

وَقُلْ رَبِّ زِدْنِي عِلْمًا



# RESPIRATORY SYSTEM

## HAYAT BATCH



SUBJECT : Microbiology

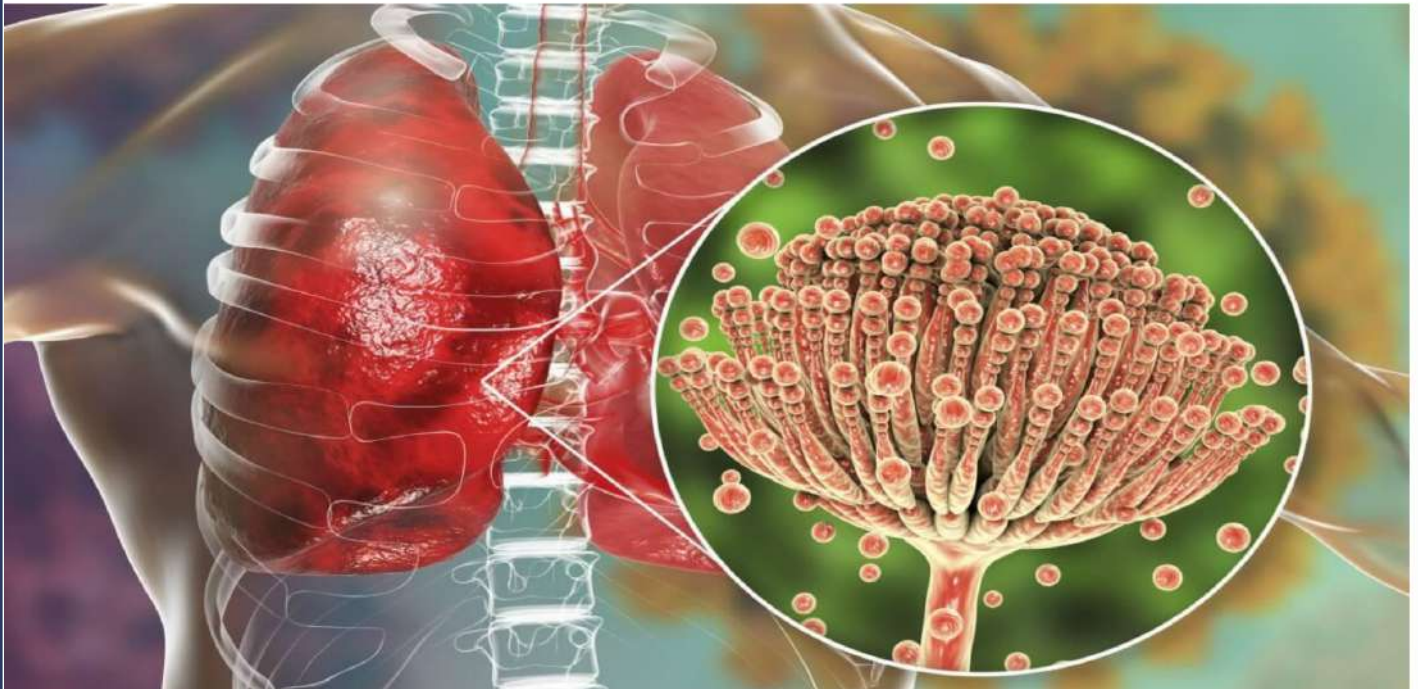
LEC NO. : 8

DONE BY : Ruba Almshaqba



# Respiratory System

## 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*
- *Paracoccidioides brasiliensis*
- *Blastomyces dermatitidis*
- *Coccidioides immitis*

Primary infections

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# Respiratory System

fungal infections caused by organisms that typically do not cause disease in healthy individuals, but can become pathogenic in people with weakened immune systems

