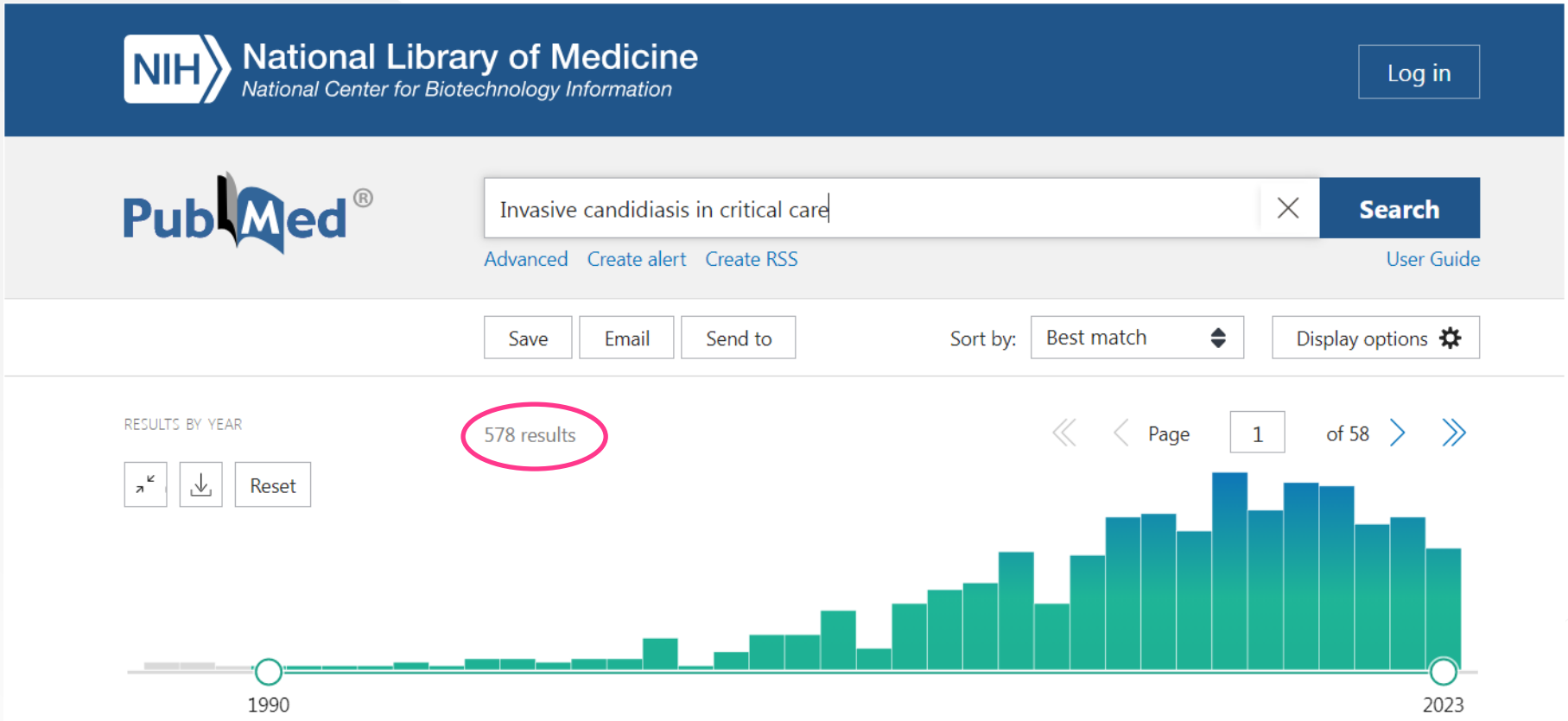
CANDIDOSES SYSTÉMIQUES EN RÉANIMATION

A. TRIFI
REA MED – CHU, La RABTA, Tunis

Hammamet, Dec 02-2023

Candidose systémique (Invasive candidiasis (IC))



RCT 28
Métatanalyses 9
Revues 182
Systematic revues 187

Candidose systémique (Invasive candidiasis (IC))

- **Infection grave** causée par plusieurs espèce de ***Candida (spp.)***
- *Candida spp.*: organismes commensaux de **l'intestin et la peau**
- Infection **fongique la plus courante en hospitalier** (USI et non USI)
  - Prévalence mondiale: 250 000 à 700 000 patients / an
- Mortalité = 40 % et 55 %
- **Candidémie** et **candidose profonde**(abdomen, péritoine ou os)

Soriano A, Honore PM, Puerta-Alcalde P, et al. Invasive candidiasis: current clinical challenges and unmet needs in adult populations. J Antimicrob Chemother. 2023 Jul 5;78(7):1569-1585. doi: 10.1093/jac/dkad139.

Candidose systémique (Invasive candidiasis (IC))

- **5 agents pathogènes** :
  - *C. albicans*
  - *Nakaseomyces glabrata (C. glabrata)*
  - *C. tropicalis*
  - *C. parapsilosis*
  - *Pichia kudriavzevii (C. krusei)*

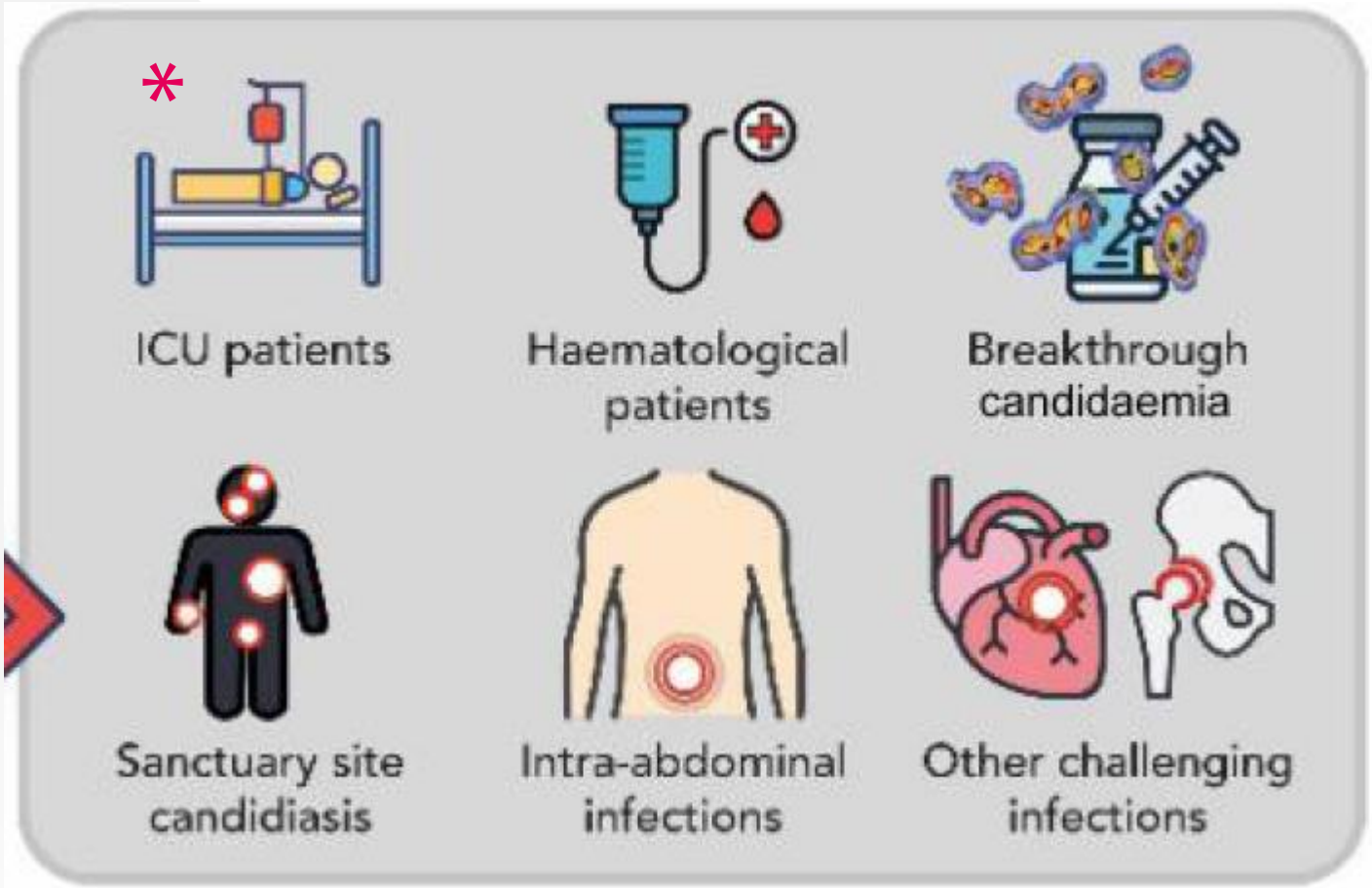
S Kidd, A Abdolrasouli, F Hagen, **Fungal Nomenclature**: Managing Change is the Name of the Game, *Open Forum Infectious Diseases*, Volume 10, Issue 1, January 2023, ofac559,

- ***C. albicans***: l'espèce la plus commune
- **Espèces non albicans**:
  - En augmentation
  - > 50 % dans certaines séries

- ***C. auris***: apparu en 2009 (Japon): épidémies (transmission environnementale), résistance AF+

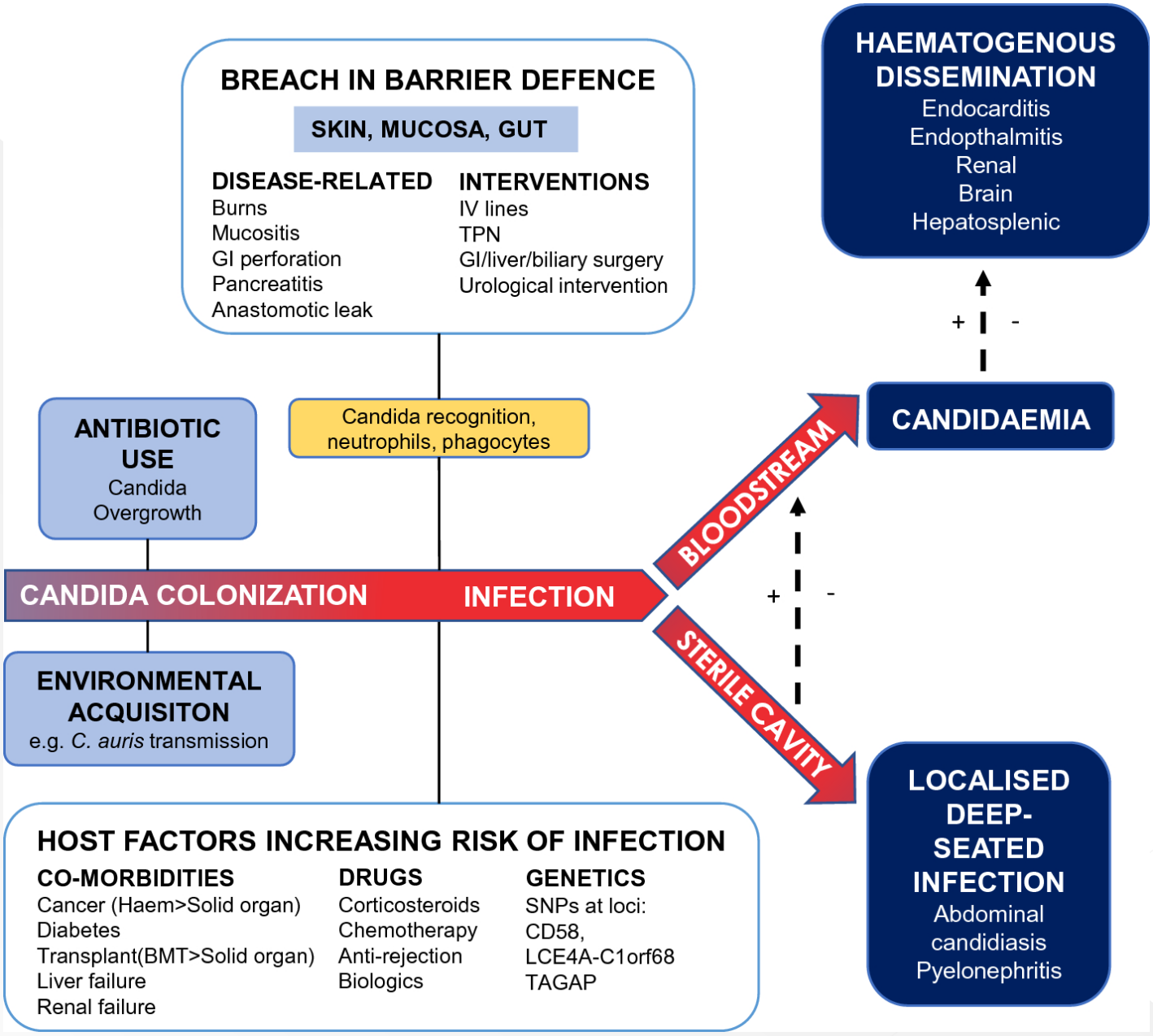
Du H, et al. Candida auris: epidemiology, biology, antifungal resistance, and virulence. PLoS Pathog 2020; 16: e1008921

FORMS OF INVASIVE CANDIDIASIS



Soriano A, Honore PM, Puerta-Alcalde P, et al. Invasive candidiasis: current clinical challenges and unmet needs in adult populations. J Antimicrob Chemother. 2023 Jul 5;78(7):1569-1585. doi: 10.1093/jac/dkad139.

