**Opportunistic Systemic Mycoses**

Opportunistic mycoses: Caused by organisms that are generally harmless unless individual has weakened defenses:

 -AIDS and cancer patients

- Individuals treated with broad spectrum antibiotics

 -Very old or very young individuals (newborns) Examples:

-Aspergillosis: Inhalation of Aspergillus spores.

- Candidiasis or Yeast Infections: Caused mainly by Candida albicans. Part of normal mouth, esophagus, and vaginal flora.

**1-Candidiasis**

Candidiasis or thrush is a fungal infection (mycosis) of any species from the genus Candida (one genus of yeasts). *Candida albicans* is the most common agent of Candidiasis in humans. Also commonly referred to as a yeast infection,

Candidiasis infections that range from superficial, such as oral thrush and vaginitis, to systemic and potentially life-threatening diseases. Candida infections also referred to as candidemia or invasive candidiasis, and are usually confined to cancer, transplant, and AIDS patients.

Superficial infections of skin and mucosal membranes by Candida causing local inflammation. Since yeasts from the Candida genus are usually present as part of the gastrointestinal flora in humans, candidiasis is considered an opportunistic infection that only occur when the immune system fails to keep the yeast population under control.

## Classification

## Candidiasis may be divided into the following types:

## • Mucosal candidiasis

##  Oral candidiasis (thrush, Oropharyngeal candidiasis)

##  Candidal vulvovaginitis (vaginal yeast infection)

## • Cutaneous candidiasis

## • Onychomycosis (nail infection) caused by Candida

## • Invasive candidiasis



Skin candidiasis Nail candidiasis (onychomycosis)

**Signs and symptoms**

Symptoms of candidiasis vary depending on the area affected. Most candidial infections result in minimal complications such as redness, itching and discomfort, though complications may be severe or even fatal if left untreated in certain populations. In immunocompromise persons, candidiasis is usually a very localized infection of the skin or mucosal membranes, including the oral cavity (thrush), the pharynx or esophagus, the gastrointestinal tract, the urinary bladder, the fingernails or toenails (onychomycosis), and the genitalia

***Candida albicans***

Candida yeasts are generally present in healthy humans, particularly on the skin, but their growth is normally limited by the human immune system, by competition of other microorganisms, such as bacteria occupying the same locations in the human body, and in the case of skin, by the relative dryness of the skin, as Candida requires moisture for growth.

Candida species are frequently part of the human body's normal oral and intestinal flora. Treatment with antibiotics can lead to eliminating the yeast's natural competitors for resources, and increase the severity of the condition.

Oral candidiasis in an immunosuppressed patient Nappy rash" candidiasis in an infant which spread to the mouth area.

**Laboratory diagnosis**:

1. Clinical Material: Skin and nail scrapings; urine, sputum and bronchial washings; cerebrospinal fluid, pleural fluid and blood; tissue biopsies from various visceral organs and indwelling catheter tips.

2. Direct Microscopy: (a) Skin and nails should be examined using 10% KOH and Parker ink or calcofluor white mounts; (b) Exudates and body fluids should be centrifuged and the sediment examined using either 10% KOH and Parker ink or calcofluor white mounts and/or gram stained smears; (c) Tissue sections should be stained using PAS digest, Grocott'smethenamine silver (GMS) or Gram stain. Note *Candida* may be missed in H&E stained sections. Examine specimens for the presence of small, round to oval, thin-walled, clusters of budding yeast cells (blastoconidia) and branching pseudohyphae

3. Culture: Colonies are typically white to cream colored with a smooth, glabrous to waxy surface.



Typical moist colonies of *Candida*.

4. Serology: Various serological procedures have been devised to detect the presence of *Candida* antibodies, ranging from immunodiffusion to more sensitive tests such as counter immunoelectrophoresis (CIE), enzyme-linked immunosorbent assay (ELISA), and radioimmunoassay (RIA).

**Treatment of Candidiasis**

Some of the most common antifungal agents used against Candida infections are **clotrimazole, nystatin, fluconazole and ketoconazole**.

**2- Cryptococcosis**

Cryptococcosis is a chronic, subacute to acute pulmonary, systemic or meningitic disease, initiated by the inhalation of basidiospores and/or desiccated yeast cells of *Cryptococcus neoformans*. Primary pulmonary infections have no diagnostic symptoms and are usually subclinical. On dissemination, the fungus usually shows a predilection for the central nervous system, however skin, bones and other visceral organs may also become involved. Although *C. neoformans* is regarded as the principle pathogenic species,. *Cryptococcus* is an encapsulated basidiomycete yeast-like fungus with a preference the respiratory and nervous system of humans and animals. Two species, these yeasts are distinguishable biochemically and by molecular techniques.

**Clinical manifestations:**

**1. Pulmonary Cryptococcosis**:

Subclinical cryptococcosis may result of environmental exposure, normal individuals may experience a self-limiting pneumonia. Most primary infections of this type have no diagnostic symptoms and are usually discovered only by routine chest x-ray. When present, symptoms include cough, low-grade fever and pleuritic pain.