## ASPERGILLOSIS

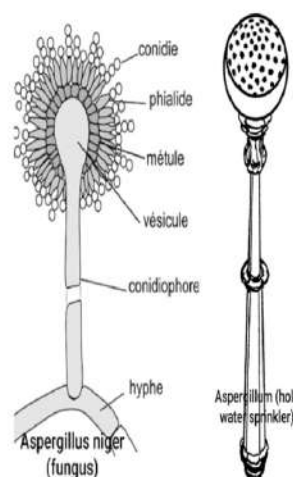
- It is a group of **opportunistic mycoses** caused by *Aspergillus* Fungi which are common **saprophytic molds** frequently found on soil, decaying vegetation, buildings,...

fungi that obtain nutrients by decomposing dead organic matter

- Medically important species that cause RTIs are:

1- **Aspergillus Fumigatus.**

2- **Aspergillus Niger.**



“Aspergillus” means “holy water sprinkler.”

رشاش الماء المقدس

“fumigatus” means “to smoke” or “to fumigate.”

“niger” means “black.”

### 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).**

meaning it appears as a dense, white mass against a darker background due to its composition and density compared to surrounding tissues.



#### 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.** Invaded the blood



# Respiratory System

## 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:

في المحاضرة 2 حكينا عنها  
III- Infections of the ear:  
Otitis Externa:  
- *Pseudomonas aeruginosa*.  
- *Aspergillus niger*

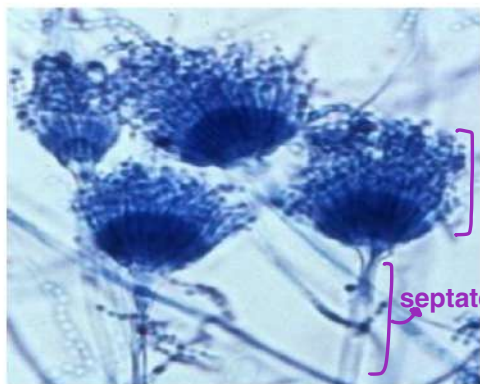
- Causes **otomycosis**, chronic infection of the **external auditory meatus**.
- Manifested by pain, itching and ear discharge.



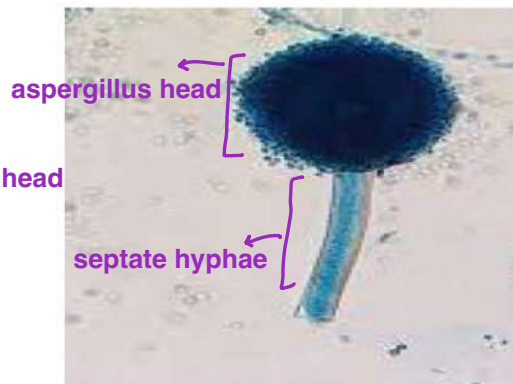
## Laboratory Diagnosis:

- **Specimen:** **Sputum**, **Ear discharge**
  - pulmonary Aspergillosis
  - otomycosis
- **Direct Microscopy:-**

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



***A. Fumigatus***  
**Flask shaped head**



***A. Niger***  
**Rounded head**





# Respiratory System

➤ **Culture:-** On **Sabouraud's** agar, **بده تقريبا 3 أسابيع**

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 disseminated diseases:

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

- In otomycosis: **Nystatin ear drop.**

- **Surgical removal in case of fungal ball is helpful** + **Antifungal Drugs**

- Patients with **ABPA** can be treated with **corticosteroids and antifungal agents.**

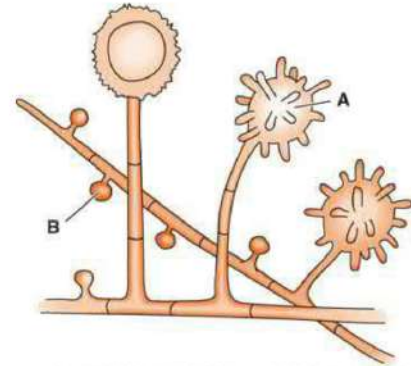


# Respiratory System

## HISTOPLASMA CAPSULATUM “HISTOPLASMOSIS”

Histoplasma capsulatum is an intracellular pathogen, meaning it can live and replicate inside macrophages

- 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)



Source: W. Levinson, P. Chin-Hong, E.A. Joyce, J. Nussbaum, B. Schwartz: Review of Medical Microbiology & Immunology: A Guide to Clinical Infectious Diseases, Seventeenth Edition: Copyright © McGraw Hill. All rights reserved.

