

Parasitic and fungal infections of respiratory tract

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Learning objectives

At the end of the session, the students will be able to understand:

- Examples of parasites & fungi that cause infections of respiratory tract.
- Epidemiology, pathogenesis, clinical manifestations, lab diagnosis and treatment of **Paragonimiasis, TPE, Pneumocystis pneumonia, Zygomycoses, Aspergillosis, Penicilliosis.**

Parasitic infections of respiratory tract

- *Paragonimus westermani* (Lung Fluke)

- Parasites passing through lungs: ***Ascaris***, hookworm, ***Strongyloides***

- Parasites causing hypersensitivity in lungs: **Filarial nematodes -TPE.**

- Parasites that infect elsewhere, rarely infect lungs: *E. histolytica*,
Toxoplasma, *Balantidium coli*, *Cryptosporidium parvum* and
Echinococcus granulosus

- Parasites of lower animals, that rarely infect man, e.g. *Mammomonogamus*.

1.Paragonimiasis

- *Paragonimus westermani* (oriental lung fluke)- a trematode.
- Causes endemic hemoptysis in man



EPIDEMIOLOGY

- 10 species of *Paragonimus* infect humans
- Global prevalence of 22 million.
- World: *P. westermani* - in the Far East (Korea, Japan, Taiwan, China, Philippines)
- **India:** Paragonimiasis is endemic in **Northeast states** of India. Many cases from Manipur- prevalence-6.7%.

LIFE CYCLE

- Similar to other trematodes, except schistosomes.

MORPHOLOGY:

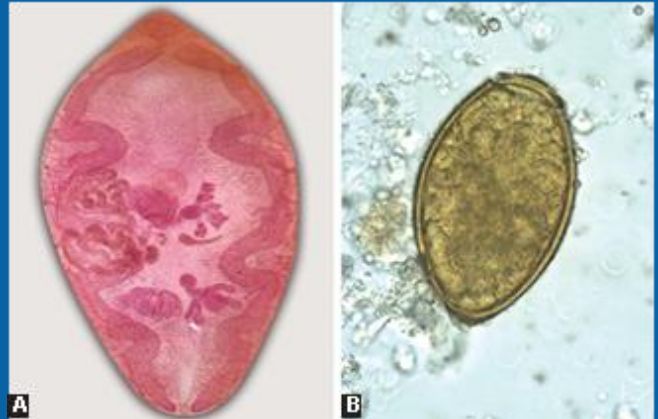
- A. adult worm (leaf-like),
- B. eggs (Operculated)
- C. larvae (five stages).

