

# **Mycobacteria & Fungal Respiratory Tract Pathogens**

Prof. Dr. Asem Shehabi

Faculty of Medicine

University of Jordan

# Global Prevalence of Tuberculosis

- The World Health Organization (WHO) estimates that approximately one-third of the global population is infected with *M. tuberculosis* (TB).
- Around **10 million new cases** of TB are being reported each year, **2-3 million deaths** occur each year worldwide.. 95% in developing countries
- After emerging (HIV)/AIDS, TB is the second most common cause of death in AIDS patients due to an infectious disease.

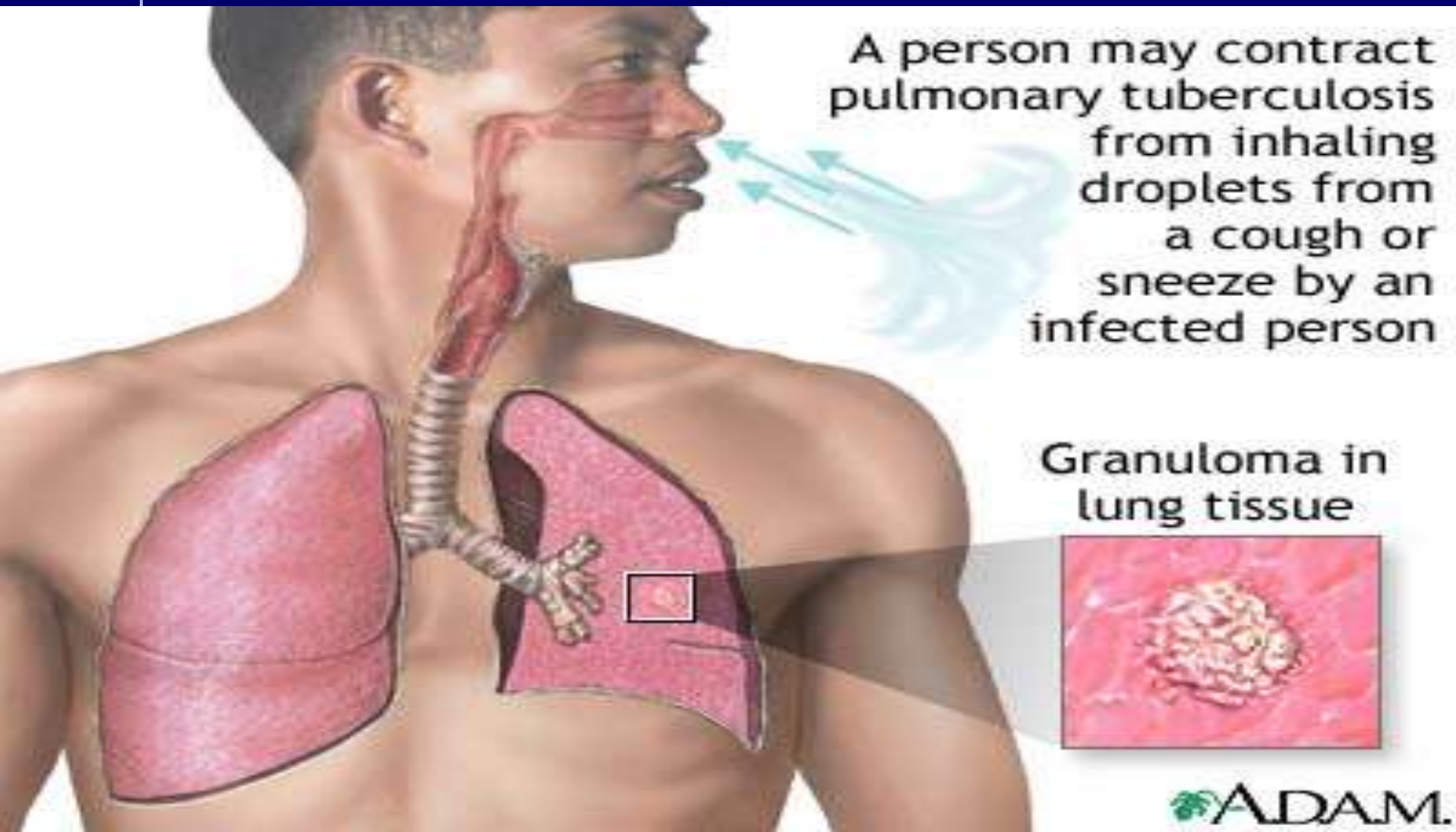
# Mycobacterium Tuberculosis

- Tubercle Bacilli.. Acid-Fast Bacilli.. Widely distributed in Human, Animals, Birds, Environment.. TB bacilli grow slowly, Resistant to Dryness, low Acidity.. survive years in nature.. But Susceptible to UV-light, Heat.
- **M. tuberculosis**.. Causes 95% of human TB cases.. mostly pulmonary .. Respiratory infection .. Few cells.. Lung positive person may infect hundred of susceptible person.. All ages.. mostly children.. with malnutrition .
- **Optimal conditions for transmission include:** overcrowding, Large cities, poor conditions & Low standard public hygiene..

# **Acid Fast Bacilli Stained by Ziehl-Neelsen (AF Stain)**



# Infection With Mycobacteria mostly through RT air droplets



# Pulmonary Infection

- **Primary Tuberculosis**: 90% Pulmonary TB , Children, Asymptomatic, TB Bacilli infect Alveolar macrophages.. Develop small lung lesions..Fibrosis, Calcification, Hypersensitivity.. Infected person becomes **Positive for Tuberculin Skin test**.
- Few cases Primary TB infection may spread from Lesion by direct extension to lymphatic system, bronchi, blood, Kidneys Gastrointestinal, Meningitis (children).. rarely developing **Military tuberculosis**.



