

# İnvazif Kandida İnfeksiyonlarının Yönetiminde Güncel Yaklaşımlar

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Süheyla SERİN SENER

Haziran 2023

# IFI Epidemiyolojisi



OUR VISION A WORLD FREE FROM DEATH AND SUFFERING CAUSED BY FUNGAL DISEASE.

English

SEARCH

HOME WHY WHO WHERE & HOW RESOURCES GLOBAL IMPACT CONTACT LATEST NEWS ANNUAL REPORTS  
BOOK - AMBROSIO ETOILE GAFFI PODCASTS



**1,400,000**

eyes infected by a fungus  
each year. Most eyes affected

## Global Action For Fungal Infections

Hedef,  
2025 yılına kadar,  
ciddi mantar hastalığı olan kişilerin %95'inin teşhis edilmesini ve  
%95'inin tedavi edilmesini sağlamak

# IFI Epidemiyolojisi

Fungal Infection	No. Affected	Case Fatality Rate	Estimated Deaths	Comments
Cryptococcal meningitis	223,000 in AIDS	15%-20% in US > 50% in developing world	180,000 in AIDS	CDC estimate
Pneumocystis pneumonia	> 400,000 in AIDS > 100,000 in non-AIDS	~15% in AIDS with best treatment ~50% in non-AIDS	> 200,000 in AIDS > 50,000 in non-AIDS	Most cases in Africa not diagnosed and 100% mortality
Disseminated histoplasmosis	~100,000	15%-30% if diagnosed and treated	> 80,000	Most common in the Americas
Invasive aspergillosis	> 1,000,000	~30% mortality in leukemia in HICs ~45%-70% in COPD ~30% mortality if treated in HICs in AIDS ~50% non-AIDS in HICs	> 500,000 > 30,000 in AIDS > 125,000 in non-AIDS	Many missed diagnoses globally
Invasive candidiasis	> 750,000	~40% mortality treated	> 350,000	
Chronic pulmonary aspergillosis	> 3,000,000	15%-40% mortality in HICs ~15% mortality in the developed world	> 450,000 in nonhospitalized populations	Underdiagnosed and mistaken for TB
SAFS	> 6,500,000	<1%. but no good figures	350,000-489,000 asthma deaths ~50% related to SAFS	Uncertain
Fungal keratitis	1-0-1.4 million	Blinding > 60%	> 600,000 blind eyes	Diagnosis often late
Total	~13,500,000		> 1,600,000	Probably a significant underestimate

ABPA, allergic bronchopulmonary aspergillosis; CDC, Centers for Disease Control and Prevention; COPD, chronic obstructive pulmonary disease; HIC, high-income country; IFI, invasive fungal infection; M, million; SAFS, severe asthma with fungal sensitization; TB, tuberculosis.

Global Action for Fungal Infections. Accessed March 23, 2023. <https://gaffi.org/why/fungal-disease-frequency/>

# İnvazif Kandidoz

- Tüm dünyada en yaygın IFI nedeni
- Kateter kullanımında artış
- İmmünsüpresif ajan kullanımında artış
- Geniş spektrumlu antibiyotik kullanımında artış
- Abdominal cerrahi
- Nötropeni (öz. mukozit varlığında), hematolojik malignite
- TPN
- YBÜ yatış

# İnvazif Kandidoz

- Kandidemi en sık görülen invazif kandidoz
- Mortalite %22-75 arasında deęiřiyor
- En fazla görülen etkenler: *C. albicans*, *C. glabrata*, *C. krusei*, *C. tropicalis* ve *C. parapsilosis*

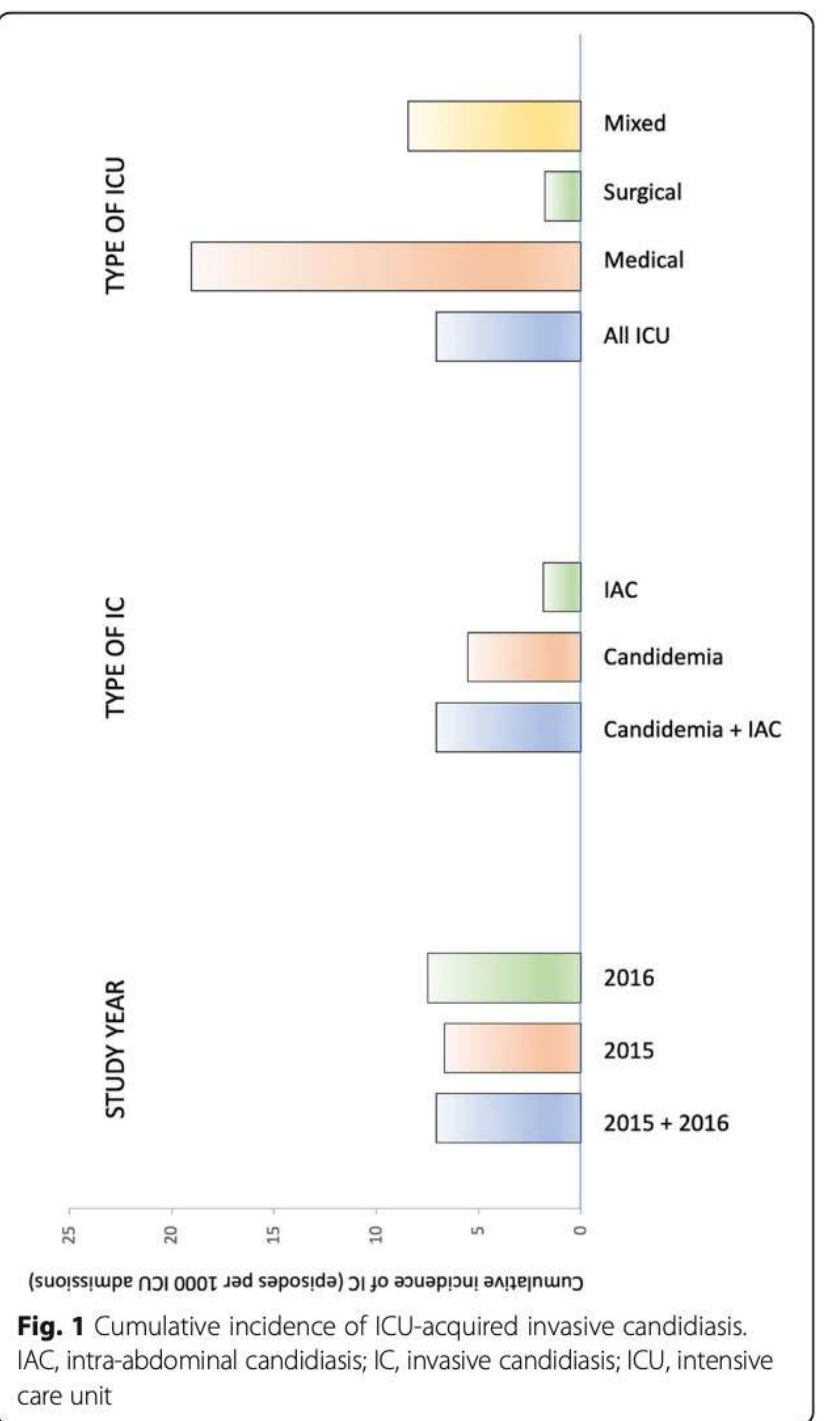
**RESEARCH**

**Open Access**

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



- Amaç: Avrupa YBÜ'lerinde invazif kandidoz kümülatif insidansını değerlendirmek
- 9 Avrupa ülkesindeki 23 YBÜ, çok merkezli, retrospektif
- Avrupa YBÜ kandidemi/karın içi kandidoz projesinin (EUCANDICU) ilk aşaması
- 570 YBÜ kaynaklı invazif kandidoz epizodu
- Her 1000 yoğun bakım yatışında 7,07 epizod
- 30 günlük mortalite %42
- YBÜ'nde uzamış yatış süreleri bağımsız risk faktörü



# İntraabdominal Kandidoz

- Klinik:
  - Peritonit
  - Abse
  - Pankreatit, pankreatik abse
  - Gangranöz kolesistit
  - Kandida fungus topu ile safra yolunda obstrüksiyon
  - Peritoneal diyaliz hastasında fungal peritonit
- Mortalite: %25-60

