

Current Strategies in Treating **INVASIVE FUNGAL INFECTIONS**

A breakfast symposium being held at the
2009 BMT Tandem Meetings

Friday, February 13, 2009
7:15 AM - 8:15 AM

Ballroom B-C
Tampa Convention Center
Tampa, Florida



CME
program

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activity is sponsored by the
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Current Strategies in Treating Invasive Fungal Infections

Target Audience

The program will be oriented to a targeted audience of physicians and medical care professionals specializing in oncology, hematology, immunology, and microbiology.

Needs Assessment

Because the prognosis of fungal infection is poor and with the recent development of new antifungal agents, knowledge of the risk factors and the types of patients at risk will allow physicians to identify groups in which antifungal prophylaxis is useful and warranted. This program's end result is to discuss the challenges and the current developments in the diagnosis and treatment of invasive fungal infections (IFI) and to optimize treatment strategies and improve patient outcomes by focusing on the appropriate use of antifungal agents.

Learning Objectives

After completion of this activity, participants should be able to:

- Summarize the characteristics of the newer antifungal agents and clinical trial results utilizing those agents
- Discuss the challenges in diagnosis and management of fungal infections through case examples
- Identify current and future treatment options for invasive fungal infections in normal and at-risk patients

Accreditation Statement

The Medical College of Wisconsin is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Designation of Credit Statement

The Medical College of Wisconsin designates this educational activity for a maximum of 1.0 *AMA PRA Category 1 Credit(s)*[™]. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Faculty Disclosures

Consistent with the current Accreditation Council for Continuing Medical Education policy, the CME Provider must be able to show that everyone who is in a position to control the content of an individual educational activity has disclosed all relevant financial relationships. The CME Provider has a mechanism in place to identify and resolve any conflicts of interest discovered in the disclosure process. The presenting faculty members have all made the proper disclosures, and the following relationships are relevant:

John R. Wingard, MD: receives honoraria, is on the speaker's bureau, and is a consultant to: Pfizer, Merck, Astellas, and Viracor.

Shmuel Shoham, MD: is on the advisory board and receives research support from Merck; participates in the speaker's bureau and receives research support from Pfizer; is on the advisory board, participates in the speaker's bureau and receives research support from Enzon; and participates in the speaker's bureau and receives research support from Advandx; participates in the speaker's bureau and receives research support from Astellas; receives research support from Quintiles; is on the advisory board and receives research support from Baxter; is a co-founder, minority stock holder, and member of board of directors for Medonyx.

Current Strategies in Treating Invasive Fungal Infections

Symposium Faculty

CHAIR

John R. Wingard, MD
Price Eminent Scholar and Professor of Medicine
Director, Bone Marrow Transplant Program
Division of Hematology/Oncology
University of Florida Shands Cancer Center, Gainesville, FL

SPEAKERS

John R. Wingard, MD
Price Eminent Scholar and Professor of Medicine
Director, Bone Marrow Transplant Program
Division of Hematology/Oncology
University of Florida Shands Cancer Center, Gainesville, FL

Shmuel Shoham, MD
Scientific Director, MedStar Clinical Research Center and
Director, Transplant Infectious Diseases
Washington Hospital Center
Washington, DC

Program Agenda

6:45 – 7:15 am: Breakfast

7:15 – 7:20 am: Introduction

7:20 – 7:45 am: John R. Wingard, MD
Case 1: The Diagnostic Challenges of Immune Reconstitution
Cases 2-4: What Invasive Fungal Infections Do These Three Patients Have
(Aspergillosis, Candidiasis or Fusariosis)?

7:45 – 8:05 am: Shmuel Shoham, MD
Case 5: A Patient with Zygomycosis After SCT

8:05 – 8:15 am: Discussion/Q&A

John R. Wingard, MD

**Price Eminent Scholar and Professor of Medicine
Director, Bone Marrow Transplant Program
Division of Hematology/Oncology
University of Florida Shands Cancer Center, Gainesville, FL**



John R. Wingard, MD is Price Chair of Medicine and director of the University of Florida's Blood and Bone Marrow Transplant Program. A former President of the American Society of Blood and Marrow Transplantation, Dr. Wingard is also a past chair of the steering committee of the National Heart, Lung & Blood Institute and National Cancer Institute's (NHLBI/NCI) Blood and Marrow Transplant Clinical Trials Network.

