

# Clinical Guidance

## ***Neonatal Manual Chapter 6: Infection***

### **Summary**

*This manual contains clinical guidelines developed by the Neonatal Unit multidisciplinary team over recent years. This chapter contains guidelines on infection. It is linked to and should be used in conjunction with the completed neonatal manual details of which are contained in the introductory chapters.*

Document Detail	
Document Type	Clinical Guideline
Document name	Neonatal Manual Chapter 6: Infection
Document location	GTi Clinical Guidance Database
Version	4.0
Effective from	January 2019
Review date	July 2019
Owner	Clinical Lead, Neonatal Unit
Author	Timothy Watts, Consultant Neonatologist
Approved by, date	Neonatal Patient Safety and Quality Group, December 2018 Evelina Clinical Guidelines Group, January 2019
Superseded documents	Neonatal Manual Chapter 6: Infection 3.0
Related documents	Neonatal Manual Chapters 1-15
Keywords	Neonatal, Neonatology, Neonatal Unit, Newborn, NNU, NICU, SCBU, group B strep, sepsis, antibiotic, meningitis, conjunctivitis, MRSA, hygiene, fungal, candida, toxoplasma, rubella, hepatitis B, hepatitis C, HIV, CMV, rubella, perinatal, congenital infection, chickenpox, VZIG, TB, BCG, immunisation, vaccination, rotavirus
Relevant external law, regulation, standards	NICE guideline CG149: Antibiotics for the prevention and treatment of early-onset neonatal infection

Change History		
Date	Change details, since approval	Approved by
	Section 6.14 Updated	Evelina Clinical Guidelines Group, Jan 2019

	Page
6 <u>Infection</u>	
6.1 Investigation of suspected sepsis	3
6.2 General antibiotic policy	4
6.3 Early onset bacterial infection	6
6.4 Prevention and treatment of Group B Streptococcal (Streptococcus agalactiae, GBS) infection	8
6.5 Prolonged rupture of membranes	10
6.6 Meningitis	11
6.7 Urinary tract infection	13
6.8 Sticky eyes and conjunctivitis	14
6.9 Umbilical sepsis	15
6.10 Osteomyelitis and septic arthritis	16
6.11 MRSA and other resistant organisms / hand hygiene	17
6.12 Fungal sepsis	20
6.13 Congenital infection – general protocol	23
6.14 Babies at risk of hepatitis B	25
6.15 Babies born to HIV positive mothers	28
6.16 Babies born to hepatitis C positive mothers	31
6.17 Babies born to mothers with positive tests for syphilis	32
6.18 Cytomegalovirus (CMV)	35
6.19 Congenital Rubella	36
6.20 Congenital Toxoplasmosis	37
6.21 Herpes simplex virus infection	39
6.22 Perinatal chickenpox	41
6.23 Tuberculosis and BCG	44
6.24 Immunisations relevant to the Neonatal Unit	48

## 6.1 INVESTIGATION OF SUSPECTED SEPSIS

Basic screen:

- FBC, Blood film
- CRP
- Blood culture (peripheral and from indwelling lines): should be taken by trained staff only
- Triglyceride level (if on TPN)

+ when clinically indicated:

- CXR (if respiratory signs)
- Request placental swab +/- placental pathology in setting of congenital sepsis
- Skin swabs if skin breakdown, rash, pustules or purulent discharge/exudates (consider viral swabs if vesicular or pustular rash)
- LP – If neurological signs / symptoms or proven sepsis (raised septic markers or blood cultures positive for organisms other than coagulase negative staphylococci). Ensure adequate sample size for viral studies if viral aetiology suspected. Separate samples are required for microbiological and virological investigations.
- Generalised sepsis – individual orifice swabs in virus transport medium for herpes simplex detection (mouth, throat, ears, eyes, anal, vulval)
- Urine - Preferably SPA, & request microscopic exam for yeasts if fungal sepsis is suspected
- AXR – if abdomen distension
- ETT secretions – may need BAL if chest infection with collapse/consolidation
- Throat and rectal swab for viral infections
- Tip of umbilical / central lines and ETT when removed

## 6.2 GENERAL ANTIBIOTIC POLICY

- When prescribing antibiotics, ensure guidelines for antibiotic stewardship are followed
  - Document the indication for starting antibiotics on the drug chart
  - Document the 'valid period' of antibiotic until time of next review: this will usually be 36-48 hours from when antibiotics are first prescribed
- At 36 hour review, stop antibiotics if cultures and septic markers negative
- If a decision is made to continue antibiotics for >36 hours, always document indication for doing so and length of antibiotic course on the drug chart

### For empiric treatment of suspected sepsis:

Early-onset sepsis (onset within 72 hours of birth): i.e. perinatally-acquired sepsis

- Benzylpenicillin and gentamicin
- Gentamicin must be prescribed with utmost care. Refer to Paediatric Formulary for advice on dosing and monitoring of blood levels
- Consider amoxicillin instead of benzylpenicillin if there is thought to be a significant risk of Listeriosis e.g. meconium-stained or discoloured amniotic fluid in < 32 weeks gestation baby
- Aciclovir if herpes simplex suspected eg hepatitis or specific perinatal risk factors. Discontinue only on advice of Virology, which will depend on results of sepsis investigations.
- Cefotaxime for babies on Postnatal Ward. (Babies should always be changed to cefotaxime when being transferred from NNU to PNW.)

Late-onset sepsis (onset > 48 hours after birth): i.e. nosocomial sepsis

- Usual first line is flucloxacillin and gentamicin. However, this does not cover enterococcus, so amoxicillin may be considered for presumed abdominal sepsis, or for marked clinical deterioration.
- Gentamicin must be prescribed with utmost care. Refer to Paediatric Formulary for advice on dosing and monitoring of blood levels
- Consider changing flucloxacillin to vancomycin if (i) blood culture grows Coagulase Negative Staph. (CONS), or (ii) failure to respond clinically to flucloxacillin and gentamicin, especially if central lines are in place.
  - If blood cultures grow CONS, take further central and peripheral blood cultures, as isolates may be skin contaminants. This is particularly true if there is no central line.
  - True CONS bacteraemia is unlikely unless there is > 1 positive blood culture with a microbiologically indistinguishable CONS isolate.
  - Vancomycin may be prescribed as intermittent bolus doses or as continuous infusion down the central line: the latter method is preferred when treating a CoNS bacteraemia as the line is the usual source. Refer to Paediatric Formulary for advice on dosing and monitoring of blood levels.
- Lines should be removed if there is no or slow clinical improvement or blood cultures are persistently positive despite adequate antibiotic treatment.
- Change antibiotics according to sensitivities after a positive culture, especially in presence of positive inflammatory markers.

- The antibiotic of choice for gram negative infections is gentamicin. However, consideration should be given to escalating therapy to include drugs with better tissue penetration eg ceftazidime (with or without gentamicin) or meropenem in very sick or poorly responding babies.
- Discuss with the attending consultant and with the microbiology department where there is failure of clinical response after 48 hours and/or good evidence of invasive disease, such as:
  - definite pneumonic changes
  - central nervous system disease (or we haven't been able to exclude this by adequate CSF examination)
  - persistent positive blood cultures
- Consider fungal sepsis in culture negative sepsis.
- Stop all antibiotics after 36 hours if cultures and septic markers negative
- Suspected NEC: add metronidazole. If baby is on flucloxacillin, also consider changing to amoxicillin.
- Umbilical flare: see 'Umbilical sepsis' guideline
- Duration of antibiotic course in proven infection depends on many factors e.g. type of infection, condition of the baby, change in inflammatory markers, but usually it ranges from 5-10 days. Meningitis should be 14-21 days depending on the organism.
- Microbiology advice can be obtained from:
  - John Klein, Consultant Microbiologist on extension 83109
  - Infection SpR on bleep 0132
- In severe sepsis other agents may reduce mortality when given with antibiotics. There is some evidence that G-CSF may reduce mortality when given to babies with acute sepsis and severe neutropenia ( $< 1.0 \times 10^9/L$ ). Dose for G-CSF is 10 micrograms/kg/day by SC injection, given for 3 days or until the neutrophil count is  $> 5.0 \times 10^9/L$ . Use of these agents should be discussed with Consultant +/- Dr Jay Alamelu in Haematology.

### 6.3 EARLY ONSET BACTERIAL INFECTION

Defined as infection presenting in the first 72 hours of life.

These guidelines are based on a combination of local practice and NICE guidance. Further information on NICE guideline, 'Antibiotics for the prevention and treatment of early-onset neonatal infection', is at <http://guidance.nice.org.uk/CG149>.

#### Aetiology

- Vertical acquisition from mother
- Organisms can invade baby via placenta & membranes or by aspiration of infected liquor
- Important organisms include GBS (*Strep agalactiae*), *E coli* and *Listeria*

#### Risk factors

Risk factors to consider when deciding whether to investigate/treat for early onset sepsis:

- Maternal GBS colonization or on MSU in this pregnancy
- Previous baby with GBS disease
- Premature delivery (<37 weeks) following spontaneous labour
- Prolonged (PROM) or pre-labour rupture of membranes. PROM is considered >18 hours
- Maternal pyrexia (e.g. >38°C for >1 h) or other evidence of maternal sepsis (positive blood culture, raised WBC or CRP)
- Co-twin with proven infection

#### Symptoms & Signs

- Respiratory distress (congenital pneumonia), apnoea
- Tachycardia, bradycardia, hypotension
- Temperature instability, pyrexia, hypothermia
- Lethargy, poor feeding, hypotonia
- Irritability, seizures (meningitis)
- Hypoglycaemia, jaundice (particularly <24 hours), metabolic acidosis
- Septic shock, with rapid deterioration and death.

#### Management

Decision to investigate/treat is based on risk factors and clinical symptoms/signs.

NICE guidance describes 'red flags', which are risk factors or 'clinical indicators of possible infection' that in isolation necessitate immediate investigation and treatment:

- Maternal IV antibiotics in labour for suspected chorioamnionitis (does not include GBS prophylaxis)
- Co-twin with proven or suspected sepsis
- Respiratory distress >4 hours after birth

- Seizures
- Need for respiratory support in term baby
- Signs of shock

In the absence of red flags, manage as follows:

- 1 risk factor as above without clinical symptoms / signs → observe hourly for 2 hours, 2 hourly until 12 hours of age
- 2 risk factors as above without clinical symptoms/ signs → investigate & treat, with ongoing observations as above
- Symptoms / signs → review history for risk factors & clinical assessment, with low threshold for investigation & treatment, continue observations as above

### Investigations

- Blood cultures, FBC and CRP
- CRP may be low at initial septic screen – consider repeating at 18-24 hours
- LP: ask senior for advice if unsure whether LP is indicated; the following indications pertain
  - Culture-proven sepsis
  - Symptoms/signs highly suspicious of sepsis or meningitis
  - Well, but previously symptomatic, babies with elevated CRP >20 mg/L

### Antibiotics

Antibiotics should be given as soon as possible after decision to treat & always within 1 hour.

