

Syphilis: The Great Masquerader



Andréa Sciberras, DO, AAHIVS, FACOI, FACP

Medical Director

Division of Disease Control and Health Protection

Florida Department of Health



**Florida
HEALTH**

October 2023

Disclosure

Disclosure: There are no conflicts of interest or financial incentives



Objectives



- **Background**
- **Signs, Symptoms, Stages of Syphilis**
- **Interpreting Laboratory Diagnostics**
- **Current Treatment Guidance**
- **Special Concerns in Pregnancy and Congenital Syphilis (CS)**
- **Summary (Key Points)**

Clinical Manifestations

“He who knows syphilis, knows medicine”

bjcardio.co.uk/2011/04/he-who-knows-syphilis-knows-medicine-the-return-of-an-old-friend/

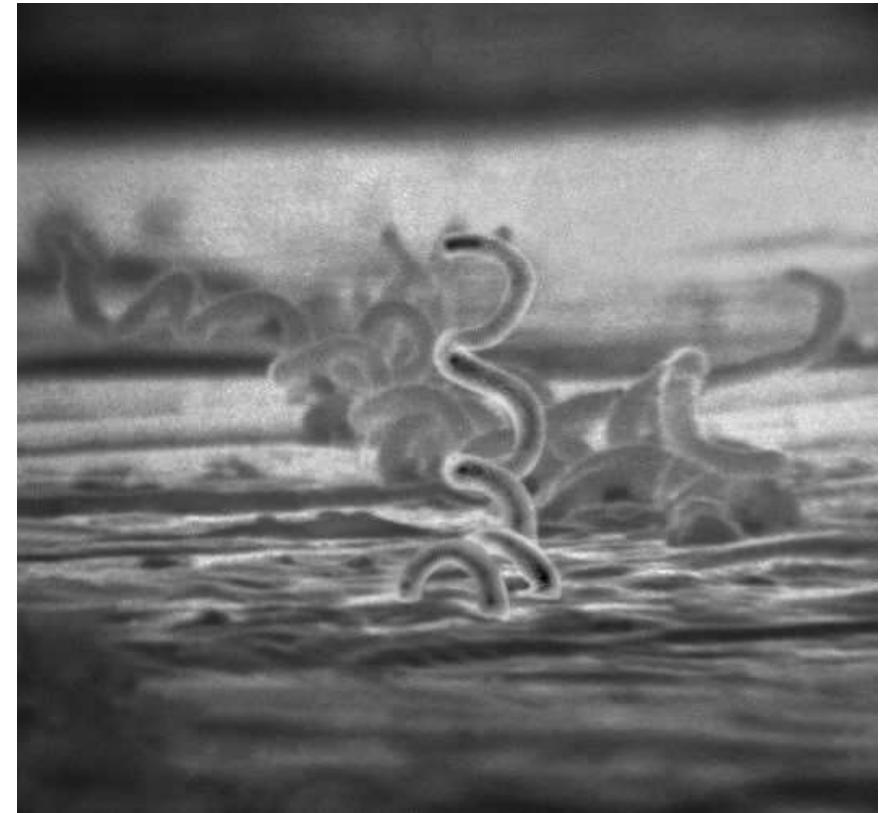


commons.wikimedia.org/wiki/File:William_Osler_1880.jpg

What is Syphilis?

A bacterial infection caused by the spirochete *Treponema pallidum*.

Transmitted primarily through sexual activity, transplacental or vertical transmission from mother-to-child during pregnancy.

