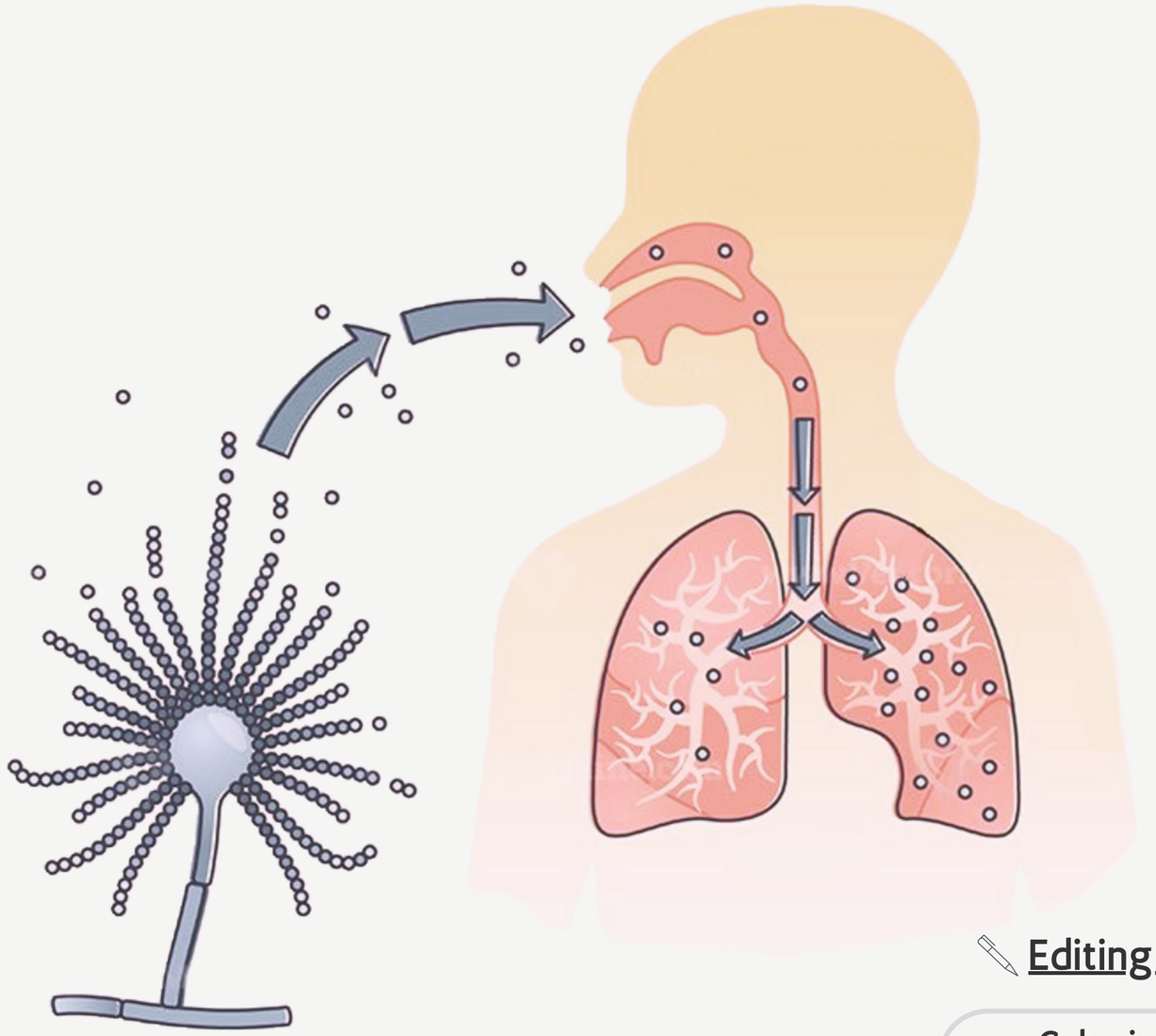
(اللَّهُمَّ انْفَعْنِي بِمَا عَلَّمْتَنِي، وَعَلِّمْنِي مَا يَنْفَعُنِي، وَزِدْنِي عِلْمًا)

RESPIRATORY FUNGAL INFECTIONS

Lecture no.7



Editing File

Color index:

Main text	Girls' slides
Important	Boys' slides
Dr. notes	Extra

ETIOLOGY OF RESPIRATORY FUNGAL INFECTIONS

Fungi

Primary Infections

Opportunistic Infections

Dimorphic fungi

439:Have 2 forms depending on environmental factors
1- it grows as yeast at body temperature
2- grows as mould at room temperature