- Benzylpenicillin and gentamicin in NNU
- Cefotaxime on PNW: 100mg BD for birth weight 2.3-4.5kg; otherwise 50mg/kg 12 hourly
- Antibiotics should be stopped at 36 hours if low clinical suspicion of infection, cultures negative and CRP <20mg/L
- Duration of course in suspected/proven sepsis should be discussed with senior
  - With proven or high clinical suspicion of sepsis, treat for 7 days
  - If baby is well, particularly if treating for isolated raised CRP, 5 days is adequate
  - Longer courses may be indicated with certain organisms, or with slow clinical response – discuss with Microbiology.

### Parent advice

- If there are concerns about early-onset infection prior to discharge from postnatal ward, advise parents to watch for signs / symptoms:
  - Abnormal behaviour eg abnormal cry, reduced activity
  - Hypotonia
  - Poor feeding
  - Abnormal temperature
  - Rapid breathing colour change

## 6.4 PREVENTION AND TREATMENT OF GROUP B STREPTOCOCCAL (GBS) INFECTION

- Maternal carriage in UK ~25%
- Early onset neonatal GBS disease diagnosed in ~0.05% of newborns
- Mortality of identified invasive GBS disease ~10%
- Intrapartum antibiotics reduce incidence of invasive GBS disease by up to 70% with risk factor strategy
- If baby is well at 12 hours despite having no intra-partum or neonatal antibiotics, there is a very low chance of developing GBS disease

### Risk factor strategy for mother

At GSTT, intrapartum antibiotic prophylaxis (IAP) is with IV benzylpenicillin 4hrly and is given for:

- Previous baby with GBS disease
- Urine or vaginal swab positive for GBS this pregnancy
- Maternal pyrexia  $>38^{\circ}$  for more than 1 hour (mother will get co-amoxiclav plus amoxycillin for this as treatment for chorioamnionitis)
- Preterm labour
- Prolonged rupture of membranes  $> 24$  hours

Not indicated if elective Caesarian Section with no labour and intact membranes.

### Management of babies in whom intrapartum treatment was indicated

(Also refer to guideline 6.3 Early onset bacterial infection.)

Risk factors to consider when deciding whether to investigate / treat for sepsis:

- GBS in this pregnancy
- Previous baby with GBS disease
- Prematurity ( $<37$  weeks)
- PROM  $>24$  hours
- Maternal pyrexia  $>38^{\circ}\text{C}$  for  $>1$  hour
- Evidence of maternal sepsis (positive blood culture, raised WBC or CRP)

#### 1. Term

- If mother has a single risk factor (above)
  - 2 hourly TPR for 12 hrs
  - If symptomatic, screen (blood culture, FBC and CRP) and treat
- If mother has at least 2 risk factors (above) and has had no treatment or antibiotics  $<4$  hours before delivery:
  - Screen and treat
- If mother has had at least 1 dose IV benzylpenicillin or amoxicillin/co-amoxyclov  $>4$  hours before delivery, GBS has been adequately treated and GBS is removed as a risk factor. Therefore treat as in 1. and 2. above, taking the GBS treatment into account. This does not pertain to maternal IV antibiotics for suspected chorioamnionitis.
- If twin has GBS disease, screen and treat.

## 2. Preterm

- Follow protocol for term babies taking prematurity as a risk factor e.g. baby needs only 1 further risk factor to be screened and treated if intra-partum treatment was inadequate

Treatment

- Broad spectrum cover: NICU/SCBU – IV benzylpenicillin and gentamicin  
Postnatal wards – IV cefotaxime
- If culture positive for GBS continue with penicillin alone
- If CSF culture positive for GBS and no improvement in clinical condition and/or markers of sepsis within 48 hours, consider repeating LP (see meningitis protocol)
- Stop treatment after 36 hours if blood culture and septic markers negative

### Duration of treatment

## 6.5 PROLONGED RUPTURE OF MEMBRANES (>24 hours)

(Also refer to guideline 6.3. Early onset bacterial infection.)

### Risk factors to consider when deciding whether to investigate for sepsis in PROM

- GBS in this pregnancy
- Previous baby with GBS disease
- Prematurity (<37 weeks)
- Maternal pyrexia >38°C for >1 hour
- Evidence of maternal sepsis or clinical chorioamnionitis (positive blood culture, raised WBC or CRP, fetal tachycardia)

### Term

- If well and **NO** risk factors
  - 2 hourly TPR for a complete 12 hours
  - After discharge, advise parents and GP to contact unit if worried.
- If symptomatic or if 2 or more risk factors
  - Screen (blood culture, FBC, CRP) and treat
  - Symptomatic babies should also have LP if no contra-indications
  - Consider admission to NNU
- If NICE red flags present (see guideline 6.3), screen & treat

### Preterm (<37 weeks)

- If well
  - Screen and treat
- If symptomatic
  - Screen and treat
  - LP if no contra-indications
  - Consider admission to NNU

### Treatment

- NICU/SCBU – IV benzylpenicillin and gentamicin
- Postnatal wards – IV cefotaxime
- Stop treatment after 36 hours if blood culture and septic markers negative
- Duration of antibiotic course in proven infection depends on many factors e.g. type of infection, condition of the baby, change in inflammatory markers. Usually it ranges from 5-10 days but in meningitis it can be up to 14-21 days.

## 6.6 MENINGITIS

### Organisms

- Group B Streptococcus and E coli are responsible for over 60% of cases.
- Other causes: Listeria, other Gram negative organisms, Coagulase Negative Staphylococcus (especially if a V-P shunt is in situ), Candida
- Enterovirus, parechovirus, herpes simplex virus

### Clinical features

- Non-specific signs of sepsis eg temperature instability, apnoea, hyperglycaemia etc.
- Bulging fontanelle, seizures, altered level of consciousness etc are late signs and associated with long term neurological sequelae.

### Investigations

#### 1. CSF analysis

In general, there should be a low threshold for performing lumbar punctures.

If the CSF is mild-moderately blood-stained, discuss with laboratory staff regarding obtaining a cell count, as this can be very important if the baby has already been started on antibiotics.

Contraindications to performing LP:

- baby too sick – treat with appropriate antibiotics anyway and defer LP until condition improved
- severe coagulopathy or thrombocytopenia – consider platelet transfusion prior to LP
- local sepsis over LP site
- known non-communicating hydrocephalus – ventricular tap is then necessary

Interpretation of CSF results (refer to Defining Cerebrospinal Fluid White Blood Cell Count Reference Values in Neonates and Young Infants, Kestenbaum LA et al, *Pediatrics* 2010;125;257)

Normal values:

CSF WCC in term babies aged  $\leq 28$  days  $\leq 20 \times 10^6/L$

CSF WCC in term babies aged  $> 28$  days  $\leq 9 \times 10^6/L$

CSF WCC in preterm babies  $\leq 27 \times 10^6/L$

CSF protein in term babies  $\leq 0.6$  g/L

CSF protein in preterm babies  $\leq 1.0$  g/l

Viral PCR: detection of virus in CSF is diagnostic. A negative result does not necessarily exclude these viruses. Discuss with Virology.

#### 2. Blood culture

Neonatal meningitis is usually secondary to bacteraemia

### Treatment

- Choice of antibiotics: Empirical therapy (organism unknown) – amoxicillin AND cefotaxime → once the organism is known, treatment can be changed as necessary

- Consider acyclovir (20mg/kg tds) if viral, particularly herpes simplex, aetiology suspected
- For bacterial pathogens, consider repeating LP after 48 hours of treatment to document adequacy of treatment, particularly if clinical signs and / or markers of infection have not improved. Also consider repeating LP and neuroimaging if deterioration occurs during antibiotic course. This is recommended because persistent infection may indicate a focus, such as obstructive ventriculitis, subdural empyema or multiple small vessel thrombi. This may indicate a poorer prognosis.
- Consider cranial CT / MRI scan to exclude abscesses or subdural collections if there is a delay in treatment response (e.g. failure to sterilise the CSF within 48 hours as above).
- Cranial ultrasound 1-5 days into treatment and prior to discharge. Consider MRI scan if concerns re. neurological status or cranial ultrasound scan. Timing of the MRI scan should be discussed with a Consultant Neuroradiologist
- Length of treatment
  - GBS – usually 2 weeks (may need more if delayed response)
  - Gram negative organisms – 3 weeks
  - More prolonged treatment may be indicated if there has been delayed sterilisation of CSF (i.e. > 48 hours)
  - Viral aetiology – discuss with Virology
- Adjunctive treatment: anticonvulsant treatment, ventilation and inotropic support may be needed. Electrolytes need to be monitored to assess for SIADH
- Baby will require long term monitoring for hydrocephalus and hearing screen. This will need to be a repeat screen if the baby has had routine hearing screen prior to meningitis presentation.

## 6.7 URINARY TRACT INFECTION

### Suspected UTI

- A diagnosis of UTI can only be confidently made from a supra-pubic aspiration, clean catch or catheter specimen of urine from a newly inserted catheter. M, C & S result from a bag specimen of urine is only of use if the result is negative
- Check urinalysis using Multistix and send specimen to microbiology for urgent M, C & S. The sample should be sent to the lab urgently.
- Start IV antibiotics: amoxicillin and gentamicin while awaiting sensitivities
- Check basic neonatal profile, FBC and CRP repeating daily if any concerns

### Confirmed UTI

As above, +

- Arrange renal tract u/s scan
- Change the antibiotics according to sensitivities from M,C & S
- Continue antibiotics for 7 days
- Once treatment antibiotics discontinued, start prophylactic antibiotics: If baby on feeds, start oral trimethoprim 2mg/kg once at night; if baby not on feeds, start cefotaxime 50mg/kg once at night.
- Consider MCUG at 4-6 weeks post completion of treatment +/- DMSA subsequently. Guidance for further imaging can be found in the NICE guideline CG54 'Urinary tract infection in children' at <http://www.nice.org.uk/guidance/cg054/chapter/1-guidance#/imaging-tests>.
- Arrange Neonatology follow-up appointment 2 weeks after MCUG
- Referral to Paediatric Nephrology team will be made following Neonatal appointment

## 6.8 STICKY EYES AND CONJUNCTIVITIS

Mucoid discharge or "sticky eye" in the 1st week of life is common and is not usually infection.

- If mild discharge persists it is likely to be due to a non-canalised lacrimal duct, 96% of which spontaneously resolve by 1 year of age.
- If the discharge is heavy, purulent, needs cleaning more than 4 hrly, obviously involves the conjunctiva or if the eye is red or swollen then send a swab for M,C&S and prescribe topical chloramphenicol or Fucidin drops or ointment every 4 hrs for 5 days. Check result of swab after 24-48 hrs and change antibiotics according to sensitivities if necessary.