Facteurs clés contribuant au développement des CI en USI



Logan C, et al. Invasive candidiasis in critical care: challenges and future directions. Intensive Care Med. 2020 Nov;46(11): doi: 10.1007/s00134-020-06240-x. Epub 2020 Sep 29. PMID: 32990778.

BMT bone marrow transplant, *GI* gastrointestinal, *Haem* haematological, *IV* intravenous, *SNPs* single-nucleotide polymorphisms, *TPN* total parenteral nutrition

Table 1. Risk Factors for Invasive Candidemia.

Risk Factors
1. Major Risk Factors
Intravascular devices (biofilms)
Recent surgery (particularly abdominal surgery)
Broad-spectrum antibiotics/antifungals
Immunosuppressive therapy (corticosteroids and chemotherapy)
Malignancies (solid tumors and hematologic)
Diabetes mellitus
2. Other Risk Factors
Hyperalimentation fluids
Previous ICU stay
Mechanical ventilation
Urinary catheterization
Prior *Candida* colonization/infection
Concomitant bacterial infections
Solid organ transplant patients
Hemodialysis
HIV-associated low CD^{4+} T cell counts

Alves, J.; Alonso-Tarrés, C.; Rello, J. How to Identify Invasive Candidemia in ICU—A Narrative Review. *Antibiotics* **2022**, *11*, 1804. https://doi.org/10.3390/antibiotics11121804

Challenges…

- **Challenge 1**: Évolution de l'épidémiologie et émergence de résistances aux AF
- **Challenge 2:** Est-ce une CI? culture et non culture, Rôle des scores de risque…
- **Challenge 3:** Quand commencer le ttt AF ?
- **Challenge 4:** Choisir l'AF optimal pour un patient en USI
- **Challenge 5:** Quand arrêter le ttt AF ?
- ……..

CHALLENGE 1: Évolution de l'épidémiologie et émergence de résistances aux AF

Clinical Microbiology and Infection 25 (2019) 1200–1212

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Systematic review

Morbidity and mortality of candidaemia in Europe: an epidemiologic meta-analysis☆

P. Koehler [1, 2], M. Stecher [1, 3], O.A. Cornely [1, 2, 3, 4], D. Koehler [5], M.J.G.T. Vehres
J. Bohlius [7], H. Wisplinghoff [8, 9, 10], J.J. Vehreschild [1, 3, 11, *]

Recherche Web: janvier 2000 - février 2019
9 pays europ (107 études)
43 799 cas de candidémie
Taux d'incidence global =3,88/100 000
En USI=5,5 (4,1-7) /1 000 admissions
79 cas /j dont environ 29: issue fatale à J 30.

Bassetti et al. Critical Care (2019) 23:219
https://doi.org/10.1186/s13054-019-2497-3

Critical Care

RESEARCH Open Access

Incidence and outcome of invasive candidiasis in intensive care units (ICUs) in Europe: results of the EUCANDICU project

Results

Primary analysis—cumulative incidence

During the study period, the 23 ICUs (median number of beds 18, interquartile range 14–43) had 80,645 admissions and 570 episodes of ICU-acquired IC, corresponding to an incidence of 7.07 episodes per 1000 ICU admissions

J Antimicrob Chemother 2018; **73** Suppl 1: i4–i13
doi:10.1093/jac/dkx444

Journal of Antimicrobial Chemotherapy

Changes in the epidemiological landscape of invasive candidiasis

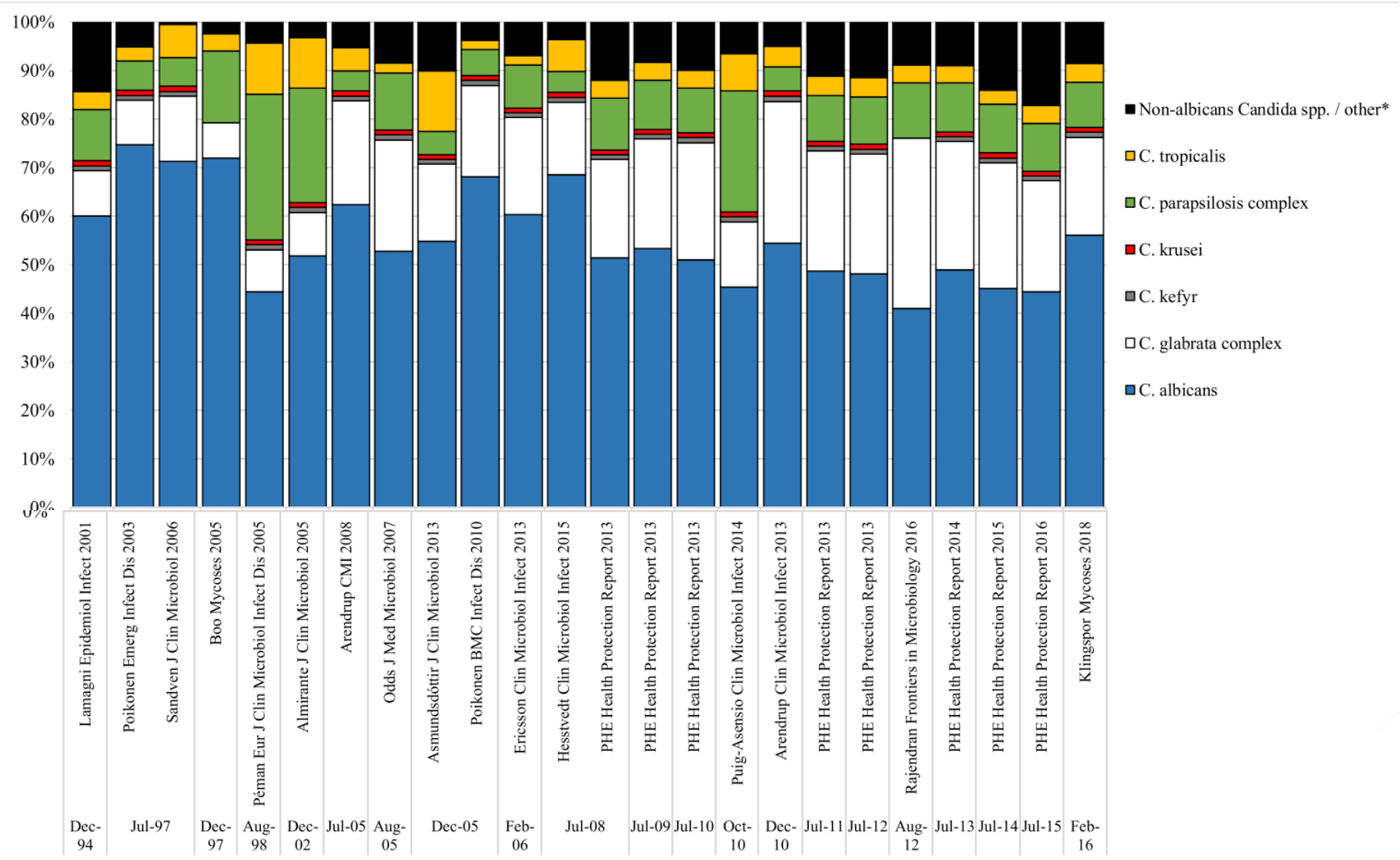
Frederic Lamoth[1,2]†, Shawn R. Lockhart[3]*†, Elizabeth L. Berkow[3] and Thierry Calandra[1]

[1]Infectious Diseases Service, Department of Medicine, Lausanne University, Lausanne, Switzerland; [2]Institute of Microbiology, Lausanne University Hospital, Lausanne, Switzerland; [3]Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, GA, USA

Table 1. Candidaemia epidemiology from population-based or multicentre studies

Country	Years covered	Number of candidaemia episodes	Annual incidence rate	Proportion *C. albicans*/ non-*albicans*	Rate of azole resistance	30 day mortality rate	Reference
USA	2008–11	2675	13.3–26.2/100000 population *	37/63	7%	28%–29%	7
USA	2013	515	9.5–14.4/100000 population	35/65	5%–7%	NA	8
Canada	2003–05	453	3.0/100000 population	62/38	4%	NA	143
Norway	2004–12	1677	3.9/100000 population	68/32	7%	NA	11
Finland	2004–07	603	2.9/100000 population	67/33	NA	35%	144
Iceland	2000–11	208	5.7/100000 population	56/44	3%	30%	145
Denmark	2004–09	2649	8.6/100000 population *	58/42	NA	NA	13
France	2001–10	15 570	3.6/100000 population	NA	NA	NA	146
Spain	2010–11	773	8.1/100000 population *	45/55	21% *	31%	14
Belgium	2013–14	338	0.4/1000 admissions	50/50	8%	NA	28
Scotland	2007	242	4.8/100000 population	50/50	2%	NA	29
Australia	2001–04	1095	1.8/100000 population	47/53	NA	28%	147
Australia	2014–15	527	2.4/100000 population	44/56	6%	NA	10
Brazil	2007–10	137	NA	34/66	9%	72%	30
Peru	2013–15	157	2.0/1000 admissions	28/72	3%	40%	148
Latin America	2008–10	672	0.3–2.0/1000 admissions	38/62	3%	41%	31
South Africa	2009–10	2172	NA	46/54	18% *	NA	33
Asia-Pacific	2010–11	1601	0.3–2.9/1000 discharges	41/59	NA	NA	20
India	2011–12	1400	6.5/1000 admissions[a] *	21/79	12%	45%	35

