





# ***MEDICAL MYCOLOGY***

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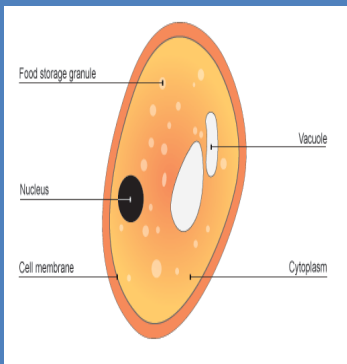
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# Medical Mycology





# Medical Mycology



- Fungi were discovered earlier than **bacteria and viruses**.
- In the past, most fungi cause skin infections or cosmetic infections, where bacteria and viruses cause serious fatal diseases, so there was no interest of studying fungi.
- In **1980**, when **HIV** infection was discovered, increasing number of **immunocompromizing conditions**, they found that fungi produce fatal diseases; from that time, fungi return to be in focus again.

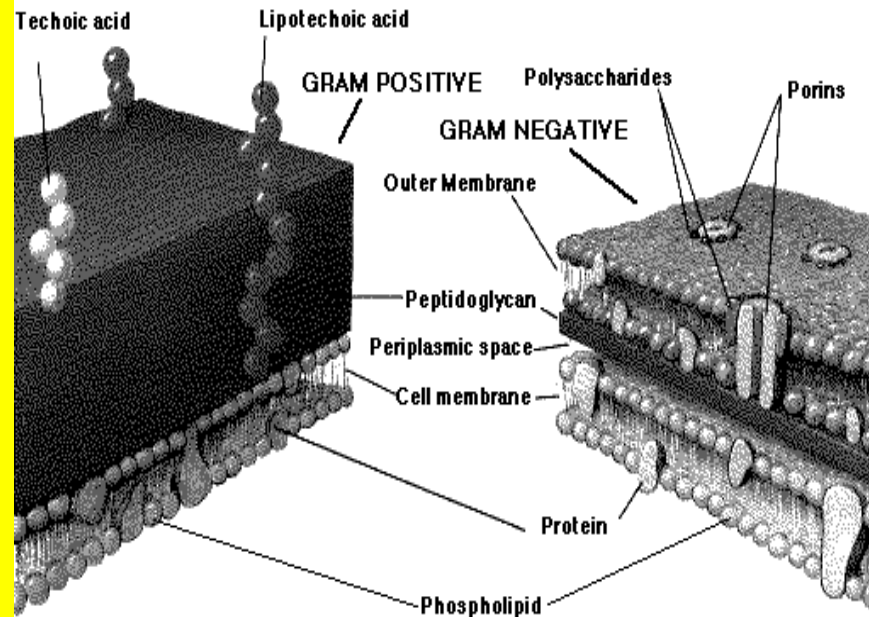
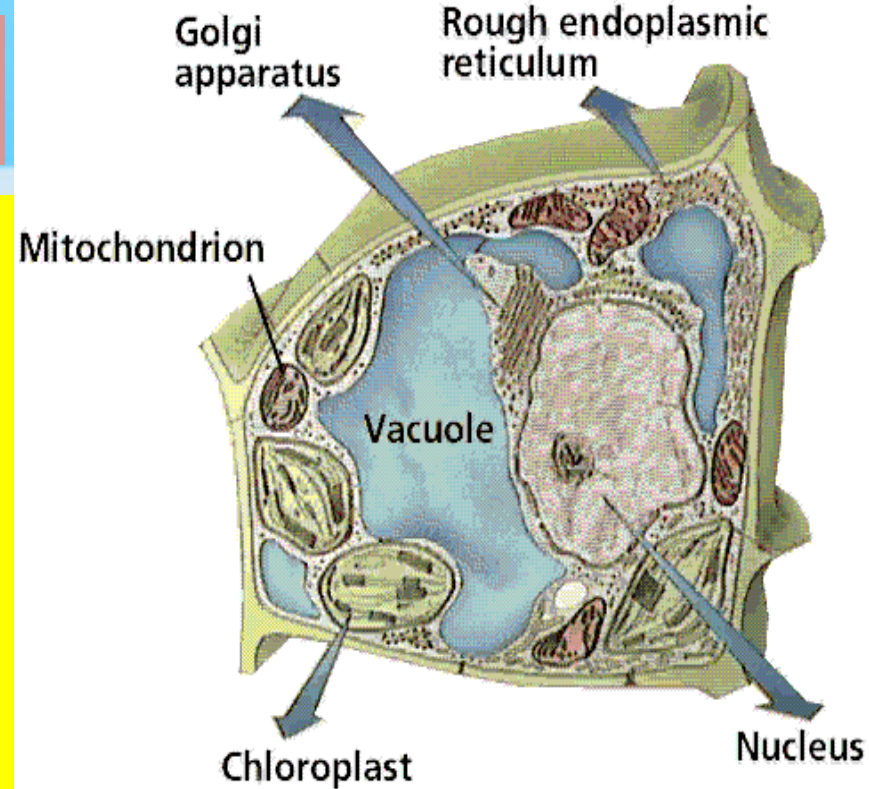
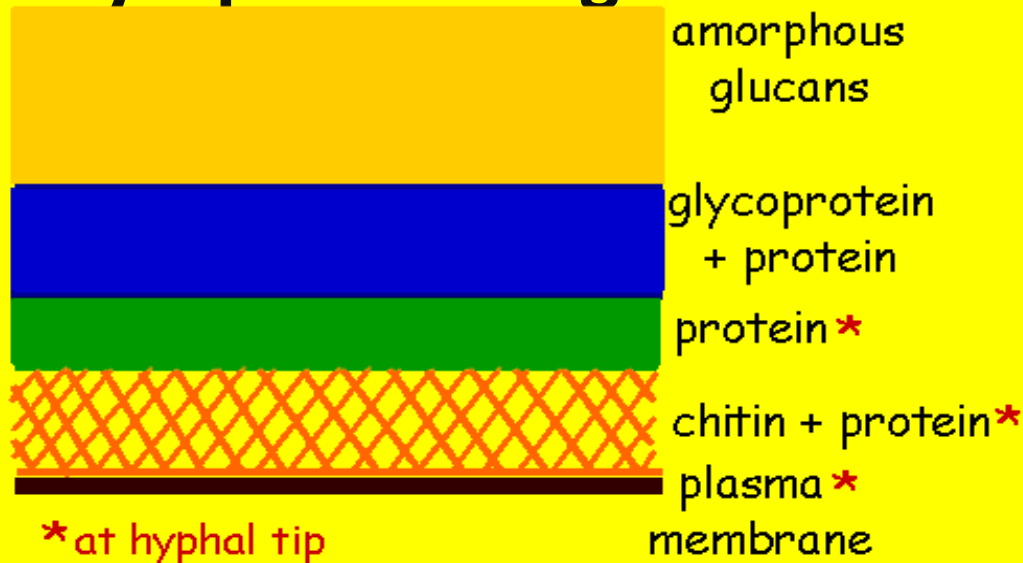
# Medical Mycology

- It is the science that deals with the study of **pathogenic fungi** that produce diseases.



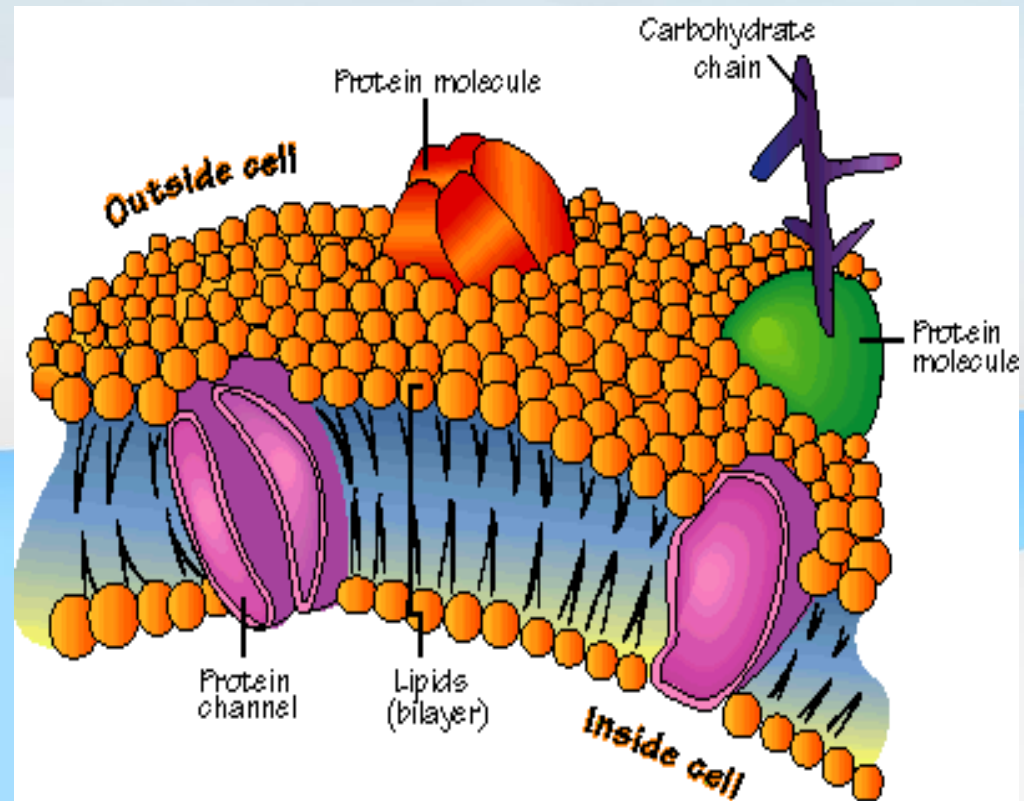
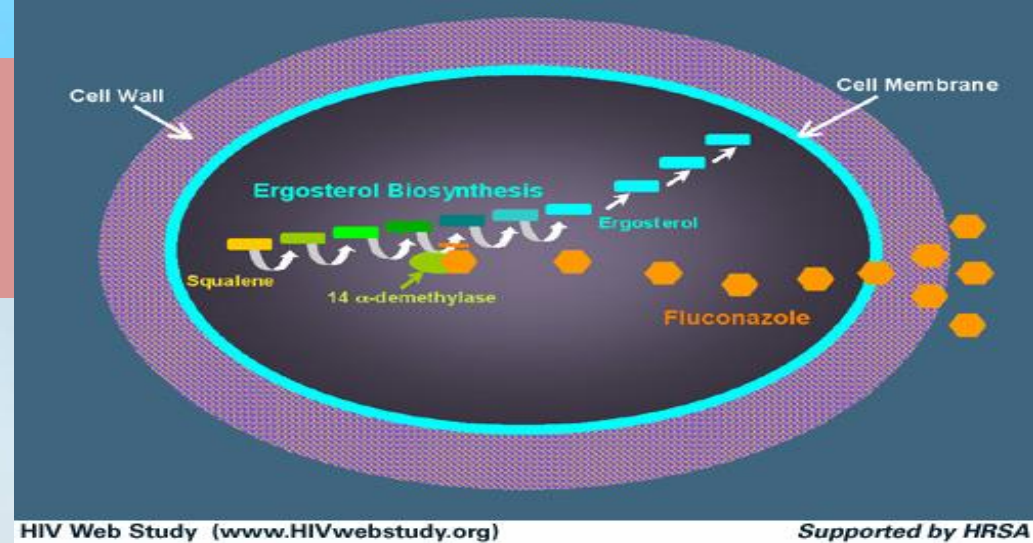
# Structure

- Fungi are **eukaryotic** organisms have **true nuclei** with definite **nuclear membrane, nucleolus, cytoplasmic organelles.**



# Structure

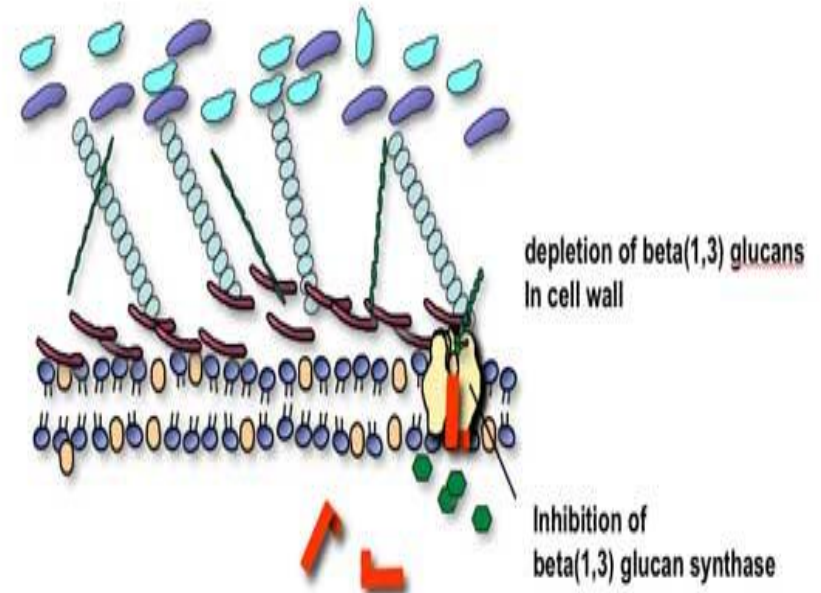
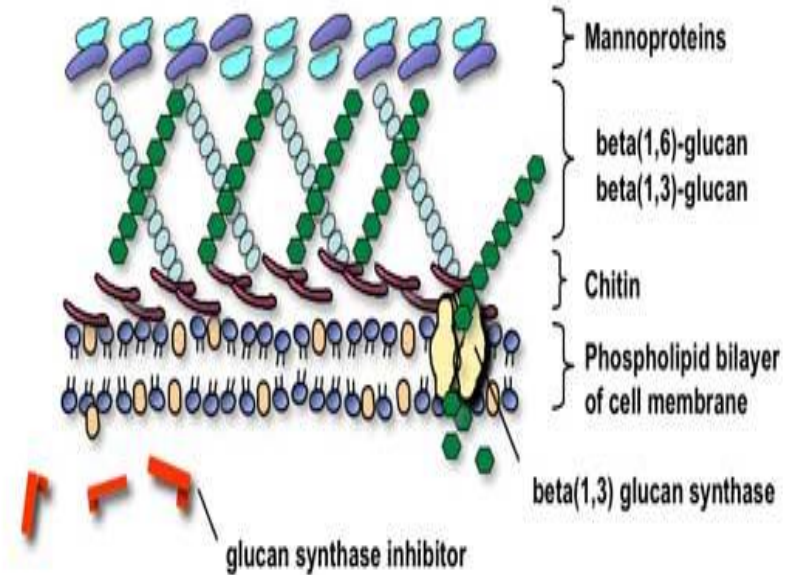
- Cell membrane of fungi has **sterols**, which is the target of action of antifungal agents. **Ergosterol** dominates in contrast to cholesterol in mammalian membrane.





# Structure

- **Cell wall of fungi lacks:**
  - Peptidoglycan
  - Glycerol & ribitol teichoic acid
  - Lipopolysaccharide
- **Cell wall composed of:**
  - Chitin.
  - Glucan (important for new antifungal agent).
  - Mannan.



# Fungal metabolism:

- All fungi are **heterotrophic** organism need to parasite or saprophyte (on plant, animal or human) to obtain organic source of carbon or nitrogen.
- All fungi are **aerobic**.
- Some are **facultative anaerobes**.
- None are **strict anaerobes**.

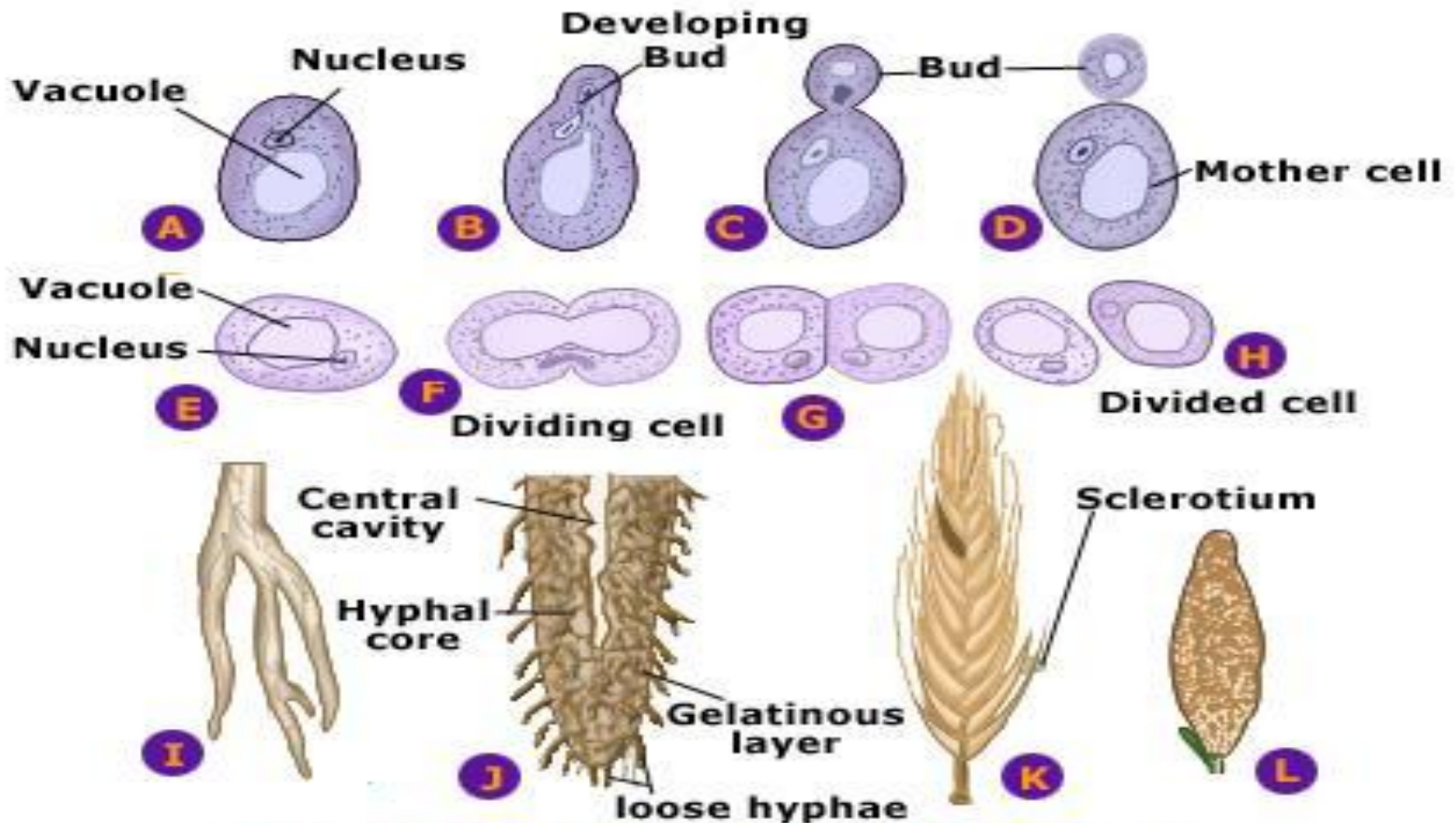


# Fungal metabolism:

- Optimum temperature of growth **25 – 30 °C** (because most are saprophyte live in the environment).
- Some are **thermophilic**, and can grow at higher temperature.
- Fungi can tolerate a wide range of pH (**2 – 9**), but generally they prefer **acidic** media.



# Reproduction



Modes of vegetative reproduction in fungi.

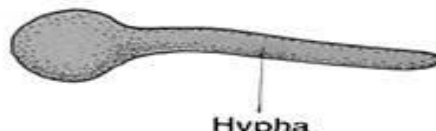
A-D. Budding. E-H. Fission. I-J. Rhizomorph; K-L. Sclerotia

# Sexual reproduction:

- Involve the union of 2 nuclei or 2 sex cells or 2 sex organs.



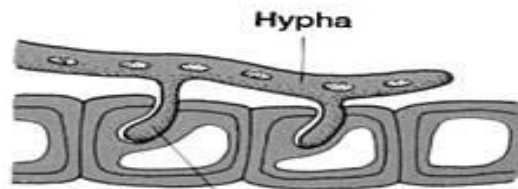
Spore



Hypha



Mycelium



Hypha

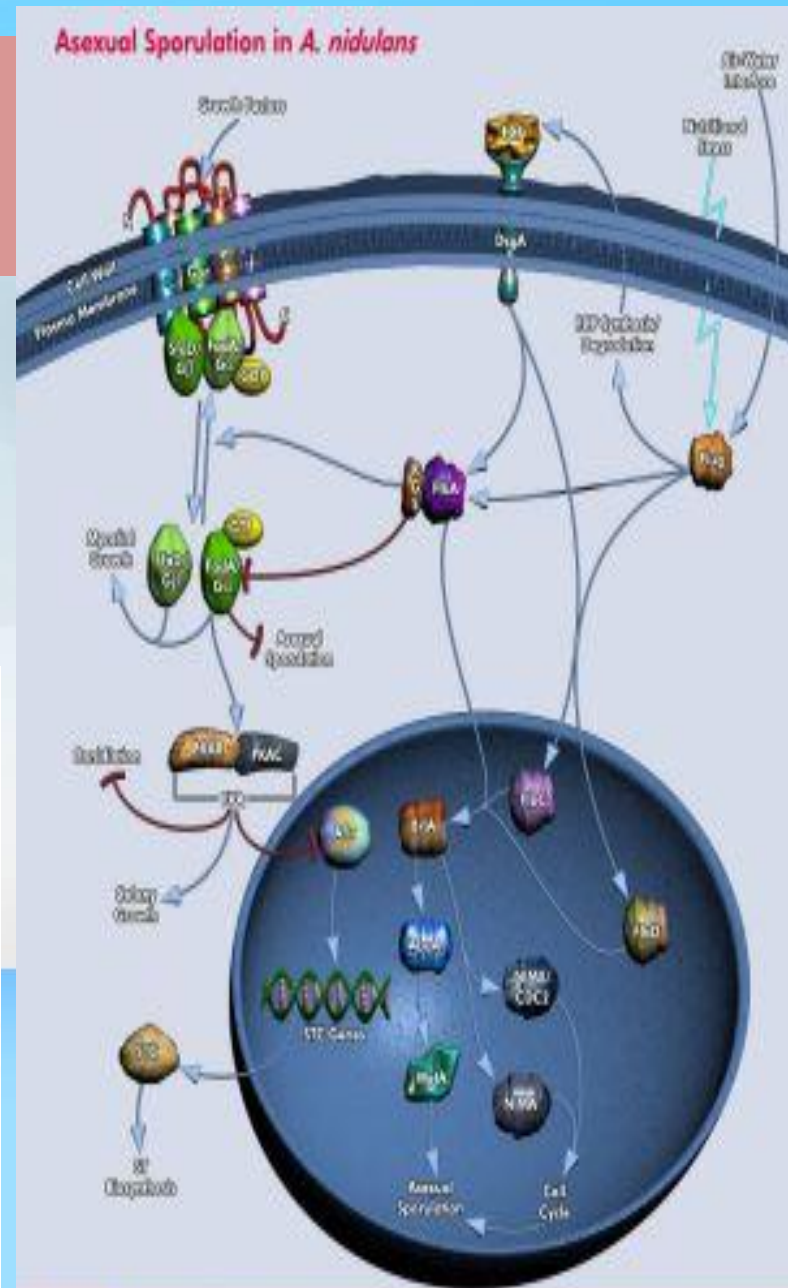
Haustorium



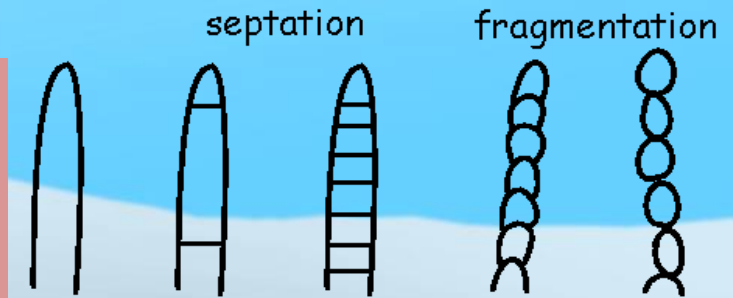
Coenocytic hypha



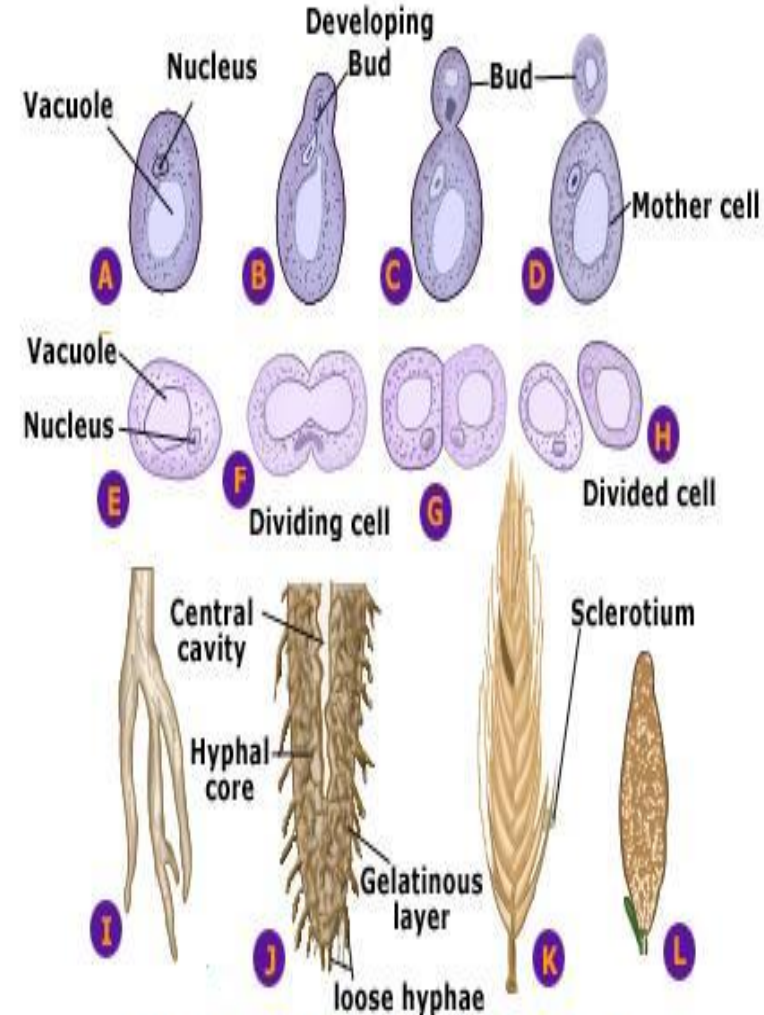
Septate hypha



# Asexual reproduction:



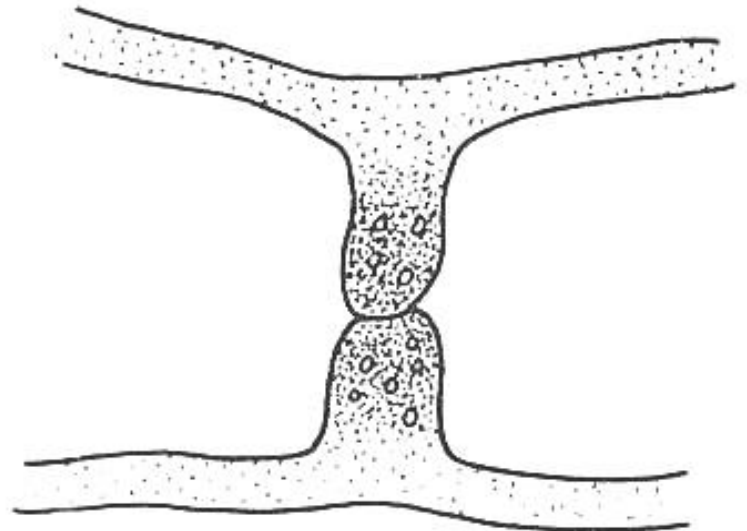
- ❑ It is the **main** method of reproduction.
- ❑ It includes:
  - **Fragmentation** of hyphae & each fragment grows into a new individual fungus.
  - **Fission** of cell into 2 daughter cells (similar to binary fission in bacteria).
  - **Budding** of cells, each bud produce new individual (e.g. Candida).
  - **Formation of asexual spores.**



Modes of vegetative reproduction in fungi.

