

## ANTENATAL CARE

## INFECTIONS IN PREGNANCY

## SYPHILLIS IN PREGNANCY AND THE NEWBORN : DIAGNOSIS AND TREATMENT

## PURPOSE

- To detect syphilis in pregnant women and offer treatment prior to delivery.
- To detect syphilis in the newborn and to treat before complications develop.

## BACKGROUND

Syphilis is a sexually transmitted bacterial infection caused by the spirochaete *Treponema pallidum*. Vertical transmission from mother to fetus can occur during pregnancy. Congenital syphilis infection can result in premature birth, low birth weight, fetal death in- utero, perinatal death and physical malformations.

**NB - Syphilis is a notifiable disease. A diagnosis of Syphilis should be reported to the State Health Department using the Notifiable Infectious Diseases form.**

## TRANSMISSION

Syphilis is primarily transmitted from person to person through direct contact with a syphilis ulcer or *chancre* through vaginal, anal or oral intercourse. Chancres occur predominantly on the external genitalia and in the vagina but can also occur in the perianal area or within the rectum. Chancres may also occur on the lips and in the oral cavity.

Vertical transmission from an infected mother to the fetus is an important mechanism of infection. Untreated maternal infection can result in adverse pregnancy outcomes, including early fetal loss, stillbirth, prematurity, low birth weight, neonatal and infant death, and congenital disease of the newborn. Clinical manifestations of congenital syphilis are influenced by gestational age, stage of maternal syphilis, maternal treatment, and the immunological response of the fetus.

## SYMPTOMS

## Primary Syphilis

Incubation period of 14 days to 3 months.

Following infection, a single painless, erythematous papule initially develops, usually on the external genitalia, but occasionally on the mouth, anus or within the rectum. This ulcerates to form a painless "punched out" ulcer or *chancre*. Multiple lesions can occur, particularly in HIV positive patients. Chancres are highly infectious and may be associated with regional lymphadenopathy. Without effective treatment the infection can progress to the secondary stage.

## Secondary Syphilis

Organisms disseminate from the primary chancre causing symptoms 1-6 months later.

*Rash* – localised or diffuse mucocutaneous rash, can be macular, papular, pustular or mixed, involving the trunk, limbs, palms of hands or soles of feet. Mucosal ulcers may also occur. Other features may include fever, sore throat, oral ulcers, lymphadenopathy, hepatitis, iritis, arthritis, glomerulonephritis. Signs and symptoms resolve with or without treatment, but without effective treatment, infection will

progress to the latent and late stages of disease. Spontaneous resolution of secondary syphilis occurs at 3-12 weeks.

### **Latent infection**

Usually asymptomatic. During this period infectivity is low, but up to one-quarter of patients will experience recrudescence of disease.

### **Tertiary stage**

This stage of disease occurs rarely in developed countries and follows a period of latency of up to 20 years. It is characterised by chronic inflammation, including gummatous syphilis (granulomatous lesions of the skin, mucous membranes, bone or organs), cardiovascular syphilis and neurosyphilis.

### **SYPHILIS IN PREGNANCY AND THE NEONATE**

During pregnancy *T.pallidum* can cross the placenta to cause fetal infection, this may occur throughout the course of pregnancy. Spirochaetes are released into the circulation and disseminate to the organs, producing an inflammatory response. Frequency of vertical transmission increases with gestational age whilst the severity of fetal infection decreases with gestational age. Pregnancies complicated by untreated maternal syphilis are at increased risk of adverse outcomes such as intrauterine growth restriction, premature birth, stillbirth, neonatal death and congenital deformities.

Infection can be transmitted to the fetus at any stage of maternal disease. The rate of transmission is 60-100% during primary and secondary syphilis and decreases with later stages of maternal infection; approximately 40% in early latent infection and 8% in late latent infection. Treatment of early maternal syphilis at least 30 days before delivery is the most important factor influencing the risk of congenital infection. 70 - 100% of infants born to untreated mothers will be infected compared to 1% - 2% of those born to women adequately treated during pregnancy.

**Early congenital syphilis** – defined as onset of symptoms before 2 years of age. Clinical manifestations can be varied, however persistent rhinitis (snuffles) is often the earliest presenting symptom occurring in up to 40% of affected neonates.

