Syphilis

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Congenital Syphilis — Reported Cases and Rates of Reported Cases by State, Ranked by Rates, United States, 2021

Rank*	State†	Cases	Rate per 100,000 Live Births
1	Arizona	181	232.3
2	New Mexico	44	205.7
3	Louisiana	110	191.5
4	Mississippi	64	182.0
5	Texas	680	182.0
6	Oklahoma	85	175.6
7	South Dakota	16	140.7
8	Arkansas	50	139.0
9	Nevada	45	133.6
10	Hawaii	20	128.0
11	California	518	123.2
12	Missouri	66	95.0
13	West Virginia	15	87.2
14	Florida	180	83.2
15	Montana	9	80.1
	US TOTAL‡	**2,855**	**77.9**
16	Georgia	93	75.0
17	Oregon	27	66.0
18	Alabama	37	63.7
19	Washington	53	63.2
20	Alaska	5	53.4
21	Kentucky	25	47.9

Congenital Syphilis Transmission

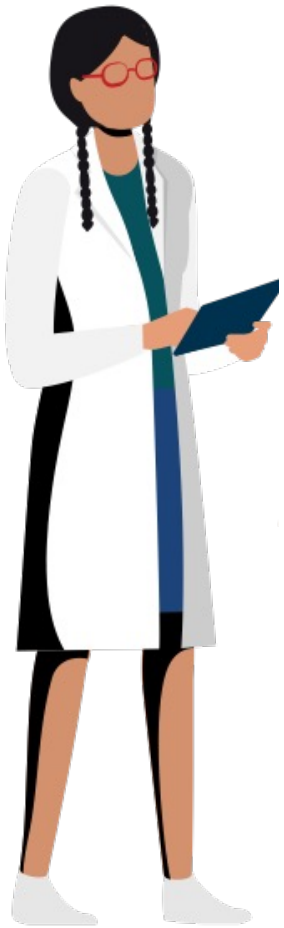
- **How**
  - Transplacental during maternal spirochetemia
  - Direct contact with an infectious lesion during birth
  - Not transferred into breast milk

- **When during gestation?**
  - At any time during gestation with increasing frequency as gestation advances.

- **Transmission according to syphilis stage:**

• Primary or secondary syphilis:	**60% to 90%**
• Early latent:	**40%**
• Late latent syphilis:	**10% (2% after four years)**

Questions that We Need to be Answer to Evaluate A positive RPR in a Newborn



Was the mother properly **diagnosed**, **staged** and **treated** for syphilis during pregnancy?

Was the treatment initiated 30 days before delivery?

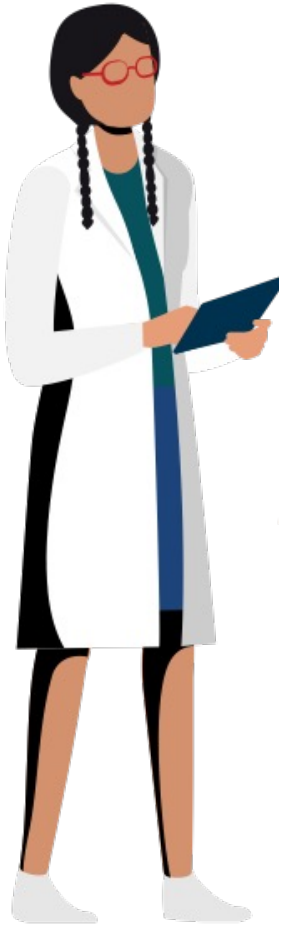
What is the neonates RPR titer?

- Is it ≥ 4-fold compared to the mothers RPR (obtained at delivery)?

Was the neonate's physical exam normal?

Does the neonate need any further workup such as LP, imaging, etc.?

