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Office hours MWF 11:30 – 12:20 or by arrangement

| Date/Time             | Topic                           | Readings                 |
|-----------------------|---------------------------------|--------------------------|
| Mon May 5             | Antifungal agents               | <b>Foye's Chapter 40</b> |
| Wed May 7             | Antifungal agents               |                          |
| Fri May 9 (8:30 AM)   | Antifungal/antiviral agents     |                          |
| Fri May 9 (10:30 AM)  | Clinical applications           |                          |
| Mon May 12            | Anti viral agents               | <b>Foye's Chapter 43</b> |
| Wed May 14            | Anti viral agents               |                          |
| Fri May 16 (8:30 AM)  | Vaccines Introduction           | CDC pink book Ch 1,2,    |
| Fri May 16 (10:30 AM) | Strategies and safety           | Chapters 3, 4            |
| Mon May 19            | Diphtheria, tetanus & pertussis | CH 5, 6, 7               |
| Wed May 21            | Polio, pneuno and mening        | Ch 8, 17, 18             |
| Fri May 23            | Measles, Mumps and Rubella      | CH 10, 11, 12            |
| Mon May 26            | Holiday                         |                          |
| Wed May 28            | <b>Exam</b>                     |                          |
| Fri May 30            | Varicella, Hep A and Hep B      | Ch 13, 14, 15            |
| Mon June 2            | Hib and Influenza               | Ch 9 and 16              |
| Wed June 4            | HPV, rotavirus                  | CH 19 and 20             |
| Fri June 6            | Wrap up and Review              |                          |

Exam questions will be mainly from lecture notes. Multiple choice and short answer questions.

Final on June 9<sup>th</sup> comprehensive

### **Texts**

**Lemke, TL and Williams, DA.** *Foye's Principles of Medicinal Chemistry*, Lippincott Williams and Wilkins, 6th Edition, 2007.

**CDC Pink Book.** Centers for Disease Control and Prevention National Immunization Program 10th Edition (2<sup>nd</sup> printing, March 2008). This is available for free viewing via

<http://www.cdc.gov/vaccines/pubs/pinkbook/>

# **Mycology (Study of Fungi)**

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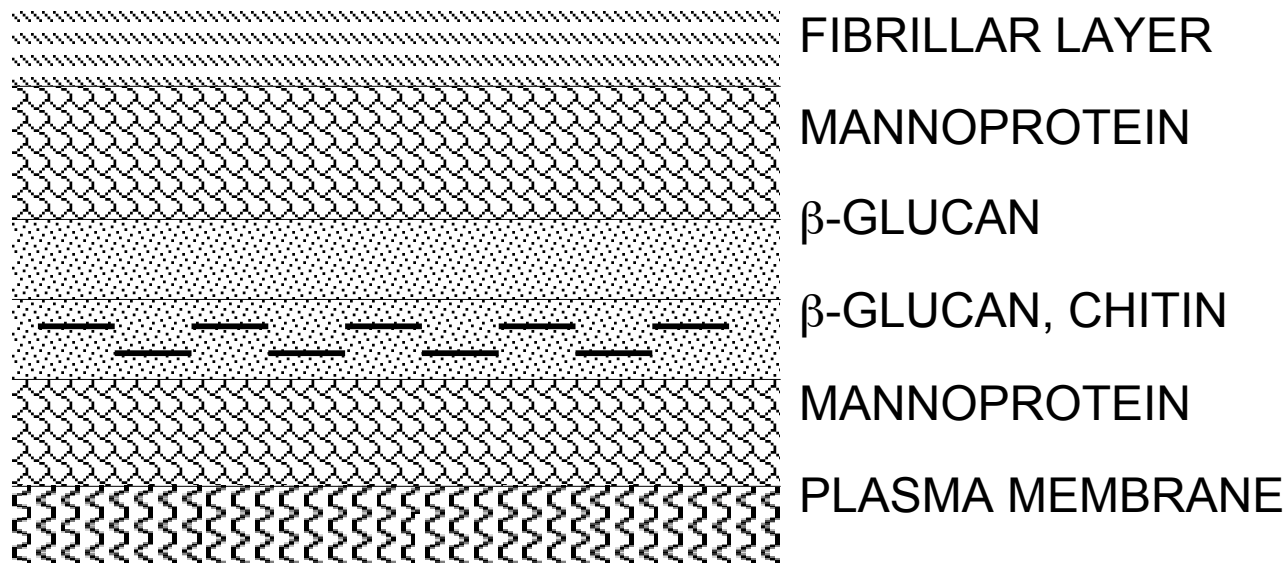
- Fungi are eukaryotic cells and as such contain nuclei, mitochondria, ER, golgi, 80S ribosomes, etc., bound by a plasma membrane.
- The fungal kingdom includes yeasts, molds, rusts and mushrooms. In general most fungi are beneficial and are involved in biodegradation. A few can cause opportunistic infections if they are introduced into a human through wounds or by inhalation.
- The importance of fungi as pathogens is increasing due to aging population, HIV, immunosuppression in organ transplant and unknown factors.

