

The Global Crisis of Congenital Syphilis: Vulnerable and Disenfranchised Women Most at Risk

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Abstract: Congenital syphilis (CS), previously considered by many paediatricians as a “historical disease”, has re-emerged as a significant preventable neonatal infection. While low-income countries have the highest burden of disease globally, notifications have increased in many high-income countries (HIC) in recent years. This literature report provides an overview of the current strategies for testing and treating syphilis in pregnancy (SIP) and CS and describes the changing global epidemiology of SIP. National SIP guidelines are reviewed with reference to testing in pregnancy and treatment of CS. The report highlights that there is an ongoing crisis of CS in HICs worldwide and a disproportionate burden is being experienced by vulnerable populations in these countries. Action is needed to address this crisis, and interventions aimed at overcoming social and structural barriers to antenatal care access for vulnerable populations should be prioritised.

Keywords: syphilis, pregnancy, congenital, epidemiology

Introduction

Despite an estimated decrease in the global incidence of CS of 12% between 2012 and 2016, the disease has re-emerged as a major public health concern in HIC where rates have historically been very low.^{1–6} Data suggests that the rise in CS disproportionately affects the vulnerable populations in these countries.^{1,2,7–16} While the African region holds the highest burden of the disease – estimated by the World Health Organization (WHO) as 62% of the worldwide CS burden, this review will focus on this trend in HIC.¹⁷

Congenital syphilis (CS) is caused by the vertical transmission of *Treponema pallidum*. Syphilis has been named “the great mimicker”, and the consequences of CS are both varied and devastating. In cases where SIP goes untreated, 67% of women will have an adverse outcome of pregnancy, including 26% who will have a fetal loss or stillbirth.¹⁸ Infants that survive may develop serious short- and long-term health consequences including meningitis, anaemia, bone abnormalities, and other disability.¹⁹ Diagnosis can be difficult given that neonates are often asymptomatic at birth. In addition to specific syphilis testing, investigations for an infant at risk of CS should include ophthalmology examination, chest and long bone radiographs, assessment of cerebrospinal fluid (CSF), full blood count (FBC), and blood chemistry (see Figure 1).²⁰

With universal antenatal screening, SIP can be effectively treated with administration of penicillin, and thus CS is entirely preventable.²¹ The WHO EMTCT program is a global initiative for the elimination of mother-to-child transmission (MTCT) of HIV, syphilis, and hepatitis B virus.²² In 2014, WHO released the first edition of the global EMTCT guidance, the “Orange Book”,²³ to provide guidance for quality healthcare provision, interventions, and monitoring in order to make progress towards elimination. As of 2023, 17 countries have been validated by WHO to have achieved elimination of MTCT of syphilis to a level where it is no longer a public health threat – most of which are lower- and upper-middle income countries, as well as some small HIC including Oman and Anguilla.²⁴

