Kimberley Aboriginal Health Planning Forum

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Protocol Review: Evidence Used and Rationale

Protocol name: Congenital Syphilis Protocol

Rationale: The Kimberley Region is experiencing a syphilis outbreak. Syphilis was previously endemic to the Kimberley region however, between 2012 and 2013 there were no new cases of syphilis. From June 2014 to June 2018 there were 165 new cases of Syphilis diagnosed, of which 15 were pregnant women diagnosed with syphilis. For this reason, it is important that clear, evidence based guidelines are in place for antenatal screening for syphilis and for investigation and treatment of infants at risk of congenital syphilis. The intent of this protocol is to guide health professionals providing antenatal, postnatal and infant care, assess the risk for congenital syphilis and initiate appropriate treatment and follow up.

This protocol differs from King Edward Memorial Hospital (KEMH) guidelines because it identifies all Kimberley pregnant women as high risk for syphilis because it is an outbreak region. The KEMH guideline syphilis screening recommendation for high risk women is at booking or in the first trimester and again at 34 weeks or at delivery if testing has not taken place during pregnancy.

This protocol follows the Northern Territory (NT) congenital syphilis guideline and recommends syphilis testing at booking, 28 weeks, 36 weeks, delivery and 6 weeks postnatal. The Kimberley protocol further recommends cord serology from all Kimberley infants with no risk factors for congenital syphilis as a safety check. Cord serology is not used as a definitive test to diagnose congenital syphilis. This recommendation was endorsed by Kimberley Regional Paediatric Team and the Maternal and Child Health Subcommittee (M&CH SubC). The NT congenital syphilis guideline does not recommend cord serology from no risk infants.

Defining no risk, low risk and high infants is not in the KEMH guidelines. The Kimberley protocol provides information on how to categorise the infant (no risk, low risk and high risk) and follow up and treat recommendations for these cases. These definitions follow the NT congenital syphilis guideline.

Initial Working Group: Katy Crawford (KPHU Senior Public Health Nurse STI), Megan Pilkington (KAMS GP registrar), Laura Korte (Kimberley Regional Paediatrician), Gavin Cleland (Kimberley Regional Paediatrician), Kerr Wright (Medical Director KAMS), Jeanette Ward (Consultant Public Health Medicine) Donna Mak (Public Health Physician, Communicable Disease Control).

Further review from: Janice Forrester (KPHU Clinical Nurse Specialist – Public Health STI), Sarah Woodland KAMS, Maternal and Child Health Subcommittee (M&CH SubC), Sexual Health Subcommittee (SHSC), and Kimberley Aboriginal Health Planning Forum (KAHPF).

Discussion points

The initial working group recommended adapting the Northern Territory (NT) congenital syphilis guidelines into a Kimberley congenital syphilis guideline with the addition of continuing the practice of taking cord sera from all Kimberley infants. The Regional Paediatric Team, Regional Obstetrician and the M&CH SubC further endorsed the recommendation of taking cord sera from babies not deemed at risk of syphilis in November 2017 and again in August 2018.

Antenatal screening;

The current Kimberley recommendation for syphilis screening in pregnancy is at booking, 28 weeks and 36 weeks. This protocol increases screening in pregnancy to booking, 28 weeks, 36 weeks, at delivery and 6 weeks postpartum. This is in keeping with the NT guidelines.

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All women with positive syphilis serology during pregnancy should be considered infected and provided treatment and follow up unless there is documented evidence of previous adequate treatment appropriate to the stage of syphilis and no evidence of reinfection.

Previously treated infection is classified as treatment with penicillin regime appropriate to the stage of infection prior to current pregnancy. Document adequate serological response is classified as a 4-fold/2 titre decline in RPR, within 12 months or if treated during late latent stage without a drop in RPR but all titres during current pregnancy are low (none-<1:4) and there is no suspicion of syphilis infection during pregnancy.

If a woman is treated in pregnancy for syphilis, a repeat RPR test is required monthly during their pregnancy and at birth and 6 weeks post-partum. This follows the NT congenital syphilis guidelines

Diagnosis and staging

The Kimberley syphilis database based at Kimberley Population Health Unit (KPHU) can provide patient information on syphilis testing and treatment for Kimberley patients. This information can assist in classifying the stage of syphilis.

Early syphilis is defined as acquisition of syphilis within the past 2 years. Clinical feature of early syphilis may include genital or muscosal ulceration, genital lumps, rash, lymphadenopathy, patchy hair loss, fever, hepatitis, arthritis meningitis, ophthalmic problems, headache and myalgia. Case definition requires any of the following laboratory evidence: positive Treponema pallidum PCR from ulcers or muccoutaneous lesions, reactive syphilis treponemal serology on at least 2 different treponemal tests and a negative serology within the past 2 years, a 4-fold or greater increase in RPR titre within the past 2 years.

Late or unknown during of syphilis is classified as positive serological tests without other evidence of disease in women without documented evidence of previously adequately treated infection or who acquired syphilis more than 2 years ago.

Tertiary syphilis may occur in approximately a third of untreated patients 20 – 40 years following initial infection and can cause neurological symptoms, aortic regurgitation, aortic aneurysms and destructive lesions of bones and soft tissue

Syphilis treatment during pregnancy

Penicillin is the only drug that reliably treats syphilis during pregnancy. Women with penicillin allergy should be referred to hospital for in-hospital desensitisation. If penicillin cannot be used then treatment must be considered inadequate for the purposes of determining adequate neonatal follow up.

Repeat RPR is required on the day of treatment to ensure a peak RPR reading is obtained to allow accurate documentation of a post treatment response.