**([www.doctorfungus.org](http://www.doctorfungus.org))**

## Mycology (continued)

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- Fungi possess a rigid cell wall containing chitin, glucans and other sugar polymers. Arrangement of the biomolecular components of the cell wall accounts for the individual identity of the organism. Although, each organism has a different biochemical composition, their gross cell wall structure is similar.
- Fungal cell wall differs greatly from bacterial cell wall. Therefore, fungi are unaffected by antibacterial cell wall inhibitors such as  $\beta$ -lactams and vancomycins.



# Mycology

## (Classification of Fungi)

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Fungi are classified as

- **Yeasts** - round/oval cells that divide by budding. (e.g. *Candida*, *Cryptococcus neoformans* )



- **Molds** - tubular structures (*hyphae*) that grow by longitudinal extension and branching. A mass of hyphae is called a *mycelium*. (*Aspergillus*)



## **Mycology** **(Infections caused by Fungi)**

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Fungal infections are classified depending on the degree of tissue involvement and mode of entry:

1. *Superficial* - localized to the skin, hair and nails.
2. *Subcutaneous* - infection confined to the dermis, subcutaneous tissue, or adjacent structures.
3. *Systemic* - deep infections of the internal organs.
4. *Opportunistic* - cause infection only in the immunocompromised.

# Mycosis

## 1. Superficial

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### The Dermatophytes

Superficial infections are caused by a variety of fungi, especially the dermatophytes (causing infection of the skin, hair and nails) belonging to 40 related fungi of three genera: Microsporum, Trichophyton, Epidermophyton. Dermatophytic infections known as Tinea and are named for the site of infection rather than the causative organism.

- Epidermophyton spp.
- Trichophyton spp.
- Microsporum spp.
- *tinea capitis* (scalp)
- *tinea barbae* (beard/hair)
- *tinea pedis* (athlete's foot)
- *tinea cruris* (jock itch)

# Mycosis

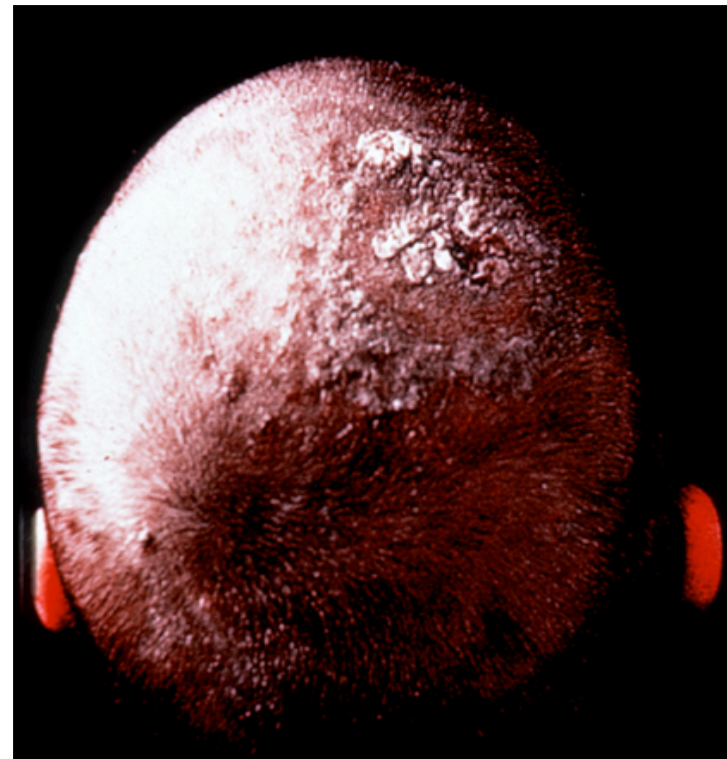
## 1. Superficial

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# The Dermatophytes



*Tinea pedis*  
“athletes foot”  
*Epidermophyton spp.*



*Tinea capitis*  
*Microsporum spp.*

# Mycosis

## 1. Superficial

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***Ringworm***, dermatophyte infection (zoophilic)



# Mycosis

## 1. Subcutaneous

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Subcutaneous infections are confined to the dermis, subcutaneous tissue, or adjacent structures; there is no systemic spread.

