The fungus Aspergillus was first described in 1729 by Micheli, who, in naming the fungus, acknowledged the resemblance of the conidial head of Aspergillus, with its radiating chains of spores, to an aspergillum, a brush used for sprinkling holy water. The first human case of aspergillosis was described in 1842 by Bennett who observed regular “vegetable structures” in tuberculous cavities in a patient who had died from pulmonary tuberculosis. Many early cases were found in patients with tuberculosis, or those with a high occupational risk, such as in pigeon-crammers and wig-combers. Some of these cases were invasive, but most were aspergillomas. The ability of Aspergillus species to cause opportunistic infection in immunocompromised patients was first described by Rankin. His report of disseminated aspergillosis and candidiasis in a patient with agranulocytosis in the United Kingdom was published in 1953. However, it was not until 1970, when the clinical and histopathologic features of this disease were described in 98 patients, that the stage was set for any modern concepts of this devastating opportunistic infection.

Since 1970, a number of autopsy studies have been published which indicate that the epidemiology of invasive fungal infections in immunocompromised patients is changing. Twenty years ago autopsy studies found Candida to be the predominant pathogen. However, studies of autopsy cases from Europe, the United States, and Japan show that the number of patients dying from invasive aspergillosis has increased significantly over the past 20 years. A recent remarkable autopsy study, performed in Germany, of more than 8000 cases showed Aspergillus to have become the leading pathogen, causing up to 60% of fungal infections in the most recent period studied, while the number of cases with invasive candidiasis had declined. This was a relatively unbiased sample, as the autopsy rate in the institution was 70% and microscopic evidence of fungal infection was sought in all cases. A significant increase was noted for all high-risk populations and fungal infections were detected in 7% of all (unselected) autopsies in 1992. The increase in the number of cases among patients with hematologic malignancies in consolidation or maintenance phase and among those treated with corticosteroids is particularly notable. The underlying disease or condition greatly determines the level of risk for patients to become infected by Aspergillus species (Table 1).

Invasive aspergillosis usually affects the lungs, sinuses, or tracheobronchial tree. Pulmonary or sinus disease may be acute or chronic, and the pace with which the disease progresses varies greatly. Some patients die within 7 to 10 days of first symptoms or radiologic abnormality; others can present 2 or 3 months after symptoms first appear. The pattern and degree of immunosuppression usually determines the rapidity of the course, so that invasive aspergillosis in corticosteroid-treated and profoundly neutropenic patients progresses more rapidly. A large number of unusual manifestations of invasive aspergillosis continue to be reported, including, for example, postoperative ocular and neurosurgery infections, Aspergillus prostatitis and peritonitis, breast implants and catheter device infections, and infection of the posterior mediastinum and unusual bony sites. Patients without conventional risk factors, including neonates or patients with systemic lupus erythematosus, or following drowning, or those with multiple myeloma are acquiring the disease.

The diagnosis of invasive aspergillosis is difficult to establish since specimens for histology and culture, necessary to prove tissue invasion by the fungus, are often difficult to obtain in clinical practice. Although, over a period of 14 years the number of patients diagnosed ante-mortem increased from 7% to 32%, at present, the majority of Aspergillus infections still remain undetected during life. Circumstantial evidence of infection can be obtained by culture and cytology of respiratory tract...
The detection of in vitro and in vivo resistance among A. fumigatus to itraconazole has added to the factors that may reduce the probability of surviving the infection. The autopsy performed on the first reported granulocytopenic patient with disseminated invasive aspergillosis, in 1953, revealed that besides invasive aspergillosis the patient had suffered from a concurrent disseminated infection by Candida species (moniliasis). Although now, 45 years later, both pathogens still account for the majority of invasive fungal infections, the changes in epidemiology indicate that attempts to control fungal infections have been partially successful for Candida but have thus far failed for Aspergillus. The increasing number of cases and the high mortality associated with invasive aspergillosis underscores the necessity for further development and evaluation of rapid diagnostic techniques for different patient groups, the development of reproducible and meaningful in vitro susceptibility tests, and randomized studies for prevention of and treatment for invasive aspergillosis.

## REFERENCES

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