

# **Biological diversity of fungi of medical interest**

# Definition of the kingdom of fungi

→ Fungi are neither plants nor animals → Constitute a distinct unique kingdom

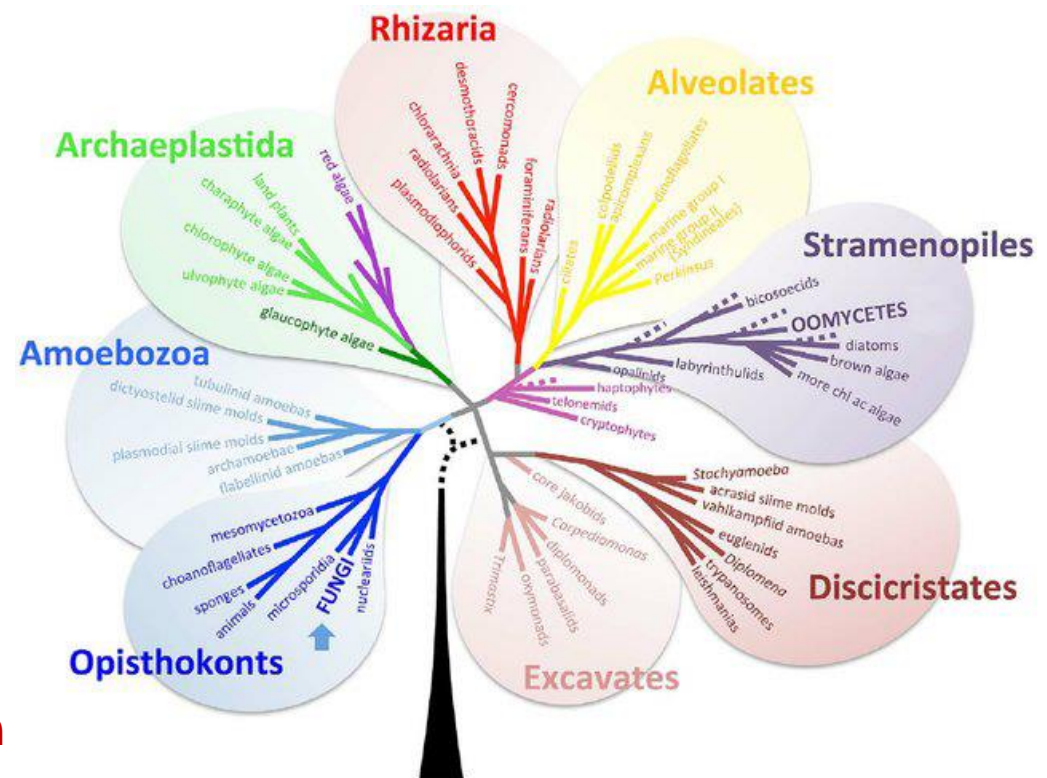
→ Uni- or multicellular **eukaryotes** (with individualized nucleus within the cell)

→ **Heterotroph**: no photosynthesis

→ Sexual and asexual reproduction with the production of **spores**

→ Thallophyte: constituted of filaments (thallus)

→ Contain a **cell wall** made up of **chitin**



# Definitions and fungal terminology

<b>Taxonomic rank</b>	<b>Termination</b>
Division	-MYCOTA
Sub-division	-MYCOTINA
Class	-MYCETES
Sub-class	-MYCETIDAE
Order	-ALES
Sub-order	-INEAE
Family	-ACEAE
Sub-family	-OIDEAE
Tribe	-EAE

# Many ways to classify fungi

→ More than 100,000 known pathogenic species

→ Classification using:

→ Mode of nutrition

Or

→ Pathologies

Or

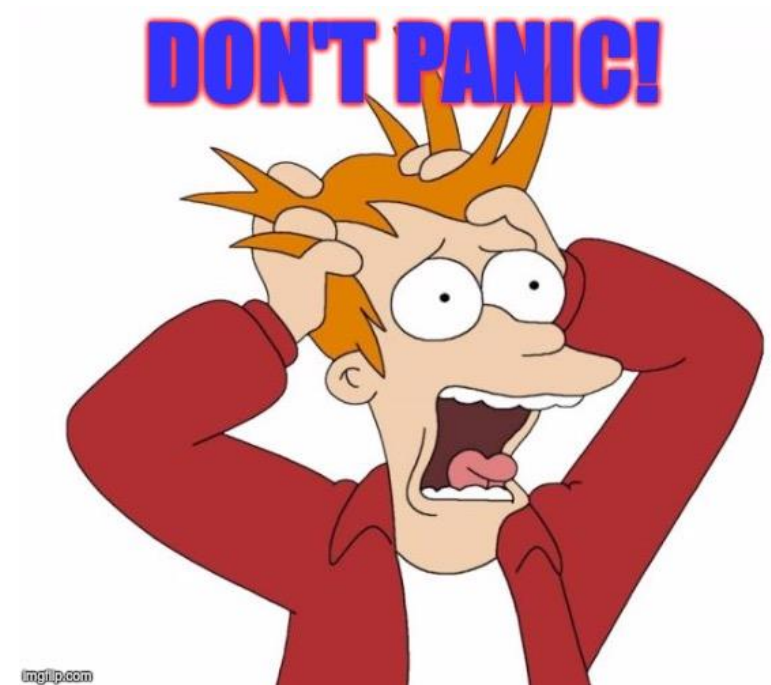
→ Mode of reproduction

Or

→ DNA sequence

Or

→ Cellular organization



# Classification by modes of nutrition

## → Symbionts

## → Saprobes (most pathogenic fungi)

→ Opportunistic saprobes: yeast, molds

→ Pathogenic saprobes: dimorphic fungi

→ yeast phase: endemic mycoses

→ mycelial phase: saprophytic in nature

## → Parasites




→ Dermatophytes

**Fungi of medical importance**

# Classification by pathologies

Infections	Example of pathologies	Fungi
CUTANEOUS	Tinea versicolor	<i>Malassezia furfur</i>
	Dermatophytosis	<i>Microsporum</i> <i>Trichophyton</i> <i>Epidermophyton</i>
SUB-CUTANEOUS	Candidiasis (skin, nails, mucosa)	<i>Candida albicans, ...</i>
	Sporotrichosis Chromoblastomycosis Mycetome	<i>Sporothrix schenckii</i> <i>Fonsecaea pedrosoi</i> <i>Madurella</i>
INVASIVE	Histoplasmosis Blastomycosis Coccidioidomycosis Paracoccidioidomycosis	<b><u>Pathogens:</u></b> <i>Histoplasma capsulatum</i> <i>Blastomyces dermatitidis</i> <i>Coccidioides sp.</i> <i>Paracoccidioides brasiliensis</i>
	Candidiasis Cryptococcosis Aspergillosis Mucormycosis	<b><u>Opportunists:</u></b> <i>Candida albicans, ...</i> <i>Cryptococcus neoformans</i> <i>Aspergillus fumigatus</i> <i>Mucor, Rhizopus, ...</i>
DIVERSE CLINICAL FORMS	Hyalohyphomycosis Phaeohyphomycosis	<i>Fusarium, Verticillium...</i> <i>Alternaria, Cladophialophoria</i>

# Classification by modes of reproduction

Reproduction	Division	Class	Genus
Sexual	<b>ZYGOMYCOTA</b>  (zygospores; coenocytic hyphae)	<b>ZYGOMYCETES</b> (Ex: order of mucorales)	<i>Rhizopus, Mucor...</i>
	<b>ASCOMYCOTA</b>  (spores contained in ascus; septate hyphae)	<b>ASCOMYCETES</b>	<i>Trichophyton</i> (dermatophytes) <i>Histoplasma, Blastomyces...</i>
	<b>BASIDIOMYCOTA</b>  (spores supported by basides; septate hyphae)	<b>BASIDIOMYCETES</b>	<i>Filobasidiella neoformans</i> (= sexual stage of <i>Cryptococcus neoformans</i> )
Asexual	<b>DEUTEROMYCOTA</b> (Imperfect fungi)  <b>Outdated classification</b>	<b>BLASTOMYCETES</b>	<i>Candida, Cryptococcus, Rhodotorula, Trichosporon...</i>
		<b>HYPHOMYCETES:</b> Moniliaceae	<i>Aspergillus, Coccidioides, Fusarium...</i>
		Dematiaceae	<i>Alternaria, Cladosporium...</i>
		<b>COELOMYCETES</b>	<i>Phoma</i>

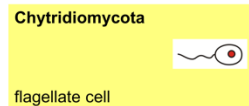
# Phylogenetic classification of fungi

→ **Molecular phylogenetics** (DNA sequence):  
« one fungus, one name », regardless their anamorph or teleomorph stage

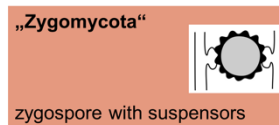
→ **Suppression of the Deuteromycota division**

→ **5 major groups:**

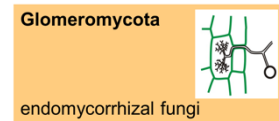
→ **CHYTRIDIOMYCOTA**: coenocytic hyphae;  
flagellated spores (Chytrids)



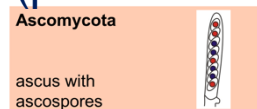
→ **ZYGOMYCOTA (\*)**: coenocytic hyphae;  
unflagellated spores (Bread molds)



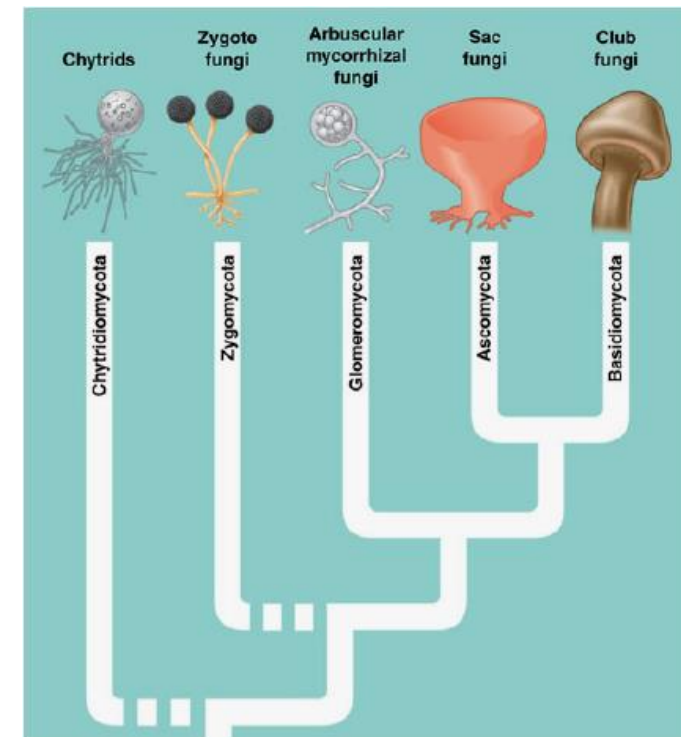
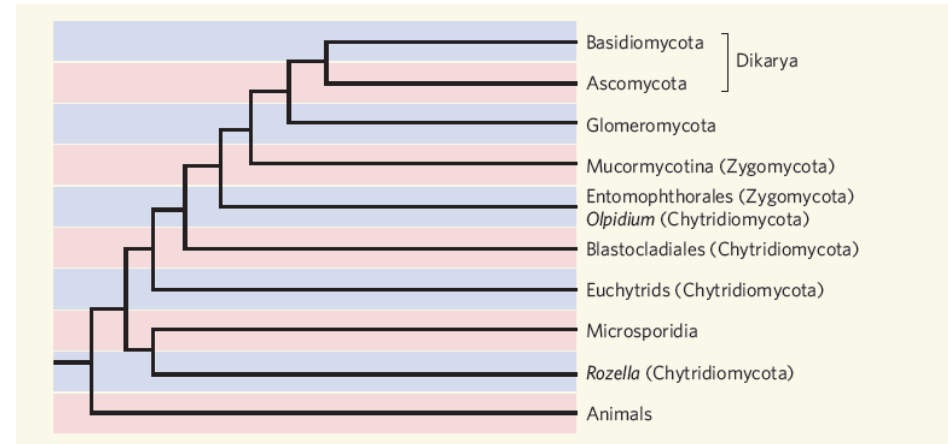
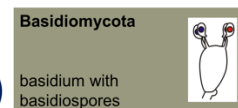
→ **GLOMEROMYCOTA**: coenocytic hyphae;  
unflagellated spores (Endomycorrhizae)



→ **ASCOMYCOTA (\*)**: septate hyphae; unflagellated spores; dikarya (part of the life cycle with paired nuclei)  
(« Sac fungi »)



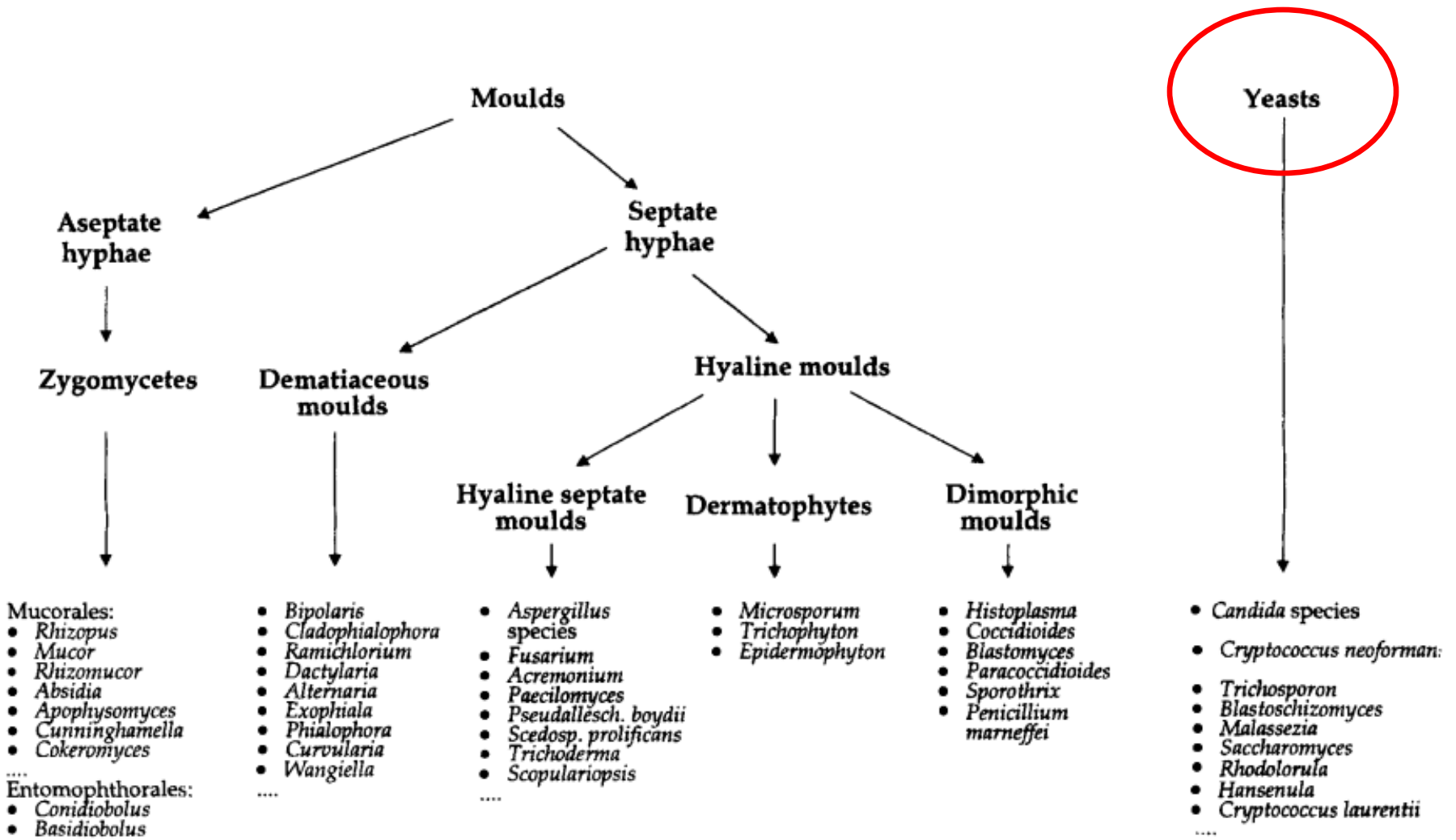
→ **BASIDIOMYCOTA (\*)**: septate hyphae, unflagellated spores; dikarya (« Club fungi »)



**\*: Fungi of medical importance**



# Classification as a function of cellular organization



# Definitions and fungal terminology

**Hyphae:** individual filaments, structural units of fungi

→ **Septate:** Divided by cross walls

→ **Coenocytic:** Lacking cross walls

**Mycelium:** mass of hyphae

**Thallus:** vegetative body of a fungus

**Mold:** filamentous (multicellular) fungus

**Dematiaceous mold:** mold with pigmented hyphae

**Yeast:** unicellular fungus

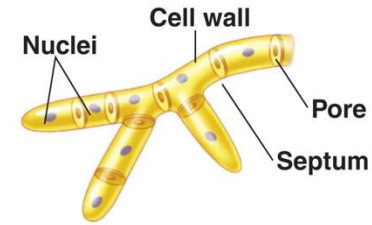
**Germ tube:** hyphal extension arising from a yeast cell, with no constriction at the point of origin, no nucleus. Important for the identification of *Candida albicans*.

**Pseudohyphae:** chain of incomplete budding yeast cells marked by constrictions rather than septa at the junctions (ex: *C. albicans*)

**Dimorphic fungi:** group of fungi characterized by two forms:

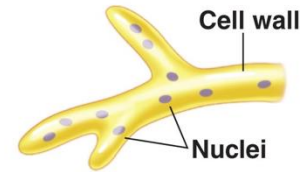
→ Mold with septate hyphae in their natural reservoir (e.g. soil) or when incubated at 25°C.

→ Yeast in animal/human tissues or when incubated at 37°C.



(a) Septate hypha

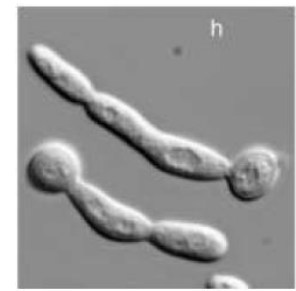
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(b) Coenocytic hypha



Germ tube



Pseudohyphae

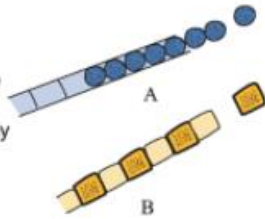
Wightman  
et al., 2004,  
J. Cell Biol.

