

# Pathology of Fungal Infection

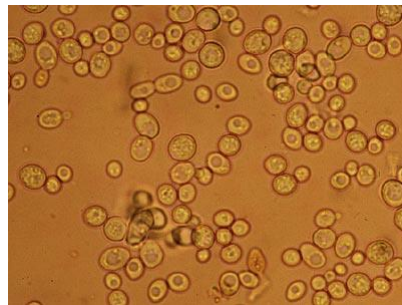
Julintorn Somran, MD.

## Growth form of fungi

Filamentous or hyphae



Yeasts



## Dimorphic fungi

- **Presence of both filamentous forms and yeasts in their cycle**
  - **Histoplasma spp.**
    - Hyphae at environmental temperatures and yeast form in the body
  - **Candida spp.**
    - Hyphae, pseudohyphae, and yeast form in the body

## Three types of fungal infection (Mycoses)

- 1. Superficial mycoses:**
  - Skin, hair, and nails
- 2. Cutaneous and Subcutaneous mycoses:**
  - deeper layer of skin
- 3. Systemic or deep mycoses:**
  - internal organ involvement
  - Including **opportunistic infection**

## Superficial mycoses

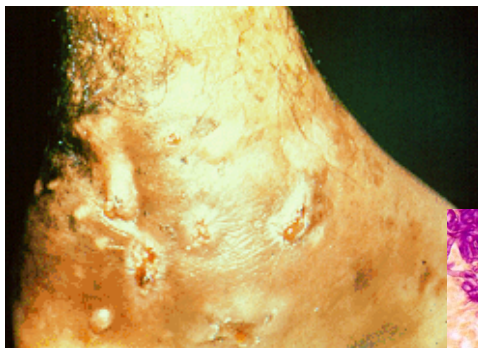
**Tinea (Ringworm)**



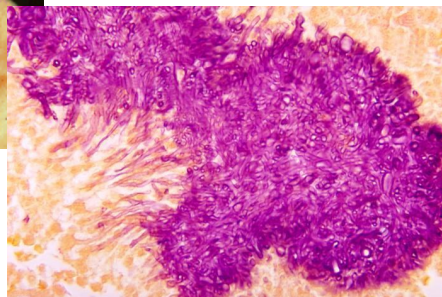
**Pityriasis versicolor**



## Cutaneous and Subcutaneous mycoses



**Eumycotic mycetoma**



## Systemic or deep mycoses



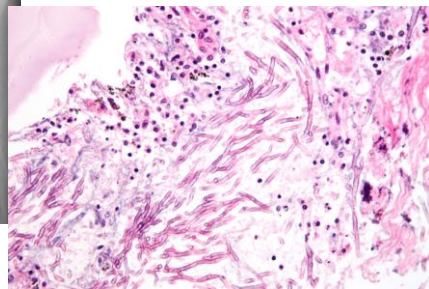
**Mucormycosis or  
Zygomycosis**



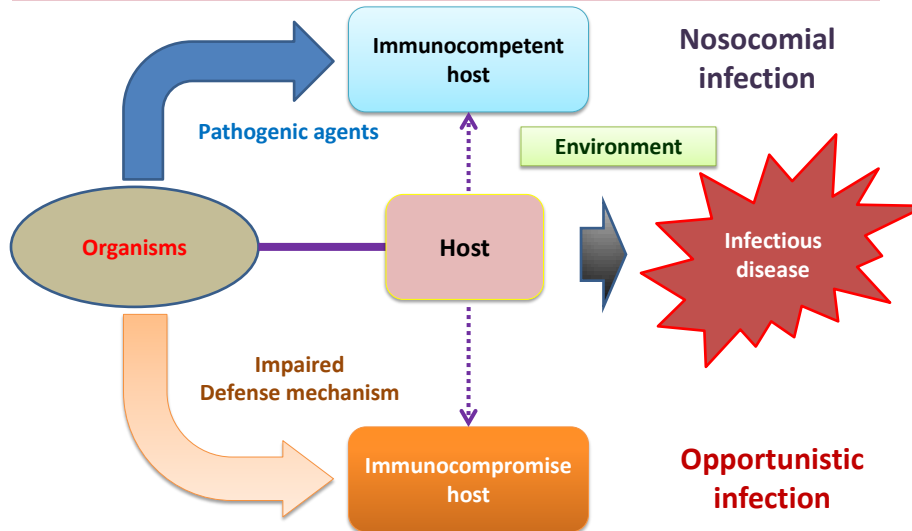
## Systemic or deep mycoses



**Pulmonary  
aspergillosis**



## Host – Agent relationship



## Superficial mycoses

Representative disease	Causative organisms	Growth form in Tissue
Dermatophytosis	Microsporum, Trichophyton, and Epidermophyton	Filamentous form
Pityriasis versicolor or skin infection via malassezia	Malassezia	<u>Yeast and filamentous form</u>
Tinea nigra or keratomycosis nigrican palmaris	Exophiala (Phaeoanellomyces) werneckii	Filamentous form (pigmented)
Onychomycosis	Microsporum, Trichophyton, Epidermophyton etc.	Filamentous form

## DERMATOPHYTOSIS

- **Definition and Epidemiology:**
  - Common superficial infection caused by fungi that able to invade keratinized tissue – stratum corneum, hair, and nails.
  - World wide in distribution
  - The source of infection – another person, animal or soil
- **Etiologic agents:**
  - Microsporum, Trichophyton, and Epidermophyton
  - *T rubrum* – most common for tinea pedis and onychomycosis in temperate climate, and tinea cruris and tinea corporis in the tropics.

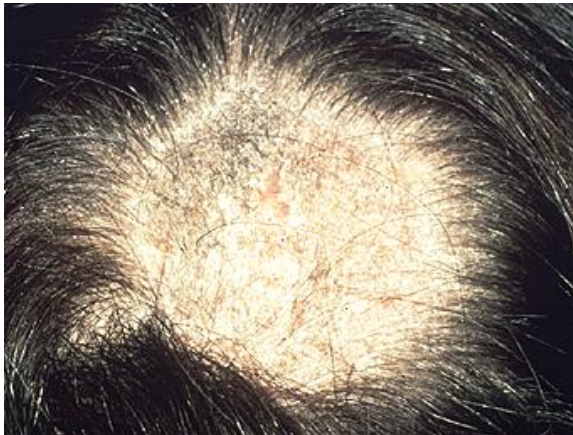
### Clinical Presentations of Dermatophytosis

Infection	Clinical Site
Tinea capitis	Scalp
Tinea favosa	Scalp
Kerion	Scalp, Hair
Majocchi Granuloma	Hair
Tinea faciei	Face
Tinea barbae	Beard
Tinea corporis	Skin (general)
Tinea cruris	Groin
Tinea manuum (manus)	Hand
Tinea pedis	Feet
Tinea unguium	Nails



### **Ringworm – Tinea corporis**

A ring inflammation scaling with diminution of inflammation toward the center



### **Tinea capitis**

Fungi invade the hair shaft producing scaling and hair loss





## Pathology of Dermatophytosis

- Routine or H&E stain in typical cases:
  - Unaffected epidermis or mild hyperkeratosis with patchy parakeratosis
  - Mild to intense perivascular infiltrate with lymphocytes and plasma cells in dermis
  - **Fungal hyphae not seen in H&E stain**
- Special stains:
  - Gomori's methenamine silver (GMS) and periodic acid-Schiff (PAS) demonstrate **filamentous elements or hyphae in stratum corneum** or hair follicles





### Confirmational Testing and Diagnosis

Direct microscopy of skin scrapings, nail clippings, or hair samples mounted in 10% potassium hydroxide (KOH) demonstrates **septate hyphae**

## PITYRIASIS VERSICOLOR

- **Synonyms:** - Tinea versicolor
- **Definition and Epidemiology:**
  - An asymptomatic benign infection of **the stratum corneum layer of skin** – flat or slightly raised macules which are oval, may be hypo or hyperpigmented with scaling on the upper trunk, shoulder, arm, and neck.
  - Worldwide in distribution but common in warm climate
- **Etiologic Agents:**
  - ***Malassezia furfur*** and other *Malassezia* sp.

