

Antibiotics for Neonatal Infection UHL Neonatal Guideline

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March 2019 - 2022
Trust Ref C54/2019

Scope:

This guideline is aimed at all Health Care Professionals involved in the care of infants within the Neonatal Service. These guidelines detail the recommended antibiotic treatment for patients in UHL neonatal units, and those neonates transferred from NNU to the postnatal wards for ongoing management.

Key Points:

- Neonatal sepsis requires prompt diagnosis and treatment with antibiotics administered within 1 hour of the decision to treat
- Be aware of risk factors and clinical indicators-Start antibiotic treatment in babies with any 'red flags' or with two or more 'non-red flag' risk factors or clinical indicators.
- Measure C-reactive protein 18-24 hours after starting antibiotics.
- Consider viral infections, especially Herpes Simplex Virus (HSV), when evaluating any baby with signs of infection
- Microbiology authorisation code is required beyond recommended antibiotic duration.

Related UHL documents:

| Documents | ID Number (if applicable) or Appendix No. |
|--|---|
| Antibiotic guideline for surgical prophylaxis and infection | C29/2015 |
| Gentamicin: Procedure for routine intravenous administration | |
| Gentamicin Therapeutic drug monitoring | |
| Prescription chart for: IV gentamicin only | |
| Audiology referral pathway for high gentamicin levels | C30/2015 |

Antibiotic Guideline for Early-Onset Neonatal Infection

Background:

Early-onset neonatal bacterial infection (infection with onset within 72 hours of birth) is less common than late-onset neonatal infection (infection with onset after 72 hours of birth) but is often severe. It is usually caused by organisms from the mother's genital tract. It can be due to Group B beta-haemolytic streptococci (leading cause in UK with overall mortality of 10% and is even higher in premature babies), Escherichia coli, Pseudomonas, Klebsiella, Streptococci other than Group B, Staphylococcus aureus, Haemophilus influenzae, Listeria monocytogenes, Gram negative anaerobes, Chlamydia trachomatis. Early-onset sepsis may develop suddenly and rapidly, and mortality is high, particularly in premature babies and those with low birth weight (birth weight between 1500 and 2499 grams). Even with antibiotic treatment, the mortality rate for early-onset infection in low birth weight babies is up to 26%. Babies who survive early-onset infection have prolonged hospital stays. Up to 7% of babies who survive GBS infection have a consequent disability [1].

Guidelines/Recommendations:

Review the maternal and neonatal history and carry out a physical examination of the baby including an assessment of the vital signs without delay.

Intravenous antibiotic therapy should be started as soon as possible and always within the first hour of the decision to treat, after appropriate cultures and investigations have been taken.

All antimicrobials should be reviewed daily. Microbiology authorisation code is required beyond recommended antibiotic duration ([Refer to Table 8](#)).

Recent maternal and infant microbiology results (where available) should be reviewed to identify if the patient is at risk of sepsis with a more resistant organism, which may not respond to standard first line therapy.

Follow guidance on timing of gentamicin assays and dosing provided in the IV monographs and pre-printed on the NNU prescription charts.

For recommended doses of antibiotics please refer to the neonatal drug doses policy and individual drug monographs available on NNU, Badgernet library and document management system. If in doubt, contact your Pharmacist for further advice.

For information on contraindications, cautions, drug interactions and adverse effects refer to the British National Formulary for children or the drug Summary of Product Characteristics.

Indications to commence antibiotics in early-onset neonatal sepsis

Use table 1, 2, 3, and 4 to identify 'Red Flag' and 'Non red flag' risk factors and clinical indicators for early-onset neonatal infection.

In babies with any red flags ([Table 1](#) and [Table 2](#)), or with two or more 'non-red flag' risk factors or clinical indicators ([Table 3](#) and [Table 4](#)), perform investigations (see below) and start antibiotic treatment.

In babies without red flags and only one risk factor or one clinical indicator, using clinical judgement, consider

- whether it is safe to withhold antibiotics, and
- whether it is necessary to monitor the baby's vital signs and clinical condition for at least 12 hours

In babies being monitored for possible infection

- if clinical concern increases, consider performing necessary investigations and starting antibiotic treatment.

Do not delay starting antibiotics pending the test results. If a baby needs antibiotic treatment it should be given as soon as possible and always within 1 hour of the decision to treat.

Use intravenous benzylpenicillin with gentamicin as the first choice antibiotic regimen for empirical treatment of suspected early-onset infection. Refer to Chart 1a, 1b and 1c for antibiotic guideline for suspected early-onset neonatal sepsis and necrotising enterocolitis (NEC).

Purulent eye discharge may indicate the presence of a serious infection (e.g. Chlamydia or Gonococcus) - start systemic treatment for possible gonococcal infection while awaiting the swab microbiology results ([Refer to Table 8](#)).

In babies with clinical signs of umbilical infection (for example, redness, increased skin warmth or swelling) - start intravenous flucloxacillin and gentamicin. Stop gentamicin if microbiology results do not indicate gram-negative infection.

Table 1. 'Red Flag' risk factors of possible early-onset neonatal infection

| | Red Flag Risk Factors |
|---|--|
| 1 | <p>Parenteral antibiotic treatment given to the woman for <u>confirmed or suspected invasive bacterial infection (such as septicemia)</u> at any time during labour, or in the 24-hour periods before and after the birth (this does not refer to intrapartum antibiotic prophylaxis)</p> <p>Follow the pathway in the Pyrexia and Sepsis in Labour guideline (C21/2017), discuss with obstetrician, and review maternal history, clinical status, antibiotic treatment and investigations (including CRP, blood culture if available)</p> |
| 2 | <p><u>Suspected or confirmed infection in another baby in the case of a multiple pregnancy</u></p> |

Table 2. 'Red Flag' clinical indicators of possible early-onset neonatal infection (observations and events in the baby)

| Red Flag Clinical Indicators | |
|-------------------------------------|---|
| 1 | Respiratory distress starting more than 4 hours after birth |
| 2 | Seizures |
| 3 | Need for mechanical ventilation in a term baby |
| 4 | Signs of shock |

Table 3. 'Non Red Flag' risk factors of possible early-onset neonatal infection

| Non Red Flag Risk Factors | |
|----------------------------------|--|
| 1 | Invasive (GBS bacteraemia and/or meningitis, GBS pneumonia) group B streptococcal infection in a previous baby |
| 2 | Maternal GBS colonisation, bacteriuria or infection in the current pregnancy |
| 3 | Prelabour rupture of membranes |
| 4 | Preterm birth following spontaneous labour (before 37 weeks) |
| 5 | Suspected or confirmed rupture of membranes for more than 18 hours in a preterm birth |
| 6 | Intrapartum fever higher than 38 deg C, or confirmed or suspected chorioamnionitis |