- **Hosts: three** hosts

▀ Definitive host: **Humans**

▀ Intermediate hosts: First : **Snails**

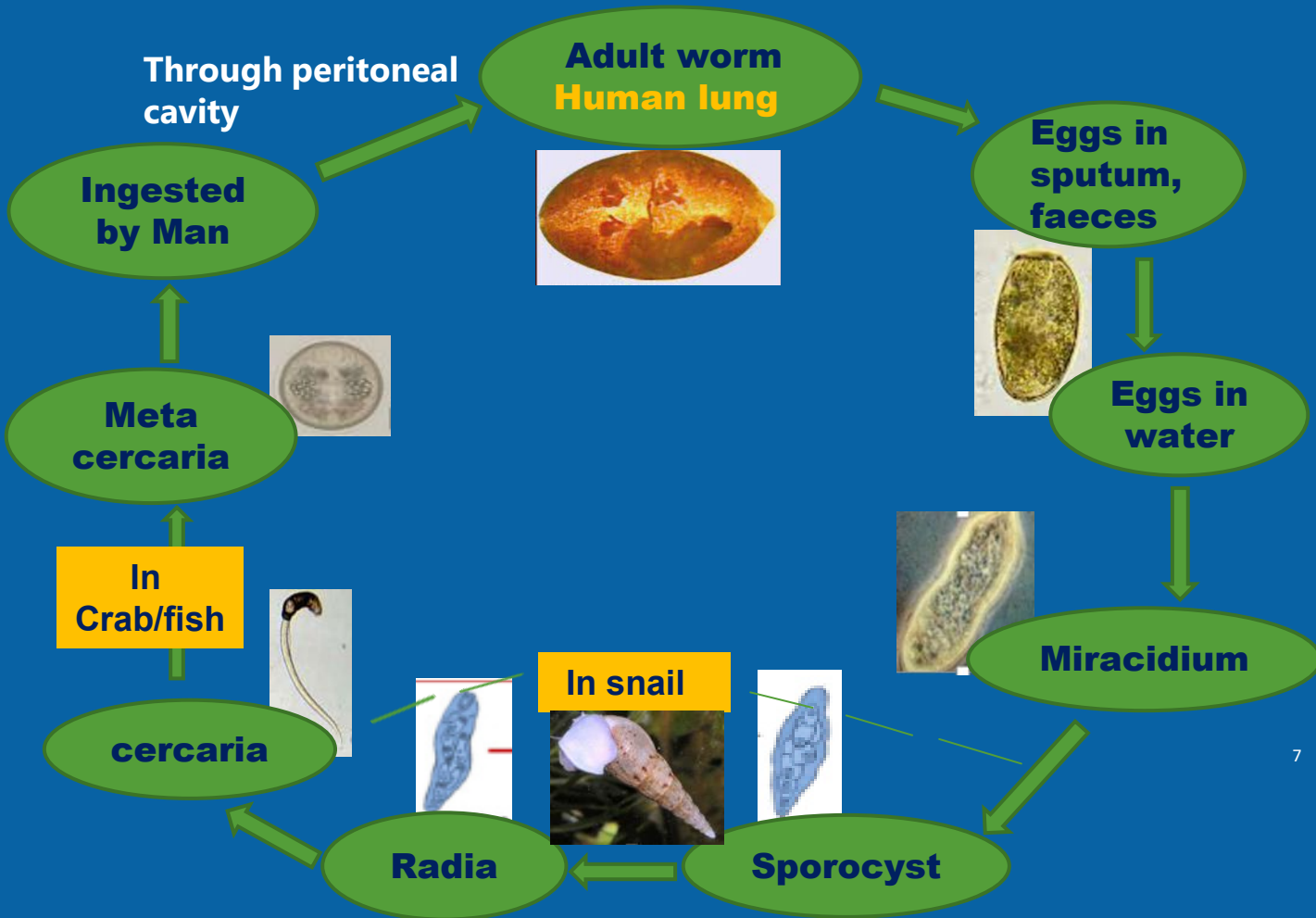
second : **crabs or crayfishes.**



A. Adult worm (carmine stained)

B. Egg (in sputum wet mount)

LIFE CYCLE-



PATHOGENESIS AND CLINICAL MANIFESTATIONS

Due to multiplication of adult worm in lungs

Pulmonary paragonimiasis (ENDEMIC HEMOPTYSIS)

- Adult worm causes eosinophilic granulomatous inflammation in the lungs-forms cyst surrounding the worm - commonly found in right lung.
- Productive cough ,brownish blood tinged rusty sputum with an offensive fishy odor
- Frank hemoptysis with peripheral blood eosinophilia
- Chronic cases-bronchitis, bronchiectasis, pneumonia or lung abscess.

Extrapulmonary Paragonimiasis

- Worms migrate from the ruptured cysts to various sites - liver, spleen, abdominal wall and sometimes brain.
 - Cerebral paragonimiasis
 - Cutaneous paragonimiasis

Laboratory Diagnosis – Sputum Microscopy

■ Early morning, deeply coughed sputum sample.



■ Saline mount of sputum - operculated eggs.

■ If the egg burden is less, then:



- Check multiple sputum samples (up to seven samples)
- Sputum -concentrated by formalin-ether sedimentation technique, but not by floatation method

Laboratory Diagnosis - Serological Tests

■ Antibody detection:

- DIGFA: dot-immunogold filtration assay
- ELISA to detect parasite specific IgG or IgE
- Western blot

■ Antigen detection: Dot ELISA

Treatment of Paragonimiasis

- Praziquantel (25 mg/kg/dose, three doses/day for 2 days)
- Surgical management -for pulmonary or cerebral lesions

Prevention

- i) sanitary disposal of sputum
- ii) control of snails
- iii) treatment of cases
- iv) health education.

2. Tropical pulmonary eosinophilia (TPE)

- Distinct syndrome, develops in some infected individuals with *Wuchereria bancrofti* and *Brugia malayi* in endemic places.
- Also called as occult filariasis or Weingarten's syndrome.

Differences between classical & occult filariasis

Characters	Classical filariasis	Occult filariasis
Probable etiology	Inflammatory changes to adult worm	Hypersensitivity reaction to microfilaria antigen
Diagnostic form	Microfilaria present in blood & in fluid	Microfilaria absent in blood
Organs affected	Lymph nodes, lymphatic vessels	Lungs, liver and spleen
Pathology	Lymphangitis and lymphadenitis	Eosinophilic granuloma
Serology	Ab detection is not diagnostic	IgE detection is diagnostic

Pathogenesis-

- Due to hypersensitivity reaction to microfilaria antigen.
- Microfilariae are rapidly cleared from the blood stream, filtered, lodged and destroyed in lungs - allergic response

Clinical Features-

- Nocturnal paroxysmal cough, wheezing, weight loss, low-grade fever.
- Microfilariae entrapped in other organs - spleen, liver and lymph node –hepatosplenomegaly, lymphadenopathy.
- Sometimes called as **Meyers Kouwenaar Syndrome**.

