Emerging infectious diseases with cutaneous manifestations

Fungal, helminthic, protozoan and ectoparasitic infections

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Learning objectives
After completing this learning activity, the participant should be able to describe the cutaneous manifestations of emerging fungal, helminth, protozoan, and ectoparasite infections and identify appropriate therapy for case studies of emerging fungal, helminth, protozoan, and ectoparasite infections with cutaneous manifestations.

Disclosures
Editors
The editors involved with this CME activity and all content validation/peer reviewers of the journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Authors
The authors involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Planners
The planners involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s). The editorial and education staff involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Given increased international travel, immigration, changing climate conditions, and the increased incidence of iatrogenic immunosuppression, fungal, protozoan, helminthic, and ectoparasitic infections that were once uncommon are being seeing more frequently in the Western hemisphere. However, the diagnosis and management of these infections is fraught with a lack of consistency because there is a dearth of dermatology literature on the cutaneous manifestations of these infections. In addition, delays in the diagnosis and treatment of these diseases can lead to significant patient morbidity and mortality. We review the epidemiology, cutaneous manifestations, diagnostic modalities, and treatment options for emerging fungal, protozoan, helminthic, and ectoparasitic infections. It should be noted, however, that throughout this review we cite statistics documenting their increased incidence to back-up these infections as emerging, and although some of the diagnoses are clinical, others rely on newer laboratory tests, and the possibility exists that the increased incidence could be caused by better detection methods. (J Am Acad Dermatol 2016;75:19-30.)

Key words: balamuthia; Chagas disease; cysticercosis; emerging infections; fusariosis; leishmaniasis; myiasis; phaeohyphomycosis; toxocariasis; zygomycosis.

Although many of the fungal, protozoan, helminthic, and ectoparasitic infections we highlight in this article were once thought to primarily affect individuals in developing countries, these infections are also present in the United States and Europe. Because of increased travel, globalization, immunosuppressive drugs, and immigration from endemic areas, the number of cases is increasing. We highlight some of these emerging diseases with which dermatologists should be

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Funding sources: None.

Conflicts of interest: None declared.
Accepted for publication April 12, 2016.

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0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2016.04.032
Date of release: July 2016
Expiration date: July 2019

Abbreviations used:

BAE: *Balamuthia* amoebic encephalitis
CD: Chagas disease
CDC: Centers for Disease Control and Prevention
CL: cutaneous leishmaniasis
CT: computed tomography
ELISA: enzyme-linked immunosorbent assay
PCR: polymerase chain reaction
PHM: phaeohyphomycosis
TES: *Toxocara* excretory–secretory

particularly familiar in order to minimize the risk they pose to public health (Table I).

EMERGING FUNGAL INFECTIONS

Zygomycosis

Key points

- **Most commonly caused by *Rhizopus* spp**
- **Increasingly seen in patients who have undergone hematopoietic stem cell transplants**
- **Presents as necrotic plaques and darkly colored nodules**

Zygomycosis is caused by fungi from the genera *Rhizopus* (most common), *Lichtheimia*, and *Mucor*.[1] The spores of these fungi are ubiquitous in nature and can be acquired most commonly by direct inoculation and also from ingestion or inhalation.[2] Although zygomycosis is rare, the incidence in patients who have undergone hematopoietic stem cell transplants (HSCTs) is increasing. Data from the Transplant-Associated Infection Surveillance Network in the United States shows an increased annual incidence of zygomycosis in HSCT patients from 1.7 per 1000 patients in 2001 to 6.2 per 1000 patients in 2004.[3] Similar increases have been noted in Europe, with 1 study in France showing an increase from 0.7 per million in 1997 to 1.2 per million in 2006.[4]

The major risk factors for zygomycosis after HSCT are steroids, diabetes, iron overload, neutropenia, malnutrition, and severe graft-versus-host disease.[4,5] Prophylaxis with antifungal agents without activity against Zygomycetes, such as voriconazole, is implicated in breakthrough infection.[1] Many infections occur >100 days after HSCT,[3] which some hypothesize may be an unintended result of protocol-driven posttransplant antifungal prophylaxis with voriconazole.[6] Zygomycosis has 5 classic clinical presentations: rhinocerebral, pulmonary, gastrointestinal, disseminated, and cutaneous. The cutaneous manifestations and course of zygomycosis are varied. The disease can have a gradual onset with slow progression or can be fulminant. Cutaneous findings are polymorphous and include dark pink violaceous or yellow nodules, black discoloration with surrounding edema, tinea corporis–like lesions, targetoid plaques, "fuzzy discharge" at the borders of a wound, gangrene, necrotizing fasciitis, and cutaneous abscesses (Fig 1). Lesions often have a typically rapid evolution to a necrotic eschar caused by vascular invasion and infarction.[7] The arms and legs are more commonly involved,[2] and lesions have a predilection for occluded or traumatized locations, such as catheter placement sites.

Cutaneous zygomycosis can be diagnosed via fungal culture, histopathology, and direct observation of characteristic hyphae on microscopy. Testing for Zygomycetes DNA using a polymerase chain reaction (PCR) study is also available. Prompt treatment of zygomycosis, often initiated empirically, is essential. In localized disease, surgical debridement and systemic antifungals are recommended. Disseminated infection has a poor prognosis. Antifungal drugs that are approved for the treatment of zygomycosis are amphotericin B and isavuconazonium sulfate, the latter of which was approved in 2015.

Fusariosis

Key points

- **Second most common mold infection in immunocompromised patients**
- **Presents as erythematous subcutaneous nodules and tender red or gray papules or macules**
- **Treatment consists of surgical debridement and amphotericin B or voriconazole**

Fusariosis causes a broad spectrum of infections in humans, particularly in immunocompromised patients, such as those with hematologic malignancies and in patients who have undergone HSCT. The introduction of fluconazole as standard prophylaxis in the setting of HSCT has led to a decreased incidence of yeast infections in this population, namely *Candida* species, and an increase in mold infections (against which fluconazole has no use). In addition, the increased incidence can also be attributed to increasing numbers of HSCT, solid organ transplantation, and newer and more potent chemotherapeutic agents that have dramatically increased the pool of immunocompromised patients.[8-10] *Fusarium* spp are now the second most common cause of mold infections, behind only *Aspergillus* spp.[8] Many authors contend that since the first case in 1973, the incidence of invasive fusariosis has dramatically increased.[8-11] According