A-D. Budding. E-H. Fission. I-J. Rhizomorph; K-L. Sclerotia

- A single fungus may contain **both** modes of reproduction (sexual and/or asexual).



# Fungal Spores

❑ It is the method of reproduction in fungi unlike bacteria.

❑ Two types:

**1-Sexual**

**2-Asexual**

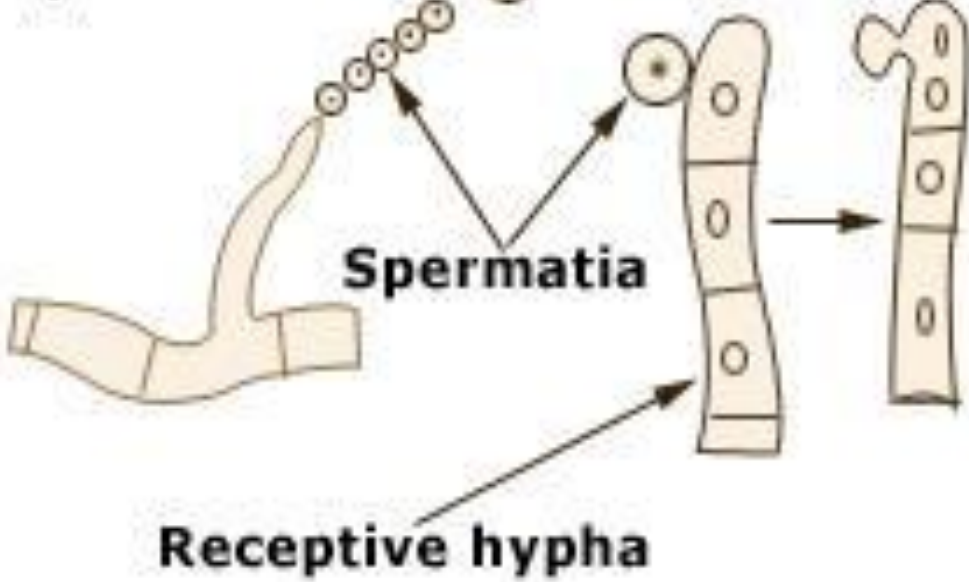




# ***1) Sexual***

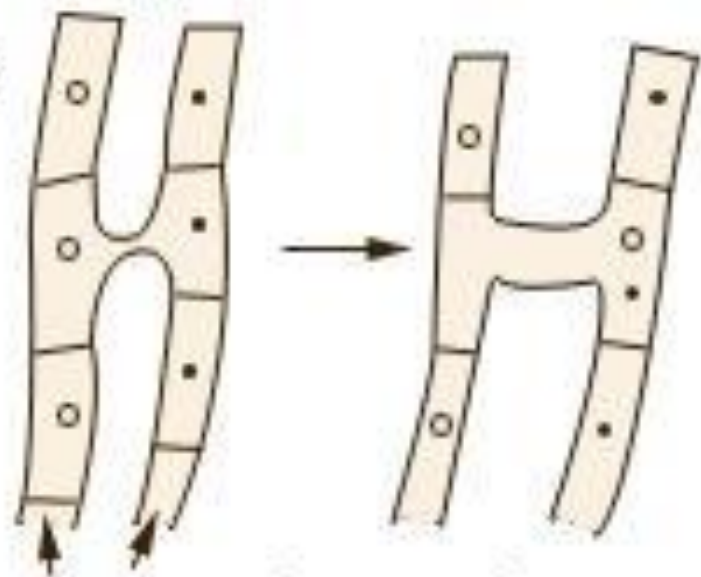


# Spermatization



Sexual reproduction

# Somatogamy



Hyphae of opposite mating types

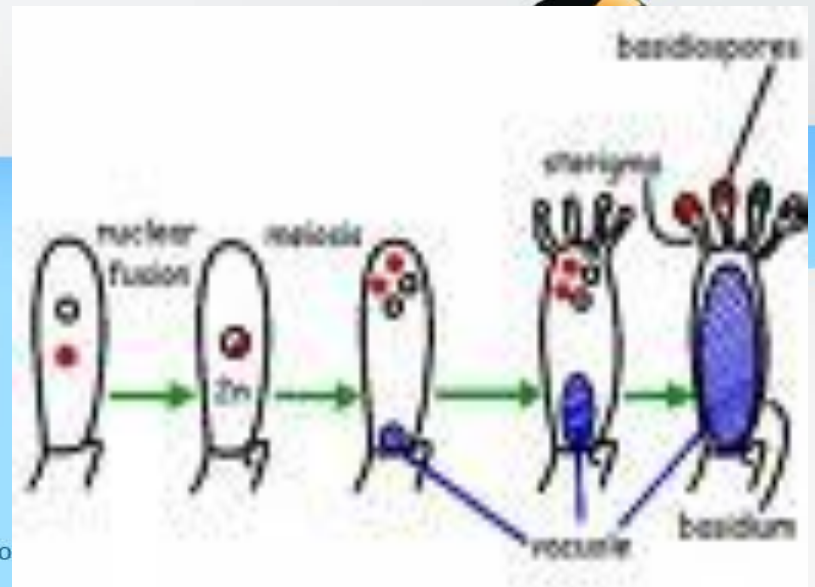
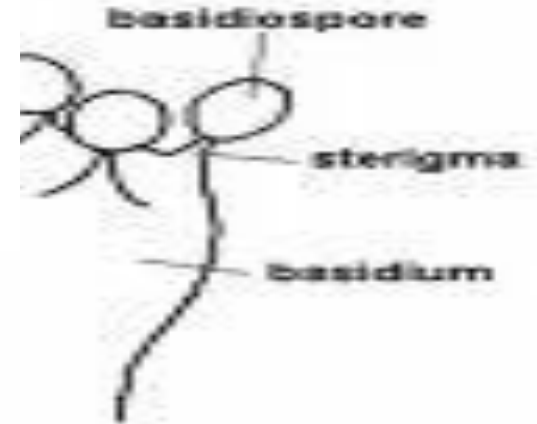
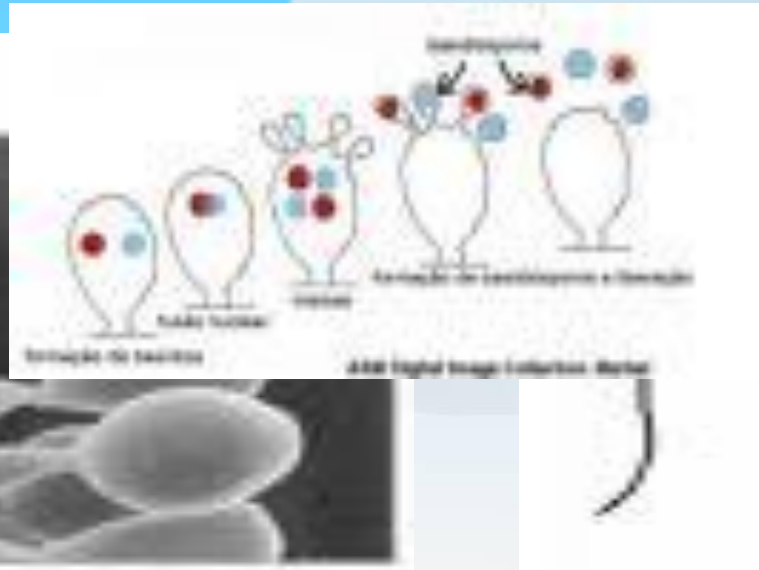
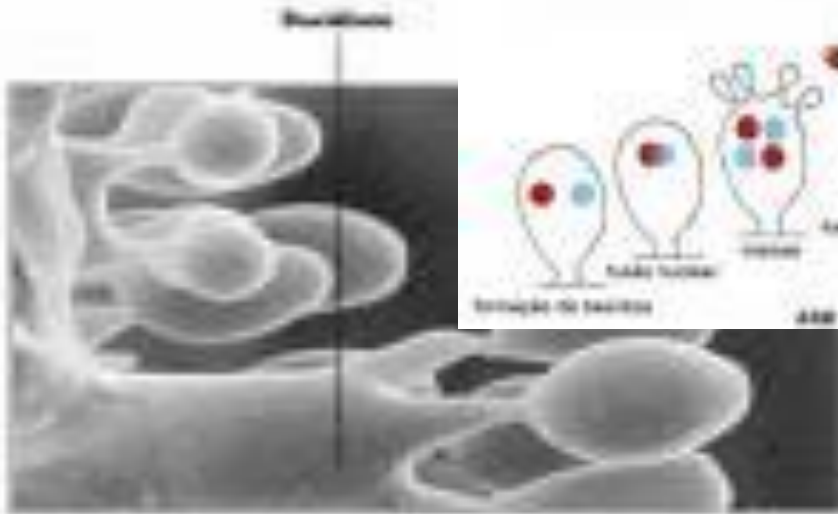
# Sexual:

–Zygospore



zygospore is a special type of [chlamydospore](#) arising from sexual conjugation between two [fungi](#).

# Basidiospore



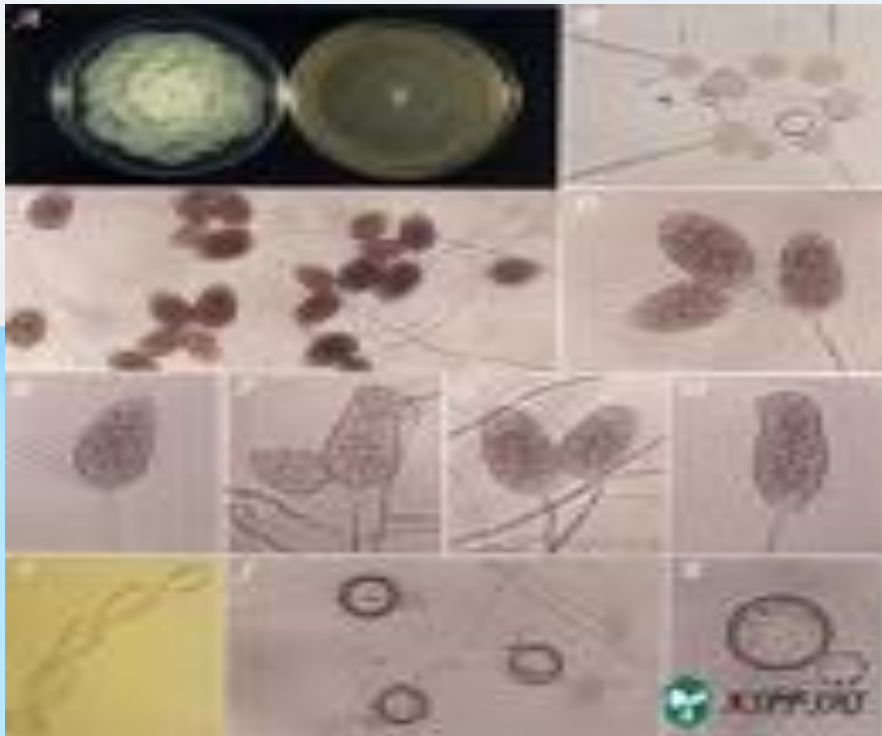


# ASCOSPORE FORMATION



# Oospore

female cell  
fertilized by male  
cell.

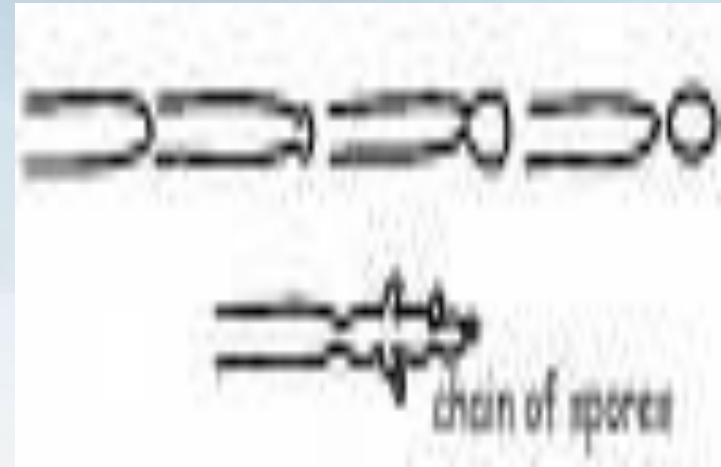
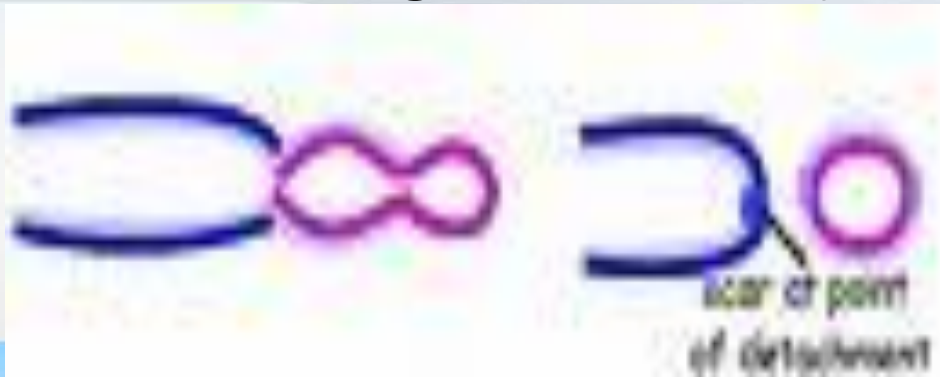


# 2) Asexual



# 2) Asexual:

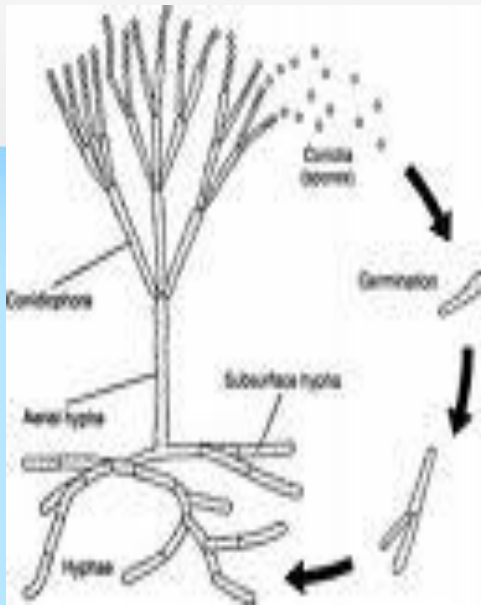
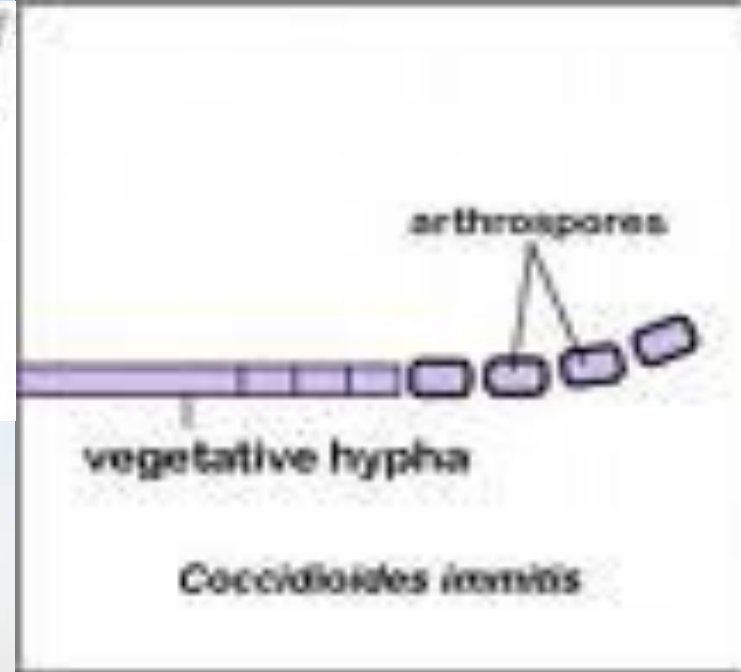
- **Thallospore:**
  - **Blastospores** (by budding from thallus).



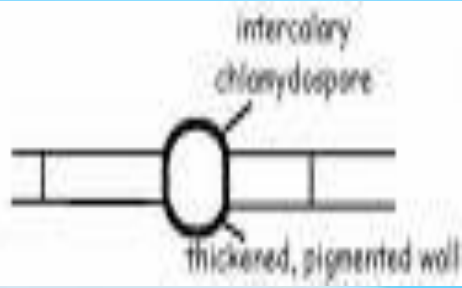


# Thallospore:

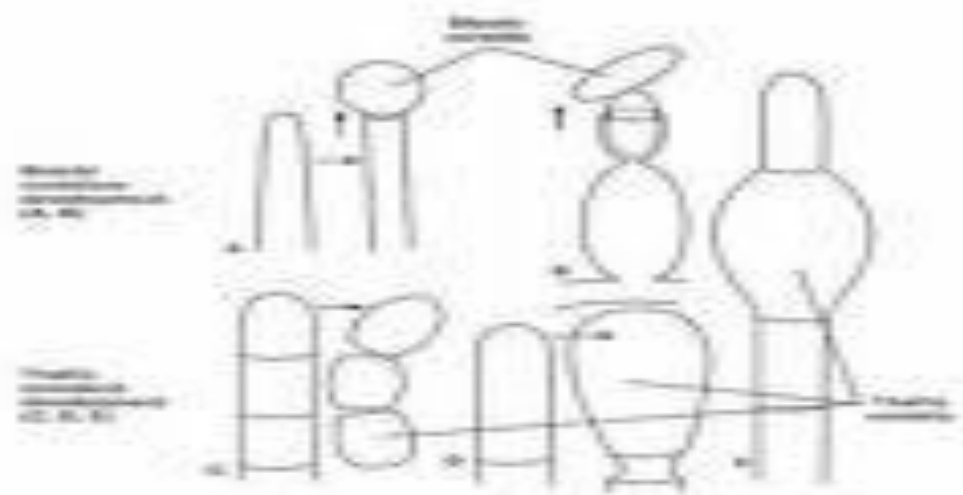
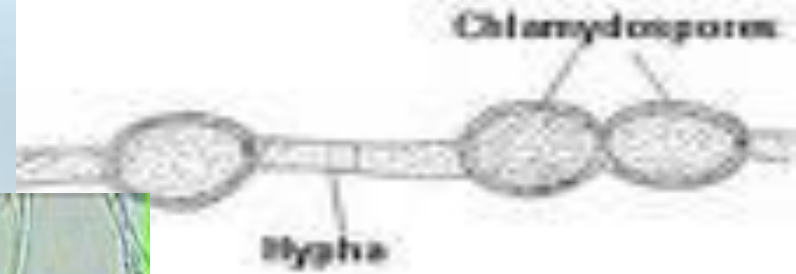
## – Arthrospores



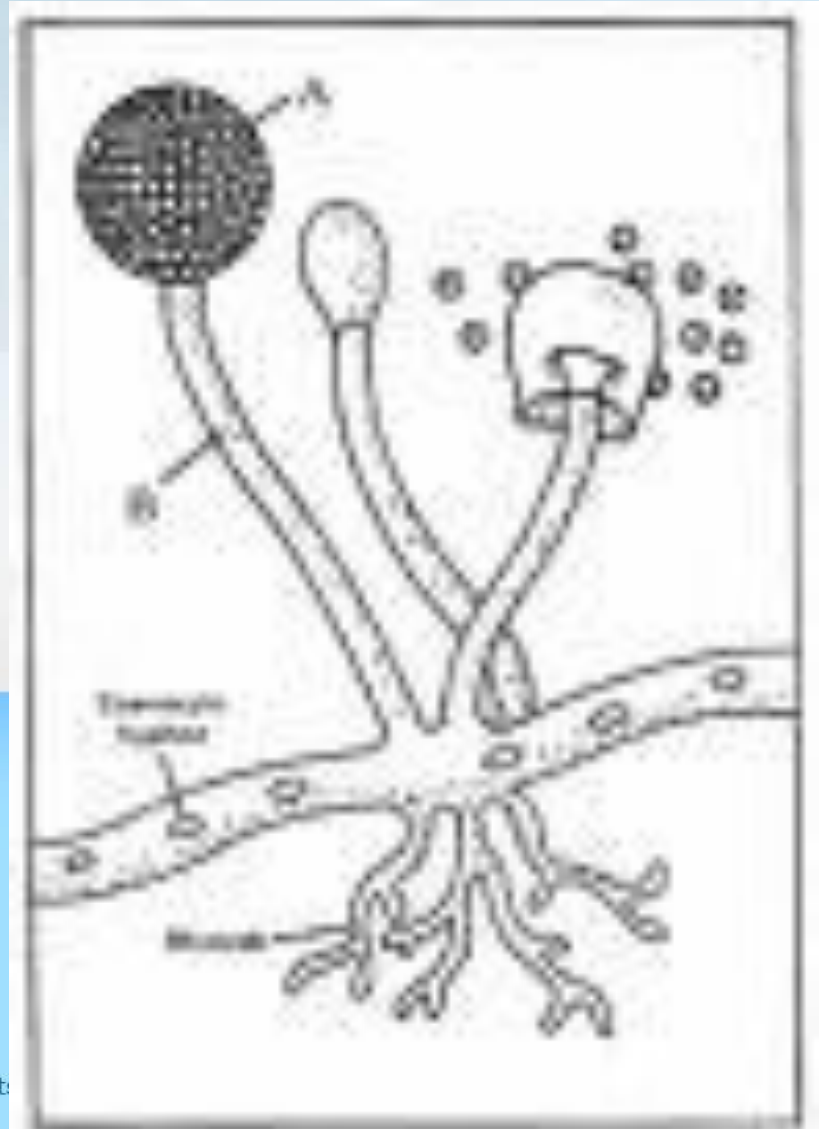
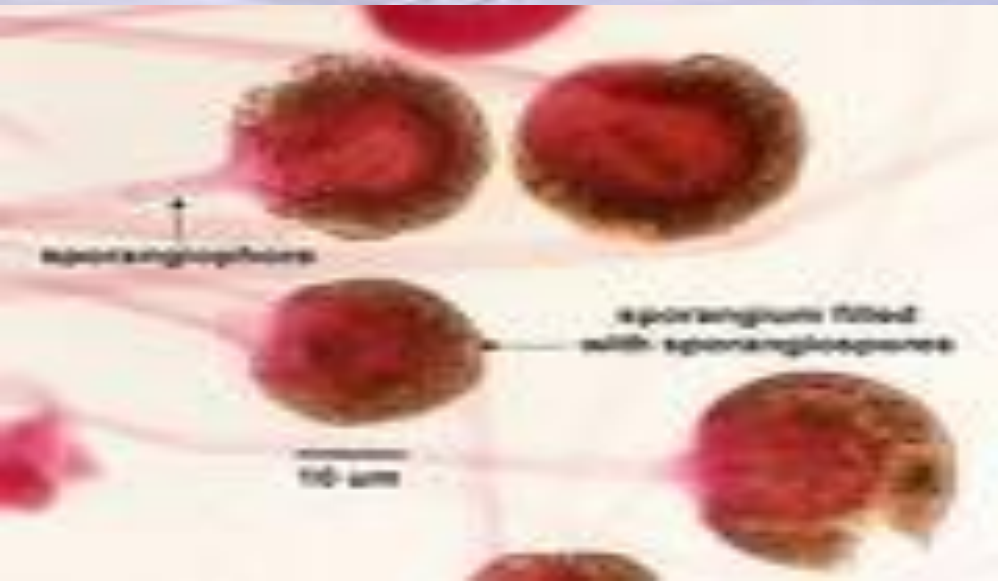
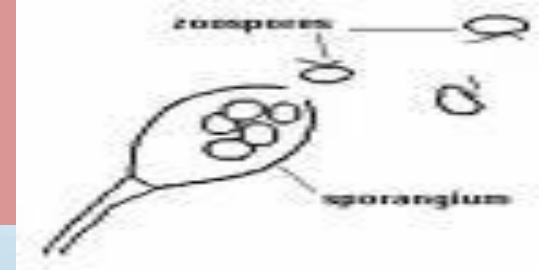
# Chlamydozooids



- ▶ spores that arise from the thallus by pulling or swelling of mycelium filaments.

