BC Children's Hospital and
BC Women's Hospital + Health Centre

Congenital Syphilis-Its back!

Dr Chelsea Elwood MD MSc FRCSC
Dr Laura Sauve MD MPH FRCPC

Land Acknowledgement

I respectfully acknowledge that the land I work and live on is the unceded territory of the Coast Salish peoples, including the territories of the Səl̓ílwətaʔ/Selilwitulh (Tsleil-Waututh), the xʷməθkwəy̓əm (Musqueam) and Skwxwú7mesh (Squamish) Nations.

Those nations have cared for and nurtured the lands and waters around us for all time.

Disclosure

- The authors have no conflict of interest to disclose.
- LJS has research funding from PHAC, CIHR
- LJS is currently the Vice President of the Canadian Pediatric Society

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Key Objectives

- Be able to interpret syphilis diagnostics in pregnancy – and understand the resources that can help with that interpretation
- Identify which infants need a full workup and treatment
- Understand the follow up implications

Case: Mother

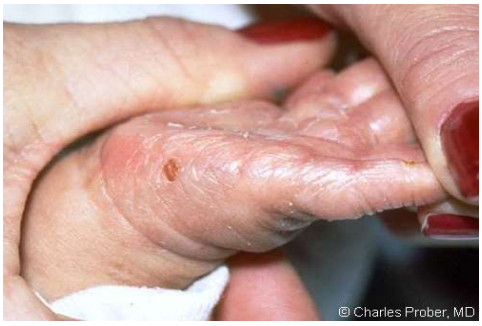
- 32 yo multipara from a rural area of BC
- substance use prior to pregnancy, stable relationship since diagnosis of pregnancy
- First trimester screening – Syphilis EIA negative
- 9w2d Dating USS – normal
- 18w: Illness with fever, diffuse rash (including palms and soles).
- Workup
  - Throat culture: No group A strep identified
  - Heterophile ab neg for mononucleosis, EBV IgG reactive
- USS 28w2d to assess for LLP detected FL < 10th centile (prev 70th centile at 20 week USS)
- Presented in spontaneous preterm labour at 31w2d- underwent emergency c/s for delivery due to breech presentation

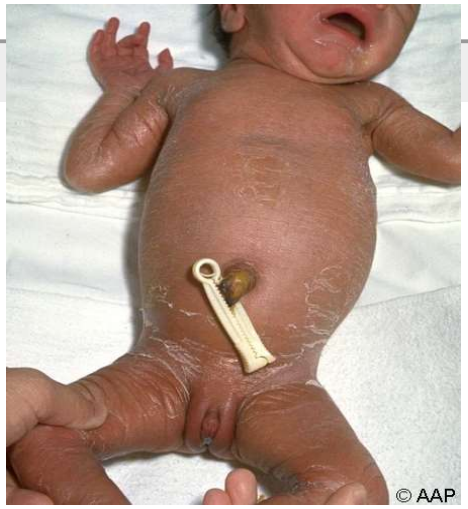
Case: Baby

- Baby born with respiratory distress and low apgars
- 12H required intubation and ventilation, anemic
- Progressive worsening hyperbilirubinemia, thrombocytopenia and anemia
- Hepatosplenomegaly
- Desquamation, especially extremities
- T/f to BCCH 1 day of life-> blood transfusion, 2x exchange transfusion

Red Book® Online

Red Book® 2018, 2018





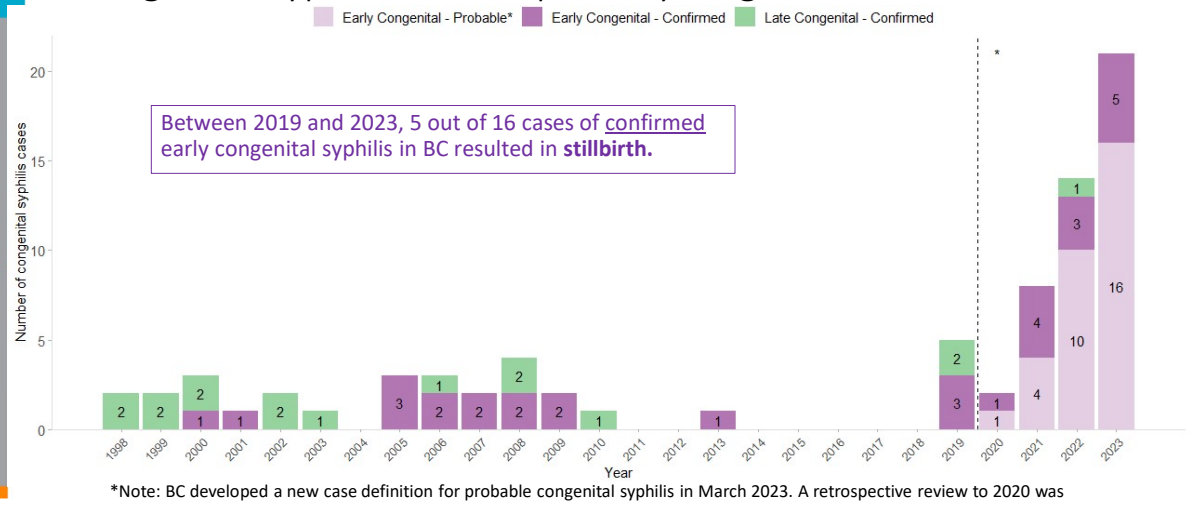
Marked generalized desquamation.

