Chapter

Systemic mycoses

-- These infections result from **inhalation of spores** of **dimorphic fungi** that have their **mold forms in soil**.

-- In the lungs **spores differentiate into yeasts** or other specialized forms such as **spherules**.

-- Though **mostly asymptomatic** and self limiting, in some persons **disseminated disease** develops causing **destructive lesions in other organs** and **may be fatal**.

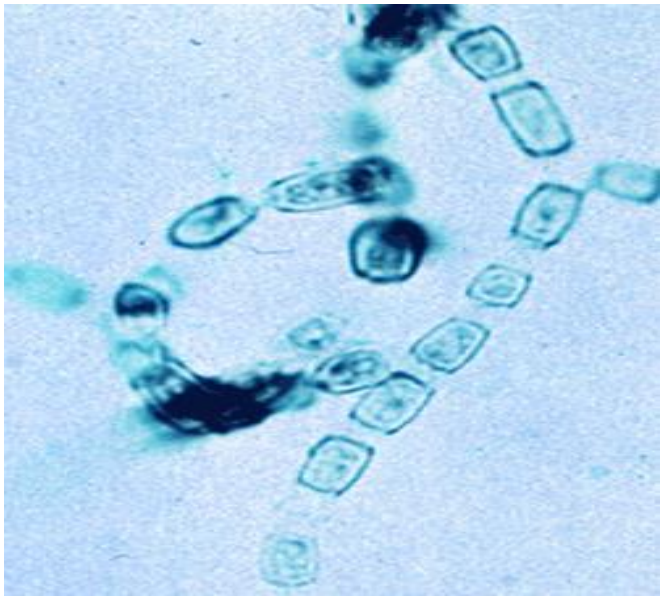
Coccidiodes

C. immitis causes **coccidomycosis**.

It is **dimorphic** and exists as **mold in soil** and as a **spherule in tissues**.

In soil it forms **hyphae** with alternating **arthrospores** and empty cells.

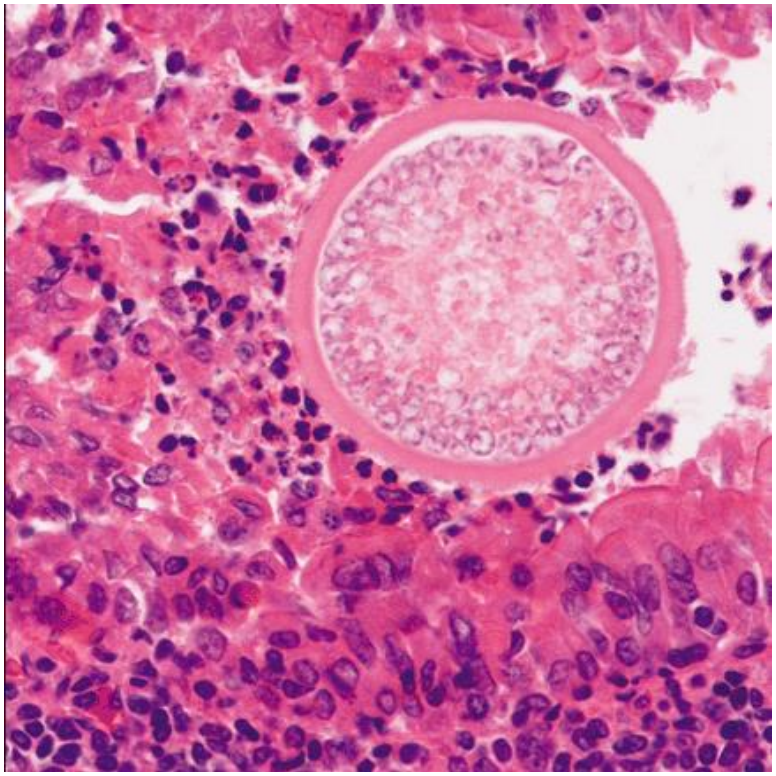
Arthrspores are inhaled and cause disease.