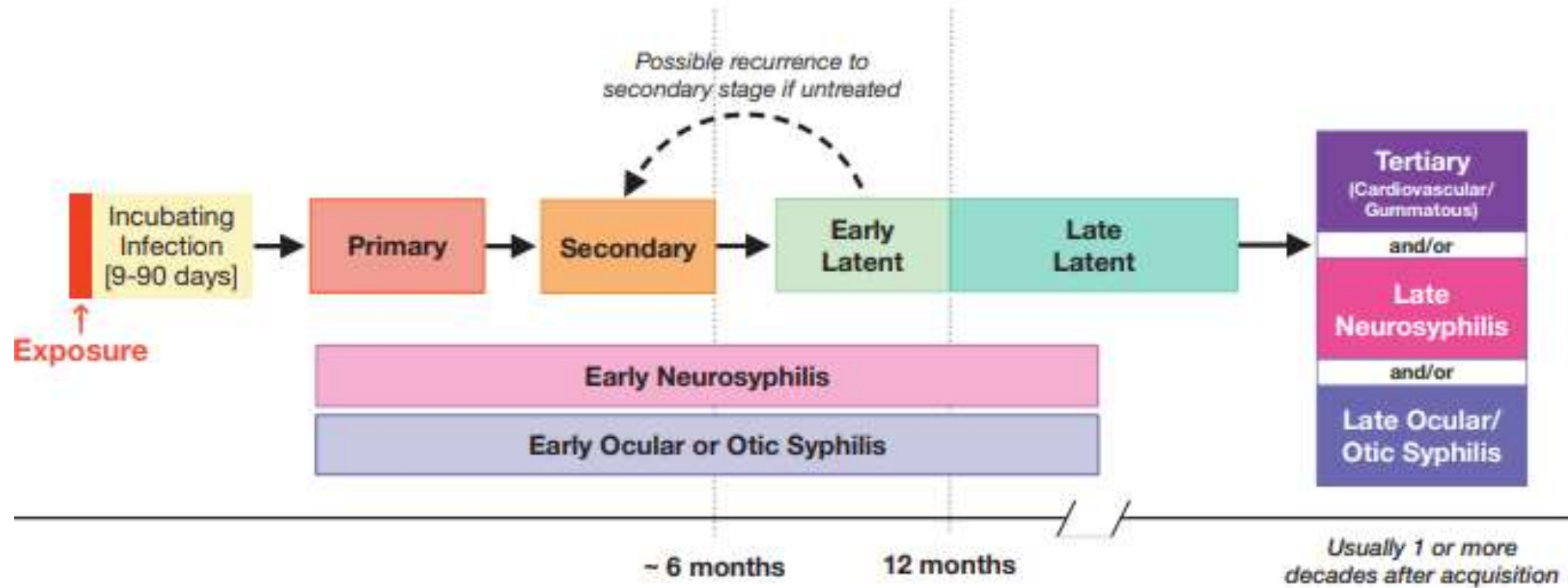


Source: https://en.wikipedia.org/wiki/Treponema_pallidum#/media/File:Treponema_pallidum.jpg

Staging: Syphilis

- Primary Syphilis
- Secondary Syphilis
- Latent
 - Early latent (1 year or less)
 - Late Latent (>1 year or unknown)
- Tertiary Syphilis
- Neurosyphilis, Ootosyphilis, Ocular syphilis (can occur at any stage)

Disease Progression



https://www.nycptc.org/x/Syphilis_Monograph_2019_NYC_PTC_NYC_DOHMH.pdf

Primary Syphilis

- Incubation: 10–90 days; average 3 weeks
- Lesion/Chancre usually occur 2–3 weeks after infection
- Typically, painless indurated ulcer with smooth firm borders

Highly infectious

Primary Syphilis, continued

- Penis, vulva, cervix, anus, mouth, nipples, fingers or other sites—may be hidden
- Regional non-tender lymphadenopathy



Source: Public Health Agency of Canada



Source: Negusse Ocbamichael, Seattle STD/HIV Prevention Training Center



Source: Dr. John Toney, Southeast STD/HIV Prevention Training Center

Primary Syphilis, continued

- Heals spontaneously within 1 to 8 weeks
- Multiple chancres in 25% of cases—
unnoticed in 15–30%



cdc.gov/std/syphilis/images/chancre-oral.htm



cdc.gov/std/syphilis/images



cdc.gov/std/syphilis/images

Secondary Syphilis

- Represents hematogenous dissemination of spirochetes
- Rash occurs in 75–100% of secondary cases
- Usually 6–8 weeks after chancre appears (may overlap)
- Signs and symptoms (S&S) usually resolve 2–10 weeks

