Lecture PowerPoint to accompany

Foundations in Microbiology
Seventh Edition

Talaro

Chapter 22
The Fungi of Medical Importance

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.
22.1 Fungi as Infectious Agents

- Molds and yeasts are widely distributed in air, dust, fomites, and normal flora
- Humans are relatively resistant
- Fungi are relatively nonpathogenic
- Of the 100,000 fungal species, only 300 have been linked to disease in animals
- Fungi are the most common plant pathogens
- Human mycoses are caused by true fungal pathogens and opportunistic pathogens
### TABLE 22.1 Representative Fungal Pathogens, Degree of Pathogenicity, and Habitat

<table>
<thead>
<tr>
<th>Microbe</th>
<th>Disease/Infection*</th>
<th>Primary Habitat and Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I. Primary True Pathogens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Histoplasma capsulatum</em></td>
<td>Histoplasmosis</td>
<td>Soils high in bird guano; Ohio and Mississippi valleys of U.S.; Central and South America; Africa</td>
</tr>
<tr>
<td><em>Blastomyces dermatitidis</em></td>
<td>Blastomycosis</td>
<td>Presumably soils, but isolation has been difficult; southern Canada; Midwest, Southeast, Appalachia in U.S.; along drainage of major rivers</td>
</tr>
<tr>
<td><em>Coccidioides immitis</em></td>
<td>Coccidioidomycosis</td>
<td>Highly restricted to alkaline desert soils in southwestern U.S. (California, Arizona, Texas, and New Mexico)</td>
</tr>
<tr>
<td><em>Paracoccidioides brasiliensis</em></td>
<td>Paracoccidioidomycosis</td>
<td>Soils of rain forests in South America (Brazil, Colombia, Venezuela)</td>
</tr>
<tr>
<td><strong>II. Pathogens with Intermediate Virulence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Sporothrix schenckii</em></td>
<td>Sporotrichosis</td>
<td>In soil and decaying plant matter; widely distributed</td>
</tr>
<tr>
<td>Genera of dermatophytes (Microsporum, Trichophyton, Epidermophyton)</td>
<td>Dermatophytosis (various ringworms or tineas)</td>
<td>Human skin, animal hair, soil throughout the world</td>
</tr>
<tr>
<td><strong>III. Secondary Opportunistic Pathogens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Candida albicans</em></td>
<td>Candidiasis</td>
<td>Normal flora of human mouth, throat, intestine, vagina; also normal in other mammals, birds; ubiquitous</td>
</tr>
<tr>
<td><em>Aspergillus spp.</em></td>
<td>Aspergillosis</td>
<td>Soil, decaying vegetation, grains; common airborne contaminants; extremely pervasive in environment</td>
</tr>
<tr>
<td><em>Cryptococcus neoformans</em></td>
<td>Cryptococcosis</td>
<td>Pigeon roosts and other nesting sites (buildings, barns, trees); worldwide distribution</td>
</tr>
<tr>
<td><em>Pneumocystis (carinii) jiroveci</em></td>
<td><em>Pneumocystis pneumonia (PCP)</em></td>
<td>Upper respiratory tract of humans, animals</td>
</tr>
<tr>
<td>Genera in Mucorales (Rhizopus, Absidia, Mucor)</td>
<td>Mucormycosis</td>
<td>Soil, dust; very widespread in human habitation</td>
</tr>
</tbody>
</table>

*Specific myotic infections are usually named by adding -mycosis, -tasis, or -osis to the generic name of the pathogen.

**As a result of some recent DNA studies in the organism that causes *Pneumocystis pneumonia* (PCP), the name of the organism is in the process of being changed from *Pneumocystis carinii* to *Pneumocystis jiroveci*. Because this change in nomenclature has not been widely accepted, we refer to this organism as *Pneumocystis (carinii) jiroveci.*
• **True or primary** fungal pathogen can invade and grow in a healthy, noncompromised host.

• Most striking adaptation to survival and growth in the human host is the ability to switch from hyphal cells to yeast cells.