### Gonococcal ophthalmitis (Ophthalmia neonatorum)

This presents with early and profuse discharge usually within 1st week of life.

- Send urgent swab and gram stain (Gram –ve diplococci); also send chlamydial swabs in all cases of suspected/confirmed gonococcal infection (as co-infection common)
- 1 hrly eye irrigation with sterile normal saline.
- Give ceftriaxone 20-50mg/kg IV stat (single dose)
- Check sensitivities and discuss antibiotic regimen with Infection registrar (bleep 0132) if necessary
- Ask for ophthalmology opinion and consider empirical treatment for Chlamydia (see below)
- Refer mother and partner for treatment to the GU clinic.

### Chlamydial conjunctivitis

This tends to occur towards the end of the 1st week of life. Suspect if not improving on chloramphenicol or if concomitant respiratory symptoms.

- Swab each eye with chlamydial swabs. During office hours contact the Virology Chief BMS (ext 83129) and/or the Virology registrar (ext 83140) to arrange collection of swabs from Virology. Out of hours, contact the on-call Microbiology BMS - bleep 1802).
- Treat with oral azithromycin for 3 days
- Ensure mother and partner are referred to Genito-urinary Medicine clinic

## 6.9 UMBILICAL SEPSIS

- Umbilical cord care is important to prevent infection, particularly with *Staphylococcus aureus*. The cord should be kept clean and dry.
- If the umbilicus is unduly “sticky” the area cleaned with an alcohol swab or other antiseptic solution – further treatment is unnecessary. Swabs for MC&S are not useful.
- If there is a purulent discharge or the surrounding skin is erythematous, arrange the following:
  1. Bacterial swab
  2. Blood culture
  3. Start IV flucloxacillin and gentamicin (if baby is on NNU) or cefotaxime alone (if baby on Posnatal Ward) until culture results are known and review antibiotic combination according to culture and sensitivity results. Continue antibiotics for 5-7 days. If good response to IV and swab grows *Staph aureus*, consider changing to oral flucloxacillin, particularly in babies on PNW.

## 6.10 OSTEOMYELITIS AND SEPTIC ARTHRITIS

### Aetiology

- Most commonly *Staphylococcus aureus* or Group B Strep
- May also be due to Gram negative bacilli or *Candida*
- May coexist with a septic arthritis
- Commonest mechanism of infection is the haematogenous route
- It is important to consider septic arthritis in a baby with sepsis, particularly in *Staphylococcus aureus* sepsis and/or when osteomyelitis is suspected

### Clinical Features

- Non-specific signs of sepsis
- Pseudoparalysis of the affected limb
- Incidental finding on Xray of a baby with multisystem disease. Multiple sites may be affected
- Consider if a baby has persistently positive blood cultures despite adequate antibiotic treatment

### Investigations

- Blood culture and inflammatory markers (although CRP is normal in about 50% of cases)
- Bone biopsy or joint aspiration
- Xray – abnormalities often appear within 7 days (earlier than in older children)
- Ultrasound should be used to look for subperiosteal abscesses and to assess adjacent joints for septic arthritis. MRI scan may also be useful.
- Bone scan – is often not helpful in neonates
- Consider skeletal survey, as neonatal osteomyelitis may be multifocal
- Urine and CSF culture – likelihood of metastatic spread is high

### Management

- An orthopaedic opinion should be sought as soon as possible. Septic arthritis is an orthopaedic emergency
- Antibiotics – be guided by gram stain of pus etc – if there is no organism found, then start IV flucloxacillin and gentamicin empirically
- Treatment should last for 4-6 weeks

### Prognosis

- Worse than for older children – 30-50% develop limb shortening

## 6.11 INFECTION CONTROL, HAND HYGIENE, MRSA AND OTHER RESISTANT ORGANISMS

Bacterial and viral infections readily spread around neonatal units so require vigilant attention from all staff. Consult attending virology and microbiology consultants with specific concerns, especially concerns re outbreaks.

### Infection Control Nurse

Bleep 1751.

### Handwashing, hand decontamination and disinfection

- Sleeves must be worn above the elbows at all times in clinical areas
- Hands and forearms must be washed with liquid soap each time the NNU is entered.
- After handwashing, always apply disinfectant foam/gel and allow to dry before handling babies.
- Use disinfectant foam/gel on entering and leaving all clinical areas and before and after each patient contact
- No rings (except wedding rings) or watches to be worn.
- If hands become contaminated (body fluids etc.) they must be washed vigorously with soap and water.
- If you have trouble with condition of your skin, the procedure should be as follows:
  - Wet hands
  - Wash hands with liquid soap and rinse
  - While hands still wet, apply moisturiser (in dispensers)
  - Dry hands with paper towel
  - Rub in disinfectant foam/gel

### Surveillance

- On admission to NNU, all babies should have screening swabs performed
  - nose, throat, groin and any wounds requested for MRSA Routine Clinical Screen
  - throat and rectum swabs for Gram Negative Resistance Screen
- For ex utero transfers, ask referring hospital to establish multi-resistant organism status prior to transfer (this does NOT mean we will refuse transfer if the baby is positive). This includes MRSA and Carbapenem-resistant organisms.
- Microbiology/infection control will inform us of positive swab results.
- Inform Infection Control of any positive results or concerns
- When there are any babies on the unit colonised with multi-resistant organisms, including MRSA, all babies should be screened weekly on Sunday nights and on discharge for the relevant organism.
- When weekly unit screening is for the presence of MRSA, it should continue until all previously positive babies have either had 3 negative swabs each one week apart, or are discharged, whichever comes first.
- When weekly unit screening is for the presence of other multi-resistant organisms, it should continue until advised by the Infection Control team

### Prevention

Avoid introduction of MRSA positive patients where possible – is admission absolutely necessary?

Hand hygiene to prevent transmission of all bugs

### Management once MRSA isolated

- The Infection Control Team will inform the Unit immediately a positive result is known by contacting the nurse and consultant in charge for the relevant clinical area. In addition, an email will be sent to the NNU Infection Prevention & Control email group (:2NICU).
- Hand hygiene (handwashing and the use of disinfectant foam/gel) is the mainstay of prevention.
- Full MRSA screen on all NNU babies (nose, throat and groin and wounds)
- While there is an MRSA positive baby on NNU, weekly (no more frequently) swabs of affected baby(ies) and all other babies (nose, throat, groin and wounds).
- Barrier nurse colonised / infected baby(ies). Consider isolation and cohort nursing – discuss with Infection Control
- Biopatch should be used under long line and surgically inserted central line dressings. Apply at the time of insertion (if MRSA status know), or at the time of next dressing change.
- The consultant and nurse in charge should decide on the site in which the baby is managed considering the current NNU disposition of staff
- Discharge baby as soon as possible
- Where possible, staff should not work between colonised and non-colonised babies.
- Colonised babies should not be handled without gloves and plastic apron.
- Hands should be decontaminated and / or disinfected on entering the baby(ies) clinical area, before and after contact and prior to leaving the clinical area.
- Gloves and yellow apron should be provided at the baby's cot space. They should be put on at the baby's cot space, while handling baby's notes and must be worn while handling the baby.
- When babies are held (eg for bottle feeding), long sleeved gown should be worn
- All colonised babies to have disinfectant foam/gel beside his/her cot, which must be used each time the baby is handled.
- Care should be taken not to touch surfaces unless necessary.
- Use baby's own cotside pens – not your own.
- All waste and linen must be treated as infectious and the Trust Waste Disposal Policy must be followed.
- Appropriate MRSA documentation must be completed
- Any questions regarding management should be directed to a Consultant Microbiologist (eg Dr Klein) or Dr Newsholme (Infection Control Doctor and ID physician)
- Decolonisation
  - All MRSA-positive babies on the Neonatal Unit should be decolonised
  - Institute 5 days of Octenisan skin wash daily and Bactroban nasally 3 time daily, then continue with daily Octenisan thereafter
  - Monitor surveillance swabs weekly

- After 3 consecutive negative MRSA swabs:
  - If baby has no long line and no skin breach, STOP Octenisan
  - If baby has no skin breach but has a central line, STOP Octenisan and ensure a Biopatch is applied to the central line site under the Opsite/Tegaderm dressing
  - If baby has skin breach(es), continue Octenisan until skin considered intact or until discharge
- A 'skin breach' is defined as a wound prior to full healing. A mature stoma is not considered a skin breach.
- Barrier nursing precautions can be stopped once Octenisan is discontinued
- Parents of MRSA-positive babies should also be decolonised as per Trust guidance. Liaise with Infection Control Nurse.

## 6.12 FUNGAL SEPSIS

With the current policy of fluconazole prophylaxis, this is very rare in our unit.

### Commonest pathogens

- *Candida albicans* (~75% cases)
- *Candida parapsilosis*
- Aspergillosis, *Trichophyton*, *Malassezia furfur*

### Risk factors

- Extreme prematurity
- Fungal colonisation (may occur at birth)
- Central lines
- Postnatal steroids
- TPN (*Malassezia furfur* especially associated with prolonged use of IV lipid)
- Antibiotic use (broad spectrum antibiotics / prolonged use)

### Prevention

- Handwashing
- Minimise invasive procedures
- Early enteral feeding
- Minimal and rational use of antibiotics
- Anti-fungal prophylaxis – see below

### Presentation

1. Fungal amnionitis
  - Can be treated prior to birth with intra-amniotic amphotericin
2. Congenital fungal sepsis
  - Associated with intra-uterine contraceptive devices and cervical suture
  - Spreads over mucocutaneous surfaces (not blood borne) and present with skin involvement and pneumonia
3. Nosocomial fungal sepsis
  - As with bacterial sepsis, may present with:
    - Temperature instability
    - Erythematous maculopapular rash
    - Jaundice
    - Abdominal distension / aspirates / vomiting
    - Respiratory deterioration
    - Cardiovascular instability
    - Carbohydrate +/- lipid intolerance

### Diagnosis

Remember to consider fungal infection, especially in at risk babies who present with signs of sepsis and fail to respond to antibiotics. Early diagnosis and treatment are more likely to lead to a favourable outcome. Look for clinical signs of mucocutaneous infection during daily examination and treat promptly.

### Investigations

To confirm diagnosis and location(s) of fungal infection:

- FBC & film – WBC changes and thrombocytopenia may not be present at the onset of infection
- Skin swabs of all suggestive skin lesions in babies at risk of invasive fungal sepsis
- Chase placental swabs and placental pathology
- Blood cultures (peripheral and from indwelling lines)
- Supra-pubic aspirate of urine (or catheter specimen)
- Lumbar puncture
- Endotracheal aspirates
- Cranial ultrasound (poor outcome with parenchymal lesions)
- Abdominal ultrasound scan looking at renal tract and for fungal abscesses
- Ophthalmology review
- Echocardiogram

### Prophylaxis

Use for preterm infants born before 26 completed weeks gestation, or birth weight <800g, especially those with immature skin.

