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45th National Conference on Pediatric Health Care

The Great Imitator: Congenital Syphilis What Every NP Should Know

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1

Speaker Disclosure

- No conflicts to disclose
- Permissions obtained for all images used in this presentation

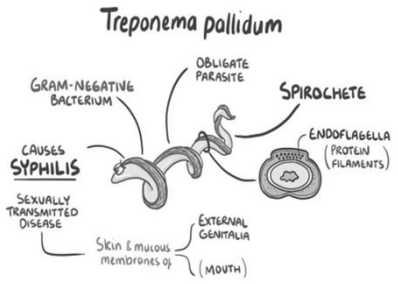
2

Learning Objectives

- Discuss the epidemiology, risk factors and diagnosis of Congenital Syphilis
- Identify the signs and symptoms of Congenital Syphilis
- Describe current management and treatment guidelines for use in practice

3

Brief Review



4

Stages and treatment of syphilis.

Stage	Symptom Onset	Clinical Features	Treatment
Primary	3 weeks	Painless chancre; spontaneous resolution in several weeks	Benzathine penicillin IM x 1
Secondary	1 to 4 months	Flu-like illness, generalized lymphadenopathy, myalgias, arthralgies, rash, condylomata lata; spontaneous resolution in 3 to 12 weeks	Benzathine penicillin IM x 1
Early latent	≤ 1 year	None	Benzathine penicillin IM x 1
Late latent	> 1 year	None	Benzathine penicillin IM x 3 (dosed one week apart)
Tertiary	10 to 30 years	Gumma (granulomatous growths), aortitis, dementia, tabes dorsalis	Benzathine penicillin Im x 3 (dosed one week apart)
Neurosyphilis Ocularsyphilis Otosyphilis	Any time	Meningitis, seizures, uveitis, optic atrophy, hearing loss	Aqueous penicillin IV x 10 to 14 days

Fang et al., 2022

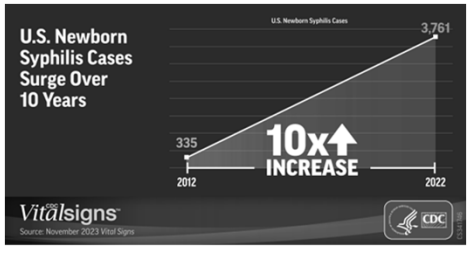
5

6

Background

- First described by Gaspar Torella in 1497
- In the U.S. syphilis was close to elimination in the 1990s
- In 2022 the rate of congenital syphilis in the United States was the highest it has been in nearly 30 years
- More than 10,000 people who gave birth in 2022 had syphilis → increase from 3,400 cases in 2016
- The largest increase in syphilis rate has been in persons younger than age 20 → from 107.3 to 418.6 per 100,000 births (CDC,2024)
- 3,761 babies born with CS in 2022 → a 10-fold increase over a decade

7



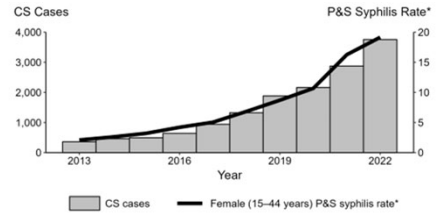
8

Epidemiological Trends

- Evolving in the United States – multifactorial
- MMWR (2023)
  - NNDSS, 2022 data – cohort women 15-44 years of age
  - 3761reported cases of CS
    - 84% livebirths
    - 39.7% no prenatal care
    - 88% received no testing, untimely testing or lack of adequate treatment
      - Lack or untimely testing 36.8% (N=1385)
      - Inadequate treatment 39.7% (N=1494)
    - 20% no treatment
- Geographically CS rates
  - "No or untimely testing"
    - West 56.2% / South 55% / Northeast 50.0% / Midwest 40.4%

9

Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Women Aged 15–44 Years, United States, 2013–2022



* Per 100,000

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

10

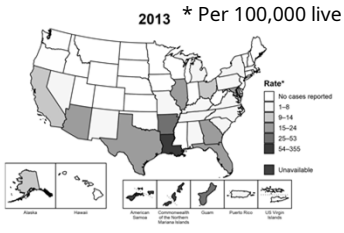
CS Trends

R/E birth person	TESTING – NONE / UNTIMELY	INADEQUATE TREATMENT	NO TREATMENT
NH/OPI	61%	24.4%	7.3%
AI/AN	47.4%	23.4%	15.8%
WA	40.8%	35.8%	12.2%
H/L	34.8%	47.4%	8.1%
B/AA	31.5%	39.2%	13.6%
UNK	45.3%	39.9%	6.1%

