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MED437  
KING SAUD UNIVERSITY



# Respiratory Fungal Infection



MICROBIOLOGY  
437

**Important!**  
Doctor's Notes  
Only found in females' slides  
Only found in males' slides  
Extra Notes

*"I'm not telling you it's going to be easy. I'm telling you it's going to be worth it."*

# Respiratory Fungal infections

A+B are opportunistic  
C is primary infections

## Etiology

- ❖ Respiratory System: Nose to alveoli
- ❖ Route of infection?
  - Inhalation of the spores
  - Aspiration like Candida
  - Hematogenous spread (blood)
- ❖ Oral Cavity, any role?
- ❖ Respiratory fungal infections are less common than viral and bacterial infections.
- ❖ Have significant difficulties in diagnosis and treatment.

### A) Yeast

- Candidiasis (Candida and other yeast)
- Cryptococcosis (Cryptococcus neoformans, C. gattii)

### B. Mould fungi

- Aspergillosis (aspergillus species)
- Zygomycosis (Zygomycetes, e.g. Rhizopus, Mucor)
- Other mould

### C. Dimorphic fungi it existence depends on temperature; body temp. 37 → yeast / room temp. 25 → mould

- Histoplasma capsulatum
- Paracoccidioides brasiliensis
- Blastomyces dermatitidis
- Coccidioides immitis

# Primary Systemic Mycoses

- ❖ Infections of the respiratory system (**Inhalation**)
- ❖ Dissemination seen in **immunocompromised hosts**
- ❖ Common in North America and to a lesser extent in South America. Not common in other parts of the World
- ❖ **Etiologies are dimorphic fungi**
  - In nature found in soil of restricted habitats.
  - Primary pathogens
  - They are highly infectious
- ❖ **They include:**
  - Histoplasmosis
  - Blastomycosis
  - Coccidioidomycosis
  - Paracoccidioidomycosis

# Aspergillosis

Aspergillosis is a **spectrum of diseases** (group of diseases) of humans and animals caused by member of genus *Aspergillus*

## These include:

1. **Mycotoxicosis** (like poisoning caused by toxins) we have many types of mycotoxins which depends on concentration, time of exposure) e.g **aflatoxin** which mostly poison the kidney
2. **Allergy**
3. **Colonization** (without invasion and extension) in preformed cavities
4. Invasive disease of lung (spread locally)
5. Systemic and disseminated disease (**extrapulmonary**) → hematogenous

## Risk Factors :

1. Bone marrow/ organ transplantation
2. Cancer: leukemia/ lymphoma
3. AIDS
4. Drugs: cytotoxic drugs, steroids
5. Diabetes

**Aetiological Agents:** Aspergillus species → *A.fumigatus*, *A.flavus*, *A.niger*, *A.nidulans*, *A.terreus*

### Classification

Invasive aspergillosis

Chronic aspergillosis:

1- Aspergilloma of lung

2- Maxillary (sinus) aspergilloma

Allergic aspergillosis:

1- Allergic bronchopulmonary (ABPA)

2- Allergic aspergillus sinusitis

Persistence without disease colonisation of the airways or nose/ sinuses

# Aspergillosis

## ★ Chronic Aspergillosis (Colonizing aspergillosis) (Aspergilloma OR Aspergillus fungus ball)

### Signs:

- Cough
- Hemoptysis
- variable fever

### Radiology:

will show mass in the lung,  
**radiolucent crescent**

## ★ Invasive pulmonary Aspergillosis

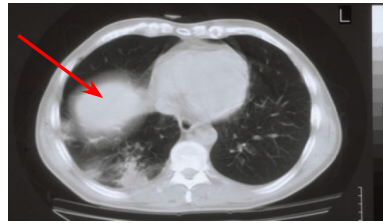
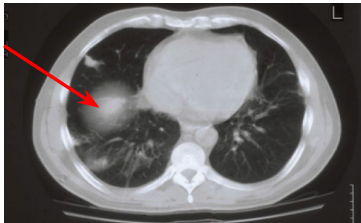
### Signs:

- Cough
- Hemoptysis
- Fever
- Leukocytosis**

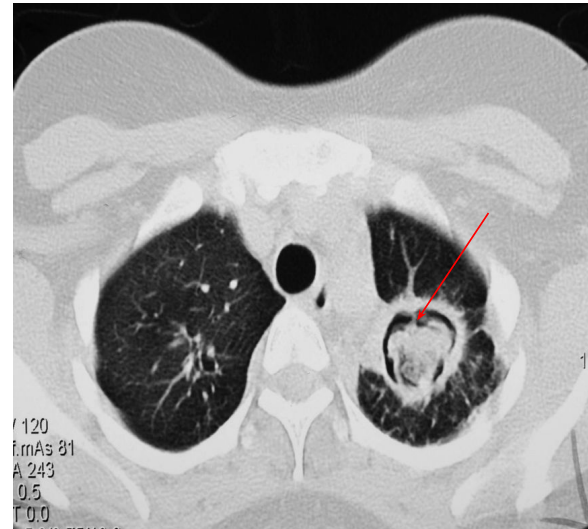
### Radiology:

will show **lesions** with  
**halo sign**

## Invasive pulmonary Aspergillosis **Note the Halo sign**



Simple (single) aspergilloma **Note the air crescent** as we can see the ring shape means that this area is filled with air which means that its recovering



# Allergic bronchopulmonary (ABPA)

## Symptoms of Asthma

- ❖ Bronchial obstruction
- ❖ Fever, malaise
- ❖ Eosinophilia
- ❖ Wheezing +/-

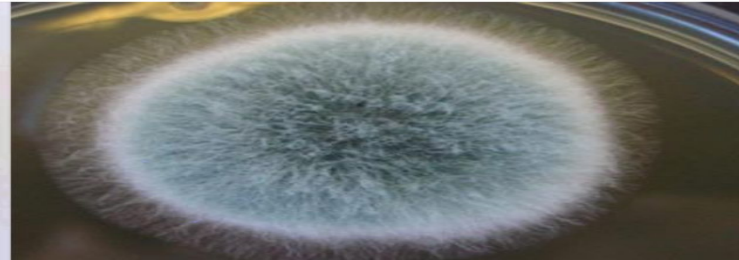
## Also:

- ❖ Skin test reactivity to *Aspergillus* (positive)
- ❖ Serum antibodies to *Aspergillus*(positive)
- ❖ Serum IgE > 1000 ng/ml
- ❖ Pulmonary infiltrates

## Common Airborne Fungi differ by color after culturing



*Aspergillus niger* (black-brownish)



*Aspergillus fumigatus* (greenish-yellow)

# Fungal sinusitis

## Clinical:

- ❖ **Nasal polyps** and other symptoms of sinusitis, **also headache and nasal stuffiness.**
- ❖ In immunocompromised, **could disseminate to eye** > cranium (Rhino cerebral)
- ❖ The most common cause in KSA is **aspergillus flavus**
- ❖ In addition to aspergillus there are other fungi that can cause fungal sinusitis
- ❖ Aspergillus sinusitis has the same spectrum of aspergillus disease in the lung

## Diagnosis:

- ❖ Clinical and radiology
- ❖ Histology
- ❖ Biopsy
- ❖ Culture
- ❖ Precipitating antibodies useful in diagnosis
- ❖ **Measurement of IgE level, RAST test**

## Treatment:

Depends on the type and severity of the disease and the immunological status of the patient



# Diagnosis of Aspergillosis

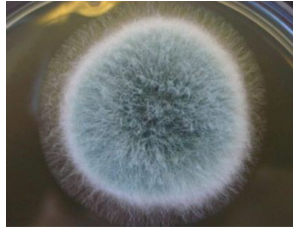
## Lab investigations

- **Direct Microscopy:**  
Giemsa Stain, Grecoth methenamine silver stain (GMS)  
Will show fungal septate hyphae
- **Culture on SDA**
- **Serology:**  
Test for Antibody or Antigen  
ELISA test for galactomannan  
Antigen
- **PCR:**  
Detection of Aspergillus DNA in clinical samples

## Specimen

- **Respiratory specimens:**  
  
Sputum, BAL, Lung biopsy,
- **Other samples:**  
  
Blood, etc.