They tend to be slow in onset and chronic in duration.

These mycoses are rare in the US and are primarily confined to tropical regions (the Americas, South Africa, Australia).

Variety of fungi involved. Infection starts with trauma inoculation from soil or plants.



***Lobomycosis***

# **Mycosis**

## 3. Systemic

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Systemic mycoses are invasive infections of the internal organs.

The organism typically gains entry via the lungs, GI tract, or through intravenous lines.

Examples include:

- Histoplasmosis
- Coccidiomycosis
- Blastomycosis

# Histoplasmosis

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Histoplasmosis is caused by *Histoplasma*, a ***dimorphic*** fungus (grows as a mold at 25°C and as a yeast form at 37°C)

*Histoplasma* soil fungus causing an intracellular mycosis of the reticulo-endothelial system. Central and Eastern USA. It is endemic in the Ohio-Mississippi river basins, where it is found in soil contaminated with bird droppings and bat excrement.

The infection is acquired through inhalation of the mold form and the lungs are thus the most frequently affected site.

Chronic pulmonary infection is frequently associated with pre-existing chronic lung diseases (i.e.- emphysema).

All stages of this disease may mimic tuberculosis.

The majority of acute cases (50%-90%) follow a subclinical course (asymptomatic to flu-like symptoms).

## Histoplasmosis continued

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The spectrum of the disease is wide, however, varying from an acute benign pulmonary infection to a chronic pulmonary infection and even a fatal disseminated disease.

Dissemination and a fatal course are more common in immunocompromised, children less than 2 years, the elderly.



Discoloration of the skin caused by *Histoplasma capsulatum*



Oral lesions following hematogenous dissemination

# Coccidiomycosis

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An infection caused by the dimorphic fungus  
*Coccidioides immitis*.

The disease is endemic only in regions of the Western Hemisphere (Arizona, California, New Mexico and Texas).

Coccidioidomycosis is acquired from inhalation and an acute respiratory infection occurs 7 to 21 days.

Most patients (50%) are asymptomatic.

Symptoms, when they occur, typically resolve rapidly.

# Coccidiomycosis

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Occasionally, infection may result in a chronic pulmonary condition and/or disseminate to the meninges, bones, joints, subcutaneous, or cutaneous tissues.



Skin lesions resulting from dissemination from the lungs



The lesion on the nose resulted from dissemination from the lungs

About 25% of patients with disseminated disease have meningitis.

# Blastomycosis

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A disease caused by the dimorphic fungus *Blastomyces dermatitidis*

It is endemic in the southeastern and south United States.

Infection is acquired via inhalation.

At least 50% of primary infections are asymptomatic.

An acute pulmonary disease indistinguishable from a bacterial pneumonia may occur after 30-45 days post exposure.



Skin lesion following dissemination from the lungs

# 4. Systemic Mycoses, Opportunistic

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Opportunistic fungi are normally of marginal pathogenicity, but can infect the immunocompromised host.

Patients usually have some serious immune or metabolic defect, or have undergone surgery.

Examples include:

- Aspergillosis

- Candidosis

- Cryptococcosis

# Candidiasis

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***Candidiasis*** - an infection caused by a *Candida* spp.

*Candida* is a yeast and is part of the normal flora (commensal) of the skin, mouth, vagina and GI tract.

Antibiotic treatment can alter the normal bacterial flora allowing *Candida* to flourish.

***Thrush*** - a superficial *Candida* infection of the mouth or vagina.

# Candidiasis

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*Candida* is the most common cause of opportunistic mycoses worldwide.

*Candida albicans* is the most pathogenic and most commonly encountered species

Systemic candidiasis is common in the immunocompromised (AIDS, chemotherapy, post-surgery)

Disseminated infections arise from hematogenous spread from the primarily infected locus

# Candidiasis

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**Oral Thrush-** the white material consists of budding yeast cells and pseudohyphae.