On day of life 4….

- RPR 1:512

Slide adapted from Dr R Stimpson

Congenital Syphilis Case Reports by Stage



Between 2019 and 2023, 5 out of 16 cases of confirmed early congenital syphilis in BC resulted in **stillbirth.**

*Note: BC developed a new case definition for probable congenital syphilis in March 2023. A retrospective review to 2020 was completed to identify cases that met the new probable congenital syphilis case definition. As a result, there are no probable congenital syphilis cases reported prior to 2020; trends should be interpreted with caution.

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Case data were extracted on February 10, 2024 from Intrahealth Profile EMR. Data are preliminary and subject to change.

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Syphilis in Pregnancy

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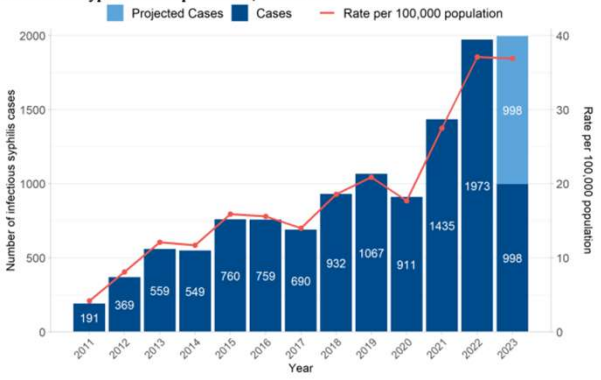
Syphilis in BC

1. Infectious syphilis case reports in BC, 2011-2023*



*Projected case counts/rates assume that the average number of reported cases per month year to date (YTD) will remain constant throughout 2023. See technical appendix (calculations) for more details.
Note: 2018 to 2023 case counts are subject to change. Infectious syphilis case reports exclude congenital syphilis cases.

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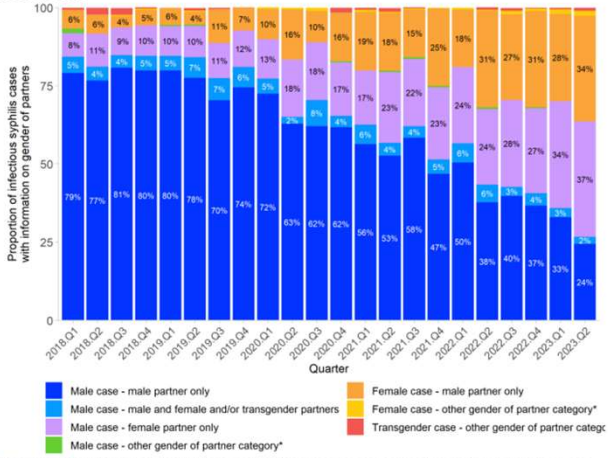
Syphilis in BC

14. Proportion of infectious syphilis case reports by gender of sexual partner and by quarter, 2018 to 2023



Note: Gender of sexual partner is based on the "gender of sexual partners" variable values collected in Intrahealth Profile EMR which is structured as male, female, transgender and unknown. Data shown reflect male, female, and transgender responses only.

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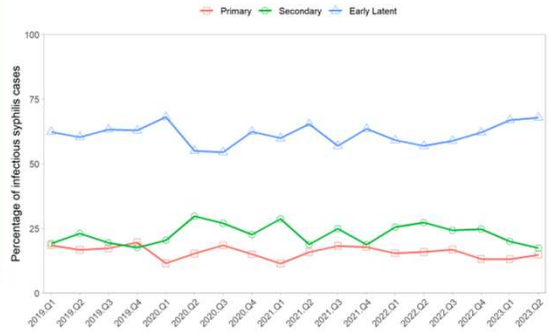
Syphilis in BC

Infectious Syphilis in by Stage of Infection

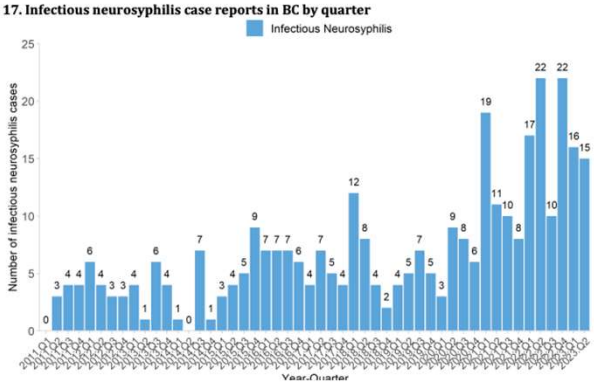
16. Proportion of infectious syphilis case reports in BC by stage of infection and by quarter



