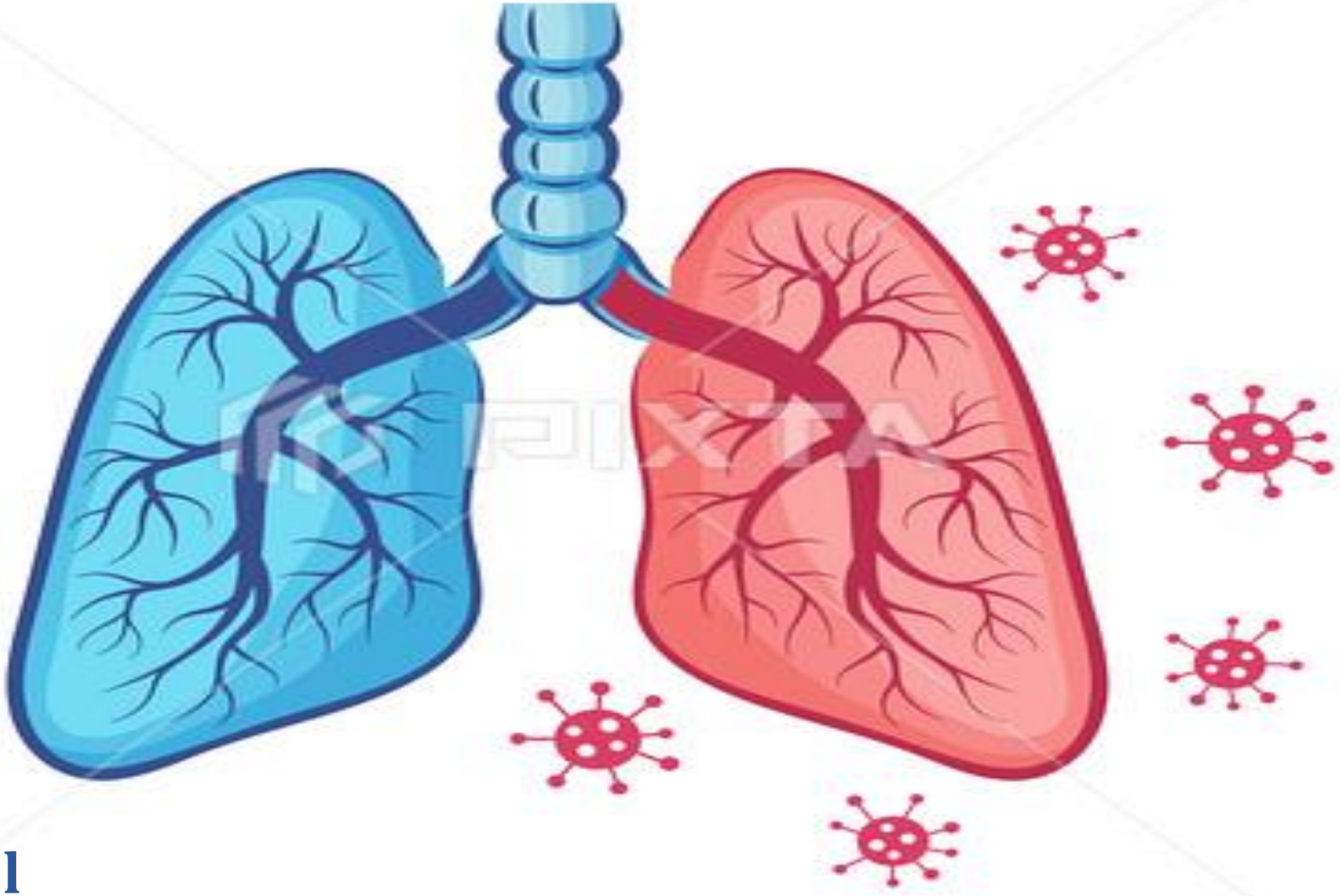
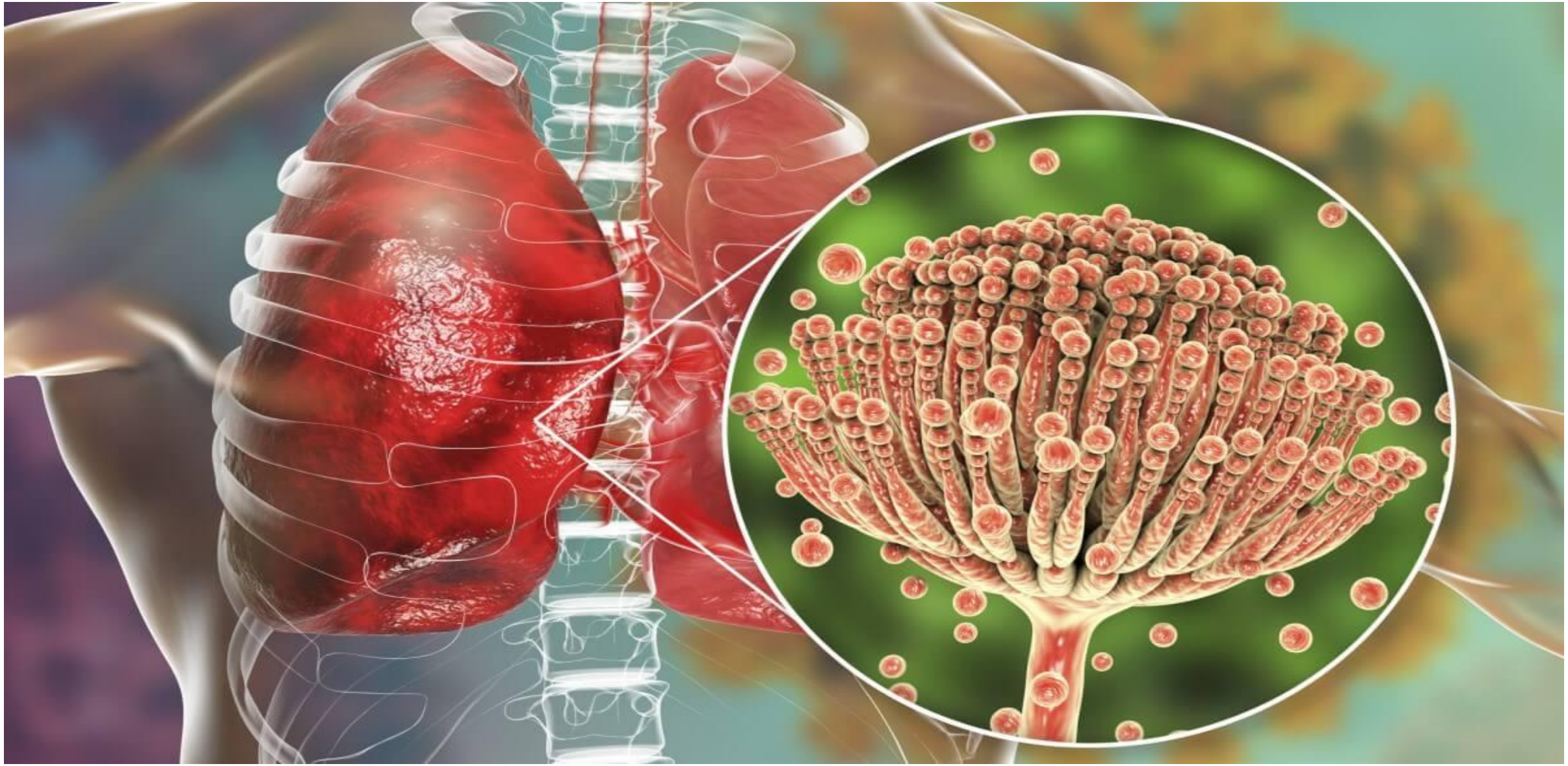
RESPIRATORY TRACT INFECTIONS - VIII