## 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.**







# Respiratory System

## 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** <sup>تذكروا هون</sup> It is a **dimorphic** fungus (exists as a **mold** in soil and as a **yeast** in tissue)

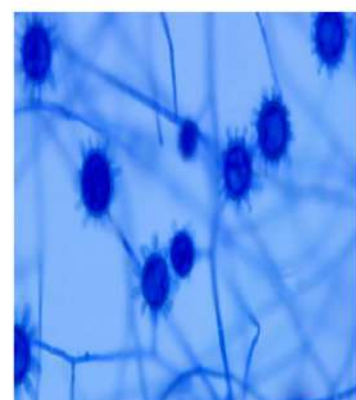
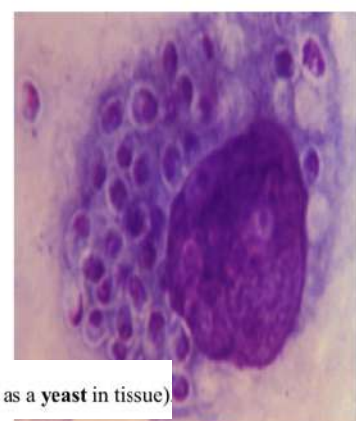
- At room temperature, produce **filamentous growth**.

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

- At **37°C** produce the yeast form (budding cells)

**Antigen detection:** in serum and urine by **ELISA**

**PCR**





# Respiratory System

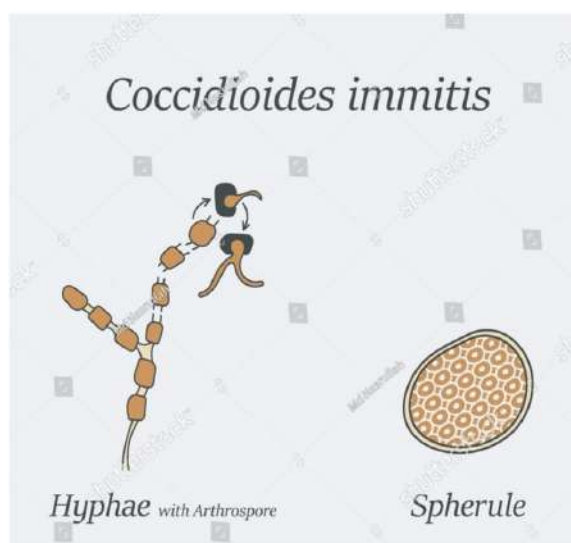
## Treatment

With progressive lung lesions, oral itraconazole is effective.

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

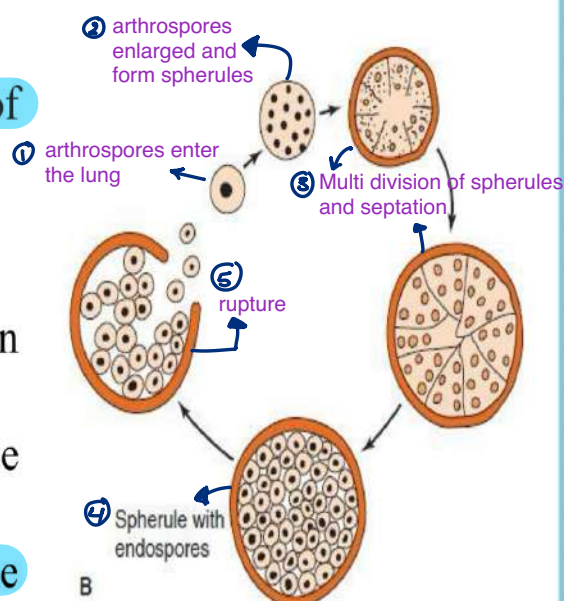
## COCCIDIODES IMMITIS “Coccidioidomycosis”

- 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.