- Fluconazole
- dose 3mg/kg IV
  - 72 hourly for 2 weeks, then
  - 48 hourly for 2 weeks, then
  - daily to 6 weeks unless ETT and all invasive lines removed before that
  - monitor LFT's weekly whilst on prophylaxis

### Treatment

1. Oropharyngeal and or topical Candidiasis
  - Nystatin liquid 100,000units/mL, 1mL in mouth 4-6 hourly
  - Clotrimazole 1% cream applied twice a day or Nystatin (Nystaform) cream 2-3 times a day.

Continue for 7 days after lesions have healed
2. High index of suspicion or positive blood cultures
  - Remove invasive lines
  - Liaise closely with microbiology and confirm sensitivities
  - Repeat blood cultures until negative

#### Antifungal treatment

- Fluconazole
  - Inhibits fungal cytochrome p450, but has some effect on human cytochrome p450

- Good urinary penetration (excreted via kidneys)
- Bone marrow depression with high serum levels
- Some resistance in non-albicans sp.
- < 2 weeks old 6-12mg/kg every 72 hours
- 2-4 weeks old → 6-12mg/kg every 48 hours
- > 4 weeks → 6-12 mg/kg daily
- treat for 21 days or until cultures negative

OR

- Liposomal Amphotericin
  - Acts by disrupting cell membrane
  - Side effects include:
    - Fever / rigors
    - Renal impairment
    - Hypokalaemia
    - Hypomagnesaemia
    - Bone marrow suppression
  - 1mg/kg/day, increasing to 3mg/kg/day
  - Remember to prescribe increasing dose over first 3 days when writing up initial prescription
  - May need to consider increasing to higher dose (maximum 5mg/kg/day), depending on clinical picture
  - Continue treatment for 21 days or until cultures negative

### 3. Disseminated Candidiasis

Isolation of fungi from sterile body sites eg CSF or retina/renal involvement

- Combined therapy – liposomal amphotericin (dose as above) and flucytosine
  - Flucytosine
    - interferes with fungal protein synthesis
    - synergistic effect with amphotericin
    - good CSF penetration
    - excreted by kidneys
    - can depress liver and bone marrow function
    - dose 50mg/kg BD
  - continue both amphotericin and flucytosine for minimum 4 weeks
  - take blood cultures at least 5 days before planned discontinuation date

## 6.13 CONGENITAL INFECTION - GENERAL PROTOCOL

- The subheading of congenital infection has traditionally described as the “TORCH” infections: toxoplasmosis, rubella, cytomegalovirus (CMV), herpes simplex (HSV). However, not all are truly congenital, but more often perinatal (e.g. HSV) and the whole group of pathogens associated with neonatology should be extended to encompass syphilis, group B streptococcus (GBS), human immunodeficiency virus (HIV), varicella-zoster virus (VZV), human T-cell leukaemia virus (HTLV), hepatitis B and C, parvovirus B19, enteroviruses including parechoviruses.
- Take care in requesting congenital infection investigations in babies, as there are a number of reasons why they may be inappropriate:
  - some of these infections can usually be ruled out on clinical evidence alone e.g. perinatal hepatitis B and C are almost always asymptomatic and thus are unlikely causes of neonatal jaundice
  - serological diagnosis may be better made on mother's blood, and some viral infections can be ruled out by testing mother (e.g. hepatitis B, C, HIV, HTLV)
  - baby's serology may simply reflect mother's long-term past infections
  - babies make their own IgM, but this is not always reliable as a marker of true congenital infections (e.g. CMV)
- Much of the positive diagnosis of true viral congenital infection is best done by direct detection (rather than serology), either through molecular techniques such as PCR to detect viral genomes, rapid culture and/or immunofluorescence for viral proteins.
- In the absence of positive evidence for a congenital infection, for some diseases the baby will need follow-up for up to 18 months before maternal antibody has decayed, allowing more confidence in the assessment that a particular infection has not occurred e.g. toxoplasmosis, syphilis, hepatitis C, HIV.
- Discuss with Virology if unsure of appropriate tests. Advice can be obtained from the Virology SpR on ext 83140 or bleep 0348, or the duty Consultant Virologist.
- For clinical advice contact Dr Esse Menson or Dr Nuria Martinez-Alier, Consultant Paediatricians and Infectious Diseases Specialists (ext. 84677). Outpatient follow-up in most circumstances will be in Dr Martinez-Alier's clinic. After discussion with one of the neonatal consultants, send a referral proforma letter (available from the secretaries) to Dr Martinez-Alier (or Dr Menson in all HIV cases) at ECH.

### Clinical features of the so-called “TORCH” infections

Consider congenital/perinatal infection in infants with the following features:

- Unexplained IUGR/low birth weight – particularly if IUGR symmetrical (CMV, rubella, toxoplasma). However, a congenital infection as a cause of growth retardation usually manifests with other signs present eg microcephaly, hepatosplenomegaly, thrombocytopaenia, etc.
- Cardiac structural defects – mainly rubella, also CMV, toxoplasma
- Cardiac inflammation – parvovirus B19, enterovirus and, rarely, CMV
- Ocular defects: cataract, retinitis, conjunctivitis (mainly rubella)
- Jaundice and hepatitis (CMV is commonest, but also toxoplasmosis, rubella, HSV, bacterial sepsis)

- Thrombocytopenia
- Purpura or petechiae (usually first day) especially in CMV infection but also toxoplasmosis, rubella, syphilis and HSV
- Hepatosplenomegaly – CMV, rubella, toxoplasma
- Pneumonitis – consider in preterm infants with unexpectedly severe chronic lung disease
- Central nervous system involvement
  - Microcephaly in toxoplasmosis, rubella, CMV
  - Cerebral calcification: wide spread in toxoplasmosis, periventricular in CMV
  - Hydrocephalus especially parvovirus B19, toxoplasmosis
  - Seizures: HSV, enterovirus, parechovirus
  - Sensorineural hearing loss

### Investigations

- If congenital/perinatal infection suspected test blood, urine, throat/rectal virus swab and viral mouth swab as early as possible. Taking relevant samples as soon as possible after delivery is important as post-natal acquisition of many viral infections is common so a positive result taken in later infancy would not necessarily indicate congenital infection.
- Take blood from mother and try to obtain results (or the sample) from bloods taken in early pregnancy
- Do not request a "TORCH screen". Use the above features to make a presumptive diagnosis and send appropriate laboratory investigation requests. Refer to specific guidelines for GBS, syphilis, hepatitis B & C, CMV, rubella, toxoplasmosis, and HSV
- Always order investigations using 'congenital/perinatal infection serology' or 'sample for molecular investigations' in the neonatal congenital infection order set on EPR. Detailed clinical information is essential for Virology to decide upon priority for testing. Maternal demographic details for assisting in the laboratory diagnosis are essential.

## 6.14 BABIES AT RISK OF HEPATITIS B

See also 'Immunisations relevant to the Neonatal Unit' protocol

Refer to the Public Health England Green Book hepatitis B immunisation guidance:

<https://www.gov.uk/government/publications/hepatitis-b-the-green-book-chapter-18>

### Hepatitis B immunisation

- There is routine antenatal screening of mothers for hepatitis B (Hep B) in an attempt to avoid vertical transmission from mother to baby
- The development of chronic infection after perinatal transmission can be prevented in over 90% of babies by vaccination starting immediately at birth (accelerated schedule – see below).
- Hep B vaccination is now also part of the universal routine vaccination schedule with hexavalent combination vaccine containing diphtheria/tetanus/acellular pertussis/ inactivated polio/Haemophilus influenzae type b/hepatitis B (DTaP/IPV/Hib/Hep B). In the routine immunisation programme, a total of three doses of vaccine at the appropriate intervals (8, 12 and 16 weeks of age) gives satisfactory long term protection.
- Only babies of mothers who are infected with Hep B are entered into the accelerated schedule starting at birth with additional monovalent Hep B vaccine (see Table 1). These infants will receive monovalent Hep B vaccine at birth and 4 weeks, before receiving the routine hexavalent Hep B-containing vaccine at 8, 12 and 16 weeks. They then receive a further dose of monovalent Hep B vaccine at one year of age. See Table 2.
- Hep B vaccine is kept in the fridges in Hospital Birth Centre, Home From Home Birth Centre, Postnatal Ward, Westminster Suite and SCBU
- At birth, the midwife informs the Neonatology SHO that the baby requires Hep B immunisation.
- Vaccine (and Hep B immunoglobulin (HBIG) if required – see below) should be given ASAP, and certainly within 24 hours of birth. This must be documented on the clinical record (BadgerNet Maternity or Neonatal).
- **Hep B vaccination notification must also be completed on EPR by the person who gives the monovalent Hep B immunisation.** This is automatically electronically forwarded to the Liaison Health Visitor office and the neonatal secretaries. The notification form can be found in EPR under 'Orders' as 'Neonatal Hepatitis B Vaccination Notification'.
- The subsequent doses of monovalent Hep B vaccine required after transfer to the community will be carried out by the GP, but this **will only be done** if the Hep B vaccination notification has been completed so that the GP notification letter can be sent.
- Parents should be provided with an information leaflet about Hep B (copies are kept in the Postnatal Surgery and with other information leaflets on NNU) and advised to register the baby as soon as possible after discharge so that the second vaccine can be given at 4 weeks.
- A list of pregnant carriers, with details of their **infectivity status**, is updated monthly and sent to the NNU, Midwifery Management, the Birth Centre, Pharmacy and the Liaison Health Visitor.
- Where a pregnant woman is determined to have Hep B infection of **high infectivity**, or there is **increased acquisition risk** antenatally (see Table 1 and HBIG section below), HBIG is supplied on a named patient basis so that the baby can receive as a single dose at birth. Emergency doses are also supplied for cases where high risk status has been recognised late. Both are available 24 hours a day from pharmacy. See also HBIG section below.

- Babies who have a **close household contact** who is infected with Hep B, but whose mother is not, are offered a single dose of monovalent Hep B vaccine at birth. They are not offered the accelerated programme, but subsequently complete their Hep B vaccination through the routine universal schedule.
- Emergency maternal serology is available every day, including weekends, and should be requested in any situation where maternal Hep B sero-status is unknown at the time of birth. Contact on-call infection registrar to arrange out of hours testing. There should be < 24 hours delay before knowing whether immunisation is necessary and whether it should include HBIG.

Interpreting maternal hepatitis serology (also see table 1 below)

- Antenatal screening is with HBsAg; a positive result indicates the woman is a Hep B carrier
- HBsAg +ve women should then have HBeAg, HBeAb and Hep B viral load assayed and these results will ascertain whether there is high or low infectivity (ie high or low risk of perinatal transmission)
- Babies of women who have had previous Hep B infection, but are no longer carriers (HBsAb positive, HBsAg negative and undetectable viral load) do not need to have the Hep B accelerated schedule
- If there is any doubt about the interpretation of infectivity, contact Infection/Virology doctor.