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

Yeasts

- **Candidiasis**
- **Cryptococcosis**
- **Causative microbes:**

1- Cryptococcus neoformans
2- C.gattii

Moulds fungi

- **Aspergillosis**: Causative microbes: Aspergillus species
- **Zygomycosis:** Causative microbes: Zygomycetes (e.g. Rhizopus, Mucor)
- Other mould

PRIMARY SYSTEMIC MYCOSIS

Overview	- They cause Infections of the respiratory system, (Inhalation) -Dissemination in immunocompromised hosts. (Immuno**competen**t : **Mild** symptoms, Immuno**compromised** : **Severe** symptoms - Common in North America and to a lesser extent in South America. Not common in other parts of the World.
Etiologies	**Dimorphic fungi, including:** **-**Histoplasmosis **-**Blastomycosis **-**Coccidioidomycosis **-**paracoccidioidomycosis
Features Of Dimorphic Fungi	- Primary pathogens - Found in nature in soil of restricted habitats - Highly infectious

Blastomycosis infection

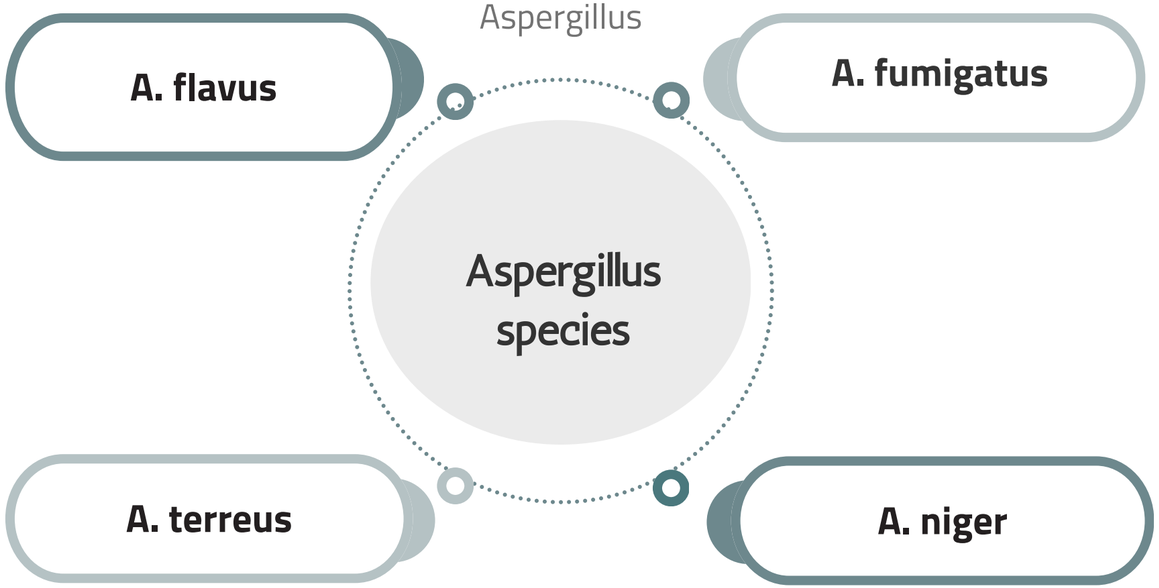
ASPERGILLOSIS

Aspergillosis is a spectrum of diseases of humans and animals caused by members of the genus Aspergillus. They include

- **Mycotoxicosis** (produce toxins)
- **Allergy**
- **Colonization** (without invasion & extension) in preformed cavities
  E.g. it will line TB cavities and cause a mass (aspergilloma)
- **Invasive disease of lungs**
- **Systemic and disseminated disease.**

AETIOLOGICAL AGENTS

A refers to :
Aspergillus



CLASSIFICATION OF ASPERGILLOSIS

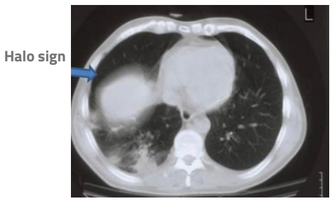
Airways/nasal exposure to airborne Aspergillus:

We are repeatedly exposed to fungal spores and our immunity can eradicate them but in cases where it is weakened diseases can happen

Persistence without disease	Invasive aspergillosis	Chronic aspergillosis	Allergic
-colonisation of the airways or nose/sinuses	In immunocompromised patients	-Aspergilloma of lung - Maxillary (sinus) aspergilloma	- Allergic bronchopulmonary (ABPA) - Allergic Aspergillus sinusitis

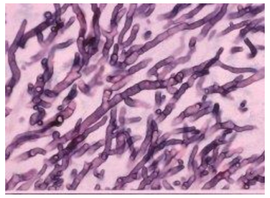
CLASSIFICATION OF ASPERGILLOSIS CONT...