# Post-Pulmonary Infection-2

- **Post primary tuberculosis:** Reactivation old lesions/infection .. Common in young adults & elderly persons.. Developing Large Lung lesions.. Cavities , Less lymphatic involvement , intensive **Granuloma & Caseation**.. May spread rapidly to other body part, CNS, Gastrointestinal/Urinary Tract .
- **Clinical Features Pulmonary TB:** Productive Cough..bloody sputum, Low continuous Fever, Night-sweating , Loss weight & Appetite.. General weakness, Breath shortness, Lesions/ Cavities can be detected easily by **Chest x-ray, Sputum culture , Tuberculin test positive**

# Tuberculin Test

- Symptomatic/ asymptomatic infected persons.. develop positive Tuberculin skin test.. Reaction to TB glycerol extract ( **Mycolic acids + lipoproteins** )
- Mantoux -Tuberculin skin test.. Specific TB antigens produced from boiling culture of *M. tuberculosis*.
- The test consists an intradermal injection of 5 tuberculin units (0.1 ml) of PPD in the forearm.. The test is read after 48-72 hours.
- **Positive tuberculin:** Indurations, Edema & Erythematic skin > 1 cm, Interpretation
- Vaccination with **BCG** ..Protection 30-78%..result in positive Tuberculin test.



# Tuberculin (PPD) Skin Test



# Other Human Pathogenic Mycobacteria species

- **M. bovis:** common in domestic animal.. rare human.. Infection.. source: milk, dairy products, meat.. begins mostly intestinal infection.. may spread to other parts.. Slow grower
- **Atypical mycobacteria:** Widely distributed in nature.. water, soil, birds, animals , mostly slow grower (1-3 weeks)
- **M. kansasii:** Soil, Photochromogenic, Produce yellow/orange color during incubation in light.. Mostly Lung tuberculosis.. immuno-suppressed persons, AIDS.
- **M. marinum :** Water ,Fish , localized Skin, ulcers-soft tissues, Swimming pool, **aquarium granuloma**.. Lymph nodes.
- **M. avium complex :** Animals, water,,Skin Lesions, rarely Pulmonary disease..
- **M. ulcerans:** Soil in Tropical countries, Skin lesions, necrosis, More Resistant to anti-tuberculosis drugs..