Table 1 Babies eligible for Hepatitis B immunisation by accelerated schedule

Hepatitis B status of mother	Baby should receive	
	HB vaccine	HBIG
Mother HBsAg + and HBeAg +	Yes	Yes
Mother has acute Hep B during pregnancy (HBc IgM +)	Yes	Yes*
Low birth weight baby < 1500g and mother HBsAg+ (regardless of e-antigen status or viral load)	Yes	Yes
Mother HBsAg +, e-markers not determined	Yes	Yes
Mother HBsAg +, HBeAg -, HBeAb -, no viral load available	Yes	Yes
Mother HBsAg +, HBeAg -, HBeAb -, viral load > 1,000,000 units/ml at any time during pregnancy	Yes	Yes
Mother HBsAg +, HBeAg -, HBeAb +, viral load > 1,000,000 units/ml at any time during pregnancy	Yes	Yes
Mother HBsAg +, HBeAg -, HBeAb -, viral load < 1,000,000 units/ml throughout pregnancy	Yes	No*
Mother HBsAg +, HBeAg -, HBeAb +, viral load < 1,000,000 units/ml throughout pregnancy	Yes	No
Mother HBsAg +, HBeAg -, HBeAb +, no viral load available	Yes	No

\* this advice may depend on the precise level of the viral load, so always discuss with Virology

**Table 2** Hep B immunisation schedule for routine childhood  
and selective neonatal immunisation programmes

Age	Routine	Babies born to Hepatitis B infected mothers	Where
<b>Birth</b>	†	Monovalent Hep B	At St Thomas This should be entered as notification on EPR
<b>4 weeks</b>		Monovalent Hep B	Health Visitor/GP
<b>8 weeks</b>	DTaP/IPV/Hib/Hep B	DTaP/IPV/Hib/Hep B	Health Visitor/GP
<b>12 weeks</b>	DTaP/IPV/Hib/Hep B	DTaP/IPV/Hib/Hep B	Health Visitor/GP
<b>16 weeks</b>	DTaP/IPV/Hib/Hep B	DTaP/IPV/Hib/Hep B	Health Visitor/GP
<b>1 year</b>		††Monovalent Hep B	Health Visitor/GP

† Newborn infants born to a Hep B negative woman but known to be going home to a household with another Hep B infected person may be at immediate risk of Hep B infection. In these situations, a monovalent dose of Hep B vaccine should be offered before discharge from hospital. They should then continue on the routine childhood schedule commencing at eight weeks.

††A further dose of monovalent Hep B vaccine is given at one year of age, alongside a blood test for HBsAg. Testing at one year of age is important to identify babies who have become chronically infected with Hep B despite vaccination, and will prompt referral for further management.

### HBIG

- Give ASAP after birth and certainly within 24 hrs
- The dose is 200 units intramuscularly for all babies, regardless of birth weight or gestation (recommended by Department of Health Joint Committee on Vaccination and Immunisation)
- If the volume of 200 units is considered too large for low birth weight babies <1500g, Virology have advised that 100 units of HBIG can be given.
- The volume of HBIG solution varies from vial to vial. If administering less than a whole vial (vials come in 500 units and 200 units), the volume of administration must be calculated from information on the vial and provided by Pharmacy.
- To arrange supply of either named patient or emergency HBIG in working hours contact the Women's Services pharmacists on bleep 0690 or 1727 (Monday-Friday) or St Thomas' dispensary on extension 85054 (7 days/week). Out of hours, contact the on-call pharmacist on bleep 0462.
- The paperwork included with the HBIG vial must be completed by the Neonatologist administering the immunoglobulin and returned to Public Health England (PHE) in the envelope provided. The empty box in which the vial was supplied should be returned to PHE in the included plastic bag.
- Give in contra-lateral thigh to vaccine (and document on BadgerNet and EPR as described above)
- If need for HBIG is not recognised at birth, a dose may be given up to a week after birth.

## 6.15 BABIES BORN TO HIV POSITIVE MOTHERS

- When a baby is born to a HIV positive mother, the midwife should contact the Neonatologist carrying the Birth Centre bleep (0678) to inform them of the birth. All cases should be discussed with the registrar and / or consultant. Consult the Antenatal File on NNU and the 'Neonatal care plan for babies of mothers with retroviral illness' document in the maternal notes for information about baby's planned treatment.
- If women present to Birth Centre without booking bloods, emergency HIV serology is available and should be requested by the maternity staff. This should be organised through Virology registrar during working hours and on-call infection registrar out of hours. Results should be available within 1 hour of the sample being received in the lab regardless of the time of day.
- Blood should be taken from the **baby** (NOT cord blood) for:
  - (i) Virology                      HIV antibody  
   HIV DNA PCR

These tests are automatically requested if 'HIV Virology Child <18 months' is requested from the 'Neonatal Unit – Congenital Infection' order set on EPR. Do not alter the test order when requesting on EPR.

Send minimum 2-3mL blood in EDTA bottle – in separate specimen bag from FBC sample.

- (ii) Full blood count, LFTs
- (iii) CMV screening – by **salivary swab** (using viral swab kit) for CMV PCR. Use EPR request 'Saliva for CMV virus' or 'Sample for Molecular Investigations in the EPR orderset 'Neonatal Unit - Congenital Infection' specifying 'Saliva swab' for 'CMVPCR'.
- Breast feeding is contraindicated
- BCG should not be given
- Babies should be commenced on Hepatitis B vaccination schedule and an EPR notification form completed
- Attention should be paid to whether the mother has disclosed her status to her partner, family or GP and care should be taken as far as possible to maintain confidentiality

### Neonatal treatment

- These are general treatment guidelines and planned treatment may vary according to maternal viral load, CD4 count, maternal antiretroviral treatment and compliance. Always consult the 'Antenatal File' on NICU and the most recent 'neonatal care plan' in the mother's notes.
- Antiretroviral drug(s) for the baby should be prescribed immediately after birth to ensure treatment within 4 hours of birth. Zidovudine (AZT) is available on Hospital Birth Centre for the baby's first dose.
- All babies admitted to the Neonatal Unit should have at least their first dose of Zidovudine given IV. IV Zidovudine is kept as stock on NICU. Route of subsequent doses should be decided after NNU consultant and Paediatric Infectious Diseases input.

### 1. Presumed low risk of transmission

- Most HIV positive mothers will have a low viral load (<40 copies/mL) due to treatment to reduce vertical transmission.
- Commence AZT for baby as soon as possible after birth (within 4 hours)
- Dose regimen
  - Babies > 34 weeks: 4 mg/kg/12 hourly orally for 4 weeks
  - All babies admitted to NNU (unless they do not need IV access) should be started on IV AZT: term 1.5mg/kg/6 hourly; preterm 1.5mg/kg/12 hourly
  - Subsequent oral dosing of preterm babies as follows:  
Babies 30-34 weeks: 2 mg/kg/12 hourly for 2 weeks, then 2mg/kg/8 hourly for 2 weeks;  
Babies < 30 weeks: 2 mg/kg/12 hourly for 4 weeks

### 2. Concern about high risk of transmission

- A plan for neonatal treatment should have been made antenatally and this should be followed
- If no plan is evident, discuss treatment with
  - Neonatal attending consultant;
  - Paediatric Infectious Diseases Consultant (Dr Menson, Dr Martinez-Alier or Dr Bamford) ext. 84677;
  - Sexual Health Specialist Midwives ext. 86868; or
  - Angela Callaghan, Family Clinic CNS: ext. 84621, mobile 07780227496
- Consider 'combination post-exposure prophylaxis' for the baby postnatally for the following:
  - the mother is found to be HIV positive on rapid testing in labour
  - maternal viral load unknown due to late presentation or failure to attend clinic
  - inadequate maternal treatment in pregnancy
  - high maternal viral load (>40 copies/mL, unless mother on effective treatment and higher threshold agreed antenatally)
  - prematurity (<36 weeks), ruptured membranes >18 hours prior to delivery (unless planned vaginal delivery), chorioamnionitis, placental abruption.

Always discuss with consultant if considering combination therapy.

- Combination post-exposure prophylaxis will generally consist of triple antiretroviral therapy (ART):
  - AZT 4mg/kg/12 hourly for 4 weeks (unless admitted to NNU and requiring IV – see above)
  - Lamivudine 2mg/kg/12 hourly for 4 weeks (there is only an oral preparation)
  - Nevirapine 2mg/kg once daily for 1 week, then 4mg/kg once daily for 1 week, then stop (there is only an oral preparation). If mother has had > 3 days Nevirapine in the 3 weeks preceding delivery, the dose should be 4mg/kg once daily for 2 weeks. Chart the dose in whole milligrams.

### Discharge

- It is quite common for partners and GPs not to be aware of the mother's diagnosis. Check whether the mother wants to maintain this degree of confidentiality before writing the discharge summary or TTOs for the baby's prophylaxis. Inform midwife, ward clerk or neonatal secretary NOT to send the GP copy in this circumstance.
- Prescribe the TTOs for the baby to complete the 4 week course

- Follow-up in the Family Clinic (1st or 3rd Tuesday of the month) at 6 weeks (or 3 weeks if on triple ART). Email or fax (84612) referral letter to Angela Callaghan. A yellow outpatient request form should be attached to the notes with a request for the Family Clinic and the Postnatal Ward ward clerk should ensure the notes are sent to Central Appointments.

For further information, contact Paediatrician Infectious Diseases Consultants (Dr Menson, Dr Martinez-Alier or Dr Bamford) on ext. 84677, or Angela Callaghan, ext. 84621 or bleep 2279.

For maternity liaison, contact the Sexual Health Specialist Midwives ext. 86868.

A list of upcoming deliveries is also available from Dr Tim Watts, Consultant Neonatologist, on NNU and in the 'Antenatal File' on NICU.

See also BHIVA management of HIV infection in pregnancy at <http://www.bhiva.org> (May 2012).

## 6.16 BABIES BORN TO HEPATITIS C POSITIVE MOTHERS

Mothers found to be HepC Ab positive antenatally should have been tested for HepC RNA.

- Babies of mothers who are HepC RNA positive have a 2.5-12% risk of acquiring Hep C perinatally.
- Babies of mothers who are HepC Ab positive with undetectable HepC RNA throughout pregnancy are probably not at risk. However, the majority of these babies will require follow-up as it may not be possible to be sure that the infection was cleared before pregnancy. Where there is doubt, discuss with Dr Menson or Dr Martinez-Alier (see below).

Hepatitis C is unlikely to present in the neonatal period and usually causes a low grade chronic hepatitis in childhood. At the present time, the natural history of the progression of vertically transmitted hepatitis C is not known.