Laboratory Diagnosis

- Blood eosinophilia (absolute eosinophil count more than 3000/ μ L)
- Chest X-ray: Shows diffuse infiltration
- Elevated serum IgE levels
- Pulmonary function test - obstructive changes in lungs.

Treatment of Occult filariasis-

- Diethylcarbamazine (DEC), 4-6 mg/kg for 14 days.
- Relapse may occur in 12-25% of cases.

3.Migratory stage of intestinal nematodes

a. In Ascariasis

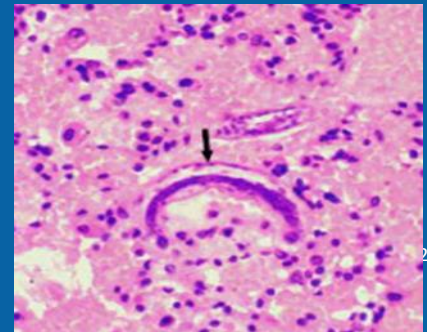
- Pulmonary symptoms seen in 2nd week after ingestion of eggs
- Eggs hatch - larvae in the duodenum - molt to L3 larvae - penetrate the intestine - reach right side of heart via portal circulation - lungs via pulmonary capillaries.
- Migrating larvae in lungs- hypersensitivity response.
- Common symptoms - non-productive cough, chest discomfort, fever

In Ascariasis- LOEFFLER'S SYNDROME:

- Severe cases develop dyspnea. Transient patchy infiltrates seen on chest X-ray with peripheral eosinophilia.
- Called as eosinophilic pneumonia (Loeffler's syndrome)

Diagnosis:

- Eosinophilia prominent early but disappears later.
- Charcot-Leyden crystals in sputum & stool - nonspecific finding.
- Larvae - found in sputum or gastric aspirates.
- Eggs are characteristically absent in stool examination



b. In Hookworm Infection-

- Migrating larva through the lungs occasionally cause mild transient pneumonitis, asthma and bronchitis.
- Severity and frequency of lung manifestation is less compared to ascariasis

c. In Strongyloidiasis

- Pulmonary symptoms -uncommon compared to ascariasis and hookworm.
- Occurs only secondary to underlying chronic obstructive lung disease.

Rare parasitic pulmonary infections

- ☐ Pulmonary **amoebiasis**
- ☐ Pulmonary **toxoplasmosis**
- ☐ Pulmonary **balantidiasis**
- ☐ Respiratory **cryptosporidiosis**
- ☐ Pulmonary **hydatidosis** →
- ☐ Parasites of lower animals



Fungal infections of respiratory tract

Opportunistic fungal agents: causing RTI

- ☐ Pneumocystis jirovecii
- ☐ Zygomycoses
- ☐ Aspergillosis
- ☐ Penicillosis.

Fungi causing systemic mycoses:

- ☐ Blastomyces dermatitidis
- ☐ Histoplasma capsulatum
- ☐ Paracoccidioides brasiliensis
- ☐ Coccidioides immitis.
- ☐ Yeast: Cryptococcus neoformans

PNEUMOCYSTIS PNEUMONIA

Taxonomy

- In 2002 the taxonomy of Pneumocystis has been changed
- Once thought to be a protozoan
- Now under fungus, based on nucleic acid sequence studies.
- ***Pneumocystis jirovecii*** (previously *Pneumocystis carinii*)

Pathogenesis

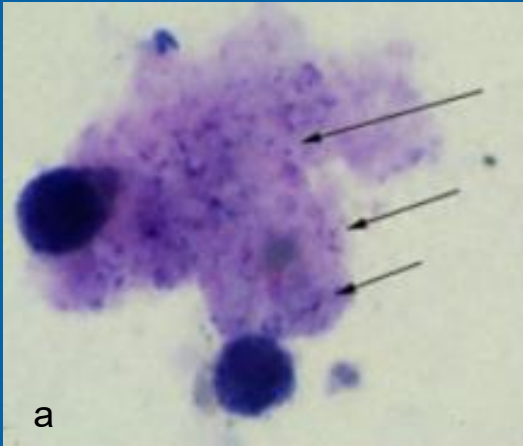
■ Pneumocystis exists in **cyst and trophozoite** forms.

Cysts -found in environment.

