Regional Guidelines for the Management of Syphilis during Pregnancy and the Perinatal Period

These regional guidelines aim to standardize the management of syphilis cases in pregnant women and newborns exposed during pregnancy. The guidelines were written following consultations with various specialists from the MUHC involved in syphilis management, as well as with clinician doctors and midwives from Nunavik's health centers.

Prepared by: Audrey Jade Paris-Migneault and Dr. Jean-Sébastien Touchette, STBBI team, Nunavik Public Health Department

Consulted for the preparation of these regional guidelines: Dr. Claire-Elise Burdet, UTHC, Dr. Amira El-Messidi, CUSM, Dr Christos Karatzios, CUSM, Kimberley Moorhouse, MW IHC, Mme Arian Navickas, MW IHC, Geneviève Lamarche, MW UTHC, Dr. Isabelle Laverdière, IHC, Dr. Joanie Tremblay-Pouliot, IHC, Vicki Van Wagner, MW IHC and Dr. Cedric Yansouni, CUSM.

Pregnant women

Reminder

In Nunavik, it is recommended that all pregnant women undergo four syphilis screenings during pregnancy, in addition to a postpartum screening, according to the following schedule:

- First visit
- Second trimester (6-8 weeks after the first screening)
- Third trimester
- Around 34-36 weeks
- 6-8 weeks postpartum

Management and treatment

When syphilis is confirmed or strongly suspected in a pregnant woman, the following treatment is recommended:

Benzathine Penicillin G 2.4 million units IM for 3 doses at 7-day (maximum 10-day) intervals.

Additional Information:

- ***Three doses of Benzathine Penicillin G are recommended in Nunavik for pregnant women, both for early and late syphilis*** *(excluding neurosyphilis). This recommendation was made due to concerns about the effectiveness of a single-dose treatment in pregnant women and to reduce the risk of early reinfection.*
- *For late syphilis, if the interval between two doses exceeds 10 days, the entire treatment series must be restarted. For early syphilis, the ideal interval between doses is also 7 to 10 days, but the treatment can be considered complete even if the interval between doses exceeds 10 days, as long as three doses have been received. In case of doubt about treatment completion, consult the adult infectious disease specialist.*
- *There is no recognized alternative antibiotic for the treatment of syphilis during pregnancy to prevent congenital syphilis. In case of penicillin allergy, consider a challenge and desensitization of the patient if*

necessary. If an alternative antibiotic is administered, the patient will not be considered adequately treated to prevent transmission to the fetus, and newborn management will be affected.

- *It is recommended to perform a syphilis serology on the day treatment begins if more than one week has passed since the initial serology.*
- *Inform the patient of the risk of a Jarish-Herxheimer reaction during antibiotic treatment for syphilis. The risk of reaction is highest at the time of the first dose. The reaction can cause fetal distress and preterm labor. The presence of fever, contractions, or decreased fetal movements should be flagged as reasons for consultation.*

Specific considerations for pregnant women identified as contacts of a syphilis Case

- 1 dose of Benzathine Penicillin G is recommended for all pregnant women identified as contacts of a syphilis case, regardless of the timing of exposure.
    - Upon receiving the syphilis serology results, if it is confirmed that the pregnant woman is infected, she must then be treated with three doses of Benzathine Penicillin G.
- If the syphilis serology cannot be performed, the pregnant woman should be treated as a presumptive case, receiving 3 doses of IM Benzathine Penicillin G, even if she is only identified as a contact.

Recommended post-treatment serological follow-up

- **Monthly** until delivery, starting 8 weeks after the administration of the first dose
- At delivery or in the immediate postpartum period
- 6-8 weeks post-partum (during post-partum visit or ABCdaire visit at 2 months)
- Ensure that syphilis serology are performed at least at 3, 6, and 12 months post-treatment (and at 24 months in cases of late or tertiary syphilis)

Additional information:

- *RPR are monitored to detect reinfection, which would require new treatment, as well as treatment failures.*
- *The desired evolution of RPR in pregnant women with syphilis is as follows:*
    - *Fourfold decrease in RPR before birth[1] (e.g. from 1:64 to 1:16)* ***OR***
    - *Achievement of an RPR of ≤ 1:8*

Ultrasound follow-up

- Obstetric ultrasound 1 month post-diagnosis, but no earlier than 18-20 weeks
- Follow-up obstetric ultrasound at 28-32 weeks

Ultrasounds can be performed in Nunavik, but the clinical request should include "Rule out signs of congenital syphilis".

Additional information:

- *If the pregnant woman has not been adequately treated and/or shows abnormal RPR evolution, consult with a maternal-fetal medicine specialist to determine the appropriate ultrasound follow-up.*

[1] In the case of late infection, the mother's RPR may not decrease as much if it was already low to begin with.

Place of delivery and placenta analysis

- Determine the planned place of delivery during the perinatal committee meeting around 32-34 weeks, in consultation with the pediatric infectious disease specialist and other specialists as needed. Delivery in Nunavik is possible for a pregnant patient treated for syphilis if the overall follow-up is normal.
- Systematically request a pathological analysis of the placenta with the mention of syphilis in pregnancy.

Medical consultations[2]

Always involve the village physician or nurse practitioner (IPS) as soon as syphilis is diagnosed or suspected in a pregnant woman.

