

Pathology of Fungal infection

☒ Definition of Fungi:

Fungi are microscopic plant single-celled or multicellular organism. are not always pathogenic. Many fungi are saprophytes (living off dead organic matter). Fungi can be **true pathogens** that cause infections in healthy persons or they can be **opportunistic pathogens** that cause infections in immunocompromised persons. Others are used for the development of antibiotics, antitoxins, and other drugs used to control various human diseases.

☒ Diseases Caused by Fungi

Fungal infections or mycoses can be classified depending on the degree of tissue involvement and mode of entry into the host. These are:

- **Superficial & cutaneous:** localized to the skin, the hair, and the nails & mucosa. Examples include oral **candidiasis** (thrush), vaginal candidiasis, athlete's foot (tinea pedis), and diaper fungal infections of babies.
- **Subcutaneous infection:** Are rare conditions, in which Infection may arise following the wounding of the skin and the introduction of soil saprophytes. The infection is chronic, localized, confined to the dermis, subcutaneous tissue or adjacent structures, leading to ulcerative lesion. **Madura foot** is an example of this type of affection.
- **Systemic Mycoses:** These are invasive infections of the internal organs. They are uncommon in normally healthy persons. They may be caused by:
 - 1) **Primary pathogenic fungi:** These are fungal infections of the body caused by fungal pathogens which can overcome the physiological and cellular defenses of the normal human host by changing their morphological form. The primary site of infection is usually pulmonary. Infection by **Histoplasma capsulatum** (**histoplasmosis**) is an example of this type of affection.
 - 2) **Opportunistic fungi** that are of marginal pathogenicity (non pathogenic or of low virulence) but can infect the immunocompromised host causing potentially fatal infections. Examples include **systemic Candidiasis**. In this condition candida albicans - which is part of the normal human flora - can proliferate and disseminate throughout the body of severely immunocompromized host.

☒ Pathogenesis of fungal infections: Fungi produce their pathological effects through the following mechanisms.

- 1) Surface factors that help in adherence to host tissue.
- 2) Enzymes which facilitate tissue invasion.

- 3) The ability to change their morphology to overcome host defense mechanisms.

☒ **Immunological response against fungi:** immunological reaction against pathogenic fungi may be mediated by:

1. Cell mediated immunity.
2. Humoral immunity against cell membrane antigens.

☒ **Spectrum of inflammatory responses to fungal infection:** Tissue reaction to pathogenic fungi may be extremely variable, depending on the type of invading fungus and the host immune response. With fungi we can find any of the following inflammatory responses.

1. Acute and chronic suppurative inflammation.
2. Chronic inflammation with mononuclear inflammatory infiltrate.
3. Granulomatous inflammation.
4. Necrotizing inflammation.

Any form of tissue reaction certainly may be associated with **necrosis** and **scarring**.

Candida albicans

☒ **Candida albicans (also called Monilia)** is the **most common** fungal pathogens of mankind. These are normal inhabitants of oral cavity, GI tract, & vagina. Fungi are yeast-like cell with pseudohyphae & hyphae.



☒ **Disease spectrum of Candida albicans:** Depending on the immunological status of the host, Candida can cause **superficial & cutaneous** affection in healthy individuals, and can cause **systemic opportunistic** affection in immunocompromised patients.

1) Superficial & cutaneous candidiasis: may occur in healthy individuals. The normal flora starts to invade mucosal surfaces and skin. Predisposing factors include pregnancy, with oral contraceptives, diabetes, and prolonged antibiotic intake.

Sites: Oral candidiasis (thrush), vulvovaginal candidiasis & folds of skin & nail bed (paronychia).

Gross: Mucosal surfaces showed superficial white friable patches composed of organism and inflammatory debris. When detached, it leaves red inflamed surface and in severe cases there is surface ulceration.



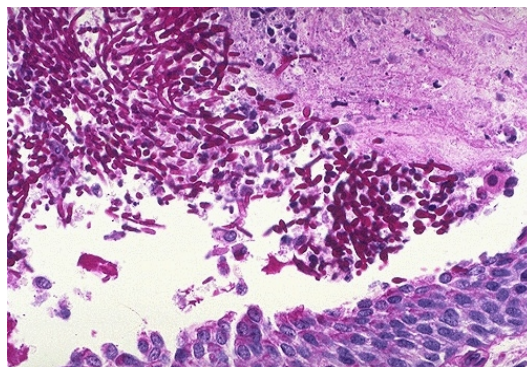
Microscopic: Ranges from acute diffuse neutrophilic infiltration with microabscesses within the epithelium, to chronic granulomatous inflammation. Fungal bodies, hyphae and spores may be detected by PAS stain.