Hepatomegaly, rash, generalised lymphadenopathy, placental and umbilical cord or skeletal abnormalities may also be seen. Skin lesions may contain spirochaetes and can transmit infection. Central Nervous System (CNS) involvement may be symptomatic or asymptomatic. Asymptomatic CNS syphilis is diagnosed by abnormalities of the Cerebral Spinal Fluid(CSF).

**Late congenital syphilis** – defined as onset of clinical manifestations after 2 years of age.

Manifestations are related to persistent inflammation or scarring in affected tissues. Late congenital syphilis occurs in approximately 40% of infants born to women with untreated syphilis in pregnancy. Manifestations include facial deformities, keratitis, sensorineural hearing loss, dental deformities (for example, Hutchinson teeth, mulberry molars), gummas of the skin and mucous membranes, intellectual impairment, hydrocephalus and skeletal deformities (“sabre shins”, arthritis).

### **ANTENATAL SYPHILIS SCREENING**

All women should have syphilis serological testing performed during the first trimester or at the first antenatal visit. Women at risk of acquiring syphilis should have further testing in the third trimester (34 weeks) or if testing is not performed, at delivery. An initial negative test does not exclude infection as it may take 10-45 days following exposure for sero-conversion to occur.

There are two main types of serological test performed together on maternal blood specimens (testing of cord blood is not recommended):

### **Treponemal Tests (TPPA, EIA IgG and IgM, FTA-Abs)**

Reported as *reactive* or *non-reactive*. When reactive these tests (with the exception of IgM) usually remain reactive for life even following adequate treatment. They indicate previous exposure to syphilis and are not an indicator of disease activity.

### Non-treponemal Tests (RPR, VDRL)

Reported as a titre (1:2, 1:4 etc). They have a moderate false positive rate and supplemental testing should be performed using a treponemal test. Reactive tests usually revert to non-reactive following treatment but frequently revert to non-reactive over a period of time even without treatment. Non-treponemal tests are useful in determining disease activity and response to therapy. For example a four-fold increase in titre (2-dilution rise) from a previous result (1:2 increasing to 1:8) suggests re-infection; a four-fold fall in titre (2-dilution fall) after treatment (1:32 decreasing to 1:8) suggests an adequate response to treatment.

### ASSESSMENT AND MANAGEMENT OF POSITIVE SYPHILIS SEROLOGY

For mothers with positive syphilis serology, (assuming false positives have been considered and excluded), it is critical to establish the stage of disease (i.e. when infection occurred) and whether effective treatment has been given previously. If effective treatment has been given it is important to exclude re-infection.

This usually requires three steps:

#### 1. Past and present history of syphilis including treatment and risk of re-infection.

It may be necessary to contact the public health unit in the patient's current and/or past area of residence where diagnosis and treatment history is recorded in specialised databases:

Communicable Disease Control Directorate (Perth):	9388 4999
Kimberley Population Health Unit (Broome):	9194 1646
Pilbara Population Health Unit (South Hedland):	9172 8306
Geraldton Population Health Unit:	9956 1958
Kalgoorlie-Boulder Population Health Unit (Boulder):	9080 8200
Wheatbelt Population Health Unit (Northam):	9622 4320
South West Population Health Unit (Bunbury):	9781 2350

#### 2. Clinical examination for stigmata of syphilis.

#### 3. Previous serology results.

These are easily obtained by phoning the State Reference Serology Laboratory at Pathwest Nedlands on 6383 4418. Electronic records are stored from 1995 onwards and paper records prior to 1995.

### TREATMENT OF THE MOTHER ACCORDING TO STAGE OF DISEASE

**Early syphilis** (less than 2 years duration, based on serology results) can be primary, secondary or latent (asymptomatic)

- **Benzathine penicillin 1.8g (2.4 million units) IM as single dose\*.**

OR

- **Procaine penicillin 1.5g IM, daily for 10 days**

*\*Some experts also recommend a second dose of IM Benzathine penicillin 1 week later*

*For patients with a history of penicillin hypersensitivity, a penicillin desensitisation protocol can be found in Australian Therapeutic Guidelines, version 15, 2014*

*For patients who are hypersensitive to penicillin and where desensitisation is not possible, discuss with a Clinical Microbiologist or Infectious Diseases Physician.*

Advise the patient to avoid sexual activity until lesions are healed. Sexual contacts in the last 3 months should receive the same treatment regardless of serology results.