Secondary Syphilis, continued

May involve the palms and soles



Source: Dr. John Toney, Southeast STD/HIV Prevention Training Center



Source: Dr. John Toney, Southeast STD/HIV Prevention Training Center

Secondary Syphilis, continued

- Macular, papular, squamous, pustular (rarely) or a combination
- Non-pruritic
- Generalized or localized
- May cover entire body



Source: Cincinnati STD/HIV Prevention Training Center



Source:
CDC/NCHSTP/Division of
STD Prevention, STD
Clinical Slides

Secondary Syphilis, continued

Mucous patches
(6–30%) oral/genital



Source: Seattle STD/HIV Prevention Training Center

Nickel/Dime
Lesions



Source: CDC/NCHSTP/Division of STD Prevention, STD Clinical Slides

Secondary Syphilis, continued

Condylomata lata (10%–20%) moist, wart-like, and intertriginous

HIGHLY INFECTIOUS



Source: Connie Celum, Walter Stamm, Seattle STD/HIV Prevention Training Center



Source: Dr. John Toney, Southeast STD/HIV Prevention Training Center

Secondary syphilis: other symptoms

- Lymphadenopathy – generalized, non-tender 50-86%
- Fever, malaise and myalgias
- Patchy rapid onset alopecia (including eyebrows)
- Liver and kidney involvement can occur
- Splenomegaly is occasionally present
- Less common: periostitis, arthralgias, meningitis, nephritis, hepatitis, proctitis, ulcerative colitis

Latent Syphilis

No signs or symptoms; Positive serology

- **Early** Latent (non-primary, non-secondary) = **<1 year**
- **Late** Latent (unknown duration or late) = **>1 year**
(not likely infectious)

Treatment is different for early vs. late

If unsure, treat for late latent

Early Latent

- Documented seroconversion or (in those previously treated) a sustained (>2 week) fourfold increase in non-treponemal test titers (NTTs)
- Unequivocal symptoms of primary or secondary syphilis
- Sex partner documented to have primary, secondary or early latent syphilis
- Only possible exposure occurred in the last 12 months

Late Latent

Unknown Duration or Late

- The absence of conditions associated with the early latent stage
- Because treatment is different for early verses late **if unsure**, treat unknown duration syphilis as if it were late infection with three doses of benzathine penicillin

Tertiary Syphilis

10–30 years after initial infection

Occurs in one third of untreated latent cases

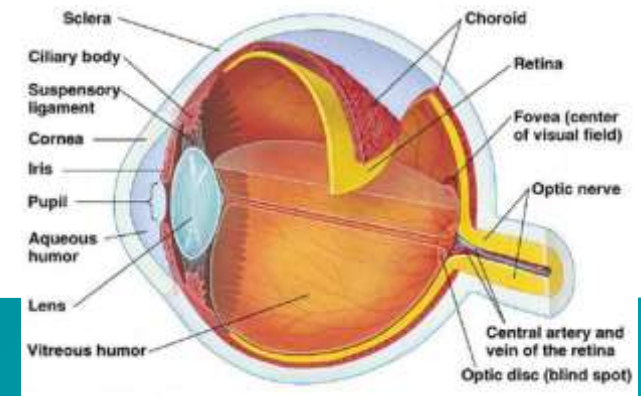
Manifestations

- Cardiovascular system (e.g., aortitis, coronary vessel disease) 20–30 years
- Skin (e.g., gummatous lesions may affect any organ system (lung, stomach, liver, spleen, genitals, breast, brain and heart) 10–15 years
- Bone (e.g., osteitis) and other tissues



Ocular syphilis

- The Centers for Disease Control and Prevention (CDC) defines ocular syphilis as “**clinical symptoms or signs consistent with ocular disease (i.e. uveitis, panuveitis, diminished visual acuity, blindness, optic neuropathy, interstitial keratitis, anterior uveitis, and retinal vasculitis) with syphilis of any stage**”
- There has been a **78% increase** (over 200 cases) of optic syphilis in the last two years



