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MICROBIOLOGY WITH DISEASES BY TAXONOMY, THIRD EDITION

Chapter 22 Pathogenic Fungi



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- Understand the importance of medical mycology.
- Understand the general characteristics of systemic mycoses by
 - Pathogenic fungi
 - Opportunistic fungi
- Understand the general characteristics of superficial, cutaneous, and subcutaneous mysoses

- Concerned with diagnosis, management, and prevention of fungal diseases or mycoses
- Mycoses are among the most difficult diseases to diagnose and treat
 - Signs of mycoses are often missed or misinterpreted
 - Fungi are often resistant to antifungal agents

- The Epidemiology of Mycoses
 - Fungi and their spores are almost everywhere in the environment
 - Most people will experience a mycosis at some time
 - Typically acquired via inhalation, trauma, or ingestion
 - Infrequently spread from person to person
 - Most mycoses are not contagious
 - Dermatophytes are the major exception

- The Epidemiology of Mycoses
 - Epidemics result from mass exposure to environmental source of fungi
 - Mycoses are generally not reportable
 - Adequate information on their occurrence is often lacking

- Categories of Fungal Agents: True Fungal Pathogens and Opportunistic Fungi
 - Only four fungi usually considered true pathogens
 - Other fungi are opportunistic
 - Certain factors increase risk for opportunistic mycoses
 - Invasive medical procedure
 - Medical therapies
 - Certain disease conditions
 - Specific lifestyle factors
 - Endemic to certain regions, primarily in the Americas

- Clinical Manifestations of Fungal Diseases
 - Three categories of clinical manifestation
 - Fungal infections
 - Most common mycoses
 - Caused by presence of true pathogens or opportunists
 - Toxicoses
 - Acquired through ingestion
 - Occurs when poisonous mushrooms are eaten
 - Allergies
 - Most often result from the inhalation of fungal spores

- The Diagnosis of Fungal Infections
 - Patient's history is critical for diagnosis of most mycoses
 - Definitive diagnosis often requires morphological analysis of the fungus involved
 - Sabouraud dextrose agar used to culture fungi

- This medium favors fungal growth

- Various techniques used to detect fungal cells in patient specimens
- Difficult to distinguish fungal infections from simple exposures
- Opportunistic infections especially challenging

Fungal Stains





Antifungal Therapies

- Mycoses are among the most difficult diseases to heal
 - Fungi often resist T cell-mediated immune responses
 - Fungi biochemically similar to human cells
 - Antifungal drugs can harm human tissues
 - Ergosterol is often a target of antifungal drugs
- Amphotericin B is gold standard of antifungals
- Opportunistic infections require two-step treatment
 - High-dose treatment to reduce pathogens
 - Low-dose maintenance therapy

Antifungal Vaccines

- Antifungal vaccines have been difficult to develop
 - Fungal metabolism similar to our own
- Scientist have developed vaccines against some fungi
 - Coccidioides
 - Candida
 - Blastomycosis

- Infections spread throughout the body
- Caused by one of four pathogenic fungi of the division Ascomycota
 - Blastomyces, Coccidioides, Histoplasma, and Paracoccidioides
- Acquired through inhalation
 - Begins as generalized pulmonary infection
 - Disseminates via the blood to the rest of the body
- All are dimorphic
- Individuals working with these fungi must take precautions to avoid exposure to spores

Dimorphic nature of true fungal pathogens



Histoplasmosis

- Histoplasma capsulatum is the causative agent
- Most common fungal pathogen affecting humans
- Mostly in the eastern United States but also in Africa and Asia
- Fungi found in moist soils containing high nitrogen levels
- Most common infection route is inhalation of spores into the lungs
- *H. capsulatum* is phagocytosed by alveolar macrophages
 Dispersed beyond the lungs via the blood and lymph