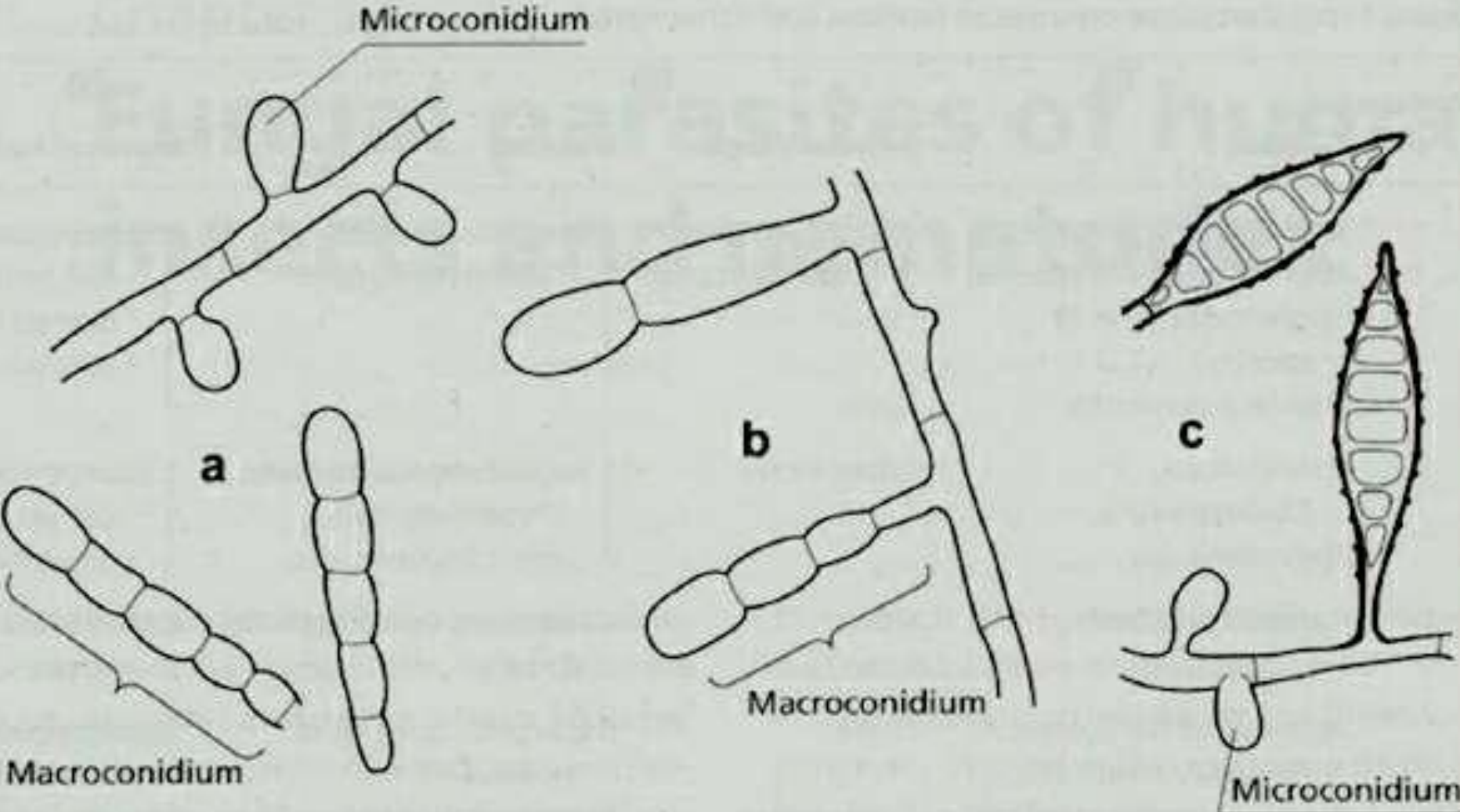
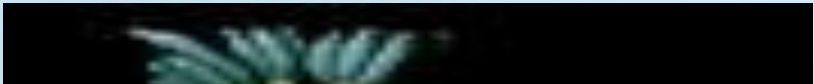


## 2) Asexual: Sporangiospore:



# Exogenous asexual spores:

- **Conidia:**



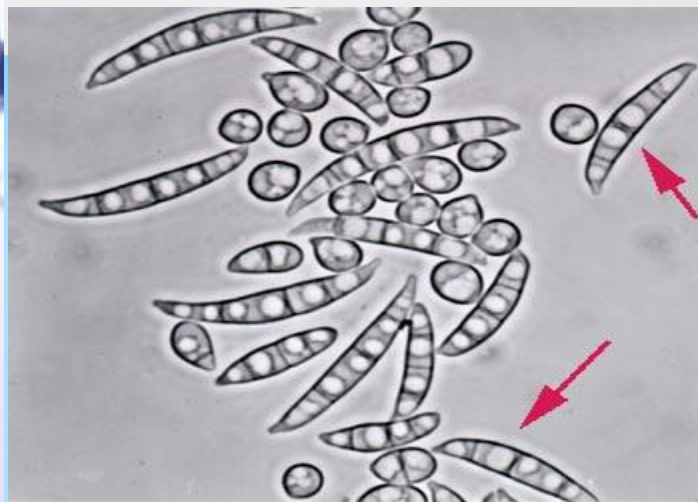
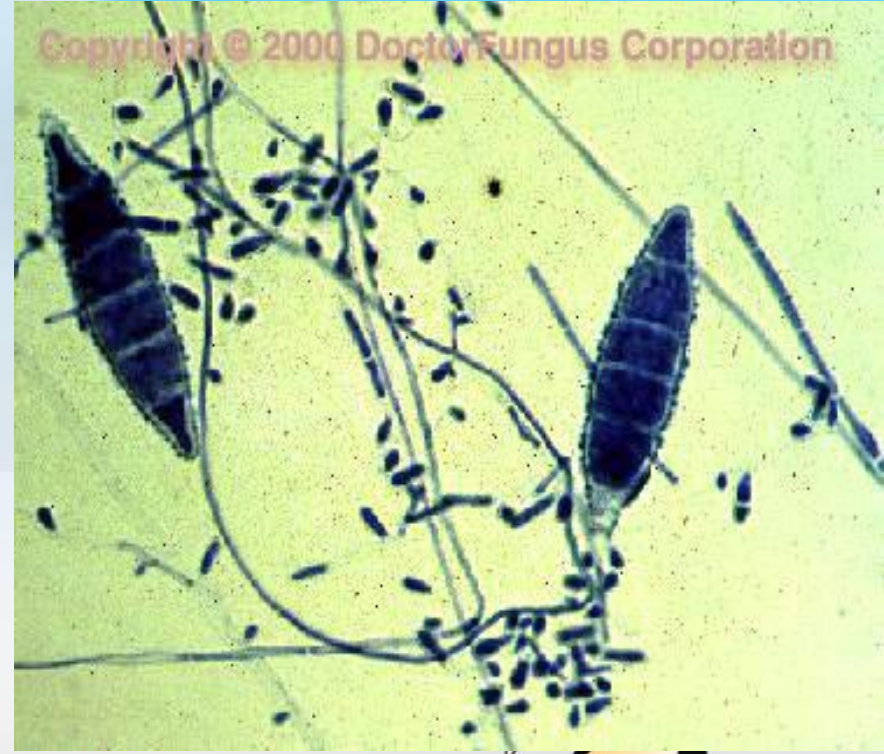
# Microconidia

- Unicellular, asexual external spores.



# Macroconidia:

➤ **Multicellular,**



# Source of infection:

## □ Endogenous:

- **Normal flora** and it is the main source in nosocomial infection (because those people in hospitals are **immunocompromized**).



# Source of infection (cont.):

## □ Exogenous:

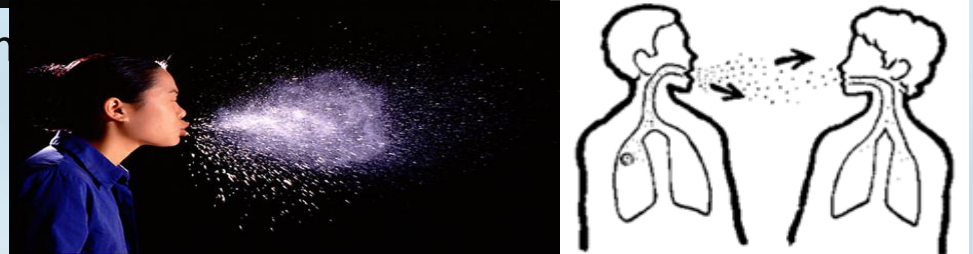
- This is the main source of fungal infection mainly from the **environment**.
- Few fungal infections are communicable between human or between animals.





# Mode of transmission:

- Respiratory tract (air borne infection)



- GIT (food & water borne infection).

- Blood stream injection.



- Skin = contact.
- Most fungal diseases are not communicable between human or animals.



# Most fungi are opportunistic:

- Produce diseases in immunocompromized patients.
- Little is primary pathogen (cause disease in person with intact immune system).



# Steps of infection:

- **I. Adherence:**

- By adhesions, e.g. **Candida**, but filamentous fungi have no adhesions.
- **Fibrinonectin** of epithelial cell is the receptors.
- Virulence usually associated with adherence.



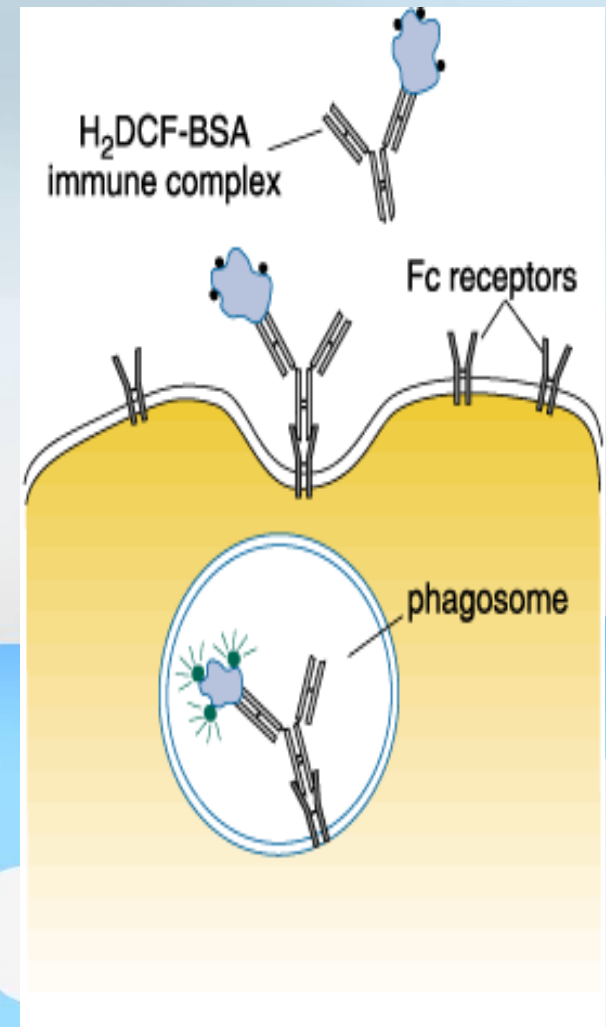
# Steps of infection:

- **ii. Invasion:**
  - **Mechanical trauma** to skin or mucosal surface is an essential step in fungal infection, because most of the infective element in fungi is the spore and it is non-invasive.
  - Some fungi have invasive power like Candida by the formation of hyphae and pseudohyphae.



# Steps of infection:

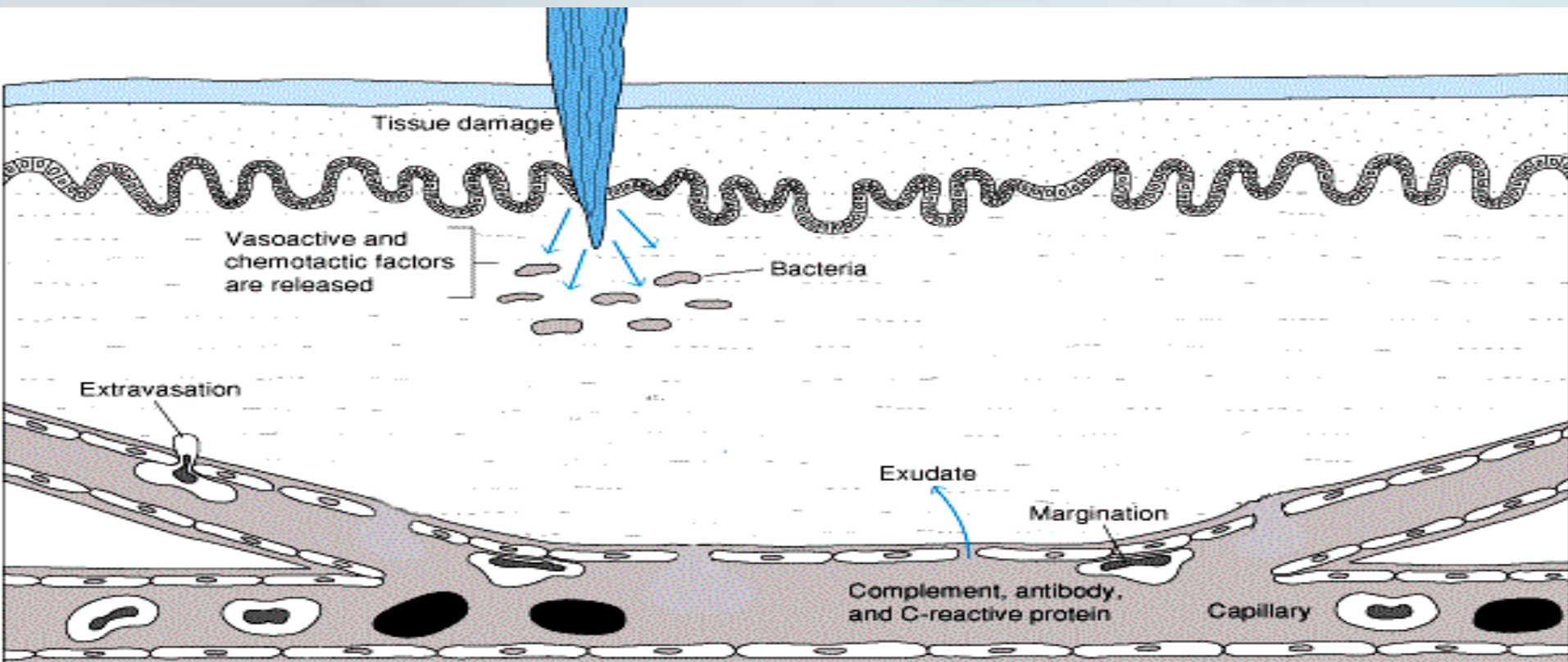
- **iii. Phagocytic interactions:**
  - Some fungi especially **dimorphic** fungi show resistance to phagocytic killing.
  - Some fungi are **capsulated** and can resist phagocytosis (Cryptococcus).



# Immunity to fungal infections

## □ Innate immunity:

- Non-specific works against all microorganisms.



# Immunity to fungal infections (cont.)

## ❑ **Acquired immunity:**

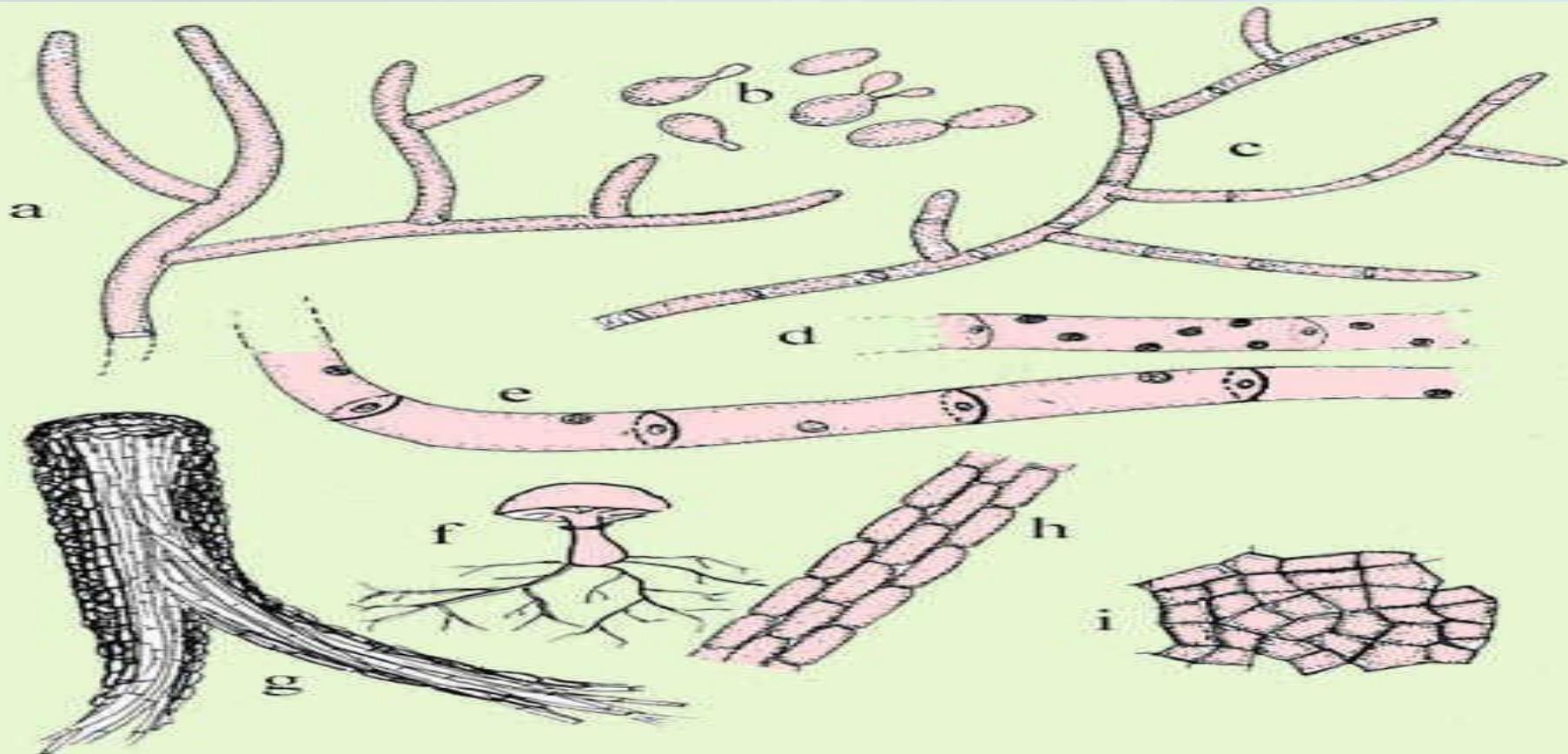
The main immunity is cellular immunity because fungi stay inside the host cell.

Antibodies have limited role in some fungal diseases.



# Fungal Classification

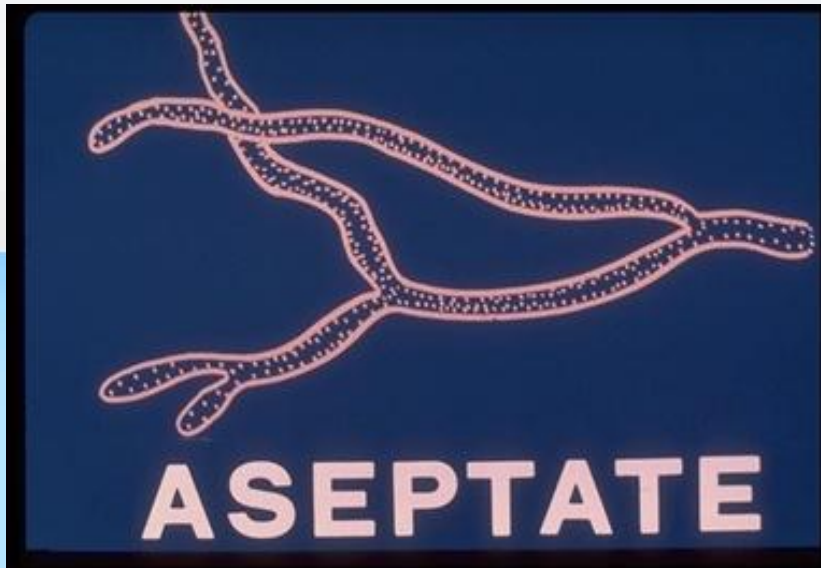
## a. According to morphology:





# Moulds (Filamentous fungi):

- Grow with formation of hyphae, which may be septated or non-septated.



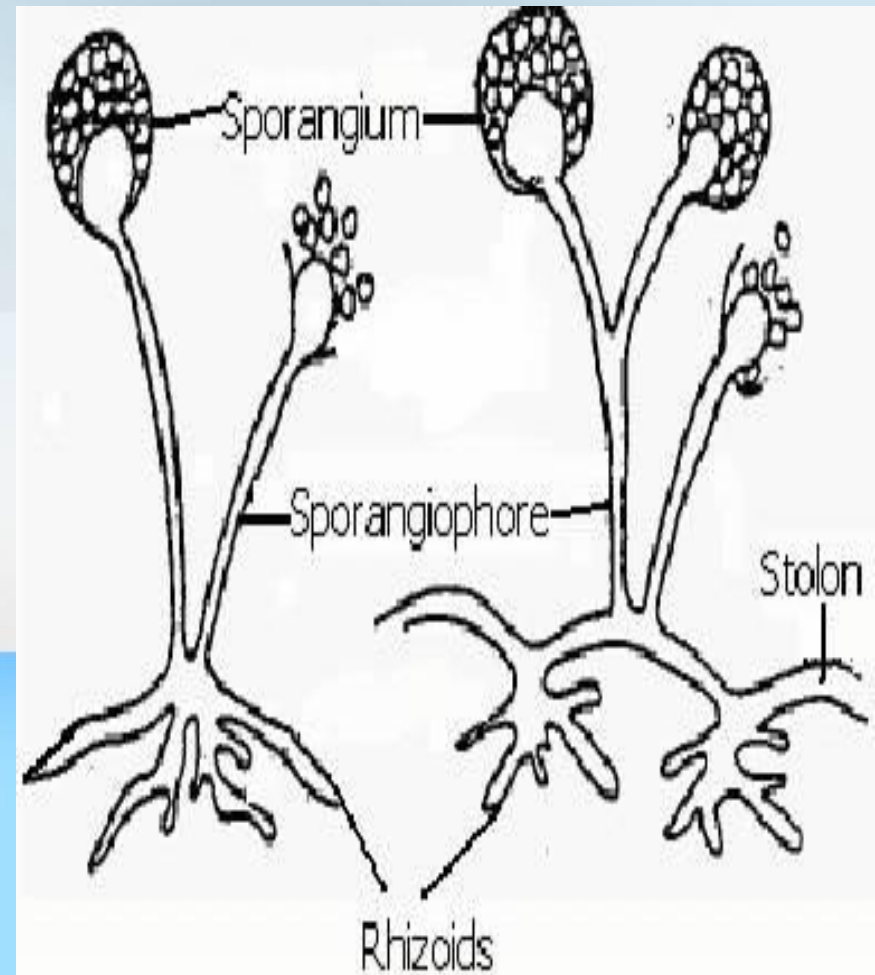
# Moulds (Filamentous fungi):

## – *Vegetative mycelium:*

- Some hyphae will penetrate the media.
- Some hyphae present at the surface of the media.

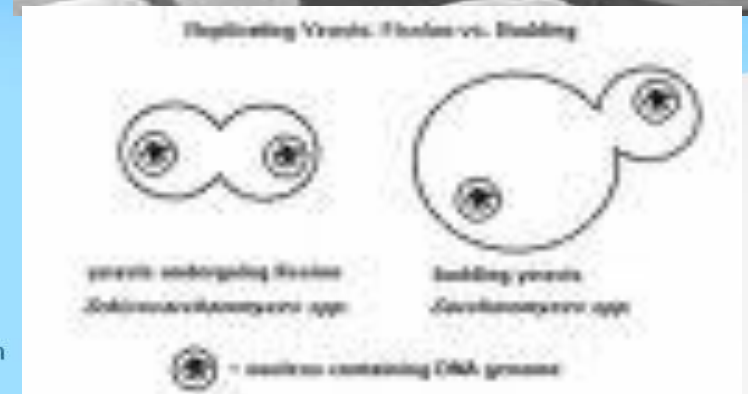
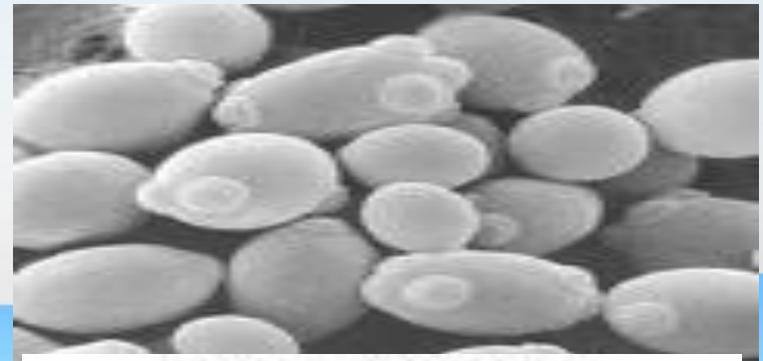
## – *Aerial mycelium:*

- Some hyphae may be directed upward & carry the different types of spores that produced by this fungus.