Pathogenesis

In **lungs** arthrospores transform into **large (30 um) spherules** which have **thick wall** and are **filled with endospores.**

On rupture, endospores are released and form new spherules.



-- Spread to other organs is by **direct extension** or **bloodstream**.

-- **Granulomatous lesions** can form **anywhere** but particularly in **bones, meninges, skin** and **CNS**.

-- **Dissemination from lungs to other organs occurs in cases of deficient CMI.**

-- Otherwise **delayed hypersensitivity is developed** which restricts the growth of organism.

-- There is a skin test which if positive indicates **adequate immunity**.

Clinical findings

-- Lung infection is often **asymptomatic** and only a **positive skin test** or **presence of antibodies** can detect the disease.

-- There may be non-specific **influenza like symptoms**.

-- About **50% cases show changes in lungs** detected by chest X-ray and **10% develop erythma nodosum or arthralgias.**

-- **Dissemination is rare** and occurs in only 1% infected persons though in some races such as **Filipinos and African Americans**, it can be up to 10%.

-- Women in **third trimester** of pregnancy are also susceptible.

Erythma nodosum manifests as **red tender nodules (“desert bumps”)** on extensor surfaces such as the skin over the tibia and ulna.

It is a **delayed cell mediated hypersensitivity response to fungal antigens** and is indicator of **good prognosis.**

There are no organisms in nodules.

EN is not specific for this disease.

It may also be seen in **histoplasmosis**, **TB** and **leprosy**.

-- In infected persons, skin tests with **fungal extracts** (coccidiodin or spherulin) cause **at least a 5 mm induration 48 hours after infection** (delayed hypersensitivity reaction).

-- Skin tests become positive **within 2-4 weeks and remain so for many years** but are often negative (**anergy**) in patients with **disseminated disease**.

Laboratory Diagnosis

In **tissue specimens**, **spherules** are seen microscopically.

Cultures on Sabouraud's agar incubated at 25°C show **hyphae with arthrospores**.

These arthrospores are **highly infectious by inhalation** so care should be taken.

In serologic tests, **IgM and IgG precipitins appear within 2-4 weeks of infection** and then decline in subsequent months.

Treatment and Prevention

-- No treatment is needed for **mild or asymptomatic infection**.

-- **Amphotericin B** is used for persisting **lung lesions or disseminated disease**.

-- **Ketoconazole** is also effective.

-- In meningitis, **fluconazole** is drug of choice.

-- Patients who have recovered need **long-term suppressive therapy with fluconazole** to prevent recurrence.

Histoplasma

-- ***H. capsulatum*** causes **histoplasmosis**.

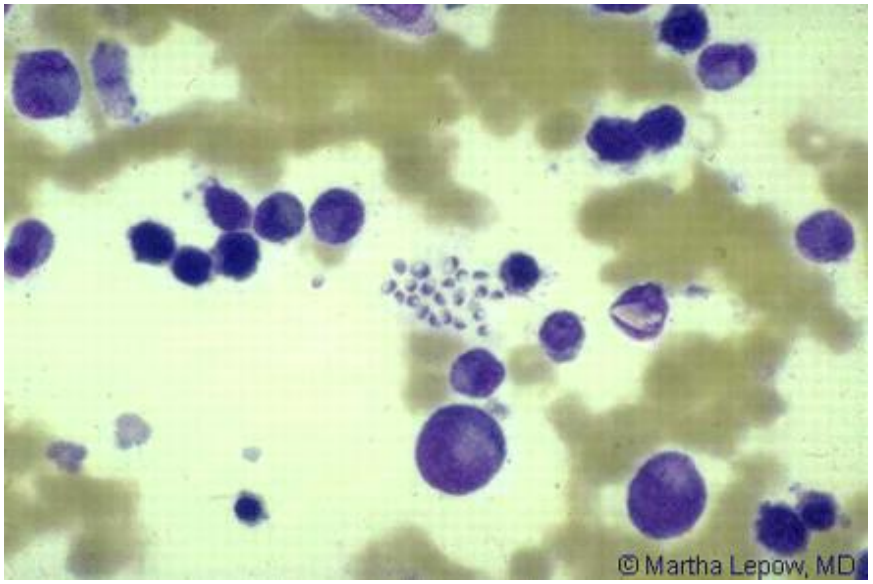
-- It is **dimorphic**.

