

Mycotic Infections

Prof. Dr. Adnan AL-Hamdani

Mycotic Infections

- **ORGANISM:**

- Genus/Species: There are a large number of different genera and species of fungi that cause human diseases. Only a few of these specific agents will be presented and discussed .

- **GENERAL CONCEPTS:**

- The fungi represent a diverse, heterogeneous group of eukaryotes. Most of these organisms are plant pathogens and relatively few cause disease in humans.
- In nature, fungi generally grow by secreting enzymes that digest tissues but some are actually predacious.
- The growth of the fungi generally involves two phases; **vegetative** and **reproductive**.

- **In the vegetative phase**, the cells are **haploid** and divide **mitotically**. Most fungi exist as **molds with hyphae** but some fungi exist as **unicellular yeast cells**. Some fungi can change their morphology and are termed **dimorphic**. For example, *Candida* is found in the yeast form at 37°C but changes to the mold form at 25°C.
- In the **reproductive phase**, fungi may undergo either **asexual or sexual reproduction**. **Asexual** reproduction involves the generation of **spores**; sexual reproduction requires specific cellular structures that are used for taxonomic differentiation.

The fungi are classified based on the characteristics of their **sexual phase.**

For the kingdom Fungi, there are two phyla; **Zygomycota** and **Dikaryomycota.**

The phylum Dikaryomycota is further divided into **two subphyla; Ascomycotina** and **Basidiomycotina.**

A third group of the fungi for which a sexual phase **has not been observed is termed Deuteromycotina.**

Group Representative Genera:

Phylum Zygomycota *Rhizopus, Absidia, Mucor*

Phylum Dikaryomycota

•Subphylum **Ascomycotina** *Trichophyton, Histoplasma, Blastomyces*

•Subphylum **Basidiomycotina** *Cryptococcus*

Form-class **Deuteromycotina** *Candida, Epidermophyton, Coccidioides*

DISTINCTIVE PROPERTIES

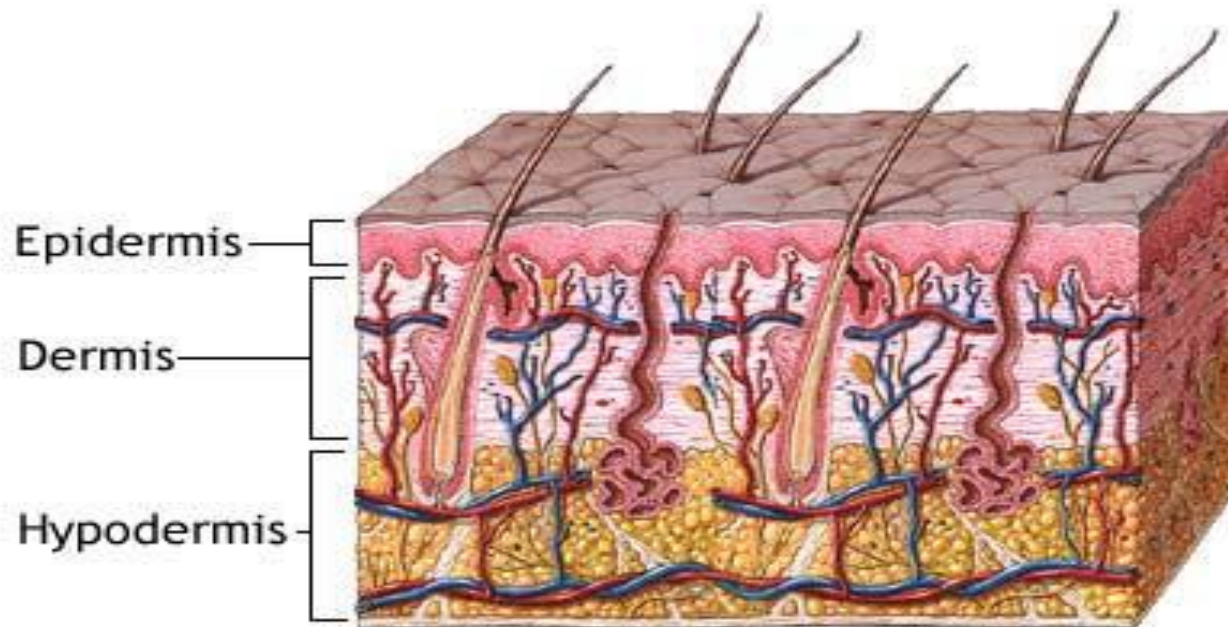
Mycotic infections are classified by the tissue levels that are colonized.