By
Prof. Hala Tabl

Fungal Infections Of Respiratory Tracts



Respiratory fungal infection - Etiology

- YEAST
  - Candidiasis (*Candida* and other yeast)
  - Cryptococcosis (*Cryptococcus neoformans*, *C. gattii*)

- Mould fungi
  - Aspergillosis (*Aspergillus* species)
  - Zygomycosis (*Zygomycetes*, e.g. *Rhizopus*, *Mucor*)
  - Other mould

Opportunistic

- Dimorphic fungi
  - Histoplasma capsulatum
  - Blastomyces dermatitidis
  - Paracoccidioides brasiliensis
  - Coccidioides immitis

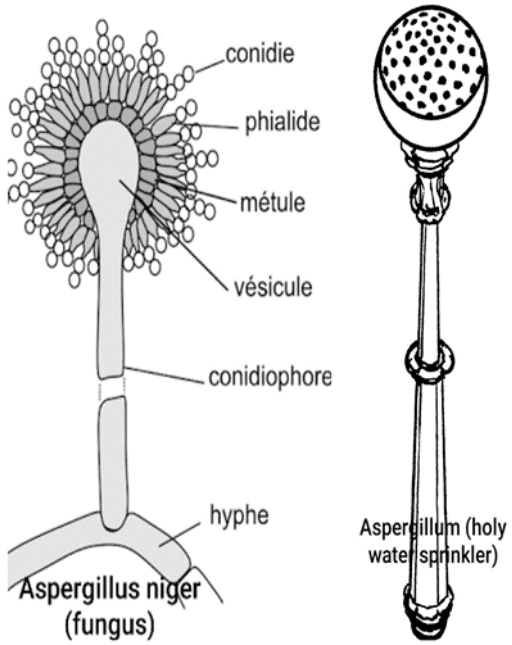
Primary infections

ASPERGILLOSIS

- It is a group of **opportunistic** mycoses caused by Aspergillus Fungi which are common **saprophytic molds** frequently found on soil, decaying vegetation, buildings,...
- Medically important species that cause RTIs are:

1- Aspergillus Fumigatus.

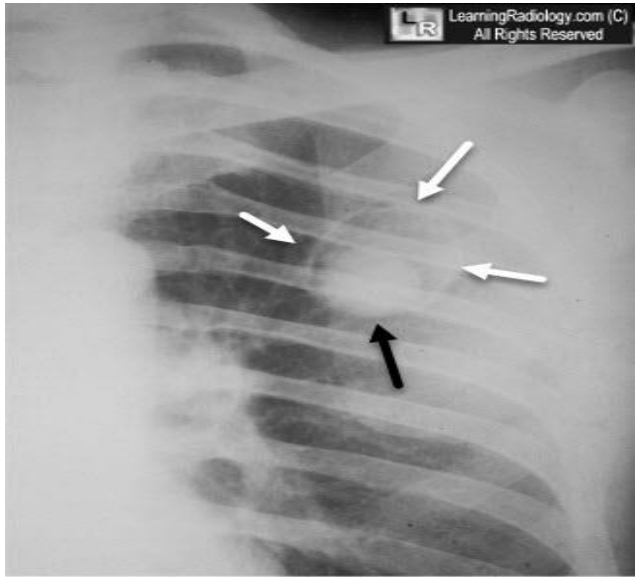
2- Aspergillus Niger.



Aspergillus Fumigatus:-

Causes **pulmonary Aspergillosis,** (in patients with a pre-existing lung disease).

Infection acquired by inhalation of conidia (spores) which commonly associated with certain occupational settings e.g. construction works.



1- Aspergilloma or " Fungus ball":

- Fungus grow in a pre- existing cavity e.g. T.B. cavity.
- X- ray shows fungus ball (radiopaque structure).

2- Invasive Aspergillosis:

- Mainly occurs in **immunocompromised** persons, and usually fatal.
- Fungus invades lung tissues giving rise to pneumonia and hemoptysis.
- Dissemination to other organs occur leading to **disseminated Aspergillosis.**

3- Allergic bronchopulmonary aspergillosis (ABPA).

- Leads to asthmatic attacks (coughing and wheezing) with high level of IgE in serum. Usually occur in hypersensitive persons who repeatedly exposed to dust contaminated with its spores, they expectorate brownish bronchial plugs containing hyphae.