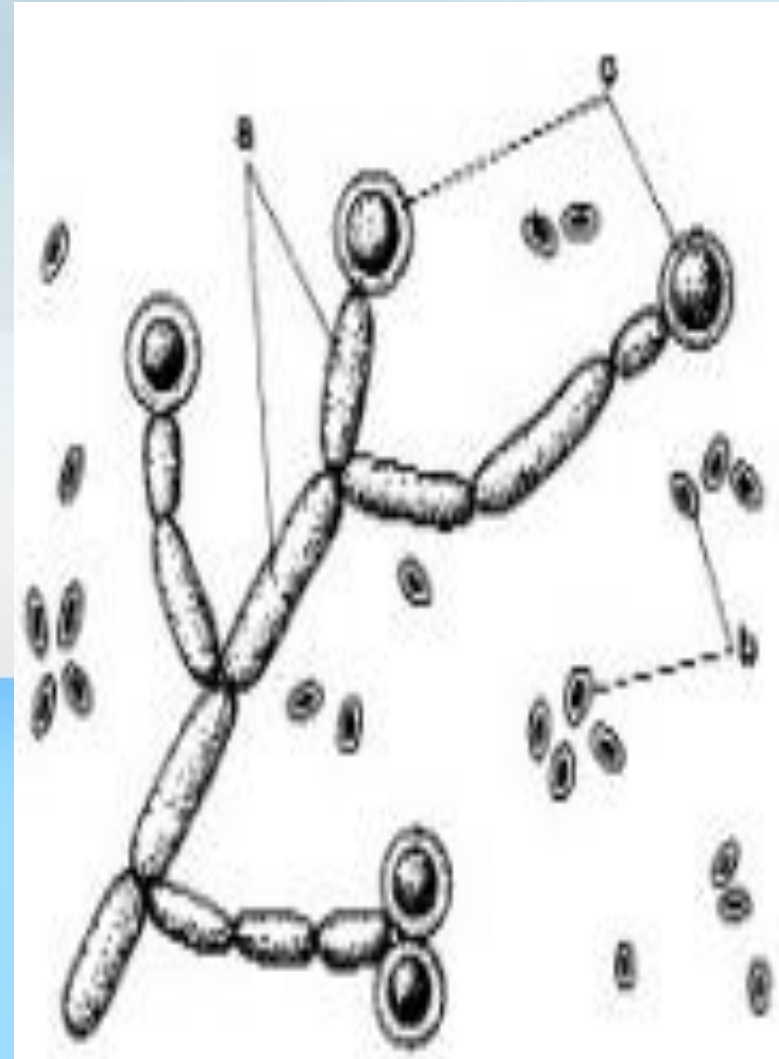
# Yeasts

- **Unicellular** fungi (rounded or oval in shape).
- Reproduce by **budding**.
- The only example of pathogenic yeasts is **Cryptococcus neoformans**.



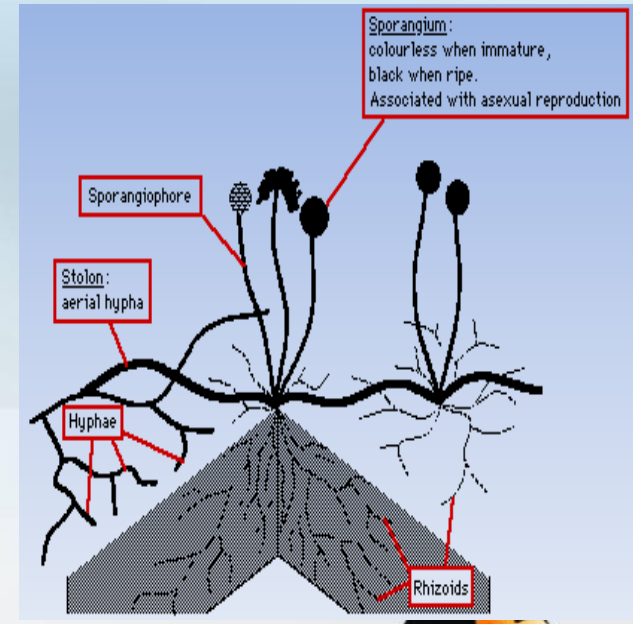
# Yeast-like

- Unicellular fungi (rounded or oval in shape).
- Reproduce by budding.
- But during infection it produces **pseudohyphae**.
- Example: Candida.



# Dimorphic fungi:

- Can grow as **yeast** during infection in the body & on incubating culture at 37 °C.
- Can grow as **moulds** or filaments when inoculated at room temperature.
- Example: *Histoplasma capsulatum*.



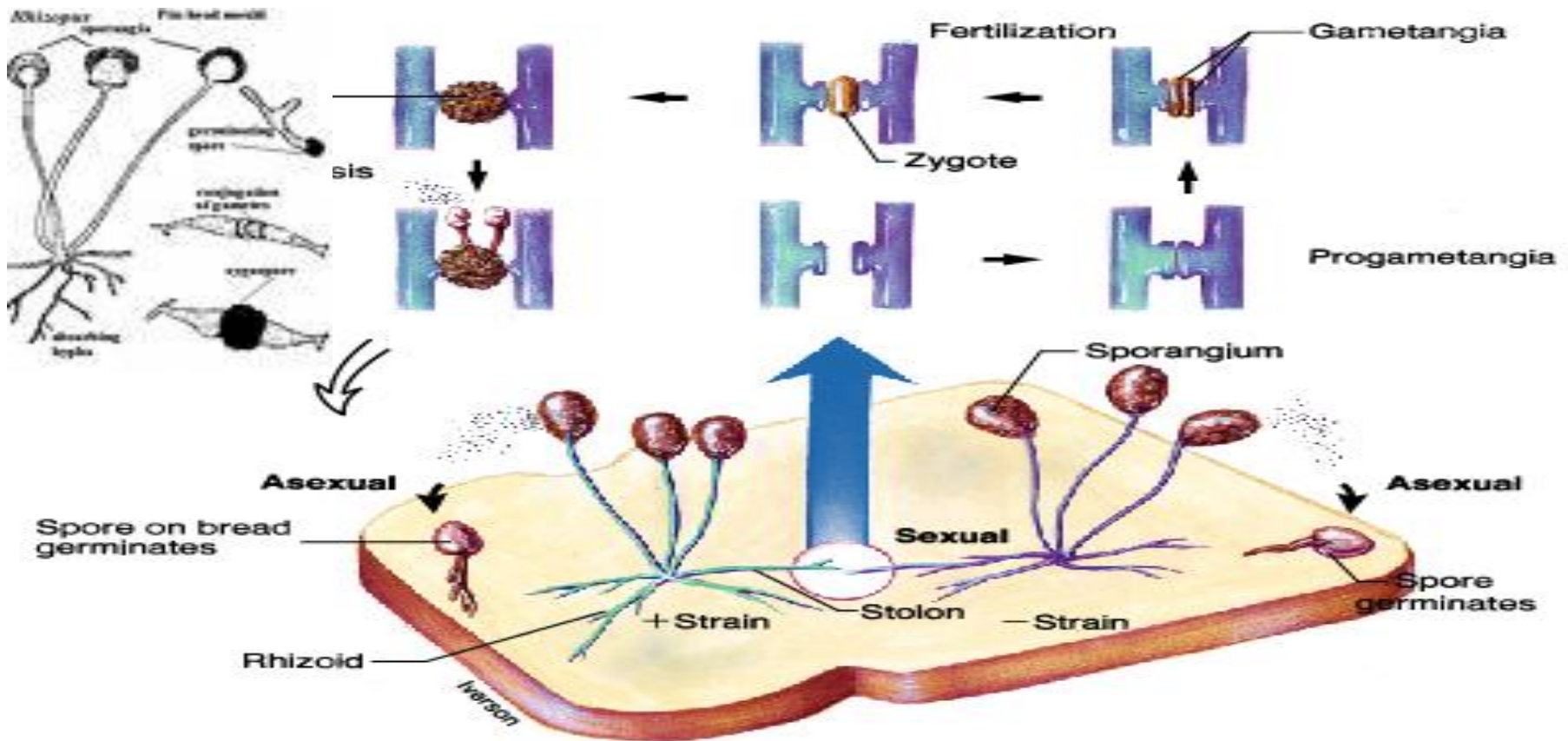
# Fungal Classification

B-According to nature of their sexual spores:



# Phycomycetes (Zygomycetes):

- ❑ Sexual spores are of 2 types:
  - **zygospores & oospores.**
  - Usually **non-pathogenic.**



# Ascomycetes

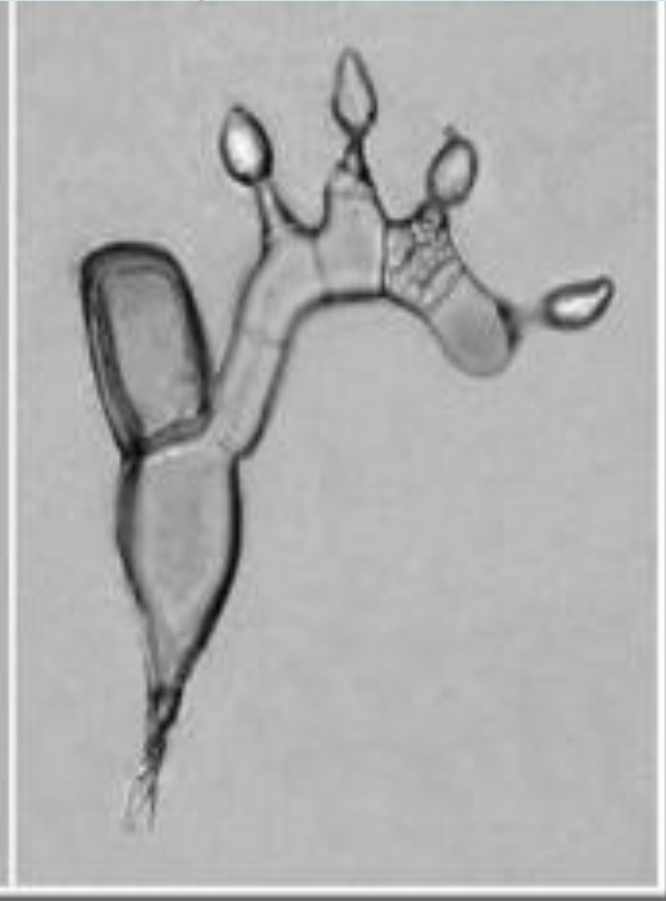
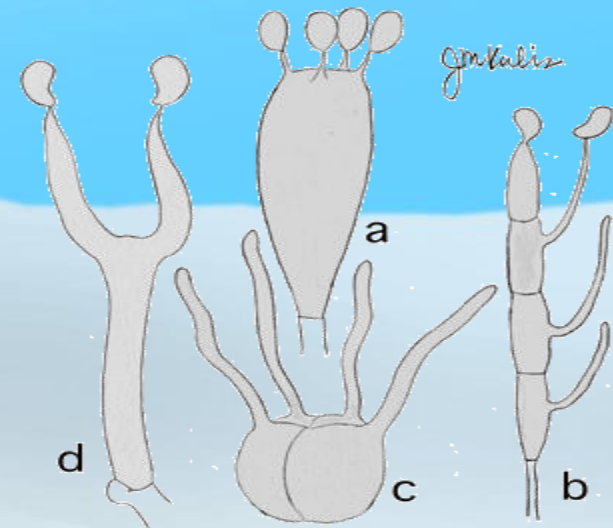


**Michael Kuo**

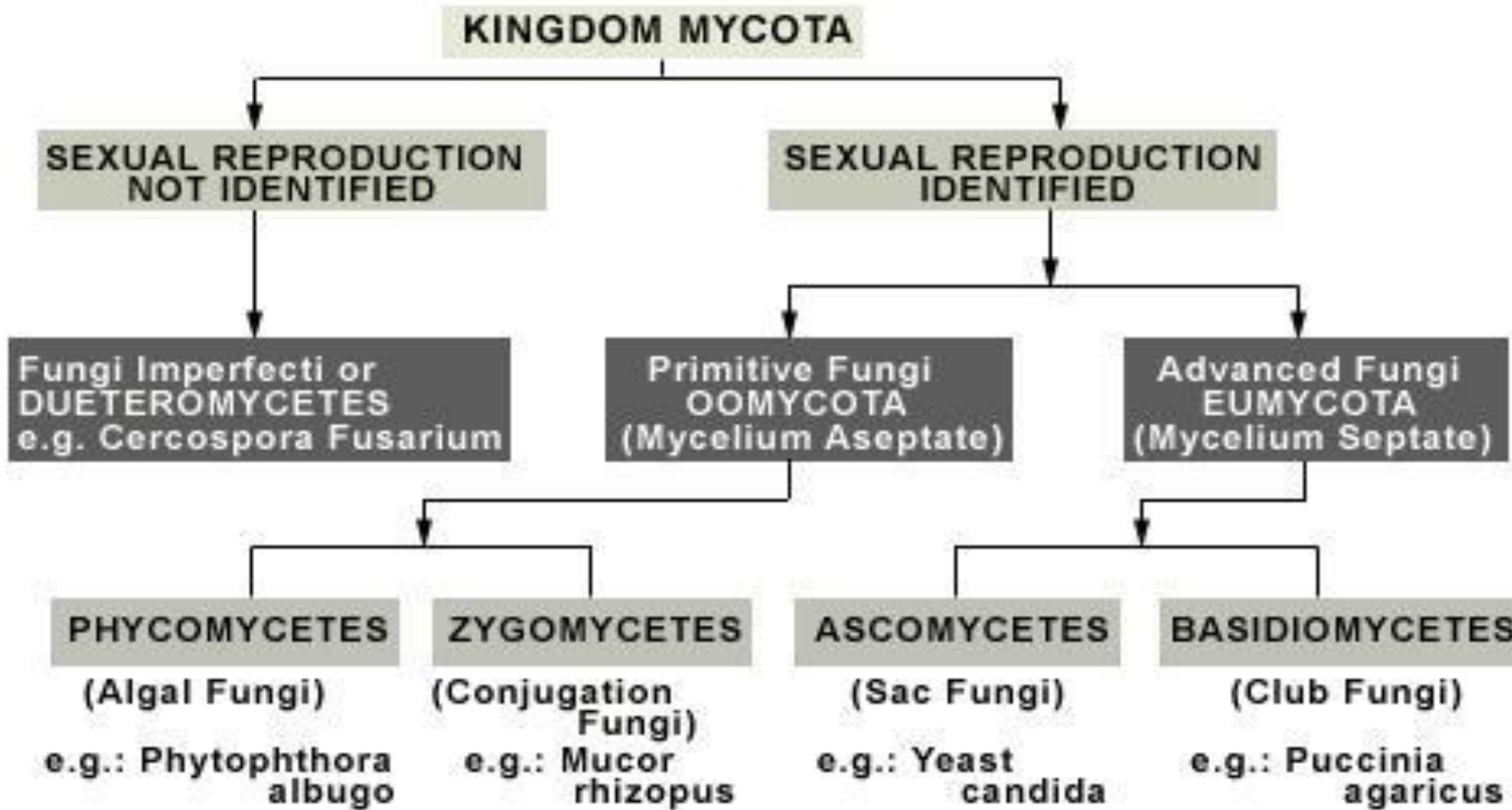


# Basidiospores

- Sexual basidiospores.
- Non-pathogens.



# Fungi imperfecti



# Human mycosis terminology



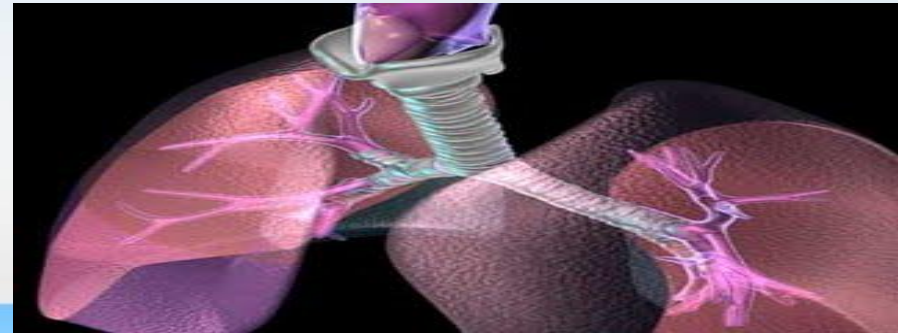
# A. Anatomical terminology

## (According to the site of infection):

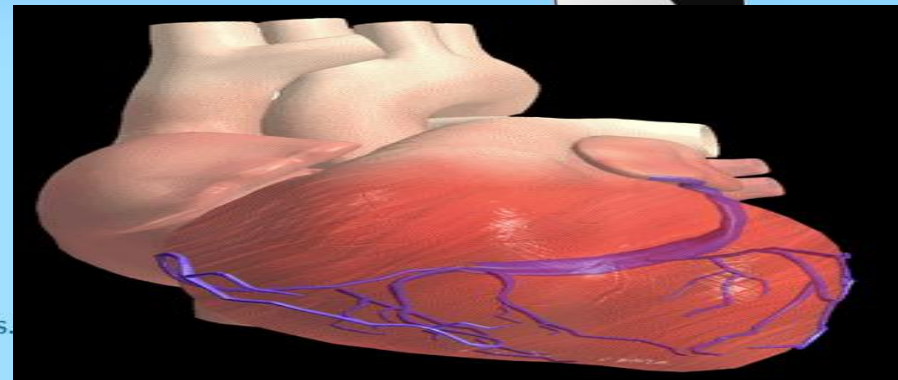
- Dermatomycosis: Fungal infection of the skin.



- Pulmonary mycosis: Fungal infection of the lung.



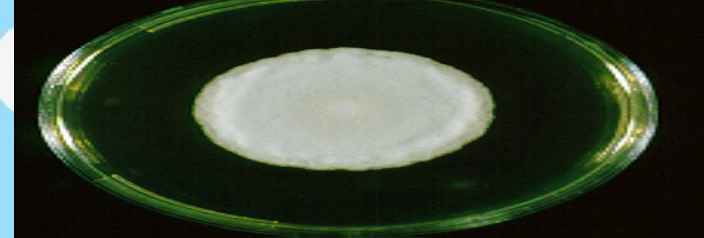
- Cardiovascular mycosis: Fungal infection of the cardiovascular system.



# B. Mycological terminology (According to the etiology):

- Candidiasis (= Candidosis): Fungal infection by Candida.
- Aspergillosis: Fungal infection by Aspergillus.
- Cryptococcosis: Fungal infection by Cryptococcus.
- Histoplasmosis: Fungal infection by Histoplasma.

Cryptococcus



# Types of human mycosis



# *Superficial mycosis*

- ▶ Infection restricted to upper most **horny** layer of skin, hair and nails e.g. **Pitryasis versicolor**.



## ***2 - Cutaneous mycosis:***





## 3- Subcutaneous mycosis (Implantation mycosis):

- Most of fungi are **non invasive**.
- Occurs by implantation of spores into wounds.
- e.g. **Mycetoma** (madura foot), **thorn pricks** mycosis.



# 4- Systemic mycosis:

- Multi organs affected.

## Mode of infection:

- Inhalation of spores of saprophytic fungi.
- Spread of local mycosis.

## Examples:

- Cryptococcosis.
- Histoplasmosis.
- Candidiasis.



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# 5- Opportunistic mycosis:

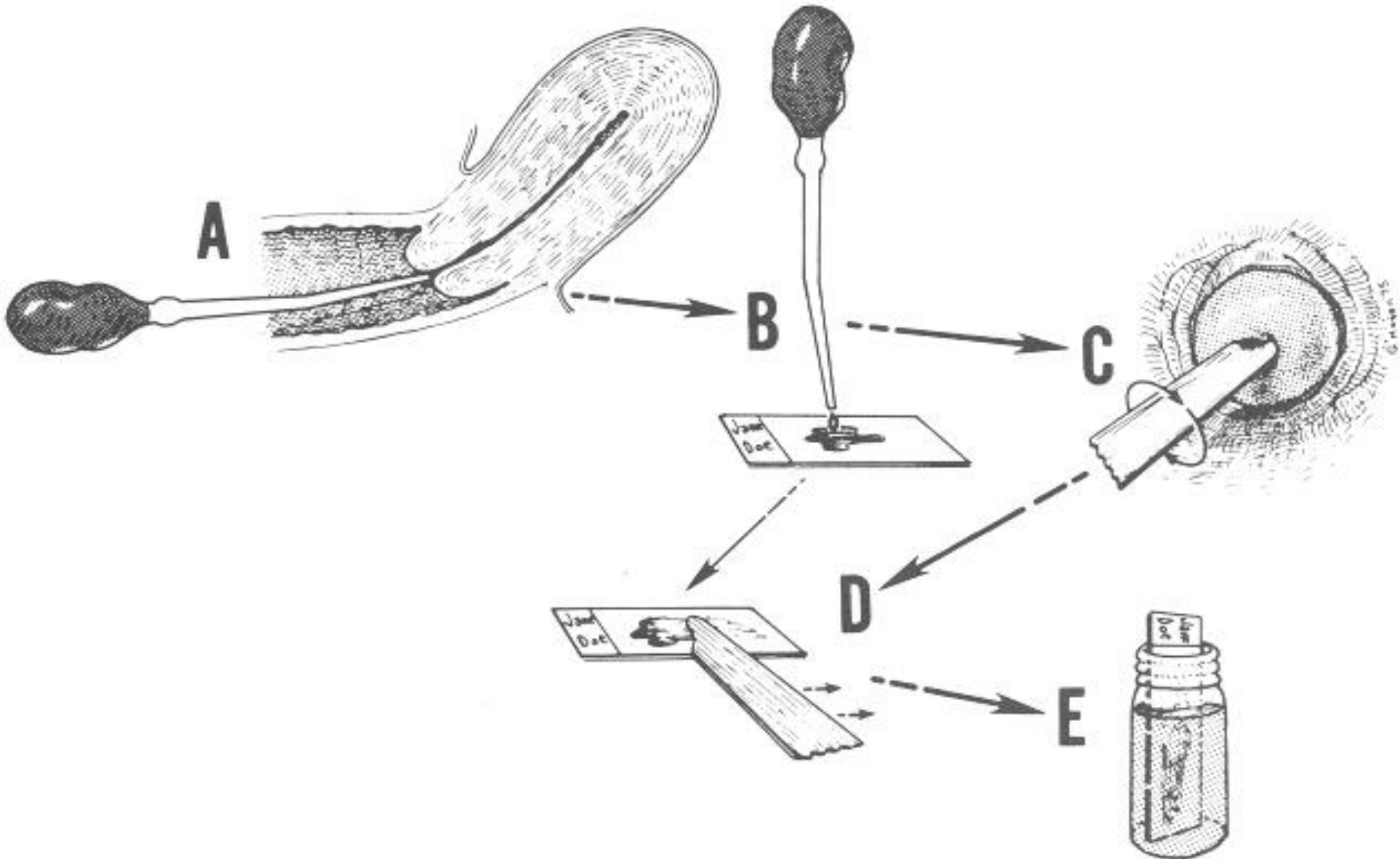
- **Fungal infection by:**
  - Fungal flora (Candida).
  - Saprophytic fungi in the environment (Aspergillus).
- **This infection occur in:**
  - Immunocompromised host (Both innate and acquired immunity).
  - Opportunistic conditions like:
    - Diabetic patients.
    - Cancer patients.
    - Corticosteroid & other immunosuppressive therapy (e.g. Cytotoxic drugs).
    - Prolonged antibiotic therapy.



