Systemic fungi
Histoplasmosis

- Thermally dimorphic fungus: *Histoplasma capsulatum*
- Two varieties: Capsulatum & Duboisii

- Soil enriched with bird or bat droppings

- Wide spectrum of clinical manifestations:
  - Asymptomatic pulmonary infection
  - Acute or chronic disease of the lungs
  - More widespread disseminated disease

Healthy individuals
Low-level exposure

High-level exposure
Underlying condition
Acute pulmonary histoplasmosis

- Fewer than 5% develop symptomatic disease

- **In immunocompetent individuals:**
  - Non-specific flu-like illness
  - Chest radiographs: small, scattered, bilateral, nodular infiltrates
  - The infiltrates: heal over several months & scattered calcifications
Chronic pulmonary histoplasmosis:

Underlying lung damage, (chronic obstructive pulmonary disease)

- First manifests: transient, segmental pneumonia
- Heals without treatment
- Progresses to fibrosis and cavitation
As lesions heal, **peripheral fibrosis** and **central calcification** may occur.
Disseminated histoplasmosis

- **older adults, infants and immunosuppressed patients**
  
  - The liver and spleen are enlarged
  
  - Anaemia, leucopenia and thrombocytopenia
  
  - Mucosal lesions can occur
  
  - CNS involvement (10-20%)
African histoplasmosis

- *Histoplasma capsulatum* var. duboisii

- **lungs**

- **Skin and bones**
  - Painless papular lesions
  - Osteomyelitis

- **Joints**
  - arthritis

- **liver, spleen** and other organs
- Sputum, BAL, Blood, urine, lymph node, bone marrow

- **Wet preparations** of clinical material?

- Wright-stained
- Stained tissue sections of lung, liver, lymph node

- **Yeast cells with narrow-based buds**

- **The definitive diagnosis**: isolation of the fungus

- 25–30°C for 4–6 weeks on Sabouraud’s dextrose agar + cycloheximide
- 37°C on brain heart infusion agar
- Rapid identification: **AccuProbe test**
yeast forms of *Histoplasma capsulatum* in alveolar macrophage
Monocytes in peripheral blood with phagocytosed yeast forms of *Histoplasma capsulatum*
Skin tests
- Not recommended for diagnosis

Serological tests
- Sub-acute pulmonary histoplasmosis
- Chronic pulmonary histoplasmosis
- Disseminated disease?

- Immunodiffusion (ID) test
- Complement fixation (CF) test

Antigen detection tests
- For?
## Treatment

**Mild symptoms:**
- Self-limited

**Progressive disseminated disease:**
- Oral itraconazole (200 mg once or twice daily for 6–12 weeks)
- Amphotericin B (3–5 mg/kg per day for 1–2 weeks)
Blastomycosis
“Chicago’s disease’

*Blastomyces dermatitis*

- In nature as a *mould*
- In tissue as large, round budding *yeast* cells

- Following *inhalation*: wide spectrum of clinical manifestations

- Occasional: *traumatic* cutaneous inoculation

*Geographical distribution*

- Overlap with the endemic region for histoplasmosis
Clinical manifestations

**Pulmonary blastomycosis**

At least 50% of individuals: asymptomatic

- Symptomatic pulmonary disease
  - Similar to histoplasmosis
  - Non-specific flulike illness
  - The radiological findings: **Hilar lymphadenopathy is uncommon**
  - Spontaneous resolution

- Chronic infection
  - Cavitation is less common
Disseminated blastomycosis

▶ Cutaneous blastomycosis

- 40-80% of cases
- Raised, crusted verrucous lesions with an irregular shape and sharp borders
- Face, neck and scalp

▶ Osteomyelitis & Arthritis

- 25-30%
- The spine, pelvis, skull, ribs and long bones

▶ Genitourinary blastomycosis

- The prostate, epididymis or testis in 10-30%
Essential investigations

**Microscopy**
- Wet preparations
- Yeast cells with thick refractive walls and broad-based single buds

**Culture**
- 25-30°C for 1-3 weeks on Sabouraud’s dextrose agar + cycloheximide
- 37°C on brain heart infusion agar

More rapid identification: **AccuProbe test**
- The AccuProbe test produces a positive result with *P. brasiliensis*
Yeast form in the lungs
Serological tests