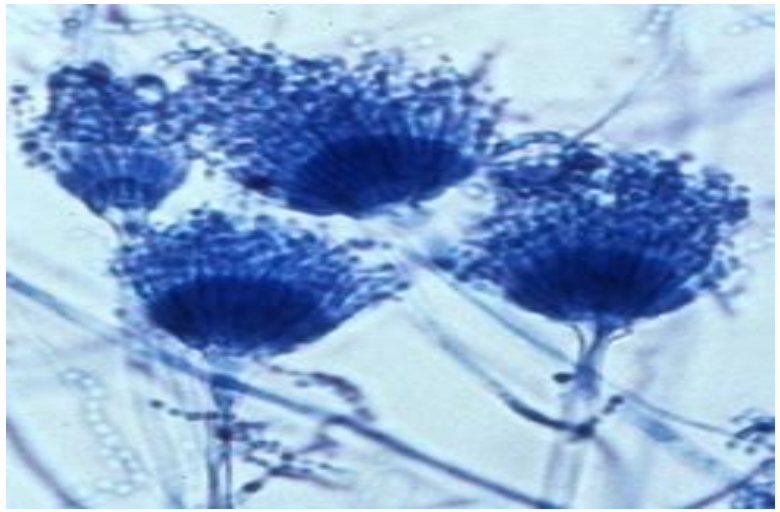
Aspergillus Niger:

- Causes **otomycosis,** chronic infection of the external auditory meatus.
- Manifested by pain, itching and ear discharge.

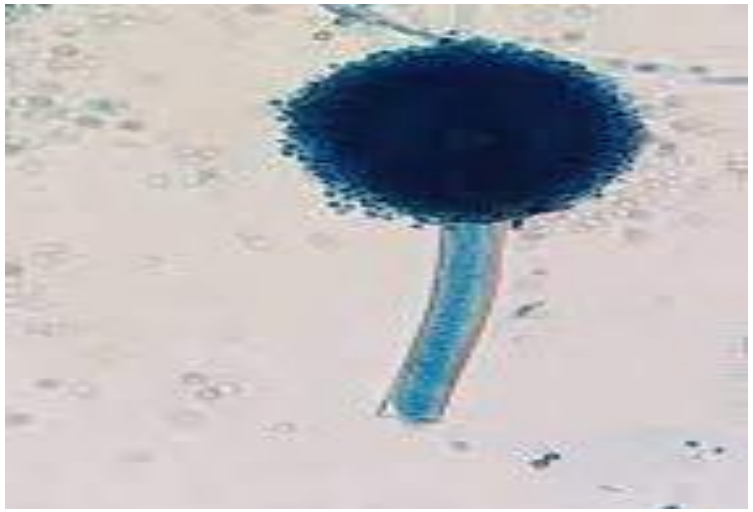
Laboratory Diagnosis:

- **Specimen:** Sputum, Ear discharge
- **Direct Microscopy:-**

Shows **filamentous septate hyphae** with characteristic **aspergillus head** in lactophenol cotton blue preparations.



A. Fumigatus
Flask shaped head

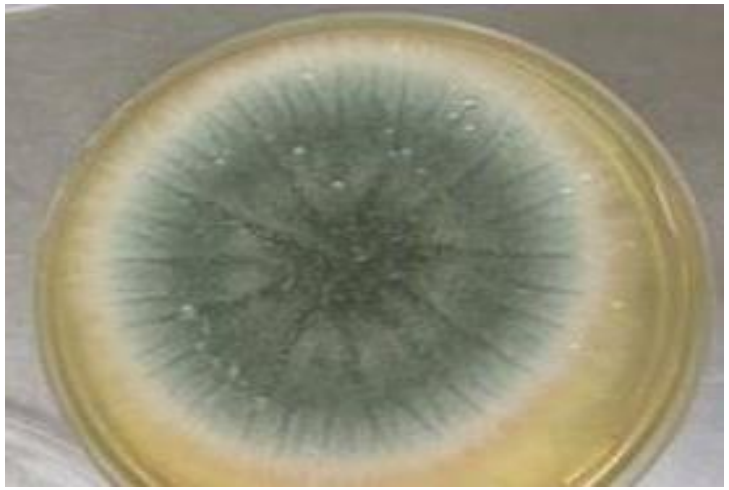


A. Niger
Rounded head

➢ **Culture:-** On **Sabouraud's** agar,

Pigmentation of **aerial growth** can identify the Aspergillus species:

- *A. Fumigatus* →White filaments with **smoky green** spores.
- *A. Niger* →White filaments with **black** spores.



A. Fumigatus

A. Niger

➢ **Antigen detection in serum:** is of value in invasive aspergillosis,

Treatment:

- In invasive pulmonary Aspergillosis and dissiminated diseases:

  Combined treatment with: I.V. Amphotericin B, itraconazole, caspofungin.

- In otomycosis: Nystatin ear drop.
- Surgical removal in case of fungal ball is helpful
- Patients with ABPA can be treated with corticosteroids and antifungal agents.

HISTOPLASMA CAPSULATUM

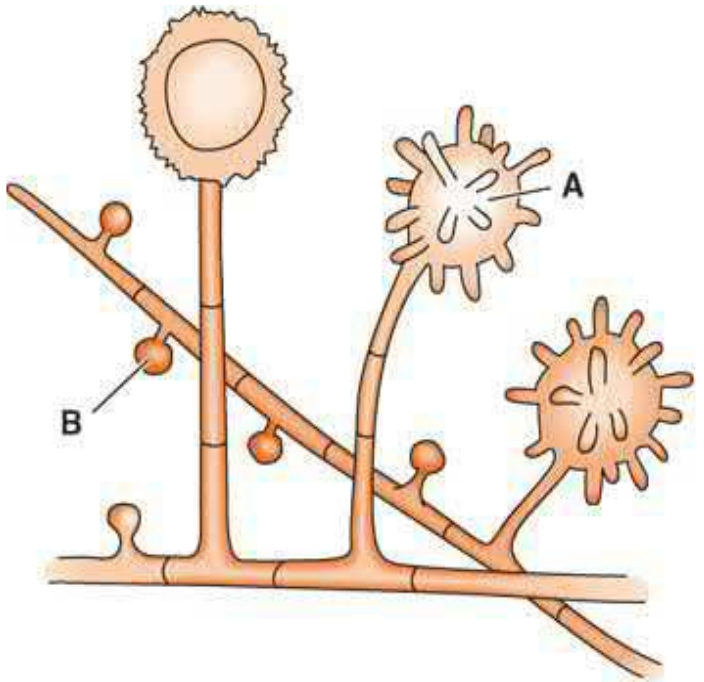
"HISTOPLASMOSIS"

- It is a **dimorphic** fungus (exists as a **mold** in soil and as a **yeast** in tissue).
- The mold forms two types of asexual spores:

(1) Tuberculate macroconidia, with thick walls (important in laboratory identification).