Syphilis

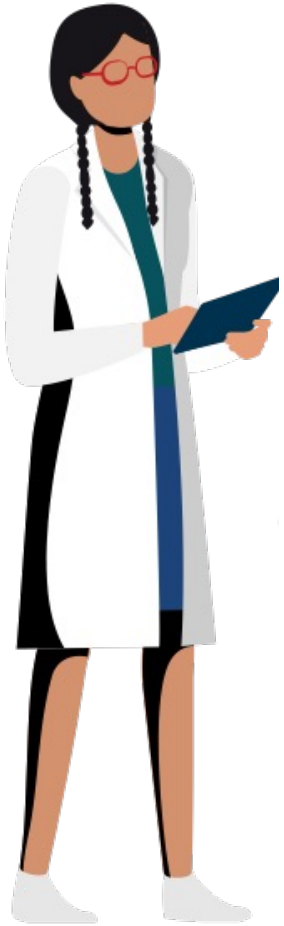


- ***Treponema pallidum***

- Sexual, vertical, and horizontal transmission
- **Curable with penicillin**
- 4 stages

1. Primary
2. Secondary
3. Early (non-primary, non-secondary)
4. Unknown duration or late

Syphilis



1. Stages start with primary, then may not progress linearly.
2. Characterized by episodes of active disease interrupted by periods of latency.
3. Signs/symptoms and transmission risks vary by stage.

Case Definitions: Primary Syphilis

Clinical Description

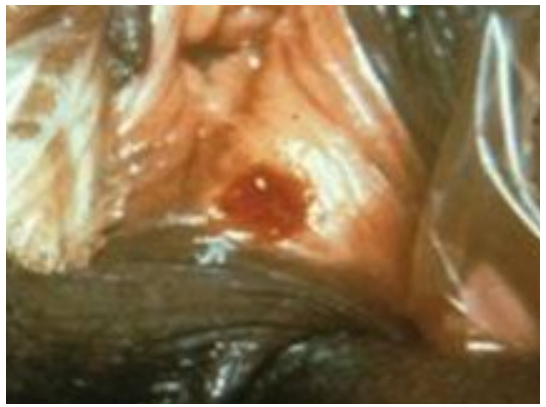
Characterized by one or more ulcerative lesions (e.g. chancre), which might differ in clinical appearance.

Classic Presentation

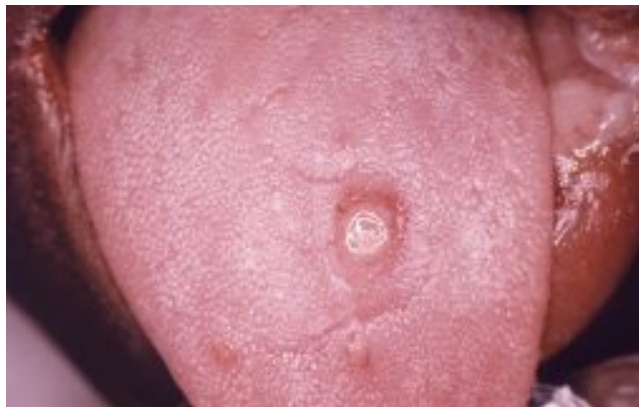
Single painless ulcer or chancre at the site of infection

Atypical Presentation

Multiple, atypical, or painful lesions at the site of infection



Vaginal



Tongue

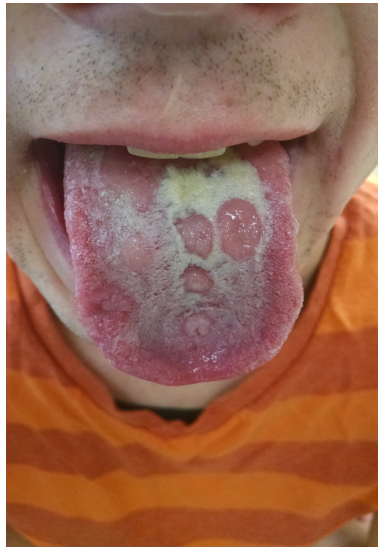
Penile

https://www.cdc.gov/std/syphilis/images.htm and https://www.cdc.gov/std/statistics/2019/case-definitions.htm