# Diagnosis of fungal infections

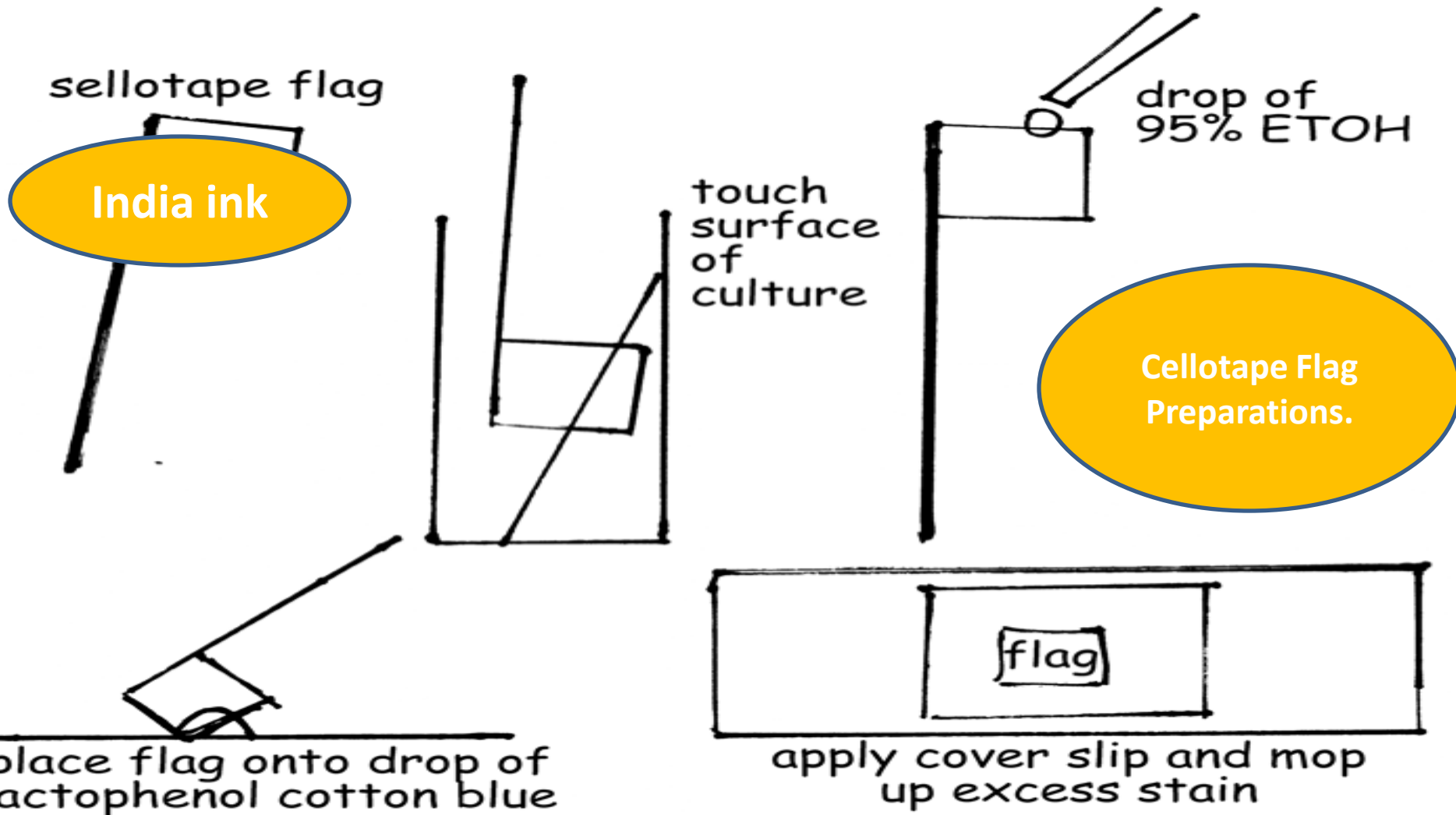


# 1. Direct Microscopic Preparation:



# 1. Direct Microscopic Preparation:

- b) Stained preparation:



## 2. Culture for isolation of fungi:

- *Sabouraud`s dextrose agar (SDA):*

- Composed of agar + dextrose + peptone.
- Disadvantage: Bacteria can grow on it.



## 2. Culture for isolation of fungi:

- ***SDA + Chloramphenicol (0.05%):***
  - Chloramphenicol is added to inhibit bacterial growth.





## 2. Culture for isolation of fungi:

- ***SDA + Chloramphenicol + Cyclohexamide (0.5%):***
  - Cyclohexamide is added to inhibit the growth of saprophytic fungal contaminants.



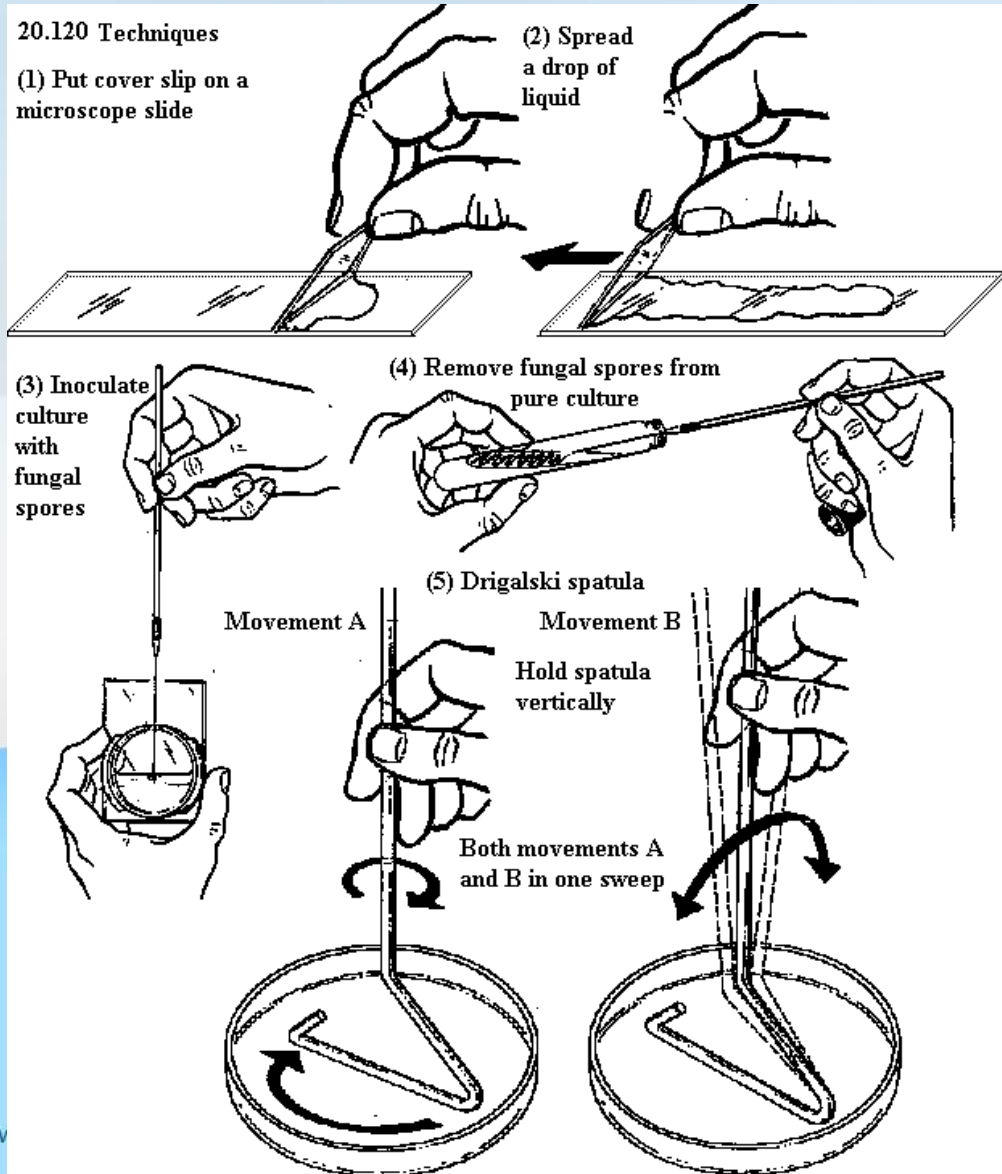
## 2. Culture for isolation of fungi:

- ***Blood agar:***
  - Some fungi as yeast, and yeast like (Candida and Cryptococcus) grow rapidly as bacteria after 4 weeks from incubation.



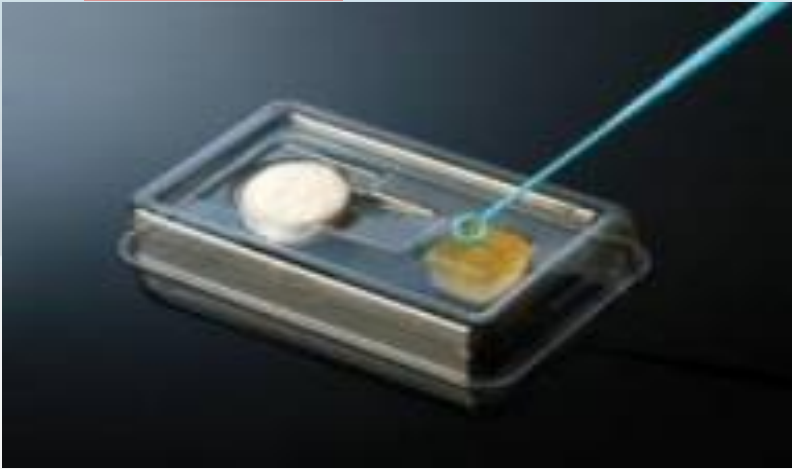
# Growth is identified by:

- **Macroscopic characters:** e.g. colour from both sides (recto – verso examination), shape, size and texture of the colony.
- **Microscopic stained preparation.**
- **Biochemical reaction:** Sugar fermentation and assimilation (especially in yeast).



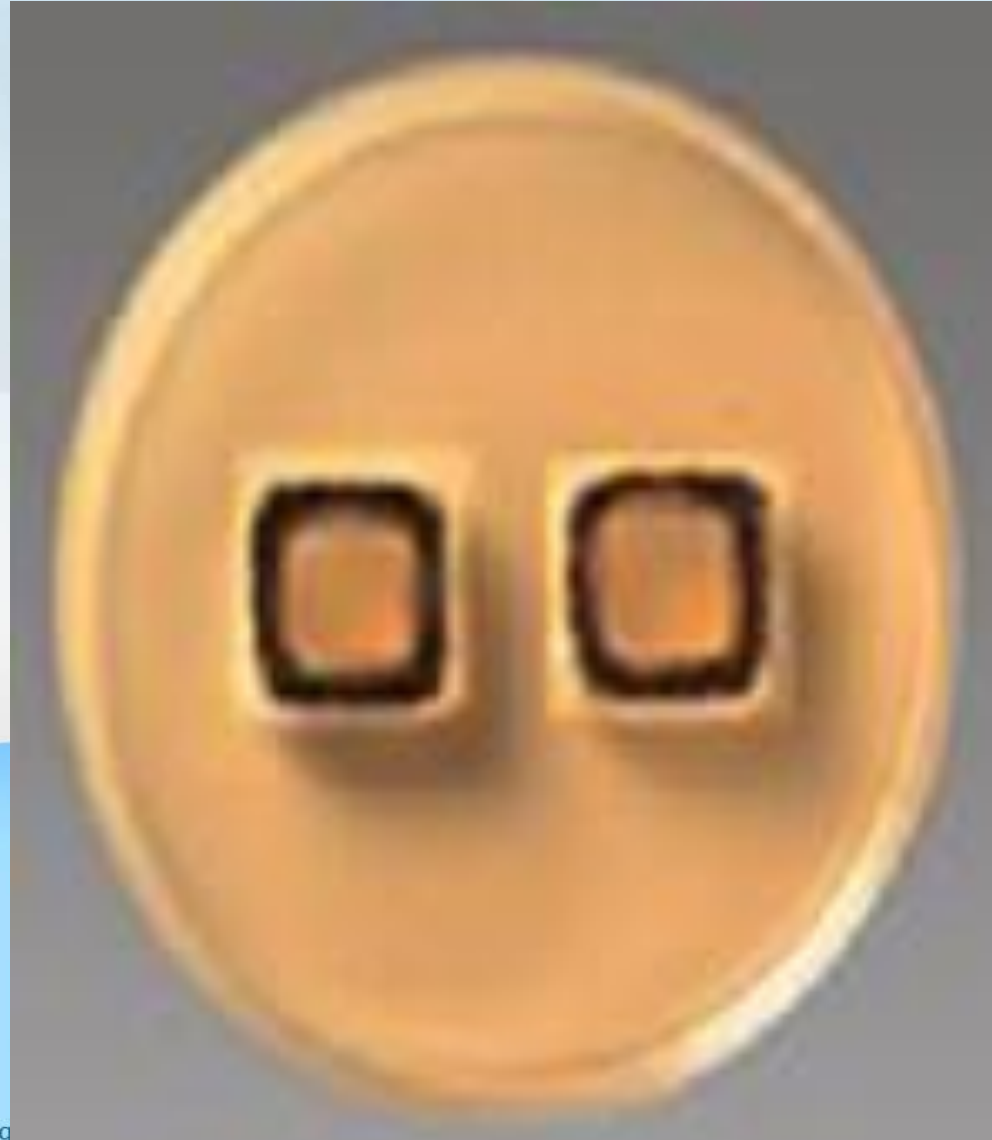
# 3. Microculture:

Used to:



It has 2 types:

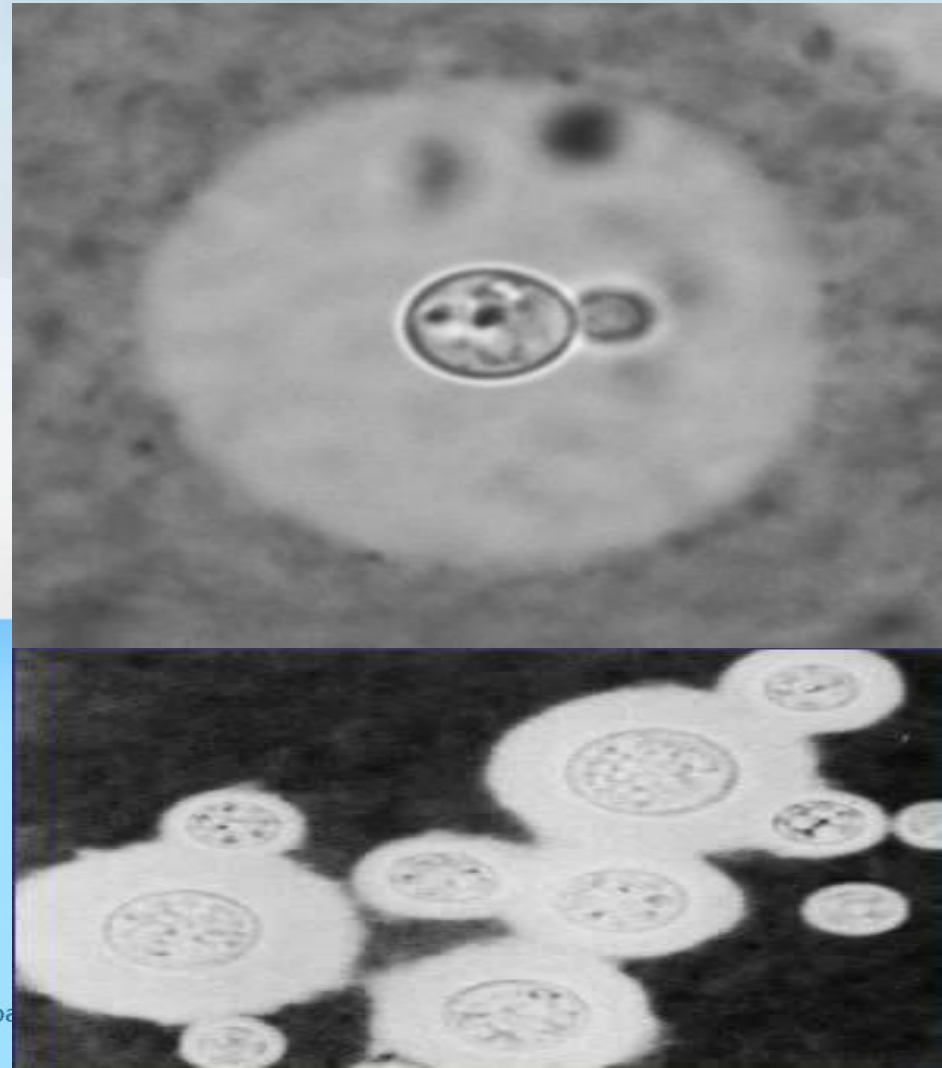
- Direct evaluation of a culture in an open petri dish under the microscope.
- Slide culture technique.



## 4. Histopathology:

### Yeast cells:

- They may be intracellular small yeast: e.g. *Histoplasma capsulatum*.
  - They may have a large distinguishing capsule: e.g. *Cryptococcus*.



## 4. Histopathology:

- Spherules:
  - Intact spherules are large **sac-like structure** filled with **sporangiospores**.



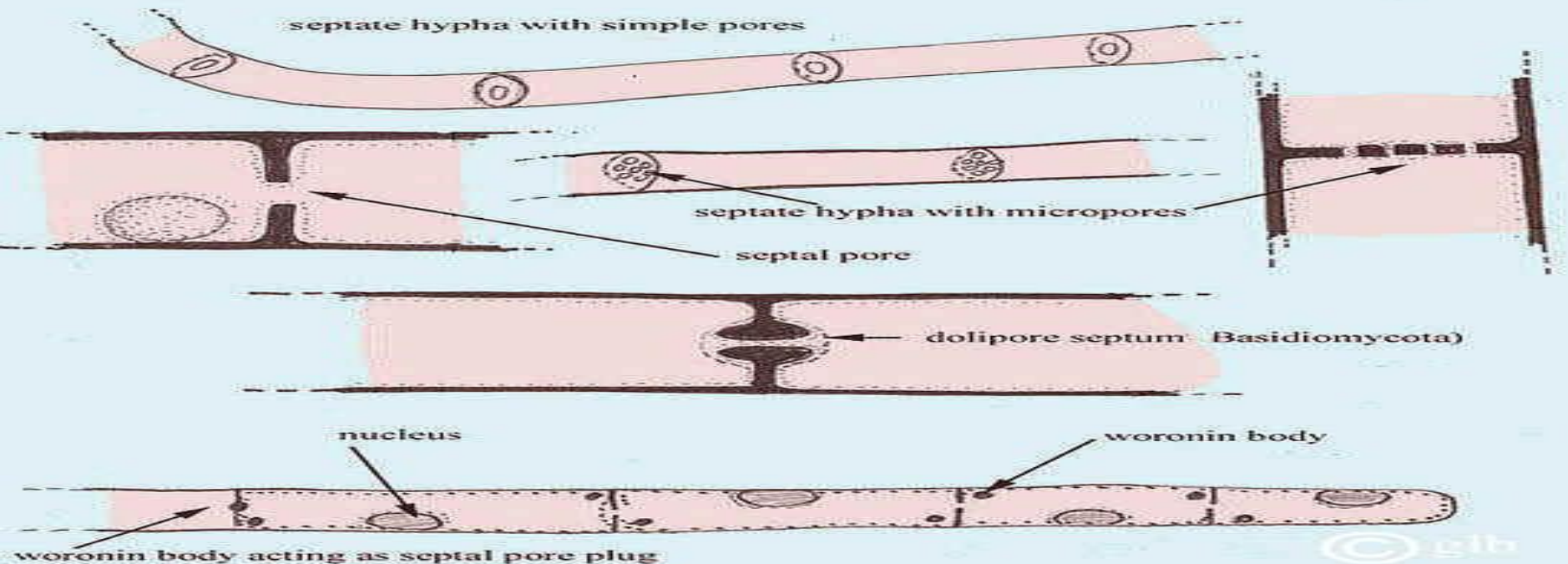
Left: A patient showing the disseminated stage of disease (coccidioidomycosis).

Top right: spherules.

Bottom right: chains of arthrospores interspersed with empty cellular compartments.

# 4. Histopathology:

- Hyphae:
  - They may be **brown** in colour or **non-coloured**.
  - They may be **septated** or **non-septated**.



# 4. Histopathology:

- Granules:

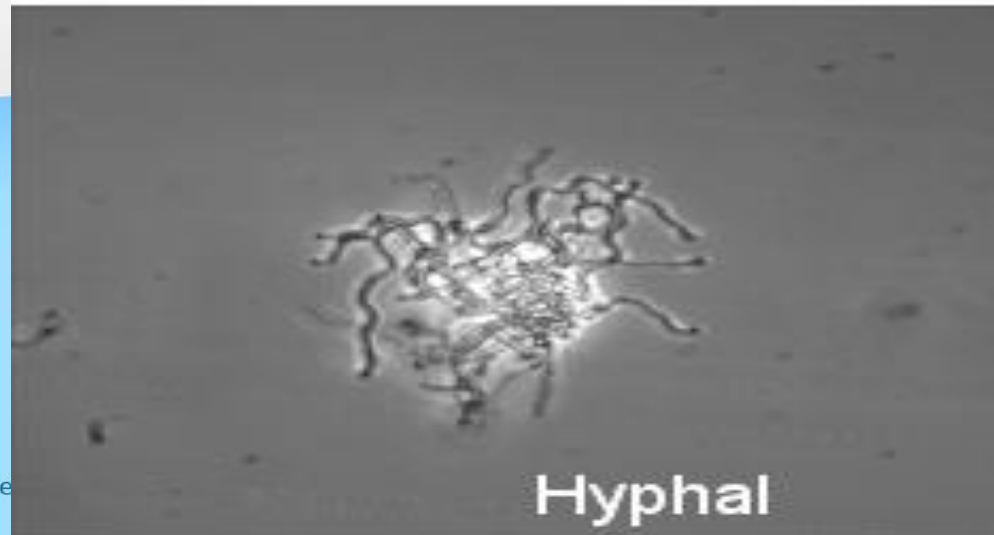
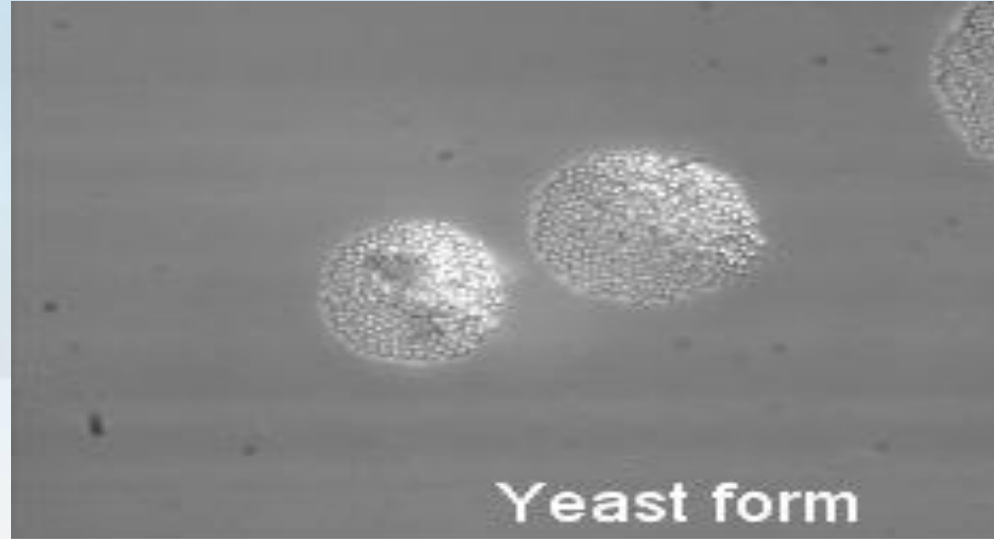
- They are tightly packed masses of **hyphae or filaments**, which are surrounded by **tough outer rind**.





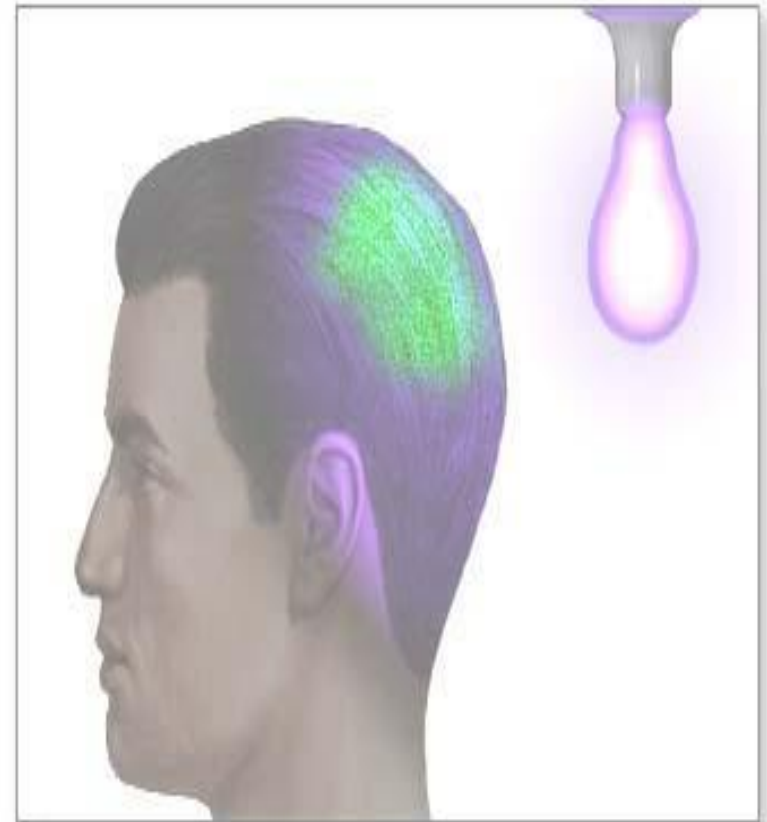
# 4. Histopathology:

- ▶ *Combination of yeast cells and hyphae:* As in Candida.



## 5. Woods light:

- Helps in clinical diagnosis.
- Long wave ultraviolet rays (black rays) which when come in contact with mycotic areas of skin and hair produce fluorescent colours.
- **Disadvantage:** it occurs in some mycotic infections only.



Infectious organisms glowing under Wood's lamp illumination

## 6. Indirect method of diagnosis:

- *Detection of circulating antibodies (Serological diagnosis):*
- It has limited role.
- Used in diagnosis and follow up of Cryptococcus and Candida with limits.



