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 or VDRL titer drawn at delivery

Infant Criteria:
• CS findings on physical exam
• Infant titer ≥4 fold higher than mother’s titer
• + darkfield or PCR of placenta, cord lesion, or body fluid
• + silver stain of placenta or cord

Yes to any

Scenario 1: Proven or Highly Probable CS

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

No to all

Addtional Maternal Criteria:
• Adequately treated with benzathine penicillin G appropriate for stage, initiated ≥30 days before delivery AND
• No concern for reinfection or treatment failure

No to all

Scenario 2: Possible 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.

Yes to any

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

No abnormalities AND follow-up§ uncertain

No abnormalities AND follow-up uncertain

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 or VDRL<1:2)

Yes to either AND follow-up§ certain

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

No to both OR follow-up§ uncertain

No to both OR follow-up§ certain

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

Scenario 3: Less Likely CS

Infant Evaluation:
Any abnormalities, results not available, OR follow-up§ uncertain

No abnormalities AND follow-up§ certain

No additional infant evaluation

Infant Criteria:
• CS findings on physical exam
• Infant titer ≥4 fold higher than mother’s titer
• + darkfield or PCR of placenta, cord lesion, or body fluid
• + silver stain of placenta or cord

Yes to any

Scenario 1: Proven or Highly Probable CS

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

No to all

Addtional Maternal Criteria:
• Adequately treated with benzathine penicillin G appropriate for stage, initiated ≥30 days before delivery AND
• No concern for reinfection or treatment failure

No to all

Scenario 2: Possible 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.

Yes to any

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

No abnormalities AND follow-up§ uncertain

No abnormalities AND follow-up uncertain

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 or VDRL<1:2)

Yes to either AND follow-up§ certain

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

No to both OR follow-up§ uncertain

No to both OR follow-up§ certain

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

Scenario 3: Less Likely CS

Infant Evaluation:
Any abnormalities, results not available, OR follow-up§ uncertain

No abnormalities AND follow-up§ certain

No additional infant evaluation

Infant Criteria:
• CS findings on physical exam
• Infant titer ≥4 fold higher than mother’s titer
• + darkfield or PCR of placenta, cord lesion, or body fluid
• + silver stain of placenta or cord

Yes to any

Scenario 1: Proven or Highly Probable CS

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

No to all

Addtional Maternal Criteria:
• Adequately treated with benzathine penicillin G appropriate for stage, initiated ≥30 days before delivery AND
• No concern for reinfection or treatment failure

No to all

Scenario 2: Possible 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.

Yes to any

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

No abnormalities AND follow-up§ uncertain

No abnormalities AND follow-up uncertain

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 or VDRL<1:2)

Yes to either AND follow-up§ certain

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

No to both OR follow-up§ uncertain

No to both OR follow-up§ certain

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

Scenario 3: Less Likely CS

Infant Evaluation:
Any abnormalities, results not available, OR follow-up§ uncertain

No abnormalities AND follow-up§ certain

No additional infant evaluation

* Scenario 4 – in which an infant at delivery has a normal physical exam and titer < 4-fold mother’s titer, AND the mother was adequately treated prior to becoming pregnant and sustains RPR titers <1:4 or VDRL<1:2 throughout pregnancy – is not included.
† CSF test results obtained during the neonatal period can be difficult to interpret; normal values differ by gestational age and are higher in preterm infants.
‡ Alternative: Procaine penicillin G 50,000 units/kg/dose IM in a single daily dose for 10 days.
§ Benzathine Penicillin G (BPG or Bicillin-LA), administered according to stage of disease and initiated at least 30 days prior to delivery is the only adequate treatment for syphilis during pregnancy.
II Evaluation is not necessary if a 10-day course of parenteral therapy is administered, although such evaluations might be useful. If the neonate’s nontreponemal test is nonreactive and the mother’s risk for untreated syphilis is low, a single IM dose of BPG can be considered without evaluation.
¶ All neonates with reactive nontreponemal tests should receive careful follow-up examinations and serologic testing (i.e., a nontreponemal test) every 2–3 months until the test becomes nonreactive. Neonates with a negative nontreponemal test at birth whose mothers were seroreactive at delivery should be retested at 3 months to rule out serologically negative incubating congenital syphilis at the time of birth.
FOR MORE INFORMATION ABOUT SCENARIO 4 MANAGEMENT, TREATMENT OF SYPHILIS IN PREGNANCY, NEONATAL CSF INTERPRETATION, AND CS INFANT FOLLOW-UP, PLEASE REFER TO THE CDC 2021 STI TREATMENT GUIDELINES.