sex partner with primary, secondary, or early latent syphilis.
3. Neurosyphilis, ocular, and otic syphilis can occur at any stage. Patients need a full neurologic exam including ophthalmic and otic; If clinical evidence of neurologic involvement is observed (e.g. cognitive dysfunction, motor or sensory deficits, cranial nerve palsies, or symptoms or signs of meningitis or stroke), a CSF examination should be performed before treatment. If only ocular/otic manifestations without other abnormalities on neuro exam, CSF evaluation not necessary before starting treatment for neurosyphilis.

Adapted with permission from CDPH/CAPTC

Last Updated: 3/31/22

Important Considerations for Syphilis Treatment in Pregnancy

Screen early, treat as soon as possible
Treatment failure, and subsequent congenital syphilis, has been associated with treatment later in the pregnancy

Treatment is safe and highly effective for both the pregnant person and fetus

Benzathine Penicillin G (Bicillin L-A) is the ONLY recommended therapy for syphilis during pregnancy

Someone with signs, symptoms, or exposure to syphilis should receive treatment for early disease regardless of whether serology results are available

ADDITIONAL RESOURCES

- **For detailed treatment guidelines,** including penicillin allergy recommendations, see the CDC 2021 STI Treatment Guidelines: www.cdc.gov/std/treatment-guidelines
- **For clinical questions:**
  - Contact Dr. Tim Menza at the Oregon Health Authority (TIMOTHY.W.MENZA@dhsoha.state.or.us), or
  - Enter your consult online at the STD Clinical Consultation Network: stdccn.org

What if my patient is allergic to penicillin?

- **Verify the nature of the allergy.** Approximately 10% of the population reports a penicillin allergy, but less than 1% of the whole population has a true IgE-mediated allergy.
- **Symptoms of an IgE-mediated (type 1) allergy include:** Hives, angioedema, wheezing and shortness of breath, and anaphylaxis. Reactions typically occur within 1 hour of exposure.
- **Refer for penicillin skin testing** if the nature of the allergy is uncertain or cannot be determined.
- **Refer for desensitization with penicillin** if the skin test is positive or the patient has a true penicillin allergy.
- **Desensitization should be performed.** Serious allergic reactions can occur. Consult an allergist.
- **Treat the patient with benzathine penicillin G.** Treat according to appropriate stage of syphilis (see opposite page for treatment regimen).

FOR MORE INFORMATION ABOUT IgE-MEDIATED PENICILLIN ALLERGY:
www.cdc.gov/antibiotic-use/community/pdfs/penicillin-factsheet.pdf
www.cdc.gov/std/treatment-guidelines/penicillin-allergy.htm

Sources
Workowski KA, Bachmann LH, Chan P et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep 2021;70 (No.4); Assessment, U. Screening for syphilis infection in pregnancy: US Preventive Services Task Force reaffirmation recommendation statement. Ann Intern Med, 2009. 150: p. 705-709; Alexander JM, Sheffield JS, Sanchez PJ, et al. Efficacy of treatment for syphilis in pregnancy. Obstetrics & Gynecology 1999;93(1):5-8; Plotzker RE, Murphy RD, Stoltey, JE. "Congenital Syphilis Prevention: Strategies, Evidence, and Future Directions." Sexually Transmitted Diseases (2018); Wendel GO, Jr, Stark BJ, Jamison RB, Melina RD, Sullivan TJ. Penicillin Allergy and Desensitization in Serious Infections During Pregnancy. N Engl J Med 1985;312:1229–32.

Oregon Health Authority

AETC AIDS Education & Training Center Oregon AETC

END HIV

Case 2 continued.

- You treat immediately with Bicillin LA
- She recalls a bump near her anus 4-6 weeks ago; it was hard and bled sometimes when she wiped with toilet paper. It went away in about 2 weeks.
- She's had anal, vaginal, and oral sex with one male sex partner who has been in and out of her life over the past 2 years
- She's thinking about moving to another state to be with family during the rest of the pregnancy

Case 2 continued.

- RPR (nontrep test) is 1:64 with a reactive T pallidum EIA (trep test)
- You arrange for an ultrasound to assess for fetal signs of CS in the next 1-2 weeks and for follow-up lab testing in 2 months

- What else do you want to do now that you have a clear diagnosis of secondary syphilis?