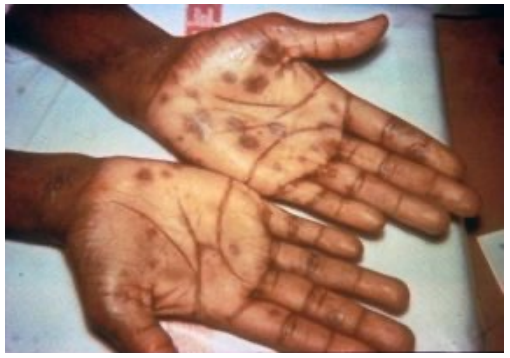
Case Definitions: Secondary Syphilis

Clinical Description

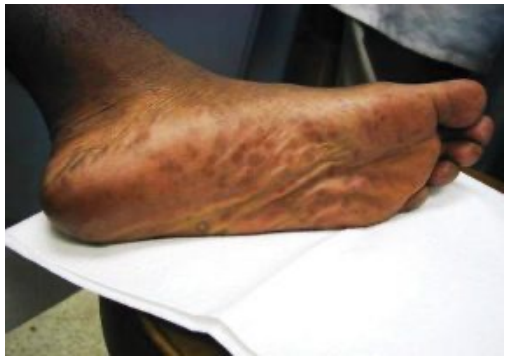
Characterized by localized or diffuse mucocutaneous lesions (e.g., rash – such as non-pruritic macular, maculopapular, papular, or pustular lesions), often with generalized lymphadenopathy. Other signs can include mucous patches, condyloma lata, and alopecia. The primary ulcerative lesion may still be present.

