

Systemic mycoses

- fungal infections or diseases which involve the inner tissues including internal organs
- may be grouped as
 1. infections caused by a group of fungi referred to as true pathogenic fungi

- include

disease	causative organism
a. Histoplasmosis	<i>Histoplasma capsulatum</i>
b. Coccidioidomycosis	<i>Coccidioides immitis</i>
c. Blastomycosis	<i>Blastomyces dermatitidis</i>
d. Paracoccidioidomycosis	<i>Paracoccidioides brasiliensis</i>

2. opportunistic systemic fungal infections

- causative agents are naturally saprophytes or normal human flora
 - fungi of very low virulence
- disease production is determined by compromised human immunological defense mechanisms
- include
 - a. systemic candidiasis
 - b. cryptococcosis
 - c. mucormycosis
 - d. aspergillosis
 - e. penicilliosis
 - f. pneumocystis pneumonia
 - g. less commonly encountered specific saprophytic fungi including *Fusarium* species

3. disseminated infection from other sites

Systemic infections due to true pathogenic fungi

- Infect immuno-competent as well as immuno-compromised people
- encountered mostly in parts of America
- causative fungi
 - A. exhibit two morphological forms
 - phenomenon referred to as **dimorphism**
 1. filamentous fungi or moulds in
 - a. the saprophytic state
 - b. cultures incubated at a temperature 25°C
 2. yeasts in
 - a. infected tissues and specimens
 - b. cultures incubated at a temperature of 37°C

- dimorphism is a result of several factors including temperature at which growth occurs
 - partly temperature dependent
- B. majority of human infections are acquired through inhalation of spores into the lungs resulting in a primary infection

Primary infection due to dimorphic fungi

- tends to remain asymptomatic with a small number associated with symptoms of the illness
- some of the asymptomatic infections progress and develop into symptomatic illness after several years
- symptomatic illness is characterized by
 - a. local b. lymphatic c. haematogenous
 - spread to other parts including the skin mucous membranes subcutaneous tissues and bone

Histoplasmosis

- causative agent is *Histoplasma capsulatum*
- two varieties of the species cause disease in humans
 1. *Histoplasma capsulatum capsulatum*
 2. *Histoplasma capsulatum duboisii*
- the varieties 1) and 2)
 - a. are similar morphologically in cultures and microscopy of the mould
 - b. yeast cells or tissue phases are significantly different morphologically
 - c. produce different clinical manifestations
 - d. different in geographical distribution

H. capsulatum capsulatum

- saprophyte mostly found in soil contaminated with birds' and bats' droppings
- causative agent of **classical histoplasmosis**
 - encountered in all parts of the world
 - highly endemic in parts of America
 - majority result from reactivation of asymptomatic primary infection
 - reactivation may or may not be precipitated by other underlying diseases
- manifests mostly as
 1. chronic lung disease with formation of cavities
 2. disseminated illness involving other tissues and internal organs

- opportunistic classical illness may manifest as
 1. an acute disseminated disease
 2. chronic illness involving multiple organs including the liver and spleen
- microscopy of infected tissues shows *Histoplasma capsulatum capsulatum* as small intra-cellular budding yeasts inside different types of phagocytic cells
- macroscopic and microscopic examination of filamentous organism in culture shows specific identification features including
 - macroconidia which are spherical with fingerlike spines described as tuberculate macroconidia

2 *Histoplasma capsulatum duboisii*

- causative agent of African histoplasmosis
 - uncommonly encountered in specific countries in central parts of Africa
 - clinically manifests as chronic inflammatory swellings and ulcerative lesions
 - may involve the skin and subcutaneous tissues including bones
 - *Histoplasma capsulatum duboisii* in specimens is observable as yeast cells which are larger than those of *H. capsulatum capsulatum*
- lungs are not commonly infected
- source and route or routes of infection are not clearly identified

