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**Chapter 31**

# Deep Fungal Infections

**Wendi E. Wohltmann, MD**

## Key Points: Deep Fungal Infections

1. Deep fungal infections can be divided into subcutaneous (localized), systemic, and opportunistic categories.
2. Neutropenic patients are particularly at risk for systemic phaeohyphomycosis, aspergillosis, fusariosis, and mucormycosis.
3. Patients with impaired cellular immunity are particularly at risk for disseminated sporotrichosis, histoplasmosis, coccidioidomycosis, penicilliosis, *Cryptococcus,* and *Candida*.
4. The differential diagnosis of lymphocutaneous (sporotrichoid) spread includes **SLANTS**: **S**porotrichosis, **L**eishmaniasis, **A**typical mycobacteria, ***N****ocardia,* **T**ularemia, and cat **S**cratch disease.

## *1. What is a deep fungal infection?*

In contrast to the superficial dermatophytes, which are typically confined to dead keratinous tissue, certain mycotic infections have the capacity for deep invasion of the skin or production of skin lesions secondary to systemic infection. They are typically acquired through direct inoculation, ingestion, and/or inhalation of spores from soil or other organic matter. In this chapter, the deep fungal diseases are organized into three categories based on clinical presentation (Table 31-1).

**Subcutaneous Fungal Infections**

***2. Discuss the characteristics of subcutaneous mycotic infections.***

Subcutaneous mycotic infections are caused by a heterogeneous group of fungi and are infections of implantation (inoculated directly into the skin through local trauma). The four most important infections are sporotrichosis, chromomycosis, phaeohyphomycosis, and mycetoma. Lobomycosis and rhinosporidiosis are significantly less common. As a group, these infections involve primarily the skin and subcutaneous tissues and rarely disseminate in the immunocompetent host. These organisms are ubiquitous in soil, plants, and trees.

***3. What is a dimorphic fungus?***

Dimorphic fungi are capable of growing in both the mold and yeast forms. Examples of diseases caused by dimorphic fungi include sporotrichosis, histoplasmosis, blastomycosis, paracoccidioidomycosis, and penicilliosis.

***4. What occupations are at increased risk of sporotrichosis?***

Sporotrichosis is caused by a dimorphic fungus, *Sporothrix schenckii.* This organism is found worldwide, except in the polar regions and is most common in subtropical and tropical climates. It is endemic in Africa and Central and South America. In the United States, infection is most common in the Midwest. The habitat includes soil, thorny plants (especially roses), hay, sphagnum moss, and animals. Cats may carry *Sporothrix* on their paws and can cause infection by scratching their owners or animal handlers. Occupations at risk of cutaneous inoculation include farmers, gardeners (especially rose), florists, masonry workers, Christmas tree farmers, veterinarians, and animal handlers (especially cats, rodents, and armadillos).

***5. Describe the clinical manifestations of sporotrichosis.***

The classic form of sporotrichosis (lymphocutaneous) begins at the site of inoculation (most commonly, upper extremity) as a painless pink papule, pustule, or dermal nodule, which rapidly enlarges and ulcerates (Fig. 31-1A). Without treatment, the infection ascends along the lymphatics, producing secondary nodules and regional lymphadenopathy that may ulcerate (Fig. 31-1B). The fixed cutaneous variant is confined to the site of inoculation. The organisms rarely disseminate hematogenously to the joints, bone, meninges, or eye.

***6. How is the diagnosis of cutaneous sporotrichosis made?***

A strong clinical suspicion is most important. Skin biopsy shows granulomatous inflammation with neutrophilic microabscesses. In the immunocompetent patient, fungal elements are only found in about 60% of cases even when special stains are utilized. When suspecting sporotrichosis, cultures (of tissue or pus) on Sabouraud's medium are both more specific and sensitive. Colonies grow rapidly in 3 to 5 days.

