Systemic Mycoses Caused by Dimorphic Environmental Molds (Endemic Mycoses)

The major pathogens included in this group are ***Blastomyces dermatitidis***, ***Coccidioides*** species, ***Histoplasma capsulatum*** , and ***Paracoccidioides brasiliensis***.

The characteristics shared by these fungi are several:

1. An endemic area in which they are found in the environment in the soil.
2. Production of airborne conidia which are inhaled when the environment is disturbed by human activity or weather patterns.
3. The ability to infect immune normal as well as immunocompromised human and lower animal hosts.
4. Exposure is believed to be common but disease is usually subclinical or self-limited. More serious disease is related to the infectious dose and host factors.
5. The property of dimorphism by which they undergo morphogenesis from the mold form in the environment to a distinctive tissue form during infection.
6. They are classed in the family **Ajellomycetaceae** within the **Onygenales**.

Blastomycosis

Disease definition: A chronic, suppurative, and granulomatous pulmonary mycosis initiated by inhaling conidia of the soil-dwelling mold, *Blastomyces dermatitidis*. Doges also are affected and are a sentinel species. *Blastomyces dermatitidis* converts to yeast forms in the lung, causing lesions. Skin is frequent site of dissemination.

Geographic distribution: Ohio-Mississippi River Valley area, Southeast and Midwestern states of the United States and Southern Canada. Small foci in Africa and India.

Ecologic niche: Blastomycosis is mostly rural but the mold is difficult to isolate from nature.

Epidemiology: The extent of subclinical exposure is unknown. Blastomycosis is notable for outbreaks.

Risk group/Factors: Farmers, hunters, campers, and other outdoor vocations or avocations.

Transmission: Respiratory-inhaling conidia from the environment.

Determinants of pathogenicity: Mold to yeast dimorphism; adhesion "BAD1" is an immunodominant antigen; cell wall α-(1→3)-glucan.

Clinical forms: Pulmonary: infiltrates, nodules, cavities, pleuritic, and pneumonia. Chronic pulmonary; Disease may disseminate especially to skin, bones, prostate, and CNS.

Therapy: Itraconazole (ITC), with amphotericin B (AmB) reserved for treatment failures or rapid progression. Voriconazole (VRC) is promising for CNS disease.

Laboratory detection, Recovery, and Identification: Direct exam and culture from early morning sputum and from scrapings or aspirates of skin lesions: direct smear, histopathology, culture. Identify culture with gene probe "AccuProbe". Serology test for antibodies.

Coccidioidomycosis

Disease definition: A community acquired pneumonia that is acute, self-limited, or progressive. Also known as "cocci", "Valley fever", and desert rheumatism.

Etiologic agent: Soil-dwelling molds, ***Coccidioides immitis, C. posadasii***

Geographic distribution: Major area for *C. immitis* – Central Valley of California; *C. posadasii* occurs in Arizona near Phoenix, in Mexico, and in smaller foci in Central America and South America.

Ecologic Niche: Lower Sonoran life zone, semiarid, very hot summers, little rain, few freezes.

Epidemiology: Majority of infections are subclinical, 40% have symptoms ("flu", "desert rheumatism"), 2% develop chronic pulmonary disseminated forms, and 0.5 – 1% develop extrapulmonary disseminated forms.

Risk groups/Factors: Persons with AIDS, archeologists, diabetics, elderly retirees, farmers, the immunosuppressed, military personnel on maneuvers, pregnant women.

Transmission: Disturbance of desert soil or dust storms; inhaled arthroconidia in dusts; handling materials shipped from endemic areas.

Determinants of pathogenicity: Dimorphism – the tissue form consists of spherules + endospores. The spherule outer wall lipids and glycoprotein are pathogenic factors.

Clinical forms: A cute or chronic pulmonary; extrapulmonary – skin, bones, meninges.

Therapy: Most recover without therapy. Fluconazole (FLC), 400 mg/day; amphotericin B (AmB) for treatment failures or rapid progression. Meningitis requires higher doses, intrathecal AmB, and consideration of combined therapy with an azole and AmB.