Montravers P, et al. J Antimicrob Chemother. 2009;63(4):785.  
de Ruiter J, et al. Infection. 2009;37(6):522.  
Bassetti M, et al. Intensive Care Med. 2015 Sep;41(9):1601-10



# Kandidemi ve Septik Şok

Bassetti *et al. Critical Care* (2020) 24:117  
<https://doi.org/10.1186/s13054-020-2793-y>

Critical Care

**RESEARCH**

**Open Access**

**Factors associated with the development of septic shock in patients with candidemia: a post hoc analysis from two prospective cohorts**



# Kandidemi ve Septik Şok

- 317 kandidemik hasta, 99 (%31.2) septik şok eşlik etmiş
- Risk analizi:
  - Yaş >50 (OR 2.57, 95% CI 1.03–6.41, p = 0.04)
  - İntraabdominal infeksiyon (OR 2.18, 95% CI 1.04–4.55, p = 0.04)
  - 30 günlük mortalitede septik şok gelişmesi bağımsız faktör

# Epidemiyolojide Değişim



AMERICAN  
SOCIETY FOR  
MICROBIOLOGY

Journal of  
Clinical Microbiology®

MYCOLOGY



## Update from a 12-Year Nationwide Fungemia Surveillance: Increasing Intrinsic and Acquired Resistance Causes Concern

K. M. T. Astvad,<sup>a</sup> H. K. Johansen,<sup>b,c</sup> B. L. Røder,<sup>d</sup> F. S. Rosenvinge,<sup>e</sup> J. D. Knudsen,<sup>f</sup> L. Lemming,<sup>g</sup>  H. C. Schönheyder,<sup>h,i</sup>  
R. K. Hare,<sup>a</sup> L. Kristensen,<sup>g</sup> L. Nielsen,<sup>j</sup> J. B. Gertsen,<sup>g</sup> E. Dzajic,<sup>k</sup> M. Pedersen,<sup>j\*</sup> C. Østergård,<sup>l</sup> B. Olesen,<sup>j</sup> T. S. Søndergaard,<sup>m</sup>  
M. C. Arendrup<sup>a,b,c</sup>

# Epidemiyolojide Değişim

- Danimarka Ulusal Fungemi Sürveysans verileri

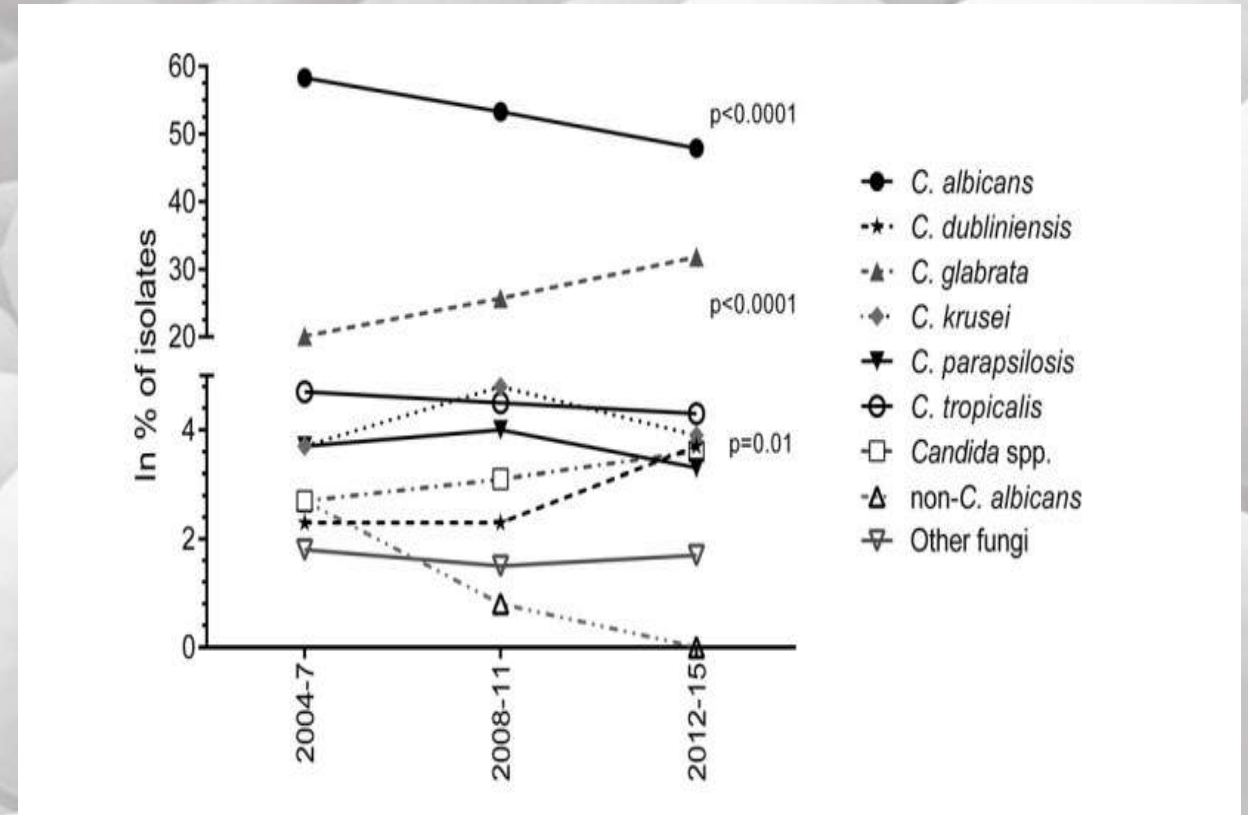
- 2004-2015

- *Candida albicans*

%64.4 → %42.4

- *Candida glabrata*

%16.5 → %34.6



# Antifungal Direnci

- Flukonazol duyarlılığında azalma
  - 2004-2007: %68.5
  - 2008-2011: %65.2
  - 2012-2015: %60.6
- Ekinokandin direnci:
  - 2004-2007: %0
  - 2008-2011: %0.6
  - 2012-2015: %1.7
- Amfoterisin B duyarlılığı: %98.7

