Fungi of Medical Importance

Prof. Md. Akram Hossain 2012
Objectives

- Types of fungal pathogens
- Classification and definition of fungal diseases
- Major fungal infections
- Risk factors for opportunistic mycoses
- Laboratory diagnostic aspects
Fungi - Morphological Classification

- **Moulds**
  - Aspergillus
    - *A. fumigatus*
  - Mucorales
    - *Mucor* spp.
    - *Rhizopus* spp.
  - Dermatophytes

- **Yeasts & Yeast like**
  - *Cryptococcus*
    - *C. neoformans*
    - *C. gattii*
  - *Candida*
    - *C. albicans*
  - Malassezia
    - *M. furfur*
    - *M. globosa*

- **Dimorphic**
  - Moulds 25°C
  - Yeasts/other phases (37°C)
  - *Histoplasma capsulatum*
  - *Coccidioides immitis*
  - *Blastomyces dermatitidis*
  - *Sporothrix schenckii*
Basic growth forms

A. Mould form:
Is a vegetative growth of fungal filament known as hypha (Pl. Hyphae). Mass of hyphae is known as mycelium. Fungi may be hyaline or coloured (dematiaceous), multicellular.

B. Unicellular or Yeast form:
Single-celled fungus that reproduce by budding to form blastoconidia. Colonies are moist or mucoid. Examples: Candida, Cryptococcus.
Thermal dimorphism

Dimorphic fungi (*Histoplasma capsulatum*, *Blastomyces dermatitidis*) produce yeast form (parasitic/tissue form) at 37°C (nutritional requirements more complex) and mould form (saprophytic form) at 25-28°C. Sabouraud agar 25°C - mould form. Brain heart infusion agar with 5% blood 37°C - yeast form.

*H. capsulatum*, yeast form

*H. capsulatum*, mould form
## Habitat for pathogenic fungi

<table>
<thead>
<tr>
<th>Location</th>
<th>Fungi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soil</td>
<td><em>Coccidioides immitis</em>, keratinophilic fungi, Dermatophytes (geophilic)</td>
</tr>
<tr>
<td>Soil associated with bird and bat faeces</td>
<td><em>Histoplasma capsulatum</em></td>
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<tr>
<td>Soil associated with pigeon faeces</td>
<td><em>Cryptococcus neoformans</em></td>
</tr>
<tr>
<td>Soil and vegetable matter</td>
<td><em>Aspergillus, Mucorales</em></td>
</tr>
<tr>
<td>Human body</td>
<td><em>Candida albicans, Malassezia spp.</em></td>
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**Common fungal diseases**

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**Common fungal diseases**
1. Mycotoxicosis - caused by ingested toxins

2. Allergic - Asthma, allergic bronchopulmonary disease, IgE and or IgG mediated

3. Colonization and invasion
   - Superficial and cutaneous
   - Subcutaneous
   - Deep seated, disseminated
     - Opportunistic mycoses
     - True (endemic) mycoses
Common fungal diseases

1. Superficial/cutaneous mycoses
   - Tinea versicolor
   - Dermatophytoses

2. Opportunistic mycoses
   - Candidiasis
   - Cryptococcosis
   - Pneumocystosis
   - Aspergillosis
   - Zygomycosis

3. True (endemic) mycoses
   - Coccidioidomycosis
   - Histoplasmosis
A superficial fungal disease characterized by well-demarcated white, pink lesions often coalescing and covered with scales. The colour of the lesion varies according to the patient’s colour and exposure to sunlight. It is caused by *Malassezia* species, a lipophilic yeast.
Laboratory diagnosis

Direct microscopic examination of skin scraping reveal yeast cells and hyphal element (spaghetti meat ball appearance) of *M. furfur*. It requires lipid (olive oil) supplementation on SDA agar for growth.

LCB mount of skin scrapings from a case of Tinea versicolor

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Dermatophytoses

It is a superficial infection of the keratinized structures of the body (i.e. skin, hair and nails) caused by a closely related keratinophilic fungi known as dermatophytes. The fungus colonizes stratum corneum. The arthrospores adhere to keratinocytes, germinates and invade. The typical lesion of dermatophyte infection (ring worm) is a scaling patch with a raised margin. The main symptom is itching.
Dermatophytes

*Microsporum, Trichophyton, Epidermophyton*

- Infect keratinised tissue
- Produce keratinase enzyme
- Colonizes stratum corneum
- Allergic and inflammatory lesions
- Severity varies depending upon species or strain involved
Diagnosis

Visual examination of the lesion

Proper sample collection

KOH microscopy

Fungal culture (SDA + chloramphenicol + cycloheximide)
Laboratory diagnosis

Skin scraping, nail clippings and epilated hairs

Direct microscopy in 10-20% KOH
Candidiasis

A primary or secondary mycotic infection caused by members of the genus *Candida*. The clinical manifestations may be localized to the mouth, throat, skin, scalp, vagina, or the gastrointestinal tract, or become systemic as in septicaemia, endocarditis and meningitis.
Candidiasis and other yeast infections

Etiology: The major causative species are:

