Emerging Health Threats in Infants

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Congenital Syphilis

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This presentation contains images that may be uncomfortable for some viewers.

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Learning Objectives

- Explain the pathophysiology of congenital syphilis.
- List at least three possible sequelae of untreated congenital syphilis.
- Describe and interpret screening tests for congenital syphilis.
- Describe diagnostic considerations and clinical decision-making for congenital syphilis in inpatient and outpatient settings.
- Discuss the management of congenital syphilis.
- Describe pertinent education points and care coordination needed for caregivers of patients with this condition.
- Apply diagnostic criteria and clinical guidelines to a case example.

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Introduction and Background

- **What is congenital syphilis (CS)?**
  - A preventable infection where the spirochete *Treponema pallidum* is transmitted from a pregnant person to a fetus.
  - Can be transmitted to the fetus as early as the 9th week of gestation (McCance & Huether, 2022).
  - In 2022, congenital syphilis affected over 700,000 births globally (WHO, 2024).
  - In 2023, 3,882 cases of congenital syphilis were reported in the U.S., including 279 congenital syphilis-related stillbirths and neonatal/infant deaths. This is the largest number of cases of congenital syphilis since 1992
- **Pathophysiology:** Congenital syphilis is caused by the *Treponema Pallidum* bacterium that is only able to live within a human body.
  - Vertical transmission can occur during any stage of syphilis infection during pregnancy
    - It is most likely to happen during early syphilis (World Health Organization [WHO] 2024).
  - The bacterium enters fetal circulation and inflames almost all organs.
  - The bones, liver, pancreas, intestine, kidney and spleen are most severely affected.

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Serologic Tests: Non-treponemal and Treponemal

What is a non-treponemal test?
- Rapid Plasma Reagin (RPR) or Venereal Disease Research Lab antigen test (VDRL)
- Demonstrate presence of syphilitic antigens
- Both can detect positive results in 50% of primary syphilis cases and 100% of those with secondary syphilis (McCance & Huether, 2022)
- False positives are common and can result from acute or chronic infections, with autoimmune and immunosuppressive conditions, or pregnancy

What is a treponemal test?
- Because of the high false-positive rate in non-treponemal testing, this type of testing includes serologic-specific tests that are used to assess antibody response to T. pallidum (CDC, 2021).
- Confirmatory testing through ELISA has a high rate of sensitivity and specificity (McCance & Huether, 2022).

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Untreated Syphilis in Pregnancy

Screening:
- Congenital syphilis features are detectable by ultrasound as early as 18-22 weeks gestation

Birthing parent risk factors include:
- Sex with multiple partners
- Sex in conjunction with drug use or transactional sex
- Late entry to prenatal care (i.e., first visit during the second trimester or later) or no prenatal care
- Methamphetamine or heroin use
- Incarceration of the woman or her partner
- Unstable housing (CDC, 2021)

Possible outcomes:
- Miscarriage
- Stillborn births
- Premature births
- Low birthweight infants (<2500 grams)

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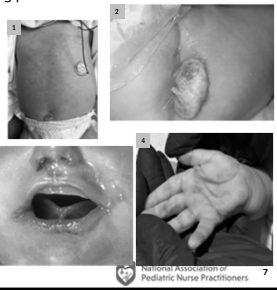
Untreated Congenital Syphilis

- **Newborn:** Transmission via placenta or birthing process
  - Maculopapular rash
  - Snuffles from spirochete proliferation
  - Hepatosplenomegaly
  - Optic neuritis
  - Nonimmune hydrops
  - Sensorineural hearing loss
  - Saddle nose



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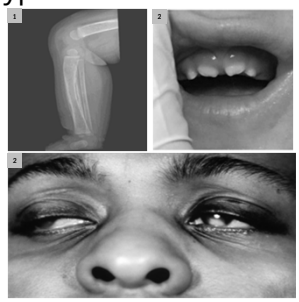
Untreated Congenital Syphilis

- **Later complications** - usually after 2 years of age
  - Saber shins
  - Hutchinson teeth
  - Hearing and vision loss
  - Seizures
  - Pseudoparalysis of extremity due to pain from a bone lesion



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[2]CDC Public Health Image Library - https://phil.cdc.gov/Default.aspx

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Screening and Assessment

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Relevant Patient Considerations

Pregnant People
- First prenatal care visit
- 28 weeks
- At delivery
- All individuals delivering a stillborn infant

Additional Considerations
- All pregnant people should be tested for syphilis early in pregnancy.
- Most states mandate testing at the first prenatal visit.
- Consider testing at the time of pregnancy confirmation if follow up may be an issue.

