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Formal Education

- **Universitas Indonesia**, Subspesialis / Konsultan Penyakit Tropik dan Infeksi, Lulus 2013
- **Universitas Indonesia**, Spesialis Penyakit Dalam (Internist), Lulus 2009
- **Universitas Trisakti**, Dokter Umum, Lulus 2002
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Organization

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- **Bendahara**, Perhimpunan Ilmu Kedokteran Tropis dan Penyakit Infeksi Indonesia (PETRI) Jakarta, sejak 2016 - 2023
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Invasive Fungal Infections (IFIs) – *Candida* spp & Others

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Issue : When to Start the Systemic Antifungal Treatment?

Invasive Fungal Infections (IFIs)

Considering

Host Factor

Risk Factor

Approach

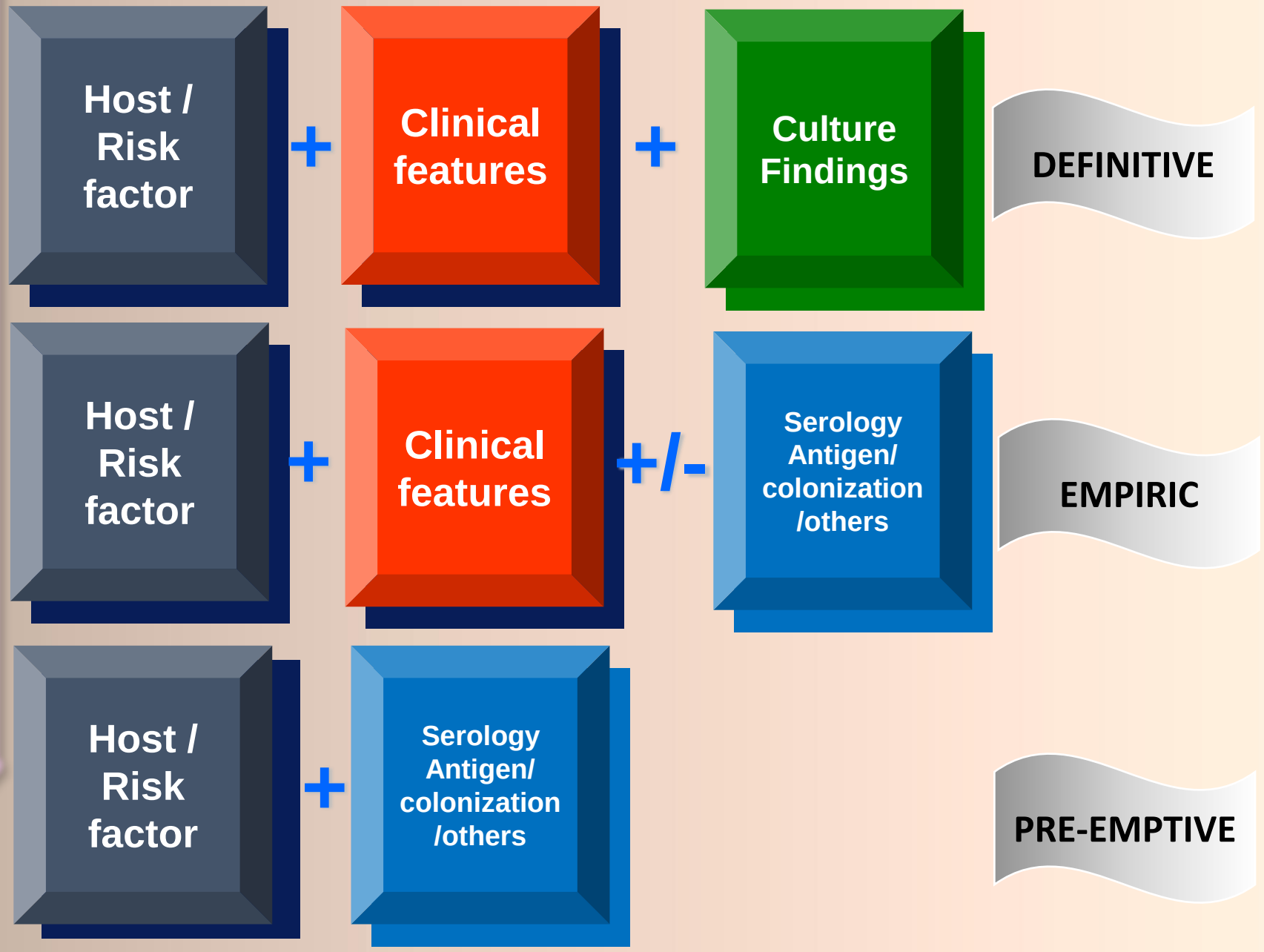
Definitive
Empiric
Pre-Emptive
(Prophylaxis?)