# Tests used for detecting fungal antibodies:

## Step 1

Microbial antigen is dried on a glass slide and treated with a chemical fixative



## Step 2

Dilutions of patient serum are incubated with the antigen on the slide, and then rinsed



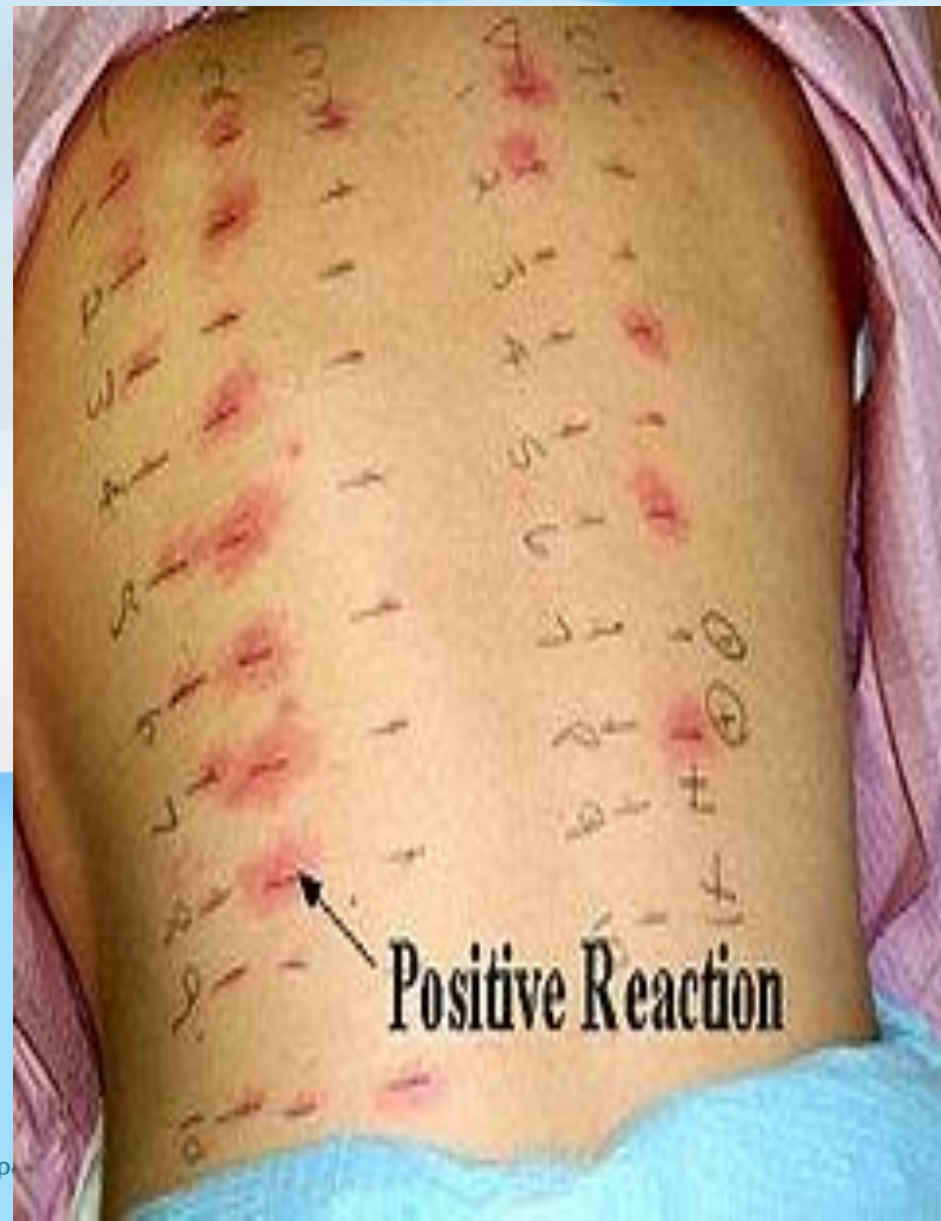
## Step 3

A fluorescein-labeled antibody (conjugate) is added



# Fungal skin tests:

- It has **no value** in diagnosis.
- It does not differentiate between active and past infection.
- Mainly used for **epidemiological study**.
- It is observed by formation of **induration and swelling** due to reaction between injected antigen and T cells.
- **e.g. Histoplasmin, Candidin, Tricophyтин tests.**



# Antifungal therapy

- *Topical antifungals:*
  - Polyenes e.g. nystatin, fungizone
  - Azoles (e.g. miconazole, Ketoconazole, econazole, clotrimazole).
  - Miscellaneous e.g. tolnaftate, allylamine, iodine.



# Systemic antifungals:

- **Polyenes** (e.g Amphotericin-B).
- **5-flucytosine.**
- **Azoles** (e.g itraconazole, fluconazole).
- **Terbinafine.**
- **Griseofulvin**
- **Iodine.**
- **New antifungal**
  - Echinocandins e.g caspofungin
  - New triazole e.g voriconazole



# Mechanism of action of antifungal

## Cell membrane

Polyenes  
Azoles



## Nucleic acid synthesis

5-Flucytosin  
Griseofulvin



Cell wall  
Cuspofungin



# 1) Polyenes

- Bind to **ergosterol** in the fungal cell membrane → altered permeability → leakage of  $K^+$ ,  $Mg^{++}$ , Sugar → Cell death
- It is **fungicidal**, has broad Spectrum usage until now
- **Hepatotoxic** and **nephrotoxic**
- **Lipid preparations** (as liposomal amphotericin-B) are more tolerable and less toxic.



## 2) Azole

- Inhibits **ergosterol** biosynthesis via binding to cytochrome p- 450 dependent enzyme 14 $\alpha$  demethylase  $\rightarrow$  accumulation of 14  $\alpha$  sterol  $\rightarrow$  depletes sterols.
- **Hepatotoxic, spermatogenesis inhibitor** so its usage restricted
- **Fluconazole** crosses blood brain barrier so used in treatment of **cryptococcal meningitis.**



# 3) Criseofulvin

- Exact mechanism is unknown
- Inhibit **nucleic acid synthesis**
- Have **antimitotic** activity by inhibiting microtubules assembly "microtubules called cytoskeleton that support shape, transport of substrates of eukaryotic cell"
- Inhibit synthesis of **cell wall chitin.**



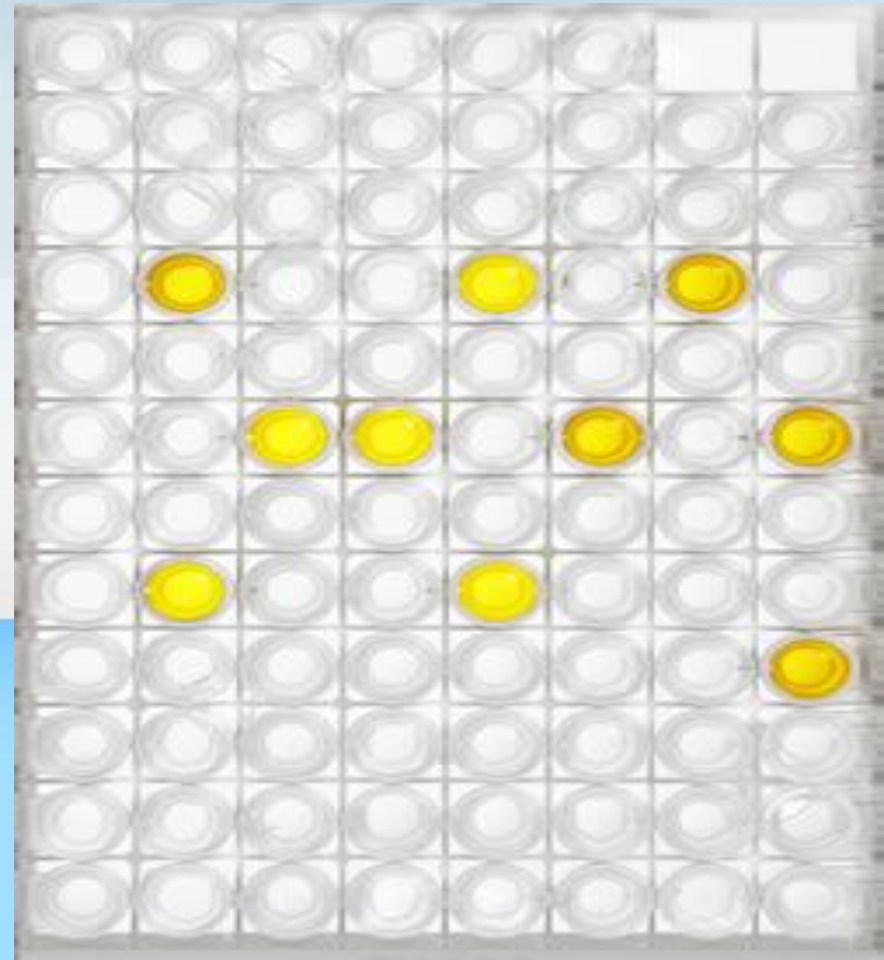
## 4) 5- Flucytosin:

- ▶ Deaminated in cell to **5- fluorouracil**, which replace uracil base in RNA → **disruption of protein synthesis.**



# How to select proper antifungal drug?

- We can select proper antifungal drug via susceptibility testing method e.g
  - *Broth dilution method*
  - *Agar diffusion method*



# I. Superficial fungal infection



# A. Ring worm fungi (Tinea = dermatophytosis)

## *Dermatophytosis*

- Fungal infection by dermatophytes of keratinous structures (skin, hair, nails)



## A. Ring worm fungi

### Common clinical types:

#### 1. Tinea Corporis:

- Dermatophyte infection of the glabrous skin (trunk, back, dorsum of the hand).







## A. Ring worm fungi

### Common clinical types:

#### 2. Tinea Capitis:

- Fungal infection of the skin of the scalp and hair.
- This takes 3 forms of hair involvement:
  - a) Endothrix:
    - There is abundant fungus growth inside the hair shaft.
  - b) Ectothrix:
    - The spores surround the hair shaft from **outside** lead to weakness and falling of the hair.
  - c) Favic type:
    - Some fungal mycelia are present inside the shaft with air space.



## A. Ring worm fungi

### Common clinical types:

#### 3. Tinea Barbae:

- Fungal infection of the beard and moustache skin area in male.





## A. Ring worm fungi

Common clinical types:

### 5. Tinea Manum:

- Fungal infection of the **palm** of the hand and **inter-digital areas**.



## A. Ring worm fungi

Common clinical types:

### 7. Tinea cruris

- Fungal infection of the **crural** area and **perineum**.

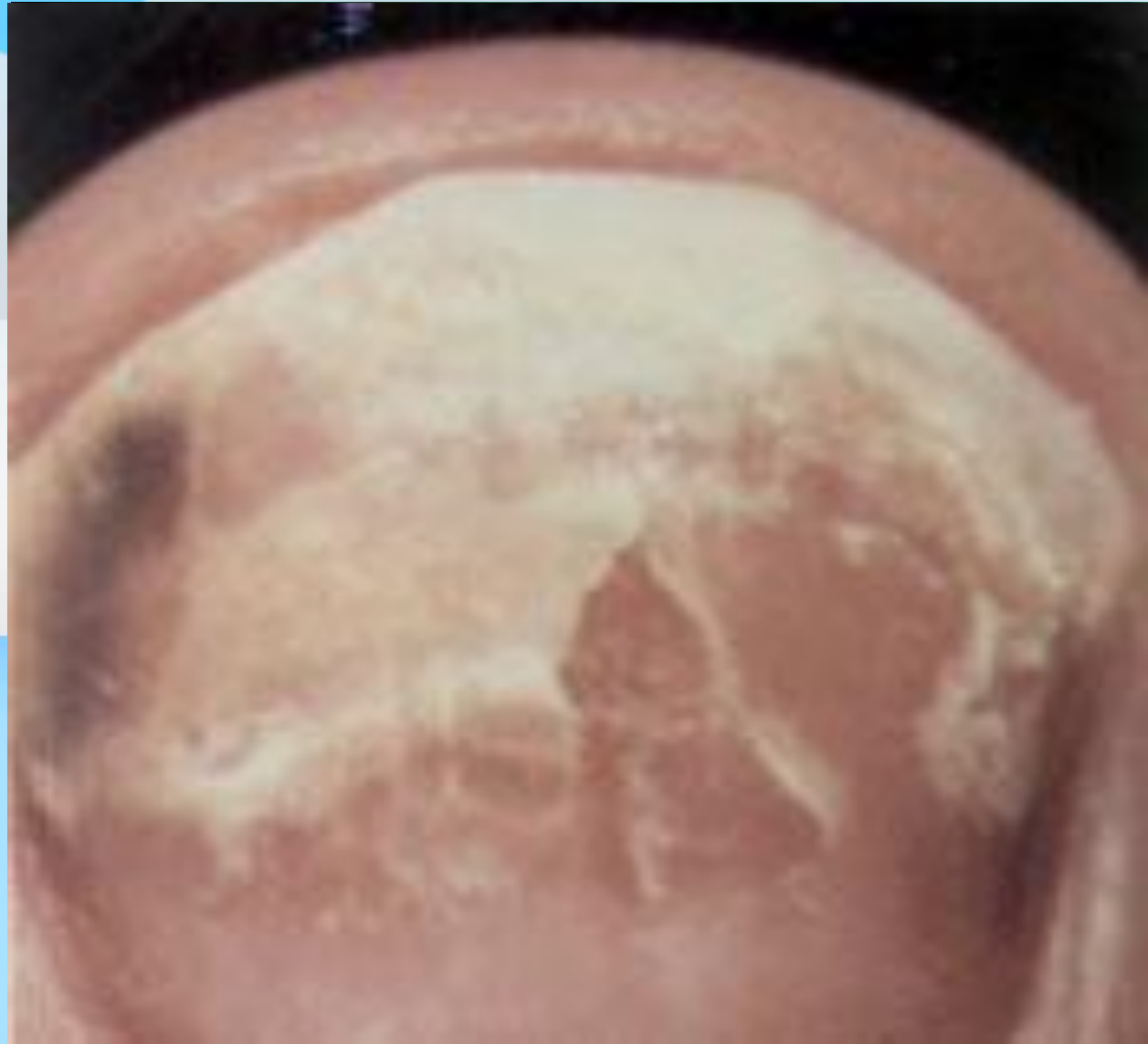


## A. Ring worm fungi

Common clinical types:

### 7. Tinea Unguim:

- Fungal infection of the **nail** of the hand.



# Epidemiology

According to the source of infection



# ***1- Anthrophilic:***

– From human to human.

– e.g.

**Epidermophyton floccosum.**

Epidermophyton





## 2- Zoophilic:

– From animal to human.

– e.g.

**Microsporium canis.**



Microsporium canis



# 3- Geophilic:

– Spores found in soil.

– e.g.

**Microsporium  
gypseum.**

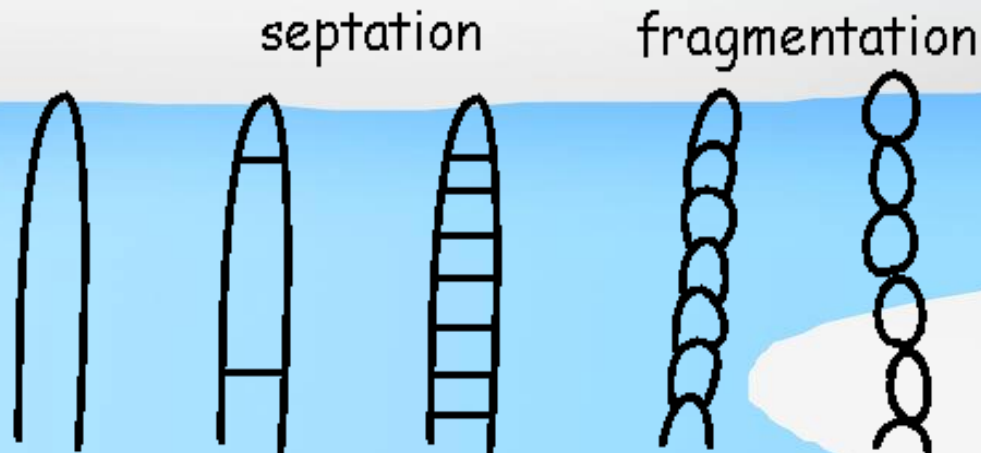
Microsporium  
gypseum



K. Nishimura

# Pathogenesis:

1. Infective stage is **arthrospore** of fungus or keratinous material containing fungus element.
2. Needs **direct or indirect contact** (indirect by the use of the same items of the patient).
3. Need slight **trauma**.
4. Active infection restricted to the **basal keratinocytes of the epidermis**.



# Causative fungus:

## **Dermatophytes include 3 genera:**

- 1. Epidermophyton. e.g. *E. floccosum*.
- 2. Trichophyton. e.g. *T. rubrum*.
- 3. Microsporum. e.g. *M. canis*.



# Diagnosis of dermatophyte infection:



# Diagnosis of dermatophyte infection:

- 1. **Clinical picture.**
- 2. **Wood's light** (negative result doesn't exclude fungal infection).
- 3. **Direct examination by KOH preparation:**

Diagnostic element in skin & nail is the septated hyphae and arthrospores.

Diagnostic element in hair is the **endothrix, ectothrix or favic.**



# Diagnosis of dermatophyte infection:

## 4. Culture:

- On **Sabouraud's dextrose agar** with chloramphenicol & actidion (cyclohexamide).
- Dermatophyte test medium that is **yellow** in colour (if turned red, this indicate positive test).



# Diagnosis of dermatophyte infection:

## Growth is examined by:

- **Macroscopic** examination.
- **Microscopic** examination: In order to differentiate between the three genera of dermatophytes according to the type of macroconidia present





# Diagnosis of dermatophyte infection:

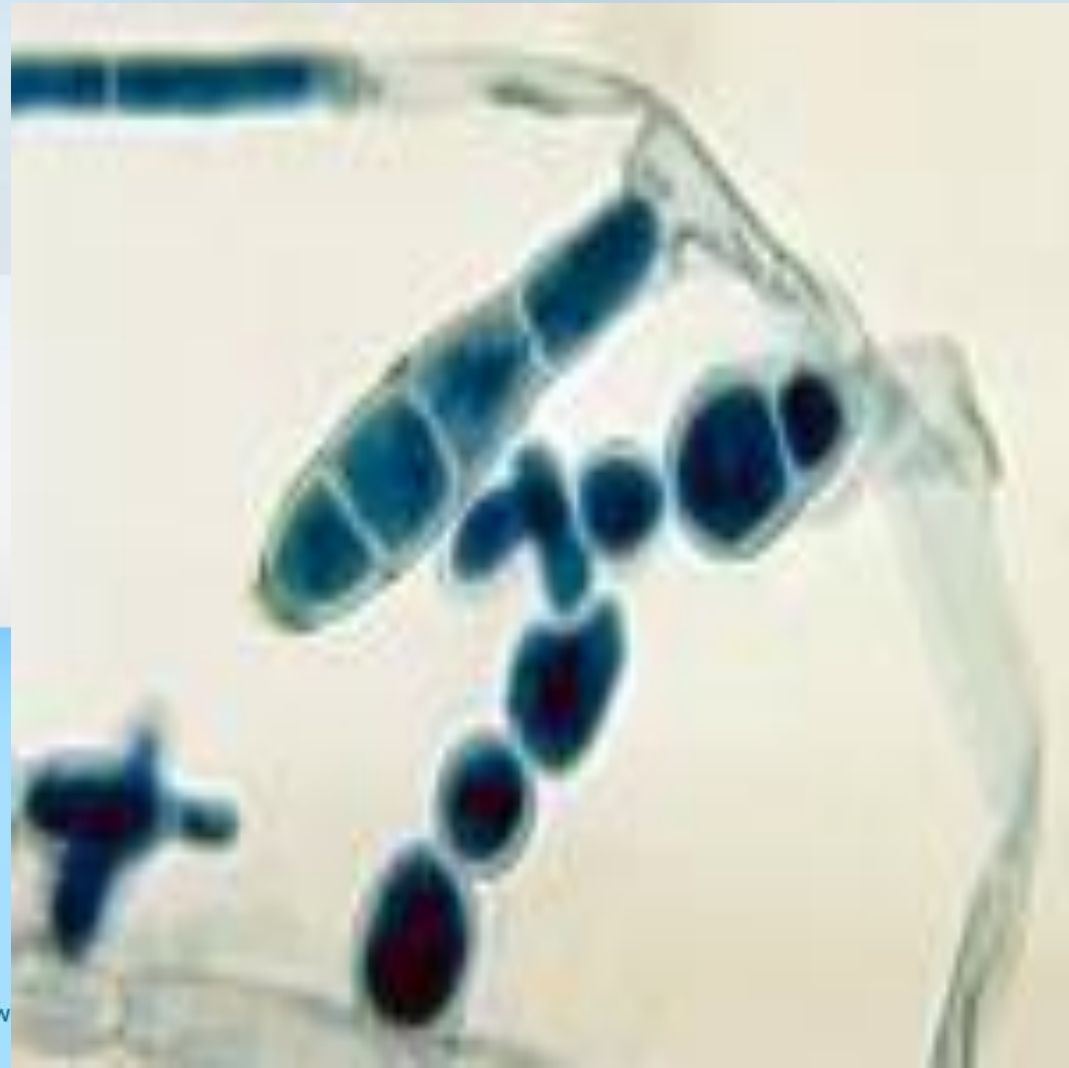
## Growth is examined by:

- **Microsporum: Spindle** shape, **multicellular** with **rough** surface.



# Diagnosis of dermatophyte infection: Growth is examined by:

**Epidermophyton:**  
**Clup shape (racket)**  
**with smooth**  
**surface.**

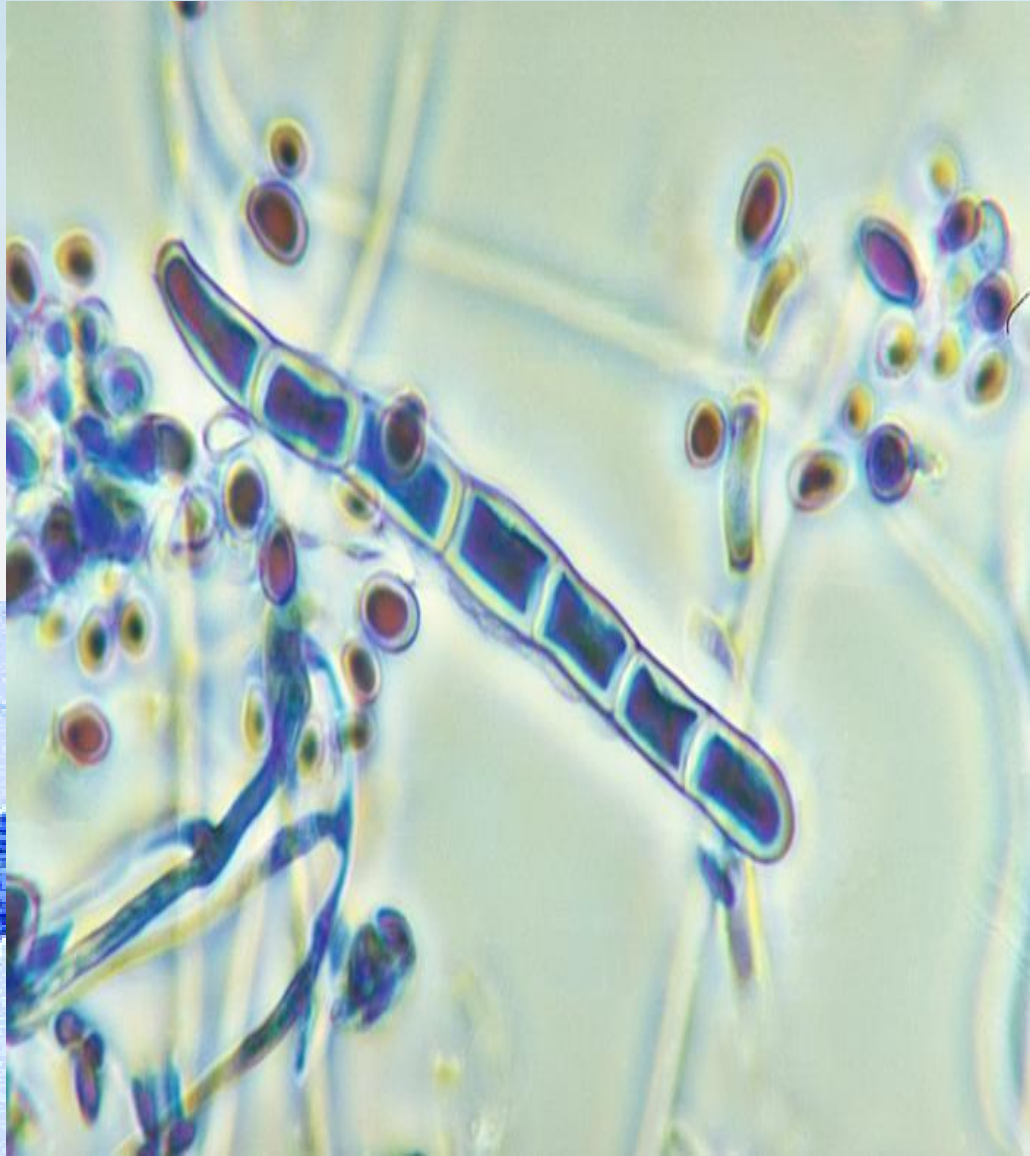


# Diagnosis of dermatophyte infection:

Growth is examined by:

## Trichophyton:

- pencil shape with smooth surface.



# Treatment

- **A. Systemic agents (oral):**

- ❖ Griseofolvin (drug of choice).
- ❖ Itraconazole.
- ❖ Allylamine (Lamisil).
- ❖ Ketoconazole (not used now).

- **B. Topical agents:**

- ❖ White field.
- ❖ Clotrimazole (Canesten).
- ❖ Miconazole (Daktarin).

- **Prohylaxis against Tinea pedis:**

- **Keep the feet dry.**

- ❖ Rub between toes by dry piece of gauze & alcohol.



**B. *Pityriasis versicolor***

**(*Tinea versicolor*)**



# *Pityriasis versicolor*

## Definition:

- **Chronic superficial** fungal infection of the **upper most horny layer of the epidermis**.
- Main area affected is the **trunk** but it can appear in any site of the skin
- Infection causes nothing except **loss of the normal skin pigmentation** may result in hypo- or hyper-pigmentation (blotchy appearance).