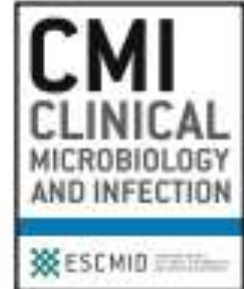


ELSEVIER

Contents lists available at ScienceDirect

# Clinical Microbiology and Infection

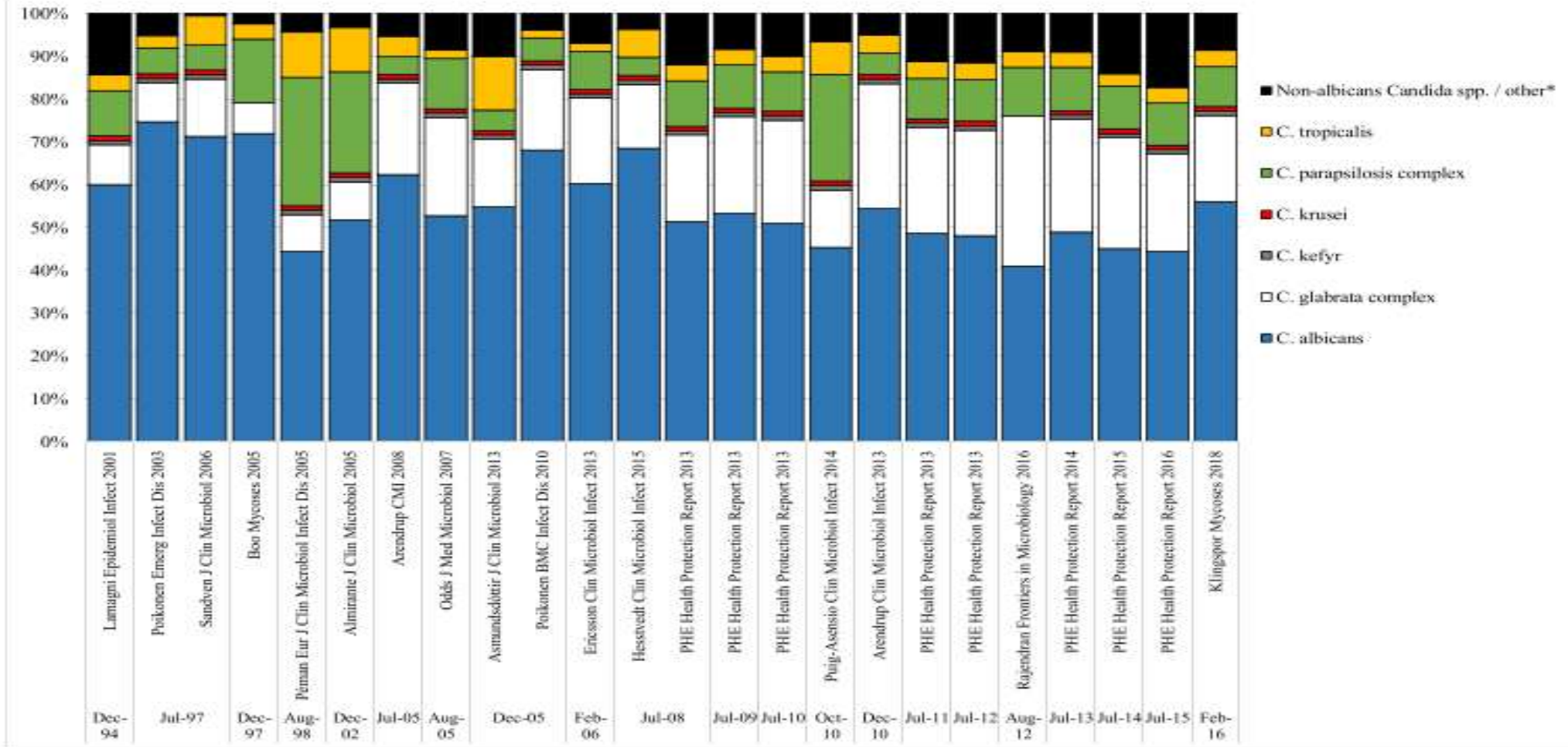
journal homepage: [www.clinicalmicrobiologyandinfection.com](http://www.clinicalmicrobiologyandinfection.com)



Systematic review

## Morbidity and mortality of candidaemia in Europe: an epidemiologic meta-analysis<sup>☆</sup>

P. Koehler<sup>1,2</sup>, M. Stecher<sup>1,3</sup>, O.A. Cornely<sup>1,2,3,4</sup>, D. Koehler<sup>5</sup>, M.J.G.T. Vehreschild<sup>1,3,6</sup>,  
J. Bohlius<sup>7</sup>, H. Wisplinghoff<sup>8,9,10</sup>, J.J. Vehreschild<sup>1,3,11,\*</sup>



**Fig. 3.** *Candida* species differentiation by population-based studies. Studies are identified by the name of the first author, the journal and year of publication. Sorted by chronologically by median of study period from left to right. \**C. ciferrii*, *C. dubliniensis*, *C. famata*, *C. guilliermondii*, *C. humicola*, *C. inconspicua*, *C. kefyr*, *C. lipolytica*, *C. lusitaniae*, *C. norvegensis*, *C. pelliculosa*, *C. rugosa*, *C. sake*, *C. utilis*, unidentified, declared as other or *Candida* spp., or non-specified *Candida*.

- 43.799 kandidemi olgusu (Ocak 2000-Şubat 2019)
- Mortalite %37-38

Open Forum Infectious Diseases

SUPPLEMENT ARTICLE



Infectious Diseases Society of America



hiv medicine association



# Twenty Years of the SENTRY Antifungal Surveillance Program: Results for *Candida* Species From 1997–2016

Michael A. Pfaller,<sup>1,2</sup> Daniel J. Diekema,<sup>2</sup> John D. Turnidge,<sup>3</sup> Mariana Castanheira,<sup>1</sup> and Ronald N. Jones<sup>1</sup>

<sup>1</sup>JMI Laboratories, North Liberty, Iowa; <sup>2</sup>University of Iowa College of Medicine, Iowa City, Iowa; <sup>3</sup>Departments of Pathology and Molecular and Cellular Biology, University of Adelaide, Adelaide, SA, Australia



# SENTRY Antifungal Sürveyans Programı

Year	No. Tested	% by Species				
		CA	CG	CP	CT	CK
1997–2001	5067	57.4	16.0	12.3	9.1	2.5
2006–2008	2647	51.2	15.9	16.8	10.7	2.1
2009–2011	4080	45.3	18.9	17.6	10.0	2.6
2012–2014	4928	46.3	19.3	15.1	8.6	3.2
2015–2016	3653	46.4	19.6	14.4	8.3	2.8

Abbreviations: CA, *C. albicans*; CG, *C. glabrata*; CK, *C. krusei*; CP, *C. parapsilosis*; CT, *C. tropicalis*.

- 1997-2016
- 39 ülke, 20.788 invazif kandidoz izolatu

# Increasing number of cases and outbreaks caused by *Candida auris* in the EU/EEA, 2020 to 2021

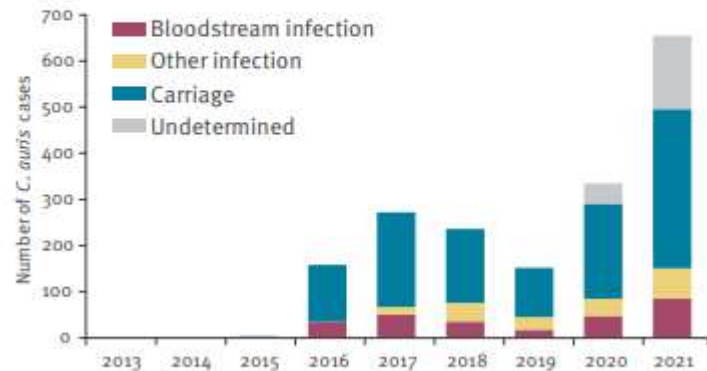
Anke Kohlenberg<sup>1</sup>, Dominique L Monnet<sup>2</sup>, Diamantis Plachouras<sup>2</sup>, *Candida auris* su  
 1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden  
 2. The members of the *Candida auris* survey collaborative group are listed under Col  
 Correspondence: Anke Kohlenberg (anke.kohlenberg@ecdc.europa.eu)

**FIGURE 2**

Epidemiological stage of *Candida auris* spread<sup>a</sup>, assessment by survey respondents in EU/EEA countries, 2022 (n = 30 countries)