-- It forms **tuberculate macroconidia with typical thick walls and finger like projections** and **infectious microconidia which are smaller, thin, smooth walled spores.**

-- It grows in **soil** heavily contaminated with **bird droppings**.

-- In African countries, ***H. duboisii*** is the main causative agent.

Tuberculate macroconidia



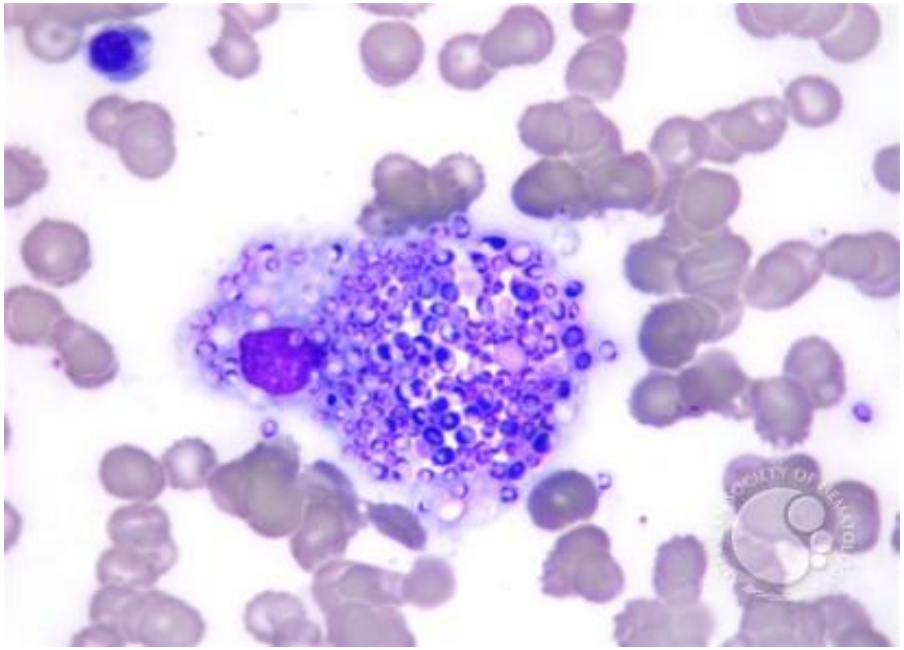
Microconidia

Pathogenesis and Clinical findings

Inhaled spores are engulfed by macrophages and grow into yeast form.

In **tissues**, it occurs as **oval budding yeast inside macrophages**.

They produce **alkaline** substances which **degrade enzymes of phagolysosome**.



-- The organisms spread widely throughout the body **especially to liver and spleen**.

-- Most infections remain **asymptomatic** and the **small granulomatous foci heal by calcification**.

-- Severe **disseminated histoplasmosis** develops in a **minority of infected persons**, especially in infants and immunocompromised persons (typical lesions on tongue).

-- A skin test using **histoplasmin** (a mycelial extract) becomes positive within 2-3 weeks and remains so for many years.

-- There are many **false positive results** but it is useful for epidemiologic studies.

Laboratory diagnosis

-- In **tissue biopsy** or **bone marrow aspirates**, **oval yeast cells within macrophages** are seen microscopically.

-- **Tuberculate macrochonidia** from **culture at RT** and **yeasts at 37°C are diagnostic**.

-- **ELISA** and **PCR** can also be useful.

-- In immunocompromised persons, tests for ***Histoplasma*** **antigen in urine** are especially useful because antibody tests may be negative.

-- An antibody titer of **1:32** in complement fixation test is useful.

-- These titers **fall in inactive disease** and **rise in disseminated disease**.

-- **Immunodiffusion** test is also available which is **more specific** but **less sensitive.**

Treatment and Prevention

-- No therapy is needed in asymptomatic or mild cases.