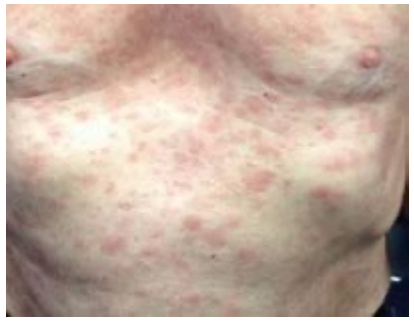


Mucous patches

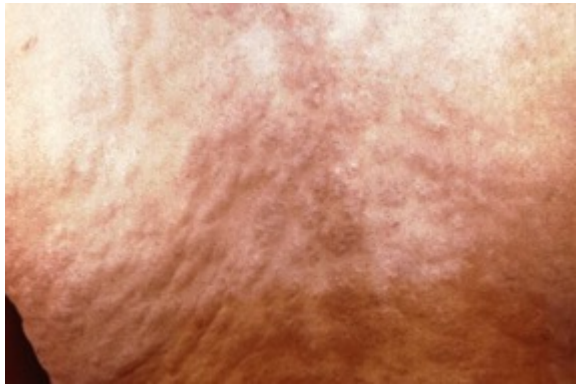


Palmar/plantar rash

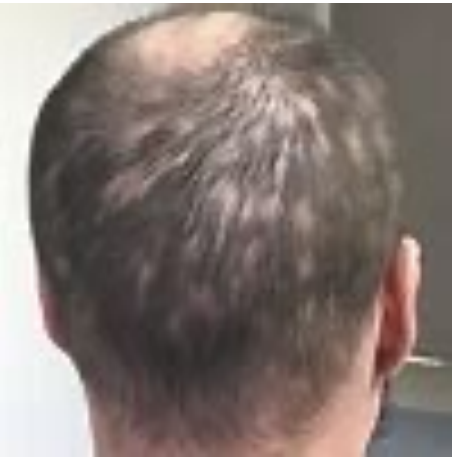




Torso/back rash



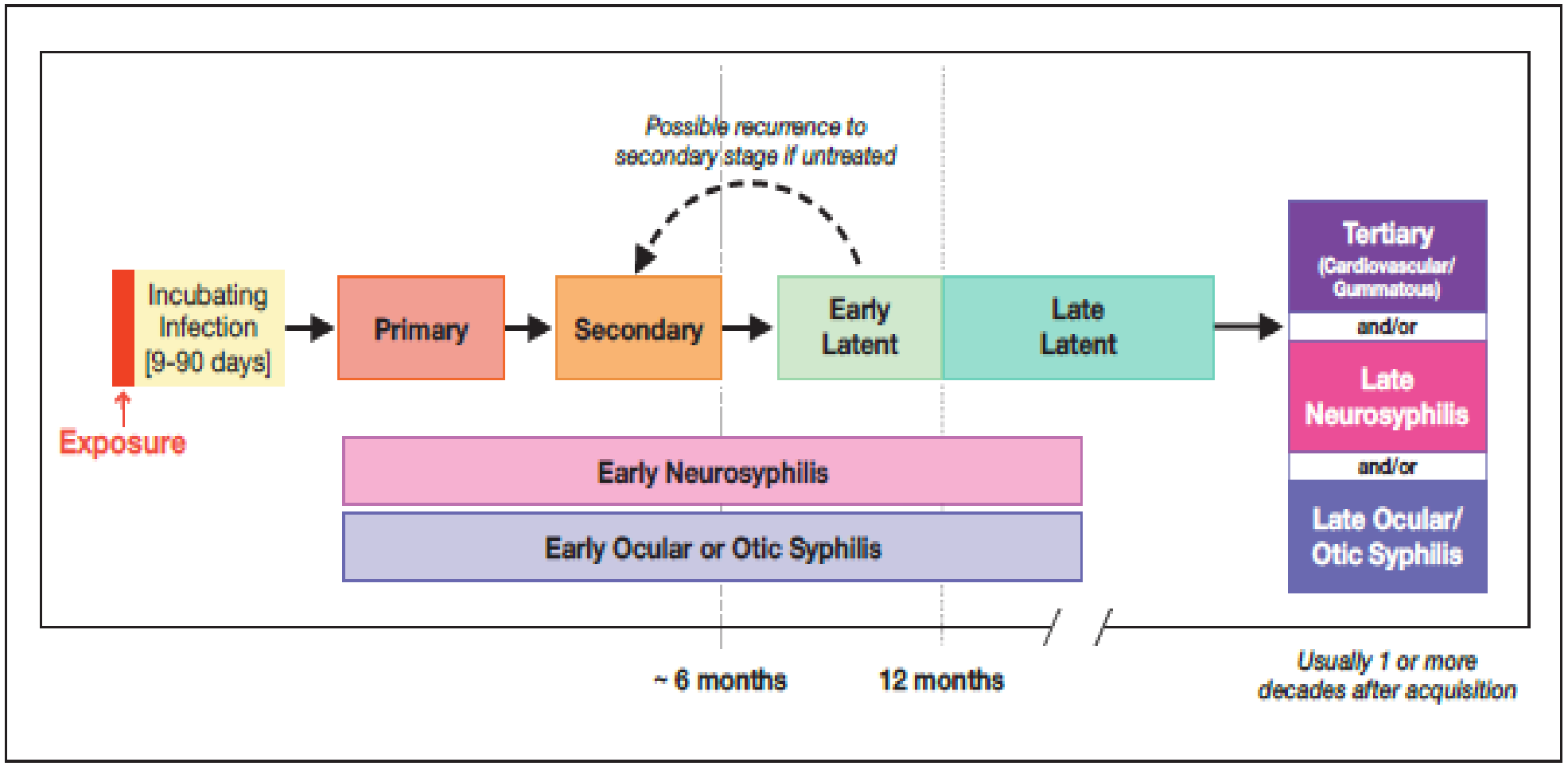
Condyloma lata



Alopecia

1. https://www.cdc.gov/std/syphilis/images.htm
2. https://www.cdc.gov/std/statistics/2019/case-definitions.htm

Natural History of Untreated Syphilis



The Diagnosis, Management and Prevention of Syphilis An Update and Review. New York City Department of Health and Mental Hygiene Bureau of Sexually Transmitted Infections and the New York City STD Prevention Training Center . May 2019. https://www.nycptc.org/x/Syphilis_Monograph_2019_NYC_PTC_NYC_DOHMH.pdf

Case Definitions: Early Latent (non-primary non-secondary)

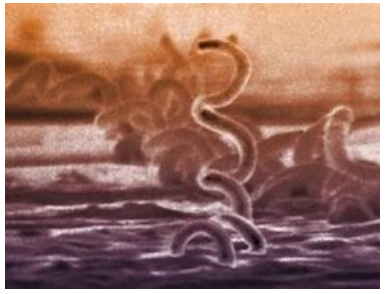
Clinical Description

Stage of infection caused by *T. pallidum* in which initial infection has **occurred within the previous 12 months**, but there are no current signs or symptoms of primary or secondary syphilis.

Less than 12 months duration by

(1) Interval from prior negative syphilis test (or 4-fold titer increase)
OR
(1) Report of symptoms consistent with syphilis within prior 12 months
OR
(1) Sexual contact with a known case (or sexual debut) within prior 12 months

https://www.cdc.gov/std/statistics/2019/case-definitions.htm)



Case Definitions: Late Latent or Unknown

Clinical Description

Stage of infection caused by *T. pallidum* in which initial infection has **occurred >12 months** previously or in which there is insufficient evidence to conclude that infections was acquired during the previous 12 months.

