Chapter 22 – The Fungi of Medical Importance*

*Lecture notes are to be used as a study guide only and do not represent the comprehensive information you will need to know for the exams.

22.1 Fungi as Infectious Agents

I. Fungal Infections Overview

Our planet is completely blanketed in fungi and their spores. Fortunately, of the 100,000 fungal species, only about 300 have been linked to disease in animals. Fungi have their own kingdom in the Whitaker 5 kingdom system of classification (see Ch.1). Fungi are eukaryotes that exist in two different morphological forms: multicellular forms that form hyphae (fig. 5.15) and unicellular forms collectively termed yeasts (fig. 5.16).

Human disease resulting from fungal infections, primarily by yeasts and molds, are termed mycoses (mycosis, s.). Infectious fungi occur in groups based upon the virulence of the pathogen and the degree of invasion: systemic, subcutaneous, cutaneous, or superficial (fig. 22.5). See also Systems Profile 22.1

Note: The fungi of medical importance to human pathology are divided into two groups: true pathogens and opportunistic pathogens (Tables 22.1 & 22.2). A true pathogen is a species that can invade and grow in a healthy, non-compromised animal host. Opportunistic fungal pathogens have weak, nonexistent invasiveness or virulence and the host’s defenses must be compromised to some degree before infection can occur. Between true and opportunistic pathogens exist a category of species not inherently invasive, but which can grow when inoculated into skin wounds and abrasions of otherwise healthy people. These agents are known as dermatophytes (e.g. athlete’s foot).

Primary / True Fungal Pathogens

II. Systemic Mycoses Caused by True Pathogens

True fungal pathogens can invade and grow in healthy hosts due to their ability to cycle between two morphological and physiological forms. Growing as molds with hyphae\(^1\) at 30ºC and as yeasts\(^2\) at 37ºC. This is called thermal dimorphism (fig. 22.1).

Treatment: amphotericin B is the principal drug prescribed for most all systemic mycoses with fluconazole as a second choice. See table 22.4 for antifungal drug comparison.

Emerging Fungal Pathogens

Opportunistic mycotic infections are an emerging medical concern. Fungal infections account for ~10% of nosocomial infections. Fungi can survive many disinfecting procedures. Also, some patient’s fungal infections come from their normal habitat. See table 22.3 for common opportunistic fungal infections.

Epidemiology of the Mycoses

Many opportunistic fungal pathogens do not require a host and they are non-communicable, with the exception of some dermatophytes and Candida. True fungal pathogens are distributed in a predictable pattern (fig. 22.2). Not many fungal infections are reported to the CDC. Epidemics of fungal infections can occur by mass exposure to a common source, by sharing clothing, or through sexual intercourse and during birth.

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\(^1\) hyphae are long threadlike cells which form extensive mesh networks; can be either vegetative or produce two types of reproductive structures: sporangia or conidia (fig. 5.19)

\(^2\) yeasts are single, round cells that can reproduce asexually by budding (fig. 5.16).
Pathogenesis of the Fungi

Fungi can enter the body, portal of entry, by various routes such as respiratory, mucous and cutaneous. Once in the body, fungi can tolerate higher temperatures (thermal dimorphism) and low oxygen tensions of the body. Different fungi produce a variety of virulence factors. The body can resist most fungal invasions by normal, healthy skin, cilia, and the specific immune system.

Diagnosis of Mycotic Infections

There are a number of laboratory techniques that can be used to diagnose a fungal infection. Almost any type of body fluid/tissue can be used for diagnosis. The samples can be used to inoculate fungal-specific media, PCR, and test for the presence of antibodies to the fungal pathogen (fig. 22.3 and 22.4).

Control of Mycotic Infections

A summary of anti-fungal drugs is given in table 22.4. Prevention measures include the use of masks and protective clothing.

22.2 Organization of Fungal Diseases

Fungal diseases are organized by:

1. True pathogens: systemic, subcutaneous, cutaneous, and superficial
2. Opportunistic mycoses

Systemic Infections by True Pathogens

They are located in a geographic region, disturbed spores are inhaled, they cause primary pulmonary infection (PPI), can become systemic in susceptible hosts, can infect the skin and cause granulomatous lesions, can elicit long term immunity.

Histoplasmosis: Ohio Valley Fever

_Histoplasma capsulatum_

Distributed worldwide, _H. capsulatum_ causes histoplasmosis (Ohio Valley fever). Associated with humans who practice agriculture.

Biology and Epidemiology of _Histoplasma capsulatum_ Most prevalent in eastern and central regions of the United States. Approximately 500,000 cases per year, several thousand of which require hospitalization and a small number being fatal.

Infection and Pathogenesis of _Histoplasma_ Infection is related to soil disturbance and guano; inhaled conidia\(^3\) produce primary pulmonary infection (PPI) that may progress to systemic involvement of a variety of organs and chronic lung disease (fig. 22.7). AIDS patients and children are most susceptible. Yeast form grows intracellularly in macrophages. Most severe systemic forms occur in immuno-compromised patients and children. Liver and spleen enlargement, anemia, circulatory collapse, and death are possible consequences.

Diagnosis and Control of Histoplasmosis Appears as “fish-eye” yeast intracellularly in macrophages. The presence of the microbe is can be detected by a sometimes weak serological tests. Most exposed to the yeast recover, but those with systemic infections are treated with amphotericin B. See also Pathogen Profile #1 _Histoplasma capsulatum_

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\(^3\) _conidia_ are free spores not enclosed by a spore-bearing sac.
Coccidioidomycosis: Valley Fever

*Coccidioides immitis* has recently demonstrated the greatest virulence of all mycotic pathogens.

