NEONATAL GUIDELINES

Postnatal Infection Guidelines

Version 2018.4.3

Specialty:	Neonatal Medicine
Revision date:	26th April 2022
Revised by:	Dr. Jamie Evans, Dr Sree Nittur
Edited by:	Dr. Jamie Evans
Approved by:	Perinatal Forum
Date Approved:	8th April 2022
Date Implemented	26th April 2022
Date for Review:	31st October 2022

Directorate of Child Health

Checklist for Clinical Guidelines being submitted for Approval by SBUHB Perinatal Forum

Title of Guideline:	**Postnatal Infection Guidelines**
Name(s) of revising author(s):	Dr Sujoy Banerjee, Dr. Geraint Morris, ANNP Gemma Davies and Steph Cannell
Chair of Group or Committee supporting submission:	Perinatal Forum – Sujoy Banerjee
Issue / Version No:	Postnatal ward Infection guidelines v2018.4.2
Next Review / Guideline Expiry:	31st October 2022
Details of persons included in consultation process:	Neonatal Consultants, Neonatal junior doctors, Nursing Managers, Midwives
Brief outline giving reasons for document being submitted for ratification	Only change is splitting the postnatal Chapter into sections – updated Oct 2021 to change Hep B immunoglobulin dose only and remove SRC which is elsewhere in postnatal Chapter. This update includes minor changes to Hep B and Hep C policy only
Name of Pharmacist (mandatory if drugs involved):	Katherine Wilson
Please list any policies/guidelines this document will supercede:	Postnatal ward guidelines 2018.4.2
Keywords linked to document:	**Postnatal, Infection**
Date approved by ABMU Perinatal Forum:	April 2022

Contents

Guidelines on management and risk assessment of Early Onset Sepsis for infants ≥34 weeks gestation on Postnatal Ward

(Midwifery led units may choose to risk assess and continue to follow existing guidelines. Families should be informed of this so that they can make an informed choice of the place for delivery)

Purpose:

To provide guidance on risk assessment and management of early onset sepsis (EOS) in neonates of greater than or equal to 34 weeks gestation, including the use of the Kaiser Permanente Sepsis Risk Calculator (SRC). In Wales, SRC will be implemented from 1st April 2019 as per the following guidance.

Background:

Culture proven EOS in the UK in term and near-term infants is infrequent (about 0.5/1000 live births) but is associated with high morbidity & mortality. Group B streptococcus (GBS) is the commonest organism identified in EOS followed by Gram-negative infections. Nearly 15-20% infants on the postnatal wards are screened by traditional univariate risk-based algorithms (e.g. NICE and RCOG guidelines) and offered prophylactic antibiotics, until investigations clear the infant of infection. These risk-based strategies can identify only 50-60% of all EOS cases. In addition, a significant proportion of EOS cases are symptomatic at birth and do not require any algorithm for identification. Thus, the number of infants needing treatment to identify a case of culture proven sepsis in the early asymptomatic phase is estimated as 1 in 600-800 near- term live births.

Developed in the USA, The Kaiser Permanente Sepsis Risk Calculator (SRC) is a multivariate model of assessing the risk of EOS using maternal risk factors and the infant's clinical state after birth (https://neonatalsepsiscalculator.kaiserpermanente.org). The use of SRC in the USA has been shown to reduce antibiotic initiation in newborn infants by 50% without missing additional cases of true sepsis and this finding has been replicated in other parts of the developed world with consistent results. For more information, please review references at the end of this document.

No sepsis algorithm can function without excellent clinical care and professional judgment. **The following generic principles apply in all situations and supercede any sepsis algorithm-**

1. All infants symptomatic of sepsis must be investigated and treated promptly with antibiotics within 1 hour of the decision to treat. This is irrespective of their sepsis risk score. See appendix 1 for common signs of clinical sepsis. If you are unsure, seek senior help.

2. Investigations for sepsis should include a blood culture **(a minimum of 1ml of blood must be inoculated into the blood culture bottle)**, FBC and a CRP. The latter should be repeated in 18-24 hours.

3. Where there is a history of confirmed Group B Streptococcal sepsis or death of a neonate in previous pregnancy, and the mother has not received adequate intrapartum prophylaxis in this pregnancy, the newborn infant should be screened and presumptively treated irrespective of the sepsis risk score.

For the full guidance on SRC please see the separate section in the postnatal Chapter dedicated to SRC

Investigations needed for sepsis screen:

- Sepsis screen should include a FBC, CRP and a blood culture. CRP should be repeated at 18 – 24 hours
- Chest X-Ray may be indicated if symptoms refer to the respiratory system.
- Lumbar puncture should be performed initially if -
  1. **there is a strong clinical suspicion of infection and not just risk factors**
  2. there are clinical symptoms and signs suggesting meningitis
  3. If blood culture is positive

If lumbar puncture would delay the start of antibiotics, then it should be performed as soon as possible after starting antibiotics.

- The ideal volume of blood for culture is 1 – 2 ml. It is important to state the volume collected on the request form as well as clinical notes
- Skin swabs are only performed if there are signs of localized infection. Routine skin swabs are misleading.
- Swabs should be taken if there is conjunctivitis with **purulent** eye discharge to identify Chlamydia or Gonococcus.
- When a line infection is suspected, blood specimens should be collected both from the line (only through Hickman Line) and a peripheral vein.

Antibiotic Policy:

- Babies with suspected early onset neonatal sepsis should be treated **as soon as possible and definitely within 1 hour of the decision to treat.**
- Explain to the parents where possible the reason for treatment, observation and investigations needed and likely duration of treatment. Treatment and care should take into account the needs and preferences of parents and carers, as appropriate. Parents and carers whose babies are at risk of or have an early-onset neonatal infection should have the opportunity to make informed decisions about their baby's care and treatment, in partnership with their healthcare professionals. Where parents cannot be contacted, continue management without delay.
- Please remember to discuss with the obstetricians and the laboratory staff the results of any swabs or cultures taken from the mother, particularly if the mother has received antibiotics prior to delivery.

First Line Antibiotics:

These are usually used within the first 72 hours or after birth for a presumed or suspected early onset sepsis

- **Benzyl Penicillin** - 60mg/kg/dose
- Use one dose 12 hourly in the first week.
- One dose 8 hourly in babies 1-4 weeks and
- One dose 6 hourly in babies of 4 weeks or more

The dosage interval should be increased in renal failure

AND

- **Gentamicin -** The dose is as follows
- Babies less than 1 week old - 5mg/Kg every 36 hourly
- Babies greater than 1 week old - 5mg/Kg every 24 hourly
- Babies > 28 days old - 7mg/Kg every 24 hourly

The interval may be shortened, based on clinical judgement, for example if the baby appears very ill or the blood culture shows a Gram-negative infection. Increase interval between dosages in renal failure. If drug levels are not available do not withhold gentamicin

unless there is suspicion of renal dysfunction (anuria / raised Creatinine)

- **Amoxicillin** and **Gentamicin** should be used if Listeria is considered on clinical grounds
  - Maternal pyrexia and flu-like symptoms prior to delivery
  - Meconium-stained liquor in a preterm infant
  - Macular rash or other signs of sepsis
- **Flucloxacilin and gentamicin** is recommended if there are signs of umbilical infection (purulent discharge or periumbilical cellulitis)

Initial choice and modification of antibiotics in babies with suspected meningitis:

If causative organism not known	Treat with Amoxicillin and Cefotaxime

Therapeutic drug level monitoring of Gentamicin:

Generally only trough levels are required. Check trough levels 4-6 hours before the 3rd dose, if Gentamicin needs to be continued beyond the 36 hours. **If more than 3 doses of Gentamicin are used, check trough levels every 3rd dose.**

Trough (pre-dose) <2 mg/L

If trough levels >2 mg/L increase interval by 12 hours

If adjustment are needed please recheck the levels after the 6th dose. If renal function is compromised, Gentamicin may need to be withheld until trough levels are back to normal.

If more than 3 doses of Gentamicin are to be given then trough level of < 1 mg/ L is advised.

Consider measuring peak blood gentamicin concentrations in selected babies

- oedema
- macrosomia (birth weight more than 4.5 kg)
- an unsatisfactory response to treatment
- proven Gram-negative infection.

Measure peak concentrations 60 minutes after gentamicin administration, if given by bolus or infusion.

If a baby has a Gram-negative or staphylococcal infection, consider increasing the dose of gentamicin if the peak concentration is less than 8 mg/litre (such babies should normally be on the neonatal unit).

How to write up 36 hourly Gentamicin?

When an infant needs Gentamicin to be prescribed 36 hourly, this needs to be written as below:

1. Write on the 'once only and pre-anaesthetic medical' area of the prescription chart.
2. Each dose must be written separately and the date & time for each dose to beclear.
3. Write on the regular medications side of the prescription chart – 'GENTAMICIN' – please see once only'.
4. As for all medications, print clearly and sign.

Prescription writing

- Drug dosage given in the Neonatal Formulary is used unless stated otherwise in our protocols
- Observe the principles of safe prescribing
- Give the first dose immediately and always within 1 hour of the decision totreat.
- Prescribe in a realistic manner – an easily measurable amount of the drug. It is pointless prescribing volumes to an accuracy of one thousandth of a ml (e.g. prescribe Gentamicin to the nearest 100 microgram and Benzyl Penicillin to the nearest milligram)
- In renal failure check the pre-dose before giving any further doses.

How to decide the duration of the antibiotic treatment?

- Prolonged and unnecessary use of antibiotics leads to the development of drug resistance and should be avoided. All babies on antibiotics on the postnatal ward should be reviewed daily and the need for continuing antibiotics discussed with a senior. If needed, discuss with the microbiologist
- During antibiotic treatment, measure CRP at 18 - 24 hours after presentation.
- Lumbar puncture should be considered in a baby on antibiotics who did not have this

investigation at presentation if blood culture is positive or who is not responding to the treatment either clinically or through persistent rise of inflammatory markers

- The duration of antibiotic treatment should be determined by whether or not infection is confirmed on bacteriological culture, the nature of the infecting organism, the focus of infection and the clinical condition of the baby.
- NICE recommends having a system in hospitals that can provide blood culture results 36 hours after starting antibiotics to support timely antibiotic discontinuation and hospital discharge.
- If cultures are negative at 36 hours, CRP levels are normal or falling satisfactorily from the peak level and the baby is well with no signs of infection, antibiotics may be discontinued.

IF IN DOUBT – DISCUSS.

Remember that all drugs have side effects, and it is not good practice to continue antibiotics without a good reason

The following are "best practice" guide on antibiotic treatment duration in different clinical scenarios.

Scenario	Duration
Low suspicion / well baby / Negative culture/ No rise in CRP > 10 on 2 samples 24 hours apart	Stop at 36 hours if blood culture still negative.
Strong suspicion of infection with rise in CRP and WBC, Good clinical and laboratory response to treatment / Negative blood culture	Use clinical judgement and response to treatment as a guide. Discuss with Senior regarding length of treatment.
Pneumonia with negative blood culture	5 days
Other scenarios	See NNU guidelines

Follow up:

1. **When a baby who has had a confirmed GBS infection is discharged from hospital**
    - ***advise the woman that if she becomes pregnant again (document in notes):***
        - there will be an increased risk of early-onset neonatal infection
        - she should inform her maternity care team that a previous baby has had a GBS infection

    - ***inform the woman's GP in writing that there is a risk of:***
        - recurrence of GBS infection in the baby, and
        - GBS infection in babies in future pregnancies.