# Diagnosis & Treatment-1

- **Rapidly growing Mycobacteria species:** Rarely cause skin ulceration, mostly non-pathogens.. *M. smegmatis* .. Found in on extragenital tract.. May contaminate urine culture.
- **Diagnosis & treatment:** Tuberculosis is confirmed by positive Direct AF Smear/ Culture, PCR X-ray, Positive tuberculin Test.
- **Clinical specimens:** Sputum, Urine, CSF, Tissues, Culture Loewenstein-Jensen Agar.. 4-8 Weeks.. No Blood Serological test.
- **Treatment Multiple Antibiotics:** 6-24 Months.. Rifampicin, Isonaized, Pyrazinamid, Ethambutol, development of Multidrug resistant MB tuberculosis.. At present 1-5% worldwide.. **Completing treatment is essential for cure**

# Nocardiosis

- **Nocardia asteroides/ N. brasiliensis**. Aerobic G+ve Pleomorphic Bacilli & Branched short Filaments.. Slightly Acid Fast.. Common as Environmental Saprophytes.
- Human Exogenous Infection.. Mostly **Pulmonary localized abscesses**.. Necrosis.. small Cavities.. spread to Brain, Kidneys.. Common in Immunosuppressed & Lung malignancy
- **Chronic suppuration**.. Abscess.. Granulomas, Draining sinuses containing granules.. Muscles, Bones, Feet, Hands and other body parts.
- **Diagnosis & Treatment**: Sputum/biopsies culture on blood 1-4 weeks at room temperature, Co-trimoxazole, Rifampicin, Amikacin.. 4-6 Weeks.

# Respiratory Fungal Agents

- **Fungal respiratory diseases** can be divided into:
- Fungal agents ..Widely distributed in Environment.. Cause mostly infection in immunocompromised individuals.. receiving immunosuppressive therapy.. undergoing bone marrow transplantation or solid-organ transplant .. HIV infection.
- **Clinical presentations** : Fungal respiratory infections are non-specific .. often overlap with other infectious and non-infectious processes..mostly without fever
- The causative agents can be opportunistic endogenous **Yeast** or exogenous **filmentous Fungi /Molds**