Ocular syphilis

- Variable clinical presentation
- Posterior uveitis and panuveitis are most common, but any eye structure can be affected
- Anterior uveitis, optic neuropathy, retinal vasculitis, interstitial keratitis
- Can lead to decreased visual acuity (rapid) with subsequent permanent blindness

Otic syphilis

- Sensorineural hearing loss, tinnitus, vertigo
- Hearing loss can be unilateral or bilateral
- Sudden onset, progresses rapidly
- Can lead to permanent hearing loss



Neurosypphilis

- A full neurologic exam especially including cranial nerves including II (optic), III (oculomotor), VI (abducens), VII (facial) and VIII (auditory) must be done when a patient is diagnosed with syphilis (any stage)
- Early signs (first few months to years)
 - Cranial nerve dysfunction, meningitis, altered mental status, stroke, meningovascular syphilis
- Late signs (10-30 years post infection)
 - Tabes dorsalis
 - General paresis



Interpreting Laboratory Diagnostics



news-medical.net/life-sciences/Microsphere-Assisted-Microscopy-Advantages-and-Limitations.aspx

Laboratory Diagnosis

Two classes of serologic tests:

- Non-treponemal (RPR/VDRL)
- Treponemal (Darkfield, PCR, Fluorescent treponemal antibody absorption [FTA-ABS], Treponema pallidum particle agglutination assay [TP-PA], Enzyme Immunoassays [EIA])

Non-Treponemal Assays

Non-treponemal tests:

- RPR
- VDRL

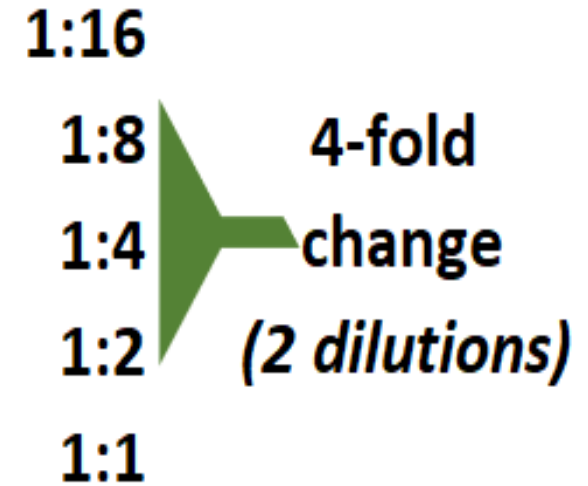
Titers—What do They Mean?

- * Higher numbers correspond to higher level of antibodies in the patient's serum 1:1024
1:512
 - * Number is determined by progressive dilution of serum until it becomes non-reactive 1:256
1:128
 - * Two-fold change 1:64
Generally considered within margin of test error 1:32
- 2-fold change

"2-fold" = "2 times" = "double"

Titers—What do They Mean?

- * Sustained four-fold change
 - Considered to be significant
- * Compare titer using same serologic test
(RPR is often higher than VDRL)