## Pathology of Pityriasis versicolor

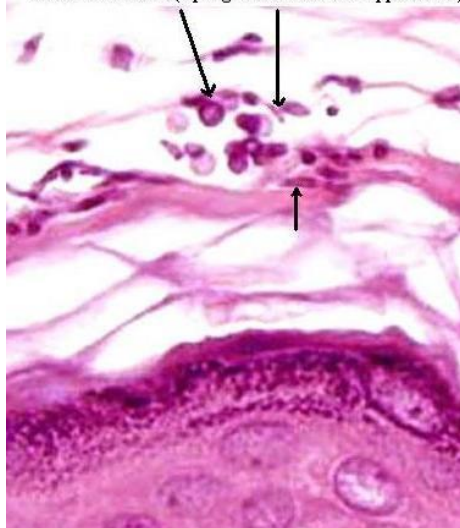
- Routine or H&E stain in typical cases:
  - Minimal epidermal change with mild hyperkeratosis, follicular plugging and acanthosis
  - **Oval yeast form and short curved hyphae (2.5-4 um wide) not easily seen in H&E stain**
  - Diagnosis rarely require for tissue biopsies
- Special stains:
  - Gomori's methenamine silver (GMS) and periodic acid-Schiff (PAS) demonstrate **fungal elements**
- Confirmational Testing and Diagnosis:
  - Direct microscopy of skin scrapings mounted in 10% potassium hydroxide

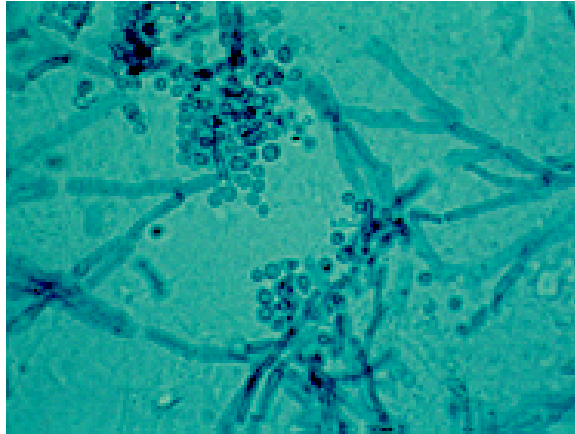
### Pityriasis (Tinea) Versicolor

Multiple hypopigmented oval to confluent macules



Numerous budding yeasts (blastocnidia) and short septate hyphae (pseudomycelium) in the stratum corneum (sphaegetti and meatball appearance)





#### Confirmational Testing and Diagnosis

**Oval yeast form and short curved hyphae**  
(2.5-4 um wide) are demonstrated by 10% KOH

### Other forms of Malassezia infection

- **Malassezia folliculitis:**
  - Yeast forms occupying the hair follicles causing perifollicular infiltrate of neutrophils and, in later stages, lymphocytes.
- **Seborrheic dermatitis:**
  - Particularly in AIDS, this **be precipitated , but not caused by these organism**
- **Fungemia and systemic infection:**
  - *M furfur* rarely cause aggressive deep infection.
  - **Reported in new born in ICU or patients receiving intravascular lipid infusion.**

## TINEA NIGRA

- **Synonyms:**
  - Pityriasis nigra, Keratomycosis nigricans palmaris, Microsporiasis nigra, and ladosporiosis epidermica
- **Definition and Epidemiology:**
  - Superficial mycosis - **asymptomatic, minimal scaly, pigmented macules on palms or/ and soles**
  - Tropical and subtropical areas
- **Etiologic Agent:**
  - Exophiala (Phaeoanellomyces) werneckii – pigmented mycelial fungus

## TINEA NIGRA



10% KOH preparation found  
septate hyphae

## Pathology of Tinea Nigra

- **Routine or H&E stain in typical cases:**
  - Hyperkeratosis and mild mononuclear perivascular infiltrate in dermis
  - Presence of pigmented hyphae in the stratum corneum – not need to do the special stains
- **Confirmational Testing and Diagnosis:**
  - Direct microscopy of skin scrapings mounted in 10% potassium hydroxide

## ONYCHOMYCOSIS

- **Definition:**
  - Fungal infection of nail plate material
- **Etiologic Agents:**
  - Microsporum, Trichophyton, Epidermophyton, Trichosporon, Candida etc.
- **Clinical and Pathologic features:**
  - Irregular, discolored, and distorted nails
  - Nail biopsies with GMS and PAS confirm the presence of fungus in nail tissue.

## ONYCHOMYCOSIS



## Cutaneous & Subcutaneous mycoses

Representative disease	Causative organisms	Growth form In Tissue
Mycetoma (Eumycotic)	White grain: <i>Acremonium falciforme</i> , <i>Aspergillus nidulans</i> , <i>Fusarium moniliforme</i> , <i>pseudallescheria boydii</i> etc.	Filamentous forms
	Black grain: <i>Chaetosphaeronema larense</i> , <i>Medurella grisea</i> etc.	
Chromoblastomycosis	<i>Fonsecaea pedrosoi</i> , <i>Cladophialophora carrionii</i> etc.	Muriform cell and Filamentous forms
Sporotrichosis	<i>Sporothrix schenckii</i>	Yeast form

## MYCETOMA

- **Definition and Epidemiology:**
  - Chronic, localized, progressive infection of skin, subcutaneous tissue, muscle, fascia, and bone caused by **a wide variety of free-living or exogenous aerobic actinomycetes or fungi.**
  - Not contagious but infected from sources in nature by **traumatic percutaneous implantation** of the causal organism into those parts of body (usually foot or hand)
  - Most prevalent in tropical and subtropical regions

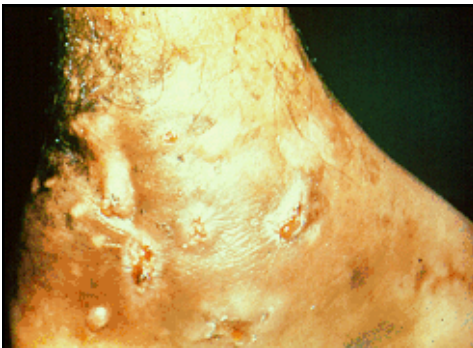
## MYCETOMA

	Eumycotic Mycetoma	Actinomycotic Mycetoma
Causative agents	Fungus: Several species depend on the geographical areas	Filamentous bacteria: Actinomadura madurae, Nocardia asteroides, Streptomyces somaliensis etc.
Clinical features	Chronic, localized, progressive infection of skin, subcutaneous tissue, muscle, fascia, and bone with multiple abscesses and sinus drainage and presence of granules or grain (0.2 to 5 mm)	
Grain colors	White or Black	White, red, or yellow

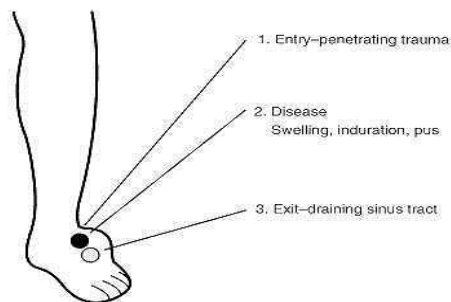


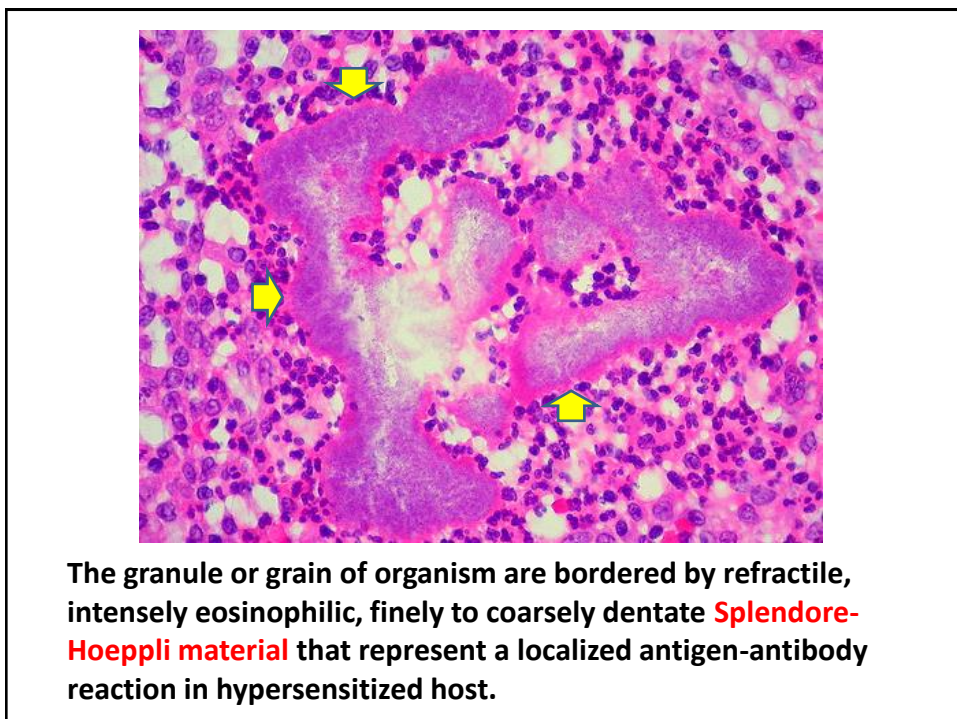
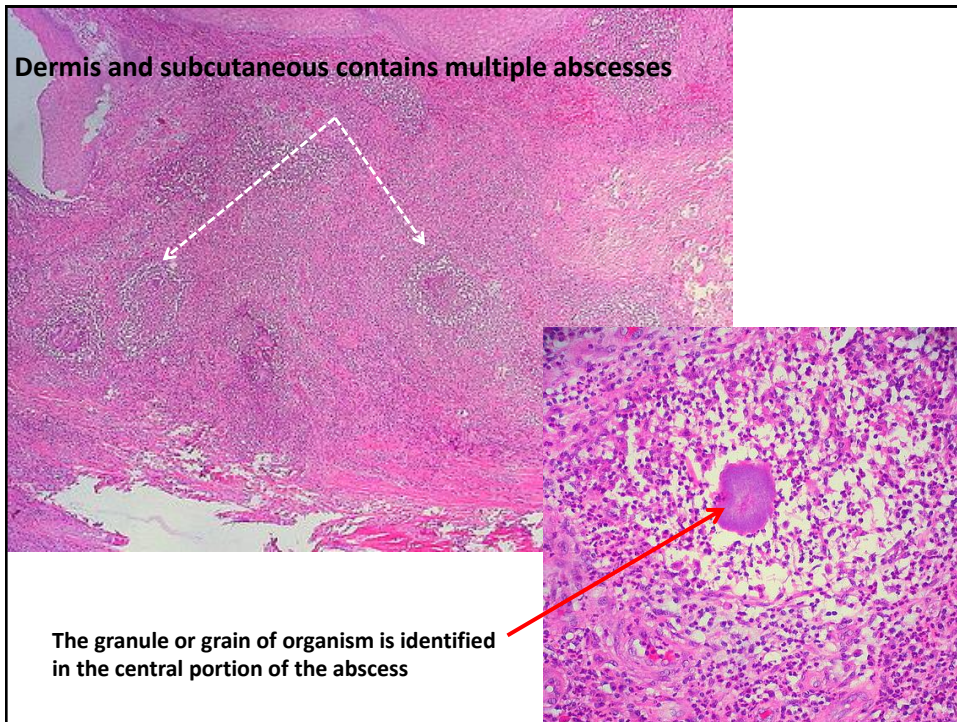
# MYCETOMA

