Solid Organ Nakli Hastalarında Antifungal Yönetim (AFY) Programı

Dr. Özlem Kurt Azap

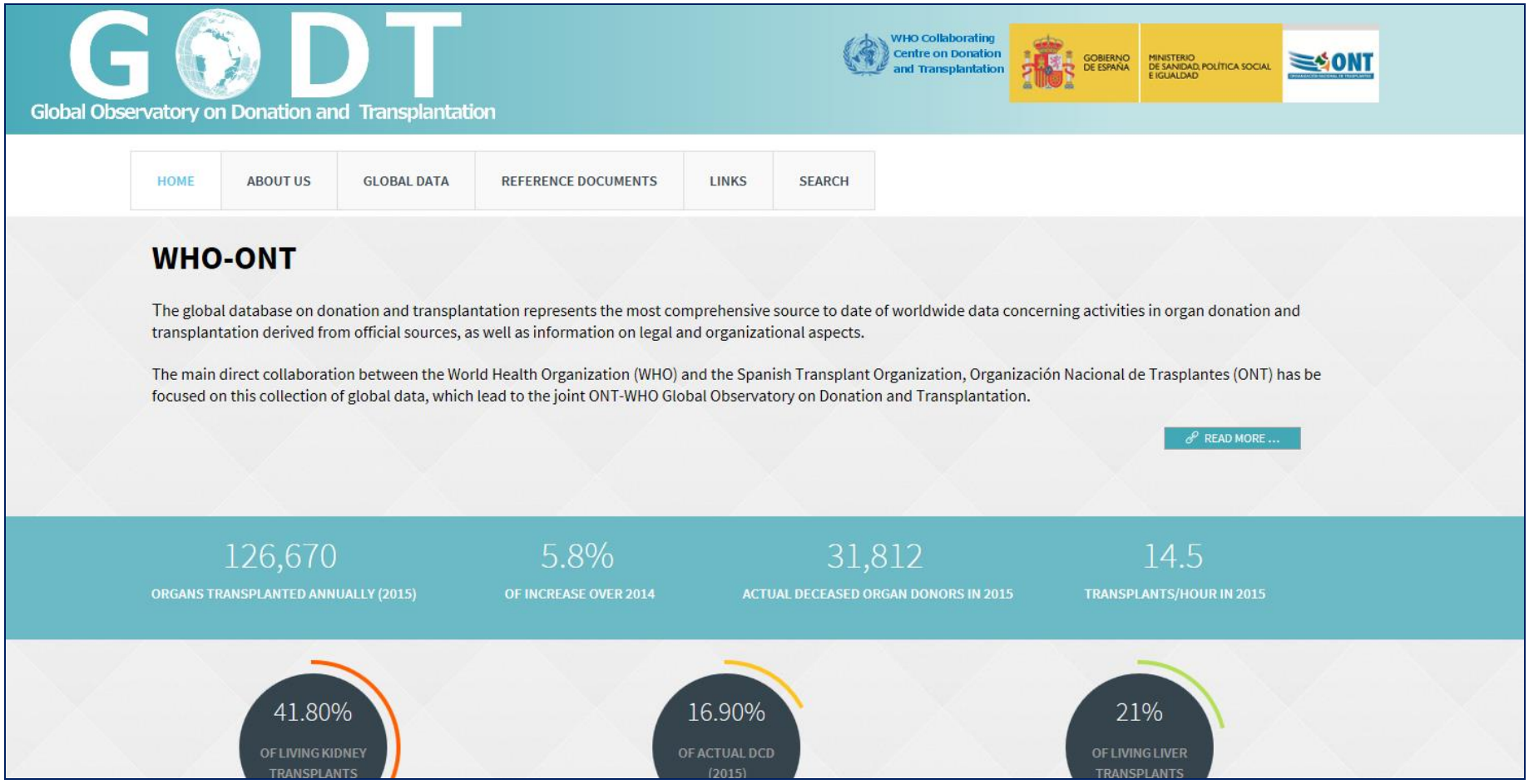
Başkent Üniversitesi Tıp Fakültesi

Enfeksiyon hastalıkları ve Klinik Mikrobiyoloji AD

SOT Hastalarında Antifungal Yönetim (AFY) Programı

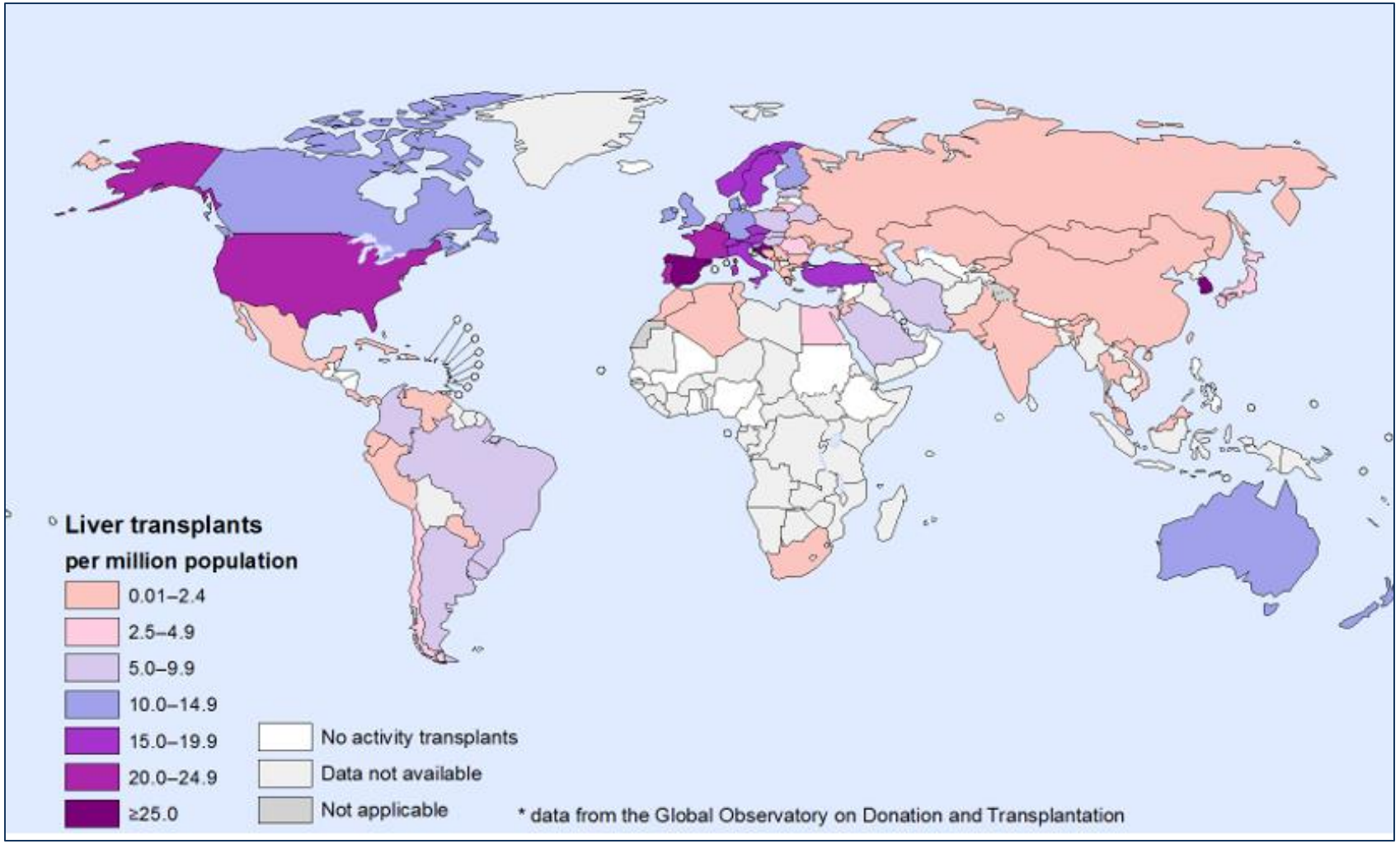
- Giriş
- Nedir? Gerekli mi? İşe yarıyor mu?
- Nasıl bir yol izlenebilir?
  - Tanımlar
  - Örnekler
  - Veriler: Türkiye, Dünya
  - Rehberler: Kandidiyazis, aspergilloz

Dünya- SOT Olguları



http://www.transplant-observatory.org/

KARACİĞER



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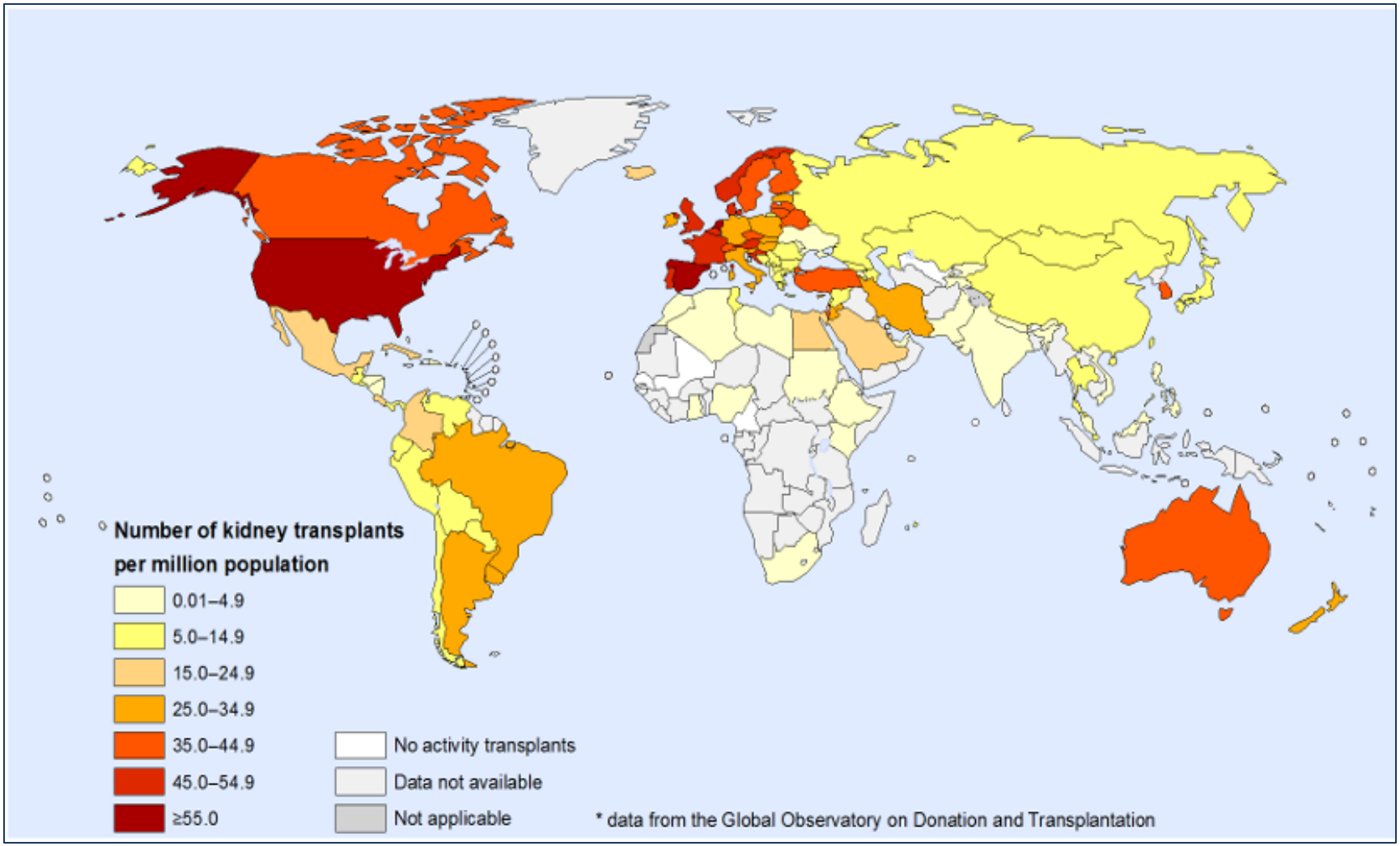
BÖBREK