# Definitions and fungal terminology

## Asexual spores

### Arthroconidia (arthrospores)

Spores which are formed and subsequently released during the process of hyphal fragmentation. Spores may be formed successively as in dermatophytes (A), or with intervening empty cells as in *Coccidioides immitis* (B)



### Macroconidia

Large multi-celled conidia which are produced by dermatophytes in culture



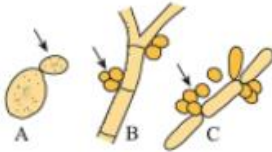
### Microconidia

Small conidia which are produced by certain dermatophytes



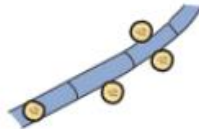
### Blastoconidia (blastospores)

Conidia (arrows) which are produced by budding, as in *Candida albicans*, from a mother cell (A), from hyphae (B) or from pseudohyphae (C)



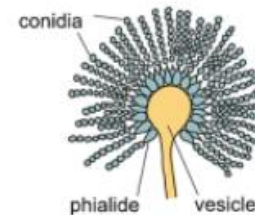
### Chlamydoconidia (chlamydospores)

Thick-walled, resistant spores which contain storage products. These structures are formed by some fungi in unfavourable environmental conditions



### Phialoconidia

Conidia produced from phialides. The phialides of *Aspergillus* species arise from a vesicle



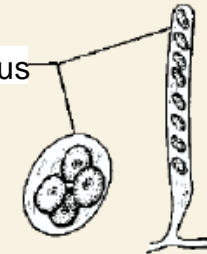
### Sporangiospores

Spores (arrow), formed by zygomycetes such as *Rhizopus* species, are released when a mature sporangium ruptures



## Sexual spores

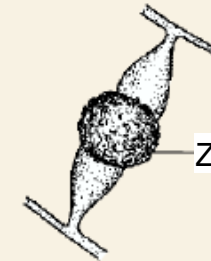
Ascus



Basidium



Zygosporangium



## Ascospore:

sexual spore formed in a sac-like cell named **ascus**  
→ often 8 spores formed (**Ascomycetes**)

## Basidiospore:

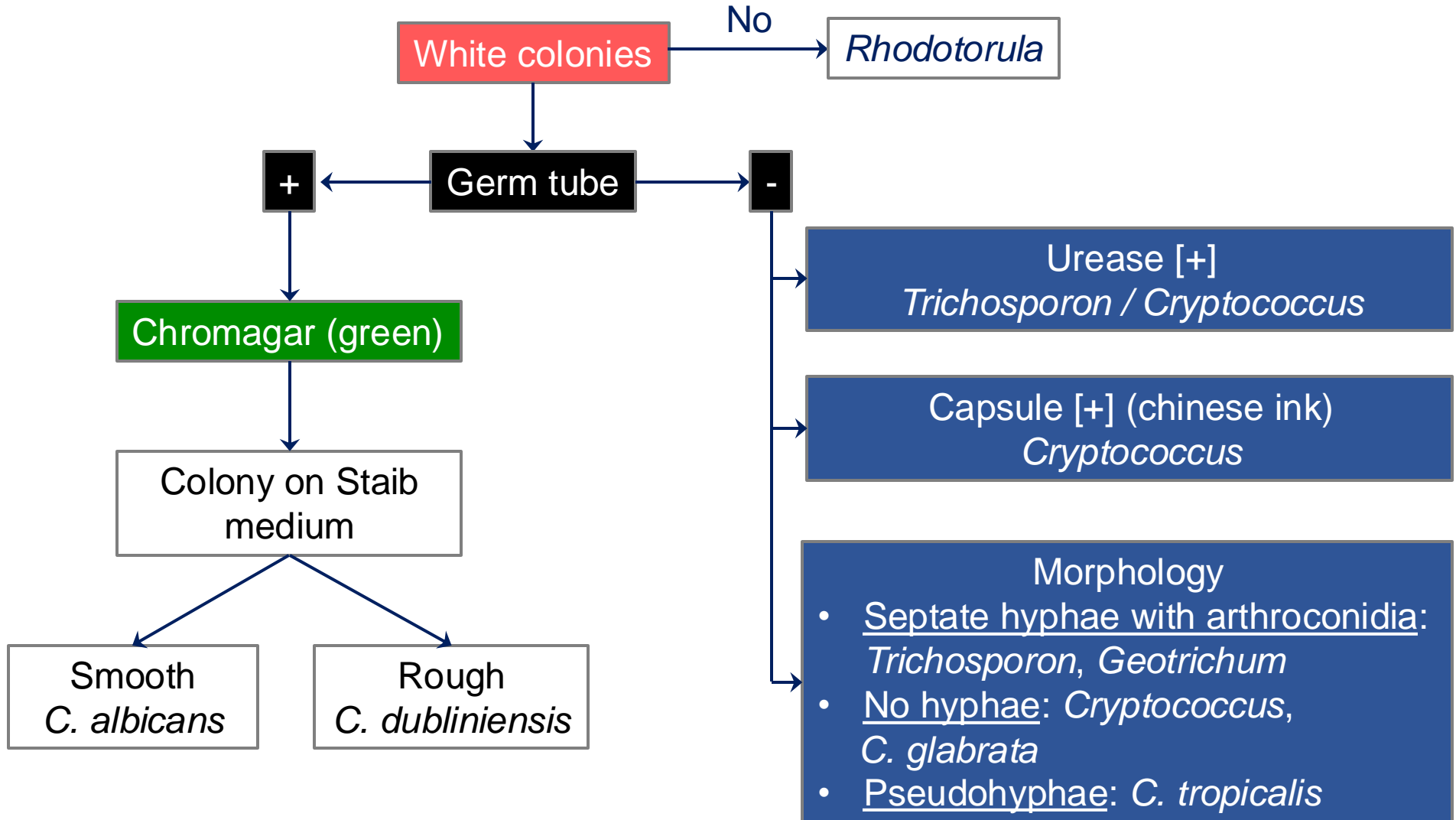
sexual spore produced on a specialized club-shaped structure, called a **basidium** (**Basidiomycetes**)

## Zygospore:

sexual spore formed in a **zygosporangium** after the fusion of mycelia from different mating types (**Zygomycetes**)

# Yeasts

## Scheme of yeast identification by conventional method



# Yeasts

- **Candida species**

- **Ascomycota**

- **Saprobe** in the digestive, respiratory or vaginal mucosa

- Can cause **candidiasis** when it multiplies uncontrollably (**risk factors:** weak immune system, age, overuse of antibiotics, poor hygiene, hot weather, overweight...)

- Oral (thrush)

- Vaginal

- Cutaneous (skin / nails)

- Invasive (disseminated) infection



# Yeasts

- **Candida species**

Ovoid cells → **Blastoconidia** with multipolar budding

→ **Pseudohyphae** (except for *C. glabrata*)

→ Chromogenic colour change on Chromagar

→ Green : *C. albicans*

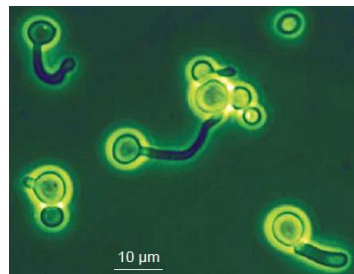
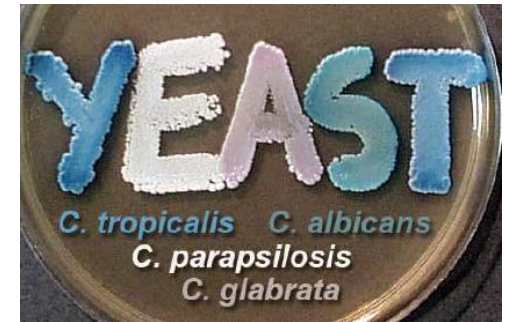
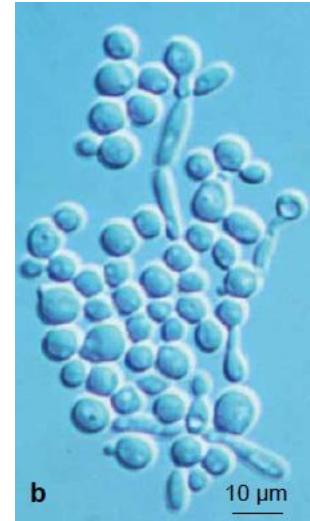
→ Blue: *C. tropicalis*

→ White: *C. parapsilosis*

→ Purple: *C. glabrata*

→ ...

→ **Germ tube** for *C. albicans* and *C. dubliniensis*





# Yeasts

- ***Cryptococcus neoformans***

- **Basidiomycota**

- Ubiquitous, **saprophyte** in the environment

- Ovoid cells → **Blastoconidia** with unipolar budding

- **Presence of a capsule**; no pseudohyphae, no germ tube

- **Production of melanin** (virulence factor)

- Contamination by inhalation of spores

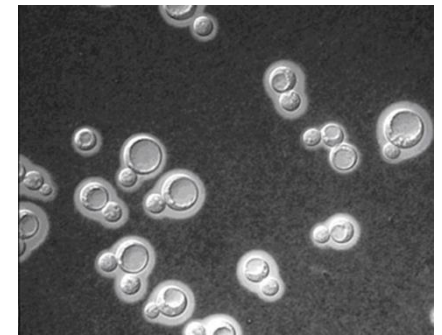
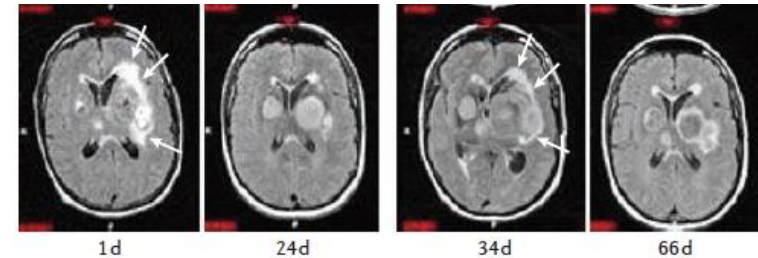
- Can cause **cryptococcosis** mostly in immunocompromised patients, rarely in immunocompetents

- **Invasive Fungal Infection (IFI):**

- Development in the lungs → hematogenous dissemination → cutaneous lesions, CNS tropism → meningoencephalitis

- Common and highly lethal in HIV patients

- 1 million new cases each year; >600 000 deaths / year



# Yeasts

- *Trichosporon sp.*

- **Basidiomycota**

- **Saprophytic** on soil and some species on human skin

- Development of **hyaline septate hyphae** → fragment into oval or rectangular **arthroconidia**

- Formation of polymorphic blastoconidia

- Urease [+]; growth on medium containing cycloheximide

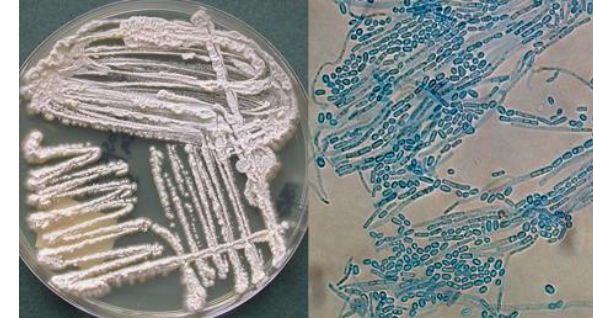
- Can cause:

- **White piedra** (infection of the hair shaft)

- **IFI in immunocompromised patients**

- Fulminant and widespread: liver, spleen, lungs, gastrointestinal tract

- Associated with leukaemia, organ transplantation, myeloma, aplastic anaemia, lymphoma, solid tumour, AIDS



White piedra



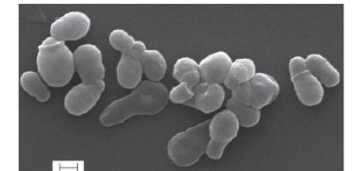
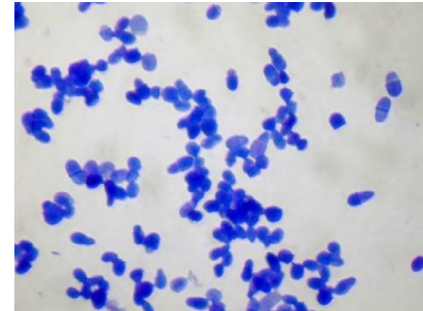
# Yeasts

- *Malassezia sp.*

- Basidiomycota

- **Saprobe** on human skin; lipophilic and keratophilic yeast

- Ovoid to ellipsoidal cells → Blastoconidia with **unipolar budding**, hyphae



- Responsible of several frequent, superficial and recurring skin diseases  
(**risk factors**: oily skin, hot weather, humidity, sudation, pregnancy, hypercorticicism, immunodepression...) → not contagious

- Hypopigmentation / hyperpigmentation without inflammation (**pityriasis versicolor**)

- Red, scaly, greasy and inflamed skin in areas rich in sebaceous glands (**seborrheic dermatitis**)

- Cutaneous inflammation with itchy, red, swollen and cracked skin in the bends of arms or legs, face and neck (**atopic eczema**) or with rash, itching and pustules on the trunk (**folliculitis**)

# Yeasts

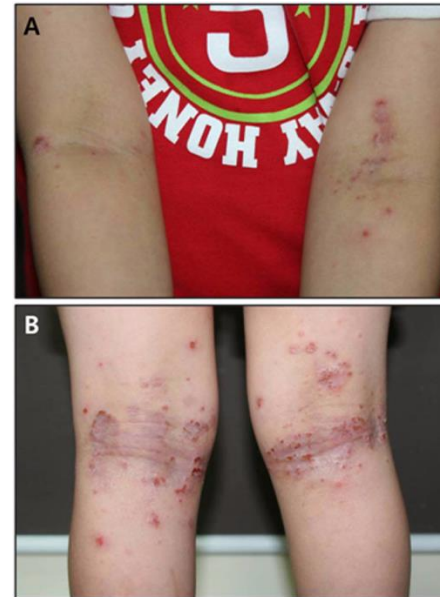
- *Malassezia sp.*



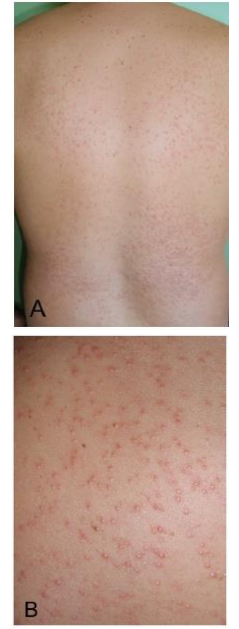
**Pityriasis versicolor**



**Seborrheic dermatitis**



**Atopic eczema**



**Folliculitis**

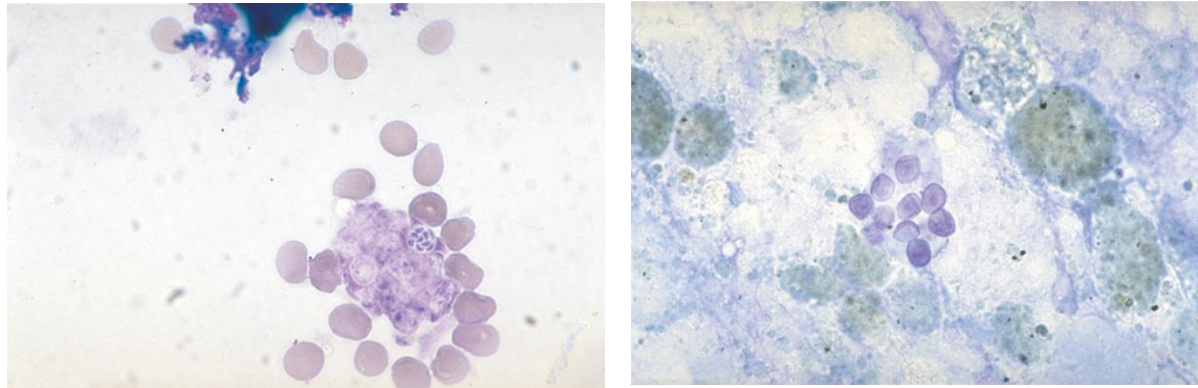
# Yeasts

- *Pneumocystis jirovecii*

→ Previously classified in protozoa (similar life cycle)

→ Classification in the **kingdom of fungi**: molecular biology / trilamellar cell wall rich in chitin → **Ascomycota**

→ **Ubiquitous parasitic fungus specific to human**; no environmental species of *Pneumocystis* characterized



Broncho-alveolar lavages containing *P. jirovecii* cysts

# Yeasts

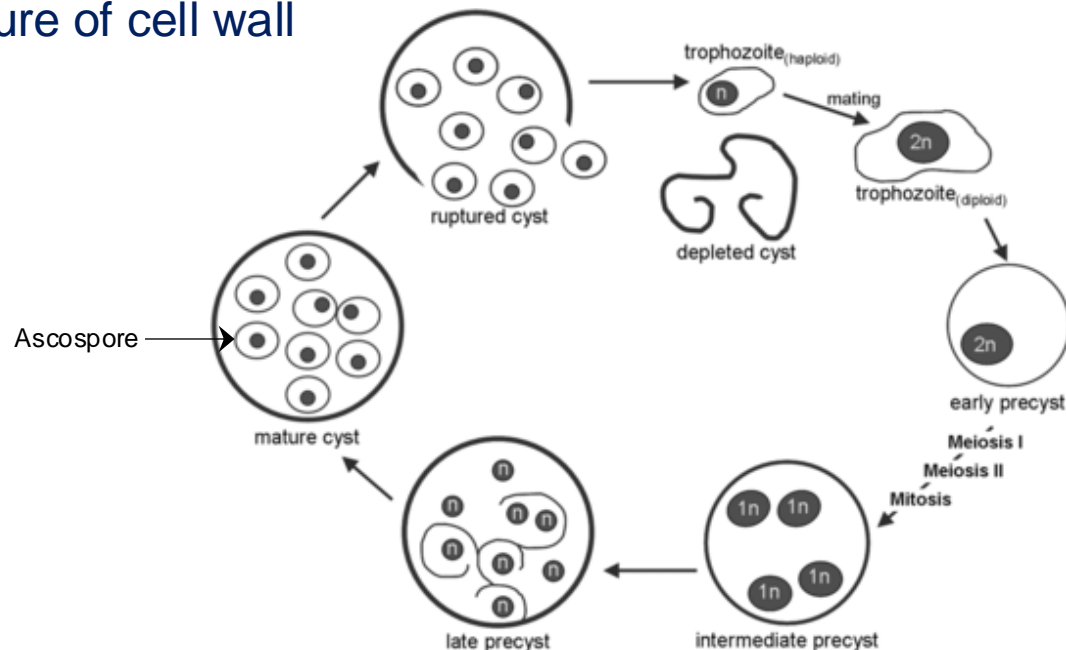
- *Pneumocystis jirovecii*

→ Life cycle not completely elucidated; 3 life stages:

→ **Mature cyst:** thick-walled structure containing 8 ascospores which are further released and differentiate in trophozoites

→ **Trophozoite:** thin-walled mononucleated vegetative form with amoeboid shape, will differentiate in precyst

→ **Precyst:** mononucleated first, become multinucleated in 3 steps (early, intermediate and late) as a function of the number of nuclei (1 to 8) and the structure of cell wall



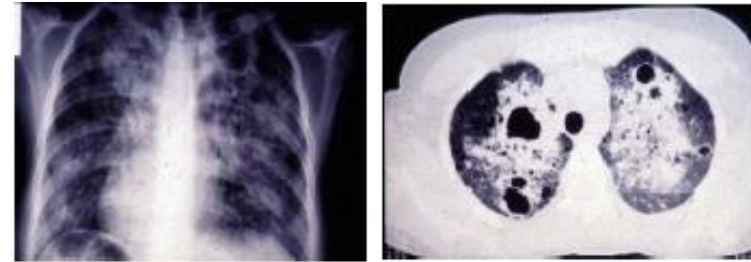
# Yeasts

- ***Pneumocystis jirovecii***

→ Can cause **pneumocystosis**, mostly in immunocompromised patients

→ **Airborne transmission** presumably

→ **Pulmonary form: severe pneumonia** with fever, dry cough, dyspnea with increasing intensity



→ **Extra-pulmonary forms** (rare): due to dissemination of *P. jirovecii*  
→ main localization in the spleen, but can also reach the liver, bone marrow, pleura, ganglia, thyroid, retina...