Note: Early Latent cases include both Early Latent and Early Latent Probable Stages

Infectious Neurosyphilis

17. Infectious neurosyphilis case reports in BC by quarter



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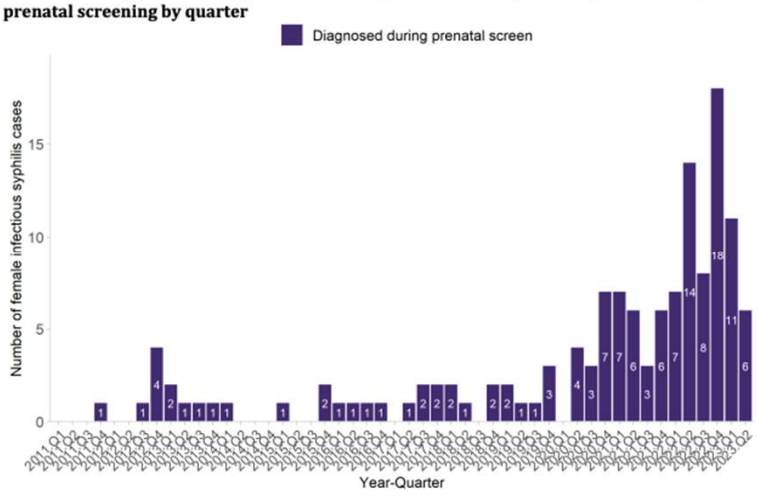
Infectious Syphilis Diagnosed During Prenatal Screening

22. Infectious syphilis case reports in BC among females 15-49 years diagnosed during prenatal screening by quarter



Note: Includes maternal infectious syphilis cases aged 15-49 years from STI-IS (cases prior to March 13, 2018) and female infectious syphilis cases aged 15-49 years who were indicated as being pregnant at their time of diagnosis in Intrahealth Profile EMR (cases from March 13, 2018 onwards).

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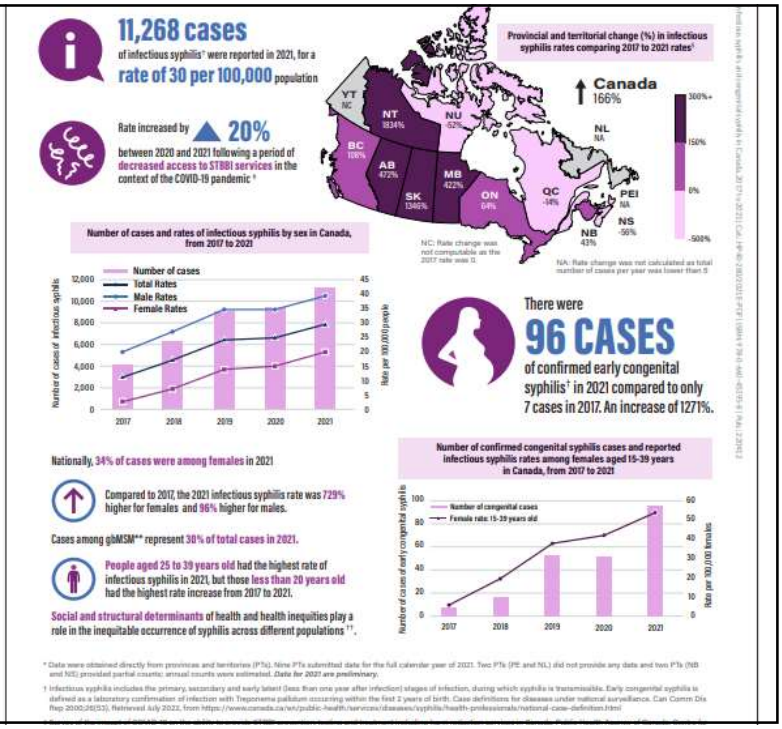
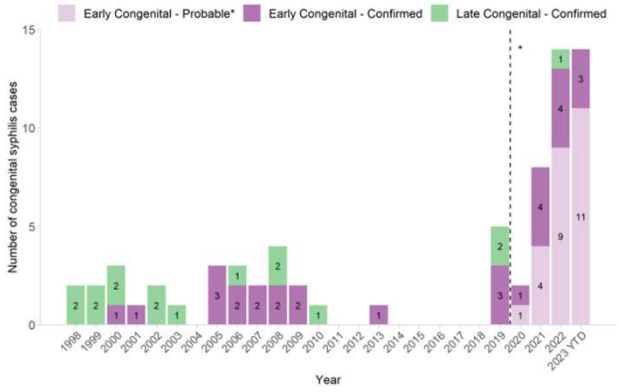
Congenital syphilis in Canada



Congenital Syphilis

From 2019 – present, there have been at least 5 fatal cases (either stillbirth or death in the first 7 days of life)



YTD = January to June 2023

*BC developed a new case definition for probable congenital syphilis in March 2023. A retrospective review to 2020 was completed to identify cases that met the new probable congenital syphilis case definition. As a result, there are no probable congenital syphilis cases reported prior to 2020; trends should be interpreted with caution.