# Respiratory System

## 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.**

في حالات disseminated disease



## Treatment:

➤ **In severe or disseminated cases: Amphotericin B & itraconazole.**

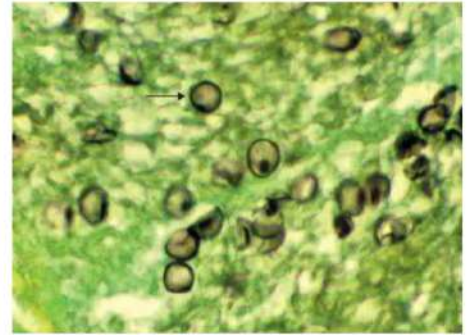
➤ **In meningitis: Fluconazole**



# Respiratory System

## Pneumocystis jiroveci

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

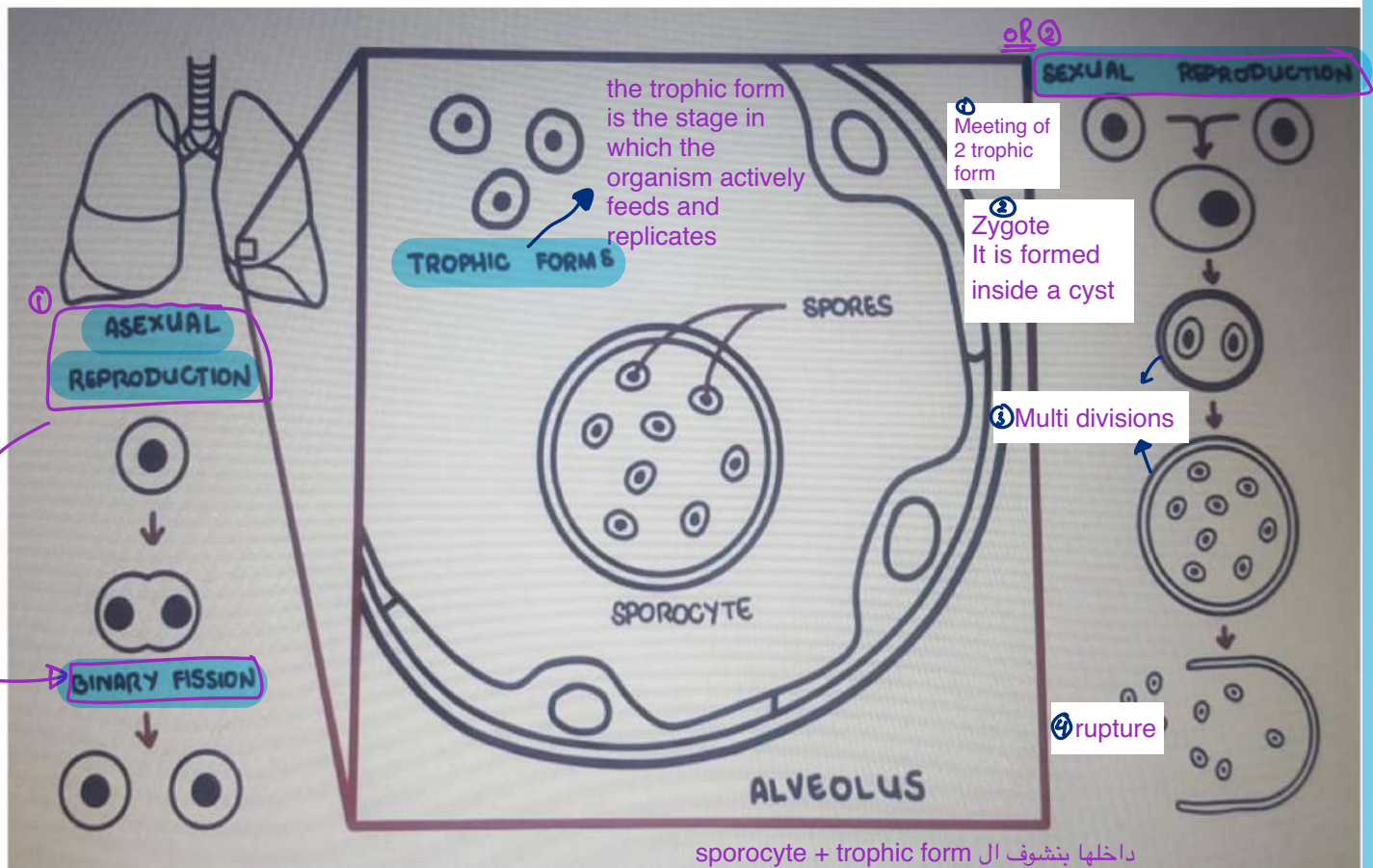


➤ However, molecular and biochemical analysis indicate that it is a **yeast**, and its cell wall contain  **$\beta$ -glucan**, although,

*component of fungal cell membranes*

- It lacks **ergosterol** so, antifungal drugs targeting ergosterol are ineffective
- It does not grow on fungal media.