- **Superficial infections** are generally limited to the outer layers of the skin and hair.
 - **Cutaneous infections** are located deeper in the epidermis, hair and nails.
 - **Subcutaneous infections** involve the dermis, subcutaneous tissues and muscle.

In addition, mycotic infections may be **systemic**, generally originating in the lungs and other organs.

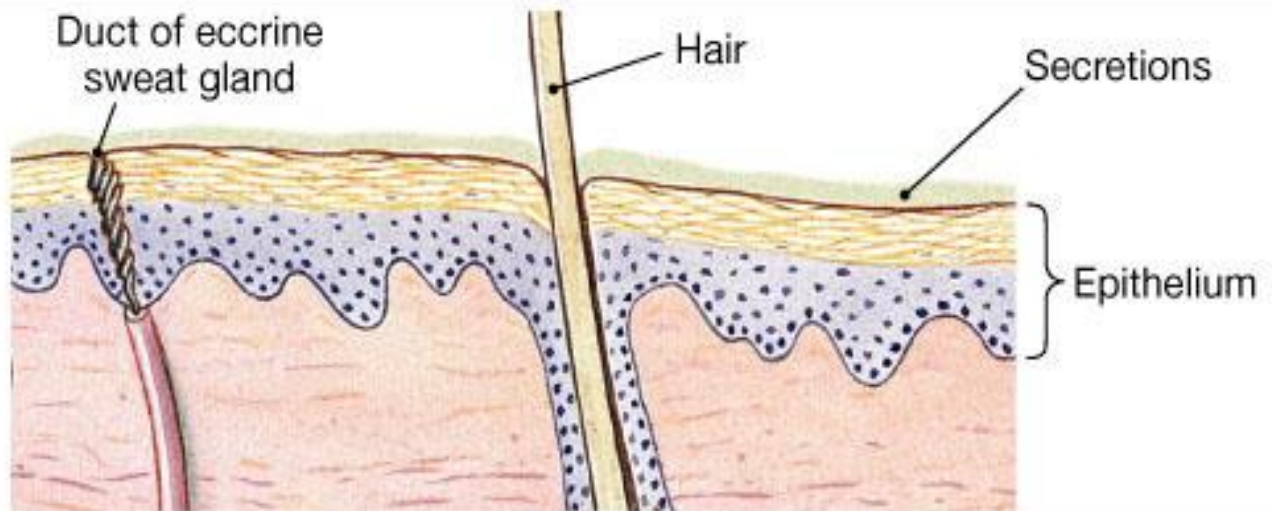
Finally, some mycoses are termed **opportunistic**, and these may involve a variety of body sites.

The following outlines these different types of mycotic infection, giving examples of representative agents.



PHYSICAL BARRIERS

Prevent approach of and deny access to pathogens



Superficial: Limited to outer layers of skin and hair.

Pityriasis versicolor (skin)

Tinea nigra (skin)