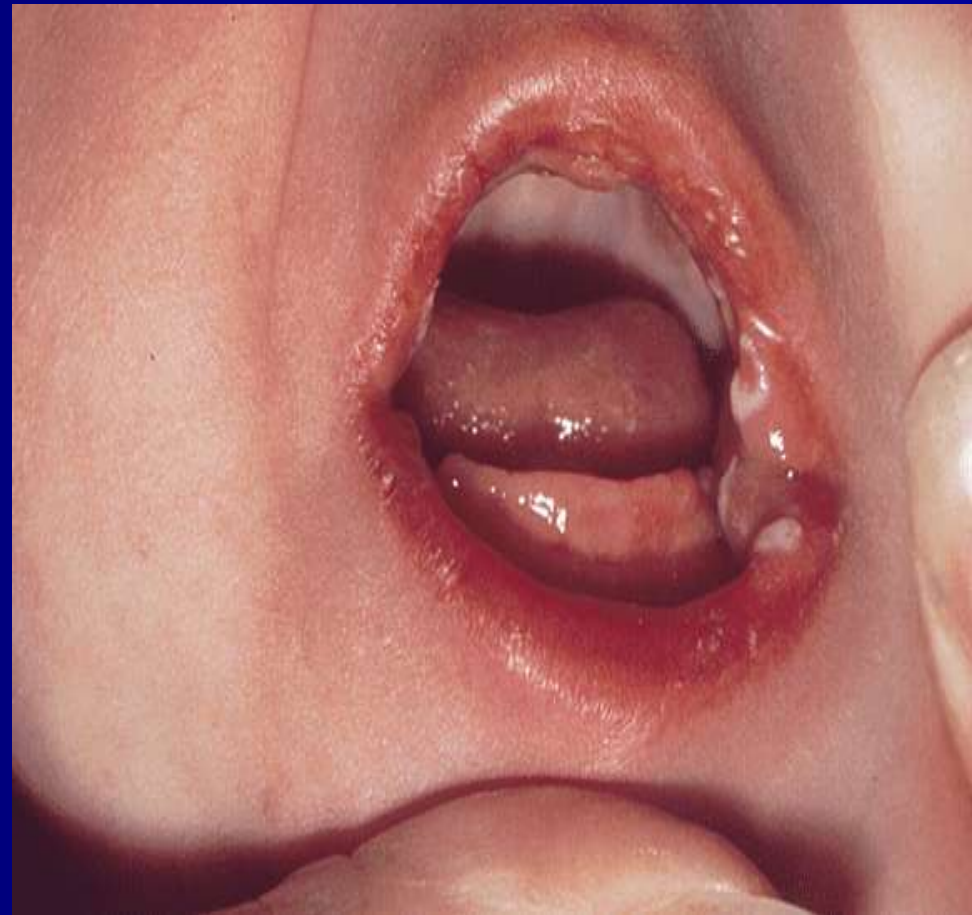


# Yeast Form: Oral Candidiasis

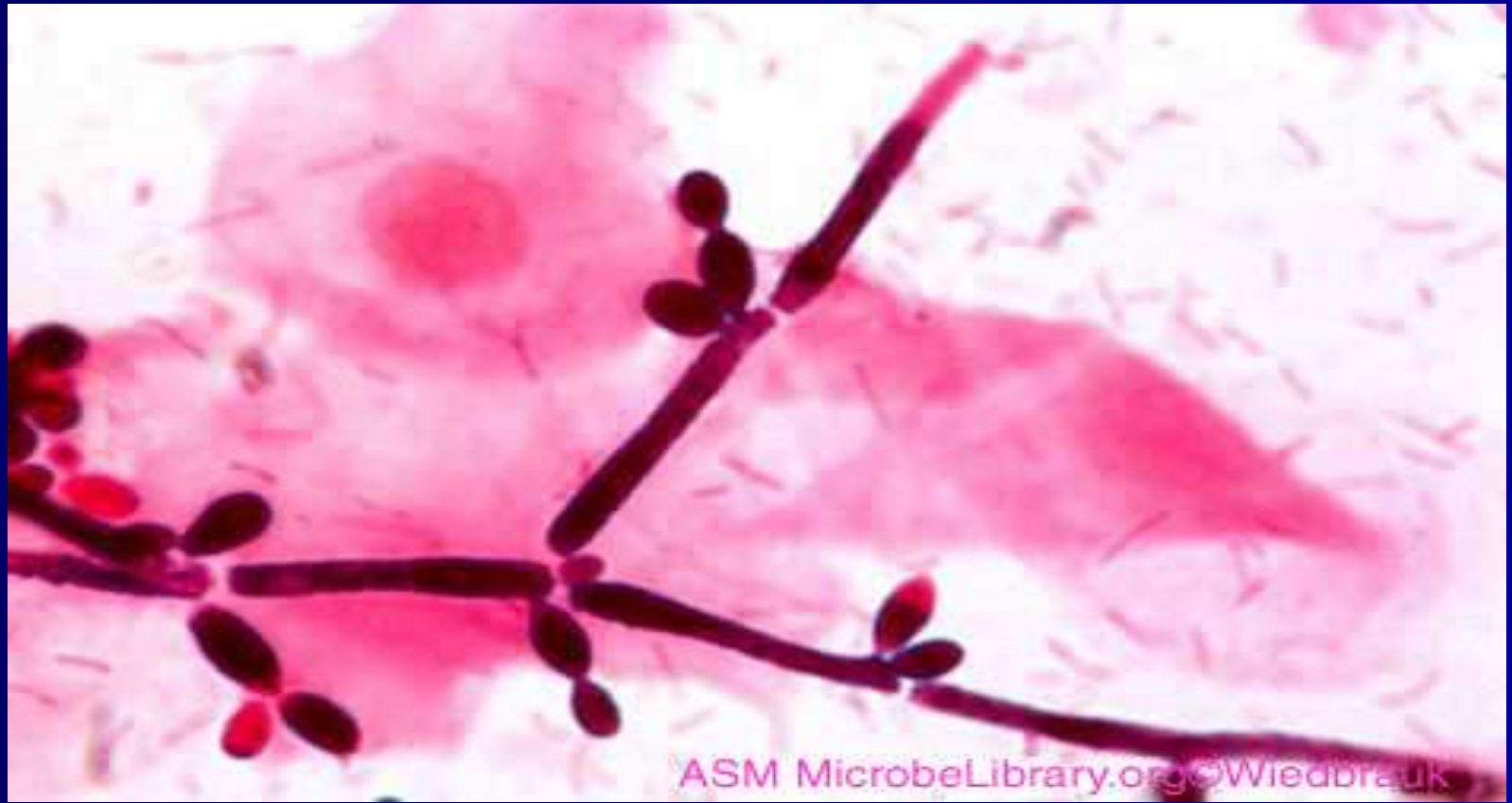
- **Part of oral /intestinal/vaginal flora..** causes characteristic mucosa patches of a creamy-white to grey pseudomembrane composed of **Blastospores** and **Pseudohyphae** .
- **Candidiasis** often develop after long antibiotics treatment .
- Oral candidiasis may spread.. Esophagus, Bronchi, Lungs, Gastro-intestinal tract, or become systemic .. Candidaemia, may results in endocarditis..meningitis.
- **Systemic Candidiasis** is common in patients with cell-mediated immune deficiency, receiving aggressive cancer, immunosuppression, transplantation therapy.
- ***C. albicans, C.glabrata,C. tropicalis, C. krusei,***

