ASIA FUNGAL WORKING GROUP
an ISHAM working group

ISHAM
INTERNATIONAL SOCIETY FOR HUMAN AND ANIMAL MYCOLOGY

MMTN
MEDICAL MYCOLOGY TRAINING NETWORK

# REGIONAL MMTN CONFERENCE 2023

## Asia Pacific Medical Mycology Training Network (MMTN) Conference

4th–6th AUG 2023
Bangkok, Thailand

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The Asia Fungal Working Group is an official working group of the International Society for Human and Animal Mycology (ISHAM).

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# Start antibiotic or antifungal?

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# Case presentation

- 73/M, UK-born, residing in the Philippines

- Recent work up showing pancreatic and hepatic masses (abdominal CT) → presumed metastatic cancer
- Comorbid: ❤️ Coronary Artery Disease S/P PCI 16 years ago

- **Chief complaint: vomiting**
  - No fever
  - Poor appetite
  - Chest and upper abdominal pain

# Case presentation

- Drowsy, weak
- Normotensive and afebrile

- Admitting CBC: WBC 44.6, 95 segmenters
  - Hemoglobin 9.6; Platelet 394
- Baseline creatinine: 2.23 mg/dL
- Electrolyte imbalance
- Chest x-ray: bilateral pneumonia

# Would you start antifungal? (Y/N)

On admission

E.R. level

# Initial Course

- A: Intraabdominal infection
  - Blood, sputum, urine cultures
  - Started on antibiotics: piperacillin-tazobactam; *levofloxacin and metronidazole further added*

- 1st hospital day: fever
  - Procalcitonin: 8.82

- 3rd hospital day: hypotension → pressor support
  - Intubated → ventilatory support

# With patient now in septic shock, would you add an antifungal? (Y/N)

Critically ill,

Non-neutropenic patient

# At 72 hours from admission

- Microbiologic work-up:
  - Blood cultures – negative
  - Urine culture - <10,000 CFU yeast cells
  - Sputum culture
    - Gram stain: 0-1 WBC, rare Gram + cocci in pairs
  - Endotracheal aspirate culture
    - Gram stain: 0-1 WBC, few Gram + bacilli and few budding yeast cells
- Chest x-ray: resolving bilateral pneumonia &/or congestion

