

SELECTED POSTER PRESENTATIONS

The following summaries are based on posters presented at the 45th Annual Meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy in Washington, DC

POSACONAZOLE IS HIGHLY EFFECTIVE SECOND-LINE AGENT IN ZYGOMYCOSIS

Based on a poster presented by Kontoyiannis DP, Hare RS,[†] Solomon HF,[‡] Corrado ML,[‡] Van Burik JA[§]*

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The current standard treatment for zygomycosis infections is amphotericin B (ampB, liposomal and lipid derivatives), but treatment data, in general, are sparse and ampB is not always well tolerated. Posaconazole has shown activity against *Zygomycetes* in animals, in humans who have failed other therapies, and in vitro, but is available only for compassionate use in the United States. Posaconazole is an extended-spectrum, oral triazole. This study was designed to evaluate the efficacy of posaconazole as a second-line agent; the study emerged from a compassionate use study of posaconazole. Questionnaires were sent to approximately 103 participating investigators; 99 were returned from 47 sites. Patients included in this retrospective review had proven or probable zygomycosis and were refractory to or intolerant of prior antifungal therapy. Of the 99 cases, 91 met criteria for this study. The primary efficacy variable was clinical response, evaluated at 12 weeks (the test-of-cure point) or earlier. Clinical response was assessed by the treating investigator and successful outcomes were defined as complete (resolution) or partial (clinically meaningful improvement). Nonsuccessful outcomes were defined as stable disease (no deterioration, no improvement) or treatment failure (deterioration or attributable death). Posaconazole was administered as a suspension in divided doses

(400 mg twice daily or 200 mg 4 times daily) orally or enterally with meals and/or nutritional supplements; most received the drug for at least 30 days.

Of the 91 study patients, 69 had proven and 22 had probable zygomycosis. Forty-eight were refractory, 10 were intolerant, and 33 were refractory and intolerant to prior antifungal therapy. Most of the patients (85%) had failed lipid ampB. The main sites of zygomycosis infections were sinuses (46%), pulmonary (41%), cutaneous (14%), brain (12%), and orbit (12%); 39% were infected at more than 1 site.

Success at 12 weeks was achieved in 60% of the patients (14% complete response, 46% partial response) and an additional 21% had stable disease. In 13 heavily immunosuppressed patients who received posaconazole and lipid ampB, response rates were similar (46% partial response, 23% stable disease) to those who only received posaconazole.

The investigators also compared success rates by underlying predisposing condition: leukemia, 63%; chronic steroids, 52%; diabetes, 60%; neutropenia, 62%; and hematopoietic stem cell transfer, 52%. Success rates were similar regardless of the infection site or *Zygomycetes* species.

Most patients (70%) underwent adjunctive surgical debridement prior to or after treatment with posaconazole. Success rates were also similar for patients who did (61%) and did not (62%) undergo the adjunctive surgical procedures, regardless of whether the procedures were carried out before (59%) or before or during treatment (41%).

The investigators note that these success rates are comparable to the survival rates seen with ampB treatment: 61% for ampB-deoxycholate and 69% for lipid formulations. Of the 34 deaths in patients taking posaconazole, 43% were attributed to zygomycosis. Thus, posaconazole, with further study, may be an alternative to ampB treatment for zygomycosis infections.

A PROFILE OF CANDIDIASIS IN BURN UNIT PATIENTS

Based on a poster presented by Chen AY,* Buhari M,† Boikov D,† Diezken B,† White M,† Ebricht J,† Vazquez JA*†

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As the fourth most common nosocomial pathogen, *Candida* species play a significant role in nosocomial infections. The source of hospital-acquired *Candida* remains unclear, with some studies suggesting exogenous acquisition from the environment, whereas others point to nosocomial transmission from the hands of healthcare workers. However, few studies have specifically examined candidiasis in burn units.