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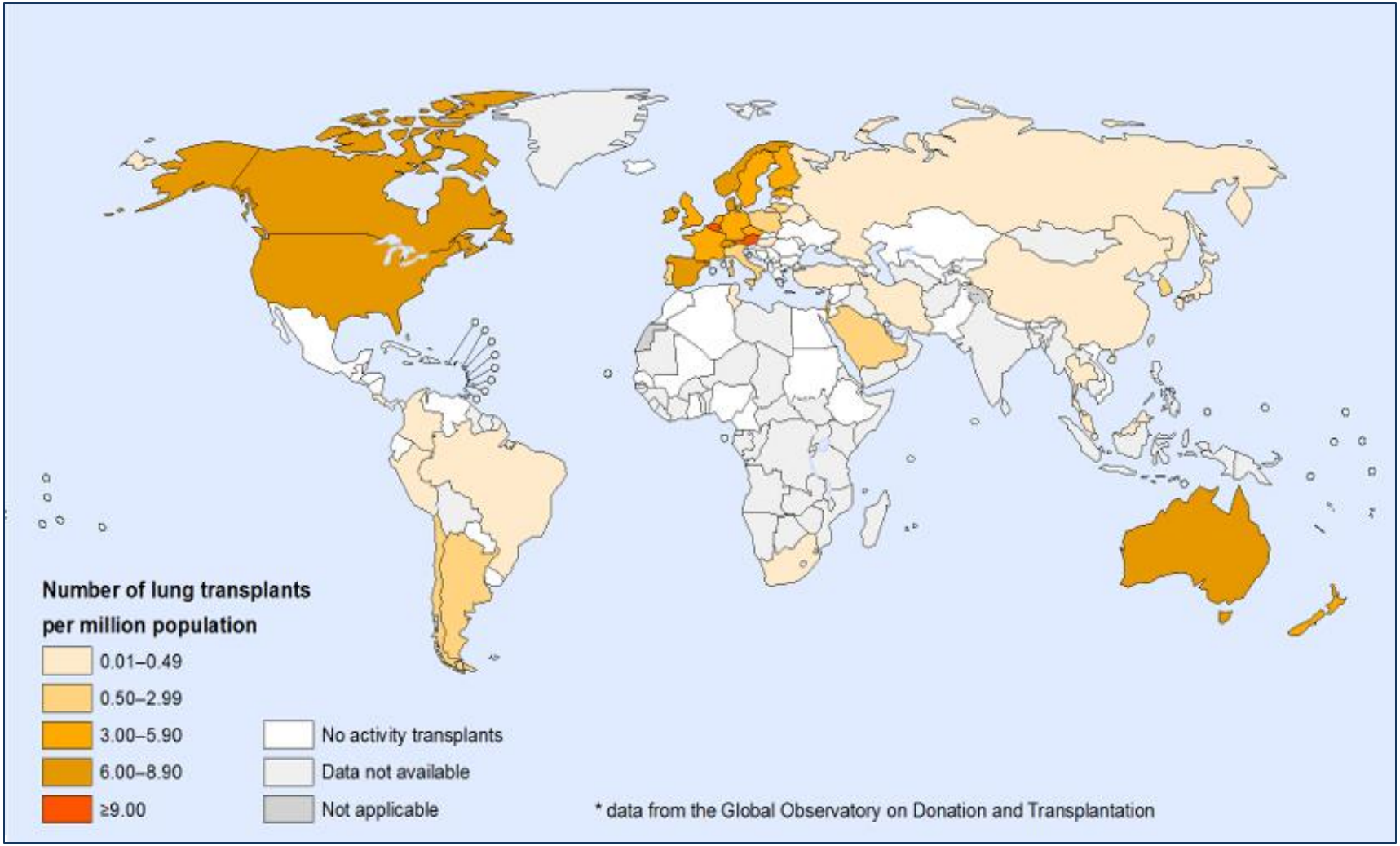
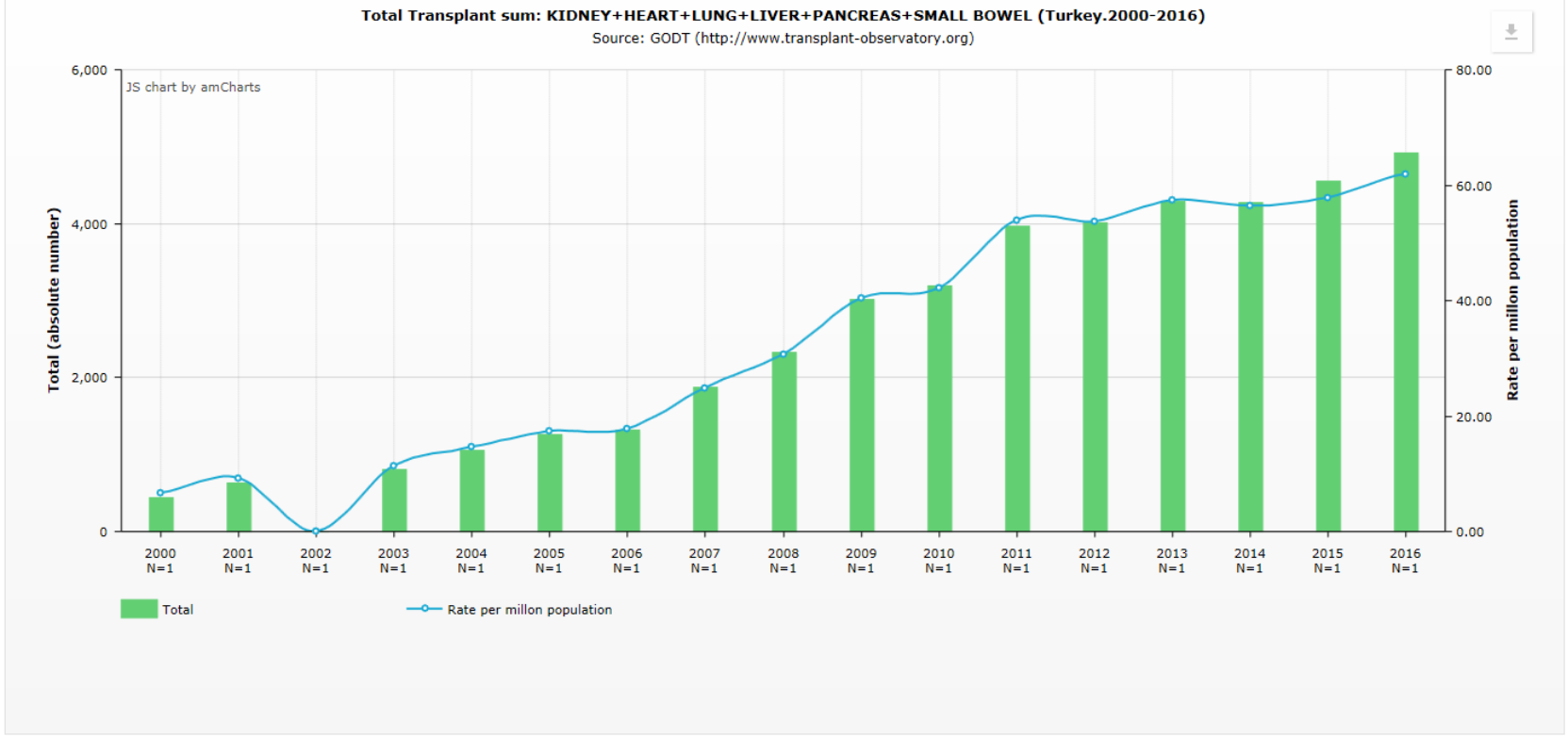
AKCİĞER



http://www.transplant-observatory.org/

Türkiye- SOT Olguları



http://www.transplant-observatory.org/data-charts-and-tables/chart/

AFY Programı Nedir?
Gerekli midir?
İşe yarıyor mu?

Antimikrobiyal "Stewardship"

- Management: Yönetim
- Stewardship: İdare

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY APRIL 2012, VOL. 33, NO. 4

SHEA/IDSA/PIDS POLICY STATEMENT

Policy Statement on Antimicrobial Stewardship by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Infectious Diseases Society (PIDS)

sequences of antimicrobial use. Antimicrobial stewardship has been defined as "coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration." [2] Given new regulatory requirements and political sup-

- Uygun endikasyon
- Uygun ilaç
- Uygun doz
- Uygun yol
- Uygun süre

Antimikrobiyal Yönetim- Amaç

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY APRIL 2012, VOL. 33, NO. 4

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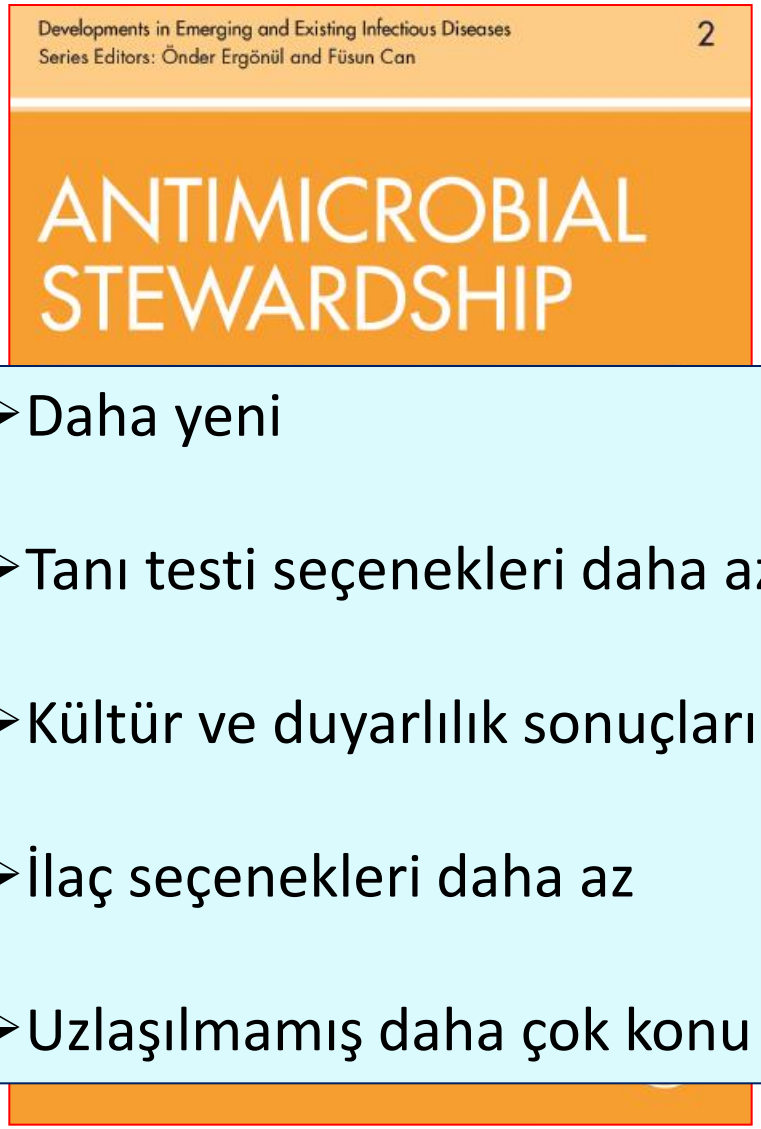
therapy, and route of administration. The major objectives of antimicrobial stewardship are to achieve best clinical outcomes related to antimicrobial use while minimizing toxicity and other adverse events, thereby limiting the selective pressure on bacterial populations that drives the emergence of antimicrobial-resistant strains. Antimicrobial stewardship may also reduce excessive costs attributable to suboptimal antimicrobial use.

- **"En iyi klinik sonuç"**
- Tanı yöntemlerinin uygun kullanılması
- Kesin tanıya ulaşma sıklığının artması
- İlaç kullanımının azalmasına bağlı yan etkilerin azalması
- Tedavi modifikasyonu ile yatış süresinde kısalma
- Direncin azalması
- Maliyette azalma

Antifungal Yönetim vs Antibakteriyel Yönetim




Chapter 12

Antifungal Stewardship

Ozlem K. Azap* and Önder Ergönül**

*Başkent University, Ankara, Turkey

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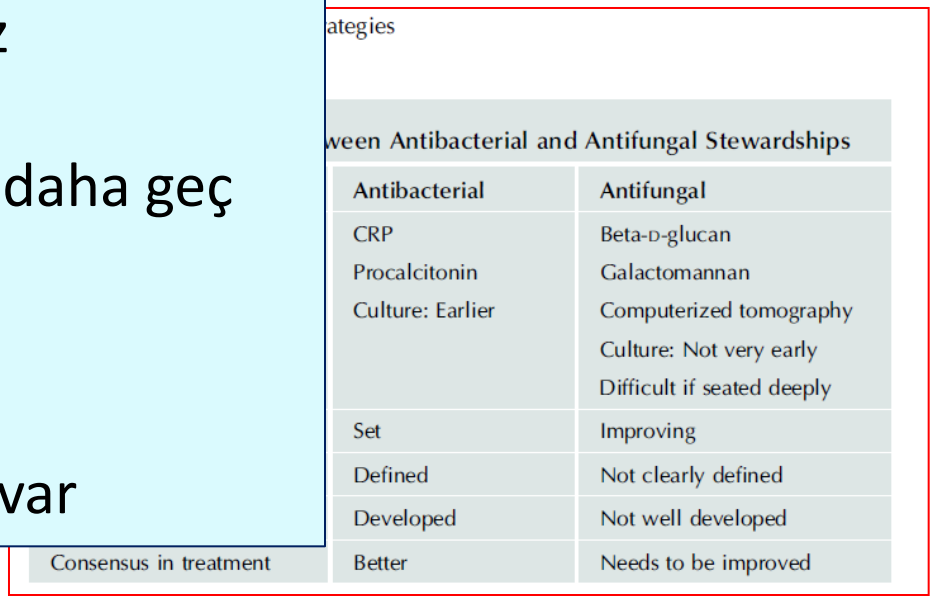
INTRODUCTION

...ns are commonly detected because of increasing num-...nised patients. New diagnostic tools and increasing ...lrug choices require clear decision-making process. ... a tertiary center, antifungal prescriptions were inap-...pphylaxis prescriptions, 78.6% of empirical prescrip-...ptive prescriptions, and 25% of tailored therapy ...7% of antifungal prescriptions were inappropriate [1].

- Daha yeni
- Tanı testi seçenekleri daha az
- Kültür ve duyarlılık sonuçları daha geç
- İlaç seçenekleri daha az
- Uzlaşılmamış daha çok konu var


...ategies

...ween Antibacterial and Antifungal Stewardships

	Antibacterial	Antifungal
	CRP	Beta-D-glucan
	Procalcitonin	Galactomannan
	Culture: Earlier	Computerized tomography
		Culture: Not very early
		Difficult if seated deeply
Set		Improving
Defined		Not clearly defined
Developed		Not well developed
Consensus in treatment	Better	Needs to be improved

Antifungal yönetime ihtiyaç var mı?

Evaluation of antifungal use in a tertiary care institution: antifungal stewardship urgently needed

Maricela Valerio[1,2], Carmen Guadalupe Rodriguez-Gonzalez[2,3], Patricia Muñoz[1,2,4]*, Betsabe Caliz[2,3], Maria Sanjurjo[2,3] and Emilio Bouza[1,2,4] on behalf of the COMIC Study Group (Collaborative Group on Mycoses)†

Table 4. Adequacy of antifungal therapy for different indications

	Prophylaxis ($n=15$)	Empirical ($n=42$)	Pre-emptive ($n=20$)	Tailored ($n=20$)	Overall ($n=100$)
Score, mean ± SD	9.1 ± 1.3	6.6 ± 2.7	8.3 ± 2.2	9.5 ± 1.9	7.7 ± 2.6
Inappropriate prescription, *n* (%)	6 (40)	33 (78.6)	10 (50)	5 (25)	57 (57)
Reason for inappropriate prescription, *n* (%)					
no microbiological adjustment	1 (6.7)	21 (50.0)	7 (35.0)	3 (15.0)	35 (35.0)
inappropriate antifungal selection	1 (6.7)	20 (47.6)	3 (15.0)	4 (20.0)	31 (31.0)
inappropriate duration	2 (13.3)	18 (42.9)	4 (20.0)	2 (10.0)	27 (27.0)
inappropriate administration route	1 (6.7)	12 (28.6)	4 (20.0)	3 (15.0)	20 (20.0)
unnecessary prescription (incorrect indication)	1 (6.7)	9 (21.4)	2 (10.0)	1 (5.0)	16 (16.0)
inappropriate dosage	2 (13.3)	9 (21.4)	2 (10.0)	1 (5.0)	16 (16.0)

➢Kullanılan antifungallerin yarısı UYGUN DEĞİL!

J Antimicrob Chemother 2014; **69**: 1993 – 1999

SOT hastalarında fungal enfeksiyonların tedavisi…

American Journal of Transplantation 2015; 15: 1141–1147
Wiley Periodicals Inc.

doi: 10.1111/ajt.13186

Minireview

Emerging Issues With Diagnosis and Management of Fungal Infections in Solid Organ Transplant Recipients

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[2]*Infectious Disease Section, Baylor College of Medicine, Houston, TX*
** Corresponding author: Dimitrios P. Kontoyiannis, dkontoyi@mdanderson.org*
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acid fluorescent *in situ* hybridization; SOT, solid organ transplant(ation); VOC, volatile organic compounds

Received 14 July 2014, revised and accepted for publication 19 December 2014

Introduction

The incidence of invasive fungal infections (IFIs) in solid organ transplant (SOT) recipients is likely underrecog-

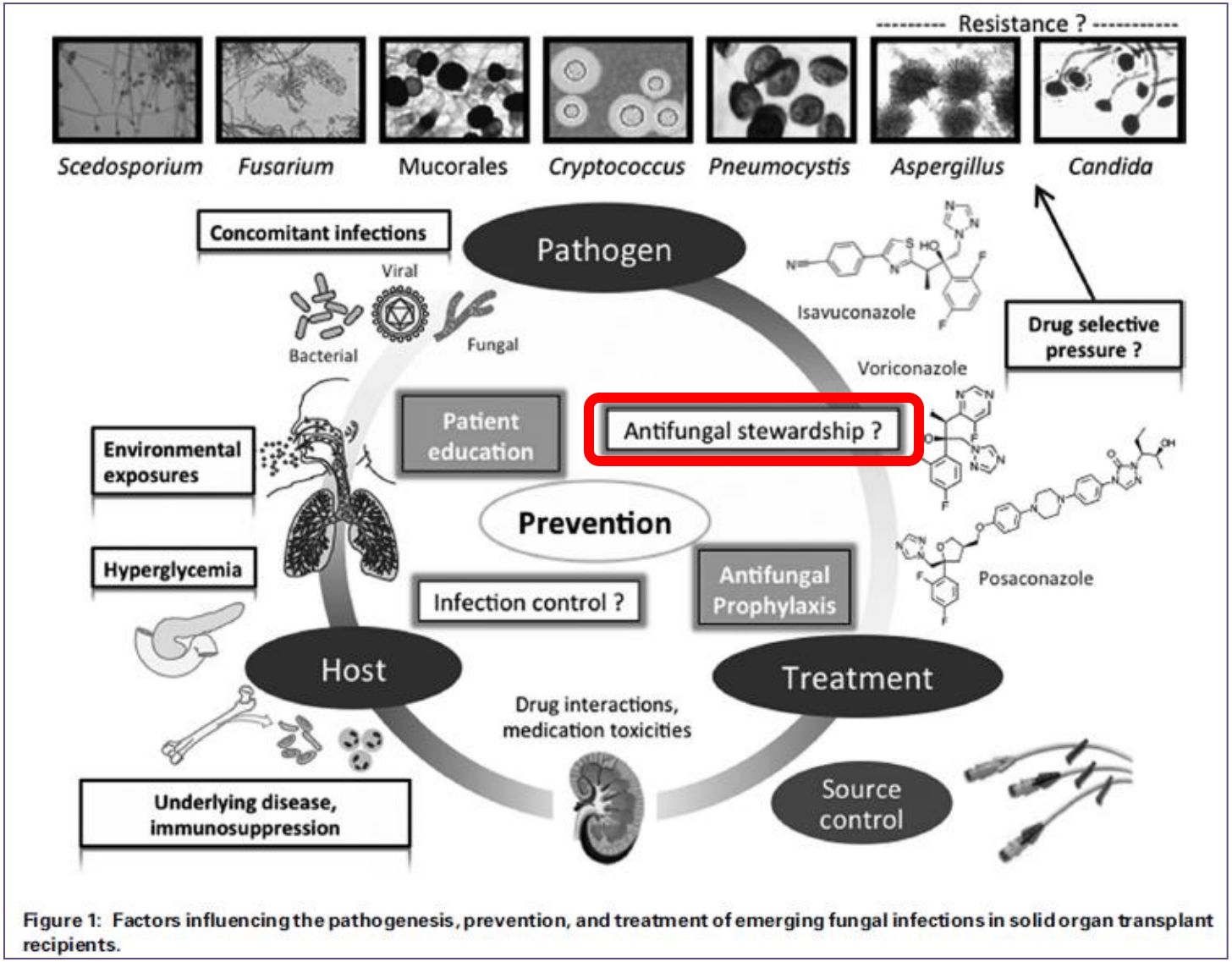

Figure 1: Factors influencing the pathogenesis, prevention, and treatment of emerging fungal infections in solid organ transplant recipients.

