Neonatal Guidelines

Chapter 6: Infection v2024

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Contents Page

Guideline for the management of infection in the Newborn 4
Antibiotics usage reduction in neonatal unit – A quality improvement initiative 5
Guidance for non- initiation of antibiotics 6
Antibiotic Policy and Therapeutic Drug Level Monitoring: 11
Initial choice and modification of antibiotics in babies on NNU with meningitis: 14
How to decide the duration of the antibiotic treatment? 16
Pseudomonas in a Blood Culture – Information and procedure to follow 19
Selective Fluconazole Prophylaxis in High-Risk Preterm Infants in NICU to reduce invasive fungal infection ..23
Management of suspected or confirmed fungal infection in the VLBW infants 27
Guideline for the management of Neonatal Herpes Infection 35
Hepatitis C infection in pregnancy and the newborn period 43
Management of Perinatal Hepatitis B transmission 47
Guidelines for Palivizumab (Synagis®) 52
Neonatal Care of the baby who has been born to a HIV Positive Mother 56
Guideline for the management of suspected and proven congenital CMV (cCMV) infection 64
Management of infants at risk of Congenital Toxoplasmosis 70
Approach to Diagnosis and Management of Newborns at Risk of Congenital Syphilis 77
Methicillin-Resistant Staphylococcus Aureus (MRSA) Guidance for NICU 80
Infection control on the Neonatal Unit – General Guide 83
HeRO monitoring – A guide for the clinicians 94

Guideline for the management of infection in the Newborn

Background:

Infection is a major cause of morbidity and mortality in the neonatal period. The UK NeonIN data demonstrate that, with the inclusion of CoNS, the incidence of all neonatal infection is 0.8% of live births and 7.1% of neonatal admissions. The mortality rate from neonatal infection is 13-30% with a higher rate in premature and VLBW infants. The combination of immature immune system, non-specific symptoms and signs together with ever changing infective pathogens leads to greater incidence of infection and consequent mortality and morbidity. Traditionally, neonatal infection is divided into congenital and acquired or early & late onset infection. The mortality rate for early-onset infection is 15% and for late-onset infection is 9%, according to a study reported in Australia. The incidence of late infection is now about 20 times that of early infection in VLBW babies (<1.5Kg)

Early-onset infection (EOS) occurs in the first 72 hours. The organisms involved are usually acquired from the mother. This may be due to haematogenous spread, or more commonly due to ascending infection from the vagina. The organisms responsible could be both Gram positive and Gram-negative bacteria that include GBS, E Coli, H Influenzae, Listeria etc. The overall incidence of EOS in the UK is 0.9/1000 of all live births and 0.9% of all neonatal admissions. GBS and *Escherichia coli* are the most common causative organisms, if CoNS are excluded, and account for 58% and 18% of bacteraemia respectively in the UK. Common risk factors are chorioamnionitis, maternal pyrexia (Temp >38^{o}C), premature rupture of membranes, preterm labour, maternal UTI or bacteriuria and GBS colonisation.

Late-onset infection (LOS) occurs after 72 hours. The incidence of LOS among VLBW infants ranges between 16% and 30%. LOS risk is directly proportional to their birth weight and gestational age and mortality rates vary between 17% and 21%. Incidence of LOS in the UK is 0.7% of live births and 6.1% of neonatal unit admissions. The organisms are usually acquired from the hospital environment or nosocomial infection. The usual organisms include CONS (45% - 55%), Staph aureus, Enterococcus, E Coli, Enterobacter, Klebsiella, GBS, Pseudomonas and Candida species.

Antibiotics usage reduction in neonatal unit – A quality improvement initiative

There is no doubt that infectious diseases remain a major cause of morbidity and mortality in neonates and that, antibiotics are life-saving. Early-onset sepsis and nosocomial sepsis persist, despite the remarkable progress in prevention over the last decade. Antibiotics are the most- prescribed medications in neonatal intensive care. These agents are begun empirically based on risk factors such as maternal chorioamnionitis or nonspecific signs and symptoms of hospital-acquired infection. Our ability to discern the need to initiate or terminate antibiotic use is limited. Results of blood cultures (the most definitive of diagnostic tests for sepsis) may be negative due to previous antibiotic exposure, low colony count sepsis, and difficulty obtaining an adequate volume of blood for culturing. In the absence of positive culture results, continuation of antibiotics is often based on concern regarding the consequences of inadequate treatment, a judgment call that can easily lead to varied opinions among qualified neonatologists. Neonatal antibiotic exposure is associated with increased risk of necrotizing enterocolitis (NEC), nosocomial infection (NI), and mortality, as well as with asthma later in life. Additionally, antimicrobial use is associated with the selection of multidrug-resistant pathogens, themselves associated with increased morbidity, mortality, cost, and length of stay. In a study published from California, there was a fortyfold variation in NICU antibiotic prescribing practice across 127 NICUs with similar burdens of proven infection, NEC, surgical volume, and mortality indicates that a considerable portion of antibiotic use lacks clear warrant; in some NICUs, antibiotics are overused.

Following the success of the antibiotic reduction quality improvement initiative, we have incorporated the following criteria for not starting antibiotics in babies who get admitted to the neonatal unit at Singleton Hospital. This policy does not apply to SCBU in Bridgend yet.

Guidance for non- initiation of antibiotics

For babies admitted to NICU at Singleton Hospital only, consider withholding antibiotics with enhanced monitoring in following scenarios

(Only applicable for babies admitted to the NICU in first 24 hours of life)

Babies should meet all of the criteria below in each of their gestational age categories

≥ 34 weeks gestation	≥ 32 weeks gestation	≥ 28 weeks gestation
Respiratory distress in keeping with gestational age	All of criteria of ≥ 34 weeks gestation	All of criteria of ≥ 32 weeks gestation
No history of chorioamnionitis or sepsis in mother	No pre-labour rupture of membranes	Baby delivered by section for maternal reasons (e.g. PET, APH)
No previous siblings affected by GBS		
If GBS isolated from HVS, Mother must have had IAP at least 4 hours prior to delivery		

All babies who meet the above criteria:

- Full examination of the baby by a clinician, including temperature, heart rate, perfusion, blood pressure and blood gas soon after admission
- Take CRP, FBC, blood gas and culture (take at least 1 ml for blood culture and clearly document in notes)

At 6 hours (earlier, if clinical concerns):

- Repeat clinical examination by clinician, documenting (perfusion, BP, HR, temp, alertness, wellbeing and HeRO score)
- Repeat CRP and blood gas
- Consider 1st line antibiotics if there are concerns regarding worsening respiratory or haemodynamic status, rising CRP or metabolic acidosis or other concerns of sepsis

At 6-24 hours:

- Continue close review and document every 6 hours for the first 24 hours
- Repeat CRP at 18-24 hrs

Please ensure all the findings and decisions are clearly documented in the notes and be aware of clinical symptoms and signs of evolving sepsis (see next page)

Table 1: Clinical indicators suggestive of early onset sepsis (EOS) in babies admitted to neonatal unit:

Altered behaviour or responsiveness
Altered muscle tone (for example floppiness)
Feed intolerance (vomiting, excessive gastric aspirates, bilious aspirates, abdominal distension)
Abnormal heart rate (bradycardia or tachycardia)
Increase in respiratory support requirements
Onset of respiratory distress after 4 hours
Apnoeas (Red flag)
Signs of neonatal encephalopathy or seizures (Red flag)
Need for cardiopulmonary resuscitation (Red flag)
Need for mechanical ventilation (Red flag)
Persistent pulmonary hypertension
Temperature instability (<36 degree C or > 38 degree C) unexplained by environmental factors
Signs of shock (Red flag)
Unexplained excessive bleeding, thrombocytopenia, abnormal coagulation
Jaundice within 24 hours of birth
Altered glucose homeostasis (hypoglycaemia or hyperglycaemia)
Metabolic acidosis (base deficit of 10 mmol/l or more)
Local signs of infection (for example eye, skin)

- Babies presenting **with any of the above red flag signs, consider starting appropriate antibiotic treatment after performing partial or full sepsis screen.**
- **For babies not assessed on the SRC pathway for early onset sepsis i.e. ≤34 weeks gestation, 2 or more non-red flag clinical indicators will require evaluation for sepsis investigation and treatment**
- **In babies without red flags and only one non-red flag indicator, use clinical judgement to decide whether it is safe to withhold antibiotics.**
- **In babies where it's being considered safe to withhold antibiotics,** take CRP, FBC, blood gas and blood culture (at least 1 ml of blood for blood culture). Monitor vital signs closely and document clinical review including temperature, heart rate, perfusion, blood pressure and blood gas for 24 hours (NEWTT2 or electronic monitoring as appropriate).

- Continue close clinical monitoring, have a low threshold of starting antibiotics and repeat CRP in 18 – 24 hours

- **Where clinical suspicion of infection is high, please do not wait for the results of the investigations before starting antibiotic**
  - Urine culture is not routinely indicated.
  - Do not perform skin swab microscopy or culture as part of investigation of EOS, if there are no clinical signs of localised infection.
  - Lumbar puncture in EOS to obtain CSF should only be performed if there is strong clinical suspicion of early onset neonatal infection (not risk factors) or there are clinical signs or symptoms suggesting meningitis
- **Treat and stabilise any of the following before performing a lumbar puncture**
  1. Unprotected airway
  2. Respiratory compromise
  3. Shock
  4. Uncontrolled seizures
  5. Bleeding risk
- **Contraindications for performing lumbar puncture are**
  1. Extensive or rapidly spreading purpura
  2. Infection at the lumbar puncture site
  3. Risk factors for an evolving space occupying lesion e.g. extra parenchymal bleeding
  4. Any symptoms or signs indicative of raised intracranial pressure including new focal neurological features, abnormal pupillary reaction and a progressive or rapid fall in level of consciousness
- **Measure blood glucose in babies immediately before LP.**

<u>CSF investigations to be sent in babies with suspected meningitis:</u>

1. Cytology and Gram stain
2. Culture and sensitivities
3. Glucose and Total Protein
4. PCR for relevant pathogens including HSV

Store the remaining CSF in case more tests are required (metabolic work up)

Ensure CSF cell count, total protein and Glucose concentration are **<u>available within 4 hours of LP</u>**.

When interpreting CSF results, take into account

1. Presence of red cells in the sample suggest blood contamination or a different diagnosis
2. Whether earlier antibiotics may have reduced the diagnostic reliability of these investigations
3. Interpret cerebrospinal fluid results in babies alongside the clinical presentation and maternal history
4. If cerebrospinal fluid results are abnormal, consider alternative viral, mycobacterial, fungal or non-infectious causes as well as bacterial meningitis

Evidence:

CSF WCC	Gram stain	CSF glucose	CSF : serum glucose ratio	Protein conc.
Threshold of ≥26 cells/ µL for preterms and ≥ 23 cells/µL for term infants – **moderate sensitivity and specificity**	**Not sensitive but very specific for bacterial meningitis**	• At a threshold of < 1.11 mmol/L – **not sensitive but very specific** • < 1.89 mmol/L – **moderately sensitive and specific** • < 3.33 mmol/L – **moderately sensitive but not specific**	Ratio of < 0.4 – **moderately sensitive but very specific for bacterial meningitis**	• > 40 mg/dL **– very sensitive but not specific** • > 90 mg/dL **– moderately sensitive but not specific** • > 120 mg/dL **– moderately sensitive but very specific**

Advice for site specific infection

Eyes

- Beware that minor conjunctivitis with encrusted eyelids is common and often benign, a purulent discharge may indicate a serious infection (e.g., chlamydia or gonococcus).
- In babies with purulent eye discharge take *swab samples urgently for microbiological investigations using methods that can detect chlamydia and gonococcus. Start systemic antibiotic treatment for possible gonococcal infection (Cefotaxime 100mg/Kg, single dose IV along with normal saline irrigation)
- If disseminated gonococcal disease is suspected continue Cefotaxime 50mg/Kg TDS for 7 days (14 days for meningitis). Seek microbiology advice.
- If chlamydia is confirmed or suspected from history, start oral erythromycin (12.5 mg/kg/dose 4 times daily for 14 days). Alternatively, Azithromycin can be given for 3 days (20mg/kg OD) as second line.

