Pathology of Fungal Infection

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

Pulmonary aspergillosis
Host – Agent relationship

Organisms

Host

Immunocompetent host

Immunocompromise host

Pathogenic agents

Impaired Defense mechanism

Environment

Nosocomial infection

Infectious disease

Opportunistic infection

Superficial mycoses

<table>
<thead>
<tr>
<th>Representative disease</th>
<th>Causative organisms</th>
<th>Growth form in Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatophytosis</td>
<td>Microsporum, Trichophyton, and Epidermophyton</td>
<td>Filamentous form</td>
</tr>
<tr>
<td>Pityriasis versicolor or skin infection via malassezia</td>
<td>Malassezia</td>
<td>Yeast and filamentous form</td>
</tr>
<tr>
<td>Tinea nigra or keratomycosis nigrican palmaris</td>
<td>Exophialia (Phaeoanellomyces) wernekii</td>
<td>Filamentous form (pigmented)</td>
</tr>
<tr>
<td>Onychomycosis</td>
<td>Microsporum, Trichophyton, Epidermophyton etc.</td>
<td>Filamentous form</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Infection</th>
<th>Clinical Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tinea capitis</td>
<td>Scalp</td>
</tr>
<tr>
<td>Tinea favosa</td>
<td>Scalp</td>
</tr>
<tr>
<td>Kerion</td>
<td>Scalp, Hair</td>
</tr>
<tr>
<td>Majocchi Granuloma</td>
<td>Hair</td>
</tr>
<tr>
<td>Tinea faciei</td>
<td>Face</td>
</tr>
<tr>
<td>Tinea barbae</td>
<td>Beard</td>
</tr>
<tr>
<td>Tinea corporis</td>
<td>Skin (general)</td>
</tr>
<tr>
<td>Tinea cruris</td>
<td>Groin</td>
</tr>
<tr>
<td>Tinea manumm (manus)</td>
<td>Hand</td>
</tr>
<tr>
<td>Tinea pedis</td>
<td>Feet</td>
</tr>
<tr>
<td>Tinea unguium</td>
<td>Nails</td>
</tr>
</tbody>
</table>
**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

Multiple hypopigmented oval to confluent macules
Numerous budding yeasts (blastocladia) and short septate hyphae (pseudomycelium) in the stratum corneum (spaghetti 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, Microsporosis 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:
  – Exophialia (Phaeoanellomyces) werneckii – pigmented mycelial fungus

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

ONYCHOMYCOSES

• 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

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

<table>
<thead>
<tr>
<th></th>
<th>Eumycotic Mycetoma</th>
<th>Actinomycotic Mycetoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Causative agents</strong></td>
<td>Fungus: Several species depend on the geographical areas</td>
<td>Filamentous bacteria: Actinomadura madurae, Nocardia asteroides, Streptomyces somaliensis etc.</td>
</tr>
<tr>
<td><strong>Clinical features</strong></td>
<td>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)</td>
<td></td>
</tr>
<tr>
<td><strong>Grain colors</strong></td>
<td>White or Black</td>
<td>White, red, or yellow</td>
</tr>
</tbody>
</table>
# MYCETOMA

<table>
<thead>
<tr>
<th></th>
<th>Eumycotic Mycetoma</th>
<th>Actinomycotic Mycetoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morphology of</strong></td>
<td>Septate, fungal hyphae (2 to 6 um or more width) and some pigmented (black grain)</td>
<td>Delicate, branched, gram-positive and sometime beaded or fragmented bacterial filaments (&lt; or = 1 um)</td>
</tr>
<tr>
<td><strong>organisms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pathologic features</strong></td>
<td>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</td>
<td></td>
</tr>
<tr>
<td><strong>Special stains</strong></td>
<td>GMS and PAS</td>
<td>Gram stain</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Surgical excision or Amputation</td>
<td>Antibiotic treatment</td>
</tr>
</tbody>
</table>

## Medura Foot Or Maduromycosis

1. Entry-penetrating trauma
2. Disease:
   - Swelling, induration, pus
3. Exit-draining sinus tract
Dermis and subcutaneous contains multiple abscesses

The granule or grain of organism is identified in the central portion of the abscess

The granule or grain of organism are bordered by refractile, intensely eosinophilic, finely to coarsely dentate Splendore-Hoepli material that represent a localized antigen-antibody reaction in hypersensitized host.
**Actinomycotic Mycetoma**

Delicate, branched, gram-positive and sometime beaded or fragmented bacterial filaments (< or = 1 um)

**Eumycotic Mycetoma**

Septate, fungal hyphae (2 to 6 um or more width) and some pigmented (black grain)

**Eumycotic Mycetoma**

Black grain

White grain
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 um) demonstrated by GMS or PAS
- Budding yeasts - Teardrop or pipe stem configuration

**The asteroid body**

- Yeast formed organism enveloped by Splendore-Hoepli material - intense eosinophilic material with elongated and radiated spicules
- Asteroid body almost always in microabscess
# Systemic or deep mycoses

<table>
<thead>
<tr>
<th>Representative disease</th>
<th>Causative organisms</th>
<th>Growth form In Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histoplasmosis Capsulati</td>
<td><em>Histoplasma capsulatum var capsulatum</em></td>
<td>Yeast form</td>
</tr>
<tr>
<td>Blastomycosis</td>
<td><em>Blastomyces dermatitidis</em></td>
<td>Yeast form</td>
</tr>
<tr>
<td>Coccidioidomycosis</td>
<td><em>Coccidioides immitis</em></td>
<td>Endospore in spherule</td>
</tr>
<tr>
<td>Paracoccidioidomycosis</td>
<td><em>Paracoccidioides brasiliensis</em></td>
<td>Yeast form</td>
</tr>
</tbody>
</table>