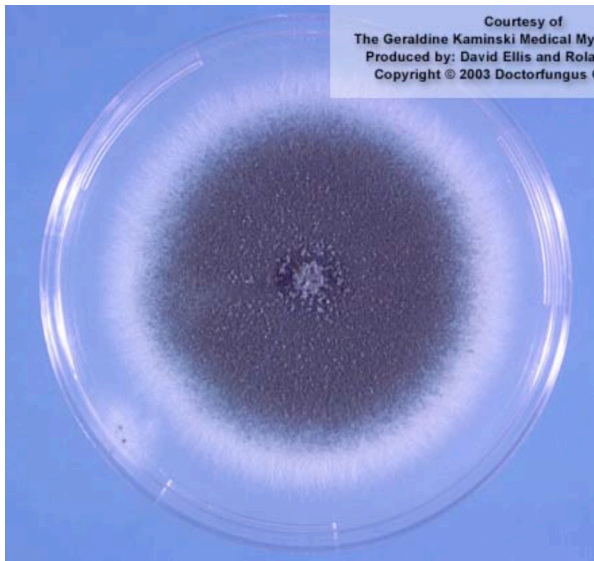
**Mucocutaneous Candidiasis-** granulomatous lesions involving the hands.

# Aspergillois

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*Aspergillus* is a filamentous mold and is a ubiquitous fungus found in nature (soil, plant debris, and indoor air)

Aspergillois is a large spectrum of diseases caused by members of the genus *Aspergillus*.



# Aspergillosis

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Aspergillus is the second most commonly recovered fungus in opportunistic mycoses (following *Candida spp*).

Colonization of the respiratory tract is common.

The organism can infect the lungs, inner ear, sinuses and, rarely, the eye of previously healthy persons.

The three principal entities are:

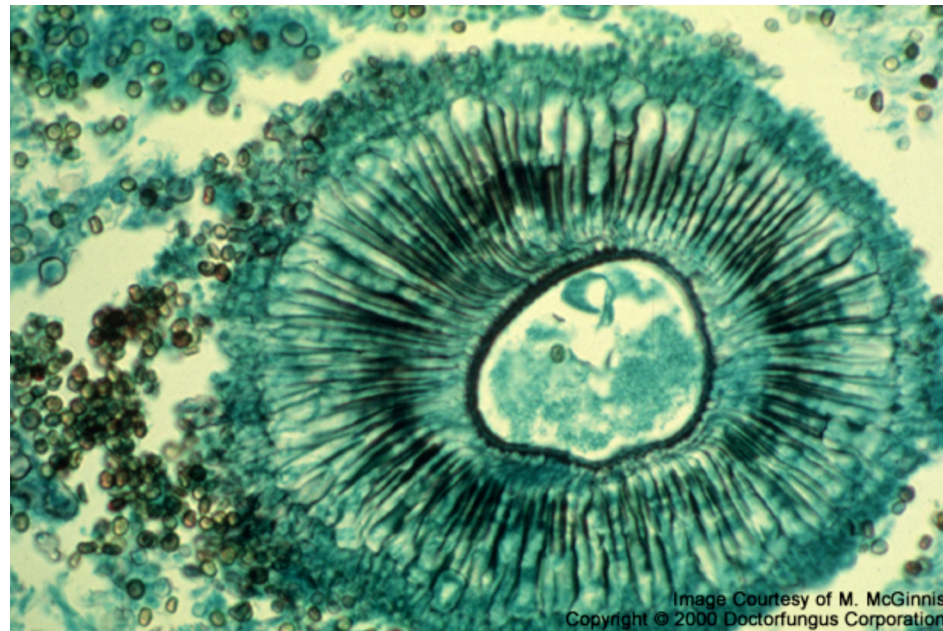
- allergic bronchopulmonary aspergillosis
- pulmonary aspergilloma
- invasive aspergillosis

Nosocomial occurrence of aspergillosis due to catheters and other devices is also frequently observed.

# Pulmonary Aspergilloma

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*Aspergillus* spp. may also be local colonizers in previously developed lung cavities due to diseases such as tuberculosis and emphysema (*aspergilloma* or *fungus ball*).



Fruiting body in a lung cavity

# Aspergillosis

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The clinical manifestation and severity of the disease depends upon the immunologic state of the patient.

Lowered host resistance:

- debilitating disease
- neutropenia
- disruption of normal flora

Almost any organ or system in human body may be involved.