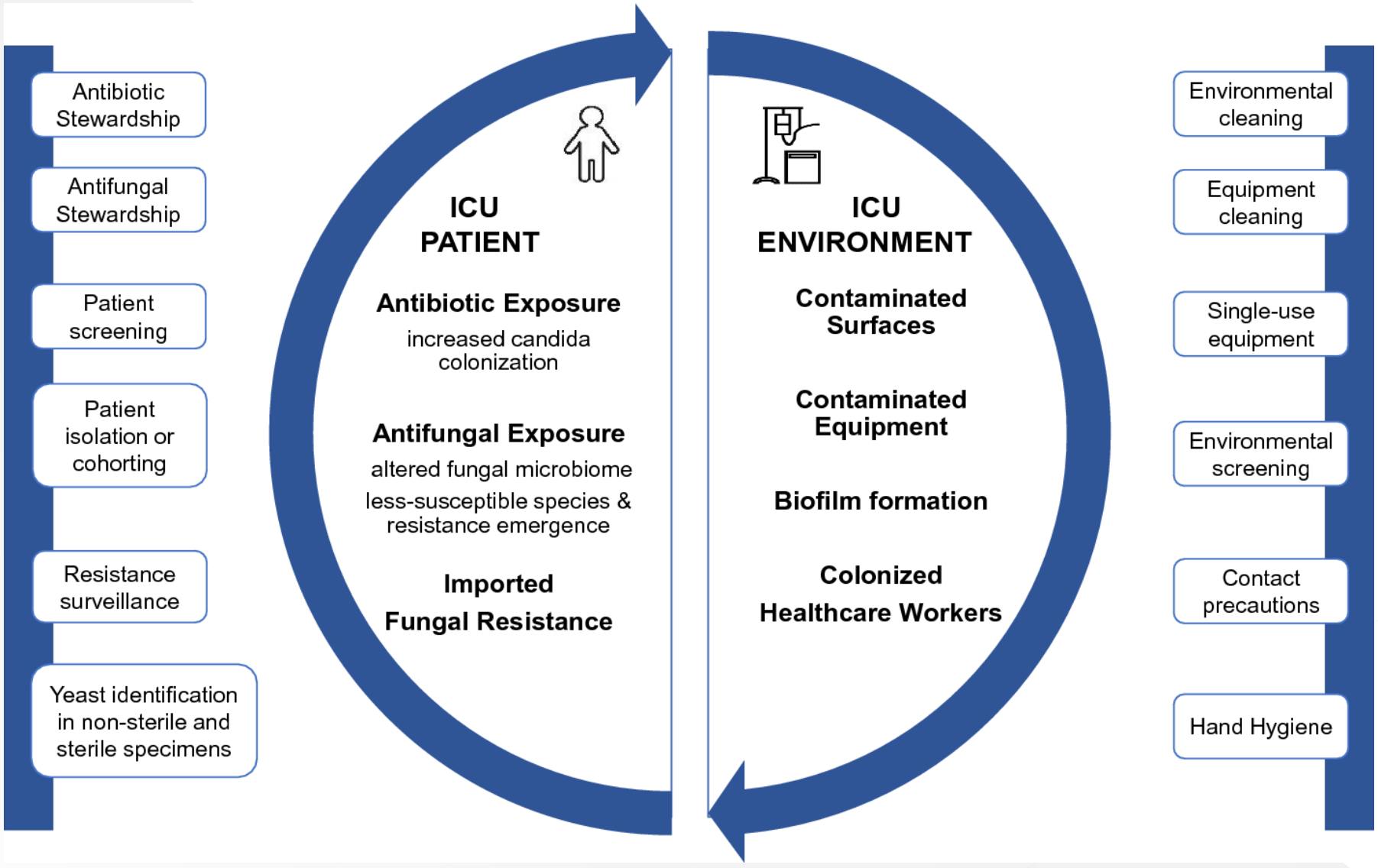
Espèces de *Candida*



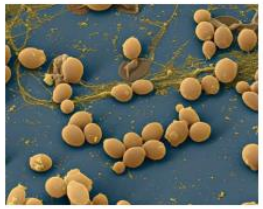
Candida non spécifiés: *C. ciferrii, C. dubliniensis, C. famata, C. guilliermondii, C. humicola, C. inconspicua, C. kefyr, C. lipolytica, C. lusitaniae, C. norvegensis,C. pelliculosa, C. rugusa, C. saké, C. utilis,

Species	Antifungal agent	No. (%) of isolates resistant to each antifungal agent by region[a]				
				Asia-Pacific	L. America	Europe
C. albicans	Anidulafungin	29 (0.0)	161 (0.0)	414 (0.2)	406 (0.0)	1,010 (0.1)
	Micafungin	29 (0.0)	161 (0.0)	414 (0.2)	406 (0.0)	1,010 (0.1)
	Fluconazole	29 (3.4)	161 (0.0)	414 (0.0)	406 (0.0)	1,010 (0.1)
	Posaconazole	29 (0.0)	161 (0.0)	414 (0.0)	406 (0.0)	1,010 (0.0)
	Voriconazole	29 (0.0)	161 (0.0)	414 (0.0)	406 (0.0)	1,010 (0.0)
C. glabrata	Anidulafungin	7 (0.0)	18 (0.0)	131 (1.5)	220 (3.2)	376 (2.4)
	Micafungin	7 (0.0)	18 (0.0)	131 (0.8)	220 (2.7)	376 (1.9)
	Fluconazole	7 (0.0)	18 (0.0)	131 (2.3)	220 (8.2)	376 (5.6)
	Posaconazole	7 (0.0)	18 (0.0)	131 (1.5)	220 (5.5)	376 (3.7)
	Voriconazole	7 (0.0)	18 (0.0)	131 (0.0)	220 (5.9)	376 (3.5)
C. parapsilosis	Anidulafungin	7 (0.0)	89 (0.0)	103 (0.0)	160 (0.0)	359 (0.0)
	Micafungin	7 (0.0)	89 (0.0)	103 (0.0)	160 (0.0)	359 (0.0)
	Fluconazole	7 (0.0)	89 (6.7)	103 (3.9)	160 (5.0)	359 (5.0)
	Posaconazole	7 (0.0)	89 (0.0)	103 (0.0)	160 (0.0)	359 (0.0)
	Voriconazole	7 (0.0)	89 (0.0)	103 (0.0)	160 (0.0)	359 (0.0)
C. tropicalis	Anidulafungin	6 (0.0)	59 (0.0)	55 (0.0)	98 (1.0)	218 (0.5)
	Micafungin	6 (0.0)	59 (0.0)	55 (0.0)	98 (0.0)	218 (0.0)
	Fluconazole	6 (0.0)	59 (1.7)	55 (3.6)	98 (4.1)	218 (3.2)
	Posaconazole	6 (0.0)	59 (0.0)	55 (0.0)	98 (2.0)	218 (0.9)
	Voriconazole	6 (0.0)	59 (1.7)	55 (3.6)	98 (2.0)	218 (2.9)
C. krusei[b]	Anidulafungin	1 (0.0)	5 (0.0)	19 (0.0)	15 (0.0)	40 (0.0)
	Micafungin	1 (0.0)	5 (0.0)	19 (0.0)	15 (0.0)	40 (0.0)
	Posaconazole	1 (0.0)	5 (0.0)	19 (0.0)	15 (0.0)	40 (0.0)
	Voriconazole	1 (100.0)[c]	5 (0.0)	19 (0.0)	15 (0.0)	40 (2.5)

Réservoirs de résistance en USI et interventions pour prévenir



Epidémiologie et spectre des levures isolées en Tunisie (Etude multicentrique nationale)

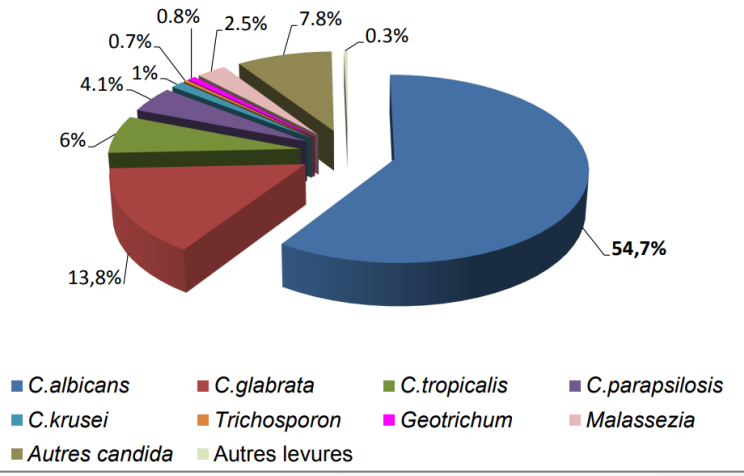


6 centres participants

CHU Habib Bourguiba; CHU Farhat Hached; Hôpital Rabta; Hôpital Charles Nicolle; Institut pasteur; Hôpital militaire

(5 ans:2011-2015)

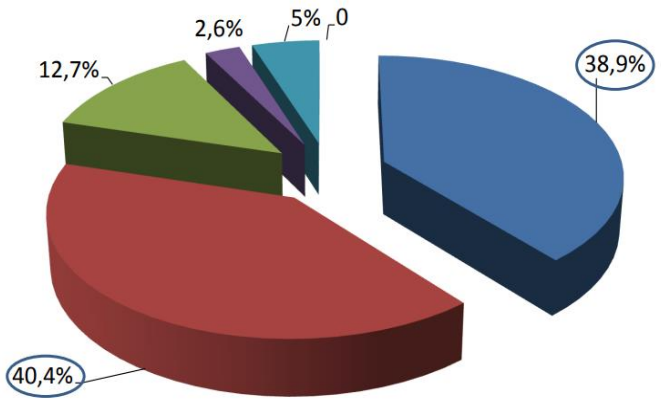
Distribution globale des levures isolées



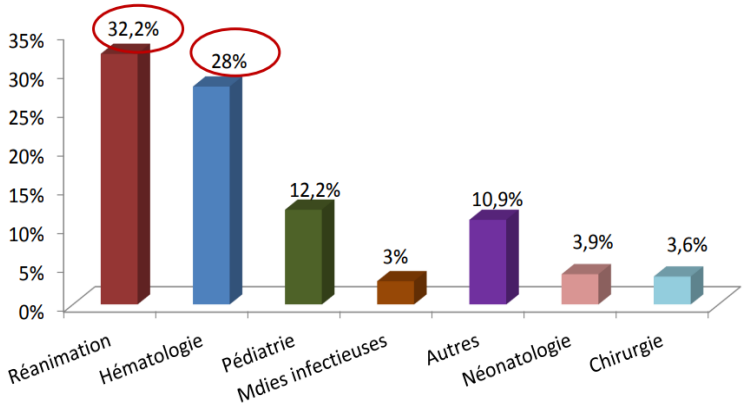
Distribution des candidémies selon les espèces et les régions géographiques

Espèces	% des espèces par région		
	Tunis (482)	Sousse (48)	Sfax (331)
C.albians	30,9	**48**	**29,3**
C.tropicalis	14,3	18,7	20
C.glabrata	12,2	3,5	7
C.parapsilosis	**33,4**	12,5	10,5
C.krusei	1,4	6,2	3
C.lipolytica	-	-	23,2

Distribution des septicémies à levures selon les centres: 935 cas



Distribution des levures isolées des hémocultures selon les services

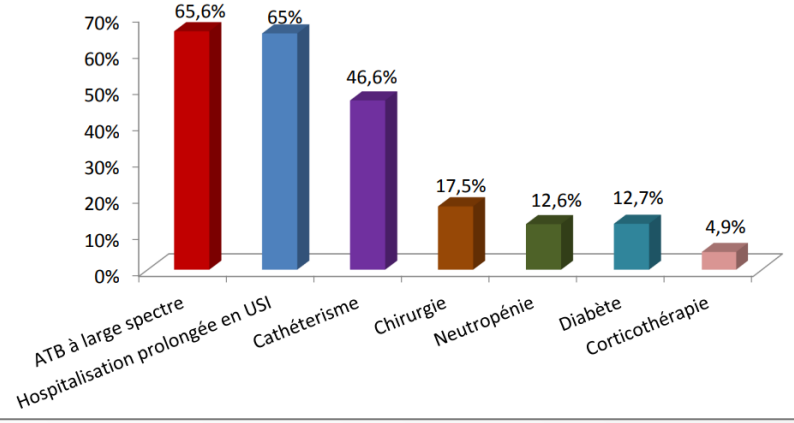


H.B. Sfax, hop. militaire et Charles Nicolle: Réanimation +++

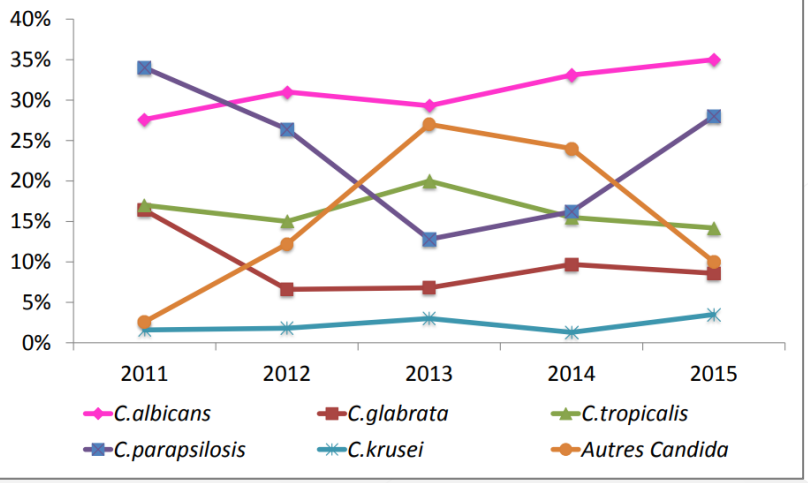
Hop. Rabta: Hématologie (centre de greffe)++

Sousse: Néonatologie+++

Distribution des septicémies à levures selon les facteurs de risque



Evolution des espèces de *Candida* isolées des hémocultures selon les années



Localement: « REA MED LA RABTA »

- **2001 – 2010**
  - **18 / 1000 ad** (délai moy de 20.7 j)
  - C.albicans : 53,3%
  - C.parapsilosis : 23,3%
  - C.glabrata : 13.3%

Thèse Mbarki Mars 2012

- **2006 - 2017**
  - **16.6 / 1000 ad** (délai med oy de 10.2 j)
  - C.albicans : 42%
  - C.parapsilosis : 33,3%
  - C.glabrata : 16%
  - C.tropicalis : 14%

Thèse Klai Dec 2019

CI/COVID?