- Check mothers HepB and HIV status from antenatal testing.
- Baby should receive Hepatitis B vaccine course regardless of mother's HepB status (see Protocol for management of babies born to Hepatitis B positive mothers and remember to complete Liaison health Visitor notification form on EPR).
- Breast feeding should not be discouraged (unless the mother is also HIV positive) as the risks are likely to be negligible.
- Arrange outpatient follow-up with Dr Nuria Martinez-Alier, Consultant Paediatrician and Infectious Diseases Specialist by completing a Perinatal/Congenital Infection proforma referral letter. Outpatient follow-up in most circumstances will be in Dr Martinez-Alier's clinic.
- Investigations should be as follows:
  - 6-8 weeks Hep C RNA (this sample is not necessary if mother is Ab positive, but RNA negative)
  - 6 months Hep C RNA
  - 12 months Hep C RNA, Hep C Abs
  - 18 months If Hep C Abs +ve at 12 months repeat Hep C RNA, Hep C Abs
- Refer to Paediatric Hepatology Clinic at KCH if Hep C RNA +ve at any time or if Hep C Abs still detectable at 18 months

## 6.17 BABIES BORN TO MOTHERS WITH POSITIVE TESTS FOR SYPHILIS

Syphilis is caused by the spirochete, *Treponema pallidum*. All mothers are screened for syphilis at booking by testing for the presence of treponemal specific antibodies. If the initial test is positive, further tests are performed, and, if confirmed, the women are referred to Genito-urinary Medicine (GUM) (usually the Lydia clinic at St.Thomas' Hospital). The current confirmed positive rate at GSTT is 1 in 120.

- Some women will be known to have had effective treatment in the past and will not be treated again during the pregnancy.
- Some women will not be known to have had treatment or considered likely to have late latent disease. These women will receive three IM doses of Penicillin during the pregnancy.
- A minority of women will be found to have active disease (primary or secondary syphilis) and will be treated with a slightly different penicillin regime.

Parenteral (IM) Penicillin treatment for syphilis completed at least a month before delivery prevents most congenital syphilis.

There are a few difficulties for neonatal practice:

- Congenital syphilis can be asymptomatic, but cause significant (preventable) problems for the child later.
- None of the available tests are perfect
  - There is no test to define at birth if an infant has been infected
  - There is no test to ensure a mother has not been reinfected since treatment

This guideline is deliberately simple and conservative.

### Infants needing only clinical and serological screening at birth, 3, 6, and 12 months:

Maternal syphilis serology confirmed positive and one of the following:

- 1) Treated during this pregnancy with penicillin AND completed treatment at least 1 month (30 days) before delivery
- 2) Effectively treated prior to this pregnancy

The information about treatment should be in the mother's notes. If not it may be necessary to contact the GUM clinic in which she was seen. (If GSTT: Lydia Clinic Health Adviser: Ext 82631)

On occasion, the GU doctors will have decided that the mother definitely has previously successfully treated syphilis and that this poses no risk to the baby. If there is clear written documentation from Lydia Clinic that this is the case, then the baby can be discharged without follow-up.

### Infants needing investigation and treatment:

1. Infant asymptomatic but "inadequate" maternal treatment i.e.:
  - Never treated
  - Treated during this pregnancy but not with parenteral penicillin
  - Concern from GUM that maternal treatment during this pregnancy ineffective
  - Parenteral Penicillin treatment incomplete or completed less than 1 month (30 days) before delivery

2. Infant unwell with symptoms consistent with congenital syphilis:

- Signs and symptoms suggestive of congenital syphilis include: IUGR, hydrops, rhinitis, rashes (especially soles and palms, perioral and perianal), osteochondritis and periostitis, hepatosplenomegaly, thrombocytopenia and anaemia, meningitis, renal impairment.

For the symptomatic infant there will also need to be investigation and treatment for differential diagnoses.

#### Investigation

- Serology. On EPR: in Children's Services select Neonatal Unit-Congenital Infection, then order Congenital Syphilis Serology. Send a large sample (2 tubes: send infant blood, not cord blood) and also request repeat maternal serology. Inform the laboratory.
- FBC and neonatal profile
- X-rays: Request long bone films
- Lumbar puncture. On EPR, request through Neonatal Unit-Congenital Infection, order CSF for virological investigations, and specify syphilis

#### Treatment

- Benzylpenicillin 30mg/kg IV 12hrly for 7 days then 8hrly for 3 days

In certain circumstances where inpatient management is considered not desirable, the following alternatives may be considered:

- Procaine Penicillin 30mg/kg IM daily for 10 days or
- Benzathine Penicillin 30mg/kg (or 50,000 units/kg) IM x1 can be considered in the asymptomatic infant: discuss with consultant

All treated infants should follow the same schedule for follow-up and repeat serology as those not treated.

Symptomatic infants with negative IgM should have repeat IgM at 4 and 8 weeks as there can be a delayed IgM response in infants.

Repeat lumbar puncture is indicated if the initial CSF was positive.

#### Serological and clinical screening

- Screening is done at birth, repeated at 3 months, 6 months and 1 year
- Follow-up and 3, 6 and 12 month serology is undertaken by Dr Nuria Martinez-Alier, Consultant Paediatrician and Infectious Diseases Specialist, in Outpatients in ECH. A Perinatal/Congenital Infection proforma referral letter should be sent after discussion with the neonatal consultant for Postnatal Ward.
- For all tests, on EPR in Children's Services, select Neonatal Unit-Congenital Infection, then order Congenital Syphilis Serology. Give all relevant clinical information, especially maternal details.
- IgM will be prioritised at birth, then TPPA / IgG / RPR during follow-up

If the infant is IgM positive at birth the infant should be recalled for full investigation and treatment.

- Particular signs of late syphilis are developmental delay, 8th nerve deafness, interstitial keratitis, abnormal bones and joints, abnormal teeth

- Maternal antibodies will disappear over the first year. Once an infant is negative (TPPA/IgG and RPR) no further testing is necessary.
- Infants should be investigated and treated or re-treated if titres are rising. Treated infected infants may have persistent low levels of IgG/TPPA but other tests should be negative i.e. RPR.
- The outlook for congenital syphilis treated at birth is good, but treponemes may remain in the eye (interstitial keratitis) and referral to Paediatric Ophthalmologist is indicated.

#### Other issues

- Ensure parents are aware of when follow-up appointments will be held and why, and that accurate address details are in the notes
- If the maternal serostatus is unknown it is possible to do a manual EIA on the infant's blood for IgG, prior to IgM. This needs discussion with the laboratory and is only going to be necessary in exceptional circumstances.
- Full information about the maternal diagnosis and treatment is fundamental to this management outline. There is no urgency to treat the asymptomatic infant and contacting the GUM team where there are doubts may prevent unnecessary investigation.
- If there are concerns that parents will not comply with follow-up then treatment can be given, after discussion with the consultant
- Negative syphilis serology at booking does not exclude congenital syphilis as the mother could become infected after the initial serology
- Thought may need to be given to arranging screening for other family members, especially siblings

#### Quick guide to available serological tests for syphilis

All infants requiring testing should have congenital syphilis serology ordered on EPR, with full clinical and maternal details. The laboratory will then prioritise which tests are performed.

IgM EIA:	enzyme immunoassay for treponemal IgM: presence highly suggestive of active infection; absence does not exclude active infection
IgG EIA:	enzyme immunoassay for treponemal IgG: presence suggestive of infection, does not distinguish previous or latent infection, and likely to be due to maternal antibody transfer in the infant unless levels are increasing.
RPR:	rapid plasma reagin: non-treponemal test that has replaced the VDRL (venereal disease reference laboratory test). Both are raised in acute infection, and titres fall in response to effective treatment. Mother to child transmission of syphilis from mothers who are RPR negative is very unusual (many countries still rely on this as a screening test).
TPPA:	Treponema pallidum particle agglutination test. Does not distinguish between active and previously treated infection

EIA (IgG) is used as the booking blood screen, and the extended tests if this is positive are RPR, RPR titre, and TPPA.

### 6.18 CYTOMEGALOVIRUS (CMV)

Commonest congenital infection (~3 per 100 live births).

Babies can be severely ill at birth (~10%) or asymptomatic. All babies, including those initially asymptomatic, are at risk of developing progressive sensorineural hearing loss (SNHL) (~15% of those without symptoms at birth), neurological impairment (less common), or chorioretinitis (also rare).

For further information including signs associated with congenital CMV, see section 6.12.

Postnatally acquired CMV is also common in very premature babies on NNU. It is usually acquired via mother's breast milk. It can cause sepsis-like symptoms, pneumonitis, hepatitis and/or thrombocytopenia. There is no evidence of association with long term impairments.

For the diagnosis of congenital CMV, it is imperative to collect urine and/or CMV-specific salivary swab within the first 2 weeks of life, otherwise perinatal infection (as opposed to congenital infection) cannot be ruled out.

#### Investigations

- Cranial ultrasound scan (and consider need for MRI or CT scan)
- Ophthalmology assessment
- Hearing screening – see separate protocol
- Virology tests
  - send salivary swab or urine for CMV virus PCR (this test is definitive in the first 2 weeks of life) from EPR orderset 'Neonatal Unit – Congenital Infection'.
  - EDTA blood for CMV DNA PCR
  - clotted blood for CMV IgM
  - also check maternal CMV serology (IgG and IgM)
  - It may be helpful to test maternal booking and current blood for CMV IgG avidity - discuss with Virology as congenital infection is most likely if the mother acquired CMV during pregnancy.
- LFT's, clotting and FBC

#### Treatment

- Ganciclovir has been used for life threatening infection in individual cases. Evidence has emerged recently that progressive hearing loss in babies born with congenital CMV central nervous system disease may be prevented with a regimen of IV ganciclovir; and there are on-going trials of oral valganciclovir. Such cases should be discussed with Dr Esse Menson or Dr Nuria Martinez-Alier, Consultant Paediatricians and Infectious Diseases Specialists, and a Virology consultant. The dose and length of treatment is debatable. Suggested dose of ganciclovir is 5mg/kg BD IV for 6 weeks. Neutropenia and thrombocytopenia are possible side effects.
- Arrange outpatient follow-up with Dr Menson or Dr Martinez-Alier by completing a Perinatal/Congenital Infection proforma referral letter.

Infection control

Most babies congenitally infected with CMV shed virus in urine and body secretions. Barrier nursing is indicated with rigorous attention to hand hygiene. Pregnant staff do not need to use more stringent precautions.

## 6.19 CONGENITAL RUBELLA

For further information including signs associated with congenital rubella, see section 6.12.

Congenital rubella is still of concern due to a significant population of Rubella non-immune women becoming pregnant.

Classical congenital rubella exhibits a triad of cataract, congenital heart disease and nerve deafness.

Confirmation of maternal rubella immune status and immunisation history and whether there has been a rubella-like illness in pregnancy is important.

