this category since it is impossible to distinguish colonization from lower or upper urinary tract infection. If the isolate is *C. albicans*, most clinicians use oral fluconazole rather than a bladder washout with amphotericin B, which was more commonly used in the past. Caspofungin has been used with success; although echinocandins are poorly excreted into the urine, they may be an option, especially for non-*albicans* isolates. The doses and duration are the same as for disseminated candidiasis. The significance of the recovery of *Candida* from abdominal drains in postoperative patients is unclear, but again the threshold for treatment is generally low because most of the affected patients have been subjected to factors predisposing to disseminated candidiasis.

Removal of the infected valve and long-term antifungal therapy constitute appropriate treatment for *Candida* endocarditis. Although definitive studies are not available, patients usually are treated for weeks with a systemic antifungal agent (Table 240-2) and then given chronic suppressive therapy for months or years (sometimes indefinitely) with an oral azole (usually fluconazole at 400–800 mg/d).

Hematogenous *Candida* endophthalmitis is a special problem requiring ophthalmologic consultation. When lesions are expanding or are threatening the macula, an IV polyene combined with flucytosine (25 mg/kg four times daily) has been the regimen of choice, although comparative studies with other regimens have not yet been reported. As more data on the azoles and echinocandins become available, new strategies involving these agents are developing. Of paramount importance is the decision to perform a partial vitrectomy. This procedure debulks the infection and can preserve sight, which may otherwise be lost as a result of vitreal scarring. All patients with candidemia should undergo ophthalmologic examination because of the relatively high frequency of this ocular complication. Not only can this examination detect a developing eye lesion early in its course; in addition, identification of a lesion signifies a probability of ~90% of deep-organ abscesses and may prompt prolongation of therapy for candidemia beyond the recommended 2 weeks after the last positive blood culture. Although the basis for the consensus is a very small data set, the recommended treatment for *Candida* meningitis is a polyene (Table 240-3) plus flucytosine (25 mg/kg four times daily). Successful treatment of *Candida*-infected prosthetic material (e.g., an artificial joint) nearly always requires removal of the infected material followed by long-term administration of an antifungal agent selected on the basis of the isolate's sensitivity and the logistics of administration.

PROPHYLAXIS

The use of antifungal agents to prevent *Candida* infections has been controversial, but some general principles have emerged. Most centers administer prophylactic fluconazole (400 mg/d) to recipients of allogeneic stem cell transplants. High-risk liver transplant recipients also are given fluconazole prophylaxis in most centers. The use of prophylaxis for neutropenic patients has varied considerably from center to center; many centers that elect to give prophylaxis to this population use either fluconazole (200–400 mg/d) or a lipid formulation of amphotericin B (AmBiSome, 1–2 mg/d). Caspofungin (50 mg/d) also has been recommended. Some centers have used itraconazole suspension (200 mg/d). Posaconazole (200 mg three times daily) also has been approved by the FDA for prophylaxis in neutropenic patients and is gaining in popularity.

Prophylaxis is sometimes given to surgical patients at very high risk. The widespread use of prophylaxis for nearly all patients in general surgical or medical intensive care units is not—and should not be—a common practice for three reasons: (1) the incidence of disseminated candidiasis is relatively low, (2) the cost-benefit ratio is suboptimal, and (3) increased resistance with widespread prophylaxis is a valid concern.

Prophylaxis for oropharyngeal or esophageal candidiasis in HIV-infected patients is not recommended unless there are frequent recurrences.

241 Aspergillosis

David W. Denning

Aspergillosis is the collective term used to describe all disease entities caused by any one of ~50 pathogenic and allergenic species of *Aspergillus*. Only those species that grow at 37°C can cause invasive infection, although some species without this ability can cause allergic syndromes. *A. fumigatus* is responsible for most cases of invasive aspergillosis, almost all cases of chronic aspergillosis, and most allergic syndromes. *A. flavus* is more prevalent in some hospitals and causes a higher proportion of cases of sinus infections, cutaneous infections, and keratitis than *A. fumigatus*. *A. niger* can cause invasive infection but more commonly colonizes the respiratory tract and causes external otitis. *A. terreus* causes only invasive disease, usually with a poor prognosis. *A. nidulans* occasionally causes invasive infection, primarily in patients with chronic granulomatous disease.

EPIDEMIOLOGY AND ECOLOGY

Aspergillus has a worldwide distribution, most commonly growing in decomposing plant materials (i.e., compost) and in bedding. This hyaline (nonpigmented), septate, branching mold produces vast numbers of conidia (spores) on stalks above the surface of mycelial growth. Aspergilli are found in indoor and outdoor air, on surfaces, and in water from surface reservoirs. Daily exposures vary from a few to many millions of conidia; the latter high numbers of conidia are encountered in hay barns and other very dusty environments. The required size of the infecting inoculum is uncertain; however, only intense exposures (e.g., during construction work, handling of moldy bark or hay, or composting) are sufficient to cause disease in healthy immunocompetent individuals. Allergic syndromes may be exacerbated by continuous antigenic exposure arising from sinus or airway colonization or from nail infection. High-efficiency particulate air (HEPA) filtration is often protective against infection; thus HEPA filters should be installed and monitored for efficiency in operating rooms and in areas of the hospital that house high-risk patients.

The incubation period of invasive aspergillosis after exposure is highly variable, extending in documented cases from 2 to 90 days. Thus community acquisition of an infecting strain frequently manifests as invasive infection during hospitalization, although nosocomial acquisition is also common. Outbreaks usually are directly related to a contaminated air source in the hospital.

Global aspergillosis incidence and prevalence have been estimated (Table 241-1). However, given the inadequate diagnostic capability in almost all low- and middle-income countries, the accuracy of these estimates is uncertain. The frequency of different manifestations of aspergillosis varies considerably with geographic location; most notably, chronic granulomatous sinusitis is rare outside the Middle East and India, and fungal keratitis is particularly common in Nepal, Myanmar, Bhutan, and India (800 and 113 cases/100,000 population, respectively). The potential effects of chronic pulmonary aspergillosis after pulmonary tuberculosis have only recently been appreciated and include life-threatening hemoptysis, misdiagnosis of smear-negative tuberculosis, and general exacerbation of posttuberculosis morbidity.

RISK FACTORS AND PATHOGENESIS

The primary risk factors for invasive aspergillosis are profound neutropenia and glucocorticoid use; risk increases with longer duration of these conditions. Higher doses of glucocorticoids increase the risk of both acquisition of invasive aspergillosis and death from the infection. Neutrophil and/or phagocyte dysfunction also is an important risk factor, as evidenced by aspergillosis in chronic granulomatous disease, advanced HIV infection, and relapsed leukemia. An increasing incidence of invasive aspergillosis in medical intensive care units suggests that, in patients who are not immunocompromised, temporary abrogation of protective responses as a result of glucocorticoid use or a general anti-inflammatory state is a significant risk factor. Many