***7. How do you treat cutaneous sporotrichosis?***

Itraconazole (100 to 200 mg/day) for 3-6 months is the treatment of choice for lymphocutaneous and fixed cutaneous sporotrichosis, with a success rate of 90% to 100%. Terbinafine (250 mg/day) is second-line treatment, and because potassium iodide (SSKI) is less costly than other agents, it is still recommended, especially in developing-world epidemics. Local hyperthermia has also been shown to be effective. Children may be safely treated with itraconazole. The treatment of choice for disseminated disease is itraconazole 300 mg twice a day for 6 months, followed by 200 mg twice a day for 6 months.

***8. What other organisms may present with lymphocutaneous disease?***

Several other diseases may present with a distal ulcer, proximal secondary nodules along the lymphatics, and regional lymphadenopathy. The most important include nontuberculous *Mycobacterium* (*Mycobacterium marinum, Mycobacterium kansasii, Mycobacterium fortuitum* complex), *Nocardia,* leishmaniasis, cat scratch disease, and tularemia. A patient with this clinical presentation should have tissue biopsies for routine histology and cultures to include bacteria, mycobacteria, and fungi. This pattern of disease is also called *sporotrichoid* and can be remembered using the **SLANTS mnemonic: S**porotrichosis, **L**eishmaniasis, **A**typical mycobacteria, **N**ocardia, **T**ularemia, cat **S**cratch disease.

***9. What are dematiaceous fungi?***

Dematiaceous fungi are brown or black pigmented fungi. The pigment is due to melanin. They are slow growing and can be found in the soil, decaying vegetation, rotting wood, and the forest carpet. Subcutaneous-cutaneous disease is caused by traumatic inoculation into the skin. There are three broad categories of dematiaceous fungal infections including chromoblastomycosis, phaeohyphomycosis, and eumycotic mycetoma (Madura foot).

***10. How do you differentiate chromoblastomycosis from phaeohyphomycosis?***

Chromoblastomycosis (also called chromomycosis) is a chronic subcutaneous infection characterized by the appearance in tissue biopsies of an intermediate, vegetative, pigmented fungal form with a yeastlike appearance that is arrested between yeast and hyphal formation. These pigmented, thick-walled fungal elements are called Medlar bodies (Fig. 31-2). Medlar bodies, also called **copper pennies** or sclerotic bodies, are diagnostic of chromoblastomycosis,

differentiating it from phaeohyphomycosis. Tissue biopsies of phaeohyphomycosis are characterized by lightly pigmented filamentous hyphae.

***11. Which organisms may cause chromoblastomycosis?***

Five fungal species account for most infections. The most frequent organism worldwide is *Fonsecaea pedrosoi.* Other organisms include *Phialophora verrucosa, Fonsecaea compactum, Rhinocladiella aquaspersa,* and *Cladophialophora carrionii.* **Memory device: Compact** *(Fonsecaea compactum)* **dead** *(Cladophialophora carrionii)* **wet** *(Rhinocladiella aquaspersa)* **warty** *(Phialophora verrucosa)* **feet** *(Fonsecaea pedrosoi).*

***12. Which organisms cause phaeohyphomycosis?***

Phaeohyphomycosis may occur in both immunocompetent and immunocompromised patients, and has been attributed to over 60 genera and more than 100 species. The most important genera include *Scedosporium (Pseudallescheria), Alternaria, Bipolaris, Curvularia, Exophiala, Phialophora,* and *Wangiella*.

***13. How does chromoblastomycosis present?***

Chromoblastomycosis is a chronic cutaneous and subcutaneous infection that is usually present for years with minimal discomfort. The inciting injury is often not recalled. The infection is most common on the lower extremity and 95% of cases occur in males. The typical patient is a barefoot, rural agricultural worker in the tropics. At the inoculation site, red papules develop that eventually coalesce into a plaque, which slowly enlarges and acquires a verrucous or warty surface. Lesions can evolve into a cauliflower-like mass, leading to lymphatic obstruction and elephantiasis-like edema of the lower extremity (Fig. 31-3) if left untreated. Neoplastic transformation to squamous cell carcinoma can occur.