Black/white piedra (hair) Malassezia

Exophiala

Piedra/Trichosporum

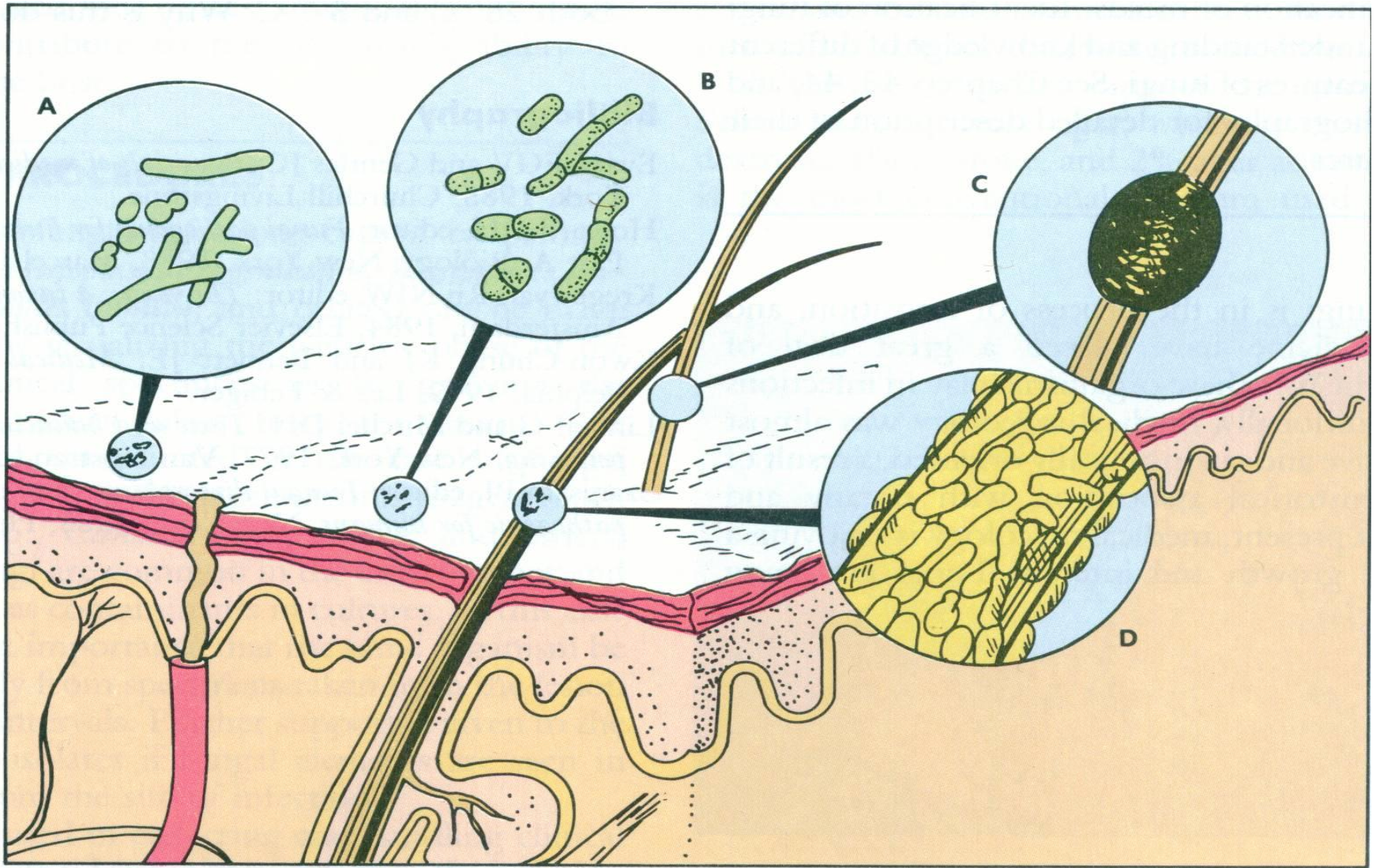


FIGURE 43-1 Schematic illustration of superficial fungal infection and tissue involvement. **A**, Pityriasis versicolor; **B**, tinea nigra; **C**, black piedra; **D**, white piedra.



FIGURE 43-2 Clinical presentation of pityriasis versicolor.