Coccidioidomycosis

- mostly asymptomatic or mild illness of the lower respiratory system
 - can manifest as mild pneumonia
- occasionally occurs as a severe illness
- inhaled spores of *Coccidioides immitis* in the lungs develop into spherical large structures referred to as spherules each spherule
 - a. contains numerous spores
 - b. develops and ruptures releasing its spores in the adjacent tissues and each of the released spore develops into a spherule
 - occurs repeatedly resulting in local spread
- severe illness is characterized by cavities in the lungs
- dissemination to extra-pulmonary sites is uncommon

Blastomycosis

- endemic in parts of America also isolated in parts of Asia and Africa
- manifestations of disseminated illness include chronic cutaneous swellings on exposed parts and involvement of other tissues
 - swellings occasionally ulcerate
- *Blastomyces dermatitidis* in infected tissues is observable as yeast cells with each cell producing a single bud

Paracoccidioidomycosis

- manifestations include ulceration of the mouth and nose with extension to the local lymph nodes
- spreads via lymphatic and haematogenous routes
- *Paracoccidioides brasiliensis* is observable microscopically in infected tissues as large yeast cells with each cell producing multiple buds

Laboratory investigation of systemic infections due to dimorphic fungi

specimens

- highly infectious
 - necessary safety methods required in specimen handling and laboratory procedures
- include
 - a. sputum
 - b. discharge or pus
 - c. skin scrapings
 - d. infected tissue
 - e. blood for serology

procedures

1. detection of the organism in yeast phase by microscopy using potassium hydroxide mount or special staining methods in tissues
2. cultures for isolation and identification

- a. cultures incubation at 25°C for filamentous fungus
 - specific colonial features are noted
 - Lactophenol blue stain used to show microscopic characteristics
- b. culture to confirm dimorphism
 - isolated filamentous fungus is sub-cultured on a suitable medium and incubated at 37°C for the yeast phase
 - specific cultural and microscopic features are useful in identification
3. serological tests may be useful in some infections
 - associated with difficulties in
 - a. differentiation of past exposure and current illness
 - b. cross-reactions

4. detection of fungal antigens in
 - a. specimens
 - b. identification of cultured organisms
5. fungal DNA based laboratory techniques

Management methods of systemic mycoses due to dimorphic fungi

- methods depend on several factors including
 - a. manifestations
 - b. predisposing factors
 - c. causative fungus and its antifungal susceptibility
- include
 1. surgical procedures
 2. antifungal agents administration including
 - a. amphotericin B as main agent
 - b. others including itraconazole and fluconazole

Mucormycosis or Zygomycosis

- uncommon opportunistic fungal infection
- predisposing conditions include
 1. metabolic derangements including acidosis
 2. other illnesses or treatment which suppress the immune responses to infection
 3. trauma
- causative fungi are rapidly growing saprophytes which release spores in air and dust mainly species of genera 1. Rhizopus 2. Absidia 3. Mucor
- most infections result from spores acquired through the respiratory tract
 - initial manifestations commonly involve head and neck regions

- specific manifestations depend on the site(s) involved
- commonest initial lesion is a swelling of variable size
- progresses rapidly as the causative organisms grow rapidly and invade tissues including blood vessels resulting in necrosis and thrombosis
 - associated with marked local and or haematogenous spread
- head and neck lesions may involve orbital area part of the face or nasal area
 - illness is named according to the site(s) affected including rhinocerebral zygomycosis
- other parts infected occasionally include lungs gastrointestinal tract skin

Laboratory investigation of mucormycosis

specimens from lesions include

- a. discharge
- b. tissue
- c. sputum

procedures

- a. microscopy for observation of characteristic hyphae
- b. culture
 - rapidly growing fungi with cottony colonies
 - microscopy shows characteristic sporangia and other specific differentiating characteristics

Management

- methods include
 - a. surgical procedures
 - b. amphotericin B administration
 - c. treatment of predisposing condition

Penicilliosis

- causative agent is *Penicillium marneffe*
 - uncommon dimorphic fungus encountered in parts of S.E. Asia
 - route of infection is not clearly defined
- an opportunistic infection in the immunocompromised people
- disseminated disease is characterized by
 - a. fever
 - b. weight loss
 - c. skin lesions including ulcers
 - d. abscesses
 - e. enlarged lymph nodes and other organs