• **Thermal dimorphism** – grow as molds at 30°C and as yeasts at 37°C.
Figure 22.1 Thermal dimorphism

1. When fungal spores from the environment gain entrance to a warm-blooded animal, they germinate into yeasts and remain in this phase in the host.

2. Yeast cells leaving the animal host return to the environment and revert to the sporulating hyphal state. These conversions can be demonstrated on artificial media in the laboratory.
Emerging Fungal Pathogens

• Opportunistic fungal pathogen has little or no virulence; host defenses must be impaired
• Vary from superficial and colonization to potentially fatal systemic disease
• An emerging medical concern; account for 10% of all nosocomial infections
• Dermatophytes may be undergoing transformation into true pathogens
<table>
<thead>
<tr>
<th>Characteristic of Fungus/Disease</th>
<th>True Pathogenic Infections</th>
<th>Opportunistic Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degree of Virulence</td>
<td>Well-developed</td>
<td>Limited</td>
</tr>
<tr>
<td>Condition of Host</td>
<td>Resistance high or low</td>
<td>Resistance low</td>
</tr>
<tr>
<td>Primary Portal of Entry</td>
<td>Respiratory</td>
<td>Respiratory mucocutaneous</td>
</tr>
<tr>
<td>Nature of Infection</td>
<td>Usually primary pulmonary and systemic; often asymptomatic</td>
<td>Varies from superficial skin to pulmonary and systemic; usually symptomatic</td>
</tr>
<tr>
<td>Nature of Immunity</td>
<td>Well-developed, specific</td>
<td>Weak, short-lived</td>
</tr>
<tr>
<td>Infecting Form</td>
<td>Primarily conidial</td>
<td>Conidial or mycelial</td>
</tr>
<tr>
<td>Thermal Dimorphism</td>
<td>Highly characteristic</td>
<td>Absent</td>
</tr>
<tr>
<td>Habitat of Fungus</td>
<td>Soil</td>
<td>Varies from soil to flora of humans and animals</td>
</tr>
<tr>
<td>Geographic Location</td>
<td>Restricted to endemic regions</td>
<td>Distributed worldwide</td>
</tr>
<tr>
<td>Pathogen</td>
<td>Associated With</td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td><em>Candida</em></td>
<td>Antibiotic therapy, catheters, diabetes, corticosteroids,* immunosuppression**</td>
<td></td>
</tr>
<tr>
<td><em>Aspergillus</em></td>
<td>Leukemia, corticosteroids, tuberculosis, immunosuppression, IV drug abuse</td>
<td></td>
</tr>
<tr>
<td><em>Cryptococcus</em></td>
<td>Diabetes, tuberculosis, cancer, corticosteroids, immunosuppression</td>
<td></td>
</tr>
<tr>
<td><em>Zygomycota Species</em></td>
<td>Diabetes, cancer, corticosteroids, IV therapy, third-degree burns</td>
<td></td>
</tr>
</tbody>
</table>

*Anti-inflammatory drugs are often given for chronic lung diseases and to transplant patients to prevent rejection.

**Includes AIDS and genetic conditions that compromise host defenses.
Epidemiology of the Mycoses

• Most fungal pathogens do not require a host to complete their life cycles and infections are not communicable
• Dermaphytes and *Candida sp* naturally inhabit human body and are transmissible
• True fungal pathogens are distributed in a predictable geographical pattern – climate, soil
• Dermaphytoses most prevalent
• Cases go undiagnosed or misdiagnosed
Figure 22.2 Distribution of the four true fungal pathogens
Pathogenesis of the Fungi

• Portal of entry
  – Primary mycoses – respiratory portal; inhaled spores
  – Subcutaneous – inoculated skin; trauma
  – Cutaneous and superficial – contamination of skin surface

• Virulence factors – thermal dimorphism, toxin-like substances, capsules and adhesion factors, hydrolytic enzymes, inflammatory stimulants
• Antifungal defenses are the integrity of the barriers and respiratory cilia
• Most important defenses are cell-mediated immunity, phagocytosis, and inflammation
• Long-term immunity can only develop for some
Diagnosis of Mycotic Infections

• Diagnosis and identification require microscopic examination of stained specimens, culturing in selective and enriched media and specific biochemical and serological tests
Figure 22.3 Identifying fungal isolates