Unknown or greater than 12 months duration by:

(1) Interval from prior negative syphilis test (or 4-fold titer increase)
OR
(2) Report of symptoms consistent with syphilis occurring > 12 months ago
OR
(1) Sexual contact with a known case > 12 months ago
OR
(1) Neurologic, ocular, otic signs without evidence of acquiring infection in prior 12 months.

https://www.cdc.gov/std/statistics/2019/case-definitions.htm)

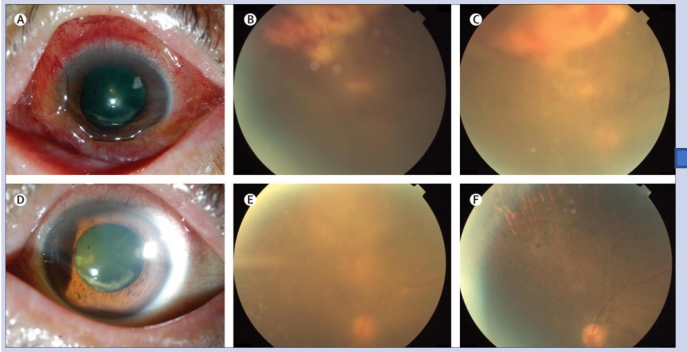
Neurologic Manifestations can occur at any stage

https://www.cdc.gov/std/statistics/2019/case-definitions.htm)

Neurosyphilis

Infection of the central nervous system with *T. pallidum,* as evidenced by manifestations including:

1. Syphilitic meningitis,
2. Meningovascular syphilis,
3. General paresis,
4. Dementia,
5. Tabes dorsalis



https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(13)70198-1/fulltext

Ocular syphilis

Infection of any eye structure with *T. pallidum.*
Manifestations can involve any structure in the anterior and posterior segment of the eye including:

1. Conjunctivitis
2. Anterior uveitis
3. Posterior uveitis
4. Panuveitis
5. Posterior interstitial keratitis
6. Optic neuropathy
7. Retinal vasculitis

Ocular syphilis may lead to decreased visual acuity including permanent blindness.

Otosyphilis

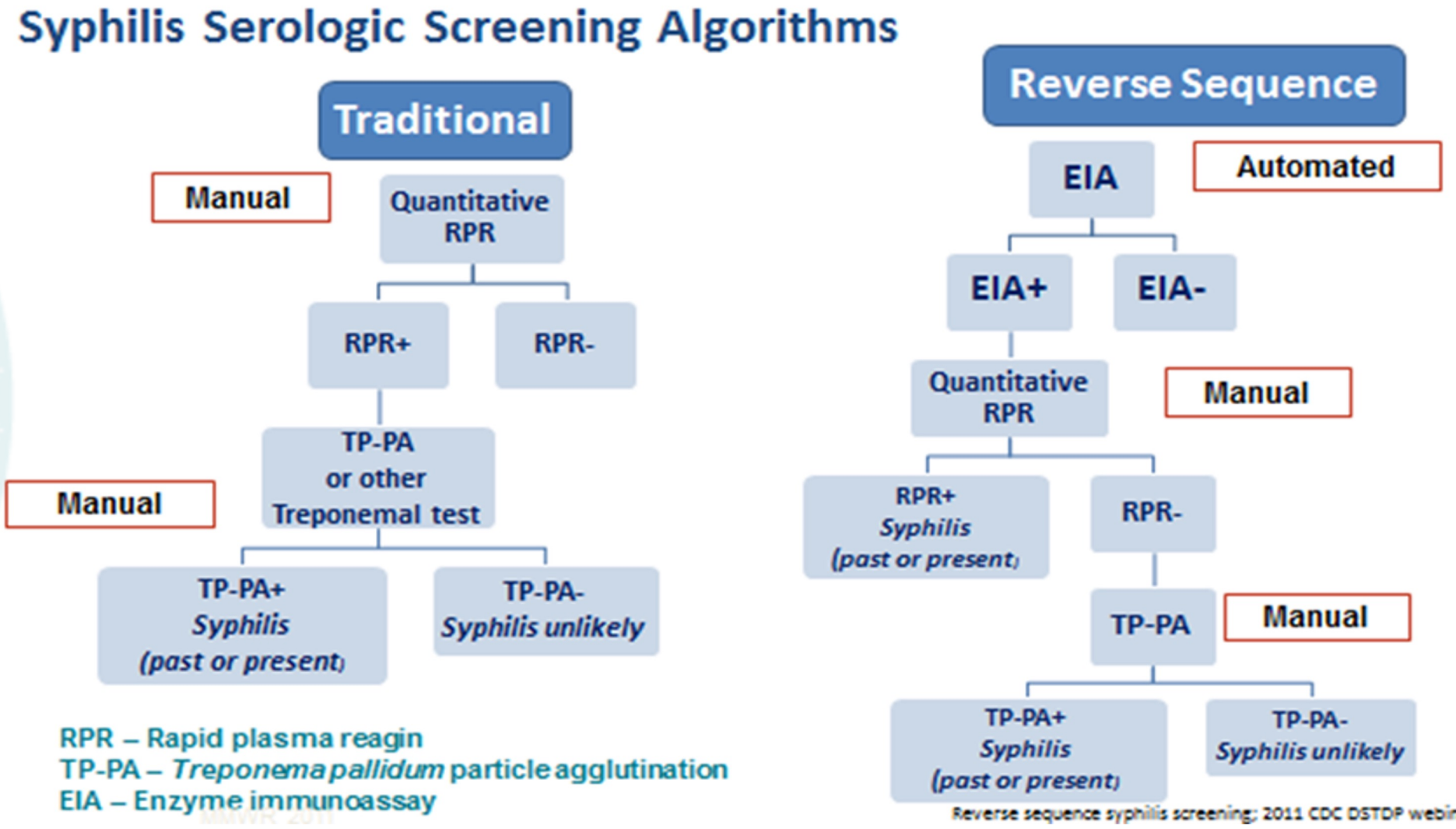
Infection of the cochleovestibular system with *T. pallidum,* as evidenced by manifestations including sensorineural hearing loss, tinnitus, and vertigo.