Clinical Infectious Diseases® 2021;73(7):e1634–44

Clinical Infectious Diseases

MAJOR ARTICLE

A National Strategy to Diagnose Coronavirus Disease 2019–Associated Invasive Fungal Disease in the Intensive Care Unit

P. Lewis White,[1] Rishi Dhillon,[1] Alan Cordey,[1] Harriet Hughes,[1] Federica Faggian,[1] Shuchita Soni,[1] Manish Pandey,[2] Harriet Whitaker,[3] Alex May,[1] Matt Morgan,[2] Matthew P. Wise,[2] Brendan Healy,[4] Ian Blyth,[4] Jessica S. Price,[1] Lorna Vale,[1] Raquel Posso,[1] Joanna Kronda,[1] Adam Blackwood,[1] Hannah Rafferty,[1] Amy Moffitt,[1] Alexandra Tsitsopoulou,[5] Soma Gaur,[6] Tom Holmes,[2] and Matthijs Backx[1]

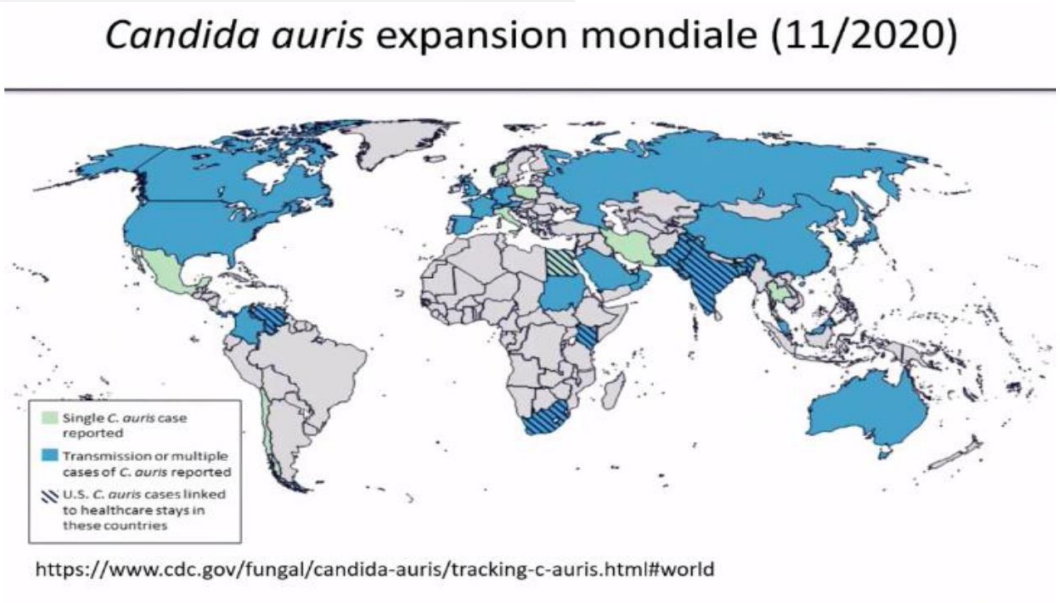
[1]Public Health Wales Microbiology Cardiff, University Hospital of Wales, Cardiff, UK, [2]Intensive Care Medicine, University Hospital of Wales, Heath Park, Cardiff, UK, [3]Department of Pharmacy, University Hospital of Wales, Cardiff, UK, [4]Public Health Wales Microbiology Swansea, Singleton Hospital, Swansea, UK, [5]Cwm Taf Microbiology Department, Royal Glamorgan, Ynysmaerdy, Rhondda Cynon Taf, UK, and [6]Aneurin Bevan Microbiology Department, Royal Gwent Hospital, Newport, Gwent, UK

- Evaluation de cohorte prospective MC d'une stratégie de test pour diagnostiquer une IFI chez les patients COVID-19 en USI

- **Résultats:**
  - **135** adultes (57 ans, H/F : 2,2) dépistés
  - IFI : 26,7 % (**aspergillose (14,1 %)** et **CI (12,6 %)**)
  - Mortalité globale= 38 % (IF:53 % et sans IF: 31 % , p=0,03)
  - Risque ↗:
    - corticostéroïdes (p=0,007)
    - ATCD d' IRpC (p= 0,05)

Épidémiologie : récapitulation

- Incidence ↗↗
- USI, centres d'oncologie et unités de transplantation ++
- Dernière décennie: augmentation des souches *non albicans*
- Résistance aux AF de plus en plus diagnostiqués
- **C. auris+++**
  - Menace mondiale provoquant des épidémies sur tous les continents
  - Connu pour survivre sur la peau humaine et les surfaces environnementales pd plusieurs sem
  - Résistance élevée au fluconazole, l'amphotéricine B et échinocandines
  - Propagation et mortalité élevée+



Diapositive: ME Bougnoux RICAI 2020

Du H, Bing J, Hu Tet al. . Candida auris: epidemiology, biology, antifungal resistance, and virulence. PLoS Pathog 2020; 16: e1008921. 10.1371/journal.ppat.1008921

CI: Mortalité à 30 J

- **Taux de mortalité le plus élevé parmi les IN (40 - 55 %)**

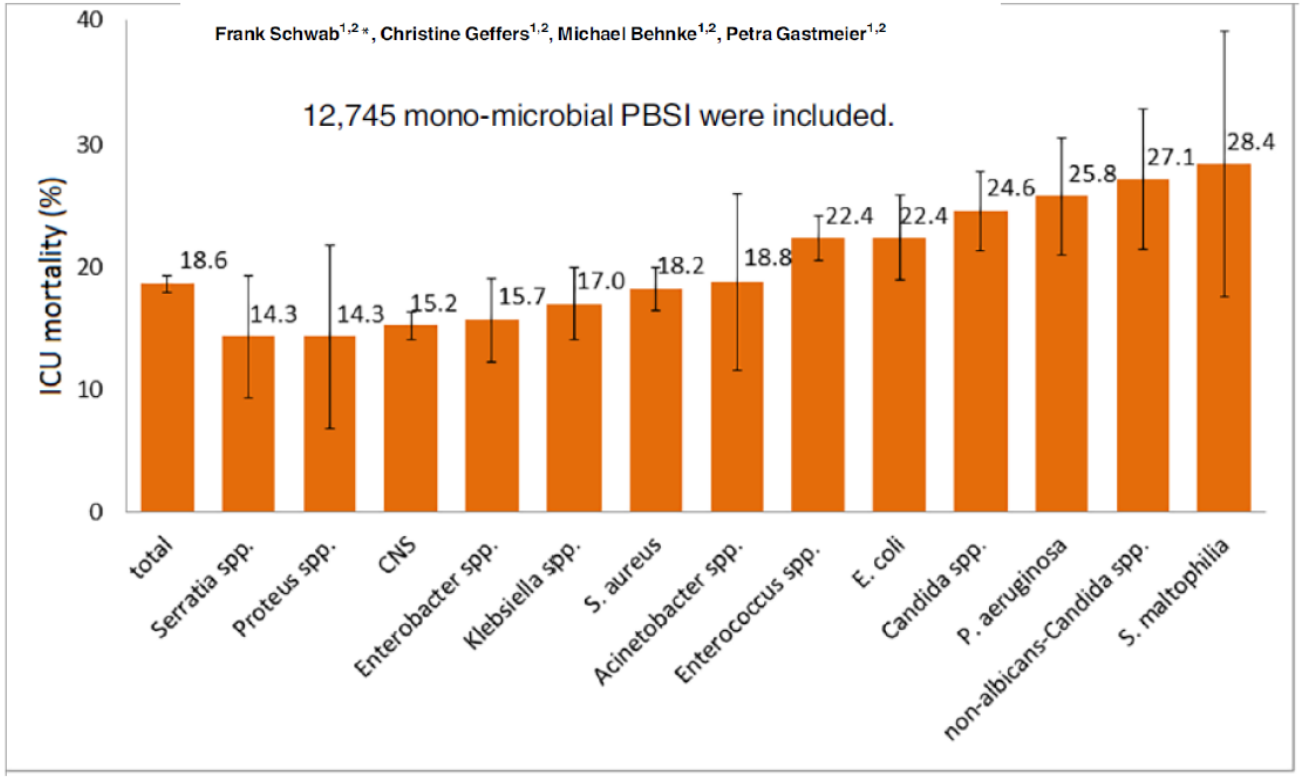
RESEARCH ARTICLE

ICU mortality following ICU-acquired primary bloodstream infections according to the type of pathogen: A prospective cohort study in 937 Germany ICUs (2006-2015)

March 8, 2018

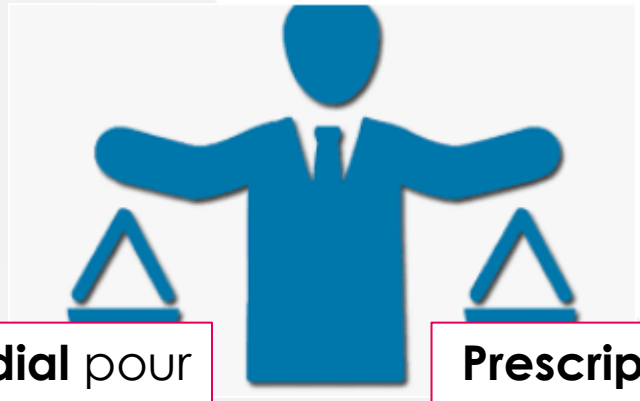
Frank Schwab[1,2]*, Christine Geffers[1,2], Michael Behnke[1,2], Petra Gastmeier[1,2]

12,745 mono-microbial PBSI were included.



Challenge 2 : Est-ce une CI? culture et non culture, Rôle des scores de risque…

DILEMME



Dg précoce= primordial pour ttt rapide et tout retard : risque de mortalité et des coûts

Prescription abusive des AF :

- toxicités médicamenteuses
- émergence de résistances

Challenge 2 : Est-ce une CI? culture et non culture, Rôle des scores de risque…

- **Hémoculture: référence diagnostique**
  - Sensibilité 63 % et 83 % pour candidémie
  - Moindre en cas de candidose profonde (21 % et 71 %)
  - Variable selon: *candida spp.*, Et l'utilisation d'af
  - Délai d'obtention: 2 à 3 jours
- **Techniques rapides (spectrométrie de masse: MALDI-TOF):**
  - Identification rapide et précise
  - Outil prometteur pour la détection de la résistance acquise aux AF
  - Pas universellement disponible
- **Tests non basés sur la culture:** Degré de sensibilité variable
  - Mannane - anti-mannane
  - Détection d'anticorps
  - Détection de BDG
  - Détection par PCR
- **Tests combinés: perspective…..**

Infection
https://doi.org/10.1007/s15010-023-02053-4

RESEARCH

The added value of (1,3)-β-D-glucan for the diagnosis of Invasive Candidiasis in ICU patients: a prospective cohort study

Martin Christner[1] · Beya Abdennadher[1] · Dominic Wichmann[2] · Stefan Kluge[2] · Amra Pepić[3] · Martin Aepfelbacher[1] · Holger Rohde[1] · Flaminia Olearo[1]

Received: 9 November 2022 / Accepted: 14 May 2023

- 174 patients en USI
- TTT empirique par échino pour suspicion de CI (dont 25,7 % CI prouvée)
- série BDG effectuée: J1 du ttt puis toutes les 24 à 48 H

- **Sensibilité modérée (74 %, [59-86 %])**
- **Faible spécificité (45 %,[36-54 %])**

Conclusions: In our study of critically ill intensive care patients at high risk for candidemia or invasive candidiasis, diagnostic accuracy of BDG testing was insufficient to inform treatment decisions. Improved classification was only achieved for cases with very high BDG values

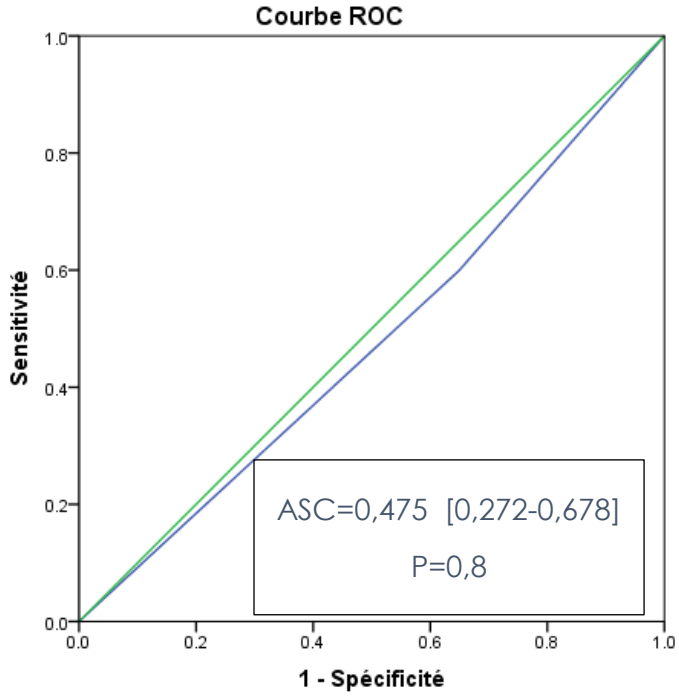
Notre expérience avec BDG

- **Conception:**
  - Étude prospective évaluative
  - REA MED/ parasitologie-mycologie
  - sur 4 mois (de février au mai 2023)
  - Patients hospitalisés en réa à risque de CI
  - Dosages de BDG à rythme hebdomadaire (en plus de l'HC, IC et calcul de CS)
  - Statut VP: CI confirmée ou fort probable et un test BDG positif (> 80 pg/mL).

