O-11	MANAGEMENT of INVASIVE *CANDIDA* INFECTIONS

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Candida spp., have emerged as important nosocomial pathogens. Most of the patients who acquire serious *Candida* infections are severely immunocompromised such as transplant recipients and patients undergoing therapy for hematological malignancies. Less immunocompromised patients at risk include patients with intravascular catheters, patients who have received prolonged therapy with multiple antibiotics, patients in intensive care units and patients who have undergone extensive or multiple gastrointestinal surgeries.

For many years about 80% of serious infections were caused by *Candida albicans* and were derived from the patients endogenous flora. At the present time, *Candida albicans* accounts for only about 45-60% of invasive infections. The second most common infecting species varies among different patient populations: *C. parapsilosis* in children, *C. tropicalis* in some hematology units and *C. glabrata* in some intensive care units. The relative frequency of different species in transplant and hematology units is influenced by the use of fluconazole prophylactically, which generally decreases the frequency of *Candida* infection but changes the predominant infecting species to *C. glabrata* and, to lesser extent, C. *krusei*. Also, hospital epidemics are being identified, sometimes linked to colonized personnel.

Difficulties in establishing the diagnosis of serious *Candida* infection remain on obstacle to successful management. Despite improvements in blood culturing techniques, as many as 25% of patients with disseminated infection never have positive blood cultures, although this is rarely a problem in catheter-related infections. Isolation of *Candida* spp. from multiple body sites is suggestive, but not diagnostic, of *Candida* infection, since patients receiving antibiotics are frequently colonized. Diagnosis of pneumonia, urinary tract infection and peritonitis are especially difficult, based on culture results. Unfortunately, little progress has been made in developing a reliable non-cultural diagnostic test. Hence, it is often necessary to institute antifungal therapy without a proven diagnosis.

For many years, Amphotericin B (AMB) was the only therapeutic option. It is associated with significant acute and chronic (nephrotoxicity) side-

effects and is of marginal benefit in neutropenic patients. Several lipid formulations of AMB are now available that reduce its toxicity, primarily to the kidney, permitting the administration of higher doses. Animal models suggest that higher doses of AMB are more effective, but a randomized trial failed to detect any improvement in efficacy with a lipid preparation, given at much higher doses. The azole, fluconazole, has been compared to AMB in several randomized trials and has been found to be as effective and less toxic. One study suggested that it was more effective in neutropenic patients. Of concern is in vitro data showing variable susceptibility of *C. glabrata* to fluconazole. Most clinical data has not supported this concern, especially when doses of 400-600 mg daily have been used. *C. krusei* is resistant to fluconazole, but infection with this species is uncommon. Itraconazole has not been studied extensively for the treatment of invasive *Candida* infections because the original preparation was a variably absorbed oral capsule. There are now an intravenous formulation and oral solution, but no comparative trials with fluconazole or AMB have been published. Its in vitro activity against. *C. glabrata* appears to be less than that of fluconazole.

Several new azole preparations and other unique chemical structures, such as echinocandins, are undergoing clinical trials. However, improved therapies need to be coupled with better diagnostic tests, in order to maximize our ability to manage these infections most successfully.