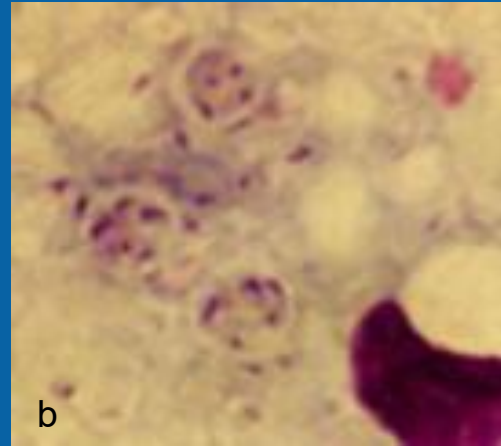
■ Inhaled- carried to lungs- transform into trophozoite

Trophozoites induce inflammatory response – recruitment of plasma cells-frothy exudate -also called ***plasma cell pneumonia***.

■ In human tissues both cysts & trophozoites (containing 4-8 sporozoites) are found



a. Trophozoite



b. Cyst from BAL

Laboratory Diagnosis

- Histopathological examination of lung tissue - cysts.

- Gomori's methenamine silver (GMS) staining -cysts.

-black colored crushed ping-pong balls, against the green background

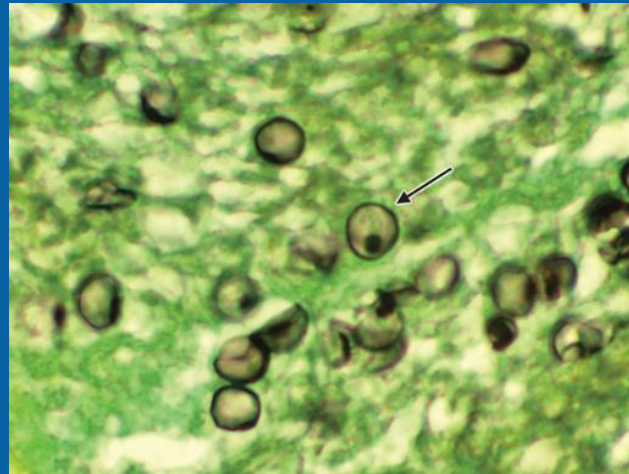
Other Tests-

- Pneumocystis is **not cultivable**

- No serological test available

- PCR detects specific genes

- Detection of 1, 3 β -D-glucan in serum



Laboratory Diagnosis (Cont..)

- Radiology: Chest X-ray - classical finding of bilateral diffuse infiltrates.
- CT of the lung -ground-glass opacities at the early stage.
- Atypical manifestations - nodular densities, cavitary lesions



CT scan of lungs suggestive of Pneumocystis pneumonia (soft tissue density nodule with reverse halo sign in the right upper lobe).

Treatment of *Pneumocystis pneumonia*

- Cotrimoxazole (trimethoprim/sulfamethoxazole)
- For 14 days in non-HIV patients and 21 days in patients with HIV.
- Also recommended for primary and secondary prophylaxis in patients with HIV

ZYGOMYCOSIS (Opportunistic)

Life-threatening infections caused by aseptate fungi belonging to phylum Zygomycota

1. Order mucorales (causes **mucormycosis**)

- Rhizopus (*R. arrhizus* and *R. microsporus*)
- *Mucor racemosus*, *Rhizomucor pusillus*

2. Order entomophthorales (causes entomophthoromycosis)

- *Basidiobolus ranarum*
- *Conidiobolus coronatus*

Mucormycosis - Pathogenesis

- Spores found ubiquitously
- Transmission-inhalation, inoculation, rarely ingestion of spores
- Mycelial form angioinvasive –results in spread of infection

Predisposing factors:

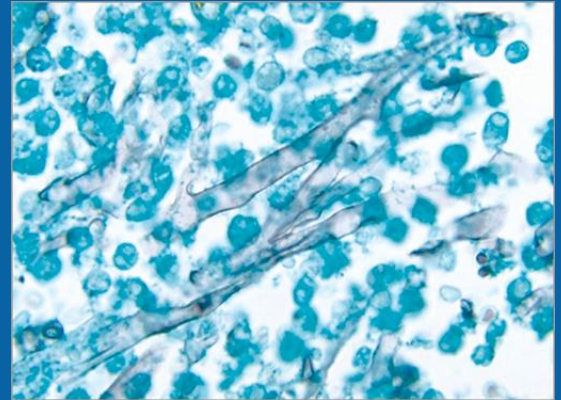
- Conditions with increased iron load
- Diabetic ketoacidosis
- End stage renal disease
- Iron therapy or deferoxamine
- Defects in phagocytic functions