Treponemal Assays

Detected 2–3 weeks before non-treponemal antibodies

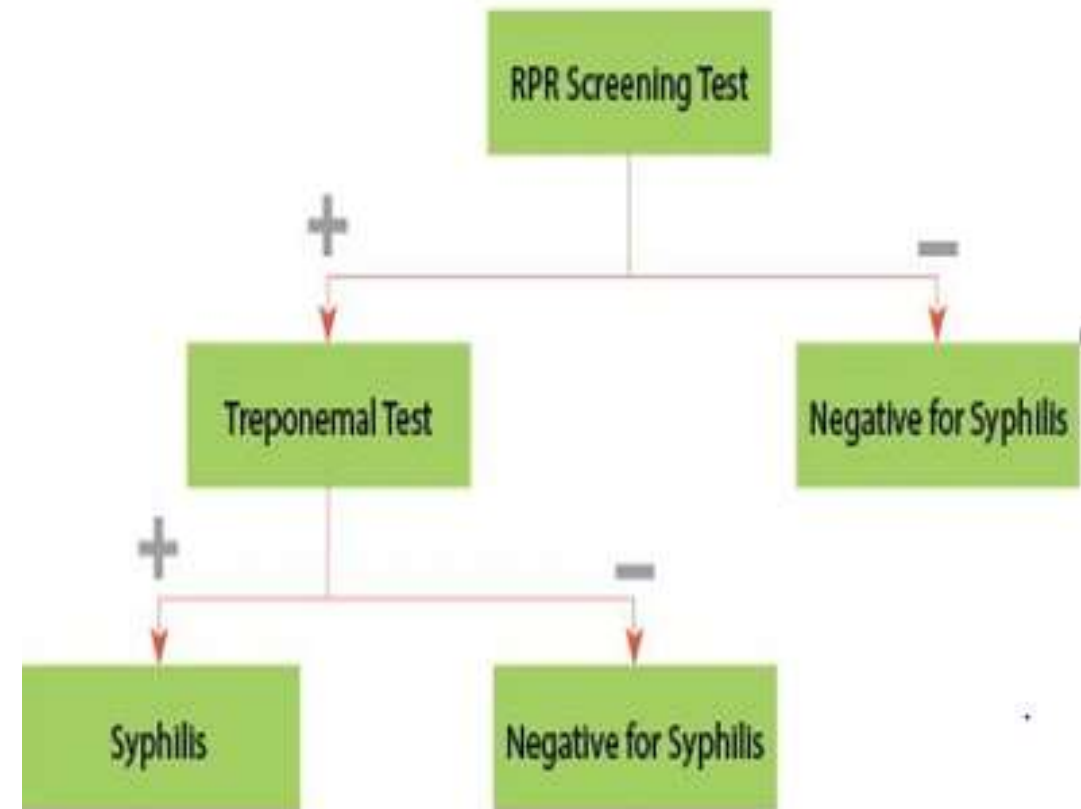
- Fluorescent treponemal antibody absorption (FTA-ABS)
- Treponema pallidum particle agglutination assay (TP-PA)
- Enzyme Immunoassays (EIA)

These all remain positive despite treatment and **cannot** be used to monitor response to therapy