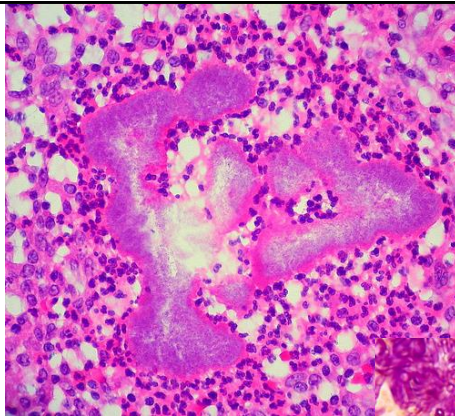
	Eumycotic Mycetoma	Actinomycotic Mycetoma
Morphology of organisms	Septate, fungal hyphae ( 2 to 6 um or more width) and some pigmented (black grain)	Delicate, branched, gram-positive and sometime beaded or fragmented bacterial filaments (< or= 1 um)
Pathologic features	Multiple abscesses in dermis containing neutrophilic exudates and clusters or grains of organism and surrounded by chronic inflammation with epithelioid histiocytes and multinucleated giant cells, and fibrosis	
Special stains	GMS and PAS	Gram stain
Treatment	Surgical excision or Amputation	Antibiotic treatment



## Medura Foot Or Maduromycosis





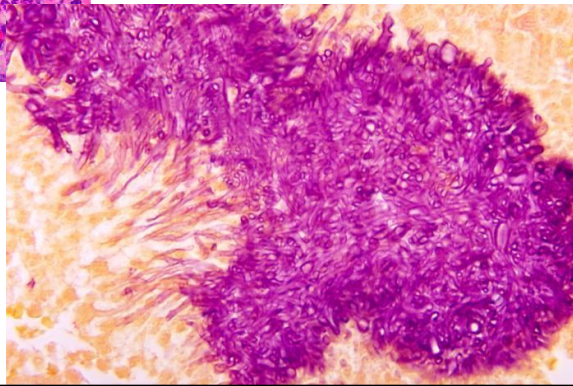


### Actinomycotic Mycetoma

Delicate, branched, gram-positive and sometime beaded or fragmented bacterial filaments ( $\leq 1 \mu\text{m}$ )

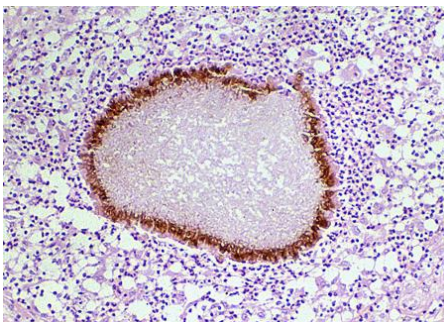
### Eumycotic Mycetoma

Septate, fungal hyphae (2 to 6  $\mu\text{m}$  or more width) and some pigmented (black grain)



## Eumycotic Mycetoma

### Black grain



### White grain

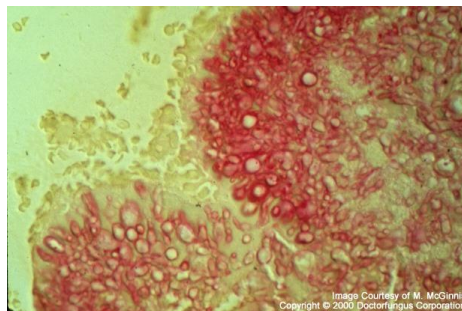
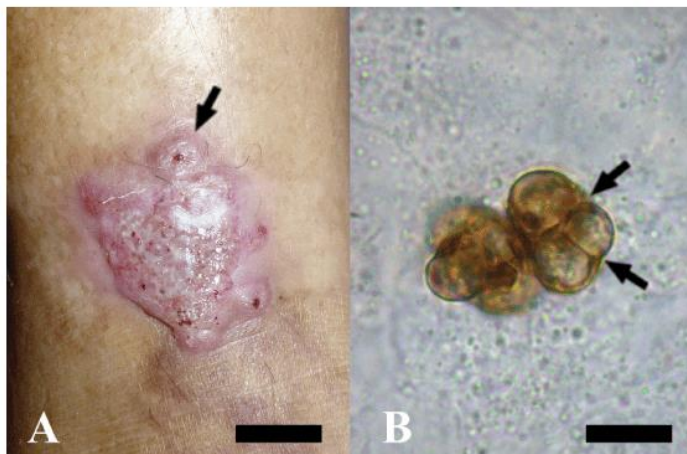


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# CHROMOBLASTOMYCOSIS

- **Definition:**
  - Chronic fungal infection of the skin and subcutaneous tissue by dematiaceous (pigmented) fungi.
  - No report of person to person spread, but most infected by **traumatic implantation of certain organisms**
- **Etiologic agents:**
  - Most common causative agents - ***Fonsecaea pedrosoi* and *Cladophialophora carrionii***



**Morphologic features of organisms:**  
Cells with internal septation; vertical and horizontal lines or Muriform cells and hyphae that are chestnut brown in color

# CHROMOBLASTOMYCOSIS

- **Epidemiology:**
  - World wide in distribution, but most common in tropical or subtropical areas especially in bare-footed agriculture workers.
- **Clinical features:**
  - Chronic, pruritic, progressive, indolent lesion spreading by patient scratches and cutaneous lymphatics; **a small scaly papule → superficial nodule → irregular plaque → large papillomatous lesion involving large portion of the limb**



Inflammatory reaction in dermis consist of suppurative and granulomatous inflammation with dermal fibrosis and pseudoepitheliomatous hyperplasia

## SPOROTRICHOSIS

- **Definition and Etiologic agent:**
  - Chronic cutaneous or systemic mycosis caused by the thermally dimorphic fungus “*Sporothrix schenckii*”, but mostly confined to skin, subcutaneous, and contiguous lymphatics
  - Infected via the accidental percutaneous inoculation of organisms growing in soil and on plant materials – **occupational disease (gardener, farmer, etc)**
- **Epidemiology:**
  - Worldwide in distribution, but most in temperate as well as tropical region

## SPOROTRICHOSIS

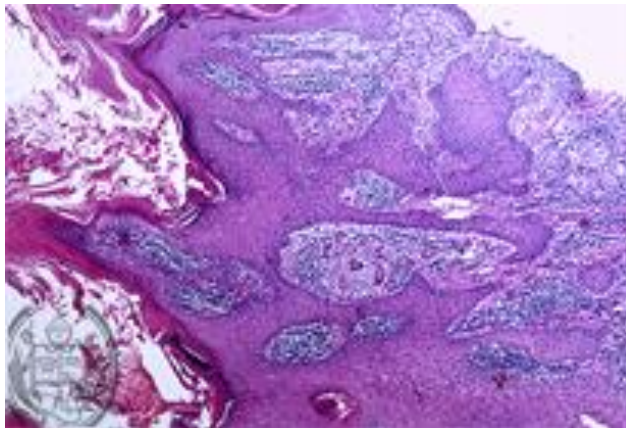
- **Clinical features:**
  - Cutaneous (Lymphocutaneous) form; most familiar clinical features consisting of a linear chain of painless subcutaneous nodules that extend indolently along the course of lymphatic drainage from the primary nodular-ulcerative lesion developing at the site of traumatic percutaneous inoculation of fungus
  - Systemic form; often localized in a single organ system such as bone, joint, or lower respiratory tract