Mucormycosis – Clinical Manifestations

1. Rhinocerebral mucormycosis: Most common form, Orbital cellulitis, proptosis and vision loss
2. **Pulmonary mucormycosis** - in patients with leukemia
3. Cutaneous mucormycosis
4. Gastrointestinal mucormycosis – necrotizing enterocolitis
5. Disseminated mucormycosis: Brain
6. Miscellaneous forms

Mucormycosis – Laboratory Diagnosis

- Histopathological staining or methenamine silver stain of tissue biopsies shows-
broad aseptate hyaline hyphae with wide angle branching



Zygomycosis—histopathology of tissue section shows aseptate broad hyphae (Methenamine silver stain).

Mucormycosis –Laboratory Diagnosis (Cont..)

- Culture on SDA at 25°C: White cottony woolly colonies with tube filling growth (hence called lid lifters).
- Rhizopus - colonies become brown black later, due to sporulation, giving rise to salt and pepper appearance

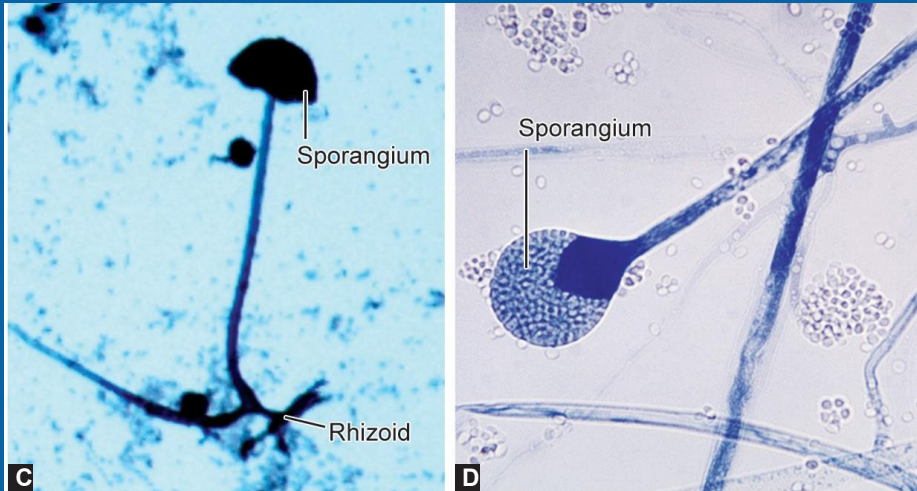


- A. Rhizopus colony on SDA shows white cottony woolly colonies with black spores (salt and pepper appearance);
- B. Mucor on SDA-white cottony woolly colonies

Mucormycosis – Laboratory Diagnosis (Cont..)

■ Microscopy: LPCB mount - broad aseptate hyaline hyphae, with sporangiophore – sporangium – sporangiospores.

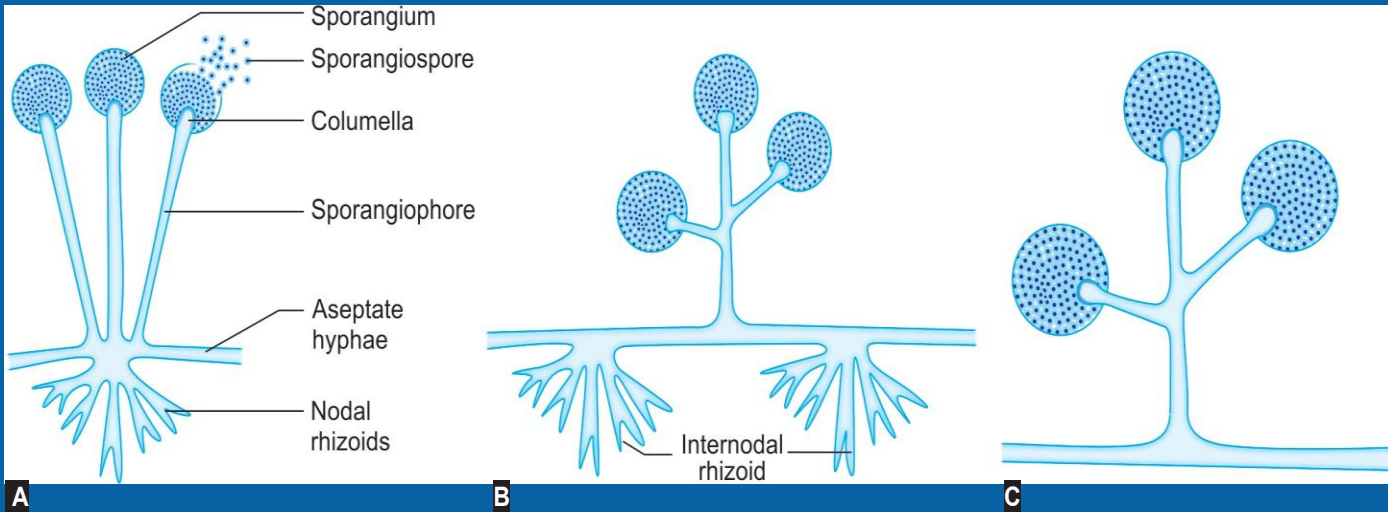
■ Rhizoid: Root like growth arising from hyphae