Table 4. 'Non Red Flag' clinical indicators of possible early-onset neonatal infection (observations and events in the baby)

| Non Red Flag Clinical Indicators | |
|---|---|
| 1 | Altered behaviour or responsiveness |
| 2 | Altered muscle tone (e.g. floppiness) |
| 3 | Feeding difficulties (e.g. feed refusal) |
| 4 | Feed intolerance including vomiting, excessive gastric aspirates and abdominal distension |
| 5 | Abnormal heart rate (bradycardia and tachycardia) |
| 6 | Signs of respiratory distress |
| 7 | Apnoea |
| 8 | Signs of neonatal encephalopathy |
| 9 | Hypoxia (e.g. central cyanosis or reduced oxygen saturation level) |
| 10 | Jaundice within 24 hours of birth |
| 11 | Need for cardio-pulmonary resuscitation |
| 12 | Need for mechanical ventilation in a preterm baby |
| 13 | Persistent fetal circulation (Persistent pulmonary hypertension) |
| 14 | Temperature abnormality (<36 deg C or >38 deg C) unexplained by environmental factors |
| 15 | Unexplained excessive bleeding, thrombocytopenia, or abnormal |

| | |
|----|---|
| | coagulation (INR > 2.0) |
| 16 | Oliguria persisting beyond 24 hours after birth |
| 17 | Altered glucose homeostasis (hypoglycaemia or hyperglycemia) |
| 18 | Metabolic acidosis (base deficit of 10 mmol/Litre or greater) |
| 19 | Local signs of infection (e.g. affecting the skin or eye) |

Investigations for suspected early-onset sepsis to consider before administering the first dose of antibiotics include:-

- Blood Culture
- Full blood count (FBC) and C - reactive protein (CRP) (repeat 18-24 hours)
- CXR only if clinical signs suggestive of pneumonia
- Lumbar puncture (LP) before starting antibiotics if it is thought safe to do so and there is a strong clinical suspicion of infection, or there are clinical symptoms or signs suggesting meningitis.
- Eye swab for Chlamydia and Gonococcus (purulent eye discharge)
- Perform surface/local swab only in the presence of purulent discharge or signs of periumbilical cellulitis

Do not routinely perform urine culture/microscopy or surface/skin swabs as part of the investigation for early-onset neonatal infection in the absence of clinical signs.

If performing the lumbar puncture would unduly delay starting antibiotics, perform it as soon as possible after starting antibiotics. Contact microbiology to arrange urgent investigation.

Do not perform a repeat lumbar puncture in neonates who are receiving the antibiotic treatment appropriate to the causative organism and are making a good clinical recovery and/or before stopping antibiotic therapy if they are clinically well.

Meningitis should be diagnosed when there are clinical signs of sepsis and positive cerebro-spinal fluid (CSF) findings (increased white cells). Decreased CSF glucose & positive culture are additional features of meningitis. Refer to [Appendix 1](#) for normal (mean and range) CSF values in preterm and term infants.

Pneumonia needs to be considered in infants with clinical signs of respiratory distress with x-ray changes. Always complete diagnostic investigations as above but in addition send endotracheal tube (ETT) secretions if baby is intubated. Antibiotics are in line with early-onset sepsis as appropriate (Refer to [chart 1a](#), [1b](#), [1c](#) and [Table 8](#)).

If the ETT secretions are culture positive treat according to the organism. If no improvement, consult Microbiology and Neonatal Consultant.

If ETT secretions are culture negative and no improvement after 48 hours of early-onset sepsis antibiotics, consider changing antibiotics after discussion with Microbiology and Neonatal consultant.

If there is still no improvement, consider a) Ureaplasma, b) Chlamydia, c) pertussis: - and d) Viruses – take NPA and viral cultures. It is important to take appropriate samples sooner than later for investigation

If positive ETT secretions, but clinically well/asymptomatic – no treatment is required.

Ureaplasma urealyticum (UU)- is known to colonise women's genital tract and has been shown to be associated with preterm neonates with bronchopulmonary dysplasia (BPD). Macrolide antibiotics are known to be effective against Ureaplasma species. The potential of azithromycin as a chemoprophylactic agent for BPD in preterm neonates is still under exploration. PCR from ET aspirates helps in the diagnosis.

Macrolide antibiotics-Oral administration of erythromycin, particularly in the first 2 weeks of life, has been shown to increase the risk of developing infantile hypertrophic pyloric stenosis (IHPS). Intravenous erythromycin is also known to cause thrombophlebitis. Because of the advantages of once-daily dosing, and a shorter required course, azithromycin has seemingly replaced erythromycin as the macrolide of choice in the newborn period. However it is to be noted that IHPS is also reported with early use of azithromycin.

Investigations during antibiotic treatment in early-onset sepsis

Measure the C-reactive protein concentration at 18-24 hours after presentation and first CRP

Consider performing a lumbar puncture to obtain CSF sample, if it is thought safe to do so, if the baby is receiving antibiotics and did not have a lumbar puncture at presentation and:

- has a CRP of 10 mg/litre or greater, or
- has a positive blood culture, or
- does not respond satisfactorily to antibiotic treatment

Decision 36 hours after starting antibiotic treatment in early onset sepsis

Stop antibiotics at 36 hours if:

- the blood culture is negative, and
- the initial clinical suspicion of infection was not strong, and
- the baby's clinical condition is reassuring with no clinical indicators of possible infection, and
- the levels and trends of CRP are < 10.

Duration of antibiotics in early onset sepsis without meningitis

The usual duration of antibiotic treatment for babies with a positive blood culture, and for those with negative blood culture but in whom there has been strong suspicion of sepsis, should be 7 days. Refer to [table 8](#) for further details and point at which microbiology authorisation code is required.

Consider continuing antibiotic for more than 7 days if:

- the baby has not yet fully recovered, or
- this is advisable, based on the pathogen identified on blood culture (seek expert microbiological advice if necessary)

If continuing antibiotics for longer than 36 hours despite negative blood cultures, review the baby at least once every 24 hours. On each occasion using clinical judgement, consider whether it is appropriate to stop antibiotic treatment, taking account of:

- the level of initial clinical suspicion of infection and
- the baby's clinical progress and current condition, and
- the levels and trends of CRP.

Management of early-onset meningitis in neonatal unit

If a baby is admitted to NNU and meningitis is suspected but the causative pathogen is unknown (e.g. CSF is uninformative), treat with intravenous amoxicillin and cefotaxime.

If a baby's meningitis is shown to be due to gram negative infection either by CSF gram stain or culture, stop amoxicillin and treat with cefotaxime alone.

