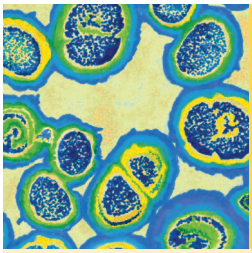

CE/CME Newsletter

Antimicrobial Resistance: A Practical Guide for Physicians and Pharmacists with a Case-Based Approach

Case 4: Managing Nosocomial Bloodstream Infections

A 4-part continuing-education newsletter series offered free of charge to physicians and pharmacists

RELEASE DATE: June 2009
EXPIRATION DATE: June 30, 2010

Contents

Target Audience

The target audience for this CME activity includes, but is not limited to, infectious disease specialists, microbiologists, hospital pharmacists, critical-care specialists, emergency room physicians, and other healthcare personnel who participate in the empiric and pathogen-specific selection of antibiotics for the treatment of patients with infections caused by MRSA, CAP, HAP, and VAP.

Learning Objectives

After participating in this activity, physicians will be better able to:

- List some of the risk factors found to be associated with nosocomial bloodstream infections
- Identify the pathogens associated with nosocomial bacteremia and fungemia and describe their impact on mortality
- Explain the clinical indications, efficacy, and safety of the echinocandin class of antifungals
- Describe the consequences of the declining number of new antibiotics entering the market and the effects on treatment of drug-resistant organisms and antibiotic stewardship

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Program Overview

This newsletter is the fourth in a 4-part accredited continuing medical education (CME) series entitled, "*Antimicrobial Resistance: A Practical Guide for Physicians and Pharmacists with a Case-Based Approach*." This CME program uses real-life patient case studies to discuss the growing prevalence of drug-resistant bacterial pathogens in healthcare and community settings and review the microbiology of drug-resistant pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), penicillin- and macrolide-resistant *Streptococcus pneumoniae*, and beta-lactamase-producing strains of *Haemophilus influenzae*. The patient cases presented in this series include complicated skin and skin-structure infections (cSSSIs), community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), and nosocomial bloodstream infections. In addition to increasing awareness of these resistant pathogens, this 4-part program will also review the various antimicrobial agents clinicians can use in empiric and pathogen-focused therapy (PFT) in an environment of increasing drug-resistant pathogens.

Activity Rationale and Purpose

Serious, life-threatening infections, particularly those with highly resistant bacteria, continue to cause infections resulting in considerable morbidity and mortality. In addition, the evolution of MRSA and the development of new antibacterial treatments have spurred physicians to reconsider previously established management strategies. To help stem the high morbidity and mortality rates associated with MRSA and other resistant bacterial infections, healthcare professionals require an update on potential pathogens involved in various types of infections.

The purpose of this educational activity is to enhance physicians' and pharmacists' understanding of the challenges in the management of serious, life-threatening infections, the microbiology of resistant bacterial pathogens, the efficacy and safety of a variety of antibacterial agents that are used to combat these serious infections, and the concept and rationale for PFT, including methods for effectively employing PFT in the clinical setting.

Continuing Education Information

Accreditation Statement

PHYSICIANS. This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of Dannemiller and Exemplar CE, LLC. Dannemiller is accredited by the ACCME to provide continuing medical education for physicians.

Dannemiller designates this educational activity for a maximum of 0.25 *AMA PRA Category 1 Credit(s)*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Pharmacists. This program is comprised of four 15-minute modules. The participant will receive a statement of credit of 1.0 contact hour (0.1 CEU) upon completion of all modules plus program evaluation.

Purdue University School of Pharmacy and Pharmaceutical Sciences is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This program is a continuing education activity of Purdue University, an equal access/equal opportunity institution. Universal Program Universal Program Number (UPN): 018-999-08-115-H01, Release Date: June 2009, Expiration Date: June 30, 2010.