C. *Rhizopus* (sporangium with rhizoid)

D. *Mucor* sporangium (absence of rhizoid).

Mucormycosis – Laboratory Diagnosis (Cont..)



A. Rhizopus; B. Lichtheimia; C. Mucor

- ☐ Rhizopus - nodal rhizoids
- ☐ Lichtheimia(Absidia)- internodal rhizoids
- ☐ Mucor - rhizoids absent.

Treatment of Zygomycosis

- Amphotericin B deoxycholate - drug of choice for all forms of mucormycosis.
- Posaconazole or isavuconazole - given alternatively.
- For mild localized skin lesions in immunocompetent patients, which can be removed surgically.

Entomophthoromycosis

- Subcutaneous lesions produced by members of the order Entomophthorales, i.e. *Conidiobolus* and *Basidiobolus*.
- Latter is also associated with visceral involvement.

ASPERGILLOSIS

- ❑ Aspergillosis refers to the invasive and allergic diseases caused by a hyaline mold named *Aspergillus*.
- ❑ >35 pathogenic and allergenic species of *Aspergillus*, important ones -*A. fumigatus*, *A. flavus* and *A. niger*

Pathogenesis

- Widely distributed in nature -on decaying plants
- Transmission – inhalation of airborne conidia
- Risk factors for invasive aspergillosis are:
 - Glucocorticoid use (the most important risk factor)
 - Profound neutropenia
 - Neutrophil dysfunction
 - Underlying pneumonia, COPD, tuberculosis or sarcoidosis
 - Anti-tumor necrosis factor therapy.

Clinical Manifestations

Incubation period - 2 to 90 days.

■ **Pulmonary aspergillosis:** Most common form

- Allergic bronchopulmonary aspergillosis (ABPA)
- Severe bronchial asthma
- Aspergilloma (fungal ball)
- Acute angioinvasive pulmonary aspergillosis
- Chronic cavitary pulmonary aspergillosis

■ **Invasive sinusitis**

- Chronic granulomatous sinusitis
- Maxillary fungal ball
- Allergic fungal sinusitis

Clinical Manifestations (Cont..)

- **Cardiac aspergillosis:** Endocarditis and pericarditis
- **Cerebral aspergillosis:** Brain abscess, hemorrhagic infarction and meningitis
- **Ocular aspergillosis:** Keratitis and endophthalmitis
- **Ear infection:** Otitis externa
- **Cutaneous aspergillosis**
- Onychomycosis (Nail bed infection)
- Mycotoxicosis

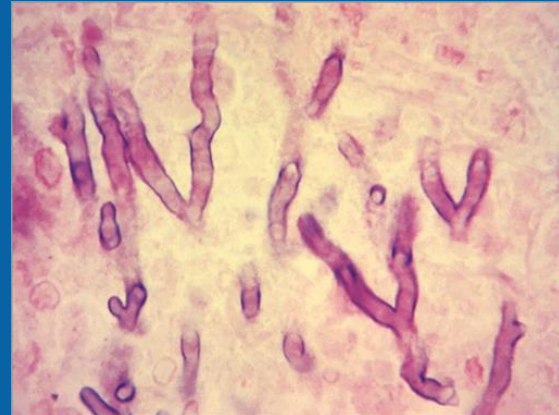
Laboratory Diagnosis - Direct examination

- Specimens - Sputum and tissue biopsies

- KOH (10%) mount or histopathological staining- narrow septate hyaline hyphae with acute angle branching