## Life Cycle







# Respiratory System

## Pathogenesis:

- Pneumocystis jiroveci is an important cause of pneumonia in immunocompromised 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%.



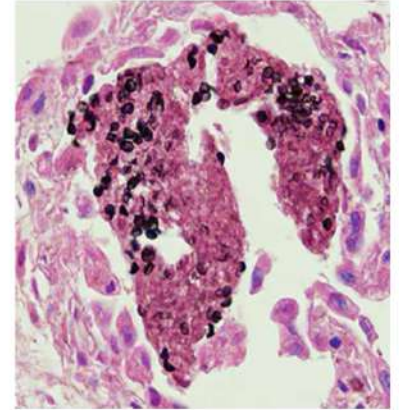
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# Respiratory System

## 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  $\beta$ -glucan.**
- **PCR**



## Treatment:

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

## Trematode of the lung (lung fluke)

تذكير من الفصل الاول

General characteristic

- \* unsegmented
- \* flattened, leaf-shaped bodies
- \* hermaphroditic

**PARAGONIMUS WESTERMANI**

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# Respiratory System

## Morphology:

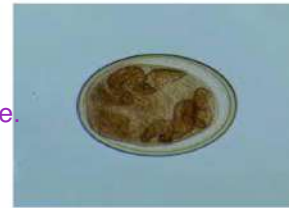
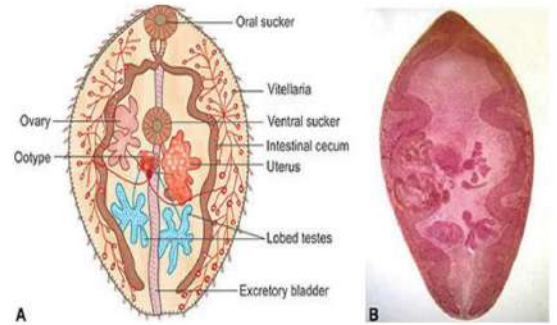
**Adult:** Short, reddish brown in color, resembles a coffee bean.

