Medical mycology Le.6 **Dr.Hamzia Ali**

Dimorphic Systemic Mycoses

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, following the inhalation of conidia.

-1 Histoplasmosis

Histoplasmosis is an intracellular mycotic infection of the reticuloendothelial system caused by the inhalation of conidia from the fungus *Histoplasma capsulatum*. Histoplasmosis has a world wide distribution, however, the Mississippi-Ohio River Valley in the U.S.A. is recognized as a major endemic region. Africa, Australia and parts of East Asia, in particular India and Malaysia are also endemic regions. Two varieties of *H. capsulatum* are recognized, depending on the clinical disease: var. *capsulatum* is the common histoplasmosis, and var. *duboisii* is the African type. The two varieties are identical in their saprophytic mould form but differ in their parasitic tissue morphology.

Clinical manifestations:

Approximately 95% of cases of histoplasmosis are in apparent, subclinical or benign. Five percent of the cases have chronic progressive lung disease, chronic cutaneous or systemic disease or an acute fulminating fatal systemic disease. All stages of this disease may mimic tuberculosis .

Histoplasmosis may be divided into the following types:

Primary pulmonary histoplasmosis

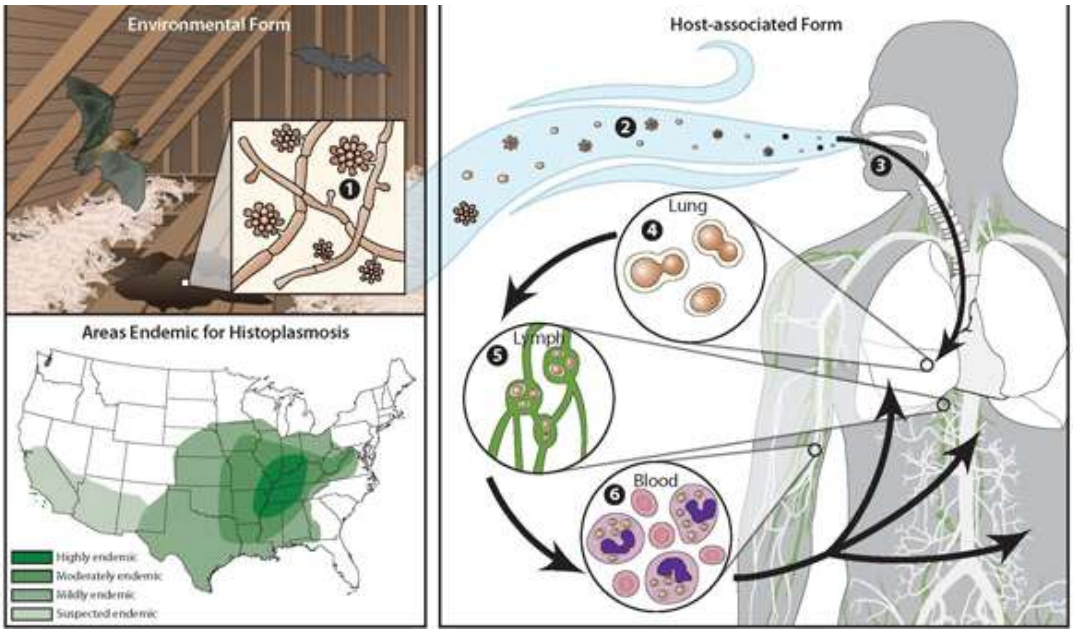
Progressive disseminated histoplasmosis

Primary cutaneous histoplasmosis

.Histoplasmosis of the lower gum showing ulcer around base of the teeth

Disease mechanism

H. capsulatum grows in soil and material contaminated with bird or bat droppings.The fungus has been found in poultry house litter, caves, areas harboring bats, and in bird roosts (particularly those of starlings). The fungus is thermally dimorphic: in the environment it grows as a brownish mycelium, and at body temperature (37 °C in humans) it morphs into a yeast. Histoplasmosis is not contagious, but is contracted by inhalation of the spores from disturbed soil. The inoculum is represented principally by microconidia. These are inhaled and reach the alveoli. In the alveoli, macrophages ingest these microconidia. They survive inside the phagosome. As the fungus is thermally dimorphic, these microconidia are transformed into yeast. They grow and multiply inside the phagosome. The macrophages travel in lymphatic circulation and spread the disease to different organs.



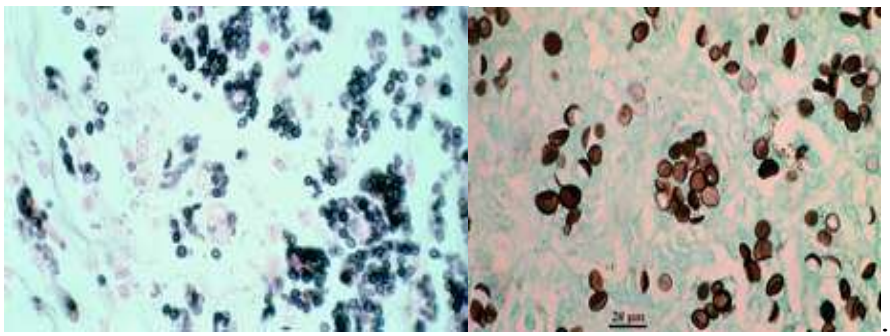
Laboratory diagnosis:

.1-**Clinical material:** Skin scrapings, sputum and bronchial washings, cerebrospinal fluid, pleural fluid and blood, bone marrow, urine and tissue biopsies from various visceral organs.

