FNU FIJI NATIONAL UNIVERSITY

COLLEGE OF MEDICINE, NURSING & HEALTH SCIENCES

MLS 602 : Medical Microbiology
LECTURE 7: Systematic & Opportunistic Mycosis

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Expected Student Outcomes

- List of fungi causing Systematic Mycoses
- Describe different species of fungi and the type of diseases
- Discuss laboratory diagnostic methods.
- Explain the treatment regime for fungi

Introduction

- Fungal infections infecting internal organs
- Fungi enter the host body via lungs, gut, paranasal sinuses or skin
- Later spread through bloodstream to multiple organs including skin
- Health problems: digestive difficulties, skin problems, asthma and breathing difficulties.
- Further complications: multiple organ failure and death

Two types of Systematic Mycoses

- Systematic mycoses due to primary pathogens
- Systematic mycoses due to opportunistic pathogens

Systematic Mycoses Due to Primary Pathogens

- Originate primarily in lungs and may spread to many organ systems
- Pathogens are dimorphic
- **Endemic infections**-always present in a certain population and region

Four Types

- *Histoplasma capsulatum* (Histoplasmosis)
- *Coccidioides immitis* (coccidioidomycosis)
- *Blastomyces dermatitidis* (Blastomycosis)
- *Paracoccidioides brasilensis* (paracoccidioidomycosis)

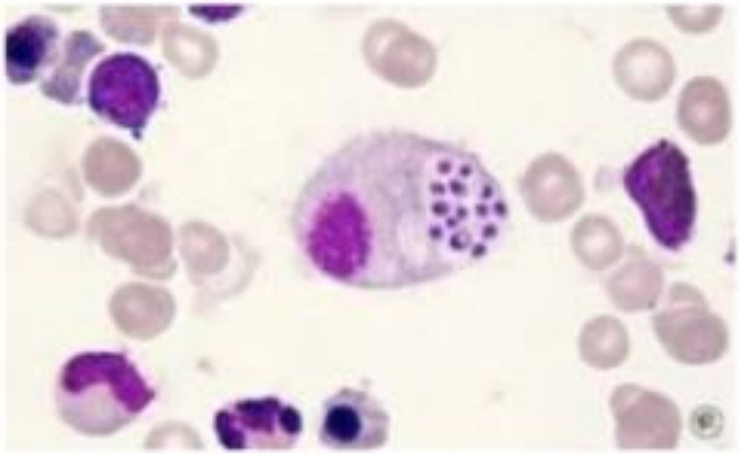
Histoplasmosis

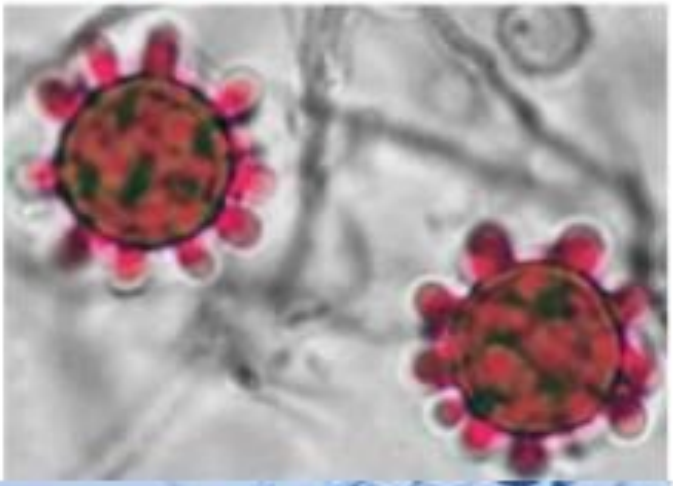
- Intracellular infection of reticuloendothelial system
- Acquired by inhalation
- Most infection remain asymptomatic.
- Infected person may develop:
  - **Pulmonary disease-** resembling TB
  - **Disseminated infection-** most affected are old age and infancy
  - **Skin and mucosa-** granulomatous and ulcerative lesions