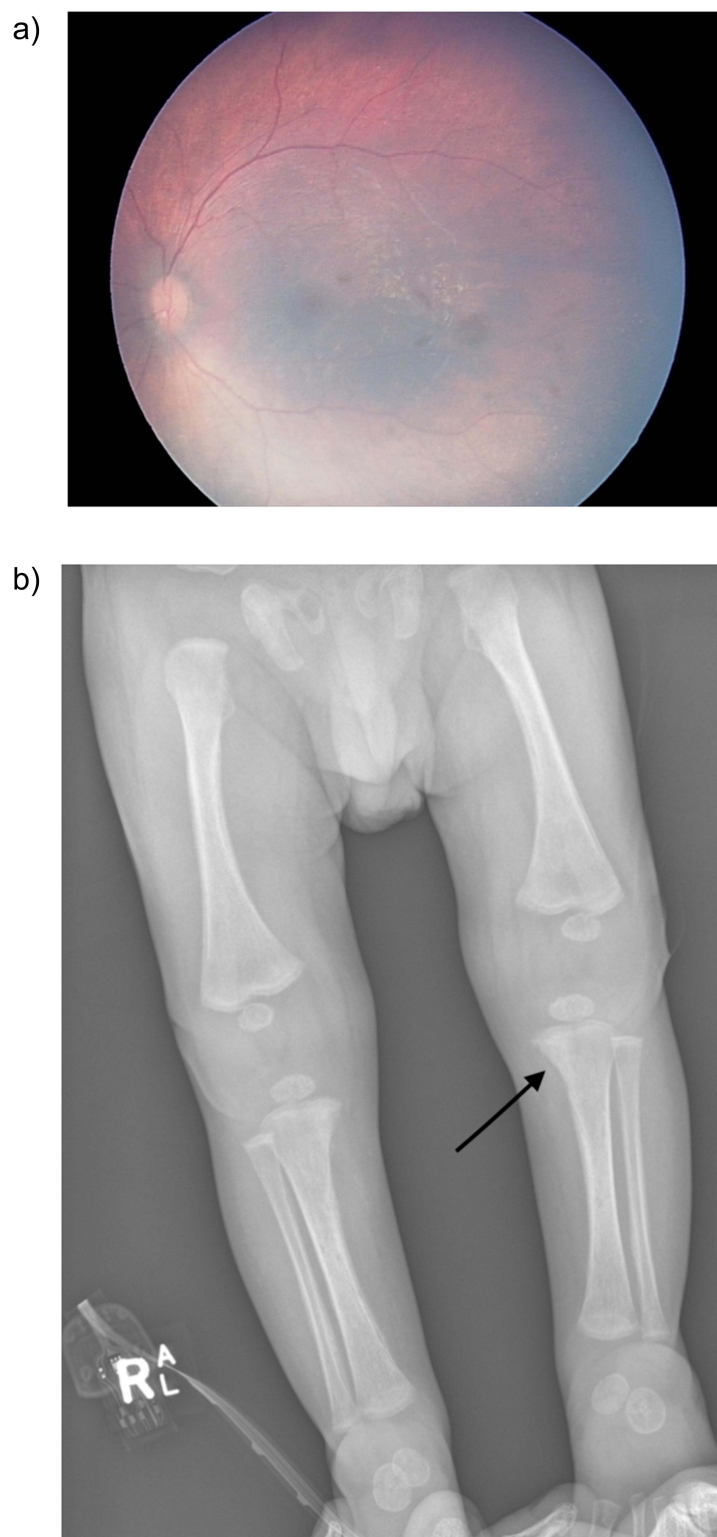


Figure 1 Typical features of congenital syphilis. **(a)** Chorioretinitis as evidenced by mottled “salt and pepper” pigmentary retinal changes on fundoscopy. **(b)** Early erosions of the mid metaphysis of the distal femur and medial proximal tibia (Wimberger’s sign – see arrow) and generalised periostitis on long bone X-ray. Reprinted from Wu MX, Moore A, Seel M, et al. Congenital syphilis on the rise: the importance of testing and recognition. *Med J Aust.* 2021;215(8):345–346 e341. © 2021 AMPCo Pty Ltd.¹⁹

Methodology

An exhaustive literature search was performed of databases including PubMed, Cochrane Library, UptoDate, CINAHL, and ClinicalKey. Papers published in the last decade were screened for review in more detail based on the relevancy of their titles and abstracts. Relevant epidemiological data were extracted and collated for the review.

Epidemiology of Congenital Syphilis – Rising Numbers in High Income Countries

Western Pacific Region

In Australia, 2020 marked the highest number of cases (n=17) diagnosed in one year since 2001.⁷ Twenty-four cases of CS were reported in New Zealand from 2017 to 2021 where prior to 2016, there had been only one reported case which was in 2011.²⁵ In China, CS rates have increased from 0.01/100 000 live births in 1991, to 19.68/100 000 live births in 2005, which is an average yearly rise of 71.9%.²⁶ This prompted the 2010 issue of the 10-year Plan for Syphilis Control and Prevention in China, with a goal to reduce CS to <15/100 000 live births. As a result, increased coverage of testing for pregnant women, increased treatment of SIP and prophylactic treatment of newborns born to women with SIP were effectively implemented.²⁷ Between 2011 and 2018, CS incidence in China reduced from 91.6/100 000 cases per live births to 18.4/100 000.²⁷ During this time, rates of SIP continued to increase, however MTCT and CS decreased.²⁷ In Japan, syphilis cases have increased to levels not seen since the 1970s, including a pronounced increase in cases in heterosexual men and women and a concomitant rise in CS.^{5,6}

Region of the Americas

In the United States (US), CS rates have increased almost every year since 2012.² From a record low of 8.4 cases per 100 000 live births in 2014, there has been a 927% increase to 77.9 cases per 100 000 live births in 2021. This is a 319% increase in 5 years alone, from 24.4/100 000 live births in 2017.² In 1998, Canada announced a national goal of maintaining syphilis rates less than 0.5/100 000 population.²⁸ Despite this, syphilis cases began to steadily increase in the early 2000s, with a more rapid increase since 2017. From 2016 to 2020, infectious syphilis rates among females alone increased by 773%, compared to a 73% increase in rates among males. Ninety-six CS cases were reported in 2021²⁹ – a massive increase from 4 reported cases in 2016 (2400% increase), and a maximum of 10 reported each year between 2011 and 2017.¹ Mexico reported an increased incidence of syphilis between 2010 and 2019, most concentrated in the population of reproductive age, with a notable increase in cases in women aged 24–29 years old.³ Alongside this, an exponential growth in CS cases has been reported, with 372 cases reported in 2019 compared to 62 cases in 2010.³

European Region

In England, infectious syphilis cases are increasing among women in particular, with rates in 2022 the highest since 1948, and demonstrating a 236% increase since 2014.³⁰ The rate of SIP has been steadily increasing, with a rise from 56/100 000 women between 2016 and 2017 to 72/100 000 women between 2020 and 2021. There were 39 confirmed cases of CS in England between January 2015 and December 2021.^{15,31} In 2019, 72 confirmed cases of CS were reported in the European Union/European Economic Area (EU/EEA), marking the 2nd consecutive year in which case numbers have notably increased. Previously, CS rates across the EU/EEA had been steadily declining since 2010, with just 44 cases in 2016. The vast majority of cases in recent years occurred in Bulgaria, followed by Portugal.⁴

Testing in Pregnancy (See Table 1)

WHO guidelines recommend testing all pregnant women for syphilis during the first antenatal care visit.²¹ Trinh et al reviewed 62 STI treatment guidelines published during 2003–2017, representing 128 countries. Fifty-seven (92%) of the guidelines recommended universal syphilis testing in pregnancy and 46 (81%) recommended initial testing early in pregnancy. In addition to universal testing at the first antenatal visit, 21 (46%) guidelines recommended repeat syphilis testing in the third trimester or at delivery.^{44,45} Many guidelines include repeat syphilis testing for at-risk populations in the third trimester and at delivery, with most guidelines specifying risk factors that would meet this criterion. Common