American Journal of Transplantation 2015; 15: 1141–1147

The Journal of Infectious Diseases
PERSPECTIVE

The *Candida auris* Alert: Facts and Perspectives

C.auris'in beklenmeyen çıkışı ve hızla yayılması: **bir şey yapmalı!**

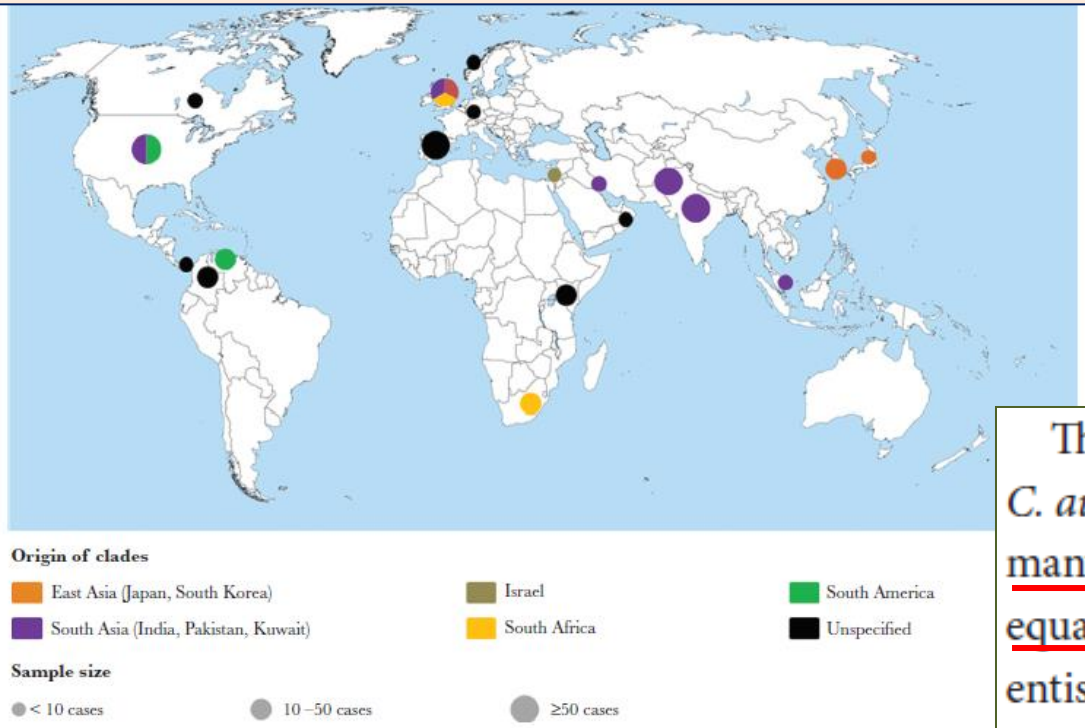

Figure 1. Geographical distribution of *Candida auris* cases and outbreaks reported in the world. Only cases reported in the medical literature are shown. circles is representative of the number of cases. The colors represent the different clades that have been described. Cases from the United States and Great tributed in different clades.

The unprecedented emergence of *C. auris* is a timely reminder that, as with many bacteria, fungal pathogens deserve equal attention from policy makers, scientists, drug developers, and treating physicians.

Antifungal yönetim işe yarıyor mu?

Antifungal stewardship in a tertiary-care institution: a bedside intervention

- YBÜ'de antifungal ilaç kullanımı %50 azalmış

TABLE 4. Impact of the antifungal stewardship on clinical and demographical characteristics

	Pre-AFS	During AFS			
	2010	2011	2012	2013	p
Candidaemia incidence/1000 admissions	1.49	1.76	1.44	1.14	0.08
Candidaemia albicans	0.87	0.83	0.67	0.48	**0.01**
Candidaemia parapsilosis	0.27	0.53	0.38	0.35	0.75
Candidaemia tropicalis	0.09	0.13	0.24	0.12	0.35
Candidaemia glabrata	0.16	0.19	0.16	0.08	0.29
Non-albicans *Candida*	0.62	0.93	0.77	0.66	0.97
Non-albicans *Candida* (%)	41.5	52.7	53.5	58.2	**0.05**
Fluconazole resistance in candidaemia (%)	6.1	4.3	4.2	3.6	0.53
Candidaemia-related mortality (%)	28.0	23.7	22.5	16.4	0.12

Significative p values are in bold.

Clin Microbiol Infect 2015; 21: 492.e1–492.e9

J Antimicrob Chemother 2018; **73**: 297–305
doi:10.1093/jac/dkx388 Advance Access publication 16 November 2017

Journal of Antimicrobial Chemotherapy

A systematic review of interventions and performance measures for antifungal stewardship programmes

Results: A total of 97 studies were identified and 14 were included. Only five studies reported an antifungal stewardship team composed of all the recommended members. The main intervention was the formulation of recommendations to change treatment (12 of 14). The main performance measure collected was antifungal consumption (10 of 14), followed by antifungal expenditure (7 of 14), adherence to therapeutic advice (4 of 14) and impact on mortality (4 of 14). Antifungal consumption was reduced by 11.8% to 71% and antifungal expenditure by as much as 50%. Adherence to therapeutic advice ranged from 40% to 88%, whereas antifungal SPs had no impact on mortality.

- Antifungal tüketimi %11-71 oranında azalmış
- Antifungallere yapılan harcama %50 azalmış
- Önerilere uyum %40-88 oranında olmuş
- Mortaliteye etkisi GÖSTERİLEMEMİŞ

Conclusions: All antifungal SPs had an impact, in particular on antifungal consumption and antifungal expenditure. Active intervention including a review of prescriptions seems to have more impact than implementation of treatment guidelines only. According to available published studies, antifungal consumption appears to be the most achievable performance measure to evaluate the impact of an antifungal SP.

Nasıl bir yol izlenebilir?

Tanımlar konusunda ortak terminoloji

EORTC-MSC Kriterleri

Yıl: 2003

Yıl: 2018

Galaktomannan FDA onayı aldı!

Kriterler

Table 2. Criteria for probable invasive fungal disease except for endemic mycoses.

- Host factors[a]
  - Recent history of neutropenia (<0.5 × 10^9 neutrophils/L [<500 neutrophils/mm^3] for >10 days) temporally related to the onset of fungal disease
  - Receipt of an allogeneic stem cell transplant
  - Prolonged use of corticosteroids (excluding among patients with allergic bronchopulmonary aspergillosis) at a mean minimum dose of 0.3 mg/kg/day of prednisone equivalent for >3 weeks
  - Treatment with other recognized T cell immunosuppressants, such as cyclosporine, TNF-α blockers, specific monoclonal antibodies (such as alemtuzumab), or nucleoside analogues during the past 90 days
  - Inherited severe immunodeficiency (such as chronic granulomatous disease or severe combined immunodeficiency)
- Clinical criteria[b]
  - Lower respiratory tract fungal disease[c]
    - The presence of 1 of the following 3 signs on CT:
      - Dense, well-circumscribed lesions(s) with or without a halo sign
      - Air-crescent sign
      - Cavity
  - Tracheobronchitis
    - Tracheobronchial ulceration, nodule, pseudomembrane, plaque, or eschar seen on bronchoscopic analysis
  - Sinonasal infection
    - Imaging showing sinusitis plus at least 1 of the following 3 signs:
      - Acute localized pain (including pain radiating to the eye)
      - Nasal ulcer with black eschar
      - Extension from the paranasal sinus across bony barriers, including into the orbit
  - CNS infection
    - 1 of the following 2 signs:
      - Focal lesions on imaging
      - Meningeal enhancement on MRI or CT
  - Disseminated candidiasis[d]
    - At least 1 of the following 2 entities after an episode of candidemia within the previous 2 weeks:
      - Small, target-like abscesses (bull's-eye lesions) in liver or spleen
      - Progressive retinal exudates on ophthalmologic examination
- Mycological criteria
  - Direct test (cytology, direct microscopy, or culture)
    - Mold in sputum, bronchoalveolar lavage fluid, bronchial brush, or sinus aspirate samples, indicated by 1 of the following:
      - Presence of fungal elements indicating a mold
      - Recovery by culture of a mold (e.g., *Aspergillus, Fusarium,* Zygomycetes, or *Scedosporium* species)
  - Indirect tests (detection of antigen or cell-wall constituents)[e]
    - Aspergillosis
      - Galactomannan antigen detected in plasma, serum, bronchoalveolar lavage fluid, or CSF
    - Invasive fungal disease other than cryptococcosis and zygomycoses
      - β-D-glucan detected in serum

- Konak faktörleri
- "Klinik" kriterler
- Mikolojik kriterler

Clinical Infectious Diseases 2008; 46:1813–21

Kanıtlanmış IFH

(EORTC-MSG kriterleri)

Steril materyalde

- Histopatolojik, sitopatolojik, direkt mikroskopik **incelemede mantar görülmesi**
- **Kültür**de üreme olması

Table 1. Criteria for proven invasive fungal disease except for endemic mycoses.

Analysis and specimen	Molds[a]
Microscopic analysis: sterile material	Histopathologic, cytopathologic, or direct microscopic examination[b] of a specimen obtained by needle aspiration or biopsy in which hyphae or melanized yeast-like forms are seen accompanied by evidence of associated tissue damage
Culture	
Sterile material	Recovery of a mold or "black yeast" by culture of a specimen obtained by a sterile procedure from a normally sterile and clinically or radiologically abnormal site consistent with an infectious disease process, excluding bronchoalveolar lavage fluid, a cranial sinus cavity specimen, and urine
Blood	Blood culture that yields a mold[d] (e.g., *Fusarium* species) in the context of a compatible infectious disease process
Serological analysis: CSF	Not applicable

[a] If culture is available, append the identification at the genus or species level from the culture results.
[b] Tissue and cells submitted for histopathologic or cytopathologic studies should be stained by Grocott-Gomori meth
fungal structures. Whenever possible, wet mounts of specimens from foci related to invasive fungal disease should be s
[c] *Candida, Trichosporon,* and yeast-like *Geotrichum* species and *Blastoschizomyces capitatus* may also form pseudohyp
[d] Recovery of *Aspergillus* species from blood cultures invariably represents contamination.

- BAL'da üreme kabul edilmez
- GM, BDG, PCR pozitifliği kabul edilmez

Clinical Infectious Diseases 2008; 46:1813–21

Probable (Muhtemel) IFH

(EORTC-MSG kriterleri)

- SOT yapılmış hastada
- Klinik kriterler (BT bulguları…)
- Mikolojik kriterler;
  - direkt (BAL veya balgam kültüründe görülme/üreme
  - indirekt: GM, BDG

- PCR?

Table 2. Criteria for probable invasive fungal disease except for endemic mycoses.

Host factors[a]
- Recent history of neutropenia (<0.5 × 10^9 neutrophils/L [<500 neutrophils/mm³] for >10 days) temporally related to the onset of fungal disease
- Receipt of an allogeneic stem cell transplant
- Prolonged use of corticosteroids (excluding among patients with allergic bronchopulmonary aspergillosis) at a mean minimum dose of 0.3 mg/kg/day of prednisone equivalent for >3 weeks
- Treatment with other recognized T cell immunosuppressants, such as cyclosporine, TNF-α blockers, specific monoclonal antibodies (such as alemtuzumab), or nucleoside analogues during the past 90 days
- Inherited severe immunodeficiency (such as chronic granulomatous disease or severe combined immunodeficiency)

Clinical criteria[b]
- Lower respiratory tract fungal disease[c]
  - The presence of 1 of the following 3 signs on CT:
    - Dense, well-circumscribed lesions(s) with or without a halo sign
    - Air-crescent sign
    - Cavity
  - Tracheobronchitis
    - Tracheobronchial ulceration, nodule, pseudor
  - Sinonasal infection
    - Imaging showing sinusitis plus at least 1 of
      - Acute localized pain (including pain radiatir
      - Nasal ulcer with black eschar
      - Extension from the paranasal sinus across
  - CNS infection
    - 1 of the following 2 signs:
      - Focal lesions on imaging
      - Meningeal enhancement on MRI or CT
  - Disseminated candidiasis[d]
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      - Small, target-like abscesses (bull's-eye les
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Mycological criteria
- Direct test (cytology, direct microscopy, or culture)
  - Mold in sputum, bronchoalveolar lavage fluid, bronchial brush, or sinus aspirate samples, indicated by 1 of the following:
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      - β-D-glucan detected in serum

- Konak faktörleri
- "Klinik" kriterler
- Mikolojik kriterler

NOTE. Probable IFD requires the presence of a host factor, a clinical criterion, and a mycological criterion. Cases that meet the criteria for a host factor and a clinical criterion but for which mycological criteria are absent are considered possible IFD.

[a] Host factors are not synonymous with risk factors and are characteristics by which individuals predisposed to invasive fungal diseases can be recognized. They are intended primarily to apply to patients given treatment for malignant disease and to recipients of allogeneic hematopoietic stem cell and solid-organ transplants. These host factors are also applicable to patients who receive corticosteroids and other T cell suppressants as well as to patients with primary immunodeficiencies.

[b] Must be consistent with the mycological findings, if any, and must be temporally related to current episode.

[c] Every reasonable attempt should be made to exclude an alternative etiology.

[d] The presence of signs and symptoms consistent with sepsis syndrome indicates acute disseminated disease, whereas their absence denotes chronic disseminated disease.

[e] These tests are primarily applicable to aspergillosis and candidiasis and are not useful in diagnosing infections due to *Cryptococcus* species or Zygomycetes (e.g., *Rhizopus, Mucor,* or *Absidia* species). Detection of nucleic acid is not included, because there are as yet no validated or standardized methods.