Treatment for early syphilis during pregnancy is benzathine penicillin 1.8g (2.4 million units) intramuscularly as a single dose. Late and unknown duration of syphilis during pregnancy requires benzathine penicillin 1.8g (2.4 million units) intramuscularly weekly for 3 weeks.

Treatment follow-up in pregnancy

Monthly RPR test is required and again at delivery and 6 weeks post-partum (ASID; 2014)

Women who are treated for syphilis after 20 weeks of gestation should have a foetal and placental ultrasound examination to evaluate for congenital syphilis.

Jarisch-herxheimer Reaction (JHR)

This is a common occurrence in the treatment of early syphilis in adults consisting of fever, chills, malaise, hypotension and tachycardia. Up to 45% of adults experience these symptoms that occur within 2 hours of treatment and peaks at 8 hours and disappears 24-36 hours after treatment. Management is supportive care. It may precipitate uterine contractions; preterm labour, and or non-reassuring foetal heart rate tracings in pregnant women treated in the second half of pregnancy. Foetal monitoring should be considered in women receiving treatment after 26 weeks gestation.

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Risk assessment for neonates;

Neonates born to mothers with positive syphilis serology are categorised as no risk, low risk and high risk.

The definition for no risk neonates is defined as mother completed a documented penicillin regime appropriate to stage of infection prior to pregnancy and has an adequate serological response of either a 4-fold decrease in RPR titre, or for late/unknown duration of syphilis without a 4-fold drop, the maintenance of stable titres below 1:4 and no suspicion of reinfection. Cord-sera only is collected and no further follow up is required.

The definition of low risk is, if the maternal history does not meet all the criteria for no risk neonates and the mother has all the following criteria:

1. Mother treated during the current pregnancy with a penicillin regimen appropriate to her stage of syphilis
2. Treatment completed more than 30 days prior to birth
3. Documented adequate serological response to treatment
4. No clinic suspicion of syphilis acquisition later in pregnancy
5. The neonate has no signs of congenital syphilis on examination
6. RPR of infant venous blood is the same or less than the maternal titre at delivery.

The definition of high risk is if the mother or neonate do not meet the criteria for no or low risk they are considered high risk of congenital syphilis.

Investigations

The major clinical features of early congenital syphilis are: ulceration of nasal mucosa with nasal discharge, skin lesions (usually maculo-papular rash but almost any form of rash can occur including scaling, mucous patches, condylomata lata and paronychia). The rash can affect palms and soles of feet. Other signs and symptoms include, fever, low birth weight, hepato-splenomegaly, jaundice, generalised lymphadopathy, glomerulonephritis, nephrotic syndrome, pancreatitis, haematological abonormalities (anaemia), osteochondritis or periostitis, central nervous system abnormalities, chorioretinitis, uveitis and glaucoma.

Venous blood is collected from the high-risk infant for (FBC,EUC, LFT syphilis and IgM) and immediate paediatric review arranged for high risk infants. Further tests including CSF examination, *Treponema pallidium* PCR from skin lesions and nasal secretions (if present), placental tissue and or amniotic fluid, histology of placenta and X-rays of long bones should be discussed with the Paediatrician.

Low risk infants require physical examination for signs of congenital syphilis and venous blood for syphilis serology including RPR.

No-risk babies will continue to have cord serology as a Kimberley safety-net as advised by Kimberley Paediatricians, Kimberley Obstetrician, CDCD expert opinion, KPHU Consultant Public Health Medicine, KAMS Medical Director and endorsed by the KAHPF M&CH SubC in August 2018.

Treatment for infants

Treatment for low risk neonates is a single dose of benzathine penicillin 37.5mg/kg (50,000 units/kg) intramusculary (IMI).

Treatment of high risk neonates is Benzyl penicillin 50mg/kg IV 12 hourly for 10 days and paediatric review.

Follow up

Low risk neonates require paediatric follow up at 3 months and 18 months and venous syphilis serology obtained and reviewed at 3, 6, 12 and 18 months.

High risk neonates require paediatric following up at 3 months, 6 months and 15-18 months and venous syphilis serology obtained and reviewed at 3, 6, 12 and 15-18 months.

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Glossary Syphilis Serology

Terminology	Explanation
Cord Blood/Cord Sera	Cord blood is a sample of blood taken from a newborn baby's umbilical cord. Cord sera results can be difficult to interpret because the maternal antibodies can contaminate the foetal cord sera producing a false positive result. In the context of a history of maternal adequate past treatment, a positive cord blood result alone is not an indication for antibiotic treatment for the infant.
Titre	The concentration of an antibody, as determined by finding the highest dilution at which it is still able to cause agglutination of the antigen
Treponemal Antibody tests	Include TPPA, EIA, TPHA, FTA-Abs • Either reported as reactive or non reactive • Once reactive usually remains reactive for life even with adequate treatment • Indicate if a person has ever had syphilis and does not indicate current disease activity • For an infant this will usually revert to negative by 12-18 months of age if adequately treated
Non-treponemal tests	Examples include RPR and VDRL • Reported as a titre (eg. 1:1, 1:2, 1:4) • Have a moderate false positive rate and need to be confirmed by a reactive treponemal test • Used to ascertain disease activity • May revert to non-reactive after treatment, may revert to no- reactive after many years even without treatment, or may never revert to non-reactive even with treatment • 2 titre or 4 fold rise over a previous result (eg. 1:2 increasing 1:8), indicates new infection • 2 titre or 4 fold decline after treatment (eg 1:32 decreasing to 1:8), indicates an " adequate response" to treatment. • In the special case of pregnancy, the titre must also fall to below 1:4 to indicate an adequate response
Immunoglobulin M antibodies (IgM)	These do not cross the placenta and are more indicative of neonatal infection

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Resources and references

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