If a baby's meningitis is shown by CSF gram stain to be due to gram positive infection, continue treatment with intravenous amoxicillin and cefotaxime while awaiting the CSF culture result and seek expert microbiology advice.

If CSF culture is positive for GBS consider changing antibiotic treatment to benzylpenicillin for at least 14 days (Maximum 21 days). NICE guidance also suggests the addition of gentamicin treatment for 5 days. However UHL microbiology guidance does not recommend gentamicin as it does not cross blood brain barrier.

If the blood culture or CSF culture is positive for Listeria, stop cefotaxime and treat with amoxicillin. NICE guidance also suggests addition of gentamicin treatment. However UHL microbiology guidance does not recommend gentamicin as it does not cross blood brain barrier.

If the CSF culture identifies gram positive bacterium other than GBS or Listeria seek expert microbiological advice on management.

Chart 1a: Antibiotic guideline for early-onset neonatal sepsis (<3 days)

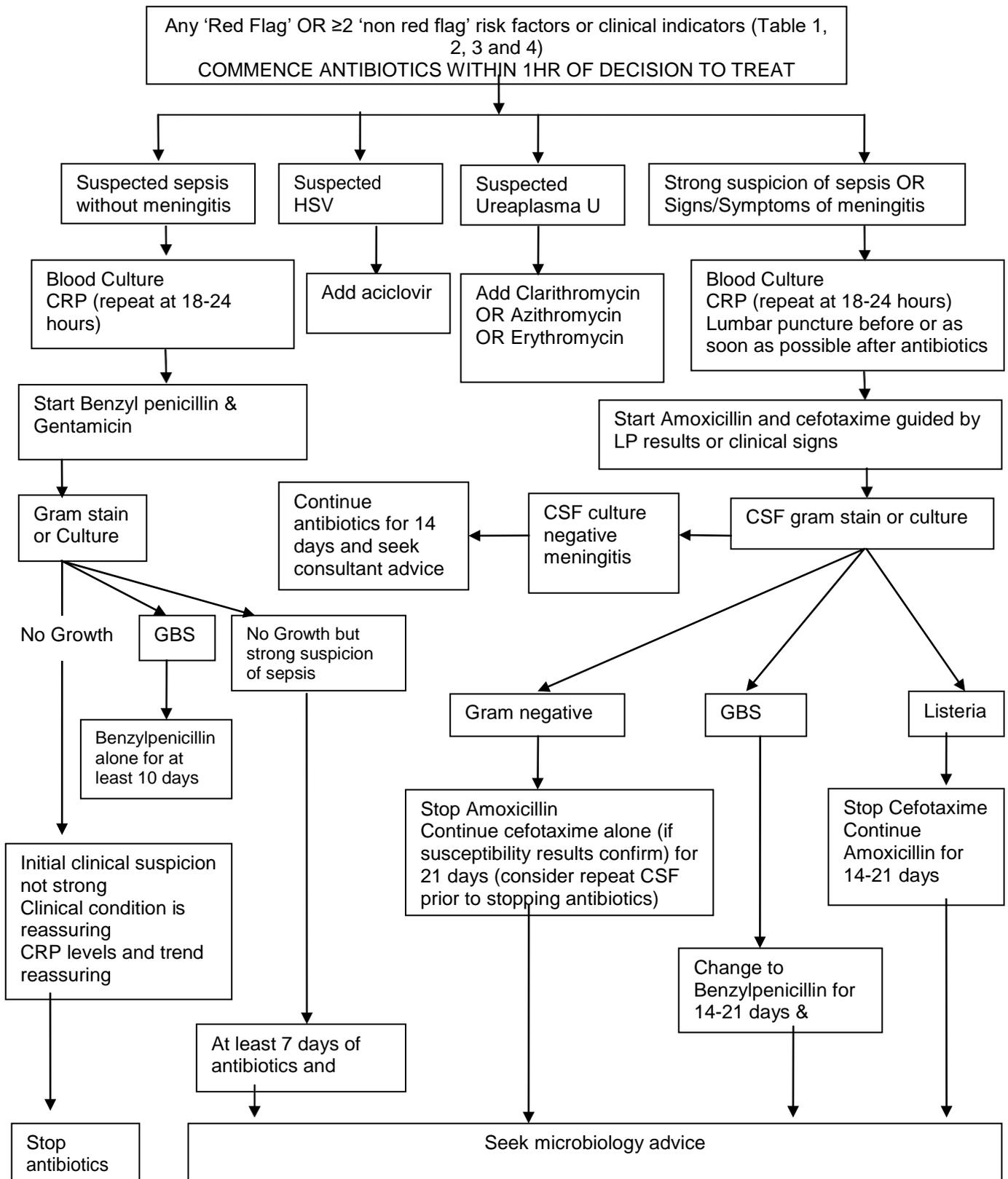


Chart 1b: Antibiotic guideline for possible early-onset neonatal sepsis (<3 days)

