Systemic Mycosis

Systemic mycotic agents are inherently virulent and can cause disease in healthy humans. Four fungi are included in this group.

1. *Histoplasma capsulatum*
2. *Blastomyces dermatitidis*
3. *Paracoccidiodes brasiliensis*
4. *Coccidiodes immitis*

They are dimorphic fungi and grow in filamentous at 25C, however when they infect human or cultured at 37 C using special media and techniques, they transform to a unicellular morphology. The first three are characterized by the presence of budding yeast cells, whereas C. immitis infections are characterized by the production of spherules (sporangium-like structures filed with endospores).

The primary infection for all four systemic mycotic agents is the lung, in which the infections in most cases are a symptomatic or of very short duration, resolve without treatment and accompanied with a host specific resistance to reinfection. Frequently, it is the secondary spread of systemic disease that causes the patient to seek medical attention.

The severity of infection depends on the organism and the host immune status. The four agents tend to be restricted to particular geographical regions, but the ease of travel and increase in reactivation disease are starting to blur these distinctions.

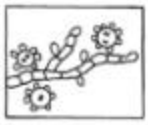
Histoplasmosis:

Etiologic agent:

The asexual phase of Histoplasma capsulatum and the state is Ajellomyces capsulatum.

Mycology:

Dimorphic fungi and possess a mycelial form at 25 C with typical tuberculate macro and microconidia. At 37 C and in host tissue this organism is budding yeast found predominantly in histocytes.



Epidemiology and ecology:

Occur throughout temperate, subtropical tropical areas and the organism has been isolated from soil samples those contaminated by bats, chicken and starling droppings. Unique clinical forms occur in Africa caused by H. capsulatum var duboisii.

Clinical diseases:

There are two form of disease:

a. In normal hosts:

Mild-flu-like illness occurs with normal exposure or acute pulmonary histoplasmosis occurs with heavy exposure.

b. Opportunistic infection:

Usually disseminated histoplasmosis occurs in individuals who have an immune defect or chronic pulmonary histoplasmosis occurs in individuals who have a structural defect.

Laboratory diagnosis:

Is based on serologic finding, direct histopathology examination of infected tissue and culture. The antigenic reagents are derived from the cell-free culture filtrate from the mycelial phase of the growth or inactivated whole yeast phase cells and called histplasmin. Both reagents are used since; neither type detects antibodies in all cases.

Treatment:

Amphotericin B is the mainstay of treatment for disseminated infection and other forms.

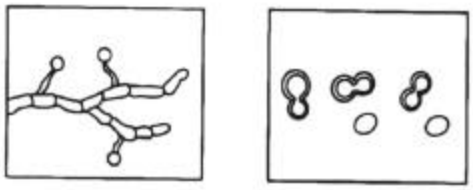
Blastomycosis:

Etiologic agent:

A sexual phase is *Blastomyces dermatitidis* and the sexual phase is called *Ajellomyces dermatitidis*.

Mycology:

A dimorphic fungus with mycelial form at 25 C has typical pyriform microconidia. At 37 C and in host tissue this organism is yeast in diameter with buds produced singly or is attached to parent cell by a broad base.



Epidemiology and ecology:

North America continent and parts of Africa, the fungi is an important veterinary problem and dogs develop a similar disease. There are a few reports of successful isolation of the organism from soil.

Clinical disease:

Primary infection in the lung is often unapparent and chronic cutaneous diseases are the most common clinical presentation.

Laboratory diagnosis:

Serologic using *B. dermatitidis* cell-free culture filtrate of both the medial and yeast phase (Blastomycin) to detect immune response to infection. However the reagents tend to have high degree of cross reactivity with other mycosis, particularly Histoplasmosis and coccidioidomycosis. An immuno-diffusion test has been developed based on the availability of a yeast phase culture filtrate possess a high degree of sensitivity and specificity.

Diagnosis requires identification of the organism in infected tissue or isolation in culture. Microscopic examination of potassium hydroxide-treated fluid from abscesses will reveal broad-based budding yeast cells. The organism grows readily in culture and identification based on conversion to the yeast or an antigen test.

Treatment:

Can be achieved using Amphotericin B or Ketaconazole.

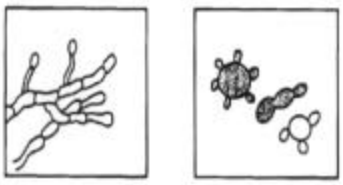
Paracoccidioidomycosis:

Etiologic agent:

A sexual phase *Paracoccidiodes brasiliensis* and the sexual phase have not been known.

Mycology:

Dimorphic and has mycelial at 25, with no typical pattern of sporulation. At 37 and tissue the fungi is a yeast form with several budding cells attached to the parent cell taking a pilot's wheel arrangement.



Epidemiology and ecology:

Limited to Central and South America (Brazil) and the clinical incidence in males is higher than females, also the fungi has been isolated from soil on rare occasions.

Clinical diseases:

Primary pulmonary disease is often unapparent and disseminated infections usually causes ulcerative lesions of the buccal, nasal and occasionally gastrointestinal mucosa.

Laboratory Diagnosis:

It is based on detection of specific antibodies, the visualization of the organism in histopathology material and isolation of fungus in culture. The antigen is called paracoccidiodin and the fungus can be seen in KOH preparation of the infected material or using silver-stained histological section.

Treatment:

Can be treated using Amphotericin B, ketaconazole and the newer azoles such as Itraconazole and floconazole.

Coccidioidomycosis:

Etiologic agent:

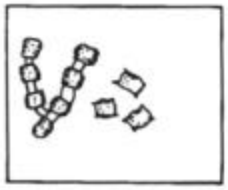
Coccidiodes immitis

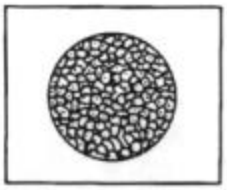
Mycology:

Dimorphic with mycelial at 25 and as the culture ages the septate hyphae matures in a manner such that alternate cell develop into arthroconidia being separated by vocalized cells. The arthroconidia separated readily and have a barrel-shaped appearance. In tissue and at 37 the organism develops into large spherical structure called spherules (sporangia) that are filled with endospores.

Epidemiology and ecology:

The disease is geographical restricted to North, Central and South America. Natural infections occur in domestic and wild animals. The fungus also has been isolated from soil samples in endemic area.





Clinical diseases:

About 60% of infections are asymptomatic and the most common symptoms of primary disease are cough, fever and chest pain. An epidemiologic history should be taken to find out whether the patient has been in an endemic area.

Laboratory diagnosis:

Two sources of antigens including both cell-free culture filtrates are used in the preparation of serologic reagents. The mycelial phase (coccidiodin) and the spherules phase (spherulin). C. immitis spherules can be seen in infected tissue stained with hematoxylin and eosin. The mold phase resemble several saprophytic fungi and therefore definitive identification is based on conversion to spherules or a specific exoantigen test.

Treatment:

Using Amphotericin B or ketaconazole, however relapses occur following cessation of therapy.

Dimorphic Systemic Mycoses

These are fungal infections of the body caused by dimorphic fungal pathogens which can overcome the physiological and cellular defenses of the normal human host by changing their morphological form. They are geographically restricted and the primary site of infection is usually pulmonary, following the inhalation of conidia.

Disease	Causative organisms	Incidence
Histoplasmosis	*Histoplasma capsulatum*	Rare*
Coccidioidomycosis	*Coccidioides immitis*	Rare*
Blastomycosis	*Blastomyces dermatitidis*	Rare*
Paracoccidioidomycosis	*Paracoccidioides brasiliensis*	Rare*

*more common in endemic areas