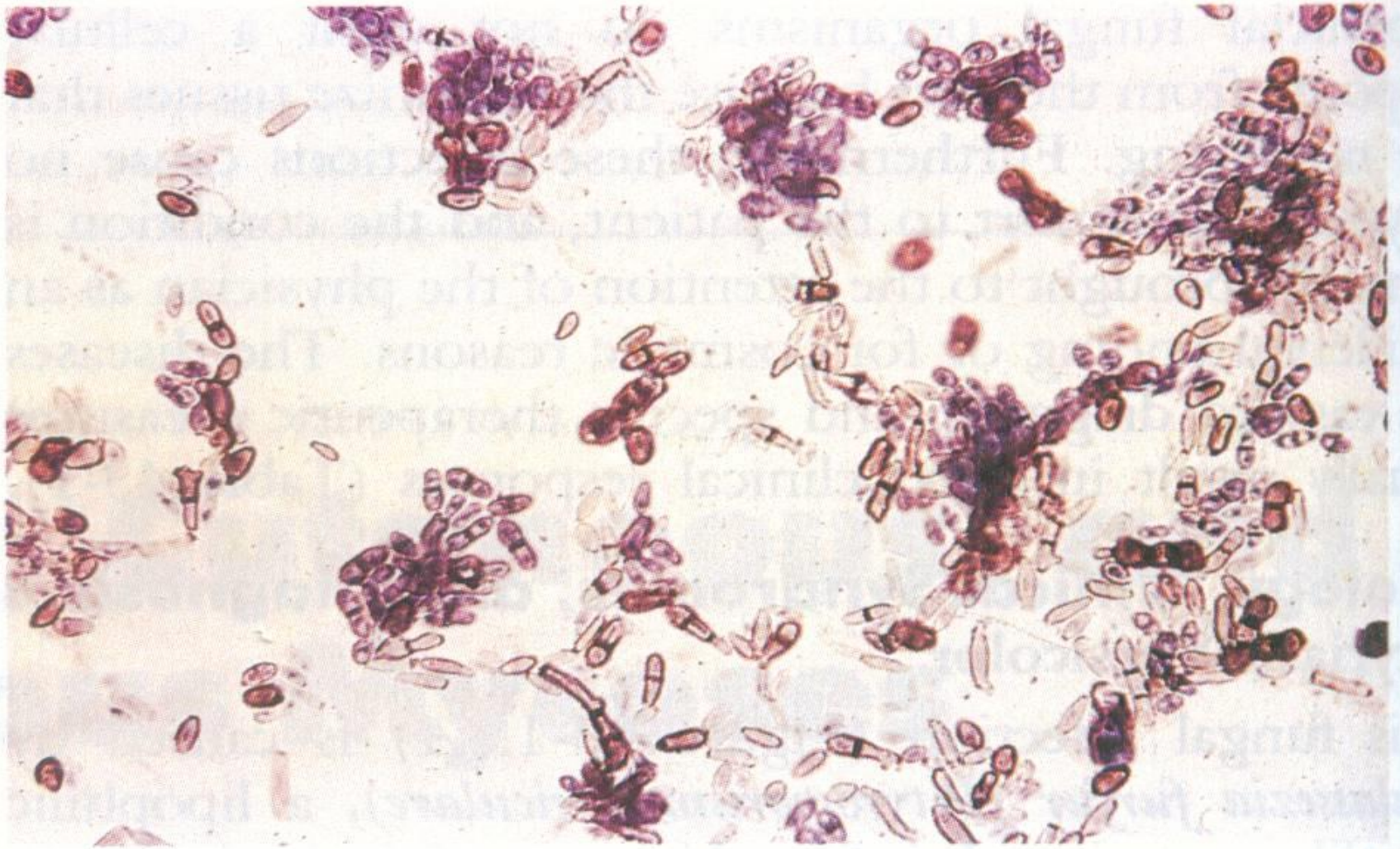


FIGURE 43-4 Yeastlike cells of *Exophiala werneckii*, the causative agent of tinea nigra.