The newsletters were released once per quarter, starting with the first in August 2008 and the last being released in June 2009. Each newsletter will be available for continuing education credits for 1 year and will be posted online at www.IDCME.org. For physicians, each newsletter will be available for 0.25 credits, with all 4 newsletters resulting in an overall accrual of 1 *AMA PRA Category 1 Credit(s)*™. For pharmacists, the completion of the series of newsletters (4 activities) is required to receive 1.0 contact hour. No partial credit will be awarded.

Method of Participation

Each newsletter should take approximately 0.25 hours to complete. The participant should, in order, read the activity rationale and purpose, the objectives, the continuing education information, and the newsletter, and answer the 5-question multiple choice learning assessment, placing the answers on the Evaluation Form on page 7. The evaluation form provides each participant with the opportunity to comment on the quality of the instructional process, the perception of enhanced professional effectiveness, the perception of commercial bias, and his/her views on future educational needs. Physicians must receive a score of 70% to obtain credit for this activity. Pharmacists must receive an aggregate score of 70% from the four quarterly learning assessments to obtain credit for this activity.

Faculty and Staff Disclosures

In accordance with the Accreditation Council for Continuing Medical Education (ACCME), Dannemiller requires that any person who is in a position to control the content of a CME activity must disclose all relevant financial relationships they have with a commercial interest. Accordingly:

George Sakoulas, MD, has received research funding from Cubist and Pfizer Pharmaceuticals, speaking honoraria from Cubist, Pfizer, and Wyeth Pharmaceuticals, and consulting fees from Cubist, Pfizer, and Ortho-McNeil Pharmaceuticals.

Cynthia L. Kryder, MS, Medical Writer, has nothing to disclose.

The Dannemiller staff and Exemplar CE, LLC staff that was involved in the development of this activity have no financial relationships with any commercial interest that are relevant to this activity.

To resolve identified conflicts of interest, the educational content was fully peer reviewed by a physician member of the Dannemiller Clinical Content Review Committee who has nothing to disclose. The resulting certified activity was found to provide educational content that is current, evidence-based, and commercially balanced.

Product Disclosure

This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The opinions expressed in the educational activity are those of the faculty. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings. Further, participants should appraise the information presented critically and are encouraged to consult appropriate resources for any product or device mentioned in this program.

Disclaimer

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Bacteremia and Fungemia

Nosocomial bloodstream infections caused by bacteria and fungi represent a major growing healthcare threat in the United States, especially among critically ill patients. Vascular catheters such as central venous and arterial lines that are fundamental tools in intensive care medicine intuitively pose a major risk factor for bloodstream infections, as approximately 90% of primary bloodstream infections develop in patients with intravascular devices.[1] Surveillance statistics suggest that primary bloodstream infections affect approximately 1% of all hospitalized patients in the United States, correlating with an incidence rate of 5 per 1000 central-line days.[2,3] Associated mortality rates range from 20% to 50%.[4-6] Among patients in medical/surgical intensive care units (ICUs), the pooled mean incidence rate of central-line-associated bloodstream infections is 1.5 per 1000 central-line days.[7]

For surveillance purposes, the Centers for Disease Control (CDC) defines systemic infections based on whether or not they can be microbiologically documented (i.e., positive blood culture or not). Systemic infections that cannot be microbiologically defined are labeled as clinical sepsis, which can be further subdivided into categories based on severity of illness.[8] These definitions suggest that detection of the infection-causing microbe is not possible in all patients with presumed bloodstream infections who demonstrate clinical signs of fever, hypotension, oliguria, or other manifestations of organ dysfunction. This is confirmed by clinical study data showing that the source of bacteremia or fungemia is undetermined in one-quarter to one-third of patients.[9]

The following case highlights issues surrounding the treatment of patients with prolonged hospital stays who develop nosocomial infections, including bloodstream infections, in light of the concerns associated with the increasing prevalence of drug-resistant pathogens.

Patient Case Study

A 60-year-old man with type II diabetes mellitus and mild obesity develops left lower abdominal pain, fever, anorexia, malaise, and diarrhea. After 3 days, he presents to the local emergency room where he is diagnosed clinically and radiographically with diverticulitis and associated abscess. After a 5-day trial of bowel rest and intravenous (IV) levofloxacin and metronidazole, the treatment team decides that he would benefit from surgical therapy and, thus, he undergoes a partial colectomy without complication. He is discharged home on postoperative day 5.