### Investigations

- Cranial ultrasound scan (and consider need for MRI scan)
- Cardiology opinion and echocardiogram
- Ophthalmology assessment
- Hearing screening (see separate protocol)
- Blood tests
  - LFT's, clotting and FBC
  - viral serology on baby for rubella IgM (EPR order 'congenital/perinatal infection serology')
  - check maternal booking viral serology and order current maternal IgG and IgM
  - further specialist tests such as rubella PCR may be advised by Virology

### Treatment

There is no safe, proven, effective treatment for congenital rubella.

### Infection control

Most babies congenitally infected with rubella shed virus in urine and body secretions. Barrier nursing is indicated.

## 6.20 CONGENITAL TOXOPLASMOSIS

For further information see section 6.12.

Consider a diagnosis of congenital toxoplasmosis in infants with:

- Unexplained IUGR (particularly if asymmetrical)
- Hydrocephalus
- Microcephaly
- Hepatosplenomegaly
- Hepatitis
- Petechiae
- Thrombocytopenia
- Chorioretinitis

Evaluation of suspected case should proceed following discussion with a Virology consultant and Dr Esse Menson or Dr Nuria Martinez-Alier, Consultants in Paediatric Infectious Diseases. Evaluation will usually involve the following:

### Mother

- Maternal history during pregnancy including possible exposure (travel, handling or ingestion of previously uncooked meat, kittens/cat litter) and illness (lymphadenopathy, fatigue, infectious mononucleosis-like illness). Note that such illness prior to conception is unlikely to be relevant to a diagnosis of congenital toxoplasmosis.
- Maternal serology results if available – liaise with Obstetricians
- Send maternal serology as indicated by Virology
- Results of antenatal ultrasound scans

### Baby

- Physical examination looking for above signs
- Discuss with consultant virologist and send clotted and EDTA blood samples to Virology as advised (requested on EPR as 'acute save serum' and 'sample for virologic testing', respectively)
- FBC and film
- LFT and clotting
- Urinalysis and serum creatinine
- Eye examination by a Paediatric Ophthalmologist
- Cranial ultrasound scan (and consider need for MRI scan)
- Hearing screening (see separate protocol)

### Treatment

Even in moderately affected babies, considerable improvement can occur with aggressive treatment.

### Symptomatic babies

- Pyrimethamine 1mg/kg BD for 2 days, then 1mg/kg OD for 6 months, then 1mg/kg three times a week for 6 months

- Sulphadiazine 50mg/kg BD for 12 months
- Folinic acid 1mg/kg, 2 times per week

Continue all 3 for one year. Monitor LFT's and FBC every 4-6 weeks (risk of myelosuppression and hepatitis).

Asymptomatic infants with positive serology

- Treatment of these babies is not straightforward. Discuss individual cases with Virologists and Paediatric Infectious Diseases is essential.

#### Follow up

Infants born to women with a definite toxoplasma infection in pregnancy will need to be followed up for up to 18 months. Frequency of testing will be determined by rate of maternal antibody decay or appearance of infant's intrinsic immune response to toxoplasma.

Discuss and arrange outpatient follow-up with Dr Esse Menson or Dr Nuria Martinez-Alier, Consultants in Paediatric Infectious Diseases, by completing a Perinatal/Congenital Infection proforma referral letter.

- Toxoplasma antibodies and/or PCR
- Monitor liver and marrow function as above
- Ophthalmology review as suggested by Paediatric Ophthalmologists
- Audiology assessment according to hearing screening result or clinical indication
- Neurosurgical referral if hydrocephalus occurs

N.B.

- Breastfeeding by an infected mother poses no risk to her infant
- Infected babies are not infectious

## 6.21 HERPES SIMPLEX VIRUS (HSV) INFECTION

Neonatal HSV is rare in the UK (1–2 per 100,000 newborn babies)

- Congenital (transplacental) HSV infection in the neonate is rare, but has a high mortality and morbidity unless treated.
- More often, infants acquire HSV at the time of delivery, through direct contact with infectious secretions or lesions (perinatal acquisition).
- Postnatal (nosocomial) HSV infection also occurs from cold sores or asymptomatic shedding from the mother, family or staff; occasional fatal cases are reported so staff need to be vigilant.

Primary maternal genital HSV infection, especially in the third trimester, is far more dangerous than is secondary, since there is no maternal antibody to afford to the baby some protection. Vaginal delivery following third trimester primary genital HSV infection is associated with a 30-60% risk of perinatal HSV infection.

### Prevention

Mothers with active genital lesions in the third trimester that are thought to be a primary infection should be advised to have elective caesarean section. If vaginal delivery is unavoidable or if the membranes have been ruptured for more than 4 hours before caesarean section, the case should always be discussed with the duty Virology/Infection doctor: x83140 or, out-of-hours, via switchboard. Otherwise vaginal delivery is reasonable.

Breast-feeding is not contraindicated as long as there are no breast lesions.

Mothers should be given treatment with aciclovir if they are noted to have active HSV.

Maternal HSV antibody status should be determined if primary HSV infection in the third trimester is suspected.

### Investigation of babies born to mothers with active genital HSV

Send swabs for viral HSV detection by PCR from:

- the conjunctiva (separately)
- oropharynx
- axillae, groin and umbilicus

### Management

#### 1. Observation

Neonatal herpes can infect the baby's skin alone; or also eyes and mucous membranes; or invasive infection can include liver and or CNS. The baby may present acutely septic +/- seizures and death can ensue rapidly.

Monitor for:

- skin or scalp rashes (especially vesicular lesions)
- respiratory distress (neonatal HSV infection may cause pneumonitis),
- seizures
- signs of sepsis eg fever, lethargy, poor feeding

Babies born to mothers without genital lesions or those born by caesarian section may be discharged early, but parents should be instructed to look out for any rashes or signs of viraemia.

Babies born vaginally to mothers with active lesions should be observed for at least 4 days.

2. Babies with suspected HSV infection

NB Consider neonatal herpes in all sick newborns with abnormal liver function tests and clotting profiles

Additional investigations:

- (i) Any vesicular skin lesions for urgent HSV DNA PCR
- (ii) EDTA blood and CSF for HSV DNA PCR
- (iii) FBC, neonatal profile, clotting

If signs of viraemia are present or the diagnosis is strongly suspected

- Contact the duty Virology/Infection doctor (extension 83140 or, out-of-hours, via switchboard.)
- Start aciclovir promptly (20mg/kg daily IV 8 hourly for 14-21 days)
- Barrier nurse, preferably in an isolation room

## 6.22 PERINATAL CHICKENPOX

### A) Maternal varicella infection

- Herpes zoster (shingles) infection in mother is not an indication for concern in the newborn.
- Maternal chickenpox during early pregnancy is associated with embryopathy (microcephaly, microphthalmia, limb atrophy etc) – risk: 2-12 weeks ~0.5%, 12-28 weeks ~1.4%, >28 weeks 0%
- If maternal chickenpox occurs 1-4 weeks before delivery, up to 50% of babies are infected and 23% of these develop clinical varicella despite high titres of transplacentally acquired maternal antibody.
- If mother develops chickenpox at term, this carries significant risk for the baby and elective delivery should be avoided for 5-7 days if possible.

### Management

- If mother develops chickenpox  $\geq 7$  days before birth, the baby is likely to have received some maternal antibodies transplacentally, therefore varicella zoster immunoglobulin (VZIG) or other prophylaxis is not indicated.
- If mother develops chickenpox from **< 7 days before birth until 7 days after birth**, VZIG should be given to the neonate. Contact the duty Virology/Infection doctor to discuss any such cases: extension 83140 or bleep 0348 during working hours or via switchboard on-call. (50% of these babies will develop neonatal chickenpox despite receiving VZIG but mortality rates are low.)

In addition

- Arrange neonatal ophthalmic examination.
- Breastfeeding is **not** contra-indicated; the mother can express and feed the EBM by bottle if there are lesions close to the nipple.
- Monitor the baby for signs of chickenpox until 28 days after onset of maternal rash (although baby does not need to be an inpatient for this).
- The appearance of any vesicular lesions in an infant should be treated with IV aciclovir whether VZIG has been given or not.
- VZIG is of no benefit once neonatal chickenpox has developed
- The mother and baby must be isolated from other mothers and babies.

### B) Chickenpox contact (healthy baby within 1 month of birth or baby of any age still requiring intensive or prolonged special care nursing)

- Contact is defined as being in the same room for 15 minutes or more or face-to-face conversation for 5 minutes or more or living in the same house. Chickenpox is infectious from 48 hours before the rash and until ~5-7 days after (traditionally taken as when all lesions have become scabs).
- Contact the duty Virology/Infection doctor to discuss: extension 83140 or bleep 0348 during working hours or via switchboard on-call
- If baby is  $\leq 28$  weeks gestation and/or  $\leq 1000$ g at birth, regardless of mother's previous chickenpox history, he/she is unlikely to have received adequate antibody transplacentally and should be given VZIG.

- If baby is >28 weeks gestation, check maternal chickenpox serology, regardless of her history of chickenpox (this may be done on booking blood samples).
  - If mother is seropositive for VZV, the baby is likely to be immune and will not need prophylaxis or treatment. However, babies over 60 days old or who have had repeated blood sampling with replacement by packed red cells may have lost maternal antibody and therefore these babies may need to be tested themselves.
  - If maternal serology is negative, the baby requires VZIG.
- Anyone with chickenpox infection can only visit NNU when no longer infectious (see above).
- Any chickenpox contacts must not visit the NNU from days 7 to 21 after the contact (days 7 to 28 after contact if they have received VZIG).
- Babies who are contacts should be isolated (and cohorted) from days 7 to 21 after contact (or from days 7 to 28 after contact if they received VZIG). Mothers who have chickenpox or who have had contact with someone with chickenpox should not be isolated from their babies.
- Breastfeeding of babies exposed to maternal chickenpox should be encouraged. If the mother has chickenpox lesions close to the nipple, milk should be expressed until the lesions have crusted. The baby should be protected from chickenpox by VZIG, and so can receive expressed breast milk.
- Babies who are contacts should be nursed by staff who are immune to chickenpox.
- When indicated, VZIG should be given as soon as possible, as far as possible within 72 hours of contact if possible, but is recommended up to 10 days following contact.
- If other family members have chickenpox at home, and the mother is seronegative, discharge should be delayed until the baby is at least 7 days old.

#### C) Management of chickenpox in neonates

- Take viral swab of lesions for VZV DNA PCR.
- Treat with IV aciclovir (20mg/kg 8 hourly) if within first 1 month of life, regardless of previous provision of VZIG or maternal chickenpox status.
- Shingles in infancy or childhood may occur following perinatal chickenpox

## 6.23 TUBERCULOSIS AND BCG

TB is due to infection with *Mycobacterium tuberculosis*

Consult with Paediatric Infectious Diseases Team, the Adult TB team or paediatric TB nurse on ext 85811. There is a monthly paediatric TB clinic at ECH run by Dr Nuria Martinez-Alier Consultant in Paediatric Infectious Diseases. Information can also be found in updated NICE guidelines (<http://guidance.nice.org.uk/CG117/Guidance>, March 2011). If multi-drug resistant (MDR) TB, refer case to Adult TB team.