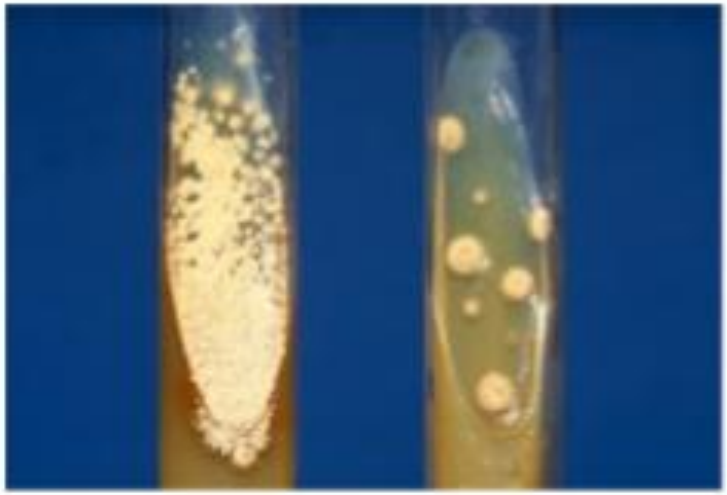
LAB DIAGNOSIS

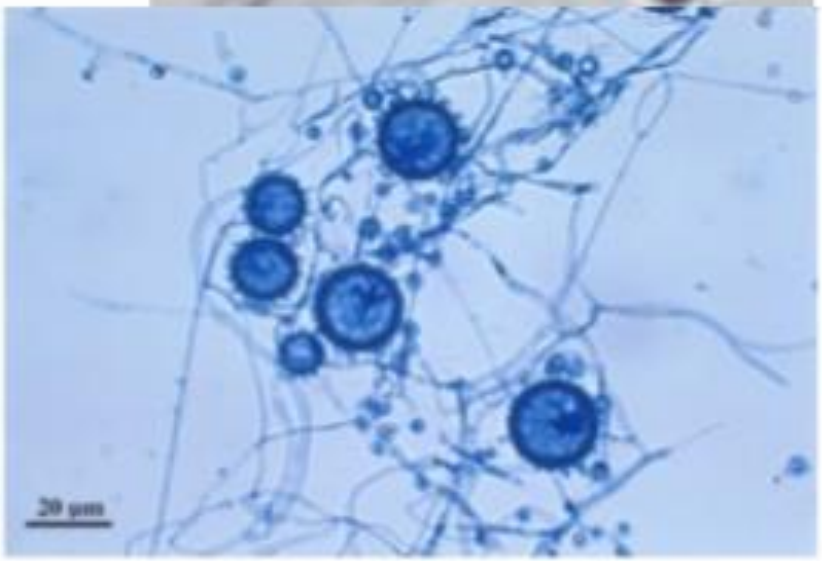
- Thermally dimorphic fungus
- SDA – White cottony mycelial growth at 37 degrees, **Tuberculate spores** at 25 degrees
- Microscopy with Giemsa or Wright stain of blood, bone marrow, lymph node biopsy or skin lesions
- Serology – Histoplasmin antigen test (DTH)

Treatment: Amphotericin B followed by oral Iitraconazole in immunocompromised patients









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Coccidioidomycosis

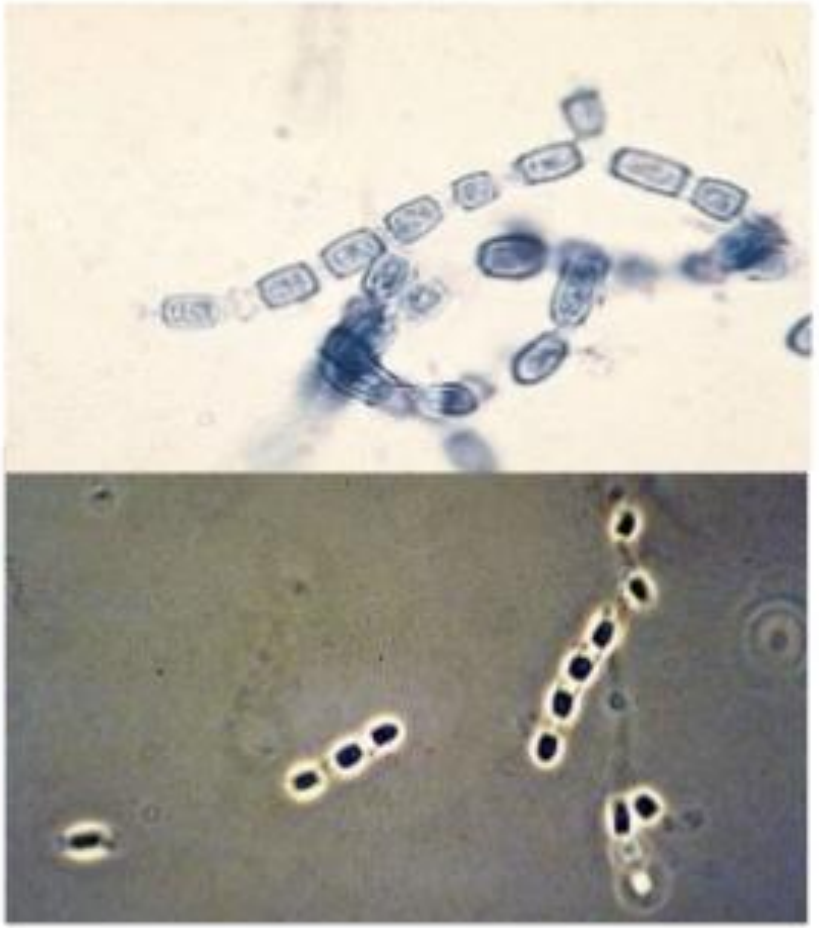
- *Coccidiodes immitis* is considered to be the most virulent of fungal pathogens.
- Restricted to hot, semi-arid areas of SW USA and Mexico.
- Grows in the soil, but inhalation of a single spore can initiate infection.
- In a small percentage of cases, organism disseminates from the lungs to a variety of organs, particularly the CNS, meninges, skin, soft tissues, and bone
- In infected tissues, *C. immitis* appears as a mixture of hyphae and *spherules.*

Lab Diagnosis

- Direct microscopy
- Serological test
- Culture

- Sabaraud's Agar incubated at 20-30C
- **Colony:** white, gray or brownish color with powdery, wooly or cottony texture (extreme caution should be exercised)