# Yeasts

- *Rhodotorula sp.*

- **Basidiomycota**

- Skin and environmental **saprobe** with low virulence

- **Orange/red colonies** on Sabouraud

- Ovoid or ellipsoid cells → Blastoconidia with multipolar budding

- *Rhodotorula* infections generally associated with immunosuppression:

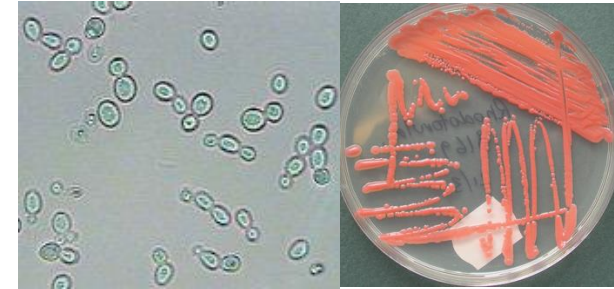
- Most common risk factor: presence of a central venous catheter

- **Fungemia** (fungi in the blood) → fever

- Possibility to cause cerebral, cutaneous, ocular or peritoneal infections

- 215 cases reported since 1960

- Incidence between 0.5 % to 2.3 % in USA and Europe





# Yeasts

- *Geotrichum sp.*

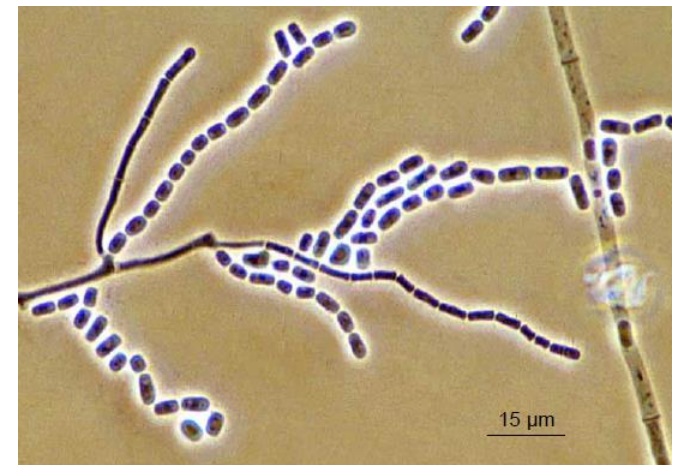
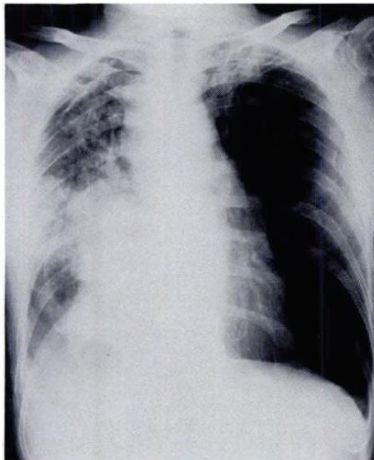
- Ascomycota

- **Saprobe** on soil, air, water, milk, plant tissues or human digestive tract

- Development of **hyaline septate hyphae** → fragment into oval or rectangular **arthroconidia**

- **No formation of blastoconidia**

- Can cause infections of the **bronchopulmonary** (more frequently), bronchial, oral, vaginal, gastrointestinal and skin **epithelia**, mostly in immunocompromised patients



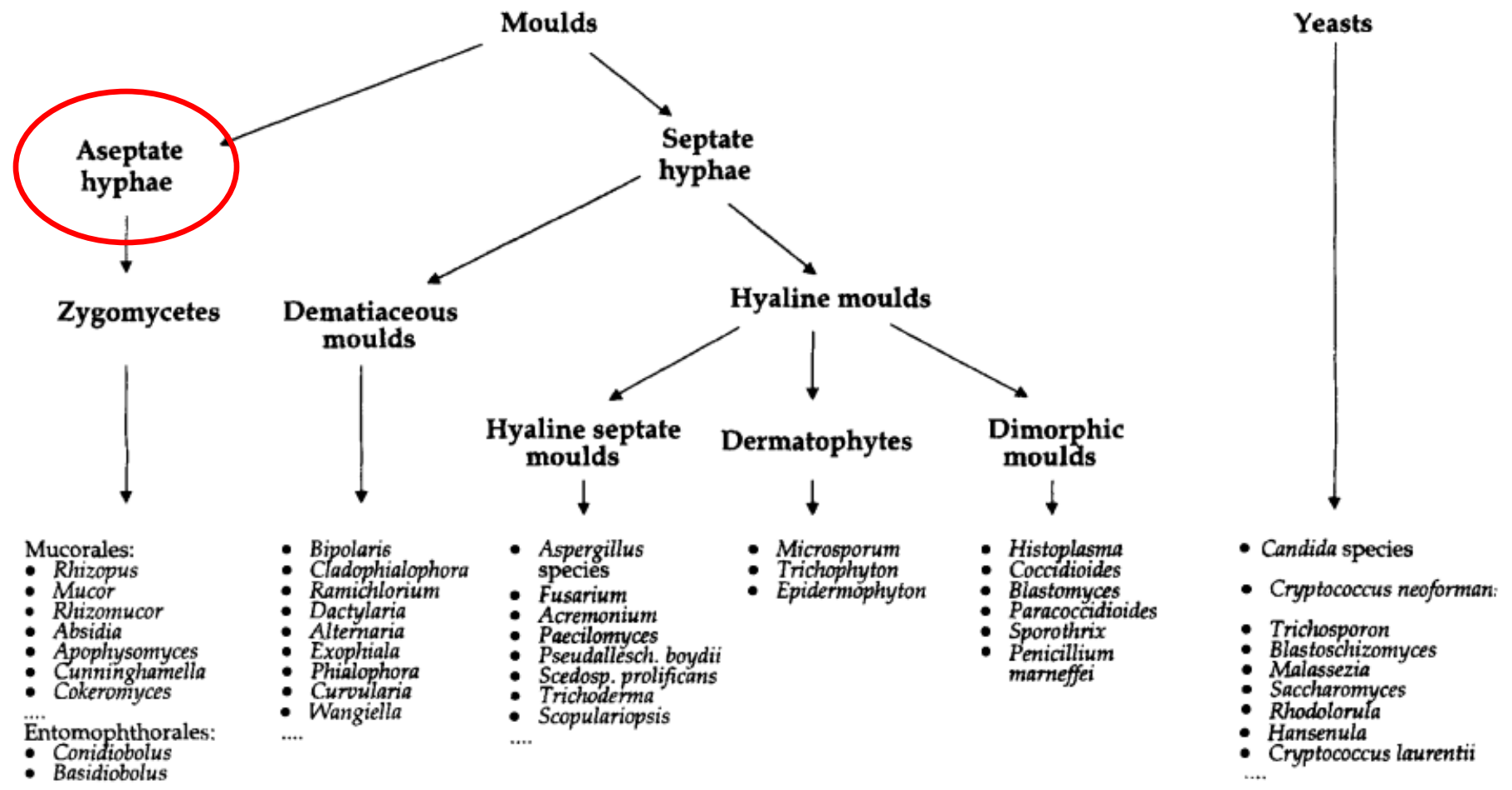
# Yeasts

## Morphological and physiological characteristics of yeasts of medical importance

	Morphology						Fermentation					Other		
Species	Pseudohyphae	True hyphae	Chlamydoconidia	Germ tube	Capsule	Arthroconidia	Glucose	Maltose	Sucrose	Galactose	Trehalose	Urease	Growth at 37°C	Growth at 40°C
<i>Candida albicans</i>	+	+	+	+	-	-	+	+	+/-	+/-	+/-	-	+	+
<i>Candida dubliniensis</i>	+	+	+	+	-	-	+	+	-	+/-	?	-	+	+
<i>Candida glabrata</i>	-	-	-	-	-	-	+	-	-	-	+	-	+	+
<i>Candida krusei</i>	+	-	-	-	-	-	+	-	-	-	-	-	+	+
<i>Candida parapsilosis</i>	+	-	-	-	-	-	+	-	-	-	-	-	+	+/-
<i>Candida tropicalis</i>	+	+/-	-	-	-	-	+	+	+	+	+	-	+	+
<i>Cryptococcus neoformans</i>	-	-	-	-	+	-	-	-	-	-	-	+	+	-
<i>Geotrichum capitulum</i>	-	+	-	-	-	+	-	-	-	-	-	-	+	+
<i>Geotrichum candidum</i>	-	+	-	-	-	+	-	-	-	-	-	-	+/-	-
<i>Rhodotorula mucilaginosa</i>	-	-	-	-	+/-	-	-	-	-	-	-	+	+/-	-
<i>Malassezia furfur</i>	+	+	-	-	-	-	-	-	-	-	-	+	+	+
<i>Trichosporon sp.</i>	-	+	-	-	-	+	-	-	-	-	-	+	+/-	+/-



# Classification as a function of cellular organization



# Aseptate molds

→ **Former Division of Zygomycota**

→ Composed of 10 Orders, with 2 of medical importance:  
**Mucorales** and **Entomophthorales**

→ **Entomophthorales**: mostly insect pathogenic fungi

→ Members of the genera *Basidiobolus* and *Conidiobolus*  
occasionally pathogenic to humans

→ Production of a single conidium forcibly ejected upon maturation

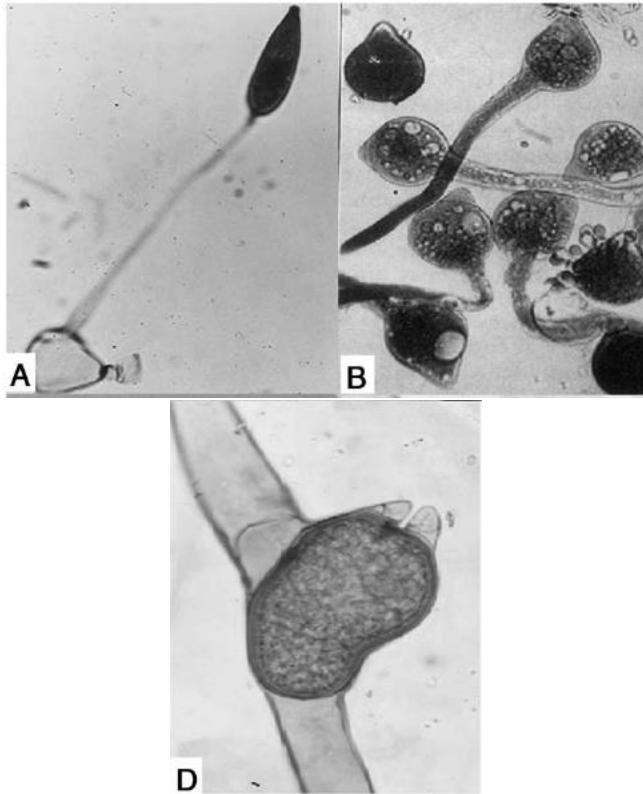
→ Waxy folded and compact mycelium

→ **Mucorales: most clinically important**

→ Production of numerous spores in a sporangium

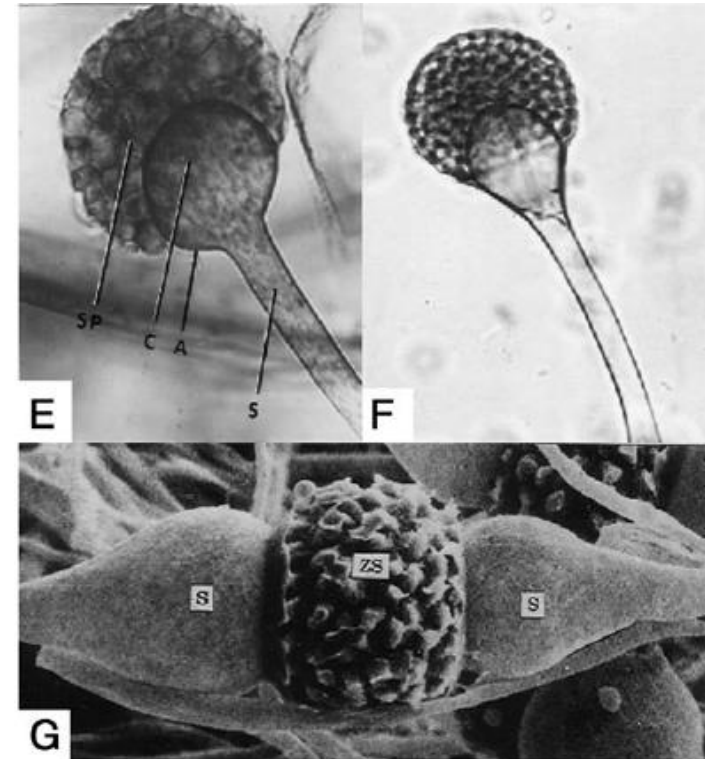
→ Floccose aerial mycelium

# Aseptate molds



## Morphology of conidia and zygospores in Entomophotrales

- A) Conidium of *Basidiobolus raranum*
- B) Conidia of *Conidiobolus incongruus*
- D) Zygospore of *Basidiobolus raranum*



## Morphology of conidia and zygospores in Mucorales

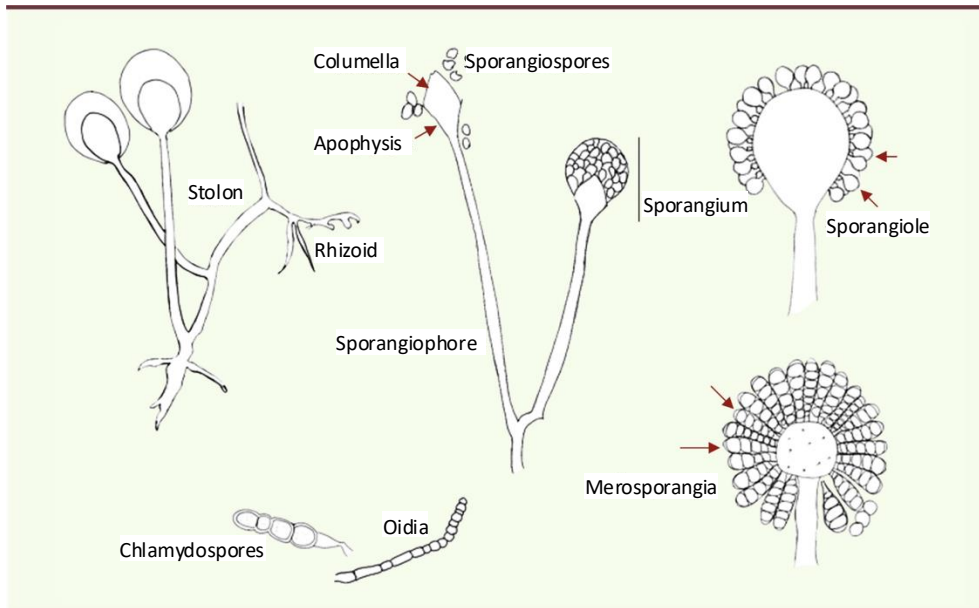
- E) Sporangial structure of *Rhizopus* species
- F) Sporangium of *Lichtheimia corymbifera*
- G) Electron microscopy of zygospore of *Rhizopus* species

# Aseptate molds

- **Mucorales**

→ Includes genera such as *Rhizopus*, *Mucor*, *Rhizomucor*, *Lichtheimia*, *Cunninghamella*, *Saksenaea*, *Cokeromyces*, *Apophysomyces*, *Syncephalastrum*, *Mortierella*...