Please send the eye swab in yellow fluid filled contained for chlamydia and gonococcal testing.

Umbilicus

- In babies with clinical signs of umbilical infection such as purulent discharge or signs of periumbilical cellulitis (redness, swelling, increased skin warmth), perform blood culture, swab for microscopy and culture and start IV antibiotics with Fluclox and Gentamicin. If microbiology swab is negative for Gram negative organism stop gentamicin.

Late onset sepsis:

When assessing or reviewing a baby:

- Check for, the possible clinical indicators of late-onset neonatal infection shown in table 2.
- Take into account that prematurity, mechanical ventilation, history of surgery and presence of a central catheter are associated with greater risk of late-onset neonatal infection.
- Think about infection in the other babies when one baby from a multiple birth has infection.

Table 2.Clinical indicators of possible late onset neonatal infection: (observations and events in the baby)

Category	Indicators
Behaviour	Parent or care-giver concern for change in behaviour Appears ill to a healthcare professional Does not wake, or if roused does not stay awake Weak high-pitched or continuous cry
Respiratory	Raised respiratory rate: 60 breaths per minute or more Grunting Apnoea Oxygen saturation of less than 90% in air or increased oxygen requirement over baseline or level of support
Circulation and hydration	Persistent tachycardia: heart rate 160 beats per minute or more (threshold may be higher in premature babies, please discuss with senior clinician Persistent bradycardia: heart rate less than 100 beats per minute
Skin	Mottled or ashen appearance Cyanosis of skin, lips or tongue Non-blanching rash of skin
Other	Temperature 38°C or more unexplained by environmental factors Temperature less than 36°C unexplained by environmental factors Alterations in feeding pattern Abdominal distension Seizures Bulging fontanelle Rising HeRO score from baseline or absolute score > 2 should trigger a clinical review (see HeRO guideline)

Investigations:

Investigations for LOS are similar to that for EOS.

Consider lumbar puncture if strong clinical suspicion or clinical symptoms and signs suggestive of meningitis.

Antibiotic Policy and Therapeutic Drug Level Monitoring:

- 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 and investigations needed and likely duration of treatment.

- Prior to starting (or changing) antibiotic treatment, every baby should have blood cultures, The results should be chased at 36 hours and the choice and need to continue antibiotics may need to be reviewed based on results and antibiotic sensitivities.
- 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. Maternal antibiotics can reduce the isolation of organisms from the baby even though the baby is infected.

First Line Antibiotics (EOS): These are usually used within the first 72 hours or after birth for a presumed or suspected EOS.

- **Benzyl Penicillin** – *25/kg/dose. Use one dose every**12 hours in the first week.

Dose to be increased to 50 mg/kg in case of confirmed GBS on blood c/s and GBS meningitis

****Consider shortening the interval to 8 hourly based on clinical judgement (if the baby appears to be unwell***

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

Age	Dose	Initial Dosing Interval	Route
< 7 days	5mg/kg	***Every 36 hours	Slow IV bolus over 3-5 minutes
7 – 28 days	5mg/kg	Every 24 hours	
> 28 days	7mg/kg	Every 24 hours	IV infusion

****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)

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 before every 3rd dose. **Trough (pre-dose) should be <2 mg/L. If more than 3 doses of Gentamicin are to be given, trough level of < 1mg/ L is advised.**

Note: In very immature infants (≤ 24 weeks gestation), an individualised treatment strategy may be followed by measuring the serum gentamicin level 22 hours after a single dose of 5mg/kg. See the neonatal formulary for a detailed plan of dosing interval based on a 22hr level.

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.**

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 the first dose on the 'once only and pre-anaesthetic medical' area of the prescription chart.
2. Subsequent doses should then be written on the regular medications side of the prescription chart using a 'day', 'night' or '24 hour' appropriate Gentamicin drug sticker.
3. As for all medications, print clearly and sign.

- **<u>Amoxicillin</u>** and **<u>Gentamicin</u>** 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

- **Metronidazole** should be added to the Benzyl penicillin and Gentamicin if the focus of infection is within the gut. Refer to BNF / neonatal formulary for updated dosage
- **Flucloxacillin and gentamicin** is recommended if there are signs of umbilical infection (purulent discharge or periumbilical cellulitis)

<u>Initial choice and modification of antibiotics in babies on NNU with meningitis:</u>

If causative organism not known	Treat with Amoxicillin and Cefotaxime
Gram negative organism confirmed	Amoxicillin can be stopped and treat with Cefotaxime
Gram positive organism confirmed	Continue Amoxicillin and Cefotaxime and seek microbiology advice
GBS positive in CSF	Consider changing to Benzyl penicillin and Gentamicin (dosage to be discussed). Gentamicin to continue for 5 days
Listeria in CSF	Consider stopping Cefotaxime and treating with Amoxicillin and Gentamicin

Second Line Antibiotics:

- If a baby becomes unwell after 72 hrs of age **i.e. late onset sepsis** and there are no specific guiding factors, use **Flucloxacillin** and **Gentamicin****. If Gram-negative infection is suspected, add **Cefotaxime** to the existing initial antibiotic regimen. If gram negative infection is confirmed then penicillin-based antibiotics should be stopped.
- If the baby has a central line in-situ then **<u>consider</u>** removing the line. **Vancomycin and Gentamicin should** be considered if the baby is ill or if it is not practical to remove the line. As

both drugs are nephrotoxic and ototoxic, therapeutic drug levels should be monitored closely and urine output and biochemical renal function reviewed on a regular basis. **Cefotaxime** should be considered if there is a strong suspicion of meningitis on clinical examination and / or CSF analysis or if a LP could not be performed on a very sick baby

- If Necrotising Enterocolitis (NEC) is suspected after 72 hours of age use **Flucloxacillin, Gentamicin** and Metronidazole**. If suspected before 72 hours of age add metronidazole to penicillin and gentamicin.

  ***** Please note that Gentamicin should be used as described in first line antibiotics***

Third Line Antibiotics:

- **Ceftazidime** should be used in preference to Cefotaxime if Pseudomonas infection is suspected
- **Meropenem** can be used in severe multi-resistant Gram-negative sepsis. In such circumstances Metronidazole can be stopped if Meropenem is being used – **discuss with the Microbiologist.**

Teicoplanin can be used to treat CONS infection especially when vascular access is a problem - can be given IM once daily. Even if IM route is contemplated for difficult venous access, it is preferable to give a loading dose through the intravenous route. It has no other advantage over Vancomycin apart from being marginally less nephrotoxic. It is usually ineffective in Vancomycin Resistant Enterococcus (VRE) sepsis.

16mg/kg loading dose; followed after 24hours by 8mg/kg

Maintenance dose daily

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 to treat.
- 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)

Monitoring of other drug levels:

Vancomycin:

The blood levels of Vancomycin need to be monitored and dosing and frequency of administration adjusted accordingly in order to prevent toxicity. Moreover, the dosage of most drugs may need to be adjusted in certain clinical conditions like renal and hepatic failure. Remember that the Pharmacist visits the unit every weekday and is an invaluable resource for advice in such circumstances. Vancomycin levels are done in biochemistry department and sample needs to be sent in lithium heparin neonatal containers.

Acceptable levels

Trough (pre-dose) 5-15 microgram/ml Peak (post-dose) 25-40 microgram/ml

Adjustments:

< 5 mcg/ml	Increase dose and repeat in 24 - 48 hours.
5 – 15mcg/ml	Ideal range for babies on Vancomycin. Higher trough levels may be desired for invasive infections.
> 15mcg/ml	Increase interval and repeat levels with next dose. If next levels are high, dose may need to be reduced. Discus it with consultant.

- Trough level is checked before the 4th dose.
- 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. Review the need for antibiotics daily on the consultant ward round. If needed, discuss with the microbiologist on Grand round
- During antibiotic treatment, measure CRP 18 - 24 hours after presentation.
- Lumbar puncture should be considered in a baby on antibiotics, who did not have this investigation at the time of 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 and the focus of infection.
- If cultures are negative after 36 hours, CRP levels are normal 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 blood culture** / CRP remains less than 10 on 2 samples 18 - 24 hours apart	Stop at 36 hours if blood culture negative.
Strong suspicion of infection with rise in CRP and or leucopenia, Good clinical and laboratory response to treatment with **negative blood culture**	Review every 24 hours beyond first 48 hours, Decision to stop antibiotics should be based on level of initial clinical suspicion, baby's clinical progress, levels and trends of CRP i.e. a reasonable fall from baseline)
Pneumonia with **negative blood culture**	5 days
Gram positive organisms such as Group B streptococcus in blood culture without meningitis	Usually 7-10 days. If in doubt discuss with microbiologist
Coagulase negative staphylococcus isolated in blood culture in babies who are clinically well and **central line removed**.	Review every 24 hours beyond first 48 hours, Decision to stop antibiotics should be based on level of initial clinical suspicion, baby's clinical progress, levels and trends of CRP i.e. a reasonable fall from baseline)
Gram negative organisms in blood culture	Usually 14 days – If in doubt discuss with microbiologist

Group B streptococcal meningitis confirmed on CSF culture	At least 14 days of Benzyl penicillin. Stop Gentamicin after 5 days
Gram negative meningitis confirmed on CSF culture	At least 3 weeks
Necrotising Enterocolitis – Stage 2 and above	7-10 days. Review clinically and using biochemical markers
Systemic Staphylococcal infection	At least 2 weeks

References and further reading:

1. NICE clinical guideline CG195 (Updated March 2024): Neonatal Infection: Antibiotics for prevention and treatment
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Pseudomonas in a Blood Culture – Information and procedure to follow

This document is based on guidance issued by the Neonatal Gram-Negative Infection Sub-group of antimicrobial resistance and healthcare associated infection committee.

Late onset neonatal sepsis (>48h of age) affects 2-3/1000 babies and gram-negative organisms cause 20-40% of these. Pseudomonas is one of these organisms and has a high associated morbidity and mortality.

This guidance should be used in order to activate a response to a positive blood culture (or other sterile site culture) and prevent an outbreak. It can also be used alongside the outbreak guidance.

In all cases of infection by gram-negative bacteria its spread is exacerbated by high cot occupancy rates and low nurse: baby ratios. At all times we should aim to follow the Neonatal Toolkit for High Quality Neonatal Services with adequate cot spacing and optimal staffing rates.