From BCCDC Q2 Syphilis report
http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Statistics%20and%20Reports/STI/Syphilis_indicators_2023Q2.pdf

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2019 Delivery Screen for all Patients Recommended in BC

- Risk factors for a diagnosis of syphilis in pregnancy
  - Limited or no prenatal care
- 19 cases of maternal syphilis
  - 8 had a previous negative test
  - 11 had no other testing

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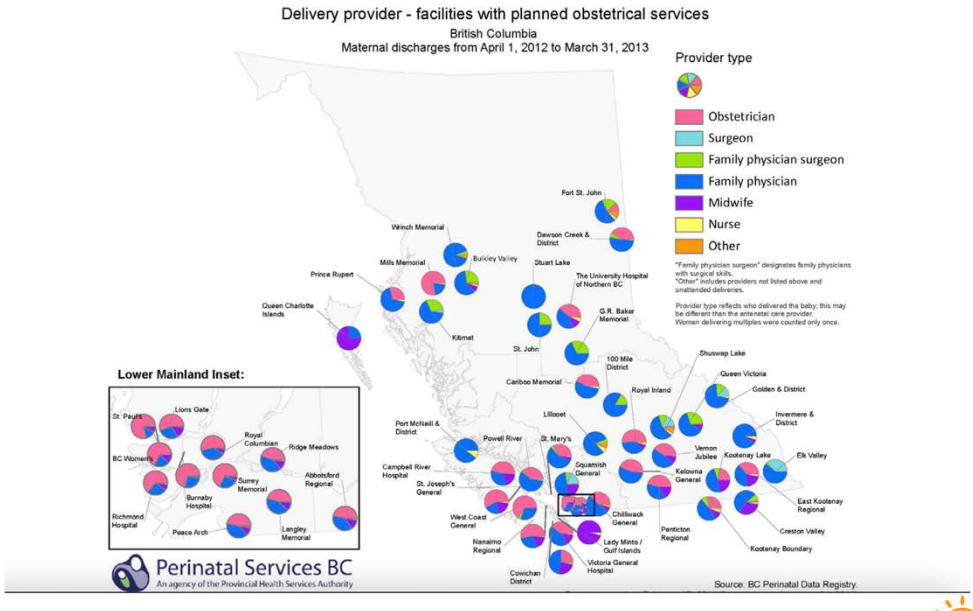

Syphilis

A. Primary
B. Secondary
C. Early latent
D. Late latent

60-90%

40%

10%

Most babies with congenital syphilis are asymptomatic at birth – so a lack of symptoms at birth is not reassuring

Risk of congenital infection and sequelae 1% if adequately treat mother

Syphilis in Pregnancy

- Spontaneous abortion
- Stillbirth (21%)
- Nonimmune hydrops
- Preterm birth (6%)
- Perinatal death (9%)
- Congenital syphilis (16%)

PLoS One. 2019; 14(2): e0211720.
Published online 2019 Feb 27. doi: 10.1371/journal.pone.0211720
PMCID: PMC6392238
PMID: 30811406

Global burden of maternal and congenital syphilis and associated adverse birth outcomes—Estimates for 2016 and progress since 2012

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Treatment in Pregnancy

- **Pregnant** women should be treated with the penicillin regimen appropriate for their stage of infection.
- Pregnant women who have a history of penicillin allergy should be desensitized and treated with penicillin.
- Penicillin G long-acting and is present for 2-4 weeks after injection in detectable levels in serum

Public Health Agency of Canada | Agence de la santé publique du Canada

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Treatment follow up

- Successful Treatment 4 fold decrease in RPR/VDRL titer over 3-6mths
- If the decline is slower, consider reinfection with syphilis
- Non-treponemal tests may revert to negative or remain “serofast’
- Treponemal Specific tests will remain positive and are thus not useful in monitoring treatment or for diagnosing reinfection

Cohen, S. E., Klausner, J. D 2013, Mattei, P. L2013

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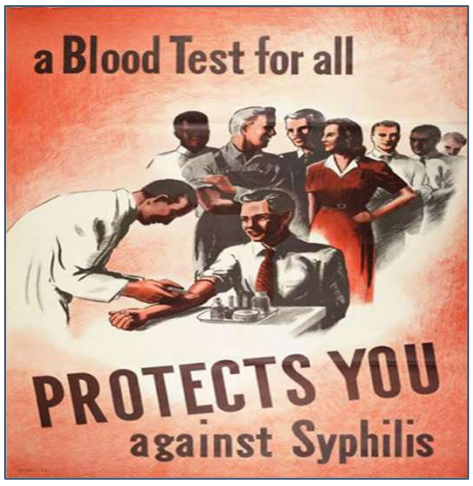
Syphilis Serology

- *Treponema pallidum* enzyme immunoassay (TP EIA)
- Rapid Plasma Reagin (RPR)
- *Treponema pallidum* Particle Agglutination (TPPA)



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Congenital syphilis manifestations

Before / At birth

- stillbirth, hydrops fetalis, IUGR, preterm birth (or may be asymptomatic at birth).