Table 1 National Guidelines for Testing and Treatment of SIP in Select HICs

Source	Testing in Pregnancy	Indication for Re-Testing	Gestation for Re-Testing	Indication for Treatment	Adequate Treatment ^a
World Health Organization (WHO) ³²	Traditional algorithm ^b Single on-site RST ^c in settings with low coverage of testing and treatment, high loss to follow up, or limited laboratory capacity	N/A	N/A	Active syphilis confirmed on testing	Primary, secondary or early latent syphilis: Benzathine penicillin G (BPG) 2.4 MU IM daily for 10 days Late or unknown stage: BPG 2.4 MU IM weekly for 3 weeks. Interval between doses should not exceed 14 days.
Centers for Disease Control 2021 ³³	Traditional or reverse sequence ^d algorithm	Lives in an area with high syphilis morbidity Sex in conjunction with drug use or transactional sex Incarceration of the woman or her sexual partner, drug misuse, unstable housing or homelessness Other STIs during pregnancy or sexual partner with STIs Multiple or new sexual partners Late or no prenatal care	28 weeks and at delivery	Active syphilis of any stage Previous syphilis without documentation of adequate treatment with serological response	Primary, secondary or early latent syphilis: BPG 2.4 MU IM single dose ± a second dose 1 week later Late latent syphilis: BPG 2.4 MU IM weekly for 3 weeks. Interval between doses should not exceed 9 days or the full course should be restarted. Desensitisation if allergic to penicillin.
Canadian Guidelines 2022 ³⁴	Traditional or reverse sequence algorithm	Lives in an area with a syphilis outbreak Ongoing risk (not defined)	28–32 weeks and at delivery	Active syphilis of any stage Clinical or serological evidence of new infection Inadequate serological response to previous treatment Recent sexual partner with infectious syphilis	Primary, secondary and early latent syphilis: BPG-LA (long acting) 2.4 MU IM single dose ± a second dose 1 week later (particularly in the third trimester). Late latent cardiovascular syphilis and gumma: BPG-LA 2.4 MU IM weekly for 3 weeks. Desensitisation if allergic to penicillin.

UK National Screening Committee ³⁵ UK Guidelines 2015 ³⁶	Traditional algorithm	Risk of re-infection (not defined)	Not defined	Active syphilis of any stage Previous syphilis without documentation of adequate treatment with serological cure	Early syphilis: 1st or 2nd trimester: BPG 2.4 MU IM once 3rd trimester: BPG 2.4 MU IM on days 1 and 8 Late latent, cardiovascular and gummatous syphilis: BPG 2.4 MU IM weekly for 3 weeks on days 1, 8 and 15 Desensitisation if allergic to penicillin
Australian National ³⁷ and state-based ^{20,38,39} Guidelines	TT ^e , confirmed with alternative TT NTT ^f in those with previously treated syphilis	Lives in an area with outbreaks or high prevalence of syphilis STI in last 12 months or previous SIP IVDU Sexual partner who is at high risk for syphilis	28–32 weeks and at delivery In areas with ongoing syphilis outbreaks, re-test at 28 and 36 weeks, delivery and 6 weeks post	Active syphilis of any stage In areas affected by an outbreak, treat without waiting for test results, particularly if at risk of loss to follow-up	Primary, secondary and early latent syphilis: BPG 2.4 MU IM once. South Australian Guidelines ³⁹ recommend an additional dose 2 weeks later if in the third trimester. Late latent or unknown duration: BPG 2.4 MU IM weekly for 3 weeks on days 1, 8 and 15.
The New Zealand Sexual Health Society (NZSHS) Syphilis in Pregnancy Antenatal Management Guidelines ^{40g}	Reverse sequence algorithm	No or inconsistent antenatal care STI in last 12 months, recreational drug use, homelessness or incarceration in the past year Multiple sexual partners, or a sexual partner with risk factors as above or is a man who has sex with men	28–32 weeks and at delivery	Active syphilis of any stage	Early syphilis: 1st or 2nd trimester: Benzathine benzylpenicillin tetrahydrate 2.4 MU IM once 3rd trimester: Benzathine benzylpenicillin tetrahydrate 2.4 MU IM on days 1 and 8 Latent or unknown stage: Benzathine benzylpenicillin tetrahydrate 2.4 MU weekly for 3 weeks on days 1, 8 and 15

Notes: ^aThis table refers to treatment of the woman with SIP. See Table 2 for treatment of CS of the infant. ^bTraditional algorithm = non treponemal test (NTT eg RPR or VDRL) for screening, followed by confirmation with treponemal testing (TT)(TTs such as FTA, TP-PA, TP-HA, and EIA detect antibodies specific to syphilis and do not distinguish between active and previously treated infections). ^cRST = rapid sequence test for treponemal antibodies. ^dReverse sequence algorithm = TT for screening, followed by confirmation with NTTs. Discordant results are resolved with an alternative treponemal test. ^eTT = treponemal test. ^fNTT = nontreponemal test. ^gAlthough official guidelines are yet to be updated, the NZSHS released a statement in December 2020 strongly recommending universal retesting for syphilis at 28–32 weeks. ^h