*Candida albicans* (> 50%) (normal flora)
*Candida parapsilosis*
*Candida tropicalis*

Other yeasts

*Malassezia furfur* (normal flora)
*Cryptococcus neoformans* (exogenous source)
Oropharyngeal candidiasis

Includes thrush, glossitis, stomatitis and angular cheilitis (perleche). Thrush exhibits creamy gray membrane covering the tongue. Newborns (5%) commonly contact this by exposure to *C. albicans* in the vagina during delivery. Thrush is often associated with patients with severe immunological impairment such as HIV, leukemia, and diabetes mellitus.
"Nappy rash" candidiasis in an infant with spread to the mouth area.
Vulvovaginal candidiasis

*Candida* is one of the important causes of vulvovaginitis. The condition is characterized by a curd-like, milky vaginal discharge, often associated with broad-spectrum antibiotics, third trimester of pregnancy, low vaginal pH and diabetes mellitus. Refractory vaginal candidiasis may be associated with HIV/AIDS.
Budding and pseudohyphae formation in *Candida* species
Laboratory diagnosis

Vaginal candidiasis:
High vaginal swabs should be taken. Direct microscopy/gram-stained smear reveals yeasts with pseudohyphae.
Cryptococcosis

A chronic, subacute to acute pulmonary, systemic or meningitic disease, initiated by the inhalation of the fungus. Primary pulmonary infections have no diagnostic symptoms and are usually subclinical. On dissemination, the fungus usually shows a predilection for the central nervous system.

Distribution: World-wide.

Etiological agent: *Cryptococcus neoformans*  
*Cryptococcus gattii*
Natural habitat and pathogenesis of \textit{C. neoformans}
Laboratory diagnosis

The demonstration of encapsulated yeast cells in CSF, tissue biopsy, BAL and urine (after prostate massage) is diagnostic.

Antigen detection:
Capsular polysaccharide

India ink preparation
Pneumocystosis

*Pneumocystis carinii (jiroveci)* is a fungus that causes pneumonia in immunocompromised patients particularly those with AIDS. It attacks the interstitial tissue of the lung causing marked thickening of the alveolar septa and alveoli leading to significant hypoxia which can be fatal if not treated. The treatment of choice is trimethoprim-sulfamethoxazole combination.
Photomicrographs of alveolar lavage stained by methanamine-silver demonstrating the typical configuration of the cyst walls on high power.

Taken from Hopkin, 1991
Aspergillosis

Aspergillosis is a spectrum of diseases of humans and animals caused by members of the genus *Aspergillus*. These include (1) mycotoxicosis due to ingestion of contaminated foods; (2) allergy and sequelae to the presence of conidia or transient growth of the organism in body orifices; (3) colonization without extension in preformed cavities and debilitated tissues; (4) invasive, inflammatory, granulomatous, necrotizing disease of lungs.

**Distribution**: World-wide.

**Etiological agents**: *Aspergillus fumigatus, A. flavus, A. niger, A. nidulans* and *A. terreus*. 

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The life cycle of Aspergillus

- Spores inhaled
- Germination
- Mass of hyphae (plateau phase)
- Hyphal elongation and branching

Common fungal diseases
Invasive pulmonary aspergillosis (opportunistic mycosis)

Risk factors for invasive aspergillosis

- Prolonged neutropenia
- High doses corticosteroids therapy of several weeks duration
- Organ transplant recipients receiving immunosuppression
- Chronic granulomatous disease (CGD).
Laboratory diagnosis

Clinical specimens:
Respiratory: Fresh sputum, bronchoalveolar lavage, biopsy etc.

Disseminated: Skin lesions biopsy

Direct microscopy: Septate, dichotomously branched hyphal fragments (digested in 10 % KOH-calcofluor) - Aspergillus/Fusarium
KOH-calcofluor mount showing septate *Aspergillus* hyphae
ZYGOMYCOSIS

- **Etiology:** Caused by members of Zygomycetes— *Rhizopus, Mucor, Absidia* etc.

- **Distribution:** Ubiquitous, inhalation of spores (sporangiospores).

- **Risk factors:**
  - Ketoacidosis and hyperglycemia (Rhinocerebral)
  - Complicate prolonged neutropenia (Pulmonary/systemic)
  - Chelation therapy with deferoxamine (Pulmonary/systemic)
  - Immunosuppressive therapy (Pulmonary/systemic)
  - Severe burns (Cutaneous)
  - Malnutritions, ulcers (Gastrointestinal)
Rhino-cerebral zygomycosis

Usually associated with uncontrolled diabetes mellitus or ketoacidosis, steroid induced hyperglycemia. Infections usually begins in the paranasal sinuses following the inhalation of sporangiospores and may include the orbit, palate, face, nose or brain. Necrotizing tissue reaction; can be fulminating. Fungus has predilection to invade blood vessels causing embolization and necrosis.

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Microscopic features: Hyphae are broad, hyaline, aseptate or with rare septa. Sporangiophores long and end in a spherical columella which is surrounded by a sac like sporangium. Rhizoids (root-like extensions from the stolon) are seen in Rhizopus and Absidia.
Happiness is a journey,
not a destination.