2) Systemic Candidiasis: is a form of opportunistic infection, occurs in immunocompromised patients.

Sites: Urinary tract (kidney & urinary bladder), GIT (oesophagus & stomach), Heart, Lung, CNS

Gross: Wide spread necrotizing lesion within the affected organ.

Microscopic: Multiple microabscesses, in which the fungal colonies occupy the center of the lesion. They are surrounded by necrosis and neutrophilic infiltrate. Fungal bodies, hyphae and spores may be detected by PAS stain.



Candida pyelonephritis, stained with PAS

Mycetoma (Madura Foot)

Definition: Madura foot or mycetoma (named because of the tumour-like mass it forms) is a chronic granulomatous infection involving the subcutaneous tissue and bone of feet and characterized by the formation of localized lesions with multiple draining sinuses. The exudates contains granules that may be yellow, white, red, brown, or black, depending upon the causative agent.

Aetiology: Mycetoma can be divided into two major categories according to the causative organism.

- **Causative agent:**
 - 1) **Eumycetoma:** which is caused by true fungi, in 40% of cases, which represent a form of **subcutaneous fungal** infection.
 - 2) **Actinomycetoma:** which is caused by filamentous bacteria, and represent 60% of cases.

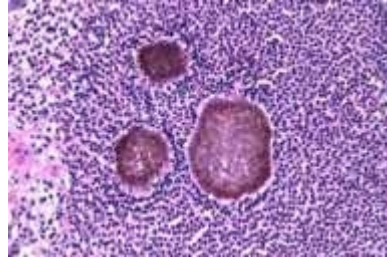
Both forms have similar gross and microscopic appearance.

- **Mode of infection:** Organisms are normally present in environment (soil & dust). Infection occurs in bare-footed persons after minor penetrating skin injury inoculating soil organisms, occurring preferentially in rural areas, usually among agricultural workers who work barefoot.
- The disease is endemic in the tropics and subtropics.
- **Risk factors:** Mycetoma typically presents in agricultural workers (hands, shoulders and back - from carrying contaminated vegetation and other burdens), or in individuals who walk barefoot in dry, dusty conditions. Minor trauma allows pathogens from the soil to enter the skin.

Gross: Both forms of mycetoma present as a progressive, cutaneous and subcutaneous swelling. Multiple nodules develop which may suppurate and drain through multiple sinus tracts that usually discharge serosanguinous fluid and, at times, grossly visible granules of various colours depending on the agent involved.



Microscopically: the dermis and subcutaneous tissue contain localized abscesses, each of which contains one or more granules in its centre. Eosinophilic, clublike material may border the granules. Between abscesses, there is extensive formation of septic granulation tissue and scarring. Infection often involve contiguous bone, resulting in destructive osteomyelitis.



Fate & Complications:

- Actinomycetoma can be cured with the appropriate antibiotic therapy but eumycetoma has a high rate of recurrence and can require amputation.
- Lymphatic or hematogenous dissemination from the primary subcutaneous lesion rarely occurs.

Histoplasmosis

Definition: is a type of primary systemic fungal affection, which is caused by *Histoplasma capsulatum*.

Aetiology: This disease is caused by a fungus called *Histoplasma capsulatum*. It is endemic in many parts of the world. It is found in the soil and growth is enhanced by the presence of bird and bat excreta. Infection by this soil fungus occurs by inhalation. So, the lungs are the main site of infection. Organisms reach alveolar spaces where it multiplies in mononuclear phagocytes (It is an intracellular pathogen of macrophages like *Mycobacterium tuberculosis*).

Clinical Presentation: The clinical presentations and morphologic features of Histoplasmosis is strikingly resemble those of tuberculosis, including:

- 1) Self limited and often latent primary pulmonary involvement.
- 2) Chronic progressive lung disease, with cavitation in lung apices.
- 3) Localized lesions in extrapulmonary sites (Liver, mediastinum, meninges and adrenals).
- 4) Widely disseminated involvement in immunocompromised patients.

Host immune response against *Histoplasma capsulatum* is mediated by cell mediated immunity, and previous sensitization can be detected by histoplasmin skin test (similar to tuberculin test).

Gross: In chronic lung affection, there are large area of consolidation (representing coagulative necrosis), which may liquefy to form apical cavities.

Microscopic features: There are multiple epithelioid granulomas, which usually undergo coagulative necrosis and coalesce to produce large areas of consolidation. The necrosis may liquefy to form cavities. Differentiation from T.B. depends on detection of fungal bodies. Older lesions showed fibrosis and calcification.