Table 2 National Guidelines for Testing for and Treatment of CS in Select HICs

Source	Indication for Testing	Neonatal/Infant Testing	Indication for Treatment	Treatment
World Health Organization (WHO) ³²	Known or suspected exposure to syphilis during pregnancy	Not defined	CS confirmed on testing Maternal SIP that was untreated or treated inadequately, within 30 days of delivery, or with non-penicillin regimen NTT ^a 4x higher than maternal NTT at delivery	IV Aqueous benzyl penicillin G (BPG) 100 000–150 000 units/kg/day for 10–15 days OR IM Procaine penicillin 50 000u/kg daily for 10–15 days
Centers for Disease Control 2021 ³³	Reactive maternal NTT and TT ^b serology at delivery Clinical, laboratory or radiographic evidence of CS	Quantitative NTT serology After treatment: repeated serologic testing every 2–3 months until nonreactive If mother seroreactive at delivery but CS unlikely: retest at 3 and 6 months	Positive testing of placenta, cord, lesions or body fluids Maternal SIP that was untreated or treated inadequately, within 30 days of delivery, or with non-penicillin regimen NTT 4x higher than maternal NTT at delivery or reactive NTT at 6 months of age	IV crystalline penicillin G 50000 units/kg/dose (12 hourly in the first 7 days of life and 8 hourly thereafter) for 10 days OR IM Procaine penicillin 50000u/kg daily for 10 days If interrupted for >1 day, restart treatment course
Canadian Guidelines 2022 ³⁴	Possible exposure to syphilis during pregnancy	NTT and TT at birth Following CS treatment: repeated testing monthly for the first three months, and then 3 monthly until 18 months of age	Clinical suspicion of CS ^c Maternal treatment inadequate, unknown, within 30 days of delivery, or inadequate serological response to treatment NTT 4x higher than maternal NTT at delivery Adequate follow up of the infant cannot be ensured 4x rise in NTT on interval testing, reactive NTT at 6 or 12 months or reactive TT at 18 months	IV crystalline penicillin G 50000 units/kg/dose (12 hourly in the first 7 days of life, 8 hourly in days 8–30, 6 hourly >30 days) for 10 days

UK Guidelines 2015 ³⁶	Mother diagnosed and/or treated for syphilis during the present pregnancy	NTT and TT tests at birth, 3 months of age, then 3 monthly until negative	Clinical suspicion of CS NTT titres remain stable or increase Maternal SIP that is untreated or treated inadequately, within 4 weeks of delivery, or with non-penicillin regimens	IV Benzylpenicillin 30mg/kg (12 hourly in the first 7 days of life and 8 hourly thereafter) for 10 days OR IM Procaine penicillin 50000u/kg daily for 10 days If interrupted for >1 day, restart treatment course
Australian STI Management Guidelines ⁴³ Queensland Guidelines ²⁰	Inadequate maternal serological response to treatment of SIP or treatment within 1 month of delivery	Following treatment: serology at 3, 6 and 12 months of age or until NTT is nonreactive to ensure treatment is effective	Clinical suspicion of CS or CS confirmed on testing of serum IgM or placenta Maternal SIP that was treated inadequately, or within 30 days of delivery NTT 4x higher than maternal NTT at delivery	IV Benzylpenicillin 30mg/kg (12 hourly in the first 7 days of life, 8 hourly in days 8–30, 4–6 hourly >30 days) for 10 days
The New Zealand Sexual Health Society (NZSHS) Syphilis in Pregnancy Antenatal Management Guidelines ⁴⁰	Mother with positive syphilis serology who does not have documentation of adequate treatment and serological response	Paired serological TT + NTT Following treatment: review at 6 weeks, 3 months, 5–6 months and 12–18 months of life	Clinical suspicion of CS Maternal treatment inadequate, undocumented, within 30 days of delivery or without documented serological response NTT 4x higher than maternal NTT at delivery Reactive TT >18 months of age	IV Benzylpenicillin 30mg/kg (12 hourly in first 7 days of life, 8 hourly thereafter) for 10 days

Notes: ^aNTT, Nontreponemal test (RPR, VDRL). ^bTT, Treponemal test (FTA, TP-PA, TP-HA, EIA). ^cClinical signs may include rash, hepatomegaly, rhinitis, generalised lymphadenopathy, pneumonitis, and/or other signs and symptoms.^{20,40}

identified risk factors include multiple sexual partners, illicit drug use, incarceration, homelessness, or living in areas with high syphilis prevalence or experiencing outbreaks.^{20,33} Numerous cases of CS have occurred after a woman tested negative on initial antenatal bloods and was not re-tested due to not being identified as “at-risk” – an assumption that can be subjective.^{8,11,46,47} WHO does not specifically recommend repeat testing in current guidelines, but an increasing number of individual jurisdictions are now recommending routine universal additional testing in the third trimester for all women. Of the 62 guidelines included in the study by Trinh et al, 57 (92%) recommend universal syphilis testing during pregnancy and 46 (74%) recommend repeat testing in pregnancy, including 21 (46%) that recommend this be done in the third trimester or at delivery. Of the 115 countries with maternal syphilis seroprevalence data available, 40 (35%) recommend universal repeat testing in pregnancy and 52 (45%) recommend repeat universal testing only for high-risk women. The study also found that countries with SIP rates 1% or higher were more likely to recommend universal repeat testing.⁴⁵