# Systemic or deep mycoses, opportunistic infection

<table>
<thead>
<tr>
<th>Representative disease</th>
<th>Causative organisms</th>
<th>Growth form In Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptococcosis</td>
<td><em>Cryptococcus neoformans</em></td>
<td>Yeast form</td>
</tr>
<tr>
<td>Candidiasis</td>
<td><em>Candida albican</em>, other candida sp</td>
<td>Yeast form</td>
</tr>
<tr>
<td>Aspergillosis</td>
<td><em>Aspergillus fumigatus</em>, <em>Aspergillus flavus</em>, <em>Aspergillus niger</em>, etc</td>
<td>Filamentous form</td>
</tr>
<tr>
<td>Zygomycosis</td>
<td>The order Mucorales, The order Entomophthorales</td>
<td>Filamentous form</td>
</tr>
<tr>
<td>Penicilliosis Maneffei</td>
<td><em>Penicillium marneffi</em></td>
<td>Yeast form</td>
</tr>
</tbody>
</table>
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
<table>
<thead>
<tr>
<th>Acute pulmonary infection</th>
<th>Chronic pulmonary infection</th>
</tr>
</thead>
</table>
| • Influenza-like symptoms and recovery in a few day to 2 weeks later  
• Rare sequelae; persistent lymphadenopathy with bronchial obstruction, granulomatous and sclerosing mediastinitis  
• Resolving need bed rest and other supportive treatment and infrequently for antifungal therapy | • Common for middle-age men  
• Symptoms and lesions similar to other chronic lung lesions – Tuberculosis; cavity and/or solitary residual nodule with central necrosis and hilar lymph node involvement - **Histoplasmosomas**  
• Residual nodule can found in CXR – coin lesion because of its calcification |

---

**Disseminated histoplasmosis capsulati**

• Severe and life-threatening  
• Usually occur in infant, elderly, and profoundly immunodeficiency patient, especially defect in CMI  
• Hematogenous dissemination to various organs via mononuclear phagocytic system  
• Mortality rate = 80% without antifungal therapy
**Pathologic Features**

**Morphology of organisms**
- Yeastlike, hyaline, spherical to oval, uniform, 2-4 um in diameter, some with single bud (narrow base) aggregate in cluster within cytoplasm of the macrophages
- Easily demonstrated by GMS

**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

**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 um in diameter, some rupture and release uninucleate endospores 2 to 5 um in diameter.

PARACOCIDIOIDIDOMYCOSIS

• 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 um 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 albicans)
  – 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 balantitis – the most
  common candida infection

• Lower urinary tract infection usually occurs in
  catheterized patients treated with antibiotics
**Classic symptoms of oral Candidiasis include the appearance of whitish, velvety plaques on the mucous membranes of the mouth and tongue.**

**Oropharyngeal candidiasis or Oral thrush**

**Vulvovaginitis candidiasis**

- Pap or cervicovaginal smear
- Vaginal smear with KOH preparation
Morphologic Features of Candida

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

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 pseudomenbranous 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 um in width with dichotomous branching, usually in acute angle
- Producing conidal head when exposed to air
- Usually visible with routine H&E, but clear hyphae demonstration via GMS and PAS

Pathology
- Allergic bronchopulmonary aspergillosis or Allergic aspergillosis sinusitis
  - Mucoid 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

www.medical-look.com/Allergies/A...sis.html
Granulomatous inflammation in Bronchogenic granulomatosis

**Pathology**

- Colonizing aspergillosis

  Characterized by presence of fungal ball (Macrocollections 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

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

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Mucormycosis</th>
<th>Entomophthoromycosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Several forms; Rhinoorbitocerebral, Pulmonary, Gastrointestinal, cutaneous, and Disseminating forms</td>
<td>Subcutaneous and Rhinofacial</td>
</tr>
</tbody>
</table>

| 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

웹사이트: webeye.ophth.uiowa.edu/eyeforum/...osis.htm
Differential diagnosis: Mucormycosis VS Aspergillosis

<table>
<thead>
<tr>
<th>Features</th>
<th>Aspergillous sp</th>
<th>Rhizopus sp and other Zygomycosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Width</td>
<td>Narrow, 3-6 um</td>
<td>Broad, 5-20 um</td>
</tr>
<tr>
<td>Caliber</td>
<td>Uniform</td>
<td>Variable</td>
</tr>
<tr>
<td>Branching</td>
<td>Regular, dichotomous branching with acute angle</td>
<td>Haphazard, and right angle</td>
</tr>
<tr>
<td>Orientation of branching</td>
<td>Parallel or radial</td>
<td>Random</td>
</tr>
<tr>
<td>Septation</td>
<td>Frequent</td>
<td>Infrequent</td>
</tr>
</tbody>
</table>
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 Penicillosis Marneffei

http://www.med.cmu.ac.th/dept/pediatrics/06-interest-cases/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*
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

<table>
<thead>
<tr>
<th></th>
<th>Non-AIDS</th>
<th>AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infected tissue</td>
<td>Lymph node, Liver, Lung, and Kidney</td>
<td>Lymph node, Skin, Bone and Bone marrow</td>
</tr>
<tr>
<td>Tissue reaction</td>
<td>Suppurative and Granulomatous</td>
<td>Necrotizing</td>
</tr>
<tr>
<td></td>
<td>Yeast-like organisms aggregate in intracellular (in macrophages) and extracellular areas with binary fission</td>
<td></td>
</tr>
</tbody>
</table>
Reference

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