Arthrospores



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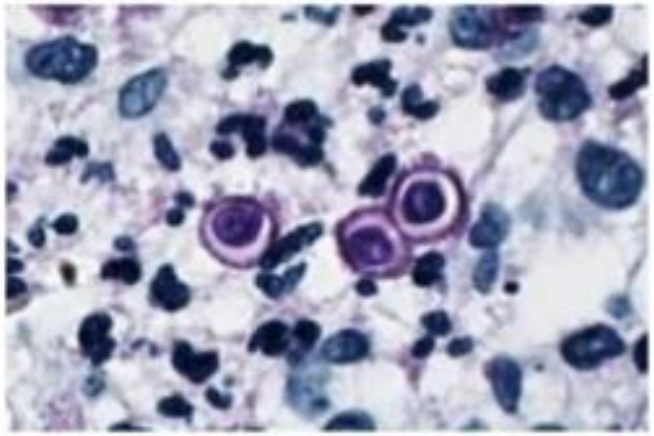
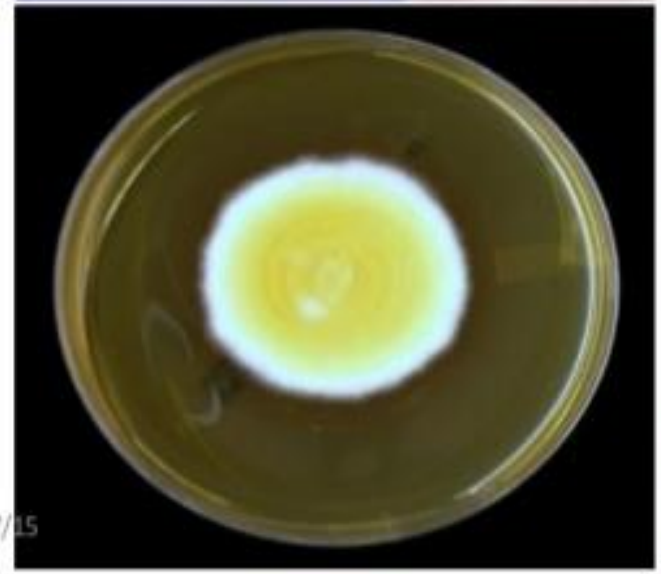
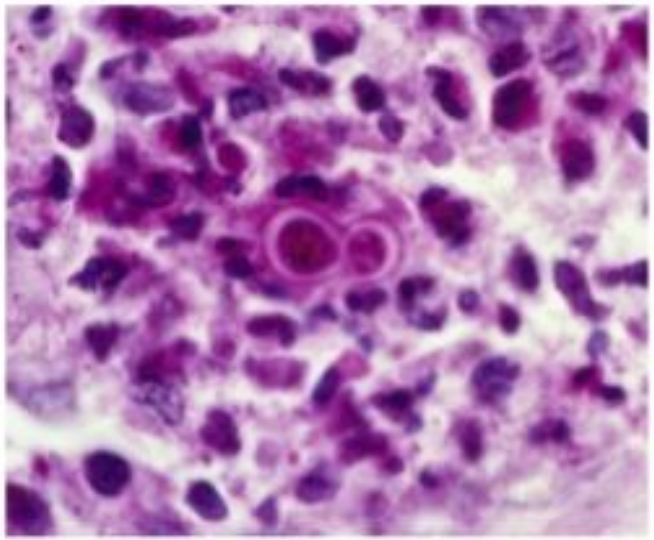
	Blastomycosis
Etiology	*Blastomyces dermatidis*
Ecology	Unknown (riverbanks?)
Geographic distribution	Endemic along Mississippi, Ohio, and St. Lawrence River Valleys and in Southeastern United States
Conidia (< 35 °C)	*YEAST FORM :* **Round yeast w/ doubly refractive wall, single broad based bud** *MOLD FORM :* Branched hyphae w/ small conidia bearing single globose to piriform conidia, 2–10 m
Tissue form	Thick-walled yeasts with broad-based, usually single buds, 8–15 m