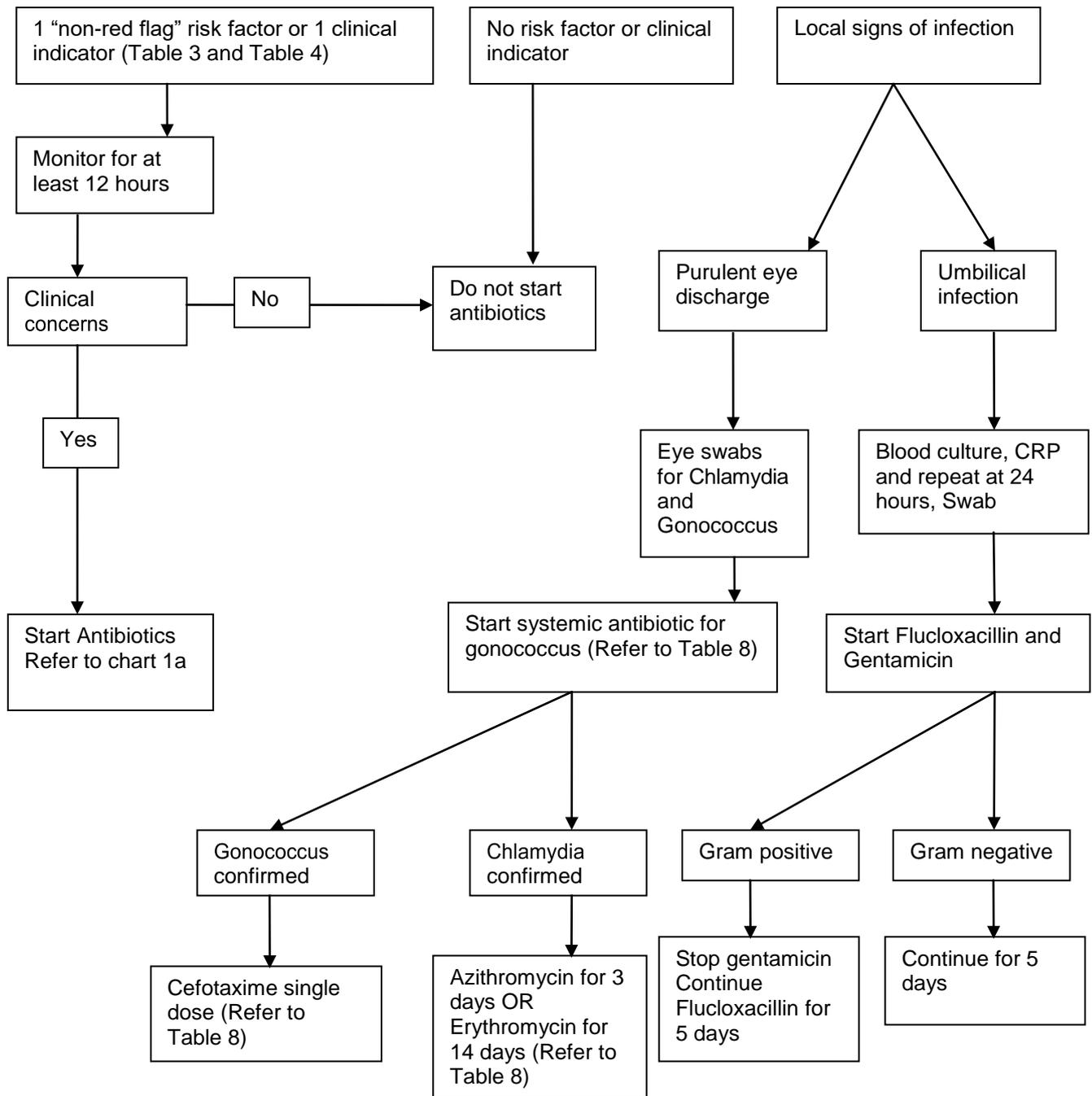
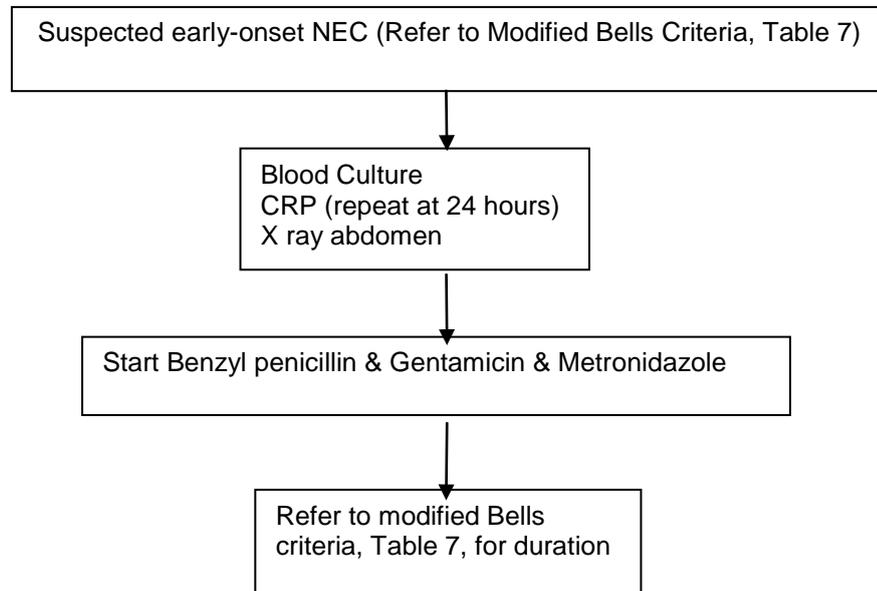


Chart 1c: Antibiotic guideline for suspected Necrotising Enterocolitis within 3 days after birth



Antibiotic Guideline for possible Late-onset Neonatal Infection

Background:

The incidence of late-onset neonatal infections (infection with onset after 72 hours of birth) is 4.4 per 1000 live births with a mortality rate of 9%. The incidence of meningitis in these infants is 9% [3]. The commonest organisms are (in order of decreasing frequency) [4]:- Coagulase negative Staphylococcus species. 55%, Staphylococcus aureus 9%, Enterococcus / group D Streptococcus 5%, Streptococcus agalactiae (Group B beta-haemolytic Streptococcus) 2%, Enterobacter 4%, Escherichia coli 4%, Klebsiella 4%, Pseudomonas 2%, Other Gram negatives 4%, Candida albicans 5%, Candida parapsilosis 2%.

Guidelines/Recommendations:

Review the maternal and neonatal history and carry out a physical examination of the baby including an assessment of the vital signs without delay.

Intravenous antibiotic therapy should be started as soon as possible and always within the first hour of the decision to treat, after appropriate cultures and investigations have been taken.

All antimicrobials should be reviewed daily. Microbiology authorisation code is required beyond recommended antibiotic duration ([Refer to Table 8](#))

Follow guidance on timing of vancomycin and gentamicin assays and dosing provided in the IV monographs and pre-printed on the NNU prescription charts.

Audiology assessment at 8 months is arranged for infants identified to have high gentamicin levels (pre dose greater than 2mg/l and/or post dose greater than 12mg/l) (Refer to guideline)

For recommended doses of antibiotics please refer to the neonatal drug doses policy and individual drug monographs available on NNU, Badgernet library and on the document management system. If in doubt, contact your Pharmacist for further advice.

For information on contraindications, cautions, drug interactions and adverse effects refer to the British National Formulary for children or the drug Summary of Product Characteristics.

Indications to commence antibiotics in late-onset sepsis

Refer to [Tables 5 & 6](#) to identify 'Strong' and 'Suggestive' clinical indicators respectively for possible late-onset neonatal infection.

In babies with clinical indicators of possible late onset neonatal infection, perform investigations and start antibiotic treatment as per [Chart 2](#).

Perform a lumbar puncture to obtain a cerebrospinal fluid sample before starting antibiotics if it is thought safe to do so and

- there is a strong clinical suspicion of infection, or
- there are clinical symptoms or signs suggesting meningitis

If performing the lumbar puncture would unduly delay starting antibiotics, perform it as soon as possible after starting antibiotics.

Do not delay starting antibiotics pending the test results. If a baby needs antibiotic treatment it should be given as soon as possible and always within 1 hour of the decision to treat

Use intravenous Flucloxacillin with Gentamicin as the first choice antibiotic regimen for empirical treatment of suspected late-onset infection. Use intravenous Cefotaxime with Vancomycin as the antibiotic regimen when empirical changing over from Flucloxacillin and Gentamicin.

