Joint Guideline for the Management of Infants Born to Mothers with Positive Syphilis Serology

A Clinical Guideline recommended for use

For Use in:	Blakeney Ward, Delivery Suite, Neonatal Unit
By:	Medical and Nursing staff
For:	For infants born to mothers with positive syphilis serology
Division responsible for document:	Women and Children's Services
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This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

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Version and Document Control:

Version Number	Date of Update	Change Description	Author
1.2	01/05/2020	Changed to include QEH	Dr Florence Walston
1.3	06/06/2022	No clinical changes. Short review given to allow another review in one year	Dr Florence Walston

This is a Controlled Document

Printed copies of this document may not be up to date. Please check the hospital intranet for the latest version and destroy all previous versions.

Glossary	
VDRL/RPR	Venereal Disease Research Laboratory test / Rapid Plasma Regain test
TPPA	Treponema pallidum Particle Agglutination Assay
IgM EIA	Immunoglobulin M Enzyme Immunoassay

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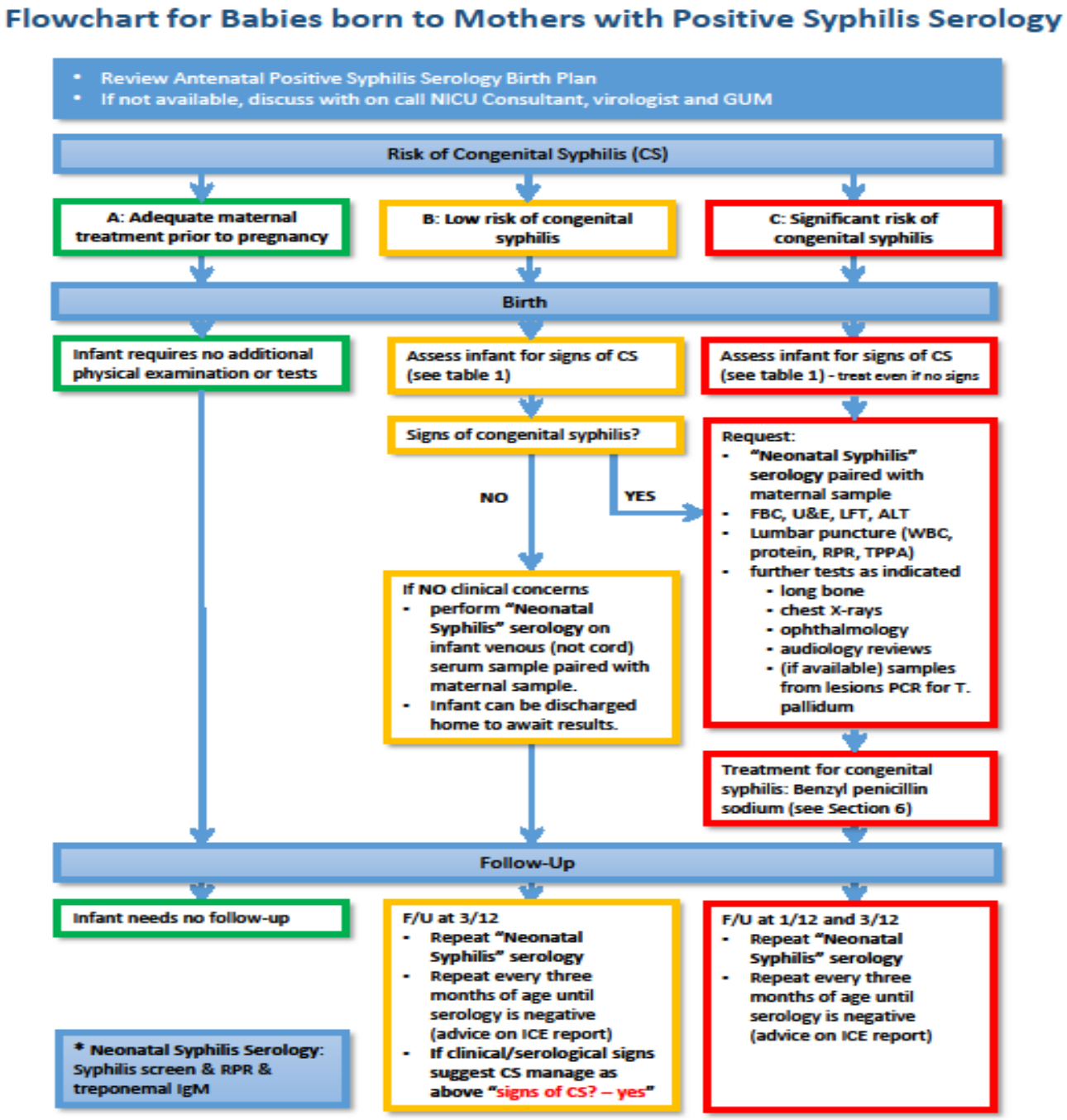
1. Quick Reference Guide *(double click picture below to expand)*