Treatment Option

Amphoterisin
5FC
Azole
Echinocandin

Approach

Definitive
Empiric
Pre-Emptive
(Prophylaxis?)



Host - Fungal Clearance

Lymphocytes (CD4+)

***Cryptococcus* spp**

***Histoplasma* spp**

Neutrophils

***Candida* spp**

***Aspergillus* spp**

GUIDELINES FOR
DIAGNOSING, PREVENTING AND MANAGING CRYPTOCOCCAL DISEASE AMONG ADULTS, ADOLESCENTS AND CHILDREN LIVING WITH HIV

World Health Organization

Since 2018, WHO guidelines have recommended that all adults and adolescents living with HIV who have a CD4 cell count <100 cells/mm^3 be screened for cryptococcal antigen before ART initiation or reinitiation; cryptococcal antigen screening may also be considered for adults and adolescents living with HIV who have a CD4 cell count <200 cells/mm^3. These recommendations were supported by evidence favouring the clinical benefit and cost–effectiveness of cryptococcal antigen screening *(20,22,24–30)*. All individuals screening positive for cryptococcal antigen should be given pre-emptive antifungal therapy (fluconazole 800–1200 mg/day for adults and 12 mg/kg per day for adolescents for two weeks), followed by consolidation and maintenance fluconazole therapy, as for treatment. The 2019 guidelines from the Southern African HIV Clinicians Society recommend 1200 mg for first 2 weeks given safety and concerns over breakthrough infection *(21)*.

PAHO
Pan American Health Organization
World Health Organization Americas
World Health Organization

GUIDELINES FOR
DIAGNOSING AND MANAGING DISSEMINATED HISTOPLASMOSIS AMONG PEOPLE LIVING WITH HIV

Prognostic factor	Weight
Burden of illness	
No or mild symptoms	5
Moderate symptoms	3
No hypotension (systolic blood pressure >90 mm Hg)	5
No chronic obstructive pulmonary disease	4
Solid tumour or no previous fungal infection	4
No dehydration requiring parenteral fluids	3
Outpatient status	3
Age <60 years	2

MASCC Risk Index score ≥21 indicates that the patient is at a low risk of complications and mortality, classified as low-risk febrile neutropenia.

Histoplasmosis has a high endemicity in certain areas of the Americas *(7)*. Although most frequently diagnosed in the Americas, it is also diagnosed in certain countries of Asia (China, India, Indonesia, Japan, Malaysia, Singapore, Thailand, and Viet Nam) and Africa (Central African Republic, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Gambia, Guinea Bissau, Liberia, Senegal, South Africa, and Uganda) *(8)*. Among people living with HIV, the most frequent clinical presentation of this disease is disseminated histoplasmosis. Symptoms of disseminated histoplasmosis are nonspecific and may be indistinguishable from those of other infectious diseases, especially TB, thus complicating diagnosis and treatment *(9)*. Most histoplasmosis reports come from the Region of the Americas, and each year there are up to 15,600 new cases and 4,500 deaths among people living with HIV *(4)*.

Risk Factors

IFIs - *Candida* spp

Evaluation of *Candida* Scoring Systems to Predict Early Candidemia: A Prospective and Observational Study at a Tertiary Care Hospital, Uttarakhand

Priyanka Gupta, Pratima Gupta, Biswaroop Chatterjee[1], Garima Mittal[1], Shashank Prateek[2], Aroop Mohanty[3]
Department of Microbiology, AIIMS, Rishikesh, [1]Department of Microbiology, Himalayan Institute of Medical Sciences, Jolly Grant, Dehradun, [2]PI Disease, Consultant Lab Medicine, Q Health Diagnostics, [3]AIIMS, Rishikesh, Uttarakhand, India