Australian guidelines are state-based, and most recommend syphilis testing for women in pregnancy at the first antenatal visit, as well as re-testing for women at high risk of infection or reinfection at 28–32 weeks and at delivery, or more frequently depending on the level of risk.^{20,37–39} Universal retesting of all women is recommended in Queensland (QLD)²⁰ and Western Australia (WA) at 28 and 36 weeks.³⁸ The New Zealand Sexual Health Society (NZSHS) official national guideline currently advises routine syphilis testing as part of first antenatal bloods, but NZSHS has since released a statement strongly recommending that all pregnant women be retested for syphilis at 28–32 weeks.⁴² A study of CS cases in the US in 2018 found that half of all reported cases that year could be attributed to gaps in prenatal testing and treatment including inadequate treatment of diagnosed SIP, inadequate testing, or acquired infection after initial negative testing in a woman not identified as high risk.⁴⁶ US guidelines now recommend testing of all pregnant women at the first prenatal visit and additionally for high risk women at 28 weeks and at delivery.³³ Studies in the US found that universal third trimester syphilis re-testing would cost an additional \$420 000 US dollars to prevent each case of CS⁴⁸ and was not cost effective in areas of low CS prevalence <3.5/100 000 live births.⁴⁹ Given the increased prevalence in recent years, at 77.9 cases per 100 000 live births in 2021,² the cost vs benefit analysis should be revisited. Canadian guidelines recommend routine testing at first prenatal visit, with re-testing at 28–32 weeks and at delivery for those at ongoing risk of infection or reinfection, or in areas experiencing outbreaks of syphilis.³⁴ UK guidelines recommend routine testing in early pregnancy. Twenty-two (56%) babies born with CS in England between 2015 and 2021 were born to women who tested negative for syphilis during initial antenatal testing.^{15,31} However, routine re-testing later in pregnancy has been considered and is not recommended, after a 2020 review by the United Kingdom National Screening Committee deemed that it would cost 1.8 million pounds to prevent one case of CS and is therefore not cost effective.³⁵

There are a number of issues that arise from retesting only high-risk women. A risk-based retesting approach is not consistently effective as this method depends on accurate and consistent identification of risk. In multiple countries employing this method, CS cases have resulted where pregnant women tested negative for syphilis at initial antenatal screening, and were not rescreened later in pregnancy due to not being identified as high-risk.^{15,31,42,50,51} A risk-based retesting approach may result in perceived stigmatization of some women^{42,52} – women may not disclose their high-risk status due to perceived stigma or a lack of awareness of high-risk demographics and sexual practices.⁵² Likewise, healthcare professionals may make assumptions of risk profiles and not thoroughly and explicitly explore all risk factors with every woman.⁴⁴ On the other hand, cost vs benefit is a consideration in most countries, and false-positive results are not insignificant, and can be a result of infection, vaccinations, autoimmune disease, older age, IVDU and pregnancy.^{36,53} In the UK in 2011, 23% of women with positive maternal treponemal serology had false-positive test results.³⁶

Given the dynamic nature of cost vs benefit assessments, limitations of risk-based re-testing, and the rapidly rising rates of CS, it is imperative that all HICs review their guidelines and consider introducing recommendations for universal syphilis re-testing for all women in the third trimester.

Treatment of SIP (See Table 1)

WHO recommends treatment of primary, secondary, or early latent syphilis in pregnancy with a single dose of benzathine penicillin G (BPG) 2.4 million units (MU) intramuscularly (IM), or if BPG is unavailable, procaine penicillin 1.2 MU IM once daily for 10 days.³² IM penicillin is recommended as first-line therapy for the treatment of syphilis in pregnant

women in 95% of the guidelines reviewed by Trinh et al.⁴⁵ Six (10%) of these recommended a single dose regardless of syphilis stage (less than WHO-recommended management), and 8 (14%) recommended 3 doses regardless of stage/duration. Depending on local laboratory capacity and clinician expertise, it can be difficult to reliably differentiate the various stages of syphilis,³⁴ and as such treatment guidelines vary. WHO recommends treatment for SIP of unknown stage/duration as per late latent syphilis, with 3 weekly doses of BPG 2.4 MU IM over 3 consecutive weeks. The WHO guideline offers oral erythromycin or IM ceftriaxone as alternative for treatment of SIP but specifies that they do not treat or prevent CS in the foetus. Forty-two (68%) of the guidelines offered at least one alternative to penicillin, and only 20 (48%) of those specified that it would not treat or prevent CS. Most guidelines (48% of those reviewed by Trinh et al) advise desensitisation for those allergic or hypersensitive to penicillin.⁴⁵

Diagnosis and Treatment of CS (See Table 2)

To assist the clinician, there are many available updated guidelines and reviews addressing the diagnosis and treatment of CS, most of which are generally in agreement.^{20,36,44} CS should be considered in any newborn with clinical suspicion of CS, or where the mother had suspected or confirmed SIP without documentation of completion of adequate and appropriate treatment at least 30 days prior to delivery. Definitive diagnosis of CS can be complex as maternal treponemal and nontreponemal IgG antibodies can be transferred via the placenta, complicating interpretation of reactive tests in neonates. Additional factors must be considered, including stage of diagnosed SIP, adequacy and timing of SIP treatment, clinical, laboratory and radiographic findings consistent with CS and comparison of maternal and neonatal nontreponemal test (NTT) titres. Serum NTTs should be performed on all neonates with suspected CS, as umbilical cord blood is at risk of contamination with maternal blood. A serum NTT titre that is 4x higher than the mothers NTT titre (on the same type of NTT) at delivery should be considered a confirmed case of CS.⁴⁰