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

**Hermaphroditic.**

**Eggs:** Oval and operculated. *a lid or covering structure.*

**Metacercaria:** Spherical in shape.



Metacercaria



Egg

## Life cycle

**Habitat:** Lung.

**Definitive host:** Man.

**Reservoir host:** Dogs, cats, pigs

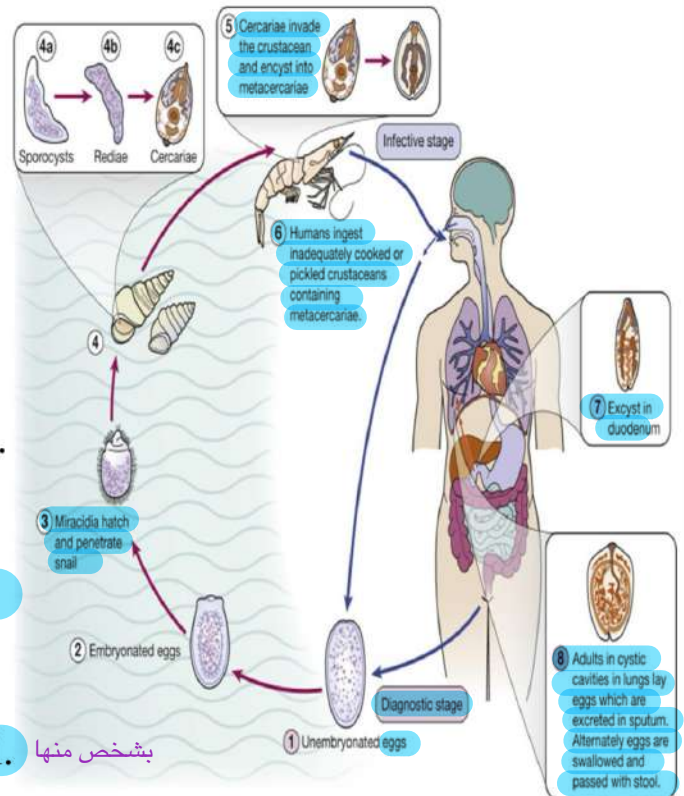
**1<sup>st</sup> Intermediate host:** Snail.

**2<sup>nd</sup> Intermediate host:** crabs and crayfish.

**Infective stage:** Metacercariae.

**Mode of infection:** eating raw freshwater crabs and crayfish.

**Diagnostic stage:** Eggs in sputum or stool. *بشخص منها*



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# Respiratory System

## 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.





# Respiratory System

## Quiz

1) A man comes to the emergency department with a history of fever, shortness of breath, productive cough, and hemoptysis for the past week. He has a history of asthma. Imaging of the chest shows bronchiectasis, and laboratory studies show an elevated total blood eosinophil count. Which of the following pathogens are responsible for this patient's condition?

- A) Actinomyces
- B) Candida albicans
- C) Aspergillus fumigatus
- D) Pneumocystis jirovecii (formerly P carinii)
- E) Mycobacterium tuberculosis

Correct answer =  
C) Aspergillus  
fumigatus

2) A patient, who had a kidney transplant six months ago, presented to his physician's office with a history of fever, chest pain, cough, and hemoptysis. A biopsy of the lung shows septate hyphae with acute angle branching. The patient has been on several immunosuppressants following his surgery. Which of the following pathogens is the most likely cause of this patient's condition?

- A) Aspergillus fumigatus
- B) Mycobacterium tuberculosis
- C) Pneumocystis jirovecii
- D) Actinomyces
- E) Candida albicans

Correct answer =  
A) Aspergillus fumigatus



# Respiratory System

3) A 48-year-old man comes to a clinic complaining of fevers, chills, headaches, and cough over the past several weeks. A chest x-ray shows enlarged hilar lymph nodes with focal infiltrates bilaterally. A lymph node biopsy reveals macrophages filled with yeast cells that bud from a narrow base. Which of the following pathogens are responsible for this patient's condition?

Correct answer =  
E) Histoplasmosis

- A) Actinomyces
- B) Candida albicans
- C) Aspergillus fumigatus
- D) Pneumocystis jirovecii
- E) Histoplasmosis

4) A 41-year-old man presents to the emergency department with a worsening cough, dyspnea, and fever for the past two days. The patient is HIV positive; the last CD4 count was 180 cells/mm<sup>3</sup>. His last viral count was 150,000 copies/mL. The patient is poorly compliant with antiviral therapy. Temperature is 39.4 C° (103 F°), pulse is 90/minute, respiratory rate 25/min, blood pressure is 120/70 mmHg, and oxygen saturation is 82% on room air. Physical examination shows diffuse lung crackles on auscultation. Chest X-ray shows bilateral "ground glass" infiltrates. Which is the most likely causative organism for this patient's condition?

Correct answer =  
D) Pneumocystis jirovecii

- A) Cytomegalovirus
- B) Mycoplasma pneumoniae
- C) Aspergillus fumigatus
- D) Pneumocystis jirovecii
- E) Mycobacterium tuberculosis





# Respiratory System

5) A farmer in Mississippi presents with a chronic cough. Chest radiograph reveals an opaque mass, and biopsy of the lung shows macrophages with multiple yeast forms. Which one of the following diagnoses is most likely?