Indian Journal of Critical Care Medicine | Volume 21 | Issue 12 | December 2017

Leon et al
- Clinical sepsis
- Surgery
- TPN
- Multifocal colonization

Wenzel et al
- Intravenous catheters
- Hemodialysis
- Antibiotic usage
- Colonization with Candida

Matteo Basseti

All Patients :
- Prior abdominal surgery
- Intravascular catheters
- Parenteral Nutrition
- Use of Broad Spectrum Antibiotic
- Immunosuppresion including corticosteroid therapy
- Acute Renal Failure
- Diabetes Melitus
- Transplantation
- Haemodialysis
- Pancreatitis

ICU patients :
- Prolong stay in ICU
- Candida Colonization particularly if multifocal
- High APACHE II Score
- Low birth weight for Neonatal ICU

Scudeller et al
- Broad spectrum antibiotic treatment ongoing for at least 5 days
- Central venous catheter (CVC) or peripherally inserted central catheter (PICC)
- Parenteral nutrition
- Chemotherapy for solid and hematological tumors (including steroids)
- Hospitalization > 10 days in previous 3 months (including nursing homes/long-term care facilities)
- Prior candidemia Candida colonization in >1 site
- Transferred from ICU Dialysis

Gupta P

Prolonged antibiotic usage ($P < 0.00001$)
Prolonged ICU stay ($P = 0.00024$)
Multifocal colonization ($P = 0.00025$),

Risk Factors IFIs - *Candida* spp

JURNAL BIOMEDIKA DAN KESEHATAN
(JOURNAL OF BIOMEDIKA AND HEALTH)
Vol. 6 No. 1 (2023) pp. 133-141 e-ISSN: 2621-5470

RASCANDIS 1.0 Form: Therapeutic Approach of Systemic Anti-Candidiasis for Non-Transplant Patients

Ronald Irwanto Natadidjaja[1,2], Aziza Ariyani[1], Hadianti Adlani[1], Anti Dharmayanti[1,3], Joyce Bratanata[1,4]