- **Sputum**
  - Digested to remove debris
  - Negative stain for capsule (fig. 22.24)
  - KOH mount (wet mount)
  - Special stains (fig. 22.11), Brighteners (fig. 22.4)
  - Grow animals
  - Culturing: Incubation for up to 8 weeks
  - Selective agar
    - Room temperature
      - 25°C or 30°C (fig. 22.6a,b)
    - Blood agar
      - 37°C
  - Demonstrate dimorphism
  - Inoculate animals

- **Blood, Cerebrospinal Fluid**
  - Concentrate
  - KOH mount
  - Negative stain for capsule
  - Direct stains of specimen
  - Isolation
  - 25°C or 30°C, selective media
  - 37°C, BHI/Blood agar
  - Stain colonies
  - Macroscopic morphology (fig. 22.11)
  - Microscopic morphology for pigment, texture (fig. 22.6)

- **Pus, Vaginal Secretions**
  - Use of Wood’s light on hair
  - Hot KOH wet mount
  - Highlight with brighteners; observe microscopically
  - Stain with periodic acid-Schiff (PAS)
  - Implant specimen on selective media; incubate for 4 weeks
  - Inoculate animals

- **Hair, Skin, Nails**
  - Implant onto media selective and differential for fungi
  - 25°C–37°C
  - Test for dimorphism (fig. 22.1)
  - Inspect microscopic morphology after staining

- **Tissue Biopsies, Punches**
  - Section
  - Grind
  - Digest
  - Perform histological stains
  - Implant onto media selective and differential for fungi

*Note: *Animal inoculation is performed only to help diagnose systemic mycoses when other methods are unavailable or indeterminant.

**Note:** Some yeasts, when incubated in serum for 2–4 hours, sprout tiny hyphal tubes called germ tubes.
Figure 22.4 Brighteners can amplify the presence of fungal elements
Control of Mycotic Infections

• Immunization is not usually effective
• Control involves intravenous amphotericin B, flucytosine, azoles, and nystatin
• In some cases surgical removal of damaged tissues
• Prevention limited to masks and protective clothing to reduce contact with spores
<table>
<thead>
<tr>
<th>Drug Target/Drug</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma Membrane</strong>&lt;br&gt;Polycenes</td>
<td>Disrupt the plasma membrane and cause leakage of the cytoplasm.</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>Amphotericin B is highly toxic but most effective for treating life-threatening infections.</td>
</tr>
<tr>
<td>Nystatin</td>
<td>Nystatin is too toxic for systemic use, but it can be used topically.</td>
</tr>
<tr>
<td><strong>Azoles</strong>&lt;br&gt;Imidazoles</td>
<td>Interfere with ergosterol synthesis, leading to defective cell membranes. Used to treat a variety of systemic and localized fungal infections.</td>
</tr>
<tr>
<td>Triazoles</td>
<td>Examples are fluconazole and itraconazole (Sporonox).</td>
</tr>
<tr>
<td><strong>Allylamines</strong>&lt;br&gt;Naftifine, terbinafine&lt;br&gt;(Lamisil)</td>
<td>Inhibit an enzyme in ergosterol synthesis. Administered topically to treat dermatophyte infections. Terbinafine can be taken orally.</td>
</tr>
<tr>
<td><strong>Cell Wall</strong>&lt;br&gt;Echinocandins&lt;br&gt;Caspofungin</td>
<td>Block the synthesis of a polysaccharide component of the cell wall in many pathogenic fungi.</td>
</tr>
<tr>
<td><strong>Cell Division</strong>&lt;br&gt;Griseofulvin</td>
<td>Used to treat skin and nail infections. Concentrates in the dead keratinized layers of the skin. Active only against fungi that invade keratinized cells.</td>
</tr>
<tr>
<td><strong>Nucleic Acid Synthesis</strong>&lt;br&gt;Flucytosine</td>
<td>Used for systemic yeast infections; inhibits an enzyme required for nucleic acid synthesis; not effective against most molds.</td>
</tr>
</tbody>
</table>
Organization of Fungal Disease

• Mycoses are presented according to type, level of infection, and degree of pathogenicity
  – True pathogens: systemic, cutaneous, and superficial mycoses
  – Opportunistic mycoses
Figure 22.5 Levels of invasion by fungal pathogens

(a) In systemic (deep) mycoses, the fungus disseminates from the lungs or other sites into the circulation. Fungemia leads to infection of the brain, kidneys, and other organs.