Conduct an ocular/otic/neuro review of systems for everyone who has a syphilis diagnosis

- Eyes: new changes in vision, seeing black spots, flashing lights, floaters, blurring, double vision, photophobia, eye discomfort, redness, burning
- ENT: new changes in hearing (hearing loss, muffled hearing), tinnitus
- Neck: stiffness
- Neuro: headaches out of the ordinary, new confusion or memory problems, trouble concentrating, change in personality, changes in coordination, trouble walking, paresthesia or numbness in limbs

Clinical manifestations of neurosyphilis

Cluster	Symptoms and signs
Early neurologic syphilis	
Syphilitic meningitis	**Headache, photophobia, neck stiffness**
Brain stem/cranial nerves	Ptosis, cranial nerve palsy, facial weakness, **hearing loss, tinnitus**
Seizure	Partial seizures with or without secondary generalization, myoclonus
Cerebrovascular accident	Acute, focal neurologic deficit (more likely in people living with HIV)
Ocular	Vision loss**, uveitis,** optic nerve dysfunction (field cuts)
Late neurologic syphilis	
Neuropsychiatric	Cognitive impairment (includes dementia and delirium), behavior change, psychosis
Myelopathy	Acute, subacute, chronic spinal cord dysfunction, includes tabes dorsalis

Case 2 continued.

- You also encourage her to tell her partner get treatment and testing

- And, you tell her that the health department may reach out to interview her and offer help in getting her partner tested and treated

Working with your local public health authority

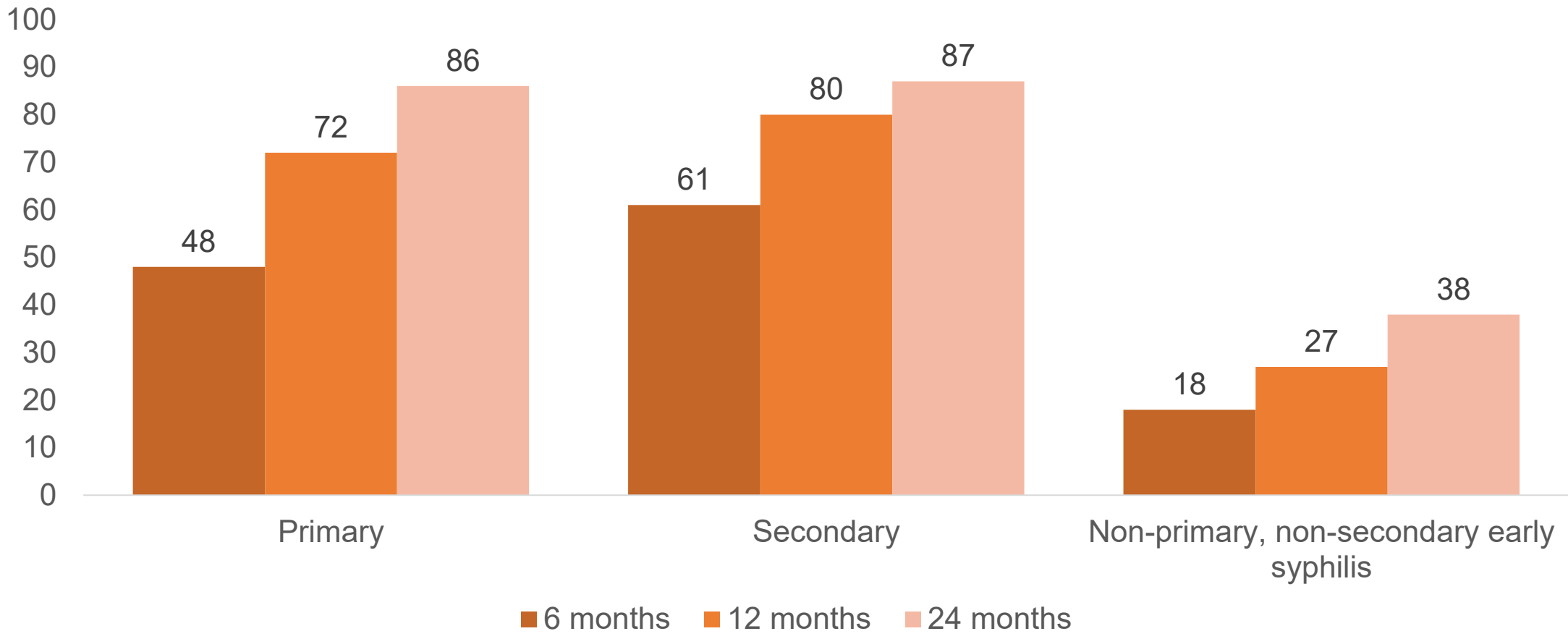
- Provide consultation on syphilis or connect you with an expert in syphilis
- Confidentially contact partners for treatment and testing
- Arrange for follow-up testing for patients and their partners
- Arrange for treatment in a public health clinic (depending on resources)
- Get records from other jurisdictions
- Provide Bicillin to clinics that do not stock it so that patients can be treated with their clinician
- Provide incentives for follow-up visits, testing, and treatment
- Address special needs, like housing, during treatment (especially for late/unknown duration syphilis)