This study was designed to evaluate the epidemiology of nosocomial candidiasis in the burn unit patient, to quantify in vitro antifungal susceptibility of *Candida* isolates, and to identify possible risk factors associated with current antifungal practices. A total of 22 patients (average age, 45 years) admitted to the Detroit Receiving Hospital Burn Intensive Care Unit were followed during their hospitalization in the burn unit (ranging from 7 to 95 days; average length of stay was 30 days). Half of the patients were discharged in under 3 weeks. During their stay in the burn unit, cultures were obtained once weekly from at least 3 surfaces in each patient (pharynx, vagina, and perineum and/or wound). Positive cultures were evaluated for fungal genus/species, in vitro susceptibilities, and genotyping. In addition, samples were obtained from the hands of burn unit healthcare workers and from various locations in the burn unit.

In total, 100 *Candida* nonsterile isolates were recovered from the 22 patients, 10 were recovered from the healthcare workers, and 4 from the environment. Although almost 50% of the patients (45%) were culture positive at baseline, 64% were culture positive by week 2 and 77% by week 3. The distribution of the *Candida* isolates from patients revealed: *Candida parapsilosis* 59%, *Candida albicans* 37%, *Candida lusitanae* 3%, and *Candida krusei* 1%. *Candida* isolates were recovered from the hands of 10/24 (42%) of healthcare workers: 7 *C parapsilosis* and 3 *C albicans*; 5 yeast isolates were recovered from the environment: 3 *C parapsilosis*, 1 *C albicans*, and 1 *Rhodotorula* spp. Most patients maintained the same strain type over their time in the burn unit. Although many patients were initially colo-

nized by *C albicans*, after 2 to 3 weeks in the unit, *C albicans* was replaced by *C parapsilosis*, which was probably acquired from the environment or the hands of healthcare workers.

The in vitro susceptibility of the *C parapsilosis* isolates was, in general, low, with high minimum inhibitory concentrations (MICs) to some antifungal agents (Table). MICs of the *C albicans* strains from the patients and healthcare workers were within the norm; they were slightly higher in the strains obtained from the environment.

Table. MICs of *Candida parapsilosis* Isolates ($\mu\text{g/mL}$)

	AmpB	FLU	VOR	ANID	CASP	MICA
Patients (MIC ₉₀)	2	64	1	2	8	16
Healthcare workers (MIC ₅₀)		2	0.06	1	1	8
Environment (MIC ₅₀)		8	0.06	0.5	1	2

AmpB = amphotericin B; ANID = anidulafungin; CASP = caspofungin; FLU = fluconazole; MIC = minimum inhibitory concentration; MICA = micafungin; VOR = voriconazole.

The investigators note that although echinocandin resistance is thought to be rare, multidrug resistance (azoles and echinocandins) was not uncommon among the colonizing isolates. *C parapsilosis* isolates from patients were found to be resistant to several antifungal agents including fluconazole, micafungin, and caspofungin. Although many of the fluconazole-resistant *C parapsilosis* isolates were also resistant to caspofungin and micafungin, they maintained susceptibility to voriconazole and anidulafungin.

Although these results may not be generalizable to other burn units, they do highlight the complexity of *Candida* colonization in burn units as well as the importance of knowing local epidemiologic trends in candidiasis and susceptibility profiles in individual burn units. This information will ultimately impact the early selection of antifungal therapy in seriously ill patients.

ZYGOMYCOSIS CULTURES IN THE DIAGNOSIS OF INVASIVE FUNGAL INFECTIONS

Based on a poster presented by Roden M,* Zaoutis T,† Buchanan W,* Knudsen T,* Sarkisova T,* Chu J,† Gea-Banacloche J,* Childs R,* Holland S,* Walsh TJ*

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Zygomycotic infections are gaining attention as etiologic pathogens of serious fungal infections. Unlike other filamentous fungi that strictly target immunocompromised patients, *Zygomycetes* can cause invasive disease in a much wider variety of hosts. Amphotericin B (which can be toxic) is the only treatment currently approved for zygomycoses and is often used in conjunction with surgical debridement. Zygomycosis is frequently diagnosed by cultures. Because of the aggressive and potentially toxic therapeutic options, clinicians must be confident of the diagnosis before committing to either amphotericin B or surgical debridement. This study was designed to determine factors that were associated with invasive disease (as opposed to colonization or superficial infection) in patients with positive cultures.