References:

1. Puopolo KM, Benitz WE, Zaoutis TE. Committee On Fetus And Newborn, Committee On Infectious Diseases. Management of Neonates Born at ≥35 0/7 Weeks' Gestation With Suspected or Proven Early-Onset Bacterial Sepsis. Paediatrics. Volume 142, number 6, December 2018:e20182894

2. Centers for Disease Control & Prevention (2010). Prevention of Perinatal Group B Streptococcal Disease: Revised Guidelines from CDC, 2010. Morbidity & Mortality Weekly Report, Nov, 19, 2010; 59(RR10); 1-32. http://www.cdc.gov/groupbstrep/guidelines/guidelines.html accessed 8/11/2015

3. Neonatal infection (early onset): antibiotics for prevention and treatment. Clinical guideline [CG149]. Published August 2012. https://www.nice.org.uk/guidance/cg149.

4. Newman T, Puopolo KM, Wi S, Draper D, Escobar GJ. Interpreting Complete Blood Counts Soon After Birth in Infants at Risk for Sepsis. Pediatrics 2010; 126:903-909.

5. Puopolo KM, Draper D, Wi S, Newman TB, Zupancic J, Lieberman E, Smith M, Escobar GJ. Estimating the Probability of Neonatal Early-Onset Infection Based on Maternal Risk Factors. Pediatrics. 2011; 128:e1155-1163.

6. Escobar GJ, Puopolo KM, Wi S, Turk BJ, Kuzniewicz MW, Walsh EM, Newman TB, Zupancic J, Lieberman E, Draper D. Stratification of risk of early-onset sepsis in newborns >=34 weeks' gestation. Pediatrics. 2014 Jan;133(1):30-6.

7. Dudhasia MB, Mukhopadhyay S, Puopolo KM. Implementation of the Sepsis Risk Calculator at an Academic Birth Hospital. Hospital Pediatrics 2018;8(5): 243-250. DOI:https://doi.org/10.1542/hpeds.2017-0180

- Not interested in feeding, or not taking feeds as well as they used to
- Vomiting
- Becoming too hot or too cold
- Looking pale
- Unusual jerking movements
- Becoming floppy
- Breathing quickly or having difficulty breathing.

If any of these things happen, or if you are concerned for any other reason, please let the nurses, midwives or doctors know.

Unless your baby becomes more unwell he/she will stay with you on the ward. You can feed, change, and care for your baby as you would normally. Your baby may need to be taken elsewhere briefly to have their antibiotics but then will be brought straight back to you.

Time to head home

Once the doctors are happy that your baby does not have an infection they will stop the antibiotics. We may advise you to stay in with your baby for another 24 hours, but in most cases we will aim to let you go home on the same day the antibiotics are stopped.

Once you get home, please try to remember the signs of infection shown in the list above. If you are concerned, ask for advice about what to do next.

You can contact your GP, call NHS 111 or go to your local Accident and Emergency department.

Any questions?

If there is anything you are not sure about, please feel free to ask one of the doctors, midwives or nurses looking after your baby.

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GIG CYMRU NHS WALES 70

Wales Neonatal Network

WALES NEONATAL NETWORK

Screening for Infection in Newborn Babies – Information for Parents

This information leaflet is for parents of babies who may need additional observations or treatment for infection in the first days following birth.

Why is my baby being observed or treated for infection?

A small number of babies become unwell after birth because of infection from bacteria. Fortunately, this is rare, occurring in only 1 in 2000 babies. There are a number of things that can put a baby at higher risk of having an infection, such as:

- The mother's waters broke more than 18 hours before the baby was born
- The mother is a carrier for a bacteria called Group B Streptococcus
- The mother has an infection at the time of delivery
- The baby is premature (born before 37 weeks)

It can be difficult to predict which babies will get an infection and become unwell, but the midwives, nurses and doctors caring for you and your baby will be able to decide whether your baby should be monitored more closely ('enhanced observations') for 24-36 hours, or have blood tests and antibiotics.

What happens if my baby is on 'enhanced observations'?

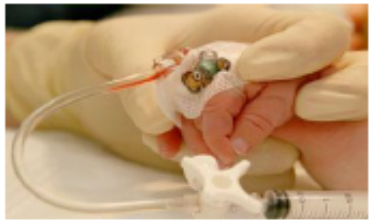
Your baby will be observed for 24-36 hours in the postnatal ward and will stay with you. The midwifery team will monitor for any early signs of infection at regular intervals and will inform the neonatal team if they are concerned. If your baby remains well, the regular observations can be stopped. However, if your baby shows any of the signs shown below, a member of the neonatal team will be asked to see your baby and to decide if he/she should have blood tests and antibiotic treatment.

Signs of an infection after birth include:

- Having difficulty with breathing
- Having too high or too low a temperature
- Being lethargic or floppy
- Feeding poorly
- Having a poor colour

Starting antibiotics

The baby's doctor will pass a small plastic tube (cannula) into a vein in your baby's hand or foot. This is used to give the antibiotics as an injection. It is better for newborn babies to get their antibiotics in this way, rather than as a medicine to swallow, because their stomachs may not absorb medicines very well.



The antibiotics we usually use are called Gentamicin and Benzylpenicillin. At the same time as putting the cannula in place, the doctors will take some blood samples to test for infection. If your baby remains well, and the blood tests are negative for infection, then the antibiotics are usually stopped after 36-48 hours. However, if the results show signs of infection, your baby may need to stay on antibiotics, and may also need more tests to find out where the infection has come from. A course of antibiotics usually last for 5-7 days, but can sometimes last longer. Please discuss this with your Neonatal team or midwife.

Your stay on the postnatal ward

As your baby will be with you most of the time it's worth bearing in mind some things you may notice which may alert you to seek help for your baby:

- Behaving different to normal, such as being irritable or tired

Chickenpox (Varicella)

If at all possible, delivery should be delayed, until after 7 days from onset of maternal rash, to allow maternal VZV immunoglobulin to be transferred across the placenta to the fetus before birth.

If delivery occurs from 7 days before to 7 days after the onset of the maternal rash (highest risk if 5 days before to 2 days after), there is a risk of developing severe neonatal chicken pox. In this situation, mother and baby should be nursed in a separate cubicle on the labour or postnatal ward. Breast-feeding is not contraindicated. Management of the infant should follow the chart below.

Maternal chicken pox rash onset: **7days before to 7 days after** delivery	→	Monitor for at least 48hrs for signs of chicken pox Give Acyclovir at earliest suspicion
Maternal chicken pox rash onset: **5 days before to 2 days after** delivery	→	**Give VZIG** Monitor for at least 48hrs for signs of chicken pox Give Acyclovir at earliest suspicion

Note:

VZIG 250 mg deep IM injection. Acyclovir is an infusion and needs to be given on NICU.

Chicken pox exposure in the first week of life on the post-natal wards or in the community:

A well newborn whose mother has no immunity to VZV (history of **not** having had chicken pox in the past), may develop neonatal infection if exposed to chicken pox in the first 7 days of life. It is recommended that these babies receive VZIG, and if any signs of chicken pox develop, they should receive a course of IV acyclovir.

In postnatally acquired chickenpox the rash begins 10-28 days after birth. The illness is generally mild and no treatment is needed.

In complicated cases discuss with infection control, virologist and the public health consultant

Guideline for the management of Neonatal Herpes Infection

Introduction - Herpes simplex virus (HSV):

HSV-1 and HSV-2 are DNA viruses that belong to Alpha herpes viridae, a subfamily of the Herpes viridae family. Both serotypes are transmitted across epithelial mucosal cells as well as through skin interruptions, and then migrate along local sensory nerves, where they persist in a latent stage.

Neonatal herpes may be caused by herpes simplex virus type 1 (HSV-1) or herpes simplex virus type 2 (HSV-2) as either viral type can cause genital herpes in a mother. In the United States and Canada, HSV-1 is now emerging as the principal cause of genital herpes. (1,2,3).

Most people are unaware they have a herpes infection and in the majority of neonatal herpes disease there is no antenatal history of herpes. (4)

Neonatal infection can follow **primary** or **recurrent** maternal infection, or be acquired postnatally through direct contact with infected secretions. Trans-placental transmission is unusual (5%), and perinatal infection in usually acquired during vaginal delivery through an infected birth canal.

The pregnant woman who acquires genital herpes as a primary infection in the latter half of pregnancy is at the greatest risk of transmitting these viruses to her newborn (25-60% risk). Whereas an infection resulting from reactivation of an infection acquired during the first half of pregnancy or earlier has a <2% risk.(3,4, 5,12)

It is estimated that 6 weeks may be required for a mother to develop and transfer immunity after a primary episode. If babies are born prematurely, then the transplacental transfer of immunity is reduced. (3)

Epidemiology:

Neonatal HSV disease is a rare but potentially devastating condition. Untreated neonatal HSV infection is associated with only a 40% survival rate. Early recognition and the early initiation of high-dose IV acyclovir can significantly improve survival and morbidity rates.

Risks of transmission:

- First episode – Primary infection – 57%
- Recurrent infection – 2%

Risk varies with:

- serotype
- mode of delivery
- rupture of membranes
- prematurity
-

Surveillance of neonatal HSV in the UK was undertaken through the BPSU in 1986-1991. The estimated prevalence of infection found was 1.65/100,000 (CI 1.3-2.0/100,000). HSV-1 and HSV-2 were reported in equal proportions, but in one third of cases the virus was not typed.(6)

However the incidence of genital herpes has increased by 89% between 2003 and 2012 and in the USA the frequency of neonatal HSV infection is 33 (3-60) per 100,000 live births.(7)

Clinical Presentations:

Congenital HSV infection is rare; it shares features such as microcephaly, hydrocephalus, and chorio-retinitis with other congenital infections and is usually manifested by clinical abnormalities at birth.

Postnatal acquisition of HSV is almost always due to HSV-1 and is associated with contact with hospital personnel or family members who are shedding HSV-1.8

Most neonatal infections result from exposure to HSV during delivery - **Perinatal acquisition.**

The clinical presentation of perinatal and postnatal infections has been divided into 3 categories, each of which is associated with different outcomes and clinical manifestations: **SEM (skin, eyes and mucosa)**, **CNS disease** and **disseminated disease** (see table)

Table: Clinical presentation of neonatal herpes

SEM disease - Cutaneous (45%)	**CNS HSV infection (30%)**	**Disseminated HSV infection (25%)**
Infection is confined to the skin, eyes and mucosa. **Disease elsewhere (disseminated and CNS) must be excluded.** Typically present by 1-2 weeks of life, but may present at birth. May be a single vesicle or group of vesicles, often in a linear distribution if affecting the limbs. Progression to extensive disease will occur in the absence of treatment. With high dose IV acyclovir, long term outcome is good. May have recurrent outbreaks of cutaneous herpes during early childhood.	Encephalitis without visceral involvement, mainly affecting temporal lobes. Associated with lethargy, poor feeding and seizures; cutaneous lesions may or may not be present. **Pleocytosis** is usually present; HSV DNA in the CSF is the most sensitive lab test for confirming the diagnosis. Samples of CSF obtained early in the illness may be falsely negative. Higher morbidity with CNS HSV- 2 infection than HSV-1. Long term morbidities - developmental delay, epilepsy and blindness. Relapses of CNS infection may occur – further increasing morbidity.	Highest fatality rate (30-80%), even with antiviral therapy. Typically present at 5-10 days with sepsis like illness involving multiple organs (liver, lungs and brain). Rash is absent in up to 50% of cases. Need to ensure blood and CSF sent for HSV PCR. May be clues in lab tests like a **raised ALT** and **coagulopathy** but may not be evident at presentation. Long term suppressive therapy may have a role in reducing morbidity.