Following identification of a positive blood culture for a Pseudomonas species, these steps should be considered:

1. If >2 sterile sites have a positive culture an outbreak should be suspected
   a. An outbreak control team meeting should be arranged including
      i. Neonatologist
      ii. Microbiologist
      iii. Infection control iv. Lead nurse
   b. Consider closure of NNU or reduction of available cots (after careful risk assessment
   c. Communicate concerns to Neonatal Network
   d. Communicate with parents
   e. Works with ABMU communications department

2. Hand Hygiene
   a. Re-education (staff and parents)
   b. Daily audits with immediate feedback on poor performance
   c. Personal Protective Equipment (PPE) should be worn for all contact with each baby (plastic apron and gloves)

3. Staffing – wherever possible, a separate group of staff members should be allocated to care for the infected/colonised infants (nursing and medical)

4. Environmental screening

Follow Department of Health guidance and advice from Estates – the following screening should be considered:

   a. Taps and sinks in every room the baby has inhabited since birth
   b. Any environmental pooled water
   c. Inside incubators
   d. Multiuse equipment
      - Blood gas machines
      - Ultrasound machine
      - Cold light
      - Phototherapy units

5. Review of Cleaning routines (this should be multidisciplinary)

6. Consider deep cleaning the environment

7. Consider screening all babies for Gram Negative Bacteria colonisation
   - Weekly rectal swabs
   - ET secretions for any ventilated baby
   - Continue for 1-2 months or until outbreak resolves
   - Feedback to staff routinely

The following table taken from the recent publication "Managing and preventing outbreaks of Gram-negative infections in UK Neonatal Units" summarises good practice points for reducing and preventing infection:

Table 1 Good practice actions to reduce Gram-negative bacteria (GNB) infections and manage outbreaks

Good practice	Number of infections		
	None	1–2/month	Outbreak
Trust engagement			
Ensure the board and executive make it a high priority to minimise GNB infections, and are supportive of all prevention and eradication measures	√	√	√
Develop a Water Action Plan	√	√	√
System-wide assurance of best practice for infection prevention, including audit and implementation of change suggested by audit findings	√	√	√
Communication			
Promptly inform and educate parents about single infections as well as outbreaks		√	√
Set up an outbreak control team			√
Once an outbreak is declared, involve the DIPC and Chief Executive			√
Inform the Strategic Health Authority about all outbreaks, but especially if there are deaths or NNU closure			√
Microbiology team to report suspected outbreak to the Health Protection Agency Health Protection Unit			√
Identify a system so that all NNUs know of any outbreak in the clinical network	√	√	√
Hand hygiene			
Use alcohol-based gels for hand hygiene (even if also wash hands)	√	√	√
Comply with advice on rings and fake nails	√	√	√
Audit hand hygiene monthly	√	√	
Audit hand hygiene twice daily			√
Ensure a system so that audit findings and action plans are translated into practice	√	√	√
Staff should wear PPE (ie, plastic apron and gloves) for every patient contact			√
Check for hand lesions, even minor, and dermatitis	(√)	(√)	√
Educate parents and visitors about hand hygiene	(√)	(√)	√
Staffing and space			
1:1 nursing qualified in service for ITU, 1:2 for HDU, 1:4 for low dependency unit	√	√	√
Aim for the recommended cot spacing	√	√	√
Ensure adequate accommodation for storage and cleaning of equipment	√	√	√
Ensure facilities for segregation of infected or colonised babies	√	√	√
Isolate infected and colonised babies, preferably in isolation cubicles		√	√
Consider deploying staff so that some only look after the infected/colonised babies			√
Consider reducing bed availability to ensure British Association of Perinatal Medicine staffing and cot spacing standards			√
Consider closing the NNU			√
Equipment and environmental contamination			
Purchase single-use or dedicated equipment (stethoscopes, laryngoscope blades, etc)	√	√	√
Robust cleaning routines for multiuse items	√	√	√
Follow Department of Health and Social Services guidance on decontamination of incubators	√	√	√
Ensure that there is a responsible person for cleaning routines	√	√	√
Sterile or filtered water to top and tail babies where the water supply has been shown to be contaminated with *Pseudomonas*	√	√	√
Follow DH advice on water colonisation by *P aeruginosa*	√	√	√
Avoid clutter of equipment and trolleys	√	√	√
Decontaminate equipment with chlorine-based agents			√
Sample potential environmental sources for specific GNB			√
Deep clean the environment			√
Audit cleaning routines and ensure findings translate to practice changes	√	√	√
Undertake a multidisciplinary review of the ward to inform cleaning routines and frequencies	(√)	(√)	√
Care bundles and information systems			
Introduce an infection-reduction care bundle, such as the Matching Michigan programme	√	√	√
Benchmark infection rates using neonIN, SEND or VON; and ensure that results are used to inform infection prevention and control improvements	√	√	√
Subscribe to a patient information system to easily track infections and antibiotic use in each patient	√	√	√
Antibiotic stewardship and microbiology			
Reduce antibiotic use, by rewriting local guidelines, to: Reduce administration at the start of life Stop antibiotics early, that is, 36 h, if no evidence of infection Reduce the duration of antibiotics for proven infection Limit the use of broad-spectrum antibiotics	√	√	√
Change the empirical antibiotic policy		√	√
Audit antibiotic use, and translate findings into practice change	√	√	√
Remove central lines in the presence of a GNB bacteraemia		√	√

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Selective Fluconazole Prophylaxis in High-Risk Preterm Infants in NICU to reduce invasive fungal infection

Background and rationale for antifungal prophylaxis:

Neonatal invasive fungal infection, primarily due to candida species, is a devastating illness in the extremely premature/very-low-birthweight infants and is associated with high incidence of mortality and morbidity. The incidence varies widely among centres providing neonatal care (2- 20%), but is inversely proportional to gestational age and birthweight. Mortality attributed to invasive fungal infection is >25%. The risk of long term neurodisability is also increased several-fold. Studies have consistently identified that most invasive fungal infection are seen in infants <27 weeks and birth weight <1000 grams. Invasive infection is usually preceded by colonisation in the bowel, skin and respiratory tract.

While acquired risk factors for neonatal fungal infection are well recognised (presence of a central line, delayed enteral feeding > 3 days, use of broad spectrum & prolonged course of antibiotics, prolonged mechanical ventilation), many are unavoidable in clinical practice in this vulnerable group of infants. While efforts to reduce these risk factors are undertaken, early prophylactic treatment has emerged as an effective strategy to reduce colonisation and subsequent invasive infection. A Cochrane review from 2015 has shown that fluconazole prophylaxis significantly reduces the risk of invasive fungal infection (RR 0.43, 95% CI 0.31 to 0.59) but has no effect on overall mortality (RR 0.79, 95% CI 0.61 to 1.0).

The effect of prophylaxis is most evident in centres with high prevalence. Infectious Diseases Society of America (2016) recommendation is to use fluconazole prophylaxis in neonatal units with incidence of invasive candidiasis > 10%. European guidelines for Candida prevention and treatment (2012) recommends fluconazole prophylaxis in neonatal units with incidence of fungal sepsis > 2% and where the incidence is less than 2% the decision to use the same should be made on case by case basis in a risk stratification strategy.

Choice of antifungal prophylaxis:

Both fluconazole and nystatin have been shown to be equally effective in clinical studies when used in targeted groups of premature and ELBW infants. Fluconazole is a potent, selective, triazole inhibitor of fungal enzymes involved in ergosterol, a constituent of cell wall.

As a group we have agreed to use Fluconazole for prophylaxis on our unit for the following reasons -

1. Fluconazole can be given both orally and intravenously thus providing prophylaxis during the most vulnerable period where infants are ill, nil by mouth and on antibiotics. There is more data on fluconazole prophylaxis in the extremely premature groups.
2. The dosage interval is infrequent (twice weekly)
3. The concern about emergence of resistant strains has not been confirmed in neonatal units using low dose (3mg/Kg) twice weekly regimen over a 12-year surveillance period. The MIC for fluconazole for the colonisation isolates had not changed either.
4. Long term follow-up over 6-8 years have established safety of fluconazole prophylaxis
5. It is cost effective in preventing invasive fungal infection and when compared to oral nystatin

   At present, about 40% of European NICUs routinely use antifungal prophylaxis with fluconazole and there is a trend towards increasing use of this practice.

   The most frequently reported side effect of fluconazole is transient elevation of plasma levels of creatinine or hepatic enzymes described in about 5% of infants treated with fluconazole.

Indication:

Fluconazole prophylaxis should be commenced on all infants 27+6 weeks and / OR <1000 grams in first 28 days of life with any additional ongoing risk factors

- Mechanical ventilation
- Central lines
- Receiving parenteral nutrition (either peripheral or central)
- Broad spectrum antibiotics use for more than 48 hours

Prescription and dosage

- Fluconazole should be commenced within 24 hours of birth
- Administer Fluconazole IV 3mg /Kg as an infusion over 20 minutes on Wednesdays and Sundays. If no IV line is available complete course orally. The oral dose of Fluconazole is also 3mg/Kg twice a week
- If a baby is born and received Fluconazole in the preceding 24 hours of a scheduled day, delay the next dose to the following scheduled day of the week.
- Side effects at this dose are extremely rare. Dose may need adjustment in renal failure. Fluconazole can increase serum levels of Phenytoin and Zidovudine. Monitor liver function (ALT and conjugated bilirubin).

Stop fluconazole prophylaxis early if:

- Creatinine > 175µmol / L **and/or** ALT > 250 IU/L

N.B. If an infant is suspected to have fungal sepsis while on Fluconazole prophylaxis you must use amphotericin B to initiate treatment until culture results are available. However, the treatment course could be completed with Fluconazole if the organism is sensitive. An audit process to monitor sensitivities of all fungal isolates should be undertaken on a regular basis to identify any emerging resistance.

When to discontinue?

Prophylaxis can be stopped once all the additional risk factors are no longer present or baby is more than 28 days old (whichever is earlier)

- *To discuss with consultant if considering restarting fluconazole prophylaxis in an infant who has previously discontinued.*

Further reading/references:

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Management of suspected or confirmed fungal infection in the VLBW infants

Introduction:

Despite prophylactic fluconazole, very low birth weight (VLBW) infants will remain susceptible to fungal infection. The signs and symptoms of invasive fungal sepsis are often indistinguishable from other causes of sepsis. A high degree of suspicion and early treatment is the key to survival and better outcome in survivors. The estimated incidence is 2% to 5% in very preterm or VLBW infants. *Candida albicans* is the main pathogen isolated in Wales in recent years and is also the commonest organism implicated in neonatal units across the UK. The attributable mortality of *Candida* bloodstream infection could be as high as 40%. In addition to fungaemia, infants may develop fungal pneumonia, meningitis, renal tract infection, ophthalmitis, osteomyelitis, arthritis, endocarditis, liver abscesses and skin abscesses.

Like other causes of neonatal sepsis, the gold standard for the diagnosis of neonatal candidemia is the blood culture. Unfortunately, the blood culture has poor sensitivity in detecting invasive infection with only 29% positive with one organ involvement rising to about 80% when 4 or more organ systems are involved. PCR techniques are oversensitive and therefore not always useful in colonised infants. Blood cultures take at least 24-48 hours before becoming positive and waiting for the result in a sick infant may result in death or severe morbidity. Therefore, an empirical approach may be required.

When to consider empirical treatment?

This is a decision based on experience and clinical judgment. For all such decisions, discuss with the most senior clinician available.

Consider empirical treatment in extremely premature infants (<28 weeks and <1000gms) who are clinically unwell and have some of the following risk factors:

- Known heavy colonisation with candida
- Unresponsive or exposed to multiple or prolonged courses of broad-spectrum antibiotics
- Unexplained severe thrombocytopenia (PLT <100)
- Refractory or unexplained hyperglycaemia
- Raised inflammatory markers
- Presence of central lines

Investigations for suspected fungal infection:

- Blood culture (peripheral & central line)
- Urine (suprapubic aspirate or catheter. Please specifically ask the laboratory to look for fungal hyphae under microscope – results should be available on the same day),
- CSF microscopy and culture
- Tracheal aspirates (in intubated babies) for culture.