MMWR, 2023
Abbreviations: AI/AN=American Indian or Alaska Native, NH/OPI=Native Hawaiian or other Pacific Islander.
WA = White American
H/L = Hispanic or Latino
UNK = Unknown

11

Congenital Syphilis — Rates of Reported Cases by Year of Birth and Jurisdiction, United States and Territories, 2013–2022



12

Risk Factors

- **Transmission in utero → transplacental**
  - 60-100% - Untreated pregnant persons with primary or secondary syphilis in 3rd trimester
  - 40% - Early latent stage
  - <8% - Late latent stage
- **Transmission during delivery → direct contact with lesion**
- **High-risk sexual behaviors**
- **Substance abuse**
- **Gaps in access to prenatal care**
  - 42% of cases
- **Health care inequality**
  - Majority of syphilis cases are diagnosed outside of STD clinics

13

Inequity

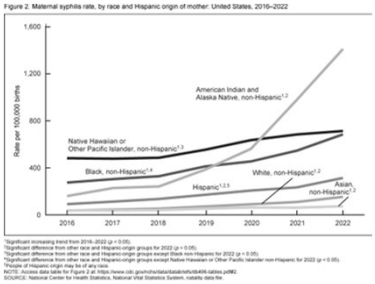
- *Variation in Patterns of Racial and Ethnic Disparities in Primary and Secondary Syphilis Diagnosis Rates Among Heterosexually Active Women by Region and Age Group in the United States.* *(Martin et al., 2022)*
  - 6.42 times higher among Black HSAW
  - 2.20 times higher among Hispanic HSAW
  - Younger women (18-24y) disproportionate burden of P&S syphilis
  - Regionally – NE had the highest Black-White and Hispanic-White disparities
  - Disproportionate CS cases among infants of Black and Hispanic persons

    - Martin et al., 2022 ASTDA
  - Highlights missed opportunities → prevention
  - STI National Strategic Plan Goals – "improve health equity"
    - Interventions tailored to age and regions

14

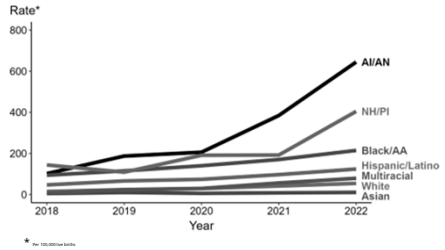
Syphilis trends:

- Maternal syphilis rates increased for all from 2016-2022
- Largest increases occurred for AI and AN followed by WNH



15

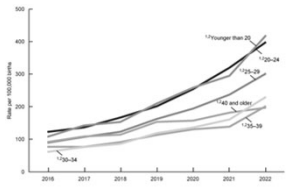
Congenital Syphilis — Rates of Reported Cases by Year of Birth, Race/Ethnicity of Mother, United States, 2018–2022



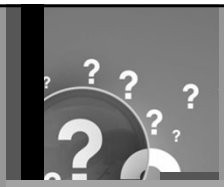
16

Syphilis trend: Age

- 2016-2022 Rate of maternal syphilis increased for each age group
- Largest increases for those younger than 20 years of age
- Highest rate in ages younger than 25yrs
- Decreased with increasing age



17



Signs & Symptoms

What to look for?

18

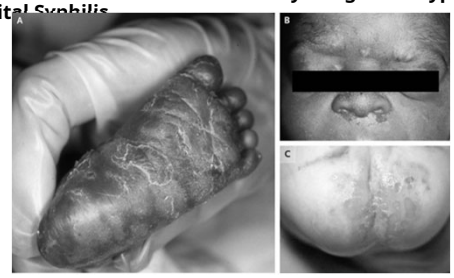
Stages – clinical manifestations

- **Early CS (< 2 years of age)**
- Asymptomatic
- "Snuffles" – rhinitis
- Hepatosplenomegaly
- Skin rash
  - Maculopapular rash
  - Hands and feet with desquamation
- Skeletal abnormalities
- Pigmentary chorioretinopathy (salt and pepper)
- Glaucoma, cataracts & interstitial keratitis
- Anemia
- Thrombocytopenia
- Hydrops