Case 2 continued.

- Neuro/ocular/otic ROS is re-assuring
- Fetal ultrasound is re-assuring
- Partner was treated and they have not had sex since prior to the syphilis diagnosis
- Repeat RPR 2 months (34 weeks EGA) after treatment is 1:32

- What is your next step?
  - Re-treat with Bicillin LA 2.4 million units weekly for three weeks
  - Re-treat with Bicillin LA 2.4 million units once
  - Repeat RPR at delivery
  - No further testing is needed at this time

When should I expect a 4-fold decrease in RPR? Romanowski et al. Ann Int Med, 1991.



Only 38% of pregnant people with syphilis experienced a 4-fold decline in RPR titer by delivery

Rac et al, CID, 2015

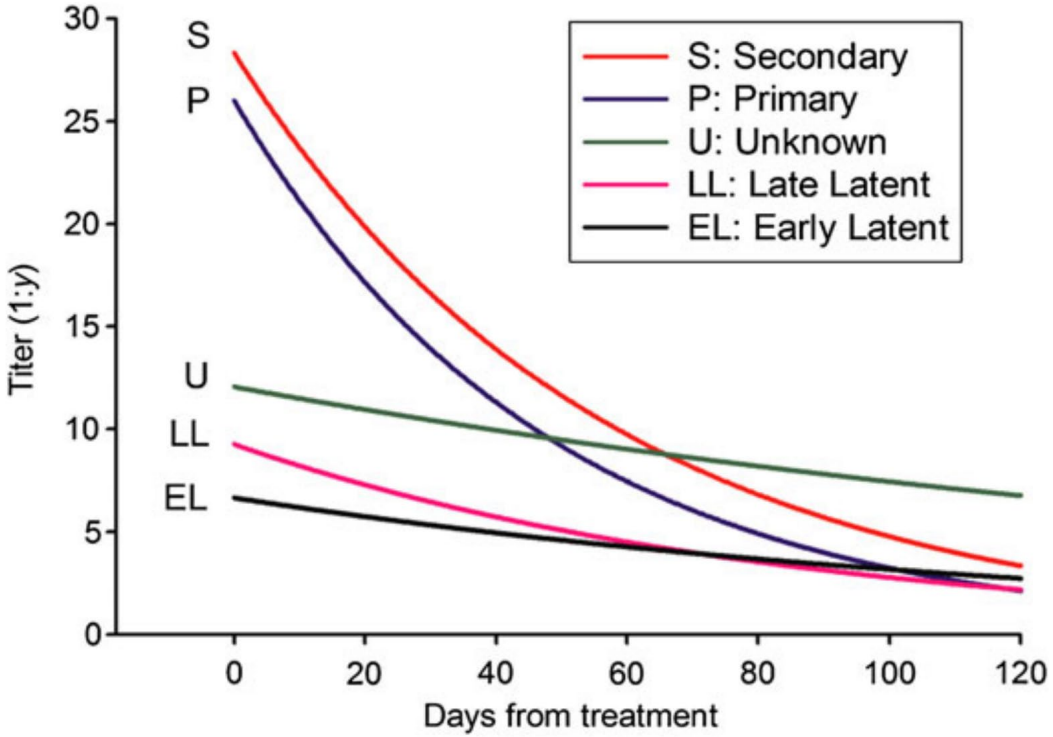


Table 2. Characteristics of Patients With and Those Without a 4-Fold Decline in Nontreponemal Titers by Delivery

