Late Onset Sepsis in the Neonate - Full Clinical Neonatal Guideline

Reference no.:CG/NICU/4075/22

1. Introduction

To optimise the antibiotic therapy in Neonatal Intensive Care

2. Aim and Purpose

For medical staff to apply this policy applies to all the neonates admitted to Neonatal Intensive Care/Postnatal ward and University Hospitals of Derby and Burton.

3.0 Main body of Guidelines

Choosing appropriate antibiotics is an important part of managing the new born infant admitted to Neonatal Intensive Care. Close liaison with the Microbiology Department is essential in optimising antibiotic therapy. The following guidelines are suggested. For guidance on the management of Early onset neonatal infection (EONI) – see guideline Trust Policies Procedures & Guidelines catalog › Details for: Management of Early Onset Neonatal Sepsis Full Clinical Guideline (koha-ptfs.co.uk)

3.1 Late Onset Neonatal Sepsis

Late onset neonatal infection (LONI) typically presents 72 hours or more after birth and is usually acquired from the care giving environment. Coagulase negative Staphylococci (CoNS) accounted for nearly 70% of isolates from babies with late-onset infection followed by Staphylococcus aureus, E coli and GBS.

When assessing or reviewing a baby:

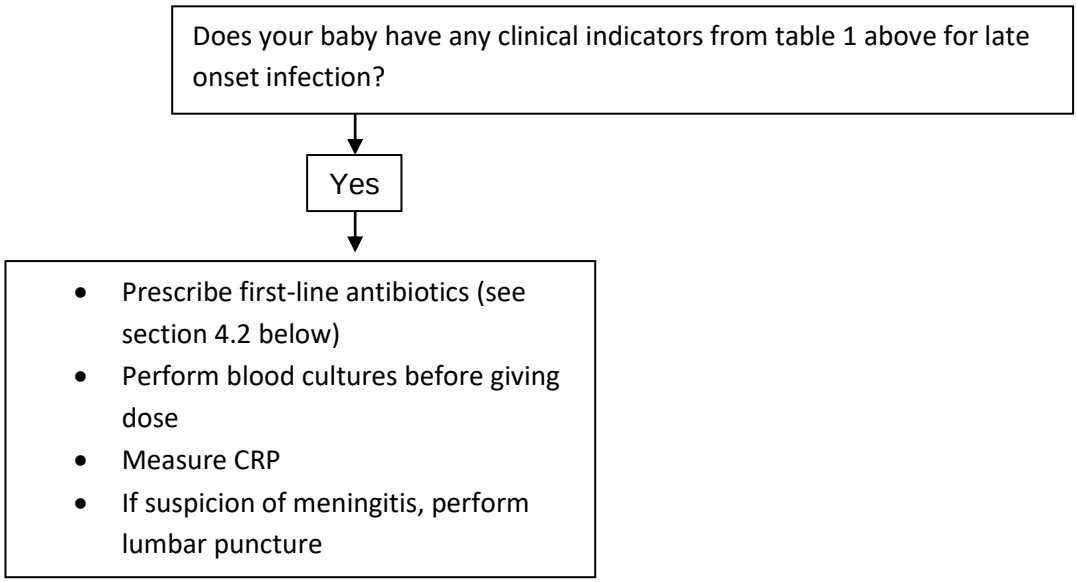
1. Check for, the possible clinical indicators of late-onset neonatal infection shown in table 1 below.
2. Consider that prematurity, mechanical ventilation, history of surgery and presence of a central catheter are associated with greater risk of late-onset neonatal infection.
3. Think about infection in the other babies when one baby from a multiple birth has infection.

	Indicators
Behaviours	• Parent or care-giver concern for change in behaviour • Appears ill to a healthcare professional • Does not wake, or if roused does not stay awake • Weak high-pitched or continuous cry
Respiratory	• Raised respiratory rate: 60 breaths per minute or more • Grunting • Apnoea • Oxygen saturation of less than 90% in air or increased oxygen requirement over baseline

Circulation and hydration	• Persistent tachycardia: heart rate 160 beats per minute or more • Persistent bradycardia: heart rate less than 100 beats per minute
Skin	• Mottled or ashen appearance • Cyanosis of skin, lips or tongue • Non-blanching rash of skin
Other	• Temperature 38°C or more unexplained by environmental factors • Temperature less than 36°C unexplained by environmental factors • Alterations in feeding pattern • Abdominal distension • Seizures • Bulging fontanelle

Table 1: Clinical indicators of possible late-onset neonatal infection (observations and events in the baby)

3.2 Investigations before starting antibiotics in babies who may have late-onset infection



3.3 Choice of Antibiotics in Late Onset Neonatal Sepsis

If a baby needs antibiotic treatment, give this as soon as possible and always within 1 hour of the decision to treat.