Table 5. 'Strong' Clinical indicators of possible late-onset neonatal infection

| | Strong Clinical Indicators |
|---|---|
| 1 | Signs of shock |
| 2 | Seizures |
| 3 | Need for cardio-pulmonary resuscitation |
| 4 | Apnoea in term baby |
| 5 | Need for mechanical ventilation in a term baby |
| 6 | Unexplained excessive bleeding, thrombocytopenia, or abnormal coagulation (INR > 2.0) |

Table 6. 'Suggestive' clinical indicators for possible late-onset neonatal infection

| | Suggestive Clinical Indicators |
|---|---|
| 1 | Altered behaviour or responsiveness |
| 2 | Altered muscle tone (e.g. floppiness) |
| 3 | Feeding difficulties (e.g. feed refusal) |
| 4 | Feed intolerance including vomiting, excessive gastric aspirates and abdominal distension |
| 5 | Abnormal heart rate (bradycardia and tachycardia) |
| 6 | Signs of respiratory distress |
| 7 | Need for mechanical re-ventilation in a preterm baby |

| | |
|----|---|
| 8 | Hypoxia (e.g. central cyanosis or reduced oxygen saturation level) |
| 9 | Need for mechanical ventilation in a preterm baby |
| 10 | Temperature abnormality (< 36 or > 38 C) unexplained by environmental factors |
| 11 | Unexplained excessive bleeding, thrombocytopenia, or abnormal coagulation (INR > 2.0) |
| 12 | Oliguria persisting beyond 24 hours |
| 13 | Altered glucose homeostasis (hypoglycaemia or hyperglycemia) |
| 14 | Metabolic acidosis (base deficit of 10 mmol/Liter or greater) |
| 15 | Local signs of infection (e.g. affecting the skin or eye) |

Investigations in Late-onset sepsis before administering the first dose of antibiotics include:-

- Blood Culture
- Full blood count (FBC) and C-reactive protein (CRP) (repeat 18-24 hours)
- CXR only if clinical signs suggestive of pneumonia
- Lumbar puncture if it is thought safe to do so and there is a strong clinical suspicion of infection, or there are clinical symptoms or signs suggesting meningitis. Contact microbiology to arrange urgent investigation
- Local skin/surface swab only in the presence of clinical signs of a localised infection (purulent discharge or signs of periumbilical cellulitis)
- Supra-pubic aspirate (SPA) is considered gold standard in the diagnosis of neonatal UTI. However a clean catch or a catheter specimen of urine may also be used. **Bag specimens should not be used for urine culture.**

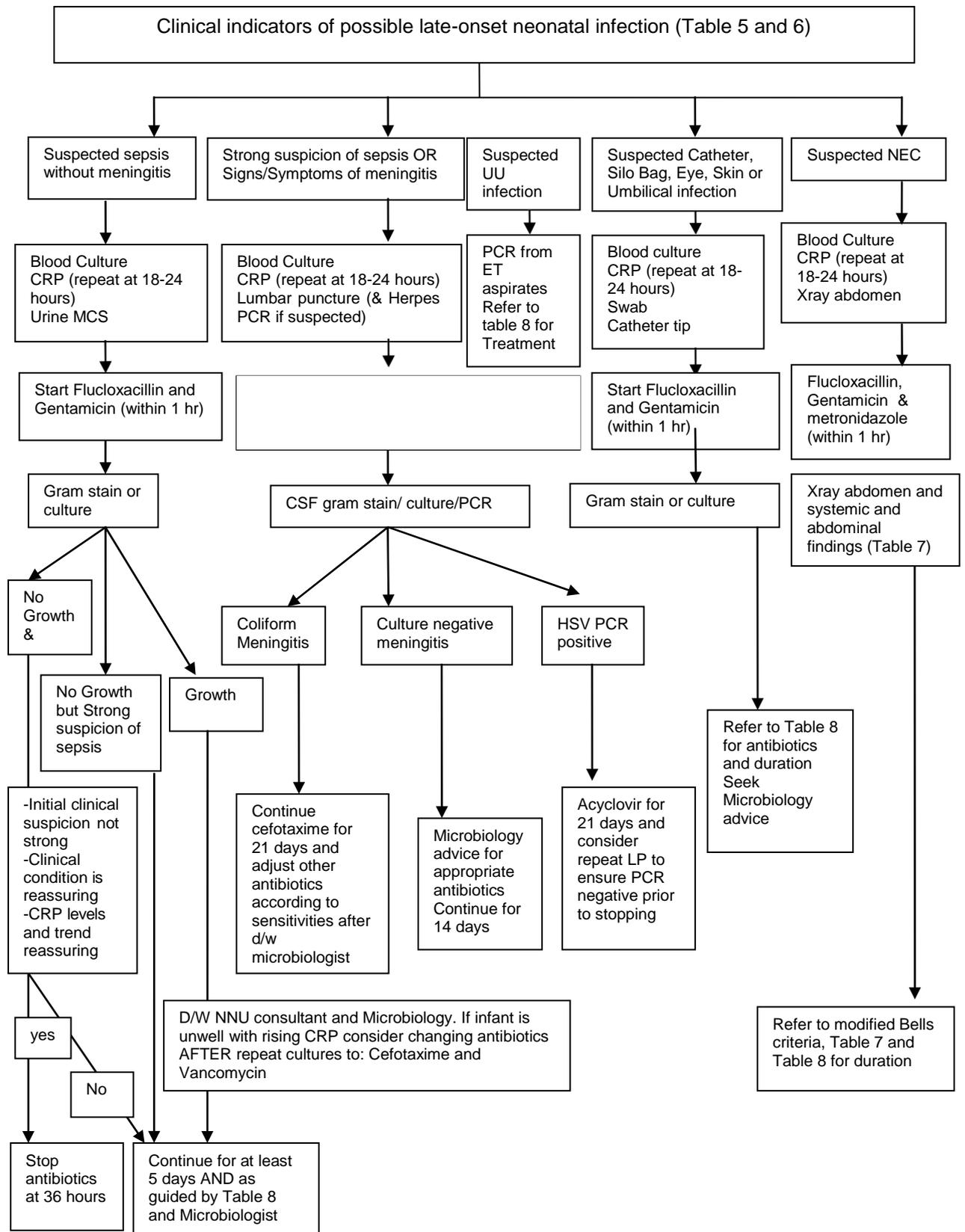
Guidance for SPA v Clean catch v Catheter urine specimen

In a very ill baby, strongly suspected of having a UTI and requiring immediate antibiotics: Collect SPA specimen, Commence antibiotics even if SPA fails, Re-attempt collection of SPA as soon as possible.