Ten days of IV penicillin is universally recommended as treatment for CS, with age-dependent dosing in most guidelines. A common scenario that occurs in infants born to mothers with SIP is when the infant has no clinical signs concerning for CS and has negative tests (NTT titre is equal to or less than the maternal titre and treponemal IgM is negative), but there is no documentation of adequate and appropriate treatment of SIP at least 30 days prior to delivery, with proven serologic response to treatment. Many guidelines from HICs recommend erring on the side of caution in this scenario and treating the newborn with 10 days of IV penicillin.^{20,41} However, some guidelines⁴¹ recommend a single dose of IM benzathine penicillin in these circumstances, provided that a complete evaluation of the infant has occurred (FBC, CSF, and imaging) and is normal, and follow up is ensured.⁵⁴

Congenital Syphilis in High Income Countries – Vulnerable Populations Disproportionately Affected

There is a common theme among many HIC, of disproportionately high rates of infectious syphilis and CS in Indigenous and socially vulnerable populations, due to social and structural barriers to care.^{1,2,7–16}

Indigenous Populations

In Australia, yearly rates of CS during the past decade are on average almost 20x higher in Aboriginal and Torres Strait Islander infants (see Figure 2).⁷ Of note, 31 (53%) of the 58 CS cases reported Australia-wide between 2011 and 2020 were Aboriginal and/or Torres Strait Islander¹⁰ and of 62 CS cases reported between 2016 and September 2022, 52 (81%) were born to mothers diagnosed with syphilis late in pregnancy, including 10 cases diagnosed within 30 days of delivery.⁷ Of the 18 deaths from CS reported between 2016 and September 2022, 12 (67%) were Aboriginal and/or Torres Strait Islander infants.⁷ A study of SIP and CS in WA reported on the 9 cases of CS diagnosed between January 2019 and June 2021. All women had infrequent, or no antenatal care. Seven of the 9 cases were born to Aboriginal and/or Torres Strait Islander women, the majority of whom had unstable housing and complex social issues.¹¹ A study examining infectious syphilis rates among different demographics in Australia from 2011 to 2019 identified factors associated with significantly higher notification rates, including Aboriginal and Torres Strait Islander communities, areas

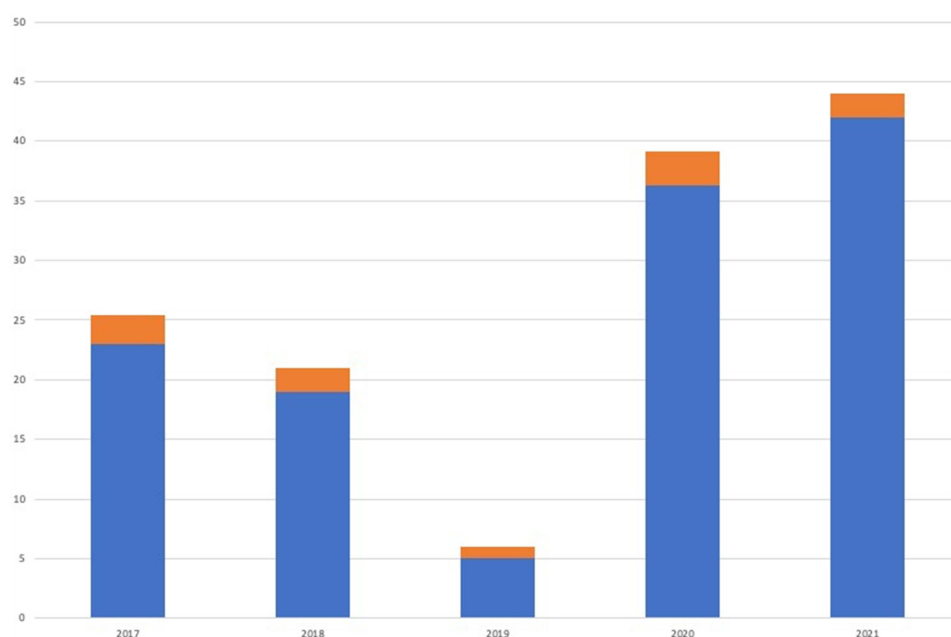


Figure 2 CS notification rates by year and Indigenous status of mother – Australia 2017–2021. Y axis = number of notifications. X axis: Aboriginal and/or Torres Strait Islander (blue), Other Australians (Orange).

of socio-economic disadvantage and IVDU.⁹ Social factors impacting the sexual health of Aboriginal and Torres Strait Islander people include barriers to healthcare access, poverty, substance use, and social and educational disadvantage.¹²

In New Zealand, 24 cases of CS were identified between 2017 and 2021. Fourteen (58%) of these occurred in women who had late, or no antenatal care and 6 (25%) were new infections in pregnancy, after initially testing negative for syphilis. The highest yearly rate was 8 cases in 2020, all of which were born to Māori (n=6) or Pacific Islander (n=2) women.⁸