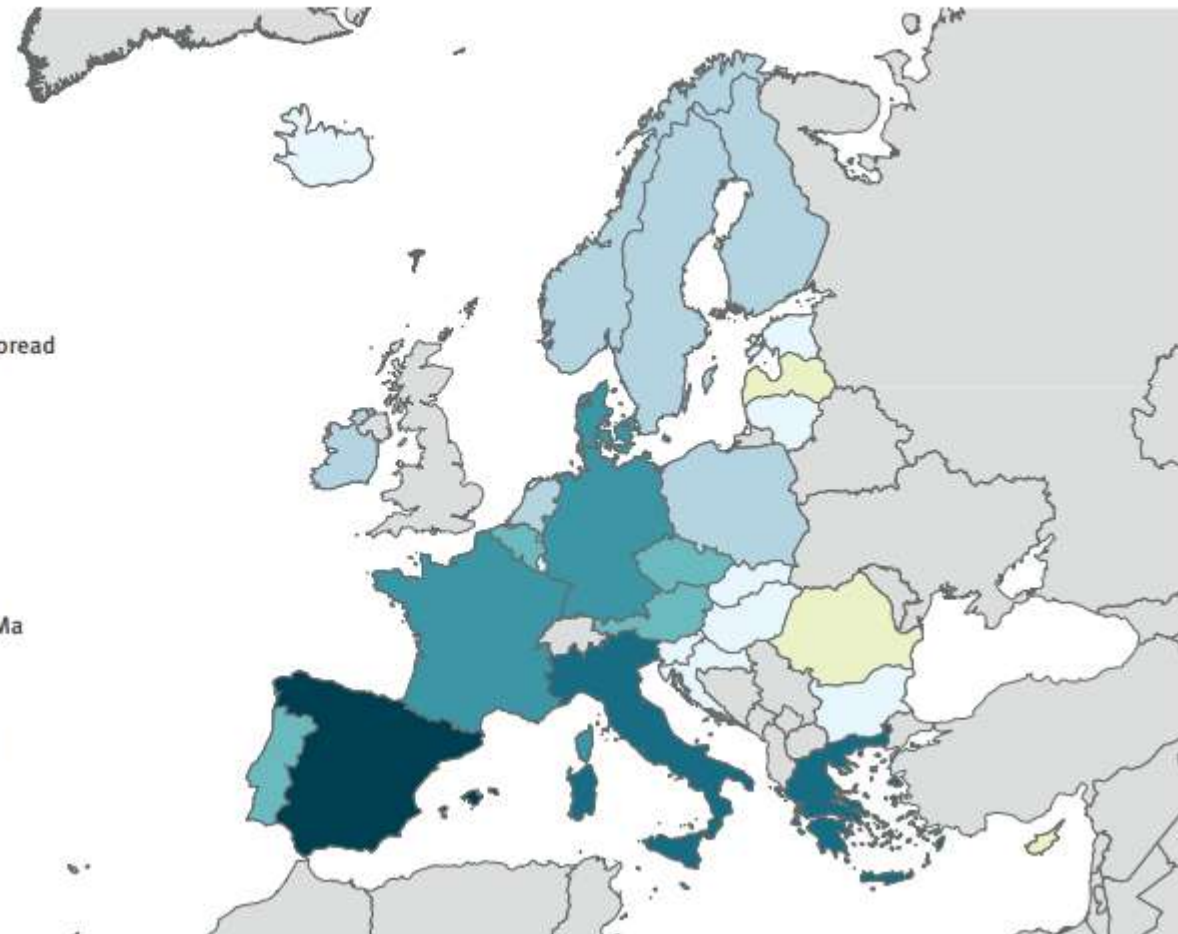
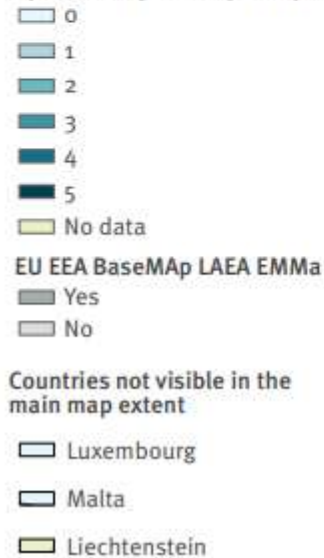
**FIGURE 1**

Reported cases of *Candida auris* infection or carriage, EU/EEA, 2013–2021 (n = 1,812)<sup>a</sup>



EEA: European Economic Area; EU: European Union.

Epidemiological stage of spread



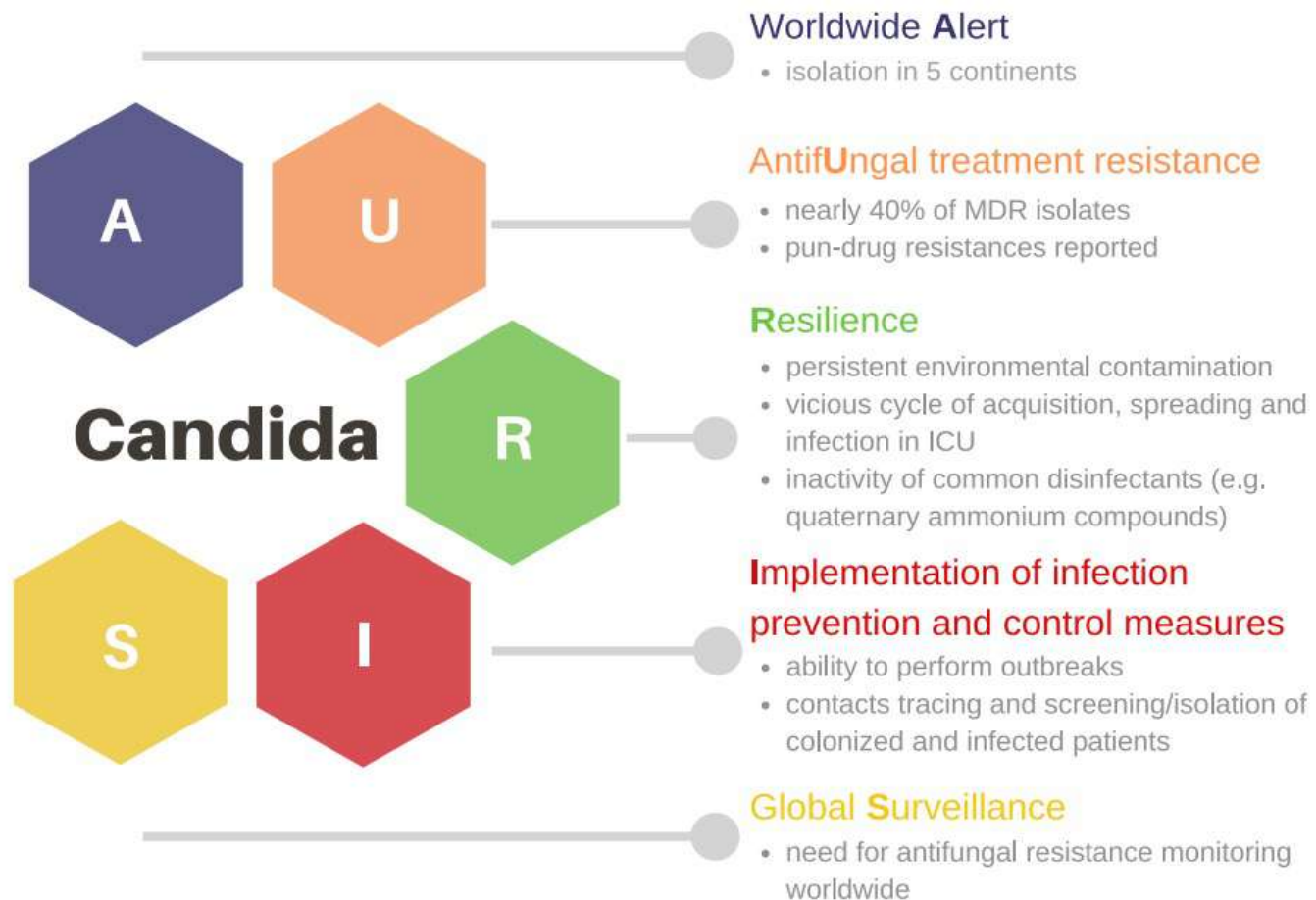
EDITORIAL

Open Access

# The global challenge of *Candida auris* in the intensive care unit



Andrea Cortegiani<sup>1\*</sup> , Giovanni Misseri<sup>1</sup>, Antonino Giarratano<sup>1</sup>, Matteo Bassetti<sup>2</sup> and David Eyre<sup>3</sup>



# MDR Candida türleri

- 10 yıllık yayınlara bakılmış
- MDR *C. glabrata* ve *C. auris* 15 ülkede bildirildi
- MDR oranları genellikle %30'un üzerinde
- Diğer potansiyel MDR Candida türleri, *C. krusei*, *C. lusitaniae*, *C. kefyr*, *C. guilliermondii* kompleksi, *Yarrowia (Candida) lypolitica* ve *C. rugosa*

# 23. ULUSLARARASI TÜRK KLİNİK MİKROBİYOLOJİ VE İNFEKSİYON HASTALIKLARI KONGRESİ

13-16 MART 2023 | GLORIA GOLF RESORT BELEK ANTALYA

SS-039

***Candida parapsilosis*'de Yükselen Azol Direnci, KLİMİK Mantar Enfeksiyonları Çalışma Grubu Çok Merkezli Gözlemsel Araştırma Ön Sonuçları**