Clip slide

BLASTOMYCOSIS







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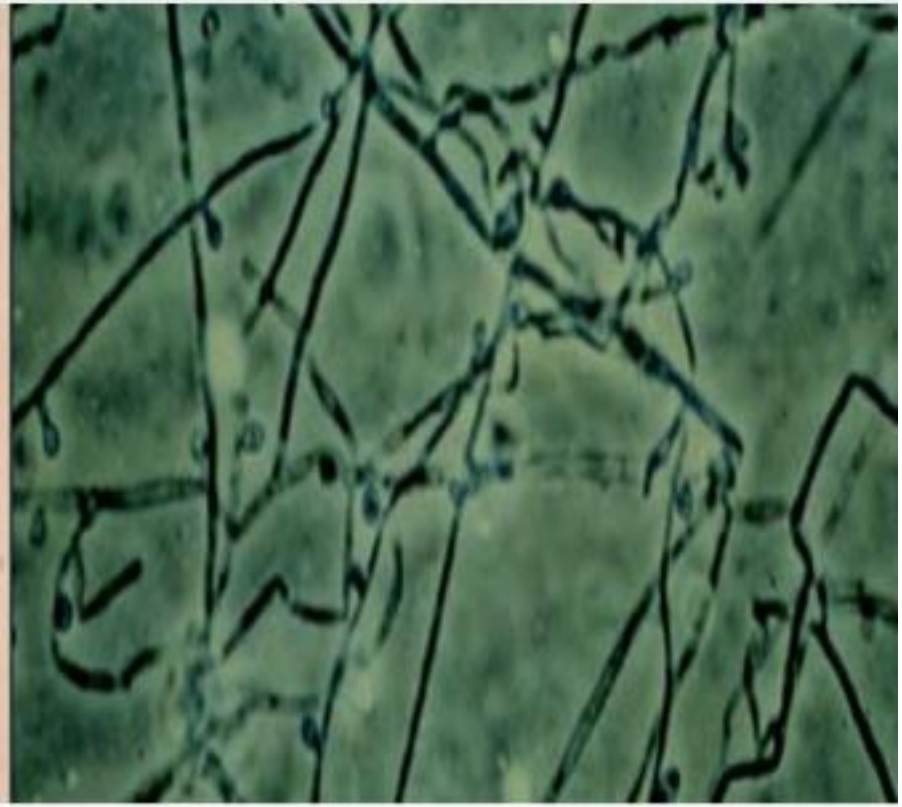
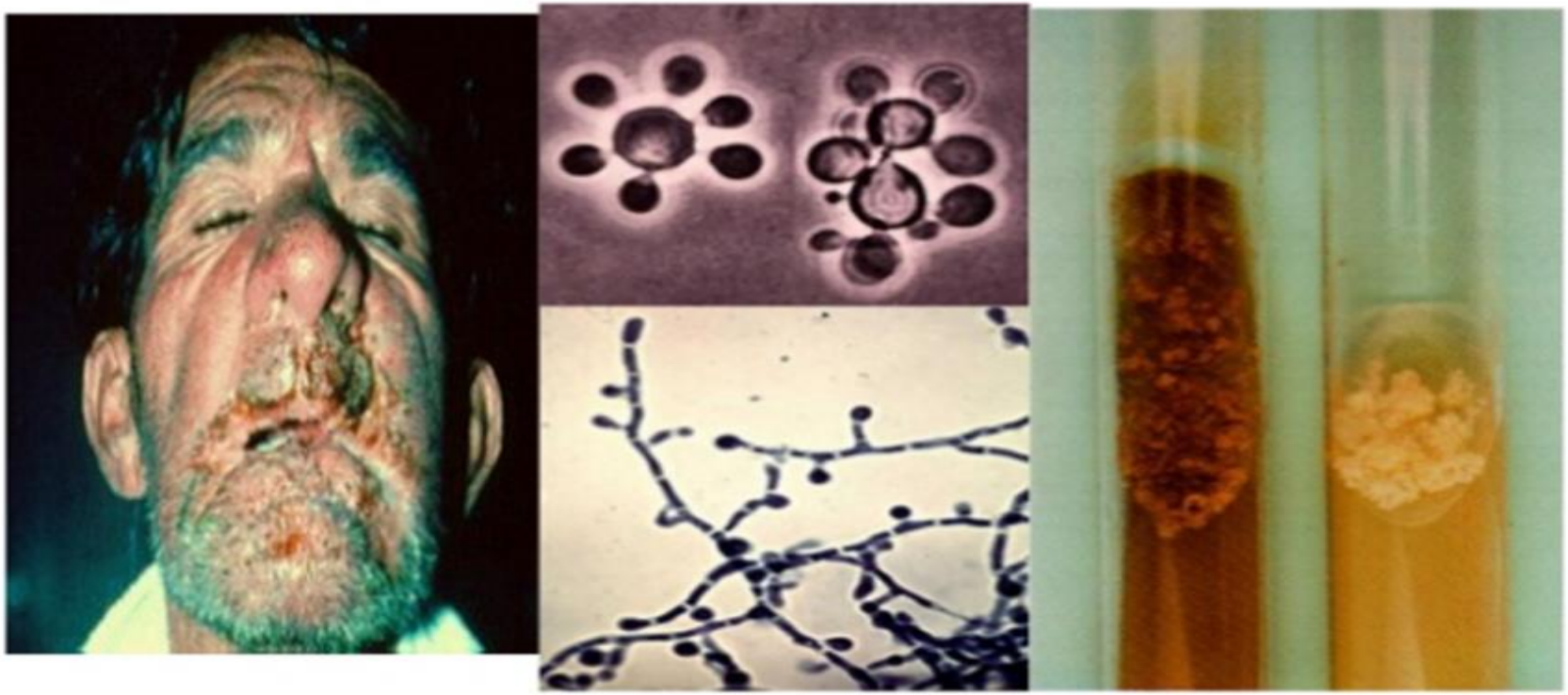
Budding yeast cells of *Blastomyces dermatitidis* in culture. When cultures are incubated at 37°C, large, broad-based budding yeast with a double-contoured all are detected which are characteristic for the yeast phase of this dimorphic fungus. (Lactophenol cotton blue stain; ×400)



Mould form of *Blastomyces dermatitidis* in culture. The lollipop appearance of the conidium on a conidiophore is characteristic of the environmental mould form for this dimorphic fungus. (Lactophenol cotton blue stain; ×400)

	Paracoccidioidomycosis
Etiology	*Paracoccidioides brasiliensis*
Ecology	Soil fungus
Geographic distribution	Central and South America **Latin America**
Conidia (< 35 °C)	Hyaline, branched septate hyphae and rare globose conidia and chlamydospores
YEAST FORM	**Round yeast w/ thick wall and** multiple buds
Tissue form	Hyaline, septate hyphae and rare globose conidia and chlamydospores

PARACOCCIDIODOMYCOSIS



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Budding yeast cells with multiple buds encircling mother cell (mariner's Wheel appearance)

Systematic mycoses due to opportunistic pathogens

- Immunocompromised people
- Aids, prolong use of broad spectrum antibiotics, immunosuppressive therapy and metastatic cancer

Main types are:

Candida spps

Aspergillus spp

Cryptococcus spps

Pneumocystic jirovesi

Candida Species

- Yeast infection of the skin, mucosa, and rarely of the internal organs, caused by a yeast-like fungus *Candida albicans,* and occasionally by other *Candida* species.
- Several species of the yeast genus *Candida* are capable of causing candidiasis.
- They also form pseudo hyphae when the buds continue to grow but fail to detach, producing chains of elongated cells that are pinched or constricted at the septations between cells.
- **Serology:** The detection of circulating cell wall mannan, using a latex agglutination test or an enzyme immunoassay, is much more specific.
- **Treatment:** Nystatin. AmphotericinB, 5-fluorocytosine and clotrimazole

What are Biofilms?

Biofilms are specific and organized communities of cells under the control of signaling molecules, rather than random accumulations of cells resulting from cell division. This characteristics allows growth of candida on medical devices.

Aspergillosis

- Inhalation of conidia
- Conidia germinate to form hyphae that invade lungs and other tissues

Types of Infection

Localized Infection

✓Sinusitis- *A.flavus and A. fumigatus*

✓Mycotic Keratitis- *A.flavus and A. fumigatus*

✓Otomycosis – *A.niger*

Pulmonary infection

- ✓Allergic asthma
- ✓Bronchopulmonary
- ✓Colonizing aspergillosis

Invasive infection

- Involves kidneys, brain and other organs.