Investigations in cases of confirmed fungal infection:

- Repeat blood culture within 48 hours of initiating treatment.
- Renal USS – must be undertaken before completion of treatment to look for fungal balls. This may need prolongation of medical treatment and very rarely surgical intervention. The scan will need to be performed earlier in those unresponsive to treatment.
- Echocardiogram to look for fungal vegetations.
- Cranial Ultrasound (and consideration of CT head if abnormalities found).
    - Fungal abscesses, when present, are seen by cranial USS/CT in around 50% of cases. There tend to be multiple abscesses present rather than solitary.
    - Periventricular leukomalacia may evolve over time and repeat, interval cranial ultrasound scans should be performed in confirmed cases of fungal sepsis.
- Ophthalmology review.
- USS of liver and spleen to look for abscess if no fungal clearance within 5 days**.**

Beta-D-glucan assay is a more recently developed test for fungal sepsis. 1,3Beta-Dglucan is a cell-wall component of several fungal species. In adult populations the beta-D glucan assay has been shown to have a variable sensitivity between 55-95%, but a more reliable specificity between 77-96%. This may be secondary to different cut-offs for a positive result being used, different assay techniques and differing populations between the studies. Specificity is improved (>95%) if two consecutive positive samples are attained. There is more limited data for the neonatal population, with the current evidence suggesting it has a more limited sensitivity but high specificity and negative predictive

value for diagnosing fungal infection. It has also been demonstrated that BetaD-glucan levels fall in neonates with effective treatment and it may have a role in monitoring antifungal therapy.

The beta-D-glucan assay is not specific for any particular fungal species and will be positive in the presence of infection with *candida, aspergillus, pneumocystis* and others. It will also be positive in bacterial sepsis with species containing the 1,3Beta-D-glucan protein in their cell wall, for example *Pseudomonas aeruginosa.* False positive results have also been reported in cases with recent intravenous immunoglobulin, albumin or IV co-amoxiclav administration. 0.5ml – 1.0ml of clotted blood sample is required to run a beta-D-glucan assay.

The reference ranges for interpretation are:

- Negative: 30 to 59 pg/mL,
- Indeterminate: 60-80 pg/mL,
- Positive: >80pg/mL

These reference ranges were developed with invasive *Candida* infections in mind and may not be applicable to other fungal species. Further advice should be sought from a mycologist as required to aid interpretation.

Treatment:

There is limited high-quality evidence available to guide optimal antifungal choice and most prospective studies have only included small numbers of infants. Fluconazole and amphotericin B are the most commonly used antifungals in neonatal practice. Caspofungin may be less nephrotoxic than amphotericin, however there is scanty pharmacokinetic, efficacy and dosing data for the neonatal population. There are also reports that prolonged use of Caspofungin can result in resistant fungal populations. Flucytosine is sometimes used as a second line treatment in CSF infections when poor response to monotherapy.

The dose of amphotericin B generally does not need be adjusted in patients with pre-existing renal impairment. However, if there is renal toxicity thought to be drug related, then the dose should be reduced (either by using alternate-day dosing or reducing the

daily dose by 50 percent). Renal toxicity secondary to amphotericin B treatment seems to be much more uncommon and milder in the neonatal population compared to adults.
The duration of treatment will depend upon the source of the fungal infection and extent of spread through other organs systems. It is generally advisable to seek expert opinion from a mycologist to determine the optimum duration of therapy in individual cases.

Central Venous Catheter Associated Infection	
Medication	Initiate treatment with intravenous liposomal amphotericin B 3-5mg/kg OD
Duration	Minimum 14 days from the first negative blood culture result.
More Info	*Central vascular access should be removed as soon as possible* as eradication with antifungals is virtually impossible in the presence of an infected central line, and delayed removal has been associated with higher mortality. IV fluconazole is an acceptable alternative once fungal sensitivities are known.

Urinary Tract Infection (UTI)	
Medication	Initiate treatment with intravenous liposomal amphotericin B 3-5mg/kg OD
Duration	10-14 days
More Info	*Any indwelling urinary catheter should be removed in cases of suspected fungal UTI.* For isolated urine infection with or without renal involvement treatment with Fluconazole can also be considered once sensitivities are known: • Isolated, uncomplicated UTI can be treated with oral fluconazole if the infant is clinically well and tolerating feeds.
	IV fluconazole is preferred for complicated UTI (e.g. presence of a renal fungal mass). If a fungal mass is present in the renal tract, *treatment will need to be continued until the mass has resolved*.

Central Nervous System (CNS) Infection	
Medication	Initiate treatment with intravenous liposomal amphotericin B 3-5mg/kg OD
Duration	A minimum of 3-4 weeks after a negative blood culture Treatment should be continued until clinical signs, CSF abnormalities, and radiographic abnormalities (if present) have resolved.
More Info	CNS devices (e.g. ventriculoperitoneal shunts and reservoirs), if present, should be removed if possible. If the CSF does not become sterile within a few days of initiating treatment, or if the infant's clinical status deteriorates, despite amphotericin B monotherapy, their case should be discussed with a mycologist to guide further, second-line antifungal treatments.

Disseminated Disease	
Medication	Initiate treatment with intravenous liposomal amphotericin B 3-5mg/kg OD
Duration	Duration of treatment will depend on organ systems affected (as described above) and clinical condition of the infant. Expert opinion should be sought to guide management.
More Info	For cases that are not responding to initial treatment further investigations will be required to determine extent of disease: • USS liver/spleen/abdomen to assess for fungal masses
	There are several cases reports of *Candida* peritonitis in VLBW/premature infants with necrotizing enterocolitis or spontaneous intestinal perforations Assess for signs of osteoarticular infections. In neonates, fungal osteomyelitis or arthritis very rarely occurs as an isolated event and usually part of a disseminated disease process. For persistent disseminated infections that are not responding to amphotericin B, there is a paucity of data on which second agent should be added. In practice, fluconazole or an echinocandin (e.g. Caspofungin) are added, but an expert opinion from a mycologist will be required to guide further treatment. In all cases of persistent infection, all potentially contaminated indwelling foreign material should be removed (e.g. CVCs, urinary catheters, ventriculoperitoneal shunts and reservoirs etc.) In serious cases, surgical resection of infected tissues may be required if systemic antifungal therapy fails.

Where intravenous access proves difficult, treatment course could be completed successfully with oral fluconazole if the infant has clinically improved and there is no evidence of fungal masses in organs. This decision should be discussed with a senior clinician.

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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 (3080%), 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:

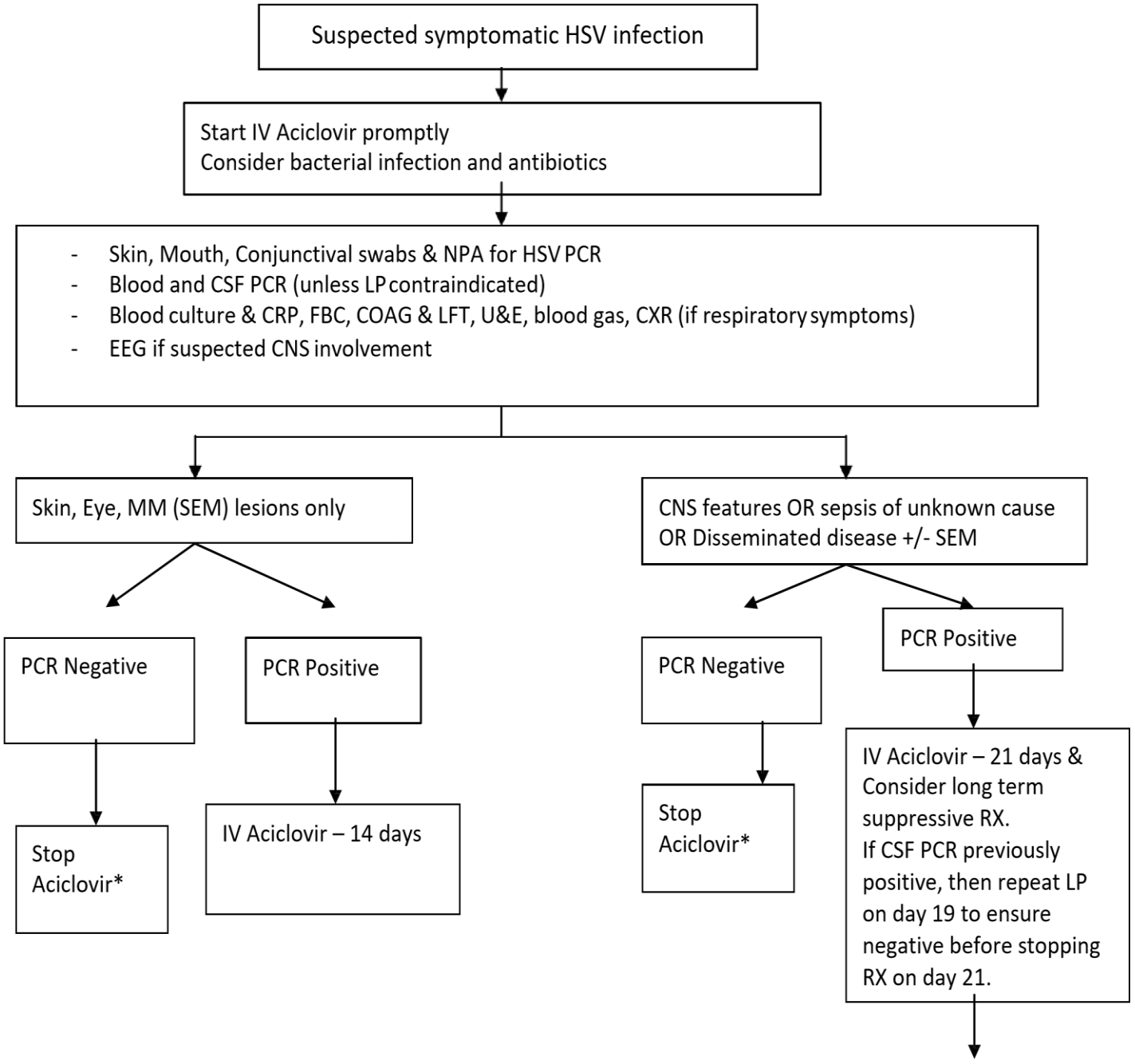
Essential diagnostic virology investigations

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 – 2472hrs
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 – 2472hrs
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 temporo- 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[10]



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.

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Hepatitis C infection in pregnancy and the newborn period

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, Consultant Gastroenterologist, 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.