Typically presents with cochleo-vestibular symptoms including

1. Tinnitus
2. Vertigo
3. Sensorineural hearing loss
4. Unilateral/Bilateral
5. Have a sudden onset
6. Progress Rapidly

Otic syphilis can result in permanent hearing loss

Serologic Diagnosis of Syphilis



Treatment of syphilis with Penicillin

Stage				
Primary	**Secondary**	**Early non-primary, non secondary**	**Late Latent/ or Unknown Duration**	**Neurosyphilis, ocular syphilis and otic syphilis**
Benzathine penicillin 2.4 million units IM in a single dose	Benzathine penicillin 2.4 million units IM in a single dose	Benzathine penicillin 2.4 million units IM in a single dose	Benzathine penicillin 2.4 million units total administered as 3 doses of 2.4 million units IM each at 1-week intervals	Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units by IV every 4 hours or continuous infusion for 10-14 days Alternative: procaine penicillin G 2.4 million units IM 1x/day PLUS probenecid 500 mg orally 4x/day, both for 10-14 days

https://www.cdc.gov/std/treatment-guidelines/default.htm

Penicillin Allergy

- **Patients often are incorrectly labeled** as allergic to penicillin
  - Evaluate what symptoms were experienced by patients with reported penicillin allergy

- **Penicillin allergy causing anaphylaxis is rare**
  - In studies that have incorporated penicillin skin testing and graded oral challenge among persons with reported penicillin allergy, the true rates of allergy are low, ranging from 1.5% to 6.1%.

- **Allergies wane over time:**
  - Approximately 80% of patients with a true IgE-mediated allergic reaction to penicillin have lost the sensitivity after 10 years

- ***Desensitization is recommended for pregnant women diagnosed with syphilis followed by treatment with penicillin.***