# With the preliminary respiratory and urine culture results, would you now start an antifungal? (Y/N)

Critically ill,

Non-neutropenic patient

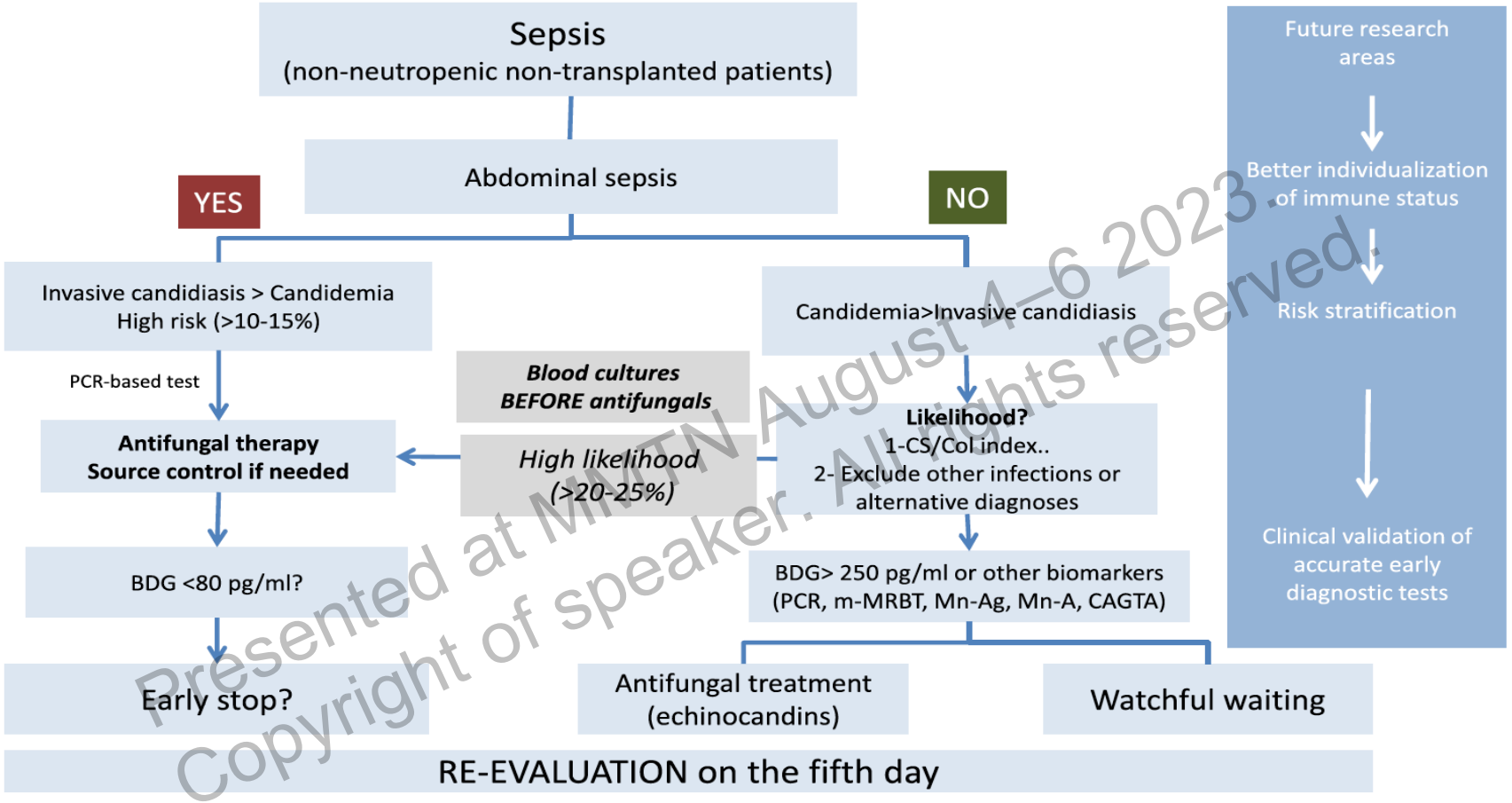




**Fig. 1** Proposed algorithm for sepsis in non neutropenic non transplanted ICU patients at risk for Candidemia and/or IC. BDG, 1-3 β-D-glucan; CS, Candida score; m-MRBT, miniaturized-magnetic resonance-based technology; Mn-Ag, mannan antigen; Mn-Ab, anti-mannan antibody; CAGTA, *Candida* species germ tube antibody; Col index, colonization index; PCR, polymerase chain reaction; Abdominal sepsis: refers to anastomosis leak, postoperative abscess, repeated surgery for recurrent abdominal sepsis or infected pancreatitis

Intensive Care Med. https://doi.org/10.1007/s00134-019-05599-w

# At 72 hours from admission

- Microbiologic work-up:
  - Blood cultures – negative
  - Urine culture - <10,000 CFU yeast cells → *Candida tropicalis*
  - Sputum culture → *Candida glabrata*
    - Gram stain: 0-1 WBC, rare Gram + cocci in pairs
  - Endotracheal aspirate culture → *Candida glabrata*
    - Gram stain: 0-1 WBC, few Gram + bacilli and few budding yeast cells
- Chest x-ray: resolving bilateral pneumonia &/or congestion

**With the respiratory and urine culture results, would you now start an antifungal? (Y/N)**

***Do these results reflect colonization?***

Critically ill,

Non-neutropenic patient

# Risk factors

1. General patient characteristics:
   - Immunosuppression (neutropenia, malignancy, organ transplant, steroid, diabetes)
2. Acquisition of candidal colonization:
   - Broad-spectrum antibiotics
   - Patients in ICU >1 week
   - Known colonization (e.g., culture of Candida from multiple sites)
3. Violation of anatomic barriers:
   - Abdominal surgery, GI perforation, anastomotic leak, necrotizing pancreatitis
   - Long-term indwelling catheters (especially hemodialysis and TPN)
   - Mucositis due to chemotherapy
   - Burns