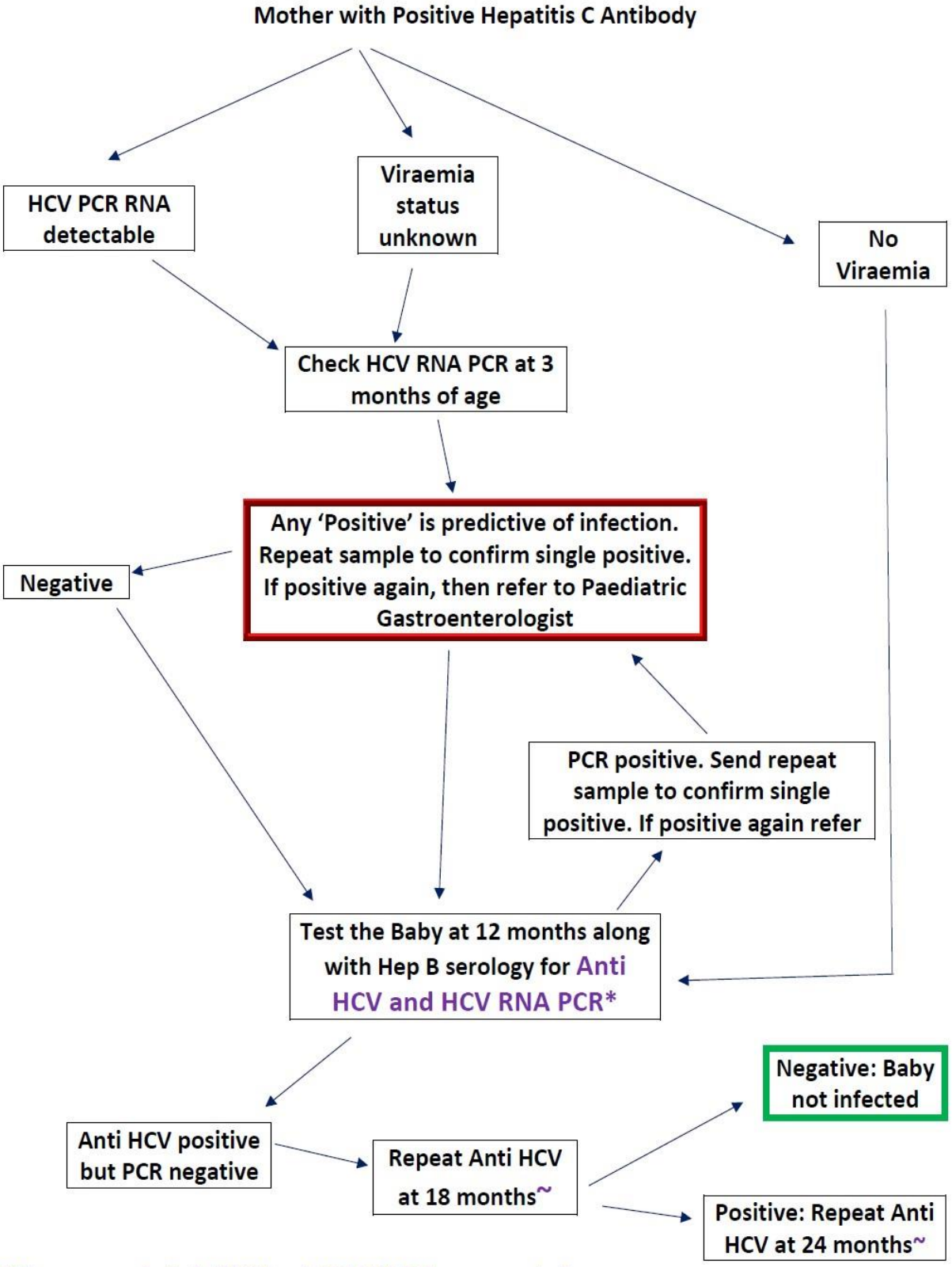
Infants born to mothers with previously documented Hepatitis C infection but with NO viraemia should have a blood test for the presence of anti HCV and HCV RNA PCR at 12 months of age. If PCR is positive, perform a repeat sample and if again positive then urgent referral to Paediatric Gastroenterologist/ Paediatrician with Gastro interest to be made.

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 urgently refer to Paediatric Gastroenterologist/Paediatrician with Gastro interest. If negative then, perform anti HCV along with Hep C RNA PCR at 12 months (refer to algorithm below).

If anti HCV is positive, but PCR is negative at 12 months, then repeat Anti HCV at 18 months of age. If still remains positive repeat at 24 months (refer to algorithm below). At this stage if Anti HCV is still positive needs a referral to Paediatric Gastroenterologist/ Paediatrician with Gastro interest. 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:



*Please ensure both Anti HCV and HCV RNA PCR are requested.

~ If still positive at 24 months please refer to Paediatric Gastroenterologist/Paediatrician with Gastro interest.

- Contact Neonatal Consultant covering SHIPs for the week for further advice. 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.**

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 Paediatric Gastroenterologist/Paediatrician with Gastro interest. 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 Hep B and against Hep A.

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Management of Perinatal Hepatitis B transmission

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. Prevalance 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 this visit 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 Postnatal Infection Guidelines Version 2018.4.3Update due 2023Page 27 of 52

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. Needs 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

HBs Ag	HBe Ag	HBe Ab	Anti HBV immunoglobulin 250IU as soon as possible following delivery	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 12 months of age when the final vaccine is done. This should be ideally explained 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 tests at 12 months for HBs Ag and AntiHBs Ag (hepatitis B immunity levels) following the final vaccination.** 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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Guidelines for Palivizumab (Synagis®)

Background:

Respiratory syncytial virus (RSV) infection in infants with chronic lung disease (or bronchopulmonary dysplasia) is associated with increased morbidity.

Palivizumab is a humanised monoclonal antibody providing passive immunity against RSV. Synagis® is the only licensed form of Palivizumab available in the UK. In a randomised double blind placebo controlled multicentre trial conducted of 1502 infants with chronic lung disease of prematurity, palivizumab resulted in a reduction in hospitalisation (4.8% vs 10.6%), fewer days hospitalisation and fewer requiring intensive care (1.3% vs 3%). *[Impact-RSV Study].* Those most at risk of developing severe, and occasionally fatal, RSV infection are very young infants born prematurely who have predisposing conditions such as chronic lung disease (CLD), congenital heart disease (CHD) or children who are immunodeficient (Wang et al., 2008). In 'high-risk' children the mortality rate is about 3% (Müller-Pebody et al., 2002).

Indications for SBU Health Board use:

Palivizumab should only be approved for use in a particular baby by a Consultant in Neonatology, Paediatric Respiratory, Cardiology or Immunology.

The objective of the passive immunisation is to protect at-risk pre-term infants for whom RSV infection is likely to cause serious illness or death. In 2010 The Joint Committee on Vaccination and Immunisation (JCVI) published guidelines on cost effectiveness. This is based on an analysis of the cost effective use of Palivizumab prophylaxis (Wang *et al.,* 2008, and 2011). JCVI recommends palivizumab to be given to all infants in the following groups. These recommendations will be adopted by Singleton neonatal unit.

1. **High Risk due to Bronchopulmonary dysplasia (BPD)** – (also known as chronic lung disease)

a) Pre-term infants who have moderate or severe BPD. Moderate or severe BPD is defined as 'preterm infants with compatible x-ray changes who continue to receive supplemental oxygen or respiratory support at 36 weeks post-menstrual age1'. Children who fall into the light and dark green shaded area of Table 1 should be offered prophylaxis.

Table 1 – Cost effective use of Palivizumab (shaded area)

Chronological age (months)	Gestational age at birth (weeks+days)						
	≤24+0	24+1 to 26+0	26+1 to 28+0	28+1 to 30+0	30+1 to 32+0	32+1 to 34+0	≥34+1
<1.5							
1.5 to <3							
3 to <6							
6 to <9							
≥9							

By date of birth, babies who qualify for treatment starting at the beginning of October are:

≤ 24 weeks	Born after 1st January
≤ 28 weeks	Born after 2nd April
≤ 32 weeks	Born after 2nd July
≤ 34 weeks	Born after 17th August

b) Infants with respiratory diseases who are not necessarily pre-term but who remain in oxygen at the start of the RSV season are also considered to be at higher risk. These infants may include those with:

- pulmonary hypoplasia due to congenital diaphragmatic hernia
- other congenital lung abnormalities (sometimes also involving congenital heart disease or lung malformation)
- interstitial lung disease

 those under 24 months receiving long term ventilation at the onset of the season.

2. **High Risk due to Congenital Heart Disease (CHD)**

a) Preterm infants with haemodynamically significant, acyanotic CHD at the chronological ages at the start of the RSV season and gestational ages at birth covered within the light green shaded area in Table 1.

b) Cyanotic or acyanotic CHD plus significant co-morbidities particularly if multiple organ systems are involved.

3. **High Risk due to Severe Combined Immunodeficiency Syndrome (SCID)** a) Children less than 24 months of age with SCID - the most severe form of inherited deficiency of immunity, who are unable to mount either

T-cell responses or produce antibody against infectious agents – until immune reconstituted.

Where **clinical judgement** of other individual patient circumstances strongly suggests that prophylaxis would prevent serious RSV infection in infants who are at particular risk of complications from RSV, use of palivizumab could be considered during the RSV season. For ABMU Health Board we will include in this category **any baby already on home oxygen on 1st October or discharged home on oxygen during the RSV season who do not fit the criteria in table 1.** Other babies can be considered after full discussion amongst the Consultants.

Preparation of Palivizumab (Synergis)

Synagis solution for injection is a clear liquid supplied in either 0.5 ml or 1.0 mls vials, with a concentration of 100mg/ml.

Handle in a similar way to vaccines - **store in fridge, do not shake.**

Dose:

- 15 mg/kg body weight given once a month
- Palivizumab should be given as a maximum of FIVE doses, given one month apart, from the beginning of the

  RSV season (within 2 weeks of the calendar week 40 i.e. 1st October).
- Where the course of treatment begins later in the RSV season (e.g. where infants are born within the RSV season) up to five doses should be given one month apart until the end of calendar week 8 (i.e. the end of February).
- As the risk of acquiring RSV infection while in the neonatal unit is extremely low, infants in neonatal units who are in the appropriate risk groups should only begin palivizumab treatment 24 to 48 hours before being discharged from hospital.
- Those infants that have begun a course of palivizumab treatment but are subsequently hospitalised should continue to receive palivizumab whilst they remain in hospital.
- Those infants who are admitted with RSV or other bronchiolitis should still receive the remainder of the injections.
- If, during the RSV season, an infant is identified to be at risk but there is no reliable history of previous palivizumab prophylaxis within the season, then doses should be started and administered monthly for the remainder of the RSV season but need not be given after the end of February.
- Where courses have been interrupted the doses should be restarted and administered monthly for the remainder of the RSV season but need not be given after the end February.

Administration:

- Palivizumab must be given in an appropriate hospital environment with the availability of drugs for the treatment of severe hypersensitivity.
- We run a specific clinic for palivizumab in order to reduce wastage.
- Palivizumab should be given intramuscularly, preferably in the anterolateral aspect of the thigh. The gluteal muscle should not be used as an injection site because of the risk of sciatic nerve damage.
- Injections over 1 ml should be given as a divided dose.
- Observation of the infant's general condition should occur for 20 minutes following administration of the dose.
- Palivizumab can be given at the same time as vaccines administered as part of the routine childhood immunisation programme.
- The site at which each injection is given and the batch numbers of the immunisations should be recorded in the individual's records.

Precautions:

See the SPC (summary of product characteristic) for a full list of special precautions.
Minor illnesses without fever or systemic upset are not valid reasons to postpone immunisation. If an individual is acutely unwell, immunisation may be postponed until they have fully recovered.

Adverse Effects:

- Common adverse drug reactions include fever, injection site reactions and nervousness.
- Report all adverse effects that occur on administration of the injection via the yellow card system.

Contraindications:

Known hypersensitivity to palivizumab, or any component of the formulation, or other humanised monoclonal antibodies is a contraindication.

Reference:

1. Impact-RSV Study Group (1998). Palivizumab, a humanised respiratory syncytial virus monoclonal antibody, reduces hospitalisation from respiratory syncytial infection in high risk infants.
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3. Green Book Chapter 27a V2.0 Respiratory Syncytial Virus Sept 2015
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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 12hourly (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

< 3 4 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

Referral Letter - Infant born to mother with retroviral infection

Date:
Re:

Affix baby sticker here	Affix maternal sticker here

Dear Dr Burke
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		Platelets		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.