Characteristic	No 4-Fold Decline (n = 103)	4-Fold Decline (n = 63)	*P* Value
Age, y	24.6 ± 5.8	21.5 ± 4.4	<.001
Race			.09
Black	54 (52)	41 (65)	
White	2 (2)	4 (6)	
Hispanic	46 (45)	18 (29)	
Other	1 (1)	0 (0)	
Nulliparity	29 (28)	25 (40)	.12
Stage of syphilis			<.001
Primary	2 (2)	4 (8)	.003[a]
Secondary	14 (14)	24 (38)	
Early latent	37 (36)	12 (19)	
Late latent	36 (35)	21 (33)	
Unknown duration	14 (14)	2 (3)	
Gestational age at treatment, wk	30.3 ± 4.6	27.3 ± 4.2	<.001
Gestational age at delivery, wk	38.1 ± 2.6	38.4 ± 2.9	.49
Congenital syphilis[b]	18 (20)	9 (16)	.63

Inadequate Treatment Response

Seña et al. BMC ID, 2015

- **Serologic nonresponse: less than 4-fold decline in non-treponemal titer at 6 or more months for early syphilis and at 12 or more months for late/unknown duration syphilis**
  - Overall, ~12% did not achieve a 4-fold decline after treatment for syphilis
    - 20% at six months after treatment (early syphilis only)
    - 11% at 12 months (or greater) after treatment (all stages)
- **Sero-fast: persistently low positive non-treponemal titer without sero-reversion after a 4-fold decline in titer**
  - 35% in late/unknown duration
  - 44% in PLWH with early and late syphilis
- **Treatment failure (hard to exclude re-infection): a greater than 4-fold increase in non-treponemal titer after treatment (0-24%)**
  - Reinfections ranged from 0.2-10% where there was evidence of a known exposure prior to the 4-fold increase in titer

Test for HIV

Test CSF for neurosyphilis

Continue to monitor titers

Retreat if unable to return

Follow-Up (for nonpregnant people): Treatment Response

Primary and Secondary	▪ Titers at [3], 6, and 12 months ▪ Expect 4-fold drop in titers at 6-12 months
Early non-primary non-secondary and unknown or late duration	▪ Titers at [3], 6, 12, and 24 months ▪ Expect a 4-fold drop in titers by 12-24 months

Follow-Up: Treatment Response in Pregnancy

- We may not observe a 4-fold decline or sero-reversion during pregnancy (there's just not enough time)

- A lack of a 4-fold decrease does not mean treatment failure or that an infant will have CS

- Post-treatment RPRs in pregnancy are most helpful for detecting possible re-infection (a sustained 4-fold increase in RPR titer)

When to re-screen after treatment?

- Re-screen no sooner than 8 weeks after treatment
  - RPRs may go up right after treatment
- For someone diagnosed at or before 24 weeks EGA
  - Test again in the third trimester
  - Test again at delivery
- For someone diagnosed after 24 weeks EGA
  - Test again at delivery
- Anytime there is concern for exposure, re-infection, symptoms related to syphilis

When to re-treat?

- A 4-fold increase in RPR titer which most likely indicates re-infection
  - Technically, a sustained response over 2 weeks
  - If you are worried about follow-up for testing again in 2 weeks, okay to just treat
- A new exposure (regardless of RPR titer) to a sexual partner with syphilis
- Evidence of prior syphilis with inadequate prior therapy

Case 2 conclusion.

- Your patient delivered a healthy baby without any signs or symptoms of CS
- RPR at delivery was 1:8 (an 8-fold decrease in titer from treatment)
  - Infant's RPR was non-reactive at delivery
- You successfully averted a case of CS!

CONGENITAL SYPHILIS (CS)

Evaluation and treatment of infants (<30 days old) exposed to syphilis in utero*

Start

INFANTS AND BIRTHING PARENT (e.g., mother) SHOULD HAVE SERUM RPR TITER DRAWN AT DELIVERY

Infant and Maternal Criteria

Infant Criteria:
- CS findings on physical exam
- Infant titer ≥fourfold higher than mother's titer
- + darkfield or PCR of placenta, cord, lesions, or body fluid
- + silver stain of placenta or cord

No to all

Maternal Criteria:
- Not treated
- Inadequately treated§
- Treatment undocumented
- Treated with a non-penicillin G regimen
- Initiated treatment <30 days before delivery

