



CLINICAL GUIDELINE	
Candida Infections	
Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, NETS WA
<p align="center">Child Safe Organisation Statement of Commitment</p> <p>The Child and Adolescent Health Service (CAHS) commits to being a child safe organisation by meeting the National Child Safe Principles and National Child Safe Standards. This is a commitment to a strong culture supported by robust policies and procedures to ensure the safety and wellbeing of children at CAHS.</p>	

This document should be read in conjunction with this [DISCLAIMER](#)

Candidiasis is an important cause of infection-related morbidity and mortality in the NICU. Most neonates are colonized by Candida species via the maternal gastrointestinal or genitourinary tract with 77.1% getting colonized within 4 weeks of life. Skin and GIT colonized first followed by respiratory tract. Candida survivors have a worse neurological outcome, especially when there is infection of the central nervous system.

Risk Factors

- Preterm infants, especially birth weight < 1000 grams and gestation <32 weeks
- Colonization of more than one body site (eg: ETT aspirates, surface swabs)
- Prolonged antibiotic use (>5 days) and exposure to ≥ two antibiotics
- Intubation and ventilation
- Parenteral Nutrition for >5 days, Intralipid infusion for >7 days
- Central catheters (for >7 days)
- Low APGARS (5 minute score <5)
- Shock
- Exposure to H2 blockers

Candida species generally colonize skin, GIT, lower female genital tract, intertriginous areas (groin, armpits) and foreskin in males.

Clinical picture

1. Mucocutaneous candidiasis: oropharyngeal thrush, diaper dermatitis, congenital cutaneous candidiasis, invasive fungal dermatitis

- **Invasive fungal dermatitis:** Presents during first two weeks of life. Risk factors include ELBW, postnatal steroids and hyperglycemia. Presents as macular, popular, vesicular or pustular lesions in dependent/ intertriginous areas, which may involve the whole back or abdomen
- **Congenital candidiasis:** rare, acquired in utero/ during delivery. Usually presents on the first day of life. Risk factors include rupture of membranes, the presence of uterine/ cervical foreign body or a history of vaginal candidiasis. Presents as

erythematous macules / papules on erythematous base, frequently involves palms and soles. Oral thrush can be present as well as papules on the umbilical cord.

2. Invasive Candidiasis (IC): Involvement of urinary tract, CNS, eyes, heart valves, bone and joints in addition to haematogenous dissemination.

Systemic candidiasis is usually a late-onset infection. Signs and symptoms are similar to bacterial sepsis and include lethargy, feed intolerance, apnoea, cardiovascular instability and respiratory distress. Persistent hyperglycemia and thrombocytopenia are strong associations with IC in ELBW neonates.

Diagnosis

Leucocytosis is usually marked, and thrombocytopenia is almost invariable. However, thrombocytopenia occurs in many cases of bacterial sepsis, so is not pathognomonic of systemic candida infection.

As candida may grow slowly in cultures (blood, urine, CSF), false-negative results of blood cultures and lumbar punctures can potentially lead to misdiagnosis or delayed diagnosis. A high index of suspicion is necessary, especially in high-risk patients.

Once the diagnosis is confirmed, a renal and cranial ultrasound is indicated. A cardiac echo may be indicated to assess for cardiac thrombi or vegetations. An ophthalmologic review is warranted.

Prophylaxis of Candida Infections

- Minimise and rationalise antibiotic use, especially broad spectrum antibiotics
- Consider early extubation
- **Nystatin:** Current practice for infants requiring any form of respiratory support (Ventilation/ CPAP/ HHF) is to administer oral Nystatin 1ml TDS until off such respiratory support (*Austin 2015, Mersal 2013, Cochrane review 2015*)
- **Miconazole:** No role as possible increased risk of developing resistance to azoles.
- **Fluconazole:** Cochrane review (Cleminson et al 2015) included 10 trials (n=1371 VLBW infants): IC incidence (6.2% vs 15.7%, RR 0.43; 95% CI: 0.31-0.59). Similar results in ELBW infants (RR: 0.30, 95% CI: 0.14-0.63). Limited data on long term outcomes of fluconazole prophylaxis suggest no adverse effects (*Kaufman et al 2011, Greenberg et al 2012*)
- **Ongoing Surveillance:** Further studies needed
- **Empiric antifungal therapy:** Further studies needed
- **Lactoferrin:** Inconclusive evidence
- **Probiotics:** Reduced rate of Candida colonization (12% vs 31%, RR: 0.43, 95% CI: 0.27-0.68) in meta-analysis of 2 studies (n=329). In another meta-analysis including 6 trials (n=1259) there was no reduction in IC (1.8% vs.2% RR: 0.88, 95% CI: 0.44-1.78)

Treatment of Invasive Candidiasis (IC)

- Consider removal of central lines.
- The drug of choice for systemic candidiasis is **Amphotericin (Fungizone)**. The drug is extremely well tolerated in neonates, with few renal adverse effects. The drug must be infused over 6 hours. In some instances where venous access is difficult, and parenteral nutrition cannot be ceased for the 6 hour infusion, consideration can be given to using **Amphotericin Liposomal (Ambisome)**. This formulation has no other specific benefits, except slightly reduced nephrotoxicity and can be infused

over 30-60 minutes. Note that Ambisome is far more expensive; seek advice from a neonatologist and/or clinical microbiologist.

- [Fluconazole](#) (12 mg/kg/day). May cause transient elevation of creatinine or hepatic enzymes (AST and ALT > 3 fold)
- [Flucytosine](#) (nucleoside analogue) may need to be added, especially in cases of meningitis.
- Length of treatment will vary (*refer to Figure 1*); systemic treatment may be continued with oral Fluconazole, but there is a paucity of data evaluating its efficacy. Oral Fluconazole may be appropriate for isolated uncomplicated UTI after discussion with microbiology.
- Newer antifungal agents, such as Voriconazole and Caspofungin (echinocandins), have also not been well studied in neonate.

Related CAHS internal policies, procedures and guidelines
Neonatology Medication Protocols Amphotericin (Fungizone) Amphotericin Liposomal (Ambisome) Fluconazole Flucytosine Nystatin

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File Path:			
Document Owner:	Neonatology		
Reviewer / Team:	Neonatal Coordinating Group		
Date First Issued:	February 2010	Last Reviewed:	21 st May 2020
Amendment Dates:		Next Review Date:	21 st May 2023
Approved by:	Neonatal Coordinating Group	Date:	2 nd June 2020
Endorsed by:	Neonatal Coordinating Group	Date:	
Standards Applicable:	NSQHS Standards: 		

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Appendix 1: Flow chart for proven invasive Candidiasis

Adapted from Kaufman et al, J Ped 2009, Bersani et al Front Pediatr 2019