Syphilis Screening Algorithms

Traditional

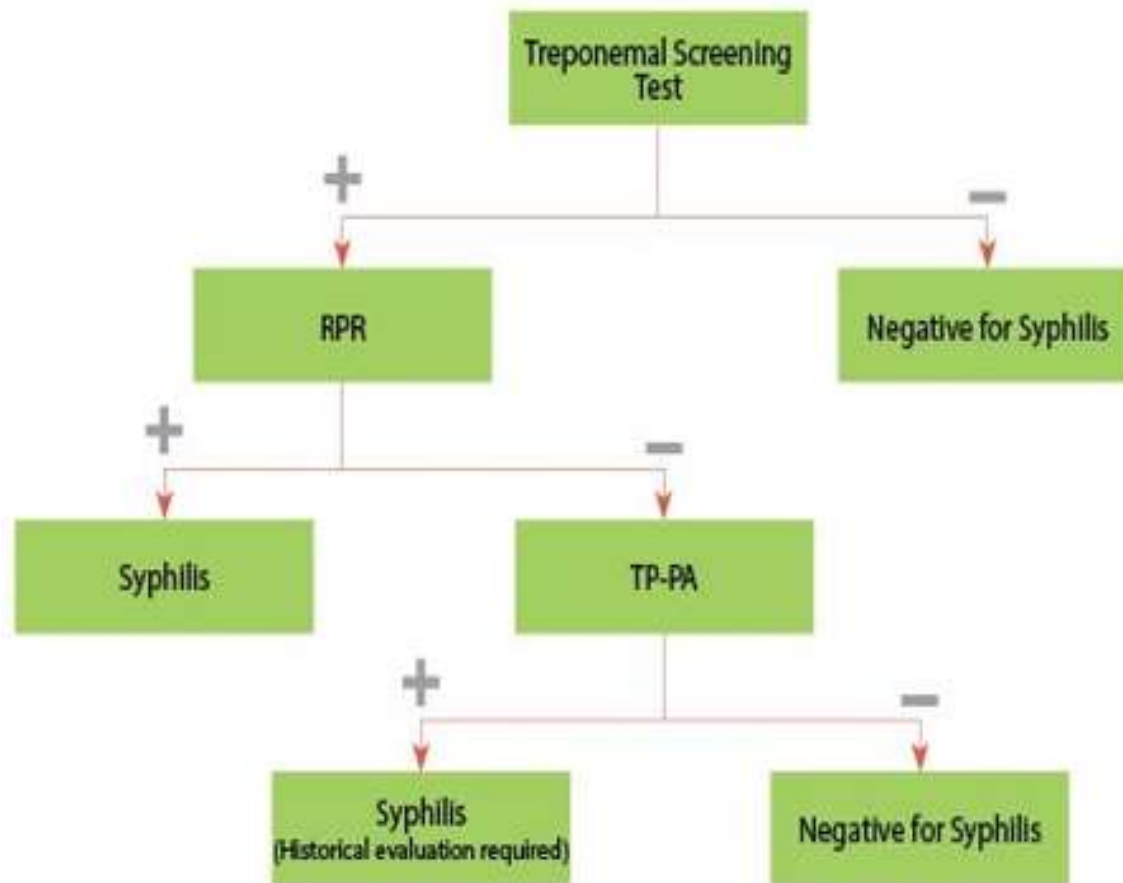
Reference Screening Algorithms



Syphilis Screening Algorithms

Reverse

Reference Screening Algorithms

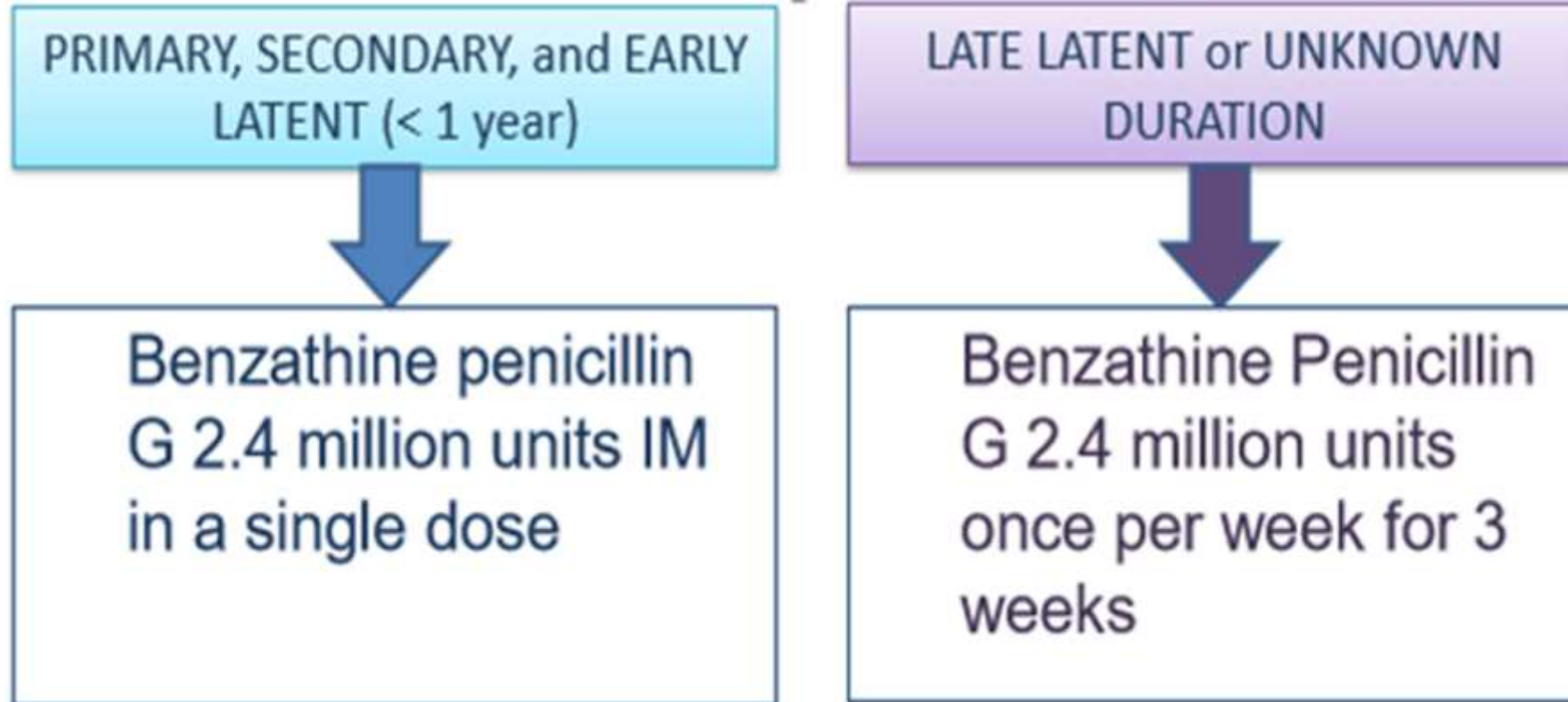


Current Treatment Guidance



**Treatment is
ALWAYS
based on the
stage of syphilis**

Treatment: Stage Based



<https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf>

May 2023: Benzathine penicillin G shortage

- Only **PREGNANT** women should be receiving **penicillin G benzathine** currently – until shortage resolved
- **ALL others:**
 - **Doxycycline** 100mg po q12h x 14d for primary, secondary, or early latent (< 1 year)
 - **Doxycycline** 100mg po q12h x 28 days for late latent (>1 year) or unknown duration
 - Remember to check pregnancy test first on female patients!
- No ifs, ands, or buts about it!



Treatment: Pregnant Patients

- **Primary and Secondary Syphilis**

Penicillin G benzathine 2.4 million units IM in a single dose

- **Early Latent Syphilis (less than one year)**

Penicillin G benzathine 2.4 million units IM in a single dose

- **Late Latent Syphilis or Latent Syphilis of Unknown Duration**

Penicillin G benzathine 7.2 million units total, administered as 3 doses of 2.4 million units IM each at **1-week intervals**

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

Treatment: Pregnant Patients

Missed doses are not acceptable for pregnant women receiving therapy for late latent syphilis

Pregnant women who miss any dose of therapy must repeat the full course of therapy. All women who have syphilis should be offered testing for HIV infection.

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

Treatment: Pregnant Patients