→ **Most frequent:** *Rhizopus*, *Mucor*, *Rhizomucor* and *Lichtheimia*



**Morphological structures in Mucorales**

**Sporangiospores:** asexual spores produced inside a closed structure named **sporangium**

**Sporangiophore:** specialized hyphae supporting the **sporangium** and emanating from a branched system named **rhizoid** anchoring the sporangiophore in a substrate

**Stolon:** hyphae connecting the rhizoids

**Columella:** Dome shaped structure located at the tip of the **sporangium**

**Apophysis:** bulge of the **sporangium**, below the **columella**

**Sporangiole:** uni-to-few spored **sporangium**

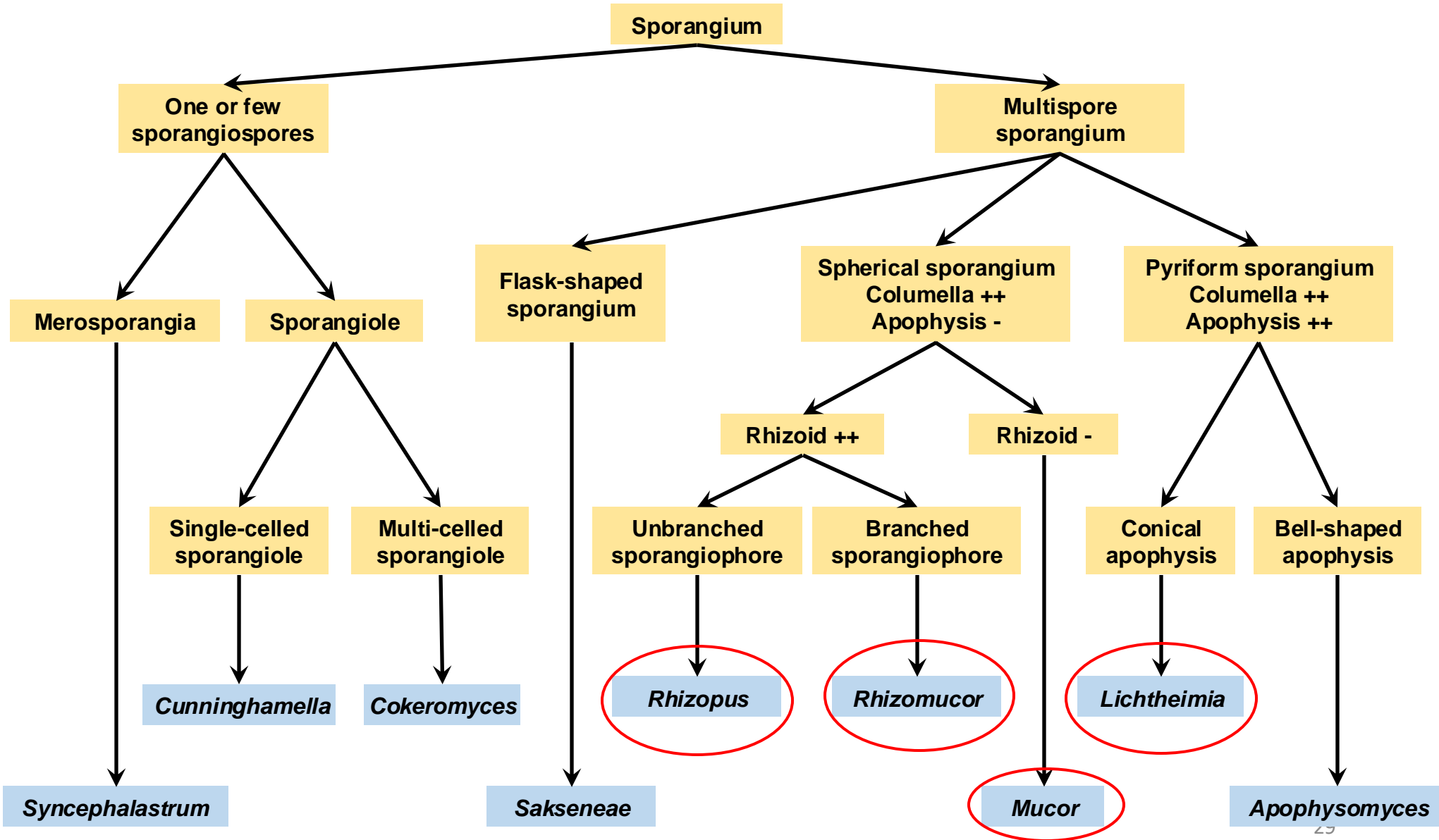
**Merosporangium:** elongated **sporangiole** with uniseriate spores

**Chlamydospore:** thick walled conidium formed within a vegetative hyphae

**Oidia:** intercalary or terminal arthrospore located through or at the end of the hyphae

# Aseptate molds

- Mucorales



# Aseptate molds

- **Mucorales**

→ ***Rhizopus sp.*** (most common *R. oryzae*) → most Mucorales cases (≈ 70% of the cases) followed by *Mucor*, *Lichtheimia* and *Rhizomucor*

→ **Ubiquitous saprobes** in soils, decaying food

→ Spherical sporangium; columella +; apophysis -; rhizoid +; unbranched sporangiophores

→ **Transmission** via the respiratory, percutaneous, or oral routes

→ **Risk factors:** diabete, immunosuppression

→ **Can cause:**

→ **Rhinocerebral infections**

→ Angioinvasion, thrombosis, infarction, necrosis

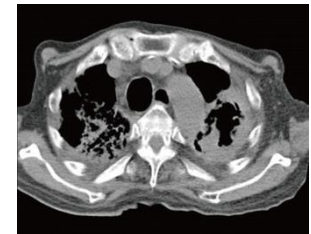
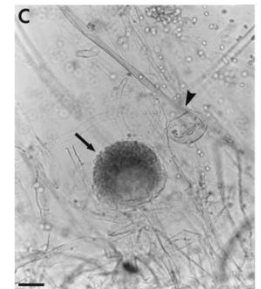
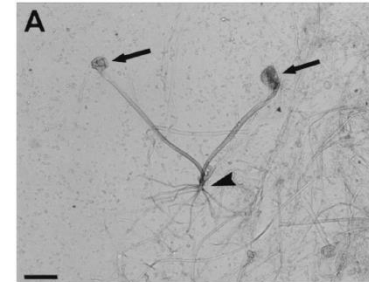
→ **Pulmonary infections**

→ Thickened alveolar walls, granulomas, interstitial infiltrate

→ **Cutaneous infections** (ex: contaminated bandages)

→ Vesicular pustules, gangrene, necrotizing fasciitis

→ **Gastric ulcers, peritonitis**



(Desoubeaux et al., Ann. Dermatol. Venerol., 2014; Kim et al., Ann. Lab. Med., 2014; Reboli and Kim, Clinical Advisor, 2019; Ribes et al., Clin. Microbiol. Rev., 2000; Ibrahim et al., Clin. Infect. Dis., 2012)



# Aseptate molds

- **Mucorales**

- *Mucor sp.*

- **Ubiquitous saprobes** in nature (soil, air, dust, food, ...)

- Spherical sporangium; columella +; apophysis -; rhizoid -

- **Transmission** via the respiratory, percutaneous, or oral routes

- **Risk factor:** immunosuppression

- **Can cause:**

- Rhinocerebral infections

- Pulmonary infections

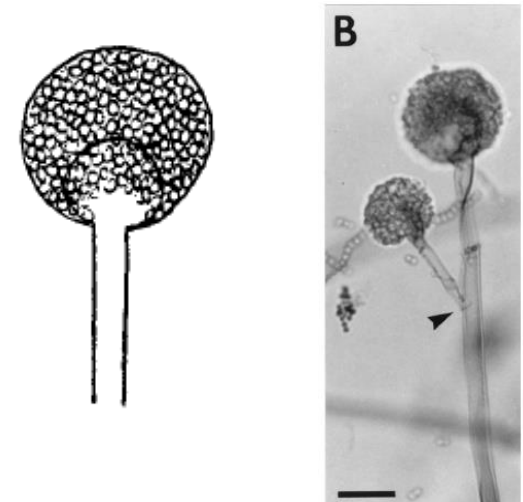
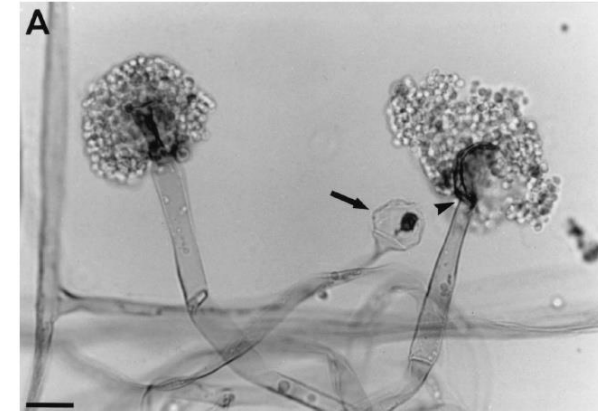
- Gastrointestinal infections

Predominantly in immunocompromised

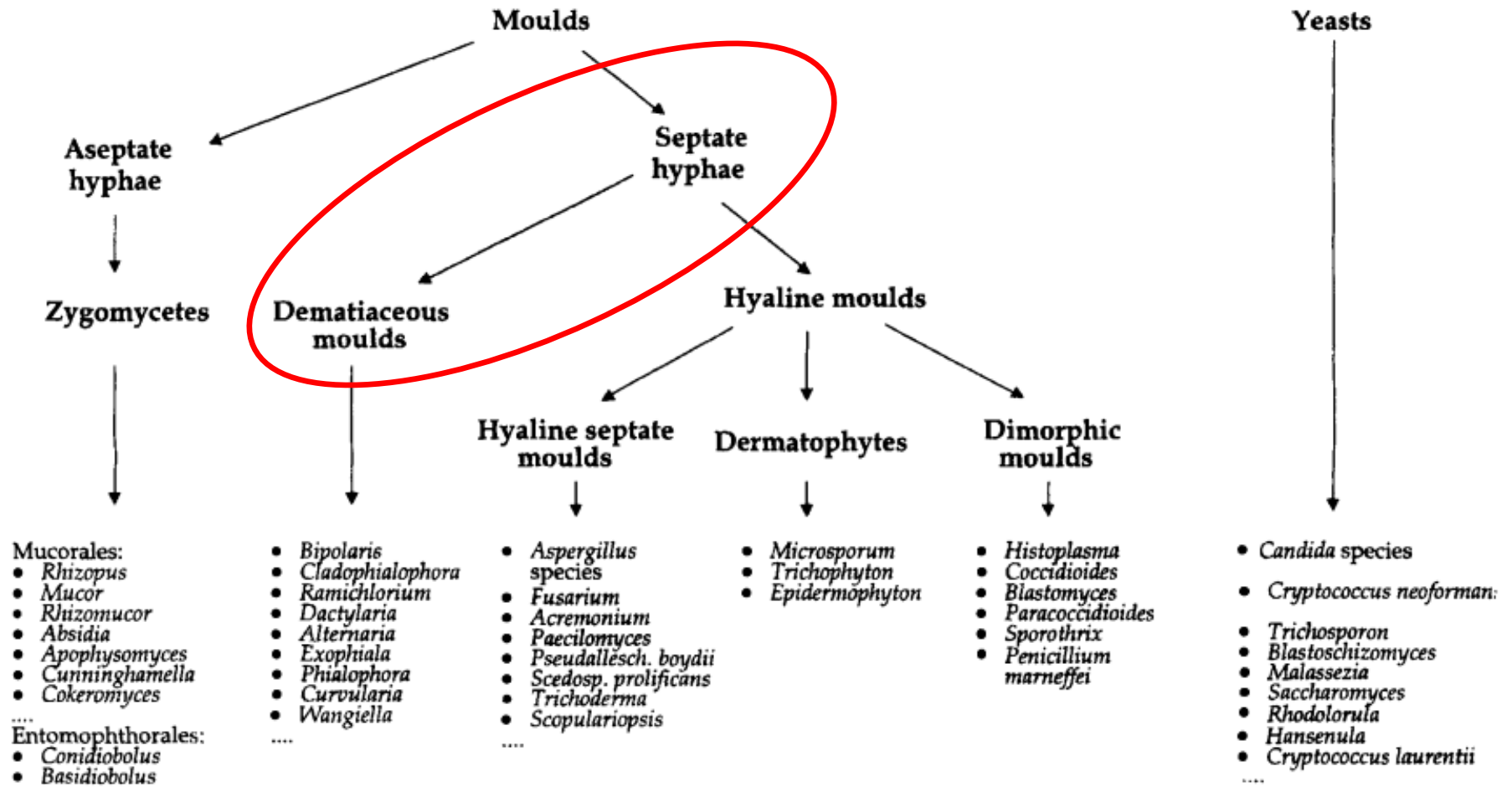
- Cutaneous infections

- Nail infections

Predominantly in immunocompetents



# Classification as a function of cellular organization





# Dematiaceous molds

- **Heterogenous group** of fungi characterized by the presence of melanin-like pigments in the cell wall → dark color of conidia, hyphae or both → brown / black colonies
- More than 150 species and 70 genera
- Melanin = virulence factor
- **Ubiquitous saprobes** in soil or decaying vegetation
- **Transmission:** breakdown of the skin or mucous membrane (ex: nasal, ocular) or inhalation
- **Phylogenetic classification** of melanized fungi:
  - **Kingdom:** Fungi
  - **Phylum:** Ascomycota
    - **Subphylum:** Pezizmycotina
      - **Class:** Dothideomycetes
        - **Orders:** Capnodiales, Dothideales (ex: *Aureobasidium sp.*), Pleosporales, Botryosphaeriales (ex: *Macrophomina sp.*)
      - **Class:** Eurotiomycetes
        - **Order:** Chaetothyriales
      - **Class:** Sordariomycetes
        - **Orders:** Sordariales (ex: *Madurella sp.*), Calosphaeriales (ex: *Phaeoacremonium sp.*)

# Dematiaceous molds

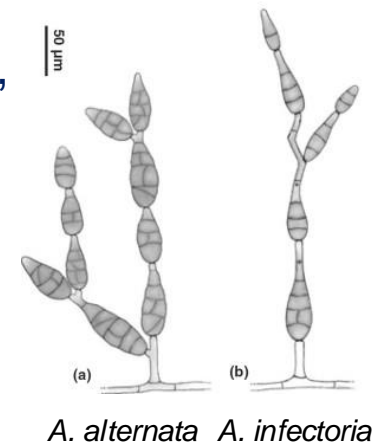
## → Dothideomycetes – Pleosporales

→ Alternaria sp.: **Large, dark, septate, muriform** (regular arrangement, as bricks in a wall) **conidia in chains**.

Most clinical isolates: ***A. alternata*, *A. infectoria***.

Can cause **allergic reactions (rhinitis, asthma, allergic sinusitis), cutaneous/sub-cutaneous mycosis**, infection of the upper respiratory tract, ocular infections, rarely onychomycosis

**Risk factors: immunosuppression** (organ transplantation...)



→ Bipolaris sp.:

**Bipolar germination, conidiophore, conidia with several distoseptations** (pseudosepta with only inner walls involved)

Responsible of **allergic fungal sinusitis** most commonly, but also sub-cutaneous lesions, keratitis, peritonitis, rarely cerebral infections

Clinically relevant species: ***B. spicifera*, *B. hawaiiensis*, *B. australiensis***



Conidia of *B. hawaiiensis* showing mostly 5 distosepta and 6 cells borne from a geniculate conidiophore



Bipolar germination of *B. spicifera*

# Dematiaceous molds

## → Clinical manifestations (1)

→ **Chromoblastomycosis**: chronic subcutaneous mycosis originating from a minor trauma with production of nodular lesions evolving in verrucous plaques. Presence of sclerotic bodies in tissues

→ Caused by *Fonsecaea pedrosoi*, *Phialophora verrucosa*, but also *Cladophialophora carrionii* or *Rhinocladiella aquaspersa*



→ **Eumycetoma**: chronic subcutaneous infection originating from a lesion with small, firm and painless nodules. Characterized by the presence of mycotic granules in tissue (white or black)

→ Caused by *Madurella mycetomatis* (most commonly), but also *Pyrenochaeta romeroi*, or *Leptospheria senegalensis*



# Dematiaceous molds

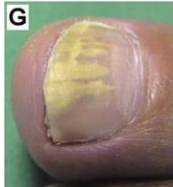
## → Clinical manifestations (2)

→ **Phaeohyphomycosis**: general term designating infections caused by dematiaceous fungi other than chromoblastomycosis or eumycetoma

### → Superficial infections:

→ Tinea nigra: infection of the stratum corneum of the skin (brownish-black macular lesions, located on the palms or soles)

Ex: *Hortaea*, *Stenella*



→ Onychomycosis: nails infection originating from a trauma (rare).

Ex: *Onychocola*, *Alternaria*

→ Subcutaneous phaeohyphomycosis: isolated cystic or papular lesions originating from a minor trauma (risk factor: immunosuppression)

Ex: *Exophiala*, *Alternaria*, *Phialophora*, *Bipolaris*



→ Keratitis: corneal infection (ulcer)

Ex: *Curvularia*, *Bipolaris*, *Exserohilum*, *Lasioidiplodia*



# Dematiaceous molds

## → Clinical manifestations (3)

### → Phaeohyphomycosis

#### → Allergic disease:

→ Fungal sinusitis: nasal polyps with the presence of allergic mucins and hyphal elements. Ex: *Bipolaris*, *Curvularia*

→ Bronchopulmonary mycosis: asthma with bronchiectasis (enlargement of part of airways with chronic mucus production), similar to bronchopulmonary aspergillosis. Ex: *Bipolaris*, *Curvularia*

→ Pneumonia: asymptomatic solitary pulmonary nodules and endobronchial lesions which may cause haemoptysis (coughing up of blood)  
Ex: *Ochroconis*, *Exophiala*, *Chaetomium*

# Dematiaceous molds

## → Clinical manifestations (4)

### → Phaeohyphomycosis

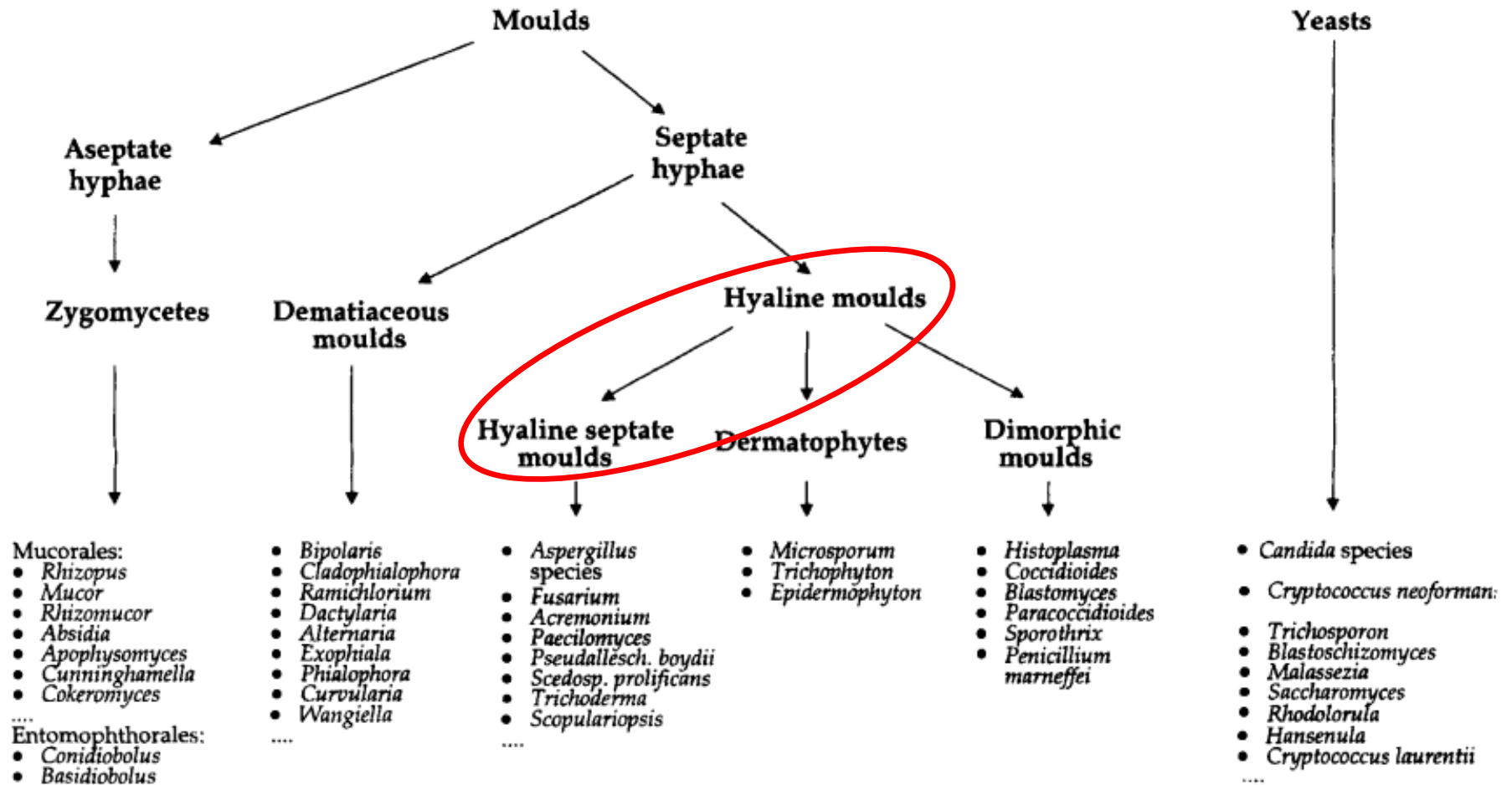
→ Brain abscess: due to hematogenous spread from an initial pulmonary focus.  
Rare but frequently fatal  
→ Ex: *Cladophialophora*, *Ramichloridium*, *Ochroconis*