### Management of baby with TB contact

- Mother has been diagnosed with 'open' TB and on treatment  $\leq 2$  weeks
  - Mother must be isolated and breast feeding is contraindicated.
  - Separate mother and baby only if mother very ill, likely poor compliance or has resistant TB
  - Perform CXR on the baby to exclude disease
  - Baby should be started on isoniazid prophylaxis immediately 10mg/kg od and pyridoxine if breast fed.
  - Refer baby to TB nurse/Paediatric Infectious Disease clinic.
  - Follow-up will include Tuberculin skin test +/- interferon gamma release assay (IGRA) at 6 weeks, +/- a repeat at 12 weeks. This will be decided by Dr Martinez-Alier in Paediatric Infectious Disease clinic.
  - Withhold BCG until 3 months as this can mask the tuberculin skin test
  - Screen household before discharge (CXR to be arranged by GP or adult chest clinic/TB nurse).
- Immediate family member with very recently diagnosed 'open' TB or 'closed' TB but other family members not yet screened.
  - Baby should be started on isoniazid prophylaxis 10mg/kg od and pyridoxine if breast fed.
  - Screen household before discharge (CXR to be arranged by GP or adult chest clinic/TB nurse).
  - Refer to TB nurse to consider tuberculin skin test/BCG depending on mother's TB screening results.
- Mother with TB disease on adequate treatment  $> 2$  weeks before birth
  - BCG for baby at birth
  - Screen household before discharge (CXR to be arranged by GP or adult chest clinic/TB nurse). Refer to Paediatric Infectious Diseases if household member infectious at screening.
  - Discuss with adult TB/Infectious Diseases team to ensure mother no longer infectious.
  - Refer to TB nurse.

### Neonatal tuberculosis

- Neonates are very susceptible to *Mycobacterium tuberculosis*.

- Virtually all infections are acquired postnatally from maternal TB, less commonly close household contacts and only rarely from staff with open TB.
- Can be rarely acquired antenatally (congenital TB) if maternal miliary TB or recent primary infection.

### Congenital tuberculosis

In congenital TB, 50% of the mothers have previously undiagnosed TB, usually a 1° infection. Pleural effusion, meningitis and disseminated infection are the commonest manifestations.

### Mode of transmission

- Infection from the genital tract is rare. Severe maternal TB usually leads to abortion or stillbirth.
- Transplacental
  - haematogenous with 1° TB in the liver
  - via amniotic fluid by ingestion or aspiration

### Presentation

- Asymptomatic at birth but most babies have an abnormal CXR and are symptomatic by 2-3 weeks.
- Symptomatic at birth, very sick and may be infectious
  - hepatosplenomegaly, lymphadenopathy, fever
  - respiratory distress
  - meningitis (present in 1/3 of cases)
  - papules and petechiae, discharging ear

### Diagnosis

- Microscopy for AFB - only 10% +ve
- PCR – 25-83% +ve
- Culture (takes 6 weeks)
- Tuberculin skin test may be –ve for 3/12. Repeat interval tuberculin skin test and/or IGRA may be indicated to completely exclude TB.
- Diagnosis often has to rely on making the diagnosis in the mother

### Treatment

Isoniazid, rifampicin and pyrazinamide + ethambutol or streptomycin - until sensitivities known.

Continue appropriate antituberculosis medication for 9-12 months. Consult with Paediatric Infectious diseases team.

Referral for follow-up should be made to Dr Nuria Martinez-Alier, consultant in Paediatric Infectious Diseases.

NB Mother generally is no longer infectious from after approximately 2 weeks of adequate treatment; beware of MDRTB.

### BCG vaccination

- Bacillus Calmette-Guerin (BCG) vaccine is a live attenuated strain of Mycobacterium bovis.
- Neonatal BCG vaccination provides 50-70% protection against all forms of TB and 70-80% protection against miliary TB and TB meningitis.
- The prevalence of TB in the GSTT catchment area is one of the highest in the UK (3x national average). Highest risk is 25-44 years but 12% are <15 years
- High risk groups are:
  - Any member of household has TB or has had it in the past
  - Any member of household born in Africa, Asia (excluding Japan but including Cyprus and Turkey), South or Central America (including Caribbean)
  - Any member of household likely to visit these areas for >1 month
  - Refugees
  - In homeless accommodation
  - Travellers
- Babies thought to be at particularly high risk (i.e. those with household members with active TB) should be offered BCG before discharge and the HV and GP informed
- BCG is available in the community for all babies in Lambeth, Southwark and Lewisham via their Health Visitor. Information leaflets are available on the Birth Centre and Post-natal Ward
- The baby's Health Visitor will ascertain whether they are high risk at the first home visit. Any high risk baby will then be given an appointment in one of the Community BCG clinics
- If the parents request BCG for their baby, they can attend one of the Community BCG drop-in clinics

### Contraindications to BCG vaccination

- Mother known to be HIV +ve
- Immunosuppressive medication or condition
- Generalised skin sepsis
- Sepsis

### Procedure for BCG vaccination

- Obtain consent from parents and give them the Community "Information for Parents" sheet
- No need for prior Tuberculin skin test <6 years of age unless resident in area of high TB incidence.

- Use intradermal BCG – draw up 0.05mL of vaccine and administer intradermally using a 26G needle. Introduce needle just under the skin over the left deltoid. There should be some resistance and it should raise a tense bleb.
- Inform HV or record in “Red Book”

#### Follow-up after BCG vaccination

This will be in the Community (inform Liaison Health Visitor) but parents should be informed that there is often a pinhead, dry, red pimple appears after 2-6 weeks and may last several months. No special treatment of the skin is required.

Skin breakdown, abscesses and lymphadenopathy also commonly occur.

BCG abscesses generally do not require treatment. However, referral to Dr Nuria Martinez-Alier, Paediatric Infectious Diseases consultant for outpatient review in TB clinic may be considered.

## 6.24 IMMUNISATIONS RELEVANT TO THE NEONATAL

### UNIT

The bulk of this is not evidence based. It follows the guidance from the Department of Health Joint Committee on Vaccination and Immunisation (the UK 'Green Book'):

[http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_079917](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_079917)

- Immunisations are offered to our population just as for the newborn in general, and at ages not corrected for gestation
- Live vaccines (BCG, oral polio and MMR) are contraindicated for 3 months following dexamethasone, because of the potential for steroid-induced immunosuppression
- All immunisations should be prescribed by their brand names on the front of the drug chart as there are multiple brands available for the same type of immunisation. It is very important that you select the right brand as they are not all licensed for the same age groups.
- Ensure parental consent for any course of immunisations. Record the administration of any immunisation in the baby's 'red book' and in the baby's casenotes, including site of administration and batch numbers. The medication chart should also be signed when the immunisation is given. Also document on SEND.
- The antero-lateral aspect (too lateral injects the fascia lata) of the thigh is most commonly used for IM injections. The deltoid may alternatively be used in bigger babies.
- When multiple immunisations are due at the same time, they should be given only when all are available to give together.

### Diphtheria, Tetanus, Pertussis, Meningococcus C, Polio, Haemophilus influenzae B, Pneumococcus

- These are administered in different combinations (see table below) at 2, 3 and 4 months, but generally delayed if baby is very unwell or deteriorating
- Diphtheria, tetanus, pertussis (acellular) (DTaP), HiB and polio come in the '5 in 1' preparation – '**Pediacel**'. Meningococcal vaccine ('**NeisVac-C**') and Pneumococcal conjugate vaccine ('**Prevenar 13**') are currently given separately.
- There is a slightly increased risk of apnoea in preterm infants for 24-48 hours following routine immunisation. This may be due to the pertussis component. Ensure adequate monitoring during this period.

### Hepatitis B

See 'Babies born to Hepatitis B positive mothers' protocol

- Preterm babies in NNU are likely to have > 1 dose of the primary course (altogether 3 injections at monthly intervals) while still in the Unit. The Hep B notification form for the Liaison HV must still be completed on EPR for these babies at birth. Liaise with the Hepatitis B programme coordinator prior to discharge home to ensure ongoing follow-up vaccinations in the community.
- It is not clear how immunogenic the vaccine is in preterm infants, so serology should be checked 6-8 weeks after the third dose, if sub-optimal a booster dose may be indicated.

## BCG

See 'Tuberculosis and BCG' protocol

## Influenza

- Indicated in infants with CLD (needing oxygen/ventilatory support by 36 wk corrected) once they have reached 6 months postnatal age.
- It is administered in two half-adult doses (i.e. 0.25ml) a month apart.
- There is central notification when the particular year's vaccine becomes available, usually in October.
- All neonatal staff should have yearly influenza vaccination from Occupational Health

## Respiratory Syncytial Virus (see also Bronchiolitis guideline 1.16)

- Humanised monoclonal antibody (IgG) against RSV – Palivizumab (Synagis®) – is available for passive immunisation. The effect lasts a month, so it must be given monthly during the RSV season (about October-February).
- Babies who will be offered Palivizumab prophylaxis are preterm infants who have chronic lung disease (CLD) at the chronological ages at the start of the RSV season and gestational ages at birth covered within the shaded area of the table below. Preterm babies with acyanotic congenital heart disease may also qualify – refer to the Green Book guidance
- Any use outside this indication must be discussed with the Dr Karen Turnock (Consultant Neonatologist, lead for chronic lung disease clinic) and agreed with pharmacy and Neonatal Outreach team

Babies who qualify for Palivizumab prophylaxis against RSV

	Gestational age at birth (whole weeks)						
Chronological age (months)	≤24	>24 to ≤26	>26 to ≤28	>28 to ≤30	>30 to ≤32	>32 to ≤34	≥35
1.0 to <1.5							
1.5-3							
3-6							
6-9							
>9							

## Rotavirus vaccine (Rotarix)

- Live attenuated oral vaccine, given at 2 and 3 months of age
- Caution is needed if the vaccine is delayed, as this increases incidence of associated intussusception. JCVI advice is to give to preterm babies regardless of gestation or whether the baby is an inpatient on NNU. Although there is no evidence for transmission of infection from live attenuated virus between babies in NNU environment, we currently do not give until the baby is going home.
- Discuss with consultant

### Summary scheme of infant immunisations

For further information on schedule and clear information regarding proprietary vaccines refer to:

[http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_122404](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_122404)

Chronological age (months unless indicated)	Hepatitis B*	Pediacel® (5 in 1)	'NeisVac-C'®	'Prevenar 13'®	Influenza*	RSV*	MMR
0	✓						
1	✓						
2	✓	✓		✓			
3		✓	✓				
6-8 wk after 3rd hep B	serology (preterm)						
4		✓		✓			
1st autumn					✓x2	✓x5	
12	✓and serology		✓ (+ HiB)				
13				✓			✓

\*where indicated—see body of text