Clinical Infectious Diseases 2008; 46:1813–21

Possible (Mümkün?) IFH

(EORTC-MSG kriterleri)

- Konak faktörleri
- "Klinik" kriterler
- Mikolojik kriterler

- SOT yapılmış hastada
- Klinik kriterler (BT bulguları…)
- **Mikolojik kriterler YOK!**

NOTE. Probable IFD requires the presence of a host factor, a clinical criterion, and a mycological criterion. Cases that meet the criteria for a host factor and a clinical criterion but for which mycological criteria are absent are considered possible IFD.

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Clinical Infectious Diseases 2008; 46:1813–21

Tanımlar tüm hastaları kapsamıyor!

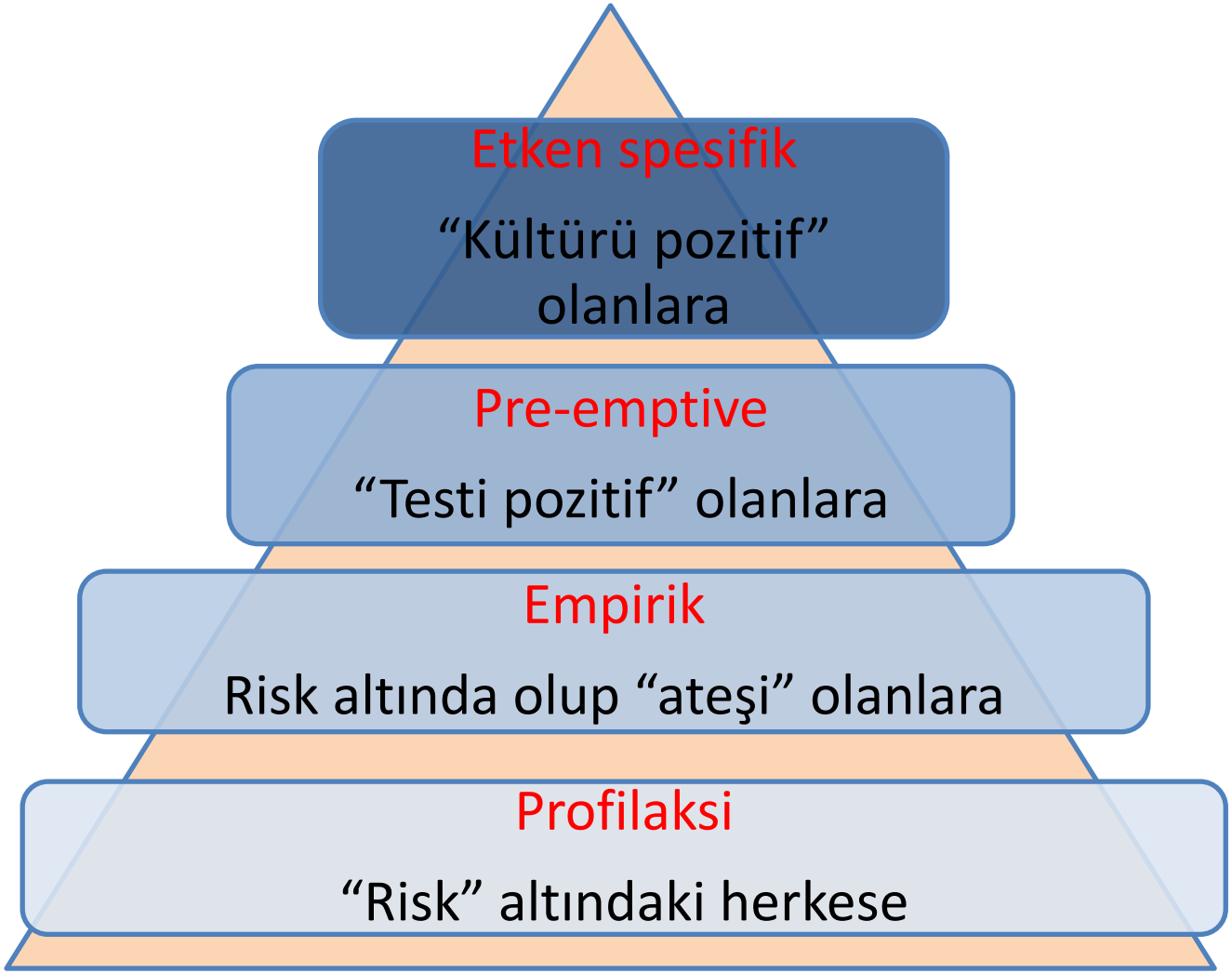
- Profilaksi

- Nötropenik ateşte empirik tedavi

  Klinik/radyolojik/laboratuvar bulgusu YOK!

- Klinik/radyolojik bulgusu YOK; SADECE biyobelirteç (GM…vb) pozitifliği olan hastalar ???

Antifungal kullanım nedenleri



Impact of the revised (2008) EORTC/MSG definitions for invasive fungal disease on the rates of diagnosis of invasive aspergillosis

Dimitris A. Tsitsikas*, Amelie Morin*, Shamzah Araf*, Bernadine Murtagh*, Gemma Johnson†, Sarah Vinnicombe‡, Stephen Ellis‡, Tamara Suaris‡, Mark Wilks†, Sarah Doffman§ & Samir G. Agrawal*†

Department of Haematological Oncology, St Bartholomew's Hospital, London, ‡Department of Diagnostic Imaging Barts and the London NHS Trust, †Blizzard Institute of Cellular and Molecular Science, Queen Mary University, London, and §Brighton and Sussex University Hospitals NHS Trust, Brighton, UK

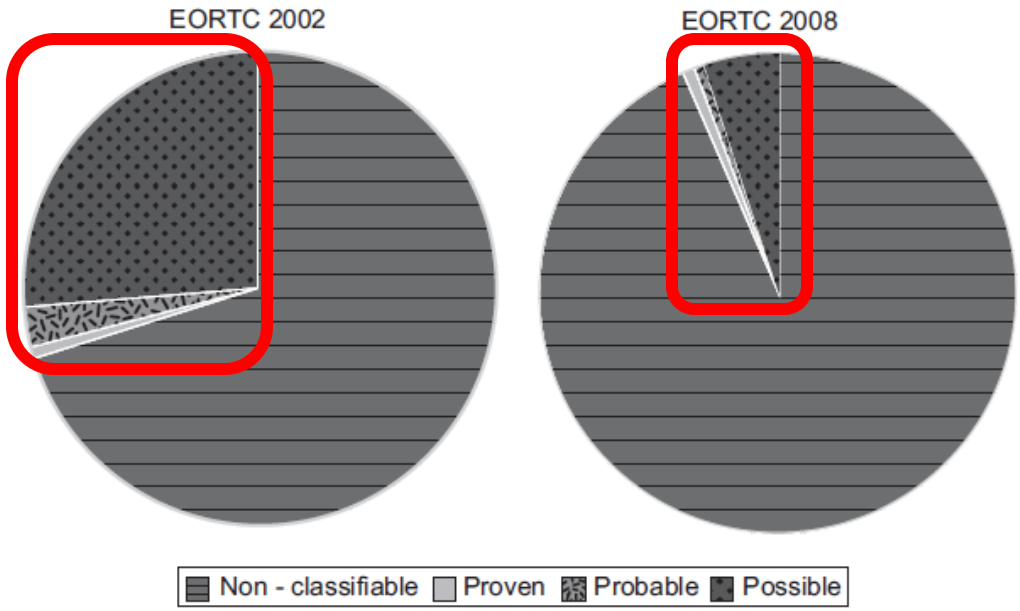


Fig. 1. Re-classification of cases of invasive aspergillosis (IA) by application of the EORTC/MSG 2008 criteria. Pie charts show EORTC/MSG classification of IFD using the 2002 and 2008 criteria. NB: all downgraded 'probable' cases get reduced to 'non-classifiable'.

 Medical Mycology, **50**, 538–542

EDITORIALS & PERSPECTIVES

The role of antifungal treatment in hematology

Johan A. Maertens,[1] Marcio Nucci,[2] and J. Peter Donnelly[3]

[1]Department of Hematology, Acute Leukemia and Stem Cell Transplantation Unit, University Hospital Gasthuisberg, K. U. Leuven, Leuven, Belgium; [2]Hospital Universitário Clementino Fraga Filho, Universidade Fedeal do Rio de Janeiro, Brazil; [3]Department of Hematology & Nijmegen Institute for Infection, Inflammation and Immunity, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

	A	B	C		D	E
				IV	-	
Radiological signs and clinical symptoms				Radiological signs on CT (dense, well-circumscribed lesions(s) with or without a halo sign, air-crescent sign, or cavity)		Not considered necessary
Mycology results				Negative	Positive biomarker or microscopy or culture	Positive tissue or specimen from a sterile site
Clinical evidence of IFD				Yes	Yes	Yes
Mycological evidence of IFI				No	Yes	Yes
Final diagnosis				Possible IMD	Probable IMD	Proven IMD
Management				ıerapy	Targeted therapy	

haematologica | 2012; 97(3)

Tanımlar tüm hastaları kapsamıyor!

- Profilaksi

- Nötropenik ateşte empirik tedavi

  Klinik/radyolojik/laboratuvar bulgusu YOK!

- Klinik/radyolojik bulgusu YOK; SADECE biyobelirteç (GM…vb) pozitifliği olan hastalar ???

EDITORIALS & PERSPECTIVES

The role of antifungal treatment in hematology

Johan A. Maertens,[1] Marcio Nucci,[2] and J. Peter Donnelly[3]

[1]Department of Hematology, Acute Leukemia and Stem Cell Transplantation Unit, University Hospital Gasthuisberg, K. U. Leuven, Leuven, Belgium; [2]Hospital Universitário Clementino Fraga Filho, Universidade Fedeal do Rio de Janeiro, Brazil; [3]Department of Hematology & Nijmegen Institute for Infection, Inflammation and Immunity, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

	A	B	C				D	E
	-	-	I	II	III	IV	-	
Radiological signs and clinical symptoms	No	Persistent febrile neutropenia	No	Clinical (any new infiltrate not fulfilling the EORTC/MSG criteria)		Radiological signs on CT (dense, well-circumscribed lesions(s) with or without a halo sign, air-crescent sign, or cavity)		Not considered necessary
Mycology results	Negative	Negative	Positive biomarker or microscopy or culture	Negative	Positive biomarker or microscopy or culture	Negative	Positive biomarker or microscopy or culture	Positive tissue or specimen from a sterile site
Clinical evidence of IFD	No	No	No	No	No	Yes	Yes	Yes
Mycological evidence of IFI	No	No	Yes	No	Yes	No	Yes	Yes
Final diagnosis			Unclassified			Possible IMD	Probable IMD	Proven IMD
Management	Prophylaxis	Empirical therapy	Diagnostic-driven (pre-emptive) therapy				Targeted therapy	

haematologica | 2012; 97(3)

EDITORIALS & PERSPECTIVES

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haematologica | 2012; 97(3)

AFY- Örnekler

INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY OCTOBER 2016, VOL. 37, NO. 10

ORIGINAL ARTICLE

Current State of Antimicrobial Stewardship at Solid Organ and Hematopoietic Cell Transplant Centers in the United States

OBJECTIVE. To assess the extent of antimicrobial stewardship programs (ASPs) at solid organ transplant (SOT) and hematopoietic cell transplant (HCT) centers in the United States.

DESIGN. An 18-item voluntary survey was developed to gauge current antimicrobial stewardship practices in transplant patients, examine the availability and perceived usefulness of novel diagnostics and azole levels to guide therapy, and identify challenges for implementation of ASPs at these centers.

PARTICIPANTS. The survey was distributed electronically to infectious disease physicians and pharmacists at adult and pediatric SOT and HCT centers during May 1–22, 2015. Facilities were deidentified.

RESULTS. After duplicate removal, 71 (56%) of 127 unique transplant centers in 32 states were analyzed. Forty-four sites (62%) performed at least 100 SOT annually, and 40 (56%) performed at least 100 HCT annually. Top 5 stewardship activities encompassing transplant patients were formulary restriction, guideline development, prospective audit and feedback, education, and dose optimization. Respiratory viral panels (66/66 [100%]), azole levels (64/66 [97%]), and serum/bronchoalveolar lavage galactomannan (58/66 [88%]) were perceived as most useful to guide therapy. Apparent challenges to antimicrobial stewardship included undefined duration for certain infections (53/59 [90%]), diagnostic uncertainty (47/59 [80%]), the perception that antibiotic-resistant infections required escalation (42/59 [71%]), prescriber opposition (41/59 [69%]), and costly drugs (37/59 [63%]).

CONCLUSIONS. ASP activities were performed at many adult and pediatric SOT and HCT centers in the United States. Diagnostic and therapeutic uncertainty in transplant patients is challenging for ASPs. Collaborative research should examine the impact of antimicrobial stewardship practices in SOT and HCT.

INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY OCTOBER 2016, VOL. 37, NO. 10

ORIGINAL ARTICLE

Current State of Antimicrobial Stewardship at Solid Organ and Hematopoietic Cell Transplant Centers in the United States

TABLE 1. Antimicrobial Stewardship Interventions and Outcomes Encompassing Transplant Patients Among 62 Medical Centers With Antimicrobial Stewardship Programs

	Hematopoietic cell transplant	Solid organ transplant	Not familiar/ not applicable
Interventions			
Formulary restriction	47 (76%)	48 (77%)	11 (18%)
Guideline development	47 (76%)	44 (71%)	12 (19%)
Prospective audit & feedback	43 (69%)	43 (69%)	16 (26%)
Education	43 (69%)	42 (68%)	17 (27%)
Dose optimization	42 (68%)	43 (69%)	17 (27%)
Prior authorization	39 (63%)	40 (65%)	18 (29%)
Antimicrobial de-escalation	36 (58%)	37 (60%)	22 (35%)
Intravenous to oral conversion	35 (56%)	36 (58%)	24 (39%)
Time-sensitive stop orders	23 (37%)	24 (39%)	38 (61%)
Computerized decision support	22 (35%)	23 (37%)	38 (61%)
Antimicrobial order forms	21 (34%)	22 (35%)	38 (61%)
Antimicrobial cycling	3 (5%)	2 (3%)	59 (95%)
None. Transplant patients are excluded.	1 (2%)	1 (2%)	61 (98%)
Outcomes			
Antimicrobial use	21 (34%)	17 (27%)	31 (50%)
Antimicrobial costs	32 (52%)	31 (50%)	19 (31%)
Rate of *Clostridium difficile* infections	40 (65%)	35 (56%)	14 (23%)
Reduction in length-of-stay	13 (21%)	13 (21%)	37 (60%)
Transplant-specific antibiogram	10 (16%)	7 (11%)	42 (68%)
None	14 (23%)	14 (23%)	38 (61%)

INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY OCTOBER 2016, VOL. 37, NO. 10

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ORIGINAL ARTICLE

Current State of Antimicrobial Stewardship at Solid Organ and Hematopoietic Cell Transplant Centers in the United States

Merkezi laboratuvar/laboratuvarlar olmalı

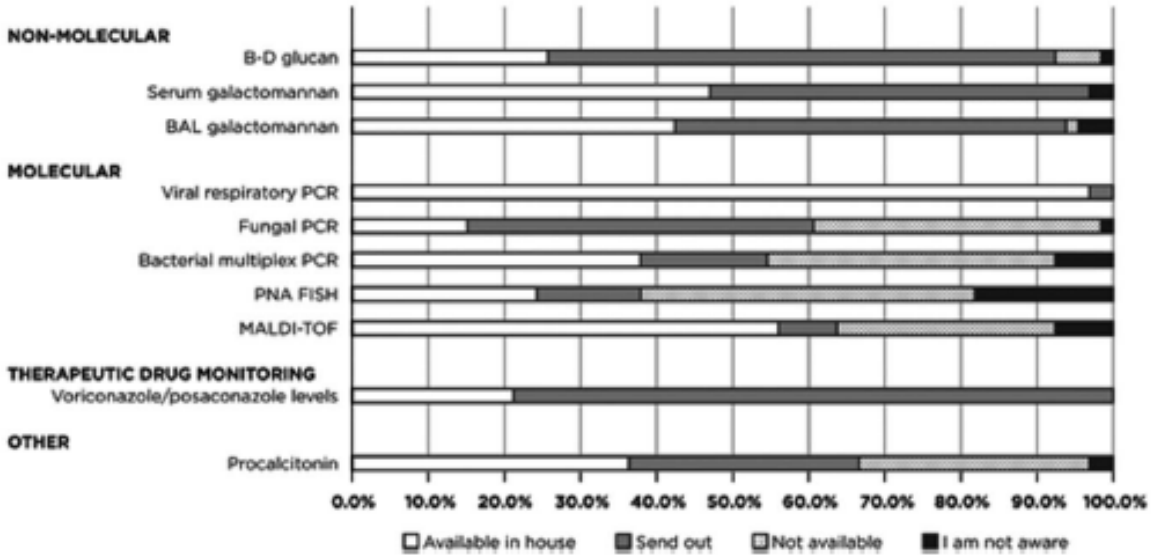

FIGURE 1. Availability of novel diagnostics and azole levels for transplant patients.
BAL, bronchoalveolar lavage; B-D glucan, (1–3)-beta-D-glucan; MALDI-TOF, matrix assisted laser desorption/ionization-time of flight; PCR, polymerase chain reaction; PNA FISH, peptide nucleic acid fluorescence in situ hybridization.

