

# Management of infants at risk of congenital syphilis



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The procedural aspects of this guideline can be found in the document entitled:-

Guideline Proforma -

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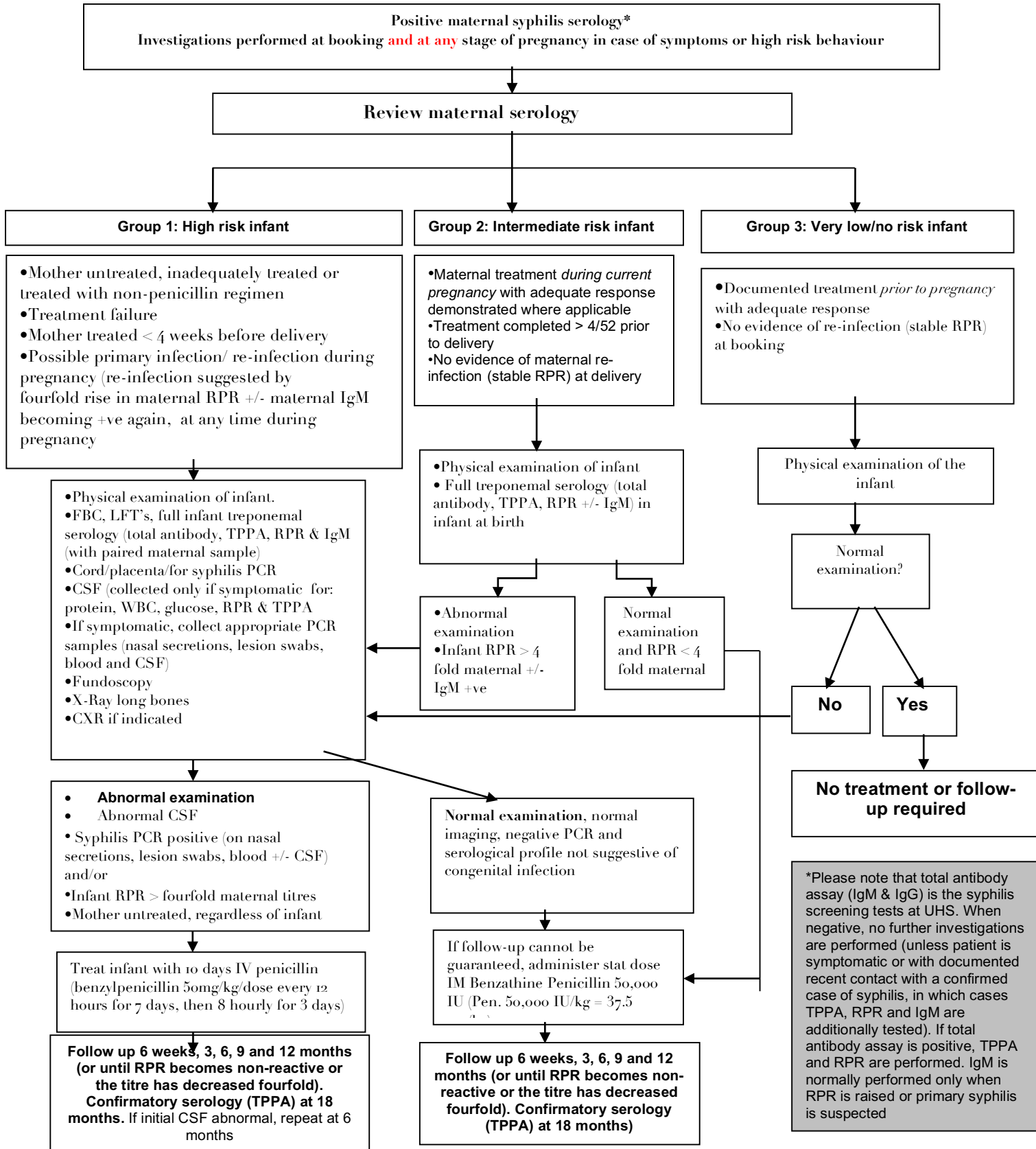
## 1. EXECUTIVE SUMMARY

There has been an increase in the diagnosis of syphilis in England since 1997. Syphilis control in pregnant women through universal screening and treatment of positive cases is important and has been established as a feasible and cost effective intervention. A large reduction in congenital syphilis is feasible with relatively simple interventions focused on maternal and newborn care.