Résultats:

- **50 tests BDG / 30 malades**
- CI retenue dans 10 cas

Performance du test BDG dans le diagnostic de CI



Mémoire Tlili B, oct 2023

	Sensibilité	Spécificité	VPP	VPN
Valeurs	60%	35%	18,75%	74,46%

Invasive candidiasis: current clinical challenges and unmet needs in adult populations

Alex Soriano, Patrick M Honore, Pedro Puerta-Alcalde ✉, Carolina Garcia-Vidal, Anna Pagotto, Daniela C Gonçalves-Bradley, Paul E Verweij

Journal of Antimicrobial Chemotherapy, Volume 78, Issue 7, July 2023, Pages 1569–1585, https://doi.org/10.1093/jac/dkad139

Published: 23 May 2023

Table 1. Overview of key diagnostics

Test	Advantages	Limitations
Microscopy	Fast turnaround[46] High sensitivity when using fluorescent brightener staining[6,51]	Inability to identify species[6]
Blood culture	Species identification[19] Susceptibility pattern	Slow turnaround[21,53] Timing of blood collection, during the course of infection[19] Necessary to culture a large blood volume (40 mL) in aerobic flasks[53] When *Candida* density is low (<1 cfu/mL), blood cultures can result in false negatives Cultures may become negative after initiating antifungal therapy[5]
Sterile site cultures	Species identification Susceptibility pattern	May require invasive procedures[19] Cultures may become negative after initiating antifungal therapy[5] Long incubation required for optimal performance (3 days)[6] For intra-abdominal candidiasis, lack of specificity to differentiate infection from colonisation[35]
Mannan antigen/anti-mannan antibodies	Early detection[22,54] Useful to rule out infection[22]	from colonisation[35] Serial determinations required[22] Lower utility in immunosuppred hosts[52] May not distinguish between past and acute infections[19] Sensitivity varies regarding *Candida* species (better for *C. albicans*, *N. glabrata* and *C. tropicalis*)[54] Decreased specificity if *Candida* colonisation is present[54] Low positive predictive value, potentially leading to antifungals overuse Limited by low serum concentrations and rapid bloodstream clearance[19] Not species-specific, requiring further tests to identify the fungus[46] No data on susceptibility pattern Not approved by FDA[19] Not universally available
CAGTA (C. albicans germ tube antibody)	Fast turnaround and low cost[5] Could be used to detect whether candidaemia originated in a catheter or deep organs[55]	May not distinguish between past and acute infections[19] Limited by low serum concentrations and rapid bloodstream clearance[19] Sensitivity varies according to *Candida* species (lower for *C. tropicalis*)[5,19] Not species-specific, requiring further tests to identify the fungus[46] Low positive predictive value, potentially leading to antifungals overuse No data on susceptibility pattern Not approved by FDA[19] Not universally available

Test	Advantages	Limitations
BDG	Early detection[22] Useful to rule out infection[22]	Not universally available Serial determinations required[22] Lower utility in patients with haematological disease[22] and immunosuppred hosts[52] Sensitivity varies according to *Candida* species (lower for *C. parapsilosis*)[19] May not distinguish between past and acute infections[19] Not species-specific, requiring further tests to identify the fungus[45] Low positive predictive value, potentially leading to antifungal overuse No data on susceptibility pattern
Nucleic acid amplification-based methods PCR	Early detection[58] Monitoring of persistence or resolution of infection[4]	Not universally available Mostly developed in-house or commercially[19] Frequently performed in reference laboratories limiting the advantage of short turnaround time[45] Data interpretation impaired by test heterogeneity[19]
T2Candida	Early detection[19,59] Automated molecular diagnosis[49,59] May detect candidaemia missed by cultures during empirical or pre-emptive AF therapy[4] Improved performance in neutropenic patients[4]	Not universally available Costs associated with the test[46] Limited to some *Candida* species (*C. albicans/C. tropicalis*, *N. glabrata/P. kudriavzevii*, and *C. parapsilosis*, groupings that are based on typical antifungal susceptibility pattern)[49,59] No data on susceptibility pattern[59] Not universally available

AF, antifungal; BDG, β-D-glucan; CAGTA, C. albicans germ tube antibody; cfu, colony forming units; FDA, Food and Drug Administration; PCR, polymerase chain reaction.

Rôle des scores de risque de CI

1/ IC

2/ CS

3/OZ

INDEX DE PITTET = nombre de sites colonisés/nombre de sites testés
>ou= 0,5
Valeurprédictive négative de 100%
Pittet et al, Annal Surg 1994

Critical Care Medicine
OFFICIAL JOURNAL OF THE SOCIETY OF CRITICAL CARE MEDICINE

"A bedside scoring system for early antifungal treatment in nonneutropenic critically ill patients with Candida colonization".

NUTRITION PARENTERALE	1
CHIRURGIE	1
COLONISATION A CANDIDA SPP	1
SEPSIS SEVERE	2

SCORE > 2,5 RISQUE DE CANDIDOSE INVASIVE x 7,75 IC95% [4,74-12,66]

Leon et al, Crit Care Med 2006

"Invasive candidiasis is highly improbable if a Candida-colonized non-neutropenic critically ill patient has a candida score < 3"

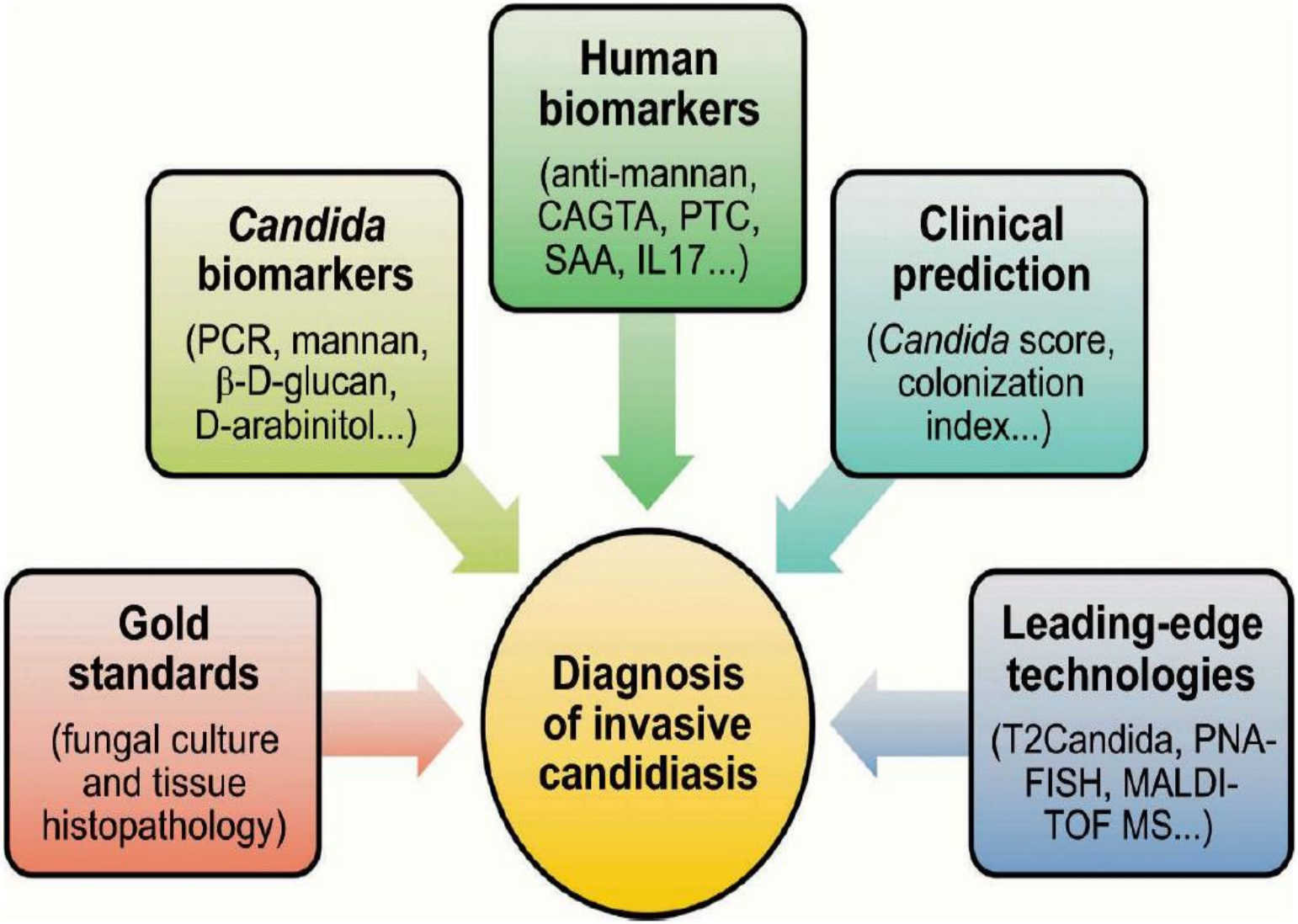
Leon et al, Crit Care Med 2009

Ostrosky-Zeichner Clinical Prediction Rule	Mechanical ventilation ≥ 48hours AND Systemic antibiotic AND CVP (on any of day 1–3 of ICU admission) plus ≥1 of: any major surgery (days 7–0), pancreatitis (days 7–0), use of steroids/other immunosuppressive agents (days 7–0), use of TPN (days 1–3), or dialysis (days 1–3)

• **CS**: largement débattu, non validé pour toutes les populations

- **VPN élevée , VPP faible: plus utiles pour exclure les patients**

Challenge 2: diagnostique



Challenge 3: quand commencer le traitement antifongique ?

Table 1 Glossary of terms: antifungal prescribing strategies

From: Invasive candidiasis in critical care: challenges and future directions

Prescribing term	Definition
Prophylaxis	AFT prescribed to prevent fungal infection in at-risk hosts
Empirical	AFT prescribed in response to signs and symptoms of infection in an at-risk ICU host
Pre-emptive	AFT prescribed in response to positive fungal non-culture-based tests or radiology
Targeted	AFT prescribed in response to microbiological evidence of proven IC

AFT antifungal therapy, *IC* invasive candidiasis, *ICU* intensive care unit

- AF empirique: 2/3 ne présentaient pas par la suite une IF

  Azoulay E, Dupont H, Tabah A, Lortholary O, Stahl JP, Francais A, Martin C, Guidet B, Timsit JF. Systemic antifungal therapy in critically ill patients without invasive fungal infection. Crit Care Med. 2012 Mar;40(3):813-22. doi: 10.1097/CCM.0b013e318236f297.*

- **Nombreux essais** (colonisation par *Candida*, scores de prédiction clinique et tests fongiques non basés sur la culture)

- Leur impact sur la pratique clinique reste vivement débattu ….

Plein d'études rétrospectives: pas de bénéfice sur la survie d'un AF empirique

Comparative Study > Clin Ther. 2010 Apr;32(4):637-48. doi: 10.1016/j.clinthera.2010.04.005.

Evaluation of caspofungin or micafungin as empiric antifungal therapy in ad… febrile neutropenia: a re… sequential cohort…

David W Kubiak [1], Julie M Bry…
Lindsey R Baden, Francisco M …

Affiliations + expand

> Eur J Clin Microbiol Infect Dis. 2022 Dec;41(12):1421-1432. doi: 10.1007/s10096-022-04507-3. Epub 2022 Oct 18.