2. Introduction

Congenital Syphilis (CS) is uncommon in the UK, with approximately 10 cases reported annually. Consequently, most paediatricians will have little or no experience of managing the condition. The diagnosis of CS can be very difficult: most infected neonates appear normal at birth and passive transfer of maternal IgG across the placenta may cause reactive neonatal syphilis serology, even in the absence of CS. Given these difficulties, it is important that paediatricians and GU physicians work closely when managing neonates.

CS is divided into early (diagnosed in the first two years of life) and late (presenting after two years). This guideline will only address early CS. The presence of signs at the time of delivery is dependent on the duration of maternal infection and the timing of treatment. Around two-thirds of infants with CS will be asymptomatic at birth but most will develop signs by five weeks.

3. Antenatal Positive Syphilis Serology Birth Plan and Flowchart

A Quick Reference Guide (Section 1) and template syphilis birth plan (Appendix A) have been developed to supplement the use of this guideline and support the appropriate management of babies born to mothers with positive syphilis serology.

4. Management of Babies Whose Mothers have Positive Syphilis Serology

All babies whose mother have had positive syphilis serology antenatally should have an **Antenatal Positive Syphilis Serology Birth Plan**. This should be in the Neonatal Alert folder as well as on the Electronic Template. If no birth plan is available, please speak to the Neonatal Consultant on call, the Virology Consultant on call and the GUM consultant (in-hours) to formulate a plan.

The baby's risk will be categorised into one of the following three options:

A. Adequate maternal treatment prior to pregnancy

Infants born to mothers where:

- Maternal syphilis was cured prior to this pregnancy.
- Maternal biological false-positive serology.

Need no investigation, treatment or follow-up.

B. Low risk of congenital syphilis

Infants born to mothers who:

- Are treated for syphilis more than four weeks prior to delivery with a penicillin regimen with no evidence of re-infection or relapse
- Decline re-treatment when it is difficult to rule out re-infection
- Were previously treated for syphilis but have a high VDRL/RPR (more than 4) will require:

Blood tests at birth:

- Request **"neonatal syphilis**" on ICE
- Ask midwifery team to send maternal sample "**paired maternal syphilis**" on ICE
- The clinical details on both requests should state the maternal and infant hospital number and also the risk of CS in the infant – low (**B**) or high risk (**C**).

- A full clinical examination (**see section 5 – Diagnosis of CS**).
  - If there is clinical suspicion of CS (**see Section 5 – Diagnosis of CS**), please treat as '**C- Significant risk of congenital syphilis'**.
  - If there is no clinical suspicion of CS, the baby can be discharged home to await the results. Please see **Section 6 – Results** and **Section 7 – Follow-Up** for further details.

C. Significant risk of congenital syphilis

In the case of:

- Infants with suspected congenital syphilis
- Infants born to mothers treated less than four weeks prior to delivery
- Infants of mothers treated with non-penicillin regimens in pregnancy
- Infants born to untreated mothers
- Infants born to mothers who were inadequately treated or who have no documentation of being treated

In all of these infants, investigation and treatment for CS should be given using the regimen detailed below (**Section 5 - Diagnosis of CS and Section 7 - Treatment of CS**).