→ Peritonitis: essentially in patients receiving peritoneal dialysis  
→ Ex: *Curvularia*, *Exophiala*, *Alternaria*, *Bipolaris*, *Aureobasidium*,  
*Phialemonium*

→ Bone and joint infections: originating most commonly from a trauma  
Ex: *Exophiala*, *Fonsecaea*, *Cladophialophora*

→ Disseminated infection: most uncommon manifestation. Sites of infection: skin, lungs, heart, brain (risk factor: immunosuppression).  
Ex: *Bipolaris*, *Wangiella*

# Classification as a function of cellular organization

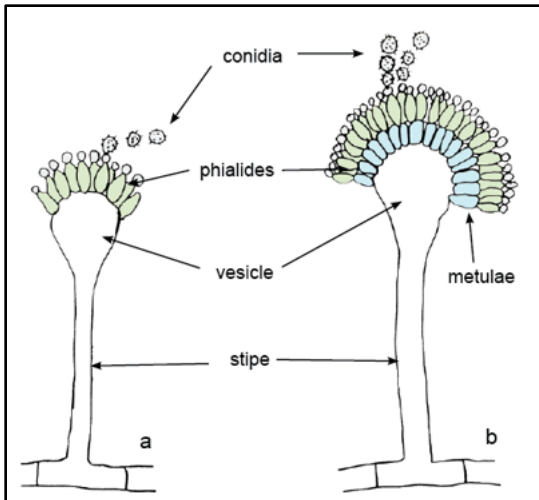
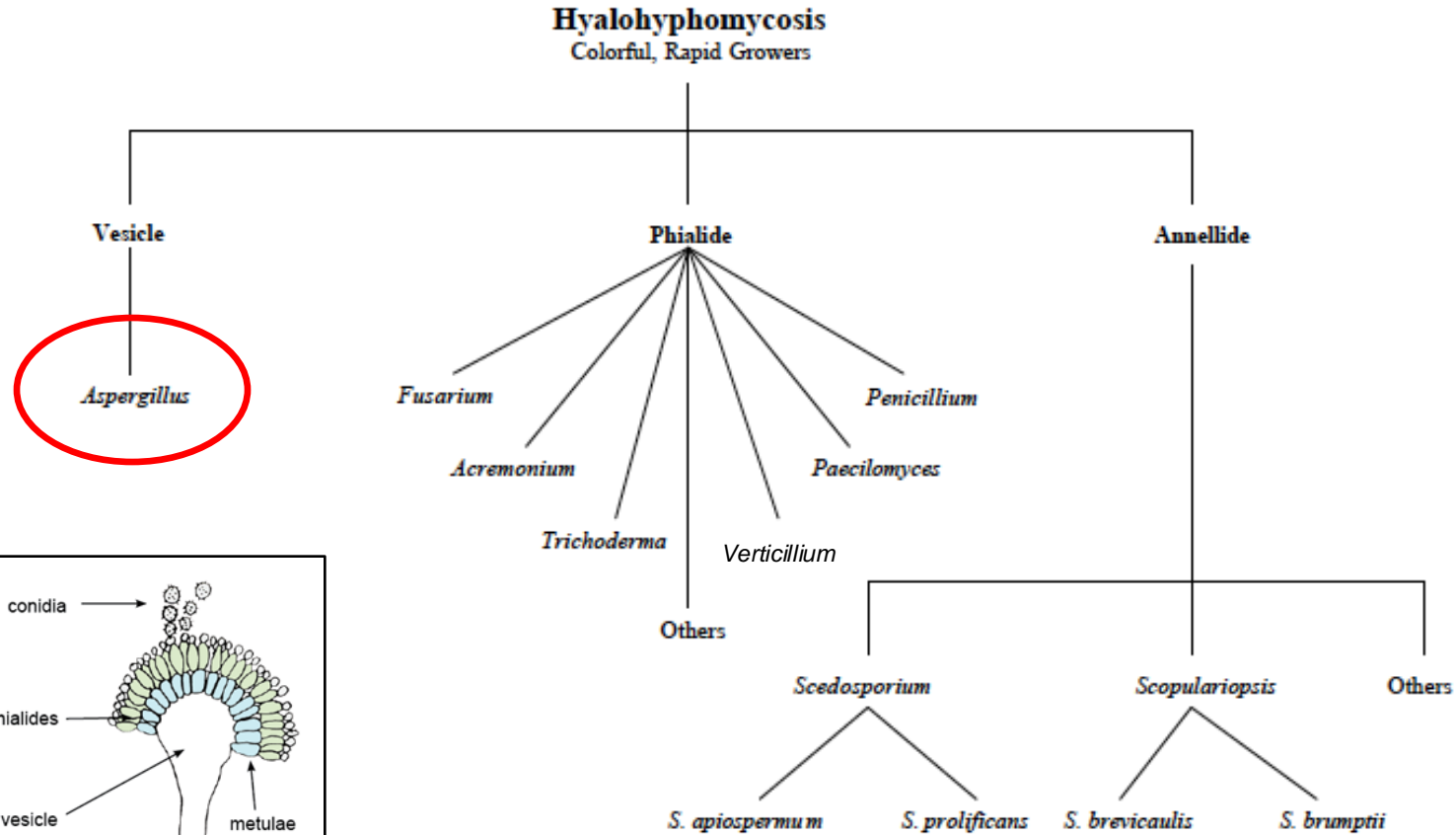


# Hyaline septate molds

- **Produce pale** (lacking melanin pigmentation in the wall) **septate hyphae**
- **Ubiquitous saprobes** in soil, or decaying vegetation
- **Transmission:** breakdown of the skin or mucous membrane (ex: nasal, ocular) or inhalation
- **Can cause (in general):**
  - Superficial / localized infections in immunocompetents (following penetrating trauma)
  - Disseminated infections in immunocompromised patients
    - Ability to disseminate hematogenously and to cause fungemia
- **Phylogenetic classification** of hyaline fungi :
  - **Kingdom:** Fungi
    - **Phylum:** Basidiomycota
      - **Class:** Agaricomycetes
        - **Order:** Agaricales (ex: *Schizophyllum sp.*)
    - **Phylum:** Ascomycota
      - **Class:** Dothideomycetes
        - **Family:** Eremomytaceae (ex: *Arthrographis sp.*)
      - **Class:** Eurotiomycetes
        - **Orders:** Eurotiales, Onygenales (ex: *Onychocola sp.*, *Chrysosporium sp....*)
      - **Class:** Sordariomycetes
        - **Orders:** Hypocreales, Microascale



# Hyaline septate molds



Conidial morphology in *Aspergillus*  
(a) uniseriate (b) biseriata

# Hyaline septate molds

→ **Ascomycota – Eurotiomycetes – Eurotiales (1)**

→ *Aspergillus sp.*:

Includes over 185 species

Around 20 species reported as causative agents of opportunistic infections in human

***A. fumigatus* most commonly isolated followed by *A. flavus* and *A. niger***

Less commonly isolated species: *A. nidulans*, *A. clavatus*, *A. glaucus*,  
*A. oryzae*, *A. terreus*, *A. ustus*, *A. versicolor*...

**Most common route of transmission:** inhalation

**Risk factor:** immunosuppression

# Hyaline septate molds

## → Ascomycota – Eurotiomycetes – Eurotiales (2)

### → Macroscopic features of *Aspergillus* sp.:

**Rapid growth** (1-9 cm in diameter at 25°C for 7 days on Czapek-Dox agar), except for *A. nidulans* and *A. glaucus* (0.5-1 cm in the same conditions).

**Downy to powdery colonies**

**Variation of color** depending on the species

**Thermotolerance for *A. fumigatus*** (unique to this species in the *Aspergillus* genus): grows well at temperatures over 40°C (can grow between 20°C and 50°C).

Species	Surface color	Reverse color
<i>A. clavatus</i>	Blue-green	White, brownish with age
<i>A. flavus</i>	Yellow-green	Goldish to red brown
<i>A. fumigatus</i>	Blue-green to gray	White to tan
<i>A. glaucus</i>	Green with yellow areas	Yellowish to brown
<i>A. nidulans</i>	Green, buff to yellow	Purplish red to olive
<i>A. niger</i>	Black	White to yellow
<i>A. terreus</i>	Cinnamon to brown	White to brown
<i>A. versicolor</i>	White at the beginning, turns to yellow, tan, pale green or pink	White yellow or purplish red

# Hyaline septate molds

→ **Ascomycota – Eurotiomycetes – Eurotiales (3)**

→ Microscopic features of *Aspergillus* sp.:

→ Common to all species:

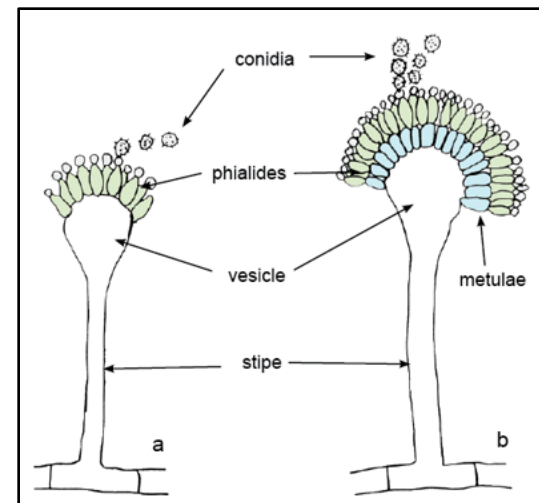
**Septate and hyaline hyphae**

**Conidiophore originates from a basal foot cell and terminates in a vesicle at the apex (vesicle: typical formation for the genus *Aspergillus*)**

Variation of morphology and color of conidiophore between species

**Uniseriate or biseriate (via a metula) flask-shaped phialides covering entirely or only partially the vesicle**

**Production of conidia in chains**



Conidial morphology in *Aspergillus*  
(a) uniseriate (b) biseriate

# Hyaline septate molds

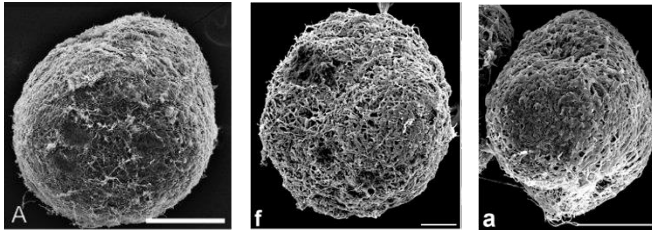
## → Ascomycota – Eurotiomycetes – Eurotiales (4)

### → Microscopic features of *Aspergillus sp.*:

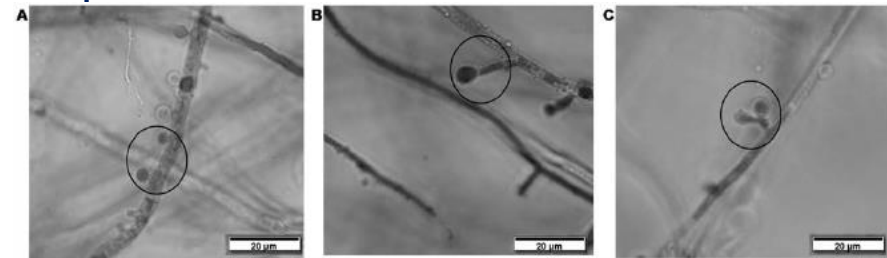
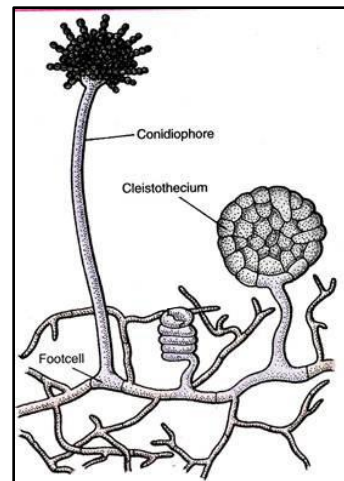
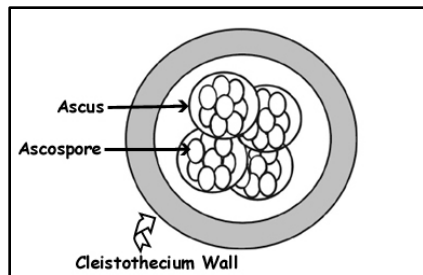
#### → Unique to certain species only:

- 1) **Sclerotia**: compact mass of hardened fungal mycelium containing food reserves
- 3) **Aleuroconidia**: conidia produced directly on the hyphae by lysis of the supporting cell. Usually larger than phialoconidia

SEM pictures of sclerotia from *A. peyronelli* (a), *A. arenarioides* (f) and *A. keratidis* (A)

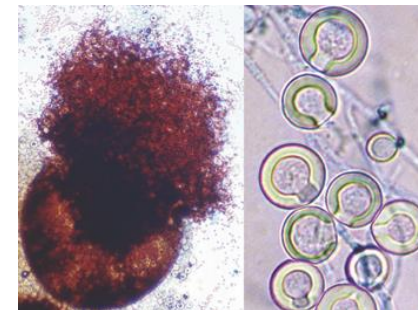


- 2) **Cleistothecium**: round, closed structure enclosing the asci, carrying the ascospores



Aleuroconidia of *A. terreus*

- 4) **Hülle cells**: large thick-walled multinucleate cell → specialized hypha-derived sexual cell



Cleistothecium (left) and Hülle cells (right) of *A. nidulans*. Cleistothecia are often surrounded by Hülle cells.

# Hyaline septate molds

→ **Ascomycota – Eurotiomycetes – Eurotiales (5)**

→ Microscopic features of *Aspergillus sp.*:

Species	Conidiophore	Phialides	Vesicle	Sclerotia	Cleistothecia	Hülle cells	Aleuroconidia
<i>A. clavatus</i>	Long, smooth	Uniseriate	Huge, clavate-shaped	-	-	-	-
<i>A. flavus</i>	Colorless, rough	Uni- / biseriate	Round, radiate head	+ (brown in some strains)	-	-	-
<i>A. fumigatus</i>	Short (< 300 µm), smooth, colorless or greenish	Uniseriate	Round, columnar head	-	-	-	-
<i>A. glaucus</i>	Variable length, smooth, colorless	Uniseriate	Round, radiate to very loosely columnar head	-	+ (yellow to orange)	-	-
<i>A. nidulans</i>	Short (< 250 µm), smooth, brown	Biseriate, short	Round, columnar head	-	+ (red)	+	-
<i>A. niger</i>	Long, smooth, colorless or brown	Biseriate	Round, radiate head	-	-	-	-
<i>A. terreus</i>	Short (< 250 µm), smooth, colorless	Biseriate	Round, compactly columnar head	-	-	-	+ (solitary, round)
<i>A. versicolor</i>	Long, smooth, colorless	Biseriate	Round, loosely radiate head	-	-	+ (in some strains)	-

# Hyaline septate molds

## → Ascomycota – Eurotiomycetes – Eurotiales (6)

### → Aspergillus sp.:

Can cause:

- **Allergic manifestations: Allergic BronchoPulmonary Aspergillosis (ABPA)** as *Aspergillus* antigens are fungal allergens. Occurs in the context of atopy (asthma) with immune hyperactivity (**Severe Asthma with Fungal Sensitisation: SAFS**)
- **Opportunistic infections: pulmonary aspergillosis**, onychomycosis, sinusitis, cerebral aspergillosis, meningitis, endocarditis, myocarditis, osteomyelitis, otomycosis, endophthalmitis, cutaneous aspergillosis, hepatosplenic aspergillosis, fungemia, disseminated aspergillosis
  - **Aspergillus nodule**: rounded opacity of up to 3 cm with or without a cavity
  - **Aspergilloma**: proliferation of *Aspergillus* in cavities previously developed in lungs (tuberculosis, sarcoidosis, bronchiectasis, pneumoconiosis, ankylosing spondylitis, neoplasms) or kidneys
    - Few symptoms (or asymptomatic) over months if aspergilloma is single (« simple aspergilloma »)



# Hyaline septate molds

→ **Ascomycota – Eurotiomycetes – Eurotiales (7)**

→ *Aspergillus sp.*:

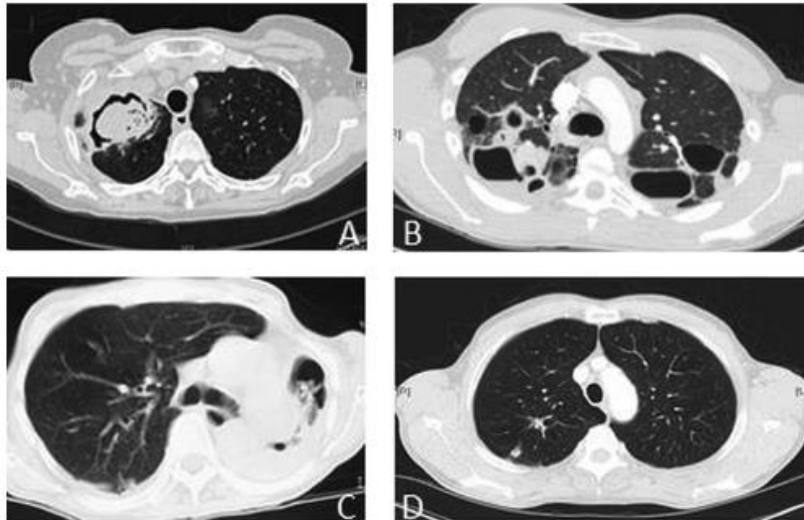
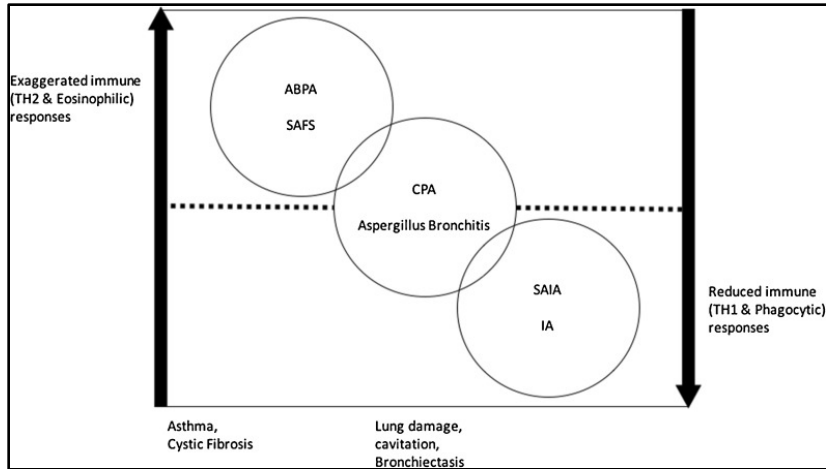
Can cause:

- **Chronic Pulmonary Aspergillosis (CPA): long-term infection (> 3 months)** with varying disease presentations ranging from **Chronic Cavitary Pulmonary Aspergillosis (CCPA)**; formerly known as « complex aspergilloma ») to **Chronic Fibrosing Pulmonary Aspergillosis (CFPA)**; when CCPA left untreated → development of extensive fibrosis).
- **Subacute Invasive Pulmonary Aspergillosis (SAIA)**; previously called chronic necrotizing pulmonary aspergillosis): form of CPA (**short-term infection: < 3 months**) usually found in immunocompromised
- **Invasive Pulmonary Aspergillosis (IPA): most severe form of aspergillosis.** Infection spreads rapidly from the lungs to other organs (brain, heart, kidneys, skin) → lethal if untreated. Risk factor: immunosuppression.