Ten days later, he returns to the hospital after developing a fever, abdominal pain, and some drainage from the surgical incision. On examination, the surgical incision exudes foul-smelling, brown drainage on deep palpation of the abdomen. The peripheral white blood cell count is 17,500/mm^3. A computed tomography (CT) scan shows a 4.5-cm fluid collection at the colonic anastomosis. The fluid is drained percutaneously by interventional radiology, the culture of which grows *Escherichia coli, Enterococcus faecalis,* and *Bacteroides fragilis*.

The patient is placed on bowel rest, IV piperacillin-tazobactam and fluconazole; a percutaneous abdominal catheter is inserted for drainage. A peripherally inserted central catheter (PICC) is placed and total peripheral nutrition is begun. The fever and leukocytosis resolve completely in 48 hours. On hospital day 7, the patient develops rigors, liquid stool, and a temperature of 103°F. The peripheral white blood cell count increases to 20,000/mm^3. In addition to urinalysis and stool samples for *Clostridium difficile* toxin and fecal leukocyes, cultures of blood and urine are obtained.

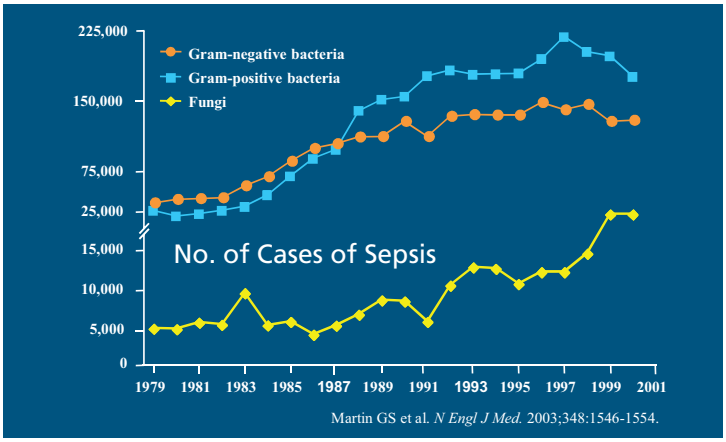

Figure 1. Change in Bloodstream Pathogens, 1979 to 2001. (Data from Martin et al, 2003[10]. Reprinted with permission from the *New England Journal of Medicine*.)

Table 1. FDA-Approved Antifungal Agents

Agent	Indications
Amphotericin	
☐ Amphotericin B Cholesteryl Sulfate Complex (Amphotec®/ Amphocil®)[21]	Invasive aspergillosis in patients where renal impairment or unacceptable toxicity precludes the use of amphotericin B deoxycholate in effective doses, and in patients with invasive aspergillosis where prior amphotericin B deoxycholate therapy has failed.
☐ Amphotericin B Lipid Complex (Abelcet®)[22]	Invasive fungal infections in patients who are refractory to or intolerant of conventional amphotericin B therapy.
☐ Amphotericin B Lipsome for Infection (AmBisome®)[23]	Empiric treatment of presumed fungal infections in febrile, neutropenic patients; cryptococcal meningitis in HIV-infected patients; *Aspergillus, Candida*, or *Cryptococcus* infections in patients who are refractory to or intolerant of amphotericin B deoxycholate; visceral leishmaniasis.
Echinocandins ☐ Anidulafungin (Eraxis™) ☐ Caspofungin (Cancidas®) ☐ Micafungin (Mycamine®)	(See Table 2 for details)
Azoles	
☐ Fluconazole (Diflucan®)[24]	Vaginal candidiasis, oropharyngeal and esophageal candidiasis (in open non-comparative studies of relatively small numbers of patients, fluconazole was effective for the treatment of *Candida* urinary tract infections, peritonitis, and systemic *Candida* infections including candidemia, disseminated candidiasis, and pneumonia), and cryptococcal meningitis. As prophylaxis, fluconazole is also indicated to decrease the incidence of candidiasis in patients undergoing bone marrow transplantation who receive cytotoxic chemotherapy and/or radiation therapy.
☐ Itraconazole (Sporanox®)[25]	Blastomycosis, histoplasmosis, and aspergillosis (patients intolerant of or refractory to amphotericin B therapy) in immunocompromised or non-immunocompromised patients; onychomycosis in non-immunocompromised patients.
☐ Posaconazole (Noxafil®)[26]	Prophylaxis of invasive *Aspergillus* and *Candida* infections in severely immunocompromised patients, 13 years of age and older, such as hematopoietic stem cell transplant recipients with graft-versus-host disease or those with hematologic malignancies with prolonged neutropenia from chemotherapy. Also indicated for treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole.
☐ Voriconazole (VFEND®)[27]	Invasive aspergillosis; esophageal candidiasis; candidemia in nonneutropenic patients and the following *Candida* infections: disseminated infections in skin and infections in abdomen, kidney, bladder wall, and wounds; serious fungal infections caused by *Scedosporium apiospermum* (asexual form of *Pseudallescheria boydii*) and *Fusarium* spp. including *Fusarium solani*, in patients intolerant of, or refractory to, other therapy.