Laboratory detection: Culture early morning sputum + genetic identification with AccuProbe®; serology – CF test (titer is prognostic = "VF titer"); ID test – diagnostic.

Histoplasmosis

Disease definition: Histoplasmosis is a community – acquired pulmonary infectious disease caused when an environmental disturbance aerosolizes microconidia of the soil – dwelling mold ***Histoplasma capsulatum***. Conidia are then inhaled and convert to yeast forms in the lung, causing an infection that may be subclinical, influenza-like, or pneumonia.

Etiologic agents: *Histoplasma capsulatum* – North America and microfloci worldwide; *H. capsulatum* var. *duboisii* – Africa; *H. capsulatum* var. *farciminosum* – Africa, causes epizootic lymphangitis in equines.

Geographic distribution: The major endemic area is in the United States bordering the Mississippi and Ohi river valleys; from the St. Lawrence River in the north to the Rio Grande River in Texas; and smaller foci worldwide.

Ecologic Niche: Soil mixed with bird droppings or bat guano; blackbird roosting sites, attics of old buildings, caves.

Epidemiology: Exposure is common, ≈20 million in the United States; 0.5 million new cases/year. Most exposed persons have a mild flu-like illness. Cases are sporadic or result from outbreaks. Outbreaks occur after disturbing the environment near bird roosts, construction, renovation, and demolition involving attics and belfries. It is a recreational risk to cave explorers.

Risk group/Factors: Cleaning contaminated sites, for example, chicken coops or bird roosting areas; demolition and construction, installing heating/air conditioning; restoring old buildings; cave exploring. Extrapulmonary disease occurs in immunosuppressed persons including people living with AIDS.

Transmission: The route of infection is via inhalation of dusts containing microconidia. Histoplasmosis is not transmissible from person to person.

Determinants of pathogenicity: Mold → yeast dimorphism; cell wall component α-(1→3) glucan; catalase; modulation of phagolysosome pH, calcium-binding protein-1, DRK1, a histidine kinase global regulator of dimorphism.

Clinical Forms: Acute pulmonary, chronic pulmonary, extrapulmonary disseminated.

Laboratory Detection and Identification: Culture early morning sputum; identify cultures with DNA probe (AccuProbe®); serology – antibody tests; urine HPA antigen test for disseminated desease.

Paracoccidioidomycosis

Disease definition: Paracoccidioidomycosis is a primary pulmonary mycosis with mucocutaneous dissemination, endemic to Central and South America. A long latent period, months or even years, may elapse between the time of infection and the development of clinical disease.

Etiologic agent: ***Paracoccidioides brasiliensis*** is a dimorphic fungal pathogen.

Geographic distribution: Central and South America, especially Brazil.

Ecologic Niche: *Paracoccidioides brasiliensis* is rarely isolated from the environment. It has been isolated from armadillos, a sentinel animal for an environmental microfocus of *P. brasiliensis*.

Epidemiology: The annual estimated incidence is 1–3/100,000 population in Brazil.

Risk group/Factors: The male sex is at increased risk; for example, farmers, coffee growers, and lumbermen.

Transmission: The route of infection is via inhalation of conidia from the environment.

Determinants of pathogenicity: Cell wall α-(1→3)-glucan resists lysis in the host; gp43 is an adhesin and a dominant antigen.

Clinical forms

- **Adults.** Mucocutaneous form: mouth ulcers, enlarged cervical nodes, adjacent skin; also chronic pulmonary disease.
- **Under 30 years old.** Infection of lymph nodes, spleen, liver, and bone marrow.

Therapy: Ketoconazole, itraconazole (ITC), AmB, role for sulfa.

Laboratory detection and identification:

- **Dimorphic:** mold at 25°C; at 37°C converts to a yeast form with multipolar budding in a "pilot wheel" shape.
- **Direct examination:** KOH prep form sputum, touch smears of mucocutaneous lesions, biopsy.
- **Culture** from sputum and from mucocutaneous lesions.
- **Identify culture** by rDNA gene sequence.
- **Serodiagnosis:** antibodies against 43 kDa protein are diagnostic.
- **Genetic identification:** gene targets are the ITS1, ITS2 regions of rDNA and exon 2 of PbGP43.