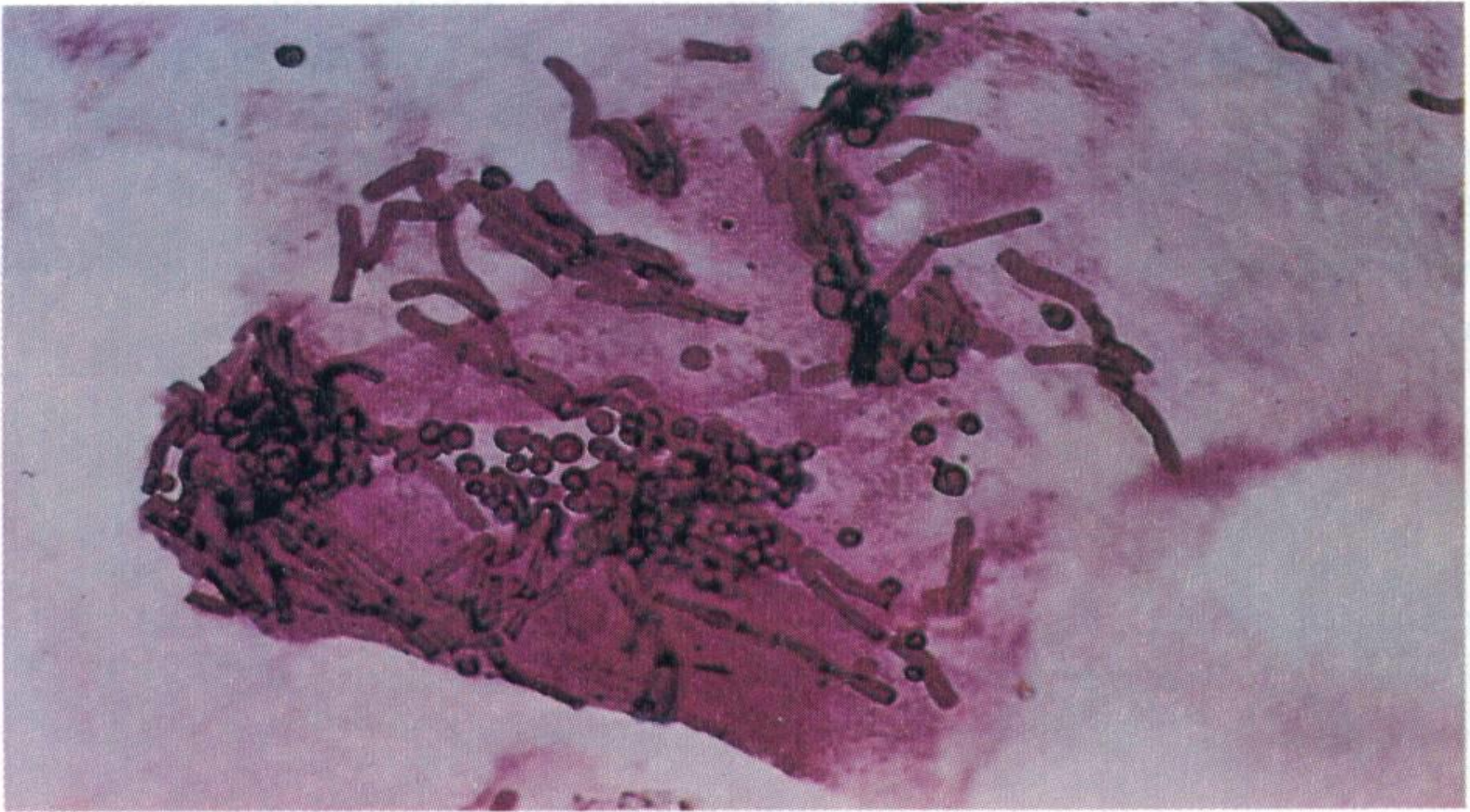


FIGURE 43-3 Skin scrapings stained with periodic-acid Schiff's stain showing typical yeastlike and hyphal fragments of *Malassezia furfur*, the etiological agent of pityriasis versicolor.