In a baby strongly suspected of having a UTI and requiring antibiotics, but not immediately: Collect SPA specimen, If SPA unsuccessful, retry after one hour, Consider use of ultrasound to aid sample collection, If SPA unsuccessful collect catheter specimen, Defer antibiotic therapy until catheter urine obtained, but do not await the result.

In a baby with an illness that might be a UTI but not immediately requiring treatment: Collect SPA specimen, If SPA unsuccessful, collect clean catch urine specimen, If clean catch urine specimen result equivocal, re-attempt SPA specimen and await the result, If clean catch urine specimen strongly suggests UTI, collect SPA specimen and commence antibiotics, Adjust therapy when SPA result known.

Chart 2: Antibiotic guideline for possible late-onset neonatal sepsis (> 3 days)



Meningitis should be diagnosed when there are clinical signs of sepsis and positive cerebro-spinal fluid (CSF) findings (increased white cells) ([Refer to Appendix 1](#)). Decreased CSF glucose & positive culture are additional features of meningitis.

Pneumonia needs to be considered in infants with clinical signs of respiratory distress with x-ray changes. Always complete diagnostic investigations as above but in addition send endotracheal tube (ETT) secretions if baby is intubated. Common organisms are coliforms, Pseudomonas, Group B Streptococcus and Staphylococcus aureus. Antibiotics are for late-onset sepsis as appropriate (Refer to [chart 2](#) and [Table 8](#) for further details).

If the ETT secretions are culture positive treat according to the organism. If no improvement, consult Microbiology and Neonatal Consultant.

If ETT secretions are culture negative and no improvement after 48 hours of late-onset sepsis antibiotics, consider changing antibiotics after discussion with Microbiology and Neonatal consultant.

If there is still no improvement, consider a) Ureaplasma, b) Chlamydia, c) pertussis:- and d) Viruses – take NPA and viral cultures. It is important to take appropriate samples sooner than later for investigation

If positive ETT secretions, but clinically well / asymptomatic – no treatment.

Ureaplasma urealyticum (UU)- is known to colonise women's genital tract and has been shown to be associated with preterm neonates with bronchopulmonary dysplasia (BPD). Macrolide antibiotics are known to be effective against Ureaplasma species. The potential of azithromycin as a chemoprophylactic agent for BPD in preterm neonates is still under exploration. PCR from ET aspirates helps in the diagnosis.

Macrolide antibiotics-Oral administration of erythromycin, particularly in the first 2 weeks of life, has been shown to increase the risk of developing infantile hypertrophic pyloric stenosis (IHPS). Intravenous erythromycin is also known to cause thrombophlebitis. Because of the advantages of once-daily dosing, and a shorter required course, azithromycin has seemingly replaced erythromycin as the macrolide of choice in the newborn period. However it is to be noted that IHPS is also reported with early use of azithromycin.

Urinary Tract Infections (UTI) in the neonate may be indistinguishable from generalised sepsis and therefore a urine sample should be considered a part of the diagnostic tests in late-onset sepsis. UTI in the neonate has long-term implications and the diagnosis must be carefully confirmed. It is essential therefore to confirm bacteria and pus cells on urine microscopy. Supra-pubic aspirate (SPA) is considered gold standard in the diagnosis of neonatal UTI. However a clean catch or a catheter specimen of urine may also be used.

Necrotising Enterocolitis [Table 7](#) below shows modified Bell's staging for NEC and provides a guide to antibiotic duration according to stage of NEC.

Table 7. Modified Bell's Staging Criteria for Necrotizing Enterocolitis (NEC)

| Stage | Systemic signs | Abdominal signs | Radiographic signs | Treatment |
|--|---|---|--|--|
| IA Suspected | Temperature instability, apnea, bradycardia, lethargy | Gastric retention, abdominal distention, emesis, heme-positive stool | Normal or intestinal dilation, mild ileus | NPO, antibiotics x 3 days |
| IB Suspected | Same as above | Grossly bloody stool | Same as above | Same as IA |
| IIA Definite, mildly ill | Same as above | Same as above, plus absent bowel sounds with or without abdominal tenderness | Intestinal dilation, ileus, pneumatosis intestinalis | NPO, antibiotics x 7 to 10 days |
| IIB Definite, moderately ill | Same as above, plus mild metabolic acidosis and thrombocytopenia | Same as above, plus absent bowel sounds, definite tenderness, with or without abdominal cellulitis or right lower quadrant mass | Same as IIA, plus ascites | NPO, antibiotics x 14 days |
| IIIA Advanced, severely ill, intact bowel | Same as IIB, plus hypotension, bradycardia, severe apnea, combined respiratory and metabolic acidosis, <u>DIC</u> , and neutropenia | Same as above, plus signs of peritonitis, marked tenderness, and abdominal distention | Same as IIA, plus ascites | NPO, antibiotics x 14 days, fluid resuscitation, inotropic support, ventilator therapy, paracentesis |
| IIIB Advanced, severely ill, perforated bowel | Same as IIIA | Same as IIIA | Same as above, plus pneumoperitoneum | Same as IIA, plus surgery |

DIC: disseminated intravascular coagulation

NPO: "nil per os" or nothing by mouth

Endocarditis should be suspected when there is evidence of systemic infection and there is either a congenital (or acquired) cardiac abnormality or when there is a central venous line in place. In general it requires clinical, laboratory and echocardiographic evidence of infection. Ensure at least three

separate blood cultures are taken prior to antibiotic therapy (but do not delay antibiotic therapy if the infant is unwell).

Special circumstances (consult microbiology department.):

Encephalopathic/seizures: Consider CSF/plasma for Herpes PCR and virology screening.

Ventriculo-peritoneal shunt in situ: Request CSF gram stain for appropriate antibiotics ([Refer to Table 8](#)).

Investigations during antibiotic treatment in late-onset sepsis

In babies given antibiotics because of clinical indicators of possible infection, measure the C-reactive protein concentration 18-24 hours after presentation.

Consider performing a lumbar puncture to obtain CSF sample in a baby who did not have a lumbar puncture at presentation is receiving antibiotics, if it is thought safe to do so and if the baby:

- has a CRP of 10 mg/litre or greater or
- has a positive blood culture, or
- does not respond satisfactorily to antibiotic treatment

Decision 36 hours after starting antibiotic treatment in late-onset sepsis

In babies given antibiotics because of clinical indicators of possible infection, consider stopping the antibiotics at 36 hours if:

- the blood culture is negative, and
- the initial clinical suspicion of infection was not strong, and
- the baby's clinical condition is reassuring with no clinical indicators of possible infection, and
- the levels and trends of CRP are reassuring

Duration of antibiotics in late-onset sepsis without meningitis

The usual duration of antibiotic treatment for babies with a positive blood culture, and for those with negative blood culture but in whom there has been strong suspicion of sepsis, should be 5 days. Refer to table 8 for further details and point at which microbiology authorisation code is required.