(b) The skin and its attendant structures provide many potential sites for invasion, including the scalp, smooth skin, hair, and mucous membranes. Differing depths of involvement are: superficial, consisting of extremely shallow epidermal colonizations; cutaneous, involving the stratum corneum and occasionally the upper dermis; and subcutaneous, occurring after a puncture wound has introduced the fungus deeper into the subcutaneous tissues.
22.2 Systemic Infections by True Pathogens

- Restricted to endemic regions of the world
- Infection occurs when matter containing conidia is disturbed
- Spores germinate in the lungs
- Infection can become systemic
- Spores may be inoculated into the skin
- All diseases result in immunity
Histoplasmosis: Ohio Valley Fever

- *Histoplasma capsulatum* – most common true pathogen; causes histoplasmosis
- Typically dimorphic
- Distributed worldwide, most prevalent in eastern and central regions of U.S.
- Grows in moist soil high in nitrogen content
- Inhaled conidia produce primary pulmonary infection that may progress to systemic involvement of a variety of organs and chronic lung disease
- Amphotericin B, ketoconazole
Figure 22.6 Dimorphic colonies of *Histoplasma capsulatum*
Figure 22.7 Events in *Histoplasma* infection and histoplasmosis
• *Coccidioides immitis* – causes coccidioidomycosis

• Distinctive morphology – blocklike arthroconidia in the free-living stage and spherules containing endospores in the lungs

• Lives in alkaline soils in semiarid, hot climates and is endemic to southwestern U.S.

• Arthrospores inhaled from dust, creates spherules, and can form nodules in the lungs

• Amphotericin B treatment
Figure 22.8 Events in *Coccidioides* infection

1. Digging in soil produces aerosol of arthrospores (inset).
2. Inhaled arthrospores establish a lung infection.
3. An arthrospore develops into a spherule that produces endospores; endospores are released in the lungs.
4. Immunocompetent persons effectively fight infection and return to health.
5. Compromised people can develop meningitis, osteomyelitis, and skin granulomas.
Figure 22.9 Disseminated coccidioidomycosis

Abscesses
Figure 22.10 Immunodiffusion test for coccidioidomycosis
Blastomyces Dermatitidis: North American Blastomycosis

- *Blastomyces dermatitidis* – causes blastomycosis
- Dimorphic
- Free-living species distributed in soil of a large section of the midwestern and southeastern U.S.
- Inhaled 10-100 conidia convert to yeasts and multiply in lungs
- Symptoms include cough and fever
- Chronic cutaneous, bone, and nervous system complications
- Amphotericin B
Figure 22.11 The dimorphic nature of *Blastomyces dermatitidis*
Figure 22.12 Cutaneous blastomycosis in the hand and wrist
Paracoccidioidomycosis

- *Paracoccidioides brasiliensis*
- Distributed in Central and South America
- Lung infection occurs through inhalation or inoculation of spores
- Systemic disease is not common
- Ketoconazole, amphotericin B, sulfa drugs
Figure 22.13 The morphology of *Paracoccidioides*
22.3 Subcutaneous Mycoses

• Subcutaneous mycoses: when fungi are transferred directly into traumatized skin, they can invade
• Most species in this group are greatly inhibited by higher temperatures of the blood and viscera
• Diseases are progressive
**Sporothrix Schenckii**

- Sporotrichosis (rose-gardener’s disease)
- Very common saprobic fungus that decomposes plant matter in soil
- Infects appendages and lungs
- Lymphocutaneous variety occurs when contaminated plant matter penetrates the skin and the pathogen forms a nodule, then spreads to nearby lymph nodes
Figure 22.14 The microscopic morphology of *Sporothrix schenckii*
Figure 22.15 Clinical appearance of lymphocutaneous sporotrichosis