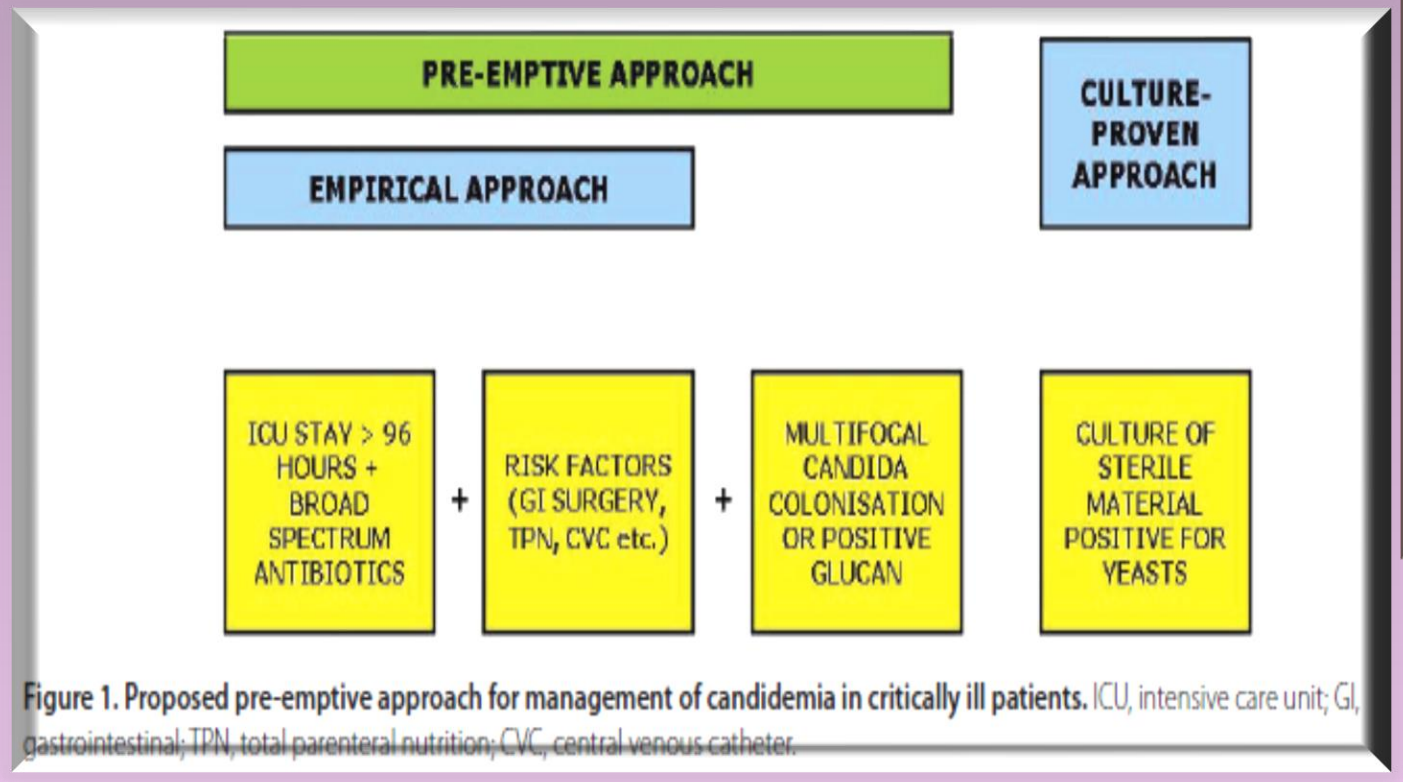


Figure 1. Proposed pre-emptive approach for management of candidemia in critically ill patients. ICU, intensive care unit; GI, gastrointestinal; TPN, total parenteral nutrition; CVC, central venous catheter.

Bassetti *et al. Critical Care 2010*

- **Sepsis**
- **Long ICU stay**
- **Using Total Parenteral Nutrition (TPN)**
- **Candida sp multifocal colonization findings**
- **Using deep vein catheters, including Central Venous Catheter (CVC)**
- **Hemodialysis**
- **History of long-term use of wide-spectrum antibiotics**
- **History of abdominal surgery**
- **Transplantation**
- **Long ICU stay**
- **Babies with low birth weight in ICU**

Gupta P, Gupta P, Chatterjee B, Mittal G, Prateek S, Mohanty A. Evaluation of Candida scoring systems to predict early candidemia: A prospective and observational study at a tertiary care hospital, Uttarakhand. Indian J Crit Care Med. 2017;21(12):830–5. doi: 10.4103/ijccm.IJCCM_159_17

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JURNAL BIOMEDIKA DAN KESEHATAN
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REVIEW ARTICLE

RASCANDIS 1.0 Form: Therapeutic Approach of Systemic Anti-Candidiasis for Non-Transplant Patients

Formulir RASCANDIS 1.0: Pendekatan Terapi Anti-Kandida Sistemik untuk Pasien Non-Transplantasi

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No.	Specification	Flow	Explanation	Approach
1	**Clinical progressive :** With positive culture finding from sterile	Yes	STOP Circle : *Blood *Liver biopsy *Spleen biopsy *Etc,...	Definitive Systemic Anti Candida
		No		
2	**Clinical progressive :** (With≥48-hours use of deep vascular catheter AND/OR TPN) without improvement with antibiotic use	Yes	STOP	Empiric Systemic Anti Candida
		No		
3	**Clinical progressive :** Post Extensive intraabdominal surgery without improvement with antibiotic use	Yes	STOP	Empiric Systemic Anti Candida
		No		
4	**Clinical progressive :** High risk neutropenia AND / OR with MASCC Index<21	Yes	STOP	Empiric Systemic Anti Candida
		No		
5	(Found ≥1 candida colonization AND/OR positive of other candida biomarker) with neutropenic condition	Yes	STOP Circle : *Oropharynx *Faeces *Skin *Etc,... *Urine	Pre-emptive Systemic Anti Candida
		No		
6	(Found ≥1 candida colonization AND/OR positive of other candida biomarker) with >48 hours of deep vascular catheterization AND/OR TPN	Yes	STOP Circle : *Oropharynx *Faeces *Skin *Etc,... *Urine	Pre-emptive Systemic Anti Candida
		No		
7	(Found ≥1 candida colonization AND/OR positive of other candida biomarker) following extensive intraabdominal surgery	Yes	STOP Circle : *Oropharynx *Faeces *Skin *Etc,... *Urine	Pre-emptive Systemic Anti Candida
		No	Systemic Anti Candidiasis is not necessary	