A linear chain of **painless subcutaneous nodules** that extend indolently along the course of lymphatic drainage

### Pathological features

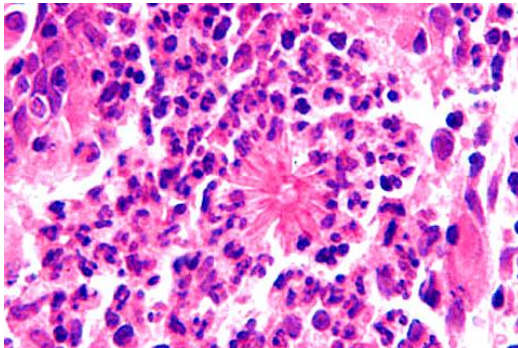
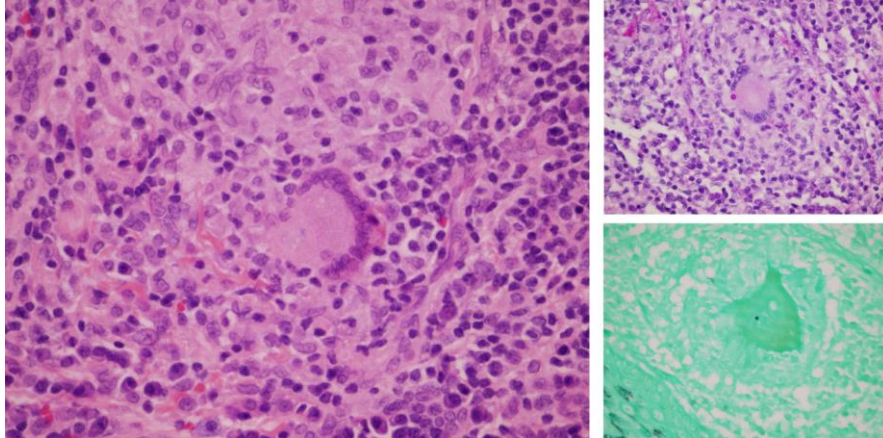
- Florid pseudoepitheliomatous hyperplasia with ulceration and intraepidermal abscesses
- Mixed suppurative and granulomatous reaction in dermis and subcutaneous tissue with fibrosis





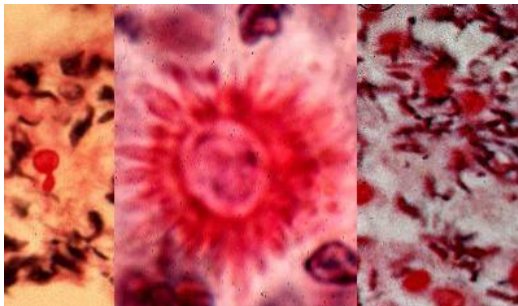
### Pathological features

- Spherical, oval, or elongated (cigar shape) single or budding yeastlike cells (2-6  $\mu$ m) demonstrated by GMS or PAS
- Budding yeasts - Teardrop or pipe stem configuration



### The asteroid body

- Yeast formed organism enveloped by Splendore-Hoeppli material - **intense eosinophilic material with elongated and radiated spicules**



- Asteroid body almost always in microabscess

## Systemic or deep mycoses

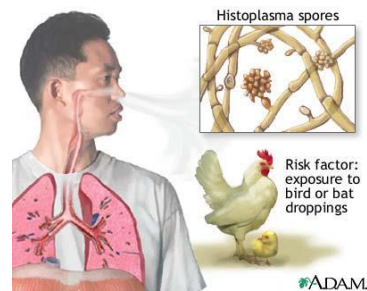
Representative disease	Causative organisms	Growth form In Tissue
Histoplasmosis Capsulati	<i>Histoplasma capsulatum</i> var <i>capsulatum</i>	Yeast form
Blastomycosis	<i>Blastomyces dermatitidis</i>	Yeast form
Coccidioidomycosis	<i>Coccidioides immitis</i>	Endospore in spherule
Paracoccidioidomycosis	<i>Paracoccidioides brasiliensis</i>	Yeast form

## Systemic or deep mycoses, opportunistic infection

Representative disease	Causative organisms	Growth form In Tissue
<b>Cryptococcosis</b>	<i>Cryptococcus neoformans</i>	Yeast form
Candidiasis	<i>Candida albican</i> , other candida sp	Yeast form
Aspergillosis	<i>Aspergillus fumigatus</i> , <i>Aspergillus flavus</i> , <i>Aspergillus niger</i> , etc	Filamentous form
Zygomycosis	The order Mucorales The order Entomophthorales	Filamentous form
Penicilliosis Maneffei	<i>Penicillium marneffe</i>	Yeast form

# HISTOPLASMA CAPSULATI

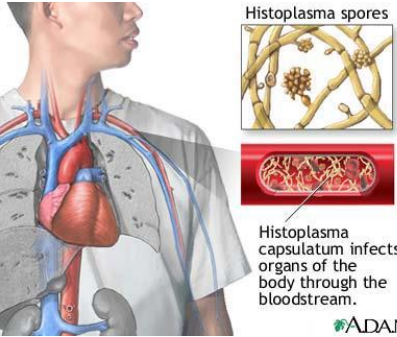
- **Definition:**
  - A systemic fungal infection by airborne infectious agents – *Histoplasma capsulatum var capsulatum*
  - Not contagious
- **Epidemiology:**
  - Primary source of these organisms – Avian but they originate from soil, enriched with feces
  - Global distribution but endemic areas including USA and South America countries



# HISTOPLASMA CAPSULATI

- **Clinical Features:**
  - 90-95% Asymptomatic or subclinical primary pulmonary lesion and heal without treatment – detected by CXR
  - 5-10% Symptomatic cases;
    1. Acute pulmonary infection
    2. Disseminated infection
    3. Chronic pulmonary infection

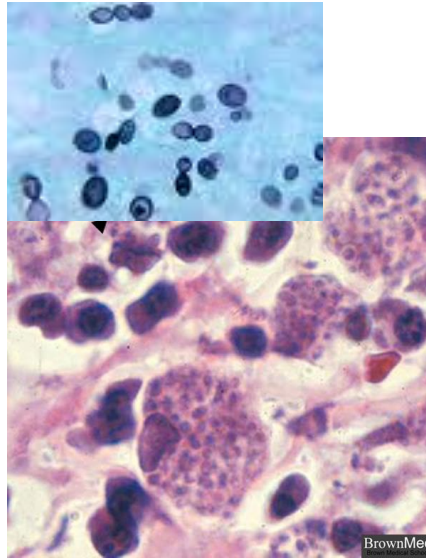
Acute pulmonary infection	Chronic pulmonary infection
<ul style="list-style-type: none"> <li>• Influenza-like symptoms and recovery in a few day to 2 weeks later</li> <li>• Rare sequelae; persistent lymphadenopathy with bronchial obstruction, granulomatous and sclerosing mediastinitis</li> <li>• Resolving need bed rest and other supportive treatment and infrequently for antifungal therapy</li> </ul>	<ul style="list-style-type: none"> <li>• Common for middle-age men</li> <li>• Symptoms and lesions similar to other chronic lung lesions – Tuberculosis; cavity and /or solitary residual nodule with central necrosis and hilar lymph node involvement - <b>Histoplasmosis</b></li> <li>• Residual nodule can found in CXR – coin lesion because of its calcification</li> </ul>

Disseminated histoplasmosis capsulati	
<ul style="list-style-type: none"> <li>• Severe and life-threatening</li> <li>• Usually occur in infant, elderly, and profoundly immunodeficiency patient, especially defect in CMI</li> <li>• Hematogenous dissemination to various organs via mononuclear phagocytic system</li> <li>• Mortality rate = 80% without antifungal therapy</li> </ul>	 <p>Histoplasma spores</p> <p>Histoplasma capsulatum infects organs of the body through the bloodstream.</p> <p>ADAM</p>

## Pathologic Features

### Morphology of organisms

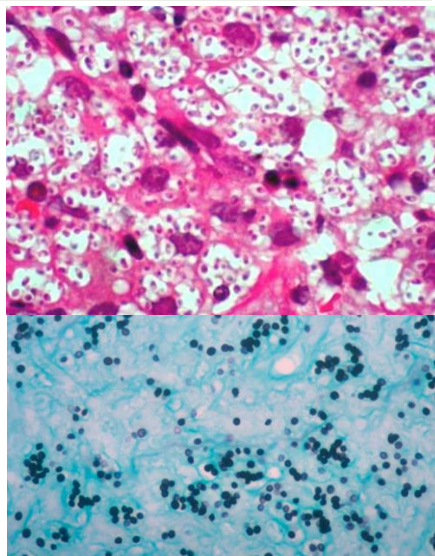
- Yeastlike, hyaline, spherical to oval, uniform, 2-4  $\mu\text{m}$  in diameter, some with single bud (narrow base) aggregate in cluster within cytoplasm of the macrophages
- Easily demonstrated by GMS