Other complications associated with aspergillus are endocarditis and paranasal granuloma

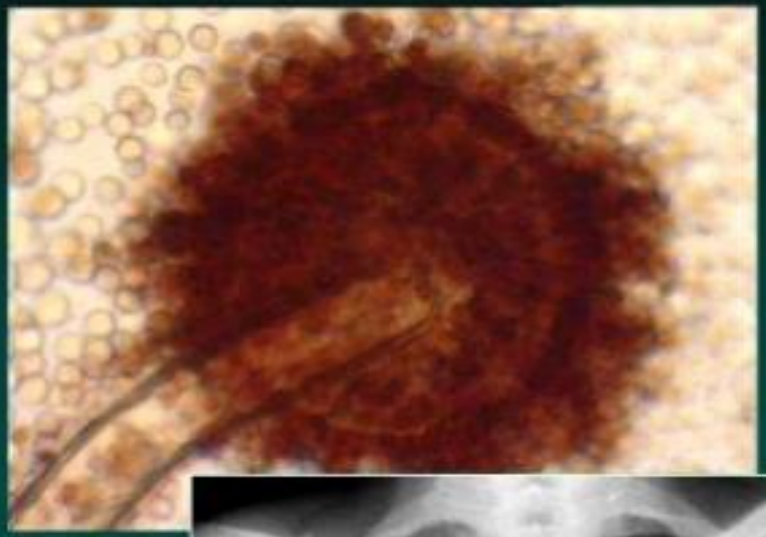
Lab Diagnosis

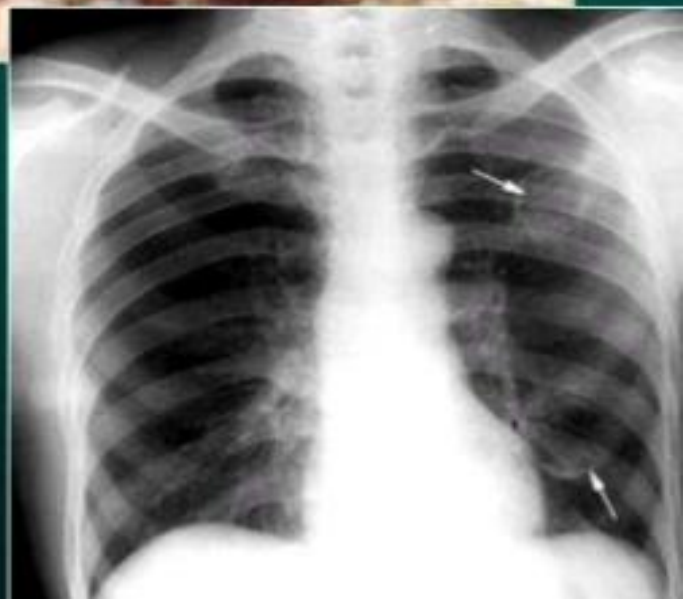
- sputum, other respiratory specimens, lung biopsies
- Microscopic examination with KOH- non-pigmented septate mycelium
- Culture and serological test

Aspergillosis

- Pulmonary infections
- Allergic pneumonitis
- Much more common among the immunosuppressed
- "Fungal ball" cavity formation
- Patients with PMN deficiency, cerebral abscess: high mortality

Aspergillus fumigatus





Cryptococcus

- ***Cryptococcus neoformans and C. gattii***
- Yeast form : oval budding yeast with thick polysaccride capsule
- No mold form
- Transmission mode is by inhalation of fungal particles, which reach the lungs and can disseminate to the brain in immunocompromised hosts.
- Natural habitat is soil with pigeon droppings
- Diseases- pneumonia, granulomas, meningitis (Lung disease and meningocephalitis)

Virulence factors

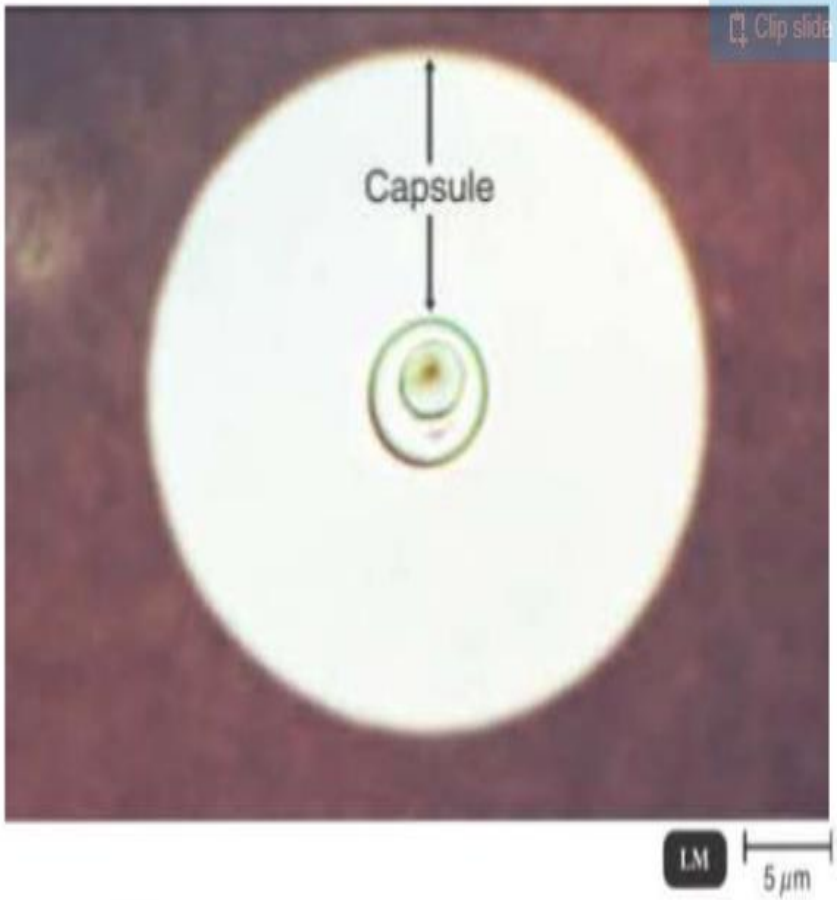
- Anti- phagocytic polysaccride capsule
- Anti oxidant melanin: melanin to the fungal cell wall
- Ability to grow at 37 °C: ability to survive at mammalian body temperature