***14. How is chromoblastomycosis diagnosed and treated?***

Diagnosis is made through potassium hydroxide (KOH) mounts from scrapings, biopsies of the lesions showing the organism with suppurative and granulomatous inflammation, and culture. Chromoblastomycosis is typically resistant to treatment. The treatment of choice for small lesions is surgical excision with a wide margin of normal skin. Chronic or extensive lesions should be treated with a combination of itraconazole therapy and surgical excision. Combination therapy with terbinafine, posaconazole, cryotherapy, and local heat therapy also appear to be effective. Treatment is continued for months.

***15. Describe the clinical features of phaeohyphomycosis.***

The spectrum of clinical infections is broad. The most typical presentation is a subcutaneous cyst or abscess at the site of trauma and *Exophiala jeanselmei* and *E. dermatitidis* are the most common organisms. The primary lesion is a painless nodule that evolves into a fluctuant abscess. Immunocompromised patients present with multiple nodules. *Scedosporium proliferans* (42% of cases), *Bipolaris spicifera* (8%), and *Wangiella dermatitidis* (7%) are the most common causes of rare disseminated disease. The primary risk factor is decreased host immunity, especially prolonged neutropenia. The outcome is poor, despite antifungal therapy, with a 79% overall mortality rate.

***16. What is Madura foot?***

Madura foot, a type of mycetoma, is a localized, destructive infection of the skin and subcutaneous tissue that eventually involves deeper structures. It may be caused by filamentous bacteria, aerobic actinomycetes (actinomycetomas), and true fungi (eumycetoma). The most common causative fungi are *Madurella mycetomatis* and *Madurella grisea.* Less frequent causes

are *Acremonium kiliense, E. jeanselmei,* and *Scedosporium apiospermum* (also called *Pseudallescheria boydii*).

***17. What are the three characteristic clinical features of Madura foot?***

The first is the formation of nodules in the skin at the site of inoculation, usually a penetrating injury. The second feature is purulent drainage and fistula formation. The third and most characteristic feature is the presence of **grains** or **granules** that are visible in the purulent drainage. Madura foot is a progressive infection leading to marked swelling and deformity in its later stages (Fig. 31-4). Additionally, the lesions have a tendency to become painful in the later stages, when bone involvement and deformity ravage the site.

**Systemic Fungal Infections**

***18. Discuss the pathogenesis of the systemic respiratory deep fungi.***

The systemic respiratory endemic fungal infections include blastomycosis, histoplasmosis, coccidioidomycosis, paracoccidioidomycosis, and penicilliosis. These infections are all due to species that show dimorphism. These diseases are similar in pathophysiology, but each has distinct clinical characteristics. The causative organisms are found in the soil, and infection occurs with inhalation of the organism into the lung. The primary infection is pulmonary. Dissemination occurs via the lymphohematogenous route, and each fungus has a predilection for particular organ systems.

***19. Where is blastomycosis endemic?***

Blastomycosis, caused by the soil saprophyte *Blastomyces dermatitidis,* is endemic in North America, especially the southeastern and south-central states bordering the Mississippi and Ohio

rivers (Kentucky, Arkansas, Mississippi, Tennessee, Louisiana, Illinois, and Wisconsin), North Carolina, and the Great Lakes region (Fig. 31-5). Sporadic cases have been reported in Colorado, Texas, Kansas, and Nebraska. The typical patient is a middle-aged male with occupational or recreational exposure to the soil.

***20. What are the clinical manifestations of blastomycosis?***

An important concept of blastomycosis is that it can mimic many other disease processes and has been called **"The Great Pretender."** The pulmonary manifestations range from a community-acquired pneumonia on one end of the spectrum to malignancy. Pulmonary disease is seen in 87% of patients, skin lesions in 20%, bone involvement in 15%, central nervous system in 5% to 10%, and less commonly the genitourinary system (prostate).