<u>When a diagnosis of cCMV confirmed – additional testing required</u>

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

<u>Considering Treatment</u>

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

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Management of infants at risk of Congenital Toxoplasmosis

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)		

Follow-up:

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:

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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:
  - Mother inadequately treated (GUM consultant will advise, see above)
  - Infant has clinical signs consistent with syphilis
  - 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.
  - Infant has positive treponemal IgM test together with corroborative history, clinical signs. GUM consultant will advise.
  - 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

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7. http://www.walesneonatalnetwork.wales.nhs.uk/sitesplus/documents/1034/congenital%20infection%20UHW%202017.pdf
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Methicillin-Resistant Staphylococcus Aureus (MRSA) Guidance for NICU

The normal habitat of *Staphylococcus aureus*, including MRSA, is human skin, particularly in the nose, axilla and perineum (groin). Clinical infection with MRSA (including MRSA bacteraemia) occurs either from the baby's own resident MRSA (if he or she is an asymptomatic carrier) or by cross-infection from mother or another person, who could be an asymptomatic carrier or have a clinical infection. MRSA is spread by direct contact or indirect contact e.g. contaminated equipment or airborne in those with sputum carriage.

Screening Policy: All babies should be screened for MRSA carriage on admission to neonatal unit and then at weekly intervals (every Monday morning) for those whose stay is prolonged.

Site of screening: The most common sites – that is the nose, axilla, groin or perineum, hairline and umbilicus need to be screened. Any superficial clinical or surgical wound, if present, should also be screened. It is advisable to screen all sites at admission however only two sites- nose and perineum should be screened weekly.

Isolation of babies: When a baby is identified as MRSA positive, either because of an MRSA infection or as an asymptomatic carrier by screening, the Infection Prevention and Control Team should be notified and correct procedures implemented to minimise risk of cross infection. The baby should be cared for in single room isolation to reduce the risk of transmission. If the latter is not available or not feasible, then the baby could be nursed in an incubator or cot (if deemed appropriate) with standard universal and contact precautions in place. Consideration could be given to separating MRSA positive patients from non-carriers in cohort bays or wards. The decolonisation regimen should be applied as soon as a positive result is known, irrespective of the availability of isolation facilities. MRSA infection or colonisation should not be a barrier to good clinical care.

Decontamination: All positive babies should receive a full decolonisation regimen. The decolonisation regimen is only 50–60% effective for long-term clearance, but as soon as the procedure is implemented the presence and shedding of MRSA are reduced significantly and the risk of the patient infecting themselves or transmitting MRSA to

another baby is much reduced. Contact precautions must be observed – see infection control guidelines.

Decontamination Regimen:

a. Bactroban (2% mupriocin) nasal ointment three times a day for 5 days.
b. Octenisan (0.3% Octenidine dihydrochloride) wash once daily for 7 days.
(Octenidine is 99.9% effective against MRSA. It can be applied undiluted using damp cotton wool, rubbed onto areas of the body to be cleansed with particular attention to groin, axilla, perineum and buttock and should be left in contact with the skin for 3 minutes before washing off. If the baby is very preterm or very low birth weight and there is difficulty in maintaining temperature, the body wash can be omitted. Once temperature control improves, this can be considered later on.)
c. Any obvious skin lesions should be covered with occlusive dressings.

Washable clothes and bedding should be changed at least daily as MRSA survives in skin scales and trapped by clothing. Bed linen should be discarded into an alginate bag within a red linen bag. Clothes should be washed the same day.

The baby should be re-swabbed 48hours after finishing the decontamination regimen. If any swabs come back as positive, repeat the decontamination regimen and re-swab in 9 days. If all swabs are negative, then no further treatment is required. Three full screens taken at weekly intervals are required before accepting that the MRSA has been cleared.

Only 2 courses of Mupriocin should be used during the hospital stay. If carriage persists, Naseptin cream (0.5% Neomycin and 0.1% Chlorhexidine) can be used four times/ day for 10 days.

Treatment: In known cases of MRSA, systemic antibiotic therapy is not indicated unless the patient is unwell or pyrexial. For systemic infection use IV Vancomycin or Teicoplanin or, occasionally, Linezolid after discussion with the Microbiology Consultant

Parental screening and Decontamination: When a baby is identified as MRSA positive, screening of parents or carers is advisable. In case of positive MRSA status in the parent/s or carers, decontamination or treatment regimen for them should be offered. (Parents can

perform cares and have skin to skin contact with the baby regardless of their status as long as they maintain good hand washing before and after touching the baby.

Policy while transferring babies to other units:

MRSA should not prevent a patient from being transferred for good clinical reasons, but unnecessary transfers should be avoided. Before transfer, the unit staff should inform the relevant ward in the receiving hospital of the baby's MRSA status and suggest that the infection control team at the receiving hospital be informed if the baby is positive for MRSA.

Policy while admitting babies from other units:

MRSA should not prevent a patient from being accepted for good clinical reasons, but unnecessary transfers should be avoided. If the baby is MRSA positive or if the MRSA status is not known, then baby should ideally be admitted in a cubicle inside neonatal unit, but if the latter is unavailable or not feasible, then babies can be nursed in an incubator with good universal precautions in place.

References:

1. MRSA Screening- Operational Guidance. Department of Health, July 2008. http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_08668
   2.pdf
2. Screening for Methicillin-resistant Staphylococcus aureus (MRSA) colonisation: A strategy for NHS trusts: a summary of best practice, Nov 2006. http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_06 318 7.pdf
3. Policy for Management of Methicillin Resistant Staphylococcus Aureus (MRSA), Section 5, Infection Control Manual, ABMU Trust.

Infection control on the Neonatal Unit – General Guide

Please Note: During the current COVID 19 pandemic, specific guidance has been written with regard to relevant infection control measures to be undertaken in relation to COVID 19 which will be updated over time. This guidance can be found in the Infection Chapter separate to this document which is a general guide

This document is written for staff of the neonatal unit. For additional information, please refer to the Infection and Control policies on the Trust intranet site http://howis.wales.nhs.uk/sites3/search.cfm?searchtext=infection+control&orgid=926 or Infection Control Manual at Sister's office.

Introduction

Staff providing care must ensure that they:

- understand and apply the principles of infection prevention and control;
- understand their responsibility for their own practice;

Every person who works on the Neonatal Unit has a duty to deliver safe infection control care. Infection in the neonate is the most common cause of death

Colonisation and/or infection of the baby by organisms acquired from the mother prior to, or during, birth is known as 'early onset infection' and usually manifests within 72 hours. Many other infections are caused by pathogens acquired from the hospital environment i.e. nosocomial infections. These usually occur after 72 hours after birth. In babies < 1500 grams birth weight, nosocomial infections are 20 times more common than those acquired congenitally.

The incidence of congenitally-acquired infections e.g. β-haemolytic streptococcus and *E. coli* appears to be relatively static or even decreasing. However, the incidence of nosocomial infection is increasing. Our neonates are uniquely vulnerable because most have immunodeficiency associated with prematurity and have many invasive procedures performed. An added problem is that multi-resistant strains of different organisms are now emerging. These are spread mainly by contact. Examples are extended-spectrum β-lactamase (ESBL) producing organism's e.g. *E. coli* and *Klebsiella sp.,* and also glycopeptideresistant enterococci (GRE) etc. These infections are becoming more common in the community e.g. a mother who has a colonisation/infection with one of these multi-

resistant bacteria may transmit the organism to her infant, who then becomes colonised. This may then be a risk factor for infection in that baby or for spreading the infection to other babies within the nursery

Prevention and control of infections – Nursery admission policies

Precise communication between Obstetricians, midwives and Neonatologists is very important. Close liaison with the microbiology laboratory and the consultant microbiologist is also essential. Nursery personnel should be notified in advance of the birth of a neonate who may have a congenital or perinatal infection or of a mother who is infected/ colonised with a significant organism. It is important to know the sensitivity of the organism e.g. if there has been an *E. coli* urinary tract infection, was it a sensitive *E.coli* or was it a multi-resistant *E. coli* ? This will have implications for the care of the baby and for antibiotic treatment should the infant develop signs of infection.

Standard universal precautions

Standard Infection control precautions (SICP) must be used by all staff, in the care of all infants in the unit whether infection is known to be present or not, to ensure the safety of those being cared for, and staff and visitors in the care environment.

SICPs are the basic infection prevention and control measures necessary to reduce the risk of transmission of micro-organisms from recognised and unrecognised sources of infection. These sources of (potential) infection include blood and other body fluids, secretions or excretions (excluding sweat), non-intact skin or mucous membranes, and any equipment or items in the care environment that are likely to become contaminated. The application of SICPs during care delivery is determined by the assessment of risk and includes the task/level of interaction, and/or the anticipated level of exposure to blood or other body fluids.

There are **ten elements** of Standard Infection Prevention and Control Precautions (SICPs):

Please refer to policy:

http://howis.wales.nhs.uk/sites3/Documents/926/CID%20892%20ABMU_Standard%20Infection%20Control%20Precautions%20Policy_V1%200_Apr_2013_Final%281%29FINAL.pdf

Hand hygiene

On arrival at the start of a shift, personnel should remove watches, rings, bracelets etc, roll up their sleeves and wash their hands and arms up to the elbows. Then rinse thoroughly and dry with paper towels. Fingernails should be kept short with no false fingernails or nail polish.

- For routine social hand-washing, (level 1) soap and water will be sufficient.
- Aseptic hand hygiene technique (level 2) , using an approved antiseptic hand cleanser or alcohol based hand rub can also be used following hand washing, should be used before and between aseptic procedures and after contact with babies in isolation, during outbreaks of infection, preparing and administrating intravenous drugs, when hands are contaminated with blood or body fluids and surgical procedures.
- Surgical scrub (level 3) should be used before surgical/invasive procedures. **Hand hygiene procedures should be performed**

  - Before touching a baby;
  - Before clean/aseptic procedures;
  - After body fluid exposure risk;
  - After touching a baby; and
  - After touching a baby's immediate surroundings.

It is very important to continue good hand hygiene to prevent cross infection into the environment, such as patients' notes, monitors, computer key boards, phones etc. Alcohol hand rub may be used up to five times following hand washing as long as hands are visibly clean. It is quick and readily available at each cot side.

Cover all cuts or abrasions with a waterproof dressing.

Dress code

Clothes worn should be clean tidy and modest and adhere to the 'Bare below Elbow' policy of the Health Board. Doctors should avoid wearing Jeans at work. Ties and lanyards will not be allowed in the clinical areas. When a neonate is held outside a basinet by nursing or other personnel, a single use long sleeved gown should be worn over the clothing. Long

hair should be restrained so that it does not touch the neonate or equipment during patient examinations or treatments.

If staff wear personal scrubs/uniform to work, they should come to work in other clothes changing into uniform at the start of their shift and out of uniform at the end of the shift before leaving the hospital

Sterile procedures

Masks & eye protection, caps, sterile gowns and sterile gloves should be worn for procedures such as insertion of long-lines, umbilical vessel catheterisation and lumbar punctures. A wide sterile field should be employed i.e. the whole of the area of the incubator.

Handling of body fluids and sharps:

Gloves ad single use aprons should be worn during the handling of body fluids and during the taking of blood. Sharp instruments should be discarded directly into the yellow sharps containers at the point of use. Please see policy on how to take blood.

Personal Protective Equipment:

Gloves must be:

- worn when exposure to blood and/or other body fluids is anticipated or likely; and when examining babies
- changed immediately after each patient, and/or following completion of a clinical procedure or task;
- changed if a perforation or puncture is suspected; and
- appropriate for use, fit for purpose, and well fitting to avoid excessive sweating and interference with dexterity.