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Physical Exam

- Most infants born with CS are asymptomatic at birth (Sankara, Partridge, & Lakshminrusimha, 2023)
- Untreated infants generally show clinical symptoms by 3 months of age
- Hepatosplenomegaly is common with hepatobiliary dysfunction causing jaundice and elevated liver function tests
- Rhinitis that has copious white discharge unresponsive to treatment often presents within the first week of life
- Generalized, non-tender lymphadenopathy
- Small red or pink maculopapular lesions may be seen on the back, buttocks, posterior thighs, and the palms and the soles of the feet which progress to desquamation and crusting
- Frontal bossing, saddle nose and short maxilla
- Hearing and vision impairment

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Diagnostic Decision Making

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Diagnostic and Laboratory Tests

- Newborns of birthing parents with documented syphilis need careful evaluation after birth.
- Birthing parent nontreponemal and treponemal immunoglobulin G (IgG) antibodies can be transferred through the placenta to the fetus.
  - Confirming CS is complicated by the presence of these birthing parent antibodies in the newborn's blood.
  - Umbilical cord blood should not be used as serological testing for CS.
- Treatment decisions are made based on birthing parent status, clinical symptoms of CS, and comparison of birthing parent and neonatal titers (CDC, 2021).
- Any infant being screened for CS should also be tested for HIV.

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Screening Algorithm – Go To Page

- https://aapca3_org/wp-content/uploads/2022/08/Syphilis-Screening_FINAL_pdf

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Diagnostic and Laboratory Tests

- CBC with differential is recommended in conjunction with non-treponemal screening of neonates.
- Reverse sequence screening is increasingly common.
- Labs may obtain a treponemal antibody test and if the result is abnormal, then a non-treponemal test is performed for confirmation and titer levels.
- Rapid point-of-care tests for mothers are now available and can provide results in 20 minutes.
  - All currently available rapid tests in the US are only using treponemal testing and require confirmation with non-treponemal testing
  - While rapid tests do not replace laboratory testing, they can be used in settings where follow-up is limited, the prevalence of syphilis is elevated, and immediate treatment is needed for positive results (Pham et al, 2022).

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Testing For Syphilis: Point-of-Care Testing

Syphilis Health Check™ (SHC) and Chembio DPP® HIV/Syphilis Treponemal Rapid Tests

	Time to Results	Shelf-life	Cost per Test	Sensitivity & Specificity
Syphilis Health Check™ (SHC)	10 min.	30 months	Approx. $10	95-99% Sensitivity 94-97% Specificity
Chembio DPP® HIV/Syphilis Test Kit	15 min.	24 months	Approx. $7-10	47-97% Sensitivity 99-100% Specificity

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Diagnostic Imaging and CSF Evaluation

- Chest x-ray may show diffuse opacification of both lung fields.
- CSF abnormalities, including reactive VDRL titers, increased leukocyte count (>25 cell/mm3), and elevated protein (> 0.15g/L).
- CSF PCR for detection of treponemal DNA.
- Darkfield microscopic examination of nasal discharge or skin lesions.
- Exceptionally high placental weight (greater than 90th percentile for birth weight).
- Histologic examination of the placenta and cord for the typical pathological changes and presence of spirochetes.
- Long bone radiographs may show findings of pathologic fractures, metaphyseal serration, localized demineralization and osseous destruction.
- Moth-eaten lesions in the long bones due to demineralization are distinguishing features of CS (David et al, 2022).

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Interpreting Assessment and Diagnostic Findings

- Examine birthing parent titers with infant titers.
- If infant has four times as high a titer as the birth mother, then congenital syphilis is likely.