***21. Describe the cutaneous findings in disseminated blastomycosis.***

The most characteristic cutaneous presentation is a single (or multiple) crusted, verrucous plaque on exposed skin (face, hands, arms) with color variation from gray to violet (Fig. 31-6). Microabscesses can form, and pus exudes when the crust is lifted off. As the plaque progresses, there is central clearing with graduated, elevated edges, an appearance likened to a sports stadium. Ulcerative lesions are a less common cutaneous presentation.

***22. Are immunosuppressed patients at increased risk of disseminated disease with blastomycosis?***

Blastomycosis behaves as an opportunistic infection in the immunosuppressed host much less commonly than other deep fungal infections. There are, however, several reports of disseminated blastomycosis in acquired immunodeficiency syndrome patients, organ transplant recipients, diabetic patients, and patients receiving glucocorticosteroids and chemotherapy.

***23. What is the treatment of blastomycosis?***

Itraconazole is the treatment of choice for mild to moderate disease. Amphotericin B is the preferred treatment of life-threatening disease, central nervous system involvement, and immunocompromised and pregnant patients.

***24. Where is histoplasmosis endemic?***

Histoplasmosis is caused by *Histoplasma capsulatum,* an environmental saprophyte. It is endemic in the Midwestern and south central United States, where 80% of the population is skin test positive. It does occur in other parts of the world, but it is not found in Europe. Soil infected with excreta from chickens, pigeons, blackbirds, starlings, and bats is inhaled, leading to a pulmonary infection. Rarely, primary cutaneous disease is contracted from traumatic inoculation.

***25. What factors are necessary for production of the disease histoplasmosis?***

The two most important factors are the number of organisms inhaled and immune status of the host. Only 1% of patients exposed to a small inoculum develop symptomatic disease; in contrast, 50% to 100% of persons exposed to a heavy inoculum develop symptoms.

***26. Discuss the clinical manifestations of histoplasmosis.***

Most patients with symptoms develop a flulike acute pulmonary illness characterized by fever, chills, headache, myalgias, chest pain, and nonproductive cough. Progressive disseminated histoplasmosis occurs in 1 of 2000 acute infections. High-risk groups for disseminated disease include patients with impaired cellular immunity such as HIV infection, lymphoma, or leukemia, and also infants and the elderly. Rarely, a primary cutaneous form is seen following direct inoculation into the skin.

***27. Describe the three different patterns of disseminated histoplasmosis (acute, subacute, and chronic).***

The acute syndrome generally occurs in immunosuppressed patients and is characterized by fever, hepatosplenomegaly, and pancytopenia, with 18% developing **mucocutaneous ulcers**. Hilar or mediastinal lymphadenopathy and focal or patchy infiltrates are the hallmarks of the subacute form, which occurs over weeks to months. Chronic disseminated histoplasmosis is characterized by involvement of the bone marrow, gastrointestinal tract, spleen, adrenals, and central nervous system (CNS); 67% have **painful ulcerations on the tongue, buccal mucosa, gingiva, or larynx** (Fig. 31-7). The treatment of choice is itraconazole and, for severe diseases and immunosuppressed patients, amphotericin.

***28. Are there any other cutaneous manifestations of histoplasmosis?***

Erythema nodosum and, less commonly, erythema multiforme may be seen in histoplasmosis, coccidioidomycosis, and, rarely, blastomycosis. These cutaneous hypersensitivity reactions are generally associated with a good prognosis.

***29. Where is coccidioidomycosis endemic?***

Coccidioidomycosis, also called San Joaquin Valley fever, is caused by *Coccidioides immitis*. It is a dimorphic fungus found in the soil of arid and semiarid regions. This organism is endemic in southern California, Arizona, New Mexico, southwestern Texas, northern Mexico, and Central and South America (Fig. 31-8).

***30. What are the clinical manifestations of coccidioidomycosis?***

Primary pulmonary infection is asymptomatic in 50% of patients. In 40%, patients present with a mild flulike illness or pneumonia. Hematogenous dissemination occurs in 1% to 5% of patients.