The guideline is applicable for people involved in the care of newborn babies born to mothers diagnosed with syphilis. It gives overview information on congenital syphilis and on the identification, investigation, treatment and follow-up of exposed and infected infants.

It has been developed in agreement with members of the neonatal, virology and paediatric infectious disease teams of the trust and is in line with the CDC congenital syphilis treatment guidelines 2010, PHE syphilis diagnostic guideline and the BASHH UK national guidelines for the treatment of syphilis 2008.

## 2. Algorithm for assessment and testing of the baby born to a mother with confirmed syphilis



### 3. INTRODUCTION

Globally, just over 2 million pregnant women test positive for syphilis every year. This accounts for 1.5% of all pregnancies worldwide, resulting in profound outcomes like stillbirth, neonatal death, prematurity, low birth weight, or congenitally infected infant, including an estimated half a million perinatal deaths each year with the vast majority of these occurring in developing countries.

In the UK in 2011, 0.15% of pregnant women tested for syphilis were positive. Regional rates ranged from 0.06% in the North West to 0.39% in London. Positive syphilis serology results do not differentiate between active and past infection.

Between 1999 and 2007, the number of women diagnosed with infectious syphilis more than doubled, from 136 to 448 (Public Health England data). As the incidence among women has risen, cases of congenital syphilis have re-emerged reflecting a failure of syphilis control programmes. Since 1999, around 10 cases have been reported each year by genitourinary medicine (GUM) clinics but this probably represents only 30% to 50% of the cases that occur.

Cases can be prevented through antenatal screening; in England in 2005, 95% of pregnant women were screened for syphilis, although this hides wide regional variation (from 77% to 100%).

([http://www.hpa.org.uk/webc/HPAwebFile/HPAweb\\_C/1245581513523](http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1245581513523) accessed 14.8.13).

Transmission can occur at any point in pregnancy, but is most common in the last two trimesters. For this reason, women are screened for syphilis between 8 and 12 weeks gestation. Rates of infection remain disproportionately high amongst men who have sex with men (MSM) and HIV infected adults.

### 4. MANIFESTATIONS OF CONGENITAL SYPHILIS

#### 1) Early Congenital Syphilis

The early stage is characterized by the appearance of signs and symptoms before the age of 2 years. Early onset of symptoms in the first few weeks of life is associated with a poorer prognosis. Signs include:

a. **Cutaneous lesions:** The skin lesions seen shortly after birth are frequently vesicular or bullous with progression to superficial crusted erosions. Skin lesions seen in later weeks are frequently papulosquamous with generalized symmetrical distribution akin secondary stage syphilis and may form typical condylomata lata (genital lesions).

b. **Mucous membrane lesions:** The mucous membranes of the nose and pharynx are frequently involved to produce a heavy mucoid discharge which is referred to as "the snuffles." A haemorrhagic nasal discharge in the newborn period is characteristic of syphilis. Both the skin and mucous membrane lesions are teeming with spirochetes, causing these lesions and their secretions to be highly infectious. A positive diagnosis can be made using PCR from samples such as nasal secretions, skin lesion fluid, blood (EDTA sample) and CSF.

c. **Bone:** Involvement occurs in 60-80% of all untreated early congenital syphilis. Radiological abnormalities may be noted in 20% of infants with asymptomatic infection. Bone lesions commonly affect the tibia and other long bones. Lesions are usually multiple and symmetrical. Skeletal lesions range from osteochondritis, osteomyelitis, periostitis, metaphysitis, osteitis and dactylitis. Bone and cartilage involvement may be evident at birth with flattening of the nasal bridge due to destruction of the cartilage or may present as asymmetric, painful flaccid paralysis of the extremities resulting in reduced spontaneous movements, referred to as Parrot's pseudoparalysis.

d. **Anemia:** Most have haemolytic anemia which is generally self-limiting.

e. **Hepatosplenomegaly:** Frequently present (two-thirds of cases) and may be associated with jaundice and abnormal liver function tests.

f. **Central nervous system:** Up to 50 percent have abnormal cerebrospinal fluid findings; however, the incidence of clinical CNS manifestations is considerably lower.

## 2) Late Congenital Syphilis

Late congenital syphilis is defined as congenital syphilis which has persisted beyond 2 years of age. In about 60 percent the disease is latent with no manifestations other than a reactive serologic test for syphilis. The titers of the serologic tests in untreated congenital syphilis may fluctuate greatly, and when such fluctuations are seen this diagnosis should be suspected.