Investigations:

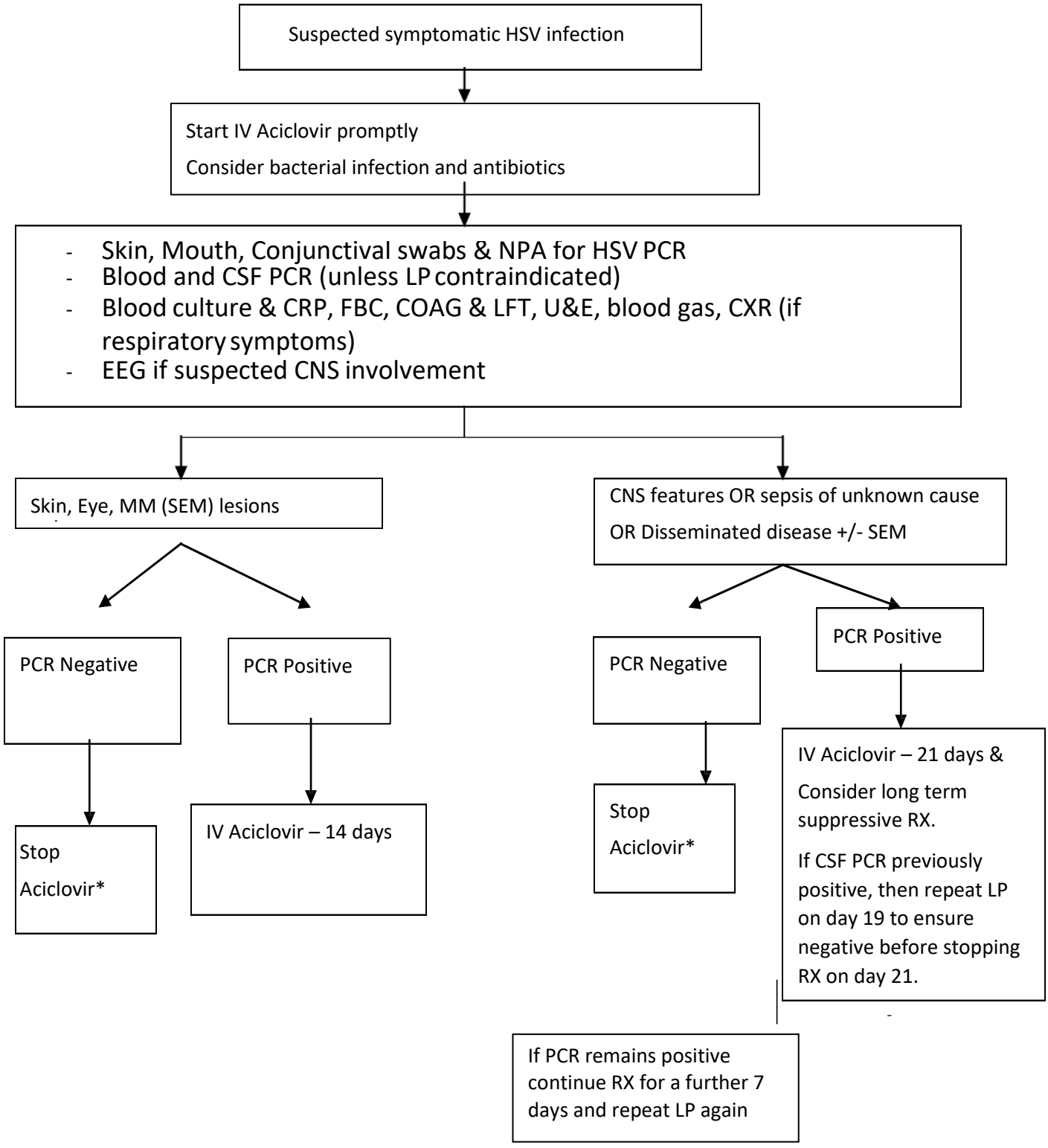
Essential diagnostic virology investigations

Type of investigation	Site	Specimen container	Expected availability or results
Herpes PCR	Skin vesicle base, de-roof and scrub the base	Dry Swab – not in Transport Medium – snap black swab into universal container	Processed in UHW -24-72hrs
Herpes PCR	Eyes, Mouth, NPA aspirates	Dry Swab – snap into universal container.	Processed in UHW – 24-72hrs
Herpes PCR	Blood	EDTA – purple top At least 1ml sample, preferably 2 mls if retesting required. Send in multiple paediatric containers	Processed in Manchester – can take up to a week – ask Singleton to send straight to Manchester to save time. Not via UHW.
Herpes PCR	CSF	Clear universal container	Processed in UHW – 24-72hrs
Please discuss with virology team for specific advice about investigations during working hours and **alert the laboratory before sending specimen asking to be processed URGENTLY (Ext: 5060/5059)** **UHW only process HSV PCR tests Monday – Friday, not over weekends.** For information on chasing results – University Hospital of Wales Cardiff Virology department: 029 2074 2178			

1. Routine blood investigations – Blood culture & CRP, FBC, LFT and COAG, U&E.
2. CXR if respiratory symptoms. Typical findings of a bilateral diffuse pneumonitis.
3. Neuroimaging may localise disease but not essential.
4. In SEM, seek ophthalmologic opinion early. In all other cases dilated ophthalmologic examination to assess chorioretinitis during the first week and at 6 months. Additional topical agent (trifluridine) is recommended for ocular disease.
5. EEG if suspected to have CNS involvement, especially if seizures observed. Typically shows characteristic tempero- parietal high-voltage low-frequency activity.

Management: Please see Table 1 and Algorithm 1 and 2 for full explanation of management pathways.

Algorithm 1. Symptomatic Neonatal HSV



- **Negative PCR results should not be used on their own to exclude invasive herpes disease, but in conjunction with the entire clinical scenario.**

Algorithm 2: Asymptomatic baby exposed to HSV[10,11]

Table 1: Assessment of Risk of Neonatal Herpes Infection, and Neonatal Plan

Risk Group	Timing of Maternal HSV	Maternal HSV Symptoms in Pregnancy	Mode of Delivery	Neonatal Plan
R1	Pre pregnancy genital HSV	No Symptoms	Any	Plan C
R2	Recurrent Infection	Recurrent genital herpes with NO active lesions at onset of labour	Any	Plan C
R3		Recurrent genital herpes WITH active lesions at the onset of labour	EL. LSCS with no ROM *	Plan C
			Other	Term baby - Plan B Preterm baby – Plan A
R4	Primary Infection	1st Episode > 6 weeks before delivery and no active lesions (if lesions present – treat as Risk group 3)	EL. LSCS with no ROM*	Plan C
			Other	Term baby – Plan B Preterm baby – Plan A
R5		1st Episode < 6 weeks before delivery	EL. LSCS with no ROM*	Plan C
			Other	Plan A

*Rupture of membranes = > 4hours before delivery

Plan A:

- Investigate and Start IV Aciclovir FBC, LFT & COAG at birth
- After 36-48hrs – send samples for HSV PCR – Blood, CSF, Surface swabs (and NPA if respiratory symptoms)
- Continue IV Aciclovir until PCR results available
- PCR Negative – Stop treatment
- PCR Positive – IV Aciclovir 14 days or 21 days if disseminated/CNS infection Term

babies can stay on the postnatal ward if asymptomatic

Plan B:

- Observe on the postnatal ward for 48hrs.
- After 36-48hrs – send samples for HSV PCR – blood and surface swabs. If well at 48hrs parents can be given option to go home to await results with the knowledge they may be required to be readmitted if positive result.

Plan C:

- Provide information for parents – http://www.nhs.uk/conditions/neonatal-herpes
- No tests indicated, unless infant is symptomatic
- Advise parents to seek medical attention if unwell in first 2 weeks

Pharmacological management:

Aciclovir dosage:

20mg/kg every 8 hours for 14 days (for at least 21 days if CNS involvement – confirm CSF negative for herpes simplex virus before stopping treatment).13

Transient neutropenia has been detected in about 20% of infants treated with these high doses of Aciclovir, but it has not been reported to result in clinically significant adverse outcomes. 9

Long Term Suppressive Treatment

Recent studies have shown that long term suppressive therapy may improve neurological outcomes. The long term oral Aciclovir treatment (300mg/m2 for six months) should be considered in disseminated and CNS cases after completion of acute treatment. These babies will need regular FBC and LFTs (suggested times at discharge, 1mo, 3mo and 6mo).

Prevention:

Infants may acquire HSV infection postnatally from contact with active HSV lesions. Therefore, the following is recommended:

A. Avoid direct contact between active lesions and neonate. Topical Aciclovir should be used by staff and family members for cold sores. Meticulous hand washing precautions.

B. Cover lesions if possible.

C. If baby is not on NICU, the baby should be isolated in a single room with mother so as to isolate from other neonates.

D. Breastfeeding is only contraindicated in the event of a herpetic lesion on the breast.

References:

1. Xu F, Sternberg MR, Kottiri BJ, McQuillan GM, Lee FK, Nahmias AJ*, et al.* Trends in herpes simplex virus type 1 and type 2 seroprevalence in the United States. *Jama*. 2006 Aug 23;296(8):964-73.

2. Gupta R, Warren T, Wald A. Genital herpes. *Lancet*. 2007 Dec 22;370(9605):2127-37.

3. Foley E, Clarke E et al. Management of Genital Herpes in Pregnancy. *Royal College of Obstetricians and Gynaecologists. NICE accredited*. October 2014.

4. Anzivino E, Fioriti D, Mischitelli M, Bellizzi A, Barucca V, Chiarini F*, et al.* Herpes simplex virus infection in pregnancy and in neonate: status of art of epidemiology, diagnosis, therapy and prevention. *Virol J*. 2009;6:40.

5. Baker DA. Consequences of herpes simplex virus in pregnancy and their prevention. *Curr Opin Infect Dis*. 2007 Feb;20(1):73-6.

6. Tookey P, Peckham CS. Neonatal herpes simplex virus infection in the British Isles. *Paediatr Perinat Epidemiol*. 1996 Oct;10(4):432-42.

7. Corey L, Wald A. Maternal and neonatal herpes simplex virus infections. *The New England journal of medicine*. 2009 Oct 1;361(14):1376-85.

8. Kimberlin DW. Herpes simplex virus infections in neonates and early childhood. *Semin Pediatr Infect Dis*. 2005 Oct;16(4):271-81.

9. Kimberlin DW, Lin CY, Jacobs RF, Powell DA, Corey L, Gruber WC*, et al.* Safety and efficacy of high-dose intravenous acyclovir in the management of neonatal herpes simplex virus infections. *Pediatrics*. 2001 Aug;108(2):230-8.