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

© Everett S. Beneke/Visuals Unlimited
Chromoblastomycosis and Phaeohyphomycosis

• Chromoblastomycosis: A progressive subcutaneous mycosis characterized by highly visible verrucous lesions
  – Etiologic agents are soil saprobes with dark-pigmented mycelia and spores
  – *Fonsecaea pedrosoi, Phialophora verrucosa, Cladosporium carrionii*
  – Produce very large, thick, yeast-like bodies, sclerotic cells

• Phaeohyphomycosis differs in the causative species and the appearance of the infectious agent
Mycetoma

• When soil microbes are accidentally implanted into the skin
• Progressive, tumor-like disease of the hand or foot due to chronic fungal infection; may lead to loss of body part
• Caused by *Pseudallescheria* or *Madurella*
Figure 22.16 Mycetoma caused by *Madurella*
22.4 Cutaneous Mycoses

- Infections strictly confined to keratinized epidermis (skin, hair, nails) are called **dermatophytoses** – ringworm and tinea
- 39 species in the genera *Trichophyton*, *Microsporum*, *Epidermophyton*
- Closely related and morphologically similar
- Causative agent of ring worm varies case to case
The Dermatophyte Genera and Diseases

<table>
<thead>
<tr>
<th>Genus</th>
<th>Name of Disease</th>
<th>Principal Targets</th>
<th>How Transmitted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trichophyton</td>
<td>Ringworm of the scalp, body, beard, and nails</td>
<td>Hair, skin, nails</td>
<td>Human to human, animal to human</td>
</tr>
<tr>
<td>Microsporum</td>
<td>Ringworm of scalp</td>
<td>Scalp hair</td>
<td>Animal to human, soil to human, human to human</td>
</tr>
<tr>
<td></td>
<td>Ringworm of skin</td>
<td>Skin; not nails</td>
<td></td>
</tr>
<tr>
<td>Epidermophyton</td>
<td>Ringworm of the groin and nails</td>
<td>Skin, nails; not hair</td>
<td>Strictly human to human</td>
</tr>
</tbody>
</table>
• Natural reservoirs – humans, animals, and soil

• Hardiness of the dermatophyte spores, presence of abraded skin, and intimate contact promote infection

• Long infection period followed by localized inflammation and allergic reactions to fungal proteins
• Ringworm of scalp (tinea capitis) affects scalp and hair-bearing regions of head; hair may be lost
• Ringworm of beard (tinea barbae) affects the chin and beard of adult males; contracted mainly from animals
• Ringworm of body (tinea corporis) occurs as inflamed, red ring lesions anywhere on smooth skin
• Ringworm of groin (tinea cruris) “jock itch” affects groin and scrotal regions
• Ringworm of foot and hand (tinea pedis and tinea manuum) is spread by exposure to public surfaces; occurs between digits and on soles
• Ringworm of nails (tinea unguium) is a persistent colonization of the nails of the hands and feet that distorts the nail bed
• Treatment of dermatophytes includes topical antifungal agents – tolnaftate, miconazole applied for several weeks
• Lamisil or griseofulvin 1-2 years
Figure 22.18 Ringworm lesions
Figure 22.19
Ringworm of the extremities
22.5 Superficial Mycoses

- **Tinea versicolor** – caused by *Malassezia furfur*; elicits mild, chronic scaling, mottling of skin; also implicated in folliculitis, psoriasis, and seborrheic dermatitis

- **White piedra** – caused by *Trichosporon beigelii*; whitish or colored masses develop scalp, pubic, or axillary hair

- **Black piedra** – caused by *Piedraia hortae*; dark-brown to black gritty nodules, mainly on scalp hairs
Figure 22.21 Examples of superficial mycoses
22.6 Opportunistic Mycoses

• All have predisposing factors

  *Candida* – dominant opportunistic pathogen
  *Aspergillus* – accounts for most lung infections
  *Cryptococcus*
  *Alternaria*
  *Paecilomyces*
  *Fusarium*
  *Rhizopus*
  *Torulopsis*
Infections by *Candida*: Candidiasis