**Late latent syphilis** - latent syphilis of more than 2 years or of indeterminate duration, in the absence of tertiary syphilis.

- **Benzathine penicillin 1.8g (2.4 million units) IM once weekly for 3 weeks (i.e. 3 doses).**

OR

- **Procaine penicillin 1.5g IM, daily for 15 days**

**Tertiary syphilis.**

- **Benzylicillin 1.8g IV every 4 hours for 15 days.**

In cardiovascular syphilis or neurosyphilis, concomitant treatment with prednisolone 20mg 12-hourly for 3 doses may be administered initially with penicillin dose to reduce the severity of the Jarisch-Herxheimer reaction (JHR)\* (see below).

Women treated for syphilis during the second half of pregnancy are at risk for premature labour and/or fetal distress if the treatment precipitates the Jarisch-Herxheimer reaction. Maternal-Fetal Medicine assessment is recommended when treating the mother during the second half of pregnancy. Some experts recommend administration of prednisolone for 24 hours prior to treatment and to continue for 48 hours following treatment in order to minimise JHR.

*Screening for other sexually transmitted diseases (ie chlamydia, gonorrhoea, HIV, HBV, HCV) must also be performed.*

Sexual partners from the last 3 months (if primary infection) and last 2 years (in the case of secondary and early latent syphilis) should also be assessed and treated. Patients with late latent and tertiary syphilis are not infectious to sexual partners.

Follow-up evaluation — RPR titres should be repeated monthly until delivery. A 4-fold decrease in titres or negative titre indicates successful therapy. Titres that decrease four-fold or become non-reactive at >4 weeks before delivery indicate successful treatment. Titres that show a four-fold rise or do not decrease appropriately suggest either treatment failure or re-infection. The treatment regimen should be repeated in these cases and lumbar puncture considered.

#### **\*Jarisch-Herxheimer Reaction (JHR)**

This reaction is a common occurrence in the treatment of early syphilis in adults (including pregnant women in up to 45%) and consists of fever, chills, malaise, hypotension and tachycardia. It begins within 2 hrs of treatment, peaks at 8 hrs and disappears in 24-36 hrs. Management is supportive care. It may precipitate uterine contractions, preterm labour, and/or non-reassuring fetal heart rate tracings in pregnant women treated in the second half of pregnancy. Women should be counselled to report symptoms of labour or decreased fetal activity. Fetal monitoring should be considered in women receiving treatment after 26 weeks gestation.

### **INVESTIGATION AND MANAGEMENT OF THE NEONATE BORN TO A MOTHER WITH SYPHILIS**

If congenital syphilis is a possibility, the following should be performed

- Infant serology (IgM, RPR) run in parallel with maternal serum specimen
- Full clinical examination: rash, mucosal lesions, nasal discharge, hepatosplenomegaly, bony tenderness, eye lesions.
- Placental histopathology plus syphilis PCR

If serology is abnormal, examination is abnormal or placental investigations suggestive of syphilis:

- **Further investigations – FBC, U&E, Creatinine, long bone X-rays, lumbar puncture for *T.pallidum* PCR, EIA / VDRL / TPPA**
- **Administer Benzylpenicillin 50mg/kg BD IV for 10 days**

**OR**

- **Procaine penicillin 50mg/kg IM for 10 days**
- Follow-up serology should be performed on the infant at 1,2,4,6 and 12 months of age, or until non-reactive on 2 occasions.
- If evidence of neurosyphilis, CSF should be re-examined at 6 months of age
- Treatment should be repeated if serology is persistently reactive or repeat CSF analysis is abnormal

*For cases of suspected or confirmed neonatal syphilis, discussion with / referral to a Paediatric Infectious Diseases Physician is recommended.*

**REFERENCES ( STANDARDS)**

1. Management of Perinatal Infections, Australasian Society for Infectious Diseases (2014)
2. Australian Therapeutic Guidelines, Antibiotic, Version 15 (2014)
3. Silver Book Guidelines for Managing Sexually Transmitted Infections – WA (2013). Govt of Western Australia Department of Health, Public Health
4. CDC Congenital syphilis - United States, 2003-2008. Centers for Disease Control and Prevention (2010)
5. CDC Sexually Transmitted Disease Treatment Guidelines. Centres for Disease Control and Prevention (2010)