	Birthing Person	Infant
Non-Treponemal Serologic Titer (VDRL or RPR)	1:16	1:64

- If an exposure to syphilis is possible or unknown in the birth parent or the birth parent requests additional evaluation to definitively rule out syphilis, repeat serology testing within 4 weeks to evaluate for early infection (CDC, 2021).

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Recognize and Differentiate

- Birth parent antibodies can interfere with the interpretation of treponemal tests up to 15 months or longer (Dalby & Stoner, 2022).
  - If results are positive, then the infant should be screened with serial non-treponemal tests every 2-3 months.
- Many uninfected infants with elevated titers will normalize their levels by 6 months old (Stafford, Workowski, & Bachmann, 2024).
- Persistently elevated titers indicate infection or insufficient treatment.
- Once treponemal antibodies become positive, they remain that way for life in approximately 85% of people
  - Non-treponemal testing will be required for any additional screening needs.

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Differential Diagnoses

- Gonorrhea
- Lyme disease
- Neonatal hepatitis
- Neonatal sepsis
- Parvovirus B19
- Enterovirus
- Erythema toxicum
- HIV
- Tuberculosis
- TORCH infections (toxoplasmosis, rubella, CMV, and HSV)

- **In seronegative neonates with a high placental weight, consider:**

- Beckwith-Weidemann syndrome
- Cerebral palsy
- Hydrops fetalis
- Birthing parent diabetes (Tudor et al, 2024).

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Treatment

- If the neonate requires treatment, penicillin is the drug of choice with titrated dosing based on neonate's weight and the day of treatment (CDC, 2021).
- Aqueous crystalline penicillin G 100,000–150,000 units/kg body weight/day, administered as 50,000 units/kg body weight/dose by IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days.
- Alternative is Procaine penicillin G 50,000 units/kg body weight/dose IM in a single daily dose for 10 days.
- If >1 day of therapy is missed, the entire course should be restarted. Data are insufficient regarding use of other antimicrobial agents (e.g., ampicillin). When possible, a full 10-day course of penicillin is preferred, even if ampicillin was initially provided for possible sepsis (*648–650*). Using agents other than penicillin requires close serologic follow-up for assessing therapy adequacy.
- If a penicillin allergy is present, then desensitization should occur with an allergy specialist (Dalby & Stoner, 2022).
  - See CDC website for most current guidelines

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Reporting Health Threats

- Congenital and syphilis in pregnancy are nationally reportable diseases for all 50 states (Leslie & Vaidya, 2024).
- The local health department should be contacted with any positive result within 3 working days.
  - An example of the case report form to fill out.


CONGENITAL SYPHILIS (CS) CASE INVESTIGATION AND REPORT

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Comorbidities

- Untreated syphilis and CS increases the risk of HIV.
- Infants born with CS may have asymptomatic neurosyphilis.
  - These infants will need a CSF evaluation.
- Pituitary abnormalities leading to diabetes insipidus and hypoglycemia.

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Involving the Patient and Family

- When a birth mother is positive for syphilis, ensure adequate treatment of sexual partners.
- Engage caregivers in discussions regarding diagnosis, treatment and future prevention.
- Education on safer sex practices for the birth parent and partners.
- Standard precautions to reduce transmission from neonatal body fluids.
- Educating families/caregivers regarding breast/chestfeeding.
  - Recommended if there are no active/open lesions on the breast.
  - Does not pass through breastmilk to the infant.

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Initiating Referral and Consultation

- Initiate consultations and referrals as indicated.
- Allergy/immunology for penicillin allergy desensitization.
- Infectious disease specialists for complicated cases.
- Online form for consultation regarding challenging cases or presentations of CS.

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Clinical Decision Making

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Clinical Practice Guidelines

- CDC Guidelines
  - https://www.cdc.gov/std/treatment-guidelines/congenital-syphilis.htm
- ACOG Practice Recommendations
  - https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2024/04/screening-for-syphilis-in-pregnancy
- American Academy of Pediatrics Toolkit
  - https://aapca3.org/cs/

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Developing Care Plans

- Inpatient management
  - Ensuring all birthing parents have a current syphilis test prior to discharge.
  - If the initial test is positive, send confirmatory testing
    - May be traditional or reverse algorithm testing.
  - Obtain CSF sample from the neonate if there is a concern for neuro-, ocular- or otosyphilis.
- Outpatient management
  - Obtain relevant neonatal and birthing parent history.
  - Ensure recent screening for syphilis and HIV based on risk factors.
  - Evaluate vision and hearing capabilities regularly.
  - Continue close observations for CS complications during the first year.
- For both: Ensure reporting of positive results within 3 working days to the public health department using state and local guidelines.