…ortality …dy

Review > Cochrane Database Syst Rev. 2016 Jan 16;2016(1):CD004920. doi: 10.1002/14651858.CD004920.pub3.

Antifungal agents for preventing fungal infections in non-neutropenic critically ill patients

Andrea Cortegiani [1], Vincenzo Russotto, Alessandra Maggiore, Massimo Attanasio, Alessandro R Naro, Santi Maurizio Raineri, Antonino Giarratano

Affiliations + expand

PMID: 26772902 PMCID: PMC6464510 DOI: 10.1002/14651858.CD004920.pub3

Free PMC article

Multicenter Study > Int…

doi: 10.1016/j.ijantimicag.201…

…):1139-46.

Impact of initia… outcome of crit… ca… …l therapy in …ients

Na … …e Orgeas, Christophe Adrie, …ca Hamidfar-Roy, Michael Darmon

Review > J Fungi (Basel). 2022 Oct 29;8(11):1146. doi: 10.3390/jof8111146.

Survival Outcome of Empirical Antifungal Therapy and the Value of Early Initiatio… Decade

Souha S Kanj [1], Ali S Omrani [2 3], Hail M Al-Abdely [4], Ahr…
Ibraheem Abosoudah [7], Hazar Kanj [8], George Dimopoulo…

Empiric antifungal and outcome in ICU patients.

Ahlem Trifi, Sami Abdellatif, Foued Daly, Rochdi Nasri, Yosr Touil, Salah Ben Lakhal

La tunisie Medicale - 2019 ; Vol 97 (n°04) : 579-587 [9042 times seen]

MSG-01: A Randomized, Double-Blind, Placebo-Controlled Trial of Caspofungin Prophylaxis Followed by Preemptive Therapy for Invasive Candidiasis in High-Risk Adults in the Critical Care Setting

Luis Ostrosky-Zeichner ✉, Shmuel Shoham, Jose Vazquez, Annette Reboli, Robert Betts, Michelle A. Barron, Mindy Schuster, Marc A. Judson, Sanjay G. Revankar, Juan Pablo Caeiro ... Show more

Author Notes

Clinical Infectious Diseases, Volume 58, Issue 9, 1 May 2014, Pages 1219–1226, https://doi.org/10.1093/cid/ciu074

- 222 adultes au moins 3 jours en USI (ventilés, ATB, cath… …gi + 1 FDR supplémentaire (nutrition parentérale, dialyse, ch… …créatite, CC ou IS)
- (1,3)-β-d-glucane x 2/ sem
- Jugement: incidence de CI prouvée o… … selon les critères EORTC/MSG (European Organization for Research and Treatment of C… …he Mycoses Study Group)

Conclusions. Caspofungin was safe and tended to reduce the incidence of invasive candidiasis when used for prophylaxis, but the difference was not statistically significant. A preemptive therapy approach deserves further study.

Table 3. Study Endpoints and Outcomes

Variable	Prophylaxis/MITT Population		
	Caspofungin (n = 102)	Placebo (n = 84)	*P* Value
Incidence of pr… …IC by DRC, %	9.8	16.7	.14
Incidence c… …DRC, %	1.0	4.8	.11
Use of antifu… …within 7 d EOT, %	13.7	17.9	.35
All-cause mortality within 7 d EOT, %	16.7	14.3	.78

Abbreviations: DRC, data review committee; EOT, end of therapy; IC, invasive candidiasis; MITT, modified intention to treat.

A Randomized, Placebo-controlled Trial of Preemptive Antifungal Therapy for the Prevention of Invasive Candidiasis Following Gastrointestinal Surgery for Intra-abdominal Infections

Wolfgang Knitsch ✉, Jean-Louis Vincent, Stefan Utzolino, Bruno François, Tamás Dinya, George Dimopoulos, İlhan Özgüneş, Juan Carlos Valía, Philippe Eggimann, Cristóbal León ... Show more

Clinical Infectious Diseases, Volume 61, Issue 11, 1 December 2015, Pages 1671–1678, https://doi.org/10.1093/cid/civ707

- Essai exploratoire, randomisé, en double aveugle et contrôlé
- Approche AF préventive avec la micafungine (100 mg/j) vs placebo
- Patients d'USI nécessitant une intervention chirurgicale pour une infection intra-abdominale.
- Jugement: incidence de CI et le temps de la première CI

Conclusions. This study was unable to provide evidence that preemptive administration of an echinocandin was effective in preventing IC in high-risk surgical intensive care unit patients with intra-abdominal infections. This may have been because the drug was administered too late to prevent IC coupled with an overall low number of IC events. It does provide some support for using βDG to identify patients at high risk of IC.

Table 2. Incidence of Invasive Candidiasis in the Full Analysis Set and Per-Protocol Set for All Patients

IC Incidence	Patient With IC/Total [illegible]		
	Placebo	Mi[illegible]	[illegible]ce [illegible]), % (95% CI)
All patients (FAS)			
IDRB-confirmed IC	11/124 (8.9)		2.24 (–5.52 to 10.20)
Investigator-confirmed IC[a]	20/121 (1[illegible]		–2.74 (–11.92 to 6.56)
Any-confirmed IC[a]	2[illegible]		–1.88 (–11.24 to 7.58)
All patients (PPS)			
IDRB-confirmed IC		[illegible]/79 (6.3)	0.65 (–7.17 to 8.95)

Abbreviations: CI, confide[illegible]; IDRB, independent data review board; PPS, per-protocol set.

[a] FAS was modified ac[illegible] confirmed IC includes IC confirmed by IDRB and/or investigator.

[b] Micafungin 100 mg/d.

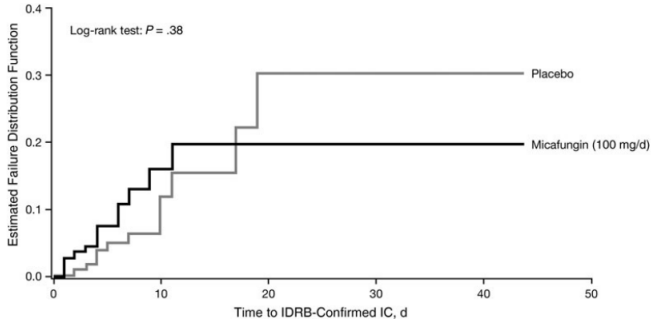


Figure 2. Kaplan–Meier failure curves of time to independent data review board (IDRB)-confirmed invasive candidiasis (IC) (full analysis set).

Original Investigation | Caring for the Critically Ill Patient FREE

October 18, 2016

Empirical Micafungin Treatment and Survival Without Invasive Fungal Infection in Adults With ICU-Acquired Sepsis, *Candida* Colonization, and Multiple Organ Failure

The EMPIRICUS Randomi- Trial

Jean-Francois Timsit, MD, PhD[1,2]; Elie A- ; et al

Conclusions and Relevance Among nonneutropenic critically ill patients with ICU-acquired sepsis, *Candida* species colonization at multiple sites, and multiple organ failure, empirical treatment with micafungin, compared with placebo, did not increase fungal infection–free survival at day 28.

- RCT multicen
- double a
- 251 pa
- A l

e vs placebo)

et CS

- Su 68 % vs 60 %, p = 0,18
- %, p = 0,07
- BD s 56 %, p = 0,19
- CS ≥ vs 55 %, p = 0,21
- IC ≥ 0,3 : 67% vs 59%, p = 0,22

Clinical Infectious Diseases

IDSA GUIDELINE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America

Peter G. Pappas,[1] Carol A. Kauffman,[2] David R. Andes,[3] Cornelius J. Clancy,[4] Kieren A. Marr,[5] Luis Ostrosky-Zeichner,[6] Annette C. Reboli,[7] Mindy G. Schuster,[8] Jose A. Vazquez,[9] Thomas J. Walsh.[10] Theoklis E. Zaoutis.[11] and Jack D. Sobel[12]

[1]University of Alabama at Birmingham; [2]Ve
Pittsburgh, Pennsylvania; [5]Johns Hopkins U
Camden, New Jersey; [8]University of Penns
Hospital of Pennsylvania, Philadelphia; and

V. What Is the Role of Empiric Treatment for Suspected Invasive Candidiasis in Nonneutropenic Patients in the Intensive Care Unit?

Recommendations

28. Empiric antifungal therapy should be considered in critically ill patients with risk factors for invasive candidiasis and no other known cause of fever and should be based on clinical assessment of risk factors, surrogate markers for invasive candidiasis, and/or culture data from nonsterile sites *(strong recommendation; moderate-quality evidence)*. Empiric antifungal therapy should be started as soon as possible in patients who have the above risk factors and who have clinical signs of septic shock *(strong recommendation; moderate-quality evidence)*.

Description et performances des outils utilisés pour l'identification précoce des patients pouvant bénéficier d'un ttt AF

Tool	Description	Performance	References
Candida Colonization Index			
Candida Colonization Index	Ratio of the number of (non-blood) sites colonized with *Candida* spp /total number of sites cultured Threshold = 0.5	PPV = 66% NPV = 100%	[45]
Clinical prediction scores			
Candida Score	Candida Score = TPN (1 point), surgery (1 point), severe sepsis (2 points), Multifocal Candida colonization (1 point). Threshold = 2.5	Sensitivity = 81% Specificity = 74% PPV = 16% NPV = 98%	[46]
Ostrosky-Zeichner Clinical Prediction Rule	Mechanical ventilation ≥ 48hours AND Systemic antibiotic AND CVP (on any of day 1–3 of ICU admission) plus ≥1 of: any major surgery (days 7–0), pancreatitis (days 7–0), use of steroids/other immunosuppressive agents (days 7–0), use of TPN (days 1–3), or dialysis (days 1–3)	Sensitivity = 50%, Specificity= 83% PPV = 10% NPV = 97%	[47]
Non-culture-based tests			
1,3-β-d-glucan (BDG)*	detection of (1–3)-beta-d-Glucan (BDG), a panfungal (incl *Candida* and *Aspergillus*) cell wall marker, in serum	Sensitivity ~ 75–80% Specificity ~ 60–85%	[48,49,50]
Candida mannan and anti-mannan*	Detection of mannan antigen (MAg) (a cell wall component) and anti-mannan IgG antibodies (Anti-Mn) in serum	Combined MAg and Anti-Mn Sensitivity ~ 79–87% Specificity ~ 80–90%	[51]
Candida albicans germ tube antibody (CAGTA)*	Detects antibodies to antigens located on the cell wall of *Candida albicans*	Sensitivity ~ 59–73% Specificity ~ 58–88%	[52]
Multiplex *Candida* real time polymerase chain reaction (PCR)*	Detection of *Candida* DNA by polymerase chain reaction	Sensitivity ~61–95% Specificity ~92–99%	[53, 54]
T2-magnetic resonance *Candida* assay (T2Candida)*	Miniaturized magnetic resonance technology to identify and speciate whole *Candida* cells of the five most common *Candida*: *albicans, glabrate, parapsilosis, tropicalis* and *krusei*	Sensitivity ~88–94% Specificity ~93–95%	[55]

Logan, C., Martin-Loeches, I. & Bicanic, T. Invasive candidiasis in critical care: challenges and future directions. *Intensive Care Med* **46**, (2020). https://doi.org/10.1007/s00134-020-06240-x

Challenge 4 : choisir l'AF optimal pour le patient en USI

3 classes :

- **Échinocandines** (anidulafungine, caspofungine, micafungine):
  - spectre d'activité plus large,
  - **activité fongicide** plus élevée pour la plupart des espèces de Candida,
  - faible interaction médicamenteuse,

- **Azoles** (fluconazole, voriconazole, itraconazole, posaconazole, isavuconazole):
  - bien tolérés
  - Bonne pénétration ds candidoses profondes (cérébrales, intraoculaires et urinaires)
  - IV ou orale

- **Polyènes : Basées sur l'Amphotéricine B :**
  - EI graves, (néphrotoxicité++)
  - formulations lipidiques++

- **Nouveaux agents:** en cours d'essais
  - Ibrexafungerp, fosmanogepix, rezafungin

Mycoses
Diagnosis, Therapy and Prophylaxis of Fungal Diseases

ORIGINAL ARTICLE

Comparative effectiveness of amphotericin B, azoles and echinocandins in the treatment of candidemia and invasive candidiasis: A systematic review and network meta-analysis

Koray K. Demir, Guillaume Butler-Laporte, Olivier Del Corpo, Taline Ekmekjian, Donald C. Sheppard, Todd C. Lee, Matthew P. Cheng

First published: 24 April 2021 | https://doi.org/10.1111/myc.13290 | Citations: 6

- 13 RCT comparant les triazoles, les échinocandines ou l'amphotéricine B
- 3528 patients inclus (1531 échinocandine, 944 amphotéricine B et 1053 triazole)
- **Échinocandines: taux de réussite thérapeutique le plus élevé**
- **La survie globale ne différait pas significativement entre les groupes.**

TABLE 3 Comparison matrix of medication classes across studies

	Amphotericin	Azole	Echinocandin
Amphotericin		0.78 (0.60, 0.99)	1.41 (1.04, 1.92)
Azole	1.29 (1.02, 1.66)		1.82 (1.35, 2.5)
Echinocandin	0.71 (0.52, 0.96)	0.55 (0.40, 0.74)	

Note: The drug in a given column is compared to the corresponding drug in the associated row. The numerical values correspond to odds ratios for the primary outcome (treatment success) with 95% confidence intervals. An odds ratio greater than one represents a favourable comparison.