A chest X-ray film shows some atelectasis without pneumonia. Blood and stool samples are collected, and IV vancomycin is added to the treatment regimen. The next day, the blood cultures yield yeast that are subsequently speciated as *Candida glabrata*. The PICC line is removed and is eventually resited to the other upper extremity once blood cultures are negative for 48 hours. Intravenous micafungin 100 mg daily is added; IV vancomycin and fluconazole are discontinued and piperacillin-tazobactam is continued. Stool is positive for leukocytes and *C difficile*. Oral metronidazole is added to the treatment regimen.

The patient spent 25 days in the hospital, which encompassed a 2-week course of micafungin, 18 days of abdominal drainage, 22 days of IV piperacillin-tazobactam, and oral metronidazole that extended for 48 hours after the piperacillin-tazobactam was discontinued.

Discussion

Bloodstream infections develop when microorganisms from the patient's own flora gain access to the bloodstream, either through drainage from a primary focus of infection (e.g., lung in the case of pneumonia) or through direct entry via intravascular devices such as catheters that have become impregnated with biofilm produced by various colonizing bacteria or fungi. The predominate classes of pathogens in bloodstream infections have seen a recent shift from Gram-negative bacteria to Gram-positive bacteria, with *Candida* species showing a recent surge (Figure 1).[10] Etiologic pathogens commonly associated with bacteremia include methicillin-resistant *Staphylococcus epidermidis* (MRSE), methicillin-resistant *Staphylococcus aureus* (MRSA), *Enterococcus* species, including vancomycin-resistant enterococci (VRE), resistant Gram-negative extended-spectrum beta-lactamase-producing (ESBL) bacilli, and *Klebsiella pneumoniae* carbapenemase (KPC)-producing organisms. Patients with long ICU stays and prolonged courses of antibiotics are at risk for infection with VRE and KPC-producing pathogens. Known risk factors for colonization and/or infection with organisms harboring ESBLs include admission to an ICU, recent surgery, instrumentation, prolonged hospital stay, and exposure to antibiotics, especially extended-spectrum beta-lactam agents.[11]

Among critically ill and immunocompromised patients, fungal infections are increasing in frequency and now represent approximately 10% of all nosocomial infections. The most common pathogen is *Candida albicans*, accounting for about 70% of all cases of fungemia, followed by C glabrata.[12] However, *C glabrata, Candida tropicalis, Candida krusei*, and *Candida parapsilosis* are occurring with increasing frequency especially when significant fluconazole use is common. Risk factors found to be independently associated with increased risk of candidemia include prior surgery (relative risk, RR, 7.3), acute renal failure (RR, 4.2), and receipt of parenteral nutrition (RR, 3.6).[13] Fungemia has been associated with attributable mortality rates that range from 5% to 71%.[13-15]

