THERAPY USING ANTIFUNGALS

Douglas Black, Pharm.D.
Associate Professor
School of Pharmacy
University of Washington
dblack@u.washington.edu

CLASSIFICATION OF FUNGI

Yeasts	Dimorphic fungi	Molds
Candida	*Blastomyces*	*Aspergillus*
Cryptococcus	*Coccidioides*	*Fusarium*
Trichosporon	*Histoplasma*	*Rhizopus*
	Sporothrix	*Mucor*
		Absidia
		Pseudallescheria (Scedosporium)

= Zygomycetes

SPECIES OF *CANDIDA* WE OFTEN SEE AROUND HERE

C. albicans

C. tropicalis

C. parapsilosis

C. glabrata

C. krusei

C. guillermondii

C. lusitaniae

HISTORY OF ANTIFUNGAL DRUGS

DRUG	CLASS	YR APPROVED
Nystatin	Polyene	1954
Amphotericin B deoxycholate	Polyene	1958
Griseofulvin	Inhibitor of mitosis	1959
Miconazole, clotrimazole	Imidazole	1969
Flucytosine	Substituted pyrimidine	1972
Ketoconazole	Imidazole	1981
Fluconazole	Triazole	1990
Itraconazole (capsules)	Triazole	1992
Terbinafine (topical)	Allylamine	1993
Terbinafine (oral)	Allylamine	1996
Amphotericin B lipid complex	Polyene	1996
Liposomal amphotericin B	Polyene	1997
Itraconazole (oral solution)	Triazole	1997
Caspofungin	Echinocandin	2001
Voriconazole	Triazole	2002
Micafungin	Echinocandin	2004
Anidulafungin	Echinocandin	2006
Posaconazole	Triazole	2006

A 75-year-old male presents to the ER with acute abdominal pain. He has been receiving long-term treatment with corticosteroids for severe COPD. He is diagnosed with acute abdomen and undergoes emergency laparotomy. A perforated cancer of the ascending colon is found, and right-sided hemicolectomy with end-to-end anastamosis is performed. IV antibiotic treatment with ampicillin-sulbactam (3.1 g IV q8h) is administered.

His postoperative course is initially uneventful. On day 7 the patient develops fever, new abdominal tenderness, increasing dyspnea, leukocytosis (22,000/mm^3, 25% band forms) and an elevated CRP. Abdominal CT scan shows a significant amount of intraperitoneal fluid. Upon second-look laparotomy a site of anastamotic leakage is found, and drainage of the operative site and a colostomy are performed.

The patient is transferred to the SICU. The antibiotics are changed to imipenem/cilastatin (500 mg IV q6h). Cultures of the peritoneal fluid grow 3+ *E. coli*, 3+ *K. pneumoniae*, 3+ *B. fragilis*, and 1+ *C. albicans*. Blood cultures are negative.

The patient is mechanically ventilated. He has a CVC in the right subclavian vein and a urinary catheter. He receives TPN. The day after surgery he is afebrile and inflammatory parameters are decreasing. Surveillance cultures of stool, urine and respiratory secretions show 1+ *C. albicans*. Three days later, he spikes a fever. Repeat peritoneal fluid tap shows 3+ *C. albicans*. **Should antifungal therapy be initiated at this time?**

The patient recovers and is sent home about two weeks later. After being at home for 48 hours, he develops fever. He returns to the hospital and is found to have leukocytosis and abdominal pain. A different *Candida* species (3+ *C. glabrata*) is found in his peritoneal fluid. The patient is mechanically ventilated and hemodynamically stable. After blood culturing, he is started on antifungal drug therapy.