- **Late CS (> 2 years of age)**
- Deconstruction of nasal cartilage
  - Saddle nose
- Frontal bossing
- Tibial thickening
  - Saber shins
- Joint swelling
  - Clutton joints
- Perforation of the hard palate
- Dental abnormalities
  - Hutchinson's teeth
  - Mulberry molars
- SN hearing loss
- Optic atrophy

19

Clinical Manifestations of Congenital Syphilisal ManifesClinical Manifestations of Early Congenital Syphilisf Congenital Syphilis



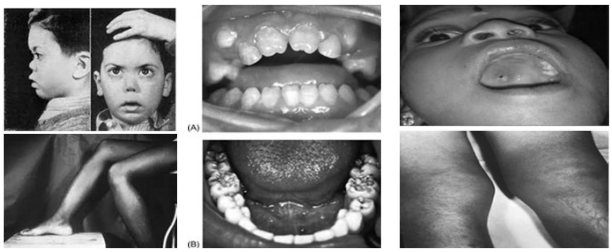
20

A. B. C.

Figures A and C. Courtesy of Pediatric Dermatology, Volume: 35, Issue: 2, Pages: e110-e113,

21

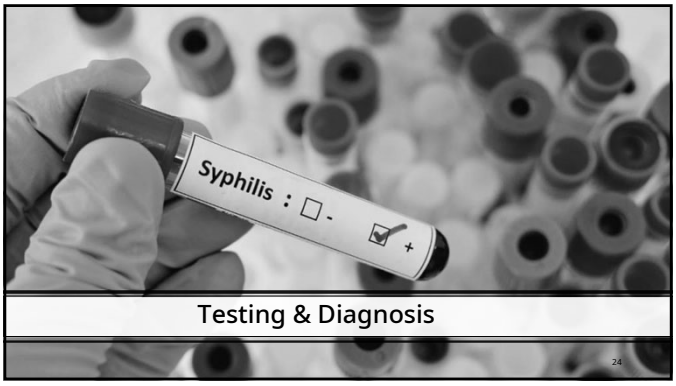
Clinical Manifestations of Late Congenital Syphilis



22

THE DIAGNOSIS OF CONGENITAL SYPHILIS SHOULD BE CONSIDERED IN ANY INFANT WITH SUSPICIOUS CLINICAL FINDINGS DESPITE MATERNAL SEROLOGICAL STATUS

23



24

Testing

Serologic Testing

- Non-Treponemal – detect lipoidal substances released from cells during syphilis infection
  - RPR
  - VDRL

  } more sensitive / less specific than trep tests
- Treponemal – detect syphilis antigens
  - TP-PA
  - FTA-ABS
  - EIA

  } more specific / do not correlate with disease activity & positive for life
- NAAT

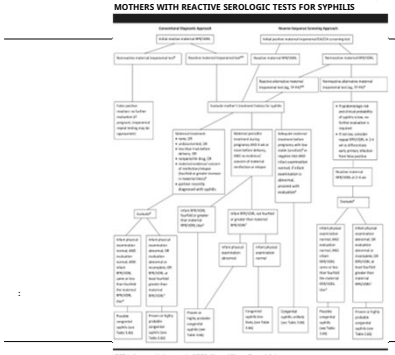
25

Diagnostic Tests

- Definitive Diagnosis
  - ~~Microscopic Darkfield exam~~
  - PCR assay
- Presumptive Diagnosis
  - Both nontreponemal & treponemal serologic tests
    - Inexpensive
    - Rapid turnover
    - Results help define disease activity & monitor response to therapy

26

ALGORITHM FOR DIAGNOSTIC APPROACH OF INFANTS BORN TO MOTHERS WITH REACTIVE SEROLOGIC TESTS FOR SYPHILIS



Red Book: 2021–2024 Report of the Committee on Infectious Diseases.