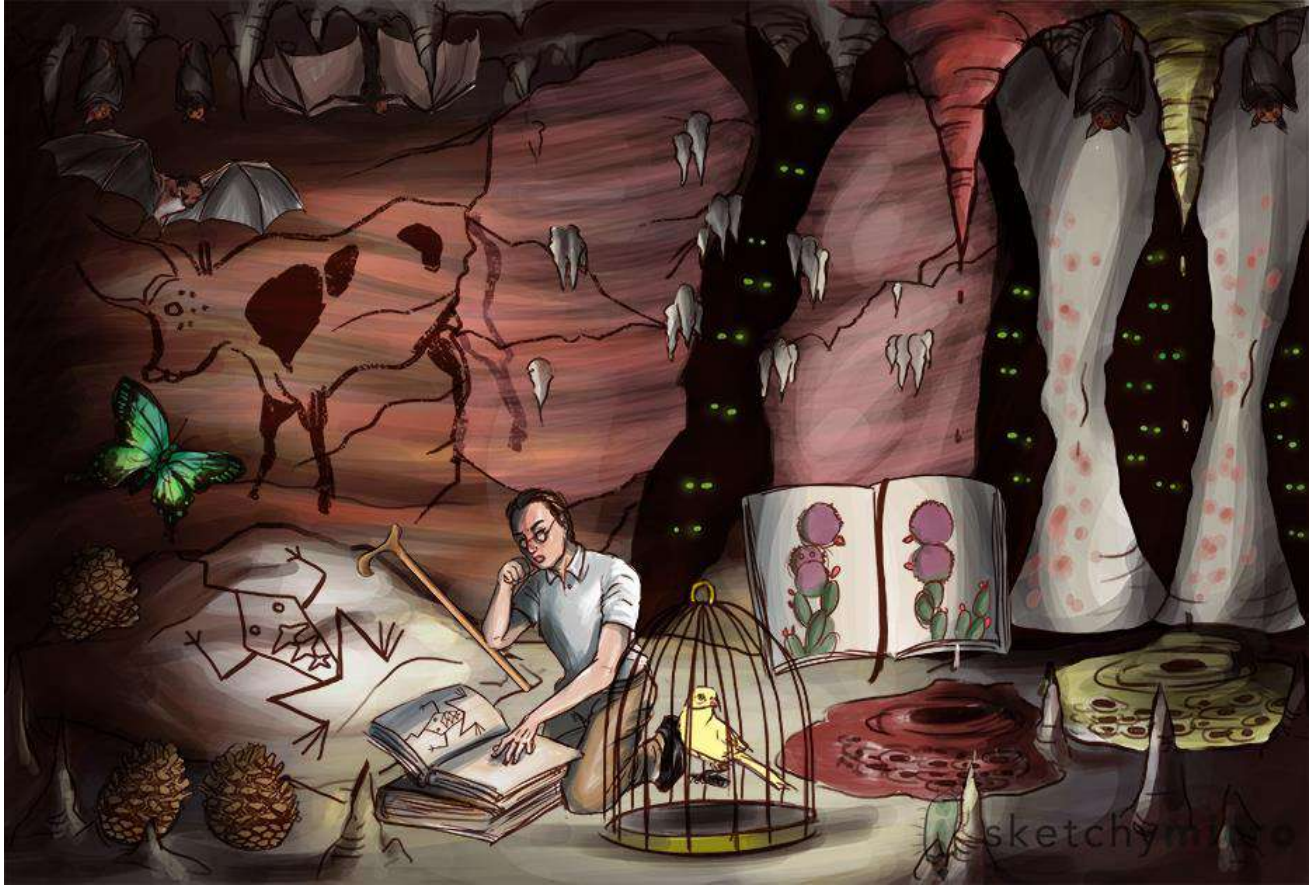
Correct answer = B. Histoplasmosis

- A) Coccidioidomycosis
- B) Histoplasmosis
- C) Aspergillus fumigatus
- D) Pneumocystis jirovecii
- E) Sporotrichosis

6) Which of the following groups of people are associated with Pneumocystis jirovecii?