# 1- Pseudohyphae , Blastospores, Chlamydospores

## 2- Oral Candida Trush



# Candida Pseudohyphae with Blastospores-Gram-stain



# Predisposing Factors for the Development of Candidiasis

- **Impaired epithelial barrier:** Burns, Wounds / abrasions, Hydration/maceration, Indwelling catheters, Foreign bodies (Dentures, etc), Increased gastric pH, Cytotoxic/ Antibiotics agents.. Radiation
- **Systemic disorders:** Diabetes mellitus, Pregnancy/oral contraceptives, Malnutrition, Malabsorption, Iron deficiency.
- **Malignancy / Haematologic disorders:** Neutropnea / Leukemia, Lymphoma, advanced cancer, AIDS all immunodeficiency conditions.
- **Systemic treatment:** fluconazole , amphotericin B, Caspofungin.
- **Local Ointment:** Nystatin, micronazole, clotrimazole

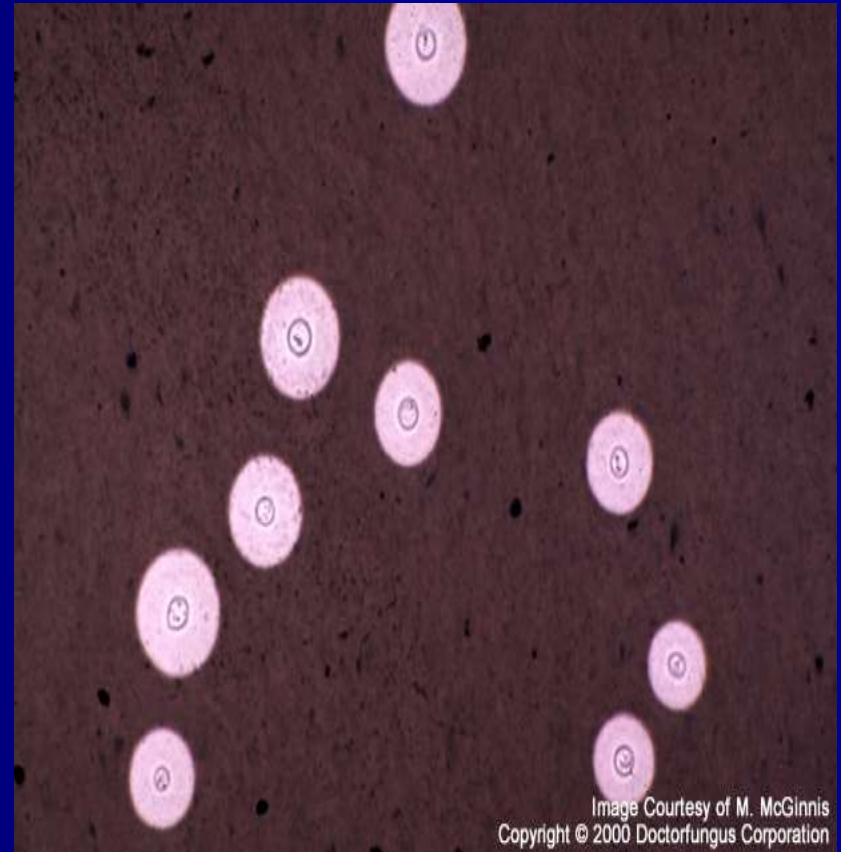


# Yeast: Cryptococcosis

- Encapsulated *C. neoformans*.. cause a chronic, subacute -acute pulmonary.. systemic or meningitic disease.. Meningoencephalitis.. Often isolated from Pigeon & Birds excreta.
- **Primary pulmonary infections:** Mostly pneumonia-like illness, with symptoms such as cough, fever, chest pain..dissemination may include central nervous system ..Lesions in brain, skin, bones and other visceral organs..Common significant opportunistic pathogens in immunodeficient humans ,AIDS patients.  
**Diagnosis: Culture + Antigens detection in Serum , CSF & Biopsy.**