Histoplasmosis

- Usually asymptomatic and resolves without damage
- Clinical histoplasmosis results in one of four diseases
 - Chronic pulmonary histoplasmosis
 - Chronic cutaneous histoplasmosis
 - Systemic histoplasmosis
 - Ocular histoplasmosis
- Infections in healthy individuals resolve on their own
- Amphotericin B is preferred drug for those who require treatment

Characteristic spores of mycelial Histoplasma

capsulatum



- Blastomycosis
 - Blastomyces dermatitidis is the causative agent
 - Endemic in the southeastern United States north to Canada
 - Fungi found in soils rich in organic matter
 - Pulmonary blastomycosis is the most common manifestation
 - Initial pulmonary lesions are mostly asymptomatic
 - The disease resolves in most people but may become chronic
 - Other conditions may result
 - Cutaneous blastomycosis, osteoarticular blastomycosis, meningitis

Geographic distribution of *Blastomyces*



Cutaneous blastomycosis



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Coccidioidomycosis

- Coccidioides immitis is the causative agent
- Almost exclusively in the southwestern United States
- Fungi in desert soil, rodent burrows, archaeological remains, mines
- If inhaled, arthroconidia germinate into spherules in the lung
- Coccidioidomycoses most often result in pulmonary conditions
 - Many patients show no or few symptoms
 - Infections in healthy individuals resolve on their own
- Dissemination to other sites occurs mostly in immunocompromised

Endemic areas of *Coccidioides*



Spherules of *Coccidioides immitis*





Coccidioidomycosis lesions in subcutaneous tissue



Paracoccidioidomycosis

- Paracoccidioides brasiliensis is the causative agent
- Found in southern Mexico and regions of South America
- Disease found most in farm workers in endemic areas
- Similar to blastomycosis and coccidiodomycosis
- Infection begins as a pulmonary condition
- The fungus almost always spreads
 - Produces chronic inflammatory disease of mucous membranes
- Treatment is with amphotericin B or ketoconazole

Paracoccidioides brasiliensis





- Opportunistic mycoses don't typically affect healthy humans
- Infections limited to people with poor immunity
- More important as the number of AIDS patients rises
- Difficult to identify because their symptoms are often atypical
- Five genera routinely encountered
 - Pneumosystis, Candida, Aspergillus, Cryptococcus, and Mucor

Pneumocystis Pneumonia

- Pneumocystis jiroveci is causative agent
 - Formerly referred to as *P. carinii*
 - Obligate parasite
- Majority of individuals exposed to *P. jiroveci* by age 5
- Infection in immunocompetent is usually asymptomatic
- Common opportunistic fungal infection of AIDS patients
 - Presence of the disease is almost diagnostic for AIDS
 - Can result in death if left untreated

Cysts of Pneumocystis jiroveci in lung tissue





Candidiasis

- Includes various opportunistic infections and diseases
- Candida albicans is the most common causative agent
- Common members of microbiota of skin and mucous membranes
- Candida is one of the few fungi transmitted between individuals
- All cases of disease result from an opportunist infection
- Can produce a wide range of diseases

Four of the manifestations of candidiasis





(a)







(c)

(d)

- Aspergillosis
 - Several diseases caused by fungi in the genus Aspergillus
 - Can be found throughout the environment
 - Disease occurs from the inhalation of the fungal spores
 - Most commonly causes only allergies

- Aspergillosis
 - Three pulmonary diseases may develop
 - Hypersensitivity aspergillosis
 - Manifests as asthma or other allergic symptoms
 - Noninvasive aspergillomas
 - Masses of fungal hyphae form in the cavities following pulmonary tuberculosis
 - Acute invasive pulmonary
 - May present as pneumonia
 - Cutaneous and systemic aspergillosis also occur

An invasive aspergilloma in the eye



Cryptococcosis

- Cryptococcus neoformans is the main causative agent
- Results from inhalation of spores or dried yeast in bird droppings
- Characteristics enhance the pathogenesis of the fungus
 - Ability to resist phagocytosis
 - Predilection for the central nervous system