Aprons must be:

- worn to protect uniform or clothes when contamination is anticipated or likely, for example, when uniform/clothing is likely to come into direct (touching) contact with a patient, patient's bedding, etc., or contact with contaminated items, waste, etc; and
- changed between patients, and/or following completion of a procedure or task.

For specific advice regarding the current COVID 19 pandemic PPE requirements please see separate guidance. **Control of the Environment:**

It is the responsibility of the person in charge to ensure that the care area is safe for practice, and this includes environmental cleanliness/maintenance. The person in charge has the authority to act if this is deficient.

Stethoscopes

Each baby should have his or her individual stethoscope kept on the cot. Doctors are **not** to use their own stethoscopes to examine babies on NICU. Stethoscopes must be carefully cleaned following use on individual babies using an alcohol wipe. Tape measures should not be shared among babies

Visitors

Wherever possible, parents of babies in intensive care, high dependency care and special care should be allowed unrestricted visits.

Parents must be instructed to decontaminate their hands on entering and leaving the unit. Parents must to wash their hands before and after handling the baby and before and after different care activities such as changing nappy and feeding. Sibling visits are currently suspended and in particular this is due to the current COVID 19 pandemic. This will be revisited at a later date. All visitors and family who are experiencing any symptoms or have recently been exposed to a known communicable disease e.g. chicken pox should not be allowed to visit.

Neonatal considerations

Catheter related infection is recognised as a significant neonatal clinical problem with a reported incidence of 4 to 18 %.

The organisms most commonly responsible are coagulase negative staphylococci, staphylococcus aureus and coliforms. The majority of infections are caused by skin micro organisms which invade the wound either at the time of insertion of the catheter or in the days following insertion. Another possible source of infection is the catheter hub.

Insertion of central catheters e.g. UAC's, UVC's and long lines should be undertaken using a strict aseptic technique (see specific guidelines). Research shows that maximal sterile barrier precautions, which include sterile gowns and surgical mask and cap significantly

reduce the CVC related infections. Before inserting the catheter, the skin must be cleaned with an appropriate cleaning solution. Clean area with 0.5% Chlorhexidine in aqueous base for infants <28 week gestation AND less than a week old. For all other infants use Chloraprep lollipop (2%) (See Chloraprep guideline). The disinfectant must then be allowed to dry before starting the procedure. Following any unsuccessful insertion attempt the catheter should be disposed of and a new sterile catheter used.

UVC's and UAC's should be firmly anchored with a suture to prevent movement and the carriage of microorganisms from the skin. Long lines must be secured with steristrips and a sterile transparent dressing. Transparent dressings facilitate continuous inspection and greater protection against exogenous wetting and contamination

Intravenous giving sets should be changed at least every 72 –96 hours using a strict aseptic technique. Hand washing including the wearing of sterile gloves and strict asepsis must be maintained when disconnecting or manipulating any part of the system. Alcohol swabs should be used on the hub and connection ports when accessing the system.

Intravascular catheters should not be left in place unless they are clearly indicated for medical management. They should be removed as soon as possible. When removing a line full asepsis should be used. **We do not routinely send line tips for culture.** Line tips should only be sent for culture if a central line infection is strongly suspected and line removed for that reason. Cut off 5 cms of the distal catheter with a sterile scissors and place into a sterile container avoiding accidental contamination. Observe the site for blood loss and apply a dressing to the site.

Whenever a UVA, UAC or long-line is inserted, please complete the form in relation to this as we wish continually to audit our long-line infection rates. Please also complete the form when the catheter or intra- venous device is removed.

Whenever a neonate is investigated for serious infection with a blood culture or CSF examination, an entry must be made on the Badgernet system and again when the culture results are chased and available. This will simplify and standardise the method to monitor serious invasive infection in the neonate.

Transmission based precautions

In addition to the standard precautions, transmission based precautions should be used when caring for patients known to have or suspected highly transmissible or epidemiologically important pathogens, such as

a) Viruses e.g. viral respiratory infection, varicella zoster, gastroenteritis,
b) Skin infections or abscesses.
c) All multi-resistant organisms e.g. multi-resistant *E. coli*, glycopeptide resistant enterococci, extended spectrum β-lactamase producing organisms such as *Klebsiella sp*., *E. coli*, *Enterobacter sp*. and MRSA. Sometimes these organisms are acquired from the mother but they can also be spread within the nursery.

82They can also arise from plasmid transfer from another patient or by the development of resistance in the patient's previously sensitive strain

Wherever possible these infants should be nursed in a single cubicle and this should definitely be implemented when the baby is in a cot or basinet.

Staff should wear appropriate PPE when coming into contact with the baby. If the baby is nursed in an incubator and is not being removed from there, a plastic apron and gloves will suffice. If the baby is in a basinet or is being weighed or removed from the incubator for any other reason, an apron with sleeves and gloves are to be worn. These must be discarded into a orange bin-bag afterwards. Hands must be washed both before putting on the gloves and especially after de-gloving. An alcohol hand-rub should be used after handling the patient and there should be very careful decontamination of the patient area after use.

It is important to realise that the environment may be heavily contaminated with the microorganisms and these organisms are often transmitted on the hands of personnel to other neonates. If more than one neonate is infected, a cohort approach should be undertaken.

If possible, the patient should be nursed in a separate room away from patients who are not infected or colonised with the relevant organism.

Shared equipment use should be minimised and avoided if possible. Where this is impossible, such as ultrasound machine, X-rays or CFM monitor, stringent infection control measures must be undertaken before and after use to avoid cross contamination. Once the equipment is cleaned and disinfected, a green sticker 'I am clean' should be attached and a log completed (see operational guideline and manufacturer's recommendation for specific instructions) When the patient is discharged the room must be thoroughly decontaminated and disinfected.

Care must be taken not to move the infant within the nursery more than is absolutely necessary and to discharge the baby home as soon as the condition allows. Clean equipment should not be stored in the clinical area close to infected baby

Specific Organisms: The following are a general guide only. For detailed advice or complicated cases consult the infection manual or contact occupational health for further expert advice

Glycopeptide resistant enterococci (GRE)

- The mode of spread is commonly by contamination of equipment and the environment, especially if the patient has diarrhoea. Other modes of spread are via the hands of health care workers and on uniforms.
- Contact precautions must be observed. These are lifelong. They must never be stepped down as long as the patient remains in hospital and during any readmissions.
- The stools of the baby should be screened for GRE. The patient should be treated after consultation with the Microbiologist e.g. Amoxicillin plus Gentamicin. (The patient's notes should be labelled 'notify infection control'). The patient must be nursed in a single room and the gloves and apron sign clearly displayed. Staff should wear gloves and aprons with disposal into yellow bags. There should be very careful hand-washing before and after patient contact. An alcohol product should also be used before leaving the patient's bed area. Equipment must be decontaminated thoroughly after use by cleaning with detergent and water and then using a chlorine releasing solution at 1,000 parts/million (or appropriate combined detergent/disinfectant, e.g. Antichlor plus). Visitors should be kept to a minimum

Droplet Spread

Droplet spread is important for pertussis, rubella, mumps, parvovirus B19, varicella zoster, respiratory viruses and bacterial meningitis. Neonates are usually ineffective disseminators of infectious bacteria or viral aerosols. Neonates with confirmed or possible infection, which could be spread by the droplet route, should be separated from other neonates by transfer from the nursery area into a cubicle or rooming in with the mother. If this is not practical or possible, the neonate the situation should be managed if possible by enclosure of all affected neonates in the area in incubators. In Singleton we have a dedicated isolation room with negative pressure facility which should be used to isolate such cases. For details refer to isolation policy. **Health Standards for Personnel**

Staff providing care must ensure that they:

- Have up to date occupational immunisations/health checks/clearances requirements as appropriate;

- Do not provide direct care while at risk of potentially transmitting infectious agents to others. If in any doubt they must consult with their line manager, Occupational Health Department or Infection Prevention and Control Team (IPCT).

  Nursery personnel should be as free of transmissible infectious diseases as possible.

- Personnel with active TB should be restricted from patient contact until adequate treatment has occurred and non-infective status verified.
- All susceptible non-pregnant hospital personnel should be offered immunisation against rubella and hepatitis B virus. All staff who do not have a good history of previous chicken pox (VZV) infection should be tested for antibody. VZV vaccine should be considered for susceptible individuals. Annual influenza immunisation is strongly encouraged.
- Individuals with respiratory, cutaneous, mucocutaneous, or gastro-intestinal infection should not have direct contact with neonates. Personnel with exudative skin lesions or weeping dermatitis should refrain from all direct patient care and should not handle patient care equipment until the condition resolves. Personnel in contact with neonates should report personal infections, inability to wash hands e.g. because of plaster-casts and other conditions to their immediate supervisors and should be medically examined to determine suitability for patient contact. Decisions to exclude the staff members from the nursery areas should be made on an individual basis.
- Transmission of herpes simplex virus from infected personnel to neonates in newborn nurseries is rare. Personnel with cold sores who have direct contact with newborns should cover their lesions and carefully observe hand-washing policies. Transmission of herpes simplex virus infection from personnel with genital lesions is not likely. Personnel with herpetic hand lesions (herpetic whitlow) should not participate in patient care until the lesions have healed.
- Personnel in Neonatal Units are likely to be exposed to infants excreting cytomegalovirus. Acquisition of cytomegalovirus infection from infants is prevented by compliance with standard precautions. Women of child-bearing age who work in the Neonatal Unit should be counselled about the relatively low risk of exposure

should they become pregnant. A routine programme of serological testing of obstetric and nursery hospital employees for immunity to cytomegalovirus is not recommended.

HeRO monitoring – A guide for the clinicians

Introduction:

HeRO is a predictive monitoring system that analyses (using a computerised analytical software) routinely acquired continuous ECG monitoring data to detect abnormal Heart Rate Characteristics (HRC) of the newborn. Using sophisticated analysis of the abnormal HRCs, it then displays to the clinicians a score every hour (The HeRO score), which indicates the risk of an infant deteriorating from late onset sepsis or other conditions such as NEC in the next 24 hours. Like most clinical tools, the HeRO score must be used within the broader context and bearing its limitations in mind. Used in this way, it helps the clinicians to make a better informed judgement for early detection and management of serious neonatal illnesses.

Pathophysiology:

In the healthy state, there are frequent physiologic small accelerations and decelerations in the heart rate called Heart Rate Variability (HRV) in response to sympathetic and parasympathetic signals to cardiac pacemaker cells. Pathological conditions such as sepsis may cause disturbances of autonomic nervous system resulting in loss or suppression of HRV at an early stage. In some cases the decreased Heart rate variability (HRV) may be accompanied by transient heart rate decelerations. This is very similar to what is seen during fetal distress on CTG.

The HeRO analyses the following parameters from an ECG trace to compute the HeRO score.

1. The standard deviation of the RR intervals on ECG as measure of HRV
2. Sample asymmetry i.e. tendency to skew towards Heart Rate decelerations
3. Sample entropy i.e. normal irregularity of Heart Rate

Low HRV, high sample asymmetry and low sample entropy raise the HeRO score. A numerical HeRO score represents the fold increase in risk that an infant will have a clinical deterioration within 24 hours. For e.g. a HeRO score of 3 represents a 3-fold increased risk of the infant manifesting a clinical deterioration from sepsis or other associated condition within 24 hours.

It is postulated that increased physician awareness, early evaluation and treatment in infants displaying the HeRO score reduced mortality.