No to all

Additional Maternal Criteria:
- Adequately treated with penicillin G regimen appropriate for stage, initiated ≥30 days before delivery

AND

- No concern for reinfection or treatment failure

Yes to any

Scenario 1: Proven or Highly Probable CS

Yes to any

Scenario 2: Possible CS‖

Yes to both

Scenario 3: Less Likely CS

Infant Evaluation

- **CSF analysis†** VDRL, cell count, and protein
- **Complete blood count (CBC),** differential, and platelet count
- **Long-bone radiographs**
- **Tests as clinically indicated by signs on physical exam**

- **CSF analysis†** VDRL, cell count, and protein
- **CBC,** differential, and platelet count
- **Long-bone radiographs**

No additional infant evaluation

Review Maternal Titers & Stage:
- ≥4 fold decrease in titer after treatment for early syphilis

OR

- Stable titer for low-titer, latent syphilis (RPR < 1:4)

Any abnormalities, results not available, *OR* follow-up¶ uncertain

No abnormalities *AND* follow-up¶ certain

No to both *OR* follow-up¶ uncertain

Yes to either *AND* follow-up¶ certain

Infant Treatment

Aqueous crystalline penicillin G‡
100,000–150,000 units/kg/day, administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days

Benzathine penicillin G
50,000 units/kg/dose IM in a single dose

No treatment indicated
with close serologic follow-up of infant every 2-3 months for 6 months

Syphilis is complicated…and preventable

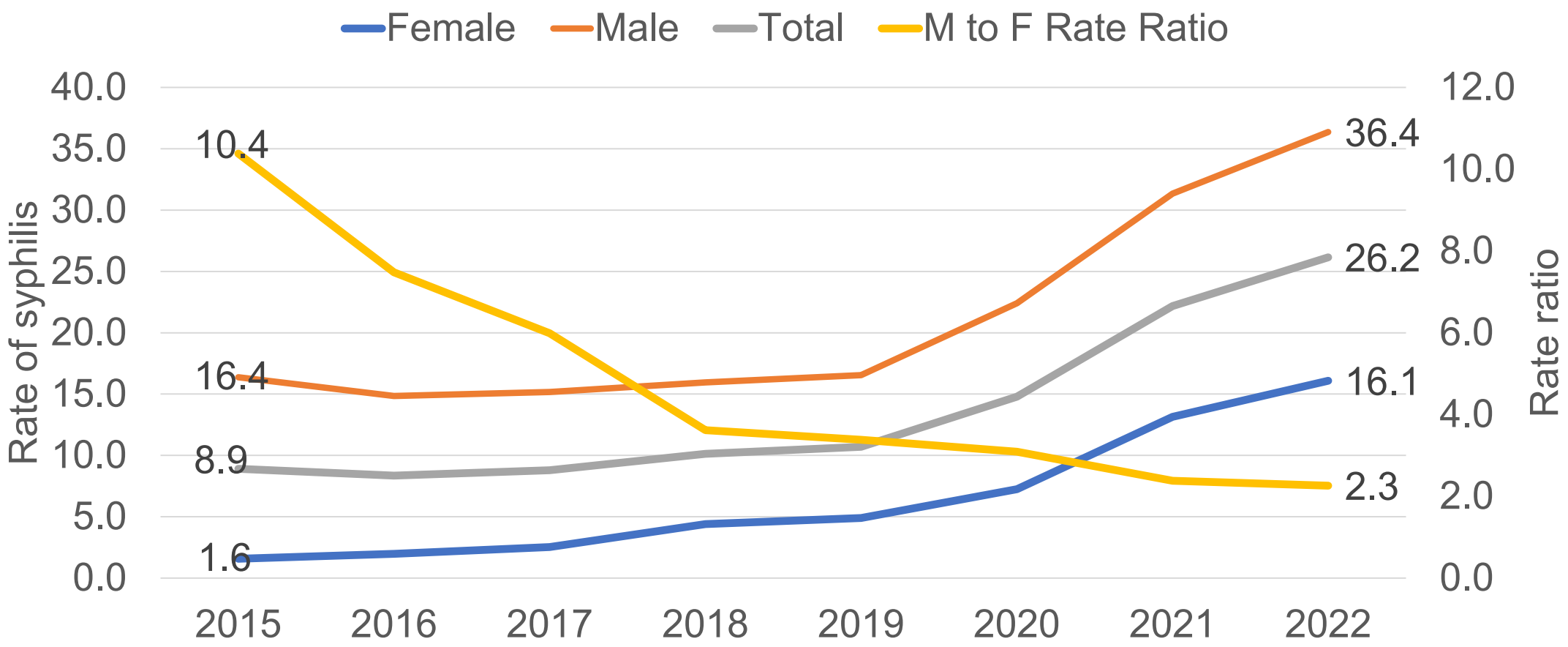
- Universal screening for syphilis
- Screen three times during pregnancy
- Clinically stage all syphilis cases with a good skin and mucosal exam
  - Neuro/ocular/otic ROS to “screen” for complicated syphilis
- Benzathine penicillin G is effective in preventing CS
- But, we don’t often observe serologic response during pregnancy
  - Re-screen according to timing of diagnosis/treatment
  - Re-treat for 4-fold increases in RPR or exposures to sexual partners with syphilis
- Partner treatment is critical, your LPHA can help