## Pathologic Features

### Tissue response

- Immunocompromise Host;
  - Diffuse aggregation of yeast-laden macrophages within tissue with or without necrosis
- Immunocompetent Host;
  - Epithelioid and giant cell granulomatous response with or without necrosis and sparse fungal cells

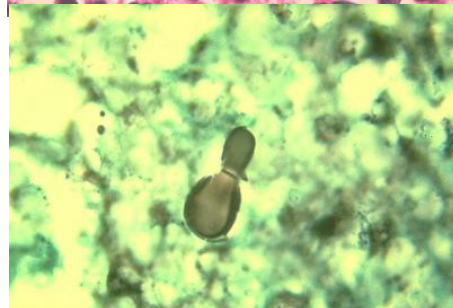
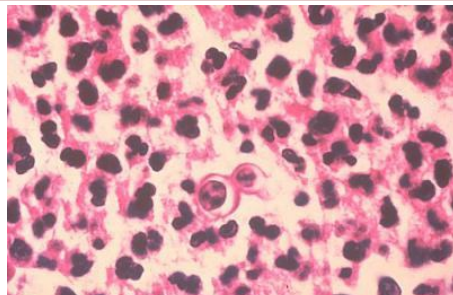


# BLASTOMYCOSIS

- **Definition and Etiologic Agent:**
  - A systemic fungal infection via *Blastomyces dermatitidis*
  - Rare primary cutaneous blastomycosis – self limited, not disseminate
- **Epidemiology:**
  - Endemic region - North America
  - Not contagious but infected by inhaling aerosolized infectious agent growing in soil
  - Primary infectious site – Lung
  - Other than human, Dogs are the most susceptible and infectious rate = 10 time more than human

## Morphology and Pathology

- **Organisms in tissue;**
  - Non-encapsulated yeastlike cells with **broad-base bud**;
  - Typical form = 8-15 um, multinucleated yeasts with vacuolated cytoplasm and thick double contoured wall
- **Tissue response:**
  - Acute form – suppurative with infiltrate of neutrophils and abscesses
  - Chronic form – Mixed suppuration and granulomatous response

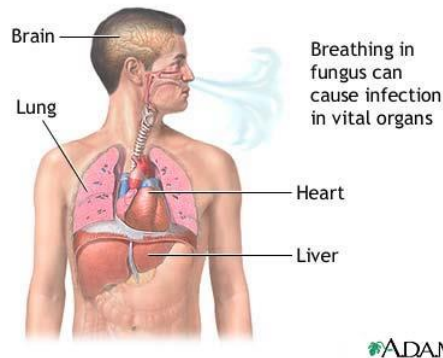




# COCCIDIOIDOMYCOSIS

- **Definition and Etiology:**

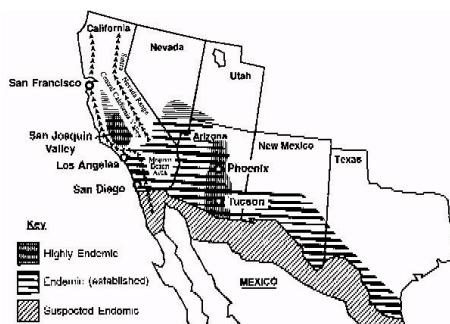
- A infectious disease caused by *Coccidioides immitis* and causing variety of lesions from silent infection (most people) to progressive infection and death
- Infected via inhaling fungal conidia



# COCCIDIOIDOMYCOSIS

## Epidemiology:

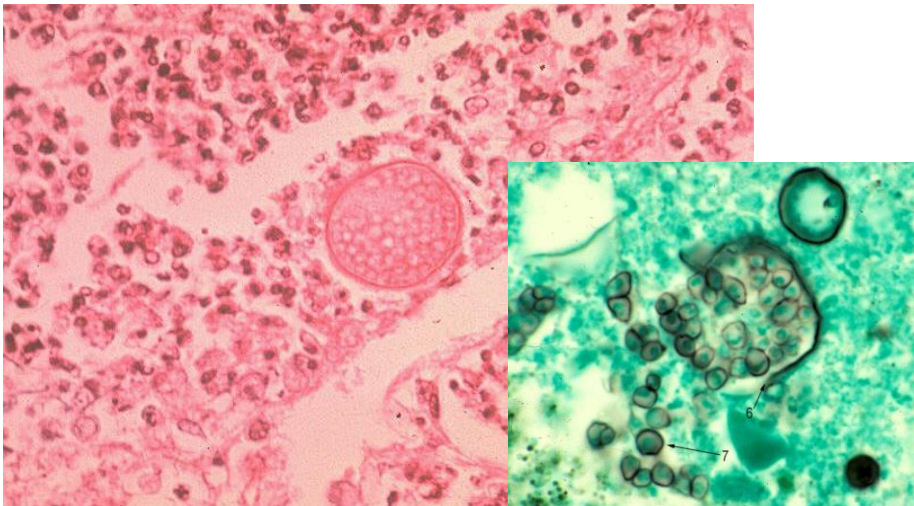
These organisms exists in soil within specific area – Northern California to Argentina



## Clinical features :

1. Pulmonary (symptomatic or asymptomatic)
2. Disseminated
3. Residual pulmonary
4. Primary cutaneous



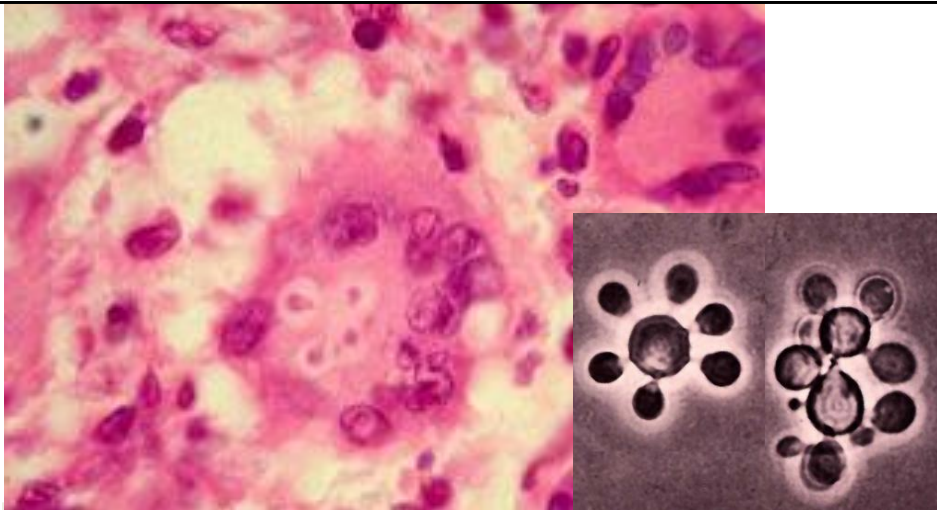


### Morphology of Organism

In host tissue, the organism form **thick-walled endosporulating spherules** 20 to 100  $\mu\text{m}$  in diameter, some rupture and release uninucleate endospores 2 to 5  $\mu\text{m}$  in diameter.

## PARACOCCIDIOIDOMYCOSIS

- **Definition and Etiologic Agent:**
  - A systemic infectious disease caused by *Paracoccidioides brasiliensis* which grow soil
  - No human to human transmission, but the organism entering the body via respiratory passage
- **Epidemiology:**
  - Numbers of case base on case reporting
  - The endemic area – along rivers from the Amazonian jungle to small forest in Uruguay
- **Clinical features – many clinical forms:**
  - Subclinical, Primary pulmonary, Acute pulmonary, Acute or subacute disseminated, chronic pulmonary, chronic disseminated, and opportunistic forms



### Morphology of Organism

In host tissue, there are diversity of organism - Large thick walled yeast cells with oval bud (narrow base), some with multiple buds

## CRYPTOCOCCOSIS

- Definition and Etiologic Agent:
  - A systemic mycosis caused by *Cryptococcus neoformans* (Most common – var *neoformans*)
  - The organisms grow in soil and more abundant in avian habitats, particularly in Pigeon excreta
- Epidemiology:
  - Worldwide in distribution
  - Infected via inhaling aerosolized fungal cells from environment
  - Infection can occurs in immunocompetent as well as immunocompromise hosts, but prominent in patients with CMI defect or severe underlying diseases including AIDS