Things are not always what they appear

Pitfalls in the Evaluation of Invasive Fungal Infections

Elias Anaissie, MD, Vice-Chair,
Myeloma Institute for Research and
Therapy, UAMS, Little Rock, AR

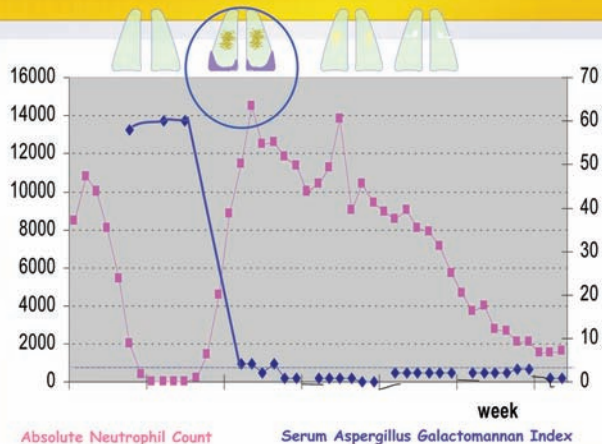
No Potential Conflict of Interest re: Asp Galactomannan or B-D-Glucan

A Patient Tells the Story

- 68 y.o male from Houston, TX, MYELOMA
- Melphalan-Auto-Tx; levofloxacin, fluconazole prophylaxis
- D+5: Fever, ANC <100, no response to Imipenem x 72 hrs
- CT: ground glass changes; CT sinus (-); Sputum samples
- POLL: What do you do next?
 - BAL?
 - Voriconazole?
 - Other?



A Patient Tells the Story (4)

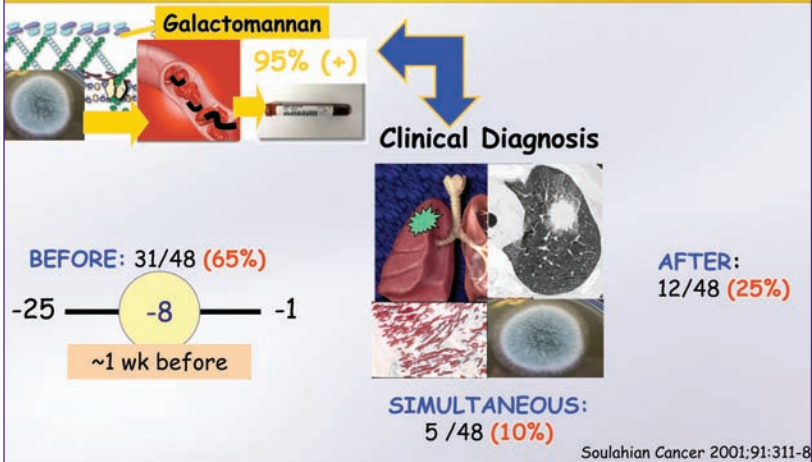


Clinical Role of Serum Aspergillus GM in the Diagnosis and Management of Aspergillosis

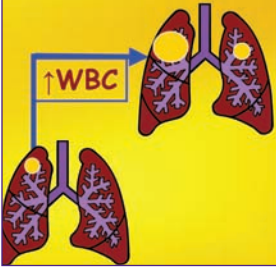
- **Good test performance**
- **Can use GM for diagnosis**
 - Same day results (in house, 7 days/week)
 - Decreases invasive procedures (BAL or VATS)
 - Clinical findings are non specific
 - CT chest findings are non specific, may be transient
- **Can use GM for outcome prediction**
 - Outcome not always predicted by clinical & radiologic findings
 - Excellent correlation with clinical outcome
- **Significant impact on management**
 - ↓ prophylaxis / empiric therapy (Cost, toxicity, interactions)




Galactomannan Index Improves Diagnosis Can Improve on CT



**Immunity
Confounds
Outcome:
P-IRIS**



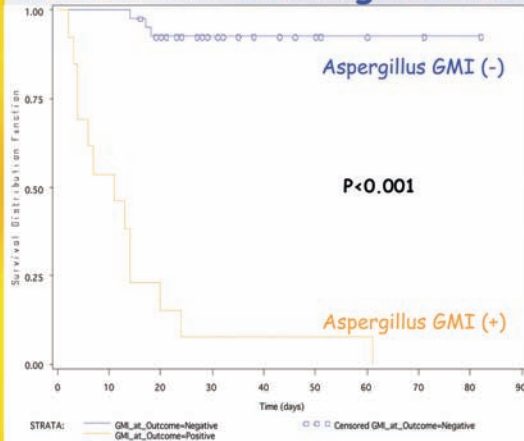
P-IRIS in Aspergillosis

- 19 Hem. ca. (04-06), neutropenia
 - ≥ 2 consecutive (+) GM (OD ≥ 0.5)
 - Aspergillosis (EORTC/MSG)
- 
- Clinical/radiologic deterioration with
 - Neutrophil recovery and
 - Microbiologic response: normal GMI
 - Complete response, survival at 3 mo
 - Same antifungal therapy
 - Addition of steroids in 2 pts.
 - Implications:
Serial GM testing to guide management