Kübra Çam<sup>1</sup>, Ahmetcan Sezen<sup>2</sup>, Doğa İlki<sup>2</sup>, Jude Husam Tubail<sup>2</sup>, Şinası Karvar<sup>3</sup>, Nuran Deliağaoğlu<sup>4</sup>, Özlem Özkan Güler<sup>5</sup>, Birsen Mutlu<sup>5</sup>, Buket Ertürk Sengel<sup>6</sup>, Arzu İlki<sup>7</sup>, Emel Gürcüoğlu<sup>8</sup>, Demet Timur<sup>9</sup>, Oğuz Evlice<sup>10</sup>, Aynur Gülcan<sup>11</sup>, Yasemin Tezer<sup>12</sup>, Semra Turan<sup>13</sup>, Çağla Karakoç<sup>14</sup>, Füsün Can<sup>1</sup>, Önder Ergönül<sup>1</sup>, Özlem Doğan<sup>1</sup>, Süda Tekin<sup>1</sup>

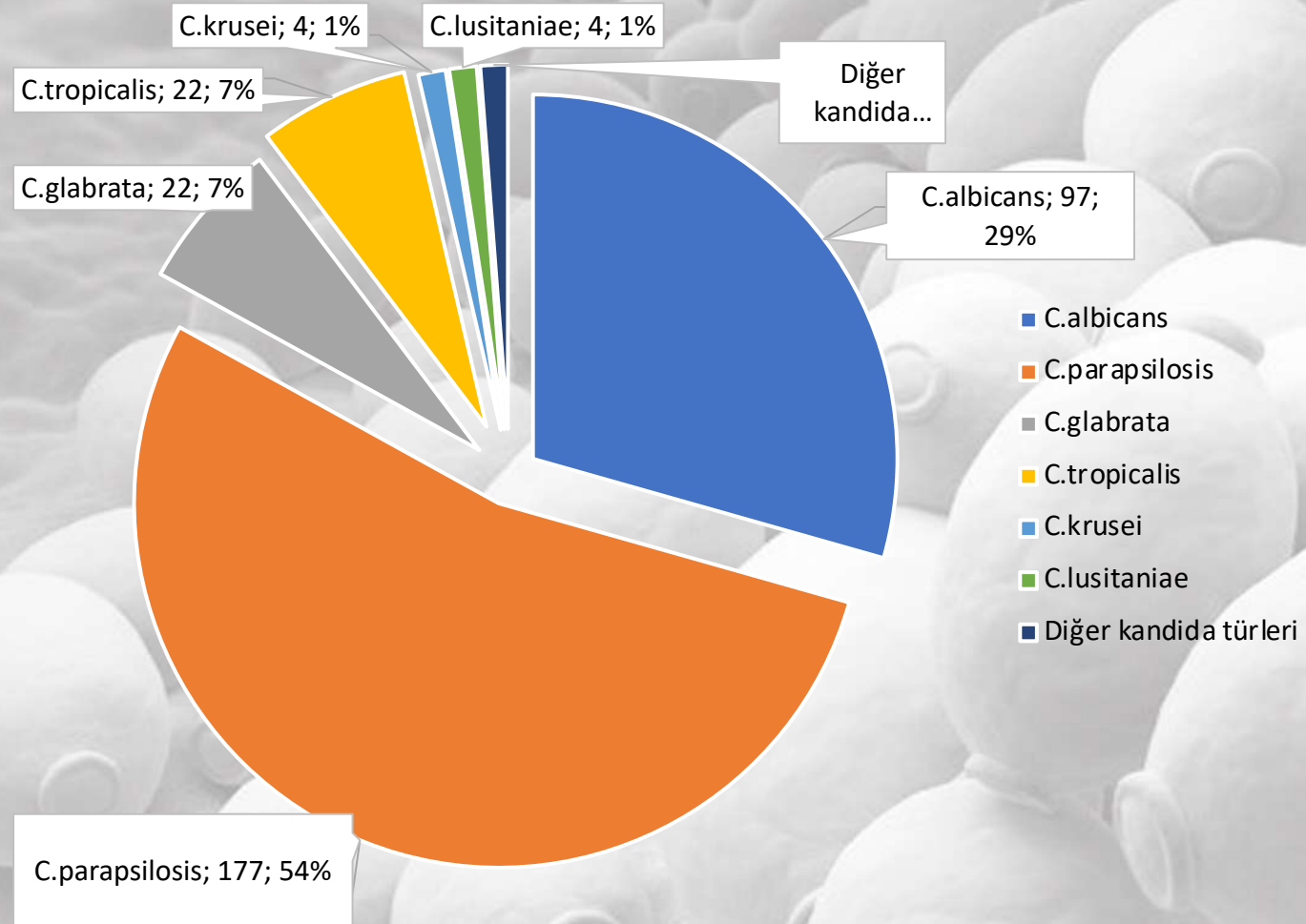
- 90 izolattan %44'ü (40/90) flukonazol'e, %27'si (24/90) vorikonazol'e, %10'u (9/90) itrakonazol'e, %4'ü (4/90) posakonazol'e dirençli

# Kendi deneyimimiz...

- SBÜ Tepecik SUAM YBÜ'lerinde 1 Ocak 2014- 31 Aralık 2021 tarihleri kandidemili hastalar
- 314 hastanın toplam 330 kandidemi atağı

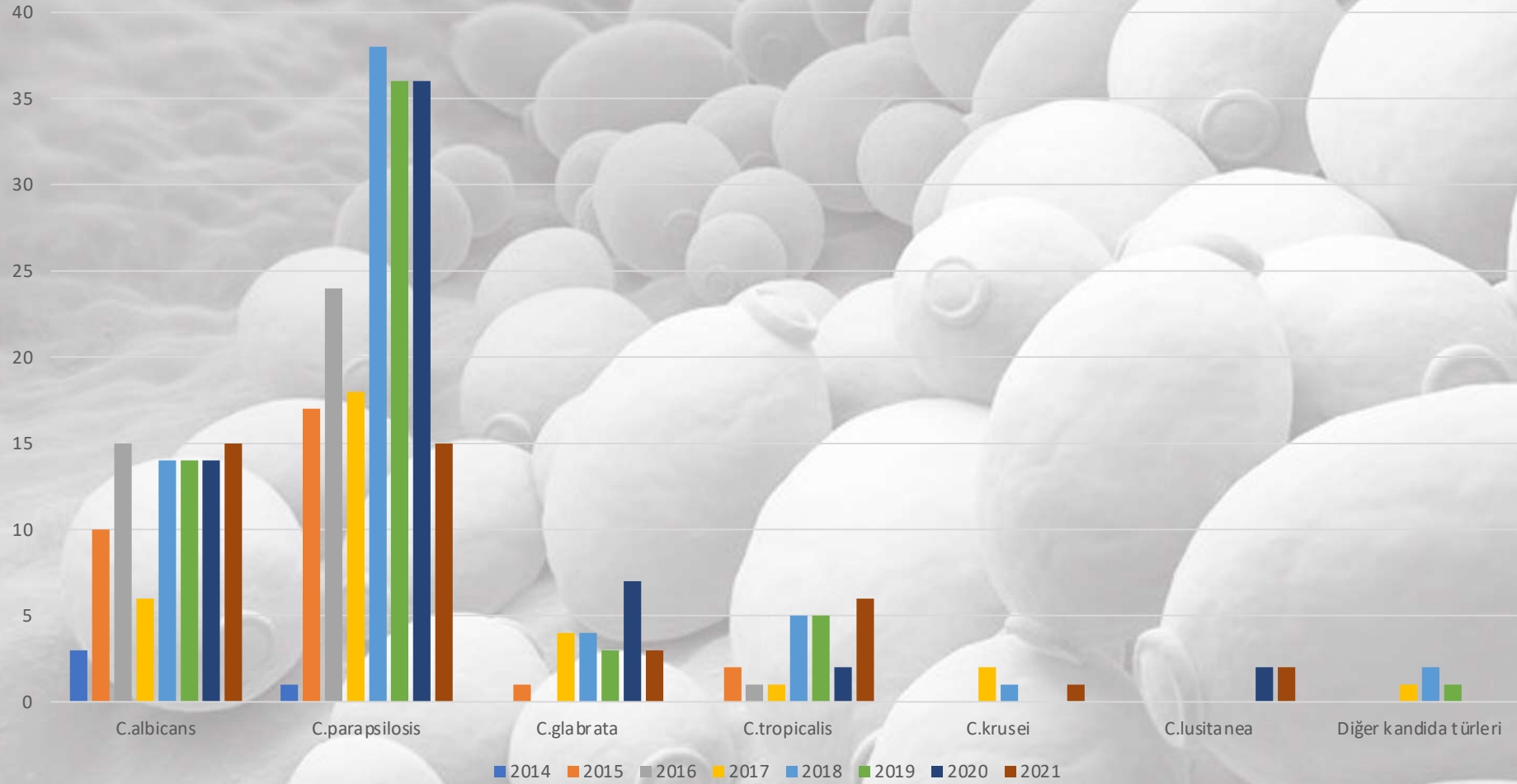
Risk Faktörleri	Sayı (n)	%
Antibiyoterapi kullanımı	324	98,2
Mekanik ventilasyon	247	74,8
Total parenteral nütrisyon	225	68,2
Santral kateterizasyon	220	66,7
Batın içi cerrahi ya da girişim	144	43,6
Hemodiyaliz	117	35,5
Malignite	97	29,4
İmmüsupresif tedavi	83	25,2
Steroid kullanımı	79	23,9
Kandidemi öncesi flukonazol kullanımı	35	10,6
Nötropeni	10	3
Organ nakli	2	0,6