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

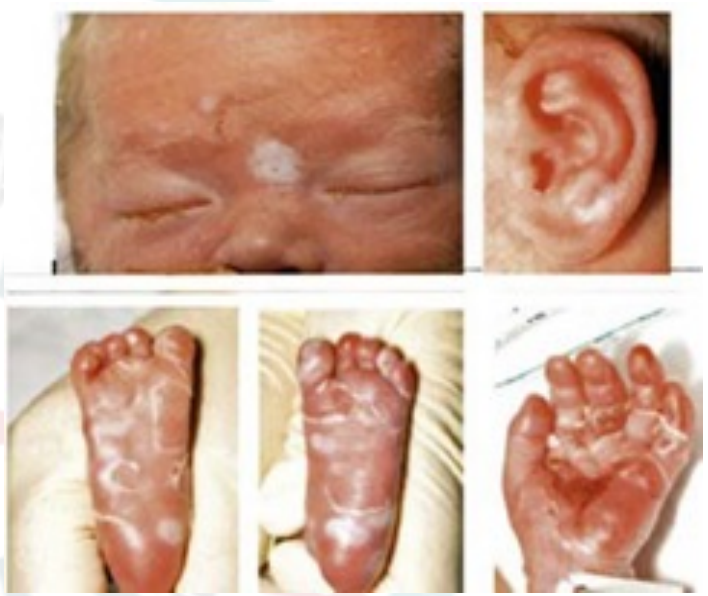
Syphilis Penicillin Shortage:

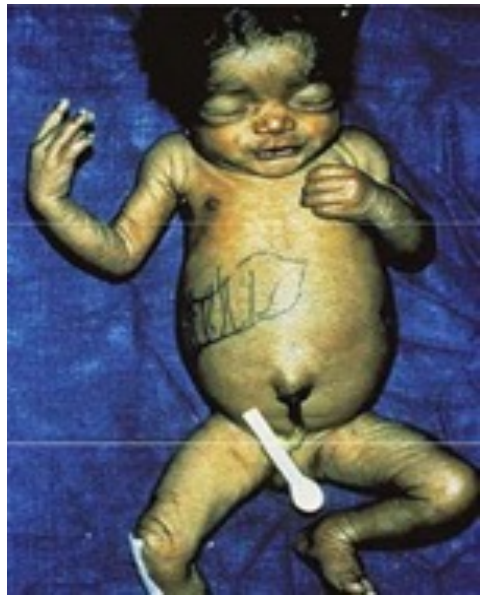
1. Pregnant persons and HIV infected persons with syphilis as well as infants with congenital syphilis should receive priority for treatment with Benzathine penicillin G.

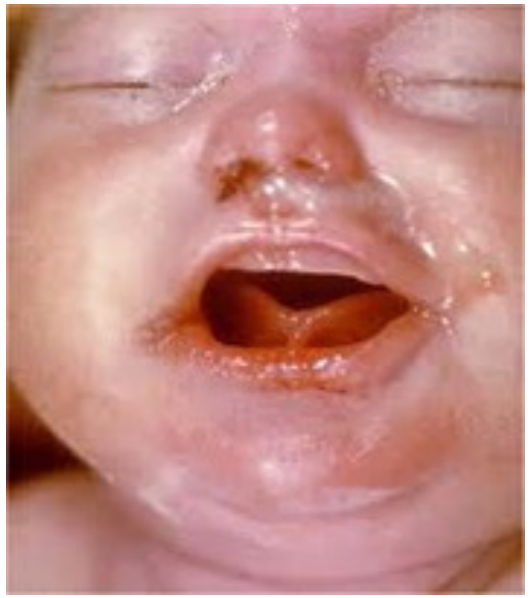
Benzathine penicillin G (Bicillin L-A®) is the only recommended treatment for pregnant people infected or exposed to syphilis.

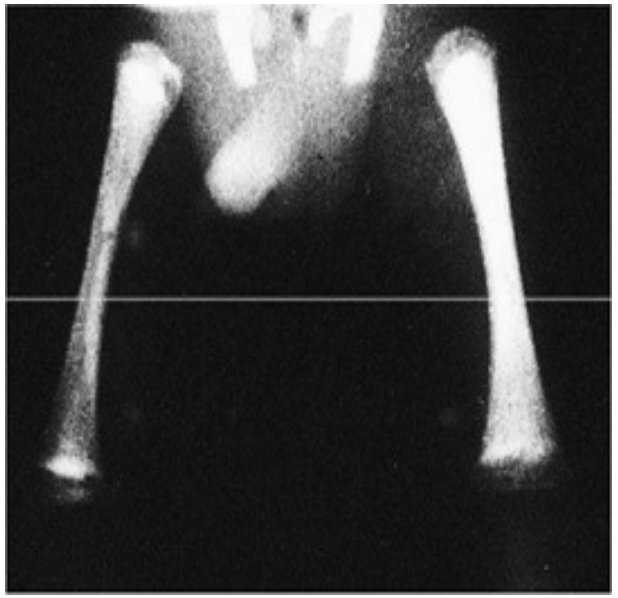
2. If Benzathine penicillin G supplies are inadequate to cover patients other than the ones listed above, treat early syphilis (primary, secondary, early latent) with doxycycline 100 mg po bid for 14 days and late latent syphilis or latent syphilis of uncertain duration with doxycycline 100 mg po bid for 28 days.