Treatment

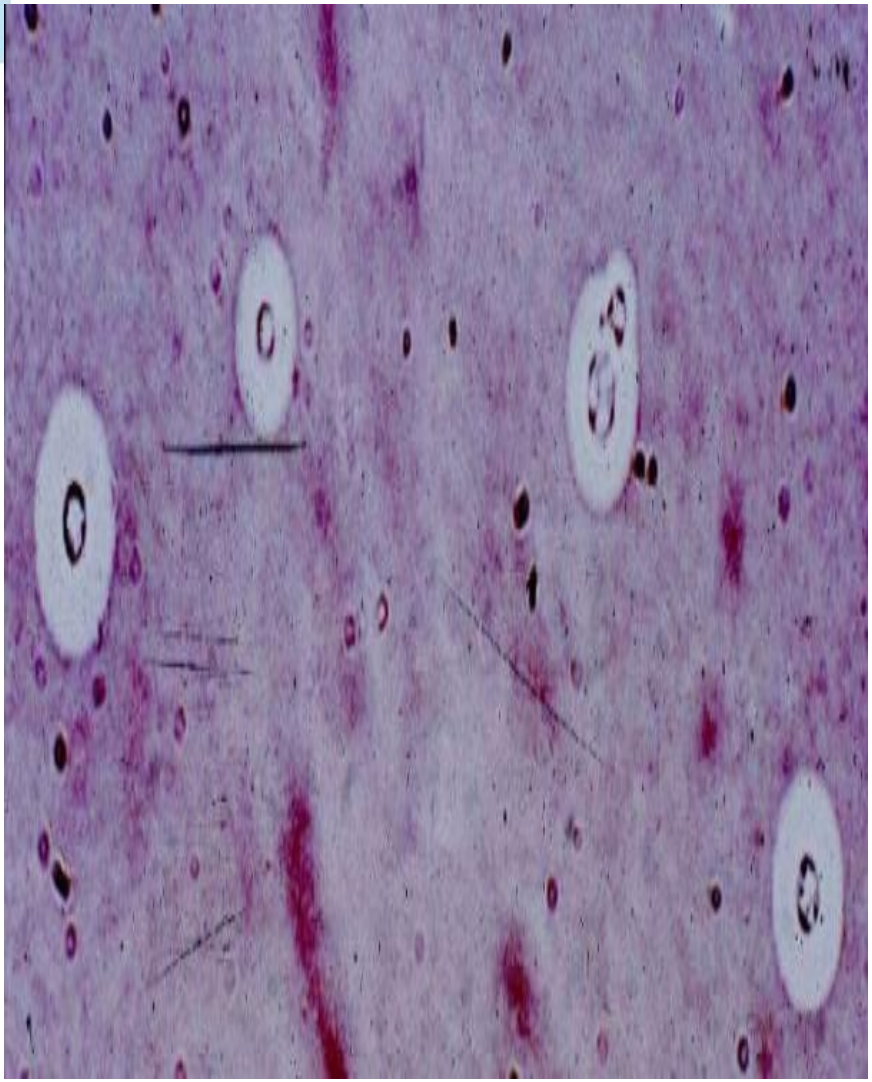
Amphotericin B, flucytosine, and fluconazole