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RASCANDIS 1.0 Form: Therapeutic Approach of Systemic Anti-Candidiasis for Non-Transplant Patients

Formulir RASCANDIS 1.0: Pendekatan Terapi Anti-Kandida Sistemik untuk Pasien Non-Transplantasi

Ronald Irwanto Natadidjaja[1,2✉], Aziza Ariyani[1], Hadianti Adlani[1], Anti Dharmayanti[1,3], Joyce Bratanata[1,4]

GUIDELINES FOR

DIAGNOSING, PREVENTING AND MANAGING CRYPTOCOCCAL DISEASE AMONG ADULTS, ADOLESCENTS AND CHILDREN LIVING WITH HIV

World Health Organization

Prevention and screening (2018 recommendations)

Screening[a] for cryptococcal antigen followed by pre-emptive antifungal therapy *(21)*[3] among cryptococcal antigen–positive people to prevent the development of invasive cryptococcal disease is recommended before initiating or reinitiating ART for adults and adolescents living with HIV who have a CD4 count <100 cells/mm³.

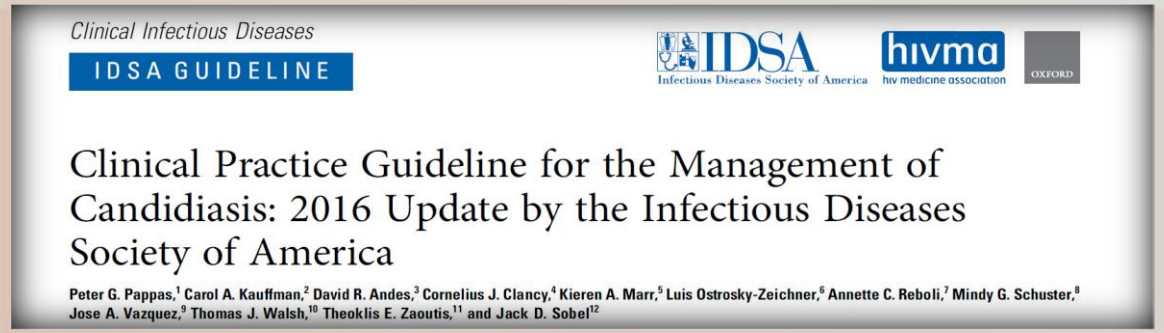
Strong recommendation; moderate-certainty evidence

This may be considered at a higher CD4 cell count threshold of <200 cells/mm³.

Conditional recommendation; moderate-certainty evidence

Cryptococcal antigen screening followed by pre-emptive therapy is preferred over providing fluconazole primary prophylaxis after considering cost, the potential for developing antifungal resistance and concerns about fetal safety among women of childbearing age without access to adequate contraception. Fluconazole primary prophylaxis should be made available in settings in which cryptococcal antigen screening is not available or there may be prolonged delays in receiving the result since cryptococcal disease and mortality peak in the first four weeks among people presenting with a CD4 cell count <100 cells/mm³ *(31)*.

Part of Guidelines

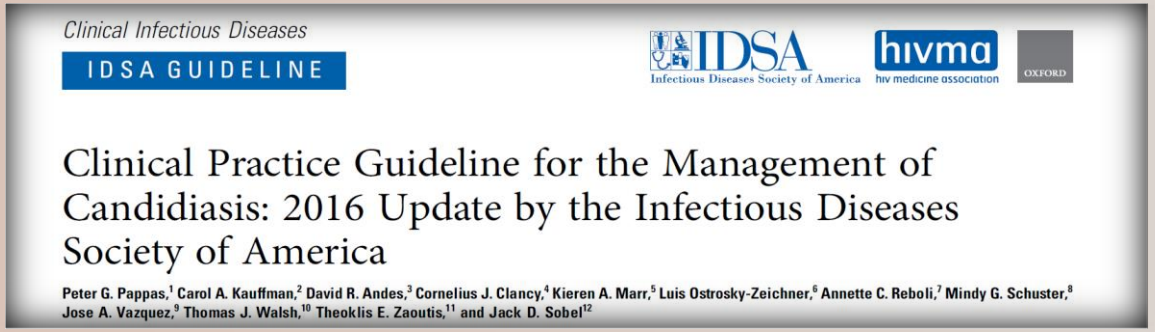


What Is the Treatment for Candidemia in Nonneutropenic Patients?