Invasive pulmonary cryptococcosis may occur in some patients when primary infections may not readily resolve in some patients, leading to a more chronic pneumonia progressing slowly over several years.

**2. Central Nervous System:**

Dissemination to the brain and meninges is the most common clinical manifestation of cryptococcosis and includes like **meningitis**

Meningitis Symptoms usually develop slowly over several months, and initially include headache, followed by drowsiness, dizziness, irritability, confusion, nausea, vomiting, neck stiffness

**3. Cutaneous Cryptococcosis**:

**4. Cryptococcosis of Bone:**

**5. Ocular Cryptococcosis**:

**Laboratory diagnosis:**

1. Clinical material: Cerebrospinal fluid (CSF), biopsy tissue, sputum, bronchial washings, pus, blood and urine.

2. Direct Microscopy: (a) For exudates and body fluids make a thin wet film under a coverslip using India ink to demonstrate encapsulated yeast cells. Sputum and pus may need to be digested with 10% KOH prior to India ink staining. (b) For tissue sections use PAS digest, GMS and H&E, mucicarmine stain is also useful to demonstrate the polysaccharide capsule. Examine for globose to ovoid, budding yeast cells surrounded by wide gelatinous capsules. Note, non-encapsulated variants, although rare, may also occur.

.


India ink preparation of CSF showing a typical yeast cell of *C. neoformans* surrounded by a characteristic wide gelatinous capsule..

3. Culture: Inoculate specimens onto primary isolation media, like Sabouraud's dextrose agar. smooth gelatinous colonies, later becoming very mucoid and cream in color..


Bird seed agar plate showing the typical brown colour effect seen with *C. neoformans*.

4. Serology: It should be noted that the detection of cryptococcal capsular polysaccharide antigen in spinal fluid is now the method of choice for diagnosing patients with cryptococcal meningitis. Note, serum specimens should be pretreated with pronase to enhance detection of antigen and avoid false negative results.

**Treatment**

Amphotericin B in combination with oralflucytosine, is indicated as initial therapy for patients Patients with less severe disease can be treated with fluconazoleor itraconazole,

**3-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 to the presence of conidia or transient growth of the organism in body orifices;

 (3) colonisation without extension in preformed cavities and weak or debilitated tissues;

 (4) invasive, inflammatory, granulomatous,

(5) systemic and fatal disseminated disease. The type of disease and severity depends upon the physiologic state of the host and the species of Aspergillus involved. The etiological agents include *Aspergillus fumigatus, A. flavus, A. niger, A. nidulans* and *A. terreus.*

**Clinical manifestations:**

1. **Pulmonary Aspergillosis**: including **allergic, aspergilloma** and **invasive aspergillosis.**

Allergic aspergillosis ranging from extrinsic asthma to extrinsic allergic alveolitis to allergic broncho pulmonary aspergillosis (hypersensitivity pneumonitis) caused by the inhalation of *Aspergillus* conidia. Features include asthma, peripheral eosinophilia,.

Non-invasive aspergillosis or aspergilloma (fungus ball), is caused by the saprophytic colonisation of pre-formed cavities.Features often include hemoptysis with blood stained sputum, positive immunodiffusion precipitin tests for antibody to*Aspergillus*, and elevated specific IgE against *Aspergillus.*.

Acute invasive pulmonary aspergillosis. Common symptoms include fever, cough and sputum production; positive serum antibody precipitins may also be detected.

**2. Disseminated Aspergillosis**:

Hematogenous dissemination to other visceral organs may occur, especially in patients with severe immunosuppression or intravenous drug addiction brain (cerebral aspergillosis), kidney (renal aspergillosis), heart, (endocarditis, myocarditis), bone (osteomyelitis), and gastrointestinal tract.

**4. Cutaneous Aspergillosis**:

Cutaneous aspergillosis is a rare manifestation that is usually a result of dissemination from primary pulmonary infection in the immunosuppressed patient. Lesions manifest as erythematous papules or macules with progressive central necrosis.

**Laboratory diagnosis:**

1. Clinical material: Sputum, bronchial washings and tracheal aspirates from patients with pulmonary disease and tissue biopsies from patients with disseminated disease.

2. Direct Microscopy: (a) Sputum, washings and aspirates make wet mounts in either 10% KOH & Parker ink or Calcofluor and/or Gram stained smears; (b) Tissue sections should be stained with H&E, GMS and PAS digest. Note Aspergillus hyphae may be missed in H&E stained sections. Examine specimens for dichotomously branched, septate hyphae.

3. Culture: Clinical specimens should be inoculated onto primary isolation media, like Sabouraud's dextrose agar. Colonies are fast growing and may be white, yellow, yellow-brown, brown to black or green in colour.

Serology:Immunodiffusion tests for the detection of antibodies to*Aspergillus*species have proven to be of value in the diagnosis of allergic, aspergilloma, and invasive aspergillosis.

### Treatment

The goal of therapy is to treat any immune problems and to control the infection with antifungal medications, antifungal therapy involved amphotericin B. Several less toxic drugs have been introduced that work against aspergillus.