27

Congenital Syphilis Evaluation & Treatment

- Confirmed Proven / Highly Probable
- Possible
- Less Likely
- Unlikely

28

Confirmed Proven or Highly Probable CS

- Abnormal physical examination consistent with congenital syphilis
- RPR or VDRL ≥ fourfold higher than mother's at delivery
- A positive darkfield test or PCR

Recommended Evaluation:

- CSF analysis for VDRL, cell count, and protein
- CBC with diff and platelets
- Long-bone radiographs
- Other tests as clinically indicated
  - (chest radiograph, liver function tests, neuroimaging, ophthalmologic examination, and auditory brain stem response)

www.cdc.gov/std/treatment-guidelines/congenital-syphilis

29

Possible CS

- Normal physical examination with RPR/VDRL ≤ fourfold of maternal titer at delivery and one of the following:
  - Mother was not treated, inadequately treated, no documentation of treatment.
  - The mother was treated with a nonpenicillin G regimen.
  - The mother received the recommended regimen <30 days before delivery.

Recommended Evaluation:

- CSF analysis for VDRL, cell count, and protein.
- CBC with differential and platelets.
- Long-bone radiographs.

www.cdc.gov/std/treatment-guidelines/congenital-syphilis

30

Less Likely CS

- Normal physical examination and RPR/VDRL ≤ equal fourfold of the maternal titer at delivery and both:
  - 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.

Recommended Evaluation:

- No evaluation is recommended

31

Unlikely CS

- Normal physical examination and RPR/VDRL ≤ fourfold of the maternal titer at delivery and both:
  - Mother's treatment was adequate before pregnancy.
  - The mother's RPR/VDRL remained low and stable (serofast) before and during pregnancy & at delivery.

Recommended Evaluation:

- No evaluation is recommended

32

Infant CS Classification & Evaluation

CLASSIFICATION	Definition	Recommended Evaluation
Confirmed proven or highly probable congenital syphilis	➢ *Any neonate with:* • *An abnormal physical examination that is consistent with congenital syphilis;* • A serum quantitative nontreponemal serologic titer that is fourfold (or greater) higher than the mother's titer at delivery EXAMPLE- maternal titer = 1:2, neonatal titer ≥1:8 or maternal titer = 1:8, neonatal titer ≥1:32 or • A positive darkfield test or PCR of placenta, cord, lesions, or body fluids or a positive silver stain of the placenta or cord.	➢ CSF analysis for VDRL, cell count, and protein ➢ CBC and differential and platelet count ➢ Long-bone radiographs ➢ Other tests as clinically indicated (chest radiograph, liver function tests, neuroimaging, ophthalmologic examination, and auditory brain stem response)
Possible congenital syphilis	➢ *Any neonate who has a normal physical examination and a serum quantitative nontreponemal serologic titer equal to or less than fourfold of the maternal titer at delivery* *EXAMPLE - maternal titer = 1:8, neonatal titer ≤1:16* *and 1 of the following:* • The mother was not treated, was inadequately treated, or has no documentation of having received treatment. • The mother was treated with erythromycin or a regimen other than those recommended in these guidelines (ie - a nonpenicillin G regimen). • The mother received the recommended regimen but treatment was initiated <30 d before delivery.	➢ CSF analysis for VDRL, cell count, and protein ➢ CBC, differential, and platelet count ➢ Long-bone radiographs
Congenital syphilis less likely	➢ *Any neonate who has a normal physical examination and a serum quantitative nontreponemal serologic titer equal or less than fourfold of the maternal titer at delivery* *EXAMPLE - maternal titer = 1:8, neonatal titer ≤1:16* *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 d before delivery. • The mother has no evidence of reinfection or relapse.	➢ No evaluation is recommended.
Congenital syphilis unlikely	➢ *Any neonate who has a normal physical examination and a serum quantitative nontreponemal serologic titer ≥ fourfold of the maternal titer at delivery and both of the following are true:* • The mother's treatment was adequate before pregnancy. • The mother's nontreponemal serologic titer remained low and stable (serofast) before and during pregnancy and at delivery EXAMPLE - VDRL ≤1:2 or RPR ≤1:4).	➢ No evaluation is recommended.

National Association of Pediatric Nurse Practitioners

CDC, 2021

33

CS Treatment
Depends on likelihood of Infection

Confirmed:

- PCN X 10 days (IV AC PCN G or IM Procaine PCN G)
- If >1 day of therapy is missed, the entire course should be restarted

Possible:

- See Above (x10 days) or
- Benzathine penicillin G = Bicillin L-A® IM x1 dose

Less likely:

- Bicillin L-A®, IM x 1 dose

National Association of Pediatric Nurse Practitioners

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

34

Treatment

Bicillin L-A® Shortage

The FDA has listed penicillin G benzathine injectable suspension products (Bicillin L-A®) on their drug shortage webpage (↗, noting limited supply due to increased demand. The FDA website includes an expected duration for the shortage. CDC continues to monitor the situation and will post updates as needed.