# Hyaline septate molds

## → Ascomycota – Eurotiomycetes – Eurotiales (8)

### → *Aspergillus* sp. pulmonary infections:



A: Simple aspergilloma; B: CCPA;  
C: CFPA; D: *Aspergillus* nodule

### Diagnosis criteria for different management of CPA

CPA subtype	Diagnostic criteria
Simple aspergilloma [14]	<ul style="list-style-type: none"> <li>Minimal symptoms or asymptomatic</li> <li>Single lung cavity containing a fungal ball</li> <li>Immunological or mycological evidence of <i>Aspergillus</i> infection</li> <li>Immunocompetent patient</li> <li>No radiological progression over at least 3 months</li> </ul>
Chronic cavitary pulmonary aspergillosis, CCPA [7]	<ul style="list-style-type: none"> <li>Significant symptoms (respiratory and/or constitutional)</li> <li>One or more lung cavities ± intraluminal material</li> <li>Immunological or mycological evidence of <i>Aspergillus</i> infection</li> <li>Radiological progression over at least 3 months</li> </ul>
Chronic fibrosing pulmonary aspergillosis, CFPA [15]	<ul style="list-style-type: none"> <li>A complication of CCPA</li> <li>Severe destruction of two lobes or more</li> <li>Major loss of lung function</li> <li>Fibrosis can manifest as consolidation or large cavities with surrounding fibrosis</li> </ul>
<i>Aspergillus</i> nodule [16]	<ul style="list-style-type: none"> <li>One or more nodules, which may or may not cavitate.</li> <li>Main differentials include tuberculosis, lung cancer, and other fungal infections.</li> <li>Histology is the gold standard for diagnosis</li> <li>Tissue invasion is not a feature, although necrosis is frequent</li> </ul>
Subacute invasive aspergillosis, SAIA [11] Formerly chronic necrotising pulmonary aspergillosis (CNPA)	<ul style="list-style-type: none"> <li>Mildly immunocompromised patients</li> <li>Occurs over 1 to 3 months</li> <li>Radiology could include cavitation, nodules and progressive consolidation with abscess formation</li> <li>Histology shows lung tissue invaded by hyphae</li> <li>Microbiological investigations reflect those in invasive aspergillosis</li> </ul>

# Hyaline septate molds

→ Ascomycota – Eurotiomycetes – Eurotiales (9)

→ Aspergillus sp.:

Can cause:

- **Toxicoses:** some *Aspergillus* species produce various mycotoxins.

Ex: Aflatoxin can cause hepatocellular carcinoma by chronic ingestion

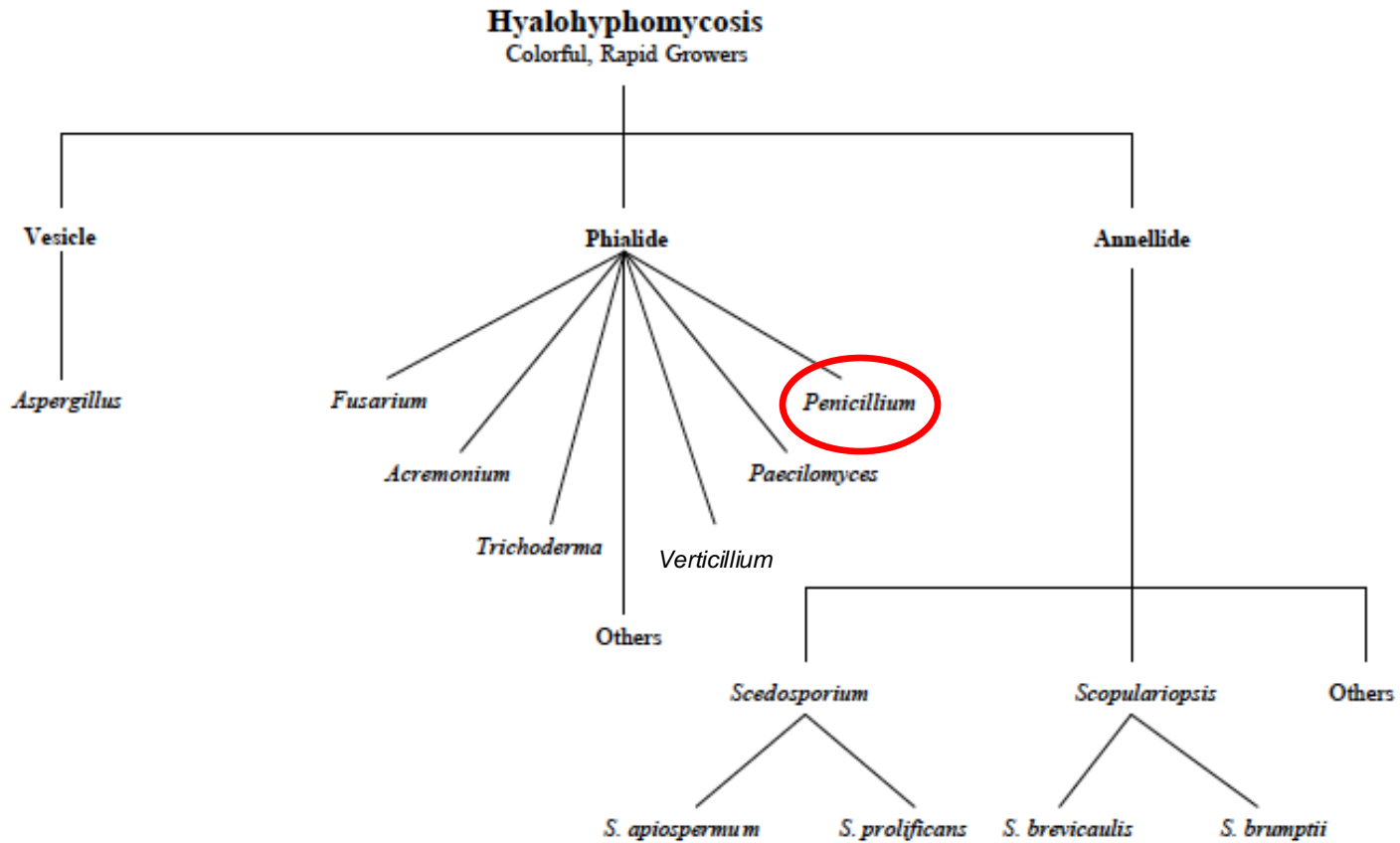
## *Aspergillus* species and mycotoxins produced

Fungal Genera	Mycotoxins Produced
<i>Aspergillus</i>	
<i>A. carneus</i>	Citrinin
<i>A. clavatus</i>	Cytochlasin E, Patulin, Tryptoquivalene
<i>A. flavus</i>	Aflatoxins, Sterigmatocystin
<i>A. fumigatus</i>	Fumagilin, Gliotoxin, Verruculogen, viriditoxin
<i>A. nidulans</i>	Sterigmatocystin
<i>A. niger</i>	Malformin, Oxalic acid, Ochratoxin A
<i>A. ochraceus</i>	Ochratoxin A, Penicillinic acid, Destruxin
<i>A. terreus</i>	Citrinin, Citreoviridin
<i>A. ustus</i>	Austdiol, Austamide, Austocystin
<i>A. versicolor</i>	Cyclopiazonic acid, Sterigmatocystin
<i>A. parasiticus</i>	Aflatoxins

## Common mycotoxins, health effects and target organs

Mycotoxins	Health Effects	Target Organs
Aflatoxins	Hepatotoxic and immune-suppressive	Liver
Ochratoxin A	Carcinogenic, teratogenic, Immuno-suppressive, nephrotoxic and causing upper urinary tract disease	Kidney, liver
Sterigmatocystin	Genotoxic, cytotoxic, immunotoxic and carcinogenic	Liver, immune system, kidney
Cyclopiazonic acid	Immunotoxic and hepatotoxic	Muscle, hepatic tissue and spleen
Gliotoxin	Immunotoxic, nephrotoxic, hepatotoxic and genotoxic	Kidney, liver, immune system
Citreoviridin	Teratogenic and immunotoxic	Not specific
Citrinin	Nephrotoxic	Kidney

# Hyaline septate molds



# Hyaline septate molds

→ **Ascomycota – Eurotiomycetes – Eurotiales (10)**

→ *Penicillium* sp.: very large and ubiquitous genus (contains more than 350 species)

**Production of chains of conidia, in basipetal succession** (basocatenate: youngest conidia at the basal end of the chain), **on flask-shaped phialides via metulae and branches giving a brush-like appearance** (penicillus)

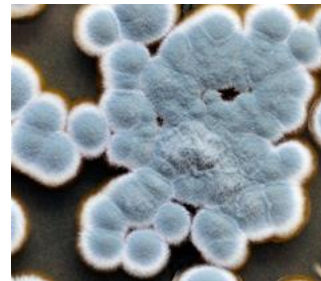
**Production of globose, ellipsoidal, cylindrical or fusiform unicellular conidia**

Most common clinical species: *P. chrysogenum*, *P. purpurogenum*, and *P. citrinum*

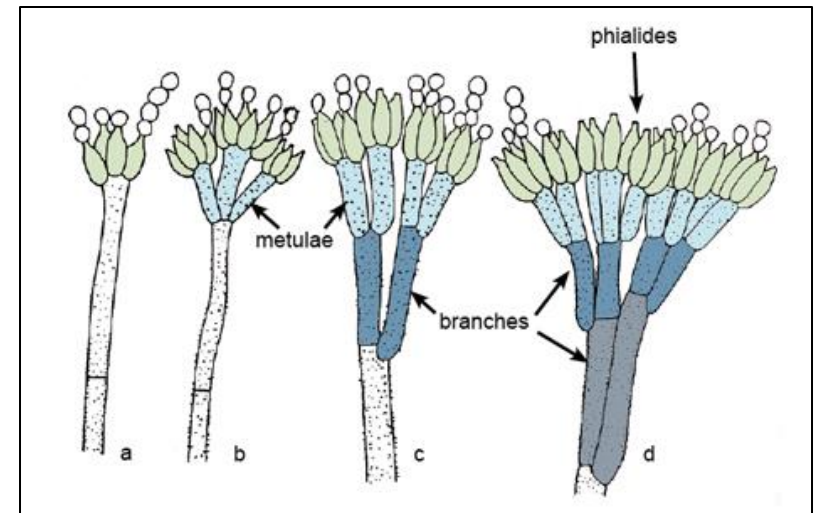
Risk factor: immunosuppression

Rare agents of **keratitis, endophthalmitis, otomycosis, pneumonia, peritonitis, and endocarditis, urinary tract infections.**

Simple conidiophore of *P. cheresanum* showing long chains of single-celled phialoconidia (left)  
conidiophores of *P. verrucosum* var. *cyclopium* showing two-stage branching



Culture of *Penicillium* sp.



Morphological structures and types of conidiophore branching in *Penicillium*. (a) Monoverticillate; (b) Biverticillate; (c) Terverticillate; (d) Quaterverticillate

# Hyaline septate molds

## → Ascomycota – Eurotiomycetes – Eurotiales (11)

### → Penicillium sp.:

Associated with **allergic reactions**: allergic rhinitis, asthma,  
Many species are potential **mycotoxin producers**

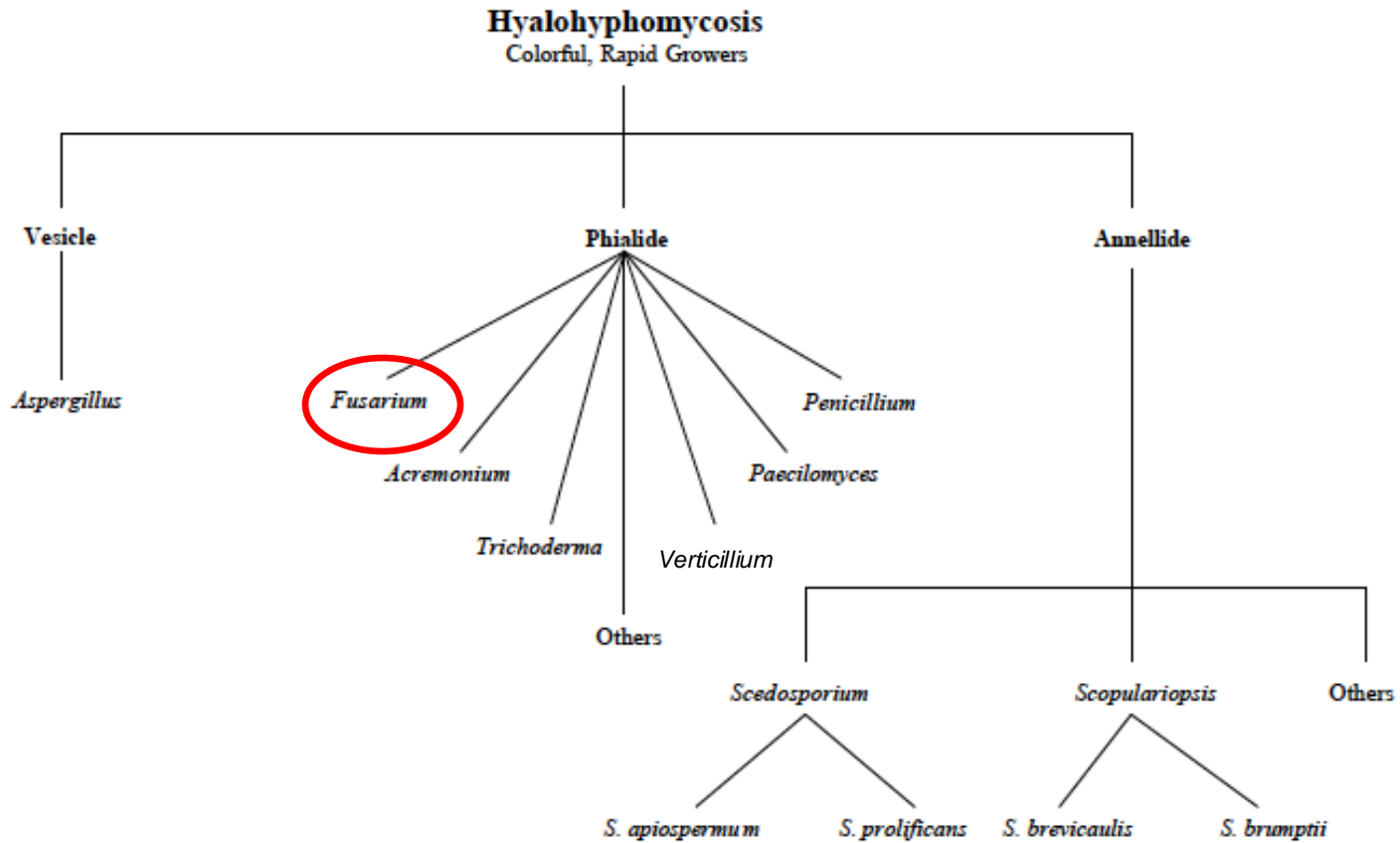
### *Penicillium* species and mycotoxins produced

<i>Penicillium</i>	
<i>P. viridicatum</i>	Ochratoxin A, Rubrosulphin, Viopurpurin, Viomellein
<i>P. citrinin</i>	Citrinin
<i>P. verrucosum</i>	Citrinin
<i>P. hirsutum</i>	Citrinin
<i>P. citreoviride</i>	Citreoviridin
<i>P. islandicum</i>	Islanditoxin
<i>P. expansum</i>	Patulin
<i>Proqueforti</i>	Patulin
<i>P. griseofulvum</i>	Patulin
<i>P. claviforme</i>	Patulin
<i>P. crustosum</i>	Penitrem, Viomellein
<i>P. rubrum</i>	Rubratoxin
<i>P. brunneum</i>	Rugulosin
<i>P. klockeri</i>	Rugulosin
<i>P. rugulosum</i>	Sterigmatocystin, Rugulosin
<i>P. aurantiogriseum</i>	Viomellein

### Common mycotoxins, health effects and target organs

Ochratoxin A	Carcinogenic, teratogenic, Immuno-suppressive, nephrotoxic and causing upper urinary tract disease	Kidney, liver
Citrinin	Nephrotoxic	Kidney

# Hyaline septate molds





# Hyaline septate molds

→ Ascomycota – Sordariomycetes – Hypocreales (1)

→ Fusarium sp. (1) :

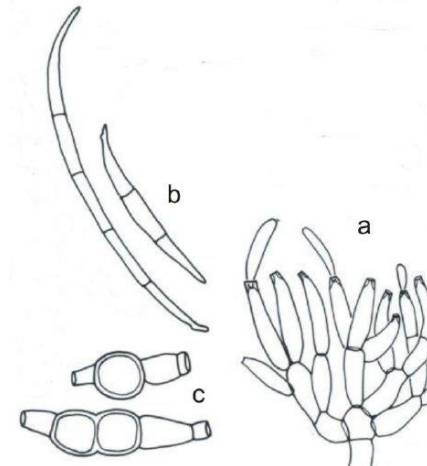
**Hyaline, septate hyphae with branch at acute or right angle**, similar to *Aspergillus sp.* in tissue.

Production of **conidiophores, phialides, macroconidia** (characteristic sickle- or banana-shaped multi-septate conidia with a foot cell at the base), **microconidia** (ovale to kidney-shaped), and sometimes **chlamydo spores**.

Most common clinical species: *F. solani* (most frequent and most virulent), *F. oxysporum*, *F. verticilloides*, *F. proliferatum* and *F. falciforme*.



Conidia produced by *F. oxysporum*: microconidia (top left), macroconidia (top right), and chlamydo spores (bottom)



Conidia produced by *F. oxysporum*: microconidia (a), macroconidia (b) and chlamydo spores (c)

# Hyaline septate molds

## → Ascomycota – Sordariomycetes – Hypocreales (2)

### → Fusarium sp. (2):

Can cause a broad spectrum of diseases:

#### → Infections:

→ **Immunocompetent**: superficial to locally invasive involving the skin (**onychomycosis**, infections typical of dermatophytes: **intertrigo**, **hyperkeratitic plantar lesions**), and eyes (**keratitis**, **endophthalmitis**), but also more occasionally sinuses, lungs, joints and bones.

**Most frequent: keratitis, onychomycosis.**

→ **Immunocompromised**: locally invasive (**pneumonia**, **sinusitis**, **rhinocerebral infection**) or more commonly cause disseminated infections.