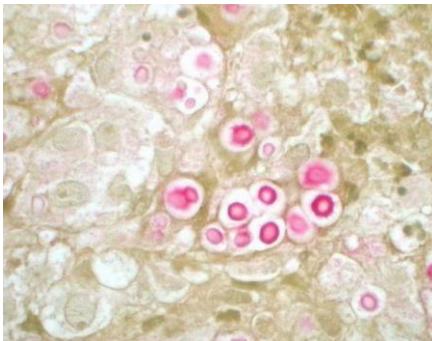
## Clinical Features

- Two basic forms;
  1. Pulmonary cryptococcosis
  2. Hematologic or lymphatic dissemination from pulmonary focus to various organs, especially cerebromeningeal
- **Cerebromeningeal cryptococcosis** – predominant clinical form, most common in AIDS
- Diagnostic testing;
  - Demonstrate fungal cells in CSF via indian ink preparation or tissue by GMS, PAS, and Mucicarmine stain
  - Detect antigen via latex agglutination in CSF

## Diagnostic test for Cryptococcosis

Presence of spherical or oval encapsulated, yeast-like cells, 2 to 20  $\mu\text{m}$  in diameter with narrow budding base and demonstrate mucinous material in capsule with

**Mucicarmine stain – pink color**

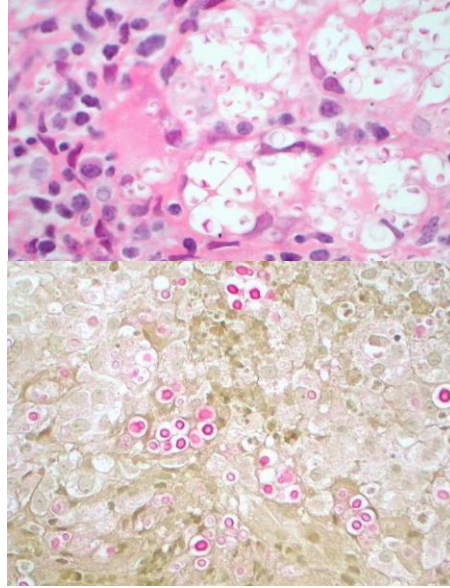


Presence of budding yeasts in CSF in dark background of india ink

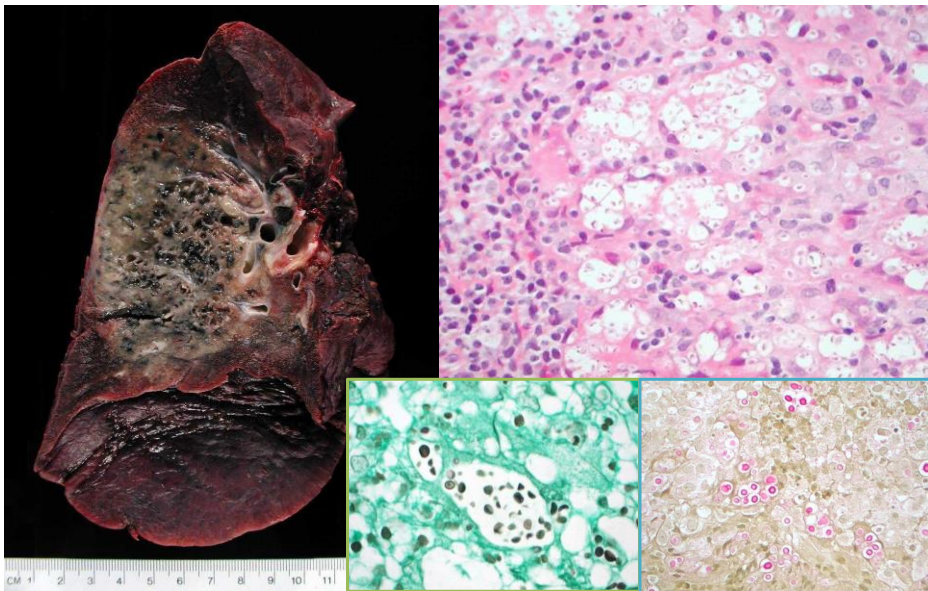


## Pathology of Cryptococcosis, depend on host immunity

- In patient with AIDS, there is a paucireactive pattern – presence of numerous and closely packed fungal cells replacing the normal tissue.
- Abundant mucoid capsule give the lesion a glistening appearance
- In immunocompetent patients, there is a mixed suppurative and granulomatous reaction with varying degree of necrosis



## Pulmonary cryptococcosis



# CANDIDIASIS

- **Definition and Etiologic Agent:**
  - An infection caused by species of the genus *Candida*  
(Most common – *Candida albican*)
  - Most candida sp are common inhabitants of respiratory, Gastrointestinal, and genitourinary tracts, but immunodeficient patients can be infected or invaded by these organisms
- **Epidemiology:**
  - Worldwide in distribution
  - *Candida* sp have human and animal reservoirs
  - Mechanical barrier, inflammation, HMI, CMI as well as bacteria normal flora restrict the growth of these fungus.

## Clinical Features

- Clinical features are so varied;
  - Depending on site or location of *Candida* infection
  - Localized or Systemic infection with candidemia
- Internal organ involvement including liver, spleen, heart, and CNS is the manifestation of disseminated infection via hematogenous spreading
- Oropharyngeal and esophageal candidiasis are common in patients with CMI defect
- Vulvovaginitis candidiasis and balanitis – the most common candida infection
- Lower urinary tract infection usually occurs in catheterized patients treated with antibiotics





[www.oralcancerfoundation.org/den...ions.htm](http://www.oralcancerfoundation.org/den...ions.htm)

### Oropharyngeal candidiasis or Oral thrush

Classic symptoms of oral Candidiasis include the appearance of whitish, velvety plaques on the mucous membranes of the mouth and tongue.

### Vulvovaginitis candidiasis



Courtesy of M. McGinnis

Copyright © 2000 Doctorfungus Co

Vaginal smear with KOH preparation

Pap or cervicovaginal smear



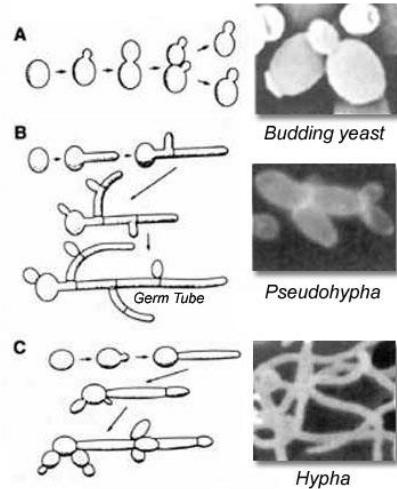
[student.ccbcmd.edu/courses/bio14...ts.html](http://student.ccbcmd.edu/courses/bio14...ts.html)

ASAP MicroLibrary.org/medunibk

## Morphologic Features of Candida

### In tissue:

- Pale blue, oval yeast cells 3 – 5  $\mu$ m, some with budding
- Pseudohyphae 3 -5  $\mu$ m wide having periodic constriction at points where budding yeast cells are joined end to end
- Occasion true hyphae
- Clear visible in GMS and PAS



[overcomingcandida.com/candida\\_al...ures.htm](http://overcomingcandida.com/candida_al...ures.htm)

## Pathology

- Three varieties
1. Superficial candidiasis
    - Most common
    - Infection limited to the lining surface , especially skin, oropharynx, GI tract, and respiratory tract and no deep tissue or vascular involvement
  2. Locally invasive candidiasis
    - In Patients with immunodeficiency
    - Local invading to deep tissue causing ulceration of GI, respiratory, and GU tracts
  3. Disseminated candidiasis
    - The most severe form with internal organ involvement – multiple organ abscesses



# ASPERGILLOSIS

- **Definition and Etiologic Agents:**
  - A disparate group of disease of varying pathogenesis, having in common their association with mycelial pathogens of the genus *Aspergillus* (**Most common – *A. Fumigatus*, *A. Flavus*, and *A niger***)
- **Epidemiology:**
  - Common throughout the world
  - Outcome of infection depending more on host factors than virulence or pathogenesis of the fungus
  - The respiratory tract – most frequent and important of entry for human infection

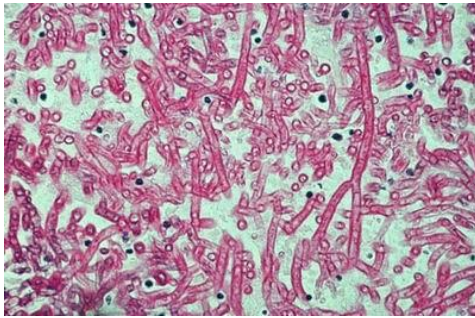
## Clinical Features

- **Allergic aspergillosis** involving the nasal cavity, paranasal sinuses, and lower respiratory tract in hypersensitized host
- **Colonizing form of Aspergillosis** include obstructed paranasal sinuses, bronchi, and preformed pulmonary cavities, with formation of fungal ball – **true aspergilloma** in persons with normal immunity
- **Necrotizing pseudomembranous bronchial aspergillosis and Chronic necrotizing pulmonary aspergillosis** - limited invasive infection of bronchi and pulmonary parenchyma in mildly immunodeficient patients
- **Invasive pulmonary aspergillosis and disseminated aspergillosis** - Frankly invasive pulmonary infection in severely immunodeficient patients with disseminated infection