# Kendi deneyimimiz...



# Kendi deneyimimiz...

Tür Dağılımı





# Kendi deneyimimiz...

## BULGULAR

Direnç	Flukonazol n (%)	İtrakonazol n (%)	Vorikonazol n (%)	Posakonazol n (%)	Anidulafungin n (%)	Amfoterisin-B n (%)
<i>C. albicans</i>	19 (19,58)	26 (26,8)	21 (21,64)	21 (21,64)	4 (4,12)	0 (0)
<i>C. parapsilosis</i>	<b>99 (55,9)</b>	57 (32,2)	67 (37,85)	45 (25,42)	7 (3,95)	2 (1,12)
<i>C. glabrata</i>	6 (27,27)	6 (27,27)	5 (22,72)	7 (31,81)	0 (0)	0 (0)
<i>C. tropicalis</i>	3 (13,63)	5 (27,27)	3 (13,63)	3 (13,63)	0 (0)	0 (0)
<i>C. krusei</i>	4 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
<i>C. lusitaniae</i>	4 (100)	4 (100)	4 (100)	4 (100)	2 (50)	0 (0)
Diğer kandida türleri	2 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Tüm etkenlerin %41,51'i flukonazole dirençli !!!

# İnvazif Kandidoz-Risk faktörleri

- Hematolojik ya da solid organ maligniteleri
- Yanık
- Major cerrahi
- Transplantasyon
- İmmünsüpresif ilaç kullanımı
- Geniş spektrumlu antibiyotik kullanımı
- Kemoterapi
- Hemodiyaliz
- TPN
- Uzamış hastane yatış süresi
- YBÜ'nde yatmak
- Yüksek APACHE skoru
- SVK

**Population-Based Active Surveillance  
for Culture-Confirmed Candidemia — Four Sites,  
United States, 2012–2016**

- Kandidemi insidansı  $\geq 65$  yaşındaki yetişkinler arasında en yüksek
- Üçte bir hastaya 90 gün içinde cerrahi işlem uygulanmış
- %77'si son 14 gün içinde sistemik antibiyotik almış
- %73'üne son 2 gün içinde santral venöz kateter (SVK) takılmış
- *C. albicans* (%39), *C. glabrata* (%28) ve *C. parapsilosis* (%15)
- Flukonazol R: %7, ekinokandin R: %1.6

*Clinical Infectious Diseases*

**IDSA GUIDELINE**



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

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

<sup>1</sup>University of Alabama at Birmingham; <sup>2</sup>Veterans Affairs Ann Arbor Healthcare System and University of Michigan Medical School, Ann Arbor; <sup>3</sup>University of Wisconsin, Madison; <sup>4</sup>University of Pittsburgh, Pennsylvania; <sup>5</sup>Johns Hopkins University School of Medicine, Baltimore, Maryland; <sup>6</sup>University of Texas Health Science Center, Houston; <sup>7</sup>Cooper Medical School of Rowan University, Camden, New Jersey; <sup>8</sup>University of Pennsylvania, Philadelphia; <sup>9</sup>Georgia Regents University, Augusta; <sup>10</sup>Weill Cornell Medical Center and Cornell University, New York, New York; <sup>11</sup>Children's Hospital of Pennsylvania, Philadelphia; and <sup>12</sup>Harper University Hospital and Wayne State University, Detroit, Michigan

Developing definitions for invasive fungal diseases in critically ill adult patients in intensive care units.

Protocol of the FUNgal infections Definitions in ICU patients (FUNDICU) project.

M. Bassetti<sup>1\*</sup>, L. Scudeller<sup>2</sup>, D.R. Giacobbe<sup>3,4</sup>, F. Lamoth<sup>5,6</sup>, E. Righi<sup>1</sup>, V. Zuccaro<sup>2</sup>, C. Grecchi<sup>2</sup>, C. Rebuffi<sup>2</sup>, M. Akova<sup>7</sup>, A. Alastruey-Izquierdo<sup>8</sup>, S. Arıkan Akdaglı<sup>9</sup>, E. Azoulay<sup>10</sup>, S. Blot<sup>11</sup>, O. Cornely<sup>12</sup>, C. Lass-Flörl<sup>13</sup>, P. Koehler<sup>12</sup>, M. Cuenca-Estrella<sup>8</sup>, D.W. de Lange<sup>14</sup>, F.G. De Rosa<sup>15</sup>, J.J. De Waele<sup>16</sup>, G. Dimopoulos<sup>17</sup>, J. Garnacho-Montero<sup>18</sup>, M. Hoenigl<sup>19,20</sup>, S.S. Kanj<sup>21</sup>, J. Maertens<sup>22</sup>, I. Martin-Loeches<sup>23</sup>, P. Muñoz<sup>24</sup>, B.J. Kullberg<sup>25</sup>, C. Agvald-Ohman<sup>26</sup>, G. Poulakou<sup>27</sup>, J. Rello<sup>28</sup>, M. Sanguinetti<sup>29</sup>, F.S. Taccone<sup>30</sup>, J-F. Timsit<sup>31,32</sup>, A. Torres<sup>33</sup>, J.A. Vazquez<sup>34</sup>, T. Calandra<sup>5</sup>

from the Study Group for Infections in Critically Ill Patients (ESGCIP) and the Fungal Infection Study Group (EFISG) of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), the European Society of Intensive Care Medicine (ESICM), the European Confederation of Medical Mycology (ECMM), and the Mycoses Study Group Education and Research Consortium (MSGERC)

# Revision and Update of the Consensus Definitions of Invasive Fungal Disease From the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium

J. Peter Donnelly,<sup>1</sup> Sharon C. Chen,<sup>2</sup> Carol A. Kauffman,<sup>3</sup> William J. Steinbach,<sup>4</sup> John W. Baddley,<sup>5</sup> Paul E. Verweij,<sup>6</sup> Cornelius J. Clancy,<sup>7</sup> John R. Wingard,<sup>8</sup> Shawn R. Lockhart,<sup>9</sup> Andreas H. Groll,<sup>10</sup> Tania C. Sorrell,<sup>11</sup> Matteo Bassetti,<sup>12</sup> Hamdi Akan,<sup>13</sup> Barbara D. Alexander,<sup>14</sup> David Andes,<sup>15</sup> Elie Azoulay,<sup>16</sup> Ralf Bialek,<sup>17</sup> Robert W. Bradsher Jr,<sup>18</sup> Stephane Bretagne,<sup>19</sup> Thierry Calandra,<sup>20</sup> Angela M. Caliendo,<sup>21</sup> Elio Castagnola,<sup>22</sup> Mario Cruciani,<sup>23</sup> Manuel Cuenca-Estrella,<sup>24</sup> Catherine F. Decker,<sup>25</sup> Sujal R. Desai,<sup>26</sup> Brian Fisher,<sup>27</sup> Thomas Harrison,<sup>28</sup> Claus Peter Heussel,<sup>29</sup> Henrik E. Jensen,<sup>30</sup> Christopher C. Kibbler,<sup>31</sup> Dimitrios P. Kontoyiannis,<sup>32</sup> Bart-Jan Kullberg,<sup>33</sup> Katrien Lagrou,<sup>34</sup> Frédéric Lamoth,<sup>35</sup> Thomas Lehrnbecher,<sup>36</sup> Jurgen Loeffler,<sup>37</sup> Olivier Lortholary,<sup>38</sup> Johan Maertens,<sup>39</sup> Oscar Marchetti,<sup>20</sup> Kieren A. Marr,<sup>40</sup> Henry Masur,<sup>41</sup> Jacques F. Meis,<sup>42</sup> C. Orla Morrissey,<sup>43</sup> Marcio Nucci,<sup>44</sup> Luis Ostrosky-Zeichner,<sup>45</sup> Livio Pagano,<sup>46</sup> Thomas F. Patterson,<sup>47</sup> John R. Perfect,<sup>14</sup> Zdenek Racil,<sup>48</sup> Emmanuel Roilides,<sup>49</sup> Marcus Ruhnke,<sup>50</sup> Cornelia Schaefer Prokop,<sup>51</sup> Shmuel Shoham,<sup>40</sup> Monica A. Slavin,<sup>52</sup> David A. Stevens,<sup>53</sup> George R. Thompson III,<sup>54</sup> Jose A. Vazquez,<sup>55</sup> Claudio Viscoli,<sup>56</sup> Thomas J. Walsh,<sup>57</sup> Adilia Warris,<sup>58</sup> L. Joseph Wheat,<sup>59</sup> P. Lewis White,<sup>60</sup> Theoklis E. Zaoutis,<sup>61</sup> and Peter G. Pappas<sup>5</sup>