Antifungal stewardship in daily practice and health economic implications

Patricia Muñoz,[1,2,3] Maricela Valerio,[1,3] Antonio Vena[1,2,3] and Emilio Bouza[1,2,3]

[1]*Clinical Microbiology and Infectious Diseases Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain,* [2]*Department of Medicine, Complutense University of Madrid, Madrid, Spain and* [3]*Instituto de Investigación Sanitaria del Hospital Gregorio Marañón, Madrid, Spain*

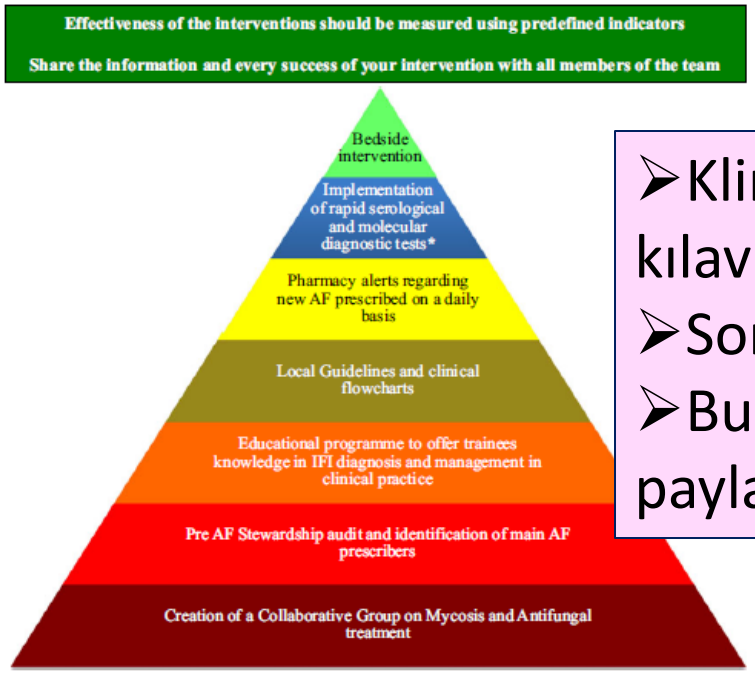

Figure 1 AF stewardship step-by-step. *Use of molecular diagnostics and/or serological biomarkers like galactomannan and beta-D-glucan for early diagnosis. Implementation of TDM for AF plasma levels and susceptibility testing. IFI, invasive fungal infection; AF, antifungal.

- Klinik uygulamalar , birimlere özgü kılavuzlar eşliğinde yürütülmeli,
- Sonuçlar izlenmeli
- Bulgular diğer bölümlerle paylaşılmalı

Mycoses, 2015, **58** (Suppl. 2), 14–25

Antifungal stewardship in daily practice and health economic implications

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Table 1 Multifaceted aspects of AFS programmes.

Intervention	Comment	References
Educational		
Restrictive prescription		
Bedside ID advice		
Bundle of care		
Pharmaceutic advice		
New diagnostic strategy		

- Eğitim
- Kısıtlama
- EHU önerisi
- Bakım demeti: order formları, geri bildirim..vb
- "Farmasötik" öneri
- Yeni tanı yöntemleri

Martinez-Jimenez *et al.* [40]
Barnes *et al.* [32]

J Antimicrob Chemother 2017; **72**: 969–974
doi:10.1093/jac/dkw506 Advance Access publication 19 December 2016

Journal of Antimicrobial Chemotherapy

Issues in antifungal stewardship: an opportunity that should not be lost

- Antifungal kullanımının optimizasyonu
- Antifungaller: Yüksek maliyet, yan etki, ilaç etkileşimi
- Antifungal direnç artıyor
- Lokal epidemiyoloji önemli
- Rehberleri uzmanlar geliştirmeli ve rehber ulaşılabilir olmalı
- **Empirik olarak başlanan antifungallerin kesilmesi veya değiştirilmesi konusu üzerinde özellikle durulmalı**
- **Multidisipliner yaklaşım önemli**
- GM, BDG, Candida ve Aspergillus PCR, BT önemli!
- Serum Vori, Posa, İtra düzeyleri izlenebilmeli
- **Antifungal tüketimi, toksisitesi ve maliyetleri düzenli olarak izlenmeli**

Issues in antifungal stewardship: an opportunity that should not be lost

Table 1. Consensus developed during interactive panel discussion

SN	Controversy	Consensus
1	Is antifungal stewardship needed?	Yes. Antifungal stewardship is needed as a central policy for the whole country, like AMR.
2	Should antifungal stewardship be part of total antimicrobial stewardship?	Yes, but antifungal stewardship should be separately addressed, though under the broad umbrella of the AMSP. However, it needs to be distinctly recognized as a separate entity.
3	Should antifungal use be monitored? (Patchy data are available across the country.)	Antifungal use data need to be collected along with the number of patients treated, to determine the baseline of antifungal use as DDD/1000 days. In resource-constrained settings, at least point prevalence studies need be done to obtain the baseline data.
4	Does local epidemiology data for IFI need to be collected?	Local epidemiology data for IFIs, including patient characteristics, spectrum of organisms and antifungal susceptibility with continuous surveillance, are necessary to develop man-
	ship can be continually improved?	be reoriented. Further initiate CME and workshops. A consensus document should be cre-
9	Should formulation of national guidelines be explored?	A year after implementation of antifungal stewardship programmes at various institutes, the collective data could be analysed and consensus guidelines be formulated and put before the Government of India for implementation. Lessons learned and further ways forward can subsequently be addressed.

AFY programı, AMY şemsiyesi altında yer alabilir ancak ayrıca ele alınmalıdır

Antifungal tüketimi DDD/1000 gün olarak izlenmeli
En azından **nokta prevelans** ile durum saptanmalı

J Antimicrob Chemother 2017; **72**: 969–974

Antifungal tüketim verileri- ATC 5 düzeyinde

	TOPLAM HASTANE kutu satış 2015	TOPLAM HASTANE kutu satış 2016	TOPLAM HASTANE kutu satış 2017	Toplam DID 2015	Toplam DID 2016	Toplam DID 2017
anidulafungin	49.716	77.429	103.253	0,0017	0,0026	0,0034
caspofungin	92.323	94.137	80.847	0,0032	0,0032	0,0027
fluconazole	1.005.893	1.137.632	1.322.625	0,0229	0,0254	0,0287
itraconazole	1.792	2.603	2.520	0,0005	0,0005	0,0006
ketoconazole	0	28	12	0	0	0
micafungin	1.149	8.551	52.119	0	0,0002	0,0013
posaconazole	6.870	9.168	9.601	0,0032	0,0042	0,0042
terbinafine	9.655	1.546	1.675	0,0048	0,0009	0,0009
voriconazole	150.899	177.191	163.521	0,0037	0,0045	0,0042
amphotericin B	112.483	391.754	441.310	0,0173	0,0185	0,0205
Genel Toplam	1.430.780	1.900.039	2.177.483	0,0574	0,06	0,0665

ATC: "*Anatomical Therapeutic Chemical*" /Anatomik, Terapötik ve Kimyasal sınıflandırma sistemi

DDD: "*Defined Daily Dose*" / Tanımlanmış günlük doz

DID: "*Defined Inhabitant Dose*"- Bir günde 1000 kişi başına düşen tanımlanmış günlük doz

J Antimicrob Chemother 2017; **72**: 969–974
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Journal of Antimicrobial Chemotherapy

Issues in antifungal stewardship: an opportunity that should not be lost

Chand Wattal[1]*, Arunaloke Chakrabarti[2], Jaswinder Kaur Oberoi[1], J. Peter Donnelly[3], Rosemary A. Barnes[4], B. L. Sherwal[5], Neeraj Goel[1], Sonal Saxena[6], George M. Varghese[7], Rajeev Soman[8], Poonam Loomba[9], Bansidhar Tarai[10], Sanjay Singhal[11], Naimish Mehta[12], V. Ramasubramanian[13], Dharma Choudhary[14], Yatin Mehta[15], Supradip Ghosh[16], Sumathi Muralidhar[17] and Ravinder Kaur[6]

[1]Department of Clinical Microbiology and Immunology, Sir Ganga Ram Hospital, Rajinder Nagar, New Delhi 110060, India;

Issues in antifungal use:

a. High cost.
b. Toxicity.
c. Drug interactions.
d. Genetic variability governing difference in pharmacokinetics.
e. Usage of generic antifungals that may be substandard in bioequivalence and can encourage resistance.

Biyoeşdeğer olmayan jenerik ilaç sorunu!

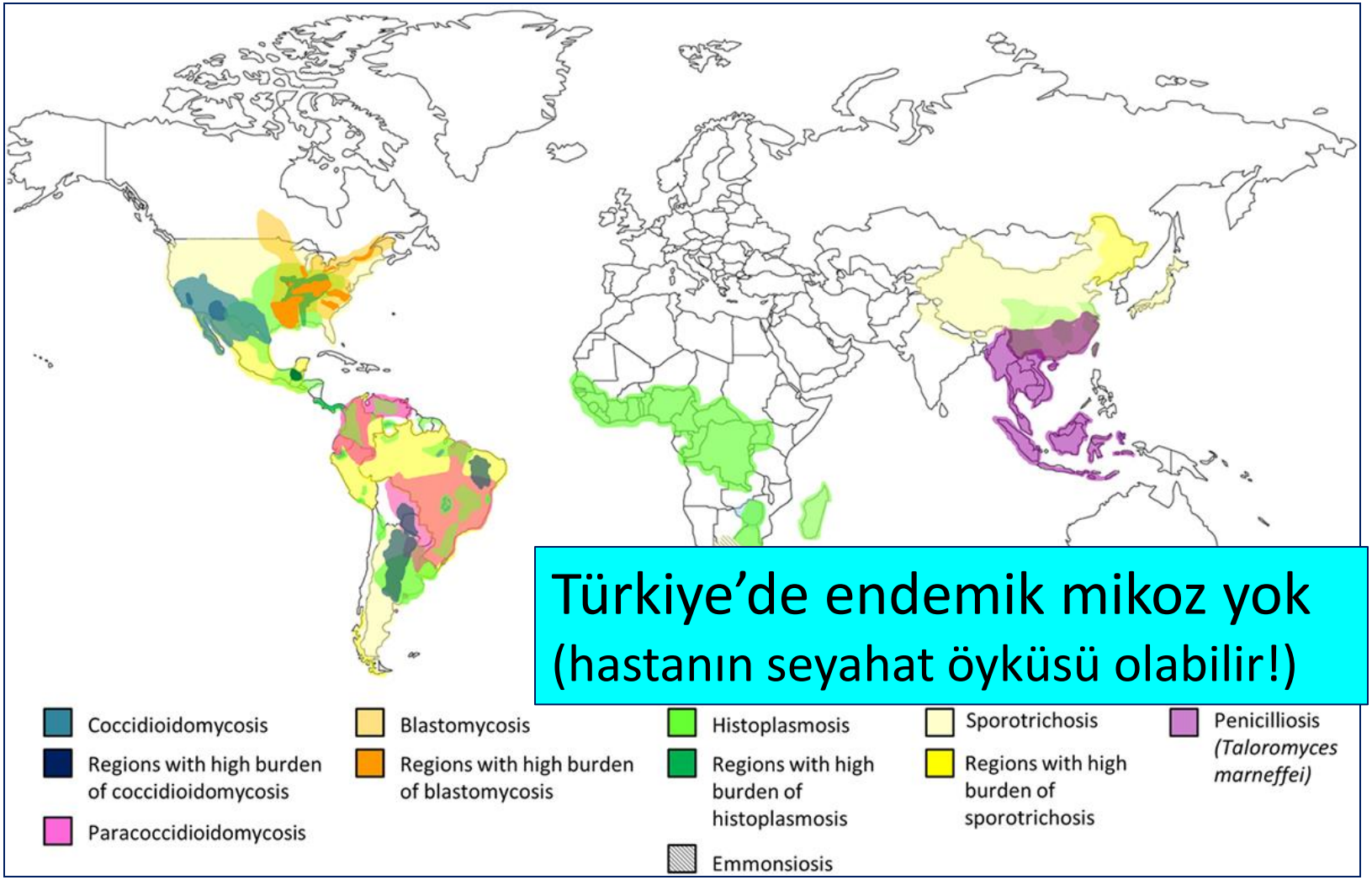
Veriler

Türkiye Verileri

?????

"Dünyada elde edilmiş olan her şey, umutla elde edilmiştir."
Marthin Luther King

Endemik mikozlar



Türkiye'de endemik mikoz yok
(hastanın seyahat öyküsü olabilir!)

Front. Immunol., 28 June 2017 | https://doi.org/10.3389/fimmu.2017.00735

Dünya Verileri

- TRANSNET: ABD
- PATH Alliance: ABD
- RESITRA: İspanya

Invasive Fungal Infections among Organ Transplant Recipients: Results of the Transplant-Associated Infection Surveillance Network (TRANSNET)

Peter G. Pappas, Barbara D. Alexander, David R. Andes, Susan Hadley, Carol A. Kauffman, Alison Freifeld, Elias J. Anaissie, Lisa M. Brumble, Loreen Herwaldt, James Ito, Dimitrios P. Kontoyiannis, G. Marshall Lyon, Kieren A. Marr, Vicki A. Morrison, Benjamin J. Park, Thomas F. Patterson, Trish M. Perl, Robert A. Oster, Mindy G. Schuster, Randall Walker, Thomas J. Walsh, Kathleen A. Wannemuehler, and Tom M. Chiller[a]

Background. Invasive fungal infections (IFIs) are a major cause of morbidity and mortality among organ transplant recipients. Multicenter prospective surveillance data to determine disease burden and secular trends are lacking.

Methods. The Transplant-Associated Infection Surveillance Network (TRANSNET) is a consortium of 23 US transplant centers, including 15 that contributed to the organ transplant recipient dataset. We prospectively identified IFIs among organ transplant recipients from March, 2001 through March, 2006 at these sites. To explore trends, we calculated the 12-month cumulative incidence among 9 sequential cohorts.