Inadequate maternal treatment is likely if delivery occurs **within 30** days of therapy, clinical signs of infection are present at delivery or the maternal antibody titer at delivery is fourfold higher than the pre-treatment titer

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

Treatment: Pregnant Patients

Treatment can prevent stillbirths and fetal infection if initiated as early as possible during pregnancy and, if **initiated at least 30 days before delivery**, effectively prevents morbidity in live-born infants **but must be:**

- with the long-acting, injectable penicillin (i.e., penicillin G benzathine) regimen
- appropriate for the mother's stage of syphilis

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

Penicillin Allergy

- Prevalence of reported penicillin allergy in the U.S. is about 8–10%
- Anaphylaxis (upper airway obstruction, bronchospasm or hypotension) can be fatal; alternative treatments are available for some
- Because **no proven alternatives are available** for neuro, CS or syphilis in pregnant women, **alternative treatment should NOT be administered to these clients**
- **They should be admitted to the hospital for penicillin desensitization**

Treatment Summary

Treatment

- Syphilis duration less than a year = BIC x 1; alternative is Doxycycline 100mg po BID x 14 days
- Syphilis duration greater than a year, or unknown = BIC x 3; alternative is Doxycycline 100mg po BID x 28 days
- Penicillin G benzathine is the **ONLY** treatment for pregnant women; treatment less than 30 days prior to delivery may be ineffective for the neonate

Special Concerns in Pregnancy and Congenital Syphilis

**Florida
HEALTH**



What is Congenital Syphilis (CS)?