-- For **progressive lung lesions, itraconazole** is beneficial and in **disseminated disease**, **amphoteicin B** is drug of choice.

-- **In meningitis, fluconazole is used.**

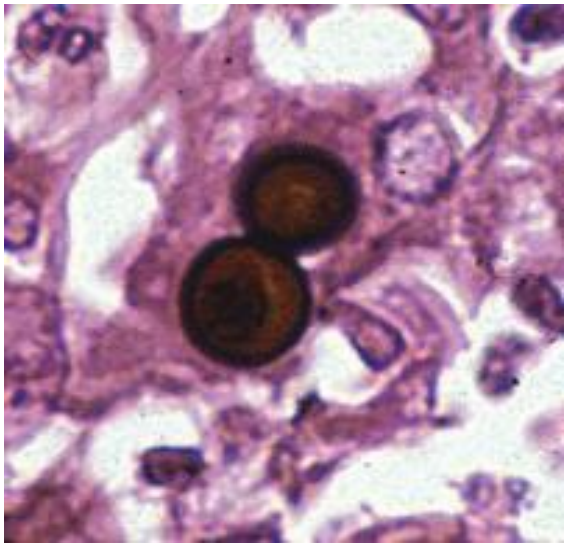
Blastomyces

-- ***B. dermatidis*** causes **blastomycosis**.

-- It is **dimorphic**.

-- The yeast in tissue is round with doubly refractive wall and a single **broad based bud**.

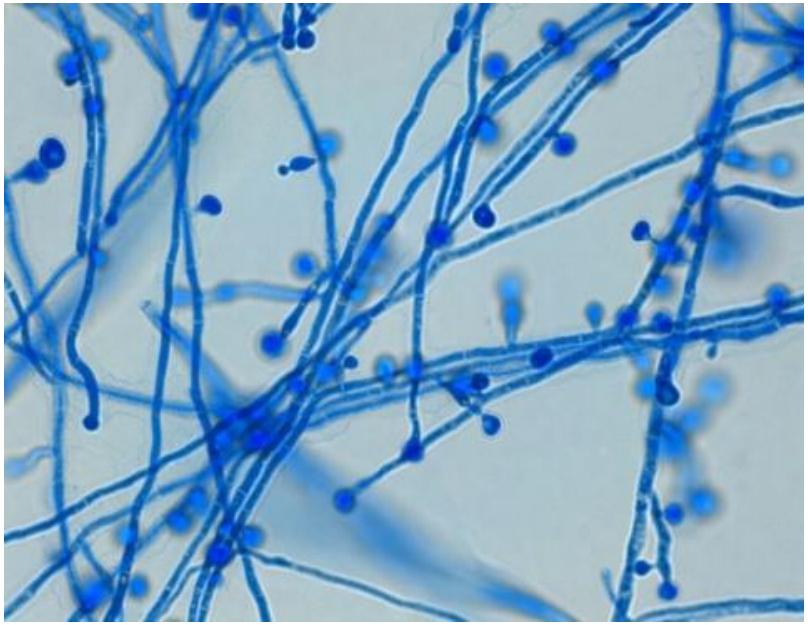
-- ***Cryptococcus neoformans*** form **narrow based bud**.



-- It mainly occurs in Americas, Africa and Middle East.

-- It grows in **moist soil rich in organic material** forming **hyphae with small pear shaped conidia**.

-- **Inhalation of conidia causes human infection.**



Pathogenesis and Clinical findings

-- Infection occurs mainly via **respiratory tract**.

-- Asymptomatic and mild cases are rarely recognized.

-- **Dissemination may result in ulcerated granuloma of skin, bone or other sites.**

Laboratory diagnosis

-- In tissue biopsy**, thick walled yeast cells with single broad-based buds** are seen.

-- In culture, **hyphae with small pear shaped conidia** can help in diagnosis.

-- Skin tests or serologic tests are not useful.

Treatment and Prevention

-- **Itraconazole** is the drug of choice but **amphotericin B** is needed for **severe cases**.


Thank You!