10. Batra D et al. Guideline for management of neonatal herpes infection. Nottingham Neonatal Service – Clinical Guidelines. July 2014.

11. Patel R, Alderson S, et al. European guideline for the management of genital herpes, 2010.

12. Kimberlin DW, Baley J et al. Guidance on Management of Asymptomatic Neonates Born to Women with Acitve Genital Herpes Lesions. *American Academy of Pediatrics Clinical Report*. February 2013, Volume 131/Issue 2.

13. British National Formulary for Children. Herpesvirus infections – Aciclovir Indications and dose. 2016.

Contributors:

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Hepatitis C infection in pregnancy and the newborn period

Introduction

Hepatitis C virus (HCV) is a small single stranded RNA virus of the family flavivirus. In the UK, the carriage of Hepatitis C is approximately 0.4% of the population and about 1 per 1,400 healthy adult blood donors. The virus may be transmitted perinatally or by blood transfusion. Blood products have been screened since 1991 but a small risk remains that the virus may be transmitted by blood transfusion in the immediate post infective period prior to the development of antibodies

Hepatitis C is the main cause of sporadic Non A Non B hepatitis. The average incubation period is 6 weeks with a range of 2 weeks to 6 months. Only a minority of patients experience symptoms during the acute stage with fever, malaise, jaundice and abdominal discomfort. Mean time from infection to presentation, usually with the complications of cirrhosis is 10-15 years. Chronic infection with the virus occurs in over 80% of cases. Hepatitis C accounts for 50% of cases of chronic hepatitis. It is a risk factor for hepatocellular carcinoma. With chronic disease, autoimmune complications are common e.g. arthritis, serum sickness and erythema multiforme.

Perinatal Transmission:

HCV infection is not screened routinely in the antenatal population, unless there are specific maternal risk factors. The risk of vertical transmission from an infected mother to her baby is low, only around 5%. Factors which increase the transmission rate are maternal viraemia with detectable HCV RNA, concurrent HIV infection (risk increased to 48%) and a lack of Anti-C 100 antibodies. Most pregnant women who are Hepatitis C positive have sub-clinical liver disease and remain well throughout pregnancy, with no deterioration in their liver function. There is no increased risk of obstetric complications or prematurity although there may be a fall in ALT and a rise in Hepatitis C virus RNA in the last trimester. There is no increased risk with vaginal delivery and there is no data to suggest that breast-feeding infants born to Hepatitis C-infected mothers affects the transmission rates.

Mothers who should be offered antenatal screening include:

- IV drug abusers(60-80% will be positive) or those with past history of drug misuse
- Those with HIV or Hepatitis B
- Those who have received haemodialysis (10-50% will be positive).
- Women whose partners are known to be Hep C positive

50% of the infected populations have no identifiable risk factor.

What to do if a mother is found to be antibody positive?

If a mother is found to be antibody positive in pregnancy then hepatitis C PCR for circulating viral RNA is needed to determine infectivity, together with liver function and coagulation studies. If hepatitis C PCR is positive, indicating an active infection as opposed to a previous infection then the

mother should be referred to Dr Chin Lye Ch'ng if from Swansea and Dr. Clem Lai if booked in POW for further assessment and consideration of treatment following pregnancy

How to manage an infant born to an infected mother?

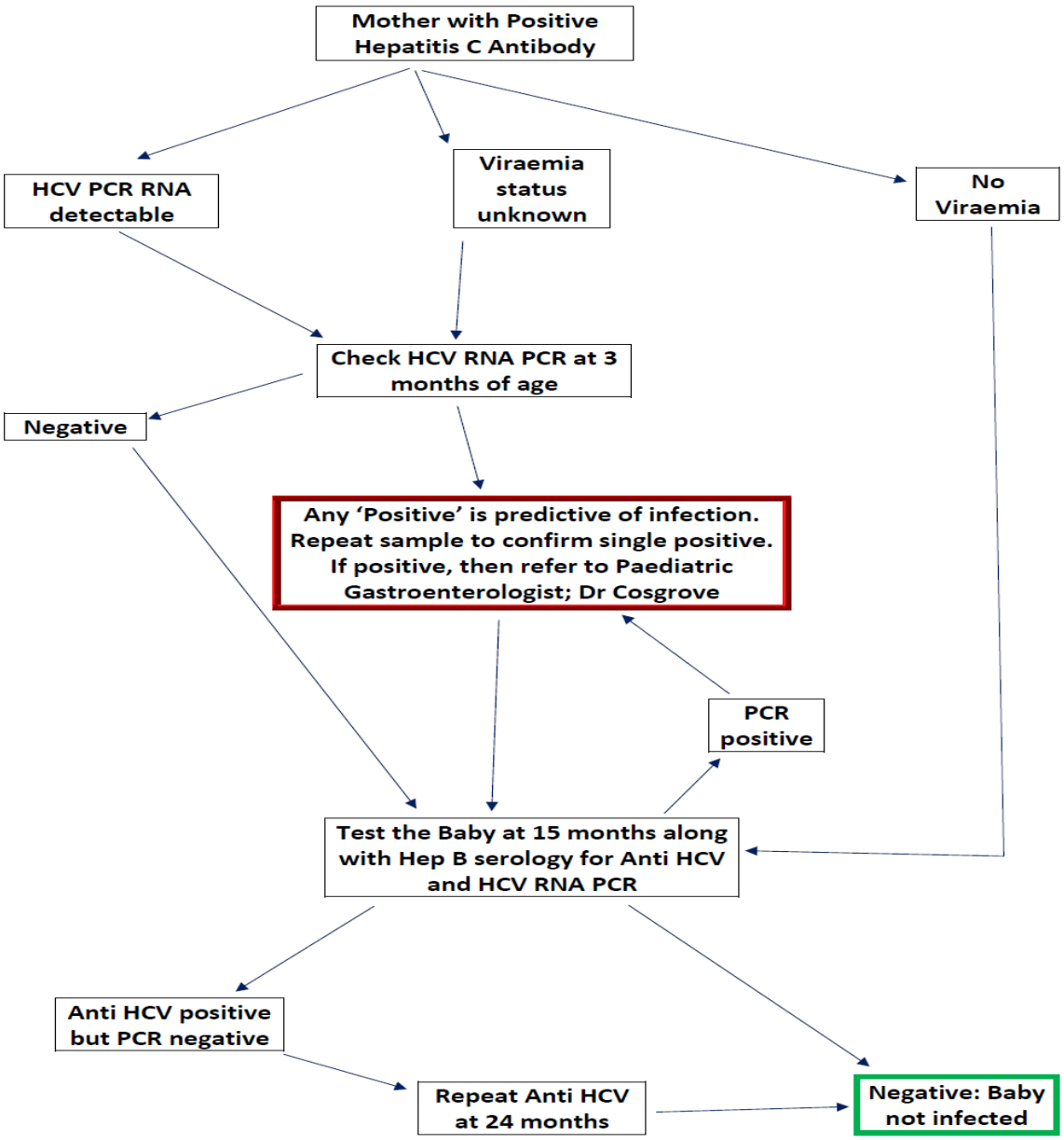
Hepatitis C infection is usually relatively silent in the newborn period and throughout childhood. HCV serology is not reliable during infancy because passively transferred maternal antibody may persist up to 18 months and sometimes beyond. Majority will be seronegative by 12 months of age. Earlier diagnosis of HCV infection is very unlikely to alter management. In view of parental anxiety and concerns on part of health care professional, that infant may be lost to follow-up, it is reasonable to check HCV RNA PCR at 3 months in high-risk cases.

Infants born to mothers with previously documented Hepatitis C infection but with NO viraemia should have a blood test for the presence of anti HCV and HCV RNA PCR at 15 months of age. If anti HCV is positive, but PCR is negative, then repeat at 24 months of age. If PCR is positive, then it needs urgent referral to paediatric gastroenterologist Dr M Cosgrove.

In case of infants born to mothers infected with HCV and with detectable HCV RNA PCR or unknown viraemia status, the infant should be tested for HCV RNA PCR at 3 months of age. If it is positive, perform a repeat sample and if again positive then refer to Dr Cosgrove. If negative then, perform anti HCV at 15 months. Persistent infection develops in around 85% of infected neonates even in the absence of biochemical evidence of liver disease.

Babies born to all Hep C positive mothers, whether current or past infection, should be offered Enhanced Hepatitis B vaccination. Please refer to the Hepatitis B guideline for further details.

The following is a suggestion for follow up and investigation:



- Refer to Neonatal Consultant of the week. In POW refer to the paediatric consultant of the week. Needs regular follow up as per above flowchart.
- If PCR positive, measure LFTs.
- NB: Antibody tests may be negative in infants who are immunocompromised.
- Every effort should be made to provide and complete Hepatitis B vaccination

Diagnosis is confirmed by positive HCV RNA PCR on two samples

OR

Anti HCV Elisa antibody test positive after 18-24 months of age

Treatment:

- Treatment of Viral Hepatitis C for adults has advanced tremendously in the last few years. Interferon with unpleasant side effects is now no longer needed. Therapy of 8 – 12 weeks with an all oral pangenotypic Direct Acting Antiviral (DAA) has shown eradication rates of nearly 100% regardless of severity and stage of liver fibrosis.
- Both European Medicine Agency and American FDA have also approved the use of Direct Acting Antiviral (DAA) without interferon for use in adolescents aged between 12-17 (weight > 35 kg). DAA may be available for children aged 3 and above soon and it is recommended to defer treatment if possible until DAA is available.
- If infection is confirmed baby will be referred in Swansea to Dr Mike Cosgrove. Referral to a liver centre for liver biopsy is of value in staging histological disease and determining response to therapy (less likely to respond if there is cirrhosis). This is usually undertaken at around 2 years of age.
- Infants who have confirmed hep C infection should be vaccinated against Hepatitis B and against Hepatitis A.

References:

1. Vertical HCV infection – Standards Unit, Evaluation and Standards laboratory, HPA , VSOP 8Ii, Nov 2007
2. Diseases of the liver and biliary system in children. Edited by Deidre A Kelly. Chapter 6 pp 104-108
3. Hepatitis C virus infection. American Academy of Pediatrics Committee of Infectious diseases. Pediatrics 1998; 101: 481- 485
4. EASL International Consensus Conference on Hepatitis C, Paris 1999. Consensus statement J Hepatology 1999; 30:956- 61
5. The silent infection: should we be testing for perinatal hepatitis C and, if so, how? W Hardiker, EJ Elliott et al MJA 2006;184(2) 54-55
6. Treating viral hepatitis c: Efficacy, side effects and complications MP Manns, H Wedmeyer Gut 2006;1350-135
7. Treatment of chronic viral hepatitis C in children and adolescents: UK experience. Abdel-Hady M et al. Arch dis child 2014; 99:505-10.
8. Excluding hepatitis C virus (HCV) infection by serology in young infants of HCV-infected mothers. England K, Pembrey L, et al. European Paediatric HCV Network. Acta Pediatr 2005.
9. http://www.cps.ca/documents/position/vertical-transmission-of-hepatitis-C

Management of Perinatal Hepatitis B transmission

Section Author Dr Sree Nittur

Hepatitis B is an infection of the liver caused by the hepatitis B virus (HBV). Hepatitis B surface antigen (HBsAg) is used to screen for the presence of this infection. It is the first detectable viral antigen to appear during infection. Shortly after the appearance of the HBsAg, another antigen - hepatitis B e antigen (HBeAg) will appear. Traditionally, the presence of HBeAg in a host's serum is usually associated with much higher rates of viral replication and enhanced infectivity. During the natural course of an infection, the HBeAg may be cleared, and antibodies to the 'e' antigen (anti-HBe) will arise immediately afterwards. This conversion is usually associated with a dramatic decline in viral replication.
Individuals who remain HBsAg positive for at least six months are considered to be hepatitis B chronic carriers. PCR tests detect and measure the amount of HBV DNA - viral load, to assess a person's infection status and to monitor treatment.
The World Health Organization (WHO) has estimated that over 350 million people worldwide are chronically infected with HBV.