Neonatal

- hepatosplenomegaly; snuffles (copious nasal secretions); lymphadenopathy; mucocutaneous lesions; pneumonia; osteochondritis, periostitis, and pseudoparalysis; edema; rash (maculopapular consisting of small dark red-copper spots that is most severe on the hands and feet); hemolytic anemia; or thrombocytopenia at birth or within the first 4 to 8 weeks of age.

Late (infancy / childhood)

- Involve the central nervous system (CNS), bones and joints, teeth, eyes, and skin.
- Includes… interstitial keratitis, eighth cranial nerve deafness, Hutchinson teeth (peg-shaped, notched central incisors), anterior bowing of the shins, frontal bossing, mulberry molars, saddle nose, rhagades (perioral fissures), and Clutton joints (symmetric, painless swelling of the knees).

https://www.cps.ca/en/documents/position/congenital-syphilis
Red Book, Syphilis chapter

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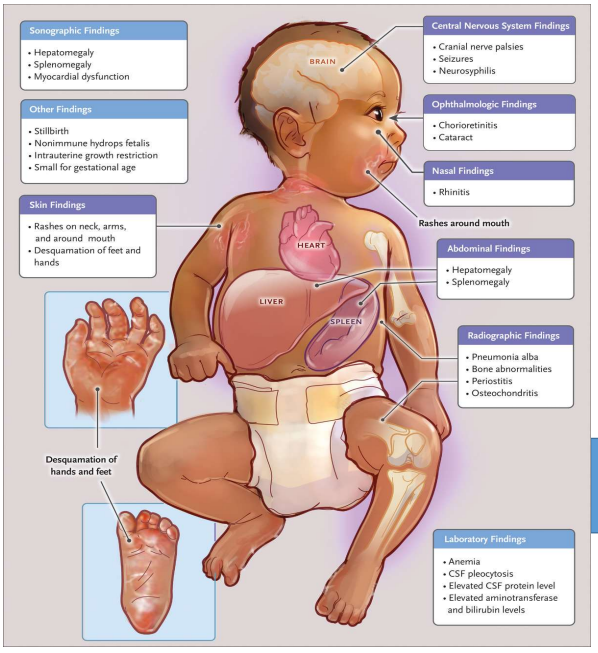
Clinical Signs of Early Congenital Syphilis



The NEW ENGLAND JOURNAL of MEDICINE

IA Stafford et al. N Engl J Med 2024;390:242-253.

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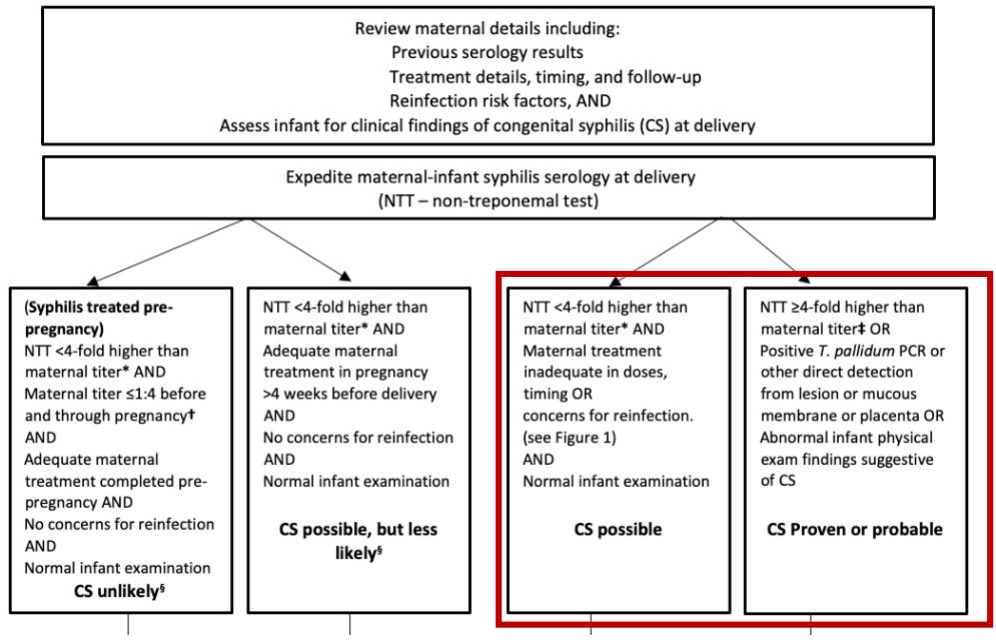
Figure 2. Initial management of infants born to mothers with positive syphilis serology



Assessment of infant born to person with syphilis in pregnancy: Key questions

Most babies with congenital syphilis are asymptomatic at birth – so a lack of symptoms at birth is not reassuring

Mother treated with penicillin?