- Altın standart: steril bölgeden pozitif kültür ya da histopatolojik inceleme
  1. Steril bölgeden alınan örneğin histopatolojik sitopatolojik ya da direkt mikroskopik incelemesinde yalancı ya da gerçek Candida hiflerinin görülmesi
  2. Klinik ya da radyolojik olarak infeksiyonla uyumlu olan, steril bölgeden alınan kültürde üreme olması
  3. Parafin emdirilmiş doku kesitlerinden PCR
  4. Kan kültür pozitifliği

**Table 3. Other Probable Invasive Diseases**

**Candidiasis**

*Host factors*

Recent history of neutropenia  $<0.5 \times 10^9$  neutrophils/L ( $<500$  neutrophils/ $\text{mm}^3$  for  $>10$  days) temporally related to the onset of invasive fungal disease

Hematologic malignancy

Receipt of an allogeneic stem cell transplant

Solid organ transplant recipient

Prolonged use of corticosteroids (excluding among patients with allergic bronchopulmonary aspergillosis) at a therapeutic dose of  $\geq 0.3$  mg/kg corticosteroids for  $\geq 3$  weeks in the past 60 days

Treatment with other recognized T-cell immunosuppressants, such as calcineurin inhibitors, tumor necrosis factor- $\alpha$  blockers, lymphocyte-specific monoclonal antibodies, immunosuppressive nucleoside analogues during the past 90 days

Inherited severe immunodeficiency (such as chronic granulomatous disease, STAT 3 deficiency, CARD9 deficiency, STAT-1 gain of function, or severe combined immunodeficiency)

Acute graft-versus-host disease grade III or IV involving the gut, lungs, or liver that is refractory to first-line treatment with steroids

*Clinical features*

At least 1 of the following 2 entities after an episode of candidemia within the previous 2 weeks:

Small, target-like abscesses in liver or spleen (bull's-eye lesions) or in the brain, or, meningeal enhancement

Progressive retinal exudates or vitreal opacities on ophthalmologic examination

*Mycological evidence*

$\beta$ -D-glucan (Fungitell)  $\geq 80$  ng/L (pg/mL) detected in at least 2 consecutive serum samples provided that other etiologies have been excluded

Positive T2Candida<sup>a</sup>



# IFI Tanımlama



# IFI Tanı-Tedavide Sorunlar

- Risk faktörlerinin iyi belirlenmesi
  - Gerçek infeksiyon/kolonizasyon ayrımı
  - Belirteçlerin doğru kullanımı
  - Antifungal duyarlılık testleri
  - Tanı konduğunda infeksiyon odaklarının tespiti ve uzaklaştırılması
  - Erken ve etkili tedavi
- 
- Kimi test edelim?
  - Kimi tedavi edelim?

# İnvazif Kandidoz Tanısında Kullanılan Testler

Test	Turnaround Time	Diagnostic Value	Sensitivity	Specificity	Notes
Culture	2–4 days	Positive	21–71%	N/A	Allows susceptibility testing
T2Candida	3–5 h	Positive	91%	99%	Approved for the detection of <i>C. albicans</i> , <i>C. krusei</i> , <i>C. tropicalis</i> , <i>C. parapsilosis</i> , and <i>C. glabrata</i> in whole blood.
$\beta$ -D-glucan (Fungitell)	1 h	$\geq 80$ ng/L	92%	81%	Can be positive in other fungal infections
$\beta$ -D-glucan + procalcitonin	1 h	$\geq 80$ ng/L <0.2 ng/mL	96%	98%	Can be positive in other fungal infections

# Tanı-Kan kültürü

- İnvazif kandidozlu olguların yalnızca % 21–71’inde kan kültür pozitifliği
- Kan kültür sayısı ya da kan miktarı arttırarak duyarlılık arttırılabilir.

> [Med Mycol.](#) 2014 Apr;52(3):270-5. doi: 10.1093/mmy/myt025. Epub 2014 Mar 23.

## Potential role of *Candida albicans* germ tube antibody in the diagnosis of deep-seated candidemia

M Carmen Martínez-Jiménez <sup>1</sup>, Patricia Muñoz, Jesús Guinea, Maricela Valerio, Roberto Alonso, Pilar Escribano, Emilio Bouza

Affiliations + expand

PMID: 24662248 DOI: [10.1093/mmy/myt025](#)

- *Candida albicans* germ tüp spesifik antikor (CAGTA) (+) kandidemi
  - %69 kateter ilişkili derin yerleşimli kandidemi (P < 0,01)
  - %4.7 derin yerleşimli olmayan kateter ilişkili kandidemi (P < 0,01)

> [Clin Microbiol Infect.](#) 2013 Feb;19(2):E129-35. doi: 10.1111/1469-0691.12096. Epub 2012 Dec 10.

## **Can microbiologists help to assess catheter involvement in candidaemic patients before removal?**

E Bouza <sup>1</sup>, L Alcalá, P Muñoz, P Martín-Rabadán, M Guembe, M Rodríguez-Créixems;  
GEIDI and the COMIC study groups

- Aynı zamanda alınan kan kültürlerinin tümünde üreme yoksa kaynağın kateter dışı olma olasılığı yüksek, başka kaynak ara !!!

# Oftalmolojik bakı

- Kandidemili tüm hastalar endoftalmit için bakılmalı
- Kandidemide endoftalmit <%1
- Nötropenik hastalarda koroidal ve vitreal infeksiyon bulguları minimal, nötropeni düzeldikten sonraki haftaya ertelenmeli
- Amerikan Oftalmoloji Akademisi, yalnızca oküler semptomları olan veya semptomları bildiremeyen hastalara bakılmasını öneriyor
- Ekinokandinlerin artan kullanımına bağı olarak insidans artabilir

Breazzano MP, et al. Ophthalmology 2022; 129:73.

Hillenbrand M, et al. Open Forum Infect Dis 2022; 9:ofac045.

# EKOKARDİYOĞRAFI

- Kandidemili hastalarda rutin EKO yapılması önerilmez
- İnfektif endokardit öyküsü olan veya damar içi uyuşturucu kullananlarda gerekli
- Kandidemi kaynak kontrolü sağlanamazsa yapılmalı
- Nötropenik hastada kaynak genellikle gastrointestinal

Sankar NP, et al. Open Forum Infect Dis 2020; 7:ofaa142.

Fernández-Cruz A, et al. Eur J Clin Microbiol Infect Dis 2015; 34:1543.