# Course

- 6th hospital day
  - AKI needing hemodialysis
  - IJ catheter insertion
  - 3rd port used as an IV access
- Antibiotic regimen shifted to meropenem, vancomycin
  - Procalcitonin: 8.82 → 7.69
- No antifungal
- Patient *stabilized* → low-dose pressor, afebrile
  - AND directive

# New events in the course

- 13th hospital day
  - New onset hypotension (was still on low dose norepinephrine)
    - Cortisol: 33.35 (N⁰ 4.3 – 22.4)
  - On 1st bag of lipid-based parenteral nutrition
- CBC:
  - WBC 49.23 (adm 44.6), 93 (95) segmenters; Hemoglobin 7.5 (9.6)
- D6 meropenem and vancomycin
  - Procalcitonin: 8.82 → 7.69 → 15.26
- No antifungal
- **Massive upper GI bleeding** → 1L bloody NGT drain



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# New Problem List

- **Hypovolemia $2^0$ to upper GI bleeding likely erosive gastropathy**
  - Blood transfusion
- **Deep vein thrombosis**
  - Venous duplex: acute to subacute proximal DVT, partially occlusive, R femoral vein
  - Enoxaparin initially given for DVT prophylaxis put on hold
- **ID**: blood cultures (peripheral, via IJ catheter)
- Broad spectrum antibiotics; No antifungal*

# Course

- 16th hospital day

  Preliminary blood cultures:

  - No growth (peripheral)
  - Gram + budding yeast cells at 72 hours of incubation (IJ catheter-drawback blood)

# What antifungal will you start?

## A. Fluconazole

## B. Echinocandin

## C. Amphotericin

Candidemia,

Likely central line-related bloodstream infection (CRBSI)

# Course

- Final blood culture results:
  - No growth (peripheral)
  - Gram + budding yeast cells at 72 hours of incubation (IJ catheter-drawback blood) → *Candida tropicalis*

- Anidulafungin
- IJ catheter remained in place**

# Issue:  central line removal

Candidemia CRBSI

# Key Takeaways (Invasive Candidiasis in the ICU)

- Antifungal treatment strategy approaches

ESICM/ESCMID task force on practical management of invasive candidiasis in critically ill patients

Ignacio Martin-Loeches[1,2*], Massimo Antonelli[3], Manuel Cuenca-Estrella[4], George Dimopoulos[5], Sharon Einav[6], Jan J. De Waele[7], Jose Garnacho-Montero[8,9], Souha S. Kanj[10], Flavia R. Machado[11], Philippe Montravers[12], Yasser Sakr[13], Maurizio Sanguinetti[14], Jean-Francois Timsit[15,16] and Matteo Bassetti[17]

# Antifungal Strategy Approach

## Prophylaxis

- Against routine and universal administration of antifungal prophylaxis in critically ill patients
  - weak recommendation, moderate quality of evidence

## Pre-emptive

- Not recommended in critically ill patients
  - weak recommendation, low-quality evidence

## Empiric

- Might be considered only in patients with septic shock and MOF who have more than 1 extra-digestive site (i.e. urine, mouth, throat, upper and lower respiratory tracts, skin folds, drains, operative site) with proven *Candida* species colonization
  - strong recommendation, low quality of evidence

Intensive Care Med. https://doi.org/10.1007/s00134-019-05599-w

# Consensus Statements

## Empiric

- Might be considered only in patients with septic shock and MOF who have more than 1 extra-digestive site (i.e. urine, mouth, throat, upper and lower respiratory tracts, skin folds, drains, operative site) with proven *Candida* species colonization
- strong recommendation, low quality of evidence

Intensive Care Med. https://doi.org/10.1007/s001

- Recommend to NOT start empirical antifungal therapy in patients without septic shock and MOF
- Isolation of *Candida* from the respiratory tract alone should not prompt initiation of treatment.
- Recommend the promotion of antifungal stewardship programs in order to limit the use of empirical therapy.

# Key Takeaways (Invasive Candidiasis in the ICU)

- Antifungal treatment strategy approaches
- Local IFI patterns (incidence and resistance rates)