**Cutaneous lesions: cellulitis** (acute inflammation of the dermis and subcutaneous tissues), **ecthyma-like lesions**, **subcutaneous nodules**

→ **similar to aspergillosis, but with fungemia** (in contrast to aspergillosis) and **higher incidence of skin lesions.**

Cellulitis secondary to interdigital fusarial infection at the dorsum of the foot of an immunocompromised patient



Intertrigo (Tinea pedis) due to *Fusarium* infection



Hyperkeratitic plantar lesion due to *Fusarium* infection



Ecthyma gangrenosum (flat ulcerating pustule) due to *Fusarium* infection

# Hyaline septate molds

## → Ascomycota – Sordariomycetes – Hypocreales (3)

### → *Fusarium sp.* (3):

Can cause a broad spectrum of diseases:

### → Mycotoxicoses

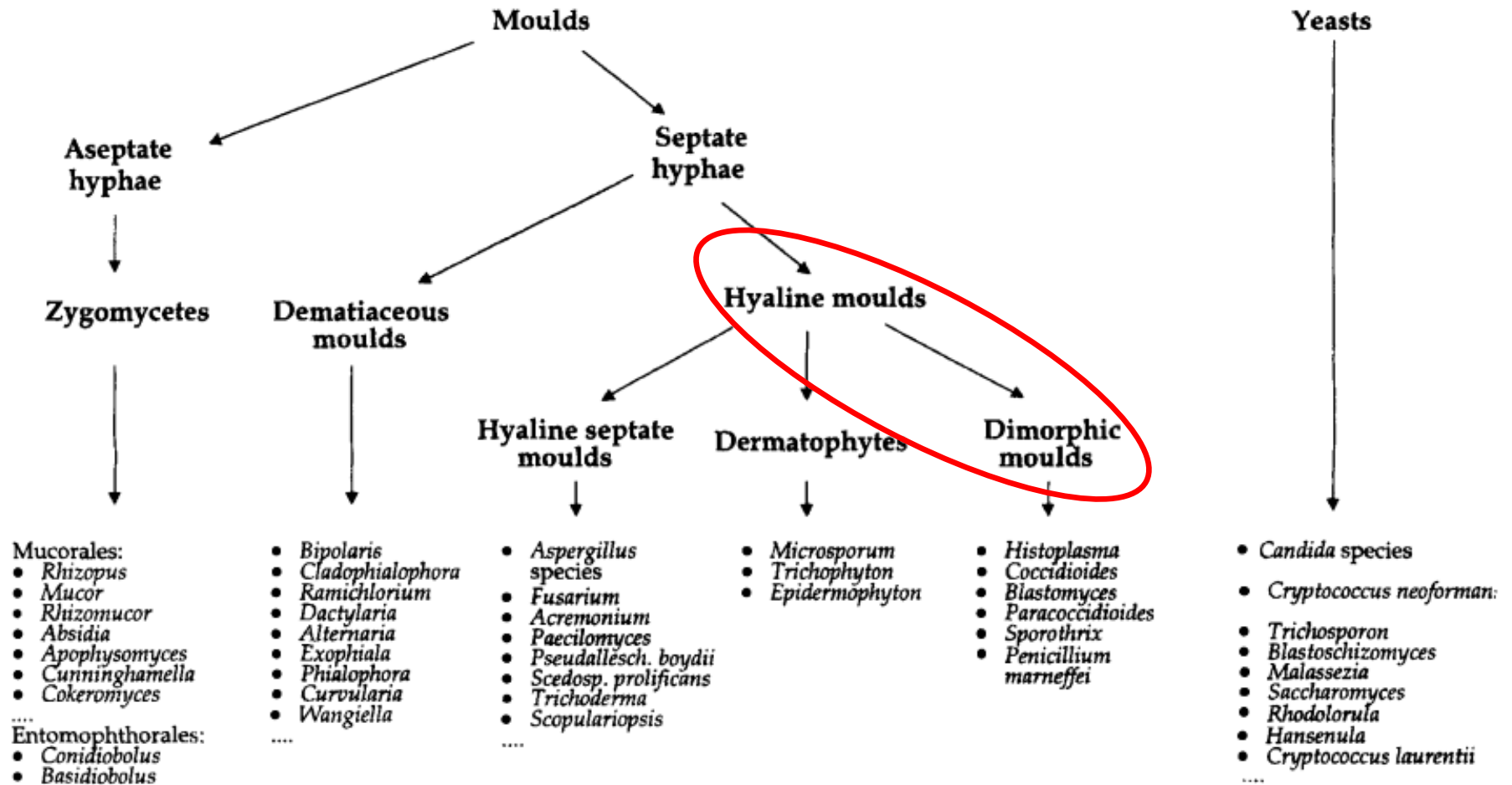
#### *Fusarium* species and mycotoxins produced

Fungal Genera	Mycotoxins Produced
<i>Fusarium</i>	
<i>F. avenaceum</i>	Enniatins, Fructagenin +1, HT-2 toxin, Ipomeanine, Lateritin +1, Lycomerasmin +1, Moniliformin, Monoacetoxyscirpenol, Neosolaniol, Nivalenol, Sambucynin
<i>F. culmorum</i>	Deoxynivalenol, Fructagenin +1, HT-2 toxin, Ipomeanine, Lateritin +1, Lycomerasmin +1, Moniliformin, Neosolaniol
<i>F. equiseti</i>	Moniliformin, Nivalenol, Monoacetoxyscirpenol, Acetoxyscirpenediol, Acetyldeoxynivalenol, Acetylneosolaniol, Acetyl T-2 toxin, Avenacein +1, Beauvericin +2, Butenolide, Calonectrin, Deacetylcalonectrin, T-1 toxin, zearalenol, T-1 toxin, T-2 toxin
<i>F. nivale</i>	Deoxynivalenol diacetate, HT-2 toxin, Ipomeanine, Lateritin +1, Lycomerasmin +1, Moniliformin, Monoacetoxyscirpenol, Sambucynin
<i>F. oxysporum</i>	Moniliformin, Monoacetoxyscirpenol, Neosolaniol, Nivalenol, Acetoxyscirpenediol, Acetyldeoxynivalenol, Acetylneosolaniol, Acetyl T-2 toxin, Avenacein +1, Beauvericin +2, Butenolide, Calonectrin, Deacetylcalonectrin, zearalenone
<i>F. roseum</i>	Fructagenin +1, Moniliformin, Monoacetoxyscirpenol, Neosolaniol, NT-1 toxin, N-2 toxin
<i>F. solani</i>	Enniatins, T-1 toxin, T-2 toxin, Sambucynin, Scirpentriol
<i>F. verticillioides</i>	Fumonisin, Monoacetoxyscirpenol, Neosolaniol, Ipomeanine, Avenacein +1, Beauvericin +2, Fusaric acid, Fusarin
<i>F. graminearum</i>	Zearalenone, Yavanicin +1

#### Common mycotoxin, health effects and target organs

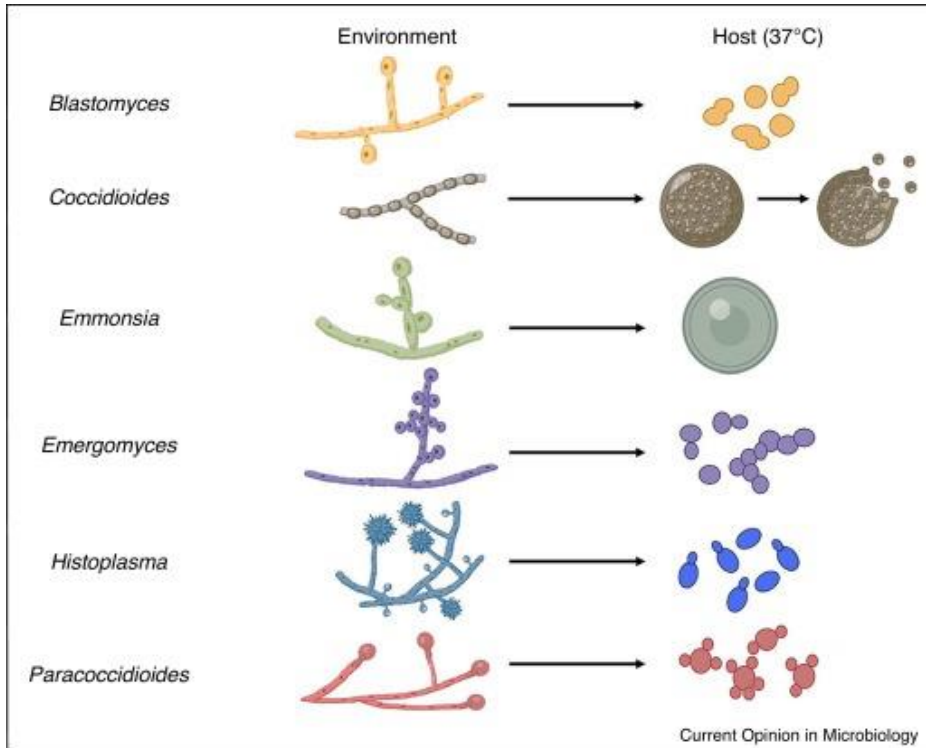
Mycotoxins	Health Effects	Target Organs
Deoxynivalenol	Nausea, vomiting, diarrhea, reproductive effects and toxicosis	Reproductive organs, GI
T-2 toxin	Hepatotoxic, genotoxic and immune-suppressive	GIT, Immune system
Zearalenone	Carcinogenic, hormonal imbalance and reproductive effects	Reproductive organs
Nivalenol	Anorexic, immunotoxic, haematotoxic and genotoxic	GIT, immune system
Moniliformin	Cardiotoxic, muscular disorders, immunotoxic	Heart, Kidney, and muscles
Enniatins	Immunotoxic, cytotoxic	Immune system

# Classification as a function of cellular organization

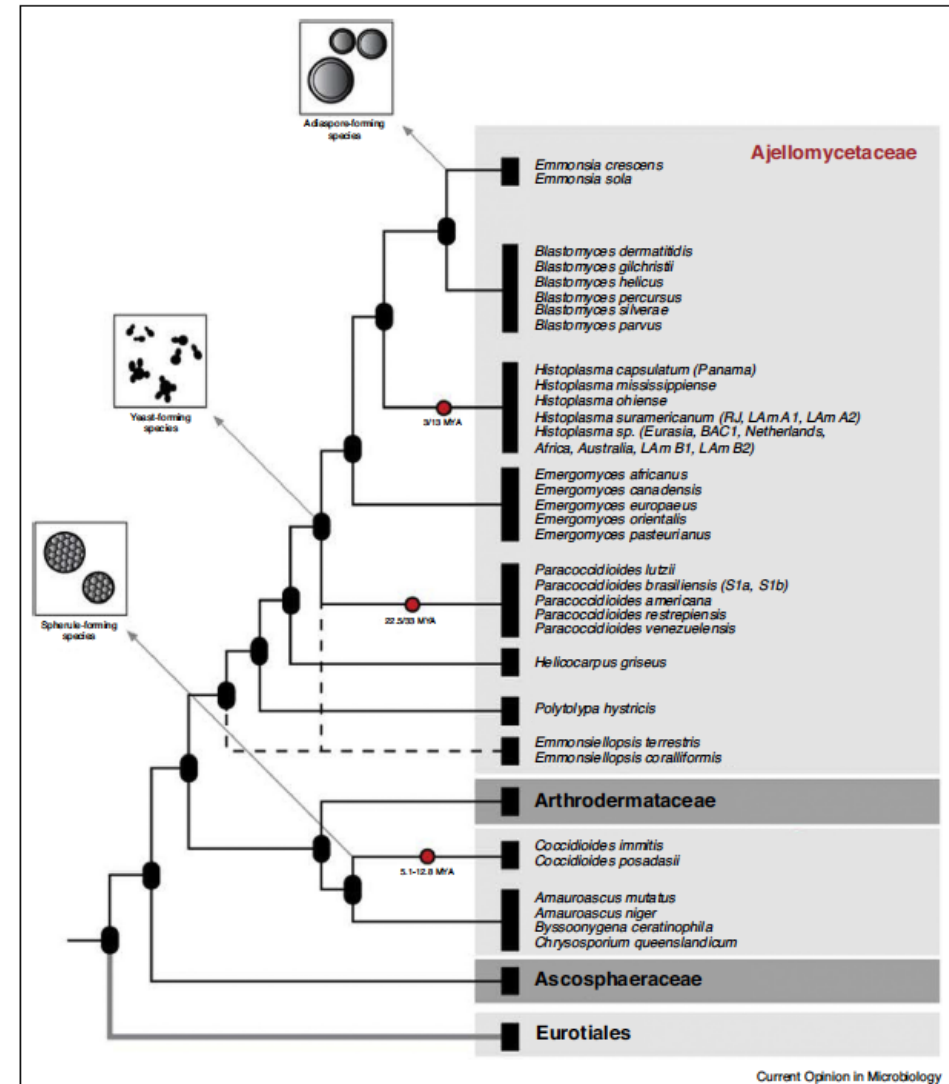


# Dimorphic fungi

- Most dimorphic fungi of medical interest are nested within the order **Onygenales**
- Characterized by **2 fungal shapes**
- Grow as **molds** in the natural environment at **25-30°C** and as **yeasts** at **37°C**



Morphological shifts of Onygenalean fungi

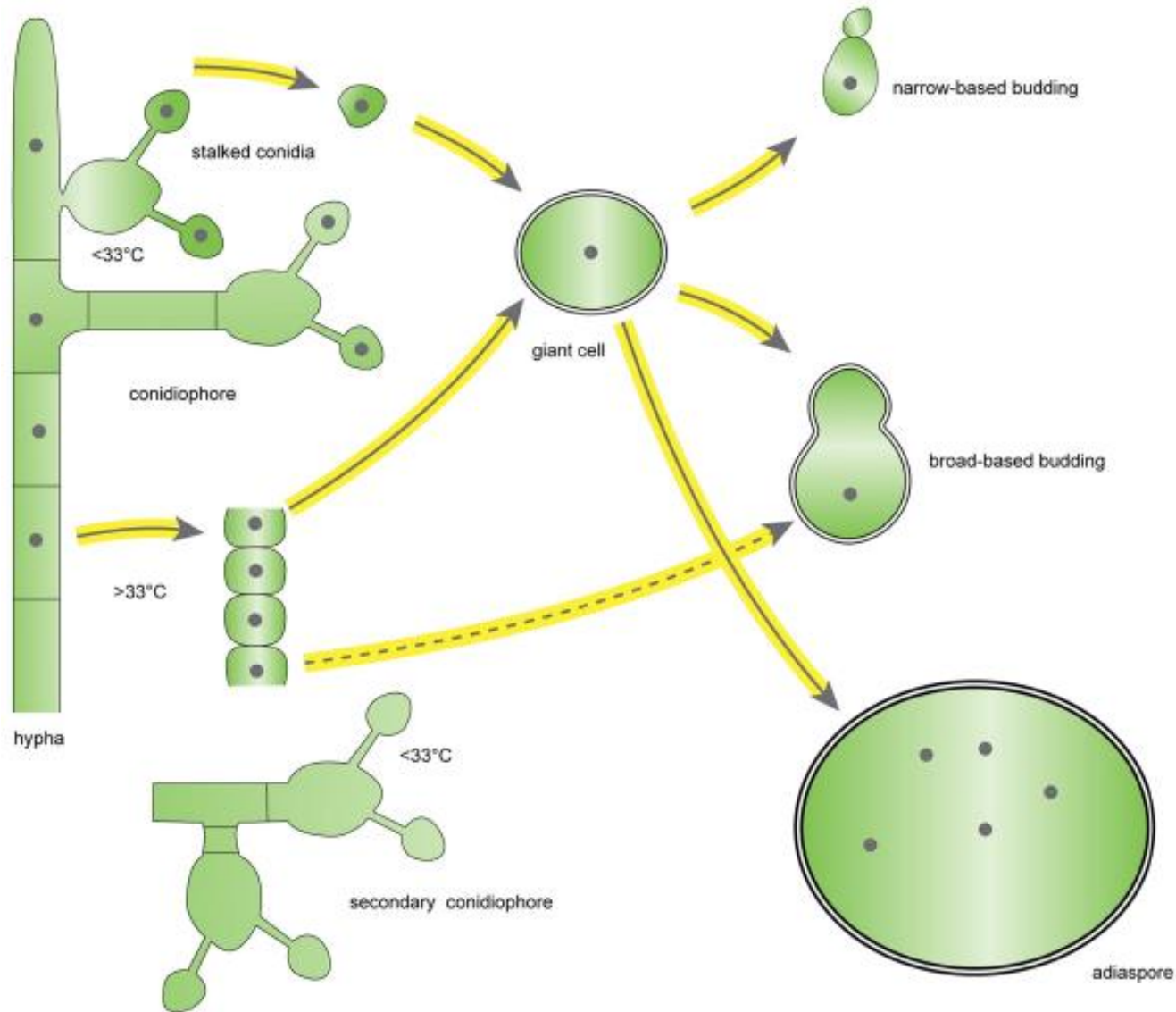


Phylogenetic representation of the evolutionary trajectory of the order onygenales



# Dimorphic fungi

→ Description of morphological changes of Onygenalean fungi



# Dimorphic fungi

→ Ascomycota – Eurotiomycetes – Onygenales (1)

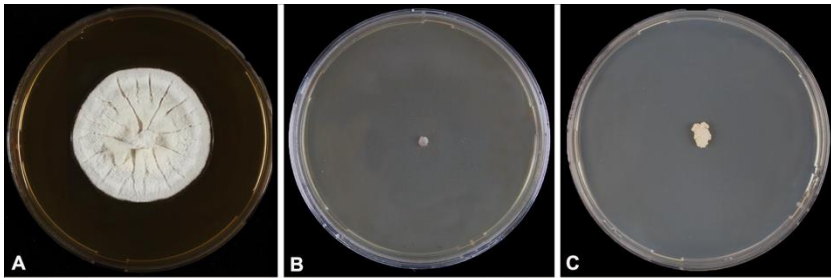
→ Emmonsia sp.:

Production of thin-walled solitary conidia (aleuroconidia) on simple or branched (secondary) conidiophores at 25°C.

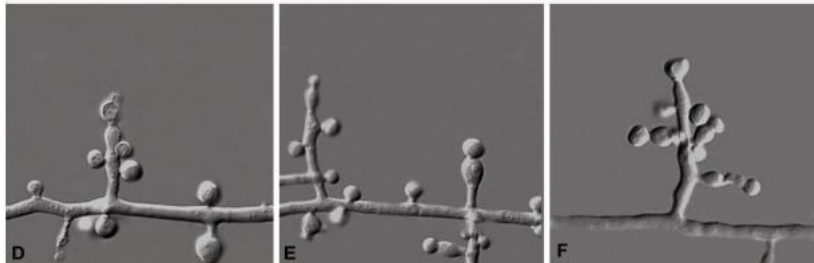
Hyphae and conidiophores swell to give rise to enlarged thick-walled cells (adiaspores) at 37-40°C.