For babies with suspected late-onset neonatal infection who are already in a neonatal unit:

- give a combination of narrow-spectrum antibiotics (such as intravenous flucloxacillin plus gentamicin – dosing below) as first-line treatment
- use local antibiotic susceptibility and resistance data when deciding which antibiotics to use
- give antibiotics that are effective against both Gram-negative and Gram-positive bacteria

- where necrotising enterocolitis is suspected, also include an antibiotic that is active against anaerobic bacteria (such as metronidazole – dosing below).

Current recommended dose:

Drug	Dose	Age	Frequency
Flucloxacillin	50mg/kg (dose rounded to the **NEAREST** 10mg)	< 7days	12 hourly
		7 – 20 days	8 hourly
		≥ 21 – 28 days	6 hourly

- *this guideline should be used in conjunction with the most up to date version of the BNFc and administration should be guided by Medusa
- **for doses in infants >28 days old – refer to most up to date BNFc

Drug	Dose	Age	Frequency
Gentamicin	5mg/kg	< 7days	36 hourly
		≥ 7 days	24 hourly
See separate Gentamicin chart for more information (RDH only)			

NOTE: When coagulase negative staphylococcus is suspected e.g. central catheters in situ, then vancomycin may be more appropriate than flucloxacillin. Please discuss with a senior colleague.

Current recommended dose (based on post conceptional age):

Drug	Dose	Age (CGA)	Frequency
Vancomycin	15mg/kg (dose rounded to the **NEAREST** 0.5mg)	≤ 28 weeks	24 hourly
		28 – 35 weeks	12 hourly
		≥ 36 weeks	8 hourly

*Frequency and doses may then be further adjusted according to pre-dose levels – discuss with pharmacist

Current recommended dose:

Drug	Loading Dose	Frequency	Maintenance Dose	Age (CGA)	Frequency
Metronidazole	15mg/kg	Once only	7.5mg/kg	≤ 26 weeks	24 hourly
				26 – 34 weeks	12 hourly
				≥ 34 weeks	8 hourly
Administer as an intravenous infusion over 20 – 60 minutes					

*this guideline should be used in conjunction with the most up to date version of the BNFc and administration should be guided by Medusa

**for doses in infants >28 days old – refer to most up to date BNF

3.4 Duration of Anti-microbial Treatment

In babies given antibiotics because of risk factors for infection or clinical indicators of possible late-onset neonatal infection, measure the C-reactive protein concentration 18 to 24 hours after starting antibiotics.

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

- the baby has a positive blood culture (other than coagulase negative staphylococcus) *or*
- the baby does not respond satisfactorily to antibiotic treatment, *or*
- there is a strong clinical suspicion of infection *or*
- there are clinical symptoms or signs suggesting meningitis.

For babies given antibiotics because of suspected late-onset infection, consider stopping the antibiotics at 48 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 C-reactive protein concentration are reassuring.

Healthcare professionals with specific experience in neonatal infection should be available every day to give clinical microbiology or paediatric infectious disease advice.

Treatment duration for late-onset neonatal infection WITHOUT meningitis

Give antibiotic treatment for 7 days for babies with a positive blood culture. Consider continuing antibiotic treatment for more than 7 days if:

- the baby has not yet fully recovered *or*
- longer treatment is needed because of the pathogen identified on blood culture *or*
- longer treatment is needed because of the site of the infection (such as intra-abdominal co-pathology, necrotising enterocolitis, osteomyelitis or infection of a central venous catheter).

Use a shorter treatment duration than 7 days when the baby makes a prompt recovery, and either no pathogen is identified or the pathogen identified is a common commensal (for example, coagulase negative staphylococcus).

If continuing antibiotics for longer than 48 hours for suspected late-onset neonatal infection despite negative blood culture, review the baby at least once every 24 hours. At each review, decide whether to stop antibiotics, 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 C-reactive protein.

4.0 Site specific Infections

Although minor conjunctivitis with encrusted eyelids is common and often benign, a purulent discharge may indicate a serious infection (for example, with chlamydia or gonococcus).

In babies with a purulent eye discharge take swab samples urgently for microbiological investigation, using methods that can detect chlamydia and gonococcus. Start systemic antibiotic treatment for possible gonococcal infection while waiting for the swab microbiology results.