High-prevalence regions:
- Sub-Saharan Africa
- Majority of Asia
- Pacific islands

Intermediate-prevalence regions:
- The Amazon
- Southern parts of Eastern and Central Europe
- The Middle East
- The Indian sub-continent

Low-prevalence regions:
- Western Europe
- North America

The Overall prevalence of HBsAg in antenatal women in the UK is around 0.4% (National Antenatal Infections Screening Monitoring**.** P**revalance** rates found in antenatal women can vary from 0.05 to 0.08% in some rural areas but rise to 1% or more in certain inner city areas where populations with origins in endemic countries are higher.
The virus is transmitted by parenteral exposure to infected blood or body fluids. Transmission mostly occurs:
- through vaginal or anal intercourse
- as a result of blood-to-blood contact (e.g. sharing of needles and other equipment by injecting drug users (IDUs), 'needle-stick' injuries)
- through perinatal transmission from mother to child.

Infants who are infected during pregnancy and birth are at high risk (90%) of becoming chronic carriers. Appropriate immunization can, however, prevent the infant developing chronic infection in over 90% of cases. (DH 2013)

Screening Pregnant Women
Screening for infectious diseases is an integral aspect of antenatal care. Occasionally women are not screened due to non-attendance at antenatal clinic or refusal to allow blood tests. In these cases, please ask the obstetric or midwifery staff to send blood from the woman urgently and ring virology to request fast tracking and let us know the results urgently.

Babies born to Hepatitis B positive women
After obtaining parental consent, immunization of babies of infected mothers should be commenced as soon as possible after birth. The immunization regime now consists of 6 doses of vaccine given intra-muscularly: (* **see changes after introduction of new 6-in-1 vaccine)**
Hepatitis B immunoglobulin, if required (see table 1 in the care pathway below), is given in a dose of 250 IU to the newborn at the time of the first vaccination. It should be given at a different site from the hepatitis B vaccination.

If mothers who are Hep B positive refuse the vaccination of their infants, then this becomes an immediate child protection issue.
We also strongly advise the immunization of babies born to **Hep B negative** women in the following high-risk groups, but this cannot be enforced against maternal wishes:
• IV drug abusers
• Current or past history of drug misuse.
• Those with HIV or Hepatitis C
• Women whose partners are known to be Hep B, Hep C or HIV positive
• Women from high and intermediate prevalence countries (see above)

***Changes after introduction of new Hexavalent vaccine (Infanrix hexa) from 1st August 2017:**
• All babies born on or after 1st August 2017 will be offered a hexavalent DTaP/IPV/Hib/HepB vaccine as part of the routine immunizations at 2, 3 and 4 months in the community at GP surgeries, thus making Hepatitis B vaccination routine for all.

• As per the Public Health Wales & England guidelines (see reference), antenatal maternal Hepatitis B screening programme and post-natal Hep B immunization of high risk infants will continue despite routine Hepatitis B vaccination in community, as follows:

- **1st dose at birth (+/- Hepatitis B Immunoglobulin as per the pathway) in hospital**
- **2nd dose at 1 month in Neonatal outpatient clinic**
- **3rd dose will now be part of routine vaccinations in community at 2 months; 4th and 5th doses at 3 and 4 months as part of routine immunizations**
- **6th – final dose at 1 year in Neonatal outpatient clinic**
- **At 15months, infants should have blood tests for HbsAg and Anti HBs Ag (hepatitis B immunity levels). Please remember to request both on the blood forms**

Care Pathway of pregnant woman who are Hepatitis B +ve

Antenatally: - Responsibility of Midwife
1. Midwife to please give woman an information sheet "Information for pregnant women who are hepatitis B positive" – available from Antenatal Screening Wales website:http://www.antenatalscreening.wales.nhs.uk/sitesplus/documents/968/Information for women who are Hepatitis B Positive English.pdf

2. Midwife to please notify **Jill Bonney – Public Health nurses - Health protection team at public Health Wales** (01792 607 387), 1st Floor, 36 Orchard Street, Swansea, SA1 5AQ, email: jill.bonney@wales.nhs.uk, of names and dates of births of other children and father of baby. They will notify the GP and undertake contact tracing if necessary. It is the GP's responsibility to ensure vaccination of these individuals and any other household contacts.

3. If other children are in care, the midwife should notify Dr Peter Barnes, Consultant Community Child Health giving names and dates of births of the children and placement if known.

4. If mother is Hepatitis B positive and HBe Ag positive or no HBe markers or HBe Ab negative, viral load will be measured by the virology lab. If there is acute hepatitis B during pregnancy, viral load is to be measured.

5. Consultant Microbiologist/Virologist will write to Dr Sree Nittur, Wendy Sunderland-Evans and Consultant Obstetrician with advice.

6. With mother's consent, her midwife should refer her to Dr Chin Lye Ch'ng stating EDD and results of tests including viral load. If high viral load mother will be treated with Lamivudine in last trimester.

7. If gamma globulin is indicated, an order form is to be completed by midwife and sent to Pharmacy so that the gamma globulin is available in Labour Ward fridge prior to delivery of baby. Order forms available in antenatal clinic. Further supplies from Katherine Wilson (Pharmacy).
8. Midwife to ensure gamma globulin is ordered and in Labour ward fridge. One spare dose of Gamma globulin to be kept in Labour ward fridge in case of emergency. (There is also one spare vial in Pharmacy emergency cupboard)

9. Information must be given to the mother by her midwife in advance in case she delivers elsewhere.

10. In an unbooked woman at the time of delivery her midwife needs to organize an urgent hepatitis B test.

At delivery
1. Paediatric doctor to give Mother Information sheet if not already given -Link: http://www.antenatalscreening.wales.nhs.uk/sitesplus/documents/968/Information for women who are Hepatitis B Positive English.pdf, and copy to be put in baby's red book. Ask mother to sign **vaccination consent for HBIG (if indicated) and first vaccination**.

2. **Hepatitis B gamma globulin (HBIG), if indicated, needs to be given as soon as possible after birth by the paediatric doctor** (**Please refer to pharmacy guideline chapter for dosage detail**). Aim to give 100% within a few hours of birth. Need written consent from parent. Record batch no. in notes. The dose is 250 IU given intramuscularly. Note if using an adult vial of 500 units you will need to draw up 1/2 of the volume of the vial. The volume is variable but is stated on the vial. Fill in form accompanying the HBIG and return to Pharmacy C/O Katherine Wilson.

Indications for Hepatitis B Immunoglobulin
All babies born to Hepatitis B positive mother with any of the following:
a) Mothers with high viral load (>1x 10_6 IU/mL) even if treated with Lamivudine.

b) Birth weight < 1.5 kg (irrespective of HBe Ag status)

c) Mothers with acute hepatitis B during pregnancy.

For all other babies: Maternal status

HBsAg	**HBeAg**	**HBeAb**	Anti-HBV Immunoglobulin 250 IU as soon as possible	HBV Vaccine
+	+	-	Yes	Yes
+	-	+	No	Yes
+	-	-	Yes	Yes
+	Not available	Not available	Yes	Yes

3. Baby given 1st hepatitis B vaccination as soon as possible after birth by paediatric doctor, (aim to give 100% within a few hours of birth). This includes extremely pre- term infants. Need written consent from parent. Dose is **0.5 ml** (**5 mcg if HBVax pro and 10 mcg if Engerix B**) given IM. (Also kept in Labour Ward fridge).

4. Vaccinations to be recorded in Red book and hospital notes. Paediatric doctor to please **send notification to the Central Clinic register** (Mrs Andrea Evans) of vaccination and batch number by completing the unscheduled immunization form. (Please see under our useful forms section).

5. Paediatrician to **explain to mother the need to complete all the vaccinations** and for testing at 15 months of age. This is done at newborn examination. Conversation is to be recorded in notes and mother's queries answered.

6. Paediatrician to arrange, before the mother is discharged, an appointment for 1 months' time for Registrar clinic (**every 2nd and 4th Wednesday morning**) with NICU receptionist. Paediatrician to write referral form and summary letter, stating indication for hepatitis B program and giving mother's serology results. **Ensure mother has date of appointment before leaving the hospital.**

7. **Babies need blood test at 15 months** for **HBs Ag and AntiHBs Ag** (hepatitis B immunity levels). Please remember to request both on the blood form.

Poor responders should receive a booster dose and *non-responders* should receive a repeat course of vaccination.

Failure to attend subsequent appointments or comply with vaccination policy. Consultant in charge is required to:

* Notify health visitor, GP and practice nurse immediately.
* Notify Helen Bartlett
* Notify CP coordinator immediately.
* Notify Social Services.

Breastfeeding

Breastfeeding should be encouraged and supported. There is no contra- indication to breastfeeding when a baby born to a carrier mother begins immunization. Mothers should not donate milk.

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References:

1. Global challenges in liver disease Roger Williams. Hepatology 2006; 521-526
2. A treatment algorithm for the management of Chronic hepatitis B infection in the United States: an update. EB Keeffe, DT Dieterich et al, Clinical gastroenterology and hepatology2006;4:936-962
3. Current management of chronic hepatitis B GV Papatheodoridis, SJ Hadziyannis Alimant Pharmacol Ther 2004; 19(1) 25-37
4. Antibody levels and protection after hepatitis B vaccination; results of a 15-year follow up BJ McMahon, DL Bruden Ann Intern Med 2005;142:333-341
5. Green book on immunization
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/503768/2905115_Green_Book_Chapter_18_v3_0W.PDF

Neonatal Care of the baby who has been born to a HIV Positive Mother

Section Author - Dr Katherine Burke

This guideline outlines the recommended care and additional considerations required when an infant is born to a mother with HIV. **Individualized birth plans should be available for known HIV positive mothers, outlining the care required for baby**. Additional considerations may arise if an infant is born preterm or if perinatal complications arise **(e.g. prolonged/premature rupture of membranes, prematurity, high risk birth)**. **Early discussion with an appropriate specialist is required.**

Delivery

Normal precautions should apply for neonatal staff attending deliveries, including gloves and apron/gown. For procedures at risk of splashing, such as cord cutting, UVC insertion or intubation, consider the use of mask and visor. Encourage skin-to-skin and normal postnatal care, including delayed cord clamping, where possible

Blood tests recommended

Infants born to mothers with HIV will have passively acquired IgG antibodies to HIV and will therefore test positive for HIV antibody. Following delivery, paired bloods must be sent from mother and baby (send together), within the first 24 hours.