**Biology and Epidemiology of Coccidioides** Present in alkaline soils in semiarid, hot climates (endemic to southwestern U.S.) *C. immitis* has free living arthroconidia which when inhaled can lead to *coccidioidomycosis* (Valley fever) ~100,000 cases/year (fig. 22.8).

**Infection and Pathogenesis of Coccidioidomycosis** The arthrospores are lightweight and are easily inhaled. In 60% of cases PPI is unapparent; in 40% it is accompanied by cold-like symptoms such as fever, chest pains, cough, headaches, and malaise. AIDS patients are most susceptible (fig. 22.9).

**Diagnosis and Control of Coccidioidomycosis** Based on the highly distinctive spherules seen in body fluid / tissue samples. Antigen tests have also been used (fig. 22.9). Patients with disseminated disease require amphotericin B. See also *Pathogen Profile #2 Coccidioides immitis*

IV. Cutaneous Mycoses

**Dermatophytopses** are fungal infections of nonliving epidermal tissues (stratum corneum) and its derivatives (hair and nails); they are known variously as *tineas* or *ringworm* (Table 22.5, pg. 673). *Ringworm is a misnomer* since these are fungal infections, *not* helmint infections. Nevertheless, several diseases of various human body sites are referred to as ringworm. For example: ringworm of the scalp (fig. 22.18a, pg. 675), ringworm of the groin (jock itch), of the foot (athlete’s foot), of the nails (fig. 22.19, pg. 676), etc. See pg. 673 of the text for an “atlas” of dermatophytopses/

Caused by species in the genera *Tichophyton*, *Microsporum*, and *Epidermophyton* – all adapted to keratinized epidermis (skin, hair, and nails) (Insight 22.1, pg. 674). Infections are *communicable* among humans and animals and are facilitated by moist, chafed skin. Inflammatory reactions to infection cause itching and pain.

**Treatment:** topical antifungal agents containing tolnaftate, miconazole, or thiabendazine are applied regularly for several weeks. Griseofulvin is prescribed in severe cases. Alternate: oral or topical terbinafine HCl (Lamisil™)

V. Opportunistic Mycoses

1. *Candida albicans*

*Candidiasis* is caused by *C. albicans* and other *Candida* species that normally reside in the mouth, vagina, and skin (fig. 22.23, pg. 679). Infection predominates in cases of lowered resistance (infants, AIDS, drug therapy) and arises from normal flora.

**Thrush** occurs as a thick, white, adherent growth on the mucous membranes of mouth and throat (fig. 22.22a, pg. 678)

**Vulvovaginal yeast infection** is a painful inflammatory condition of the female genital region that causes ulceration and whitish discharge. Sexually transmissible. Male urogenital tract infections have similar pathology.

**Cutaneous candidiasis** (fig. 22.22b, pg. 678) occurs in chronically moist areas of skin (e.g. diaper rash) and in burn patients.

**Treatment:** therapy for superficial mucocutaneous infection consists of topical antifungal agents (azoles and polyenes). Recurrent bouts of vulvovaginitis are managed by over-the-counter topical azole ointments.

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4 Recall: antibiotic therapy may alter normal bacteria flora leading to *Candida* superinfection (see Ch.12 notes).
2. *Cryptococcus neoformans*

*Cryptococcosis* is caused by *C. neoformans*, a widespread yeast (fig. 22.25, pg. 680). Common infection of AIDS, cancer, and diabetes patients. Infection of lungs (by inhalation) leads to cough, fever, and lung nodules. Dissemination to meninges and CNS can cause severe neurological disturbance and death.

**Treatment:** systemic infection requires immediate treatment with amphotericin B and fluconazole over a period of weeks or months.

3. *Pneumocystis jiroveci* (previously known as *P. carinii*)

*P. jiroveci* is a small, unicellular fungus that causes *Pneumocystis pneumonia* (PCP) – the most prominent opportunistic infection in AIDS patients (fig. 22.26, pg. 681). This form of pneumonia forms secretions in the lungs that block breathing and can be rapidly fatal if not controlled with medication.

**Treatment:** traditional antifungal drugs like amphotericin B are ineffective. Primary treatment is cotrimoxazole, a combination of sulfamethoxazole and trimethoprim (Bactrim™ or Septra™). Therapy should be applied even if disease appears mild or is only suspected. Pentamidine is another treatment, but has many side-effects.

**FYI — Additional Notes:**

3. *Blastomyces dermatitidis*

Endemic to the U.S., dimorphic morphology of *B. dermatitidis* follows that of other true pathogens (fig. 22.11). Causative agent of *blastomycosis*. Mild PPI disease is accompanied by cough, chest pain, hoarseness, and fever. Severe, chronic blastomycosis can progress to the skin and numerous other organs. Subcutaneous nodules can erupt to the skin surface (fig. 22.12). Chronic systemic blastomycosis of the spleen, liver, and urogenital tract can last for weeks to years and eventually destroy the host defenses.

III. Subcutaneous Mycoses

*Sporothrix schenckii*

*Sporotrichosis* (rose-gardener’s disease) is caused by *S. schenckii* (fig. 22.14), a free-living fungus that accidentally infects the appendages and lungs. *Lymphocutaneous* variety occurs when contaminated plant matter penetrates the skin (by a thorn prick for example) and the pathogen forms a local nodule, then spreads to nearby lymph nodes, where it can erupt to the skin surface (fig. 22.15).