Risk factors for dissemination and fatal disease include male sex, pregnancy, immunocompromised status, and race (in order of decreasing risk by race: Filipino, black, and white). Coccidioidomycosis is considered an AIDS-defining illness. The most common sites of extrapulmonary disease include the skin, lymph nodes, bones/joints, and central nervous system (meninges).

***31. What are the skin findings in coccidioidomycosis?***

Cutaneous lesions of disseminated coccidioidomycosis are protean. Warty papules, plaques, or nodules are the most characteristic (Fig. 31-9). Cellulitis, abscesses, and draining sinus tracts also may occur. Rarely, cutaneous lesions can be from primary cutaneous inoculation. Erythema nodosum is the most common reactive manifestation and indicates a robust cell-mediated immune response. Other reactive patterns include generalized morbilliform, papular, targetoid or urticarial exanthem, interstitial granulomatous dermatitis, and Sweet's syndrome.

***32. Where is paracoccidioidomycosis endemic?***

Paracoccidioidomycosis (South American blastomycosis) previously has been thought to be restricted to Latin America, especially Brazil. There have been reports of cases outside this area. The disease is confined to humid tropical and subtropical forests. *Paracoccidioides brasiliensis* is the causative dimorphic fungus.

***33. Why is paracoccidioidomycosis more common in men?***

Paracoccidioidomycosis is most common in adult men between the ages of 30 and 60 years. Skin testing indicates that the rate of infection is equal among the sexes. However, clinical disease is more common in men, with a male : female ratio of 15 : 1. It has been shown that this sex

difference is due to the inhibitory action of estrogens on the mycelium to yeast transformation necessary for infectivity.

***34. What is the most common presenting complaint of paracoccidioidomycosis?***

Painful mucosal ulcerations involving the mouth and nose are the most common findings. Patients may also have enlarged cervical lymph nodes and verrucous, crusted, edematous facial lesions. The lung is the primary site of infection; however, respiratory complaints are the least common presenting symptom.

***35. Which organism is responsible for penicilliosis?***

Penicilliosis is caused by the dimorphic fungus *Penicillium marneffei*. It is inhaled into the lungs and causes disease in both immunocompetent and immunocompromised patients, with a predilection to the latter.

***36. Where is penicilliosis endemic?***

Penicilliosis is endemic in Southeast Asia and southern China. The increase in HIV-infected individuals in these areas has led to the emergence of this organism as a cause of infection.

***37. How does penicilliosis present clinically?***

The most common clinical presentation is subacute with weeks of intermittent fevers, headache, marked weight loss, and anemia. AIDS patients have an increased frequency of septicemia and mucocutaneous lesions. Skin lesions are a common manifestation of disseminated disease and are usually found on the upper body. Abscesses, subcutaneous nodules, and reactive skin diseases such as Sweet's syndrome are seen in non-HIV–infected individuals. Cutaneous lesions are more diversified in the HIV patients and include molluscum contagiosum–like papules,

pustules, acneiform, and morbilliform eruptions. Delay in treatment is associated with 100% mortality in all patients. Biopsy and culture are used for diagnosis. Treatment options include itraconazole or amphotericin B in severe cases.

***38. What is a parasitized histiocyte?***

It is a macrophage (histiocyte) hosting an infection. Several species of bacteria and fungi infect and proliferate and actually thrive within the cytoplasm of macrophages rather than being killed by the macrophage (Table 31-2).

**Opportunistic Fungal Infections**

***39. Define opportunistic infection.***

Opportunistic infections are caused by organisms that typically produce disease in a host with lowered resistance. The four discussed in this chapter are cryptococcosis, aspergillosis, fusariosis, and mucormycosis.

***40. What are the common fungal pathogens in HIV infection?***

*Candida* and *Cryptococcus* species are the most common fungal infections in HIV-infected patients. See Table 31-3 for other fungal pathogens and their most frequent clinical presentations.