The signs of this stage represent late manifestations that occur as a result of scarring from early systemic disease. Late congenital syphilis is not infectious. The signs of late congenital syphilis can include:

a. **Interstitial keratitis:** Usually appears near puberty and eventually becomes bilateral. The cornea develops a ground glass appearance with vascularization of the adjacent sclera.

b. **Hutchinson's teeth:** Due to the poor development of the middle denticle, the permanent upper (occasionally the lower) central incisors develop a barrel-shaped and notched appearance and are smaller than normal, causing these teeth to be more widely spaced. Dental X-rays are useful in confirming the diagnosis.

c. **Eighth nerve deafness:** An unusual manifestation with onset frequently near puberty but occasionally delayed until middle age.

A combination of these interstitial keratitis, Hutchinson's teeth and eighth nerve deafness is referred to as the Hutchinson's triad.

d. **Mulberry or Moon's molars:** The first molars may show maldevelopment of the cusps.

e. **Neurosyphilis:** The congenital syphilitic may show the same manifestations of neurosyphilis as seen in adult-type (tertiary) syphilis. Tabes dorsalis is much less common and paresis is more frequent than in the adult-type disease.

f. **Bone involvement:** This may be sclerotic to produce a sabre shin appearance and frontal bossing, or it may be lytic (gummatous) and produce bony destruction, most frequently of the nasal septum (saddle nose) or the hard palate. Perforation of the palate is very suggestive of congenital syphilis. Any part of the skeletal system may be involved.

g. **Cutaneous involvement:** Rhagades (cracks or fissures around the mouth or nose) may result from infantile syphilitic rhinitis, but are rarely seen. Gummas may involve any portion of the skin or other organ systems as in the adult form of the disease.

h. **Clutton's joints:** Painless hydroarthrosis, usually of the knees, rarely involving the elbows or other large joints.

Clutton's joints, interstitial keratitis and eighth nerve deafness all have their onset near puberty and are commonly associated with each other.

#### **4. EXPLANATION OF LABORATORY INVESTIGATIONS**

Serological tests are the mainstay of screening and diagnosis. There are two types of serological tests: treponemal and non-treponemal.

##### **Treponemal tests:**

Include Treponema pallidum particle haemagglutination assay (TPPA), Treponema pallidum haemagglutination assay (TPHA), enzyme immunoassay (EIA), chemiluminescence immunoassay (CLIA) and fluorescent treponemal antibody absorption test (FTA-Abs). These tests remain positive indefinitely after primary infection

#### Non-treponemal tests:

Include Venereal Disease Research Laboratory test (VDRL) and rapid plasma reagin test (RPR). The titres decrease after effective treatment therefore these tests are beneficial in monitoring the response to treatment.

#### Interpretation of maternal serology:-

Treponemal test (EIA or CLIA or TPPA)	Non treponemal test (RPR)	Interpretation
Negative	Negative	Susceptible (no evidence of previous infection)
Positive	Negative	Infection at some time* <b>or</b> Early syphilis
Positive	Positive	Infection at some time* (RPR < 1 in 16) <b>or</b> Recent/active infection (RPR > 1 in 16)

\*Infection at some time includes treated syphilis and untreated latent syphilis: the two cannot be distinguished serologically.

**NOTE** for women at high risk of acquiring STIs, serological testing (syphilis, HIV, hepatitis B+C) should be repeated in the 3<sup>rd</sup> trimester or at delivery.

#### Interpretation of serology in the newborn:-

Treponemal serological profiles in babies born to sero-positive mothers or to recently infected mothers		
Total antibodies TPPA	RPR	Interpretation and action
Negative	Negative	<b>No serological evidence of congenital syphilis.</b> <b>However, baby could be sero-negative if mother acquired infection late in pregnancy.</b> <b>In this situation further investigations are warranted:</b> <ul style="list-style-type: none"> <li>• IgM test</li> <li>• PCR test on EDTA-blood, NPA &amp; lesions</li> <li>• Follow-up sample</li> </ul>
Positive	Positive with titre $\geq 4$ times than mothers	<b>Consistent with congenital syphilis.</b> <b>Confirm serological profile by performing an IgM test and by PCR on EDTA-blood,</b>