5. Diagnosis of CS

The clinical signs of CS include:

- Jaundice, anaemia, generalised lymphadenopathy,hepatosplenomegaly, non-immune hydrops, pyrexia, failure to move an extremity (pseudoparalysis of Parrot), low birth weight, glomerulonephritis, neurological or ocular involvement, haemolysis and thrombocytopenia
- Skin rash (usually maculo-papular, but almost any form of rash is possible); the palms and soles may be red, mottled and swollen. Vesicles or bullae may be present.
- Condylomata lata - flat, wart-like plaques in moist areas such as the perineum).
- Skeletal abnormalities - osteochondritis, periosteitis (elbows, knees, wrists).
- Ulceration of the nasal mucosa, haemorrhagic rhinitis ('bloody snuffles' usually presents after the first week of life), perioral fissures

Investigation:

- PCR of exudates from suspicious lesions, or body fluids, e.g. nasal discharge
- Serological tests - on infant's blood not cord blood - request "**neonatal syphilis**" serology on ICE. The clinical details on both requests should state the maternal and infant hospital number and also the risk of CS in the infant – low (**B**) or high risk (**C**).

- Further investigations will be required if the infant is suspected/likely to have CS:
    - Blood: full blood count, liver function, electrolytes.
    - CSF: cells, protein, serological tests.
    - If clinically indicated:
        - Ophthalmic assessment
        - X-rays of long bones
        - chest X-ray
        - audiology reviews and
        - PCR for *Treponema pallidum* from suspicious body fluids

6. Results

The results on ICE will provide information and advice about the results and necessary action. The following indicate a diagnosis of congenital infection:

- A positive IgM EIA test.
- A positive RPR/VDRL test on CSF.
- A four-fold or greater difference of RPR/ VDRL titre or TPPA titre above that of the mother.
- A four-fold or greater increase in RPR/VDRL or TPPA titre within three months of birth.
- In a child more than 18 months age, positive treponemal tests.

In order to make the diagnosis of CS more specific, a combination of clinical signs and laboratory tests are used. These are described in Tables 1 and 2, but all suspected cases **must** be discussed with the on-call virology team

(*Kaufman*)

Table 1. Criteria to be applied (in Table 2) for diagnosing congenital syphilis.

Absolute	Major	Minor	Serology
T. pallidum identified on dark ground, PCR or histology	Condylomata lata	Fissures of lips	A. Positive RPR/VDRL or TPPA/TPHA
	Osteochondritis	Skin rash	B. Positive IgM
	Periosteitis	Mucous patches	C. Negative RPR/VDRL or TPPA/TPHA
	Snuffles (haemorrhagic rhinitis)	Hepatomegaly	D. Positive RPR/VDRL not becoming negative within four months
		Splenomegaly	E. Rising RLR/VDRL over three months
		Generalised lymphadenopathy	
		Neurological signs	
		Heamolytic anaemia	
		CSF pleocytosis or raised protein	

RPR: rapid plasma reagin; VDRL: Venereal Diseases Research Laboratory; CSF: cerebrospinal fluid; TPHA: *Treponema pallidum* haemagglutination assay; TPPA: *Treponema pallidum* particle agglutination assay; PCR: polymerase chain reaction.

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Table 2. Certainty of a congenital syphilis diagnosis from assessment of the infant using the clinical criteria in Table I

Definite	Probable	Possible	Unlikely
One or more absolute criterion	Serology E or D	Serology A or B with no clinical criteria	Serology C
	One major criterion plus serology A or B		Serology A or B plus mother known to be adequately treated
	Two or more minor criteria plus serology A or B		
	One major and one minor criteria		

7. Treatment of Congenital Syphilis

All infants in **"C - Significant risk of congenital syphilis"** (**see Section 4 - Management of Babies Whose Mothers have Positive Syphilis Serology**) should be investigated and treated for possible CS, even if there are no clinical signs.

If a baby in the category **"B - Low risk of congenital syphilis"**, only treat if there is clinical or serological evidence that the baby has likely CS, including during their period of follow-up.

The treatment regimen is:

Congenital syphilis	Recommended regimens	Alternative regimen	Clinical notes
	1. Benzyl penicillin sodium - 60–90 mg/kg daily IV (in divided doses given as –30 mg/kg 12 hourly in the first 7 days of life and 8 hourly thereafter for 10 days:1C	2. Procaine penicillin 50,000 u/kg daily IM × 10 days	In children IV therapy (option one here) is preferable due to the pain associated with IM injections.