Investigators reviewed all cases with positive cultures for *Zygomycetes* identified in the Microbiology Laboratory of the Warren Grant Magnuson Clinical Center (National Institutes of Health, Bethesda, Md) from 1976 to 2004. A total of 112 positive *Zygomycetes* cultures were identified. The mean age of these patients was 38 years (55% male, 45% female). Of the 112 isolates, the infections were distributed as follows: colonization 65%, invasive disease 28%, and superficial infection 6%.

The findings illustrated 2 important points: a positive culture for a *Zygomycete* in the presence of European Organisation for the Research and Treatment of Cancer/Mycoses Study Group (EORTC/MSG)-defined infection, leukemia/lymphoma, receipt of corticosteroids, and elevated serum ferritin levels was highly predictive of invasive disease; and *Zygomycetes* are commonly associated with other fungal pathogens.

In all patients with a positive culture, the most frequent underlying conditions were (in descending order of frequency) inherited immunodeficiencies,

solid tumor, lymphoma, normal hosts, and leukemia. Invasive disease occurred most commonly in (in descending order) those patients receiving deferoxamine therapy and those with aplastic anemia/myelodysplastic syndrome, bone marrow transplantation, HIV/AIDS, leukemia, and lymphoma. Colonization was most common in (in descending order) those with chronic obstructive pulmonary disease, hepatitis/liver disease, cystic fibrosis, solid organ transplantation, other conditions (including urine and nephrostomy tube), inherited immunodeficiencies, solid tumor, normal hosts, lymphoma, and leukemia.

The most frequent organisms in those with invasive disease were (in descending order) *Rhizopus microsporus*, *Rhizomucor pusillus*, *Conidiobolus* spp, and *Cunninghamella bertholletiae*. However, the species most commonly found in those who died due to the mycotic infection were *Rhizopus oryzae*, *Rhizopus microsporus*, *R pusillus*, and *C bertholletiae*. (Of note, invasive disease is defined as having met the EORTC/MSG criteria for proven/probable disease. Mortality was assessed as zygomycosis-specific mortality up to 30 days after recovery of the positive culture.)

Colonization was characterized by roughly equal distribution of *Zygomycetes* alone (47%) and co-cultures with other filamentous fungi (53%). By contrast, infections by *Zygomycetes* alone dominated superficial infections (86% vs 14%) and invasive disease (68% vs 32%).

RISK FACTORS FOR A TOXIN GENE VARIANT STRAIN OF CLOSTRIDIUM DIFFICILE

Based on a poster presented by Owens RC,* Lyden J,* Prato S,* Medd D,* Valenti AJ,* Gerding DN,† Bhavnani SM‡

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There was an outbreak of *Clostridium difficile* during 2002 to 2003 at a hospital in Maine. During the outbreak, the investigators discovered, through restric-

tion endonuclease analysis, pulsed-field gel electrophoresis, and toxinotyping studies, a new epidemic strain of *C difficile* (toxintype III, binary toxin positive, *tcdC* gene deletion) at their institution. This strain contains putative virulence characteristics that seem to be contributing to greater disease severity and higher relapse rate. The study described here was designed to ascertain the risk factors associated with this type of outbreak—*C difficile*-associated disease (CDAD).

For this study, 103 cases of CDAD were compared with 204 controls. Severity of illness was determined by the Horn score and Charlson Comorbidity Index. Also recorded were individual comorbidities, gastrointestinal (GI) surgical history, setting from which the patient was admitted (home, long-term care, or other hospital), and whether the patient had been readmitted within the last 60 days. Days at risk were calculated as the number of inpatient days prior to the CDAD for cases, or the number of inpatient days until discharge or death (for controls).

In the univariate analysis, the risk factors for CDAD were the presence of a feeding tube, use of proton pump inhibitor, Charlson score, and exposure to cephalosporins (third and fourth generation), fluoroquinolone, macrolides, metronidazole, aztreonam, and vancomycin IV. Excluded risk factors were days at risk, previous GI surgery, Horn index, and exposure to penicillins, beta-lactamase inhibitors, linezolid, clindamycin, and aminoglycosides. The multivariate analysis for independent risk factors identified the following (in decreasing order of relative risk): cephalosporins, feeding tube, macrolides, vancomycin IV, fluoroquinolones, and proton pump inhibitors.