Thank you!

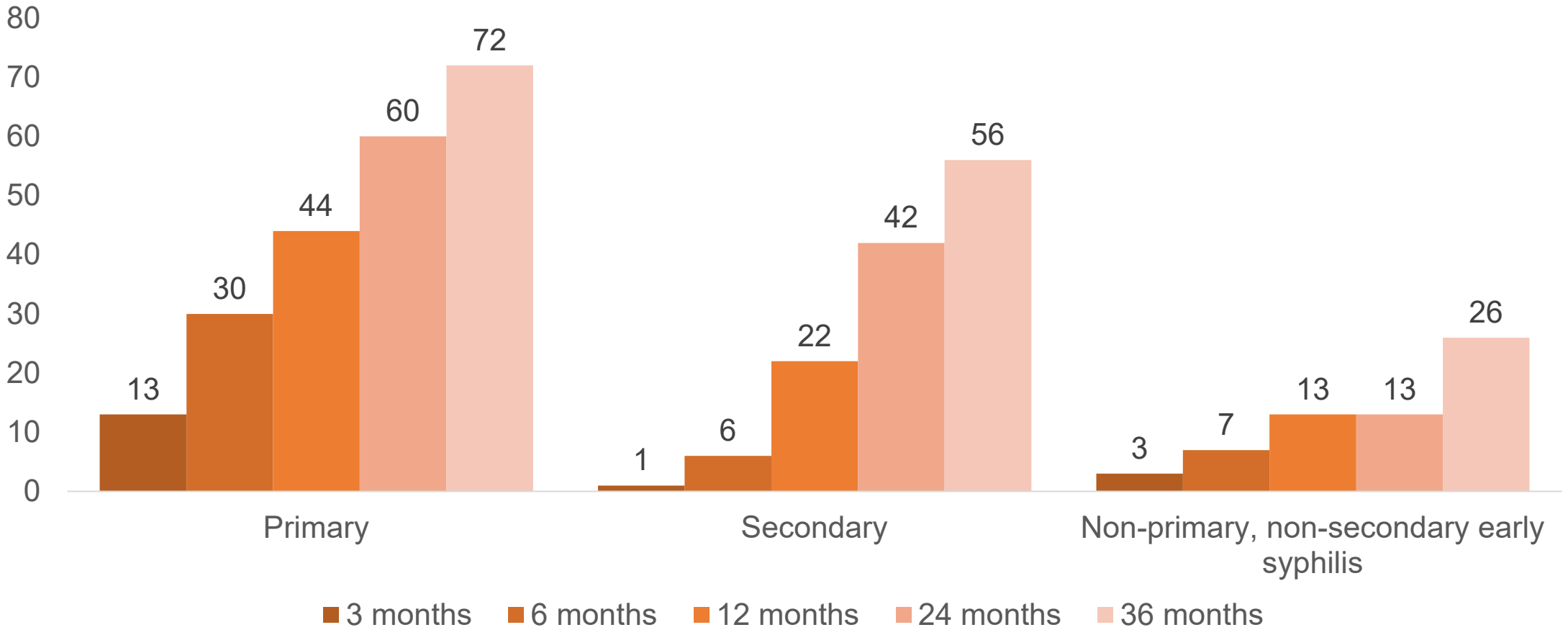
Tim W Menza, MD, PhD
timothy.w.menza@oha.oregon.gov

Resources:
OHA CS Page
OR AETC
CDC STI Treatment Guidelines
National STD Curriculum
STD Clinical Consultation Network

The M:F rate ratio of early syphilis cases has decreased from 10 to 2 from 2015 to 2022



When does the RPR revert back to non-reactive? Romanowski et al. Ann Int Med, 1991.