Baby	HIV DNA PCR	> 1ml EDTA (purple top)
	FBC	> 0.5ml EDTA (purple top)
	LFT	> 0.5ml LiHep (green top)
Mother	HIV DNA PCR	10mls – 2 x adult EDTA bottle

Medications recommended for baby (Post Exposure Prophylaxis – PEP)

In most cases, an **individualized plan is available in the medical notes**. **Following delivery, baby should receive Zidovudine (AZT) within 4 hours of birth.**

Risk Group	Criteria	Medications Required	Duration
VERY LOW RISK	Woman on cART for longer than 10 weeks **AND** 2 documented maternal HIV viral loads less than 50 HIV RNA copies/mL during pregnancy, at least 2 weeks apart **AND** Maternal HIV viral load less than 50 HIV RNA copies per mL at or after 36 weeks	Zidovudine (AZT) 4mg/kg/dose given 12 hourly (BD)	**2 weeks**
LOW RISK	If criteria for VERY LOW RISK are not all fulfilled but - maternal HIV viral load is less than 50 HIV RNA copies per mL at or after 36 weeks **AND / OR** - infant is born before 34 weeks but most recent maternal HIV viral load is less than 50 copies HIV RNA per mL	Zidovudine (AZT) 4mg/kg/dose given 12 hourly (BD)	**4 weeks**
HIGH RISK	Maternal HIV viral load unknown, or likely to be greater than 50 copies HIV RNA per mL on day of birth **OR** if concerns regarding recent maternal adherence	SEEK IMMEDIATE EXPERT ADVICE – if unavailable, commence standard three drug PEP until guidance provided (**see appendix one**)	

In infants who are unable to feed, zidovudine can be administered intravenously.

Drug	Route	Dose	Duration
Zidovudine (AZT)	Oral	4mg/kg/dose given 12 hourly (BD)	2-4 weeks (see table above, dependent on risk)
Zidovudine (AZT)	IV	1.5mg/kg/dose every 6 hours	Until feeding, then change to above

PCP Prophylaxis

As transmission rates for mothers **who fully take up interventions** in pregnancy are <1%, it is no longer necessary to routinely give these infants co-trimoxazole for pneumocystis carinii pneumonia prophylaxis. Infants at high risk of becoming infected due to inadequate control of maternal HIV viral load may still need co-trimoxazole. Please discuss before commencement. Dosing if required is in table *.

Co-trimoxazole		
< 2kg birth weight	60mg single dose	Give Monday, Wednesday, Friday
> 2kg birth weight	120mg single dose	Give Monday, Wednesday, Friday

Be cautious as co-trimoxazole displaces bound bilirubin, increasing the risk of kernicterus. Consider early testing for G6PD if infant is of high-risk ethnicity, as co-trimoxazole can cause crisis in these patients.

Recommendations regarding ongoing care for the infant born to HIV positive mother

Immunisations

Should be given as per the national schedule (see Green Book and Local guideline)

Rotavirus vaccine is not contraindicated

BCG

If infant is in the Very Low Risk or Low Risk category for HIV transmission and BCG at birth is indicated, this should not be delayed

Hepatitis B and C

Refer to unit protocols for management.

Feeding

There is no data on the risk of HIV transmission via breast milk in high income countries. A recent study in the low income setting demonstrated that for women on cART treatment throughout the breast feeding period, the transmission rate was 0.3% at 6 months, and 0.6% at 12 months.

It is currently recommended that all infants born to HIV positive mothers are formula fed. There should be provision made for financial support to alleviate the burden of this, particularly for vulnerable woman and infants.

Women who are virologically suppressed with good adherence may be supported to breastfeed if they participate in additional monitoring (monthly HIV RNA viral load testing) – discuss this with the multidisciplinary team involved in care. Factors known to increase transmission rates in women not receiving cART include detectable HIV viral load, advanced maternal HIV disease, longer duration of breast feeding, breast/nipple infection and inflammation, infant mouth or gut infection /

inflammation and early mixed feeding. It is presumed the same factors are relevant for woman on cART, albeit less so in the context of suppressed viral load and good adherence. Discuss the additional surveillance required for these infants with the local specialist.

Consider donor breast milk in high-risk infants, such as those born before 34 weeks gestation.

Medication

Medication should be dispensed in two bottles in case of spillage or breakage at home. Please check the dose and time of medication. Ensure that the mother or carer gain skills in administering medication with supervision from nursing staff prior to discharge. Ensure the instructions on the bottle are clear to the mother / carer, especially if English is not the first language.

Diagnosis

Molecular diagnostics are used – see BHIVA guidelines for more detail. In Swansea this is paired (mother and infant) HIV RNA/DNA PCR

ALL INFANTS - Soon after birth (within 24 hours)	To be sent by neonatal/postnatal team while Mother and Baby are inpatient following delivery
HIGH RISK ONLY – bloods at 2 weeks of age	Postnatal team to arrange appointment in Children's OPD and provide date/time prior to discharge *--complete forms for mother and baby and take these to Children's Outpatient department*
LOW RISK – bloods required at 6 weeks of age (2 weeks post infant PEP cessation) 12 weeks (8 weeks post infant PEP cessation)	Postnatal team to arrange appointment in Children's OPD and provide date/time for first appointment prior to discharge *--complete forms for mother and baby and take these to Children's Outpatient department*
VERY LOW RISK – bloods required at 4 weeks of age (2 weeks post infant PEP cessation) 10 weeks (8 weeks post infant PEP cessation)	Postnatal team to arrange appointment in Children's OPD and provide date/time for first appointment prior to discharge *--complete forms for mother and baby and take these to Children's Outpatient department*
ALL INFANTS, regardless of risk group	HIV antibody testing at 18-24 months of age --arranged at outpatient appointment

Discharge from Hospital (Swansea Infant)

- Full **referral letter** (see appendix 2) should be completed and placed in infants medical notes with a copy for Neonatal Secretaries to upload to Welsh Clinical Portal. Copy to Dr Webb for follow-up.
- Follow up appointment with Dr Joanna Webb OPD clinic 6 weeks
- **Book initial diagnostic blood tests** (Forms for mother and infant to Childrens outpatients – date to be confirmed with mother prior to discharge)

- If mother is an asylum seeker / refugee, please liaise with **Mrs Jean Saunders** (Specialist Health Visitor) – telephone 01792 517 882

Referral Details	
Swansea Family > Dr Joanna Webb	Appointment for 6 weeks OPD
Llanelli Family > West Wales General Paediatricians	Refer to West Wales General Paediatricians
In mothers with resistant virus (HIV2, Zidovudine resistance)	Email referral letter to Dr Kathir Yoganathan (HIV consultant) > Kathir.Yoganathan@wales.nhs.uk or Dr Helen Bradshaw Helen.Bradshaw@wales.nhs.uk

Appendix One – ART prescriptions in High Risk context

Zidovudine, Lamivudine and Nevirapine are the most commonly used medications, though other regimes may be recommended in individualized birth plans. The only medication available as an IV infusion is Zidovudine.

Greater than 34 weeks completed gestation

	Drug	Dose	Frequency	Total Duration
> 34 weeks and feeding	Zidovudine (AZT)	4mg/kg/dose	12 hourly (BD)	4 weeks
	Lamivudine (3TC)	2mg/kg	12 hourly (BD)	2 weeks
	Nevirapine (NVP) NB use 4mg/kg once daily for 2 weeks if mother has received more than 3 days neviripine	2mg/kg then 4mg/kg	Once daily for one week then Once daily for second week, then stop	2 weeks NB check LFTs on day 5, prior to increased dosing
> 34 weeks and unable to feed	Zidovudine (AZT)	1.5mg/kg IV	6 hourly	Until feeding then change to above

Less than 34 weeks completed gestation

	Drug	Dose	Frequency	Total Duration
< 34 weeks and feeding	Zidovudine (AZT)	2mg/kg/dose	12 hourly (BD) for 2 weeks, then 8 hourly (TDS) for 2 weeks	4 weeks
	Lamivudine (3TC)	2mg/kg	12 hourly (BD)	4 weeks
	Nevirapine (NVP)	2mg/kg then 4mg/kg	Once daily for one week then Once daily for second week, then stop	2 weeks NB check LFTs on day 5, prior to increased dosing

< 34 weeks and not feeding	Zidovudine (AZT)	IV	1.5mg/kg/dose every 12 hours	4 weeks or when tolerating feeds, commence oral triple therapy to complete 4 weeks therapy in total

Bwrdd Iechyd Prifysgol Bae Abertawe
Swansea Bay University Health Board

Referral Letter - Infant born to mother with retroviral infection

Date:

Re:

Affix Infant label	Affix Mother label

Dear Dr Webb,

I would be grateful if you would kindly arrange a follow up in your outpatient clinic for this baby who was born to a mother with retroviral infection. The clinical details are as follows:

Birth details

Gestation at birth		
Birth Weight		Centile
Head circumference		Centile
Mode of Delivery (include delivery details)		
Duration of membrane rupture		
Feeding Mode		

Maternal Details

Maternal diagnosis date				
Maternal ART medications, and date commenced				
Recent maternal viral load and CD4 count	Date	Gestation	Viral Load (IU/mL)	CD4 count (%)
Maternal Hepatitis B status				
Maternal Hepatitis C PCR				
Rubella Titres				
Toxoplasma Titres				
CMV Titres				
Maternal blood group				

Infant Risk Group (see guideline for details)

High risk ☐ **Low risk** ☐ **Very low risk** ☐

Medication	
Date commenced	
Dose and duration prescribed	

Infant blood results (date……)

Hb		Platlets		CD4 (%)	
WCC		Neutrophils		Lymphocytes	
ALT		Bilirubin		GGT	

Additional Considerations

Pneumocystis Carinii Pneumonia (PCP) Prophylaxis required	Yes	No
Advice given regarding immunisation?	Yes	No
Appointment date for blood tests (date/time) ➢ give to family prior to discharge ➢ forms completed and taken to Children's OPD (mother and infant paired HIV RNA/DNA PCR):		
Is a translator required for appointments? If yes, which language		

Many thanks,

Name

Guideline for the management of suspected and proven congenital CMV (cCMV) infection

Section Author - Dr Katherine Burke

CMV is the commonest congenital infection, with a prevalence of 7 per 1000 births. Around half of cCMV infected babies with clinically detectable disease at birth will have significant impairments in their development. cCMV is implicated in approximately 25% of all children with sensorineural hearing loss (SNHL). **There is an urgency to diagnose and assess infants with potential cCMV as antiviral treatment is only recommended if started in the first four weeks of life, based on current research**.

Transmission

Babies can acquire CMV during pregnancy, at delivery or postnatally through breast milk or close contact.

For congenital CMV

- The risk of transmission is higher during later pregnancy; however, transmission in early pregnancy is associated with more severe consequences for the fetus.
- The rate of transmission is 30-40% in primary maternal CMV infection, and 1% when there is maternal CMV reactivation (reactivation occurs in around 10% of seropositive women)
- In the UK 50% of woman of reproductive age are CMV seronegative, so can have a primary CMV infection during pregnancy.

Who should be investigated for CMV?