Most common clinical isolate: *E. crescens*

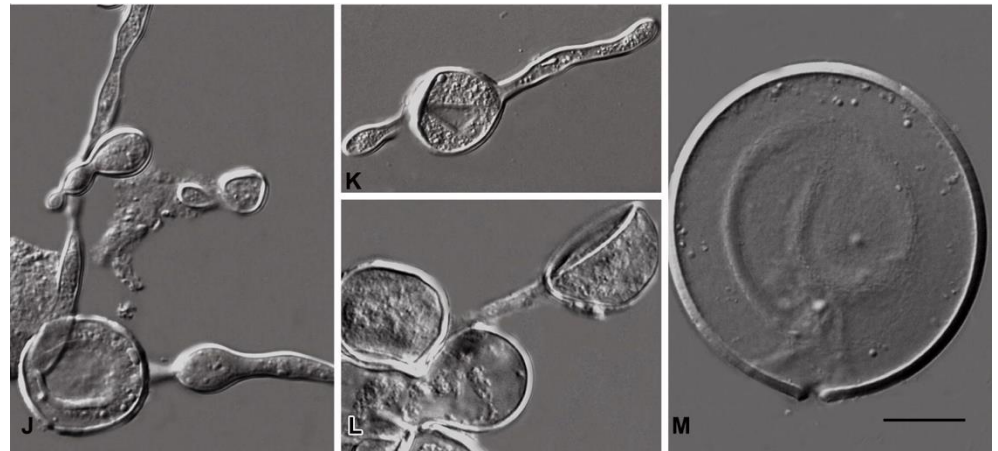
Agent of **adiaspiromycosis** (asymptomatic pulmonary infection which may disseminate in immunocompromised).



Colonies of *Emmonsia crescens* at 24°C, 33°C and 37°C



Conidiophores and aleuroconidia of *Emmonsia crescens*



Swollen hyphae of *Emmonsia crescens* (J to L) leading to adiaspores (M)



# Dimorphic fungi

## → Ascomycota – Eurotiomycetes – Onygenales (2)

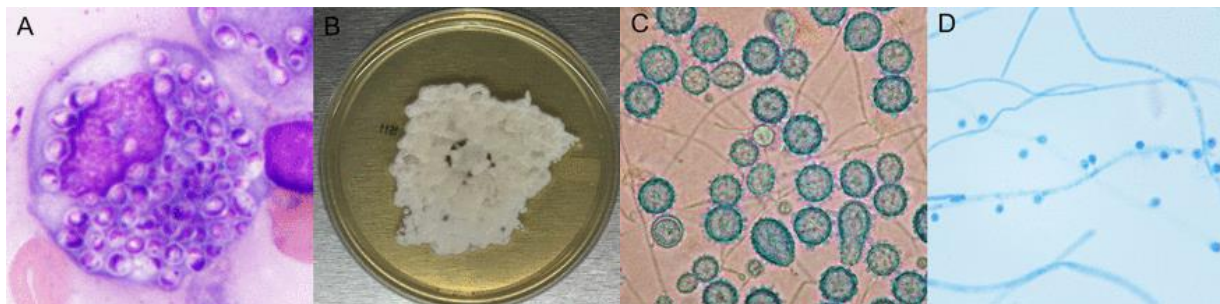
### → Histoplasma sp.:

Natural habitat: soil contaminated with bird droppings or excrements of bats

One species with 2 varieties: *H. capsulatum* var. *capsulatum* and *H. capsulatum* var. *duboisii*

At 25°C: **Conidiophores arising at right angle of hyphae producing macroconidia** (thick-walled round, large tuberculate unicellular cells = tuberculochlamydospores) **and microconidia** (thin-walled, small, globose unicellular cells = microaleuroconidia).

At 37°C: **Production of narrow-based, ovoid, budding yeast-like cells. Yeasts of *H. c. var. capsulatum* are smaller (2-4 µm) than *H. c. var. duboisii* (12-15 µm).**



*Histoplasma capsulatum* var. *capsulatum*: (A) Numerous intracellular yeast cells (2 to 4 µm) within a macrophage. (B) Cottony white colonies grown at 25°C. (C) Tuberculate macroconidia. (D) Small microconidia.

# Dimorphic fungi

→ Ascomycota – Eurotiomycetes – Onygenales (3)

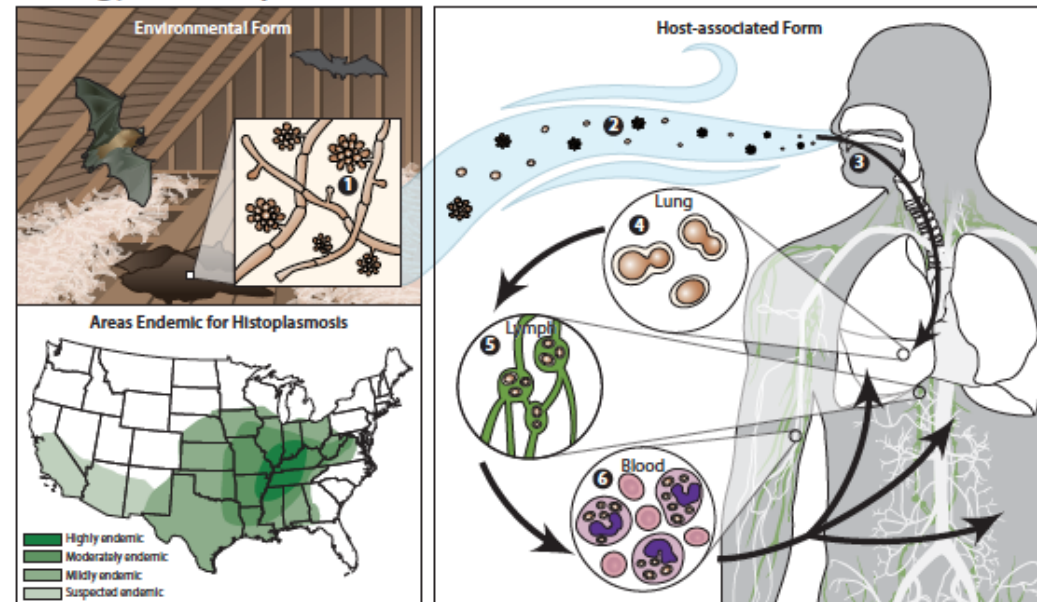
→ Histoplasma sp.:

→ Agent of **histoplasmosis** (in immunocompetents and immunocompromised): varying from **acute pulmonary infection to chronic pulmonary or fatal disseminated disease** (all stages mimic tuberculosis).

→ Dissemination of *H. c. var. capsulatum*: **involvement of the ReticuloEndothelial System (RES) most frequently** (rarely thyroid gland). May cause fungemia.

→ Dissemination of *H. c. var. duboisii*: **involvement of bones and skin**. Lungs = primary site of infection (contamination by inhalation)

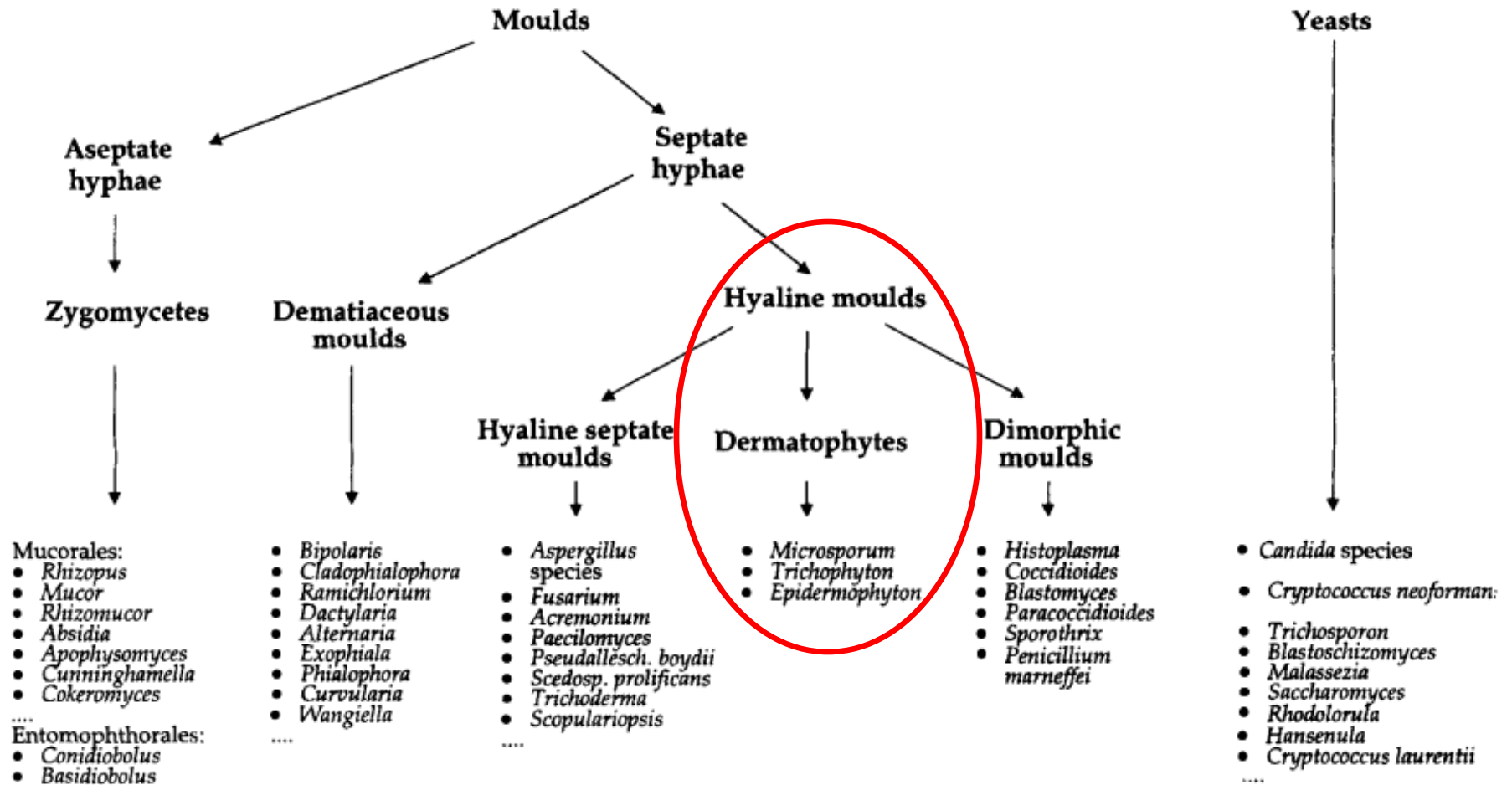
## Biology of Histoplasmosis



In the environment, *Histoplasma capsulatum* exists as a mold (1) with aerial hyphae. The hyphae produce macroconidia and microconidia (2) spores that are aerosolized and dispersed. Microconidia are inhaled into the lungs by a susceptible host (3). The warmer temperature inside the host signals a transformation to an oval, budding yeast (4). The yeast are phagocytized by immune cells and transported to regional lymph nodes (5). From there they travel in the blood to other parts of the body (6).



# Classification as a function of cellular organization



# Dermatophytes

- **Fungal pathogens (-phytes) causing skin diseases (dermato-)**
- Most common cause of fungal infections worldwide
- Occupy 3 different ecological niches: **anthropophilic** (human-associated); **zoophilic** (animal-associated) and **geophilic** (soil-associated) → all 3 associated with clinical human disease
- Agent of various cutaneous mycoses including **athlete's foot, ringworms, onychomycosis**
  - Scientific name of diseases: « *Tinea* » followed by the location of infection
    - Ex: *Tinea corporis*, *Tinea pedis* (= athlete's foot), *Tinea capitis*, *Tinea unguium*, *Tinea barbae*, *Tinea faciei*, *Tinea manuum*, *Tinea cruris* (groin area).
- Phylogenetic classification of dermatophytes
  - **Kingdom:** Fungi
    - **Phylum:** Ascomycota
      - **Class:** Eurotiomycetes
        - **Order:** Onygenales
          - **Family:** Arthrodermataceae
            - **Genera:** *Trichophyton*, *Microsporum*, *Epidermophyton* (more prevalent)  
*Arthroderma*, *Nannizzia*, *Paraphyton* (less prevalent)

# Dermatophytes



Clockwise from left: *Tinea corporis*, *Tinea capitis*,  
*Tinea unguium* and *Tinea pedis*



*Tinea manuum*



*Tinea faciei*

**Table 2.** Less prevalent and geophilic genera in the dermatophytes with currently accepted species.

<i>Nannizzia</i>	<i>Lophophyton</i>	<i>Paraphyton</i>
<i>N. aenigmaticum</i> -?	<i>L. gallinae</i> -Z	<i>P. cookei</i> -G
<i>N. corniculata</i> -G		<i>P. cookiellum</i> -G
<i>N. duboisii</i> -?		<i>P. mirabile</i> -Z
<i>N. fulva</i> -G		
<i>N. gypsea</i> -G		
<i>N. incurvata</i> -G		
<i>N. nana</i> -Z		
<i>N. persicolor</i> -Z		
<i>N. praecox</i> -?		
<b><i>Arthroderma</i></b>		
<i>Arthroderma amazonicum</i> -Z		
<i>Arthroderma ciferrii</i> -G		
<i>Arthroderma cuniculi</i> -G		
<i>Arthroderma curreyi</i> -G		
<i>Arthroderma eboreum</i> -Z		
<i>Arthroderma flavescens</i> -Z		
<i>Arthroderma gertleri</i> -G		
<i>Arthroderma gloriae</i> -G		
<i>Arthroderma insingulare</i> -G		
<i>Arthroderma lenticulare</i> -G		
<i>Arthroderma melis</i> -G		
<i>Arthroderma multifidum</i> -G		
<i>Arthroderma onychocola</i> -?		
<i>Arthroderma phaseoliforme</i> -G		
<i>Arthroderma quadrifidum</i> -G		
<i>Arthroderma redellii</i> -Z		
<i>Arthroderma silverae</i> -?		
<i>Arthroderma thuringiensis</i> -Z		
<i>Arthroderma tuberculatum</i> -Z		
<i>Arthroderma uncinatum</i> -G		
<i>Arthroderma vespertilii</i> -Z		

Note. A, anthropophilic; G, geophilic; Z, zoophilic; ?, ecology unknown because of rarity of the species.

**Table 1.** Overview of current species and species groups in genera prevalent in the routine clinical lab.

*Epidermophyton floccosum*-A

*Microsporum audouinii*-A

*Microsporum canis*-Z

*Microsporum ferrugineum*-A

*Trichophyton benhamiae* series

(*T. benhamiae*-Z, *T. concentricum*-A, *T. eriotrephon*, *T. verrucosum*-Z)

*Trichophyton bulbosum*-Z

*Trichophyton mentagrophytes* series

(*T. equinum*-Z, *T. interdigitale*-A, *T. mentagrophytes*-Z, *T. tonsurans*-A)

*Trichophyton rubrum* series

(*T. rubrum*-A, *T. soudanense*-A, *T. violaceum*-A)

*Trichophyton simii* series

(*T. quinckeanum*-Z, *T. schoenleinii*-A, *T. simii*-Z)

Note. A, anthropophilic; Z, zoophilic.



# Dermatophytes

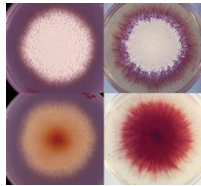
→ **Ascomycota – Eurotiomycetes – Onygenales – Arthrodermataceae**

→ *Trichophyton* sp.: 16 species in the genus on the basis of DNA sequence.

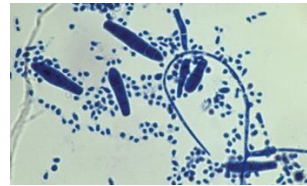
Genus characterized by the formation of smooth-walled macro- and microconidia

→ *T. mentagrophytes*: **Numerous hyaline, smooth-walled, spherical single-celled microconidia produced in clusters. Sparse production of chlamydospores, spiral hyphae and smooth, thin-walled, clavate-shaped macroconidia.**

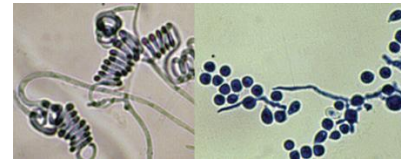
Zoophilic fungus causing ***tinea capitis*** and **kerion** (fungal ringworm infection of the scalp hair follicle with secondary suppurative bacterial infections)



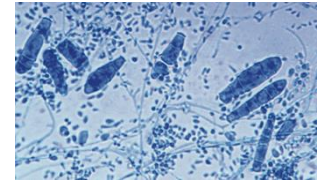
Cultures of *T. mentagrophytes*



Macroconidia, microconidia of *T. mentagrophytes*



Spiral hyphae (left) and chlamydospores (right) of *T. mentagrophytes*



Microconidia and macroconidia of *T. mentagrophytes*

→ *T. rubrum*: Moderate production of microconidia. Rare (or absence of) macroconidia. Numerous chlamydospores in old cultures.

Variation of shape and number of microconidia and macroconidia between strains.

**Most widely distributed dermatophyte in human**

Anthropophilic fungus causing ***tinea pedis***, ***tinea corporis***, **onychomycosis**



Culture of *T. rubrum*



Slender clavate microconidia of *T. rubrum*



Slender clavate microconidia and cigar-shaped macroconidia of *T. rubrum*

# Dermatophytes

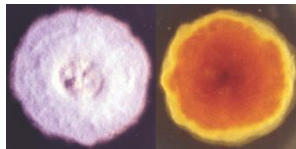
→ Ascomycota – Eurotiomycetes – Onygenales – Arthrodermataceae

→ Microsporum sp.:

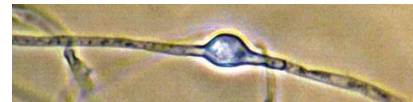
→ Restricted to 3 species: *M. audouinii*, *M. canis* and *M. ferrugineum*

→ *M. audouinii*: **Rare macroconidia** (similar to *M. canis* but longer, smoother, and irregularly fusiform) or **microconidia** (pyriform to clavate). **Occasional thick-walled terminal or intercalary chlamydospores.**

Anthropophilic fungus causing ***tinea corporis*** and ***tinea capitis***. Greenish fluorescence under Wood's UV light



Culture of *M. audouinii*



Chlamydospore of *M. audouinii*

→ *M. canis*: **Thick-walled macronidia with a terminal knob.**  
**Occasional pyriform to clavate microconidia.**

Zoophilic fungus with worldwide distribution causing frequently **ringworm** in humans (***tinea corporis***, ***tinea capitis***) and rarely **onychomycosis**. Greenish fluorescence under Wood's UV light



Culture of *M. canis*



Macroconidia and microconidia of *M. canis*



Ringworm caused by *M. canis*



# Dermatophytes

→ Ascomycota – Eurotiomycetes – Onygenales – Arthrodermataceae

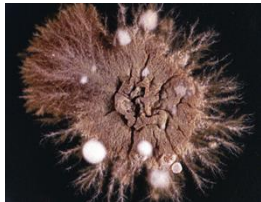
→ *Epidermophyton sp.*:

Single clinical species: *E. floccosum*

**Production of clusters of smooth, thin-walled macroconidia directly on hyphae.**

**No microconidia. Numerous chlamydospores in old cultures.**

Anthropophilic fungus with worldwide distribution causing **tinea pedis**, **tinea cruris**, **tinea corporis** and **onychomycosis**. Known to invade hair.



Culture of *E. floccosum*



Macroconidia of *E. floccosum*



Chlamydospores of *E. floccosum*

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