Factors associated with treatment response

Seña et al. BMC ID, 2015

- Age
  - Younger patients achieve serologic cure more often than older patients
- Higher baseline titers
  - Titers ≥1:32 were associated with serologic cure or decreased time to serologic response
- Stage
  - P/S > early non-P non-S syphilis > late syphilis
- HIV status
  - PLWH have an increased rate of serologic failure
    - Lower CD4 counts and patients not on ART experience greater rates of treatment failure
- Neurosyphilis
  - In one study, 6 patients with serologic non-response had an LP and CSF analysis; none had neurosyphilis (even one with an RPR of 1:32 for 4 years)

Bonus case if time

Case 3.

- 24-year-old cisgender woman G2P1 seen for initial prenatal care with a positive treponemal test and RPR of 1:1
  - No prior testing or known history of syphilis
  - HIV nonreactive, GC/CT negative
  - Unhoused, uses methamphetamine by smoking
  - FOB recently died from an overdose
- Stage?
- What is the appropriate treatment?

Case 3 continued.

- She received long-acting benzathine penicillin G 2.4 million units x 1

- She delivered 3 months later in another state, infant with a weekly positive serum VDLR, diagnosed with CS (by maternal and infant criteria)

CONGENITAL SYPHILIS (CS)

Evaluation and treatment of infants (<30 days old) exposed to syphilis in utero*

Start

INFANTS AND BIRTHING PARENT (e.g., mother) SHOULD HAVE SERUM RPR TITER DRAWN AT DELIVERY

Infant and Maternal Criteria

Infant Criteria:
- CS findings on physical exam
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- + darkfield or PCR of placenta, cord, lesions, or body fluid
- + silver stain of placenta or cord

No to all

Maternal Criteria:
- Not treated
- Inadequately treated§
- Treatment undocumented
- Treated with a non-penicillin G regimen
- Initiated treatment <30 days before delivery

No to all

Additional Maternal Criteria:
- Adequately treated with penicillin G regimen appropriate for stage, initiated ≥30 days before delivery

AND

- No concern for reinfection or treatment failure

Yes to any

Scenario 1: Proven or Highly Probable CS

Yes to any

Scenario 2: Possible CS‖

Yes to both

Scenario 3: Less Likely CS

Infant Evaluation

- **CSF analysis†** VDRL, cell count, and protein
- **Complete blood count (CBC),** differential, and platelet count
- **Long-bone radiographs**
- **Tests as clinically indicated by signs on physical exam**

- **CSF analysis†** VDRL, cell count, and protein
- **CBC,** differential, and platelet count
- **Long-bone radiographs**

No additional infant evaluation

Review Maternal Titers & Stage:
- ≥4 fold decrease in titer after treatment for early syphilis

OR

- Stable titer for low-titer, latent syphilis (RPR < 1:4)

Any abnormalities, results not available, *OR* follow-up¶ uncertain

No abnormalities *AND* follow-up¶ certain

No to both *OR* follow-up¶ uncertain

Yes to either *AND* follow-up¶ certain

Infant Treatment

Aqueous crystalline penicillin G‡
100,000–150,000 units/kg/day, administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days

Benzathine penicillin G
50,000 units/kg/dose IM in a single dose

No treatment indicated
with close serologic follow-up of infant every 2-3 months for 6 months

Case 3 continued.

- Second pregnancy in 2022
- Initial RPR was non-reactive at first presentation to prenatal care
- Repeat RPR at delivery was 1:1
- Infant had a non-reactive RPR, no exam findings concerning for CS

- Would the infant meet maternal criteria for CS?

CONGENITAL SYPHILIS (CS)

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AND

- No concern for reinfection or treatment failure

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Scenario 1: Proven or Highly Probable CS

Yes to any

Scenario 2: Possible CS‖

Yes to both

Scenario 3: Less Likely CS

Infant Evaluation

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No treatment indicated
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Exception to untreated