- **Antibody detection tests:**
  - Immunodiffusion (ID)
  - Complement fixation (CF)
    - CF: cross-reactions with *H. capsulatum* and *Coccidioides* species

- **Antigen detection tests**
Management

- **Spontaneous resolution**

- **Mild to moderate pulmonary disease**
  - Oral itraconazole
  - Posaconazole and voriconazole
  - Lipid formulation of amphotericin B

- **Disseminated blastomycosis**
  - **Amphotericin B**
Coccidioidomycosis

*Coccidioides immitis*

- Nature as a mould *(arthrospores)*
- Human and animal tissue: *spherules*
- A single arthroconidia
- Arid climate, alkaline soil, hot summers
1. Arthospore (about 5 μm long) germinates into tubular hypha

2. Hypha begins to segment into arthospores

3. Airborne arthospore is inhaled

4. Inhaled arthospore enlarges and begins to develop into a spherule

5. Endospores develop within spherule

6. Spherule releases endospores

Some arthospores become airborne

Soil

Human

Spherule in tissue (about 30 μm diameter)
Large, mature spherule containing hundreds of endospores (H &E stain)
Clinical manifestations

- **Acute pulmonary coccidioidomycosis**
  - 60%: no symptoms
  - Moderate flu-like illness
  - Up to 50% of patients: erythematous rash (trunk and limbs)

- **Erythema nodosum or erythematous multiforme:**
  - 5% of infected persons
  - More common in women
  - In joints
Disseminated coccidioidomycosis

- black, Asian or Filipino
- 1-5% of individuals
- Following reactivation in an immunosuppressed individual
- Cutaneous and subcutaneous lesions, bones, joints, and meninges
The lesion on the nose resulted from dissemination from the lungs

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Differential diagnosis:

- **Diffuse lung infiltrates in AIDS patients**
  - *Pneumocystis jirovecii* infection

- **Lung cavities**
  - Cryptococcosis, tuberculosis

- **Cutaneous form**
  - Histoplasmosis, blastomycosis, cryptococcosis, tuberculosis

- **Meningeal form**
  - Cryptococcosis
Diagnostic

Microscopy

- Stained tissue sections
- Wet preparations of pus, sputum or joint fluid: less sensitive

Spherules containing Endospore

Culture

25-30°C on Sabouraud’s dextrose agar with cycloheximide

Arthroconidia

AccuProbe test
Skin tests

Serology

- The immunodiffusion (ID)
- Complement fixation (CF)
**Paracoccidioidomycosis**

- *Paracoccidioides brasiliensis*
  
- In nature: as a mould
  
- In tissue: round cells with multiple buds
  
- Inhalation OR *traumatic* inoculation
  
- **Women** appear to be *protected* from the disease, but not from infection?
  
- Risk factors: Alcoholism and smoking, as well as *malnutrition*
Clinical manifestations

**chronic or adult form**

- Lungs (Multiple bilateral infiltrates, hilar calcified)
- Spreads through the lymphatics in immunocompromised patients
- Painful, Ulcerative mucocutaneous lesions (face, mouth and)

**The juvenile or acute form**

- Generalized lymphadenopathy
- Weight loss
- Multiple cutaneous and/or osteolytic lesions
- Lung and mucous membrane involvement is uncommon
Differential diagnosis

Mucocutaneous leishmaniasis
Round yeast cells with multiple peripheral buds
Ship's wheel
**Cultures**

- 25-30°C on Sabouraud’s dextrose agar with cycloheximide

- Mycelial cultures *seldom sporulate*

- 37°C on brain heart infusion agar with glutamine: yeast form

- No commercial DNA probe test

**Serological tests:**

- The immunodiffusion test
- The complement fixation (CF) test
- **Without appropriate treatment**

  Chronic form will die within a few years
  Acute or sub-acute disease will die within a few months

- **Three different classes:**
  - The sulphonamides (*Sulphadiazine*)
  - Amphotericin B
  - Azoles (Choice: itraconazole)