- Consider "**no**" if unknown

Maternal treatment completed >4 weeks before delivery?

Treatment adequate for stage of infection?

- Early – 1 dose penicillin IM
- Latent / unknown – 3 doses penicillin IM
- Neurosyphilis – 10-14 days penicillin IV

Adequate treatment response documented?

- Yes if >4-fold decline – eg 1:64 to 1:16 or less
- Note: latent infections may not demonstrate 4-fold decline

If no to any of these, consider infant at **high risk**

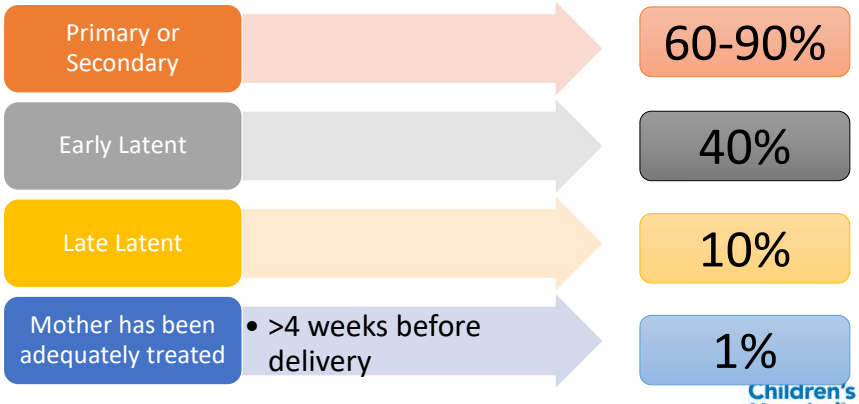
Assessment of infant born to person with syphilis in pregnancy

- Key questions - If **no** to any of the key questions – consider the infant at **high risk**
- Also high risk if:
  - Maternal reinfection or re-exposure without adequate treatment
  - Ultrasound consistent with congenital syphilis
  - Clinical concerns / features at delivery

Most babies with congenital syphilis are asymptomatic at birth – so a lack of symptoms at birth is not reassuring

https://www.cps.ca/en/documents/position/congenital-syphilis
Red Book, Syphilis chapter

A note on staging…
Be skeptical of what is written in the chart about staging. Call BCCDC for help!



Work up for infants at moderate – high risk

- Recommended for all:
  - Serology in mom (if possible) & baby
  - Complete Blood Count (CBC) with differential and platelets
  - Liver function tests (e.g ALT, AST; others as clinically indicated)
  - CSF for cell count, differential, glucose, protein, and syphilis NTT serology
  - Long-bone radiographs (e.g., bilateral femur and tibia/fibula)
  - Audiology (auditory brain stem response)
  - Ophthalmologic Assessment - Ocular syphilis can occur at any stage - more common in infants with neurosyphilis.
- Additional Investigations (Based on Clinical Indication and Availability):
  - Neuroimaging / ultrasound for organomegaly
  - Nasopharyngeal swab and swabs of any mucosal or skin lesions for T. pallidum PCR
  - Pathologic examination (+/- T. pallidum PCR) of the placenta for women with concerns for active infection at birth
- Don't forget - There is a window period, so if baby appears to have congenital syphilis even if 1st trimester screening negative, do the full work up.

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Slide adapted from Dr R Stimpson

Neonatal Serology at Delivery

- RPR only on baby (**NOT CORD BLOOD**)
- TP EIA- will be positive if mother is positive and generally uses up all the blood
- TPPA- will be done after RPR as a confirmatory test (again if mother's TPPA is reactive baby will also be reactive due to passive transfer of maternal antibodies)

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Slide adapted from
Dr R Stimpson

Syphilis PCR

- Can be obtained from nasal secretions, visible lesions, rashes, umbilical cord, placenta

Image property of BCCDC. Not for re-use

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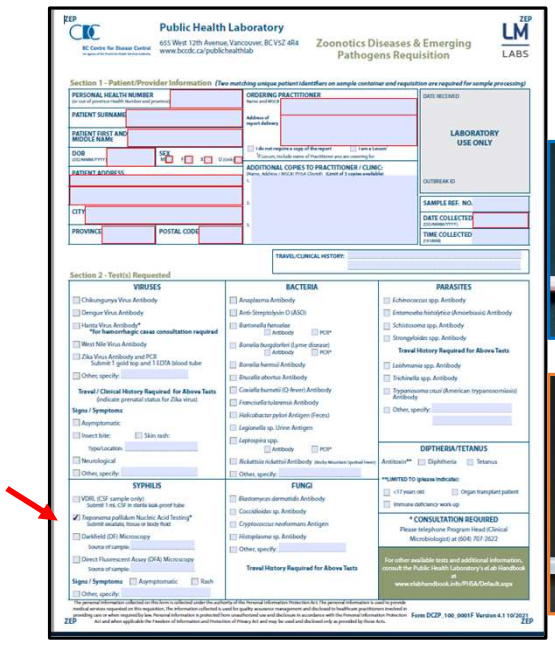
Province-wide solutions. Better health.



