Fungi as Infectious Agents

- Molds & yeasts are widely distributed in air, dust, composts & 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 both true and opportunistic pathogens

Mycoses

- Most fungal pathogens do not require a host to complete their life cycles and infections are not communicable
- Dermaphytes & Candida sp. naturally inhabit human body & are transmissible
- Dermaphytoes most prevalent
- Most cases go undiagnosed or misdiagnosed
- Levels of infection: systemic, superficial, cutaneous, subcutaneous

Emerging Fungal Pathogens

- Opportunistic fungal pathogens have little or no virulence; host defenses must be impaired
- Vary from superficial 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 22.3 Common Opportunistic Fungi and Conditions That Predispose Patients to Them

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Associated With</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candida</td>
<td>Antibiotic therapy, catheters, diabetes, corticosteroids, immunosuppression **</td>
</tr>
<tr>
<td>Aspergillus</td>
<td>Luesemia, corticosteroids, tuberculosis, immunosuppression, IV drug abuse</td>
</tr>
<tr>
<td>Cryptococcus</td>
<td>Diabetes, tuberculosis, cancer, corticosteroids, immunosuppression</td>
</tr>
<tr>
<td>Zygomycota</td>
<td>Diabetes, cancer, corticosteroids, IV therapy, third-degree burns</td>
</tr>
</tbody>
</table>

*Anti-inflammatory drugs are often given for chronic lung disease and to transplant patients to prevent rejection.
**Includes AIDS and genetic conditions that compromise host defenses.
Pathogenesis of Fungi

- Primary mycoses – spores use respiratory portal
- Subcutaneous - inoculated skin; trauma
- Cutaneous and superficial – contamination of skin surface
- Virulence factors – thermal dimorphism, toxin production, capsules and adhesion factors, hydrolytic enzymes, inflammatory stimulants

Clinical Considerations

- Immunity to fungal infections consist of nonspecific barriers, inflammation & cell mediated defenses
- Diagnosis & identification require microscopic examination of stained specimens, culturing in selective & enriched media & specific biochemical & serological tests

Control of Mycotic Infections

- Immunization is not usually effective
- Control involves intravenous amphotericin B, fluocytosine, azoles and nystatin
- In some cases surgical removal of damaged tissues
- Prevention limited to masks and protective clothing to reduce contact with spores

True Pathogens that Cause Systemic Mycoses

- **Histoplasma capsulatum**
- **Coccidioides immittis**
- **Blastomyces dermatitidis**
- **Paracoccidioidomycosis brasiliensis**

**Histoplasma capsulatum**

- Causes histoplasmosis – Ohio Valley Fever
- Distributed worldwide, most prevalent in eastern & central regions of US
- Grow in moist soil high in nitrogen content
- Inhaled conidia produce primary pulmonary infection that may progress to systemic involvement of a variety of organs & chronic lung disease
- Treat with amphotericin B, ketoconazole

Dimorphic Colonies of *Histoplasma capsulatum*
**Histoplasma capsulatum**

- Cause histoplasmosis
- Distinctive morphology: blocklike arthroconidia in the free-living stage & spherules containing endospores in the lungs
- Lives in alkaline soils in semiarid, hot climates & is endemic to southwestern US
- Arthroconidia inhaled from dust form spherules & nodules in the lungs
- Treat with amphotericin B; nikkomycin Z is under development

---

**Coccidioides immitis**

- Cause coccidioidomycosis – Valley Fever
- Distinctive morphology: blocklike arthroconidia in the free-living stage & spherules containing endospores in the lungs
- Lives in alkaline soils in semiarid, hot climates & is endemic to southwestern US
- Arthroconidia inhaled from dust form spherules & nodules in the lungs
- Treat with amphotericin B; nikkomycin Z is under development

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**Blastomyces dermatitidis**

- Causes blastomycosis
- Dimorphic
- Free-living species distributed in soil of a large section of the midwestern and southeastern US
- Inhaled 10-100 conidia convert to yeasts & multiply in lungs
- Symptoms include cough & fever
- Chronic cutaneous, bone, & nervous system complications
- Treat with amphotericin B