Systematic

Pediatric infectious disease specialist

- Consult the pediatric infectious disease specialist **systematically** during the perinatal committee around 32-34 weeks.
- Additionally, consult the pediatric infectious disease specialist in the following situations:
    - Preterm labor
    - Presence of signs of syphilis on ultrasound
    - Suboptimal progression of RPR or reinfection

As needed

Adult infectious disease specialist

- Consult the adult infectious disease specialist as needed, particularly in the following situations:
    - Uncertainty in establishing the diagnosis
    - Suboptimal progression of RPR
    - Suspected reinfection
    - Suspected neurosyphilis or tertiary syphilis
    - Proven allergy to penicillin

Maternal-fetal medicine specialist

- Consult the maternal-fetal medicine specialist as needed, particularly in the following situations:
    - Inadequate treatment regarding the risk of transmission to the fetus
    - Suboptimal progression of RPR
    - Presence of signs of syphilis on utltrasound

Allergist

- Consult the allergist in case of penicillin allergy to consider a challenge and desensitization if needed.

[2] During a consultation with a specialist involved in syphilis, always provide the following information: RAMQ number, date of birth, number of weeks of pregnancy, estimated due date, nature of symptoms if applicable, dates of administration of Benzathine Penicillin G doses, RPR progression (results and dates), information on the partner's syphilis status and treatment history, mention if the partner is untreated, and any abnormalities on ultrasound if present.

Newborns of mothers with reactive syphilis serology during pregnancy

Preliminary assessment of congenital syphilis risk

To assist the pediatric infectious disease specialist in assessing the risk of congenital syphilis for the exposed newborn, the following criteria should be evaluated:

Are the criteria for considering the mother adequately treated regarding the risk of fetal transmission met?

- Complete treatment received (3 doses administered on time) more than 30 days before delivery
- Benzathine Penicillin G received as treatment, not an alternative
- Desired progression of the mother's RPR

Are there supplementary elements raising the level of suspicion?

- Suspicion of re-exposure or inadequately treated reinfection in the mother
- Signs of congenital syphilis on ultrasound
- Clinical manifestations of syphilis in the mother at delivery

Initial evaluation of the newborn

- Perform syphilis serology at birth via venipuncture, not via the umbilical cord.
- Conduct a physical examination of the newborn at birth. Table 1 in the appendix outlines the clinical features and presentations of early congenital syphilis**.**

Consultation with the pediatric infectious disease specialist

Systematically consult with the pediatric infectious disease specialist at birth to determine the necessary serological follow-up and, if needed, additional physical and laboratory examinations[3]. Table 2 in the appendix presents the serological follow-ups that could be recommended based on the situation.

During follow-up, consult the pediatric infectious disease specialist as needed, especially in these situations:

- Presence of signs of congenital syphilis in the child
- Increase in the child's RPR
- RPR still reactive after 6 months of age
- Persistence of a reactive EIA at 18 months of age

Interpretation of serologies and expected progression in infants without congenital syphilis

- It is expected that EIA, RPR, and confirmatory tests may be positive in the newborn due to the transfer of maternal antibodies without necessarily indicating a diagnosis of congenital syphilis. These results should be interpreted with caution and correlated with the mother's RPR. The risk of congenital infection is significant when the newborn's RPR is four times higher (two dilutions) than the mother's at delivery.
- In an uninfected infant, a reactive RPR result due to passive transfer of maternal antibodies typically becomes negative by three months of age and should be negative by six months of age. Passive transfer of maternal EIA may persist longer but is often negative by 12 months of age and should be negative by 18 months of age in all uninfected infants.

[3] For example, the following tests might be recommended: CBC, liver enzymes and bilirubin, X-rays of long bones and clavicles, lumbar puncture: glucose, protein, VDRL, and cell count in cerebrospinal fluid (CSF), simultaneous blood glucose, audiogram, and ophthalmological examination.

Appendix

Table 1: Clinical features and presentations of early congenital syphilis

System	Feature
Growth	Low birth weight; failure to thrive*
General	Fever, pallor, jaundice, nonimmune hydrops, generalized lymphadenopathy, severe sepsis syndrome
Head and neck	Rhinitis, chorioretinitis, cataracts, uveitis, keratitis
Skin	Maculopapular*, desquamating*, or vesiculobullous lesions
Cardiorespiratory	Myocarditis, congestive heart failure, respiratory distress, pneumonia
Gastrointestinal	Hepatosplenomegaly*, necrotizing funisitis, pancreatitis, transaminitis
Central nervous system	Cranial neuropathies, meningitis, seizures, hearing loss
Musculoskeletal	Dactylitis, periostitis* leading to pseudoparalysis
Renal	Proteinuria, hematuria, or nephrotic syndrome
Other	May mimic other infectious diseases syndromes or congenital infections and non-infectious conditions (e.g., juvenile myelomonocytic leukemia)

*Common findings

Table 2: For reference, serological follow-ups that could be recommended based on the situation

Situation	Serological follow-ups
Newborn not treated, from a mother who was adequately treated **before** pregnancy (and without reinfection of the mother during pregnancy)	At birth 3 months * 6 months 12 to 18 months
Newborn not treated, from a mother who had syphilis adequately treated **during** pregnancy	At birth 2 months 4 months 6 months 12 to 18 months
Newborn who was treated for suspected/risk of congenital syphilis at birth	At birth 3 months 6 months 18 months
Newborn not treated, from a mother who had syphilis inadequately treated during pregnancy	At birth 1 month 2 months 3 months 6 months 12 months 18 months

* If EIA and RPR are non-reactive >3 months of age and maternal reinfection risk in late pregnancy remained low, no further testing indicate

References

INESSS – Optimal usage guide: Syphilis

Canadian Paediatric Society – Diagnosis and management of congenital syphilis

Public Health Agency of Canada – Canadian Guidelines on Sexually Transmitted Infections: Syphilis guide