Clinical Manifestations of Congenital Syphilis (CS)









https://www.cdc.gov/ncbddd/birthdefects/surveillancemanual/quick-reference-handbook/congenital-syphilis.html

Scenario 1:
Confirmed, proven or highly probable congenital syphilis

Neonate with:

- A physical exam consistent with CS: Hepatomegaly, Jaundice, Nasal discharge ("snuffles"), Rash, Generalized lymphadenopathy, Skeletal abnormalities
- A serum quantitative nontreponemal serology 4-fold greater than mother's or
- A positive darkfield or PCR test of placenta, body fluids or positive silver stain of placenta or cord

Evaluation:

CSF with VDRL, cell ct, protein, CBC/diff, long bone radiographs, neurologic eval (eye, auditory, imaging)

Treatment:

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

Procaine penicillin G 50,000 units/kg body weight/dose IM in a single daily dose for 10 days

Scenario 2:
Possible congenital syphilis

Neonate with a normal physical exam and a serum quantitative nontreponemal serologic titer equal to or < 4-fold of the maternal titer at delivery and **one** of the following:

- The mother was not treated, was inadequately treated, or has no documentation of treatment.
- The mother was treated with erythromycin, or a regimen not recommended in these guidelines
- The mother received recommended regimen, but treatment was initiated <30 days before delivery.

CSF analysis for VDRL, cell count, and protein**
CBC, differential, long-bone radiographs

Treatment:

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

Procaine penicillin G 50,000 units/kg body weight/dose IM in a single daily dose for 10 days OR

Benzathine penicillin 50,000 units/kg body wt. single IM injection

Scenario 3:
Congenital syphilis less likely

Neonate with a normal physical examination and a serum quantitative nontreponemal serologic titer equal or <4-fold of the maternal titer at delivery and **both** of the following are true:

- The mother was treated during pregnancy, treatment was appropriate for the infection stage, and the treatment regimen was initiated ≥30 days before delivery.
- The mother has no evidence of reinfection or relapse

No evaluation is recommended

Treatment:

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

* Another approach involves not treating the newborn if follow-up is certain but providing close serologic follow-up every 2–3 months for 6 months for infants whose mothers' nontreponemal titers decreased at least fourfold after therapy for early syphilis or remained stable for low titer, latent syphilis (VDRL <1:2 or RPR <1:4).

Scenario 4:
Congenital syphilis unlikely

Neonate with:

- a normal physical exam
- serum quantitative nontreponemal serology equal to or less than 4-fold mother at delivery and
- **Mother's treatment was adequate before pregnancy**
- Mother's nontreponemal titer remained low and stable before and during pregnancy and at delivery

No evaluation is recommended

No treatment recommended

- Benzathine penicillin 50,000 units/kg body weight as a single IM injection might be considered, if follow-up is uncertain and the neonate has a reactive nontreponemal test.
- Neonates should be followed serologically to ensure the nontreponemal test returns to negative

Provider Education Resources

- **CDC STD Treatment Guidelines:** https://www.cdc.gov/std/treatment-guidelines/default.htm
- **Indian Country Infectious Disease ECHO:** www.IndianCountryECHO.org
- **CDC STD Prevention Training Centers:** https://www.cdc.gov/std/training/default.htm
- **University of Washington STD CME sessions:** https://www.std.uw.edu/
- **California Prevention Training Center Online:** https://www.stdhivtraining.org/online_courses.html
- **Johns Hopkins STD Prevention Training:** https://www.stdpreventiontraining.com/
- **New York City STD/HIV Prevention Training Center:** https://www.nycptc.org/
- **CDC STD Surveillance:** https://www.cdc.gov/std/statistics/2019/default.htm
- **CDC STD Hotline:** https://www.usa.gov/federal-agencies/cdc-national-std-hotline

Follow-up

Please email the following contact with any questions, concerns, or interest in having a follow-up discussion to learn more about how we can best support your efforts:

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