## Morphologic Features of Aspergillus

### In tissue

- Homogeneous and uniform, septate hyphae 3-6  $\mu\text{m}$  in width with dichotomous branching, usually in acute angle
- Producing conidial head when exposed to air
- Usually visible with routine H&E, but clear hyphae demonstration via GMS and PAS

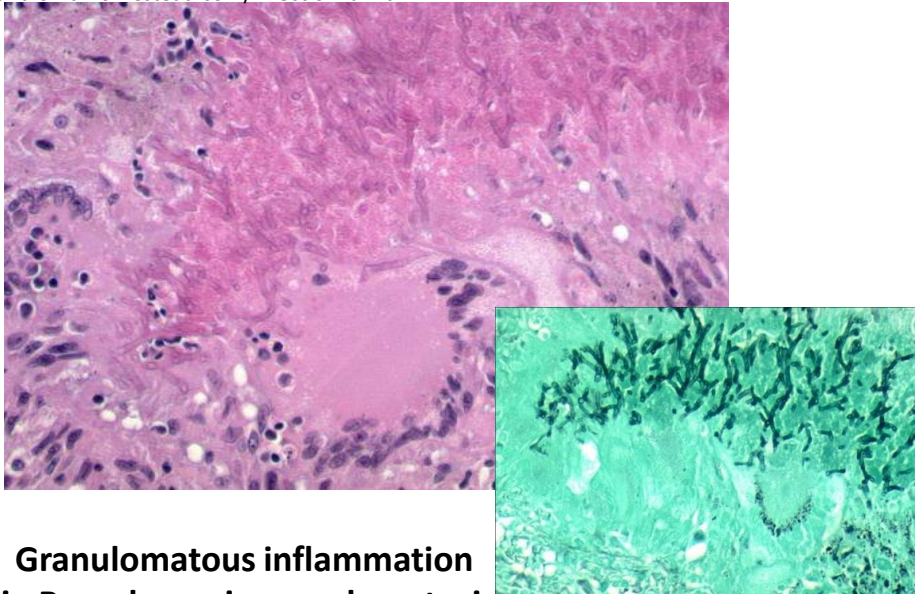


[www.medical-look.com/Allergies/A...sis.html](http://www.medical-look.com/Allergies/A...sis.html)

## Pathology

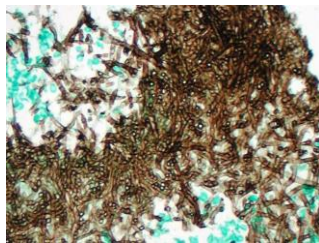
- Allergic bronchopulmonary aspergillosis or Allergic aspergillosis sinusitis
  - Mucoïd impact in bronchi or sinuses which consists of eosinophils, cellular debris, Charcot-leyden crystals, and eosinophilic mucous
  - Granulomatous inflammation with destruction of small bronchial wall – Bronchogenic granulomatosis
  - Diffuse infiltrate of inflammatory cells, predominant eosinophils in alveolar septae and spaces – Chronic eosinophilic pneumonitis

[granuloma.homestead.com/infectio...ial.html](http://granuloma.homestead.com/infectio...ial.html)



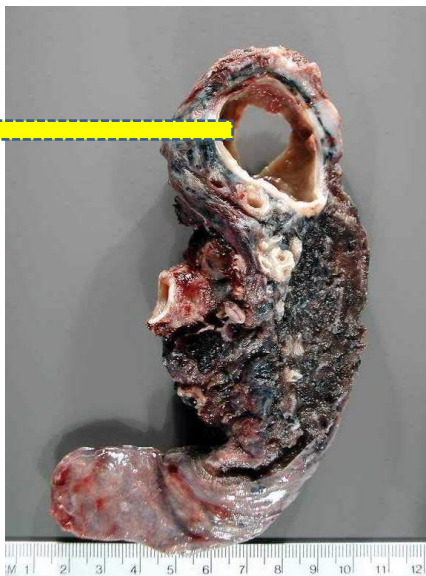
**Granulomatous inflammation  
in Bronchogenic granulomatosis**

## Pathology



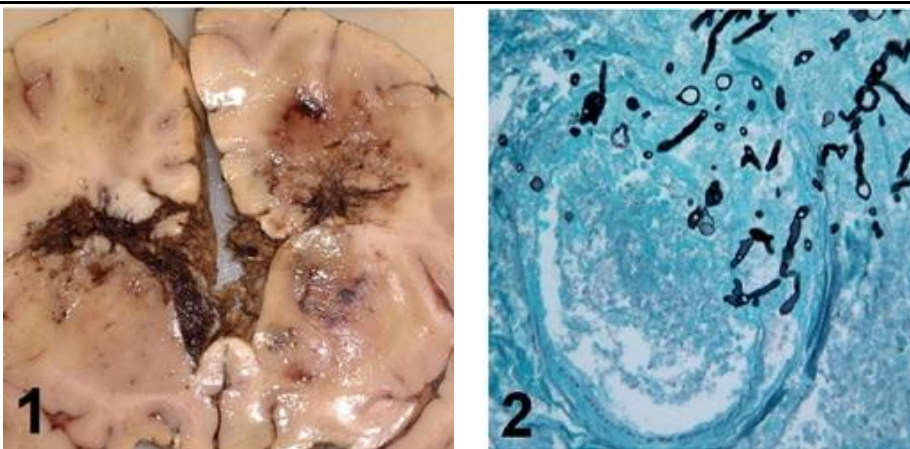
- Colonizing aspergillosis**

Characterized by presence of fungal ball (Macrocolonies of mycelium) in a preexisting lung cavity, often with focal erosion and hemorrhage



# Pathology

- **Necrotizing bronchial aspergillosis**
  - Inflamed or pseudomembrane replacing the epithelium and hyphae or inflammation extend to peribronchial parenchyma
  - No hematologic spreading
- **Invasive pulmonary aspergillosis and disseminated aspergillosis**
  - The pathologic hallmark – **vascular invasion** of fungal hyphae with thrombotic occlusion and parenchymal infarction and hemorrhage
  - Presence of septic emboli in other organs with tissue infarction and hemorrhage



1. Aspergillus invasion in the cerebrum with recent hemorrhage into bilateral ventricles.
2. GMS highlights angioinvasion of Aspergillus sp

**These lesions were observed in the patient with leukemia**

*The Internet Journal of Pathology. 2008 Volume 7 Number 2*

# ZYGOMYCOSIS

- **Definition and Etiologic agents:**
  - An infection causing various diseases which are caused by fungi of the class Zygomycetes (Phycomycetes)
  - There are two different forms of Zygomycosis;
    1. **Mucormycosis via the order Mucorales**
    2. **Entomophthoromycosis via the order Entomophthorales**
- **Epidemiology:**
  - Mucormycosis – Worldwide in distribution
  - Entomophthoromycosis – predominantly in tropical Africa, Southeast Asia, and South America

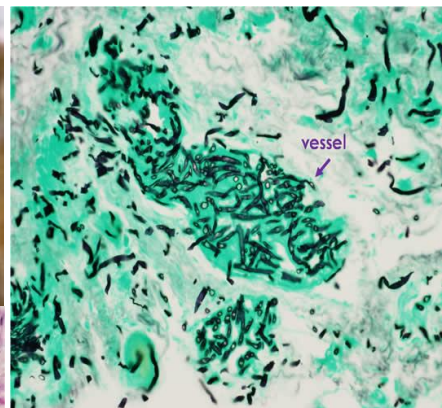
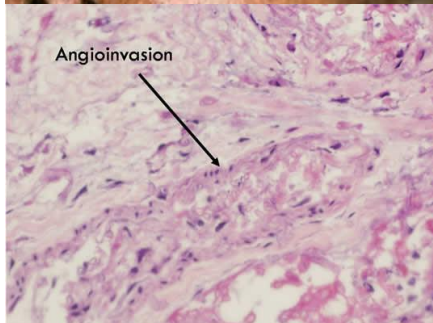
# ZYGOMYCOSIS

	Mucormycosis	Entomophthoromycosis
Pathogenic genera	<b>The order Mucorales:</b> Absidia, Apophysomyces, Cunninghamella, Mortierella, Mucor, Rhizomucor, Rhizopus, Saksenaea and Syncephalastrum <b>but the most common – Rhizopus arrhizus</b>	<b>The order Entomophthorales :</b> Basidiobolus and Conidiobolus
Host factor	Immunodeficiency, particularly in patients with acidosis, leukemia or lymphoma	Immunocompetent
Route of Entry	Exposure to sporangiospores via inhale, ingest, or deposite to the mucous membrane in burn case, but not contagious	Percutaneous implantation of fungus