Given that bloodstream infections that develop in the hospital setting frequently involve *Candida* species, it is important for clinicians to consider them in the empiric selection of antimicrobials when fever or sepsis develops in a hospital setting. In this case, the patient was already on an antifungal, fluconazole, but this did not prevent fungemia from a fluconazole-resistant *C glabrata*. Once bloodstream infections have been identified, catheter removal and repositioning may be the most important therapy in the management of candidemia since these are often line-associated infections with a low attributable mortality. In this patient, who displayed many of the risk factors for developing candidemia, removing and resiting the PICC line was an essential component of the treatment regimen, as was the addition of an antifungal agent, micafungin, to the treatment regimen. The list of antifungal agents approved by the US Food and Drug Administration (FDA) is listed in Table 1.

The duration of therapy is typically 10 to 14 days for simple cases that rapidly clear after line removal. Ophthalmologic examination is often recommended for all cases of candidemia to rule out endophthalmitis but in reality this is employed in cases of neutropenia and/or cases of persistent fungemia. If fungemia persists, complicated endovascular infection such as endocarditis or septic thrombophlebitis must be ruled out by transesophageal echocardiography and venous Doppler studies, respectively.

Echinocandins: New Options for the Treatment of Fungal Infections

The echinocandins are the newest agents approved by the FDA for the treatment of fungal infections. Echinocandins exert their mechanism of action by inhibiting the synthesis of β-(1,3)-D-glucan, an action that leads to damage of the cell walls of most fungi.[16] *In vivo* and *in vitro*, the echinocandins are fungicidal against most *Candida* species and are fungistatic against *Aspergillus* species.[16,17] The activity of echinocandins against