- *Candida albicans*
- Widespread yeast
- Infections can be short-lived, superficial skin irritations to overwhelming, fatal systemic diseases
- Budding cells of varying size that may form both elongate pseudohyphae and true hyphae
- Forms off-white, pasty colony with a yeasty odor
Candida Albicans

• Normal flora of oral cavity, genitalia, large intestine or skin of 20% of humans
• Account for 70% of nosocomial fungal infections
• Thrush – occurs as a thick, white, adherent growth on the mucous membranes of mouth and throat
• Vulvovaginal yeast infection – painful inflammatory condition of the female genital region that causes ulceration and discharge
• Cutaneous candidiasis – occurs in chronically moist areas of skin and in burn patients
Figure 22.22 Infections by *Candida albicans*
Diagnosis and Treatment

• Presumptive diagnosis made if budding yeast cells and pseudohyphae are found; germ tube
• Growth on selective, differential media differentiates *Candida* species
• Topical antifungals for superficial infections, amphotericin B and fluconazole for systemics
Figure 22.23 Detection of *Candida albicans*
Cryptococcosis and *Cryptococcus Neoformans*

- *Cryptococcus neoformans* causes cryptococcosis
- A widespread encapsulated yeast that inhabits soil around pigeon roosts
- Common infection of AIDS, cancer, or diabetes patients
- Infection of lungs leads to cough, fever, and lung nodules
- Dissemination to meninges and brain can cause severe neurological disturbance and death
Figure 22.25 Cryptococciosis
Diagnosis and Treatment

• Negative stain demonstrating encapsulated budding yeast
• Biochemical tests, serological testing
• Systemic infection requires amphotericin B and fluconazole
**Pneumocystis (Carinii) Jiroveci and Pneumocystis Pneumonia**

- A small, unicellular fungus that causes pneumonia (PCP), the most prominent opportunistic infection in AIDS patients.
- This pneumonia forms secretions in the lungs that block breathing and can be rapidly fatal if not controlled with medication.
- Pentamidine and cotrimoxazole.
Figure 22.26 *Pneumocystis (carinii) jiroveci*

Cyst, containing several boides
Aspergillosis: Diseases of the Genus Aspergillus

- Very common airborne soil fungus
- 600 species, 8 involved in human disease; *A. fumigatus* most commonly
- Serious opportunistic threat to AIDS, leukemia, and transplant patients
- Infection usually occurs in lungs – spores germinate in lungs and form fungal balls; can colonize sinuses, ear canals, eyelids, and conjunctiva
- Invasive aspergillosis can produce necrotic pneumonia, and infection of brain, heart, and other organs
- Amphotericin B and nystatin
Figure 22.27 Clinical aspects of aspergillosis
Figure 22.28 Microscopic appearance of *Aspergillus*

Conidial head  Hyphae

40 μm

© Image courtesy David Ellis, Adelaide Women's and Children's Hospital
Zygomycosis

• Zygomycota are extremely abundant saprobic fungi found in soil, water, organic debris, and food
• Genera most often involved are *Rhizopus, Absidia, and Mucor*
• Usually harmless air contaminants invade the membranes of the nose, eyes, heart, and brain of people with diabetes and malnutrition, with severe consequences
Figure 22.29 *Absidia corymbifera*
Miscellaneous Opportunists

• Any fungus can be implicated in infections when immune defenses are severely compromised

• *Geotrichum candidum* – geotrichosis; mold found in soil, dairy products; primarily involved in secondary lung infections

• *Fusarium species* – soil; occasionally infects eyes, toenails, burned skin
Figure 23.30 Common fungi that can cause uncommon infections
22.7 Fungal Allergies and Intoxications

- Fungal spores are common sources of atopic allergies
- Seasonal allergies and asthma
  - Farmer’s lung, teapicker’s lung, bark stripper’s disease
- Fungal toxins lead to mycotoxicoses usually caused by ingesting or inhaling fungal toxins
  - Aflatoxin toxic and carcinogenic; grains, corn, peanuts; lethal to poultry and livestock
- Stachybotrys chartarum – sick building syndrome; severe hematologic and neurological damage