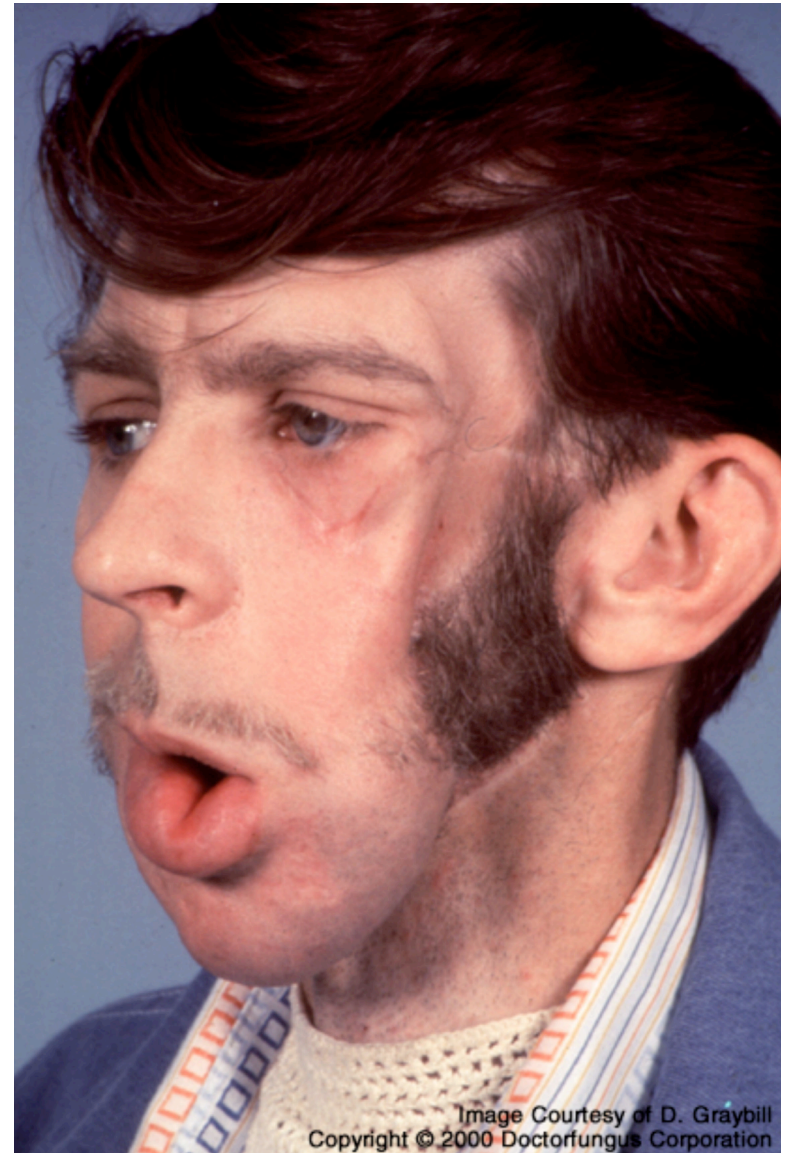
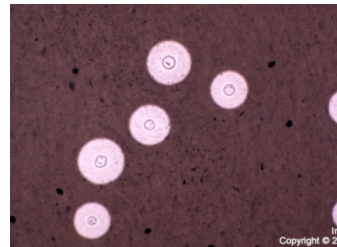


Image Courtesy of D. Graybill  
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# Cryptococcosis

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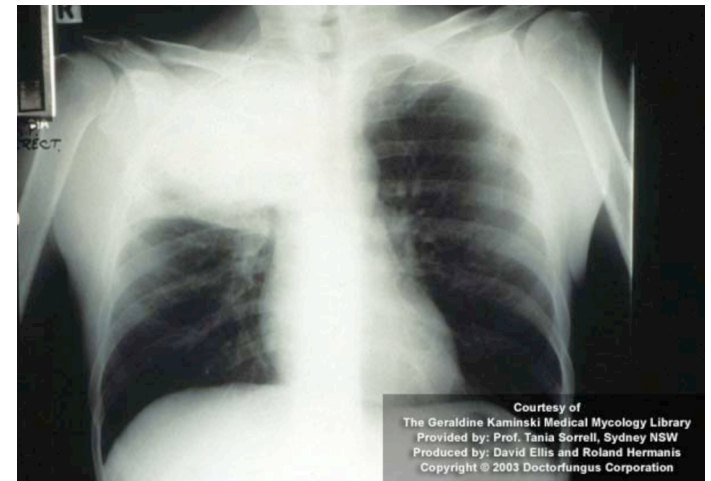
*Cryptococcus* is an encapsulated yeast found world-wide; it is found in pigeon droppings, eucalyptus trees, some fruits and contaminated milk.



*Cryptococcus neoformans* is the only species that is pathogenic to humans.

The primary port of entry is inhalation.

The course of the infection is usually sub-acute or chronic.



# Cryptococcosis

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AIDS is the most commonly encountered predisposing factor for development of cryptococcosis.



Skin lesions resulting from disseminated *C. neoformans*

*Cryptococcus* is neurotropic and the most common clinical presentation is ***meningoencephalitis***.