## Cultures of aspergillus



Smear: septate fungal hyphae. Aspergillosis



## Choice of antifungal for aspergillosis

- **Voriconazole**
- **Alternative therapy:**  
Amphotericin B, Itraconazole, Caspofungin

# Zygomycosis

## Clinical forms of Zygomycosis:

- ❖ Pulmonary zygomycosis
- ❖ Rhinocerebral zygomycosis (can extend to adjacent structures)

## Risk factors:

- ❖ Transplant patients, malignancy, AIDS, diabetic ketoacidosis, and many others.

# Pulmonary Zygomycosis



## Diagnosis:

- ❖ Acute
- ❖ Consolidation, nodules, cavitation, pleural effusion, hemoptysis
- ❖ Infection may extend to chest wall, diaphragm, pericardium.
  - Pulmonary infarction and hemorrhage
  - Rapid evolving clinical course

Early recognition and intervention are critical

## ❖ Specimen:

- Respiratory specimens: Sputum, BAL, Lung biopsy,
- Other sample

## ❖ Lab. Investigations:

- Direct Microscopy: Giemsa, Grocott methenamine silver stain (GMS)
  - Will show broad non-septate fungal hyphae
- Culture on SDA (no cycloheximide)

- ❖ **Serology:** Not available because the specie doesn't contain antigen

## Etiology:

Zygomycetes (Non-septate hyphae) e.g Rhizopus

## Treatment:

- ❖ Amphotericin B
- ❖ Surgery

# Pneumocystis (PCP)

## ❖ Pneumocystis pneumonia (PCP)

- Opportunistic fungal pneumonia
- It is **interstitial pneumonia of the alveolar area.**

- Previously thought to be a protozoan parasite, but later it has been proven to be a fungus
- **Does not grow in laboratory media e.g. SDA**
- **Naturally found in rodents (rats), other animals (goats, horses), Humans may contract it during childhood**

### Affect:

compromised host (especially common in AIDS patients.)

### Etiology:

**Pneumocystis jiroveci**

## Laboratory Diagnosis:

- **Patient specimen:** Bronchoscopic specimens (B.A.L.), **Sputum**, Lung **biopsy tissue.**
- **Histological sections or smears** stained by **GMS stain.**
- **Immunofluorescence** (better sensitivity)
- If positive will see cysts of **hat-shape, cup shape, crescent**

## Treatment: **ANTIBACTERIAL**

- Trimethoprim - sulfamethoxazole
- Dapsone
- **Cotrimoxazole**

# Summary

## Aspergillosis

<b>Aetiological Agents</b>	1- A. fumigatus -2-A. flavus 3- A. niger -4- A. terreus 5- A. nidulans	<b>Treatment</b>	Voriconazole <i>Alternative therapy:</i> Amphotericin B, Itraconazole, Caspofungin
<b>Risk Factors</b>	<ul style="list-style-type: none"> <li>○ Bone marrow - organ transplantation</li> <li>○ Cancer: Leukemia, lymphoma</li> <li>○ AIDS</li> <li>○ Drugs: Cytotoxic drugs, steroids</li> <li>○ Diabetes</li> </ul>	<b>Diagnosis</b>	<b>Specimen:</b> Respiratory: Sputum, BAL, Lung biopsy. Other samples: Blood <b>Lab:</b> <b>Direct Microscopy:</b> Giemsa Stain, GMS stain <b>Will show fungal septate hyphae</b> <b>Culture</b> on SDA <b>Serology:</b> Test for Antibody ELISA test for galactomannan Antigen <b>PCR:</b> Detection of Aspergillus DNA
<b>Classification</b>	1- Invasive aspergillosis 2-Chronic aspergillosis A-Aspergilloma of lung. B-Maxillary (sinus) aspergilloma.	3- Allergic A- Allergic Aspergillus sinusitis B - Allergic bronchopulmonary (ABPA) 4- Persistence without disease: colonization of the airways or nose/sinuses.	