- **Culture:** SDA and incubated at 25°C

- Species identification - based on macroscopic and microscopic

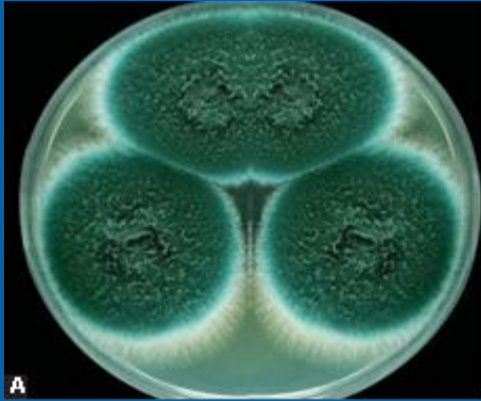


- (LPCB mount) appearance of the colonies

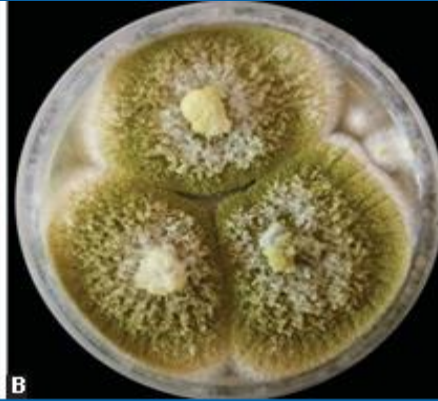
Identification of *Aspergillus* species

Species	Macroscopic appearance-colony	Microscopy of colony (LPCB mount)
A. fumigatus	smoky green, velvety to powdery, reverse is white	- Vesicle is conical-shaped - Phialides arranged in single row - Conidia arise on upper 3rd of vesicle - Conidia are hyaline
A. flavus	yellow green, velvety, reverse is white	➤ Vesicle is globular-shaped ➤ Phialides in one or two rows ➤ Conidia arise from upper two-third to entire vesicle ➤ Conidia are hyaline
A. niger	black, cottony type, reverse is white	➤ Vesicle is globular-shaped ➤ Phialides in two rows ➤ Conidia arise from entire vesicle ➤ Conidia are black in color

Aspergillus sp.



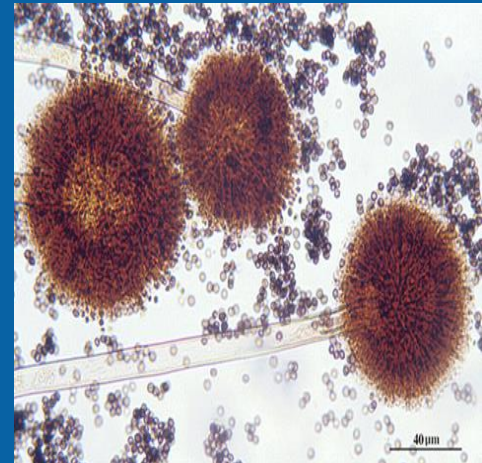
A. fumigatus,



A. flavus,



A. niger



Laboratory Diagnosis - Antigen Detection

- β -d-Glucan Ag assay: Marker of invasive fungal infections
 - Raised in most invasive fungal infection
- Galactomannan Ag: by ELISA in patient's sera or urine.

Antibody Detection-

- For chronic invasive aspergillosis & aspergilloma
- In allergic syndromes, specific serum IgE levels elevated.

Treatment of Aspergillosis

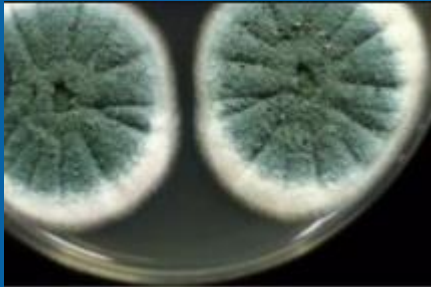
- For invasive aspergillosis-voriconazole
- For ABPA- itraconazole
- For single aspergilloma- surgery is indicated
- For chronic pulmonary aspergillosis-itraconazole/voriconazole
- For prophylaxis - posaconazole is indicated.

PENICILLIOSIS -Clinical Significance

- Penicillium has >250 species, saprophytes in nature.
- *Penicillium marneffe* - dimorphic fungus, produces wart like skin lesions
- Mycotoxicoses - toxins released by certain species such as *P. cyclopium*, *P. verrucosum*, *P. puberulum*
- Invasive penicilliosis: endophthalmitis and endocarditis
- Superficial disease: otomycosis, keratitis and Onychomycosis
- **Allergic disease: asthma and allergic pneumonitis**