National Standards – 1 Clinical Care is Guided by Current Best Practice  
Legislation - Nil

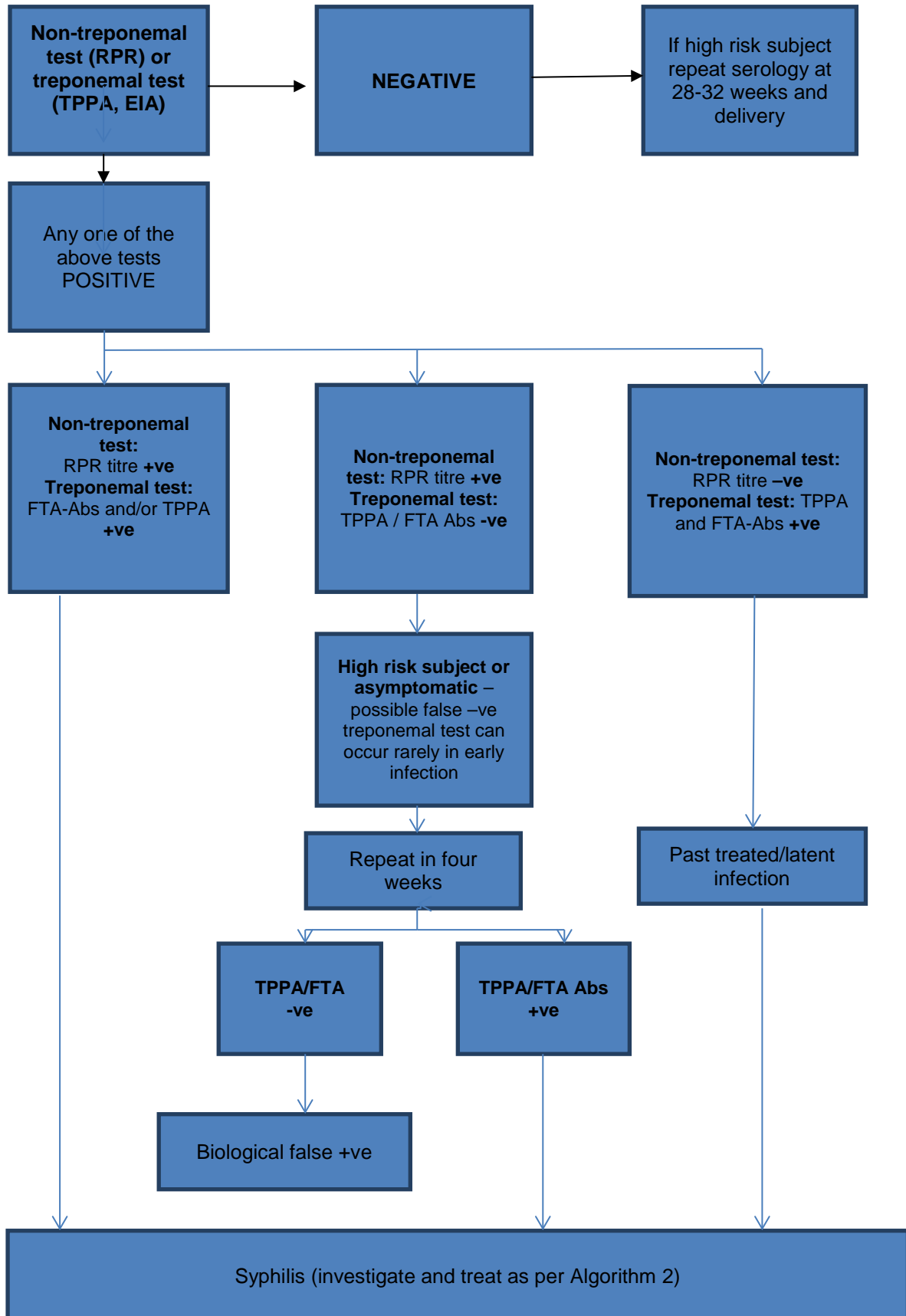
Related Policies - Nil  
Other related documents – Nil

**RESPONSIBILITY**

<b>Policy Sponsor</b>	HoD Microbiology
<b>Initial Endorsement</b>	November 2001
<b>Last Reviewed</b>	January 2015
<b>Last Amended</b>	
<b>Review date</b>	January 2018