Consider continuing antibiotic for more than 5 days if:

- the baby has not yet fully recovered, or
- this is advisable, based on the pathogen identified on blood culture (seek expert microbiological advise if necessary)

If continuing antibiotics for longer than 36 hours despite negative blood cultures, review the baby at least once every 24 hours. On each occasion using clinical judgement, consider whether it is appropriate to stop antibiotic treatment, taking account of:

- the level of initial clinical suspicion of infection
- the baby's clinical progress and current condition, and
- the levels and trends of CRP

Management of late-onset meningitis for baby's in neonatal unit

In a baby with suspected sepsis AND meningitis (CSF shows a meningitis picture) add cefotaxime IV to any current antibiotics, then adjust according to identification and sensitivities after discussion with microbiologist.

Prescribing antimicrobials

[Table 8](#) gives details of the first line antimicrobials recommended for specific neonatal infection, and the required duration of treatment. Antimicrobials used in line with these recommendations can be initiated without prior microbiologist approval. Duration of treatment is restricted to that detailed in the table. If you wish to continue treatment beyond this period authorisation MUST be sought from microbiology and documented on the drug chart and in the medical records.

Certain antimicrobials cannot be initiated without prior microbiology approval because of factors including: High risk of unwanted effects, Limited availability, Expense & Unique mechanism of action to be reserved for the treatment of organisms resistant to standard antimicrobials.

These antimicrobials, along with details of their restrictions, are listed on the Trust Antimicrobial website (search alphabetically in A-Z bugs and drugs section).

Prescribers MUST seek microbiological approval for permission to prescribe an antimicrobial from the Trust-designated 'restricted list of antimicrobials', prior to starting treatment. This approval must be sought even out of hours and must be recorded (as a verification number) on the antimicrobial prescription and in the medical notes by the prescriber.

This restricted use of antimicrobials also helps to reduce antimicrobial burden and ensure the choice of antimicrobial is clinically appropriate.

Appendix 1: Normal CSF values (Mean and Range) [2]:

| Type of Infant | WBC / mm ³ | Protein (g/l) | Glucose (mmol/l) |
|-------------------|-----------------------|----------------|------------------|
| Preterm < 28 days | 9 (0-30) | 1 (0.5-2.5)* | 3 (1.5-5.5) |
| Term < 28 days | 6 (0-21) | 0.6 (0.3-2.0)* | 3 (1.5-5.5) |

*Protein values are higher in the first week of life and depend on the red cell count. A white cell count of more than 21/mm³ with a protein value of more than 1 g/l with less than 1000 red cells is suspicious of meningitis.

NB. Plasma glucose should be taken immediately prior to the LP. CSF glucose is usually 70-80% of plasma glucose (normal). A low CSF glucose can persist for many weeks following IVH. If CSF results are suspicious then always consider a repeat LP in next 12-24 hours (discuss with Consultant). Antibiotic therapy should initially be according to the unit guidelines (Refer to Chart [1a](#), [1b](#), [1c](#)) but will subsequently be guided by the CSF Gram stain and, later, by culture results.

Table 8. Antimicrobial guidance for UHL neonatal services

| Infection | First antimicrobial(s) | Line | Recommended Duration | Notes | Point at which microbiology verification is required |
|--|---|------|--|--|--|
| <p>Presumed early onset sepsis – with signs presenting within 72 hours of birth</p> <ul style="list-style-type: none"> (Any ‘Red Flag’ OR ≥ 2 ‘non red flag’ risk factors or clinical indicators (Table 1,2,3 and 4) | <p>Benzympenicillin IV & Gentamicin IV</p> <p>Add extra gram –ve cover if gram –ve infection confirmed and stop benzympenicillin.</p> | | <p>Stop if culture negative at 36 hours. If positive continue treatment for 7 days, antibiotic choice guided by sensitivities.</p> | <p>If ongoing signs of sepsis at day 5 of treatment discuss with microbiology.</p> | <p>Treatment beyond 7 days</p> |
| <p>Presumed early onset sepsis – with signs presenting within 72 hours of birth</p> <ul style="list-style-type: none"> (1 ‘non red flag’ risk factor or 1 ‘non red flag’ clinical indicator (Table 3 and 4) and clinical concerns increases during monitoring period) | <p>Benzympenicillin IV & Gentamicin IV</p> <p>Add extra gram –ve cover if gram –ve infection confirmed and stop benzympenicillin.</p> | | <p>Stop if culture negative at 36 hours. If positive continue treatment for 7 days, antibiotic choice guided by sensitivities.</p> | <p>If ongoing signs of sepsis at day 5 of treatment discuss with microbiology.</p> | <p>Treatment beyond 7 days</p> |
| <p>Presumed late onset sepsis. Presenting after the first 72 hours of life</p> <ul style="list-style-type: none"> Clear evidence of localised infection, e.g. umbilical flare. | <p>Flucloxacillin IV & Gentamicin IV</p> | | <p>Stop if culture negative at 36 hours. If positive continue for 5 days, antibiotic choice guided by sensitivities.</p> | <p>If ongoing signs of sepsis at day 5 of treatment discuss with microbiology.</p> | <p>Treatment beyond 5 days</p> |

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| Presumed late onset sepsis. Presenting after the first 72 hours of life <ul style="list-style-type: none"> Suspected sepsis AND meningitis | Add Cefotaxime to any current antibiotics or commence Amoxicillin, cefotaxime and gentamicin | Depends upon identification and sensitivities after discussion with microbiologist. | | Treatment beyond 21 days |
| Meningitis, initial treatment when causative pathogen unknown (blind treatment) | Amoxicillin IV & Cefotaxime IV | See below | Notify public health. If subsequently confirmed gram –ve infection can stop amoxicillin | |
| Meningitis – confirmed gram –ve infection | Cefotaxime IV (guided by CSF antimicrobial susceptibilities when available) (Stop Amoxicillin) | For at least 21 days. If clinical progress is slow, consider extending duration of treatment (Consider repeat CSF prior to stopping antibiotics) | Notify public health. Seek expert microbiology advice | Treatment beyond 21 days |
| Meningitis – Group B streptococcus on culture | Benzylpenicillin IV | Benzylpenicillin for 14-21 days | Notify public health | Treatment beyond 14 days |
| Listeria meningitis - Blood or CSF culture +ve | Amoxicillin IV (Stop cefotaxime) | For 14-21 days | Notify public health | Treatment beyond 21 days |
| Culture negative meningitis | Amoxicillin IV & Cefotaxime IV | For 14 days and discuss with consultant | Notify public health | Treatment beyond 14 days |