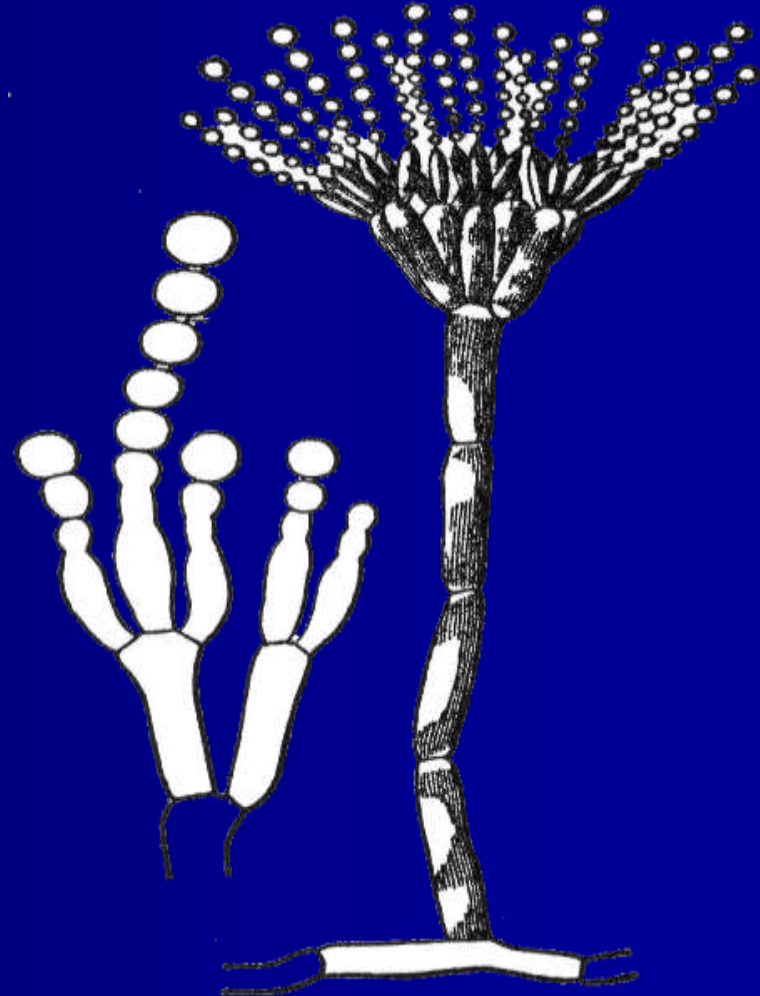
# Cryptococcus detection by India ink test



# Molds: Aspergillosis-1

- **Most common *Aspergillus* species**  
*A. fumigatus, A. flavus, A. niger.*
  - **Aspergillus** widely distributed in nature.. Survive harsh environmental conditions. Found in all dead animal, plants , Grains, soil, spread via small spores that are extremely light and float easily in the air.
- 1) **Allergic Bronchopulmonary:** Presence of conidia or fungal filaments in lung tissues, Sinuses.. often associated with **Allergic reaction** ..Eosinophilia.. Asthma..
  - 3) **Mycotoxicosis** due to ingestion of contaminated foods with fungal toxin ***A. flavus*** .. Produce Aflatoxins.. Liver cirrhosis..Death

# Septated Hyphae & Spores



## Aspergillosis-2

- 3) **Pulmonary Aspergilloma** ( Fungus Ball).. Invasive Aspergillosis.. Pre-existing lung cavity, inflammatory, granulomatous, necrotizing disease of lungs..May spread to other organs.. Causing mostly **Thrombosis.. Rhino-cerebral lesions** rarely systemic and fatal disseminated disease.
- **Treatment:** Fluconazole, Itraconazole, Caspofungin Amphotericin B ..
  - Less common Respiratory fungi: *Mucor*, *Rhizopus* *Fusarium* spp.. Common Rhino-cerebral mucormycosis