(2) Microconidia, with small thin walls (if inhaled, transmit the infection).

- It is not capsulated (had a refractive halo mimicking a capsule, hence the name)



Transmission & Pathogenesis:

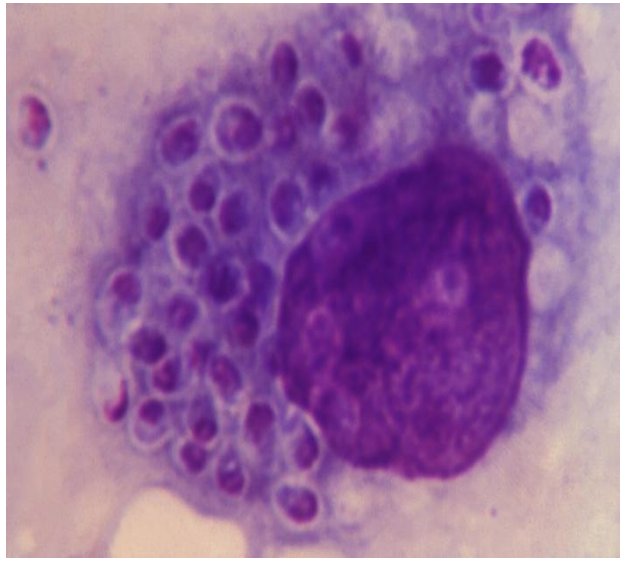
- It grows in soil, particularly if the soil is heavily contaminated with bird excreta, especially **bats**.
- Histoplasmosis is an occupational disease results from **inhalation of microconidia** during exploration of bat infested caves (for fertilizer).
- It is an **intracellular organism** which particularly infect **reticuloendothelial cells (macrophages).**
- Inhaled spores are engulfed by alveolar macrophages, resist intracellular killing and develop into **budding cells**. It may spread from the lung to other part of the body, bone marrow, liver, and the spleen.

Clinical findings:

Infection may be either:

- **Asymptomatic:** in majority of cases.
- **Acute pulmonary disease:** fever, headache, chills, cough, and chest pain.
- **Chronic progressive histoplasmosis:** fever, dyspnea, and productive cough, **cavitary lung lesions** may be seen on chest radiographs. These clinical features resemble tuberculosis and the two must be distinguished.
- **Severe disseminated histoplasmosis:**
  - Especially in infants and **immunocompromised.**
  - **Ulcerated lesions on the tongue** are typical of disseminated histoplasmosis.
  - Pancytopenia, lymphadenopathy, hepatosplenomegally.

Laboratory diagnosis



Specimen: Sputum, Bone marrow aspirate or blood.

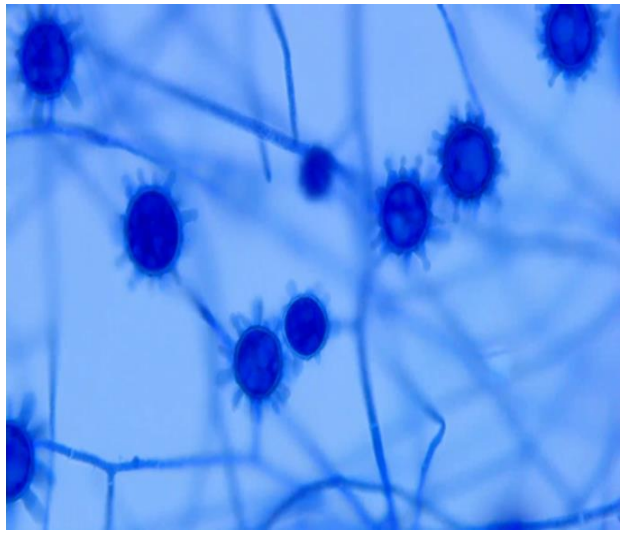
Direct Microscopy

In **Giemsa** stained preparations, **yeast form** can be seen intracellular as round or oval **budding cells**.

Culture: On sabouraud's agar

- At room temperature, produce filamentous growth.

A lactophenol cotton blue stained film from this culture shows **septate hyphae and rounded thick walled spores with finger like projections.**



- At 37ºC produce the yeast form (budding cells)