Laboratory investigation of penicilliosis

- involves
 - a. demonstration of yeast cells intra and extra cellularly in specimens
 - b. appropriate cultures for isolation and identification

Antimicrobial susceptibility

- effective antifungal agents include itraconazole and voriconazole

Aspergillosis

- a group of diseases in which species of the genus *Aspergillus* are involved
- may or may not be opportunistic

Aspergillus genus of fungus

- composed of numerous species encountered mostly as saprophytes
 - most of the species are not associated with human disease
- species and their spores are found in various places in the environment
 - a. air
 - b. soil
 - c. decaying vegetation
 - d. organic debris
 - e. construction and demolition sites
- chances of contamination of items and inhalation of airborne spores are higher than for other fungi

Aspergillus species commonly associated with human diseases

- include

- a. *A. fumigatus* responsible for the majority
- b. *A. flavus* produces mycotoxin which damages various internal organs
- c. *A. niger*

mechanisms of disease causation include

- a. colonization
- b. invasion of tissues
- c. hypersensitivity reaction to the spores
- d. effects of released fungal toxin on tissues

manifestations of aspergillosis depend on the

- a. species and mechanism of disease causation
- b. parts of the human or systems involved

aspergillosis involving the respiratory system

- basically three categories of diseases
 1. allergic aspergillosis
 - manifestations are due to hypersensitivity reaction to inhaled spores of *Aspergillus*
 - may manifest as an asthmatic attack or alveolitis
 2. colonizing aspergillosis
 - acquired by inhalation of *Aspergillus* spores
 - *Aspergillus* species grows in or colonizes pre-existing lung cavities by the inhaled species

- colonizing aspergillosis more commonly develops in lung cavities resulting from previous pulmonary tuberculosis

Aspergillus grows and its filaments intertwine and form a mycelial mass in the cavity

- also referred to as fungus ball or aspergilloma

3. invasive aspergillosis

- occasionally encountered in patients with chronic debilitating illnesses
- characterized by rapid growth and invasion of the lung by Aspergillus species
 - causes destruction of lung tissue and blood vessels

other types of aspergilloses

- a. Nasal-orbital aspergillosis
 - encountered as aspergilloma in the air sinuses including the maxillary sinus
 - possible causative species include *A. fumigatus* and *A. niger*
- b. Cutaneous aspergillosis
 - occasionally encountered as external ear infection or otomycosis
 - may be caused by *A. niger* or *A. fumigatus*
- c. uncommon causative agent of finger or toe nail infection
- d. rare causative agent of mycetoma
 - associated with *A. nidulans* and *A. glaucus*

Laboratory investigation of aspergillosis

- for manifestations due to infection by *Aspergillus* species
 - A. detection of *Aspergillus* in various specimens by
 - 1. microscopic examination of potassium hydroxide mount for specific morphological features of *Aspergillus*
 - 2. culture for isolation
 - 3. identification
 - a. as genus *Aspergillus*
 - b. of species
 - to enable differentiation of regular saprophytes from possible pathogens

identification of *Aspergillus* species

- methods include
 1. examination of the cultures
 - colonial and microscopic features
 2. *A. fumigatus* may be identified as above and its ability to grow at 43 degrees c.
- species which are not common pathogens might require repeated isolation for conclusive results
- B. serology applicable in the investigation of aspergilloma
- C. detection of *Aspergillus* antigen(s) in serum in invasive aspergillosis
- D. others methods including specific methods of investigation of hypersensitivity states and toxin mediated illnesses

Management of aspergillosis

- A. aspergillosis due to infection by *Aspergillus* species
 - 1. Antifungal agents administration
 - amphotericin B
 - others including voriconazole
casprofungin itraconazole
 - choice depends on
 - a. type of aspergillosis
and effective agent
 - b. general status of the patient
 - c. availability of the agents
 - 2. other measures including surgical procedures
and other chemotherapeutic agents
- B. hypersensitivity reactions and toxin associated
conditions are managed differently