Recommendations

1. An echinocandin (caspofungin: loading dose 70 mg, then 50 mg daily; micafungin: 100 mg daily; anidulafungin: loading dose 200 mg, then 100 mg daily) is recommended as initial therapy (strong recommendation; high-quality evidence).
2. **Fluconazole, intravenous or oral, 800-mg (12 mg/kg) loading dose, then 400 mg (6 mg/kg) daily is an acceptable alternative to an echinocandin as initial therapy in selected patients,** including those who are not critically ill and who are considered unlikely to have a fluconazole-resistant Candida species (strong recommendation; high-quality evidence).
3. Testing for azole susceptibility is recommended for all bloodstream and other clinically relevant Candida isolates. Testing for echinocandin susceptibility should be considered in patients who have had prior treatment with an echinocandin and among those who have infection with C. glabrata or C. parapsilosis (strong recommendation; low-quality evidence).
4. Transition from an echinocandin to fluconazole (usually within 5–7 days) is recommended for patients who are clinically stable, have isolates that are susceptible to fluconazole (eg, C. albicans), and have negative repeat blood cultures following initiation of antifungal therapy (strong recommendation; moderate-quality evidence).
5. For infection due to C. glabrata, transition to higher-dose fluconazole 800 mg (12 mg/kg) daily or voriconazole 200–300 (3–4 mg/kg) twice daily should only be considered among patients with fluconazole-susceptible or voriconazole-susceptible isolates (strong recommendation; low-quality evidence).
6. Lipid formulation amphotericin B (AmB) (3–5 mg/kg daily) is a reasonable alternative if there is intolerance, limited availability, or resistance to other antifungal agents (strong recommendation; high-quality evidence).
7. Transition from AmB to fluconazole is recommended after 5–7 days among patients who have isolates that are susceptible to fluconazole, who are clinically stable, and in whom repeat cultures on antifungal therapy are negative (strong recommendation; high-quality evidence).

What Is the Treatment for Candidemia in Nonneutropenic Patients?



8. Among patients with suspected azole- and echinocandin resistant Candida infections, lipid formulation AmB (3–5 mg/kg daily) is recommended (strong recommendation; low-quality evidence).
9. Voriconazole 400 mg (6 mg/kg) twice daily for 2 doses, then 200 mg (3 mg/kg) twice daily is effective for candidemia, but offers little advantage over fluconazole as initial therapy (strong recommendation; moderate-quality evidence). Voriconazole is recommended as step-down oral therapy for selected cases of candidemia due to C. krusei (strong recommendation; low-quality evidence).
10. All nonneutropenic patients with candidemia should have a dilated ophthalmological examination, preferably performed by an ophthalmologist, within the first week after diagnosis (strong recommendation; low-quality evidence).
11. Follow-up blood cultures should be performed every day or every other day to establish the time point at which candidemia has been cleared (strong recommendation; lowquality evidence).
12. Recommended duration of therapy for candidemia without obvious metastatic complications is for 2 weeks after documented clearance of Candida species from the bloodstream and resolution of symptoms attributable to candidemia (strong recommendation; moderate-quality evidence).

Part of Guidelines

The 10 most remarkable rules for developing antifungal stewardship program in ICU

1. **Restrict or avoid antifungal prophylaxis**
2. Differentiate infection from colonisation
3. Use non-culture-based diagnostics for early detection of IC
4. Limit the use of empirical therapy based on risk-factors
5. Promote early pre-emptive antifungal treatment based on risk factors and biomarkers
6. Get treatment right the first time with adequate drugs (echinocandins)
7. Have adequate source control within 48 hours (catheter removal, appropriate drainage, surgical control)
8. Use an adequate dose: low dose is associated with resistance
9. De-escalate whenever possible (if possible, within day 5)
10. Stop early useless therapy and check duration of therapy

Slide of Prof Basseti March 6th, 2021

IC, invasive candidiasis.

Bassetti M et al. Intensive Care Med 2017: DOI: 10.1007/s00134-017-4922-x.

Cetakan I, 2023

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