Antigen detection: in serum and urine by ELISA

PCR

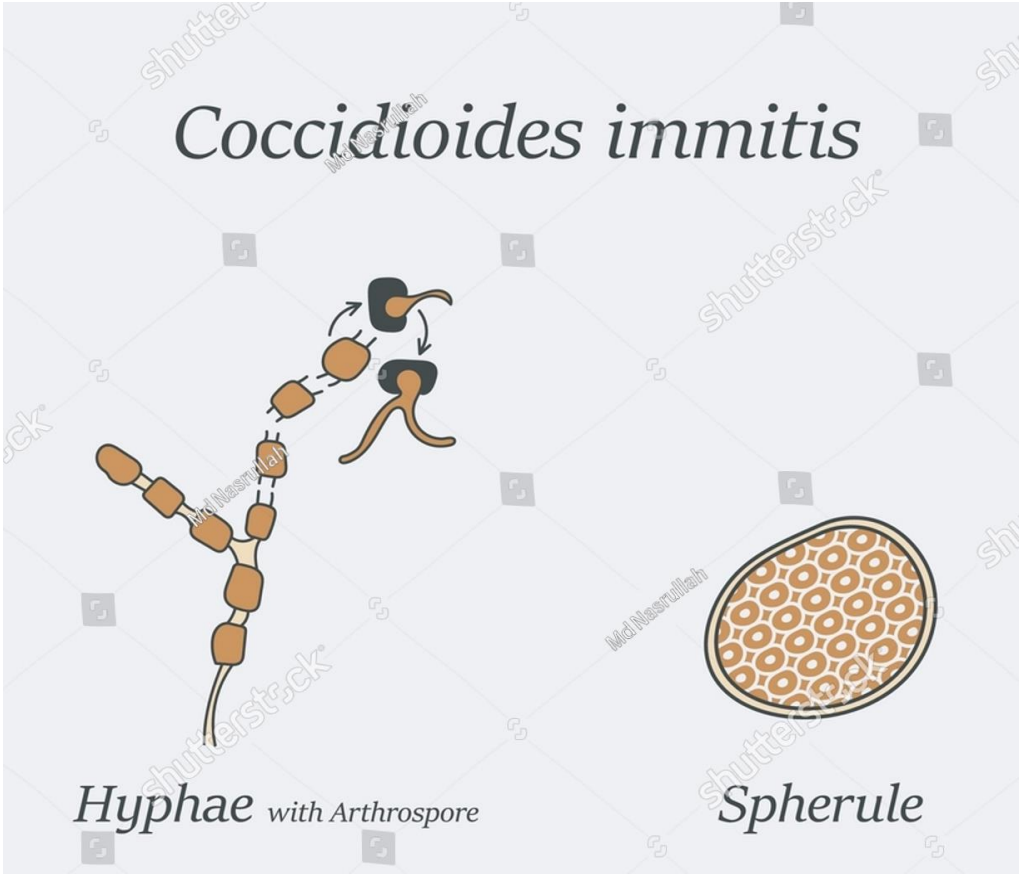
Treatment

With progressive lung lesions, oral itraconazole is effective.

In disseminated disease, parenteral itraconazole (or amphotericin B) is the treatment of choice.

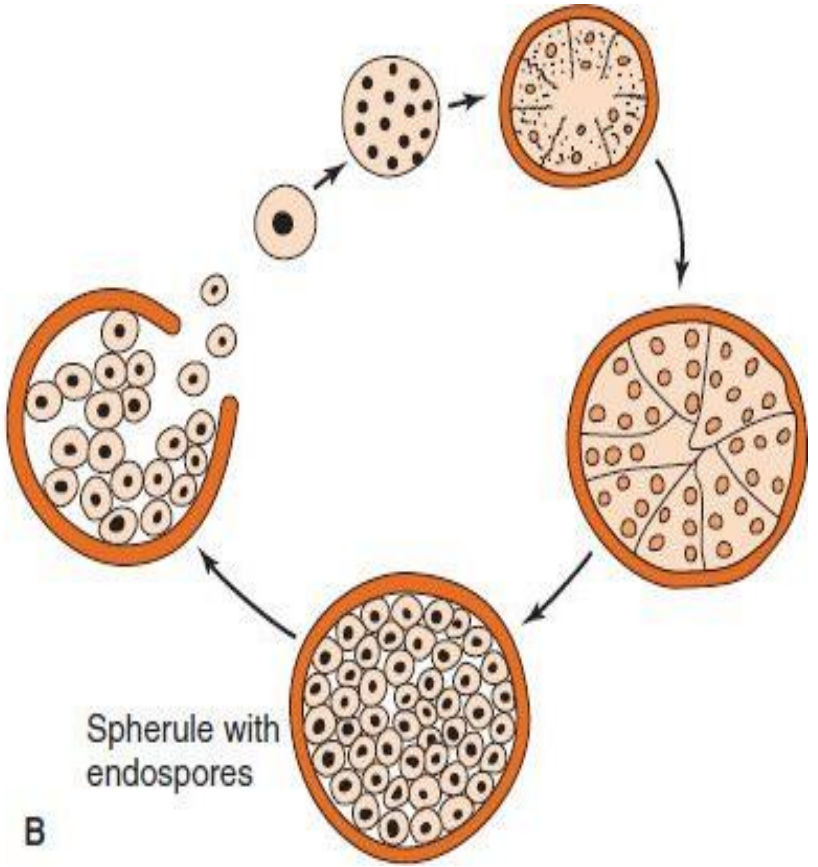
COCCIDIOIDES IMMITIS
“Coccidioidomycosis”

- It is a **dimorphic** fungus.
- In soil, as a mold, **arthrospores** (Barrel shaped, Rectangular) at the ends of hyphae.
- In tissues, as a **spherule**, have a thick, double wall, and are filled with endospores.



Pathogenesis:

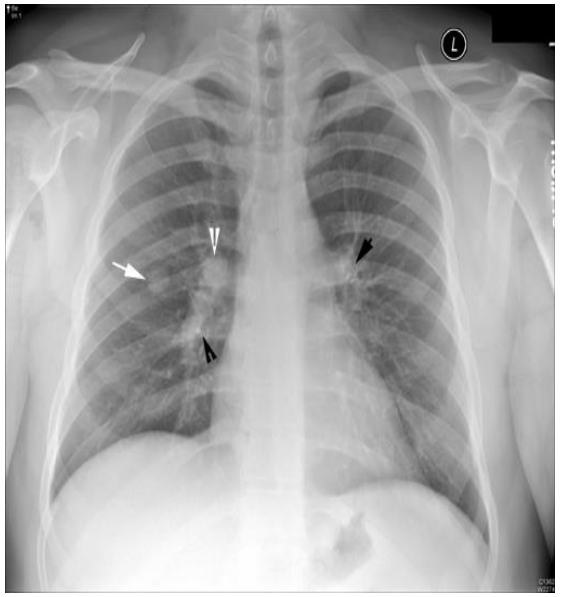
- The infection acquired by **inhalation** of arthrospores (arthroconidia).
- In the lungs, arthrospores form spherules. Upon rupture, endospores are released and differentiate to form new spherules that induce immune response in the form of granulomatous lesions.