Laboratory Diagnosis

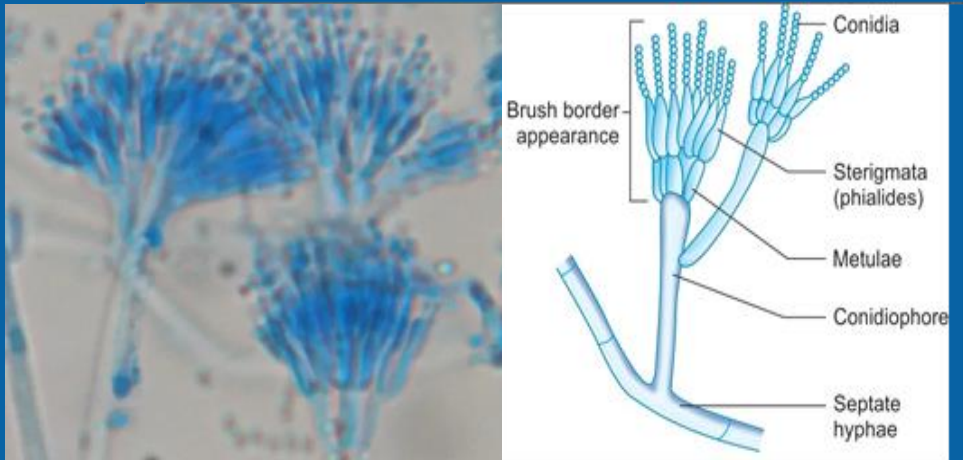
- *P. marneffei* - dimorphic fungus
- Other *Penicillium* -molds, grow easily on SDA at 25°C
- Colonies - rapid growing, flat,velvety to powdery texture and greenish colored



Laboratory Diagnosis (Cont..)

■ Microscopic appearance - LPCB mount -

Hyaline thin septate - conidiophore and its branches -
elongated metulae - flask-shaped phialides - chain of
conidia - **brush border appearance**



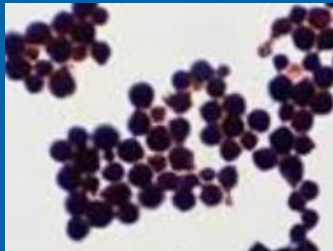
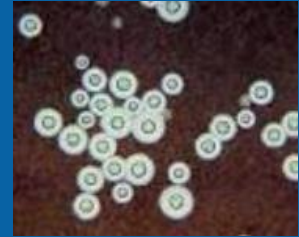
PULMONARY CRYPTOCOCCOSIS

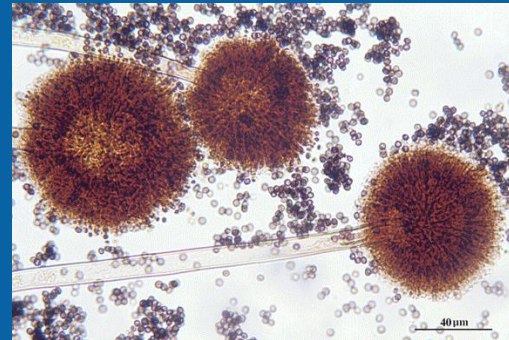
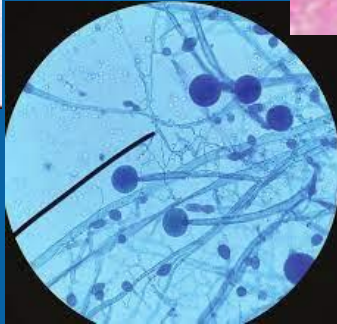
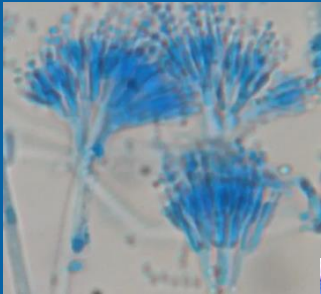
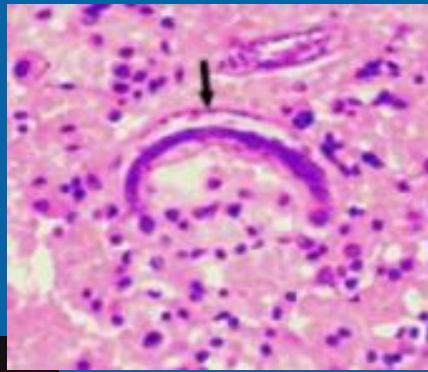
■ Cryptococcus neoformans - capsulated yeast causes meningitis in HIV-infected individuals.

■ Acquired by inhalational route

■ In immunocompetent individuals-lungs exhibit defense mechanisms.

■ In people with low immunity, pulmonary infection occurs first, followed by dissemination through blood to distant sites such as CNS.





QUESTIONS:

Q1. The drug of choice for *Pneumocystis* pneumonia is:

- a. Amphotericin B
- b. Flucytosine
- c. Cotrimoxazole
- d. Voriconazole

QUESTIONS:

Q2. Azole active against mucormycosis is:

- a. Voriconazole
- b. Fluconazole
- c. Itraconazole
- d. Posaconazole