Slide adapted from
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Do I really need to do an LP?....

Symptomatic / Probable syphilis / High risk for syphilis

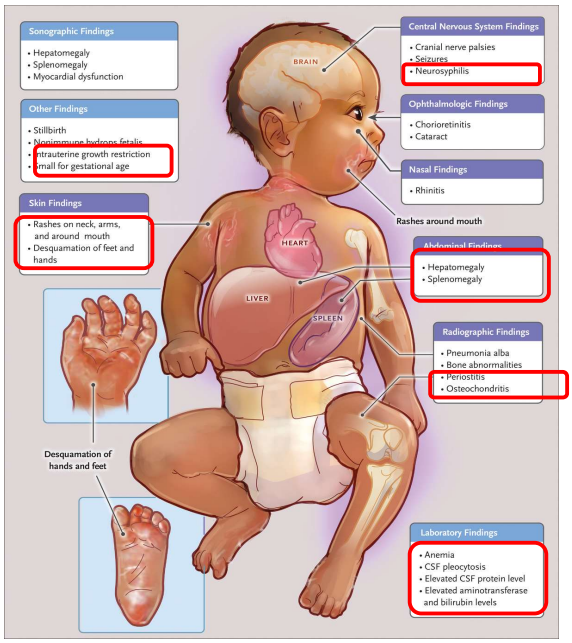
- YES
- Developmental delay, hearing, eye involvement all more likely in confirmed neurosyphilis
- If CSF VDRL is positive – ophthalmology & audiology follow up very important

Possible syphilis / Low risk

- Potentially can avoid – even if treatment planned

Lim, J., Yoon, S.J., Shin, J.E. et al. Outcomes of infants born to pregnant women with syphilis: a nationwide study in Korea. BMC Pediatr 21, 47 (2021). https://doi.org/10.1186/s12887-021-02502-9

Case



- RPR –
  - Birth: 1:512
  - 12 Weeks: 1:4
  - 6 mo: 1:1
  - 12 mo: NR

Treated with penicillin IV x 10 days

Case

- Prematurity (born at 30 weeks)
- Physical findings (rash, HSM, sepsis)
- LP – VDRL initially positive – follow up negative
- Long bones – symmetric periosteal reaction & metaphyseal changes
- Audiology – normal
- Ophthalmology – no retinitis

- RPR –
  - Birth: 1:512
  - 12 Weeks: 1:4
  - 6 mo: 1:1
  - 12 mo: NR
- Elevated liver enzymes
- Anemia & thrombocytopenia
- Jaundice (required exchange transfusion)

Treated with penicillin IV x 10 days

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Case: at 1 year

- Thriving – no further health concerns
- Development normal – connected to AIDP
- Follow up with general pediatrician
  - There were some ongoing barriers to care including transport difficulties, difficulty making appointments

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Treatment

- **IV Aqueous crystalline penicillin G 50,000 U/kg/dose IV x 10 days**
  - Under 1 week - Q12h
  - 8-28 days - Q8h
  - Above 28 days - Q6h
- While some sources recommend routinely restarting the course of therapy if >24 hours is missed, evidence behind this is not clear
- Rather than missing doses while awaiting IV replacement…
  - daily IM procaine penicillin 50,000 units/kg/dose for each of the days that intravenous access is not available may be considered (but no current availability)
  - Some experts recommend ceftriaxone but many are hesitant due to lack of documented efficacy

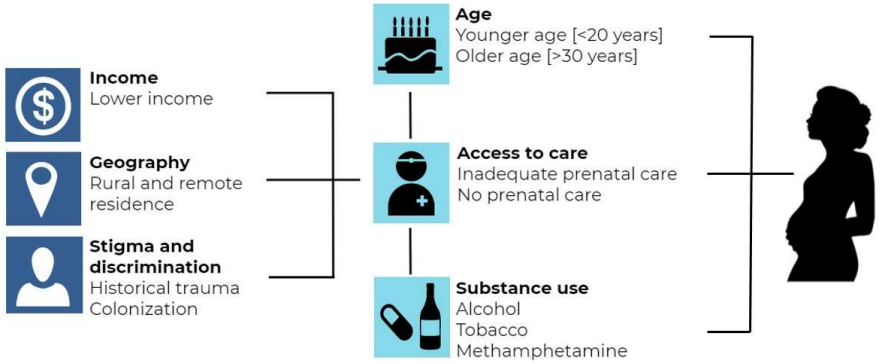
https://www.cps.ca/en/documents/position/congenital-syphilis
Red Book, Syphilis chapter