Miceli et al., Cancer 2007

**GMI Predicts
Outcome
and Survival**

Survival of 56 pts with Hem. Ca and IA according to GMI



Woods, G et al. Cancer 2007

Another Patient, Another Story

- 53 y.o male, relapsed myeloma
- Melphalan-Auto-Tx; levofloxacin, acyclovir, fluconazole
- Fever, \uparrow LFTs, blood cultures (+) yeast, normal Aspergillus EIA, elevated serum B-D-Glucan
- Skin lesions
- CT: pulmonary infiltrates (patchy, multilobar);
- POLL:
 - What is your diagnosis?
 - What is your plan?





Shmuel Shoham, MD

**Scientific Director, MedStar Clinical Research Center and
Director, Transplant Infectious Diseases, Washington Hospital Center
Washington, DC**

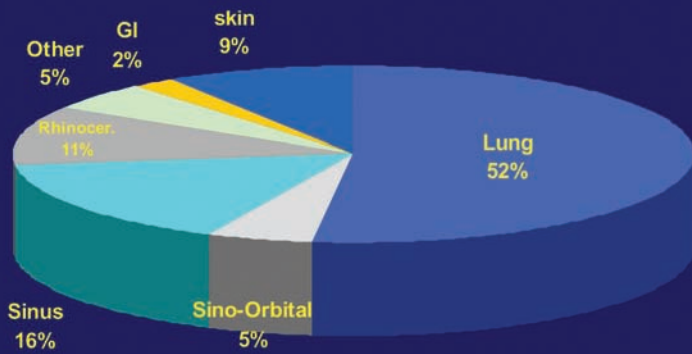
Shmuel Shoham is Director of Transplant Infectious Diseases at the Washington and serves as the Scientific Director of the MedStar Clinical Research Center at WHC.

Dr. Shoham's research interests include the prevention, diagnosis and treatment of invasive fungal infections in immunocompromised patients with a focus on translating bench research to clinical use at the patient bedside and in the community. He has served as the principal investigator for numerous federally- and commercially-sponsored clinical studies. His ongoing work focuses on improving anti-microbial use through development and application of diagnostic techniques and pharmacokinetic analysis, and prevention and treatment of infections in critically ill patients. Using in-vitro models Dr. Shoham's laboratory is currently studying the impact of small molecules upon kidney cells and on the blood-brain barrier.

As part of his focus on fostering collaboration between clinical and research interests, Dr. Shoham has partnered with colleagues at National Cancer Institute and within the Mycoses Study Group, a national consortium of academic and private researchers studying treatments for invasive fungal infections. The partnerships developed through Dr. Shoham's collaborative work with the NIH have helped establish WHC as a referral center for complex infections.

Dr. Shoham earned his medical degree from the Thomas Jefferson Medical College in Philadelphia. He went on to complete his residency in Internal Medicine and fellowship in Infectious Diseases at Boston University School of Medicine

Location of Infection in 44 HSCT Recipients with Zygomycosis



Roden et al, Clin Infect Dis. 2005, 41:634–53

Approach to Therapy

Immune reconstitution



Medical therapy

Surgical therapy

Antimicrobial Treatment Options

Agent	Study details	Response (%)	Reference
ABLC	64 patients, primary and salvage	72	1
ABCD	20 patients	60	2
LAmB	32 patients, primary therapy	32	3
AmB (any)	45 patients	45	4
AmB+CAS	6 patients	100	4

1. Larkin et al. Infect Med 2003(20):201-6.
2. Herbrecht et al. Eur J Clin Microbiol Infect Dis 2001;20(7):460-6.
3. Shoham et al. IDSA/ICCAC, 2008 Meeting, Washington, DC
4. Reed et al. Clin Infect Dis. 2008; 47:364–71