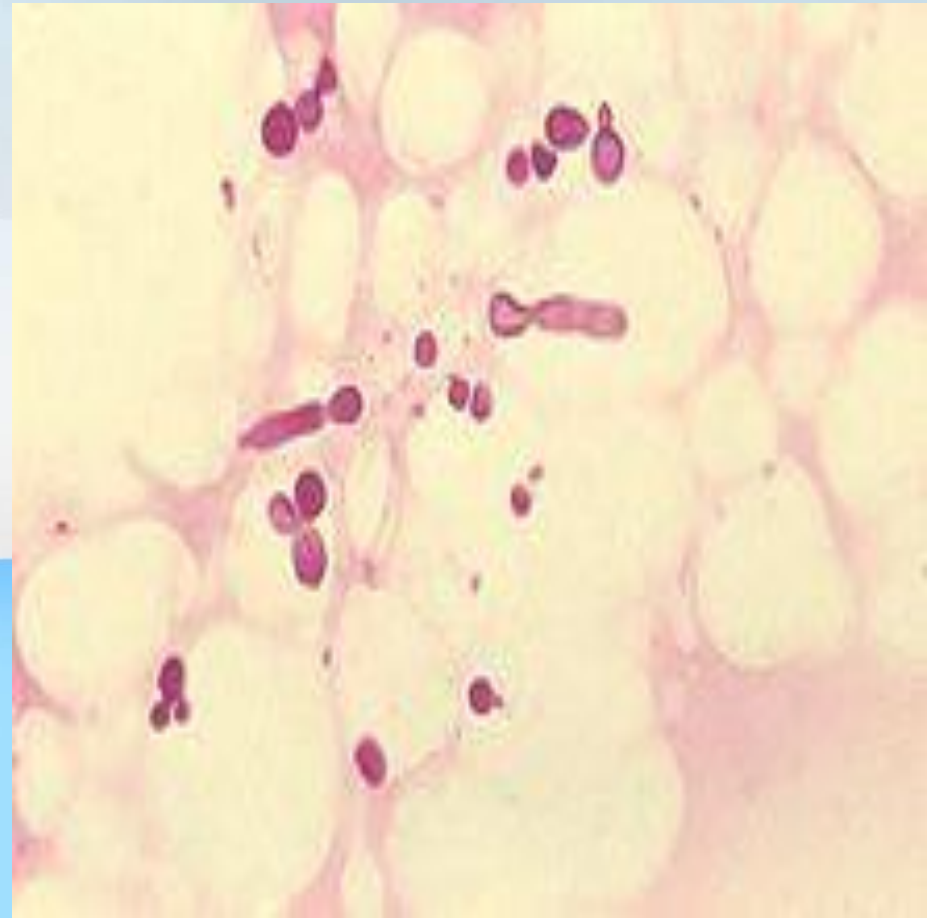
# Etiology:

- Caused by yeast flora called *Pityrosporum orbicularis*.



# Diagnosis:

- **Direct microscopic** examination of skin scrapping by KOH preparation.
- Diagnostic element is **short angular hyphae & yeast cells** (spaghetti & meat ball appearance).





## Treatment:

- Any topical **azole** is effective (e.g. Miconazole, Clotrimazole).
- If the infection is **recurrent** or widely **diffused** in the trunk: **Selenium blue Shampoo** (1% selenium sulfide).



# Candidal infection



# Source of infection:

- **Endogenous:** (autoinfection): Present as normal flora in oral cavity, GIT, female genital tract and skin which is the major source of infection.
- **Exogenous:** By sexual intercourse.



# Pathogenesis and virulence factors:

- **Adhesin:** Colonization on the mucosal surface.
- **Pseudohyphae:** inflammation and tissue destruction.
- **Protease enzyme:** invasion.
- **Endotoxin like:** Releasing of histamine leading to clinical reaction.
- **Resistance to intracellular killing of phagocytes.**



# Predisposing factors:

- **Extreme of age.**
- **Pregnancy** and **diabetes.**
- Prolonged use of **antibiotics, steroids** or **immunosuppressive drugs.**
- **Traumatic conditions** such as catheter or IV lines.



# Immunity:

- Cell mediated.
- Humoral immunity has a limited role.



# Causative agents:

❑ Candida albicans.

❑ Non-albicans

Candida:

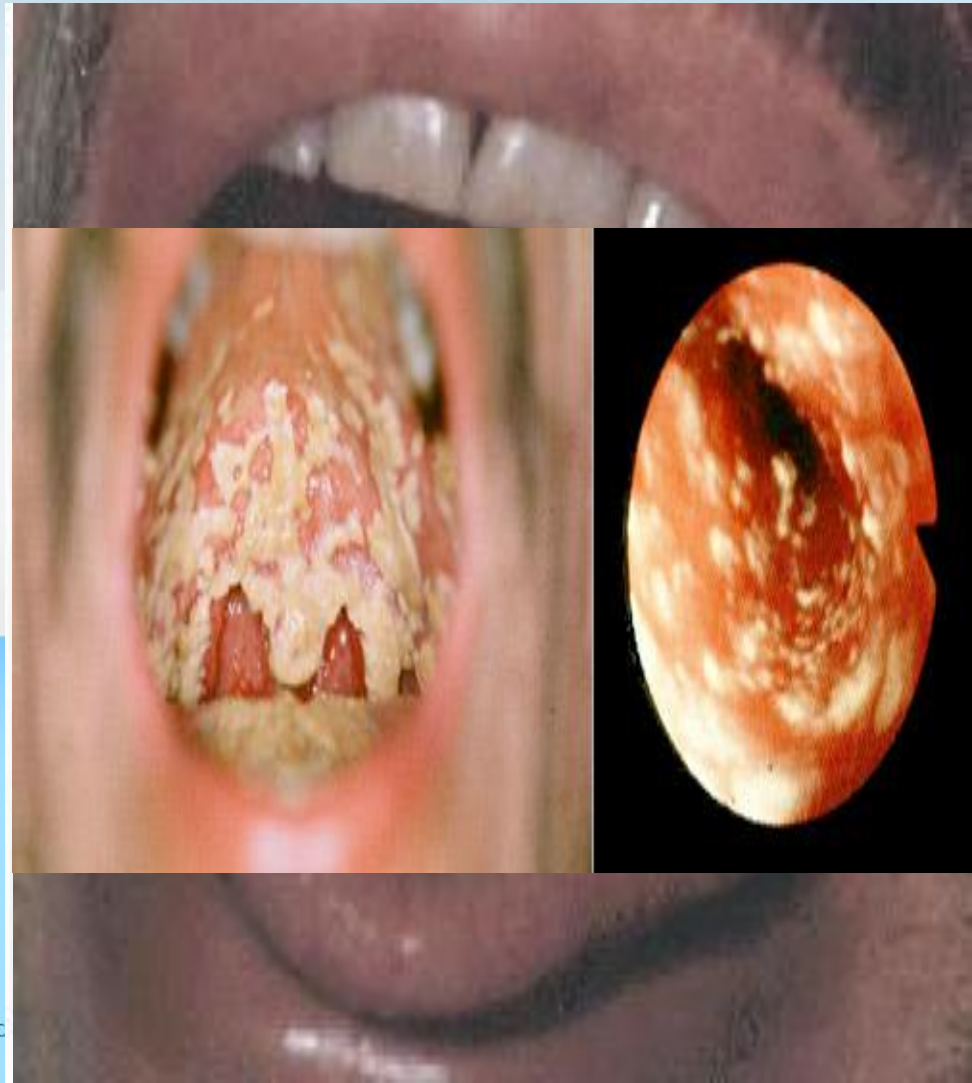
- Candida tropicalis.
- Candida glabrata (doesn't cause pseudohyphae).



# Clinical manifestations of diseases caused by Candida:

- Mucocutaneous  
infection:

- **Oral thrush:** In the mouth (cheesy covering layer), mouth angles: (stomatitis), at the lips (cheilitis).
- Vaginitis: White-milky discharge and itching.





# Clinical manifestations of diseases caused by

## Candida:

### Cutaneous infections:

- **Skin:** Napkin area in baby, axilla, groin, submammary folds, characterized by **Satellite lesions**, redness, itching and red follicles.
- **Nail:** Onychia and paronychia.



**Clinical manifestations of diseases caused**  
**by Candida:**  
**systemic infections:**

- Urinary tract infection.
- Endocarditis.
- Meningitis.
- Septicemia, fungemia.



# Laboratory diagnosis of Candidiasis:



## A. Direct:

### 1. Microscopic examination:

- Unstained preparation or stained preparation (KOH) lactophenol-cotton blue stains.
- For detection of yeast cells and pseudohyphae.



## 2. Culture:

- **On SDA medium.**
- The suspected growth is identified by:
  - **Macroscopic appearance** of: the colonies after 24 – 48 hours are white, smooth, creamy and have characteristic yeast odour.



## 2. Culture:

- ❑ **Microscopic appearance:** Spherical or oval cells.
- Gram film shows Gram-positive yeast.
- ❑ **Microculture:** Rice agar tween plates for demonstration of chlamydo spores (in *C. albicans*).

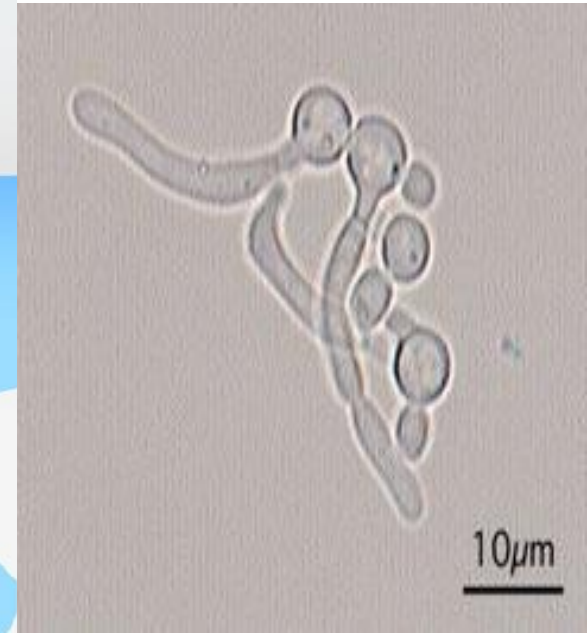
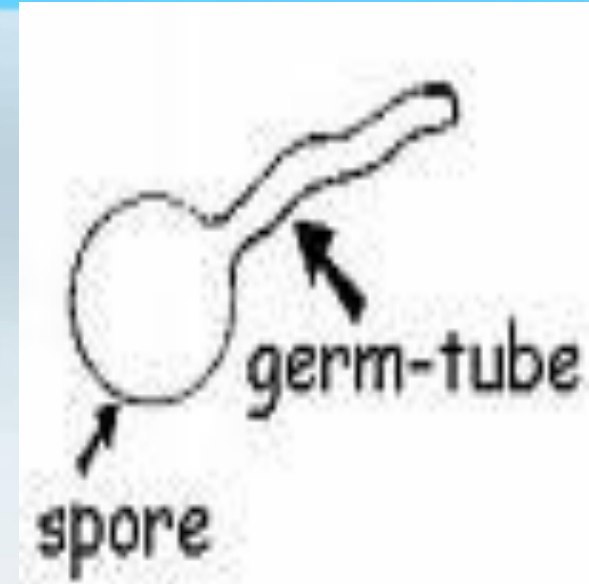
chlamydo spores



## 2. Culture:

❑ The suspected growth is identified by:

- **Biochemical reactions:** Sugar fermentation and assimilation for species differentiation.
- **Germ tube formation:** The ability of *Candida* to form filamentous growth after 2 – 4 hours when cultivated on human serum at 37°C (in *C. albicans*).
- **Chlamydoconidia formation** on Potato Carrot Bile (PCB) medium (in *C. albicans*).



## • **B. Indirect:**

- **1. Skin test:** No value in diagnosis.
- **2. Serological test:**
  - Ag detection: Important in immunocompromized patients.
- **3. Histopathology:**
  - Diagnostic element is Yeast cell & Pseudohyphae.
- **4. New tests for diagnosis:**
  - Detection of  $\beta$ -glucan antigen.
  - D-arabitol marker.
  - PCR.
  - Biofilm by scanning electron microscope.





# Treatment:

## 1. Superficial:

- Topical polyene, nystatin & amphotericin B.
- Topical imidazole as micnazole, clotrimazole.

## 2. Deep systemic infection:

- Amphotericin B.
- Fluconazole, Itraconazole.
- Caspofungin.
- Lipid preparation; liposomal Amphotericin B.



# II. Subcutaneous Mycosis



# A. Mycetoma (Madura foot = Maduromycosis)

## Definition:

- **Chronic granulomatous infection**, which produce tumour-like lesion and sinus tract formation, with the presence of **pus containing granules** affecting foot, SC tissue, fascia and bone.



# A. Mycetoma (Madura foot = Maduromycosis)

## Etiology:

### (1) Bacterial:

- **Actinomycotic** (Actinomadura, Nocardia, Streptomyces).
- The granules contain very fine delicate filaments.
- Usually the pyogenic abscess has one tract.



# A. Mycetoma

## Etiology:

### (2) Fungal (Eumycotic):

- Most saprophytic fungi can produce mycetoma e.g. Madurella.
- The granules contain large coarse septated hyphae.
- Usually the lesion has many sinuses.



# A. Mycetoma

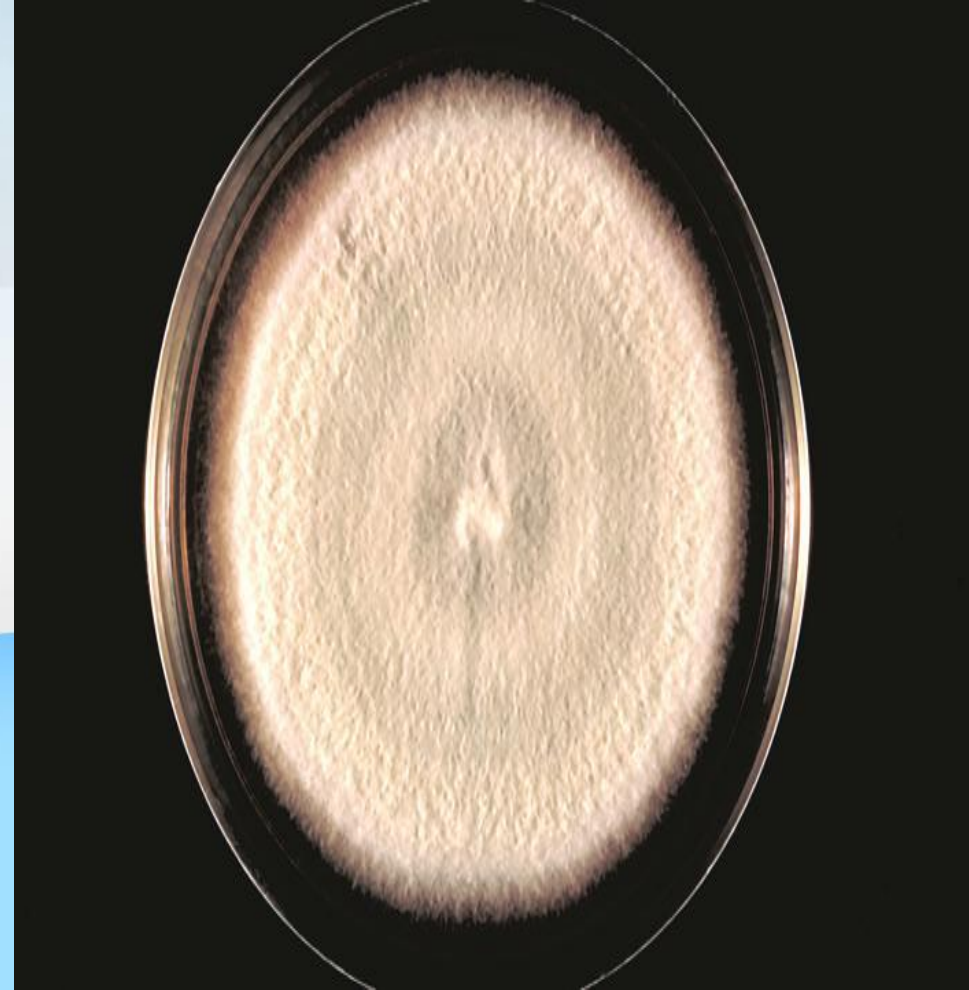
## Diagnosis:

**KOH preparation.**

If it is: Bacterial:

**Fine branching  
filament.**

Eumycotic: **Coarse  
septated hyphae.**



# A. Mycetoma

## Treatment:

### –Bacterial (Actinomycotic):

Antibacterial antibiotic.

### –Eumycotic:

❖ Amputation of the affected part.

❖ Antifungal agents can be used to prevent the amputation or to minimize it e.g. Itraconazole, Amphotericin B.



# B. Sporotrichosis





# B. Sporotrichosis

## Definition

- **Subcutaneous** fungal infection, characterized by mobile tender **nodules** forming **ulcer**, may be followed by **chronic** sporotrichosis in the form of **multiple** hard nodules along **lymphatic channels**.



## B. Sporotrichosis

### Etiology:

- Sporothrix schenckii (A dimorphic fungus).



# B. Sporotrichosis

## Diagnosis:

- 1. Sample: Exudates from lesion or LN aspirate.
- 2. Direct film:
  - In pus: Cigar shaped yeast.
  - In tissue: Asteroid body (fungus surrounded by eosinophilic infiltration).



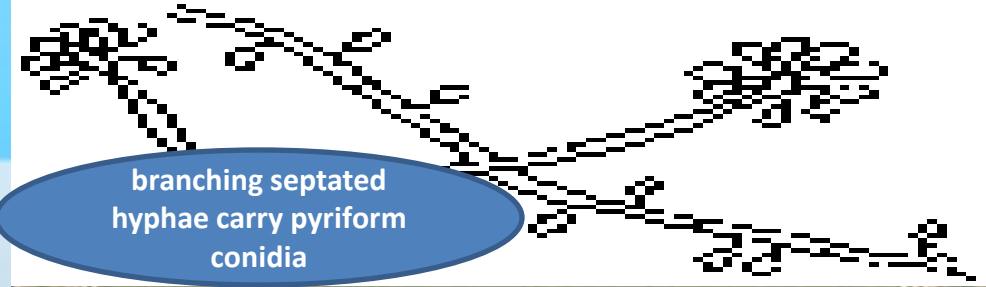
## B. Sporotrichosis

### Diagnosis:

#### 3. Culture:

- At 37 °C on enriched media giving **gray** colonies.
- Identified microscopically as Gram-positive **cigar shaped budding yeast**.
- At 27 °C on Sabouraud`s dextrose agar: **wrinkled white to black colonies**. Identified microscopically as **branching septated hyphae carry pyriform conidia**.

www.get



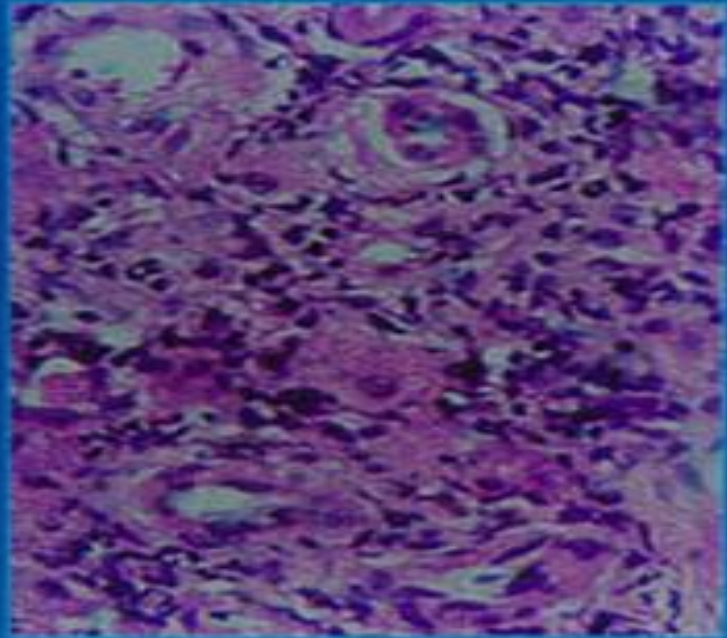
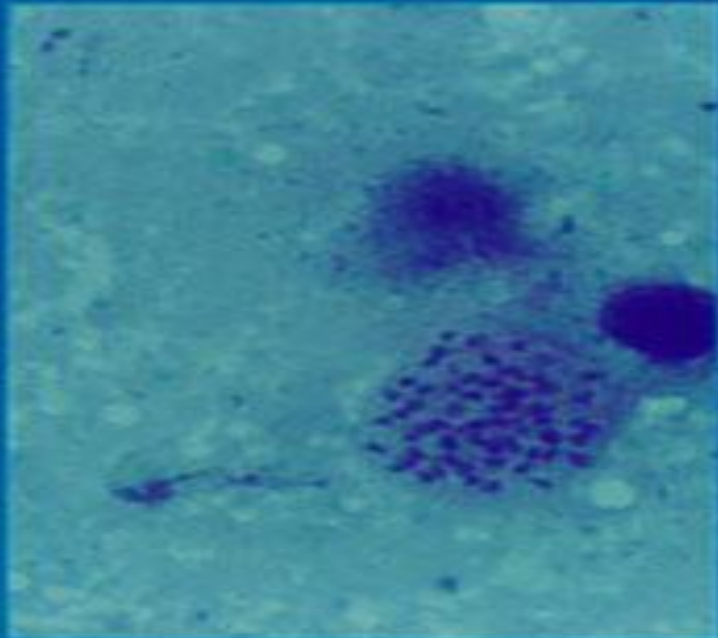
# III. Systemic Mycosis



# A. Histoplasma capsulatum

- The organism is **misnamed** because infection is not in the plasma cells but in the **macrophages**, and it is **not capsulated**.

Histoplasmosis



# A. Histoplasma capsulatum

## Microbiological characters:

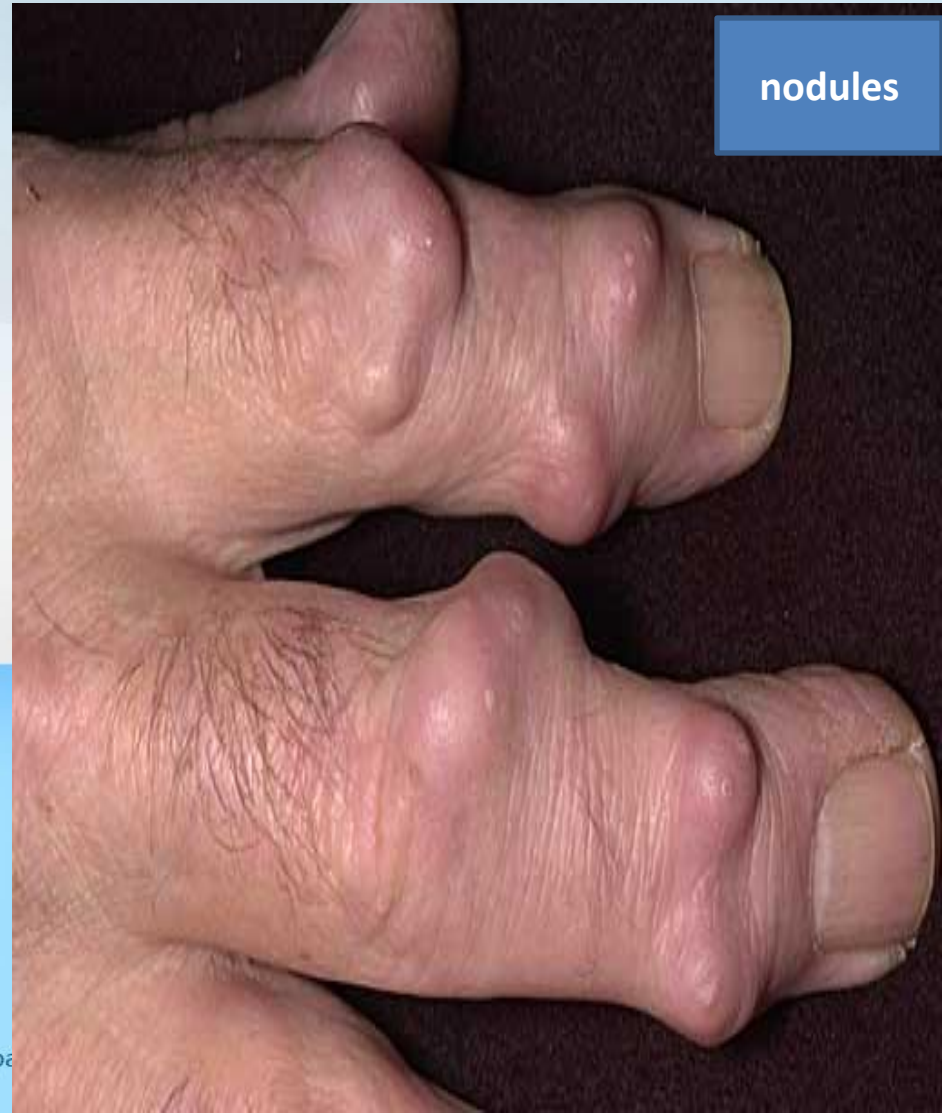
- **1. Dimorphic fungi:**
- i.e. two morphological forms:
- - **Yeast:** during infection and cultures at 37 °C
- - **Mould:** in cultures at 25 °C produce **microconidia** and **macroconidia** with **septated hyphae**.
- **2. Smallest yeast cell,** reproduce by budding.
- **3. Non-capsulated.**



# A. Histoplasma capsulatum

## Pathogenesis:

- Infection of **reticuloendothelial** system and grow intracellularly in phagocytic **macrophage**.
- Primary lesion is in the **lung, which leads to calcified nodule** and positive Histoplasmin **skin test**.
- **Immunity:** Cell-mediated immunity.





# A. Histoplasma capsulatum

## Epidemiology:

- Restricted geographical distribution.
- Source of infection: Soil containing bird or bat droppings.
- No case-to-case transmission.



# A. Histoplasma capsulatum

## Clinical picture:

Asymptomatic or respiratory infection giving flue like symptoms in immunocompetent patient.