.**2-Direct Microscopy**: (a) Skin scrapings 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, (c) Tissue sections should be stained using PAS digest, Grocott's methenamine silver (GMS) or Gram stain.

Histopathology is especially useful and is one of the most important ways of alerting the laboratory that they may be dealing with a potential pathogen.



Tissue morphology of *H. capsulatum var. capsulatum* (left) showing numerous small narrow base budding yeast cells (1-5µm diam) inside macrophages and *H. capsulatum var. duboisii* (right) .showing larger sized budding yeast cells (5-12) µm in diameter

.**3-Culture**: Clinical specimens should be inoculated onto primary isolation media, like Sabouraud's dextrose agar and Brain heart infusion agar supplemented with 5% sheep blood..

.Culture of *Histoplasma capsulatum*

4 . **-Serology**: Immunodiffusion and/or complement fixation tests for the detection of antibody have proven to be useful in the diagnosis of Histoplasmosis, especially in immunocompetent patients. However, detection of antibodies in immunosuppressed patients is often difficult, with between 20-50% of patients testing negative.

Causative agents *Histoplasma capsulatum*

Treatment In the majority of immunocompetent individuals, histoplasmosis resolves without any treatment. Antifungal medications are used to treat severe cases of acute histoplasmosis and all cases of chronic and disseminated disease. Typical

treatment of severe disease first involves treatment with amphotericin B, followed by oral itraconazole.Treatment with itraconazole will need to continue for at least a year in severe cases.while in acute pulmonary histoplasmosis, 6 to 12 weeks treatment is sufficient..

2-Blastomycosis

Blastomycosis is a chronic granulomatous and suppurative disease having a primary pulmonary stage that is frequently followed by dissemination to other body sites, chiefly the skin and bone. Although the disease was long thought to be restricted to the North American continent, in recent years more cases have been diagnosed in Africa, Asia and Europe. All available clinical and epidemiological evidence indicates that humans and lower animals contract blastomycosis from some source in nature especially soil

Pathogenesis

Inhaled conidia of *B. dermatitidis* are phagocytosed by neutrophils and macrophages in alveoli. Some of these escape phagocytosis and transform into yeast phase rapidly. In lung tissue, they multiply and may disseminate through blood and lymphatics to other organs, including the skin, bone, genitourinary tract, and brain. The incubation period is 30 to 100 days, although infection can be asymptomatic.

Clinical manifestations:

Pulmonary blastomycosis: In most individuals pulmonary lesions are asymptomatic and are not detected until the infection has spread to other organs. Others develop symptoms after an incubation period of 3-15 weeks. In most cases blastomycosis is indolent in onset and patients present with chronic symptoms such as cough, fever, malaise and weight loss. The lesions become more extensive, with continued suppuration and eventual necrosis and cavitation.

Cutaneous blastomycosis: Haematogenous spread gives rise to cutaneous lesions in over 70% of patients. These tend to be painless and present either as raised verrucous lesions with irregular ulcers. The face, upper limbs, neck and scalp are the most frequent sites involved.

.Ulcerated granuloma due to *B. dermatitidis*

Osteoarticular blastomycosis: Occurs in about 30% of patients with the spine, pelvis, cranial bones, ribs and long bones most commonly involved.

Other forms include genitourinary blastomycosis ,spread to the brain causing meningitis, and spinal or brain abscess. Other organs may also be involved

Laboratory diagnosis:

.1-Clinical material: Skin scrapings, sputum and bronchial washings, cerebrospinal fluid, pleural fluid and blood, bone marrow, urine and tissue biopsies from various visceral organs.

2 . -Direct Microscopy: (a) Skin scrapings 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, (c) Tissue sections should be stained using PAS digest, Grocott's methenamine silver (GMS) or Gram stain.

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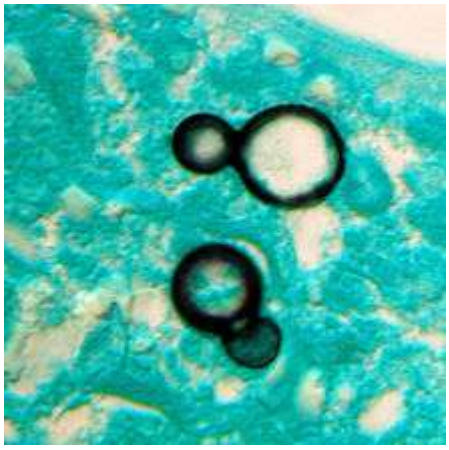
3-Culture: Clinical specimens should be inoculated onto primary isolation media, like Sabouraud's dextrose agar and Brain heart infusion agar supplemented with 5% sheep blood.

.**4-Serology**: Serological tests are of limited value in the diagnosis of Blastomycosis .



Large, broadly-based budding yeast cells characteristic of Blastomyces dermatitidis in a GMS-stained biopsy section from a human leg.

Causative agents:

Blastomyces dermatitidis

Treatment

Itraconazole given orally is the treatment of choice for most forms of the disease. Amphotericin B is used for patients with central nervous system disease.. Fluconazole has excellent CNS penetration and is useful where there is CNS involvement after initial treatment with Amphotericin B.