***41. Discuss the fungal infections seen in organ transplant recipients.***

Organ transplant recipients are at increased risk of localized and disseminated disease from dermatophytes, yeast (candidiasis, *Malassezia,* cryptococcosis, *Trichosporon*), dimorphic organisms (histoplasmosis, coccidioidomycosis, blastomycosis), and nondermatophyte molds (aspergillosis, fusariosis, mucormycosis). Skin manifestations due to *Candida* spp., *Aspergillus*

spp., dematiaceous fungi, and *Pityrosporum* typically occur shortly after transplantation. Cryptococcosis occurs 6 months or later after transplantation, and the endemic dimorphic fungi can cause disease any time following transplantation. Emerging mold pathogens in the transplant patients have included *Aspergillus fumigatus*, *Fusarium, Scedosporium,* and Zygomycetes (e.g., Rhizopus, Mucor, Rhizomucor).

***42. What causes cryptococcosis?***

Cryptococcosis is caused by *Cryptococcus neoformans,* a ubiquitous encapsulated yeast found in soil worldwide. Several strains are associated with pigeon and other avian excreta, and another strain is associated with eucalyptus trees.

***43. Discuss the important epidemiologic factors of cryptococcosis.***

During the pre-AIDS era (prior to 1980), cryptococcal infections were infrequent and about 50% occurred in patients with lymphoreticular malignancies. Cryptococcosis is rare in immunocompetent patients, and patients at risk are those with impaired cellular immunity (advanced HIV patients, organ transplants, lymphoreticular malignancies, patients receiving corticosteroid therapy). The incidence of cryptococcosis is inversely proportional to the CD4 lymphocyte count. The prevalence in patients infected with HIV has declined with aggressive antiretroviral therapy. The mortality rate of untreated disseminated disease is 70% to 80%.

***44. How is an infection with cryptococcosis acquired?***

Infection occurs primarily from inhalation of the organism leading to a primary lung infection. Immunocompetent patients generally present with a mild pulmonary infection. Disseminated disease via the hematogenous route occurs in 10% to 15% of immunosuppressed patients, with a predilection for the meninges. **It is the leading cause of fungal meningitis.** Other organs

involved include the skin (10% to 20%), eye, bone, and prostate. There are a few rare reports of primary inoculation cutaneous disease, which manifests itself as a solitary papule/nodule. However, cutaneous disease is generally indicative of disseminated disease and a poor prognosis.

***45. What are the cutaneous manifestations of disseminated cryptococcosis?***

Cryptococcosis is a great imitator of a wide variety of cutaneous diseases. These include molluscum contagiosum–like lesions (Fig. 31-10), Kaposi sarcoma–like lesions, pyoderma gangrenosum–like lesions, herpetiform lesions, cellulitis, ulcers, subcutaneous nodules, and palpable purpura. Lesions are most commonly found on the head, neck, and genitals, but can be found anywhere. Cutaneous lesions are found in 10% to 20% of HIV-infected patients. Histologic features are characteristic with periodic acid–Schiff stain with diastase demonstrating budding yeast surrounded by a clear space representing the capsule (Fig. 31-11).

***46. What patient population is at increased risk of aspergillosis?***

Neutropenia and corticosteroid therapy, especially when combined, are the two most important risk factors for aspergillosis. Solid organ and bone marrow transplant recipients, and leukemic patients, in particular, are at high risk. Other at-risk patients include HIV-infected individuals, patients on broad-spectrum antibiotics, and patients on immunosuppression therapy.

***47. How common are cutaneous lesions in aspergillosis?***

*Aspergillus* species are ubiquitous saprophytes in the air, soil, and decaying vegetation. It is primarily a respiratory pathogen, with the lungs and sinuses as the major sites of infection. Disseminated disease occurs in 30% of aspergillosis cases, and cutaneous lesions develop in fewer than 11%. There are several documented reports of primary invasive skin infections

occurring in neutropenic patients associated with intravenous catheters and adhesive tape contaminated with spores.