The evidence:

The HeRO trial, sponsored by National Institutes of Health (NIH) was undertaken in 9 centres in US and recruited 3000 VLBW infants between 2004 and 2010. All infants underwent continuous HeRO monitoring but were randomised to having their HeRO scores displayed or not displayed to the clinicians. Clinicians were educated on how the HeRO scores were developed and encouraged to evaluate infants whose scores were rising in contrast to standard care where the score was not displayed. There was a 22% relative reduction in mortality (10.4% to 8.1%, P<0.04) for infants whose HeRO scores were displayed, which translated to one extra survivor for every 48 VLBW or 23 ELBW infants monitored.

A subsequent analysis focussing on 974 episodes of late onset sepsis in 700 infants who developed the condition showed that mortality within 30 days of septicaemia was reduced by 40% in those infants whose HeRO scores were displayed (P<0.01)

Administrative guide for clinicians to manage the HeRO monitoring system:

(For more details see 'HeRO Quick Guide for Singleton Hospital' or the full manual on SharePoint under operations manual tab and within 'HeRO training' folder)

Step 1: Preparation to capture relevant data

For a HeRO score to be computed and displayed there must be a good quality ECG trace obtained continuously. The data is automatically collected in bed spaces where there is a permanent monitor. In SHIPS where a temporary M3 monitor is used in some spaces, it will be necessary to plug in the free end of the HeRO cable (Green cable) to the ECG output of the M3 monitor. The number of the bed space that is being monitored is clearly labelled on the cable.

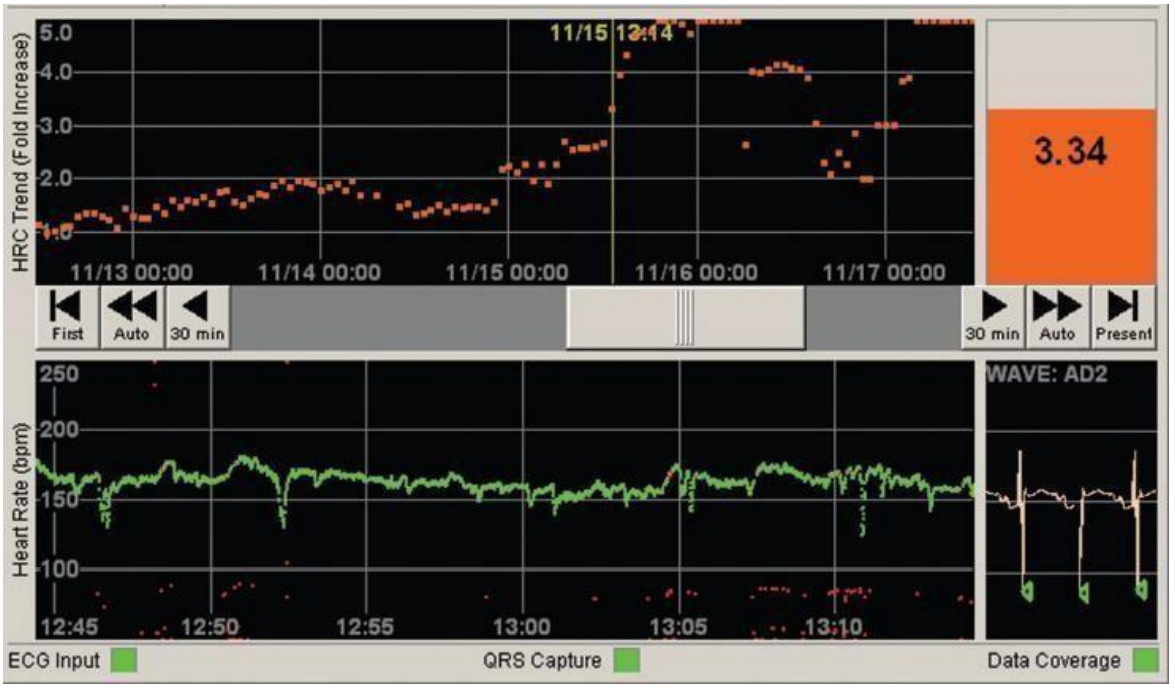
Step 2: Admit the Patient

- Open HeRO Monitor on the any PC or use the central monitoring station (touch screen)
- Click on 'Log in' at the bottom of the display window
- The User ID and password for our unit is both 'hero' (not case sensitive)
- Once you log in, go to 'patient information' tab and the 'New Patient' tab will be active. Click on this tab to admit a patient.

- Enter hospital number, last and first name and click ‘ok’. The patient is now admitted into the HeRO system in the ‘holding area’ but not yet allocated a bed space. Until this is done correctly, the HeRO score will not be displayed.

Step 3: Allocating a bed to the patient:

- Select the appropriate clinical area from the tabs i.e. ITU/HDU/SHIPS, right click on the cot space where the patient is admitted. Select ‘transfer patient’.
- In the pop up window, select the patient’s hospital no. from the drop down list and select the date and time from when monitoring was commenced. Select ‘ok’ and confirm again by selecting ‘Yes’. The patient will now be allocated this space and any ECG recording from this point of time will be used for HeRO score computing.
- To allocate a cot space to an admitted patient retrospectively, select the ‘Bed Assignment’ Tab. All the bed space will be displayed. The vertical red bar in each space indicates the duration of the ECG data available to compute the HeRO score.
- Tick the box ‘Edit Bed Assignment’. The bed space window turns blue. Right click on the red bar in the bed space you want to allocate this patient and select ‘Edit Event’.
- The ‘Bed History’ pops up. Select the date and time from which this new patient had ECG monitoring and click ok
- Go back to the display for each cot side. The current HeRO score should be displayed numerically on the right side of the window with a corresponding orange scale.



The quality of the data is satisfactory when the 'ECG input' box and the 'QRS capture' box are both green in the patient view screen for the cot. The top window displays the HeRO score trends over the last 5 days as red dots. Missing dots indicate poor or missing data. The bottom window on the left displays the HR trends over the last 30 minutes and the small window on the right shows live ECG capture.

Once sufficient data is available to compute a HeRO score (usually 4 hours), the 'Data Coverage' box turns green. The Numerical HeRO score is displayed on top right window and visually indicated by an orange column. If the score is greater than 2, a visual alarm (a yellow triangle with double exclamation) appears.

N.B. There are no audible alarms on the HeRO system.

Step 4: How to reallocate a patient following a change of cot space

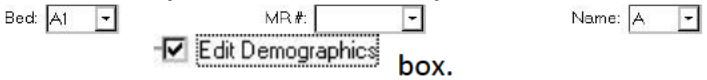
Movement of patients within the NNU is common

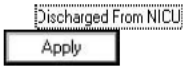
- It will be important to note the time of transfer and the time when monitoring in the new cot space was commenced.
- Ensure the previous patient in this cot has been discharged or transferred to another cot (see step 3or 5)

- Click on the area tab i.e. ITU/HDU, right click on bed space, select transfer patient and then select the new cot space by selecting a drop down list from the tab 'To'. Select the date and time when monitoring started in the new cot space following transfer. This is an important step to ensure continuity. All data of this patient will now be transferred to this cot. Please do not readmit the patient

Step 5: How to discharge a patient

- Once a patient has been discharged, click on the area tab, right click on bed space and select 'transfer patient'.
- In the new window select 'holding area' in the tab 'To'.
- The patient data will be available to view or readmit this patient for the next 14 days after which this data will be transferred to the secure server for storage up to 1 year.
- To permanently discharge patient from NICU, Go to the 

tab.
- Choose the patient from the drop-down lists: either by Bed, by Medical Record, or by Name.


- Check the box.
- Check the box, and enter the appropriate date, if necessary.
- Press the 

button.
- Ensure this process is followed to prevent misallocation of scores to another patient.
- To readmit a patient, select the new cot space and use 'transfer patient' to move from holding area to the new cot space. Do not readmit by entering the hospital number again

Guidance for clinicians:

Nurses must record the HeRO scores on observation charts hourly or as frequently as routine care dictates. The HeRO score is refreshed hourly and usually changes slowly over a few hours. If the HeRO score has changed by more than one point of the baseline or is greater than 2, reevaluate patient, review observation and trends and request a medical review.

The doctor or ANNP reviewing the patient should use the following as a guide only. The clinical context, risk factors physical examination and other laboratory and radiological parameters must be used in conjunction with the HeRO score to arrive at a decision on further management.

1) If a patient is acting sick, regardless of the HeRO score, do what is clinically indicated.
2) When a patient has an *increase* of *one point over* his/her prior baseline, or the *first time the*

HeRO score rises *above* 2, evaluate the patient. This may include -

a) physical examination, review of vital signs and review of recent test results

b) discussion with the nurse about how the patient is acting

c) consider if an event or pre-existing condition could explain the rise in HeRO score – see next section on limitations and pitfalls.

d) consideration of blood tests or studies to evaluate for infection, if appropriate

e) consideration of antibiotics if clinical and/or HeRO abnormalities support this*

f) Continue close observation: a continued rise in HeRO score after antibiotic treatment may indicate ongoing illness or inadequately treated infection

*Many patients (based on low clinical suspicion of sepsis from a and b above) may only require close observation. However if there is clinical suspicion of sepsis or a very large increase in HeRO score, testing and treatment should be considered. If in doubt, discuss with a senior colleague.

Pitfalls and limitations:

Unfortunately, the elevation in HeRO score is not specific to infection and other conditions may also affect this. There are many areas that are yet to be studied

Expected 'benign' causes of increased HeRO score

- Paralytic drugs, atropine
- ROP examination or intervention (anticholinergic medications, laser or Avastin therapy)
- Surgery(anaesthesia)
- Tachyarrhythmias

Pathological conditions associated with increased HeRO scores

- Sepsis
- NEC
- Focal infection (UTI, Pneumonia, meningitis, cellulitis, abscess)
- Acute Respiratory Decompensation (some patients with severe chronic lung disease have recurrent, self -resolved elevations in HeRO scores or so called 'spikes')
- Significant brain pathology (some patients with Grade 3-4 IVH have HeRO spikes several weeks after birth)

- Idiopathic (will probably become less as more conditions are studied)

NB: please note that HeRO scores are not generated or valid if HR is less than 80, as often seen in patients undergoing therapeutic hypothermia. It is also not validated for use in early onset sepsis as there are frequent overlaps with other conditions that disturb the autonomic control during early postnatal adaptation.

Troubleshooting:

Issue 1: Unable to obtain a HeRO score

- Ensure patient admitted to the cot space as above and has had at least 4 hours of ECG recording
- For SHIPS patients on M3 monitors, please ensure cable allocated to the bed space is connected
- Ensure that the cable is firmly connected to the network point. You should hear a 'click' when plugging
- Ensure that the ECG leads have good contact and the ECG input and QRS capture box are green
- The patient does not have a HR <80 persistently (cooled infants)
- The hospital network is active and functional **Issue 2: I am unable to log in to HeRO.**

Resolution: When the application is opened on a PC, the user must log in to HeRO to make changes. If the application is left open and minimized, the user will not have to log in again until the application is closed and re-opened.

Username: hero, Password: hero.

Further reading:

1. Hicks JF, Fairchild K. HeRO monitoring in the NICU: sepsis detection and beyond. Infant 2013;9(6):187-91
2. Hicks JF, Fairchild K. Heart rate characteristics in NICU: What nurses need to know? Advances in Neonatal Care;13(6): 396-401
3. Moorman JR, Carlo WA, Kattwinkel J, et al. Mortality reduction by heart rate characteristic monitoring in very low birth weight neonates: a randomized trial. *J Pediatr*. 2011;159(6):900.e1-906.e1.
4. Fairchild KD, Schelonka RL, Kaufman DA et al. Septicaemia mortality reduction in neonates in a heart rate characteristics monitoring trial. Pediatr Res 2013; doi:10.1038/pr.2013.136