Antenatal Considerations	Oligo/polyhdramnios, placentomegaly. Intrauterine growth restriction Fetal ascites, non-immune hydrops Echogenic bowel Brain anomalies: calcification, cysts, white matter
Physical Examination	**Hepatosplenomegaly** **Petechiae** or **purpura** or **blueberry muffin rash** in newborn **Jaundice** (prolonged or conjugated) **Microcephaly** (OFC <-2SD for gestational age) consider testing if symmetrically small for gestational age (< -2SD for GA)
Neurology	**Seizures** with no other explanation Cerebral Palsy of unknown origin / cause
Laboratory Parameters	**Hyperbilirubinaemia** causing prolonged jaundice often associated with **transaminitis** **Conjugated hyperbilirubinaemia** **Unexplained thrombocytopenia**, especially if leucopoenia or anaemia
Neuroimaging	**Intracranial calcification** (often periventricular) **Ventriculomegaly** Consider also in lenticulostriate vasculopathy, periventricular cysts
Visual Examination	Abnormal finding such as **chorioretinitis or congenital cataracts**

Audiology	**No clear response on newborn hearing screening**
Maternal Serology	Evidence of **maternal primary infection** (seroconversion or low avidity IgG)

Which tests are needed to confirm cCMV?

- Diagnosis of cCMV is by the detection of CMV DNA by PCR in body fluids in the first three weeks of life – the sooner after birth the tests are performed, the more confidently the diagnosis of cCMV can be made.
- If CMV is detected after three weeks, then there is uncertainty about whether it was congenital (antenatal infection) or acquired (postnatal infection).

Test	**Comments**
CMV PCR Urine	Can be obtained in bag or cotton wool Send in white universal container
CMV PCR Blood	Can be negative when urine positive – urine preferred Send in EDTA bottle (purple top)
CMV PCR on Guthrie Card (Call newborn screening laboratory)	Can be used for a retrospective diagnosis – negative result does not exclude CMV as sensitivity is variable (34-80%)
Maternal Booking Bloods	Can demonstrate timing of infection by: - Seroconversion if there are two sequential samples e.g. during pregnancy, or when comparing ante/peri/post natal bloods - CMV IgG avidity testing – low avidity is consistent with a recent infection

Other tests can be used (including CMV PCR saliva swabs, CMV IgG in children over 1 year and maternal CMV IgG), please discuss with virology consultant.

When a diagnosis of cCMV confirmed – additional testing required

Test	Additional Considerations
Bloods	
FBC	Thrombocytopenia (<100,000/mm^3, nadir at 2 weeks)
Urea and Electrolytes	Baseline renal function (prior to considering treatment)
Liver Function Tests	ALT >80U/L, conjugated hyperbilirubinaemia
CMV Viral Load by PCR	EDTA sample
Radiology	
Cranial USS and Brain MRI	All infants with cCMV should have neuroimaging. Some centres advocate undertaking MRI in all babies with cCMV because additional pathology can be identified as compared with CrUSS.
Referrals	
Ophthalmology	Chorioretinitis, optic atrophy, cataracts
Audiology	Through auditory brainstem response assessments, even when there are clear responses on newborn hearing screening, as the screen can miss a mild SNHL

Considering Treatment

Previously, cCMV infection is categorised as 'symptomatic' or 'asymptomatic', but the European Guidelines have suggested that we consider babies in terms of having mild, moderate or severe disease. Evidence of benefit from randomized controlled trials is only available for treatment started in the first month of life, in infants over 32 weeks gestation.

Treatment decisions should be made in discussion with a consultant virologist and/or specialist in paediatric infectious disease.

Disease Manifestation	Treatment Recommendation
Severe Disease	
CNS microcephaly CNS calcification chorioretinitis white matter changes, or other abnormalities on MRI consistent with CNV disease	Ganciclovir / valganciclovir Duration 6 months
Life threatening disease Severe multiorgan non-CNS disease Severe single organ disease i.e. significant liver abnormalities (failure, marked hepatosplenomegaly), colitis, pneumonitis, severe bone marrow suppression	Ganciclovir / valganciclovir Duration 6 weeks to 6 months (limited evidence without full consensus, consider treatment duration until underlying clinical manifestation i.e. hepatitis, resolves)
Isolated Hearing Deficit	Ganciclovir / valganciclovir Duration 6 months (limited evidence without full consensus)
Moderate Disease	
Persistent (>2 weeks duration) abnormalities of Haematological / biochemical indices More than 2 'mild' disease manifestations	Consider treatment after discussion with specialist Duration 6 weeks to 6 months
Mild Disease	
Isolated (1-2) otherwise clinically insignificant/ transient clinical findings Petechiae Mild hepatosplenomegaly Biochemical/haematological abnormalities Small for gestational age, without microcephaly No clinical or biochemical evidence of disease	No treatment

Oral valganciclovir is the medication of choice, though is used off-licence. Intravenous valganciclovir is used when infants are unable to tolerate oral medications or when gastrointestinal absorption is uncertain. Neonatal pharmacokinetic data shows that **16mg/kg/dose of valganciclovir oral solution given twice daily** provides ganciclovir exposure comparable to that of a **6mg/kg/dose of intravenous ganciclovir twice daily**, in infants born 32 weeks gestation or more.

Treatment after 4 weeks of age

Treatment of cCMV for infants older than 28 days has not been addressed in any randomized controlled trials, although it is acknowledged that the 28 day cut off is not evidence based. Retrospective case series have reported good outcomes, but no consensus was reached in the European Guidelines. Discuss with paediatric infectious disease and virology to consider treatment on a case-by-case basis.

Treatment monitoring

FBC, U and E and LFT weekly for 4 weeks, then monthly until cessation of treatment course.

Weight measurement and dose calculations and alterations to be performed with blood sampling.

Monitoring is required to identify potential toxicity. Short term toxicity can include neutropenia (50% when using ganciclovir, and 20% on valganciclovir) which usually occurs in the first month of treatment can require the interruption of treatment. Hepatotoxicity and thrombocytopenia occur in 30% of infants receiving either medication. These resolve following treatment cessation. It can be challenging to differentiate between disease and treatment associated changes. Therapeutic drug monitoring may be indicated when toxicity is a concern, particularly for high risk groups such as infants <36 weeks gestation and those with abnormal renal function. The European Guidelines do not recommend routine or serial viral load testing, though this may be considered on a case-by-case basis.

Additional considerations

Children who are on valganciclovir should have **open access to their local paediatric assessment unit**, in light of the increased risk of neutropenia and associated severe or atypical infections. In Swansea, this should be arranged via the PAU at Morriston Hospital by contacting Dawn Edwards.

Follow Up

Follow up should be considered in both treated and untreated infants. This includes

- **audiology assessment**: 3-6 months for one year, then 6 monthly until 3 years and then annually until 6 years of age
- **ophthalmology assessment**: annually until 5 years of age
- **consider neurodevelopmental follow-up and assessment to allow early intervention if indicated**

Resources for Parents

http://cmvaction.org.uk

https://www.nhs.uk/conditions/cytomegalovirus-cmv/

Relevant Contacts

Newborn Screening Laboratory, UHW	029 20 744 032
Dr Jennifer Evans / Dr Siske Struik, Paediatric Infectious Diseases, University Hospital Wales	Jennifer.evans7@wales.nhs.uk Siske.struik@wales.nhs.uk
Professor Mike Sharland, Consultant Paediatrician in Infectious Disease St George's Hospital, London	Mike.sharland@stgeorges.nhs.uk
Open Access at Morriston Hospital via Dr. Dawn Edwards	Dawn.edwards@wales.nhs.uk

References

Shah T, Luck S, Sharland M, et al. Fifteen-minute consultation: diagnosis and management of congenital CMV. Archives of Disease in Childhood - Education and Practice 2016;101:232-235.

Luck, SE; Wieringa, JW; Blázquez-Gamero, D; Henneke, P; Schuster, K; Butler, K; Capretti, MG; Cilleruelo, MJ; Curtis, N; Garofoli, F; et al. (2017) Congenital Cytomegalovirus: A European Expert Consensus Statement on Diagnosis and Management. Pediatr Infect Dis J, 36 (12). pp. 1205-1213. ISSN 1532-0987 https://doi.org/10.1097/INF.0000000000001763 http://openaccess.sgul.ac.uk/109384/

Management of infants at risk of Congenital Toxoplasmosis

Authors: Ian Morris, Sujoy Banerjee, Jennifer Evans, Matt Ryan

Background:

Toxoplasma Gondii is one of the most common parasitic infections in humans, and is acquired by ingestion of cyst-containing tissues in undercooked meat, or of oocysts excreted by cats which contaminate soil or water. If a seronegative woman acquires the infection during pregnancy, the parasite can be transmitted vertically to the foetus. This can lead to inflammatory lesions affecting the brain, retina and choroid which can cause permanent neurological and visual sequelae and, rarely, foetal or postnatal death.

Seroprevalence varies widely between countries (5-80%), and is thought to be around 8% in the UK. Incidence of congenital infection in the UK is thought to be around 1 per 10 000.

The risk of maternal-fetal transmission increases with advancing gestational age at time of maternal infection (from around 10-15% in the first trimester, to 80% just prior to delivery), with overall transmission rates being about 25%. Conversely, the risk of clinical sequelae is highest if transmitted in the early stages of pregnancy (60-80% in first trimester).

Currently, it is national policy within the UK that routine antenatal and neonatal screening for Toxoplasmosis is not performed (it is widely used in Europe). This is because of low prevalence of disease, relatively high false positive screening results, and limited evidence of the benefit of prenatal treatment in reducing transmission of infection from mother to foetus. Where antenatal infection is detected, mother may be treated with spiramycin in an attempt to reduce transmission of infection, and/or severity of its impact on the fetus / newborn.

Clinical picture:

At birth, signs are often subtle or absent, with only around 5-10% of infants born to infected mothers manifest neonatal symptoms. Mortality in this group is around 25%.

Clinical features of Congenital Toxoplasmosis:

Central nervous system disease	Microcephaly Hearing impairment Seizures Hydrocephalus Motor deficits Intracranial calcifications
Ophthalmological disease with subsequent visual impairment	Microphthalmia Chorioretinitis (usually bilateral) Retinal scarring Strabismus Nystagmus Cataract
Hepatic disease	Hepatosplenomegaly Jaundice
Cardiorespiratory disease	Pneumonitis Myocarditis
Systemic features	Rash (may be 'blueberry-muffin') Fever Bone marrow suppression (thrombocytopenia, anaemia)

When actively investigated, retinochoroiditis and/or intracranial lesions (e.g. calcifications, hydrocephalus, epilepsy) are detected in 17% of infected infants in the postnatal period. Further eye lesions can appear at any stage of life as a result of reactivation of latent cysts in the retina and choroid. Progression to severe neurological impairment is rare (less than 5%), but the extent of milder neurodevelopmental problems is uncertain.

Diagnosis:

Prenatal: Serological tests during pregnancy for evaluation of maternal infection are interpreted as shown in Table 1. In addition, PCR analysis of amniotic fluid is possible and if positive is diagnostic of congenital toxoplasmosis however negative result does not exclude infection. Foetal ultrasound looking for typical, but non-specific findings including

hydrocephalus, brain or hepatic calcifications, splenomegaly, ascites, severe IUGR, hydrops fetalis and pericardial/pleural effusions also offer diagnostic clues.