***48. Describe the cutaneous lesions in aspergillosis.***

Patients may have single or multiple lesions that begin as a well-circumscribed papule, which over several days enlarges into an ulcer with a necrotic base and surrounding erythematous halo (Fig. 31-12). The organism has a propensity to invade blood vessels, causing thrombosis and infarction. The skin lesions can be very destructive and extend into cartilage, bone, and fascial planes. Aspergillosis should be considered in the differential diagnosis of necrotizing lesions.

***49. What opportunistic fungus is clinically and histologically similar to Aspergillus?***

Patients with prolonged neutropenia, especially leukemia patients, are susceptible to *Fusarium* infections. In this patient population, *Fusarium* species are the second most common pathogenic mold. *Fusarium* is a filamentous mold found in soil and plants. Inhalation into the lungs is the primary route of infection, although primary cutaneous infection from indwelling catheters may occur. The lung is the usual site of infection; however, 75% of patients have hematogenous spread with a predilection for the skin and sinuses. The cutaneous lesions caused by *Fusarium* are similar to aspergillosis. Histologically, the two are identical (septate hyphae with acute angle branching). The treatment of choice is amphotericin B and the mortality rate is 50% to 80%.

***50. What are the most important predisposing factors for acquiring mucormycosis?***

Approximately one third of patients have diabetes, and diabetic patients in ketoacidosis are at especially high risk. Other reported associations include malnutrition, uremia, neutropenia, hematologic malignancies, corticosteroid therapy, burns, antibiotic therapy, neonatal prematurity, iron-overload syndromes, deferoxamine therapy, and HIV-positive patients with a

history of IV drug use. Neutrophils are the predominant component of host defense. Mucormycosis is caused by rapidly growing molds from several genera, including *Apophysomyces, Mucor, Rhizopus, Absidia,* and *Rhizomucor*. These organisms are ubiquitous in decaying vegetation, fruit, and bread.

***51. Can mucormycosis be acquired from contaminated dressings?***

Yes. Primary cutaneous mucormycosis can occur when the spores are directly inoculated into abraded skin. In the 1970s, there was a nationwide epidemic associated with contaminated elastic dressings. Patients presented with a cellulitis under the covered areas. Primary cutaneous mucormycosis has also been reported from gardening, intramuscular injections, intravenous lines, needle-sticks, arthropod bites, automobile accidents, and burns. Cutaneous disease accounts for approximately 10% of reported cases and can also be from hematologic spread (Fig. 31-13).

***52. What is the treatment of mucormycosis?***

The treatment of mucormycosis is multimodal and includes rapid diagnosis in conjunction with correction of any underlying diseases. Biopsy sample of necrotic tissue demonstrates thick, nonseptate hyphae branching at right angles. The microbiology lab should be alerted if mucormycosis is suspected, as gentle tissue handling is paramount to successful culture growth. Cultures are only positive in one third of cases. The treatment of choice is amphotericin B, along with aggressive surgical debridement of necrotic tissue in order to minimize mortality.

***53. For what fungal infections might patients on biologic therapies be at risk?***

Patients on tumor necrosis factor-α antagonists most commonly are at risk for histoplasmosis, candidiasis, and aspergillosis. There may be a different degree of risk with each of the agents—infliximab creating a higher risk than etanercept or adalimumab. In endemic areas, patients are also at risk for primary or reactivation of latent coccidioidomycosis. Close monitoring of current and past residents of endemic areas is indicated.

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**Figure 31-1.** Sporotrichosis. **A,** Linear lesions secondary to a cat scratch. **B,** Erythematous, crusted, ulcerated nodule in a lymphocutaneous pattern. (Courtesy James E. Fitzpatrick, MD.)

**Figure 31-2.** Chromomycosis. Diagnostic golden-brown, yeastlike fungi (Medlar bodies) within a multinucleated foreign body giant cell. (Courtesy James E. Fitzpatrick, MD.)

**Figure 31-3.** Chromomycosis. Cauliflower-like nodules and tumors on the foot and ankle with edema. (Courtesy James E. Fitzpatrick, MD.)