Cryptococcosis

- Various diseases can result from infection
 - Primary pulmonary cryptococcus
 - Asymptomatic or mild pneumonia
 - Cryptococcal meningitis
 - Most common clinical form of cryptococcal infection
 - Follows dissemination of the fungus to the CNS
 - Cryptococcoma
 - Rare condition in which solid fungal masses can form
 - Cutaneous cryptococcosis
 - Skin lesions or inflammation of subcutaneous tissues

GMS stain of Cryptococcus





• Zygomycoses

- Infections caused by genera in the division Zygomycota
- Common in the environment with worldwide distribution
- Seen in several groups
 - Individuals with uncontrolled diabetes
 - People who inject illegal drugs
 - Some cancer patients
 - Some patients receiving antimicrobial drugs
- Infections usually develop in the face and head area

- Zygomycoses
 - Can spread and cause various conditions
 - Rhinocerebral zygomycosis
 - Infection of the paranasal sinuses that can invade the brain
 - Pulmonary zygomycosis
 - Follows inhalation of spores
 - Gastrointestinal zygomycosis
 - Involves ulcers in the intestinal tract
 - Cutaneous zygomycosis
 - Introduction of fungi through the skin after trauma

- Emergence of Fungal Opportunists in AIDS Patients
 - AIDS patients vulnerable to opportunistic fungal infections
 - Permanent immune dysfunction makes cure of infections unlikely
 - Mycoses account for most deaths associated with AIDS
 - Various fungi partly define end-stage AIDS
 - Emergence of new fungal opportunists
 - Three emerging pathogens are particularly problematic
 - Fusarium species
 - Penicillium marneffei
 - Trichosporon beigelii

- Are the most commonly reported fungal diseases
- All are opportunistic infections
- Localized at sites at or near the surface of the body
- Acquired by person-to-person contact or environmental exposure
- Diseases are usually not life threatening
 - Can cause chronic or recurring infections

- Superficial Mycoses
 - Are the most common fungal infections
 - Confined to the outer, dead layers of the skin, nails, or hair

- Superficial Mycoses
 - Black piedra and white piedra
 - Superficial infection characterized by nodules on the hair shaft
 - Transmission is often mediated by shared hair brushes or combs
 - Several members of a family usually infected at the same time
 - Shaving removes infected hair

Two forms of piedra



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- Superficial Mycoses
 - Dermatophytoses
 - Fungal infections of the skin or nails caused by dermatophytes
 - Previously called ringworms
 - Fungi use keratin as nutrient source and colonize dead tissues
 - May provoke cell-mediated immune response that damages living tissues
 - Genera of asxomycetes cause most dermatophytoses
 - Dermatophytoses show a variety of clinical manifestations

22.3 Common Dermatophytoses

common Dormatophy topos			
Disease	Agents	Common Signs	Source
Tinea pedis ("athlete's foot")	Trichophyton rubrum; T. mentagrophytes var. interdigitale; Epidermophyton floccosum	Red, raised lesions on and around the toes and soles of the feet; webbing between the toes is heavily infected	Human reservoirs in toe webbing; carpeting holding infected skin cells
Tinea cruris ("jock itch")	T. rubrum; T. mentagrophytes var. interdigitale; E. floccosum	Red, raised lesions on and around the groin and buttocks	Usually spreads from the feet
Tinea unguium (onychomycosis)	T. rubrum; T. mentagrophytes var. interdigitale	Superficial white onychomycosis: patches or pits on the nail surface	Humans
		Invasive onychomycosis: yellowing and thickening of the distal nail plate, often leading to loss of the nail	
Tinea corporis	T. rubrum; Microsporum gypseum; M. canis	Red, raised, ringlike lesions occurring on various skin surfaces (tinea corporis on the trunk, tinea capitis on the scalp, tinea barbae of the beard)	Can spread from other body sites; can be acquired following contact with contaminated soil or animals
Tinea capitis	M. canis; M. gypseum; T. equinum; T. verrucosum; T. tonsurans; T. violaceum; T. schoenleinii	<i>Ectothrix invasion:</i> fungus develops arthroconidia on the outside of the hair shafts, destroying the cuticle	Humans; can be acquired following contact with contaminated soil or animals
		Endothrix invasion: fungus develops arthroconidia inside the hair shaft without destruction	
		Favus: crusts form on the scalp, with associated hair loss	