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Evidence-based Management

Prescribing
- Pharmacologic agents
- Therapies
- Interventions

Ongoing surveillance through non-treponemal testing

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Community Resources

- Local health departments
- Maternal-child health programs
- State STI programs
- Community-based organizations that raise awareness and provide sexual health education
- Perinatal case managers, doulas and community health workers

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Multidisciplinary Care Coordination

- Neonatology
- Obstetricians and midwives
- Primary care involvement
- Health Department
- Pharmacy
- Laboratory services

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Ongoing Management

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Ongoing Support, Monitoring and Counseling

Follow-up:

- If the nontreponemal test is nonreactive by the age of 6 months, no further evaluation or treatment is needed.
- If the neonate still has a reactive nontreponemal test at 6 months, they are likely to be infected and should receive treatment (Dalby & Stoner 2022).
- For well-child checks, continue monitoring for failure to thrive and developmental delays.

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Advocating for the Child and Family

- Discuss the risks, possible outcomes and prevention.
- Discuss infection prevention measures.
- Evaluate barriers to effective screening and management.
  - Inpatient hospitalization with 10-day course of IV penicillin vs. 1 dose IM regimen.

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Case Study:

A 33-year-old birth parent (assigned female at birth) arrives to the clinic with a history of primary syphilis diagnosis around 28 weeks gestation that was treated with a single dose of penicillin at the local health department. The birth parent is there to have her 2-month-old infant (who was a term birth) evaluated for syphilis. You note a history of a positive history of maternal treponemal antibodies with RPR testing and initial infant labs from birth are below:

	Birthing parent	Infant
Non-Treponemal Serologic Titer: RPR	1:16	1:32

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Case Study:

Additional history reveals that the infant was not treated with penicillin since the birthing parent received treatment during pregnancy.

- **What more would you like to know about the history?**
- **What lab/diagnostic screening tests do you anticipate ordering?**
- **Are there any additional guidance you would provide to this caregiver?**

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Case Study:

- **History:** Was there concern for neurosyphilis? Any LP/CSF obtained? What has been the growth trajectory of the infant? Any ongoing exposures? Was the birth mother's partner treated/do they have a new partner?
- **Labs/Diagnostics:** Anticipate ordering a RPR on infant today to ensure that maternal treatment was sufficient.
  - Consider a CBC if concern for anemia or infection.
  - Recommend an HIV screening test.
  - If physical exam was abnormal, could consider radiographs for extremities (pseudoparalysis), chest (ongoing respiratory concerns), culture of nasal discharge, if present, etc.
- **Guidance:** Continue to ensure access to follow-up exams and relevant screening for infant for at least the first year. Reassure parents that if infant's titer continues to decline, they are likely not infected. Educate on resolution of most positive infant titers by 6 months. Provide local screening and testing sites for birth mother and partners.

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Accessing Provider and Patient Resources - napnap.org/emerging-maternal-infant-infectious-diseases/

- Provider Resources
  - For consultation regarding challenging cases or presentations of CS
  - State prenatal syphilis screening laws and regulations
  - STI treatment mobile app
  - National STD curriculum - includes an adult syphilis module
  - Syphilis photos made available by the CDC (contains sensitive content)
- Patient Resources
  - About CS - CDC guidance
  - Testing locations by zip code
  - March of Dimes Infographic
  - Partner conversation tips

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Summary

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Summary

- Congenital syphilis is an emerging health threat that needs to be immediately recognized and treated to promote optimal outcomes for children and caregivers.
- Infant health outcomes are improved through heightened awareness of this condition.
- This preventable condition is easily treated when detected early.
- Pediatric providers play a crucial role in preventing, screening and managing this condition.

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