**Figure 31-4.** Madura foot. Swelling and deformity of the foot and ankle with purulent drainage and fistula formation.

**Figure 31-5.** Blastomycosis. Areas depicted in yellow represent the areas reporting the most cases of blastomycosis. (Courtesy Fitzsimons Army Medical Center teaching files.)

**Figure 31-6.** Blastomycosis. Classic verrucous plaques located on the forehead and eyelid. (Courtesy teaching files of Fitzsimons Army Medical Center.)

**Figure 31-7.** Histoplasmosis. Oral ulcerations in an HIV-infected patient. Histoplasmosis more commonly affects the oral mucosa than the skin. (Courtesy James E. Fitzpatrick, MD.)

**Figure 31-8.** Coccidioidomycosis. Areas depicted in red represent the regions reporting the most cases of coccidioidomycosis. (Courtesy Fitzsimons Army Medical Center teaching files.)

**Figure 31-9.** Disseminated coccidioidomycosis. Discrete verrucous papules, plaques, and nodules. (Courtesy James E. Fitzpatrick, MD.)

**Figure 31-10.** Disseminated cryptococcosis. Multiple papules and nodules that resemble molluscum contagiosum. (Courtesy James E. Fitzpatrick, MD.)

**Figure 31-11.** Cryptococcosis. Periodic acid–Schiff stain with diastase demonstrating budding yeast surrounded by a clear space representing the capsule. (Courtesy Fitzsimons Army Medical Center teaching files.)

**Figure 31-12.** Fatal case of disseminated aspergillosis in an immunocompromised patient. (Courtesy Fitzsimons Army Medical Center teaching files.)

**Figure 31-13.** Cutaneous mucormycosis due to Rhizopus at the site of an intravenous line. (Courtesy Joanna Burch Collection.)

**Table 31-1. The Deep Fungal Infections**

| SUBCUTANEOUS FUNGAL INFECTIONS | SYSTEMIC OR RESPIRATORY FUNGAL INFECTIONS | OPPORTUNISTIC FUNGAL INFECTIONS |
|---|---|---|
| Sporotrichosis<br>Phaeohyphomycosis<br>Chromomycosis (chromoblastomycosis)<br>Mycetoma (Madura foot)<br>Lobomycosis<br>Rhinosporidiosis<br>Zygomycosis | Blastomycosis<br>Histoplasmosis<br>Coccidioidomycosis<br>Paracoccidioidomycosis | Cryptococcosis<br>Aspergillosis<br>Fusariosis<br>Mucormycosis<br>Penicilliosis |

**Table 31-2. Organisms That Parasitize Histiocytes Mnemonic**

| | |
|---|---|
| Rare | Rhinoscleroma |
| Lesions | Leishmaniasis |
| Try | Trypanosomiasis |
| To | Toxoplasmosis |
| Grow in | Granuloma inguinale |
| Parasitized | Penicilliosis |
| Histiocytes | Histoplasmosis |

**Table 31-3. Fungal Pathogens in HIV Infection**

| **ORGANISM** | **CLINICAL FEATURES** |
|---|---|
| *Candida albicans* | Thrush, vaginal, and esophageal candidiasis |
| *Cryptococcus neoformans* | Pulmonary and disseminated disease, meningitis, skin, eye, prostate |
| *Histoplasma capsulatum* | Disseminated disease with fever, weight loss, and predilection for reticuloendothelial system, adrenal glands, and CNS |
| *Coccidioides immitis* | Disseminated and pulmonary disease. Predilection for skin, lymph nodes, bones/joints, and CNS |
| *Blastomyces dermatitidis* | Disseminated and pulmonary disease. Predilection for lung, skin, bone, CNS, and prostate |
| *Aspergillus fumigatus* | Disseminated and pulmonary disease |
| *Penicillium marneffei* | Disseminated disease with fever, anemia, weight loss. Mucocutaneous lesions are common |
| *Sporotrichosis schenckii* | Disseminated disease. Sites of predilection: joints/bones, eyes, and meninges |