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- Superficial Mycoses
 - Malassezia infections
 - Caused by Malassezia furfur
 - Normal microbiota of the skin
 - Causes pityriasis
 - Depigmented or hyperpigmented patches of scaly skin
 - Relapses of Malassezia infections are common

Pityriasis



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- Cutaneous and Subcutaneous Mycoses
 - Fungi are commonly found in the soil
 - Less common than superficial mycoses
 - Requires traumatic introduction of fungi beneath the outer layers of skin
 - Most lesions remain localized to subepidermal tissues in the skin

- Cutaneous and Subcutaneous Mycoses
 - Chromoblastomycosis and phaeohyphomycosis
 - Similar cutaneous and subcutaneous mycoses
 - Caused by dark-pigmented ascomycetes
 - Incidence of infection is relatively low
 - Individuals who work in the soil are most at risk
 - Chromoblastomycosis
 - Produces lesions on skin surface that progressively worsen
 - Phaeohyphomycosis
 - Involves colonization of the nasal passages and sinuses
 - Both diseases are difficult to treat

A leg with extensive lesions of chromoblastomycosis



Differences between chromoblastomycosis and

phaeohyphomycosis

Sclerotic body





LM

(b)

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- Cutaneous and Subcutaneous Mycoses
 - Mycetomas
 - Tumorlike infections of skin, fascia, and bones of hands or feet
 - Caused by mycelial fungi in the division Ascomycota
 - Fungi are found in the soil
 - Fungi introduced via wounds from contaminated twigs, thorns, or leaves
 - Nodules form at site of infection that slowly worsen and spread
 - Bone destruction can cause permanent deformity
 - Surgical removal of the mycetoma is required for treatment

A mycetoma of the ankle



- Cutaneous and Subcutaneous Mycoses
 - Sporotrichosis
 - Sporothrix schenckii is the causative agent
 - Subcutaneous infection usually limited to the arms and legs
 - Those who work with plant material at highest risk for infection
 - Cutaneous sporotrichosis
 - Produces nodular lesions around the infection site
 - Lymphocutaneous sporotrichosis
 - Secondary lesions occur on the skin along the course of lymphatic vessels
 - Effectively treated with topical agents

Lymphocutaneous sporotrichosis on the arm



- Some fungi produce mycotoxins or cause allergies
- Fungal mycotoxins can cause toxicosis
- Two types of toxicosis
 - Mycotoxicosis
 - Caused by eating mycotoxins
 - Mycetismus
 - Mushroom poisoning from eating a fungus
- Fungal allergens can elicit hypersensitivity response in sensitive individuals

- Mycotoxicoses
 - Mycotoxins
 - Produced by fungi during normal metabolic activities
 - Poisonous
 - Often consumed in grains or vegetables
 - Aflatoxins are the most well-known mycotoxins
 - Fatal to many vertebrates
 - Carcinogenic at low levels when consumed continually
 - Prevalent in the tropics
 - Some mycotoxins are used to make drugs

- Mushroom Poisoning (Mycetismus)
 - Most mushrooms are not toxic
 - Some produce extremely dangerous poisons
 - Can cause neurological dysfunction, hallucinations, organ damage, or death
 - Poisoning typically occurs when untrained individuals pick and eat wild mushrooms
 - Deadliest mushroom toxin produced by the "death cap" mushroom

Amanita phalloides, the "death cap" mushroom



- Allergies to Fungi
 - Fungal allergens are common both indoors and out
 - Determining specific cause can be difficult
 - Due to their presence in the environment
 - Fungal allergens usually cause type I hypersensitivity reactions that can result in asthma, eczema, and hay fever
 - Type III hypersensitivity reactions occur much less frequently

End of Chapter

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