Class	Chronic Aspergillosis Colonizing aspergillosis, Aspergilloma OR Aspergillus fungal ball	Invasive pulmonary Aspergillosis	Allergic Aspergillosis (ABPA)
Signs	Cough, hemoptysis,variable fever.	Cough, hemoptysis, fever, leukocytosis.	Symptoms of asthma, bronchial obstruction, eosinophilia, wheezing +/-
Radiology	Mass in the lung, radiolucent crescent.	Lesions with Halo sign -معتمة منطقة-	-
Test	-	Tissue specimen from lung biopsy is very important for diagnosis	• Skin test reactivity to Aspergillus • Serum antibodies to Aspergillus • Serum IgE > 1000 ng/ml
Risk factor	1- Bone marrow / organ transplantation 2- Cancer: Leukemia, lymphoma, etc . 3- AIDS 4- Drugs (immunosuppressive): steroids, etc.. 5- Diabetes 6- Others		
Diagnosis	• **1- Specimen:** • Respiratory specimens: Sputum, BAL (bronchoAlveolar Lavage), Lung biopsy. • Other samples: Blood, etc.. **2-Lab investigations:** 1- Direct Microscopy: - We use Giemsa Stain, Grecott methenamine silver stain (GMS). ★ It will show fungal **septate** hyphae. 2-Culture on SDA 3- PCR: Detection of Aspergillus DNA in clinical samples. 4- Serology : - Test for Antibody ★ ELISA test for **galactomannan** Antigen (specific for aspergillus).		
Treatment	★ **Voriconazole** (drug of choice) • Alternative therapy: Amphotericin B, Itraconazole, Caspofungin. -Dr skipped it-		



Halo sign
(Invasive pulmonary Aspergillosis)

Aspergilloma, air crescent.
(Chronic Aspergillosis)



Smear: Septate fungal hyphae aspergillosis

FUNGAL SINUSITIS

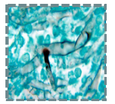
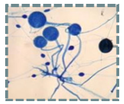
Clinical presentation	• Nasal polyps -لحمية- and other symptoms of sinusitis • In immunocompromised, could disseminate to adjacent structures (e.g. to the eye → craneum (rhinocerebral)) • In addition to aspergillus, there are other fungi that can cause fungal sinusitis • Aspergillus sinusitis has the same spectrum of aspergillus disease in the lung (see below)
Spectrum	1. Non invasive (localized) 2. Allergic 3. Chronic (all of the previous easy to remove) 4. Invasive (very critical, could extend to the brain and cause rhinocerebral aspergillosis)
Diagnosis	• Clinical and radiology • Histology • Culture • Precipitating antibodies useful in diagnosis • Measurement of IgE level, RAST test* in the case of allergic • If it was invasive or chronic we take tissue biopsy *RAST (Radioallergosorbent test) is a laboratory test performed on blood. It tests for the amount of specific IgE antibodies in the blood which are present if there is a "true" allergic reaction.
treatment	Depends on the type and severity of the disease and the immunological status of the patient

ZYGOMYCOSIS → CAUSED BY ENVIRONMENTAL FUNGI

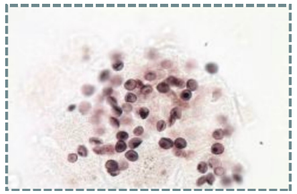
2 Types 1-Pulmonary zygomycosis less common clinical form

2- ◎ Rhinocerebral zygomycosis when it's go to sinuses & brain

Clinical presentation	• Consolidation, nodules, cavitation, pleural effusion, hemoptysis • Infection may extend to chest wall, diaphragm, pericardium. very rapidly -Tissue invasion- - Pulmonary infraction and hemorrhage - Rapid evolving clinical course • Early recognition and intervention are critical
Etiology	Zygomycetes, **non** septate hyphae (e.g. Rhizopus)
Risk factors	• Transplant patients • Malignancy • AIDS it will cause a very severe disease • Diabetes (ketoacidosis) • Many others • For immunocompromised patients, it will be very severe, high mortality rate and grows fastly. but for normal patients it is very benign
Diagnosis	**1- Specimen**: Respiratory specimens: Sputum, BAL, Lung biopsy & other sampleس **2- Direct Microscopy:** • Giemsa, Grecott methenamine silver stain (GMS): **will show broad non- septate fungal hyphae** • Culture on SDA (no cycloheximide) **3-Serology:** Not available
treatment	• **Amphotericin B** • Surgery many cases it is needed, the drug alone cannot cure