Table 2. The Echinocandins

	Anidulafungin[28]	Caspofungin[29]	Micafungin[30]
Indications and Usage	☐ Candidemia and other forms of *Candida* infections (intra-abdominal abscess, and peritonitis) ☐ Esophageal candidiasis	☐ Empirical therapy for presumed fungal infections in febrile, neutropenic patients ☐ Candidemia and the following *Candida* infections: intra-abdominal abscesses, peritonitis, and pleural space infections ☐ Esophageal candidiasis ☐ Invasive aspergillosis in patients who are refractory to or intolerant of other therapies	☐ Candidemia and other forms of *Candida* infections ☐ Acute disseminated candidiasis ☐ *Candida* peritonitis and abscesses ☐ Esophageal candidiasis ☐ Prophylaxis of *Candida* infections in patients undergoing hematopoietic stem cell transplantation
Dose Administration	☐ **Candidemia and other *Candida* infections:** Single 200-mg loading dose on Day 1, followed by 100-mg daily dose. Duration should be based on the patient's clinical response, but should continue for at least 14 days. ☐ **Esophageal candidiasis:** Single 100-mg loading dose on Day 1, followed by 50-mg daily dose. Treat patients for a minimum of 14 days and for at least 7 days following the resolution of symptoms.	**ADULTS** ☐ Administer by slow infusion over 1 hour. ☐ Single 70-mg loading dose on Day 1, followed by 50 mg daily for all indications except esophageal candidiasis. ☐ For esophageal candidiasis, use 50 mg daily with no loading dose. **CHILDREN** ☐ Base dosing on the patient's body surface area. ☐ For all indications, administer a single 70-mg/m^2 loading dose on Day 1, followed by 50 mg/m2 daily thereafter. ☐ Maximum loading dose and daily maintenance dose should not exceed 70 mg.	☐ **Candidemia, acute disseminated candidiasis, *Candida* peritonitis, and abscesses:** 100-mg dose daily ☐ **Esophageal candidiasis:** 150-mg dose daily ☐ **Prophylaxis of *Candida* infections:** 50-mg dose daily
Registry Trial Results	☐ **Candidemia and other forms of *Candida* infections:** Anidulafungin vs. fluconazole (n=256). Success rate 75.6% anidulafungin vs. 60.2% fluconazole. Superiority was maintained at the end of all treatment. ☐ **Esophageal candidiasis:** Anidulafungin vs. fluconazole (n=601). Endoscopic success (the combined rate of clinical improvement and cure) 97.4% anidulafungin vs. 98.7% fluconazole; this included cure rates of 88.3% vs. 93.6%, respectively, and improvement rates of 9.1% vs. 5.1%. At 2 weeks after treatment, subjects receiving anidulafungin experienced significantly more endoscopically documented relapses (53.3%) than subjects receiving fluconazole (19.3%).	☐ **Empirical therapy:** Caspofungin vs. amphotericin B (n=1111). Success rate 33.9% caspofungin vs. 33.7% amphotericin B. ☐ **Candidemia and other forms of *Candida* infections:** Caspofungin vs. amphotericin B (n=224). Success rate 74.3% caspofungin vs. 67.8% amphotericin B. ☐ **Esophageal candidiasis:** Caspofungin vs. IV fluconazole in 1 large randomized, double-blind trial and 2 smaller dose-response trials. Favorable overall response rates 81.5% caspofungin vs. 85.1% for fluconazole. ☐ **Invasive aspergillosis:** Open-label, noncomparative study of 69 patients refractory to or intolerant of previous antifungal treatment. 41% of patients receiving at least 1 dose of caspofungin had a favorable response. For those patients who received > 7 days of therapy with caspofungin, 50% showed a favorable response.	☐ **Candidemia and other forms of *Candida* infections:** Micafungin vs. caspofungin. Success rate 70.7% (135/191) micafungin vs. 63.3% (119/188) caspofungin. ☐ **Esophageal candidiasis:** Micafungin vs. fluconazole (n=763). Clinical cure rates were 91.9% for patients in both treatment groups. ☐ **Prophylaxis of *Candida* infections in patients undergoing hematopoietic stem cell transplantation:** Micafungin vs. fluconazole (n=882). Success in prophylaxis 80.7% micafungin vs. 73.7% fluconazole.
Notes	☐ This product has not been studied in endocarditis, osteomyelitis, and meningitis due to *Candida*, and has not been studied in sufficient numbers of neutropenic patients to determine efficacy in this group. ☐ Safety and effectiveness of anidulafungin in pediatric patients have not been established.	This product has not been studied in endocarditis, osteomyelitis, and meningitis due to *Candida*.	Safety and effectiveness in pediatric patients have not been established.

molds may be enhanced when administered in combination with amphotericin B or broad-spectrum triazoles, such as voriconazole; for this indication, mortality rates appear to be lower with combination therapy than monotherapy.[18] Echinocandins also demonstrate excellent *in vitro* activity within biofilms, a potentially advantageous characteristic in the treatment of catheter-associated candidemia.

Three echinocandins are currently available: anidulafungin, caspofungin, and micafungin (Table 2). All demonstrate dose-dependent activity against *Candida* species and are generally well tolerated. Anidulafungin and micafungin have similar minimum inhibitory concentrations (MICs) that are lower than those of caspofungin, although the clinical significance of in vitro susceptibility testing in *Candida* species is not as well defined as in bacterial infections and is not generally employed in most hospital laboratories.[18] The limited toxicity profile, low incidence of drug-drug interactions, and ease of administration with once-daily dosing make echinocandins attractive options for the treatment of invasive fungal infections. However, they are more costly than other antifungal agents on the market, which may limit their use to those institutions that have high rates of triazole-resistant *Candida* infections.

Declining Antibiotic Discovery

According to the Infectious Diseases Society of America (IDSA), the pharmaceutical pipeline for new antibiotics has been drying up over the past decade, as major pharmaceutical firms lose interest in developing less-profitable antibiotics. Because of the decline in antibiotic discovery research as well as the tightening regulatory standards required to receive approval, the FDA is approving fewer new antibiotics. Between 1998 and 2002, only 10 new FDA-approved antibiotics entered the market (Figure 2). Of these, 2 were novel, as evidenced by having a new target of action, with no cross-resistance with other antibiotics. In 2002, among the 89 new medications that entered the market, none was an antibiotic.[19] In light of the current economic climate, it is difficult to foresee an expansion in antibiotic drug discovery efforts.

