

Candida infections and antifungal treatment in the newborn unit

Guideline Responsibilities and Authorisation

Department Responsible for Guideline	NICU
Document Facilitator Name	Vinayak Kodur
Document Facilitator Title	Consultant Neonatologist
Document Owner Name	Vinayak Kodur
Document Owner Title	Acting Head of Department
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Guideline Review History

Version	Updated by	Date Updated	Summary of Changes
1	Catherine Domett	March 2022	New guideline
2	Vinayak Kodur	November 2023	Change in dose and indications of use of nystatin prophylaxis

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1 Overview

1.1 Purpose

- To identify patients in the newborn unit at risk of fungal infection prompting further investigation.
- To inform treatment of invasive fungal infections in the neonate.
- To inform when to give prophylactic antifungal treatment.

1.2 Staff group

Te Whatu Ora Waikato staff working in Neonatal Intensive Care Unit (NICU): Consultants, Registrars, Neonatal Nurse Practitioners (NNP) & Neonatal Nurse Specialists (NNS), Registered Nurses (RN).

1.3 Patient / client group

Neonates at risk of fungal infection and those with suspected or proven fungal infections.

1.4 Definitions and acronyms

Invasive candidiasis	Systemic infection with candida species
NEC	Necrotising Enterocolitis
VLBW	Very low birth weight <1500g

2 Clinical management

Proven fungal infection

2.1 Oral candidiasis (thrush)

- Treatment is with topical (not nasogastric) nystatin to the oral mucosa at a dose of 1ml Q6H for 7 days or 48 hours after lesions disappear whichever is the longer. (See [Nystatin oral liquid for neonates](#) drug guideline). Saturate a cotton bud with the required dose and paint on the inside of the mouth
- Observe closely for evidence of systemic candidiasis and investigate and treat as appropriate

2.2 Candida Dermatitis

- Generally in the nappy area
- Swab the area, then topical miconazole if well and not at high risk of invasive candidiasis
- See [Prevention and Treatment of Nappy Rash in the Neonatal Intensive Care Unit \(NICU\)](#) drug guideline

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2.3 Invasive candida dermatitis

- A condition unique to VLBW infants. There is a variable appearance of lesions typically in intertriginous areas but these may be more widespread.
- Presents in the first 14 days after birth.
- Commonly becomes invasive so fungal blood cultures must be performed. Please clearly mention 'suspected fungal infection' on the request form to allow the lab to process sample accordingly.
- Treat with IV fluconazole.
- If blood cultures positive, investigate and treat as invasive candidiasis, refer to 3.5 for relevant investigations.

2.4 Congenital candidiasis

Presents at or shortly after birth with a generalised eruption of 2-4mm papules with an erythematous base. The rash may be atypical in preterm infants. There may be associated oral thrush.

Increased risk in prolonged rupture of membranes or known maternal vaginal candidiasis.

Take skin swabs of the lesions, blood cultures, urine and cerebrospinal fluid (CSF) cultures if suspected.

May be treated with oral fluconazole in the well, term infant who is tolerating feeds, otherwise use IV fluconazole.

2.5 Invasive candidiasis

Generally late onset sepsis.

Increased risk in extremely low birth weight infants (<1000g), broad spectrum antibiotic use, central venous access device (CVAD) access, parenteral nutrition, candida colonisation, NEC or previous abdominal surgery, intubated babies or postnatal steroid treatment.

Potential sites of infection: skin, central nervous system (CNS), liver, spleen, urinary tract, bone, eyes.

Consider if signs of infection and instability not improving despite appropriate antibiotics, thrombocytopenia, leucocytosis, hyperglycaemia, conjugated hyperbilirubinemia and metabolic acidosis.

2.5.1 Investigations

Send blood culture, CSF and urine for culture, review sensitivities to determine treatment.

Poor sensitivity on blood culture therefore may need to take further cultures if clinical suspicion remains and initial culture is negative.

U+Es, LFTs, CBC at the start of suspected infection and monitor throughout infection.

Swabs of any oral or skin lesions – (full examination of skin and mucocutaneous sites) .

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2.5.2 Treatment

- Remove any potential source of infection e.g. central lines, urinary catheters, endotracheal tubes if able.
- Fluconazole is often used instead of amphotericin B conventional for treatment of invasive neonatal candida infections because of its effectiveness and low incidence of side effects.
- Treat with maximal dose IV fluconazole, providing:
 - no prior exposure to fluconazole and
 - isolate is not one with predictable/likely fluconazole resistance (C.krusei/C.glabrata)
- Alternatively, commence IV amphotericin if confirmed candida infection or if high suspicion in a high risk patient as above (See [Amphotericin B Liposomal \(AmBisome\) for neonates](#) and [Amphotericin B Deoxycholate \(Conventional\) for neonates](#) drug guidelines).
- Amphotericin liposomal has theoretical risk of poorer renal tract penetration than amphotericin conventional.
- In renal infection and CNS infection amphotericin B Conventional is preferable to amphotericin B liposomal (See [Amphotericin B Liposomal \(AmBisome\) for neonates](#) drug guideline). In renal impairment or adverse drug effects amphotericin B (liposomal) is preferred.
- Review sensitivities once available, and use caspofungin for salvage therapy. (guideline to be requested from Starship after discussion with Infectious disease specialist if required)