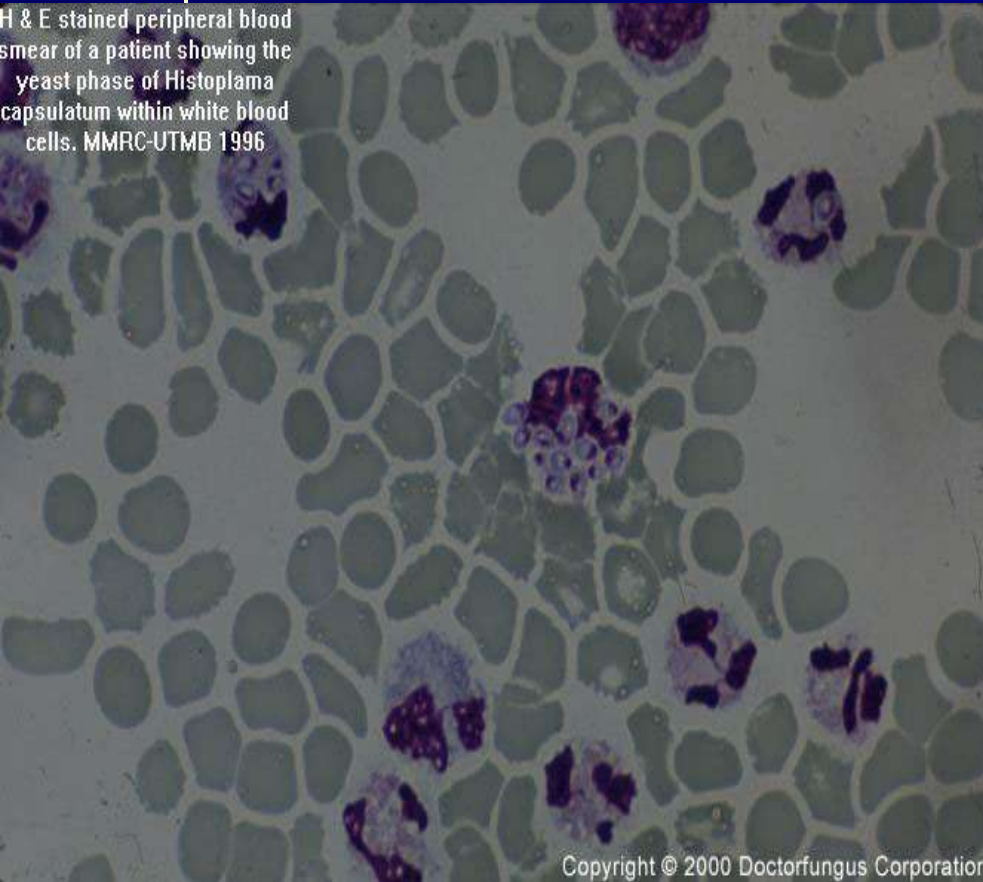
# Dimorphic Fungus: **Histoplasmosis-1**

- ***Histoplasma capsulatum***.. Dimorphic fungus with conidia and yeast forms at body temperature and hyphae & macroconidia in vitro culture.. Common in soil enriched with excreta of birds. Endemic in southern U.S.A, Australia.. Less other countries.
- The primary site of infection is usually **Lung**.. inhalation dust with microconidia.. Phagocytosed by macrophages, obligate intracellular parasites.. Causing slight inflammatory reaction.. Most cases of **histoplasmosis** are asymptomatic /subclinical, benign as Flu-like syndrome.
- Few may develop chronic **progressive lung disease**.. Granuloma & fibrosis, chronic cutaneous or systemic disease involve any internal organ.. **Fatal systemic disease**.
- All infected persons become positive by histoplasmin skin test.