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| Suspected Herpes Simple Virus (HSV)- Encephalopathy/seizures/atypical CSF | Aciclovir IV | For 21 days if herpes PCR positive and review | Discuss with Consultant Virologist | Treatment beyond 21 days |
| Group B streptococcal septicaemia (Blood culture +ve or baby symptomatic) | Benzylpenicillin IV (Stop Gentamicin IV) | For 10 days. | | Treatment beyond 10 days |
| Group B streptococcal osteomyelitis | Benzyl penicillin IV | For 4 weeks | | Treatment beyond 4 weeks |
| Congenital pneumonia - | Benzylpenicillin IV & Gentamicin IV | For 7 days, antibiotic choice guided by sensitivities. | If ongoing signs of sepsis at day 7 of treatment discuss with microbiology. | Treatment beyond 7 days |
| Staphylococcal aureus septicaemia | Flucloxacillin IV | For at least 14 days | Duration will depend on focus of infection. Discuss all cases with microbiology. | Treatment beyond 14 days |
| Coagulase negative staphylococcal septicaemia | Vancomycin IV (must request vancomycin MIC from micro) | For 7-10 days | | Treatment beyond 10 days |

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| Nosocomial infection -unknown cause | Flucloxacillin IV & Gentamicin IV | Stop if culture negative at 36 hours. If positive continue for 5 days, and review antibiotic choice guided by sensitivities. | If ongoing signs of sepsis at day 5 of treatment discuss with microbiology. | Treatment beyond 5 days |
| Nosocomial Infection -presumed catheter related sepsis | Vancomycin IV & Cefotaxime IV Consider removal of central line | Continue for a minimum of 7 days. If sensitivities indicate sensitive to flucloxacillin switch to IV flucloxacillin for remainder of course. | | Treatment beyond 7 days |
| Necrotising enterocolitis at < 72 hours of age | Benzylpenicillin IV, Gentamicin IV, Metronidazole IV | For up to 14 days | Authorisation code not required. | Treatment beyond 14 days |
| Necrotising enterocolitis at 72 hours of age or greater | Flucloxacillin IV, Gentamicin IV, Metronidazole IV | For up to 14 days | Authorisation code not required. | Treatment beyond 14 days |
| Neonatal Herpes Simplex Virus | Aciclovir IV | For 14 days. Give for 21 days if CNS involvement. Consider repeat LP to ensure herpes PCR negative prior to stopping acyclovir. Consider 6 months of oral acyclovir to prevent relapse | Discuss all cases with Virology. | Treatment beyond 21 days |

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| Silo bag infection ("silo" is a bag made from silastic or similar material which allows gravity to slowly return the exposed intestines to the abdominal cavity in conditions such as omphalocele, exomphalos and gastroschisis) | Flucloxacillin IV, Gentamicin IV and Metronidazole IV | For 14 days guided by sensitivities. | If recent course of flucloxacillin substitute cefotaxime IV | Treatment beyond 14 days |
| Candidaemia | Fluconazole IV | 14- 21 days. | Discuss with microbiology | Treatment beyond 21 days |
| Staphylococcus aureus osteomyelitis | Flucloxacillin IV | 6 weeks | | Treatment beyond 6 weeks |
| Urinary tract infection [7, 8] | Gentamicin IV & amoxicillin IV | Up to 7 days –change antibiotic if necessary once sensitivity known. | | Treatment beyond 7 days |
| Urinary tract infection prophylaxis after recurrent infection where no underlying pathophysiology | Trimethoprim oral once daily | Management guided by specialist renal clinic | | Before commencing treatment |
| Urinary tract infection prophylaxis where underlying pathophysiology known | Trimethoprim oral once daily | Management guided by specialist renal clinic. | | Not required |
| Bacterial Endocarditis | Discuss with microbiology before treatment | 4-6 weeks and review with clinical course and blood cultures | | Treatment beyond 6 weeks |
| Pseudomonas pneumonia | Ceftazidime and gentamicin | For 7 days. | | Treatment beyond 7 days |

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| Suspected Ureaplasma Pneumonia First line-Clarithromycin Second line-Azithromycin/Erythromycin | Clarithromycin IV if oral route not available OR | For 10 days Switch to oral route when appropriate | | Treatment beyond 10 days |
| | Azithromycin PO OR | For 10 days. | | Treatment beyond 10 days |
| | Erythromycin IV | For 10 days | | Treatment beyond 10 days |
| Chlamydia Pneumonia Or Conjunctivitis First line-Erythromycin Second line-Azithromycin | Erythromycin PO/IV | For 14 days | | Treatment beyond 14 days |
| | Azithromycin PO | For 3 days | | Treatment beyond 3 days |
| VP shunt Gram stain shows a <i>Staphylococcus species</i> . | Vancomycin IV Rifampicin PO | For 14 days. | | Treatment beyond 14 days |

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| VP shunt Gram stain shows Coliforms | Cefotaxime IV Gentamicin IV | For 14 days | | Treatment beyond 14 days |
| VP shunt Gram stain shows no bacteria | Vancomycin IV Cefotaxime IV | For 14 days | | Treatment beyond 14 days |
| Conjunctivitis with purulent eye discharge in 1 st 72 hours (possible congenital gonococcal infection) | Cefotaxime 100mg IV /IM | Single dose | Take swabs urgently for microbiological investigation to include Chlamydia and gonococcus. Start systemic treatment with cefotaxime whilst awaiting swab results. | Not required |
| Umbilical infection | Flucloxacillin IV and gentamicin IV | For 5 days | Stop gentamicin if swab culture indicates no gram –ve infection | Treatment beyond 5 days |

Audit standards

1. Microbiology authorisation codes requested when giving antibiotics beyond recommended duration.
2. Give intravenous antibiotics within 1 hour of decision to treat
3. Intravenous Benzylpenicillin and Gentamicin is used as first line antibiotics for early-onset neonatal sepsis
4. Intravenous Flucloxacillin and Gentamicin is used as first line antibiotics for late-onset neonatal infection
5. Stop antibiotics at 36 hours if blood culture is negative, CRP level and trend is normal, clinical condition good and initial suspicion was not strong

Annual Surveillance

1. Incidence of early, late and nosocomial infection (blood positive and negative)
2. Resident bacterial flora and sensitivities to antibiotics.
3. Long line sepsis incidence, organisms, and antibiotic sensitivities

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