Chronic lesion in lungs leads to tuberculosis like picture.

Disseminated infection: appears as febrile illness and enlargement of reticuloendothelial organs.



# A. Histoplasma capsulatum

## Diagnosis:

- **Direct examination** of sputum is useless as the organism present in few numbers.
- **Histological examination** of bone marrow to demonstrate intracellular yeast in macrophages.
- **Culture.**
- **Serology.**
- **Skin test:** Histoplasmin test; of epidemiological value only.



# A. *Histoplasma capsulatum*

## Treatment:

- Amphotericin B, followed by itraconazole.



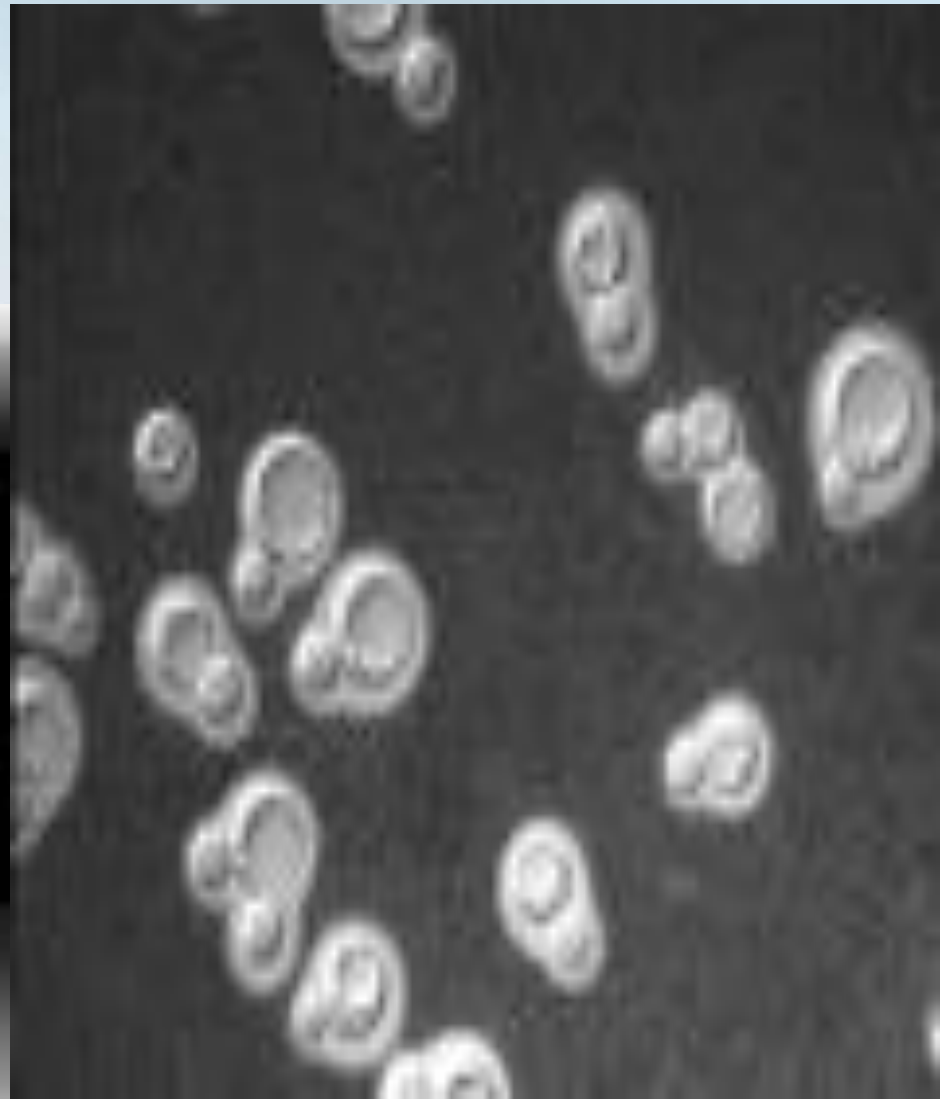
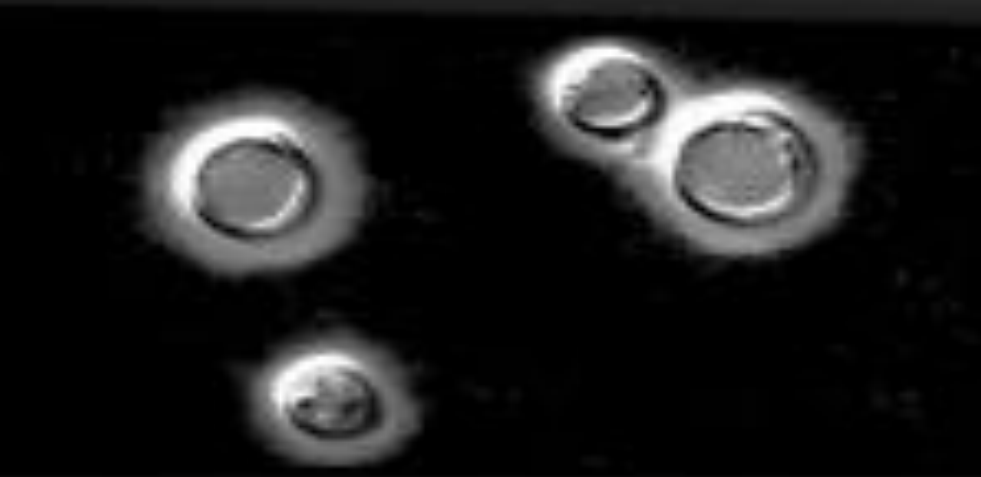
# B. *Cryptococcus neoformans*



## B. *Cryptococcus neoformans*

### Morphology:

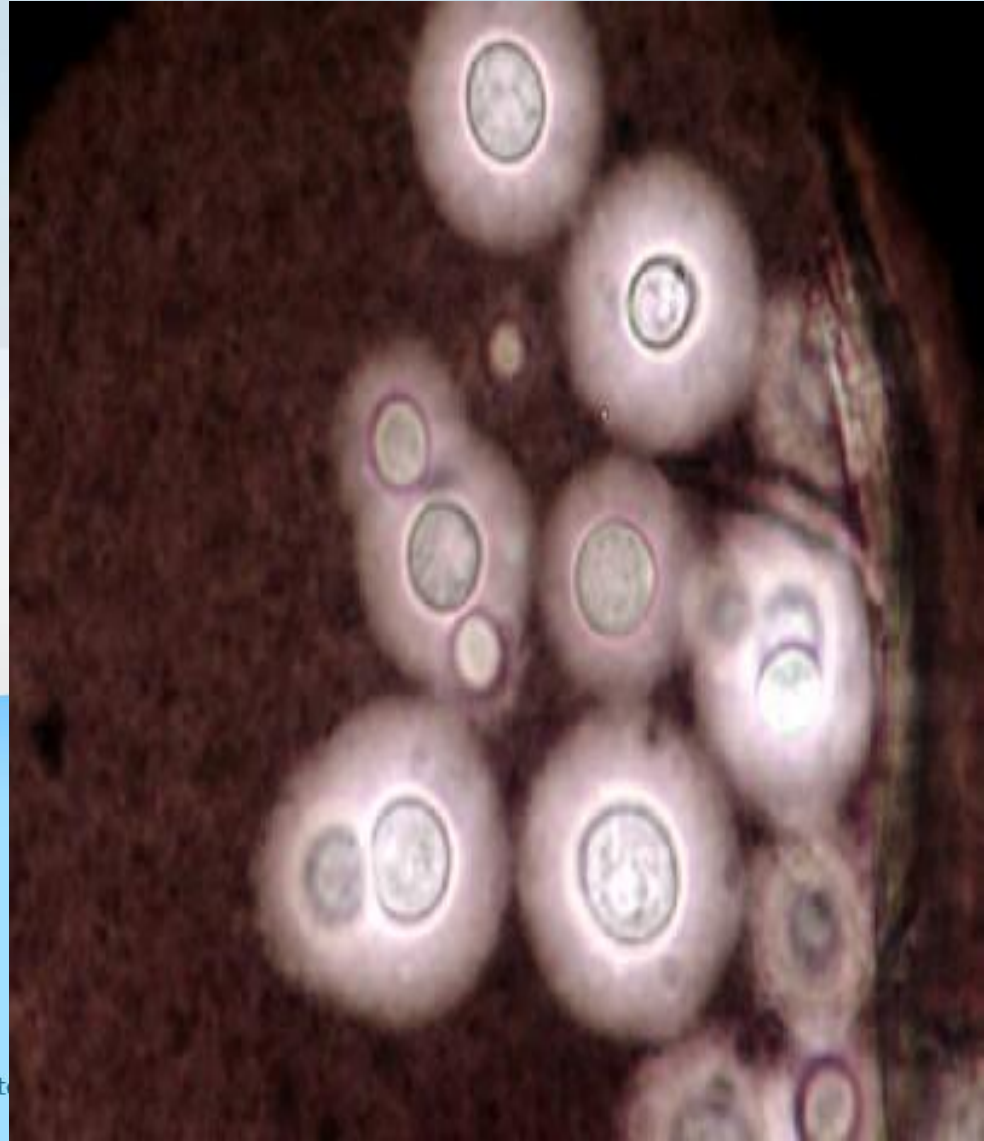
- **Capsulated** yeast.
- **Urease** positive.



# B. Cryptococcus neoformans

## Pathogenesis:

- Infection occurs by **inhalation of spores** of cryptococcus, which lead to pulmonary infection.
- Most infection **is unrecognized and self-limiting**.
- **Capsule** is the determinant of virulence.
- **Immunity:**
  - ✓ Cell-mediated immunity (in immunocompromized patients).
  - ✓ Humoral (opsonizing antibodies against capsule).



# B. Cryptococcus neoformans

## Epidemiology:

- One of the **opportunistic** mycosis.
- Source of infection: **Pigeon** or **birds** droppings and **soil** contaminated with them.
- Human infection mostly **by inhalation**.
- No case-to-case transmission.





# B. Cryptococcus neoformans

## Clinical picture:

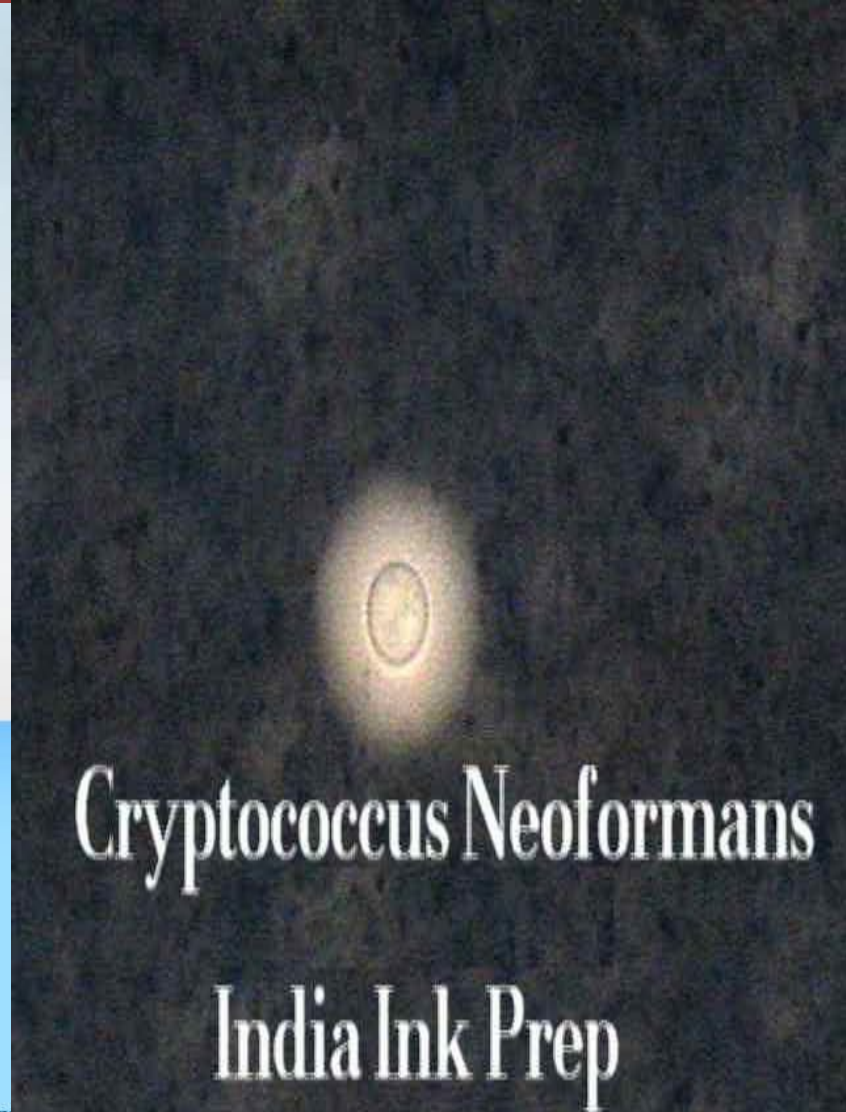
- **Pneumonia**, infection starts in the lung.
- Then followed by **meningitis**.
- In heavy infection disseminated **skin** and **bone** infections occur.



# B. Cryptococcus neoformans

## Diagnosis:

- *In Cryptococcus meningitis:*
- CSF:
  - ❖ Increased pressure of CSF.
  - ❖ Decreased glucose and increased protein.
  - ❖ Increased cell count > 100, mostly lymphocytes.
  - ❖ India ink preparation: yeast cell surrounded by huge capsule.
- **Culture** and identification of growth.
- Detection of Cryptococcus antigen in CSF by latex agglutination.



# B. Cryptococcus neoformans

## Treatment:

- **Amphotericin B**, followed by **fluconazole** (Can cross blood brain barrier).



# C. Aspergillosis



## C. Aspergillosis

- It is the fungal infection by *Aspergillus* spp.
- It is a **saprophytic** organism.
- Produces **spores** carried by air.
- Aspergillosis can be produced in immunocompromized patients as well as immunocompetent persons.



# C. Aspergillosis

Causes:

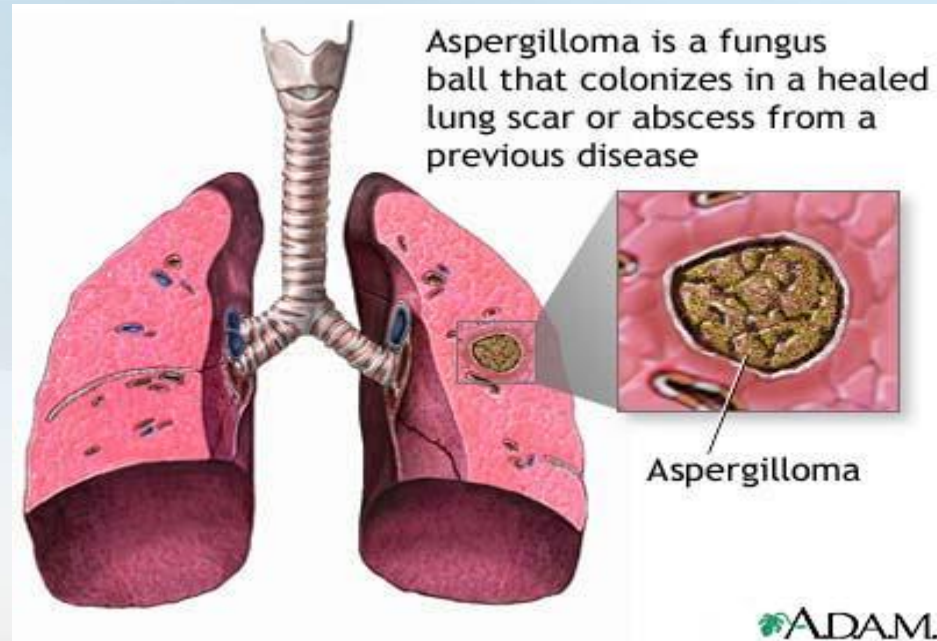
- *A. fumigatus*, *A. niger*, and *A. flavus*.



# C. Aspergillosis

## Clinical forms:

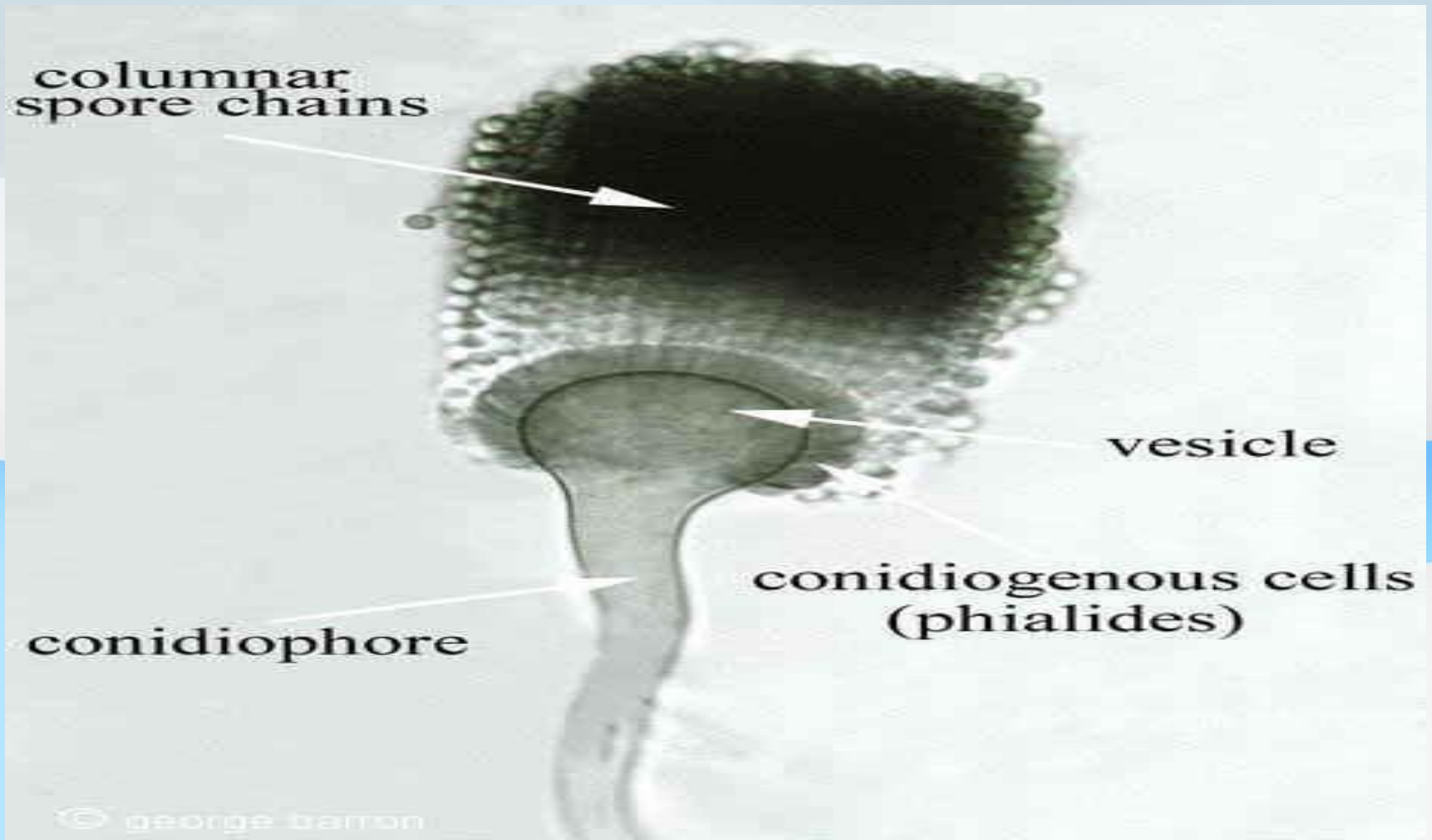
- **Granulomatous lesion:** Chronic infection in the lung.
- **Fungal ball in old TB cavity (Aspergilloma):** mass formation in the lung, which may be mistaken with bronchogenic carcinoma.  
**Allergic type:** Asthma and farmer's lung.
- **Acute pneumonia** in immunocompromized patients.



# C. Aspergillosis

## Mode of transmission:

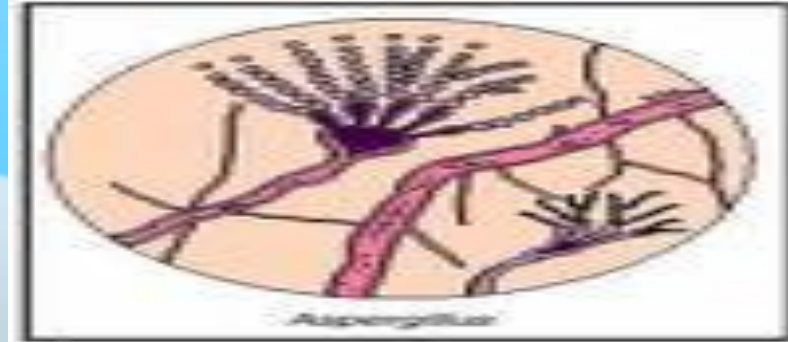
- Environmentally by inhalation of spores.



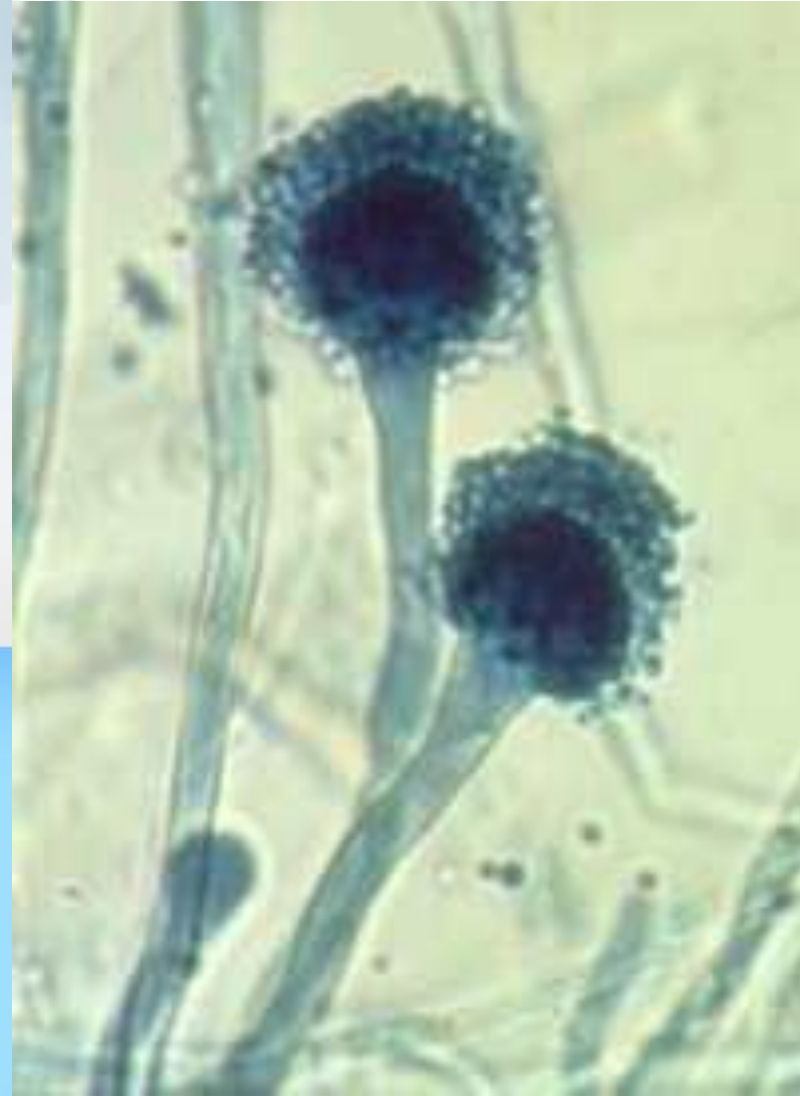


# C. Aspergillosis

## Diagnosis:



- **KOH preparation of sputum:** Hyaline, septated hyphae or dichotomously branched hyphae.
- **Culture on SDA** and examination of growth by:
  - **Macroscopically:** Black (*A. niger*), green-orange or white colonies.
  - **Microscopically:** septated filaments with characteristic aspergillar heads.



# C. Aspergillosis

## Treatment:

- **Antifungal drugs** in disseminated lesions like: Amphotericin B, Itraconazole, Voriconazole.
- **Surgical removal of fungal ball.**



# Mycotoxigenesis



# Mycotoxins

- Fungi can generate substances with direct toxicity for humans and animals.
- Ingestion of these toxins leads to mycotoxicosis, the severity depends on the **amount** and **type** of ingested mycotoxin.



# Mycotoxicosis

## General criteria of mycotoxicosis:

- Non-transmissible.
- No effect of antifungal drugs.
- Seasonal.
- Associated with food ingestion.
- The degree of toxicity depends on many host factors.
- Examination of the food reveals fungal growth.



# Mycotoxinos

## Types of mycotoxins:

- There is large number of mycotoxins according to the fungus producing it. e.g. **aflatoxin, ochratoxin, amatoxin and phallotoxin.**



# Mycotoxicosis

## Aflatoxin:

- Produced by **Aspergillus flavus**.
- Effects of aflatoxins on man:
  - Initiate **liver cell carcinoma** (Its metabolite binds DNA preventing base pairing leading to frame shift mutation).
  - **Immunosuppression.**
  - **Gastroenteritis.**



A winter landscape featuring a bright sun in the upper left corner, casting rays across a clear blue sky. The foreground and middle ground are dominated by snow-covered evergreen trees, their branches heavily laden with white snow. In the background, a valley stretches out, showing rolling hills and a small body of water, all under a soft, hazy light. The overall scene is serene and peaceful.

*thank you*