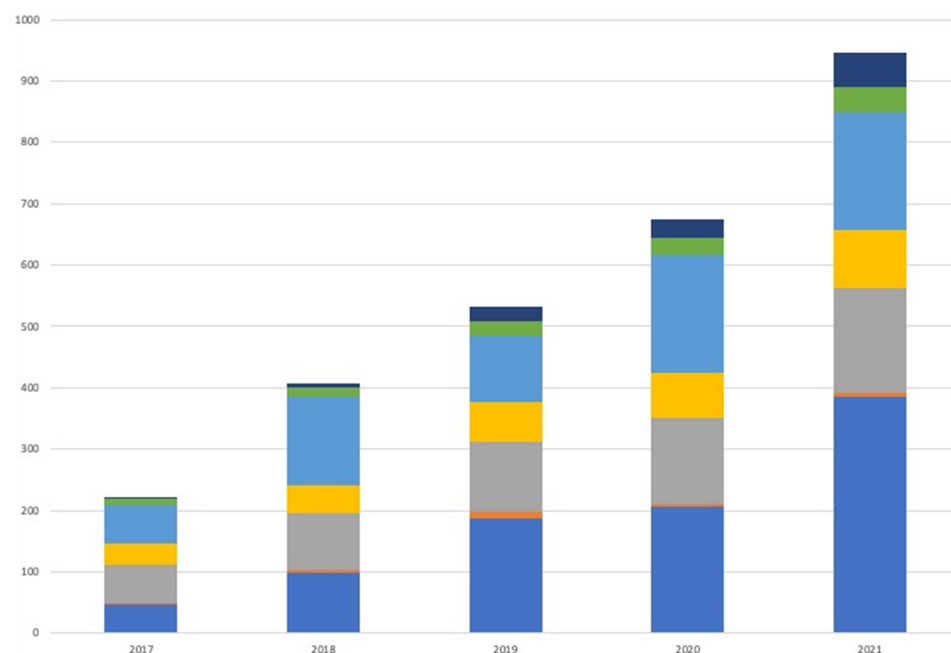


Figure 3 CS notification rates by year and race/Hispanic ethnicity of mother – US 2017–2021. Y axis = number of notifications. X axis: American Indian or Alaska Native (blue), Black or African American (gray), Native Hawaiian or other Pacific Islander (light blue), Multiracial (dark blue), Asian (Orange), Hispanic or Latino (yellow), White (green).

In the US in 2021, CS rates were disproportionately higher in racial and ethnic minority groups than in white Americans, including American Indian/Alaska Native (9.4x higher), Native Hawaiian/Pacific Islander (4.7x higher), African American (4.1x higher), and Hispanic populations (2.3x higher)² (see Figure 3). CS rates were also disproportionately high for those living in poverty, and illicit drug users.^{2,13} A recent study of CS hospitalisations in Mississippi⁵⁵ found a 1000% increase from 10 hospitalisations in 2016 to 110 in 2022 and identified significant racial and socioeconomic disparities. Over 71% of infants hospitalised with CS between 2016 and 2022 were African American, and 91% were covered by the Medicaid program, which was used in this study as an indicator for low socioeconomic status.

In recent years, syphilis outbreaks in Canada have disproportionately affected First Nations, Métis and Inuit populations.¹⁴ In Canada in 2020, 86% of all confirmed CS cases were within the three Prairie provinces alone.¹ Incomplete antenatal care has been identified as a major risk factor for CS, and this can be associated with social and structural health determinants including low income, living in rural areas, housing instability, domestic violence, cultural barriers, stigma, discrimination and racism, and substance use.¹⁴

Disproportionate rates of CS among Indigenous and disenfranchised populations are linked to structural, social, economic, and cultural barriers to care often as a result of racial and socioeconomic inequity.^{14,43,56,57} Historical racism, discrimination, and exploitation of Indigenous populations in HICs results in intergenerational trauma and mistrust of healthcare professionals and the healthcare system.^{58,59} As a result, Indigenous populations are vulnerable to missed healthcare opportunities due to avoidance and lack of engagement with the healthcare system.^{58–60} A 2022 report⁶¹ on cultural safety in health care for Indigenous Australians was based on data collated from a number of surveys of the general Australian population and of patients in Australian public hospitals. It found that in 2020, 22% of Indigenous Australians reported that they or their families had been racially discriminated against by medical professionals in the previous year and that in 2018–2019, 32% of Indigenous Australians who did not access health care when needed attributed this to cultural barriers including language, discrimination, and lack of access to culturally appropriate health care.⁶¹ A 2016 study⁶² of Inuit youth in Nunavut, Canada, identified factors affecting access to sexual and reproductive health care. Major barriers to care include lack of trust in healthcare providers, stigma and taboo surrounding sexual health, and feelings of powerlessness that particularly affect female Inuit youth, and are compounded by sexual abuse and violence.⁶² An understanding of intersectionality in these populations is important; other risk factors for syphilis (substance misuse, remote living, low education levels, socio-economic disadvantage, poverty) are more prominent in Indigenous populations and in turn contribute to their relative risk.^{62–64}