Bicillin L-A® is the first-line recommended treatment for syphilis and the only recommended treatment option for some patients.

During this time, programs should:

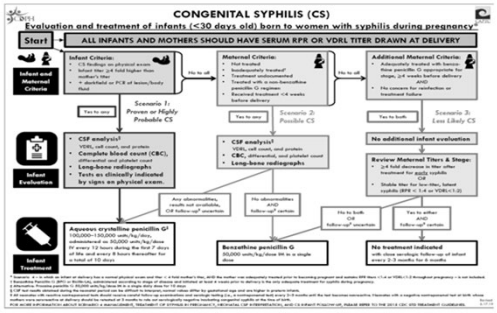
- Continue to follow CDC's treatment recommendations. Penicillin G benzathine (Bicillin L-A®) is the only recommended treatment for pregnant people infected with or exposed to syphilis.
  - Doxycycline 100mg PO BID for two weeks (for early syphilis) or for four weeks (for late latent or syphilis of unknown duration) is an alternative for the treatment of non-pregnant people with a penicillin allergy.
- Prioritize the use of Bicillin L-A® to treat pregnant people and babies with congenital syphilis.
- To help CDC continue to monitor the situation, notify DSTDP (stdshortages@cdc.gov) of:
  - Shortages or stock-outs of Bicillin L-A® in the jurisdiction.
  - Situations in which patients diagnosed with syphilis are not being treated due to the inability to procure Bicillin L-A® in the jurisdiction.
- Report any shortages to the Pfizer Supply Continuity Team at 844-646-4398 (select 1 and then select 3).

Centers for Disease Control and Prevention
Sexually Transmitted Infections Treatment Guidelines, 2021

National Association of Pediatric Nurse Practitioners

35

35



California Dept of Public Health

National Association of Pediatric Nurse Practitioners

36

36

Now What?

- Follow-Up Exam and RPR/VDRL Q 2-3 months
  - Expect titer to decrease by 3 months & non-reactive by 6 months.
- Persistent RPR/VDRL at 6-12 months
  - Consider LP
  - Possible Retreat
  - Consult ID
- Seronegative at birth
  - check RPR/VDRL at 3 months to rule out incubating CS
- If initial CSF abnormal →repeat LP not needed *unless:*
  - RPR/VDRL persist at 6-12 months
  - Consult ID

37

Evaluation and Treatment of Infants and Children

- **DEFINED AS**:
  - Infants and children aged ≥1 month
  - Reactive serologic tests for syphilis (RPR reactive, TP-PA reactive or EIA reactive)
- **RECOMMENDED EVALUATION:**
  - Thorough PE
  - Maternal serology & History reviewed (congenital or acquired??)
    - Extremely early or "incubating syphilis" at the time of delivery → all maternal serologic tests might have been negative
    - CS undetected until later
    - Any infant or child *at risk* for congenital syphilis should receive a full evaluation and testing for HIV infection.
- **SPECIAL POPULATIONS:**
  - International adoptee, immigrant, or refugee children from countries where treponemal infections (yaws or pinta) are endemic might have reactive nontreponemal and treponemal serologic tests (STD Guidelines, 2021)
  - Which cannot distinguish between syphilis and other subspecies of *T. pallidum.*
- **Recommended Evaluation:**
  - CSF analysis for VDRL, cell count, and protein
  - CBC, differential, and platelet count
  - Other tests as clinically indicated (long-bone radiographs, chest radiograph, liver function tests, abdominal ultrasound, ophthalmologic examination, neuroimaging, and auditory brain-stem response)

38

Treatment - Infants & Children

commended Regimen for Congenital Syphilis Among Infants and Children

- **Aqueous crystalline penicillin G**
  - 200,000–300,000 units/kg – IV (administered as 50,000 units/kg body weight) every 4–6 hours **for 10 days**

39

Follow- Up Infants & Children

- Thorough follow-up examinations and serologic testing (RPR or VDRL) of infants and children treated for congenital syphilis (aged >30 days)
  - Q3 months until nonreactive or the titer has decreased fourfold.
- If these titers increase at any point >2 weeks or do not decrease fourfold after 12–18 months →
  - CSF evaluated
  - Treated with a 10-day course of penicillin G
  - Consult ID

40

PCN Allergy – What do we do?