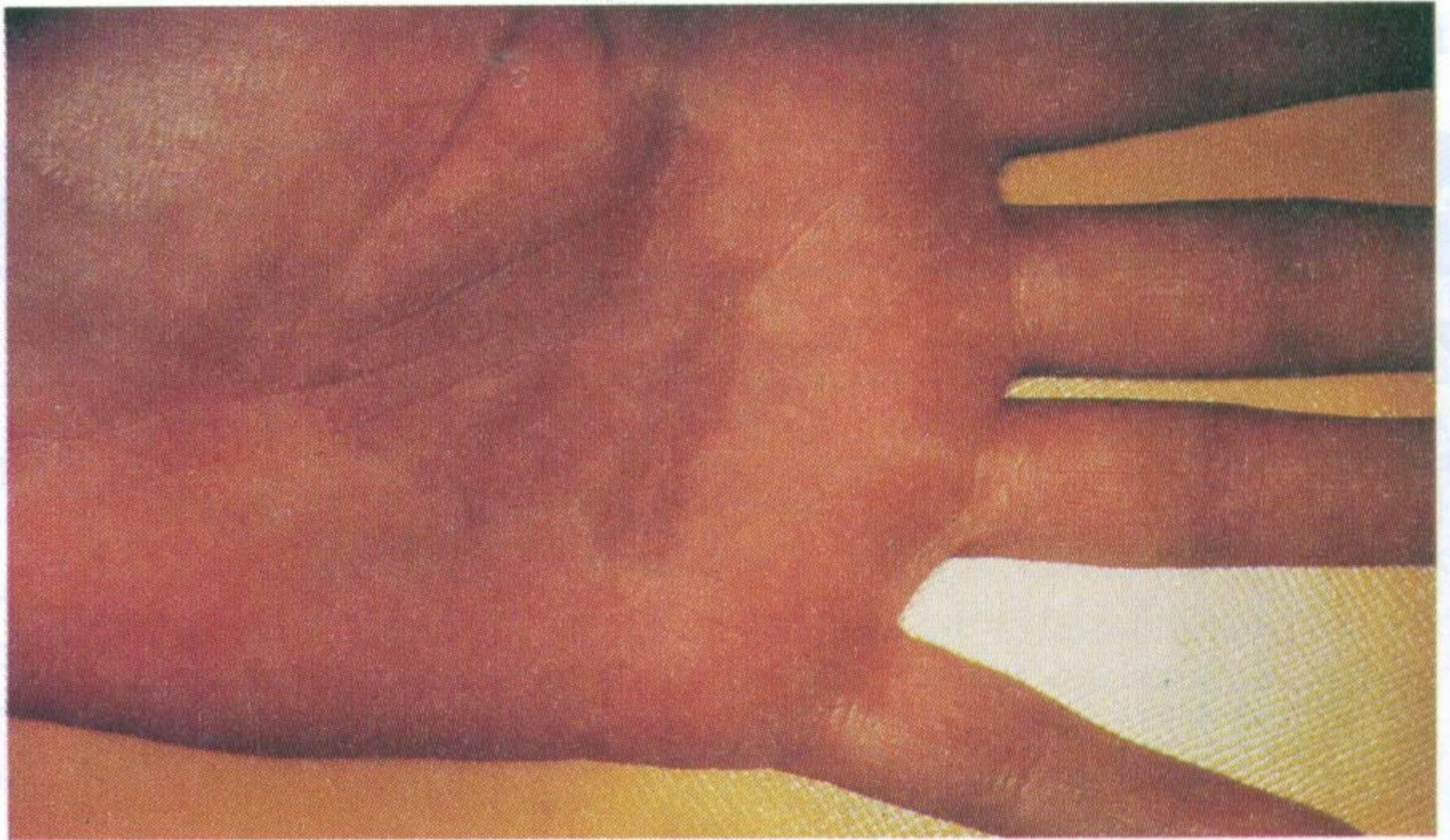


FIGURE 43-5 Clinical presentation of tinea nigra. Note dark pigmentation in the center of the palm.

Cutaneous: Involves deep epidermis and keratinized body areas (skin, hair, nails). Diseases are generally cosmetic, not life-threatening. Diseases of the skin are termed **Tinea**; Diseases of hair and nails are termed **Dermatophycoses**.

Trichophyton, Microsporum, Epidermophyton

Subcutaneous: Involves dermis, subcutaneous tissues and muscle.

Fungi are generally implanted in skin; fungal growth produces a lesion.

Lymphocutaneous sporotrichosis, Chromoblastomycosis

Eumycotic mycetoma

Sporothrix, Pseudallescheria

Many others

Systemic: Originate in lungs, phagocytosis by macrophages, spread to many organs.

Most primary infections are inapparent. Progression may produce pulmonary symptoms or ulcerative lesions. Host responses produce formation of fibrous tissue, granulomas and calcified lesions.

Representative organisms are dimorphic, except for *Cryptococcus*, which is a yeast.

Histoplasmosis: It may become endemic, most infections are **asymptomatic**.

Histoplasma capsulatus

Blastomycosis: Endemic and important veterinary problem

Blastomyces dermatitidis

Paracoccidioidomycosis: Endemic in Central and South America, primarily Brazil

Paracoccidioides braziliensis

Coccidioidomycosis: Endemic in Southwestern United States, *Coccidioides immitis*

Cryptococcosis: Worldwide distribution. Most common clinical presentation is meningitis.