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**Paracoccidioidomycosis**

- Distributed in Central & South America
- Lung infection occurs through inhalation or inoculation of spores
- Systemic disease is not common
- Ketoconazole, amphotericin B, sulfa drugs

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**Subcutaneous mycoses**

- Lymphocutaneous sporotrichosis
- Chromoblastomycosis
- Mycetoma
**Sporothrix schenckii**

- Sporotrichosis (rose-gardener’s disease)
- Very common saprobic fungus that decomposes plant matter in soil
- Infects appendages & lungs
- Lymphocutaneous variety occurs when contaminated plant matter penetrates the skin & the pathogen forms a nodule, then spreads to nearby lymph nodes

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**Chromoblastomycosis**

- Progressive subcutaneous mycosis characterized by highly visible verrucous lesions
- Etiologic agents are soil saprobes with dark-pigmented mycelia & spores
- *Fonsecaea pedrosoi*, *Phialophora verrucosa*, *Cladosporium carrionii*
- Produce very large, thick, yeastlike bodies, sclerotic cells

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**Mycetoma**

- Occurs when soil microbes are accidentally implanted into the skin
- Progressive, tumorlike disease of the hand or foot due to chronic fungal infection; may lead to loss of body part
- Caused by *Pseudallescheria* or *Madurella*

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**Cutaneous mycoses**

- Infections strictly confined to keratinized epidermis (skin, hair, nails) are called dermatophytooses—ringworm & tinea
- 39 species in the genera *Trichophyton*, *Microsporum*, *Epidermophyton*
- Communicable among humans and animals
- Infection facilitated by moist, chafed skin

- Ringworm of scalp (*tinea capitis*) affects scalp & hair-bearing regions of head; hair may be lost
- Ringworm of body (*tinea corporis*) occurs as inflamed, red ring lesions anywhere on smooth skin
- Ringworm of foot & hand (*tinea pedis* & *tinea manuum*) is spread by exposure to public surfaces; occurs between digits & on soles
- Ringworm of nails (*tinea unguium*) is a persistent colonization of the nails of the hands & feet that distorts the nail bed
Superficial mycoses

- *Tinea versicolor* causes mild scaling, mottling of skin
- White piedra is whitish or colored masses on the long hairs of the body
- Black piedra causes dark, hard concretions on scalp hairs

Ringworm Treatment

- Ointments containing tolnaftate, miconazole or menthol & camphor
- Lamisil or griseofulvin 1-2 years for intractable infections

Microbiological Achievement of the Year, 2007

DNA Sequence of *M. globosa*, Causative Agent of Dandruff

Opportunistic Mycoses

*Candida albicans*

- Widespread yeast
- Infections can be short-lived, superficial skin irritations to overwhelming, fatal systemic diseases
- 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 80% of nosocomial fungal infections
- Account for 30% of deaths from nosocomial infections in general
- Thrush – occurs as a thick, white, adherent growth on the mucus membranes of mouth & throat
- Vulvovaginal yeast infection – painful inflammatory condition of the female genital region that causes ulceration & whitish discharge
- Cutaneous candidiasis – occurs in chronically moist areas of skin and on burn patients
Diagnosis and Treatment

- Presumptive diagnosis made if budding yeast cells and pseudohyphae are found
- Growth on selective, differential media differentiates *Candida* species
- Topical antifungals for superficial infections, amphotericin B and fluconazole for systemics

**Candida albicans**

Cryptococcus neoformans

- A widespread encapsulated yeast that inhabits soils around pigeon roosts
- Causes cryptococcosis
- Common infection of AIDS, cancer or diabetes patients
- Infection of lungs leads to cough, fever, & lung nodules
- Dissemination to meninges & brain can cause severe neurological disturbance & death

**Pneumocystis carinii**

- 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 & can be rapidly fatal if not controlled with medication
- Pentamidine & cotrimoxazole

**Aspergillus**

- Very common airborne soil fungus
- 600 species, 8 involved in human disease
- Serious opportunistic threat to AIDS, leukemia, and transplant patients
- Inhalation of spores causes fungus balls in lungs and invasive disease in the eyes, heart, & brain
- *A. flavus* produces toxin which is frequent contaminant of stored grain
- Amphotericin B & nystatin