Treatment of neonatal *N. gonorrhoeae* conjunctivitis consists of a single dose of ceftriaxone (dose as per BNFc). Ceftriaxone should be used with caution in infants with clinically significant hyperbilirubinemia (since it displaces bilirubin from albumin and may increase the risk of encephalopathy), and it should be avoided in neonates receiving calcium-containing intravenous fluids including parenteral nutrition (due to risk of precipitation). Alternative agents that can be used in these circumstances include cefotaxime or ceftazidime. Topical antibiotic therapy alone is inadequate and is not necessary when systemic treatment is provided. The eyes should be irrigated frequently with saline until the discharge clears.

Initial treatment for chlamydial conjunctivitis should be based upon a positive diagnostic test. Oral azithromycin is the preferred treatment for neonatal *C. trachomatis** infections, including conjunctivitis. The dosing regimen is 20 mg/kg per day given orally once daily for three days. Erythromycin base, 50 mg/kg/day in four divided doses for 14 days, is an alternative.

**NOTE: Data on the effectiveness of azithromycin in treating* C. trachomatis *infections in infants are limited. In a case series of 13 infants with* C. trachomatis *conjunctivitis, three of five infants treated with single dose of azithromycin therapy became culture negative with resolution of symptoms. Of the eight infants treated once daily for three days, six had resolution of symptoms with negative cultures, one had improved symptoms though cultures remained positive until erythromycin was given, and one, was lost to follow-up.*

In babies with clinical signs of umbilical infection, such as a purulent discharge or signs of per umbilical cellulitis (for example, redness, increased skin warmth or swelling):

1. Perform blood culture
2. Take a swab sample
3. Start antibiotic treatment with intravenous flucloxacillin and gentamicin
   Note: If the microbiology results show that the infection is not caused by a Gram-negative bacterium, stop the gentamicin.

5.0 Antifungals to prevent fungal infection during antibiotic treatment for late-onset neonatal infection

Antifungal prophylaxis use can reduce the incidence of invasive fungal infections. Consider giving prophylactic oral nystatin to babies treated with any antibiotics other than benzylpenicillin and

gentamicin **OR** any antibiotics for more than a 5-day course for suspected late-onset neonatal bacterial infection.

Babies at higher risk include those who:

- have a birth weight of up to 1,500 g *or*
- were born at less than 30 weeks' gestation.

If oral administration of nystatin is not possible, give intravenous fluconazole. Note: off-label use of fluconazole and therefore should ALWAYS be a consultant decision.

Where anti-fungal prophylaxis is prescribed, it should be continued for 48 hours beyond the cessation of the antibiotic course.

6.0 Late onset neonatal meningitis

If a baby is in a neonatal unit and meningitis is suspected but the causative pathogen is unknown (for example, because the cerebrospinal fluid Gram stain is uninformative), treat with intravenous amoxicillin and cefotaxime.

If a baby is in a neonatal unit and meningitis is shown (by either cerebrospinal fluid Gram stain or culture) to be caused by Gram-negative infection, stop amoxicillin, and treat with cefotaxime alone.

If a baby is in a neonatal unit and meningitis is shown (by cerebrospinal fluid Gram stain) to be caused by a Gram-positive bacterium:

- Continue treatment with intravenous amoxicillin and cefotaxime while waiting for the cerebrospinal fluid culture result and seek microbiological advice.

If the cerebrospinal fluid culture is positive for group B streptococcus, consider changing the antibiotic treatment to:

- Benzylpenicillin 50 mg/kg every 12 hours, normally for at least 14 days and gentamicin treatment lasting for 5 days.

If the blood culture or cerebrospinal fluid culture is positive for listeria

- Consider stopping cefotaxime and treating with amoxicillin and gentamicin.

If the cerebrospinal fluid culture identifies a Gram-positive bacterium other than group B streptococcus or listeria, seek microbiological advice on management.

7.0 References (including any links to NICE Guidance etc.)

- Medicines for children- RCPCH 2003
- NICE, Neonatal infection: antibiotics for prevention and treatment, NICE guideline [NG195] Published: 20 April 2021 last accessed 13.04.22
- BNFc available online bnfc.nice.org.uk last accessed 13.04.22
- Up-To-Date - Prevention of Candida infection in neonates

1. Documentation Controls

Development of Guideline:	Shalini Ojha, Harriet Hughes
Consultation with:	Neonatal Consultants, Antimicrobial pharmacist, Paediatric Pharmacist, Clinical Educator
Approved By:	Women and Childrens - Oct 2022
Review Date:	November 2025
Key Contact:	Shalini Ojha