Lab Diagnosis

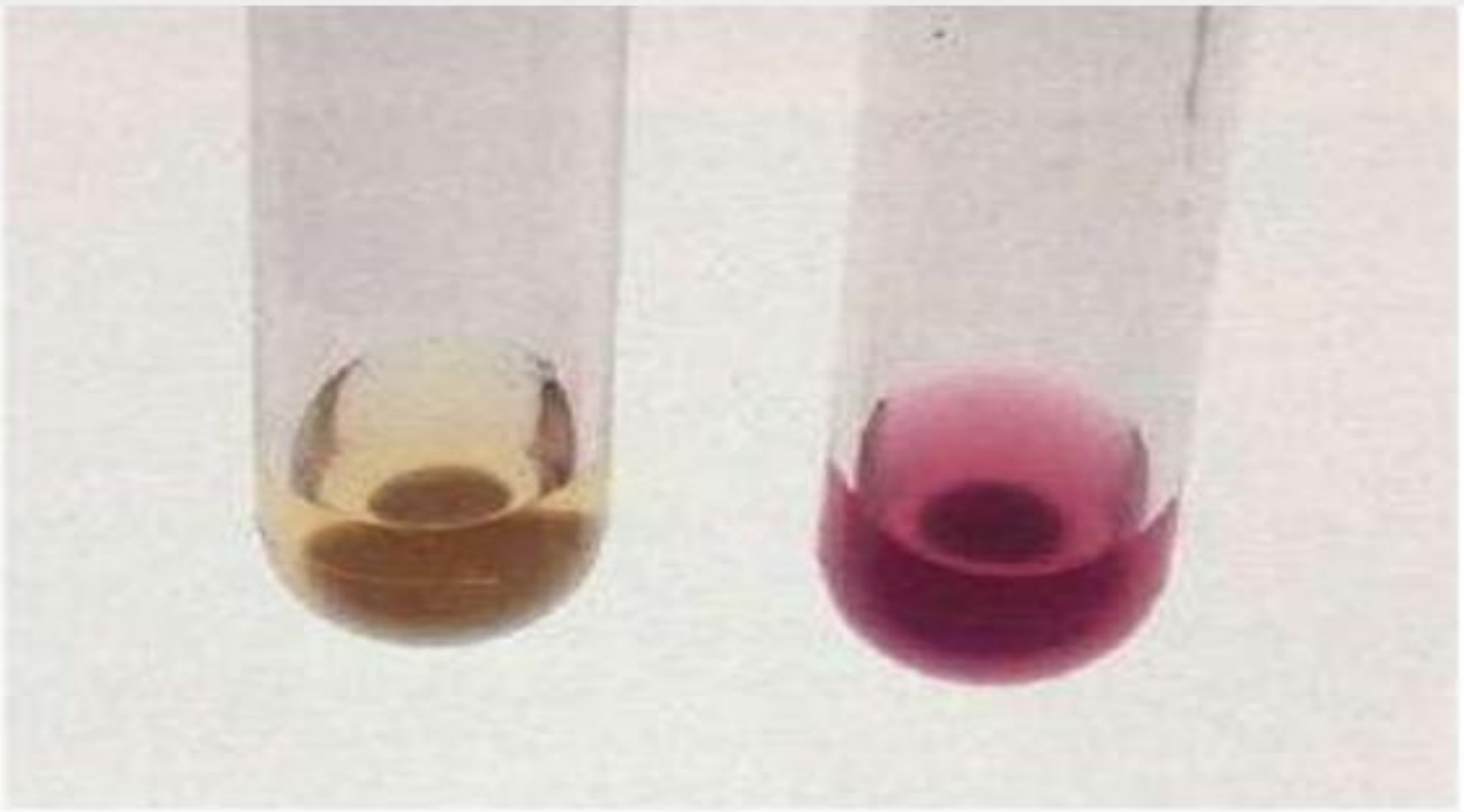
- **India Ink preparation-** is a negative stain that creates a dark background, with the yeast appearing to be surrounded by a clear halo generated by the polysaccharide capsule, which repels the India ink staining
- Sputum and other purulent samples can be treated with a 10% potassium hydroxide solution. The purpose of this sample preparation is to disrupt cellular proteinaceous debris, cleaning the specimen for easier fungal detection.
- Culture on SDA with/without antibiotics (chloramphenicol)
- Serological tests- Latex Ag-Ab slide test agglutination and immune enzymatic techniques using serum, CSF, and urine are widely available for the detection of the **capsular antigen**
- Urease test is positive (15 minutes)



Cryptococcus neoformans. This yeastlike fungus has an unusually thick capsule. In this photomicrograph, the capsule is made visible by suspending the cells in dilute India ink.



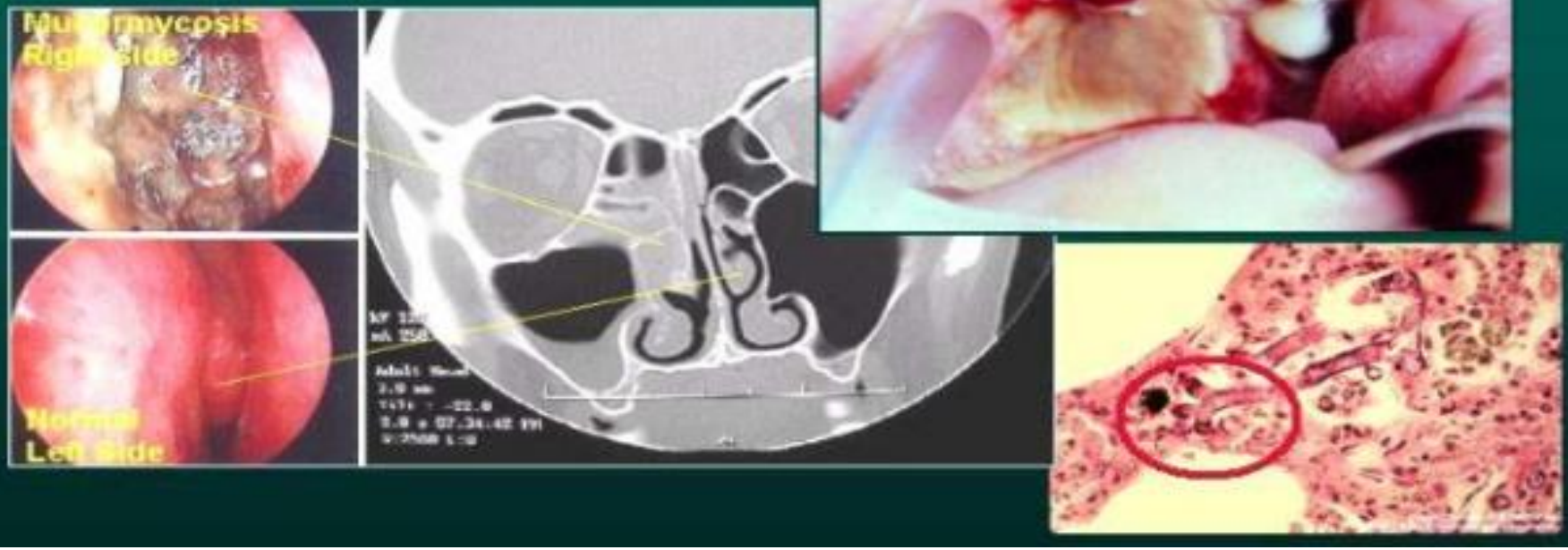
Colonies of *Cryptococcus neoformans* usually appear mucoid when first isolated. Some strains are poorly encapsulated and lack the mucoid appearance. (Sabouraud dextrose agar)



14-13 Urease test for *Cryptococcus neoformans*. Over 99% of the *C. neoformans* isolates give a positive urease test, pink-purple color, within 15 minutes, in contrast to other urease-positive species of yeast that require more than 3 hours to give a positive reaction.