- Infants and children with PCN allergy should be desensitized and treated with penicillin G
- Data are insufficient regarding use of other antimicrobial agents for CS in infants and children.
- If a nonpenicillin G is used → close clinical, serologic, and CSF follow-up is required & Consult ID

41

What are we doing?

National Syphilis and Congenital Syphilis Syndemic (NSCSS) Federal Task Force

Immediately Treat and Report Syphilis Cases

42

Screening

TEST PREGNANT PERSONS	
At 1st Prenatal Visit (or as soon as pregnancy 1st id)	✓
At 28 weeks (early 3rd trimester)	✓
At delivery	✓

43

Screening

- State dependent

44

Implications & Barriers

- "Never Event" →Public Health Crisis
- Long-term complications
- Funding / Expense
- Disparity in coverage & care
- State to State variations screening
- Missed Opportunities
- Education
- Provider gap
- Syndemic

US health officials alarmed by 'dire' rise in dangerous, preventable syphilis infections in babies

'Time to sound the alarm': Surge in babies born with syphilis draws attention to lack of care

Babies Die as Congenital Syphilis Continues a Decade-Long Surge Across the US

Infant syphilis cases are skyrocketing in the US: 'Shameful crisis'

Infants Are Born With Syphilis in Growing Numbers, a Sign of a Wider Epidemic

Newborn syphilis cases have reached 'dire levels,' CDC says

45

Role of the NP

EDUCATION | SCREENING | REPORTING | TREAT | FOLLOW-UP | COLLABORATE & ADVOCATE

46

Resources

- www.stdccn.org/render/Public
- https://www.hhs.gov/about/news/2023/11/15/readout-adm-rachel-levines-visit-georgia-learn-impacts-congenital-syphilis-syphilis.html
- https://www.cdc.gov/std/treatment-guidelines/provider-resources.htm#MobileApp
- cdc.gov/std/treatment-guidelines/wall-chart.pdf
- https://www.ncsddc.org/resource/injectable-syphilis-treatment-delivery-considerations-for-std-programs/
- https://www.cdc.gov/std/treatment-guidelines/congenital-syphilis.htm
- https://www.cdc.gov/std/treatment-guidelines/syphilis.htm

47

- Consult with the STD Clinical Consultation Network for assistance with complex cases of titer interpretation - National Network of STD Clinical Prevention Training Centers
- www.stdccn.org/render/Public

48

REMEMBER THE CHECKLIST

•Examine the neonate for:
- Face: Rhinitis (snuffles) with mucopurulent nasal discharge
- Skin: Jaundice, rash and desquamation
- Abdomen: Hepatosplenomegaly (enlarged liver and spleen)
- Eye: Chorioretinitis and pigmentary chorioretinopathy (salt and pepper type), glaucoma, cataracts, interstitial keratitis, optic neuritis

•Additional clinical examinations:
- Radiographs: Osteochondritis, diaphyseal osteomyelitis, periostitis.
- Hearing test: Hearing impairment (failed hearing screening must be followed with diagnostic testing to verify hearing loss).

•Obtain maternal medical health and pregnancy history for syphilis diagnosis.
•Collect maternal and neonatal blood samples for laboratory testing (maternal titers rapid plasma reagin [RPR] and venereal disease research laboratory [VDRL], neonatal blood count and thrombocytopenia).
•As indicated, test cerebrospinal fluid (CSF) for reactivity for VDRL test, or elevated CSF cell count or protein.
• Use darkfield microscopy or fluorescent antibody detection to detect Treponema pallidum in relevant tissue samples.
•Obtain photographs of the congenital anomalies noted.

CDC, 2021

49

Take Home

- Congenital syphilis is a major public health issue
- Repeated serology during pregnancy is recommended - especially if risk factors are present.
- The diagnosis of congenital syphilis should be considered in any infant with suspicious clinical findings despite maternal serological status
- Congenital Syphilis is preventable – education is key
- Advocate - Addressing patient and systemic barriers is essential

50

51

Questions?

Thank you for listening!

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52