Invasive candidiasis: current clinical challenges and unmet needs in adult populations

Alex Soriano, Patrick M Honore, Pedro Puerta-Alcalde ✉, Carolina Garcia-Vidal, Anna Pagotto, Daniela C Gonçalves-Bradley, Paul E Verweij

Journal of Antimicrobial Chemotherapy, Volume 78, Issue 7, July 2023, Pages 1569–1585, https://doi.org/10.1093/jac/dkad139

Published: 23 May 2023

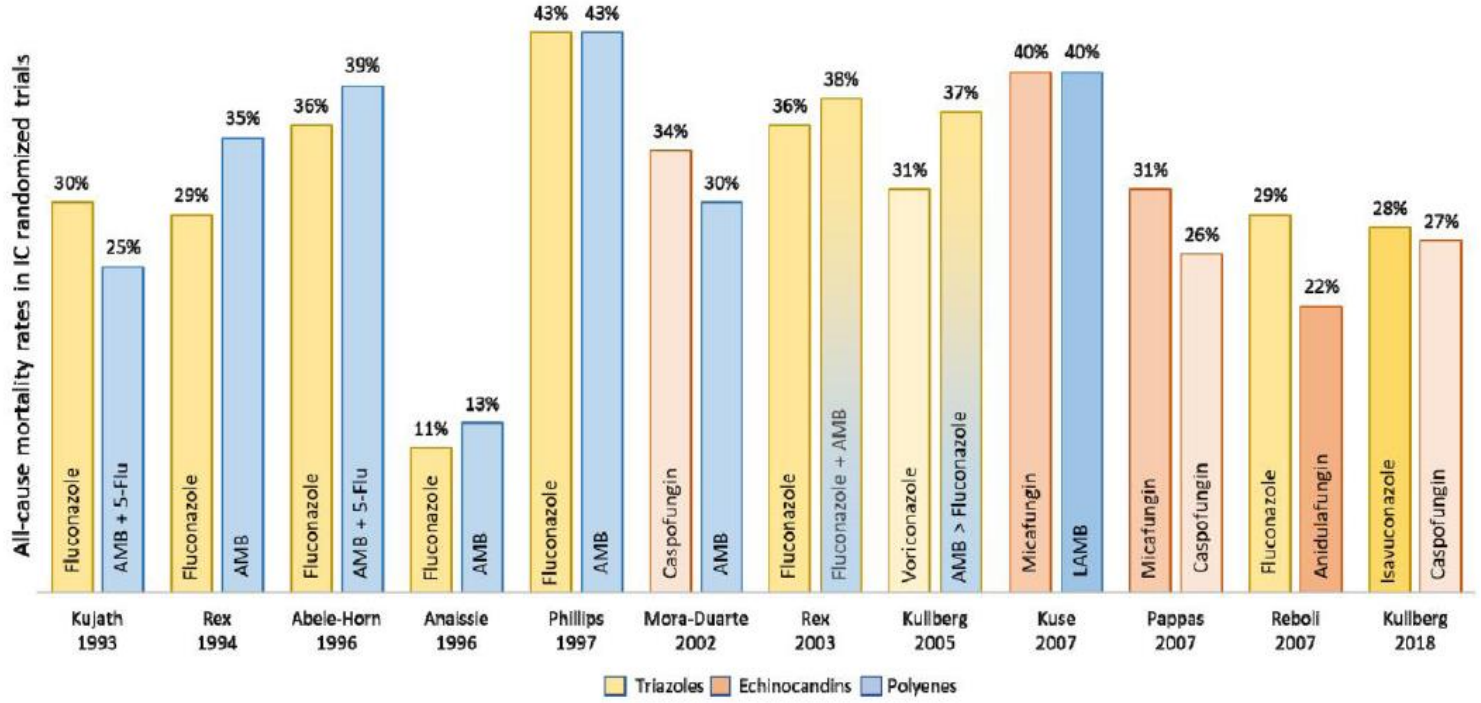


Figure 2. All-cause mortality rates in IC randomized trials (based on data reported by Demir).[18] The figure does not account for differences in study design, namely number of patients randomized, and only includes antifungals currently reimbursed. AMB, amphotericin B; 5-Flu, 5-fluorocytosine; LAMB, lipid formulation of amphotericin B.

ESCMID PUBLICATIONS | VOLUME 18, SUPPLEMENT 7, 19-37,
DECEMBER 2012

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PDF [144 KB]

ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: non-neutropenic adult patients

O.A. Cornely † • M. Bassetti † • T. Calandra † • ... C. Viscoli • A.J. Ullmann
for the ESCMID Fungal Infection Study Group (EFISG) • Show all authors • Show footnotes

Open Archive • DOI: https://doi.org/10.1111/1469-0691.12039

secretions alone should never prompt treatment. For the targeted initial treatment of candidaemia, echinocandins are strongly recommended while liposomal amphotericin B and voriconazole are supported with moderate, and fluconazole with marginal strength. Treatment duration for candidaemia should be a minimum of 14 days after the end of candidaemia, which can be determined by one blood culture per day until negativity.

Clinical Infectious Diseases

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hivma hiv medicine association

OXFORD

Clinical Practice Candidiasis: 201 Society of Amer

Peter G. Pappas,[1] Carol A. Kauffman,[2] David Jose A. Vazquez,[9] Thomas J. Walsh,[10] The

[1]University of Alabama at Birmingham; [2]Veterans Affa Pittsburgh, Pennsylvania; [5]Johns Hopkins University S Camden, New Jersey; [8]University of Pennsylvania, Phi Hospital of Pennsylvania, Philadelphia; and [12]Harper U

- Fluco++++

I. 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)*.
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 d
for
dia
11. F
or
candidemia has been cleared *(strong recommendation; low-quality 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)*.

II. Should Central Venous Catheters Be Removed in Nonneutropenic Patients With Candidemia?

Recommendation

13. Central venous catheters (CVCs) should be removed as early as possible in the course of candidemia when the source is presumed to be the CVC and the catheter can be removed safely; this decision should be individualized for each patient *(strong recommendation; moderate-quality evidence)*.

Challenge 4: recap

Table 4 Factors to be considered when choosing the most appropriate antifungal drug for ICU patients

From: Invasive candidiasis in critical care: challenges and future directions

Factor	Rationale
Clinical stability of patient	Fungicidal drug (e.g. echinocandin) preferred if clinically unstable
Previous antifungal exposure	Prior or prolonged use of azole and echinocandins associated with increased risk of resistance
Fungal colonization	Assess risk of infection with less susceptible/resistant-*Candida*
Local epidemiology	Assess risk of infection with less susceptible/resistant-*Candida* e.g *C. auris* outbreaks, echinocandin-resistant *C. glabrata*
Site of infection and dissemination	Echinocandins: poor penetration to aqueous sites (CSF, synovial fluid, anterior chamber of the eye, brain tissue, and urine) Amphotericin B: renal penetration of AmBd greater than L-AMB
Concurrent medications	Triazoles: inhibit various cytochrome P450 (CYP) isoenzymes; multiple drug-drug interactions. Caution with other hepato-toxic and cardio-toxic drugs Amphotericin: caution with other nephrotoxic drugs and drugs affecting electrolytes
Organ failure	Assess if drug and dose is appropriate in renal or liver impairment
Organ support	Assess if drug and dose is appropriate in RRT or ECMO
Therapeutic drug monitoring (TDM) requirement	essential for voriconazole and flucytosine to ensure effectiveness and prevent toxicity

Espèces R!

Ajuster les posologies+

AmBd amphotericin deoxycholate, *ECMO* extracorporeal membrane oxygenation, *L-AMB* liposomal amphotericin, *RRT* renal replacement therapy

Logan, C., Martin-Loeches, I. & Bicanic, T. Invasive candidiasis in critical care: challenges and future directions. *Intensive Care Med* 46, (2020).

Monitorage ttt: (Therapeutic drug monitoring (TDM))

- Recommandé par **IDSA** et **ESCMID:** ttt de CI avec voriconazole
- ESCMID : **+** 5-fluorocytosine et posaconazole

Pappas PG, et al. . **Clinical practice guideline for the management of candidiasis: 2016** update by the Infectious Diseases Society of America. Clin Infect Dis 2016; 62: e1–e50. 10.1093/cid/civ933 -

Cuenca-Estrella M, et al. . **ESCMID* guideline** for the diagnosis and management of Candida diseases 2012: diagnostic procedures. Clin Microbiol Infect **2012;** 18(Suppl 7):9–18. 10.1111/1469-0691.12038

- D'autres situations (absorption / excrétion d'un AF entravée)
  - Mucite, SNG, gastrostomie,
  - EER
  - Échec du ttt,
  - Inf° révolutionnaires (breakthrough infections)
  - Inf° par espèces à CMI élevé (C auris!)

Lewis RE, Andes DR. Managing uncertainty in antifungal dosing: antibiograms, therapeutic drug monitoring and drug-drug interactions. Curr Opin Infect Dis 2021; 34: 288–96. 10.1097/QCO.0000000000000740

Challenge 5: quand arrêter ttt AF?

Clinical Infectious Diseases

IDSA GUIDELINE

Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America

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33. For patients who have no clinical response to empiric antifungal therapy at 4–5 days and who do not have subsequent evidence of invasive candidiasis after the start of empiric therapy or have a negative non-culture-based diagnostic assay with a high negative predictive value, consideration should be given to stopping antifungal therapy *(strong recommendation; low-quality evidence)*.

Challenge 5: quand arrêter ttt AF?

- Stratégie axée sur les tests non basés sur la culture (BDG++)

Discontinuation of empirical antifungal therapy in ICU patients using 1,3-β-D-glucan

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Comparison of outcome variables between the three cohorts

	Candidaemia, *N*=7	Positive biomarker cohort, *N*=57	Negative biomarker cohort, *N*=21	*P*
Duration (days) of antifungal therapy, median (range)	14 (1–37)	10 (1–20)	3 (2–12)	<0.001
Breakthrough candidaemia	0	0	0	1.0
Discharged from the ICU on day 14 of study, *n* (%)	3 (42.8)	12 (21.0)	6 (28.6)	0.40
14 day mortality, *n* (%)	1 (14.3)	25 (45.6)	5 (23.8)	0.09
Discharged from the ICU on day 30, *n* (%)	4 (57.1)	18 (		
30 day mortality, *n* (%)	2 (28.6)	32 (		

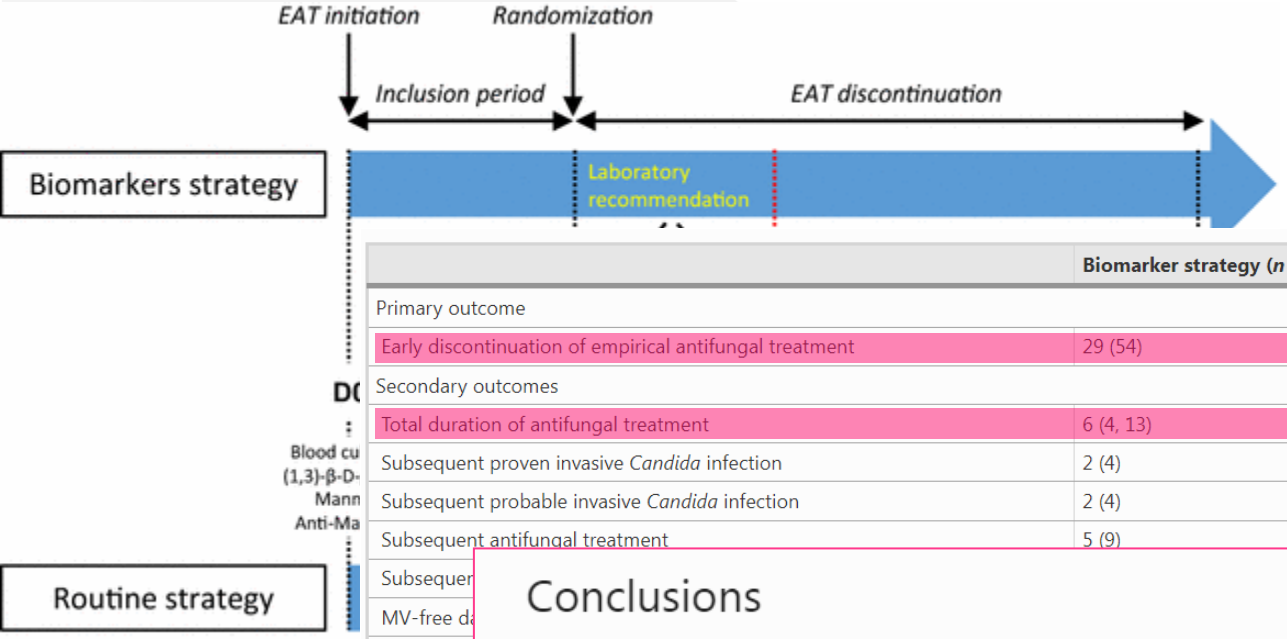
Conclusions

Early discontinuation of empirical echinocandin therapy in high-risk ICU patients based on consecutive negative BDG tests may be a reasonable strategy, with great potential to reduce the overuse of echinocandins in ICU patients. Prospective studies with a higher number of patients are needed.