Currently, the only new Gram-negative antimicrobial that has entered phase 1 (a single ascending dose) study is CB 182,804 from Cubist Pharmaceuticals. This agent demonstrates bactericidal activity against resistant Gram-negative pathogens such as *Acinetobacter baumanii, Pseudomonas aeruginosa*, and resistant Enterobacteriaciae. However, FDA approval for this

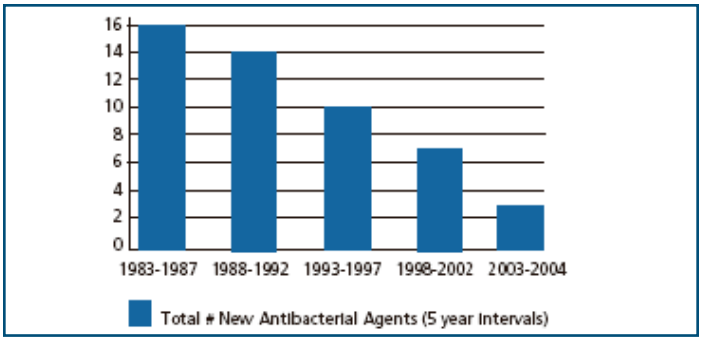

Figure 2. Number of New FDA-Approved Antibacterial Agents, 1983-2004.[19] (Data adapted from Spellberg et al[31], with permission. Reprinted with permission of the Infectious Diseases Society of America.)

agent is at least 8 years away. The lack of novel antimicrobial agents coupled with increasing antibiotic resistance forces clinicians to turn to older, more toxic antibiotics, such as colistin and polymixin, when treating critically ill patients infected with Gram-negative bacilli. Although rapidly bactericidal to Gram-negative bacteria, these agents are associated with toxicity, particularly nephrotoxicity, making them difficult to administer to patients with multiorgan system dysfunction.[20]

Summary

This case highlights some of the concerns that clinicians face in treating patients with nosocomial infections. Frequently, what are perceived as routine surgical procedures, such as a colectomy for diverticulitis, can be wrought by adverse events such as postoperative infections that are increased in frequency in patients with comorbidities such as diabetes mellitus, obesity, and increased age, ever-increasing segments of the aging population in developed countries such as the United States. Once these complications develop, longer hospitalization and antimicrobial exposure further increase the chances of other complications such as infections with resistant organisms, often in what appears to be a vicious cycle. Moving forward, the problems we will face will require a multidisciplinary approach for a definitive solution. Not only must there be changes in industry to facilitate the process of bringing novel antibiotics to market, as well as better attention to infection-control practices, there also must be changes in the healthcare system to optimize healthcare utilization, including the prescribing of antibiotics.

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Learning Assessment

Case 4: Nosocomial Bloodstream Infections

Pre-test Assessment

Prior to your participation in this activity, what was your knowledge of the etiologies and treatment of nosocomial bloodstream infections (on a scale of 1–5; 1 is the lowest and 5 is the highest)?

1 2 3 4 5

CME Test Questions

1. What dose of micafungin is recommended for the treatment of candidemia?
   - a. 50 mg daily with no loading dose
   - b. 100-mg dose daily with no loading dose
   - c. single 70-mg loading dose on Day 1, followed by 50 mg daily
   - d. single 200-mg loading dose on Day 1, followed by 100-mg daily dose
   - e. none of the above

2. What are common risk factors for the development of candidemia?
   - a. antibiotic use
   - b. steroids use
   - c. central venous catheter placement
   - d. diabetes mellitus
   - e. all of the above

3. What pathogens must be covered in sepsis that develops in a hospital setting?
   - a. *S epidermidis*
   - b. *Candida* species
   - c. MRSA
   - d. ESBL-producing Enterobacteriaciae
   - e. all of the above