Clinical findings:

- **Asymptomatic:** in endemic areas (e.g. Arizona, New Mexico, California).
- **Acute Coccidioidomycosis "Valley fever" "Desert rheumatism":** Triad,
  - Respiratory manifestations (fever and cough), erythema nodosum (EN) and arthralgias.

- **Chronic Coccidioidomycosis:** prolonged cough & **Pulmonary nodule** commonly seen on chest radiographs.

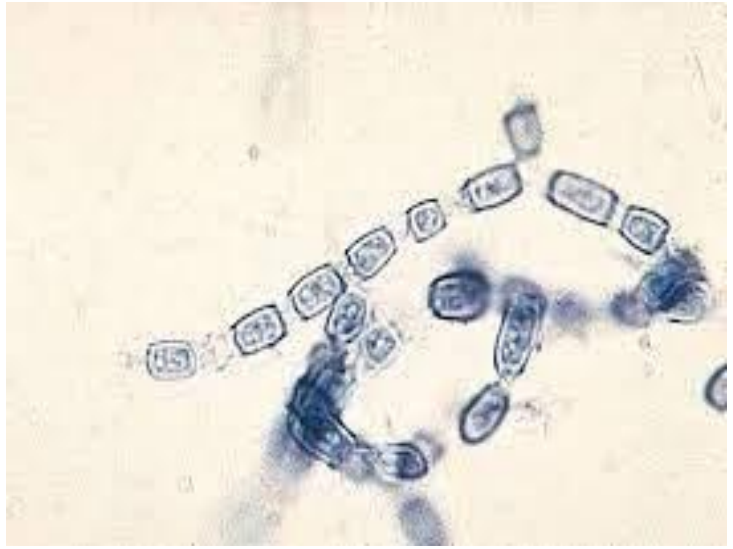


- **Disseminated Coccidioidomycosis:**

  In immunocompromised persons. Affect any organ; specially the meninges (meningitis) and bone (osteomyelitis).

Diagnosis:

- In tissue specimens, **spherules (filled with endospores)** are seen microscopically.
- Cultures on Sabouraud's agar at room temp.: show **septate hyphae with arthrospores** with lactophenol cotton blue stain.
- Serologic testing to detect specific antibodies.

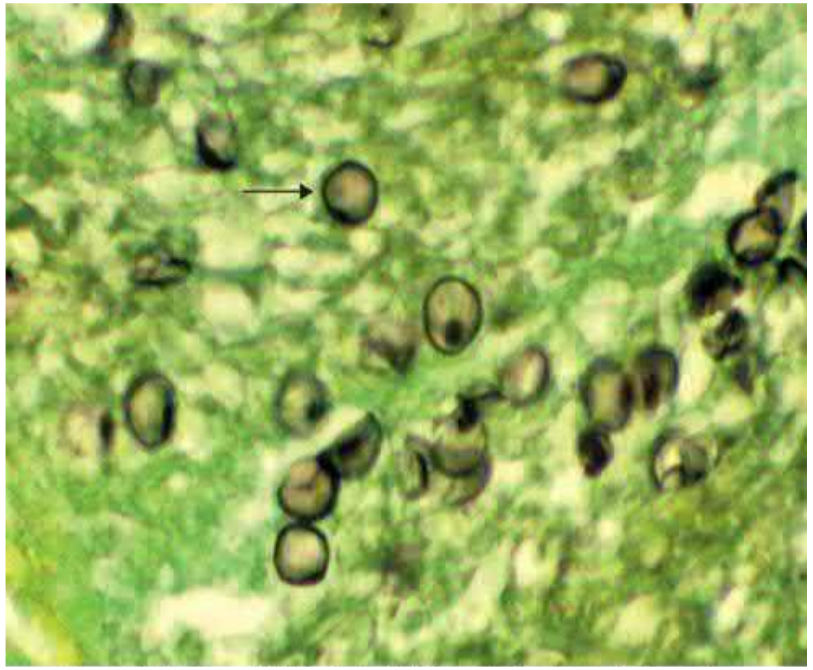


Treatment:

- In severe or disseminated cases: Amphotericin B & itraconazole.
- In meningitis: Fluconazole