Results. During the surveillance period, 1208 IFIs were identified among 1063 organ transplant recipients. The most common IFIs were invasive candidiasis (53%), invasive aspergillosis (19%), cryptococcosis (8%), non-*Aspergillus* molds (8%), endemic fungi (5%), and zygomycosis (2%). Median time to onset of candidiasis, aspergillosis, and cryptococcosis was 103, 184, and 575 days, respectively. Among a cohort of 16,808 patients who underwent transplantation between March 2001 and September 2005 and were followed through March 2006, a total of 729 IFIs were reported among 633 persons. One-year cumulative incidences of the first IFI were 11.6%, 8.6%, 4.7%, 4.0%, 3.4%, and 1.3

respectively. One-year incidence

analysis showed a slight increase

Conclusions. We detected a s

insights into the timing and incid

prevention and treatment strateg

- ABD'de 23 merkez, 15'i veri göndermiş
- 2001-2005 yılları, 16 808 SOT hastası
- 1063 hastada 1208 IFI

Clinical Infectious Diseases 2010; 50:1101–1111

Invasive Fungal Infections among Organ Transplant Recipients: Results of the Transplant-Associated Infection Surveillance Network (TRANSNET)

Table 3. Characteristics of All Patients Included in the Incidence Cohort

Characteristic	No. (%) of patients
Total no. of patients	16,808
Age, median years (range) (n = 15248)	50.3 (0.1–86.7)
Male sex (n = 16668)	10136 (60.8)
White race (n = 16512)	12816 (77.6)
Death within 12 months after receipt of transplant (n = 16,459)	1144 (7.0)
Pediatric patients (<18 years of age) (n = 15248)	762 (5.0)
Transplant type (first transplant only)	
Kidney (unrelated donor)	5506 (32.8)
Kidney (living related donor)	3166 (18.8)
Liver[a]	4468 (26.6)
Pancreas[b]	1213 (7.2)
Lung[c]	1195 (7.1)
Heart[d]	1165 (6.9)
Small bowel[e]	71 (0.4)
Other	24 (0.1)

Clinical Infectious Diseases 2010;50:1101–1111

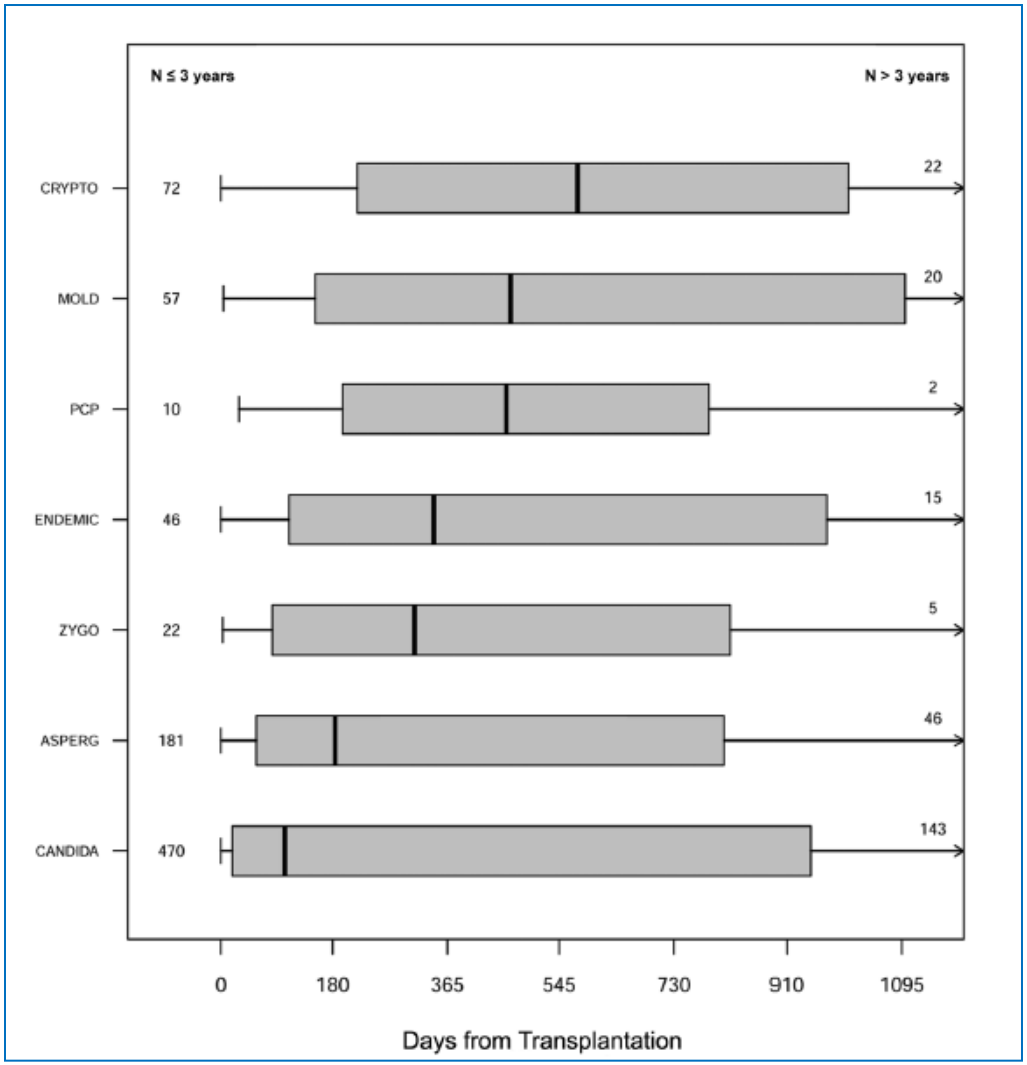
Invasive Fungal Infections among Organ Transplant Recipients: Results of the Transplant-Associated Infection Surveillance Network (TRANSNET)

Table 2. No. (%) of Invasive Fungal Infection (IFI) Cases in the Surveillance Cohort, by Transplant Type

IFI type	Kidney (n = 332)	Liver (n = 378)	Pancreas (n = 128)	Lung (n = 248)	Heart (n = 99)	Small bowel (n = 22)
Candidiasis	164 (49)	255 (68)	97 (76)	56 (23)	48 (49)	19 (85)
Aspergillosis	47 (14)	42 (11)	6 (5)	109 (44)	23 (23)	0 (0)
Zygomycosis	8 (2)	9 (2)	0 (0)	8 (3)	3 (3)	0 (0)
Other mold	10 (3.0)	9 (2.4)	4 (3.1)	49 (19.8)	7 (7.1)	0 (0.0)
Unspecified mold	7 (2.1)	8 (2.1)	0 (0.0)	7 (2.8)	2 (2.0)	0 (0.0)
Cryptococcosis	49 (15)	24 (6)	6 (5)	6 (2)	10 (10)	1 (5)
Endemic mycoses	33 (10)	17 (5)	8 (6)	3 (1)	3 (3)	0 (0)
Pneumocystosis	5 (1)	0 (0)	1 (1)	4 (2)	3 (3)	0 (0)
Other yeast	6 (1.8)	9 (2.4)	5 (3.9)	0 (0.0)	0 (0.0)	1 (5)
Unspecified yeast	3 (0.9)	5 (1.3)	1 (0.8)	6 (2.4)	0 (0.0)	1 (5)

Clinical Infectious Diseases 2010;50:1101–1111

Invasive Fungal Infections among Organ Transplant Recipients: Results of the Transplant-Associated Infection Surveillance Network (TRANSNET)



Clinical Infectious Diseases 2010;50:1101–1111

ISHAM
INTERNATIONAL SOCIETY FOR HUMAN AND ANIMAL MYCOLOGY

Medical Mycology, 2017, 55, 269–277
doi: 10.1093/mmy/myw086
Advance Access Publication Date: 4 October 2016
Original Article

Original Article

Epidemiological features of invasive mold infections among solid organ transplant recipients: PATH Alliance® registry analysis

Shahid Husain[1,*], Fernanda P. Silveira[2], Nkechi Azie[3], Billy Franks[3] and David Horn[4]

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of Toronto, 11 PMB 138,
Diseases, University of P
15213, USA, [3]Astellas Pha
[4]David Horn, LLC, Doylest

ABD, Kanada, 25 merkez
2004-2008 yılları, 333 invazif küf enfeksiyonu

PATH (Prospective Antifungal Therapy) *Alliance*

Materials and methods

The PATH Alliance® registry is a sentinel surveillance network comprising 25 medical centers in the United States and Canada, which collected data on patients with IFIs between July 1, 2004, and September 30, 2008. The methodology

Results

Epidemiology

A total of 333 cases of IMIs in SOTRs were noted in the PATH Alliance® registry. The majority, 63% (*n*/N = 209/333), were in lung transplant recipients followed by 14% (*n*/N = 45/333) in kidney transplant recipients, 10% (*n*/N = 33/333) in LTRs, 7% (*n*/N = 22/333) in heart transplant recipients, 6% (*n*/N = 20/333) in multiple-organ transplant recipients, and 1% (*n*/N = 4/333) in small bowel transplant recipients.

Concomitant bacterial infection was noted in at least one-third of the patients with IMIs, while concomitant cytomegalovirus infection (detected by PCR or p antigenemia) was noted in no more than 11% of IMI cases (Table 1).

Epidemiological features of invasive mold infections among solid organ transplant recipients: PATH Alliance® registry analysis

Table 3. Distribution of fungal infections based on category of disease.

Type of Organ	All	*Aspergillus*		*Mucorales*		Other moulds*		Unidentified moulds		Multiple	
		proven	prob	proven	prob	proven	prob	proven	prob	proven	prob
	333 (100)	114 (34.2)	132 (39.6)	12 (3.6)	1 (0.3)	20 (6.0)	13 (3.9)	2 (0.6)	1 (0.3)	14 (4.2)	23 (6.9)
Kidney	45 (100)	12 (26.7)	16 (35.6)	3 (6.7)	1 (2.2)	6 (13.3)	1 (2.2)	0 (0)	0 (0)	3 (6.7)	3 (6.7)
Liver	33 (100)	12 (36.4)	11 (33.3)	7(21.2)	0 (0)	1 (3.0)	0 (0)	1 (3.0)	0 (0)	1 (3.0)	0 (0)
Lung	209 (100)	74 (35.4)	82 (39.2)	0 (0)	0 (0)	11 (5.3)	12 (5.7)	1 (0.5)	1 (0.5)	9 (4.3)	19 (9.1)
Heart	22 (100)	4 (18.2)	14 (63.6)	1 (4.5)	0 (00)	1 (4.5)	0 (0)	0 (0)	0 (0)	1 (4.5)	1 (4.5)
Small bowel	4 (100)	4 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Multiple	20 (100)	8 (40.)	9 (45.0)	1 (5.0)	0 (0)	1 (5.0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5.0)

*Others include *Cladosporium, Chrysosporium, Exophiala, Exophiala spinifera, Exophiala jeanselmei, Ochroconis, Rhizopus, Scedosporium apiospermum, Trichophyton rubrum, and Scopulariopsis brevicaulis.*

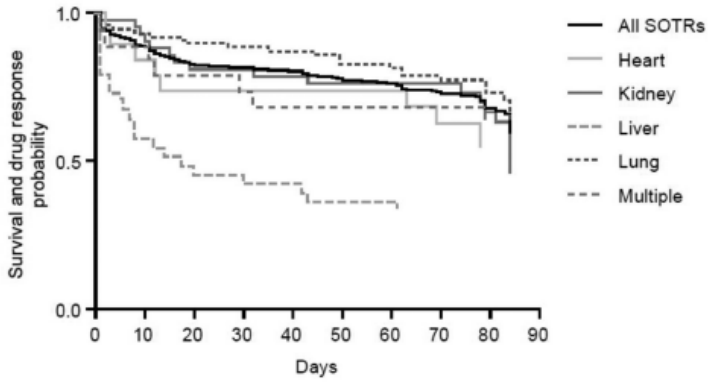

Figure 2 . Kaplan–Meier survival and therapy response probabilities for solid organ transplant recipients at 12 weeks.

Medical Mycology, 2017, 55, 269–277

Rehberler

ESGICH

ESCMID STUDY GROUP FOR INFECTIONS IN COMPROMISED HOSTS

European Society of Clinical Microbiology and Infectious Diseases

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Invasive fungal infections in solid organ transplant recipients

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spp. Candida spp. is the most frequent agent of IFD in the transplant recipient. The absence of clinical trials and the epidemiological differences in IFD in different transplant programmes mean that there are no definitive recommendations for the diagnosis, treatment and prevention of IFD in SOT, so most of the evidence must be based on clinical experience.

Keywords: Drug interactions, invasive aspergillosis, invasive candidiasis, solid organ transplantation, Transplant infectious disease
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SOT hastalarında invazif aspergilloz, enfeksiyondan daha çok bir **sendrom**dur

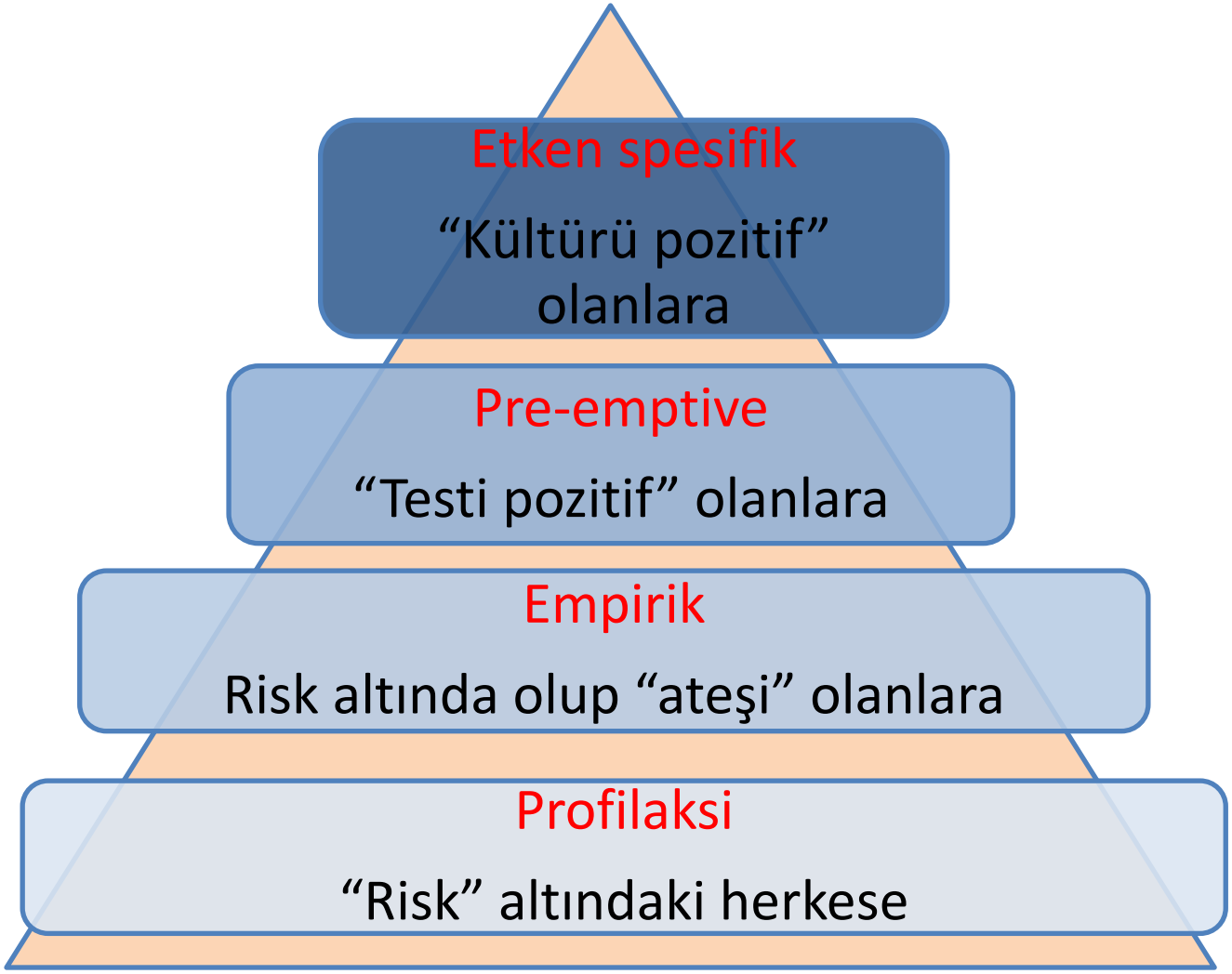
- Solid organ transplant (SOT) recipients have a significant risk of invasive fungal diseases (IFD) caused mainly by *Candida* spp. and *Aspergillus* spp.
- *Candida* spp. is the most frequent agent of IFD in the transplant recipient
- The absence of clinical trials and the epidemiological differences in IFD in different transplant programmes mean that there are no definitive recommendations for the diagnosis and prevention of IFD in SOT
- Universal prophylaxis against IFD should not be routinely used in renal, liver and heart transplantation. Guided