4. Important steps in the management of primary nosocomial bloodstream infections include:
   - a. catheter removal and repositioning
   - b. empiric therapy with fluconazole
   - c. treatment with oral metronidazole
   - d: a and b
   - e. none of the above

5. Fungal infections now represent approximately ___ of all nosocomial infections.
   - a. 5%
   - b. 10%
   - c. 12%
   - d. 15%
   - e. 18%

Antimicrobial Resistance: A Practical Guide for Physicians and Pharmacists with a Case-Based Approach
Case #4: Managing Nosocomial Bloodstream Infections

Expiration Date: June 30, 2010 **Activity Code:** 08-1017D

CME Registration/Post-Test Answer Form/Evaluation

Participant Information – Required for Certificate		
Full Name:		Degree/Title: ☐ MD/DO ☐ PharmD/RPh ☐ PA ☐ NP ☐ RN ☐ Other: _____
Street:		**RN/NP (required for certificate):** State of Licensure: License #:
City:	State:	
Country:	Zip:	Would you like your certificate sent to you via email? ☐ Yes ☐ No
Email address:		
I certify that I completed this CME activity. The actual amount of time I spent in this activity was hours minutes.		Signature:

Post-Test Answers

1. ____ 2. ____ 3. ____ 4. ____ 5. ____

6. ____ 7. ____ 8. ____ 9.____ 10. ____

Participant Demographics

1. Number of years in practice? ☐ <5 ☐ 5-10 ☐ 11-15 ☐ 16-20 ☐ >20
2. Type of practice? ☐ Private ☐ Hospital ☐ Academic
3. What is your specialty?

☐ Allergy/Immunology	☐ Anesthesiology	☐ Cardiology	☐ Dermatology	☐ Endocrinology
☐ Gastroenterology	☐ Hematology	☐ Neurology	☐ Nephrology	☐ OB/GYN
☐ Oncology	☐ Ophthalmology	☐ Pain Management	☐ Pediatrics	☐ Primary Care
☐ Pulmonology	☐ Rheumatology	☐ Surgery	☐ Other:	

Evaluation - Content

Please rate your level of agreement with the following statements and provide narrative comments where appropriate.

	Strongly Agree	**Agree**	**Neutral**	**Disagree**	**Strongly Disagree**
1. The following objectives were fully met:					
List some of the risk factors found to be associated with Nosocomial bloodstream infections					
Identify the pathogens associated with Nosocomial bacteremia and fungemia and describe their impact on mortality.					
Explain the clinical indications, efficacy, and safety of the echinocandin class of antifungals					
Describe the consequences of the declining number of new antibiotics entering the market and the effects on treatment of drug-resistant organisms and antibiotic stewardship					
2. The quality of the educational process (method of presentation and information provided) was satisfactory and appropriate.					
3. The information presented was *without* promotional or commercial bias.					
4. If you answered "disagree" or "strongly disagree" for the above question, please provide specific examples of bias that you perceived in this activity.					
5. The educational activity will result in a change in my practice behavior.					
6. Please list two ways you intend to change your practice as a result of this activity.					
7. Please assist us in planning future activities by describing any areas in which you feel you have a professional practice gap.					

In order to properly measure the effectiveness of this activity, Dannemiller will send you a website link to a follow-up survey in approximately 30 days regarding the material presented. Your information will not be sold or shared with anyone outside our organization.

*If CME/CE Credit is desired please **mail** this form to: Dannemiller, ATTN: 08-1017D, 5711 Northwest Pkwy, San Antonio, TX, 78249.*

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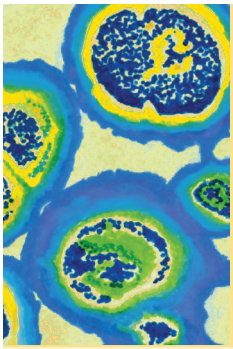

CE/CME Newsletter

Antimicrobial Resistance: A Practical Guide for Physicians and Pharmacists with a Case-Based Approach

Case 4: Managing Nosocomial Bloodstream Infections

A 4-part continuing-education newsletter series offered free of charge to physicians and pharmacists