		<b>NPA &amp; lesions</b>
<b>Positive</b>	<b>Positive with titre &lt; 4 times than mothers</b>	<b>No serological evidence of congenital syphilis, antibody likely of maternal origin. Only baby's follow up advised. If any concerns, Confirm serological profile by performing an IgM test and by PCR on EDTA-blood, NPA &amp; lesions</b>
<b>Negative</b>	<b>Positive at any titre</b>	<b>Antibody likely of maternal origin or represents a false positive result. Discuss with Laboratory and Paediatric ID Consultant</b>

## 5. WHAT TO DO AT BIRTH

- There should be a 'birth plan' on edocs for each mother diagnosed with syphilis in pregnancy outlining the investigations and treatment required.
- Examine the infant looking for signs suggestive of congenital syphilis
- Review maternal notes to get further information on the following:
  - Maternal current clinical information
  - The latest syphilis serology results
  - The previous syphilis serology results
  - Information on previous treatment
- Assign infant to a risk category and follow investigation and treatment recommendations (see below). If in doubt, discuss with the Paediatric infectious disease team on 07824417993 or Dr Emanuela Pelosi (Consultant virologist, UHS).
- Fill out the Personal child health record documenting what treatment given
- Notify the paediatric infectious disease team the next working day.
- Arrange follow up of infant with paediatric infectious diseases team on discharge (see section 5 (page 14) for timing of follow-up). Please fax referral to Chris Dyche (Paediatric infectious diseases team secretary) on 023 8079 5230.

## 6. NOTES ON TREATMENT

- If > 1 day of therapy is missed, the entire course should be restarted
- There is no evidence that treating with other antimicrobials is effective therefore a 10 day course of penicillin must be completed even if other antimicrobials such as ampicillin were used previously to treat possible sepsis.
- Always check and document maternal HIV/hepatitis B and C status and ascertain whether mother has been screened for other STIs e.g Chlamydia

## 7. NOTES ON FOLLOW UP

High risk and intermediate risk seroreactive infants (or infants whose mothers were seroreactive at delivery) should receive careful follow-up examinations and serologic testing with a non-treponemal test (RPR). IgM should be rechecked at 6 weeks and 12 weeks (may be negative at birth if infected late in pregnancy).

Non-treponemal antibody titres should decline by age 3 months and should be nonreactive by age 6 to 12 months if the infant was not infected (i.e., if the reactive test result was caused by passive transfer of maternal IgG antibody) or was infected but adequately treated. If non-treponemal titres (RPR) remain unchanged or increase after age 6-12 months, the child should be discussed with the paediatric ID team (Southampton) and evaluated (e.g., undergo lumbar puncture and CSF examination) and retreated with a 10-day course of benzylpenicillin. Re-check titre at 6 wks & 3 monthly, as necessary, until 2 consecutive RPRs are negative

Treponemal titres should gradually decrease over 12-18 months. If the TPPA is -ve (and RPR -ve) at  $\geq 12$  months, the child can be discharged with no further follow-up. If the TPPA remains +ve beyond 18 months, this supports a diagnosis of treated congenital syphilis.

Infants whose initial CSF evaluation is abnormal should undergo a repeat lumbar puncture at 6 months. A reactive CSF VDRL test or abnormal CSF indices that cannot be attributed to other on-going illness requires re-treatment for possible neurosyphilis.

## 8. REFERENCES

- (i) CDC congenital syphilis treatment guidelines 2010  
<http://www.cdc.gov/std/treatment/2010/>
- (ii) UK national guidelines for the treatment of syphilis 2008  
[www.bashh.org/documents](http://www.bashh.org/documents)
- (iii) The Northern Ireland Antenatal screening programme, Guidelines on detection and management of syphilis in pregnancy  
<http://www.dhsspsni.gov.uk/hivpreganancyguidelines.pdf>
- (iv) <http://www.healthguidance.org/entry/6790/1/Chapter-VIII--Syphilis-in-Pregnancy-and-Congenital-Syphilis>.  
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- (v) Congenital syphilis in the United Kingdom; I Simms et al, Sex trans Infect 2006;82:1
- (vi) UK standards for microbiology investigations serological diagnosis of syphilis. HPA V44, 2011  
[http://hpa.org.uk/webc/HPAwebFile/HPAweb\\_C/1317134740009](http://hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317134740009)

## APPENDIX ROLES AND RESPONSIBILITIES

**ACTION: Public Health England Southeast Regional Laboratory, UHS,  
Consultant Medical Virologist**