- Standard treatment of *Candida* infections in transplant recipients is no different from that administered to non-neutropenic patients, although some aspects related to drug–drug interactions and potential toxicities associated with the use of azoles should be considered
- Invasive aspergillosis (IA) in SOT is more a syndrome than an infection. Treatment should be individualized according to type of transplant, SOT recipient, type of IA and immunosuppression used
- Drug–drug interactions involving antifungal drugs should be evaluated very carefully in SOT

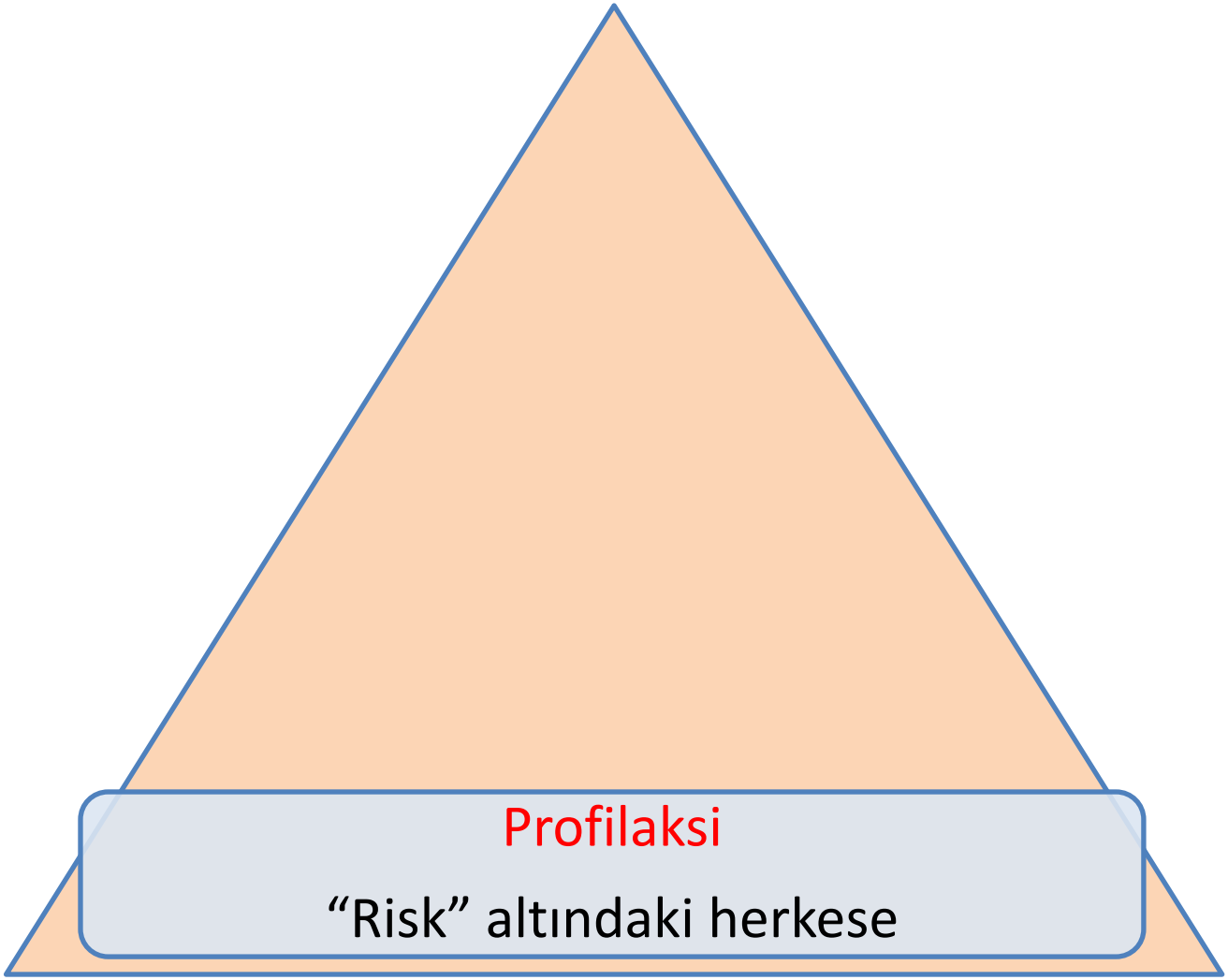
Kaynak olabilecek rehberler

- IDSA aspergilloz 2016
- IDSA kandidiyazis: 2016, SOT'a ilişkin ayrıca öneri YOK!
- ESCMID aspergilloz: Yayımlanma aşamasında
- ESCMID kandidiyazis: Nötropenik olmayan hastalar için, 2012
- Aspergillosis in SOT, American Society of Transplantation, 2013
- Candida infections in SOT, American Society of Transplantation, 2013
- ….

Antifungal kullanım nedenleri



Antifungal kullanım nedenleri



Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America

What Are the Recommendations for Antifungal Prophylaxis in Lung Transplant Patients?
Recommendations.

69. We recommend antifungal prophylaxis with either a systemic triazole such as voriconazole or itraconazole or an inhaled AmB product for 3 to 4 months after lung transplant *(strong recommendation; moderate-quality evidence).*

lung transplant recipients *(weak recommendation; low-quality evidence).*

71. We recommend reinitiating antifungal prophylaxis for lung transplant recipients receiving immunosuppression augmentation with either thymoglobulin, alemtuzumab, or high-dose corticosteroids *(strong recommendation; moderate-quality evidence).*

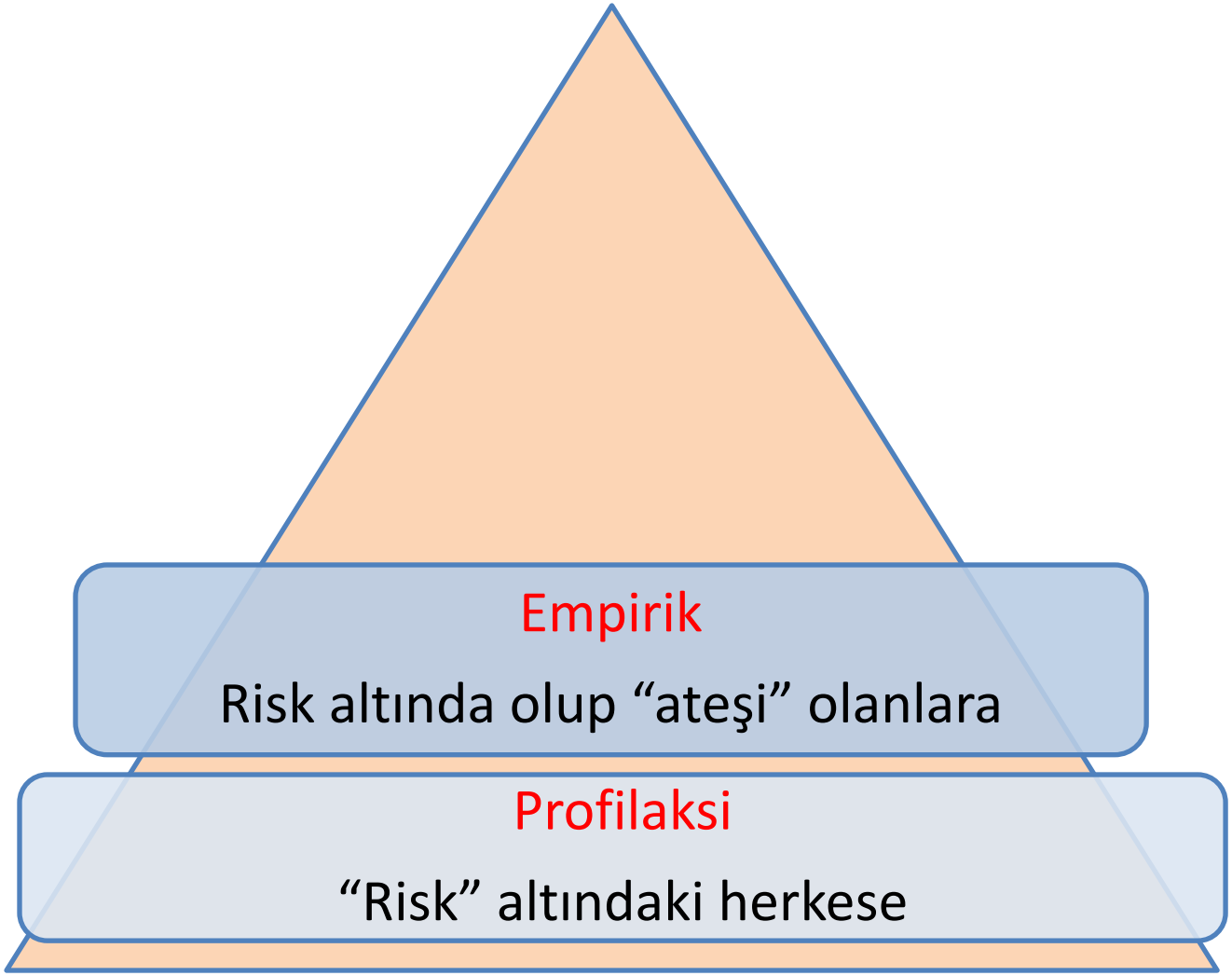
Akciğer naklinde antifungal profilaksi gerekli

What Are the Recommendations for Antifungal Prophylaxis in Nonlung Solid Organ Transplant Recipients?
Recommendation.

Diğer nakillerde birim ve/veya hasta bazında karar verilmeli

address the need for routine anti-*Aspergillus* prophylaxis other than for lung transplant recipients. Individual risk factors have been identified in cardiac (pretransplant colonization, reoperation, cytomegalovirus [CMV] infection, renal dysfunction, institutional outbreak), liver (fulminant hepatic failure, reoperation, retransplantation, or renal failure), and others with institutional outbreaks or prolonged or high-dose corticosteroid use. In such patients, the optimal duration of prophylaxis is not known.

Antifungal kullanım nedenleri



Empirik tedavi sırasında…

- Tedavinin kesilmesi veya daraltılması hep akılda tutulmalıdır

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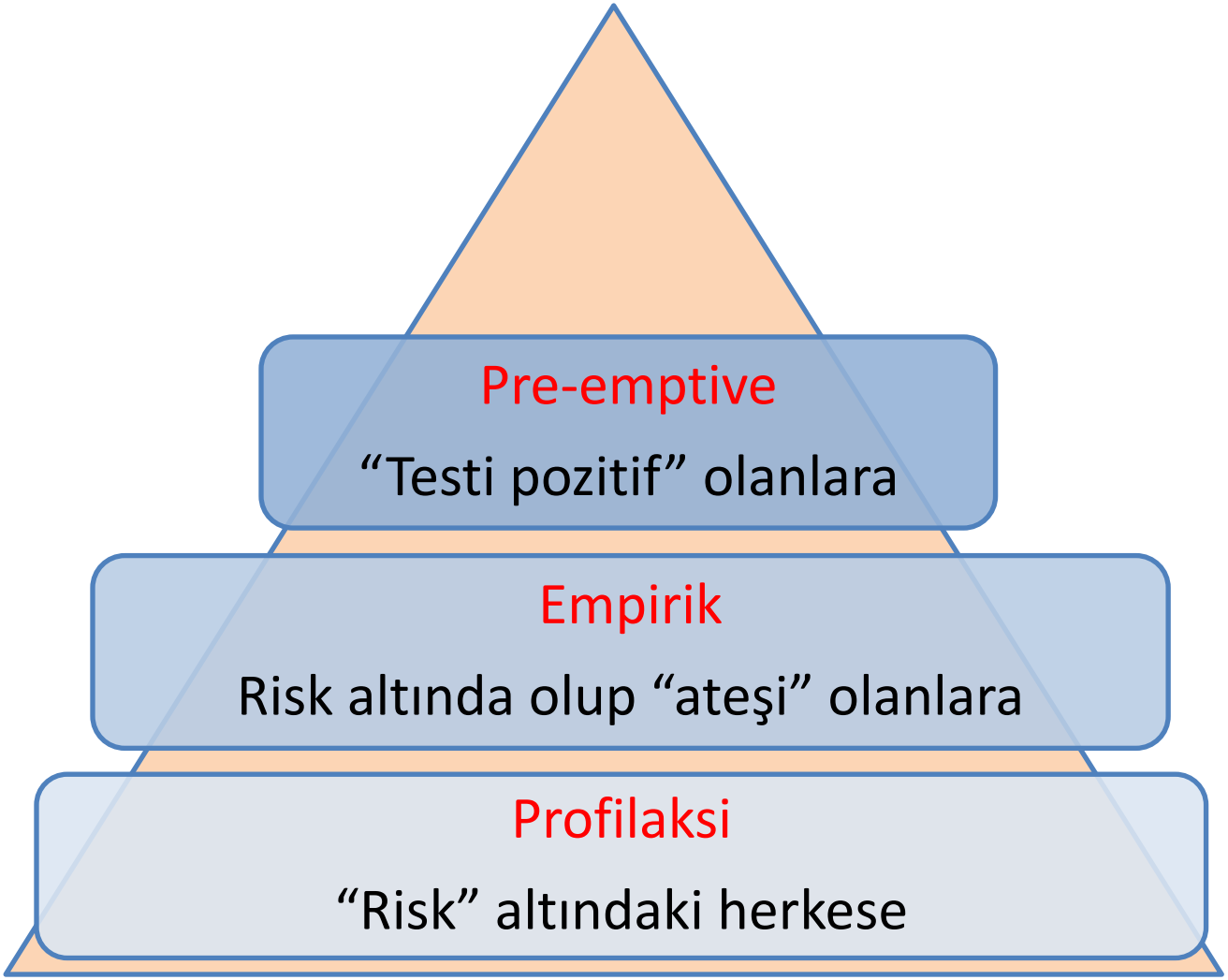
49. In lung transplant recipients, we recommend treatment with a systemic antimold antifungal for TBA, including saprophytic forms. We also recommend adjunctive inhaled AmB in the setting of TBA associated with anastomotic endobronchial ischemia or ischemic reperfusion injury due to airway ischemia associated with lung transplant *(strong recommendation; moderate-quality evidence)*. Duration of antifungal therapy is at least 3 months or until TBA is completely resolved, whichever is longer.

Akciğer nakil alıcılarında tedavi süresi **en az 3 ay**!

Antifungal kullanım nedenleri



Hangi testler?

- Hastanın günlük olarak değerlendirilmesi
- Direkt mikroskopik inceleme
- Kültür
- BAL galaktomannan
- Serum galaktomannan
- Beta D glukan
- Serum, BAL, BOS PCR
- Akciğer tomografisi
- ….

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11. GM is not recommended for screening in SOT recipients or patients with chronic granulomatous disease (CGD) *(strong recommendation; high-quality evidence).*

Serum GM:
SOT hastalarında tarama amacıyla kullanılması ÖNERİLMEZ

12. Serum assays for (1 → 3)-β-D-glucan are recommended for diagnosing IA in high-risk patients (hematologic malignancy, allogeneic HSCT), but are not specific for *Aspergillus (strong recommendation; moderate-quality evidence).*

Serum BDG:
Aspergilloz için spesifik DEĞİL

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What Is the Approach to the Radiographic Diagnosis of Invasive Pulmonary Aspergillosis?
Recommendations.