Interruptions in treatment congenital syphilis

- If drug administration is interrupted for more than one day at any point during the treatment course, it is recommended that the entire course is restarted.

8. Follow-Up

A. Adequate maternal treatment prior to pregnancy

a. Infant needs no follow-up for syphilis.

B. Low risk of congenital syphilis

a. Following investigation at birth (paired mother/baby samples – see **Section 5 – Diagnosis of CS**) the baby can be discharged home if no suspicion of CS to await the results (guidance will be provided on the ICE report from the virology team).

b. Follow-up in **Named Consultant's Clinic**

c. Review at three months of age with repeat **"Neonatal Syphilis"** serology on ICE, then three monthly until serology is negative (guidance will be provided on the ICE report from the virology team).

d. If there is clinical suspicion of CS at any point, or titres remain stable or increase, the child should be evaluated and treated for CS (**see Section 5 - Diagnosis of CS and Section 7 - Treatment of CS**). This should be done in discussion with the virology team.

C. Significant risk of congenital syphilis

a. Following investigation and treatment in hospital, follow-up should be arranged in with the **Named Consultant.**

b. Review at one month and three months of age with repeat **"Neonatal Syphilis"** serology. Assuming satisfactory results, see three monthly with repeat **"Neonatal Syphilis"**, until serology is negative (guidance will be provided on the ICE report from the virology team).

Based Upon:

BASHH UK national guidelines on the management of syphilis 2015 (https://www.bashhguidelines.org/media/1053/syphilis-2015.pdf)

Reference:

Kaufman RE, Jones OG, Blount JH, et al. Questionnaire survey of reported early congenital syphilis: problems in diagnosis, prevention, and treatment. Sex Transm Dis 1977; 4: 135–139.

Appendix A
Antenatal Positive Syphilis Serology Birth Plan *(to be formatted into a letter to GP)*

Maternal details

Estimated date of delivery.
Maternal syphilis diagnosis, treatment details and dates:
Other concerns (e.g. Re-infection risk from partner, treatment late in pregnancy, etc)

Advice for infant management:

A. Adequate maternal treatment prior to pregnancy

a. At birth: Infant requires no additional physical examination or tests for syphilis.

b. Follow-up: Infant needs no follow-up for syphilis.

B. Low risk of congenital syphilis

c. At birth: Assess infant for signs of congenital syphilis. If no concerns, request **Neonatal Syphilis** serology (with maternal samples "**paired maternal syphilis"**) on infant venous (not cord) serum sample. The clinical details on both requests should state the maternal and infant hospital number and also the risk of CS in the infant – **low risk**.

d. Follow-up: Request "**Neonatal Syphilis" serology** and repeat at three months of age then every three months until serology is negative (advice will be given on ICE report).

e. **If clinical or serological signs suggest CS**, manage according to '**option C'** below – significant risk of CS.

C. Significant risk of congenital syphilis

f. At birth: Assess infant for signs of CS (see Guideline). Request **"Neonatal Syphilis" serology** (with maternal samples "**paired maternal syphilis"**) on infant venous (not cord) serum sample. The clinical details on both requests should state the maternal and infant hospital number and also the risk of CS in the infant – **high risk**. Infant will also require FBC, U&E, LFT, ALT, lumbar puncture (request WBC, protein, RPR, TPPA). Further tests as clinically indicated; long bone and chest X-rays, ophthalmology and audiology reviews and (if available) samples from lesions PCR for *Treponema. pallidum*

g. Treatment for congenital syphilis: Benzyl penicillin sodium – 60–90 mg/kg daily IV (in divided doses given as – 30 mg/kg 12 hourly in the first seven days of life and 8 hourly thereafter for 10 days

h. Follow-up months 1 and 3: Request **"Neonatal Syphilis" serology**

i. Follow-up months 6 and repeat at three months of age then every three months until serology is negative (advice will be given on ICE report).

Please discuss all infants with suspected syphilis or requiring treatment with the NICU Consultant/On Call virologist/GUM consultant.

Local contact details:

Plan completed by:

Date:

Copies to: obstetric team, GUM, mother, neonatal alert folder