Primary Systemic Mycoses	
<b>Transmission</b>	Inhalation – highly infectious
<b>Etiology</b>	Dimorphic fungi: (Primary infections) Histoplasmosis Blastomycosis Coccidioidomycosis Paracoccidioidomycosis

Pneumocystis pneumonia (PCP): Opportunistic fungal pneumonia	
	It is interstitial pneumonia of the alveolar area.
<b>Etiology</b>	Pneumocystis jiroveci
<b>Diagnosis</b>	<b>Laboratory Diagnosis:</b> <ul style="list-style-type: none"> <li>○ specimen: BAL, Sputum, Lung biopsy tissue.</li> <li>○ Histological sections stained by GMS stain.</li> <li>○ Immunofluorescence</li> </ul> If positive will see cysts of hat-shape, cup shape, crescent
<b>Treatment</b>	Trimethoprim – sulfamethoxazole Dapsone

# Summary

Zygomycosis (Mould fungi) (opportunistic)	Pulmonary zygomycosis (Acute)	Rhinocerebral zygomycosis
<b>Clinical Findings</b>	Consolidation, nodules, cavitation, pleural effusion, hemoptysis	-
<b>Prognosis</b>	Infection may extend to chest wall, diaphragm, pericardium.	-
<b>Etiology</b>	Zygomycetes, e.g. Rhizopus	-
<b>Diagnosis</b>	1-Specimen: Respiratory specimens: Sputum, BAL, Lung biopsy 2-Lab: Direct Microscopy: Giemsa stain, GMS stain * Will show broad non- septate fungal hyphae Culture on SDA (no cycloheximide) Serology: Not available	
<b>Risk factors</b>	Transplant patients - AIDS Malignancy - Diabetic ketoacidosis	
<b>Treatment:</b>	Amphotericin B - surgery	

Aspergillosis (Mould fungi) (opportunistic)	Chronic Aspergillosis	Invasive pulmonary Aspergillosis	Allergic bronchopulmonary (ABPA)	Fungal sinusitis
<b>Symptom</b>	Cough <u>hemoptysis</u> variable fever	Cough hemoptysis fever <u>Leukocytosis</u>	Symptoms of Asthma Bronchial obstruction Fever, malaise Eosinophilia - Wheezing+/-	Nasal polyps other symptoms of sinusitis
<b>Diagnosis</b>	Radiology: mass in the lung, radiolucent crescent	Radiology: lesions with halo sign	- Skin test reactivity to Aspergillus - Serum antibodies to Aspergillus - Serum IgE > 1000 ng/ml - Pulmonary infiltrates	Clinical and Radiology Histology - Culture Precipitating Measurement of IgE level RAST test
<b>Etiology</b>	-	-	-	Aspergillus flavus
<b>complication</b>	-	-	-	In immunocompromised could lead to cranium (Rhinocerebral)
<b>Treatment</b>	-	-	-	depends on the type and severity and the immunological status of the patient

# Quiz

4-D  
3-C  
2-A  
1-C

1- which of the following is opportunistic?

A-Histoplasma capsulatum    B-Coccidioides immitis

C-Cryptococcosis                      D-Blastomyces dermatitidis

2- a patient labs shows a fungal septate hyphae he most likely has?

A- Aspergillosis                      B- Zygomycetes

C- Histoplasmosis                      D-*Pneumocystis jiroveci*

3- which of the following tests is not effective in case of patient with *Pneumocystis pneumonia* ?

A-GMS stain                                      B-IF

C-Culture    D-PCR

4- a patient with Aspergilloma radiology result should show ?

A- halo sign                                      B- nothing

C- pleural effusion                      D-radiolucent crescent

# Team Leaders

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