Cryptococcus neoformans

Opportunistic: These organisms generally have a low potential for virulence but can produce severe disease involving a variety of body tissues.

Candidiasis, Aspergillosis, Zygomycosis

Candida albicans

Aspergillus species

Rhizopus species

PATHOGENESIS:

Mycotic disease is often a consequence of **predisposing factors** including age, stress or other pathologic conditions (e.g. cancer, diabetes, AIDS).

Only the dermatophytes (*Trichophyton*, *Microsporum*) and *Candida* are communicable from human to human.

The other agents are acquired from the environment (plants, soil, etc.).

Fungi generally **cause one of three distinct tissue responses**;

- chronic inflammation** (scarring, accumulation of lymphocytes)
- granulomatous inflammation** (collections of modified epithelial cells, lymphocytes)
- acute suppurative inflammation** (vascular congestion, exudation of plasma, accumulation of PMNs).

Some of the tissue responses may be due to **mycotoxins**, which are fungal metabolites that are toxic to the host. Some agents produce LPS-like endotoxins or hemolysins or steroid-like toxins that affect the nervous system. *Aspergillus* produces a toxin called **aflatoxin** that has a strong association with liver cancer. For example, in Thailand, where people generally consume about 25-times more aflatoxin in their diets, the incidence of cancer is about 18-fold greater. **Systemic mycoses** are generally **asymptomatic** but may have generalized symptoms including low grade fever, shaking chills, night sweats, malaise or appetite loss.

HOST DEFENSES:

Host defenses against the fungi include **nonspecific** and **specific** factors:

Nonspecific defenses include the skin (lipids, fatty acids, normal flora), internal factors (mucous membranes, ciliated cells, macrophages), blood components, temperature, genetic and hormonal factors. In other words, both physical and chemical factors and phagocytic defenses play major roles in prevention and control of mycotic disease.

Specific defenses include both **humoral** and **cell-mediated**.

The role of **humoral defenses** is somewhat controversial, since certain antibodies are not protective.

It is possible that high titers of certain antibodies actually suppress the cell mediated defenses. Nevertheless, some antibodies may be protective (e.g. antitoxins or opsonins).

Generally, however, the

cell-mediated defenses are probably more important.

Acquired resistance is

usually **T-cell mediated** and persons with compromised cell-mediated defenses generally show **more disseminated disease**

EPIDEMIOLOGY

Dermatophytes may be communicated from person to person by combs, towels, etc.

These infections (termed "tineas" when affecting the skin) include ringworm, athlete's foot, jock itch, etc.

Candida is a member of the normal vaginal flora; candidiasis is often associated with **diabetes**.

In some cases of mycosis, **occupation** seems an important contributor.

For example, *Sporothrix* is normally found in woody plants; hence, agricultural workers acquire disease more often.

Similarly, *Histoplasma* is often found in bird or bat excret; hence caves workers or persons involved in community clean up may acquire more often.

DIAGNOSIS

Clinical: For the dermatophytes, appearance of the lesions is usually diagnostic. For systemic mycoses, the epidemiology and symptomology are useful clues.

Laboratory: Treatment of skin scrapings with 10% potassium hydroxide can reveal hyphae or spores. Most fungi can be grown on Sabouraud's dextrose agar

but they are often very difficult to speciate. Some fungi show a yellow fluorescence under 365 nm ultraviolet light.

Skin testing for a delayed hypersensitivity response is useful for epidemiologic purposes but often not for diagnosis.

CONTROL

Sanitary: Control by sanitary means is difficult, but the incidence of communicable disease can be reduced by good hygiene.

Immunological: No vaccines are currently available.

Chemotherapeutic: Many antifungals are available but some are very toxic to the host and must be used with caution.

Topical powders and creams often contain tolnaftate or azole derivatives (miconazole, clotrimazole, econazole) and are useful against superficial dermatophytes.

Sporotrichosis may be treated using potassium iodide or AMB
Systemic infections are generally treated by AMB , 5- FC, miconazole, Fluconazole or ketoconazole.