The investigators observe some important points from these results. First, this study confirmed cephalosporins as a risk factor for CDAD, as have other studies. Perhaps because most of the strains in this study were susceptible to clindamycin, exposure to this drug was not a risk factor for developing CDAD. Interestingly, multivariate analysis indicated that fluoroquinolone exposure was a risk factor for CDAD, but no differences were observed in risk for CDAD among ciprofloxacin, levofloxacin, gatifloxacin, or moxifloxacin. This study also reinforces previous findings that proton pump inhibitors are a risk factor for CDAD.

The investigators conclude that “developing CDAD depends on (1) antimicrobial exposure, (2)

contact with toxigenic strains of *C difficile*, and (3) usually the co-presence of an additional ‘wild-card’ factor, such as decreased immunity, gastric acid suppression, increased age, and resistance to the antimicrobial agent prescribed, with the sequences of events (1) and (2) being important.” For CDAD outbreak situations, improved antimicrobial stewardship efforts combined with infection control interventions should be de rigueur. In fact, as they note, the presence of a feeding tube is a presumed marker for increased healthcare worker contact and was significantly associated with CDAD. The investigators propose handwashing (vs alcohol-based hand hygiene products in the care of patients with CDAD) and use of sporocidal environmental cleaning agents (vs quaternary ammonium products), in addition to patient isolation or cohorting as infection control measures and avoiding gratuitous proton pump inhibitor exposure as a means of intervening in outbreak situations due to *C difficile*.

EFFECT OF METHODOLOGY IN DETERMINING PREVALENCE OF COMMUNITY-ACQUIRED METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*

Based on a poster presented by Furuya EY,*† Cook H,† Hyman S,* Lee M,† Miller M,† Larson E,† Della-Latta P,† Mendonca E,† Lowy F*†

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With reports of increasing incidence of community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA), the authors examined whether certain factors can affect the reported incidences, namely definition of CA-MRSA, definition of prevalence, and case-finding methodology. The investigators used 3 methods to identify CA-MRSA cases, specifically in the Columbia University Medical Center (CUMC) area: computer queries of the CUMC database to identify MRSA isolates susceptible to clindamycin, levofloxacin, and ciprofloxacin; a convenience sample of nares cultures from emergency department (ED)

patients; and nares cultures from a randomly selected population-based sample from the CUMC area. For all 3 samples, CA-MRSA was defined as susceptibility to clindamycin, levofloxacin, and ciprofloxacin, in addition to being SCCmec type IV.

When considering only the sample from the CUMC database, the prevalence of CA-MRSA varied widely based on specimen source. For this analysis, prevalence was defined in 2 ways: CA-MRSA as a percentage of all *S aureus* isolates and CA-MRSA as a percentage of all MRSA.

	CA-MRSA as a Percentage of all <i>S aureus</i> Isolates*	CA-MRSA as a Percentage of all MRSA*
All specimens	3.2%	8.9%
Skin/soft tissue	7.9%	22.8%
Nares	2.1%	5.5%

*P ≤ 0.01.

When comparing the 3 methods of specimen sampling (the CUMC database, ED samples, and community samples), prevalence was defined in 3 possible ways: CA-MRSA as a percentage of all obtained nares cultures, CA-MRSA as a percentage of all *S aureus*, and CA-MRSA as a percentage of all MRSA. The results again showed variation in prevalence among the 3 methods of sampling and between definitions of prevalence. However, the differences were only significant among sampling method for CA-MRSA as a percentage of all MRSA.