Biomarker-based strategy for early discontinuation of empirical antifungal treatment in critically ill patients: a randomized controlled trial

Anahita Rouzé, Séverine Loridant, Julien Poissy, Benoit Dervaux, Boualem Sendid, Marjorie Cornu & Saad Nseir ✉ for the S-TAFE study group

Intensive Care Medicine **43**, 1668–1677 (2017) | Cite this article



	Biomarker strategy (*n* = 54)	Routine care (*n* = 55)	*P*
Primary outcome			
Early discontinuation of empirical antifungal treatment	29 (54)	1 (2)	<0.0001*
Secondary outcomes			
Total duration of antifungal treatment	6 (4, 13)	13 (12, 14)	<0.0001
Subsequent proven invasive *Candida* infection	2 (4)	1 (2)	0.547
Subsequent probable invasive *Candida* infection	2 (4)	0 (0)	0.243
Subsequent antifungal treatment	5 (9)	1 (2)	0.113

Conclusions

The use of a biomarker-based strategy increased the percentage of early discontinuation of empirical antifungal treatment among critically ill patients with suspected invasive *Candida* infection. These results confirm previous findings suggesting that early discontinuation of empirical antifungal treatment had no negative impact on outcome. However, further studies

Challenge 5: quand arrêter ttt AF?

- Les tests de diagnostic rapide peuvent justifier l'arrêt précoce d'un traitement antifongique empirique,

- La décision de réduire la durée du ttt doit prendre en compte aussi l'état du patient

Adhérence aux guidelines?

Analyzing candidemia guideline adherence identifies opportunities for antifungal stewardship

Original Article | Published: 13 June 2018 | 37, 1563–1571 (2018)

We assessed adherence to the current guideline of the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) and the Infectious Diseases Society of America (IDSA) using the EQUAL Candida Score of the European Confederation of Medical Mycology (ECMM). Data were documented by trained medical students as part of an integrated research and teaching concept at the University of Cologne. Between January 2014 and June 2017, 77 patients had candidemia, corresponding to an incidence of 0.2 cases/1000 admissions. While 55 patients were enrolled, 22 patients were excluded due to incompletely retrievable health records. Fluconazole monotherapy was the preferred first-line treatment in cases with *Candida albicans* infection (21/29). A central vascular

- D'autres écarts: l'indication, la posologie, la voie d'administration et la durée…

Valerio M, Muñoz P, Rodriguez CGet al. . Antifungal stewardship in a tertiary-care institution: a bedside intervention. Clin Microbiol Infect 2015; 21: 492.e1–e9. 10.1016/j.cmi.2015.01.013 - DOI - PubMed

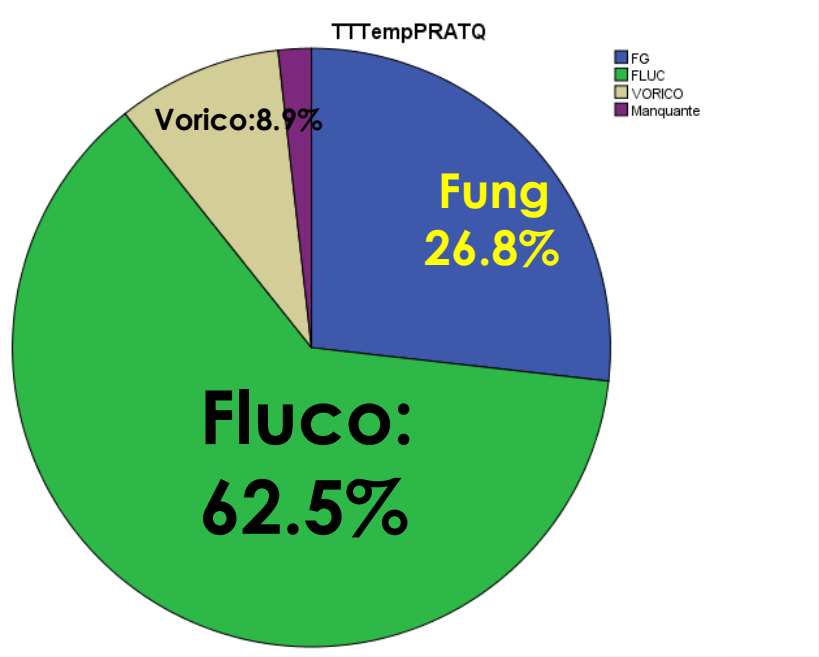
Muñoz P, Bouza E, COMIC (Collaboration Group on Mycosis) Study Group . The current treatment landscape: the need for antifungal stewardship programmes. J Antimicrob Chemother 2016; 71: ii5–ii12. 10.1093/jac/dkw391 - DOI - PubMed

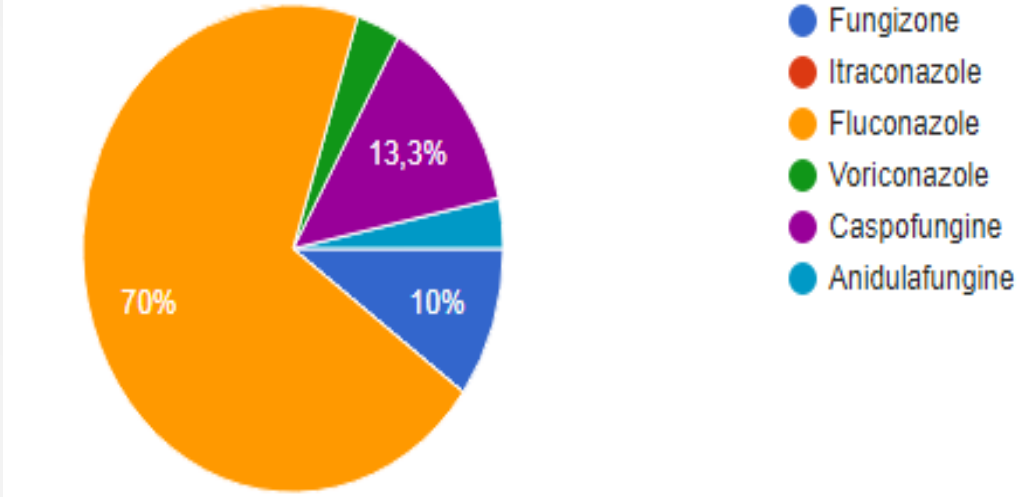
2014

2018

Enquête en ligne de l'ATR

Dans votre pratique, en cas de suspicion de CI, AF de 1ère intention?





Face aux défis

- Augmentation des IFI
- Retards dans le ttt avérées nocifs
- Le ttt empirique pour tous les patients à risque n'a pas démontré de bénéfice
- Augmentation mondiale de résistance de candida aux azoles et aux aux échinocandines
- Délai de prescription d'antifongiques ?

Antifungal Stewardship

antibiotics

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Article

Evaluation of an Antifungal Stewardship Initiative Targeting Micafungin at an Academic Medical Center

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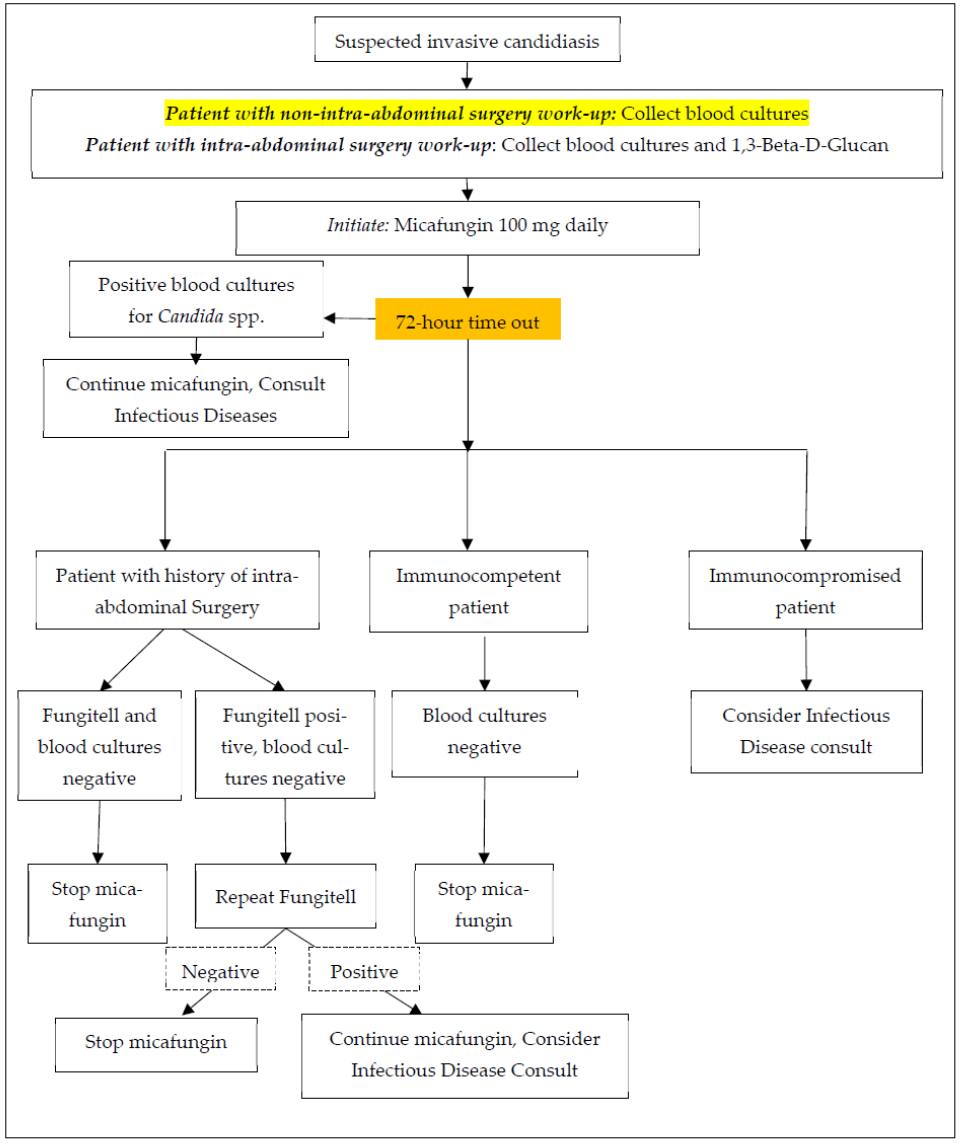

Figure 2. Micafungin Antifungal Stewardship Algorithm.

Conclusions & perspectives

- Incidence : augmentation constante
- Complication hospitalière redoutée

- Surveiller l'écologie

- Ttt empirique:
  - Pas/peu d'intérêt en population générale
  - Biomarqueurs et scores pred clinique proposés (VPN++, arrêt précoce du ttt)
  - Mieux préciser les sous populations de patients pouvant en bénéficier
  - Identifier rapidement la source

- Choix de l'AF en fct du contexte
- Utiliser de bonnes doses, TDM++

- **Antifungal Stewardship+++**

Merci pour votre attention