# ZYGOMYCOSIS

	Mucormycosis	Entomophthoromycosis
Clinical feature	Several forms; Rhinoorbitocerebral , Pulmonary , Gastrointestinal, cutaneous, and Disseminating forms	Subcutaneous and Rhinofacial
Pathology	Aggressive angioinvasion, septic thrombosis and tissue infarction, but suppurative or granulomatous may be seen	Granulomatous inflammation with presence of hyphae ensheathed by amorphous intensely eosinophilic Splendore-Hoepli material
Morphology of Organisms	Broad (5-20um wide) nonseptate , thin hyphae with irregular contour and right angle branching, some collapse or twisted.	Shorter and more conspicuous septate

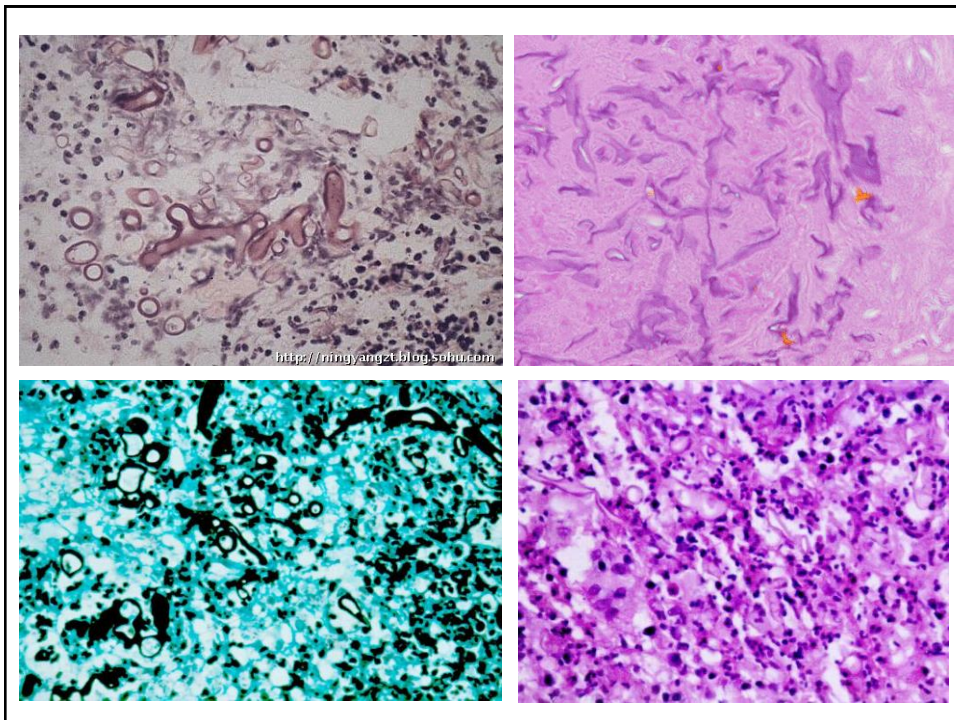
## Rhinoorbitocerebral Mucormycosis



GMS highlights fungal hyphae  
invading blood vessel - **Angioinvasion**

[webeye.ophth.uiowa.edu/eyeforum/...osis.htm](http://webeye.ophth.uiowa.edu/eyeforum/...osis.htm)





## Differential diagnosis: Mucormycosis VS Aspergillosis

Features	Aspergillous sp	Rhizopus sp and other Zygomycosis
Width	Narrow, 3-6 $\mu$ m	Broad, 5-20 $\mu$ m
Caliber	Uniform	Variable
Branching	Regular, dichotomous branching with acute angle	Haphazard, and right angle
Orientation of branching	Parallel or radial	Random
Septation	Frequent	Infrequent

## PENICILLIOSIS MARNEFFEI

- **Definition and Etiologic Agent:**
  - A disseminated fungal infection involving the mononuclear phagocytic system and caused by *Penicillium marneffei*
  - Occurring primarily in HIV-infected patients living in Thailand and South China
- **Epidemiology:**
  - Endemic in Thailand, Some provinces of China including Hong Kong, Vietnam, and Indonesia
  - Occurring in immunodeficient cases, especially in Thailand

## Clinical Features

### In AIDS patients

- Fever with or without Chills
- Respiratory signs; persistent cough and pulmonary infiltrate
- Cutaneous and Subcutaneous lesions
- Septicemia
- Gastrointestinal lesion

### In other immunocompromise conditions including poor nutrition, SLE, Lymphoma etc.

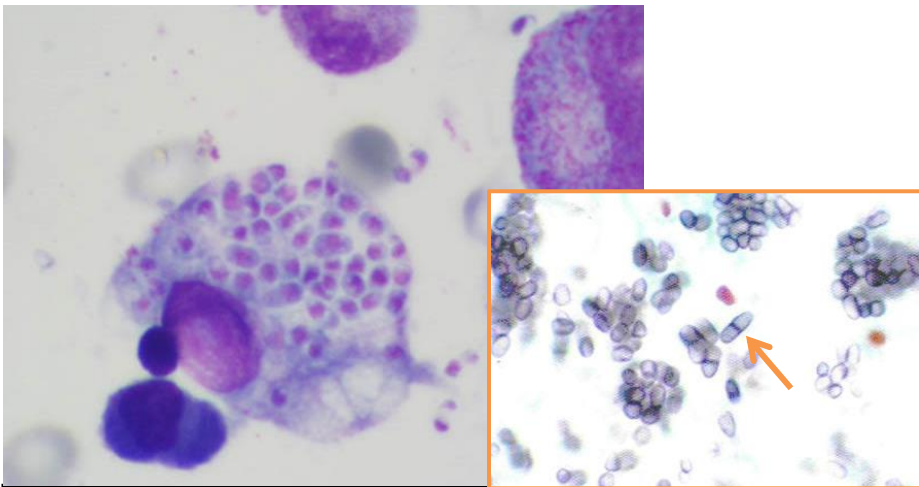
- Fever with or without Chills
- Respiratory signs
- Cutaneous and Subcutaneous lesions
- Lymphadenopathy
- Hepatomegaly and Splenomegaly
- Osteoarticular lesion



### Cutaneous lesion

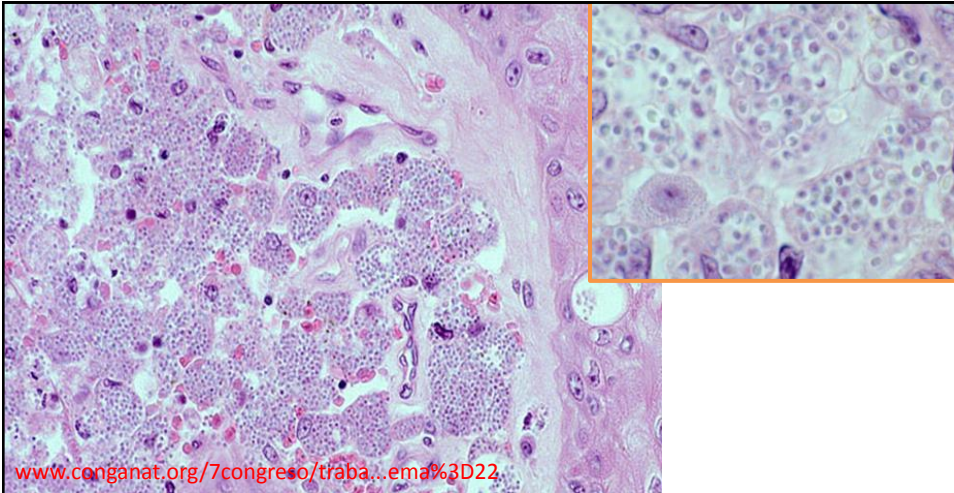
Skin papules with central necrotic umbilication or Acne-like pustules in *Penicilliosis Marneffei*

<http://www.med.cmu.ac.th/dept/pediatrics/06-interest-cases/ic-45/case45.HTM>



### Wright stain from skin lesion

Aggregation of yeast organisms, 2-4 um in cytoplasm of the macrophage. Central fission (Binary fission) is the characteristic feature of *Penicillium marneffei*



### Morphology of Organism in Tissue

In human tissue, *P marneffei* grows as a yeast with the same size as *Histoplasma capsulatum*. The difference in reproduction can separate *P marneffei* from *H capsulatum*; **Binary fission (fission at the center) in *P marneffei* but Budding in *H capsulatum***

## Pathology

	Non-AIDS	AIDS
Infected tissue	Lymph node, Liver, Lung, and Kidney	Lymph node, Skin, Bone and Bone marrow
Tissue reaction	Suppurative and Granulomatous	Necrotizing
	Yeast-like organisms aggregate in intracellular (in macrophages) and extracellular areas with binary fission	

## Reference

- **Daniel H Connor et al. Pathology of Infectious Disease ( 1997)**
- **Vinay Kumar et al. Robbins and Cotran: Pathologic Basis of Disease 7<sup>th</sup> eds.**
- **Cedric Mims et al. Medical microbiology 3<sup>rd</sup> eds.**