

# CLASSICAL HISTOPLASMOSIS

## Learning objectives

To know in detail about,

- Synonyms of classical histoplasmosis
- Natural habitat and morphology of *Histoplasma capsulatum*
- Cultural characteristics of *Histoplasma capsulatum*
- Pathogenesis and pathogenicity of classical histoplasmosis
- General approaches used to diagnose classical histoplasmosis

## INTRODUCTION

- Synonyms of this disease are small form histoplasmosis, Darling's disease and reticuloendothelial cytomycosis.
- Histoplasmosis is a chronic, granulomatous disease caused by *Histoplasma capsulatum* var *capsulatum* (Teleomorph : *Ajellomyces capsulatus*).

## NATURAL HABITAT AND MORPHOLOGY

- The organisms become heavily concentrated in the feces of birds (particularly black birds, sea gulls, starlings and pigeons); bats are also important vectors of this disease. Thus, the fungus has been isolated from soil in bat caves, bird roosts, chicken houses, and silos inhabited by pigeons.
- The organisms are facultative, intracellular parasites of macrophages.
- The tissue form cells of *H. capsulatum* var. *capsulatum* appear as small, oval yeast cells with or without buds.
- Daughter cells are attached to mother cells by a narrow attachment point.
- The yeast cells are relatively small (2-4  $\mu\text{m}$ ). A clear halo is seen around darker-staining central material.

## CULTURAL CHARACTERISTICS

- *H. capsulatum* may be cultured on the Sabouraud agar with chloramphenicol but without cycloheximide at 25° C, or on brain heart infusion agar with blood at 37° C. At 25° C, the mycelial phase has two types of conidia: small, round microconidia and large (7-18  $\mu\text{m}$ ) thick-walled, macroconidia with knob-like projections. The yeast phase grows at 37° C on blood agar.

## EPIDEMIOLOGY

- Prevalent in America, parts of Africa and Asia. Rare in Australia and Europe.
- In the United States, histoplasmosis occurs throughout the midwest and much of the eastern half of the United States.
- Infection usually occurs through inhalation of spores of the dimorphic fungus *Histoplasma capsulatum*.
- Infections may also occur through ingestion. Most infections are subclinical or benign.
- Histoplasmosis may occur commonly in animals in endemic areas.
- Dogs are particularly susceptible, but the disease has also been reported in cattle, cats, swine, horses, sheep and wild animals.
- The disease has not been reported in birds. *Histoplasma capsulatum* is not contagious.

## PATHOGENESIS

- The disease may vary from small granulomatous nodules to an acute, disseminating, rapidly fatal form.
- Usually, the disease manifests itself either as a pulmonary or intestinal infection, and may be inapparent or subclinical, mild, acute, chronic, or disseminated.
- Ulcerations and tuberculosis-type lesions may occur in many of the organ systems.
- Mice are highly susceptible to infection, whereas other laboratory animals vary in susceptibility.
- Following inhalation of spores, macrophages phagocytize the organisms and an inflammatory response ensues.
- The fungus is either killed, or local granulomas form with calcification.
- Host immunity and the number of spores inhaled determine which form the disease manifests itself as.
- The macrophages may carry the organisms to various body sites and actually help to disseminate it.
- Thus, histoplasmosis has been referred to as a disease of the reticuloendothelial system.
- Enlargement of the liver and spleen, and nodules on the tongue, ocular involvement, and abortion have also been reported.

## PATHOGENECITY

### Clinical signs

- Basically pulmonary. Most infections are asymptomatic or benign and self limiting.
- Symptomatic forms with fever, night sweats, weight loss and hemoptysis.
- In disseminated cases hepatomegaly and splenomegaly develop, with anemia and leucopenia.
- Chronic pulmonary infections associated with cough, dyspnea, chest pain, hemoptysis and weight loss.
- Cavities may develop in the apex or subapical regions of the lungs.

### Lesions

- Epithelioid and giant cell granulomas of the lung are characteristic.
- Invasion of cells of the reticuloendothelial system in the adrenal glands, bone marrow, gastro intestinal tract, liver, lymphnode and spleen. Lesions tend to become calcified.

## DIAGNOSIS

### Diagnosis

- The organisms are rarely seen extracellularly. Specimens (CSF, biopsies, bone marrow, lymph nodes, or buffy coat) stained with a variety of histological stains (Gomori methanamic or Periodic acid-schiff stains) reveal the organisms within macrophages. The yeast cells are relatively small (2-4  $\mu\text{m}$ ).
- A clear halo is seen around darker-staining central material.
- The skin test becomes positive after exposure to the fungus and remains so for the life of the animal.
- Thus, the skin test is of little usefulness in detecting active disease.
- Furthermore, skin testing may induce antibody formation, thereby, interfering with more useful serological tests.
- The complement fixation test for detection of specific antibodies is useful for diagnosis.
- Animals develop a rapid rise in titer following infection; the titer falls off gradually and disappears by nine months.
- However, cross-reactivity to antigens of the other systemic fungal pathogens may occur.

- The immunodiffusion test is a useful adjunct to the CF test; the development of 2 bands may indicate active or past infection, respectively.
- A latex agglutination test and fluorescent antibody test are useful screening tests, but complement fixation is considered the confirmatory test.

### **Treatment**

- Amphotericin B is the drug of choice, but ketoconazole, sulfonamides, and ethyl vallynate may also be effective.