# Abdominal görüntüleme (BT)

- Nadiren, karaciğer ve dalak apseleri kandideminin bir komplikasyonu olarak ortaya çıkabilir
- Abdominal semptomları, karaciğer enzim anormallikleri ve/veya inatçı ateşi olan kişilerde düşünülmelidir

# Antifungal Tedavi

- Tedavide 12-24 saatlik gecikmeler mortaliteyi %100'e kadar arttırır
- İnfeksiyon kaynağının bulunmalı ve ortadan kaldırılmalı
- Çıkarılan tüm kateter ve yabancı cisimlerin kültüre gönderilmeli
- İnfeksiyon kaynağından cerrahi debridman yapılmalı, apse varsa direne edilmeli
- Erken ve etkin bir antifungal başlanmalı
- Antifungal tedavide gecikme, uygunsuz ajan ya da yetersiz doz mortalide artışa neden olmaktadır.

# Antifungal Tedavi

**Table 2.** Therapy of invasive candidiasis and preferred medications.

<b>Etiologic Agent of Invasive Candidiasis Therapy</b>	<i>C. albicans, C. parapsilosis, C. tropicalis</i>	<i>C. krusei, C. glabrata</i>	<i>C. auris</i>
First-line therapy *	Echinocandin	Echinocandin	Echinocandin
Alternative first-line therapy	Fluconazole	Amphotericin B lipid formulations	Amphotericin B lipid formulations
Step-down therapy **	Fluconazole	Voriconazole	Susceptibility data required

Notes: \* Liposomal amphotericin B and flucytosine are used in the central nervous system or for eye infections.

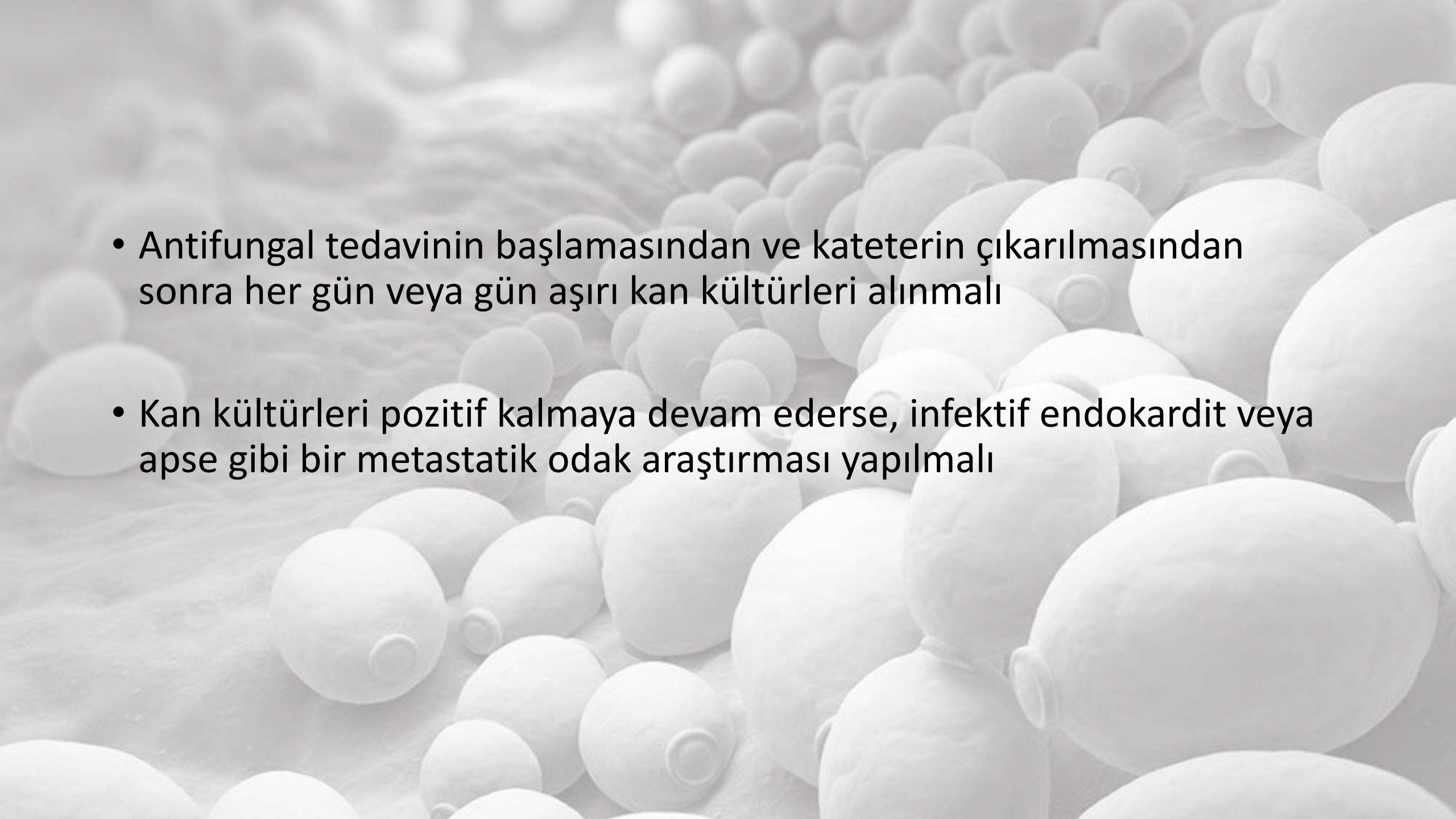
\*\* Step-down therapy is based on MIC assessment in individual cases.

# Antifungal Tedavi

- Bařlangıç tedavisi ekinokandin olmalı
  - Anidulafungin: 200 mg ykleme dozu, ardından gnde 100 mg IV
  - Caspofungin: 70 mg ykleme dozu, ardından gnde 50 mg IV
  - Micafungin: Gnlk 100 mg IV
- Ntropenik olmayan, hafif/orta seyirli ve flukonazole dirençli bir organizmaya (*C. glabrata* veya *C. krusei* gibi) sahip olmayan hastalarda, flukonazol (1. gn 800 mg [12 mg/kg] ykleme dozu, ardından 400 mg [6 mg/kg] oral veya IV gnlk) alternatif

# Antifungal Tedavi

- *C. glabrata* etken ise, duyarlı olması koşuluyla yüksek doz flukonazol günde 800 mg (12 mg/kg) günlük veya vorikonazol günde iki kez 200-300 (3-4 mg/kg) verilebilir
- Direnç ya da diğer ajanlara yan etki varsa, amfoterisin B'nin lipid formülasyonları (günde 3 ila 5 mg/kg IV)

- 
- Antifungal tedavinin başlamasından ve kateterin çıkarılmasından sonra her gün veya gün aşırı kan kültürleri alınmalı
  - Kan kültürleri pozitif kalmaya devam ederse, infektif endokardit veya apse gibi bir metastatik odak araştırması yapılmalı

# Ardışık Azaltma Tedavisi


- Klinik olarak stabil olan nütropenik olmayan ve nütropenik hastalarda, flukonazole duyarlı Candida izolatlarına sahip olan ve kan kültürleri negatifleşen hastalarda, antifungal başlandıktan 5-7 gün sonra oral flukonazole geçiş yapılabilir (400 mg (6 mg/kg) po)

# Tedavi süresi

- Metastatik komplikasyonları olmayan kandidemi için önerilen tedavi süresi, kan kültürü negatifleşmesinden ve kandidemiye atfedilebilen semptomların çözülmesinden sonra 2 haftadır
- İntraabdominal kandidoz gibi derin yerleşimli invazif kandidozda, tedavi süresi normalde birkaç haftadan 6-12 aya kadar değişir



# Yeni antifungaller

Antifungal agents	Fosmanogepix	Ibrexafungerp	Olorofim	Opelconazole	Rezafungin
 <i>Candida albicans</i>	Green	Green	Red	Green	Green
<i>Candida auris</i>	Green	Green	Red	Green	Green
<i>Candida dubliniensis</i>	Green	Green	Red	White	Green
<i>Candida glabrata</i>	Green	Green	Red	Green	Green
<i>Candida krusei</i>	Red	Green	Red	Green	Green
<i>Candida lusitanae</i>	Green	Green	Red	White	Green
<i>Candida parapsilosis</i>	Green	Green	Red	White	Green
<i>Candida tropicalis</i>	Green	Green	Red	White	Green



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**1,400,000**

eyes infected by a fungus each year, Most eyes affected go blind and some have to be removed

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