Post-discharge care

- There is a risk of failure of cure, therefore close clinical follow up needed
- CPS / AAP recommend:
  - Monthly clinical exams x3 months
  - Syphilis serology repeat at 3, 6 and 18 months
    - Note: batch bloodwork with other follow up labs (e.g. Hep B at 7mo if primary immunization series)
    - RPR should be declining by 3 months and substantially improved/resolved by 6 months
    - Maternal transplacental EIA/TPPA should resolve by 18 months but if endogenous, may persist
  - No need to repeat LP unless there is evidence of treatment failure

https://www.cps.ca/en/documents/position/congenital-syphilis
Red Book, Syphilis chapter

PHAC: Most commonly reported risk factors associated with maternal syphilis and related congenital syphilis in the Canadian literature



Teams in caring for syphilis in pregnancy & exposed / infected infants

- Genearl pediatricians / Primary care / midwife → lead the care locally.
  - No newborn should be discharged without the delivery syphilis testing!
  - Recognize the intersectionalities / barriers to care – trauma aware & antiracist care are critical.
  - All infants with CS should have some form of well child care & developmental surveillance with a healthcare provider following their course of treatment.
- BCW Reproductive ID & BCCH Pediatric infectious diseases on call available 7 days / week to answer questions
- Oak Tree Clinic outpatient consultations
  - Post discharge: BCW Oak Tree Clinic – provides shared care with community providers (available Monday – Friday to discuss cases as needed) for those who were treated for possible or confirmed syphilis
- BCCDC Syphilis program – tracks all syphilis exposed infants and available Monday – Friday to discuss cases as needed – especially assessment of maternal testing and treatment.
- Regional public health – can support connections to care when there are multiple barriers to care

How Can the BCCDC Syphilis Team support your work?

- Questions? Please call:
  - *RACE line (Sexually Transmitted Infection Service)*
  - *BCCDC Syphilis Physician- 604-707-5610 (M-F)*
- Syphilis Diagnosis and Treatment Records:
  - *BCCDC has records for the province dating back decades*
  - *Relationships with other provinces to obtain out-of-BC records*

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Resources

- BC Children's Hospital Pediatric Infectious Diseases – via locating 604-875-2212
- BC Women's Hospital Reproductive Infectious Diseases – via locating 604-875-2212
- BCCDC Syphilis Physician- 604-707-5610 (M-F)
- Oak Tree Clinic – http://www.bcwomens.ca/our-services/specialized-services/oak-tree-clinic
- Canadian Pediatric Society Infectious Diseases and Immunization Committee
  - https://cps.ca/en/documents/authors-auteurs/infectious-diseases-and-immunization-committee
  - Reducing perinatal infection risk in newborns of mothers who received inadequate prenatal care
    - https://cps.ca/en/documents/position/reducing-perinatal-infection-risk-in-newborns-of-mothers-who-received-inadequate-prenatal-care
  - The management of infants, children, and youth at risk for hepatitis C virus (HCV) infection
    - https://cps.ca/en/documents/position/the-management-of-hepatitis-c-virus
  - Congenital syphilis *(update underway)*
    - https://cps.ca/en/documents/position/congenital-syphilis
- American Academy of Pediatrics Red Book
  - Syphilis Chapter - https://publications.aap.org/redbook/book/347/chapter/5756873/Syphilis
- Perinatal Services BC
  - Guidance
    - http://www.perinatalservicesbc.ca/Documents/Resources/Alerts/FAQs-for-OB-care-providers-Syphilis-screening-in-pregnancy.pdf
  - Congenital syphilis handout for families
    - http://www.perinatalservicesbc.ca/Documents/Resources/Alerts/patient-resource-syphilis-in-pregnancy.pdf?_gl=1*t2lujj5*_ga*MTQ1NDAxMTUxMy4xNjczMzk5ODA5*_ga_ZKY1XG50LJ*MTcwMTY1MjQ1Mi4zNS4wLjE3MDE2NTI0NTMuMC4wLjA.
- BCCDC
  - Communicable Disease Manual
    - http://www.bccdc.ca/resource-gallery/Documents/Communicable-Disease-Manual/Chapter%205%20-%20STI/Non-certified%20Syphilis%20DST.pdf

Thank you!
Questions?

Routine syphilis testing in pregnancy by trimester

First	Second	Third
Serology for **all**	Serology for any with risk factors	Serology for **all**
	Serology + PCR where appropriate for symptomatic	Serology + PCR where appropriate for symptomatic

If loss to follow up a concern, ensure that 3rd trimester test results are available prior to discharge of the baby.