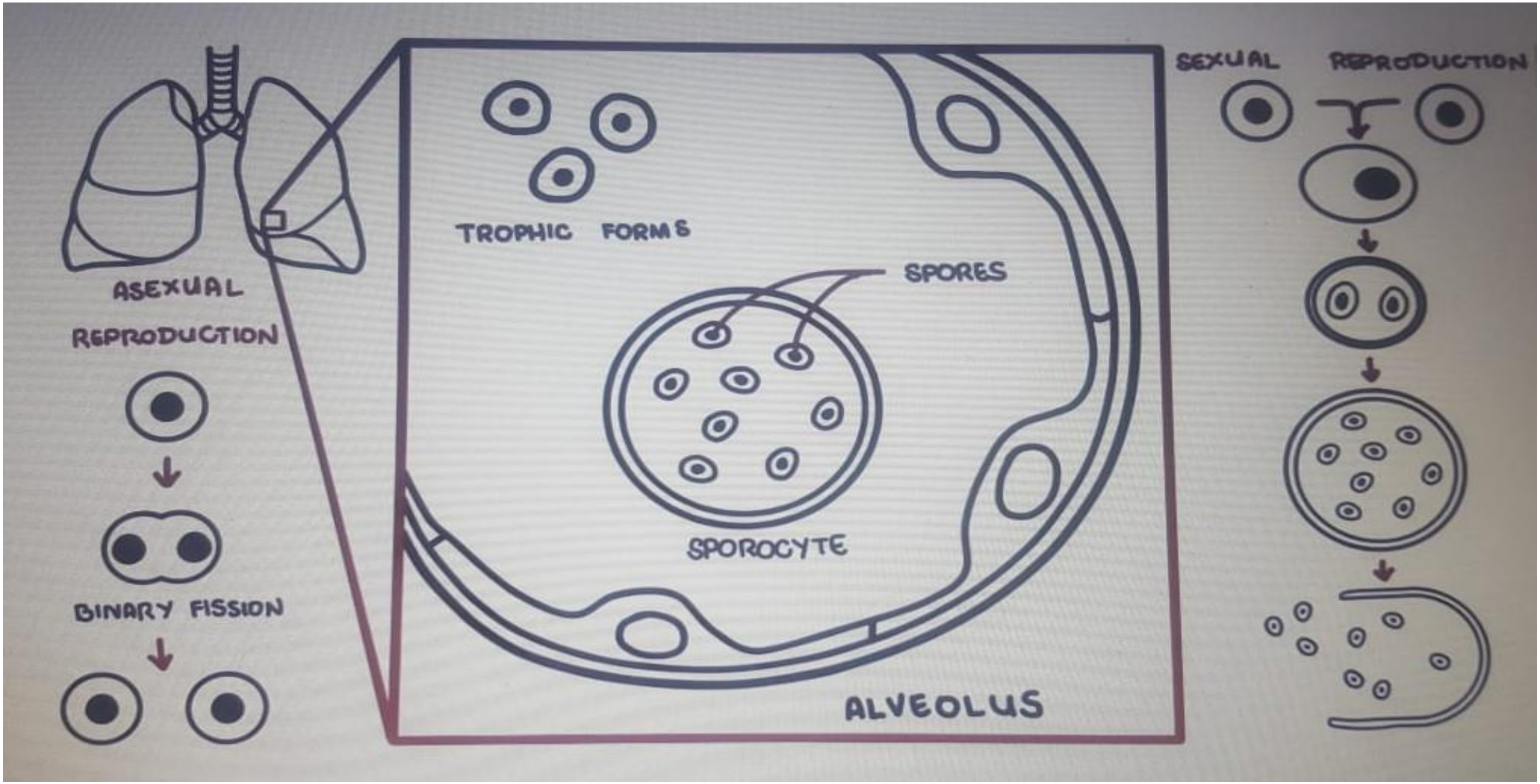
Pneumocystis jiroveci

- It was long considered **a parasite** based on morphology (In tissue, it appears as a cyst that resembles the cysts of protozoa).



- However, molecular and biochemical analysis indicate that it is a **yeast**, and its cell wall contain **β-glucan ,** although,
  - It **lacks ergosterol** so, antifungal drugs targeting ergosterol are ineffective
  - It does not grow on fungal media.

Life Cycle


ASEXUAL
REPRODUCTION
BINARY FISSION
TROPHIC FORMS
SPORES
SPOROCYTE
ALVEOLUS
SEXUAL
REPRODUCTION

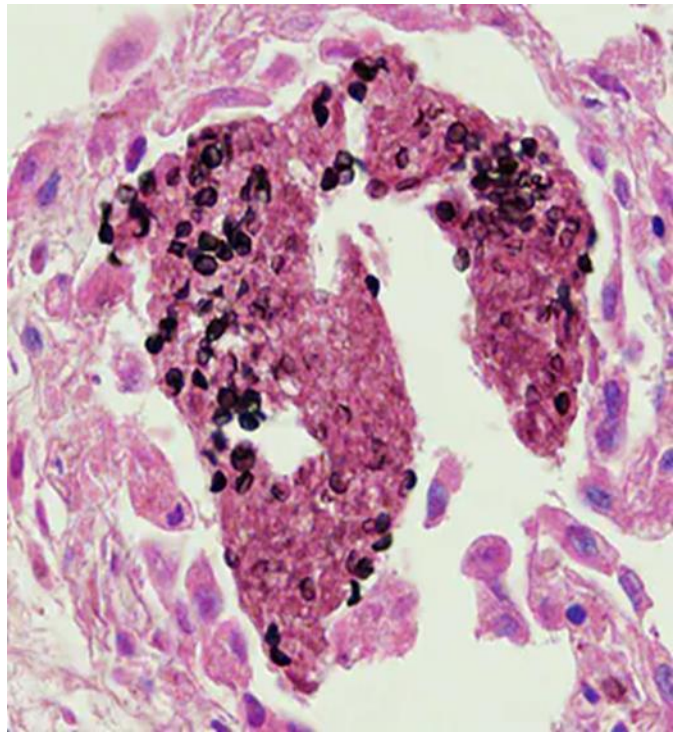
Pathogenesis:

- Pneumocystis jiroveci is an important cause of pneumonia **in immuno-compromised individuals (Pneumocystis pneumonia)**.
- The organism does not invade the lung tissue.
- The presence of cysts in the alveoli induces an inflammatory response consisting primarily of plasma cells "**plasma cell pneumonia"** and resulting in alveolar foamy exudate & edema (that blocks oxygen exchange) and interstitial fibrosis.

Clinical Findings

- Asymptomatic infection is common in normal individuals.
- The sudden onset of fever, nonproductive cough, dyspnea, and tachypnea is typical of Pneumocystis pneumonia.
- Chest X-ray shows **bilateral "ground glass"** infiltrates.
- Extra-pulmonary infections rarely occur in the late stages of AIDS and affect primarily the liver, spleen, lymph nodes, and bone marrow.
- The mortality rate of untreated Pneumocystis pneumonia approaches 100%.

Laboratory Diagnosis



- **Sample:** Broncho-alveolar lavage, or lung biopsy.
- **Microscopic examination:** The cysts can be visualized with silver, Giemsa, or other tissue stains.
- **Detection of β-glucan.**
- **PCR**

Treatment:

- The treatment of choice is a combination of trimethoprim and sulfamethoxazole.

Trematode of the lung (lung fluke)

Morphology:

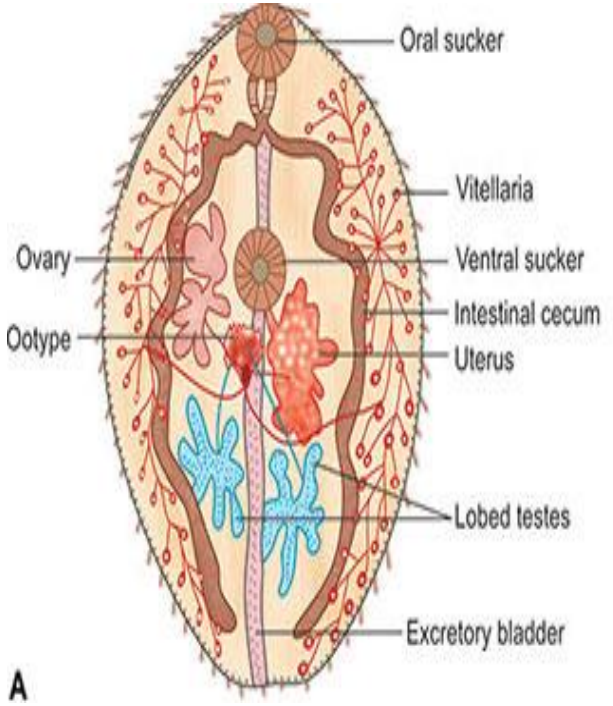
Adult: Short, reddish brown in color, resembles a coffee bean.