Correct answer = A

- A) AIDS/Immunocompromised
- B) Mexican American Culture
- C) African-American
- D) Elderly



### ***Histoplasma capsulatum*: The Historians Cave**

1. Bird or Bat droppings in a cave – Location of exposure. Mississippi and Ohio River valleys. Midwestern US
2. Histoplasmosis Indiana Jones - Indiana area "His on the Miss"
3. Coughing: transmission through respiratory.
4. Macrophage Cage and puddles - Macrophages w/ intracellular oval bodies. Canary just a reminder about the cave
5. Red Stalactite and yellow Stalactite: Diagnosis through KOH or rapid serum (red) or urine (yellow) antigen test
6. Puddles with Ovoid bodies – what it would look like on histological size
7. Many ovoid bodies inside of the puddle - Histoplasma much smaller than RBC
8. Dimorphic Butterfly - mold in the cold and yeast in the beast
9. Historian Coughing and lung symbol in the background w/ white stalactites: Pneumonia
10. Stalactites and TB Wild West scene - granulomas, can look like TB w/ calcified nodes and nodules in the hilar region.
11. Book w/ TB symbol: looks like TB
12. Long Legs: erythema nodosum
13. Cane Associated w/ immunocompromised cave drawing of bull w/ liver and spleen: disseminated to liver and spleen because fungus targets the reticuloendothelial system that has a lot of macrophages these are prevalent in the liver and spleen. Causes hepatosplenomegaly
14. Pine cones and Frogs - TXT: -Azole drugs, and systemic infections AMP B



## Fungi – Opportunistic Fungi



### Pneumocystis jiroveci – PCP Ping Pong

1. Aid for Aids – Associated with Aids CD4 counts below 200
2. 20-0 – CD4 counts below 200
3. Immunocompromised Cane player and young player – Symptoms are evident in immunocompromised individuals
4. Cracked glass ping pong tables - Will have a ground glass appearance in both lungs
5. BAL water bottle - Broncheolavar lavage for diagnosis
6. Silver discs on the table and ovoid ping pong balls - Methamine silver stain to identify fungus that looks like disc shaped yeasts
7. Backhand, and the jar of ping pong sulfa bottle- Prophylaxis begins when CD4 count is below 200, Bactrim (TMP/SMX)
8. Pentagon paddles – Pentadamine can be used with sulfa allergies

# Fungi – Opportunistic Fungi



## Aspergillus fumigatus – Asparagus Farm

1. Cat on scarecrow - Catalase Positive
2. Peanut plant in the front – Peanuts are associated with **aflatoxins produced by Aspergillus flavus**
3. Wheat field – aflatoxins associates with grain
4. Cow with liver and Crab on the tractor - Hepatocellular carcinoma
5. Plant has acute angles and septations – Aspergillus is Acute branching with septations ASpergillus
6. Fruiting bodies on the peanut plant - Conidiophores with fruiting bodies, those will be inhaled by humans
7. 3 types of infection
  - a. Crop duster with Sweaty, running, farmer running with inhaler below- Allergic bronchopulmonary aspergillus (ABPA), causing wheezing, fever, and a migratory pulmonary infiltrate.
    - i. Inhaler says IgE on it - Type I hypersensitivity, IgE response
  - b. Farmer that is coughing with a handkerchief and TB Cactus – Susceptibility increases with TB cavities. Aspergillosis causing aspergillomas
    - i. Peanuts under the ground - Aspergillomas are gravity dependent so fungus balls will be at the bottom of the cavity
  - c. Farmer on the right w/immunocompromised cane – Angioinvasive aspergillosis - Patients with neutropenia from leukemia or lymphoma –
    - i. Red sprinkler system throughout the crops - invades blood vessels and the surrounding tissues
    - ii. Scarecrow with a straw heart, kidneys, and black dots on head, black dot on nose – Kidney failure, endocarditis, ring enhancing lesions in the brain. Invades nasal sinus
8. Pine cones and vortex – Voriconazole for less serious infections
9. Frogs – Amphotericin B for angioinvasive disease