A potentially fatal infection passed from mother-to-child during pregnancy (up to 40% may result in miscarriage, stillbirth, or infant death).

Non-fatal infections can lead to severe sequelae including bone deformation, hepato-splenomegaly, severe anemia, neurological issues including blindness and/or deafness, and more.



CS: Transmission

- Transplacental (as early as 9–10 weeks gestation, but at any stage of pregnancy) or via lesion present at delivery
- Rate dependent on stage in mother
 - Primary or secondary: 60%–100% transmission
 - Late latent syphilis: 13% transmission or less

CS: Effects

- Miscarriage
- Stillbirth
- Death shortly after birth

Up to 40% of babies born to women with untreated syphilis may be stillborn or die from the infection as a newborn.

CS: CDC Recommendations

Specifically, for Screening Syphilis in Pregnant Women:

- All pregnant women at the **first** prenatal visit
- Retest **early** in the third trimester
- At delivery **if high risk**

State Statutory and Regulatory Language Regarding Prenatal Syphilis Screenings in the U.S., 2018

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

Final Summary

The logo for Florida Health is positioned on the left side of the slide. It features a circular graphic with a teal border containing a sunset scene over the ocean. The text "Florida HEALTH" is overlaid on the bottom half of the circle in a white, bold, sans-serif font. "Florida" is in a larger font size than "HEALTH".

Florida
HEALTH

- The great masquerader- complete history AND physicals need to be performed, keep an open mind in regards to diagnosis!
- Treat according to stage
- Pregnant women can ONLY get penicillin G benzathine for treatment
- Congenital syphilis cases are on the rise - use CDC guidelines when testing pregnant women



For our history buffs:

Does anyone know where the term syphilis came from??



Answer:

Name of the disease came from a poem written in 1530 by Fracostoro about an infected shepherd named **Syphilis**



CDC Passport to Partner
Services Key Disease
Concepts Unit 2: Syphilis

Thank you!

**Andréa Sciberras, DO, AAHIVS, FACOI, FACP,
Medical Director,
Division of Disease Control and Health Protection,
Florida Department of Health
(850) 756-2283
Andrea.Sciberras@flhealth.gov**



STD Clinical Resources

- CSTE guidelines
- CS Definitions
- STI Treatment Guidelines, 2021
- Red Book: American Academy of Pediatrics (Syphilis, Algorithm for evaluation and treatment of infants born to mothers with reactive serologic tests for syphilis)



STD References

- Association of Public Health Laboratories (APHL)
 - aphl.org/aphlprograms/infectious/std/Pages/STD-syphilis.aspx

CDC

- cdc.gov/National Coalition of STD Directors (NCSD) Press Release August 28, 2018; “STDs Hit Record Highs, Again, Threatening Millions of American Lives”
- cdc.gov/nchhstp/newsroom/2018/press-release-2018-std-prevention-conference.html
- cdc.gov/nndss/conditions/syphilis/case-definition/2018/
- cdc.gov/std/stats18/310702A_Congential_Syphilis_FS_Final-508.pdf

Florida Department of Health (DOH) and F.S.

- floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/index.html
- leg.state.fl.us/statutes/index.cfm?App_mode=Display_Statute&URL=0300-0399/0384/0384.html

STD References, continued

National Center for Biotechnology Information (NCBI)

- ncbi.nlm.nih.gov/books/NBK540979/
- ncbi.nlm.nih.gov/pmc/articles/PMC1779891/
- ncbi.nlm.nih.gov/pmc/articles/PMC3590030/

Other

- medicalency.com/syphilis-congenital.htm
- Effectiveness of Prenatal Screening and Treatment to Prevent Congenital Syphilis; Louisiana and Florida, 2013–2014 Statistics provided by James Matthias, MPH
- <https://jamanetwork.com/journals/jamadermatology/article-abstract/2673815>
- stdccn.org/default.aspx

References will be made available electronically