They possess oral and ventral **suckers** (organs of attachment).

Hermaphroditic.

Eggs: Oval and **operculated**.

Metacercaria: Spherical in shape.



Metacercaria

Egg

Life cycle

Habitat: Lung.

Definitive host: Man.

Reservoir host: Dogs, cats, pigs

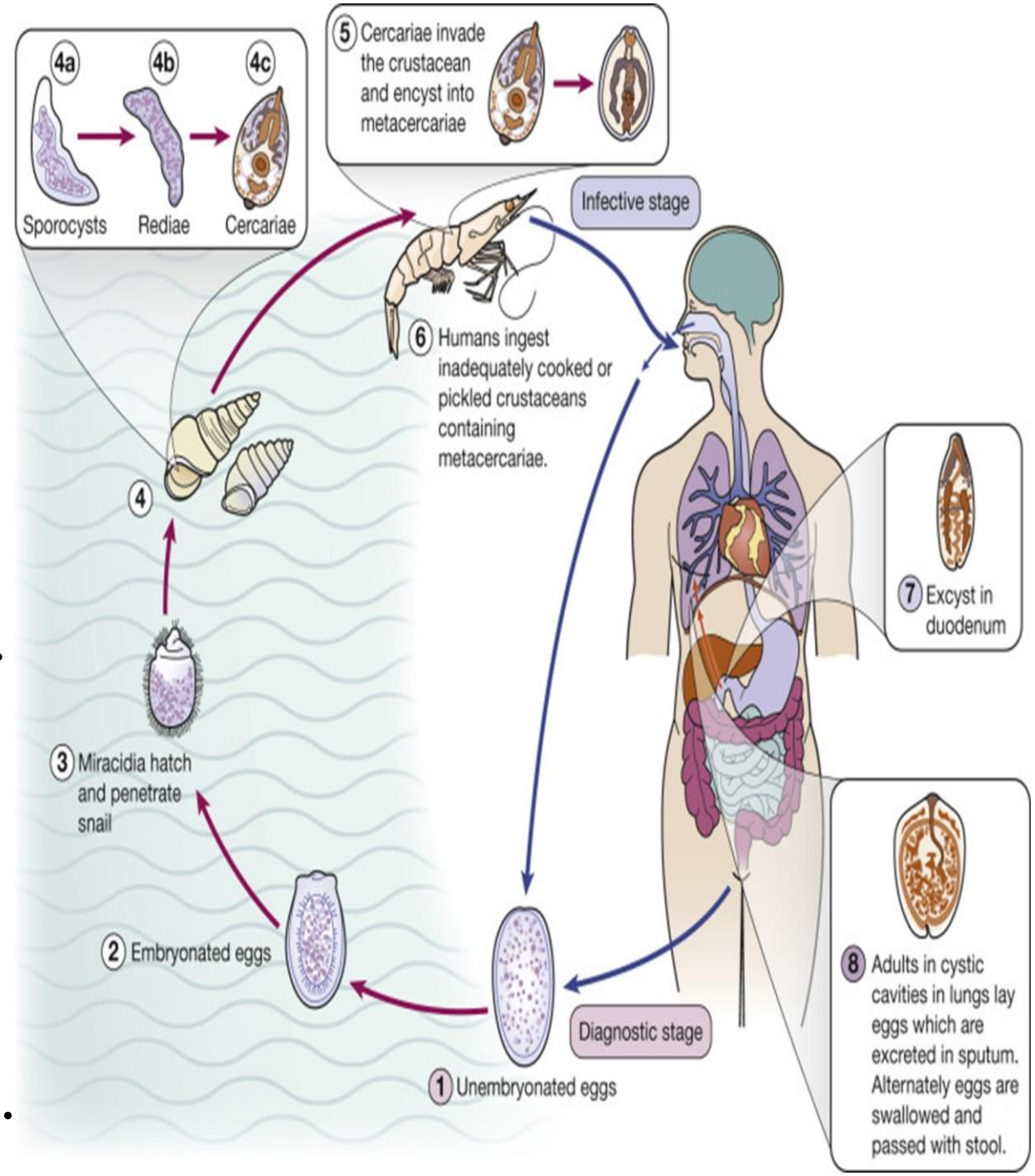
1st **Intermediate host:** Snail.

2nd **Intermediate host:** crabs and crayfish.

Infective stage: Metacercariae.

Mode of infection: eating raw freshwater crabs and crayfish.

Diagnostic stage: Eggs in sputum or stool.



Pathogenesis & Clinical findings:

- Paragonimiasis is endemic in far east countries, where eating raw, undercooked or Drunken (wine soaked) crustaceans and spitting habit is common.
- Within the lung, the worms can **persist for years** and exist in a fibrous capsule and stimulates an inflammatory response (granuloma). Secondary bacterial infection frequently occurs.
- The main symptom is a **chronic cough** with bloody sputum, dyspnea and pleuritic chest pain.
- Ectopic lesions may rarely occur e.g. brain, liver, heart, skin,..

Laboratory Diagnosis:

- Eosinophilia
- Finding the typical **operculated eggs** in sputum or feces.
- Serologic tests to detect specific antibodies e.g. ELISA (The eggs may not be present in sputum or stool until 2 to 3 months after infection).

Treatment & Prevention:

- Praziquantel is the treatment of choice.
- Cooking crabs properly is the best method of prevention.
- Snail control.

Thank you