Other Disadvantaged Populations

There is a similar theme of inequitable distribution of infectious syphilis and CS in HICs that do not have large Indigenous populations, where disproportionately high numbers occur in disenfranchised and socially vulnerable populations. In England in 2022, the rate of infectious syphilis in the population with black ethnicity was 80% higher than the rate in those of white ethnicity. The rate of infectious syphilis in the most deprived areas (index of multiple deprivation (IMD) quintile 1) was approximately 2.5x higher than that of the least deprived areas (IMD quintile 5).³⁰ A retrospective review of case reports of all confirmed and suspected cases of CS in England since 2015¹⁵ identified a number of risk factors including lifestyle (IVDU, sex work), incarceration, social inequalities, and poor engagement with health services resulting in late or no antenatal care. A third of women diagnosed with SIP in 2020 reported complicating social issues including mental health challenges (13.6%), social services involvement (12.3%), housing concerns (9.7%), domestic violence (7.7%), and substance misuse (7.2%), and half were unemployed.¹⁵ Although there are comparatively low rates of CS in England, it remains a public health concern due to the devastating outcomes, and the health inequity that it represents.^{36,65}

Geographical distribution of syphilis and CS cases in China remains disproportionately concentrated in some counties, with the vast majority of CS cases occurring within 5 provinces.^{27,66} Risk factors such as rural-to-urban migration, stigma, and suboptimal routine testing may contribute to this disparity.¹⁶ The proximate determinants of syphilis spread are poorly understood, and further research is required to assess the contributing factors.²⁷

Optimisation of antenatal testing and treatment services will not overcome the structural barriers to seeking antenatal care. The data indicates that many individuals in vulnerable populations – including but not limited to Indigenous

populations – eg victims of domestic violence and control, those who misuse substances, and those living in poverty – do not have the education, empowerment, and resources to seek antenatal care.^{67–69} Major structural barriers that these women face include (1) lack of health literacy and limited understanding of the risks of sexually transmitted infections and MTCT, (2) lack of empowerment to seek antenatal care, compounded by stigma, racism, and discrimination, and (3) poverty and a lack of resources to facilitate healthcare attendance.^{67–69} In order to address the crisis of CS and implement effective preventative strategies, the social inequity, discrimination, and intersectionality that it represents must first be acknowledged and understood. National structural strategies must be implemented to achieve locally effective change.

Public Health Initiatives

Many HICs have initiated public health campaigns in response to increasing CS rates. In Australia, the Fourth National Sexually Transmissible Infections Strategy 2018–2022 was published in 2019.⁷⁰ It aims to implement effective programs targeting priority populations with a focus on human rights, reducing stigma and discrimination and improving access and equity, as well as closing the gap between Aboriginal and Torres Strait Islander health status and that of other Australians.⁷⁰ New Zealand launched the National Syphilis Action Plan in 2019, which includes a plan for increased health promotion and awareness among high-risk groups and improving affordable and equitable health care, with a focus on addressing barriers to access for Māori women in particular.⁷¹ In January 2021, the US Department for Health and Health Services launched the Sexually Transmitted Infections National Strategic Plan in response to the rise in STIs. The five-year plan aims to improve STI prevention and treatment with a focus on public health, health disparities, stigma, and the social determinants of health.⁷² Specifically, it targets a reduction in CS rates of 15% by 2025 and 50% by 2030, with specific targets for reduction of cases in American Indian and African American populations.⁷² Multiple US state-based innovative initiatives have been launched in an attempt to address the issue of CS as a result of barriers to healthcare access. These include a podcast launched by the Department of State Health Services in Texas, strategizing sessions to address CS launched by the Oklahoma State Department of Health, and the implementation of 9 regional CS case review boards in Louisiana to identify missed opportunities for prevention.⁴³ In 2019, the Public Health Agency of Canada (PHAC) established the Syphilis Outbreak Investigation Coordinating Committee (SOICC) with the aim to share syphilis epidemiology and best practices on territorial, state, and federal levels.¹

Discussion

Syphilis screening in pregnancy, whether performed through traditional or reverse sequence algorithms, reliably picks up syphilis infections. It appears that many HICs that are experiencing increasing rates of CS have updated their guidelines to recommend additional testing following testing at first antenatal visit, particularly for high-risk women and in areas experiencing infectious syphilis outbreaks. HIC where prevalence of CS is becoming particularly high should make it a priority to update their official guidelines and consider universal re-testing for all women in the third trimester.

With these measures in place, the failure to prevent CS in HIC is largely due to missed opportunities for recommended testing, diagnosis, and treatment of SIP.²² Data from HIC indicate that many CS cases are born to women who had late, or no antenatal care and therefore would have been missed diagnoses during pregnancy regardless of guidelines that recommend repeat testing in pregnancy.^{8,11,73} Barriers to adequate antenatal care are numerous and challenging to address and include structural barriers such as financial pressure, communication and language barriers, lack of transportation and childcare, and inability to take time off work, as well as social barriers such as domestic and family violence, mental health issues, stigma, racism, discrimination, and lack of trust in healthcare providers.⁹ Inadequate contact tracing also contributes to rising numbers of SIP. Many sexual contacts remain undetected and untreated if traditional contact tracing methods are employed.

Conclusion

There is a crisis of CS in HIC worldwide, with rising cases disproportionately affecting vulnerable populations. It is unacceptable that we are seeing this trend in countries that have widespread availability of penicillin and ample resources for education, testing, and treatment. Worldwide efforts in the first decade of the century led to significant reductions in CS rates across the globe. A global effort is needed again now – with a new focus. The imperative aim in HIC should be

to address structural and psychosocial barriers that employ community-based interventions, point of care testing and peer led services – this is not a simple goal but encouragingly some countries have recognised these disparities and have begun implementation of committees and programs to address the problem.

Disclosure

The authors report no conflicts of interest in this work.

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