Zygomycosis

- *Mucor & Rhizopus* species
- Associated with poorly controlled diabetes



Penicillium marneffei

- A dimorphic fungus grow as mold at 25 °C and as arthroconidia at 37 °C
- causes tuberculosis-like disease in AIDS patients
- Drug of choice is amphotericin B
- Produces a red pigment

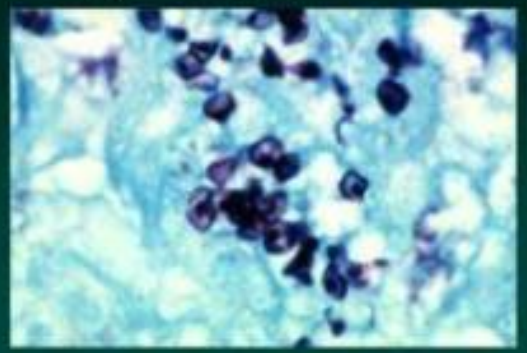
Pneumocystis jiroveci

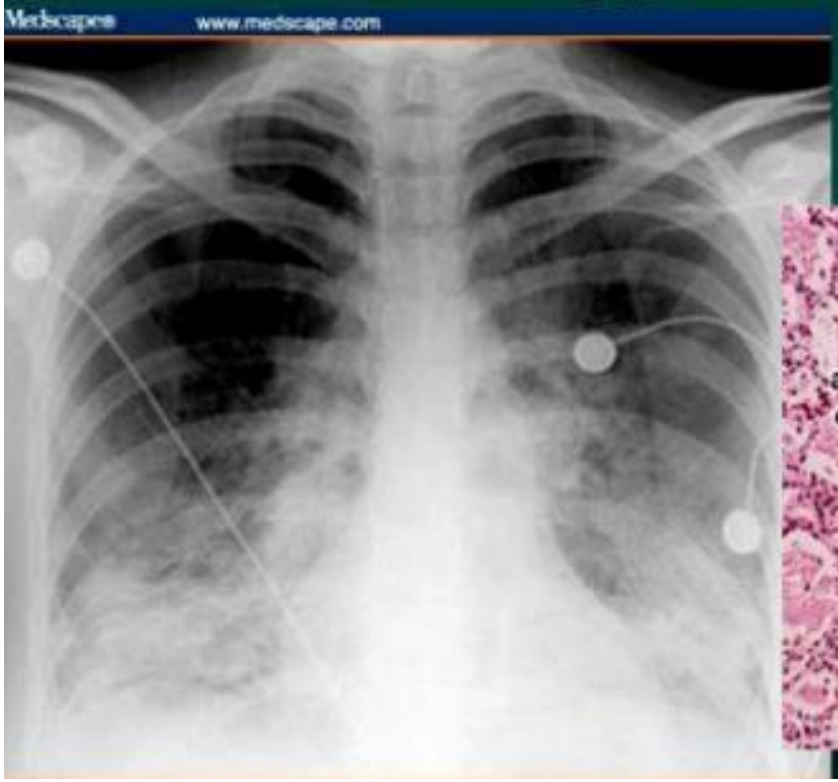
- Organism previously considered as protozoa.
- Old name was *P. carinii*
- Spread by respiratory droplet
- Causes severe life threatening pneumonia
- When stained with Giemsa stain, hyaline or foamy alveolar exudate is seem with "Honeycomb" appearance of stained section

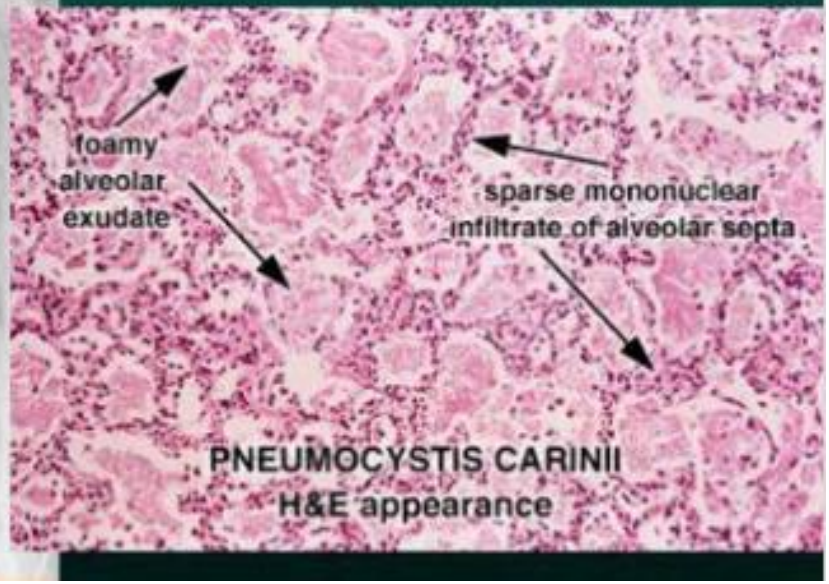
Pneumocystis carinii

- Most common cause of HIV-associated lung infection, dropped recently

Silver Stain of Bronchoalveolar lavage sample







Readings

- Some commercially yeast identification Systems
- Antimicrobial susceptibility testing for Fungi
- Mycotoxicosis

THE END