13. We recommend performing a chest CT scan whenever there is a clinical suspicion for invasive pulmonary aspergillosis (IPA) regardless of chest radiograph results *(strong recommendation; high-quality evidence)*.
14. Routine use of contrast during a chest CT scan for a suspicion of IPA is not recommended *(strong recommendation; moderate-quality evidence)*. Contrast is recommended when a nodule or a mass is close to a large vessel (*strong recommendation; moderate-quality evidence)*.
15. We suggest a follow-up chest CT scan to assess the response of IPA to treatment after a minimum of 2 weeks of treatment; earlier assessment is indicated if the patient clinically deteriorates *(weak recommendation; low-quality evidence)*. When a nodule is close to a large vessel, more frequent monitoring may be required *(weak recommendation; low-quality evidence)*.

- Aspergilloz şüphesi olduğunda AC filmi bulgularından bağımsız olarak BT çekilmelidir
- Her zaman konrastlı BT çekilmesi GEREKMEZ

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16. We recommend performing a bronchoscopy with BAL in patients with a suspicion of IPA *(strong recommendation; moderate-quality evidence).* Significant comorbidities such as severe hypoxemia, bleeding, and platelet transfusion-refractory thrombocytopenia may preclude BAL. The yield of BAL is low for peripheral nodular lesions, so percutaneous or endobronchial lung biopsy should be considered. We recommend the use of a standardized BAL procedure and sending the BAL sample for routine culture and cytology as well as non-culture-based methods (eg, GM) *(strong recommendation; moderate-quality evidence).*

Aspergilloz şüphesi olduğunda bronkoskopi ve BAL incelemesi önerilir

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What Is the Diagnostic Value of Nucleic Acid Testing in Clinical Specimens?

Recommendations.

7. There was debate among the committee members regarding the clinical utility of blood-based PCR in diagnosing IA, and experts
dations
role wh
detection assays to diagnose IA and/or reduce preemptive antifungal usage. The other group thought that PCR assays are promising but could not be recommended for routine use in clinical practice at present due to the lack of conclusive validation for commercially available assays, the variety of methodologies in the literature, and questions about the extent to which results assisted diagnosis.

PCR, diğer tanı testleri ile birlikte kullanılmalı

8. As research in the area continues, we recommend that clinicians choosing to use PCR assays employ them carefully in the management of individual patients on a case-by-case
and
and
interpret results accordingly. When PCR assays are used, results should be considered in conjunction with other diagnostic tests and the clinical context *(strong recommendation; moderate-quality evidence)*.

J Antimicrob Chemother 2013; **68** Suppl 3: iii17–iii24
doi:10.1093/jac/dkt391

Journal of Antimicrobial Chemotherapy

Triggers for driving treatment of at-risk patients with invasive fungal disease

Hangi durumda ne yapacağız?

Table 2. Recommended actions for triggers suggestive of IFD

Trigger	Action	Comments
Radiological signs (non-specific lung infiltrate)	diagnostic investigations [bronchoscopy, BAL, PCR[a], GM (serum/BAL fluid), culture/microscopy from tissue, tissue biopsy]	rule out bacterial, viral and non-infectious causes
Clinical symptoms (cough, chest pain, shortness of breath)	diagnostic investigations [bronchoscopy, BAL, PCR[a], GM (serum/BAL fluid), culture/microscopy, tissue biopsy]	rule out bacterial, viral and non-infectious causes
Any new lung infiltrate plus haemoptysis/chest pain/sudden respiratory deterioration/sinusitis	start antifungal therapy (continue with diagnostic investigations)	rule out bacterial, viral and non-infectious causes
New suggestive clinical symptom and radiological sign[b]	start antifungal therapy (continue with diagnostic investigations)	rule out bacterial, viral and non-infectious causes

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Journal of Antimicrobial Chemotherapy

Triggers for driving treatment of at-risk patients with invasive fungal disease

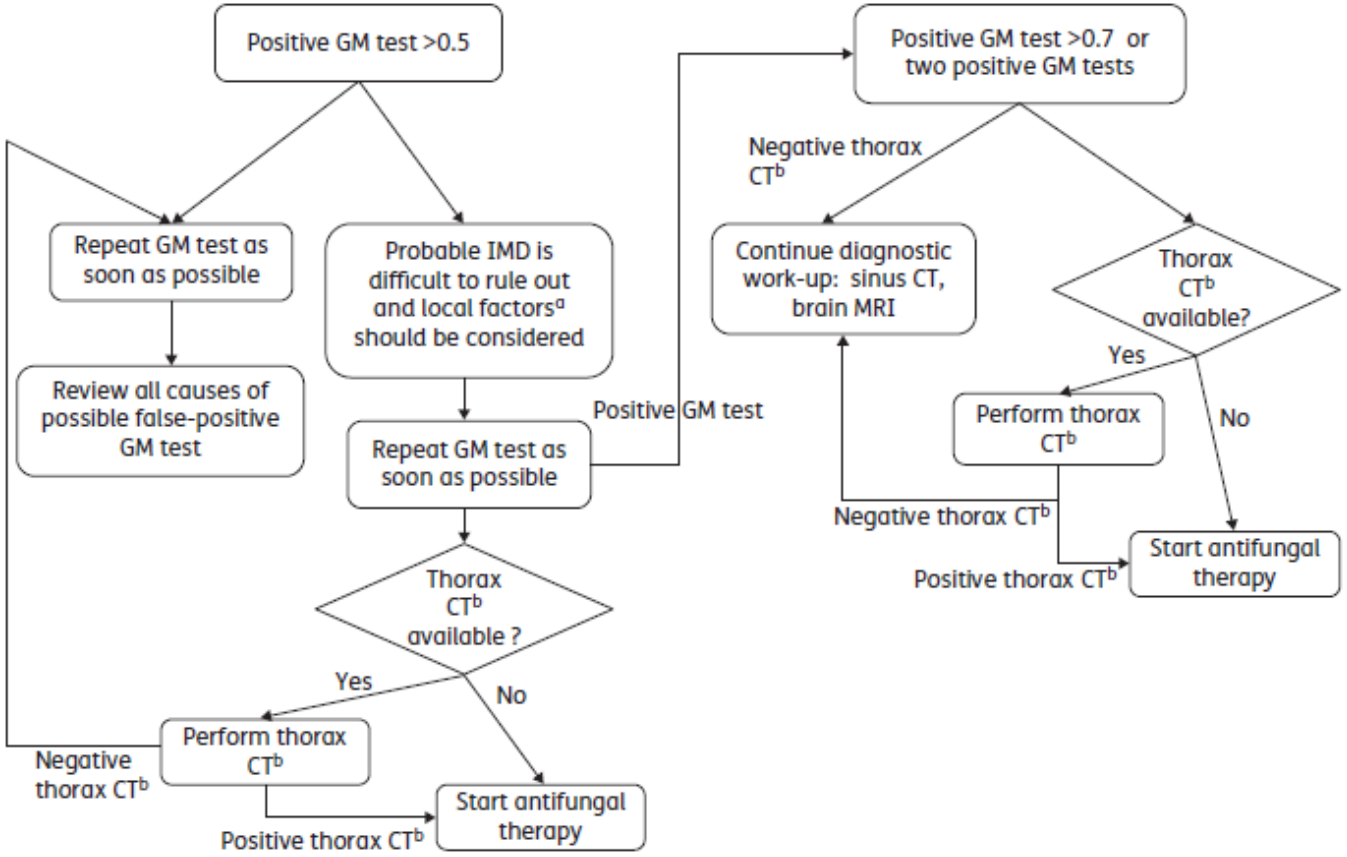
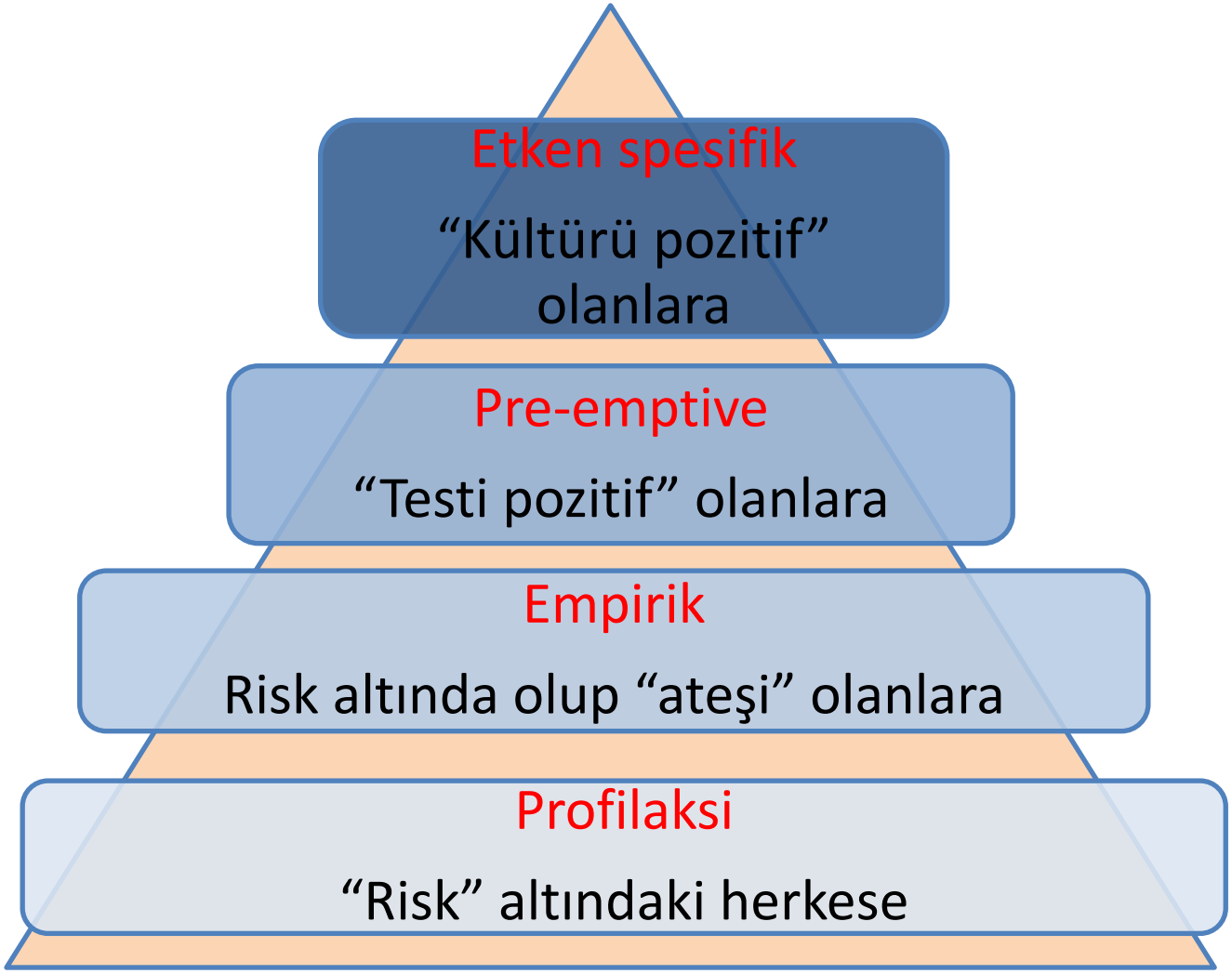


Figure 1. Triggers for driving
IMD, invasive mould disease
tomography or multislice CT.

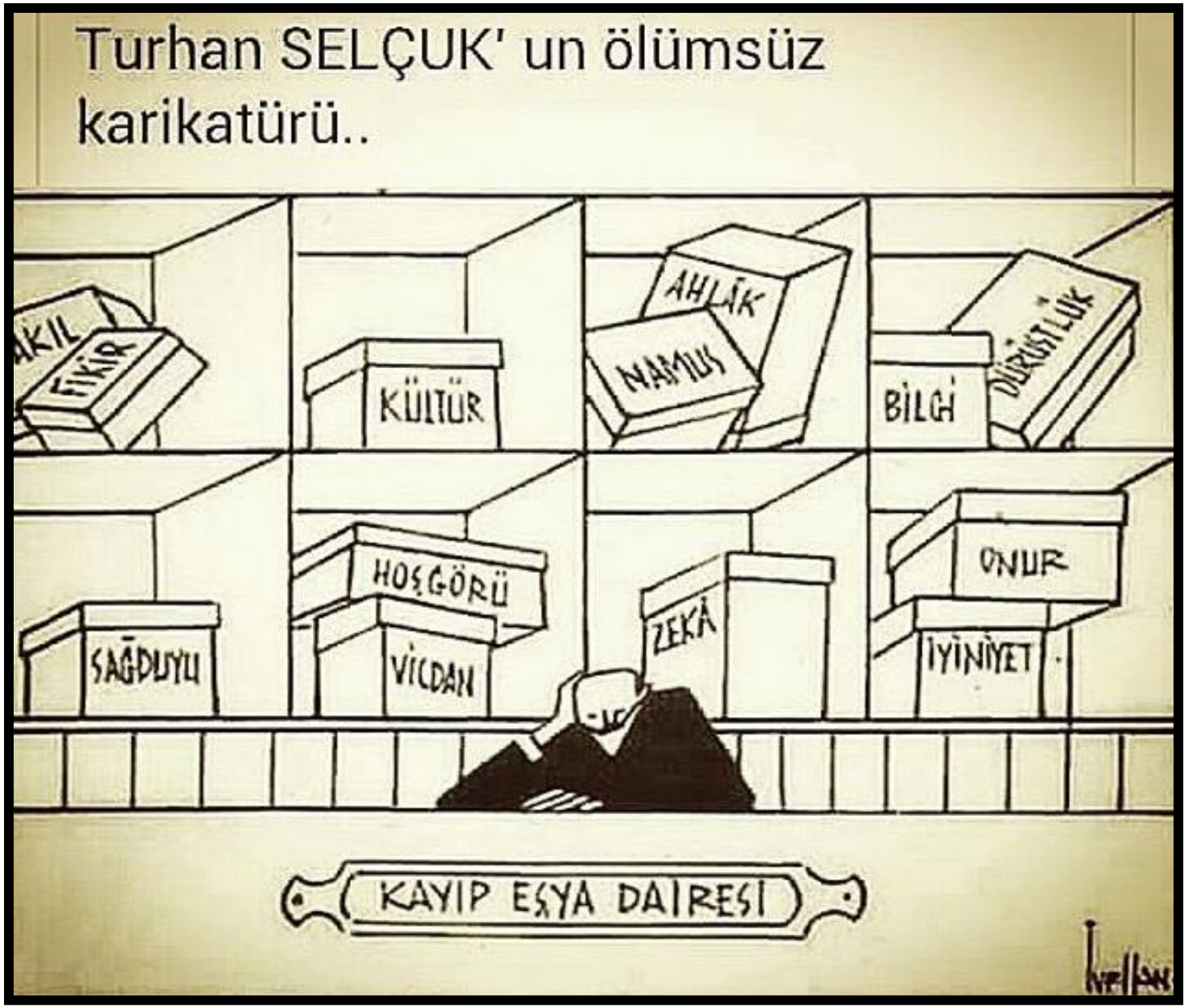
Kendi algortimalarımızı oluşturmalıyız!

Antifungal kullanım nedenleri



Kısa kısa…

- AFY programı gerekli!
- Tanı ve tedavi algoritmaları ile başlanabilir!
- Laboratuvar desteği çok önemli!
- Hastaların yatak başında değerlendirilmeleri çok önemli!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