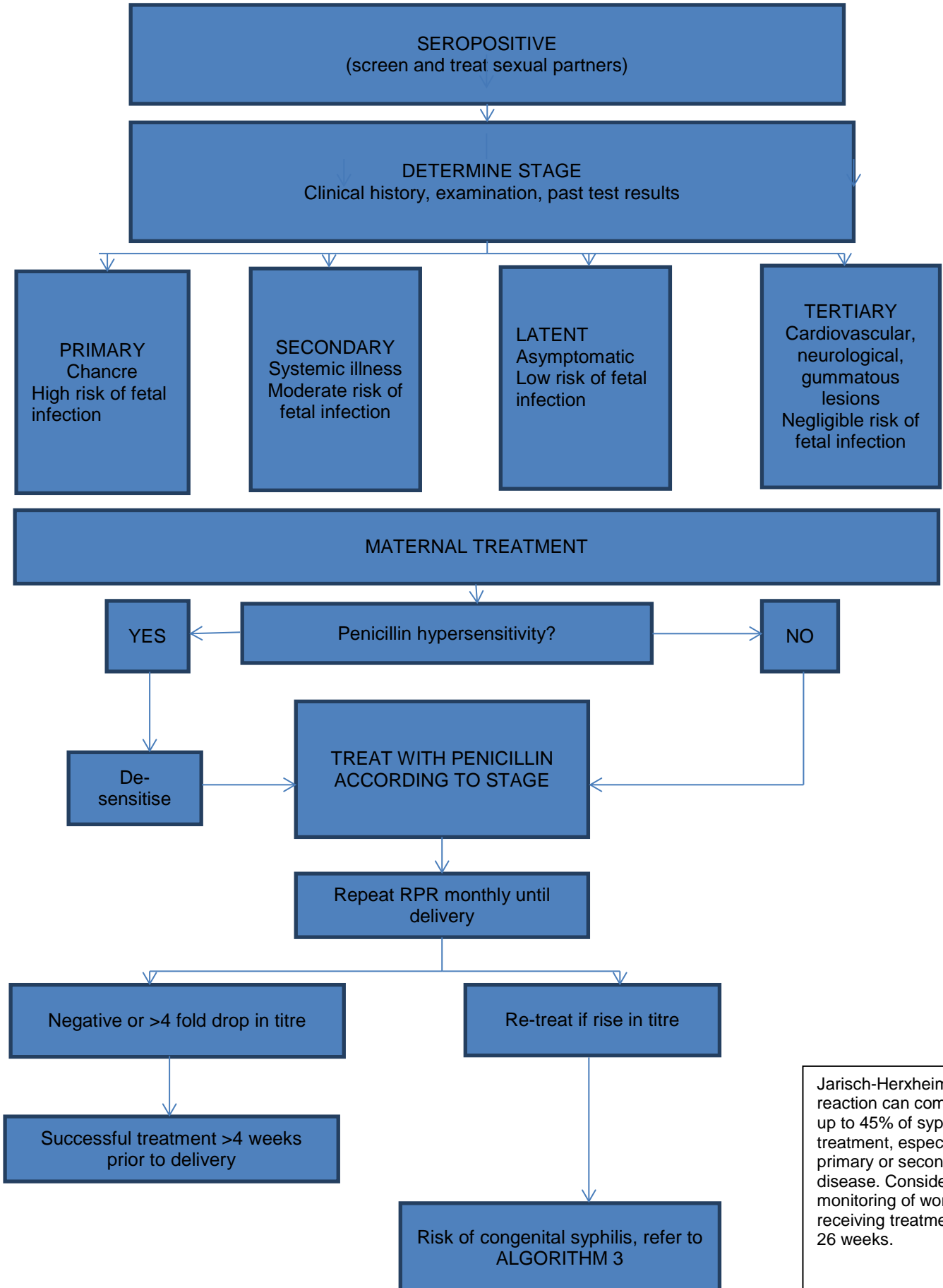


**Algorithm 1 – Antenatal Screening for Syphilis (Source: ASID Management of Perinatal Infections 2014)**





**Algorithm 2 – Investigation and Treatment of Maternal Syphilis (Source: ASID Management of Perinatal Infections 2014)**



**Algorithm 3 – Investigation and Management of a Neonate born to a mother with Syphilis (Source: ASID Management of Perinatal Infections 2014)**

