1. INTRODUCTION

Hyalohyphomycosis is the term used to designate infections caused by fungi noted to have hyaline (colorless) septate hyphae microscopically in clinical samples, similar to the use of phaeohyphomycosis for those infections caused by pigmented fungi (Chapter 11). This distinction is clinically useful when hyphal elements are seen on tissue examination but fail to grow. Hyalohyphomycosis typically includes infections caused by species of *Fusarium*, *Scedosporium*, *Acremonium*, *Paecilomyces*, *Scopulariopsis*, *Beauveria*, and *Penicillium*. Although *Aspergillus* produces similar hyaline septate hyphae microscopically, and is thus considered a member of this grouping of fungi, infection caused by this genus (aspergillosis) is generally discussed as a separate disease (Chapter 9). These agents may cause superficial or localized infection in immunocompetent hosts (usually as a result of direct inoculation of the fungus after trauma) and invasive or disseminated infections in immunocompromised hosts. In the latter setting, the clinical infection may be indistinguishable from that of invasive aspergillosis. A remarkable feature of some of these hyaline moulds is their ability to cause fungemia and to disseminate hematogenously, causing numerous embolic skin lesions. These infections may be clinically suspected on the basis of a constellation of clinical and laboratory findings. Definitive diagnosis requires isolation of the organism because histopathological examination reveals branching hyaline septate hyphae regardless of the pathogen, similar to the findings with *Aspergillus*. An accurate diagnosis at the species level is important because of the variable susceptibility to antifungal agents. An important component of therapy of localized infection is surgery and removal of infected prosthetic devices. Outcome is usually favorable in immunocompetent hosts, while usually very poor in the setting of persistent profound immunosuppression. We herein describe the most relevant characteristics of these organisms and the clinical spectrum and diagnosis and treatment of infections caused by these agents.
2. **FUSARIUM**

2.1. Introduction

*Fusarium* species recently emerged as a cause of disseminated infections in neutropenic patients and in patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT). *Fusarium* represents the second most common fungal pathogen, after *Aspergillus*, as the cause of life-threatening infection in recipients of hematopoietic transplant (1). *Fusarium* causes a broad spectrum of infections in humans, including superficial and local infections in immunocompetent hosts, while disseminated infection is seen almost exclusively in immunosuppressed patients.

2.2. Etiologic Agents

Four species are most commonly involved in human infections: *F. solani* (the most common), *F. oxysporum*, *F. moniliforme*, and *F. proliferatum* (2). *Fusarium* species are septate filamentous fungi that produce conidiophores, phialides, macroconidia, and microconidia. *Fusarium* species grow easily and rapidly in almost all fungal media. On potato dextrose agar (PDA), the colonies have a velvety or cottony surface, and are white, yellow, pink, purple salmon or gray on the surface, with a pale, red, violet, brown or sometimes blue reverse. The characteristic sickle- or banana-shaped multiseptate macroconidia with a foot cell at the base are used in identifying the genus and species of *Fusarium* (Fig. 10.1). Molecular methods may also be used for rapid identification of *Fusarium* to the species level. In tissue, the hyphae are similar to those of *Aspergillus* species, with hyaline and septate filaments that typically dichotomize in acute and right angles. In the absence of microbial growth, distinguishing fusariosis from aspergillosis and other hyalohyphomycoses is difficult, and requires the use of in situ hybridization in paraffin-embedded tissue specimens (3). *Fusarium* species are toxigenic, and may cause mycotoxicosis in animals and humans (2).

2.3. Epidemiology

*Fusarium* is ubiquitous in soil and water, taking part in water biofilms and is a human and plant pathogen (4). *Fusarium* species are causative agents of superficial and localized infections in immunocompetent hosts, most commonly onychomycosis and cutaneous and subcutaneous infections including mycetoma and keratitis, the latter in contact lens wearers (5). A recent large outbreak of *Fusarium* keratitis was reported in contact lens wearers in the United States and was linked to contaminated contact lens rinse solutions (6). Other risk factors for keratitis are trauma and use of topical corticosteroids and antibiotics. *Fusarium* endophthalmitis may arise from keratitis or by direct inoculation after cataract surgery or trauma (7). Fusariosis may also result from skin breakdown, such as burns and wounds, or the presence of foreign bodies, such as peritonitis in patients receiving continuous ambulatory peritoneal dialysis (CAPD), and catheter-associated fungemia, and thrombophlebitis (8–10). Other infections include sinusitis, pneumonia, cutaneous and subcutaneous infections, septic arthritis, and osteomyelitis (11–15).

Immunosuppressed patients may develop locally invasive and disseminated fusariosis (16). Risk factors include prolonged neutropenia such as following chemotherapy.