	CA-MRSA as a Percentage of All Obtained Nares Cultures	CA-MRSA as a Percentage of all <i>S aureus</i>	CA-MRSA as a Percentage of all MRSA
CUMC database	NA	2.1%	5.5%
ED samples	0.6%	5%	33%
Community samples	0.27%	1.2%	50%
P	.47	.45	≤0.01

The authors also note some additional important observations. Regarding definition of CA-MRSA, almost all "possible MRSA" contained SCCmec type IV, whereas more than 50% of "other MRSA" also contained SCCmec type IV. Thus, antibiotic susceptibility is not a reliable criterion for defining CA-MRSA. Also, specimen type greatly impacted prevalence, with skin and soft-tissue infections having the highest proportion of CA-MRSA.

The authors note that "epidemiological definitions of CA-MRSA using a combination of risk factors and time of diagnosis may be most appropriate, but this information may be unavailable." Although the most appropriate definition and sampling method remains unclear, these results highlight the importance of standardization and rigorous epidemiologic studies to determine the true prevalence and definition of CA-MRSA.

COMPARING ANAEROBES FROM INTRA-ABDOMINAL INFECTIONS AND DIABETIC FOOT INFECTIONS

Based on a poster presented by Citron DM, Goldstein EJC,* Lipsky BA,† Tice A,‡ Abramson MA§*

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Although there has been much interest in the emergence of resistant strains of aerobic bacteria, the effects of antibiotic overuse and the emerging antibiotic resistance among anaerobes in the skin, intestinal tract, and mucous membranes remain largely undefined. The investigators in this study examined the species and antibiotic resistance patterns of anaerobes isolated from intra-abdominal infections and diabetic foot infections during 2 prospective, double-blind, multicenter, randomized, comparator clinical trials of ertapenem versus piperacillin/tazobactam. Specimens were tested for susceptibility to ertapenem, imipenem, piperacillin/tazobactam, ticarcillin/clavulanate, amoxicillin/clavulanate, ampicillin/sulbactam, cefoxitin, ceftriaxone, lev-

ofloxacin, moxifloxacin, gatifloxacin, gemifloxacin, clindamycin, chloramphenicol, and metronidazole.

Anaerobes grew from more than 70% of the intra-abdominal specimens as part of a mixed culture or as pure cultures, compared with only 45% of diabetic foot infection specimens. In the intra-abdominal specimens, the *Bacteroides fragilis* group species were predominant (39% of anaerobes), followed by *Clostridium* species and nonspore-forming gram-positive rods of the *Eubacterium* group. In the diabetic foot infections, anaerobic gram-positive cocci were most predominant (45%), followed by *Prevotella* species, *Porphyromonas* species, and the *B fragilis* group species. The investigators also note the striking difference in distribution of anaerobic gram-positive cocci between the 2 sources of infections: in diabetic foot infection, *Fingoldia magna* was most predominant, compared to *Micromonas micros* in intra-abdominal infections.

Susceptibilities to some of the antimicrobial agents were similar between specimens from both sources (all strains)—for example (intra-abdominal, diabetic foot): ertapenem, 99%, 100%; piperacillin/tazobactam, 97%, 99%. However, there were marked differences in fluoroquinolone resistance between specimens from the 2 patient populations. For example, for all peptostreptococci, diabetic foot infections had more levofloxacin-resistant isolates than those

from intra-abdominal sources. A similar trend was also found for clindamycin.

Based on the results, the investigators note that the differences in susceptibility between anaerobes from diabetic foot infections and intra-abdominal infections might be explained by the frequent prior courses of antibiotic therapy in patients with severe diabetic foot infections (as these study patients were), which required systemic therapy. Quinolones, cephalosporins, and clindamycin are frequently used for these types of infections. Thus, the findings in this study may reflect the impact of widespread quinolone use.

Also, the presence of anaerobic gram-positive cocci in the specimens from diabetic foot infections (which were all postdebridement) is notable because these bacteria produce tissue-destroying enzymes, such as collagenases and proteases, and some species produce pro-inflammatory end-products (eg, butyric acid), all of which can prolong the infection. Therefore, these bacteria may be of greater significance than has hitherto been appreciated.

Finally, the investigators also note that because many laboratories do not culture for anaerobes (or do not identify anaerobes at the species level) and do not perform susceptibility testing, these study results should prompt clinicians to consider these types of tests before choosing an antibiotic regimen for intra-abdominal or diabetic foot infections.