2.5.3 Length of treatment

- 14 days post negative culture in systemic infection
- 3 weeks in CNS infection
- 4-6 weeks of treatment may be recommended for focal infection of the eyes, heart, liver, kidney, spleen or bones. - Discuss with the Paediatric Infectious diseases team at Starship as a combination therapy with 5-flucytosine and amphotericin Liposomal may be beneficial.

2.5.4 Follow up

- Repeat cultures (blood, urine, CSF) after 72 hours to assess for clearance. If the repeat fungal blood is positive as well, consider adding or changing antifungal agent in consultation with Starship Hospital Paediatric ID specialist. Urine may take more time to clear especially in presence of renal fungal balls.
- If still infected, consider:
 - Eye examination
 - USS kidney, head, liver, spleen

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- Scan for osteomyelitis/ septic arthritis
- Echocardiogram
- Please note advice for adverse effects monitoring during treatment within this guideline.

2.6 Candida Urinary Tract Infection

- Fluconazole is particularly useful for urinary tract infections, obtaining high concentrations in the urine. A loading dose should be given to obtain therapeutic serum concentrations in a timely manner.

2.7 Other non-candida fungal infection

- These are less common but do occur with species such as aspergillosis, cutaneous and intestinal zygomycosis, Malasseziasepsis, trichosporonosis, Pichia sepsis, cryptococcosis, coccidioidomycosis, blastomycosis, and dermatophytosis.
- These cases should be discussed with paediatric infectious disease team. Treatment should be based on results of cultures and sensitivities. If sensitivities are uncertain, treatment should be commenced with amphotericin conventional (See [Amphotericin B Deoxycholate \(Conventional\) for neonates](#) drug guideline).

3 Summary of Treatment Options

Condition	Recommended first treatment choice
● Oral candidiasis	● nystatin
● Candida dermatitis	● Topical miconazole
● Invasive candida dermatitis	● fluconazole
● Congenital candida dermatitis	● fluconazole
● Invasive candidiasis	● fluconazole - if no prior exposure - if not C. krusei / C. glabrata ● amphotericin conventional / amphotericin liposomal
● Invasive candidiasis with focal infection	● 5-flucytosine plus amphotericin liposomal
● Renal infection, CNS and side effects/intolerance	● amphotericin conventional better than amphotericin liposomal
● Candida UTI	● fluconazole
● Non-candida / mould	● amphotericin conventional – discuss with Paediatric Infectious Diseases team

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4 Prophylaxis of fungal infection in babies at risk of systemic candidiasis:

- All infants \leq 30 weeks irrespective of risk factors until they are $>$ 30 weeks of corrected gestational age.
- Any infant $>$ 30 weeks with risk factors such as,
 - On intravenous nutrition via central catheter (UVC, or CVAD)
 - On dexamethasone for prevention or treatment of chronic lung disease of prematurity
 - Inhaled steroids for chronic lung disease of prematurity
 - Systemic antibiotics (chart along with the first dose of antibiotics and not to wait till 36 hours)

Please refer to the nystatin guideline for prophylaxis dose (1ml q 8 hourly, Saturate a cotton bud with the required dose and paint on the inside of the mouth). (See [Nystatin oral liquid for neonates](#) drug guideline).

5 Evidence base

5.1 Bibliography

- UpToDate: Epidemiology and risk factors for Candida Infection in Neonates, 2019. Available from <https://www.uptodate.com/contents/epidemiology-and-risk-factors-for-candida-infection-in-neonates>
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- Al-Matary A, Almahmoud L, et al. Oral Nystatin Prophylaxis for the Prevention of Fungal Colonization in Very Low Birth Weight Infants: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Cureus. 2022 Aug 24;14(8):e28345. doi: 10.7759/cureus.28345. PMID: 36168346; PMCID: PMC9505707.

5.2 Associated Te Whatu Ora Waikato Documents

- [Nystatin Oral Liquid for neonates](#) drug guideline (Ref. 6443)
- [Prevention and Treatment of Nappy Rash in the Neonatal Intensive Care Unit \(NICU\)](#) drug guideline (Ref. 2836)
- [Amphotericin B Deoxycholate \(Conventional\) for neonates](#) drug guideline (Ref. 0570)
- [Amphotericin B Liposomal \(AmBisome\) for neonates](#) drug guideline (Ref. 2901)

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