PNEUMOCYSTOSIS (PCP)

overview	• It is interstitial pneumonia of the alveolar area • Affect **compromised** host
Etiology	• Pneumocystis jiroveci • Previously thought to be a protozoan parasite, but later it has been proven to be a fungus • Naturally found in rodents (rats), other animals (goats, horses) • Humans may contract it during childhood
Risk factors	Especially common in AIDS patients, once AIDS patient comes with pneumonia it is very important to test for this disease *might be seen in other immunocompromised patients, like organ transplant
Diagnosis	**Specimen:** • Bronchoscopic specimens (Bronchoalveolar lavage) • Sputum • Lung biopsy tissue **Histological section or smears stained by:** • GMS stain • Immunofluorescence (better sensitivity) * If positive will see cysts of hat-shape, cup shape, crescent Does not grow in laboratory media (e.g. SDA) 
treatment	• Trimethoprim-sulfamethoxazole (Trisulfa) NOTE: it is an antibiotic not an antifungal • Dapsone

SUMMARY

Disease	Aspergillosis			Fungal sinusitis	Zygomycosis	pneumocystosis
	Chronic	Invasive	Allergic			
Overview	Cough, hemoptysis, variable fever. *for people with cavities	Cough, hemoptysis, fever, leukocytosis.	Symptoms of asthma, bronchial obstruction, eosinophilia, wheezing.	in **immunocompromised,** could disseminate to adjacent structures	▪ present with consolidation, nodules, cavitation, pleural effusion, hemoptysis ▪ **rapidly** progressive	▪ interstitial pneumonia ▪ Affect compromised host ▪ acquired during childhood
Etiology	**A. fumigatus & A. flavus**			**the most common cause in KSA is Aspergillus flavus**	**Zygomycetes**	**Pneumocystis jiroveci**
Risk factor	▪ Bone marrow / organ transplantation ▪ Cancer: Leukemia, lymphoma, etc.. ▪ AIDS ▪ Drugs (immunosuppressive) ▪ Diabetes			-	▪ Transplant patients ▪ Malignancy ▪ AIDS ▪ Diabetes (ketoacidosis)	common in **AIDS** patients
Diagnosis	▪ Microscopy: Septate hyphae ▪ ELISA test for galactomannan Antigen ▪ Culture			▪ Histology ▪ Biopsy ▪ culture	▪ microscopy: broad non-septate hyphae - GMS stain - Giemsa ▪ culture	▪ microscopy: Cup shaped (cyst) - immunofluorescence - GMS stain ▪ culture: does not grow
treatment	**Voriconazole**			depend on the type and severity	**-Amphotericin B** - surgery	**Trimethoprim-sulfamethoxazole**

Q1: D
Q2: B
Q3: B

MCQs:

Q1/ Which of the following is the drug of choice for pneumocystosis ?

A	Amphotericin B	B	Voriconazole	C	itraconazole	D	Trisulfa

Q2/ 2- a patient came to the ER with symptoms of asthma, later he was diagnosed with allergic aspergillosis, what is the characteristic of the fungi under the microscope?

A	non-septate hyphae	B	septate hyphae	C	cup shaped	D	none of the above

Q3/ an AIDS patient came to the ER with symptoms of pneumonia, which of the following organisms might be the cause?

A	A. fumigatus	B	Pneumocystis jiroveci	C	Zygomycetes	D	S. pneumoniae

Q4: A
Q5: A

MCQs:

Q4/ Which of the following organisms we use ELISA test for galactomannan antigen?

A	A. flavus	B	Pneumocystis jiroveci	C	Zygomycetes	D	C. gattii

Q5/ 5- The most common cause of Fungal sinusitis in KSA is?

A	A. flavus	B	Pneumocystis jiroveci	C	Zygomycetes	D	C. gattii

SAQs:

Q1/ Primary systemic disease are caused by?

dimorphic fungi

Q2/ What special feature that can be seen in radiologic scan in a patient with invasive pulmonary aspergillosis?

Halo sign

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