Table 1: Interpretation of maternal serological tests in pregnancy for toxoplasma infection

IgG	IgM	IgA	IgG avidity	Interpretation
Negative	Negative			Seronegative
Positive (<200 IU)	Negative			Previous infection
Positive (any)	Positive	Positive	< 15%	Acute infection
Positive (>300 IU)	Positive	Negative		Probable recent infection
Positive (<300 IU)	Positive	Negative		IgM chronic carrier
Positive (>300 IU)	Negative	Negative	> 30%	Probably reinfection
Negative	Positive	Negative		Natural IgM

Postnatal:

Postnatal diagnosis is challenging.

For infants with maternal history of Toxoplasmososis or clinical concern of congenital toxoplasmosis the following investigations are indicated:

1. Paired infant and maternal T.Gondii specific IgM, IgA and IgG (repeat testing may be required)
2. cranial ultrasound +/- MRI brain looking for calcifications, hydrocephalus, cortical atrophy, microcephaly and major structural abnormalities
3. Urgent ophthalmology and audiology review
4. Any infant with findings consistent with congenital toxoplasmosis should have a lumbar puncture for CSF protein, glucose, cell count, culture and T.Gondii NAAT (PCR).

   Detection of neonatal IgM and IgA by enzyme immunoassay and/or by immunosorbent agglutination assay is considered diagnostic of neonatal infection. However, current assays often fail to detect IgM in neonatal serum, and passively acquired IgG makes interpretation of routine serology difficult. Therefore, where primary maternal infection during pregnancy cannot be excluded, serial infant specimens should be analysed over the first 12 months of life. Passive infection will lead to disappearance of IgG by 1 year of age. Persistence confirms congenital infection.

Management:

Treatment of congenitally infected children should always be initiated after detailed discussion with microbiologist and a paediatric infectious disease specialist. Optimum treatment regimen and duration are not well established but most standard regimens consist of a combination of pyrimethamine and a sulphonamide (sulphadiazine or sulphadoxine). These treatment regimens can cause bone marrow toxicity and at least twice monthly FBC is advised to monitor for neutropenia, and thrombocytopenia.

Treatment regimens	Mildly affected[a]	Severely affected[b]
Pyrimethamine AND Sulphadiazine AND Folinic acid	1mg/kg BD for 2 days then 1mg/kg/d for 2 months then 1mg/kg 3 times per week for 10 months 50mg/kg BD for 12 months 5-20mg (age dependent) 3 times weekly	1mg/kg BD for 2 days then 1mg/kg/d for 6 months then 1mg/kg 3 times per week for 6 months 50mg/kg BD for 12 months 5-20mg (age dependent) 3 times weekly
Pyrimethamine / sulphadoxine combination (25/500mg) – Fansidar AND Folinic acid	1.25mg/kg & 25mg/kg every 15 days for 1-2 years 50mg once weekly	1.25mg/kg & 25mg/kg every 7 days for 1-2 years 50mg once weekly
a - ≤ 1 ocular lesion and/or ≤ 3 intracerebral calcifications b – neurological signs and/or > 1 ocular lesion and / or > 3 intracerebral calcifications (more commonly used dosing)		

<u>Follow-up</u>:

No specific guidance is available and will depend on the nature and extent of organ involvement. As a minimum the child should have regular follow up with:

- Ophthalmologist
- Neuro-developmental paediatrician
- Paediatrician with a special interest in infectious diseases

References:

1. Saso A, Bamford A, Grewal K, et al. Fifteen-minute consultation: Management of the infant born to a mother with toxoplasmosis in pregnancy *Arch Dis Child Educ Pract Ed.* E-pub ahead of print 18/2/2020 doi:10.1136/edpract-2018-316603
2. Serranti D, Buonsenso D, Valentini P. Congenital toxoplasmosis treatment. *Eur rev med and pharm sciences* 2011;15:193-198.
3. Robert-Gangneux F, It is not only the cat that did it: How to prevent and treat congenital toxoplasmosis, *J Infect* (2013), http://dx.doi.org/10.1016/j.jinf.2013.09.023 UK national screening committee. *Screening for toxoplasmosis* January 2011.

Approach to Diagnosis and Management of Newborns at Risk of Congenital Syphilis

Section Author – Dr Lucinda Perkins

Background

Syphilis is a bacterial infection, which can be sexually transmitted, caused by the spirochete bacterium Treponema pallidum. Syphilis has become more prevalent in the United Kingdom (UK) in recent years, increasing by 160% in England between 2008 and 2018.[1] Syphilis in pregnancy increases the risk of miscarriage, intra-uterine growth restriction, non-immune hydrops fetalis, stillbirth and preterm delivery. If not adequately treated vertical transmission can occur at any time during pregnancy. Accurate data on congenital syphilis cases in the UK is not available, but from 2020 surveillance will become part of the Infectious Diseases in Pregnancy Screening Programme. We do know that an 153% increase in congenital syphilis was observed in the US in parallel with increasing rates among women.[2]

The British Association of Sexual Health and HIV (BASHH) syphilis birth plan provides clear guidance on the identification, treatment and follow-up of infants born to mothers with confirmed or suspected syphilis. This guideline is adapted from BASHH guidelines published in 2015 and should be used alongside the BASHH syphilis birth plan.

In Swansea Bay University Health Board, antenatal syphilis cases should be referred to the GUM team, FAO Dr Helen Bradshaw, GUM Consultant, by the obstetric team for management. Mothers should also be added to the High Risk Antenatal List, FAO Dr Lucinda Perkins, Consultant Neonatologist, to ensure timely communication of a completed BASHH birth plan to the neonatal team. The individualised birth plan will clearly state the pathway to be followed under the section 'GUM advice to paediatricians'.

Management of Infants at Risk of Congenital Syphilis

Signs and Symptoms

Approximately half of all neonates with congenital syphilis are normal on initial examination. The commonest early abnormality in babies with congenital syphilis is hepatitis, so syphilis serology should be requested on any baby with unexplained abnormal liver function tests. If not treated, surviving infants develop early-stage and late-stage symptoms of syphilis.

Full blown symptomatic congenital syphilis is rare in the UK. Early-stage symptoms include anaemia, oedema, jaundice, irritability, failure to thrive, non-specific fever, rash and condyloma lata on the borders of the mouth, anus, and genitalia. The rash can vary but is usually maculopapular. Palms and soles can be red and mottled. Bullae and vesicles can also be seen. A small percentage of infants have rhinitis with watery nasal discharge ('snuffles') usually after the first week. Ulceration of nasal mucosa can also occur. Osteochondritis is a frequent and typical manifestation and may present as dactylitis, fracture or pseudoparalysis (pseudoparalysis of Parrot).

Later signs appear as tooth abnormalities (Hutchinson teeth), bone changes (sabre shins), neurological involvement, interstitial keratitis, and sensorineural deafness.

Please note that, if present, the rash and secretions in congenital syphilis is highly infectious and full universal precaution must be taken to prevent transmission to members of staff and others caring for the infant.

Management of Infants

- All infants born to seropositive mothers should be considered exposed to Syphilis unless good evidence of complete treatment and response in mother is documented.
- Paired blood samples should be taken from mother and baby for IgM and RPR after birth. This should NOT be cord blood.
- If lesions are present a red top swab should also be send for Treponema pallidum Polymerase Chain Reaction (PCR) from the lesions. Dark Ground Microscopy (DGM) is not available locally.
- Indications for further tests and treatment are:
  a) Mother inadequately treated (GUM consultant will advise, see above)
  b) Infant has clinical signs consistent with syphilis
  c) Infant's RPR/VDRL titre 4 x mother's on two occasions (e.g mother's RPR 1:4, infant's RPR 1:16). Sample from mother to be taken no greater than 4 weeks before that of infant.
  d) Infant has positive treponemal IgM test together with corroborative history, clinical signs. GUM consultant will advise.
  e) Infant has positive T pallidum PCR test together with corroborative history, clinical signs. GUM consultant will advise.
- If treatment is indicated further tests should be undertaken as detailed in the birth plan
- Consider the need for treatment for all siblings and mother's sexual partners
- Other treponemal diseases, such as Yaws, are prevalent in certain countries and so should be considered in those from or travelling to these areas
- If any concerns or queries arise then early discussion with the GUM team is advised
- Confirmed cases of congenital infection should, additionally, be discussed with Dr Jennifer Evans, Paediatrician with interest in infectious disease at UHW.
- Suspected or confirmed cases of congenital syphilis should be reported to CARIS

Treatment

Benzyl penicillin sodium 30 mg/kg BD intravenously (IV) in the first 7 days of life and 30mg/Kg 8 hourly if older than 7 days. The total duration of treatment is 10 days (If drug administration is interrupted for more than one day at any point during the treatment course, the entire course should be restarted.

Infant Follow-up

It is very important that infants are appropriately followed-up. There are 3 follow-up pathways that are made clear in the BASHH Syphilis Birth Plan.
For Swansea Bay University Health Board patients follow-up should be arranged in the 'Registar led' clinic overseen by Dr Sree Nittur. A referral letter should be sent to Dr Nittur's secretary stating the follow-up required at the time of discharge. The 3 follow-up pathways are:

***Pathway 1: Infants treated for syphilis at* birth**
Months 1 and 3: check RPR and treponemal IgM.
Month 6: check RPR
Month 12: check RPR.Discharge if RPR has achieved sustained 4x drop from peak level.

Pathway 2: Infant not treated for syphilis
RPR <4 x mother's, IgM negative at birth

Month 3: check RPR and treponemal IgM.
Month 6: check RPR- if negative discharge, if positive repeat at 12 months.
Month 12: RPR negative, no further follow-up.
Month 12: RPR still positive, discuss with GUM colleague.
(Note: the RPR is usually negative by six months).

Pathway 3: Infant not treated for syphilis and RPR and IgM negative at birth
Month 3: repeat RPR and IgM and discharge if still negative.
Month 3: RPR and/or IgM positive-discuss with GUM colleague.
Of note, the neonatal RPR should be negative by 6 months of age and the TPPA by 18 months of age when they are reactive as a result of passive transfer of maternal antibodies.

Appendix

BASHH Birth Plan

https://www.bashhguidelines.org/media/1196/syphillis-bp_print_2016_p3.pdf

References:

1. Public Health England https://www.gov.uk/government/statistics/sexually-transmitted-infections-stis-annual-data-tables. Table 1: STI diagnoses and rates in England by gender, 2009 to 2018
2. CDSC. Sexually transmitted diseases surveillance 2017 https://www.cdc.gov/std/stats17/syphilis.htm
3. https://www.gov.uk/government/publications/integrated-screening-outcomes-surveillance-service-isoss/infectious-diseases-in-pregnancy-screening-programme-isoss
4. Townsend, CL, Francis, K, Peckham, CS, Tookey, PA. Syphilis screening in pregnancy in the United Kingdom, 2010–2011: a national surveillance study. *BJOG* 2017; 124: 79– 86.
5. https://www.bashhguidelines.org/media/1196/syphillis-bp_print_2016_p3.pdf
6. Wales Neonatal Network Congenital Infection Guideline
7. http://www.walesneonatalnetwork.wales.nhs.uk/sitesplus/documents/1034/congenital%20infection%20UHW%202017.pdf
8. UK National Guidelines on the Management of Syphilis 2015. International Journal of STD & AIDS. December 31, 2015; 1-26 – most up-to-date version
9. UK National Guidelines on the Management of Syphilis 2015. International Journal of STD & AIDS.