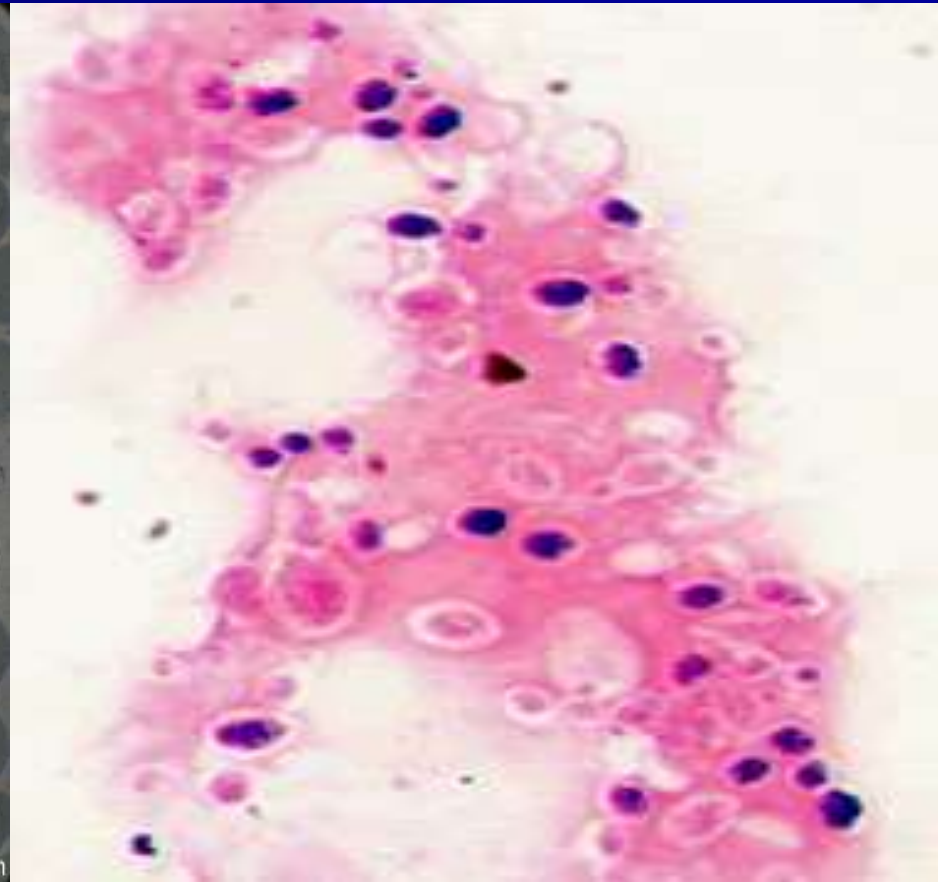


# ***Histoplasma capsulatum*** ***in infected White Blood cells***

H & E stained peripheral blood smear of a patient showing the yeast phase of *Histoplasma capsulatum* within white blood cells. MMRC-UTMB 1996



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# Coccidioidomycosis & Blastomycosis-2

- ***Coccidioides immitis* & *Blastomyces dermatitidis***.. soil inhabiting **Dimorphic Fungus**.. Endemic in south-western U.S.A., northern Mexico and various parts South America.
- Respiratory infection.. inhalation of microconidia, often resolves rapidly leaving the patient with a strong specific immunity to re-infection.
- Some individuals the disease may progress to a **chronic pulmonary** condition or a **systemic disease** involving the meninges, bones, joints, subcutaneous, cutaneous tissues.. Antigen Skin test positive.. Not significant in diagnosis.

# Laboratory Diagnosis

- **Direct microscopy and culture** should be performed on all specimens (sputum, bronchial washings, CSF, pleural fluid tissue biopsies from various visceral organs ).
- wet mounts in 10% KOH with india ink.. Ovoid-budding yeast cells (b) Gram-stain smear..
- Cultures on **Sabouraud dextrose agar** should be maintained for one month at 25C.... fungal growths & Wet Mount.. Identification ..produces hyphae-like conidio-phores & Spores.. Color of fungal growth
- **Serological tests are of limited value**.. not significant
- Detection of Histoplasma antigen in blood & urine is significant

# Pneumocystis (carinii, Rats type)

## P. jiroveci (Human type)

- Small Yeast like Cells ..No filaments or Capsules
- **Pneumocystis** infection occurs by inhalation contaminated dust .. It is commonly found in the lungs of healthy individuals. .without symptoms
- **Asymptomatic Infection** mostly started in children & increased in Adults .. Worldwide.
- **Clinical Disease** occurs only associated with both decrease of cellular immunity and humoral immunity, suppressed immunity .
- **Infectious trophic form** of the organism attaches to the lung alveoli.. Encyst & multiple in host tissues.



# Pneumocystis-2

- **Clinical disease .. Pneumonia..** Organism is usually found in the interstitial fluid in the lungs, Lung tissue.. of **immunocompromised patients..** AIDS ..may disseminate to other internal body organs.. Associated with high mortality.
- Sputum /lung biopsy specimens are usually used for PC detection.
- **Silver – Giemsa-, Stain.. Immunofluorescent Antigen (IFA)..** Treatment: **Cotrimoxazole** alone or with intravenous Pentamidine in sever cases.